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Extended Research Article

Effects and costs of a group-based educational intervention to reduce opioid use in people with chronic pain: I-WOTCH RCT

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[†]In Memoriam

To Colin Bernard Tysall, thank you for your valuable contribution to this study which would not have been a success without you.

Disclaimer: This report contains transcripts of interviews conducted in the course of the research, or similar, and contains language which may offend some readers.

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This article

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Abstract

Background: The long-term use of strong opioids for chronic non-cancer pain puts people at risk of serious harm.

Objectives: To test the effectiveness and cost-effectiveness of a multicomponent intervention targeting opioid use for the treatment of chronic pain.

Design: A multicentred randomised controlled trial with embedded process evaluation.

Setting: Primary care.

Participants: Adults using strong opioids for non-malignant chronic.

Interventions: Participants were randomised 1 : 1 (using a minimisation programme stratified by geographical locality, baseline pain intensity score and baseline morphine equivalent dose) to either usual care (an educational booklet and relaxation compact disc) or usual care plus the I-WOTCH intervention; 3 day-long group sessions delivered by a nurse and lay facilitator, plus a one-to-one session and ongoing telephone contact from the nurse to support opioid tapering.

Main outcome measures: The two primary outcomes were Patient-Reported Outcomes Measurement Information System Pain Interference Short Form (8A), and proportion using no opioids, at 12 months.

Results: We randomised 608 people. At 12 months, there was no between-group difference in Patient-Reported Outcomes Measurement Information System Pain Interference Short Form (8A) scores; mean difference, −0.52 (95% confidence interval −1.94 to 0.89). At 12 months, 65/225 (29%) of people in the intervention group and 15/208 (7%) of people in usual-care group reported using no opioids [odds ratio 5.55 (95% confidence interval 2.80 to 10.99)], absolute difference, 21.7% (95% confidence interval 14.8 to 28.6). Over a lifetime horizon, I-WOTCH is on average associated with an incremental cost of £9277 per person, and provides an additional 0.314 quality-adjusted life-years. The deterministic incremental cost per quality-adjusted life-year gained was £29,543. The I-WOTCH intervention may be cost-effective compared to best usual care. The process evaluation suggested group support and shared experience were important to those trying to taper.

Limitations: The opioid use analysis is based solely on participant self-report. The findings only apply to people willing to consider opioid reduction and may not apply to a more complex secondary care population. The results may not be applicable to people using very high opioid doses.

Conclusions: The I-WOTCH intervention helps substantially more people stop opioids than best usual care without adversely affecting pain interference.

Future work: The I-WOTCH intervention should be tested in different healthcare settings and other populations.

Trial registration: This trial is registered as Current Controlled Trials ISRCTN49470934.

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Supplementary material can be found on the NIHR Journals Library report page (https://doi.org/10.3310/GJHS2715).

Supplementary material has been provided by the authors to support the report and any files provided at submission will have been seen by peer reviewers, but not extensively reviewed. Any supplementary material provided at a later stage in the process may not have been peer reviewed.

The supplementary materials (which include but are not limited to related publications, patient information leaflets and questionnaires) are provided to support and contextualise the publication. Every effort has been made to obtain the necessary permissions for reproduction, to credit original sources appropriately, and to respect copyright requirements. However, despite our diligence, we acknowledge the possibility of unintentional omissions or errors and we welcome notifications of any concerns regarding copyright or permissions.

List of abbreviations

ADL	activity of daily living
AE	adverse event
BNF	*British National Formulary*
CCA	cost–consequences analysis
CEA	cost-effectiveness analysis
CEAC	cost-effectiveness acceptability curve
CEM	cost-effectiveness model
COPERS	COping with persistent Pain, Effectiveness Research into Self-management
COVID-19	coronavirus disease 2019
CRF	case report form
DMC	Data Monitoring Committee
EQ-5D-3L	EuroQol-5 Dimensions, three-level version
EQ-5D-5L	EuroQol-5 dimensions, five-level version
EVPI	expected value of perfect information
GLM	generalised linear model
GLMM	generalised linear mixed model
GP	general practitioner
HADS	Hospital Anxiety and Depression Scale
ICC	intercluster correlation
ICER	incremental cost-effectiveness ratio
IPD	individual patient data
IST	intervention supported tapering
ITT	intention to treat
I-WOTCH	Improving the Wellbeing of People with Opioid Treated Chronic Pain
LTOT	long-term opioid therapy
MED	morphine equivalent dose
NICE	National Institute for Health and Care Excellence
NIHR	National Institute for Health and Care Research
NIST	non-intervention supported tapering
NMB	net monetary benefit
NRTT	non-responder to treatment
OF	successful opioid free management of pain
ONS	Office of National Statistics
PMM	predictive mean matching
PMP	pain management programs
PP	per protocol
PPI	patient and public involvement
PROMIS-PI-SF-8A	Patient-Reported Outcomes Measurement Information System Pain Interference Short Form (8A)
PROs	patient-reported outcomes
PSA	probabilistic sensitivity analysis
PSS	Personal Social Services
PSSRU	Personal Social Services Research Unit
QALY	quality-adjusted life-year
RCT	randomised controlled trial
REC	Research Ethics Committee
SAE	serious adverse event
SF-12	Short Form questionnaire-12 items
ShOWS	Short Opioid Withdrawal Scale
TMG	Trial Management Group
TSC	Trial Steering Committee
VAS	visual analogue scale
WCTU	Warwick Clinical Trials Unit
WTP	willingness to pay

Plain language summary

What was the problem?

Many people use strong opioid drugs to help them to live with chronic (long-lasting) pain. But they are addictive and can have serious side effects.

What did we want to find out?

Does the I-WOTCH support programme for people using strong opioid drugs for chronic pain both help people live better with their pain and reduce their opioid use?

How did we do this?

We worked with 191 general practices in England to find people taking strong opioid drugs for non-cancer pain. Using a computer, we randomly allocated participants into two groups. Both received best current care including an advice booklet and relaxation compact disc. The other group were also offered the I-WOTCH intervention. This consists of 3-day-long group discussion/education sessions on pain management and opioid use, led by a nurse and someone with pain who had stopped using opioids, followed by a 1-hour session with a nurse to discuss opioid dose reduction, and ongoing telephone support. One year after receiving treatment, we wanted to know if people had reduced their opioid drugs and if we had changed how pain affected their lives.

What did we find out?

In total, 608 people joined the study. At 1 year, there was no difference between the groups in how pain affected their lives. In the best usual-care group, 1 in 14 people (7%) were taking no opioids at 1 year. While in the I-WOTCH group, one in four people (29%) were taking no opioids at 1 year. How pain affected people was neither better nor worse in either group. The I-WOTCH intervention may represent good value for the NHS.

What does this mean?

The I-WOTCH intervention can help people living with chronic non-malignant pain stop using strong opioids without affecting how pain interferes with their lives.

Scientific summary

Background

Chronic non-malignant pain is the leading cause of years lived with disability globally and is defined as pain that persists or recurs for longer than 3 months. Despite a lack of evidence that they improve pain, function or quality of life, opioids are widely used to treat chronic non-malignant pain. Adverse effects from opioids include sedation, nausea, respiratory depression/sleep apnoea, depression, abdominal pain, hormone imbalance, overdose and death. Up to 80% of opioid users report at least one adverse effect. In 2017, there were 110,000 deaths from opioid overuse disorder worldwide — a 77% increase from 2007 with further increase reported during the COVID-19 pandemic. Data published in 2020 from a retrospective cohort study using UK primary care electronic health records from the Clinical Practice Research Data Link found that between 2006 and 2017 a total of 1,968,742 new adult patients with chronic non-malignant pain were prescribed an opioid. Codeine was the most commonly prescribed opioid, with use increasing fivefold from 2006 to 2017, reaching 2456 prescriptions/10,000 people/year. Prescribing of other opioids such as morphine, buprenorphine, and oxycodone also continued to increase during this period. At the time we were developing this study, there were few data supporting interventions that assist people to reduce opioid doses. A 2017 Cochrane review found one randomised controlled trial of acupuncture (*N* = 35) and one of computerised therapeutic voice support (*N* = 51). The reviewers were unable to make recommendations for practice. This review also identified five observational studies (*N* = 1800) from one unit suggesting that an intensive 3-week pain management programme can substantially reduce opioid use.

There have been three subsequent systematic reviews. Two reviews focused on opioid reduction interventions. They identified 10 randomised controlled trials of patient focused opioid de-prescribing interventions (*n* = 835). These trials did not show evidence of reduced opioid consumption or increased opioid cessation. The third review, looking at the wider pain management literature, included two trials of pain self-management (*N* = 238) in a meta-analysis that found positive effects on opioid cessation [odds ratio (OR) 2.15, 95% confidence interval (CI) 1.02 to 4.53] and five (*N* = 428) that found a reduced daily morphine equivalent dose of 14.3 (95% CI 7.1 to 21.6)]. These data suggest that a pain management programme might have some potential to reduce opioid use by people living with chronic non-malignant pain.

An effective pain management programme that specifically targeted opioid use could be expected to help people live better with their pain both directly through its effect on pain self-efficacy and indirectly through an improved quality of life from reduced opioid use. However, an alternative outcome could be that successful opioid tapering leads to increased pain, and worse quality of life due to loss of their analgesic effect. This means that any trial of an opioid reduction intervention needs to consider both any changes in opioid uses and how pain affects people.

Tapering opioids too quickly without a lack of alternatives to manage pain can cause substantial harm. Individuals motivated to reduce their opioid use need appropriate advice on how to do this safely. In the Improving the Wellbeing of People with Opioid Treated Chronic Pain (I-WOTCH) study, we tested the combination of a pain management approach and an individualised and supported opioid tapering plan on pain interference and opioid use.

Aims

The aim of the I-WOTCH study was to test the clinical and cost-effectiveness of a patient-centred multicomponent self-management intervention (targeting withdrawal of opioids and assessing impact of their withdrawal on pain interference with daily living) for people living with chronic non-malignant pain, compared with a best usual care (i.e. the control group intervention) in a two-arm pragmatic randomised controlled trial. An embedded process evaluation was used to inform the interpretation of the findings and, if indicated, implications for the implementation of the intervention.

Study objectives were:

1. To develop and refine a patient-centred, group-based, multicomponent, self-management intervention for people living with chronic non-malignant pain.
2. To assess the acceptability of the intervention and to optimise participant recruitment during the internal pilot phase.
3. To conduct a pilot accompanied with a process evaluation to establish efficient recruitment.
4. To run a multicentre trial to examine the clinical effectiveness and resource use implications of the I-WOTCH intervention versus usual care over a 12-month follow-up period.
5. To develop an initial decision-analytic cost-effectiveness model and value of information analysis based on existing evidence.
6. To update the decision-analytic cost-effectiveness model and value of information analysis with the data from the definitive trial and model the long-term cost-effectiveness of the I-WOTCH intervention versus usual care.
7. To conduct process evaluation of the trial which will aid interpretation of the trial findings and, if indicated, to inform the implementation of the intervention across the NHS.
8. To disseminate the findings from the trial and, where necessary, results providing materials to support wider implementation of the intervention.

Methods

We conducted a pragmatic, multicentre, 1 : 1 randomised controlled trial design to test the superiority of a multicomponent, psychologically informed, group self-management support programme, including a one-to-one discussion with a trained nurse and the development of an opioid tapering programme, against enhanced usual care for reducing opioid consumption in people with chronic non-malignant pain. The trial was approved by the Yorkshire and The Humber – South Yorkshire Research Ethics Committee on 13 September 2016 (16/YH/0325) and sponsored by the University of Warwick, UK. It was conducted according to good clinical practice guidance and overseen by an independent Trial Steering Committee, with an independent Data Monitoring and Ethics Committee.

Participants were adults (aged ≥ 18) using strong opioids as defined in the *British National Formulary* (BNF) published at the time of the study design, for at least 3 months for chronic non-malignant pain, and on most days in the preceding month. Since the study was developed, the BNF has changed its approach and no longer makes a distinction between weak and strong opioids.

To identify potential participants, general practices searched their records for people aged 18 years and over, who had more than one prescription for a strong opioid (buprenorphine, dipipanone, morphine, diamorphine, fentanyl, hydromorphone, methadone, oxycodone, papaveretum, pentazocine, pethidine, tapentadol and tramadol) in the previous 3–6 months and in the previous 0–3 months as indicated by their health record.

General practices invited potentially eligible people to express an interest in the study. They excluded people known to be using opioids for malignant pain, care home residents, the housebound, and those using methadone not prescribed for chronic pain. People could also self-refer. Posters were placed in general practitioner surgeries, pharmacies, pain clinics and musculoskeletal physiotherapy clinics and the study website had details of the trial. We confirmed eligibility in a subsequent telephone call. Eligible participants then completed baseline questionnaires and returned signed consent forms. In a further telephone call, medication use, as reported in the baseline questionnaire, and consent to join the study were checked and confirmed.

Participants were randomised 1 : 1 to either usual care or the I-WOTCH intervention. Both groups received enhanced usual care, including a booklet ‘My Opioid Manager’ based on the 2010 Canadian Opioid Guideline, a self-help guide containing information about pain, opioids and tapering, and a relaxation compact disc. The intervention group was offered the I-WOTCH intervention package.

Two primary outcomes were Patient-Reported Outcomes Measurement Information System Pain Interference Short Form (8A) (PROMIS-PI-SF-8A) (T-score range 40.7–77, 77 indicates worst pain interference) and the proportion of participants who discontinued opioids at 12 months, measured by self-report. Secondary outcomes were Patient-Reported Outcomes Measurement Information System Pain Intensity Short Form 3a (PROMIS-PI-SF-3A), severity of opioid withdrawal symptoms [Short Opiate Withdrawal Scale (ShOWS)], health-related quality of life [SF-12v2 health survey and EuroQol-5 Dimensions, five-level version (EQ-5D-5L)], sleep quality (Pittsburgh Sleep Quality Index), emotional well-being [Hospital Anxiety and Depression Scale (HADS)], self-efficacy (Pain Self-Efficacy Questionnaire), and proportion of patients who reduced opioids by 50% from baseline. All outcomes were collected at baseline, 4, 8 and 12 months.

Sample size

As originally designed, we sought to demonstrate a 3.5-point difference in PROMIS-PI-SF-8A at 1 year at a significance level of 5% with 90% power as a single primary outcome. To show this with a simple sample size calculation requires data on 346 participants. Allowing for the possibility of clustering effects in the intervention group, we inflated this to 374. Allowing for 20% loss to follow-up, we aimed to recruit 468 people. We anticipated recruiting from around 100 practices in the West Midlands, The North East of England and London: 33 from each area. We were unable to run the study in London because we could not secure excess treatment costs from London Clinical Commissioning Groups and therefore the study ran in the wider midlands area and the North East.

Due to the nature of the recruitment process, and the need to have sufficient participants to populate an intervention group in a particular locality, we substantially exceeded our original recruitment target. Since we considered that if the intervention were to have no impact on pain interference but did reduce opioid usage this could be an important benefit, we sought approval to add difference in opioid use as a second primary outcome. This was agreed by the Trial Steering Committee and Data Monitoring Committee while data collection was still in progress. The actual group sizes were less than expected reducing the sample size inflation needed to account for clustering effects. Recalculating the sample size, accounting for this, and a significance level of 2.5% required to assess the two primary outcomes, opioid reduction and pain interference, was 542 participants (271 per group).

Health economics

We conducted a prospective within-trial cost–consequences analysis and a model-based long-term cost-effectiveness analysis (CEA) to assess the value for money of the I WOTCH intervention compared with the best usual care to support withdrawal of strong opioids, among those living with chronic non-malignant pain.

Process evaluation

An embedded process evaluation was also conducted to better understand people's experiences of the intervention and assess fidelity of the intervention. We interviewed 18 intervention facilitators, 20 intervention and 20 control group participants. Fidelity of group sessions and 1 : 1 consultations were evaluated, assessing adherence and competence. Participant feedback forms were also utilised. Interviews were analysed using framework analysis and feedback forms analysed using thematic analysis.

Results: clinical

Between 17 May 2017 and 30 January 2019, we randomised 608 people after screening in 191 general practices, 3 hospitals, and allowing self-referrals. We randomised 303 to control and 305 to intervention; we ran a total of 35 intervention groups in 25 locations.

At 12 months, 29% (65/225) in the intervention group and 7% (15/208) in the usual-care group had fully tapered off opioids [OR 5.55 (95% CI 2.80 to 10.99); $p < 0.001$]. At 12 months, the PROMIS-PI-SF-8A scores did not show a statistically significant between-group difference [adjusted mean difference −0.89 (95% CI −2.12 to 0.33); $p = 0.15$]. Over the 12-month study period, PROMIS-PI-SF-8A scores did improve in both groups: −4.1 (95% CI −4.98 to −3.22) in the intervention group and −3.17 (95% CI −4.10 to −2.24) in the usual care group.

At 12 months, 57% (129/225) in the intervention group and 27% (57/208) in the usual-care group had reduced their daily opioid usage by ≥ 50% from baseline [adjusted OR 3.76 (95% CI 2.47 to 5.71); $p < 0.001$]. Similar results were also seen at 4 and 8 months follow-up. No other secondary outcomes showed meaningful differences between the intervention group and usual-care group at 12 months. At 4 months, statistically significant differences were found between groups for the SF-12 mental component [adjusted 2.29 (95% CI 0.30 to 4.27); $p = 0.02$], HADS depression score [adjusted −0.94 (95% CI −1.63 to −0.25); $p = 0.01$], pain self-efficacy [adjusted 4.19 (95% CI 1.97 to 6.41); $p < 0.001$], EQ-5D-5L utility score [adjusted 0.57 (95% CI 0.01 to 0.10); $p = 0.02$] and EQ-5D-5L visual analogue scale score [adjusted 4.43 (95% CI 0.70 to 8.16); $p = 0.02$], with all differences favouring the intervention.

There were 36 adverse events (AEs; 25 intervention, 11 usual care) reported by 30 participants (22 intervention, 8 usual care). Fifty-two serious AEs (32 intervention, 20 usual care) were reported by 41 participants (25 intervention, 16 usual care). The serious adverse events (SAEs) included five deaths (four intervention, one usual care), all five of which were unrelated to the trial intervention. The causes of death were metastatic prostate cancer, aortic dissection, subdural empyema secondary to otitis media, lymphoma complication and one unknown. In the intervention group, there was one probably related and expected SAE (hot flushes and shooting pains in limbs after tapering) of moderate severity and three possibly related SAEs, two unexpected (small intestinal bleed, and pain surges and hot sensations after tapering) and one expected (hospitalisation due to joint/back pain). There was one possibly related SAE in the usual-care group (hospitalised for arthritis flare-up).

Results: health economics

The complete case analysis results indicate that in the short term, I-WOTCH is a cost-incurring but a similarly effective (i.e. maintaining measures of health benefit at a similar level to that experienced while on strong opioids) management strategy for tapering opioids in patients with non-malignant chronic pain compared to best usual care. Individuals who are able to self-regulate their use of strong opioids, however, could also achieve a reduction in their exposure to the excess mortality rate associated with long-term consumption of strong opioids. Modelling these results as part of the base-case CEA indicates that in the long term the I-WOTCH intervention may be cost-effective compared to best usual care [deterministic incremental cost-effectiveness ratio (ICER): £29,594; probabilistic ICER: £34,614]. The model results reflect the large uncertainty in the model parameters. Scenario analyses confirm these conclusions. Overall, the findings suggest that there is value in conducting further research to reduce the uncertainty associated with the results of the health economics analysis.

Results: process evaluation

Four themes emerged from the data: (1) the right time to taper, (2) the backdrop of a complex life with chronic pain, (3) needing support and (4) the group effect. Being in a group was an important aspect of the process.

This process evaluation revealed the I-WOTCH intervention was well delivered and well received. Being ‘the right time’ to taper and having support throughout emerged as important aspects within the context of living with chronic pain.

Conclusions: implications for healthcare

The I-WOTCH intervention (incorporating group sessions and one to one support) achieved a substantial and sustained cessation in opioid use with no increase in pain, or pain-related disability with no drug or device substitution. Our recommendations for future research are

1. Replication of I-WOTCH in different populations and different settings.
2. Adaptation and evaluation of the I-WOTCH intervention for use in people who do not speak English.
3. Comparing I-WOTCH to alternative tapering interventions.

Trial registration

This trial is registered as Current Controlled Trials ISRCTN49470934.

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Chapter 1 Introduction

Background

Chronic pain is defined as pain that persists for more than 12 weeks.[6] Globally, chronic non-malignant pain is the leading cause of years lived with disability.[7] In the UK, between one-third and one-half of the population are affected by chronic pain, which equates to just under 28 million adults.[8] Some of the most frequent causes of persistent pain include musculoskeletal problems such as low back, neuropathic pain, fibromyalgia and postsurgical pain.

Chronic pain treatment and treatment-related side effects

People with chronic non-malignant pain and general practitioners (GPs) find the pharmacological management of chronic pain unsatisfactory.[9] People on long-term opioid treatment often report inadequate analgesia and little benefit to help with their activities of daily living (ADLs) and social engagement.[10]

In the UK, around 1 million people are opioid users.[11] However, opioids are not effective in the long term and can cause a range of adverse effects such as sedation, nausea, respiratory depression/sleep apnoea, depression, abdominal pain, hormone imbalance, overdose and death; up to 80% of opioid users report at least one adverse effect.[12]

Prescription data from the UK showed that there were substantial increases in opioid prescribing for chronic non-cancer pain with a 466% increase in the number of strong opioid users between 2000 and 2010. During this decade, only 12% of the opioid prescribing in the UK was cancer related, while 88% of prescriptions were issued to non-malignant chronic pain patients. While morphine remained the most frequently prescribed drug both for cancer and non-cancer pain, the greatest increase in annual number of prescriptions was for oxycodone in both the non-cancer (11,265%, from 764 to 86,833 daily doses/1000 of population) and cancer groups (8939%, from 124 to 11,209 daily doses/1000 of population).[13] More recent data from a retrospective cohort study using UK primary care electronic health records from the Clinical Practice Research Data Link found that between 2006 and 2017 a total of 1,968,742 new adult patients with chronic non-malignant pain were prescribed an opioid.[14] Codeine was the most commonly prescribed opioid, with use increasing fivefold from 2006 to 2017, reaching 2456 prescriptions/10,000 people/year. Other opioids such as morphine, buprenorphine, and oxycodone also continued to increase during this period.[14] A spatial analysis of the association of opioid prescribing in primary care in England examined the 2018–9 national primary care prescribing data. In total, 624,411,164 defined daily doses, as defined by the World Health Organization, of opioids were prescribed.[15] The prevalence of rheumatoid arthritis had a strong positive effect on prescribing with no impact from other conditions. Prescribing in the least deprived areas of the North of England was 2.8 times higher than least deprived parts of London. Highest levels of prescribing were found in the most deprived areas of the North of England where prescribing was 3.3 times higher than the most deprived parts of London. A positive association was observed between deprivation and opioid prescribing with prescribing in urban areas being on average 1.85 times higher than rural. The authors argued that the highest prevalence of prescribing in the north of the country mirrors the wider inequalities between the North and the South. While the association of deprivation with opioid prescribing was clear, the association at an area (Clinical Commissioning Group) level was less clear cut. In some cases, opioid prescribing was higher in less deprived areas.[16]

Evidence for the effect of self-managed interventions on withdrawal of opioids

At the time of study development, there was limited evidence supporting interventions that assist patients to reduce opioid doses. A 2017 Cochrane review found one randomised controlled trial (RCT) of acupuncture (*N* = 35) and one of computerised therapeutic voice support (*N* = 51).[17] The reviewers were unable to make recommendations for practice. This review also identified five observational studies (*N* = 1800) from one unit suggesting that an intensive 3-week pain management programme can substantially reduce opioid use.

Rationale for the I-WOTCH trial

Data for the National Drug Treatment Monitoring System 2011–2 suggested an increase (around 8%) in the number of patients seeking help for analgesic dependency, with or without additional use of illicit drugs.[18] Less intense self-management interventions for people with chronic low back pain that do not target opioid use can have sustained benefits on pain and disability.[19] At the time this study was developed, there was no formal UK guidance on reducing opioid use in this population, and there was no clear evidence supporting a particular tapering speed. In the absence of validated protocol, empirical plans have been proposed based on expert consensus opinion; such plans have been recommended by the Mayo Clinic and Washington University. There was no clear rationale for switching a patient treated long term with one opioid onto another opioid nor was there clear guidance on drugs use in facilitation of opioid taper in this group. Furthermore, we struggled to define what constituted usual care or best standard care due to the lack of awareness and lack of formal UK guidance.

Evidence demonstrating the use of self-management and cognitive–behavioural interventions in supporting opioid tapering is sparse and largely relevant to health systems in North America. Subsequently, I-WOTCH was created to assist patients in managing pain interference, lower their opioid consumption and strengthen their overall quality of life.

Literature update

Since staring the I-WOTCH project three new relevant systematic reviews have been published. Mathieson (2020) identified 10 randomised trials of patient-focused opioid de-prescribing interventions (*n* = 835). They did not find evidence of reduced opioid consumption, increased opioid cessation, or adverse events (AEs).[20] Avery (2022) looking at the wider pain management literature included two trials of pain self-management (*N* = 238) in a meta-analysis that found positive effects on opioid cessation [odds ratio (OR) 2.15, 95% confidence interval (CI) 1.02 to 4.53] and five (*N* = 428) that found a reduced daily morphine equivalent dose (MED) of 14.3 mg (95% CI 7.1 mg to 21.6 mg). Three trials (*N* = 92) were included in meta-analyses of pain and function and found a positive effect on pain intensity (−0.59, 95% CI −1.02 to −0.16) but no effect on function (−0.27, 95% CI −0.69 to 0.15).[21] De Kleijn (2022) identified four individually randomised trials (*N* = 200) of opioid reduction in primary care, and none of these, or the one cluster randomised trial identified (*N* = 985), found any statistically significant benefits.[22] An updated search in June 2023 did not identify any further published RCTs.

Aims and objectives of the I-WOTCH Trial

The aim of the I-WOTCH study was to test the clinical and cost-effectiveness of a patient-centred multicomponent self-management intervention targeting withdrawal of strong opioids on ADLs for people living with chronic non-malignant pain.

Study objectives:

1. To develop and refine a patient-centred, group-based, multicomponent, self-management intervention targeting the withdrawal of strong opioids, for people living with chronic non-malignant pain.

2. To assess the acceptability of the intervention and to optimise participant recruitment during the internal pilot phase.
3. To conduct a pilot accompanied with a process evaluation to establish efficient recruitment.
4. To run a multicentre trial to examine the clinical effectiveness and resource use implications of the I-WOTCH intervention versus usual care over a 12-month follow-up period.
5. To develop an initial decision-analytic cost-effectiveness model and value of information analysis based on existing evidence.
6. To conduct process evaluation of the trial which will aid interpretation of the trial findings and examine the implementation of the intervention across the NHS, if indicated.
7. To update the decision-analytic cost-effectiveness model and value of information analysis with the data from the definitive trial and model the long-term cost-effectiveness of the I-WOTCH intervention versus usual care.
8. To disseminate the findings from the trial and where necessary results providing materials to support wider implementation of the intervention.

Overview of report

This report is structured across 11 chapters. The methods are presented in conjunction with the development of the I-WOTCH intervention. Trial results are reported followed by the health economic evaluation and then qualitative findings from the study. Finally, we present an overarching discussion and conclusion for the trial.

Chapter 2 Methods

Trial design and setting

I-WOTCH was a definitive RCT incorporating an internal pilot study and parallel process evaluation and health economics analysis. Participants living with chronic non-malignant pain prescribed strong opioids were recruited from primary care; general practice, community pain services, local musculoskeletal services and pharmacies across the North East, East Midlands, West Midlands and South Central areas of England. When originally planned, we intended to recruit in London. However, failure to secure agreement to fund excess treatment costs meant we were unable to set up, recruit and deliver the trial in this region. The trial protocol has been published elsewhere[2] and the final version (2.0) is available here: www.fundingawards.nihr.ac.uk/award/14/224/04.

Participants

Definition of regular strong opioid use

In this study, we utilised the *British National Formulary* (BNF)[23] definition of strong opioids current at the time of set up: buprenorphine, dipipanone, morphine, diamorphine, fentanyl, methadone, oxycodone, papavertum, pentazocine, pethidine, tapentadol, or tramadol. Individuals using methadone for purposes other than to manage pain were excluded. Individuals who regularly injected opioids were also excluded. Those taking opioids orally or via transdermal preparations were included. Subjects who primarily had a headache disorder were excluded due to the variation in approach used to treat chronic migraine and the potential for medication overuse headache, neither of which align with the treatment model used in this study.

For the purpose of the current study, careful consideration was given to the definition of opioid use. If the intervention was to be meaningful, it was necessary to recruit regular opioid users. A definitive description of regular opioid use does not exist among current guidance. For example, epidemiological definitions for use include 'several days a week for a month or more', or 'at least five days per week for at least four continuous weeks'.[24,25] However, these definitions are likely to capture individuals using opioids to manage an acute problem and therefore discontinue use shortly after. These definitions therefore did not extend to our population of interest, which was individuals with long-term strong opioid use. Therefore, we set the duration of regular opioid use at 3 months in line with the criteria for pain to become chronic. Nonetheless, in line with earlier definitions, the previous 4 weeks determine if use was regular. Our entry criteria were using strong opioids to treat non-malignant pain for at least 3 months, and to have used a strong opioid on at least half of the days in the preceding 4 weeks.

Intervention venues and inclusion/exclusion criteria

The intervention venues were selected to ensure easy access on public transport. Individuals who could not attend due to travel arrangements or who were physically unable to attend were also excluded. Individuals with mental health or substance misuse issues (e.g. alcohol abuse) were not automatically excluded unless they were unable to participate in the group process or there could have been potential disruption to other members in the group. If multiple individuals from the same household completed an expression of interest form, the project team would ensure a suitability assessment was provided to both. If both were suitable to participate, the project team requested that the individuals decide between themselves who would like to participate in the study.

Inclusion criteria

Participants were eligible if they were aged 18 years old or above, using opioids for chronic non-malignant pain, report using strong opioids for at least 3 months and on most days in the preceding month, were fluent in written and spoken English and willing for their GP to be informed of participation. All participants provided written informed consent.

Exclusion criteria

Participants were excluded if they regularly injected opioids or were using opioids for malignant pain, recorded chronic headache as their primary pain disorder, had a mental health condition that would prevent participation in the group intervention or were unable to physically attend group intervention sessions. Participants were also excluded if they had taken part in clinical trial on the investigational medicinal product within the last 90 days. Individuals that were pregnant at the time of the assessment or actively trying to conceive were also excluded.

Recruitment and consent

Recruitment

For the study, potential participants were identified using the following methods:

1. Screening of electronic GP or pain clinic records or musculoskeletal physiotherapy clinic records

Search algorithms identified individuals who (1) had been prescribed strong opioids in the preceding 3–6 months and (2) had received a prescription for strong opioids in the preceding 0–3 months. Individuals who were using methadone to manage their substance misuse or were using opioid treatment to manage malignant disease were excluded. Potential participants who were identified but had a cancer code were marked for review. Individuals who were using opioids to manage malignant pain were excluded. The Clinical Research Network supported practices to identify and screen individuals who were not suitable and should not be contacted by the study team.

2. Referrals received by GPs or other relevant healthcare professionals

Healthcare professionals such as GPs and those providing care at pain clinics and musculoskeletal physiotherapy clinics were able to refer individuals to participate in the study by providing them with a project information sheet, an expression of interest form and contact details for the study team.

3. Posters were also displayed in GP practices (see *Report Supplementary Material 1*), pharmacies, pain clinics and musculoskeletal physiotherapy clinics outlining information about the study and providing contact details for the project team.

Eligibility assessments were carried out prior to enrolment on the trial and established through screening of healthcare records and confirmation from the GP or appropriate healthcare professional, and via a telephone interview with a member of the study team. Any clinical matters that required further clarification were addressed by a clinical member of the study team.

The study planned to recruit from three locations: North East England, London and the West Midlands. This strategy was used due to its proven success in other large community-based studies of people managing chronic pain [BEAM, BEST, COping with persistent Pain, Effectiveness Research into Self-management (COPERS)].[26–28] Originally, the team sought to recruit from approximately 33 general practices across each of these three locations providing an estimated 850,000–900,000 potential participants. In addition to general practices, the recruitment strategy would also include

community pain and musculoskeletal services and pharmacies. Recruitment was planned in waves with clusters of general practices in similar proximity so that treatment groups could be established in a timely manner.

Those who found out about the study via practice clinicians, or the study poster, were advised to contact the study team directly and provided with an invitation pack (see *Report Supplementary Material 1*) by the practice. Individuals were also able to refer themselves after having seen, for example, the study web page or press releases. To aid recruitment and ensure that the target was met, community-based musculoskeletal services, community pain services and pharmacies in the surrounding area to the participating practices were also approached. However, it was acknowledged that access to information on opioid prescribing for this subgroup could be difficult and therefore the individuals themselves would need to be approached to ascertain their opioid use as part of the recruitment.

Individuals who contacted the project team were assessed for their suitability, using the inclusion and exclusion criteria. Eligibility forms were completed (see *Report Supplementary Material 1*), outlining reasons for exclusion where necessary.

Consent

Recruitment to the study consisted of two steps: an expression of interest and consent to participate in the study.

1. Expression of interest

Individuals identified as being eligible to participate following screening of electronic GP records or following a telephone interview with a member of the project team were sent an information sheet and an 'expression of interest' form, along with a letter inviting them to take part in the study (see *Report Supplementary Material 1* for recruitment documents). Those who wanted to take part were able to return the form along with their contact details in a pre-addressed envelope back to the study team. A reminder was issued via post 10–14 days after the initial invitation.

2. Consent to participate

Once the study team had received an 'expression of interest' form, a recruitment pack was dispatched to the potential participant. The pack (see *Report Supplementary Material 1*) comprised an I-WOTCH cover letter, information sheet, consent form, baseline questionnaires (see *Report Supplementary Material 2*) and a pre-addressed envelope. By consenting to take part in the study, the participant was also agreeing to the use of their anonymised data, the recording and observation of group sessions and engaging in individual consultations.

Individuals who expressed an interest in participating from the displayed posters (see *Report Supplementary Material 1*) or self-referred were asked to contact the Warwick Clinical Trials Unit (WCTU) directly. They were then contacted by a member of the study team to assess their suitability over the telephone and collect GP details for those deemed eligible. A recruitment pack was then dispatched to these individuals (see *Report Supplementary Material 1*).

Following receipt of a signed consent form and baseline questionnaire from a potential participant, an assigned member of the study team then made telephone contact with the individual for the purpose of conducting a final eligibility assessment. This was completed based on the medication and self-reported information on the returned baseline questionnaire from the initial project pack. Any outstanding queries pertaining to the information provided by the participant were resolved at this stage. If the details regarding medications fulfilled the eligibility criteria, and the individual's consent was deemed valid and informed, the consent form (see *Report Supplementary Material 1*) was countersigned by the member of the study team. The participant was also able to ask any questions. Following countersigning, the participant was officially enrolled in the trial.

Individuals were also told of their right to withdraw, and asked if they required more time to decide on taking part in the study, for which they were then given the option to provide consent at a later date – typically within 14 days of being contacted by a member of the study team. If the participant decided to take part within this period, they were asked to

contact a member of the study team via the details provided on the information sheet in the project pack. A copy of the countersigned consent form was returned to the participant and sent to their GP.

Additional consent for qualitative interviews

Individuals who gave consent to be approached for qualitative interviews and were selected for interviews received a further invitation letter, information sheet interview consent form (see *Report Supplementary Material 1*) through the post. Participants selected for interview were telephoned between 7 and 10 days after the initial invitation letter was sent to ascertain whether they wished to be interviewed and allow the opportunity for any questions to be asked. If they consented to be interviewed, a suitable date was arranged. Prior to interview, the interviewer checked and countersigned the interview consent form.

Additional consent for missing data calls

Questionnaires at the 4-, 8- and 12-month time point in the study contained a *Missing data* section (see *Report Supplementary Material 2*). Participants were asked to provide consent for a member from the study team to contact them to discuss any information provided on the questionnaires that was unclear or absent over the course of the trial.

Overview of intervention development

The I-WOTCH intervention consisted of a number of key elements including evidence-based interventions for self-managing chronic pain.[19] Central to its development was coproduction with individuals who had experience of chronic non-malignant pain and using opioids to manage this pain and further patient and public involvement (PPI) groups. Members of the trial management team who had experience of working with individuals with chronic pain and managing these individuals also provided input. Feedback was also provided during the pilot phase of the trial from participants and those delivering of the invention. We used The Medical Research Council Framework[29] to inform the intervention development and psychological theories of self-efficacy[30] theory of planned behaviour and reasoned action[31,32] and group-based interventions[33] to inform content and structure around beliefs and attitudes towards pain management and opioid tapering, confidence in perceived skills and abilities to taper and incorporating peer support. The bio-psychosocial framework[34] was adopted to capture the interaction between physical, psychological and social factors of living with chronic pain and opioid use, in particular, the interaction of opioids on pain mechanisms and impact on mental health, mood/emotions and social factors such as family, relationships and work. A cognitive–behavioural approach[35] was applied to the course structure which included interactive sessions to address cognitive appraisal, reframing of unhelpful thoughts for predicted outcomes of pain and opioid tapering and behavioural activation through the tailored one-to-one sessions. A 2020 systemic review on psychological therapies in the pain management found that cognitive–behavioural therapy had the largest evidence base with 59 studies and over 5000 participants found a small or very small benefit for reducing pain, disability and distress in chronic pain, with overall moderate level evidence.[36]

The Behaviour Change Wheel and the Capability, Opportunity, Motivation – Behavior model[37] of behaviour change further informed the behavioural techniques adopted for the intervention for opioid tapering and specific intervention functions within the group and one-to-one sessions. In particular, the one-to-one sessions were guided by motivational interviewing[38,39] to help and support participants through withdrawal and decision to taper. The intervention development has been published elsewhere.[3]

Final trial intervention

I-WOTCH is an 8- to 10-week programme which consists of a combination of group sessions delivered by two trained facilitators (a nurse and a person with lived experience of chronic pain and opioid withdrawal/tapering) and one-to-one sessions, face to face and via phone with the I-WOTCH nurse. Key components of the intervention are highlighted in *Table 1*.

TABLE 1 Detailed course content

I-WOTCH group-based sessions day 1 (week 1)	Aims
Introductions, group work, aims	To allow participants to introduce themselves to the group, encourage participation in a safe and relaxed environment, explore expectations and discuss the I-WOTCH course aims
What causes pain? (Pain information)	To increase understanding about long-term pain
Living with pain (opioid education I)	To increase understanding about use of opioids for long-term pain and encourage participants to start questioning their own knowledge and beliefs about opioids and why they take them
Acceptance	To understand and start to accept pain, with a view to implementing self-management strategies as reduction of opioids occurs
Attention control and distraction	To learn how to focus the mind away from pain thoughts and use of opioids
Distraction activity – drawing	An opportunity to practise distraction activity and socially interact with group informally
Good days, bad days – pain, bearable or not?	To reinforce that pain is not just physiological, it is a psychological, social and an emotional phenomenon
The pain cycle (including opioids) and breaking the pain cycle	To explain and identify unhelpful factors in the pain cycle and learn strategies to break the cycle
Posture and movement	To promote body awareness, posture and muscle weakness (managing pain without opioids)
Relaxation and breathing	To reduce muscle tension and introduce breathing as a relaxation technique
Summary of the day	To consolidate learning of the day and outline aims for group day 2
I-WOTCH group-based sessions day 2 (week 2)	**Aims**
Reflections from day 1	To understand and empathise with the group
Stress-busting for Health: Action planning, problem-solving, pacing, SMART goal setting	To help the participants logically and systematically identify problems, free think solutions, set achievable goals and create action plans, as a means of escaping the pain cycle
Withdrawal symptoms, case studies (opioid education II)	To discuss potential withdrawal symptoms that participants might experience if their taper is too quick
Distraction activity – origami	To learn how to focus the mind away from pain thoughts and use of opioids
Identifying and overcoming barriers to change	Introduce ideas about unhelpful thoughts, automatic thoughts and errors in thinking. To identify reasons why people stay in the pain cycle, and barriers to change. Introduce positive reframing
Mindful attention control	To introduce mindfulness as a tool to train attention and distract from pain
Balance and stretch	To promote body awareness and core strength
Summary of the day	To consolidate learning of the day and outline aims for final group day 3. A reminder to attend the one-to-one appointment with the clinical facilitator
I-WOTCH group-based sessions day 3 (week 3)	**Aims**
Reflections from day 2	To understand and empathise with the group and ascertain current thoughts
Anger, irritability and frustration	Identifying reasons for negative emotions and implementing goal setting and action planning
Relationships: getting the most from your healthcare team (part 1)	To reflect on consulting behaviour and promote effective communication and constructive consultations
Relationships (part 2) listening skills	To improve listening and communication skills
Managing setbacks and non-drug management techniques	To know what to do when experiencing a setback or a flare-up

TABLE 1 Detailed course content (*continued*)

I-WOTCH group-based sessions day 1 (week 1)	Aims
Mindful distraction activity – colouring	To learn how to focus the mind away from pain thoughts and use of opioids
Stretch	To learn how to stretch muscles gently with low risk of injury and pain
Mindfulness of thoughts and senses	To learn how to apply mindfulness of thoughts by detaching emotion from reality, to appreciate 'the now'
Summary of the day	To consolidate the days learning.
Summary of the course	To clarify learning from past 3 group days and motivation to continue with opioid reduction
One to one session	**Aims**
Interaction one: face to face with clinical facilitator	To reflect on group learning days, agree tapering goals and generate tapering plan
Interaction two: 30 minutes via telephone call with clinical facilitator	To reflect on progress and offer support during the tapering process
Interaction three: 30 minutes via telephone with clinical facilitator	To reflect on progress and offer support during the tapering process
Interaction four: face to face with clinical facilitator	To reflect on progress so far and discuss goals for future

SMART, specific, measurable, achievable, relevant, time-bound.

Source
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The three group sessions of the intervention were delivered on a weekly basis. The study team ensured that intervention venues were accessible from public transport and had disabled parking. Refreshments were provided for participants during group sessions. In line with PPI feedback, the 3 days for group sessions were split into 2 consecutive days, followed by a subsequent group day after participants had a one-to-one delivered in person with the nurse to discuss and mutually agree a tapering plan. Participants were given a copy of the tapering plan to discuss with their GPs. This sheet advised the GP on the plan to taper opioids and minimise withdrawal effects. Following this, participants were offered two telephone consultations with the I-WOTCH nurse and a face-to face consultation during weeks 8 and 10 of the programme.

When delivering the group intervention, a variety of methods were utilised, including group discussion, sharing ideas and experiences, problem solving, engaging in role play and viewing educational DVDs. Activities also included considering the potential challenges and barriers during opioid withdrawal and creating means by which to overcome these barriers. Techniques such as mindfulness were also used. We ran the group session in community facilities proximate to the recruiting general practices to ensure these were accessible for those randomised to the intervention group. The intervention included the integration of pain management topics and opioid-specific topics (*Table 2*).

Opioid tapering

Participants were tapered as, a first choice, on their drug of presentation. In case of participants presenting on long-acting preparations such as fentanyl transdermal patches, these could be tapered in decrement of 12 mcg/hour patches and an oral formulation of alternative opioid with equianalgesic potency introduced when the lowest increment of the patch is reached.[40] To minimise the likelihood of participants having serious withdrawal symptoms and to facilitate adherence to the tapering plan, a slow tapering regime was used based upon the experience of the Mayo Clinic.[40] This involved a 10% decrease in the original opioid does every 7 days up until the point that a 30% dose is reached. Once

TABLE 2 Key components of the I-WOTCH group sessions

General pain management topics include	Opioid-specific topics include
Acute vs. chronic pain	The rationale of prescribing in chronic pain
Coping and pacing skills	Opioid-induced tolerance and need for dose escalation
Posture and movement advice	Evidence of usefulness of opioids short and long term
Communication skills	Side effects of opioids short term and long term
Relaxation techniques	Case studies of successful discontinued opioid therapy
Mindfulness	Opioid withdrawal symptoms
	Advantages of slow supervised taper
	Symptom management during tapering
	Pain control after opioids

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this 30% dose is reached, it will further be decreased by 10% every 7 days. To suit prescribing, 10% of the dose may be rounded up. Tapering was tailored and individualised as necessary.

Equianalgesic dosing

For the calculation of equianalgesic doses, we used the data provided by the Faculty of Pain Medicine.[41] These recommendations changed during the lifetime of the study. Training was given on calculating the equianalgesic dose calculation in conjunction with electronic methods of calculating and communicating the tapering plan to participants and GPs. Nurses were supported by an android App developed by JN and SE working with the University of Warwick's Clinical Trials Unit programming team. The App enabled the calculations of tapering regimes, as well as equianalgesic doses of systemic opioids when switching from patch preparations. Where appropriate, 'weak' opioids (codeine/dihydrocodeine) were used as part of the tapering regime.

Frequency of usage

People utilising opioids, as rescue analgesia at a frequency of less than one dose per day, did not require a formal tapering regime were still supported to completely withdraw from opioids.

Planning of, and support for, tapering regime

The withdrawal plan and tapering regime were discussed by participants at their first one-to-one consultation with the intervention nurse. Participants were asked to communicate their preferences during this process to allow for flexibility in the approach taken with each individual participant. The three subsequent one-to-one consultations between week 4 and week 10 of the programme were used to support and encourage participants and will allow study nurses to examine progress in accordance with the agreed tapering plan.

Control intervention

All participants were offered 'best usual care' a comprehensive self-help booklet, My Opioid Manager™ (Toronto Rehabilitation Institute, University Health Network, Canada) on opioid tapering for chronic pain and a relaxation CD. The My Opioid Manager Book and App is a tool designed for clinicians prescribing opioids for patients with chronic non-malignant pain and was developed by Toronto Rehabilitation Institute, University Health Network in 2010 by Dr Andrea Furlan.[42] The aim of My Opioid Manager is to prepare individuals for consultations with their healthcare provider. The information presented in the app includes understanding the causes of various types of pains, uses of opioids and the associated side effects and risks, managing pain by tracking opioid trials, and tips on using opioids. For the purpose of this study, the language used was modified to represent a UK population. The names of medication brands and pictures were also altered to reflect the UK population. In addition to this, as part of the control intervention participants were also provided with a relaxation CD.

Facilitator training

All facilitators for the intervention were provided with 2 days training which covered a step-by-step approach to use of the course manuals and intervention materials such as case studies to support learning. I-WOTCH trainers had the intervention manual and all participant materials. During training days, facilitators were encouraged to ask any questions and clarify any of the material covered and completed a short assessment to assess their knowledge on the material covered in the training. Lay facilitators also completed a brief assessment. All assessments were then marked by a member of the I-WOTCH team. Facilitators were contacted via telephone if they did not achieve a mark of 70% or above and offered further training.

Facilitators were observed by a member of the process evaluation team (VN) during their first initial group sessions on day 1 and day 2 of delivering the intervention by an independent member of the study team as part of the quality assurance process. Where possible facilitators were also observed on day 3 of group sessions. They were provided with the opportunity to reflect upon delivering the intervention. Continuous support was given to trainers throughout the duration of the study.

Feasibility and piloting

Prior to the start of the I-WOTCH study, the intervention was piloted within the pain service at South Tees Hospital NHS Trust, Middlesbrough UK. This was funded by the Hambleton and Richmond Clinical Commissioning Group. We trained seven facilitators (three community team clinicians, two nurses and two volunteer patients). Observation of two courses (with five patients in total) allowed the study team to evaluate the delivery of content as well as gain feedback from the facilitators and the patients of what worked well and what could be adapted and changed moving forward. The main suggestions included structure of course (length and when the sessions were delivered), and content on certain topics such as use of case studies, relaxation and mindfulness and distraction techniques as well as opioid-specific education.

An internal pilot was also conducted to test the feasibility of the trial. Thirty-six people from 10 general practices across Coventry and Warwickshire were recruited to a randomised internal pilot. The number of participants for the pilot was similar to two practice clusters and the proximity of the site to the trial team enabled close oversight and evaluation. The location was also situated centrally, with respect to prescribed opioid use, to the three proposed localities for current opioid prescribing providing a benchmark for recruitment for the full trial. The number of participants in the pilot enabled the formation of two intervention groups of nine. Data collected from the pilot also provided vital information on recruitment and individuals baseline characteristics enabling where necessary adjustments to be made to the sample size (included in report below), recruitment procedures and time frame. The success indicators for the pilot study were to have randomised participants in a timely manner and delivered the essential components of the I-WOTCH intervention within 3 months to 70% of randomised participants. Essential components of the intervention were outlined as participants having attended a minimum of half of the group sessions, and agreeing to an opioid tapering plan within the initial one to one consultation. A meeting with the Trial Steering Committee (TSC) was held as the pilot phase was drawing to a close to ascertain whether there were adequate grounds to support undertake the full study.

A process evaluation was also conducted on the pilot phase to examine the acceptability of randomisation and control condition, feasibility of group intervention delivery, the burden of outcome assessments and to assess any problems that may have presented during administering the intervention. Interviews were also conducted with individuals who were eligible to participate but did not. During delivery of the trial intervention, the number of sessions attended by each participant was recorded, including the number of follow-up calls completed.

Process evaluation

A process evaluation was conducted to examine any potential barriers and enablers to the intervention becoming integrated into everyday behaviour, from the stance of those delivering the intervention and those in receipt of the

intervention. Observational data were collected from audio recordings of all interactions that occurred during the intervention; 10% of these were analysed to determine fidelity to the study protocol and examine interactions between intervention facilitators and the participants. Further details of the process evaluation are outlined in Chapter 6.

Data collection

Baseline data

Demographic data collected at baseline included age, gender, ethnic group, age upon leaving full-time education, education, occupation and current employment status. The clinical measures outlined in *Table 3* were also collected at baseline and the time points across the follow-up period. All baseline data were collected prior to randomisation (see *Appendix 5*, *Tables 81–84*).

Outcomes measures

Activities of daily living

Individuals maintained on opioids to manage chronic pain frequently describe poor pain control and limited functioning and a reduced quality of life. Therefore, a vital long-term aim in treating individuals with chronic pain is to improve or maintain functioning in daily living. Experimental pain testing protocols imply that sensory hyperalgesia presents immediately after discontinuation of opioids resulting in an exacerbation of pain. Research investigating long-term opioid tapering has demonstrated an improvement in function without an increase in pain.[52,53]

To measure ADLs the study used the Patient-Reported Outcomes Measurement Information System (PROMIS) Pain Interference Short Form (8A)(PROMIS-PI-SF-8A) eight-item tool.[43] Data were collected at baseline, 4, 8 and 12 months after randomisation.

Opioid use

The I-WOTCH intervention was designed to facilitate complete withdrawal from opioids. Initially, opioid use was outlined as a secondary outcome, but an amended recruitment plan and increasing the number of participants meant that opioid use could be a second primary outcome in conjunction with ADLs. Opioid use was measured as daily MED (mg), collected 4 weeks prior to the to the 1-year follow-up time point by patient-reported questionnaire. Daily MED

TABLE 3 Outcome measures

Outcome measures	Tool
ADL[a]	Patient-Reported Outcomes Measurement Information System (PROMIS) Pain Interference Short Form (8A)(PROMIS-PI-SF-8A)[43]
Opioid use[a]	Opioid consumption over the last 4 weeks
Opioid prescriptions	Prescribed opioid medication from GP records expressed as average daily morphine equivalent
Pain severity	PROMIS-3A Scale v1.0 – Pain Intensity Short-Form 3A[44,45]
Symptoms	Severity of Opioid Withdrawal (Symptoms): Short Opiate Withdrawal Scale (ShOWS)[46]
Health-related quality of life	• Short Form questionnaire-12 items V2[47] • EuroQol-5 Dimensions, five-level version[48]
Sleep quality	Pittsburgh Sleep Quality Index[49]
Emotional well-being	Hospital Anxiety and Depression Scale[50]
Self-efficacy	Pain Self-Efficacy Questionnaire[51]

a Primary outcome measure.

was calculated using conversion values found by taking the mode of conversion values published by national authorities (see *Appendix 2*, *Tables 38* and *39*).

Originally, the opioid use primary outcome was to be reported as a continuous variable of daily MED (mg); however, the final opioid use data did not satisfy the normality assumptions of linear regression, due to zero-inflated positively skewed data, with Shapiro–Wilk test statistic 0.75 ($p < 0.001$) (see *Appendix 3*, *Figures 11* and *12*). Removal of the zero values was not an option, as the aim of the trial was to taper participants off opioids; therefore, the zero values were the aim of the trial and true values. There are numerous non-parametric ways to handle non-normal continuous data (log transform, Poisson, negative binomial); however, the literature of how to handle non-parametric zero-inflated data are scarce. The best option was to use a Gamma generalised linear mixed model (GLMM); however, this method fitted the positive skewness, but still did not account for the inflation of zero-values. After discussion with a senior independent statistician, Data Monitoring Committee (DMC), TSC and I-WOTCH Trial Management Group (TMG), it was decided to categorise the continuous opioid use measure into two groups: MED = 0 and MED > 0, that is participants who have fully tapered off opioids, and those still taking opioids. This was discussed to be the most clinically meaningful interpretation of the data, and also solved the zero-inflation modelling issues. Therefore, this primary outcome was changed to the proportion of participants reporting no opioid use. We also performed a sensitivity analysis on the opioid use outcome, modelling it as a continuous outcome using the same modelling as for the PROMIS-8A outcome (see *Appendix 3*, *Table 54*).

Although for initial recruitment purposes the study sought to screen data on opioid prescribing, medication used was the focus for outcome assessment. Therefore, participant self-report data on medication use in the preceding 4 weeks were used to examine this outcome. Previous clinical experience indicates that participants using strong opioids often have reliable recall of medication use and dose. While our study entry criterion is participant-reported use of using strong opioids on most days in the preceding 4 weeks, our continuous measure of opioid use was planned to be mean morphine equivalents of opioid used in the preceding 4 weeks. This included all opioids used, including any weak opioids used.

Participant data of self-reported opioid use were collected at baseline, 4, 8 and 12 months after randomisation. Postal reminders were sent at each time point. Where no responses were received, the participant was contacted by telephone to obtain clinical outcomes and opioid use information and the EuroQol-5 Dimensions, five-level version (EQ-5D-5L). All participants were contacted to confirm opioid use data provided in the questionnaires. Staff making these calls were blind to treatment allocation, although on occasion participants divulged their treatment allocation during the call.

Other secondary outcomes

Data on other secondary outcomes collected are outlined in *Table 3*. Selection of secondary measures was guided by the suggestions for core outcome domains for trials of the efficacy and effectiveness of treatments for chronic pain by the Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials group.[54] *Table 4* details the time point at which each measure was collected. Where participants had not returned questionnaires, postal reminders were sent 10–14 days later. If questionnaires were not received following this initial reminder, a member of the trial team contacted the participant via telephone to obtain the data on ADLs, opioid use and the EQ-5D-5L.

An additional secondary measure of proportion of participants who reduced opioids by 50% MED from baseline, measured at 4, 8, and 12 months post randomisation was also reported after being requested by the TMG, for clinical importance.

Data collection and management

The electronic study database was created by the Programming Team at the WCTU in collaboration with members of the study team including the statistician to decide upon the variables to be included, the necessary validation checks

TABLE 4 Summary of outcome measures and delivery time points

Type of data	Outcome measures	Time points				
		1[a]	2[b]	3[c]	4[d]	5[e]
Demographic	Age, gender, ethnic group, age at leaving full-time education, current work status	X				
ADLs[f]	PROMIS-PI-SF-8A[43]	X	X	X	X	
Opioid use[f]	Opioid consumption over the last 4 weeks by questionnaire. The dosage of opioids will be expressed as average daily morphine equivalent.	X	X	X	X	
Opioid prescriptions[g]	Prescribed opioid medication from GP records expressed as average daily morphine equivalent.	X	X	X	X	
Pain severity	PROMIS Scale v1.0 – Pain Intensity Short-Form 3a[44,45]	X	X	X	X	
Symptoms	Severity of Opioid Withdrawal (Symptoms): Short Opiate Withdrawal Scale (ShOWS).[46]	X	X	X	X	X
Health-related quality of life	Short Form questionnaire-12 items V2, and EQ-5D-5L.[47,48]	X	X	X	X	X EQ-5D-5L only
Sleep quality	Pittsburgh Sleep Quality Index.[49]	X	X	X	X	
Emotional well-being:	Hospital Anxiety and Depression Scale.[50]	X	X	X	X	
Self-efficacy	Pain Self-Efficacy Questionnaire.[51]	X	X	X	X	
Resource use	Study participants were invited to provide self-reported healthcare resource use data on pain medication, inpatient admissions, day case admissions, and community health and social care contacts, including GP visits at surgery, GP visits at home. practice nurse, district nurse (i.e. at home), district nurse (GP surgery visit), counsellor occupational therapist, psychologist, social worker, physiotherapist, other (GP phone call) (e.g. acupuncture, physiotherapy).	X	X	X	X	

a Baseline.
b Four months after randomisation.
c Eight months after randomisation.
d Twelve months after randomisation.
e Weekly from allocation to 4 months.
f Primary outcome measure
g Due to COVID epidemic, we were unable to access and collect these data as planned.

Source
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and screens. All data were obtained from study participants by members of the I-WOTCH research team, identified individuals of the Clinical Research Network or where necessary, the appropriate NHS Trust. Data were stored in the case report form (CRF). Initial copies of the data collected were transferred to WCTU, with copies also kept by the research nurses regarding the intervention. Upon entering the study, individuals were allocated a unique study number, which paired with their initials enabled identification in the CRF. Project documentation and study records were stored by the WCTU in accordance with the necessary regulatory guidance. Access to the study data was only permitted to authorised members of the study team. For archiving purposes, documents and data pertaining to the trial will be stored for at least 10 years after completion of the trial.

Data collected from individuals began at the point of being assessed for participating in the study through to completion of the intervention and subsequent follow-up. The data collected were checked to ensure validity and quality at the point of data entry. Participants were requested to complete questionnaires for the purpose of obtaining follow-up data at 4, 8 and 12 months (see *Report Supplementary Material 2* and *Report Supplementary Material 3*). To

incentivise completion of the questionnaires, participants received an I-WOTCH pen and tea bag with the 8-month questionnaire, followed by a £10 high street voucher with their 12-month questionnaire. Questionnaires at 8 and 12 months included the key clinical outcomes. Paper copies of the baseline questionnaires, intervention evaluation sheets and follow-up questionnaires were stored safely by a member of the research team at WCTU.

Data access and quality assurance

Case report forms were developed utilising the expertise of the study team in collaboration with the TMG. Electronic participant data that are identifiable were stored on a secure password protected database which was only accessible to essential personnel. Paper forms containing participant-identifiable data were stored safely in locked filing cabinets within a restricted area of the WCTU. Access to these data was required for trial monitoring. A data management plan outlining the appropriate checks on the data was followed to provide quality assurance.

Chapter 3 Statistical analysis

Power and sample size

Initial plan

Our sample size calculation was based on our primary clinical outcome, the PROMIS-PI-SF-8A. Based on developer's values, we assumed a standard deviation (SD) of 10[43] for individuals in the control arm was used. To demonstrate a 3.5-point difference on this measure at a significant level of 5% with 90% power, using a simple sample size calculations means data were needed from 346 participants. It was anticipated that clustering effects could occur in the intervention arm, but there were limited data from other studies to assist in estimating intracluster correlations (ICCs). Previous experience from other studies on group interventions has revealed that these effects are minor or inconsequential.[26–28] Nonetheless, assuming a relatively modest ICC of 0.01 and assuming on average that 10 participants per group provide 1 year of outcome data, data from 374 participants were required. The trial needed to recruit 468 individuals to permit a potential loss of 20% to follow-up. Similar studies have indicated that when approaching the end of recruitment, there can be a need to recruit beyond the number of participants initially calculated to make sure that the final intervention group has an adequate number of participants.[19,26,27]

For the COPERS project of supportive self-management for people with chronic musculoskeletal pain, the study team recruited from 25 general practices with an overall list of 223,425. The average list size was 8937. In total, 5878 (2.6%) were approached to participate in the study, 531 (9%) of whom were recruited and 23% of whom were taking strong opioids.[19] If these recruitment numbers were achieved for the I-WOTCH study, it would equal 0.5 participants/1000 registered patients. Therefore, to recruit the 468 individuals needed for the I-WOTCH trial, a total list number of 936,000 (105 practices) would be needed. It was anticipated that recruitment in the North East of England would be advantageous due to greater opioid use. The trial aimed to recruit participants from approximately 100 practices, 33 from the 3 locations (The North East, The West Midlands and London) totalling between 850,000 and 900,000 patients. We were unable recruit in London due to operational barriers. To compensate for this, we extended recruitment to other areas contiguous with the West Midlands. Further recruitment occurred from community pain services, community musculoskeletal services and local pharmacies.

Changes to protocol

Initial replies to invitations to participate in the study were fewer than expected compared to the COPERS study recruitment rates from which the original recruitment numbers were calculated. To assist in reaching the target sample size, the population base for the study was increased, by contacting further GP practices were and hosting additional groups across both geographical areas.

As originally designed, pain interference was our single primary outcome (as measured by the PROMIS-PI-SF-8A). However, the target of the I-WOTCH intervention was to reduce opioid usage, consequentially reducing pain interference. Due to the nature of the recruitment process, and the need to have sufficient participants to populate an intervention group in a particular locality we overshot our original recruitment target. Since we considered that if the intervention was to reduce opioid usage but have no impact upon pain interference, then it could still be considered beneficial; we sought approval to add difference in opioid use as a second primary outcome. This was agreed by the TSC, DMC and the funder while data collection was still in progress. The necessary group size needed was less than expected and therefore the requirement for sample size inflation to account for clustering effects was reduced. The revised sample size required to assess the two primary outcomes, opioid reduction and pain interference, was 542 participants (271 per group). This was estimated based on changing the significance level to 2.5% and assuming a similar effect size for both outcomes.

Allocation sequence generation and randomisation

The unit of randomisation was the individual participant (1 : 1). We used the WCTU computer randomisation system, developed by WCTU programmers, to randomise and allocate participants to either the I-WOTCH intervention or

best usual care. Allocation concealment was achieved. All baseline data were collected prior to randomisation. Where possible, any data collected from GP records were done by staff blind to treatment allocation. Routine data sources such as GP prescribing data were also collected.

Initial plan

Based on the assumption that recruitment would be relatively equal in each area, it was estimated that between 75 and 80 people individuals were to be randomised to the intervention in each locality. It was anticipated that the study would need to provide seven courses in each of three localities. To ensure adequate numbers for intervention, groups are reached, groups of four to five. General practices were clustered to begin recruitment at the same time point. Participants were randomised when the target of approximately 24 participants for an intervention group was reached. This avoided any delay between randomisation and commencement of the intervention.

Along with intervention group, pain severity (low/high) and opioid use at baseline (0–29 mg, 30–59 mg, 60–89 mg, 90–119 mg, 120–149 mg, 150 mg+) were used as stratification variables in the minimisation algorithm for randomisation. These baseline data were collected from the self-report questionnaires completed by participants when obtaining consent.

It was anticipated that there could be some differences in the percentage of the population using strong opioids between regions. To mitigate this, recruitment estimates were revisited following the value of information analysis at the end of the pilot phase (described in more detail later in the document) and, if appropriate, adjust numbers required. The study initially aimed to randomise approximately 350–370 people in the Midlands Region (175–185 to the intervention) and around 180–200 people in North East England (90–100 to the intervention). The study aimed to populate 20 groups in the Midlands, and around 16 groups in North East England.

Post-randomisation withdrawals and exclusions

The study team monitored participants throughout the duration of the trial and reported any concerns to the principal investigators. If there were concerns regarding participant safety, participants were withdrawn from the trial at the discretion of the investigator and/or TSC due to safety concerns.

In accordance with the Declaration of Helsinki, each participant was free to withdraw from the study at any time, including during the follow-up period, without needing to provide a reason for withdrawal. Participants were informed of their right to withdraw on the information sheet provided to them in the initial recruitment phase.

Any data collected prior to a participant withdrawing were included in the analysis. If a participant decided to withdraw from the study after the intervention programme commenced, observations prior to withdrawal were completed as thoroughly as possible. If a participant withdrew due to a serious adverse event (SAE), they would continue to be monitored until an outcome in relation to the SAE had been achieved.

Blinding

Members of the trial team who were responsible for collecting data from GP records and managing data were unaware of treatment allocation. Due to the nature of the intervention, it was not possible to blind facilitators, and patients to their treatment allocation. The core members of the research team were blind to treatment allocation throughout the trial.

Data analyses

Statistical analyses

Statistical analyses were carried out using STATA version 16 (StataCorp, Stata Statistical Software: Release 16. College Station, TX: StataCorp LLC; 2019). The two primary outcomes used two-sided tests at the 2.5% significance

level (see *Report Supplementary Material 3*). All other statistical tests were two-sided at the 5% significance level. The estimate, 95% CI and *p*-value were reported for each test undertaken. We looked at two levels of adherence in this study: minimal adherence and full adherence. Minimal adherence with the intervention was defined as the participant attending day 1 of the intervention plus the first one-to-one session. Full adherence was defined as the participant attending all 3 days, the first one-to-one session and one or more phone calls. The primary analysis approach was 'intention to treat' (ITT). The participants were analysed according to the treatment they were randomised to, irrespective of the treatment they actually received. All participants were included in the analysis, regardless of whether they adhered to the protocol. We also undertook an instrumental variable analysis to adjust for non-adherence for the pain interference primary outcome for the two pre-defined levels of adherence to assess whether the level of compliance influenced the intervention effect.

Descriptive analysis

Participant characteristics and outcomes are summarised as mean and SD for continuous data or frequency and percentage for categorical data, summarised by treatment arm. The median and interquartile range (IQR) were presented if data are non-normal.

Primary analysis

The primary analysis approach was ITT. Partially nested mixed-effects regression models (linear for pain interference, logistic for opioid use) were used to estimate the treatment effects for both primary and secondary outcomes. The covariates that were included as fixed effects in the models were age (years), gender (male/female), geographical locality, baseline pain intensity and the baseline value of the dependent variable. To account for partial clustering, the education support group was used as the cluster variable for the intervention group, with each participant in usual-care group having individual clusters of size 1.[55,56] We anticipated the group effects and corresponding ICCs to be relatively small. Nonetheless, the models accounted for potential heterogeneity in outcome due to the group effect. The adjusted treatment effect estimates (mean difference) were presented along with their associated 95% CI. The primary analyses assessed the overall difference in the primary outcomes between the self-management (intervention) group and the usual-care group at the 12-month time point. Model assumptions were assessed as appropriate.

Secondary analyses

Secondary outcomes were also assessed using an ITT approach. The treatment effect and 95% CIs were estimated for the secondary outcomes using partially nested mixed-effects regression models adjusting for the same variables used in the primary analysis.

Missing data

The level of missingness in the primary outcomes was assessed and an inverse probability weighting analysis was conducted on the opioid use outcome as a sensitivity analysis.

Subgroup analyses

Pre-specified subgroup analyses were also conducted for the primary outcomes using formal statistical tests for interaction to examine whether baseline anxiety, depression and opioid use are moderators of treatment effect.[57] The median value was used as the cut-point to define these subgroups.[58]

Additional analysis

Participants in this trial were recruited from primary care and pain clinics. Typically, those participants recruited from pain clinics will be on more opioids and will have worse pain. For this reason, we planned to compare the baseline characteristics for participants recruited from primary care to those recruited from pain clinics and planned to adjust for this entry pathway to see if it affected the treatment effect estimate for the primary outcomes. However, only one person was recruited from a pain clinic, and this analysis was not possible. To inform future studies and to contribute to future meta-analyses, we report the effectiveness of the intervention based on the primary outcomes for people with different pain disorders, namely back pain, chronic widespread pain and multisite pain.

Sensitivity analyses

A number of participants were included in the process evaluation interviews conducted from pre-randomisation to follow-up. It is possible that discussing their expectations and experiences before and during the study may have influenced the treatment effectiveness. A sensitivity analysis was therefore performed that excluded these participants from the main analysis. An additional sensitivity analysis was performed to estimate the treatment effect size having adjusted for any imbalance in the death rates across the treatment arms.

Adverse event reporting/management

Adverse events (AEs) due to an intervention such as serious psychological disturbance are uncommon, as are those associated with engaging with an intervention, for example, a fall while attending the intervention location. Suspected AEs that may have occurred during the trial were addressed during group or one-to-one sessions in accordance with WCTU's guidance procedures.

Definitions

Adverse events

An AE was defined as an untoward medical occurrence within a participant which do not necessarily have a causal relationship with the treatment or intervention. AEs can be an unfavourable and unintended symptom or disease that presents during the time in which an individual is participating in the study, for example over the duration of a 12-month research period, irrespective of whether it is attributable to the intervention.

Examples of AEs that were expected during the trial are outlined below and were therefore not recorded on an AE form. However, they were monitored and documented through the nurse one-to-one consultations and via the 4-, 8- and 12-month follow-up questionnaires.

- Reporting mild or moderate levels of emotional distress from recounting experiences of living with opioid use while receiving the intervention.
- Symptoms associated with a reduction in opioid such as experiencing anxiety, rapid heart rate, heart palpitations, elevated blood pressure, restlessness, sweating, tremors, nausea, abdominal cramps, diarrhoea, poor appetite, dizziness, hot flushes, shivering, myalgia or arthralgia, rhinorrhoea, sneezing, lacrimation, insomnia, yawning, temporary worsening of chronic pain.

Serious adverse events

A SAE was defined as event that meets one or more of the following criteria:

- Results in death.
- Is immediately life-threatening.
- Requires hospitalisation or prolongs a period of existing hospitalisation.
- Results in persistent or significant disability or incapacity.
- Is a congenital abnormality or birth defect.
- Is an important medical condition.

For any SAEs which occurred during the research study, the study team adhered to WCTU's standard operating procedures.

Reporting related and unexpected serious adverse events

During the study, individuals were asked to report experiencing any S/AE(s) while reducing their opioid use to nurses during consultations and outline what AEs they were experiencing. Research nurses were then required to notify the trial co-ordinating centre within 24 hours of participants reporting SAEs. In conjunction with consultations, follow-up

questionnaires at 4, 8 and 12 months were screened upon receipt for any S/AEs and, if necessary, participants were contacted to confirm details or provide more information. SAEs were recorded on a SAE form. An individual's GP was not notified of a S/AE except in circumstances where there were safety concerns[52] regarding potential harm to the individual or others. Once received, the trial co-ordinator would discuss the SAE form with the investigator to gather the relevant information. The trial co-ordinating centre assumed responsibility for relaying any associated or unexpected SAEs to the sponsor and Research Ethics Committee (REC) within the stipulated time frame. All SAEs were also documented in annual study reports provided to the REC. The cause of any SAEs (i.e. relationship to trial treatment) was examined by the investigator(s) against the criteria provided on the SAE form (see *Appendix 1*, *Table 37*).

Serious adverse event information gathered over the duration of the trial was examined by the TMG. SAEs were monitored for a final outcome until completion of the follow-up period (12 months). 'Unknown' outcomes were not valid as a final outcome. Outcomes that remained unresolved were considered admissible for non-serious AEs by the end of the individual's involvement in the study and for the purpose of locking the SAE database.

Trial organisation and oversight

Sponsor and governance arrangements

The University of Warwick were the sponsor for this study, and the trial was co-ordinated by the WCTU. University policies and procedures were adhered to and followed throughout the entire duration of the project.

Regulatory authorities/ethical approval

The Integrated Research Application system was used to apply for ethical approval for the study. Each site within the trial was required to have the appropriate NHS Trust research and development department approval, evidence of which was needed by WCTU prior to enrolling individuals onto the trial. Substantial amendments that occurred over the duration of the study were submitted to the relevant organisations for approval.

Trial registration

The study was also registered on the International Standard Randomised Controlled Trial Number (ISRCTN) Register

Indemnity

For the purpose of the trial, the University of Warwick provided indemnity for any potential harm caused to participants from the design of the protocol. The University required evidence of Public Liability insurance from the non-NHS locations hosting the trial intervention. NHS indemnity covers NHS staff including medical staff possessing honorary contracts and individuals directly involved in conducting the trial.

Trial Management Group

To oversee the trial, a TMG was created. Members of this group included staff and coinvestigators who were responsible for the routine management of the trial. The TMG held regular meetings over the duration of the study to discuss trial progress. Any important matters that arose from these meetings were forwarded to the TSC or Investigators where necessary.

Trial Steering Committee

A TSC for the study comprised staff and trialists with the relevant knowledge and expertise, an independent Chairperson and a 'lay' representative. Meetings were held regularly over the course of the trial, once a year or otherwise determined by need. Outside of these meetings, communication was carried out via e-mail, post or teleconferencing. The purpose of the Committee was to provide guidance for the trial and assume overall oversight, which included making decisions pertaining to changes in the protocol, tracking the trials progress, examining information from other sources and reviewing recommendations made by the DMC.

Data Monitoring Committee

The DMC consisted of independent members with the appropriate clinical and research expertise who reviewed information on recruitment, protocol compliance, data safety and assessments of outcomes in order to make

recommendations to the TSC on whether the trial should be revised or terminated. The DMC held meetings with the TSC, which were also attended by the Trial Chief Investigator and Co-ordinator, and trial statistician.

Essential documentation

A Trial Master file was created in accordance with WCTU standard operating procedure and stored securely at the co-ordinating centre. Investigator Site Files were provided to all recruiting centres by the co-ordinating centre.

Monitoring and quality assurance of trial procedures

We performed a risk assessment and produced a monitoring plan in line with the level of risk identified.

Patient and public involvement

The I-WOTCH study has benefited from substantial amount of patient and public input from designing the overall trial to intervention development, delivery and interpretation and dissemination of results. At the initial stage of application, a meeting was held in February 2015 with the North East and North Cumbria Clinical Research Network which was attended by nine volunteers, all with lived experience of using opioids. These volunteers provided valuable insight into their personal experience of using opioids in managing chronic pain, their motives to cease or reduce opioids and the anticipated barriers to reducing or withdrawing from using opioids entirely. Further involvement and engagement were facilitated by organising a second meeting with the North East and North Cumbria Clinical research network, to which 10 volunteers attended, all with different experiences of opioid withdrawal. This group provided additional input regarding the feasibility of the intervention, focusing especially on the design of the I-WOTCH intervention.

Another valuable contribution was the delivery of the I-WOTCH intervention, with the lay facilitators having the opportunity to share their experiences of opioid withdrawal and deliver and help deliver the group component of the I-WOTCH intervention.

We have also had significant input from our PPI coinvestigators. One of whom retired during the study and the other (CT) who gave a significant and valuable contribution in the design and delivery of the intervention who was able to also share in the dissemination of final results to the British Pain Society Annual Scientific Meeting. CT was also involved in radio broadcasts and TV, in discussing the I-WOTCH study and results from a lay perspective and his experience of being a facilitator for the I-WOTCH intervention. CT died unexpectedly soon after the I-WOTCH study was completed, and results disseminated. We have dedicated this report to CT as a reflection of his valuable contribution to the success of the I-WOTCH study.

Chapter 4 Results

Study timeline

The first trial participant was recruited on 17 May 2017 and the last was recruited on 30 January 2019. Follow-up ended on 18 March 2020. The trial data were locked on 15 July 2021.

Recruiting centres

We recruited participants from 191 sites, 117 general practices from the Midlands and 71 general practices from the North East and 3 hospitals (see *Appendix 3*, *Table 40*).

Participant flow

Screening

The flow of trial participants from screening to randomisation is shown in in the Consolidated Standards of Reporting Trials diagram (*Figure 1*). A total of 21,353 people were identified from a search of 191 general practices. Of these, 20,900/21,353 (98%) people were eligible for an invitation, with 2220/20,900 (11%) replying with interest. A further nine people self-referred to the study. We assessed 1541/2220 (69%) of these people for eligibility with 1050/1541 (68%) found to be eligible. We randomised 608/1050 (58%) of these people into the trial. The main reasons for not being eligible for the trial were being unable to attend group sessions and not using opioids for the last 3 months.

Recruitment

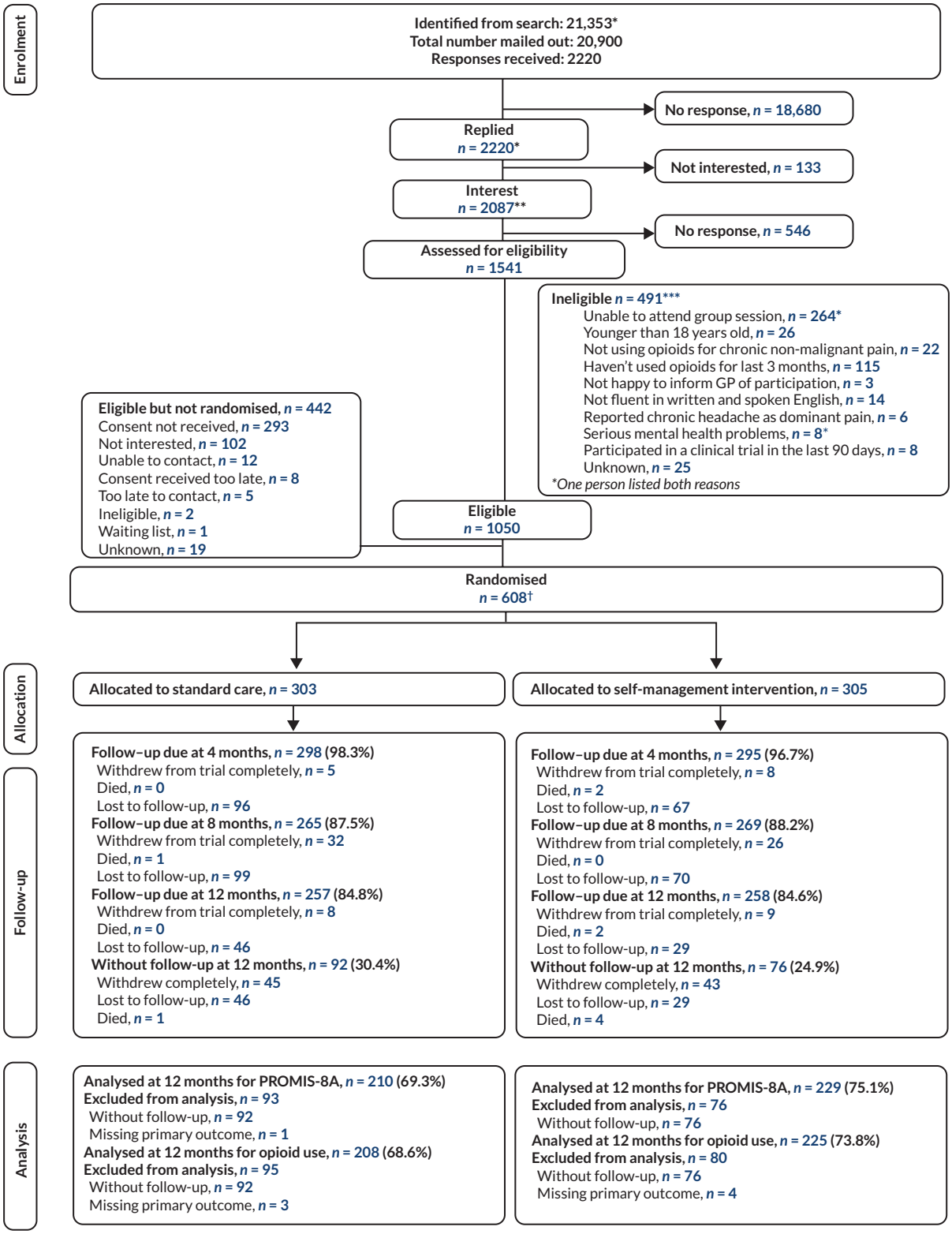
The recruitment target was 542; however, due to follow-up rates being lower than the predicted 80%, we recruited 608 participants to ensure there was not a drop in power. The total number of participants randomised was 608: 305 in the intervention group and 303 in the usual-care group. There was a total of 35 groups in 25 locations that delivered the intervention to participants. *Appendix 3*, *Table 41* shows recruitment split by these groups.

Participant characteristics

All 608 participants randomised completed a baseline questionnaire. Their mean age was 61 (12.9 SD, range 22–90) years, 362 (60%) were female and 585 (96%) were White British (*Table 5*). Over one-third of participants were retired from paid work (270/608; 44%) and (345/608; 57%) had left education between the ages of 13 and 16. Predominately, participants had been experiencing pain for more than 5 years (500/608; 82%) and most had been taking opioids for more than 5 years (365/608; 60%). Participants reported having pain in multiple areas, with the majority reporting lower back pain (490/608; 81%) and multisite pain (541/608; 89%). Overall, the baseline characteristics were well balanced between the study groups.

Participant baseline outcomes

Table 6 shows the baseline outcome measures for all 608 randomised participants by arm. At baseline, in the intervention group 34% (103/105) were in the lowest opioid band usage (0–29.9 MED) and 12% (37/305) were in the highest opioid usage band (≥ 150 MED). In the usual-care group, 32% (98/303) and 10% (29/303) were in the lowest and highest opioid usage bands, respectively. The mean pain interference (PROMIS-PI-SF-8A) score at baseline was 68.4 (SD 6.1, range 48.5–77), indicating participants had a high pain interference with their daily life. The overall pain intensity (PROMIS-PI-SF-3A) score (mean 69.1; SD 7.0, range 36.3–81.9) also indicated participants in this study had high pain intensity at baseline. The other baseline outcome scores also indicated that the study participants had low physical and mental health [Short Form questionnaire-12 items (SF-12) Mental Score mean 40.9; SD 11.1; SF-12 Physical score mean 32.0; SD 8.1], low pain self-efficacy (mean 25; SD 13.2) and low health-related quality of life (EQ-5D-5L mean 0.36; SD 0.28). Overall, baseline outcomes were well balanced between arms.



** 9 self-referrals, 5 secondary care referrals. ** 9 self-referrals, 5 secondary care referrals. ***2 self-referrals, 1 secondary care referral. †2 self-referrals, 2 secondary care referrals*

FIGURE 1 Consolidated Standards of Reporting Trials diagram.

TABLE 5 Baseline demographic characteristics of all randomised participants by treatment group

	Standard care *N* = 303	Self-management *N* = 305	Total *N* = 608
Age (years)			
Mean (SD)	60.4 (13.8) (*n* = 303)	62.1 (11.9) (*n* = 305)	61.3 (12.9) (*n* = 608)
Gender			
Male	117/303 (39%)	125/305 (41%)	242/608 (40%)
Female	184/303 (61%)	178/305 (58%)	362/608 (60%)
Other	0/303 (0%)	1/305 (< 1%)	1/608 (< 1%)
Prefer not to say	0/303 (0%)	0/305 (0%)	0/608 (0%)
Missing	2/303 (1%)	1/305 (< 1%)	3/608 (< 1%)
Ethnicity			
White	290/303 (96%)	295/305 (97%)	585/608 (96%)
Black Caribbean	3/303 (1%)	3/305 (1%)	6/608 (1%)
Black African	0/303 (0%)	1/305 (< 1%)	1/608 (< 1%)
Black Other	0/303 (0%)	1/305 (< 1%)	1/608 (< 1%)
Indian	4/303 (1%)	2/305 (1%)	6/608 (1%)
Pakistani	0/303 (0%)	1/305 (< 1%)	1/608 (< 1%)
Bangladeshi	0/303 (0%)	0/305 (0%)	0/608 (0%)
Chinese	0/303 (0%)	0/305 (0%)	0/608 (0%)
Prefer not to say	1/303 (< 1%)	0/305 (0%)	1/608 (< 1%)
Other	3/303 (1%)	1/305 (< 1%)	4/608 (1%)
Missing	2/303 (0.7%)	1/305 (< 1%)	3/608 (< 1%)
Employment status			
Employed	65/303 (21%)	67/305 (22%)	132/60 (22%)
Unemployed	6/303 (2%)	8/305 (3%)	14/608 (2%)
At school or full-time education	1/303 (< 1%)	0/305 (0%)	1/608 (0%)
At school or part-time education	1/303 (< 1%)	0/305 (0%)	1/608 (0%)
Unable to work due to long-term sickness	76/303 (25%)	78/305 (26%)	154/608 (25%)
Looking after home/family	6/303 (2%)	7/305 (2%)	13/608 (2%)
Retired from paid work	136/303 (45%)	134/305 (44%)	270/608 (44%)
Other	10/303 (3%)	10/305 (3%)	20/608 (3%)
Missing	2/303 (1%)	1/305 (< 1%)	3/608 (< 1%)
Age left full-time education			
Did not receive formal education	1/303 (< 1%)	1/305 (< 1%)	2/608 (0.3%)
Age 12 or less	1/303 (< 1%)	0/305 (0%)	1/608 (0.2%)
Age 13–16	171/303 (56%)	174/305 (57%)	345/608 (56.7%)
Age 17–19	65/303 (21%)	70/305 (23%)	135/608 (22.2%)
Age 20 or over	54/303 (18%)	55/305 (18%)	109/608 (17.9%)

TABLE 5 Baseline demographic characteristics of all randomised participants by treatment group (*continued*)

	Standard care *N* = 303	Self-management *N* = 305	Total *N* = 608
Still in full-time education	4/303 (1%)	0/305 (0%)	4/608 (0.7%)
Other	5/303 (2%)	4/305 (1%)	9/608 (1.5%)
Missing	2/303 (1%)	1/305 (< 1%)	3/608 (0.5%)
How long have you experienced pain			
< 1 year	3/303 (1%)	5/305 (2%)	8/608 (1%)
1–5 years	50/303 (17%)	47/305 (15%)	97/608 (16%)
More than 5 years	248/303 (82%)	252/305 (83%)	500/608 (82%)
Missing	2/303 (1%)	1/305 (< 1%)	3/608 (< 1%)
How long have you been taking opioids for your chronic pain			
< 1 year	18/303 (6%)	11/305 (4%)	29/608 (5%)
1–5 years	107/303 (35%)	104/305 (34%)	211/608 (35%)
More than 5 years	176/303 (58%)	189/305 (62%)	365/608 (60%)
Missing	2/303 (1%)	1/305 (< 1%)	3/608 (< 1%)
I want to reduce my opioid use			
Not at all	25/303 (8%)	21/305 (7%)	46/608 (8%)
By a little	45/303 (15%)	37/305 (12%)	82/608 (13%)
By half	36/303 (12%)	44/305 (14%)	80/608 (13%)
So I only use a little	60/303 (20%)	95/305 (31%)	155/608 (25%)
So I use no opioids	133/303 (44%)	102/305 (33%)	235/608 (39%)
Missing	4/303 (1%)	6/305 (2%)	10/608 (2%)
I expect in 4 months' time, I will have reduced my opioid use			
Not at all	45/303 (15%)	43/305 (14%)	88/608 (14%)
By a little	78/303 (26%)	82/305 (27%)	160/608 (26%)
By half	56/303 (18%)	56/305 (18%)	112/608 (18%)
So I only use a little	67/303 (22%)	82/305 (27%)	149/608 (25%)
So I use no opioids	50/303 (17%)	37/305 (12%)	87/608 (14%)
Missing	7/303 (2%)	5/305 (2%)	12/608 (2%)
I am confident I could reduce my opioid use a lot over 4 months			
Not at all confident	90/303 (30%)	90/305 (30%)	180/608 (30%)
Somewhat confident	70/303 (23%)	77/305 (25%)	147/608 (24%)
Fairly confident	79/303 (26%)	79/305 (26%)	158/608 (26%)
Strongly confident	35/303 (12%)	40/305 (13%)	75/608 (12%)
Completely confident	22/303 (7%)	15/305 (5%)	37/608 (6%)
Missing	7/303 (2%)	4/305 (1%)	11/608 (2%)

continued

TABLE 5 Baseline demographic characteristics of all randomised participants by treatment group (*continued*)

	Standard care *N* = 303	Self-management *N* = 305	Total *N* = 608
I feel that involvement in this study can help me to reduce my opioid use			
Not at all	25/303 (8%)	22/305 (7%)	47/608 (8%)
By a little	76/303 (25%)	73/305 (24%)	149/608 (25%)
By half	38/303 (13%)	46/305 (15%)	84/608 (14%)
So I only use a little	68/303 (22%)	86/305 (28%)	154/608 (25%)
So I use no opioids	86/303 (28%)	69/305 (23%)	155/608 (25%)
Missing	10/303 (3%)	9/305 (3%)	19/608 (3%)
Pain area[a]			
Lower back pain	249/303 (82%)	241/305 (79%)	490/608 (81%)
Chronic widespread pain	137/303 (45%)	154/305 (50%)	291/608 (48%)
Multisite pain	264/303 (87%)	277/305 (91%)	541/608 (89%)
Missing	3/303 (1%)	6/305 (2%)	9/608 (1%)

a More than one pain area could be chosen.

Source

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TABLE 6 Baseline outcome measures

	Standard care *N* = 303	Self-management *N* = 305	Total *N* = 608
Opioid use: total MED of all opioid pain killers taken over the last 4 weeks (daily MED)[a]			
0–29.9	98 (32%)	103 (34%)	201 (33%)
30–59.9	103 (34%)	95 (31)	198 (33%)
60–89.9	44 (15%)	42 (14)	86 (14%)
90–119.9	17 (6%)	18 (6)	35 (6%)
120–149.9	12 (4%)	10 (3)	22 (4%)
≥ 150	29 (10%)	37 (12)	66 (11%)
Median (IQR)	44.0 (25–75) (*n* = 303)	49 (25–80.6) (*n* = 305)	46.4 (25–79.3) (*n* = 608)
Pain interference (PROMIS-8A)[b]			
Mean (SD)	68.2 (6.2) (*n* = 301)	68.5 (6.0) (*n* = 304)	68.4 (6.1) (*n* = 605)
Pain intensity (PROMIS-3A)[c]			
Mean (SD)	68.8 (7.1) (*n* = 303)	69.3 (6.8) (*n* = 305)	69.1 (7.0) (*n* = 608)
SF-12 mental[d]			
Mean (SD)	41.0 (11.4) (*n* = 301)	40.7 (10.8) (*n* = 304)	40.9 (11.1) (*n* = 605)
SF-12 physical[d]			
Mean (SD)	32.1 (8.1) (*n* = 301)	32.0 (8.1) (*n* = 304)	32.0 (8.1) (*n* = 605)

TABLE 6 Baseline outcome measures (*continued*)

	Standard care *N* = 303	Self-management *N* = 305	Total *N* = 608
Pittsburgh Sleep Quality Index[e]			
Mean (SD)	12.5 (4.1) (*n* = 285)	12.3 (4.3) (*n* = 278)	12.4 (4.2) (*n* = 563)
Pittsburgh sleep quality: do you have a bed partner or roommate			
N	303	305	608
No bed partner or roommate	108/303 (36%)	112/305 (37%)	220/608 (36%)
Have partner or roommate	192/303 (63%)	191/305 (63%)	383/608 (63%)
Missing	3/303 (1%)	2/305 (1%)	5/608 (1%)
Pittsburgh sleep quality: if have partner, how often had…			
Loud snoring			
Not during past month	63/192 (33%)	56/191 (29%)	119/383 (31%)
Less than once a week	21/192 (11%)	27/191 (14%)	48/383 (13%)
Once or twice a week	29/192 (15%)	32/191 (17%)	61/383 (16%)
Three or more times a week	71/192 (37%)	67/191 (35%)	138/383 (36%)
Missing	8/192 (4%)	9/191 (5%)	17/383 (4%)
Long pauses between breaths asleep			
N	192	191	383
Not during past month	108/192 (56%)	121/191 (63%)	229/383 (60%)
Less than once a week	27/192 (14%)	16/191 (8%)	43/383 (11%)
Once or twice a week	23/192 (12%)	19/191 (10%)	42/383 (11%)
Three or more times a week	26/192 (14%)	24/191 (13%)	50/383 (13%)
Missing	8/192 (4%)	11/191 (6%)	19/383 (5%)
Legs twitching or jerking when asleep			
N	192	191	383
Not during past month	57/192 (30%)	58/191 (30%)	115/383 (30%)
Less than once a week	21/192 (11%)	22/191 (12%)	43/383 (11%)
Once or twice a week	35/192 (18%)	31/191 (16%)	66/383 (17%)
Three or more times a week	77/192 (40%)	78/191 (41%)	155/383 (40%)
Missing	2/192 (1%)	2/191 (1%)	4/383 (1%)
Episodes of disorientation/confusion during sleep			
N	192	191	383
Not during past month	123/192 (64%)	116/191 (61%)	239/383 (62%)
Less than once a week	22/192 (11%)	34/191 (18%)	56/383 (15%)
Once or twice a week	22/192 (11%)	21/191 (11%)	43/383 (11%)
Three or more times a week	22/192 (11%)	15/191 (8%)	37/383 (10%)
Missing	3/192 (2%)	5/191 (3%)	8/383 (2%)

continued

TABLE 6 Baseline outcome measures (*continued*)

	Standard care *N* = 303	Self-management *N* = 305	Total *N* = 608
HADS anxiety[f]			
Mean (SD)	9 (5.1) (*n* = 298)	9 (5.1) (*n* = 303)	9.4 (5.1) (*n* = 601)
HADS depression[f]			
Mean (SD)	9.1 (4.6) (*n* = 298)	9.1 (4.6) (*n* = 304)	9.1 (4.6) (*n* = 602)
Pain self-efficacy[g]			
Mean (SD)	25 (13.6) (*n* = 300)	24 (12.7) (*n* = 301)	25 (13.2) (*n* = 601)
EQ-5D-5L utility[h]			
Mean (SD)	0.36 (0.29) (*n* = 301)	0.35 (0.28) (*n* = 304]	0.36 (0.28) (*n* = 605)
EQ-5D-5L VAS[h]			
Mean (SD)	49.4 (21.3) (*n* = 301)	47.0 (21.4) (*n* = 304)	48.2 (21.4) (*n* = 605)
ShOWS[i]			
Mean (SD)	10.5 (4.96) (*n* = 301)	10.6 (5.49) (*n* = 303)	10.5 (5.23) (*n* = 604)

HADS, Hospital Anxiety and Depression Scale; MCID, minimal clinically important difference; PROMIS-PI-SF-3a, PROMIS Scale v1.0 Pain intensity Short Form 3a; ShOWS, Short Opiate Withdrawal Scale; VAS, visual analogue scale.

a For opioid medication by region, see *Appendix 2*, *Table 38*.

b PROMIS-PI-SF-8A measures daily pain interference using eight self-reported items. Standardised T-scores reported and calculated using the recommended Health Measures Scoring Service. Higher scores indicate greater pain interference (scores 40.7–60 are average, scores 60–77 indicate high interference). MCID 3.5 (see *eTable 33* Supplement 2 in Sandhu *et al.*).[1]

c PROMIS-PI-SF-3a measures daily pain intensity using 3 self-reported items. Standardised T-scores reported and calculated using the recommended Health Measures Scoring Service. Higher scores indicate greater pain intensity (scores 36.3–60 are average, scores 60–81.8 indicate high pain intensity). MCID 3.5 (see *eTable 37* Supplement 2 in Sandhu *et al.*)[1]

d The 12-item Short Form Health Survey measures quality of life using eight domains of daily living. Scores range from 0 to 100, higher scores reflect better physical and mental functioning. Mental MCID 3.3, physical MCID 3.8 (see *eTable 34* Supplement 2 in Sandhu *et al.*).[1]

e Pittsburgh Sleep Quality Index measures sleep quality using 19 self-reported questions, combined into 7 component scores (range, 0–3), summed to create a global score ranging from 0 to 21, with higher scores indicating worse sleep quality. This global score has been reported. MCID 3.0 (see *eTable 37* Supplement 2 in Sandhu *et al.*).[1]

f HADS anxiety/depression score is measured using 7 questions, ranging from 0 to 3, summed to create the anxiety/depression score ranging from 0 to 21, with higher scores indicating worse anxiety/depression. Anxiety MCID 1.7, depression MCID 1.7 (see *eTable 35* Supplement 2 in Sandhu *et al.*).[1]

g Pain Self-Efficacy Questionnaire score is calculated by summing 10 questions (range, 0–6) to create the reported score ranging from 0 to 60, with higher scores indicating stronger self-efficacy beliefs. MCID 7.0 (see *eTable 37* Supplement 2 in Sandhu *et al.*).[1]

h EQ-5D-5L utility scores range from <−0.594 to 1, with higher scores indicating better quality of life. Crosswalk index value calculator used to map 5L to 3L, citation. EQ-5D-5L VAS score ranges from 0 to 100 ('worst health you can imagine' to 'best health you can imagine'). The reported score ranging from 0 to 100 were self-reported by participants.[59] Utility MCID 0.07, VAS MCID 7.0 (see *eTable 36* Supplement 2 in Sandhu *et al.*).[1]

i ShOWS score measures severity of symptoms, using 10 questions (range, 0–3) summed to give reported score ranging from 0 to 30, with higher scores indicating more severe symptoms. MCID 3.0 (see *eTable 37* Supplement 2 in Sandhu *et al.*).[1]

Outcomes and analyses

Participant follow-up

Questionnaire response rates were 71% (430/608) at 4 months, 60% (365/608) at 8 months and 72% (440/608) at 12 months. Response rates were slightly higher in the intervention arm (see *Appendix 3*, *Table 43*). Time from randomisation to completing the follow-up questionnaires was 4.8 (SD 1.5), 8.5 (SD 1.2) and 12.8 (SD 1.4) months for 4-, 8- and 12-month questionnaires, respectively (see *Report Supplementary Material 4*).

Intervention adherence

For the 305 participants randomised to the intervention arm, 62% (190/305) achieved minimal compliance with the intervention, which was attending at least day 1 and the first one-to-one consultation, and 47% (144/305) achieved full compliance of the intervention, which consisted of attending all three sessions, the first one-to-one consultation and one telephone call (see *Appendix 3*, *Table 45*). A total of 54% (166/305) attended all three group sessions. For the 30% (90/305) of participants in the intervention arm that did not attend any of the group sessions, they were offered slides and handouts. The group sizes at session 1 contained on average 6.2 (SD 2.8) participants.

Withdrawals and lost to follow-up

During the study, 16% (99/608) participants withdrew from the study completely (53/303 in usual care, 46/305 in intervention) and 1% (8/608) discontinued the intervention package only (see *Appendix 3*, *Table 42*). The majority of the complete withdrawals occurred between 4 and 8 months follow-up (59%; 58/99) (see *Appendix 3*, *Table 44*). The main reason given for withdrawing from the trial was poor health (22%; 22/99).

Primary outcome completion rates

For the 12-month questionnaire, 28% (168/608) of participants had no follow-up at 12 months (*Figure 1*). Additionally, one participant was missing the PROMIS-PI-SF-8A primary outcome at 12 months. This left 439 (72%; 439/608) participants with PROMIS-PI-SF-8A primary outcome data at 12 months to be analysed. For the opioid use primary outcome, additional to the 168 participants missing 12-month follow-up data, 7 participants were also missing opioid use data at 12 months, leaving a total of 433 (71%; 433/608) participants with opioid use primary outcome data to be analysed at 12 months.

Primary outcomes

At 12 months, 29% (65/225) in the intervention group and 7% (15/208) in the usual-care group had fully tapered off opioids [OR 5.55 (95% CI 2.80 to 10.99); $p < 0.001$] (*Table 7*). At 12 months, the PROMIS-PI-SF-8A scores did not show a statistically significant between-group difference [mean difference −0.52 (95% CI −1.94 to 0.89); adjusted −0.89 (95% CI −2.12 to 0.33), $p = 0.15$], minimal clinically important difference 3.5.[1] Over the 12-month study period, PROMIS-PI-SF-8A scores did improve in both groups: −4.1 (95% CI −4.98 to −3.22) in the intervention group and −3.17 (95% CI −4.10 to −2.24) in the usual-care group.

Primary outcomes: instrumental variable analysis and missing analysis

To assess the effect of non-adherence to the intervention had on the primary outcome conclusions, an instrumental variable analysis to adjust for non-adherence was performed using both minimal and full compliance definitions. Due to the skewed distribution of the opioid use data, this analysis was only performed on the PROMIS-PI-SF-8A outcome. The findings from the instrumental variable analyses were not meaningfully different to the ITT analysis when using both the full compliance definition [adjusted mean difference −1.47 (95% CI −4.04 to 1.09); $p = 0.26$] and the minimal compliance definition [adjusted mean difference −0.99 (95% CI −2.93 to 0.96); $p = 0.32$] (*Table 8*).

Due to the large number of missing data for the opioid use primary outcome, we also conducted an inverse probability weighting analysis on the missing data for the opioid use outcome to assess whether the missing data affected the conclusions. We found no meaningful difference in conclusions (see *Appendix 3*, *Table 51*).

Secondary outcomes

Opioid use percentage reduction from baseline

The proportion of participants who reduced their daily MED opioid usage by ≥ 50% from baseline was assessed as a secondary measure. This was assessed at 4-, 8- and 12-month follow-up. At 12 months, 57% (129/225) in the intervention group and 27% (57/208) in the usual care group had reduced their daily opioid usage by ≥ 50% MED from

TABLE 7 Primary outcomes (daily opioid use and PROMIS-PI-SF-8A) at primary 12-month time point and secondary 4- and 8-month time points

	Self-management	Standard care	Unadjusted estimate (95% CI); *p*-value	Adjusted estimate (95% CI); *p*-value
Primary time point				
Opioid use (12 months)[a]			5.23 (2.87 to 9.52); $p < 0.001$[b]	5.55 (2.80 to 10.99); $p < 0.001$[c]
Fully tapered (MED = 0), *n* (%)	65/225 (29%)	15/208 (7%)		
Not tapered (MED > 0), *n* (%)	160/225 (71%)	193/208 (93%)		
PROMIS-PI-SF-8A (12 months)[d]			−0.52 (−1.94 to 0.89); $p = 0.47$	−0.89 (−2.12 to 0.33); $p = 0.15$[e]
Mean (SD)	64.2 (7.7) (*n* = 229)	64.7 (7.3) (*n* = 210)		
Secondary time points				
Opioid use (4 months)				
Fully tapered (MED = 0), *n* (%)	58/224 (26%)	7/201 (3%)	9.68 (4.30 to 21.79); $p < 0.001$[b]	11.61 (5.06 to 26.63); $p < 0.001$[c]
Not tapered (MED > 0), *n* (%)	166/224 (74%)	194/201 (97%)		
PROMIS-PI-SF-8A (4 months)[d]				
Mean (SD)	64.5 (7.5) (*n* = 227)	64.6 (7.2) (*n* = 202)	−0.09 (−1.48 to 1.31); $p = 0.90$	−0.73 (−1.93 to 0.48); $p = 0.24$[e]
Opioid use (8 months)				
Fully tapered (MED = 0), *n* (%)	57/193 (30%)	11/163 (7%)	5.79 (2.92 to 11.50) $p < 0.001$[b]	7.25 (3.46 to 15.18); $p < 0.001$[c]
Not tapered (MED > 0), *n* (%)	136/193 (70%)	152/152 (93%)		
PROMIS-PI-SF-8A (8 months)[d]				
Mean (SD)	64.5 (7.3) (*n* = 199)	64.9 (7.5) (*n* = 166)	−0.39 (−1.93 to 1.14); $p = 0.61$	−0.75 (−2.10 to 0.59); $p = 0.27$[e]

a Opioid use reported as total MED of all opioid pain killers taken over the last 4 weeks (daily MED).
b OR (95% CI) and *p*-value reported.
c Based on a partially nested mixed-effect logistic model adjusted for age, gender, baseline pain intensity, geographical location and baseline measure of the outcome. The education support group was used as the cluster variable for the intervention group, with individual clusters of size 1 used for each participant in usual care. OR (95% CI) and *p*-value reported.
d Indicative MCID, 3.5 (*eTable 33* in Supplement 2 from Sandhu *et al.*).[1]
e Based on a heteroscedastic partially nested mixed-effect model with corrected degrees of freedom, adjusted for age, gender, baseline pain intensity, geographical location, baseline opioid band and baseline measure of the outcome. The education support group was used as the cluster variable for the intervention group, with clusters of size 1 used for each participant in usual care.

baseline [adjusted OR 3.76 (95% CI 2.47 to 5.71); $p < 0.001$] (*Table 9*). Similar results were also seen at 4 months and 8 months follow-up.

Pain intensity (PROMIS-PI-SF-3A)

We found no meaningful difference in the PROMIS-PI-SF-3A pain intensity scores at 12 months [adjusted −1.31 (95% CI −2.88 to 0.26); $p = 0.10$] with similar results shown at 4- and 8-month follow-up (see *Table 9*).

Twelve-item short form survey

For the SF-12 Mental score, we found no meaningful difference at 12 months [adjusted 0.41 (95% CI −1.59 to 2.42); $p = 0.68$] (see *Table 9*). The results were similar at 8 months; however, at 4 months a statistically significant

TABLE 8 Pre-specified ITT and instrumental variable analysis to adjust for non-adherence, at each time point (using minimal compliance definition of compliance)

	ITT model		IV model	
	Mean difference (95% CI)[a]	*p*-value	Mean difference (95% CI)[b]	*p*-value
Minimal compliance: PROMIS-PI-SF-8A				
4 months	−0.73 (−1.93 to 0.48)	0.24	−0.88 (−2.63 to 0.88)	0.33
8 months	−0.75 (−2.10 to 0.59)	0.27	−0.85 (−2.89 to 1.19)	0.42
12 months	−0.89 (−2.12 to 0.33)	0.15	−0.99 (−2.93 to 0.96)	0.32
Full compliance: PROMIS-PI-SF-8A				
4 months	−0.73 (−1.93 to 0.48)	0.24	−1.27 (−3.62 to 1.07)	0.29
8 months	−0.75 (−2.10 to 0.59)	0.27	−1.24 (−3.93 to 1.45)	0.37
12 months	−0.89 (−2.12 to 0.33)	0.15	−1.47 (−4.04 to 1.09)	0.26

a Based on a heteroscedastic partially nested mixed-effect model with corrected degrees of freedom, adjusted for age, gender, baseline pain intensity, geographical location, baseline opioid band and baseline measure of the outcome. The education support group was used as the cluster variable for the intervention arm, with clusters of size 1 used for each participant in usual care.
b Based on a single equation instrumental variable regression model with outcome adjusted for age, gender, baseline pain intensity and baseline measure of the outcome. Minimal compliance is defined as attending at least day 1 and F2F#. Full compliance is defined as attending at least day 1, 2 and 3, F2F#1 and at least one phone call.

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between-group difference was found [adjusted 2.29 (95% CI 0.30 to 4.27); $p = 0.02$], with scores higher in the intervention group, suggesting those participants had better mental functioning than usual care. No meaningful difference was found for the SF-12 Physical score at 12 months [adjusted −0.02 (95% CI −1.49 to 1.44); $p = 0.98$] with similar results found at 4 and 8 months.

Pittsburgh Sleep Quality Index

No meaningful differences between the intervention and usual-care group were found for the Pittsburgh Sleep Quality Index score at 12 months [adjusted −0.10 (95% CI −0.82 to 0.63); $p = 0.80$] (see *Table 9*). Similarly, no meaningful differences were found at 4 or 8 months.

Hospital Anxiety and Depression Scale

For the Hospital Anxiety and Depression Scale (HADS) anxiety score, no meaningful differences between the intervention and usual-care group were found at 12 months [adjusted 0.11 (95% CI −0.67 to 0.89); $p = 0.78$] (see *Table 9*). Similarly, no differences were found at 4 and 8 months. For the HADS depression score, no meaningful differences were found at 12 months [adjusted −0.02 (95% CI −0.77 to 0.73); $p = 0.95$]; however, a statistically significant between-group difference was found at 4 months [adjusted −0.94 (95% CI −1.63 to −0.25); $p = 0.01$] with depression scores lower in the intervention group.

Pain Self-Efficacy Questionnaire

No meaningful differences were found between the intervention group and usual-care group for pain self-efficacy at 12 months [adjusted 1.43 (95% CI −0.87 to 3.73); $p = 0.22$] with similar results at 8 months (see *Table 9*). At 4 months, a statistically significant between-group difference was found [adjusted 4.19 (95% CI 1.97 to 6.41); $p < 0.001$] with higher scores shown in the intervention group, indicating participants in that group had stronger self-beliefs than in the usual-care group at 4 months.

TABLE 9 Secondary outcomes at time points 4, 8 and 12 months

	Intervention	Standard care	Unadjusted estimate (95% CI); *p*-value	Adjusted estimate (95% CI); *p*-value
Opioid use: % reduction in MED from baseline, n (%)				
≥ 50% reduction (4 months)	112/224 (50%)	31/201 (15%)	5.48 (3.45 to 8.72); $p < 0.001$[a]	6.12 (3.77 to 9.92); $p < 0.001$[b]
≥ 50% reduction (8 months)	110/193 (57%)	38/163 (23%)	4.36 (2.75 to 6.92); $p < 0.001$[a]	4.94 (3.04 to 8.03); $p < 0.001$[b]
≥ 50% reduction (12 months)	129/225 (57%)	57/208 (27%)	3.56 (2.38 to 5.33); $p < 0.0001$[a]	3.76 (2.47 to 5.71); $p < 0.001$[b]
PROMIS-PI-SF-3A[c]				
Mean (SD) (4 months)	65.0 (8.1) (*n* = 189)	65.9 (7.7) (*n* = 151)	−0.96 (−2.66 to 0.75); $p = 0.27$	−1.42 (−3.08 to 0.23); $p = 0.09$
Mean (SD) (8 months)	65.0 (8.7) (*n* = 182)	65.9 (7.3) (*n* = 147)	−0.92 (−2.69 to 0.85); $p = 0.31$	−1.47 (−3.03 to 0.09); $p = 0.06$
Mean (SD) (12 months)	64.7 (8.6) (*n* = 187)	65.6 (7.7) (*n* = 159)	−0.91 (−2.64 to 0.83); $p = 0.30$	−1.31 (−2.88 to 0.26); $p = 0.10$
SF-12 Mental[c]				
Mean (SD) (4 months)	45.8 (11.6) (*n* = 189)	44.4 (12.1) (*n* = 151)	1.38 (−1.16 to 3.92); $p = 0.29$	2.29 (0.30 to 4.27); $p = 0.02$
Mean (SD) (8 months)	43.9 (11.7) (*n* = 181)	44.3 (12.0) (*n* = 146)	−0.39 (−2.98 to 2.20); $p = 0.77$	0.28 (−1.79 to 2.35); $p = 0.79$
Mean (SD) (12 months)	43.4 (11.8) (*n* = 185)	44.1 (11.2) (*n* = 160)	−0.67 (−3.12 to 1.77); $p = 0.59$	0.41 (−1.59 to 2.42); $p = 0.68$
SF-12 Physical[c]				
Mean (SD) (4 months)	33.9 (10.0) (*n* = 189)	33.2 (9.3) (*n* = 151)	0.67 (−1.41 to 2.75); $p = 0.53$	0.87 (−0.62 to 2.36); $p = 0.25$
Mean (SD) (8 months)	34.2 (9.2) (*n* = 181)	33.2 (9.4) (*n* = 146)	0.97 (−1.07 to 3.01); $p = 0.35$	1.06 (−0.52 to 2.65); $p = 0.19$
Mean (SD) (12 months)	33.6 (8.8) (*n* = 185)	33.8 (9.3) (*n* = 160)	−0.24 (−2.15 to 1.66); $p = 0.8012$	−0.02 (−1.49 to 1.44); $p = 0.98$
Pittsburgh Sleep Quality Index[c]				
Mean (SD) (4 months)	11.2 (4.4) (*n* = 177)	12.1 (4.2) (*n* = 141)	−0.94 (−1.90 to 0.01); $p = 0.054$	−0.65 (−1.38 to 0.08); $p = 0.08$
Mean (SD) (8 months)	10.8 (4.5) (*n* = 170)	11.8 (4.2) (*n* = 140)	−0.97 (−1.96 to 0.02); $p = 0.05$	−0.72 (−1.46 to 0.02); $p = 0.06$
Mean (SD) (12 months)	11.3 (4.3) (*n* = 175)	11.6 (4.4) (*n* = 150)	−0.33 (−1.29 to 0.62); $p = 0.49$	−0.10 (−0.82 to 0.63); $p = 0.80$
HADS anxiety score[c]				
Mean (SD) (4 months)	8.1 (4.8) (*n* = 187)	8.3 (5.3) (*n* = 149)	−0.16 (−1.25 to 0.93); $p = 0.77$	−0.59 (−1.30 to 0.12); $p = 0.10$
Mean (SD) (8 months)	8.3 (5.0) (*n* = 176)	7.7 (5.0) (*n* = 146)	0.59 (−0.51 to 1.69); $p = 0.29$	0.27 (−0.44 to 0.99); $p = 0.44$
Mean (SD) (12 months)	8.3 (5.0) (*n* = 182)	7.8 (5.3) (*n* = 157)	0.49 (−0.61 to 1.59); $p = 0.38$	0.11 (−0.67 to 0.89); $p = 0.78$

TABLE 9 Secondary outcomes at time points 4, 8 and 12 months (*continued*)

	Intervention	Standard care	Unadjusted estimate (95% CI); *p*-value	Adjusted estimate (95% CI); *p*-value
HADS depression score[c]				
Mean (SD) (4 months)	7.6 (4.4) (*n* = 190)	8.1 (4.6) (*n* = 150)	−0.55 (−1.53 to 0.42); *p* = 0.26	−0.94 (−1.63 to −0.25); *p* = 0.01
Mean (SD) (8 months)	7.9 (4.7) (*n* = 181)	8.1 (4.5) (*n* = 147)	−0.17 (−1.18 to 0.83); *p* = 0.73	−0.35 (−1.04 to 0.34); *p* = 0.31
Mean (SD) (12 months)	8.3 (4.8) (*n* = 182)	7.7 (4.7) (*n* = 156)	0.58 (−0.45 to 1.60); *p* = 0.27	−0.02 (−0.77 to 0.73); *p* = 0.95
Pain Self-Efficacy Questionnaire[c]				
Mean (SD) (4 months)	31.2 (14.6) (*n* = 189)	28.8 (14.7) (*n* = 147)	2.39 (−0.78 to 5.56); *p* = 0.14	4.19 (1.97 to 6.41); *p* < 0.001
Mean (SD) (8 months)	30.4 (14.8) (*n* = 180)	29.0 (14.4) (*n* = 146)	1.37 (−1.84 to 4.59); *p* = 0.40	2.05 (−0.18 to 4.28); *p* = 0.07
Mean (SD) (12 months)	29.1 (15.2) (*n* = 185)	29.1 (13.5) (*n* = 159)	−0.01 (−3.08 to 3.06); *p* = 0.99	1.43 (−0.87 to 3.73); *p* = 0.22
EQ-5D-5L index score[c]				
Mean (SD) (4 months)	0.43 (0.28) (*n* = 228)	0.40 (0.30) (*n* = 199)	0.03 (−0.03 to 0.08); *p* = 0.33	0.06 (0.01 to 0.10); *p* = 0.02
Mean (SD) (8 months)	0.39 (0.28) (*n* = 197)	0.41 (0.29) (*n* = 166)	−0.02 (−0.08 to 0.04); *p* = 0.58	−0.001 (−0.05 to 0.05); *p* = 0.96
Mean (SD) (12 months)	0.42 (0.28) (*n* = 227)	0.41 (0.29) (*n* = 209)	0.01 (−0.05 to 0.06); *p* = 0.78	0.02 (−0.02 to 0.06); *p* = 0.32
EQ-5D-5L VAS[c]				
Mean (SD) (4 months)	53.3 (22.6) (*n* = 227)	51.6 (23.3) (*n* = 199)	1.66 (−2.72 to 6.04); *p* = 0.46	4.43 (0.70 to 8.16); *p* = 0.02
Mean (SD) (8 months)	53.1 (23.2) (*n* = 197)	51.5 (23.7) (*n* = 165)	1.58 (−3.28 to 6.44); *p* = 0.52	3.88 (−0.24 to 7.99); *p* = 0.06
Mean (SD) (12 months)	52.0 (24.0) (*n* = 228)	51.3 (23.7) (*n* = 209)	0.68 (−3.81 to 5.17); *p* = 0.77	2.35 (−1.62 to 6.32); *p* = 0.24
ShOWS[c]				
Mean (SD) (4 months)	9.2 (5.1) (*n* = 190)	9.6 (6.0) (*n* = 150)	−0.40 (−1.59 to 0.79); *p* = 0.51	−0.65 (−1.61 to 0.31); *p* = 0.18
Mean (SD) (8 months)	9.3 (5.4) (*n* = 181)	9.5 (5.2) (*n* = 146)	−0.20 (−1.36 to 0.97); *p* = 0.74	−0.29 (−1.20 to 0.61); *p* = 0.52
Mean (SD) (12 months)	9.3 (5.4) (*n* = 183)	9.4 (5.5) (*n* = 156)	−0.11 (−1.27 to 1.06); *p* = 0.85	−0.35 (−1.34 to 0.65); *p* = 0.49

a OR (95% CI) and p-value reported.
b Based on partially nested mixed-effect logistic model adjusted for age, gender, baseline pain intensity, geographic location and baseline opioid band. The education support group was used as the cluster variable for the intervention group, with individual clusters of size 1 used for each participant in usual care. ORs and 95% CIs are reported.
c See footnotes b–i in *Table 6* for information on scoring and calculations of secondary outcomes. Adjusted estimates are based on a heteroscedastic partially nested mixed-effect model with corrected degrees of freedom, adjusted for age, gender, baseline pain intensity, geographic location, baseline opioid band and baseline outcome score. The education support group was used as the cluster variable for the intervention group, with clusters of size 1 used for each participant in usual care.

Source
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Short Opiate Withdrawn Scale

For the Short Opiate Withdrawn Scale (ShOWS) score at 12 months, no meaningful differences were found between the intervention group and usual-care group [adjusted −0.35 (95% CI −1.34 to 0.65); $p = 0.49$] with similar results shown at 4- and 8-month follow-up (see *Table 9*).

Health-related quality of life (EuroQol-5 dimensions, five-level version)

No meaningful differences were found at 12 months between the intervention group and usual-care group for both the EQ-5D-5L utility score [adjusted 0.02 (95% CI −0.02 to 0.06); $p = 0.32$] and the EQ-5D-5L visual analogue scale (VAS) score [adjusted 2.35 (95% CI −1.62 to 6.32); $p = 0.24$] (see *Table 9*). However, at 4 months, statistically significant between-group differences were found for both the EQ-5D-5L utility score [adjusted 0.57 (95% CI 0.01 to 0.10); $p = 0.02$] and the EQ-5D-5L VAS score [adjusted 4.43 (95% CI 0.70 to 8.16); $p = 0.02$]. EQ-5D-5L utility and VAS scores were higher in the intervention arm at 4 months, indicating those participants had better quality of life at 4 months than those in the usual-care group.

None of the secondary outcomes showed any significant clinical differences.

Serious adverse events and adverse events

There were 36 AEs (25 intervention, 11 usual care) reported by 30 participants (22 intervention, 8 usual care) (see *Appendix 3*, *Table 52*). Fifty-two SAEs (32 intervention, 20 usual care) were reported by 41 participants (25 intervention, 16 usual care). The SAEs included five deaths (four intervention, one usual care), all five of which were deemed unrelated to the trial intervention (see *Appendix 3*, *Table 53*). The causes of death included metastatic prostate cancer, aortic dissection, subdural empyema secondary to otitis media, lymphoma complication and one unknown cause of death. In the intervention group, there was one probably related and expected SAE (hot flushes and shooting pains in limbs after tapering) of moderate severity and three possibly related SAEs, two unexpected (small intestinal bleed, and pain surges and hot sensations after tapering) and one expected (hospitalisation due to joint/back pain). There was one possibly related SAE in the usual care group (hospitalised for arthritis flare-up).

Sensitivity analyses

The pre-specified subgroup analyses tests for interactions, neither anxiety and depression, were statistically significant for both the PROMIS-PI-SF-8A and opioid use primary outcomes (see *Appendix 3*, *Tables 46* and *47*). All three of the pre-specified sensitivity analysis testing the treatment effectiveness of the primary outcomes with (1) the process evaluation interviewees removed, (2) adjusting for imbalance of death rates and (3) splitting by pain disorders, showed no change in conclusions to the primary analysis (see *Appendix 3*, *Tables 48–50*).

Chapter 5 Health economic evaluation: methods and results

Introduction

We conducted a prospective within-trial cost-consequences analysis (CCA) and a model-based long-term cost-effectiveness analysis (CEA) to assess the value for money of the I-WOTCH intervention compared with the best usual care to support withdrawal of strong opioids, among those living with chronic non-malignant pain. The CCA provided a framework to estimate the impact of the I-WOTCH intervention on patient-reported outcomes (PROs) and healthcare resource utilisation in the short term. A de novo state-transition cost-effectiveness model (CEM) was developed to predict the full distribution of the long-term mean costs and health benefits associated with I-WOTCH and best usual care.

Methods

The protocol for the economic evaluation of the I-WOTCH intervention was published elsewhere.[60] This was implemented as planned, with the only exception being the impossibility to access GP records data for the majority of the trial patients during the COVID-19 pandemic. As a result, in consultation with the I-WOTCH TSC/DMC, the decision was to populate the economic evaluation using the participant self-report data collected in the I-WOTCH trial only. The base-case analysis for both Economic Evaluations (Ees) was an ITT population. However, to explore the impact of compliance on the economic study results, a deterministic evaluation and a probabilistic evaluation, were also run using a per-protocol (PP) population.

Statistical analysis of the individual patient data (IPD) collected in the I-WOTCH trial directly informed both the CCA and the CEA, where feasible. All other inputs were derived from the published literature or clinical opinion. In addition, the results generated in the CCA directly informed the model inputs for the CEA.

Statistical analysis

All statistical analyses of I-WOTCH resource use and outcome IPD were implemented in R Studio version 2022.07.1 [R version 4.1.1 (2021-08-10) (R Core Team. R: A Language and Environment for Statistical Computing. In; 2014)].

Descriptive statistics

We estimated descriptive statistics for the total annual costs and all other continuous variables stratified by intervention arm. Binary and categorical variables are described as percentages.

Missing data and imputation

There was substantial missingness in the I-WOTCH self-report data (see *Appendix 4*, *Table 60*, Missing outcome data for a summary). Following recommendations by Faria *et al.*, we used predictive mean matching (PMM) to impute missing data in I-WOTCH trial data.[61] Briefly, PMM is a way to do multiple imputation for missing data, especially for imputing quantitative variables that are not normally distributed. Compared with standard methods based on linear regression and the normal distribution, PMM produces imputed values that are closer to the observed values (*Box 1*).[62] The PMM is an implicit method that does not rely on any distributional assumptions.[63]

BOX 1 Step-by-step procedure for the PMM

Step-by-step procedure for the PMM from[62]

*A data set say **D** has a single variable **x** that has some cases with missing data and set of variables **z** with no missing data. These **z** variables are needed to impute for **x**. PMM works as described below:*

*For cases with no missing data, estimate a linear regression of **x** on **z**, producing set of coefficients **b***

1. *From the posterior distribution of **b**, generate random draws to create coefficients **b***. The random draw will be from multivariate normal distribution with mean **b** and covariance matrix of **b** estimated from the regression in step 1. This step produces sufficient variability in the imputed values and is the backbone of multiple imputation methods.*
2. *Using **b***, generate the predicted values of **x** for all cases (including the non-missing values)*
3. *For each missing case of **x**, identify a set of cases with observed **x** whose **predicted** values are close to the predicted values of the case with missing data. The number cases to match usually is taken as 3.*
4. *From among the close cases, randomly choose one and assign its **observed** value to substitute for the missing value.*
5. *The steps 2–5 are repeated for each completed data set.*

The purpose of linear regression in PMM is not to generate the imputed values, but rather to construct a metric for matching cases with missing data similar to the observed data. The two random draws in the process are to include random variation in regression coefficients and to help estimate the standard errors (SEs) without inflating test statistics.

Predictive mean matching only imputes values that were observed. The range of imputed values therefore always lies between the minimum and the maximum of the observed values. Thus, as opposed to regression imputation, PMM never generates implausible values (e.g. negative incomes in the case of healthcare resource use and costs) and also can deal very heteroscedastic data. PMM was conducted using the 'mice' package in R.[64]

Regression analyses (imputed data)

Given the non-normal distribution of the longitudinal patient-level health benefit data, we used GLMMs to analyse these data controlling for baseline age, gender, duration of pain, duration of opioid usage, baseline opioid use, pain severity and trial arm (*Box 2*). GLMMs were implemented using the R package 'glmmTMB'.[57]

BOX 2 The general form for the GLMM model

The general form for the GLMM model is

$$\eta = g[E(y|X,Z)] = X\beta + Zu + \varepsilon, \tag{1}$$

Repeated measures of health benefit collected at different time points (j) during the follow-up of the I-WOTCH study are nested within individuals (i). Consequently, the GLMM final specification modelled the coefficients associated with participant 'ID' and 'follow-up time', as random effects.

The model specification for measures of health benefit for individual i are described in equation (2):

$$\begin{aligned}\eta_{ij} = {} & \beta_0 + S_{0j} + \beta_{age}\,Age_i + \beta_{intervarm}\,Intervention_i + \beta_{gender}\,Gender_i \\ & + \beta_{duration\ pain}\,Duration\ Pain_i + \beta_{duration\ Opuse}\,Duration\ OpUse_i \\ & + \beta_{base\ OpUse}\,Baseline\ Opioid\ Use_i + \beta_{pain\ severity}\,Pain\ Severity_i + (\beta_{time} \\ & + S_{1j})Time_{ij} + \varepsilon_{ij}\end{aligned} \tag{2}$$

Total annual costs were analysed using a generalised linear model (GLM) specification, which included the same set of covariates used in equation (2), except for the variable 'follow-up time', since we are analysing the cumulative costs for each participant over the 12-month I-WOTCH study period.

$$\begin{aligned}\eta_i = {} & \beta_0 + \beta_{age}Age_i + \beta_{intervarm}\,Intervention_i + \beta_{gender}\,Gender_i + \beta_{duration\ pain}\,Duration\ Pain_i \\ & + \beta_{duration\ Opuse}\,Duration\ OpUse_i + \beta_{base\ OpUse}\,Baseline\ Opioid\ Use_i \\ & + \beta_{pain\ severity}Pain\ Severity_i + \varepsilon_i\end{aligned} \tag{3}$$

Error distribution and link function assumptions varied for different measures of health benefit and total annual cost. ADL and total annual cost data are non-negative; thus, the GLMM models for ADL and total annual cost assumed gamma distributed errors and a log link function. ShOWS are count data; thus, the GLMM model for ShOWS assumed Poisson distributed errors and a log link function. Similarly, re-scaled EuroQol-5 Dimensions, three-level version (EQ-5D-3L) scores are bounded in a (0–1) interval; thus, the GLMM model assumed Beta distributed errors and a logit link function.

Cost data for the cost–consequences analysis and the cost-effectiveness analysis

Unit costs

The unit costs used in both economic evaluations of the I-WOTCH study are summarised in *Table 10*. All costs were set to 2019 prices as this was the year when I-WOTCH's follow-up ended. Unit costs of opioid medications were taken from the BNF[65] and are listed in *Appendix 4*, *Table 58*. For each strength and preparation of a given opioid-based medication, we used the BNF cost per pack (or bottle). To calculate the relevant MED per pack, we used the same algorithm used in the I-WOTCH clinical analysis. Further details on the algorithm can be found in *Appendix 2*. For each opioid-based medication reported to have been used by individuals in the I-WOTCH study, we estimated their unit cost per MED and used this to estimate a weighted average cost per MED across all opioid medications used in the trial. A detailed table with an explanation of the calculation of unit costs is listed in *Appendix 4*, *Table 58*.

Unit cost for inpatient hospital admissions and day care procedures were estimated using National Reference Costs and Healthcare Resource Group codes.[66] Referrals and consultations were costed using Personal Social Services Research Unit (PSSRU) statistics[67] and reports.[68,69] If necessary, costs were inflated to 2019 prices using inflation and price indices from the Office for National Statistics (ONS).[70] A summary of the unit costs for the other categories of resource use considered is reported in *Appendix 4*, *Table 59*.

TABLE 10 Unit costs used in the economic analyses, UK gross domestic product

Item of resource use	Base case (£)[a]	Range for sensitivity analysis (£)[b]	Source
Medications	*Appendix 4*, *Table 58*	NA	BNF[65]
Inpatient stay	3477.36	2781.89–4172.83	National Reference Cost (2019)[66]
Day case admissions	752.00	601.60–902.40	
GP visits at surgery	34.20	27.36–41.04	PSSRU (2019)[67]
GP visits at home	89.60	71.68–107.52	
Practice nurse	14.47	11.57–17.36	
District nurse (i.e. at home)	53.20	42.56–63.84	
District nurse (GP surgery visit)	36.00	28.80–43.20	
Counsellor	44.33	35.47–53.20	
Occupational therapist	24.00	19.20–28.80	
Psychologist	92.60	74.08–111.12	
Social worker	51.00	40.80–61.20	
Physiotherapist	54.00	43.20–64.80	
Other (GP phone call)	15.32	12.26–18.38	

NA, not assigned.
a Unit costs expressed at 2019 values.
b Range was assumed to vary between ± 20% of the base-case value for the unit cost of healthcare resource use.

Costing of the interventions

We conducted a prospective micro-costing of the resources required to provide the I-WOTCH intervention (the yearly cost of each intervention is shown in *Table 11*). The categories of resource use and unit costs used in the I-WOTCH micro-costing exercise are provided in *Appendix 4*, *Table 56*. Fixed costs included salary, facility and travel costs per mile. Salaries for the facilitators and trainers were estimated based on average daily salary by grade. Facility costs were based on the number of venues hired, number of days hired and daily venue hire rate. PSSRU unit costs were used to estimate nurse face-to-face and telephone consultations.[67] I-WOTCH intervention unit costs are reported per participant.

The costs associated with best usual care are shown in *Appendix 4*, *Table 57*. These included costs of both the relaxation CD (i.e. printing and production costs) and 'My Opioid Manager'.

Complete case analysis

Decision problem

The CCA aimed to estimate the total costs per arm and the health outcomes of three measures across the trial length. Since the trial was run for 12 months, a 12-month time horizon was used. In line with National Institute for Health and Care Excellence (NICE) guidelines,[71] the 12-month time horizon of the CCA meant that the within-trial cost and health benefits were left undiscounted. The total costs were estimated using a UK NHS and Personal Social Services (PSS) perspective.

Costs

Total annual costs associated with both arms were estimated by adding up the cost of (1) medication; (2) all the categories of healthcare resource utilisation (i.e. GP surgery visit, GP home visit, practice nurse, district nurse surgery visit, district nurse home visit, occupational therapist, counsellor, psychologist, social worker, physiotherapist, other); and (3) the I-WOTCH intervention or best usual care.

Total annual costs were calculated as the sum of cost of total medication used and total healthcare utilisation over the entire follow-up period.

Health outcomes

The core measures of health benefit for the CCA were the following:

- **Activities of daily living** – measured using the PROMIS-PI-SF-8A.[72] For more details, please see *Outcomes measures*.
- **Severity of ShOWS** – measured using the short opiate withdrawal scale.[73] For more details, please see *Table 4*.
- **The EQ-5D-5L** – a preference-based generic measure of health-related quality-of-life instrument typically used in healthcare economic evaluation.[48,74] The EQ-5D-5L questionnaire[48] describes health in five domains (mobility, self-care, usual activities, pain or discomfort, and anxiety or depression). Each domain has five levels of severity (1 – no problems/2 – slight problems/3 – moderate problems/4 – severe problems/5 – unable to do). A response consists of a sequence of five digits, for example 12315, 12112, which represent the level of severity on each domain reported by the respondent. Combinations of the levels of the five domains describe 3125 possible health states. Several valuation studies have been carried out to estimate value sets for a given country/region. These studies used methods consistent with economic theory to elicit the respondent's preferences towards the health states defined by the EQ-5D. A value set to calculate utility values for the EQ-5D-5L has been published recently[75] but is

TABLE 11 Cost of each intervention per year

Intervention	Base case (£)[a]	Range for sensitivity analysis (£)	Source
I-WOTCH intervention	222.57	329.11–407.58	*Appendix 4*, *Table 56*
Usual care[a]	4.10	NA	*Appendix 4*, *Table 57*

NA, not assigned.
a Costs of both the relaxation CD (i.e. printing and production costs) and 'My Opioid Manager'.

still subject to methodological controversy. Until the controversies are resolved, we followed NICE guidance and converted EQ-5D-5L responses onto the EQ-5D-3L scale using the mapping function developed by van Hout *et al.*[59] following current recommendations from NICE.[74]

Cost-effectiveness model

Decision problem

The model was constructed to determine the cost-effectiveness of the I-WOTCH intervention versus best usual care in patients with chronic non-malignant pain who are aiming to reduce opioid usage. This patient population is aligned with the population in the I-WOTCH trial, which was used to determine the majority of the model inputs. The model was developed from the perspective of the UK NHS and PSS. A 4-month cycle length and a lifetime time horizon to capture all costs and health outcomes associated with the model cohort were used. Health benefits were expressed in terms of quality-adjusted life-years (QALYs), and all benefits and costs were discounted at 3.5% per year in line with methodological guidance from NICE.[71] A summary of the key elements of the overall decision problem is presented in *Table 12*.

Model structure

A five-state cohort Markov model was developed in R. Conceptualisation and validation of the model structure were informed by iteratively consulting with the clinical experts who developed the I-WOTCH intervention. This activity was further informed by a critical review of previously published decision models that evaluated the use of opioids in chronic non-malignant- pain. An illustrative representation of the model structure is provided in *Figure 2*.

Our model assumes that at any point in time, patients' opioid intake – for chronic non-malignant- pain – can be characterised by one of five mutually exclusive states (represented as ovals in *Figure 2*), including:

1. Long-term opioid therapy (LTOT) – individuals who have been using strong opioids for more than 3 months. In the model, this is composed of two substates: responder to treatment and non-responder to treatment (NRTT).
2. Intervention-supported tapering (IST) – individuals who engage in opioid tapering, after having received the I-WOTCH intervention.
3. Non-intervention-supported tapering (NIST) – individuals who engage in opioid tapering, but who have not received the I-WOTCH intervention.

TABLE 12 Summary of CEA decision problem

Element	Details
Population	Adults with chronic non-malignant pain on long-term strong opioids
Intervention	I-WOTCH intervention
Comparators	Best usual care
Perspective on costs	UK NHS and PSS
Time horizon	Lifetime time horizon
Cycle length for Markov model	4 months
Cost outcomes	Total cost per-patient per arm
Health outcomes	Total QALYs per patient per arm
Discount rate (benefits)	3.5% per year
Discount rate (costs)	3.5% per year
Cost-effectiveness threshold	£20,000–30,000 per QALY gained
Analysis of uncertainty	Probabilistic sensitivity analysis and scenario analysis

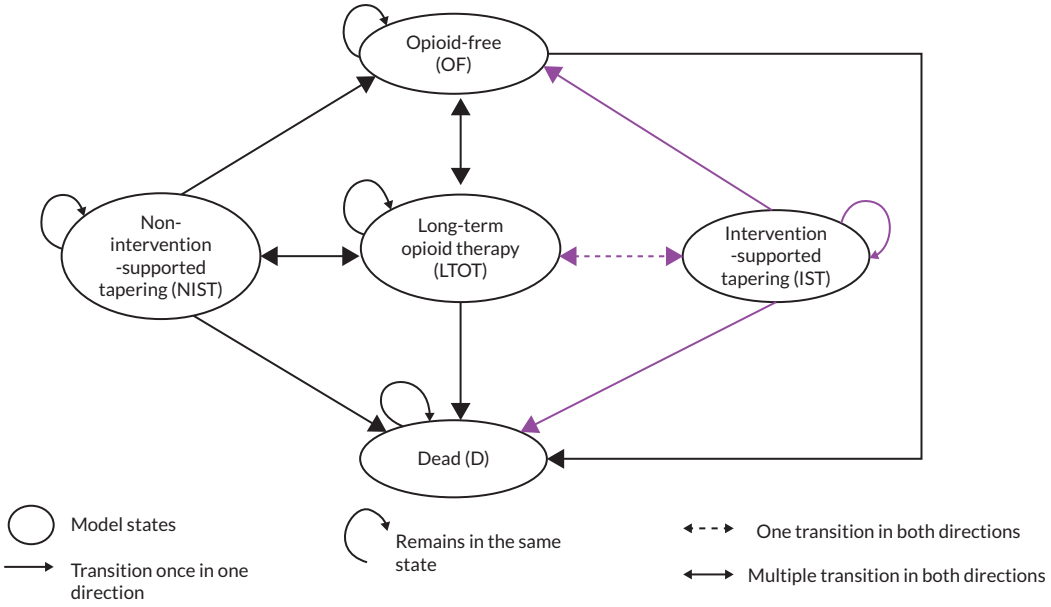

FIGURE 2 I-WOTCH CEA model structure.

4. Successful opioid free management of pain (OF) – individuals who have completely stopped opioids consumption; and
5. Dead (D).

All individuals were placed in the LTOT state at the start of the model. During each model cycle of the study period, individuals could make transitions between the above model states, as represented by the direction of the arrows in *Figure 1*. Individuals could decide to engage with NIST at any time point during the time horizon of the study. Only individuals who had received the I-WOTCH intervention could transit to the IST state. This transition could only take place once during the initial three cycles of the model (i.e. first 12 months). In other words, after the initial 12 months, individuals who reduced their intake of strong opioids – as a result of having received the I-WOTCH intervention – could only transit to the NIST state. Individuals who over the duration of the trial never make an attempt to engage with tapering (i.e. remain in the LTOT state) are defined as no responders to tapering.

Individuals in the LTOT state could experience opioid-related transient/emergent AEs or persistent/serious adverse events. At any point in time, individuals in the IST and NIST states could stop opioid tapering and return to LTOT. Only individuals in the LTOT, IST or NIST states could transit to OF (i.e. a state where they no longer consume any strong opioids). Individuals in the LTOT, IST, NIST and OF states were all at risk of death.

Populating model parameters

To estimate mean values for all key model parameters, we re-analysed the participant-reported data from the I-WOTCH trial and integrated these with the cost data from the published literature that is detailed in *Cost data for the cost–consequences analysis and the cost-effectiveness analysis*. This analysis generated cost and utility values for each of the five model states, as well as the initial transition probabilities between states. Transition probabilities from all model states to death were extracted from age- and sex-adjusted all-cause mortality statistics from the ONS.[76] The starting age for the base-case analysis was 61 years old (i.e. mean age for all patients participating in the I-WOTCH trial).

While the first three cycles of the I-WOTCH model follow the time-dependent transition probabilities observed in the trial (calculated based on participant's self-reported medication use pattern at baseline, 4, 8 and 12 months of the I-WOTCH trial follow-up), from cycle 4 the transition probabilities were no longer time dependent. The transition probabilities observed at the 12th-month follow-up (i.e. cycle 4) were extrapolated over the full lifetime horizon of the analysis. In other words, it was assumed that the self-reported consumption of strong opioids in the best usual-care arm observed at 12 months was representative of the long-term consumption of strong opioids of people with chronic

non-malignant pain. After 12 months, individuals in the I-WOTCH group could no longer transit to the IST, they could however transit to the NIST (i.e. the excess transition rate of individuals in LTOT was not directly attributed to the I-WOTCH intervention). For individuals in the I-WOTCH group, the observed excess transition probability from the LTOT into NIST was reduced over time in line with the waning rate observed in the I-WOTCH trial over its 12-month follow-up.

Table 13 provides a list all model inputs, their mean values, the probability distribution functions used to characterise each model input, and the parameters values used in the model. Inputs for the PP scenario of the cost-effectiveness model can be found in *Appendix 4*, *Table 69*.

Deterministic base-case analysis

We estimated differential costs and QALYs predicted by the decision model and calculated the incremental cost-effectiveness ratio (ICER) and net monetary benefit (NMB). An ICER is defined as the ratio between the difference in mean costs and the difference in mean QALYs between the I-WOTCH intervention and best usual care. Total costs (and QALYs) were calculated weighting the mean costs (utility values) attached to each model state by the time spent by individuals in each state. The model was run until the entire cohort reached the absorbing state Dead (lifetime time horizon). The NMB represents the value of I-WOTCH (in monetary terms) assuming a threshold value [i.e. willingness-to-pay (WTP)] per additional QALY of £30,000. This higher threshold was selected to acknowledge the healthcare system's role in the ongoing opioid use crisis.

Deterministic and scenario sensitivity analyses

Nine deterministic scenarios were considered in addition to the base case. These scenarios involved changing the base-case inputs with alternative values and rerunning the model. The scenarios which were run are shown in *Table 14*.

Probabilistic sensitivity analysis

To characterise sampling uncertainty in the estimates of the I-WOTCH model inputs, we assigned appropriate probability distributions to all long-term parameters in the model described in *Table 13*. Transition probabilities and EQ-5D-3L scores (for each of the five model states) were assigned using the van Hout algorithm. Beta distributions were characterised by alpha and beta parameters, which we estimated from the data observed in the I-WOTCH trial. Total cost for each of the five model states was assigned gamma distributions with ancillary parameters alpha and beta derived using observed mean and variance estimated from the I-WOTCH trial.

To understand the effect on the predicted mean QALYs and mean costs associated with each treatment arm, sampling uncertainty was propagated through the model using Monte Carlo simulation in the form of a probabilistic sensitivity analysis (PSA).

To estimate the probability of cost-effectiveness at different threshold levels, we combined and compared the ratio between the difference in mean costs and the difference in mean QALYs against a range of feasible cost-effectiveness thresholds. These varied between £5000 and £60,000 per QALY gained to include the values suggested by Lomas *et al.* (£5000 and £15,000) and NICE (£20,000 and £30,000).[71,77] This information was represented graphically in a cost-effectiveness acceptability curve (CEAC).[78]

Value of information analysis

To estimate the value associated with reducing the decision uncertainty associated with the long-term decision problem, we conducted a Bayesian value of information analysis. To estimate the total expected value of perfect information (EVPI) per individual, we used the package 'voi' in R.[79]

TABLE 13 Input parameters used in the state-transition model

Input	Source	Description	Control			Intervention		
			Mean value	Distribution	Parameters	Mean value	Distribution	Parameters
Transition probability (0–4 months)								
LTOT to IST	PtQ	Proportion of people engaged in IST	NA			0.593	Beta	$\alpha = 181; \beta = 124$
LTOT to NIST	PtQ	Proportion of people engaged in NIST	0.541	Beta	$\alpha = 164; \beta = 139$	0		
LTOT to OF	PtQ	Proportion of people stopping any use of opioids	0.03	Beta	$\alpha = 9; \beta = 294$	0.190	Beta	$\alpha = 58; \beta = 247$
Remaining in LTOT	PtQ	Proportion of people who do not engage in IST and remain in LTOT	0.429	Beta	$\alpha = 130; \beta = 173$	0.216	Beta	$\alpha = 66; \beta = 239$
IST to LTOT	PtQ	Proportion of people withdrawing from IST	NA			0		
IST to OF	PtQ	Proportion of people stopping any use of opioids	NA			0		
Remaining in IST	PtQ	Proportion of people who remain engaging in IST	NA			1		
NIST to LTOT	PtQ	Proportion of people withdrawing from NIST	0			NA		
NIST to OF	PtQ	Proportion of people from NIST and stop any use of opioids	0			NA		
Remaining in NIST	PtQ	Proportion of people who remain in NIST over time	1			NA		
OF to LTOT	PtQ	Proportion of people who had remained OF but then restarted	0			0		
Remaining in OF	PtQ	Proportion of people who remain OF	1			1		
Transition probability (5–8 months)								
LTOT to IST	PtQ	Proportion of people engaged in IST	NA			0.658	Beta	$\alpha = 25; \beta = 13$
LTOT to NIST	PtQ	Proportion of people engaged in NIST	0.649	Beta	$\alpha = 48; \beta = 26$	NA		
LTOT to OF	PtQ	Proportion of people stopping any use of opioids	0.068	Beta	$\alpha = 5; \beta = 69$	0.053	Beta	$\alpha = 2; \beta = 36$
Remaining in LTOT	PtQ	Proportion of people who do not engage in IST and remain in LTOT	0.284	Beta	$\alpha = 21; \beta = 53$	0.289	Beta	$\alpha = 11; \beta = 27$
IST to LTOT	PtQ	Proportion of people withdrawing from IST	NA			0.254	Beta	$\alpha = 46; \beta = 135$
IST to OF	PtQ	Proportion of people stopping any use of opioids	NA			0.072	Beta	$\alpha = 13; \beta = 168$
Remaining in IST	PtQ	Proportion of people who remain engaging in IST	NA			0.674	Beta	$\alpha = 122; \beta = 59$
NIST to LTOT	PtQ	Proportion of people withdrawing from NIST	0.262	Beta	$\alpha = 43; \beta = 121$	NA		
NIST to OF	PtQ	Proportion of people from NIST and stop any use of opioids	0.018	Beta	$\alpha = 3; \beta = 161$	NA		

TABLE 13 Input parameters used in the state-transition model (*continued*)

Input	Source	Description	Control			Intervention		
			Mean value	Distribution	Parameters	Mean value	Distribution	Parameters
Remaining in NIST	PtQ	Proportion of people who remain in NIST over time	0.720	Beta	$\alpha = 118; \beta = 46$	NA		
OF to LTOT	PtQ	Proportion of people who had remained OF but then restarted	0.444	Beta	$\alpha = 4; \beta = 5$	0.224	Beta	$\alpha = 13; \beta = 45$
Remaining in OF	PtQ	Proportion of people who remain OF	0.556	Beta	$\alpha = 5; \beta = 4$	0.776	Beta	$\alpha = 45; \beta = 13$
Transition probability (9–12 months)								
LTOT to IST	PtQ	Proportion of people engaged in IST	NA			0.143	Beta	$\alpha = 10; \beta = 60$
LTOT to NIST	PtQ	Proportion of people engaged in NIST	0.559	Beta	$\alpha = 38; \beta = 30$	0.314	Beta	$\alpha = 22; \beta = 48$
LTOT to OF	PtQ	Proportion of people stopping any use of opioids	0.059	Beta	$\alpha = 4; \beta = 64$	0.143	Beta	$\alpha = 10; \beta = 60$
Remaining in LTOT	PtQ	Proportion of people who do not engage in IST and remain in LTOT	0.382	Beta	$\alpha = 26; \beta = 42$	0.4	Beta	$\alpha = 28; \beta = 42$
IST to LTOT	PtQ	Proportion of people withdrawing from IST	NA			0.197	Beta	$\alpha = 29; \beta = 118$
IST to OF	PtQ	Proportion of people stopping any use of opioids	NA			0.048	Beta	$\alpha = 7; \beta = 140$
Remaining in IST	PtQ	Proportion of people who remain engaging in IST	NA			0.755	Beta	$\alpha = 111; \beta = 36$
NIST to LTOT	PtQ	Proportion of people withdrawing from NIST	0.289	Beta	$\alpha = 48; \beta = 118$	NA		
NIST to OF	PtQ	Proportion of people from NIST and stop any use of opioids	0.024	Beta	$\alpha = 4; \beta = 162$	NA		
Remaining in NIST	PtQ	Proportion of people who remain in NIST over time	0.687	Beta	$\alpha = 114; \beta = 52$	NA		
OF to LTOT	PtQ	Proportion of people who had remained OF but then restarted	0.385	Beta	$\alpha = 5; \beta = 8$	0.183	Beta	$\alpha = 11; \beta = 49$
Remaining in OF	PtQ	Proportion of people who remain OF	0.615	Beta	$\alpha = 8; \beta = 5$	0.817	Beta	$\alpha = 49; \beta = 11$
Transition probabilities to death								
All states to death	ONS	All-cause mortality rates from ONS[76]	Please see *Appendix 4*, *Table 68*					
Utilities (4 months)								
LTOT	CCA		0.416	Beta	$\alpha = 1.074; \beta = 1.509$	0.340	Beta	$\alpha = 0.617; \beta = 1.199$
IST	CCA		NA			0.409	Beta	$\alpha = 1.205; \beta = 1.739$
NIST	CCA		0.384	Beta	$\alpha = 0.869; \beta = 1.396$	NA	Beta	

continued

TABLE 13 Input parameters used in the state-transition model (*continued*)

Input	Source	Description	Control			Intervention		
			Mean value	Distribution	Parameters	Mean value	Distribution	Parameters
OF	CCA		0.642	Beta	α = 1.407; β = 0.785	0.581	Beta	α = 2.776; β = 2.003
Utilities (8 months)								
LTOT	CCA		0.381	Beta	α = 0.762; β = 1.238	0.347	Beta	α = 0.768; β = 1.447
IST	CCA		NA			0.372	Beta	α = 1.353; β = 2.288
NIST	CCA		0.400	Beta	α = 0.977; β = 1.467	NA		
OF	CCA		0.613	Beta	α = 5.954; β = 3.755	0.493	Beta	α = 1.584; β = 1.629
Utilities (12 months)								
LTOT	CCA		0.401	Beta	α = 0.860; β = 1.284	0.395	Beta	α = 0.984; β = 1.509
IST	CCA		NA			0.361	Beta	α = 0.850; β = 1.504
NIST	CCA		0.401	Beta	α = 0.837; β = 1.252	0.373	Beta	α = 0.967; β = 1.624
OF	CCA		0.465	Beta	α = 1.418; β = 1.631	0.518	Beta	α = 1.466; β = 1.363
Costs (4 months)								
LTOT	CCA		£1181.92	Gamma	α = 0.499; β = 2369.11	£1804.57	Gamma	α = 0.600; β = 3224.86
IST	CCA		NA			£1021.20	Gamma	α = 0.577; β = 1770.24
NIST	CCA		£1186.28	Gamma	α = 0.417; β = 2842.57	NA		
OF	CCA		£735.59	Gamma	α = 0.346; β = 2125.45	£981.28	Gamma	α = 0.310; β = 3162.97

TABLE 13 Input parameters used in the state-transition model (*continued*)

Input	Source	Description	Control			Intervention		
			Mean value	Distribution	Parameters	Mean value	Distribution	Parameters
Costs (8 months)								
LTOT	CCA		£1159.23	Gamma	α = 0.501; β = 2310.38	£1398.66	Gamma	α = 0.609; β = 2298.21
IST	CCA		NA			£1297.60	Gamma	α = 0.814; β = 1594.60
NIST	CCA		£1147.46	Gamma	α = 1.091; β = 1051.98	NA		
OF	CCA		£537.42	Gamma	α = 0.271; β = 1981.83	£802.36	Gamma	α = 0.388; β = 2070.23
Costs (12 months)								
LTOT	CCA		£746.31	Gamma	α = 0.473; β = 1575.25	£1070.97	Gamma	α = 0.320; β = 3345.03
IST	CCA		NA			£1053.06	Gamma	α = 0.403; β = 2615.22
NIST	CCA		£1098.81	Gamma	α = 0.375; β = 2931.26	£969.64	Gamma	α = 0.283; β = 3432.01
OF	CCA		£1349.19	Gamma	α = 0.497; β = 2715.24	£631.47	Gamma	α = 0.283; β = 2233.69

NA, not assigned; PtQ, patient questionnaire.

Note
Transition probabilities are obtained from the trial PtQ with no death considered. In the economic model, the cyclic dependent probabilities of death from life tables are incorporated.

TABLE 14 List of scenarios explored

#	Scenario	Description	Inputs changed
1	Fractures	Inclusion of patients experiencing fractures in the model	Additional inputs added into model: 'Incidence of fracture by age' 'Cost of fracture by age' Updated death calculations to include death from fracture
2	Discount rate (0%)	Using a lower discount rate than the base case	Discount rate for costs and QALYs set to 0% per year (was 3.5%)
3	Discount rate (6%)	Using a higher discount rate than the base case	Discount rate for costs and QALYs set to 6% per year (was 3.5%)
4	Younger starting age	A younger population being put through the model	Starting age of the population set to 23 (was 61)
5	Older starting age	An older population being put through the model	Starting age of the population set to 91 (was 61)
6	I-WOTCH costing	Optimistic costing scenario for the intervention being used	'Intervention state cost of LTOT at 4 months' changed from £1804.59 to £1716.02 'Intervention state cost of NRTT at 4 months' changed from £1895.99 to £1807.42
7	Lower waning rate	Exploring the impact of a different washout period with a lower waning rate	'Change' changed from 0.13848 to 0.02
8	Higher waning rate	Exploring the impact of a different washout period with a higher waning rate	'Change' changed from 0.13848 to 0.5
9	Excess mortality (all opioid states using same relative risk)	In addition to background mortality, excess mortality between the trial arms was included in the model.	'rr_mortality_taper' changed from 1 to 1.2 'rr_mortality_ltot' changed from 1 to 1.2
10	Excess mortality (tapering opioid state different relative risk than other opioid states)	In addition to background mortality, excess mortality between the trial arms was included in the model.	'rr_mortality_taper' changed from 1 to 1.18 'rr_mortality_ltot' changed from 1 to 1.2

Results

Complete case analysis

Baseline sociodemographic analysis

The baseline sociodemographic data of the I-WOTCH trial cohort are shown in *Tables 15* and *16*. A total of 608 participants were recruited, with 303 randomised to best usual care and 305 to the I-WOTCH group. At baseline, individuals were well balanced between groups.

Micro-costing

The results of the I-WOTCH intervention micro-costing analysis are shown in *Table 17*. Delivering the I-WOTCH intervention to the 305 individuals in the I-WOTCH group required an investment of approximately £68,000 with an average cost per individual of £222.57 when applied to the randomised to intervention population. Of the 305 who were randomised to the intervention, 204 individuals attended at least one group face-to-face session and at least one nurse appointment. However, only 164 individuals attended all elements of the I-WOTCH intervention.

Missing data and imputation

There was a substantial level of missing data in the I-WOTCH study. A complete case analysis would have reduced the sample size in the I-WOTCH group by 67.3% and the best usual-care group by 56.4%. An available case analysis per variable would have produced disparate results across variables (i.e. the set of people contributing to each estimate

TABLE 15 Baseline data for I-WOTCH's economic analysis

Variable	Best usual care (%) *n* = 303	I-WOTCH (%) *n* = 305
Gender		
Female	184 (61.13)	178 (58.55)
Male	117 (38.87)	125 (41.12)
Other	0 (0.00)	1 (0.33)
Pain duration		
< 1 year	3 (1.00)	5 (1.64)
1–5 years	50 (16.61)	47 (15.46)
More than 5 years	248 (82.39)	252 (82.89)
Pain severity		
High	282 (93.07)	283 (92.79)
Low	21 (6.93)	22 (7.21)
Opioid use band		
0–29 mg	164 (54.13)	165 (54.10)
30–59 mg	45 (14.85)	44 (14.43)
60–89 mg	27 (8.91)	26 (8.52)
90–119 mg	17 (5.61)	19 (6.23)
120–149 mg	15 (4.95)	15 (4.92)
150 mg+	35 (11.55)	36 (11.80)
Opioid intake duration		
1–5 years	107 (35.55)	104 (34.21)
< 1 year	18 (5.98)	11 (3.62)
More than 5 years	176 (58.47)	189 (62.17)

TABLE 16 Baseline data for I-WOTCH's economic analysis

	Best usual care *n* = 303			I-WOTCH *n* = 305		
Variable	**Mean**	**SD**	**Range**	**Mean**	**SD**	**Range**
Age	60.40	13.75	23–91	62.11	11.85	27–89
Measures of health benefit						
ADLs (PROMIS PI-SF-8A)	68.24	6.16	48.50–77.00	68.52	5.99	54.10–77.00
ShOWS	10.51	4.96	0–29	10.59	5.49	0–28
Generic health-related quality of life (EQ-5D-5L)	0.45	0.283	−0.285 to 1	0.44	0.274	−0.192 to 1
Healthcare utilisation						
Medications in MED	68.22	86.17	4.29–810	72.93	92.32	6.25–728.57

continued

TABLE 16 Baseline data for I-WOTCH's economic analysis (*continued*)

Variable	Best usual care *n* = 303			I-WOTCH *n* = 305		
	Mean	SD	Range	Mean	SD	Range
Hospital care (use)						
Inpatient stay (no. of admissions)	0.14	0.47	0.00–3.00	0.10	0.35	0.00–3.00
Day case admissions	0.32	0.63	0.00–3.00	0.30	0.65	0.00–3.00
Community health and social care						
GP surgery (no. of visits/contacts)	2.82	2.93	0.00–24.00	3.09	2.88	0.00–20.00
GP home (no. of visits/contacts)	0.05	0.28	0.00–3.00	0.06	0.44	0.00–6.00
Practice nurse (no. of visits/contacts)	1.02	1.41	0.00–8.00	1.06	1.70	0.00–16.00
District nurse (i.e. at home) (no. of visits/contacts)	0.17	0.86	0.00–8.00	0.18	1.34	0.00–18.00
District nurse (i.e. at surgery) (no. of visits/contacts)	0.25	1.37	0.00–16.00	0.16	0.96	0.00–10.00
Occupational therapist (no. of visits/contacts)	0.36	2.16	0.00–30.00	0.32	2.04	0.00–30.00
Counsellor (no. of visits/contacts)	0.56	2.33	0.00–16.00	0.31	1.56	0.00–16.00
Psychologist (no. of visits/contacts)	0.28	1.69	0.00–18.00	0.29	1.94	0.00–20.00
Social worker (no. of visits/contacts)	0.21	1.66	0.00–20.00	0.11	0.92	0.00–12.00
Physiotherapist (no. of visits/contacts)	0.83	2.02	0.00–16.00	1.13	3.40	0.00–32.00
GP phone call (no. of contacts)	1.75	0.96	1:00–3:00	1.5	0.58	1:00–2:00

TABLE 17 Micro-costing of the I-WOTCH intervention

Costs		Cost
Delivery	Total facilitation cost	£29,121
	Total venue cost	£9079
	Total consumables cost (targeted attendance)	£2269
	Total delivery cost[a]	**£40,469**
Training	**Total training cost**[b]	**£27,416**
Total	**Total I-WOTCH cost**	**£67,884**
Population		**Number of patients**
Target population	Potentially eligible	20,900
	Interested and eligible	1050
	Randomised	608
Randomised to intervention	Randomised to intervention	305
	Minimum attendance[c]	164
	Maximum attendance[d]	204
Average cost per individual (randomised to intervention)		**£222.57**

a Total delivery cost (across 93 days of course delivery).
b Total training cost (across 81 days of facilitator training).
c Individuals who attended one of the group face-to-face sessions of the I-WOTCH intervention and a one-to-one nurse appointment.
d Individuals who attended all elements of the I-WOTCH intervention.

TABLE 18 Annual healthcare use cost[a]

	Best usual care (£) *n* = 303	I-WOTCH (£) *n* = 305
Opioid medication		
Mean (SD) (range)	713.45 (1223.34) (19.04–9450.17)	606.88 (1104.37) (6.35–10,602.36)
Health care resource use		
Mean (SD) (range)	2845.07 (2957.76) (0–24,003.47)	3107.42 (3318.66) (0–22,828.72)
Total cost		
Mean (SD) (range)	3562.61 (3257.27) (61.19–24,143.20)	3936.87 (3625.96) (278.49–23,324.96)
Inpatient admission		
Mean (SD) (range)	1485.05 (2441.36) (0–20,864.16)	1694.22 (2714.44) (0–20,864.16)
Day case admission		
Mean (SD) (range)	814.54 (835.49) (0–5264.00)	894.51 (1005.41) (0–6768.00)
Community health and social care contacts		
Mean (SD) (range)	545.47 (445.48) (0–3007.01)	518.70 (466.50) (0–3995.92)

a After imputation.

would have differ). Consequently, we followed recommendations by Faria *et al.* and used PMM to impute missing data in I-WOTCH trial data.[61]

Table 18 reports the total annual use cost for opioid medications and healthcare resource use after imputation.

Cost–consequences analysis results

Regression analyses (intention-to-treat population)

The results of the GLMM to analyse health benefits and the GLM to analyse total annual costs, while controlling for baseline covariates (i.e. age, gender, duration of pain, duration of opioid usage, opioid use, pain severity and trial arm) are reported in *Appendix 4*, *Tables 61–67*. Opioid band use was the only covariate that was statistically significant across all GLMM and GLM models for ADL, ShOWS, EQ-5D-3L and total annual costs. The treatment arm coefficients from the GLMMs fitted to ADL, ShOWS and EQ-5D-3L indicated no statistically significant differences between I-WOTCH and best usual-care group. This finding was consistent across all the sensitivity analyses conducted.

Total costs were found to be significantly higher in the I-WOTCH group compared to the best usual-care group ($p = 0.037$) (see *Appendix 4*, *Table 65*). This result was found across all sensitivity analyses tested. The only other significant drivers of cost were opioid use band (30–59 mg) and opioid use band (≥ 150 mg) ($p = 0.042$ and $p = 0.001$ respectively).

The GLMM model output was used to derive adjusted means (and 95% CI) for each of the outcomes of interest (ADL, ShOWS, EQ-5D-3L, total annual costs) as reported in *Table 19*. The results indicate that (when adopting a 12-month time horizon for the economic analysis) I-WOTCH is a more expensive strategy for supporting strong opioid tapering in individuals with chronic non-malignant pain compared to best usual care.

TABLE 19 Cost–consequences analysis – ITT population

	Best usual care *n* = 303		I-WOTCH *n* = 305	
	Adjusted mean[a]	95% CI	Adjusted mean[a]	95% CI
ADL	61.58	59.21 to 64.04	61.75	59.33 to 64.26
ShOWS	7.55	6.06 to 9.40	7.60	6.20 to 9.31
EQ-5D-3L	0.532	0.402 to 0.643	0.527	0.400 to 0.638
Total cost of scenario 1: training only benefit those randomised to intervention (£)	1250	360 to 4345	1670	487 to 5723
Total cost of scenario 2: training benefits all potentially eligible population (£)	1231	346 to 4370	1572	449 to 5503

a Adjusted conditional mean: conditional marginal mean (averaged over other predictors).

The effect of the baseline characteristics on health benefits and annual costs cannot be estimated directly from the regression output. The reason is twofold: first because these regressions are not calculated on the natural scale and, second, for non-linear models, one would need to calculate marginal effects for each of these to avoid falling into the '*Table 2* fallacy' trap.[80] This occurs when presenting adjusted effect estimates for secondary risk factors alongside the adjusted effect estimate for the primary exposure, which implicitly suggests that all of these estimates can be interpreted similarly, if not identically.

Regression analyses (per-protocol population)

We fitted the same GLMM and GLM (that were used for the ITT population) to the PP population (see *Appendix 4*, *Table 70* and *71* for the baseline characteristics of this sample). The adjusted means (and 95% CI) for each of the outcomes of interest (ADL, ShOWS, EQ-5D-3L, total annual costs) are reported in *Table 20*. The results indicate that – when adopting a 12-month time horizon for the economic analysis – I-WOTCH is a more expensive strategy for supporting strong opioid tapering in patients with chronic non-malignant pain compared to best usual care. No statistically significant difference in mean measures of health benefit was observed between I-WOTCH and best usual care. The same coefficient patterns described for the ITT population were found in the PP population (see *Appendix 4*, *Table 65*).

Long-term model-based cost-effectiveness analysis

Deterministic base case (intention-to-treat population)

A summary of the deterministic results of the cost-effectiveness for I-WOTCH compared with usual care for the ITT population are presented in *Table 21*. The deterministic results suggest I-WOTCH is more costly while improving clinical benefits compared with usual care. Over a lifetime time horizon, I-WOTCH is associated with an incremental cost of £9277 per person, but it also provided an additional 0.314 QALYs. Therefore, the ICER was £29,543 per QALY gained.

Deterministic base case (per-protocol population)

A summary of the deterministic results of the cost-effectiveness for I-WOTCH compared with usual care for the PP population are presented in *Table 22*. The deterministic results suggest I-WOTCH is more costly and provides fewer clinical benefits compared with usual care. This means that in the PP population, the I-WOTCH intervention is dominated by best usual care.

Deterministic scenario analyses

The I-WOTCH intervention was found to be cost-effective versus best usual care at a £30,000 per QALY gained threshold in 8 of the 10 scenarios explored (see *Deterministic and scenario sensitivity analyses* above for further details

TABLE 20 Cost–consequences analysis – PP population

	Best usual care *n* = 303		I-WOTCH *n* = 144	
	Adjusted mean[a]	95% CI	Adjusted mean[a]	95% CI
ADL	60.82	57.81 to 63.97	60.53	57.57 to 63.64
ShOWS	6.54	4.63 to 9.24	6.25	4.62 to 8.44
EQ-5D-3L	0.528	0.381 to 0.651	0.542	0.398 to 0.663
Total cost of scenario 1: training only benefit those randomised to intervention (£)	938	262 to 3351	1601	454 to 5647

a Adjusted conditional mean: conditional marginal mean (averaged over other predictors).

TABLE 21 Long-term CEA (base case, deterministic, per person)

Arm	QALY	Costs	ICER	NMB @ £20,000	NMB @ £30,000
Best usual care	5.642	£35,278	£29,543	−£2997	£143
I-WOTCH	5.956	£44,556			
Incremental	0.314	£9277			

TABLE 22 Long-term CEA (PP population, deterministic, per person)

Arm	QALY	Costs	ICER	NMB @ £20,000	NMB @ £30,000
Best usual care	5.612	£42,023	Dominated	−£17,487	−£20,961
I-WOTCH	5.265	£52,574			
Incremental	−0.347	£10,551			

about the inputs altered in each scenario). The difference in QALYs per patient between the I-WOTCH intervention and best usual care remained positive in all scenarios. The I-WOTCH intervention remained cost increasing in all scenarios, with incremental cost per patient ranging from £1206 (in a scenario with an older starting age) to £16,170 (in a scenario with younger starting age). Starting age also had the greatest effect on the QALY differences from base case. The scenario analyses are summarised in *Table 23*.

Probabilistic sensitivity analysis

The PSA suggests that the I-WOTCH intervention is more effective but also more costly when compared to optimised best usual care (*Table 24*). Overall, the I-WOTCH intervention was cost-effective in ~50% of simulations (10,000 iterations) at both WTP thresholds (£20,000 and £30,000 per QALY).

The cost-effectiveness plane is presented in *Figure 3*. The spread of simulations demonstrates that there are extreme variations in both the incremental costs and the incremental health benefits of the interventions. There are a large proportion of simulations in each of the four quadrants which make it difficult to determine whether the I-WOTCH intervention is cost-effective versus best usual care. Overall, the plane suggests that there is large uncertainty in the model input parameters.

Figure 4 shows a level of WTP at which the I-WOTCH intervention or best usual care is the cost-effective alternative. The probability of cost-effectiveness for each intervention stays at around 50% as the WTP threshold increases. This demonstrates the high uncertainty of the probabilistic results.

TABLE 23 Results of the deterministic scenario analyses

#	Scenario	Δ QALY	Δ Cost	ICER	NMB @ £20,000	NMB @ £30,000
0	*Base case*	*0.314*	*£9277*	*£29,543*	*−£2997*	£143
1	Fractures	0.307	£9071	£29,592	−£2940	£125
2	Discount rate (0%)	0.488	£14,927	£30,561	−£5158	−£287
3	Discount rate (6%)	0.242	£6957	£28,757	−£2118	£303
4	Younger starting age	0.525	£16,170	£30,827	−£5679	−£420
5	Older starting age	0.058	£1206	£20,747	−£43.42	£534
6	I-WOTCH costing	0.314	£9266	£29,508	−£2986	£154
7	Lower waning rate	0.267	£4279	£16,004	£1069	£3731
8	Higher waning rate	0.328	£10,389	£31,708	−£3836	−£549
9	Excess mortality (equal opioid state risk)	0.303	£8838	£29,153	−£2778	£252
10	Excess mortality (lower taper state risk)	0.303	£8839	£29,158	−£2779	£251

TABLE 24 Probabilistic sensitivity analysis results

Item	I-WOTCH (95% CIs)	Best usual care (95% CIs)	Δ (95% CIs)
Lifetime costs	£43,985 (£4841 to £146,905)	£35,578 (£5969 to £62,349)	£8407 (−£66,501 to £114,872)
Lifetime QALYs	5.918 (1.252 to 12.218)	5.675 (1.426 to 11.298)	0.243 (−7.805 to 8.402)
ICER (cost per QALY gained)	£34,614		
NMB (£20,000 per QALY gained)	−£3547		
NMB (£30,000 per QALY gained)	−£1117		
Probability of cost-effectiveness (threshold value: £20,000 per QALY gained)	49.5%		
Probability of cost-effectiveness (threshold value: £30,000 per QALY gained)	49.6%		

Value of information analysis

Expected value of perfect information

The EVPI at each of the WTP thresholds was calculated using the simulations generated in the PSA which are shown in *Figure 5*. The EVPI per person at the £20,000 and £30,000 thresholds was £24,875 and £61,455, respectively.

The short-term findings indicate that individuals who received the I-WOTCH intervention were more likely to engage with a tapering plan to reduce their opioid consumption, but effective management of non-malignant chronic pain (i.e. maintaining measures of health benefit at a similar level to that experienced while on strong opioids) in these individuals required an increased use of healthcare resources. Consequently, in the short term, the I-WOTCH intervention was cost-incurring when compared to the best usual care with similar health benefits between the two groups. Extrapolating this effect beyond the 12-month horizon of the trial (assuming that the ability to self-regulate will reduce over time in line with the waning rate observed in the I-WOTCH trial over its 12-month follow-up) indicates that individuals who

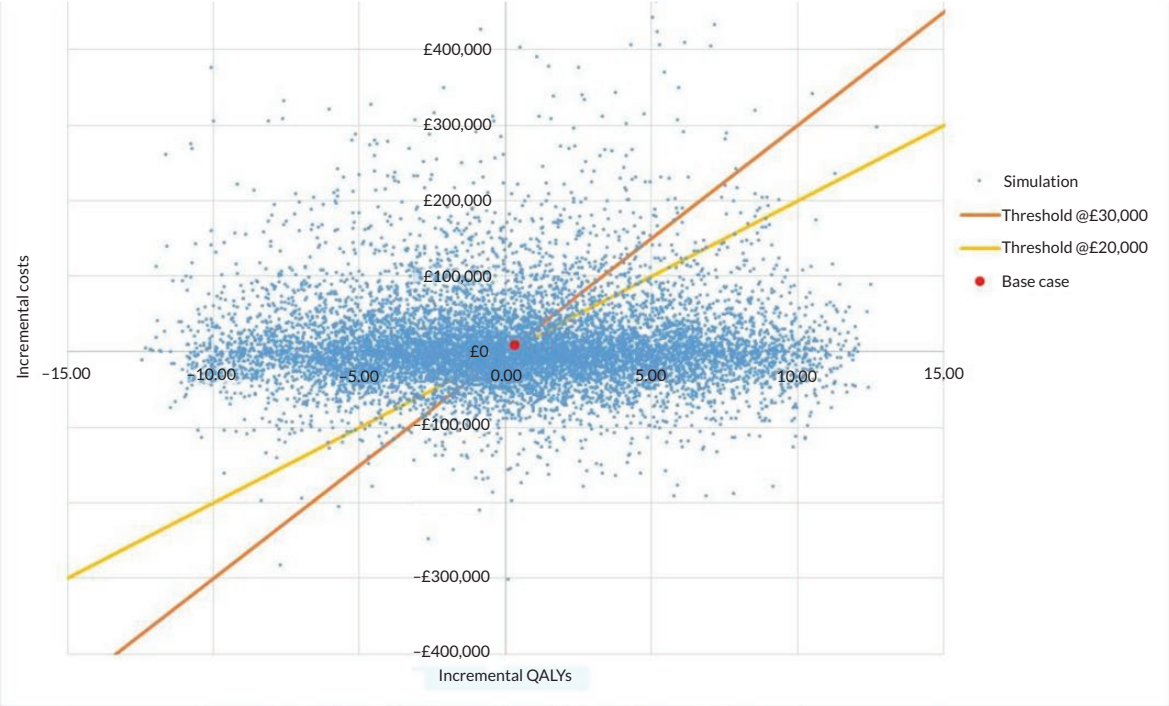

FIGURE 3 Cost-effectiveness plane.

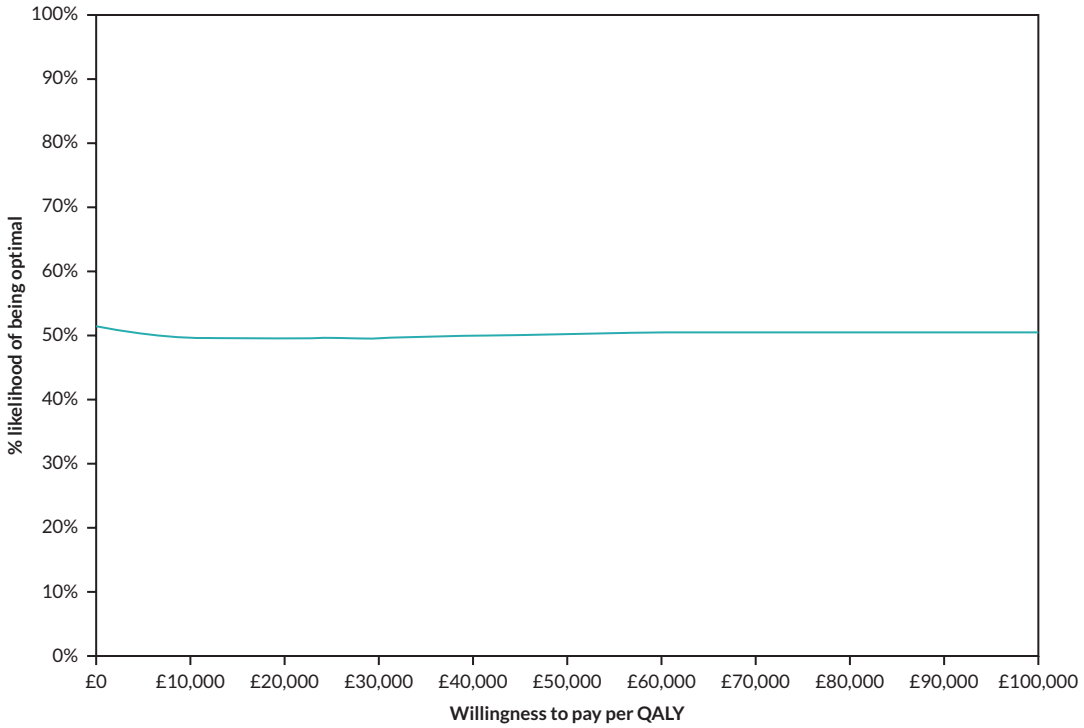

FIGURE 4 I-WOTCH CEAC.

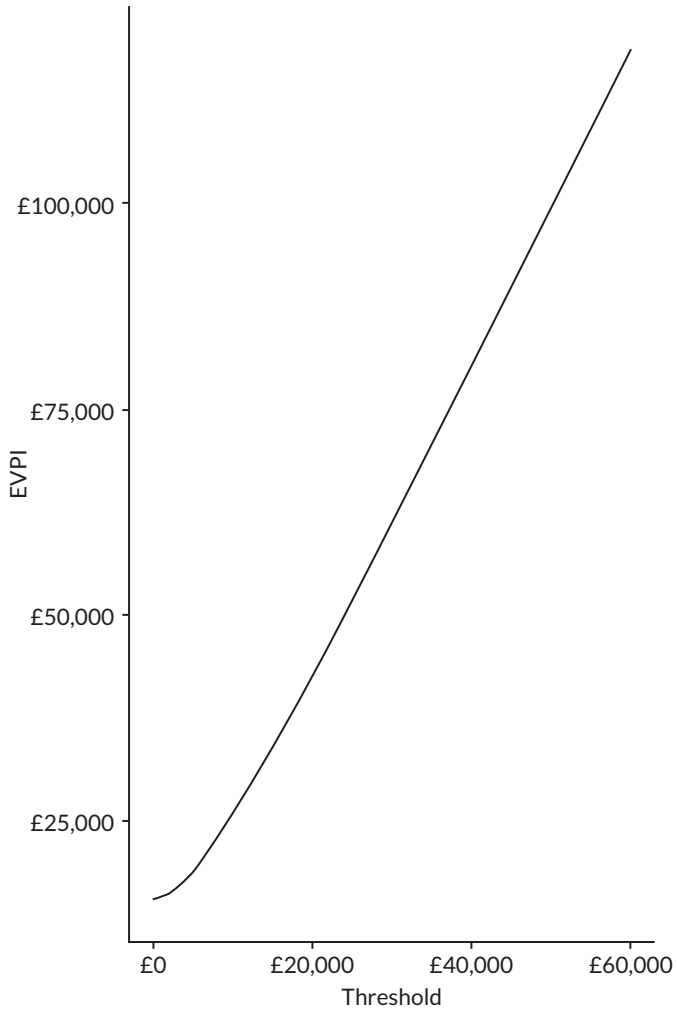

FIGURE 5 Expected value of perfect information results by threshold.

are able to self-regulate their use of strong opioids also achieve a reduction in their exposure to the excess mortality rate associated with long-term consumption of strong opioids. Modelling these results as part of the base-case analysis of the long-term CEM indicates that – adopting a lifetime horizon – the I-WOTCH intervention may be cost-effective compared to the best usual standard of care.

Chapter 6 Process evaluation: methods and results

Background

Process evaluation is embedded in trials of complex interventions to better understand how an intervention functions. The process evaluation findings were kept separate from the main trial team during data collection and prepared before the main RCT analysis was known.

Aims

1. Understand experiences of the intervention, including enablers of, and barriers to, the intervention facilitating change among participants.
2. Explore intervention implementation, including dose of the intervention delivered and received, and the fidelity of delivery.
3. Investigate change mechanism markers and whether hypothesised changes occurred.
4. Identify contextual issues that may affect the outcome or running of the study and/or intervention.

Design

The process evaluation assessed how the intervention was delivered, the 'dose' received and the fidelity of the intervention. In this study, we also explored experiences of the participants and staff and examined contextual issues.

The intervention included educational, psychological and behavioural components designed to effect change using a pain management approach. The process evaluation team used a predefined checklist to ensure we had considered all aspects of the group behaviour-change intervention.[81] We then used process evaluation theory to devise a logic model specific to this intervention, informed by The Information, Motivation and Behaviour skills Model[82] which highlights that knowledge, strong and stable motivation and prerequisite skills are needed to initiate and maintain behaviour change. See *Appendix 5*, *Table 72*.

Methods

The methods are described in more detail in our process evaluation protocol paper.[4] Briefly, we used a mixed-methods approach for the process evaluation using qualitative data collection methods as well as quantitative data collected by the trial team as outlined in the tables below (*Table 25*).

Qualitative data

Interviews

Patient participants

Potential interviewees were purposively sampled from those who had indicated on the initial trial consent that they could be contacted for an interview after their 12-month questionnaires, to ensure a range of age, opioid reduction experience and gender across the intervention and control arms. Interviews were semistructured (see *Report Supplementary Material 5*) and took place face to face in people's homes or a mutually acceptable alternative as convenient for the participant, for example their doctor's surgery.

Intervention staff interviews

Those delivering the intervention were interviewed about their experiences after all the intervention groups had been completed. After obtaining informed consent, interviews were audio-recorded and transcribed verbatim when all identifiable data were removed. They were checked for accuracy by the researcher who had conducted the interview. Home visits to conduct interviews were risk assessed, and a lone worker policy was followed.

TABLE 25 Qualitative data collected in I-WOTCH study

Key components of process evaluation	Type of data
Experiences of participants receiving the I-WOTCH interventions (intervention and control)	Interview recordings and transcripts Participant feedback forms
Experiences of staff delivering the intervention	Interview recordings and transcripts
Assess fidelity of group sessions and one-to-one consultations: • Adherence • Competence	Audio recordings of group sessions, and one-to-one sessions with nurse
One-to-one consultations To understand the issues discussed	Audio recordings of one-to-one sessions with nurse

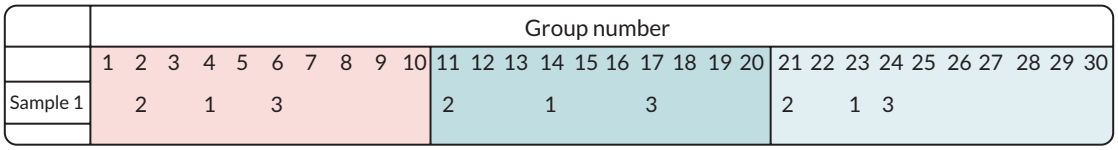

FIGURE 6 Random sampling chart.

Fidelity

All study intervention groups and one-to-one consultations were recorded. The group intervention took place over 3 days. All of the main trial groups were given a chronological number. To identify which groups would be checked for fidelity, the trial statistician allocated a random day 1, 2 and 3 per block of 10 groups, signifying early, middle and late stages of the study *Figure 6*. We also rated a 1 : 1 nurse consultation per group. We double rated 10% of the group sessions and 1 : 1 consultations using a second rater.

If audio-recordings were missing or inaudible, then the same sessions as those missing would be taken from the next group in the same area [North East (NE) or Midlands].

Fidelity of the intervention delivery was assessed for (1) adherence to the intervention content as specified in the manual and (2) competency of the facilitators in delivery of particular components, using bespoke scoring sheets (see *Appendix 5*, *Table 73*). We pre-specified 11 group sessions which were key to promoting behaviour change because of their educational and/or discursive content. Other sessions which were more practical in nature were checked to see if they took place but were not rated. *Appendix 5*, *Table 74* shows which sessions were rated.

Scores were summed and a percentage score was calculated for adherence and for competency. Face-to-face nurse consultations were also assessed for adherence and competence using bespoke categories taken from the face-to-face training manual, applying the same methods as that used for group sessions. See *Appendix 5*, *Table 75* for the forms used.

Participant feedback forms

These included questions about the course and how confident they felt that the course content would help them. They were given out after day 3 (the final day) of the intervention, to the last 10 intervention groups only due to delays in getting an ethics amendment submitted.

Quantitative data

The quantitative data used are shown in *Table 26*.

TABLE 26 Quantitative data used in process evaluation

Key components	Type of data
Number of groups run with locations	Trial data
Numbers attending each component of the three intervention days and attrition	Trial data/attendance sheets per session
Uptake of the one-to-one consultations	Trial data
Uptake of the telephone follow-up telephone calls[a]	Trial data
Patient motivations, expectation, self-efficacy and perceived credibility of the intervention	Change mechanism questions on main trial questionnaire *Box 3*.

a It was not possible to record content of telephone conversations.

BOX 3 Questions linked to potential change mechanisms

Baseline motivation (baseline and follow-up)

I want to reduce my opioid use

(not at all, by a little, by half, so I only use a little, so I use no opioids)

Baseline expectation (baseline only)

I expect that, in 4 months' time, I will have reduced my opioid use

(not at all, by a little, by half, so I only use a little, so I use no opioids)

Baseline self-efficacy (baseline only)

I am confident I could reduce my opioid use a lot over 4 months

(not at all confident, somewhat confident, fairly confident, strongly confident, completely confident)

Credibility (baseline and follow-up)

Baseline

I feel that involvement in this study can help me to reduce my opioid use

Not at all, by a little, by half, so I only use a little, so I use no opioids

Follow-up

I feel that involvement in this study has helped me to reduce my opioid use

Not at all, by a little, by half, so I only use a little, so I use no opioids

Analysis

Qualitative

All interviews were initially analysed using framework analysis and NVivo12 software used to organise the data. Participant feedback forms were analysed using content and seven-stage thematic analysis of Braun and Clarke.[83]

A mixed-methods approach described by O'Cathain *et al.* was used to combine the quantitative and qualitative data using a 'following a thread' and a 'mixed-methods matrix' across the data.[84]

Quantitative

The statistical team provided descriptive statistics, charts, tables or figures for the quantitative analysis, using STATA 16.0. The mean and SD were presented for continuous data, and the frequency and percentage for categorical data, summarised by treatment arm.

Findings

We include a headings table to present an overview of the findings and to aid navigation of the findings (*Table 27*).

TABLE 27 Headings table

Main heading		Subheadings

1	Experiences of the intervention	**Participant interviews** (*n* = 40)
		• Participant demographics
		• Motivations/barriers to taper
		• Role of the GP
		Control interviews (*n* = 20)
		• 'My Opioid Manager' manual
		• Relaxation CD
		Intervention interviews (*n* = 20)
		• Being in a group
		  • Shared experience
		  • *Social* comparisons
		  • *Support*
		  • *Being* committed *to something*
		  • *Group* numbers
		  • *Perceptions about group facilitators*
		  • *Challenges* to *establishing group cohesion.*
		• Nurse one-to-one consultations: participant perspectives
		• Group sessions of interest
		  • Opioid *Information*
		  • *Anger irritability* and *frustration*
		  • *Relaxation*
		  • *Mindfulness*
		  • *Distraction* techniques
		• Acceptability the intervention
		Intervention delivery staff interviews
		(*n* = 10 nurses, *n* = 6 lay facilitators and *n* = 2 other HCPs)
		• Characteristics
		• Training
		• Venues
		• Facilitators
		• Suggestions for changes
		• Group dynamics
		• One-to-one sessions
		• Factors affecting readiness to change across the group sessions – facilitator perspective.
		• Categories of change
		  • *Resistance to change*
		  • *Open to trying*
		  • *Not the right time*
		• Turning points
		Feedback forms

2	Implementation of the IWOTCH group intervention	**Groups run** (dose delivered) **Groups delivered** (dose received) Uptake and attendance Participant reasons for non-attendance throughout the study **Fidelity of intervention delivery**
3	Change mechanism questions	**(no subheadings)**
4	Contextual issues	**(no subheadings)**
5	Revisiting our logic model	
6	Overarching themes	

Experiences of the intervention

Participant interviews

Participant demographics

The 40 patient participants interviewed in this study had a mean age of 65, median IQR 59–72 years, 63% were female and 95% were White. There were 78% who had pain from more than 5 years and 50% had been taking opioids for more than 5 years. See *Appendix 5*, *Table 76* for full interviewee sampling characteristics and *Appendix 5*, *Table 77* as a comparison with the main study demographics. Eighteen patients declined an interview, reasons are given in *Appendix 5*, *Table 78*.

Enablers and barriers to tapering

We analysed the interview data (n = 40) to see how participants spoke about any enablers or barriers to the tapering process including any effects attributable to I-WOTCH.

Enablers to tapering There were four main themes from all the interviewee data (n = 40); readiness to start tapering, I-WOTCH as a trigger or motivator, continuing to taper and living without opioids as *Table 28* illustrates.

Barriers to tapering

The three main barrier themes are different phases of tapering: pre tapering, during tapering and being off opioids. *Table 29* gives subthemes for each phase.

Role of the general practitioner

Thirty-four out of the 40 interviewees across the control and intervention arms spoke about their GPs and the role they played in this study about tapering opioids. There was more confidence or interest in I-WOTCH when the participant had had prior discussion with their GP before being approached by the study. Some made the decision to give tapering a go at that GP consultation.

> *Talking through [with the GP] made me realise I was ready*
>
> *4*

Many spoke of a history of being put on opioids when other pain relief was not effective, and subsequent visits about pain meant many were advised to increase their dosage. Looking back they felt this advice was taken due to trust in their doctor.

> *I sort of trusted my doctor that he was doing the right thing by me …*
>
> *28*

There were examples of a good working relationship with the GP, some of which were extremely supportive of the tapering process.

> *… I'd come down an awful lot and my doctor was absolutely gobsmacked… she calls me 'her star patient…' …she's a fantastic GP … she wanted me to succeed as much as I did so it was team work but if you've got a good GP like that you're sailing aren't you but some are too busy!*
>
> *31*

Some doctors were perceived as being resistant

> *[T]hey didn't think I would get off them[opioids] (because of their pain)*
>
> *13*

> *Can't come off them we've tried all sorts*
>
> *15*

TABLE 28 Enablers to tapering

Theme 1: readiness to taper		
Theme 1 sub hemes	**Exemplar quotes – control**	**Exemplar quotes – intervention**
Already made the decision or had started to taper	*I'd already decided 015* *…made the decision probably 6 to 8 months ago …* 020 *I was thinking about it.* 033 *…now's the time to do it … if I don't do it now I'm not going to do it …* 08 *…one day I woke up and just thought … that's it I'll stop taking them!* 35	*…absolutely determined because I'd cut it by half by the time the study started and because I was already reducing it when the first lot of information arrived … 01* *and then the invitation to take part in the study so I was reasonably invested in actually engaging with the study because it was something that I'd been thinking of myself … if you understand … 29*
Didn't like the side effects	*…you're not in pain but you're not really enjoying your life … I'd sooner be the other way not quite taking enough so that at least I'm firing on three cylinders instead of two …* 24 *I knew about constipation and that's really what made me try and come off the morphine …* 33	*They weren't suiting us at all they were taking … you know as if you … you'd scratched yourself and you had little red spots … 10* *so it was a case of well I would try and see if I could reduce them or come off them and see if I wouldn't need as much other medication so it's the side-effect medication so I wouldn't be taking the anti-nausea tablets I wouldn't be having the … mmm … bowel medication … 34* *… well I was talking to my GP about forever being given larger and larger doses of opioids and the side effect of opioids … 36*
Not wanting to be on opioids	*my role in life to get off all this flipping medication … I hate taking pills! 033* *I don't want to be on them forever …* 027 *I don't like anything I don't need to take … one thing that has worried me somewhat is all the stuff in the press about how in America they are very … worried about inappropriate opioid usage … 037* *It does scare me knowing that I'm on morphine … 039* *If there was an alternative I think I'd go for the alternative … 27*	*Well it was the side effects … I mean the low moods and the depression … 05* *… it was when it was on the tele as well about being an opioid I thought I don't want to be addicted or to be totally dependent on them … 13* *I don't like taking drugs … I mean I want to get off all those drugs … they make me retch every morning when you've gotta take so many drugs … 016*
Wondering if opioids were working anyway	*Could I do without them …? 08* *Toyed with the idea 06,* *I thought, these just don't work … 19*	*I'd been sort of talking in my head with myself about Fentanyl because post-surgery there was a lot of post-surgical pain and while I was rehabilitating so it was all sort of … so I'd been talking in my head about … 'Do you really need to be on this now?' … so I was reasonably invested in actually engaging with the study because it was something that I'd been thinking of myself … if you understand … mmm … but as I say nobody else had … had raised it as a (inaudible) issue at all it was … it was just there you are! 29*
Support from GP or family to taper	*my GP … a while before I got the letter had been saying to me 'do you think you should be decreasing your morphine a bit? … you may find that you're absolutely fine without it, obviously we'll take it slowly …'* 37 *…if you find you can't cope come back in and we'll have another discussion …* 24 *…yeah try that Mum and you might be able to come off …* 08	*it's your family are pleased for you as well and I think they think you know you're more with it and so that's … that's really a nice thing yeah … 21* *…that's when I came out that day and my husband was with me because he was in when I had this face to face with (name) and he was now 'oh we know what we're doing' and he's quite good at making sure I take all the right things at the right time! 25* *…I myself thought right I don't want to be on these anymore and the doctor agreed … 25*
Positive past experience of tapering	*…and I thought well you know if I ever need to come off this again I can do it … 17*	*16–17 years ago just after I'd had my first pair of hip replacements before they started giving me problems I came straight off all the opioids I was taking then so I knew that I didn't really have a problem with … withdrawal from a previous experience … 22*

TABLE 28 Enablers to tapering (*continued*)

Theme 1: readiness to taper		
Theme 1 sub hemes	**Exemplar quotes – control**	**Exemplar quotes – intervention**
The right time to fit in with life, for example holiday, season Potential for change in pain, for example, operation	*[I]t was through the doctor there that they suggested that maybe this research thing would help … be helpful for me and I found it has cos it's part of in your mind as well I think you think 'well do I need these tablets?' and I've just had hip surgery I've just had to have a new hip done … it was after I'd come off that that the pain just seemed to go from the hip completely so I thought 'right now's maybe the time that yes I do need to come off them … stop taking them' I mean you don't do it without asking your doctor how well to do it … so my doctor advised me how to wean myself off them and that's kind of what we've done … 08*	*Because I was on the Tramadol … mmm … during and going up to my back pain … err … my back surgery we decided that we wouldn't start it off immediately … mmm … we would try it after the … the surgical pain had gone cos … cos that's one thing I did find … get from the group that there is this long term pain that I've had now and I've still got … err … and there's the short term medical intervention pain that you get as well … 09 … it was when it was on the tele as well about being an opioid I thought I don't want to be addicted or to be totally dependent on them I'd rather tinker around this like … erm … and keep it just … if I'm really, really was desperate … erm … so really the study couldn't've come at a better time … 13* *I'm trying to think back to that part of the summer … how I was like … think I was relatively well which is why I started reducing it … 34*
Theme 2: I-WOTCH as a trigger or motivator to taper		
Theme 2 sub themes	**Exemplar quotes – control**	**Exemplar quotes – intervention**
I-WOTCH as trigger	*…if I hadn't have had this research … I don't think I'd of jiggled my mind to think about coming off pain relief to be fair … 08* *…she [GP] said 'Well yes that's fine and if you're going to reduce a bit anyway then that would be a sensible thing to do and you'd be potentially doing something useful at the same time' which was my other driver for it really …' 37* *In fact when I saw this study and when they said that it was to help … hopefully help people reduce that was one of the reasons as well … because I wanted to reduce the in-take of them.20*	*I don't want to really go over there and didn't want …' and then when I really got to think about it I thought, 'Well this might be good for me you know … it might help me'21* *… but being part of the study has … mmm … enabled me not to be on them anymore whereas I don't know whether that would've been the case otherwise!29*
Information	*… there was certainly a lot of useful information … a useful … to make you think about what you're taking and why you're taking it … mmm … and yeah it was useful … see that's a good thing there … he thought the opiates were the only answer to his pain but they're not because I do think the more you take the more need … 08* *I knew it but I didn't know it as in-depth as this … 11*	*because I didn't know the Fentanyl or the MSTs was in … yeah I knew MSTs was morphine but I didn't realise they were in the Heroin range of painkillers! 10* *… and then when I was on the course I realised how damaging these things could be and I got all this information off the ladies and went through that and I got relaxation discs and all sorts of things … I found them all very useful but when I read this I thought … well there's only one thing you've got to do … you've got to come off these dam things … 30*
Support from group or nurse	N/A	*…I think because I had the support and like I say I'm into the research bit where I found it better to do it under the research bit as well. I just felt encouraged like that I could do it meself so I liked the support I suppose and the fact that they believed in me … 13*
Tools to help	*I feel that because I've had the booklet to look at I've always got something to fall back onto when I was like thinking, 'Oh is that right … is that right I am doing things right?' and just looking at obviously people must have experienced some of these things that you've put in here and the fact that you've put so much other information in the back of the groups that'll help you and things like that … I didn't even realise that half of these companies … like societies were even available! 12* *…I had the disc and I play that disc now … because well it's so relaxing and so what I do is I … put the cushions there and I lie on the floor because of the spine it's better to lie on the floor than the bed … I switch it on and it makes me relax and sometimes I go to sleep. 15*	*… point number one my goal really is which I appreciate a lot from this study my goal is not to look at Tramadol as my solution, as a solution to my you know but to adopt these other tools … mmm … and there are many it's not just relaxation or my … or meditation which are very helpful but you … you bring into … you know you bring it in to play all this … I always say, you see another thing is what I miss most here is not having people to laugh with because I feel even laughter is something that takes you away it distracts you from the pain … So am really trying hard to develop those to apply tools, not develop, to apply tools that I have. 38* *I was over the moon because I got more tips you know … it was all helpful to me. 10i*

continued

TABLE 28 Enablers to tapering (*continued*)

Theme 2: I-WOTCH as a trigger or motivator to taper		
Theme 2 sub themes	**Exemplar quotes – control**	**Exemplar quotes – intervention**
Tapering plan – given the means	N/A	*… it was a joint plan that we worked out together … mmm … and from the information I'd had from my own doctor and what he could do in the way of the tablet size and stuff like that … mmm … I went round with the knowledge of what I could get available … 09* *… I'd [tried] to do it on my own and it just didn't work and having the proper goals to follow and knowing what you have to do I'm not so frightened as to try and come off it now as I would've been because it's … it's an addiction it really … really is an addiction! 41*
Open Mindset 'give it a go'	N/A	*… and I'm getting back to the mind set as I say once I find out in August … sorry April about the liver and what I have got to have done then I think then is another time when I will be able to come down perhaps to 10 … I am still determined to come down or come off it … 07* *… but I went in with an open mind and everything we did on the group the … the practice sessions and the things we got to do at home you know the colouring and everything else that we did on the study … mmm … and listening to the relaxation CD's and everything like that … I'm … I went in with an open mind on that and listened to it and took out what … what I could from … 09*

Theme 3: Continuing to taper		
Theme 3 sub themes	**Exemplar quotes – control**	**Exemplar quotes – intervention**
Self-efficacy	*…and sometimes when I'm really in pain I think … 'No no because that's just going to disrupt everything that you've done … so I don't take it! … give yourself a pat on back* 12 *…that gives me satisfaction if I can get through [on less medication]* 23	*because I had a motivation I think as you know an innate motivation I suspect that I may have been successful as well with … in the control group in coming off the Fentanyl … 29* *… the Tramadol thing is still there I look at it at times and I sort of say 'maybe it's better that it's there instead of me throwing it away because that's training me' it's giving me enough courage to sort of say 'I'm straight I can actually see it and overcome it' and … err … I'm almost like it's like a mini training moulding myself on how to … to … to manage that … 38*
Feeling better, decreased side effects	*…when you come off it you're not Zombie like!015* *…had more energy … 04* *I'm not so wobbly … not be so drugged up … not knowing what's going on around you … 24*	*… because I knew that I wasn't getting any benefit from being on it so that was a big incentive to come off and it wasn't helping with the pain so would you want to keep putting that into your body if it's not doing anything! 01* *…yeah it's your family are pleased for you as well and I think they think you know you're more with it and so that's … that's really a nice thing yeah.21* *but it was really important to me to get rid of this … rid myself really of this drug … all I can say is this complete … having from the other side now I describe as 'un-reality' 29*
Pain similar	*'Did I need all that medication?' 15*	*Well when I think back it was just a dull time … too much pain and too much everything and then when I had reduced it and I was thinking one day. 'Oh I'm in so much pain again why did I reduce all these?' then I thought 'Well I was in this much pain when I was on them …'21* *… before I came on the study the pain level I was having then and the pain I'm having now there is no difference … 029* *… but really I can say coming off of it the pains not any worse than it was … 31*
Seeing the reduction of opioids	N/A	*…so it just shows you … you just … you know if I can do without half of them I'm going to try and get down a bit further … 21* *Well I found it easier to decrease my taking of opiates than I … I expected more trouble but I must've gone at a steady enough pace for it to be ok … 32*

TABLE 28 Enablers to tapering (*continued*)

Theme 3 sub themes	Exemplar quotes – control	Exemplar quotes – intervention
Theme 3: Continuing to taper		
Flexibility (slow) of the tapering plan	N/A	*…I knew I couldn't follow a strict pattern than that … if it was that strict then I wouldn't've be able to do it and I would've left the study! 034* *The stimulus that there's a study happening … mmm … it's not being imposed on you it's a choice that was important that it's a choice … and the notion as well that was presented that … mmm … you didn't have to come off them completely and I think that was really helpful … 29* *Mmm … I think cos I was on such a high dose it was … it was alright 'til I got to the lower and then that's when you start finding it a little bit more difficult.* *… it came down in such low you know … I can't think of the word … but the dosage didn't alter that much so you'd only come down like … mmm … 5mgs or whatever cos I went off the patches onto tablets … so it changed … mmm … when I got down cos I think it was 25 on the … mmm … on the patches and then I had to go onto the Morphine tablets … and then I had slow release ones so it … it was … it was done so … so slowly and minutely it was … I … I can't honestly say I had any side-effects!31*
Participant in control	N/A	*I thought that was helpful you know to set your goals and know what you'd set and … and then if you didn't achieve it think … well you know 'am I any worse off for it?' you know so … so she was saying there was no right or wrong … one day you will achieve what you want to do and another day obviously you won't so yeah.31*
Understanding/ weathering withdrawal effects	N/A	*I was kicking I was twitching I was … I couldn't sit still I was … Aah … me hands were going and … I'm not joking I had to run round … I was running the table or walking fast round the table 'cause I couldn't keep still … I couldn't get any comfort whatsoever or any satisfaction and I was like 'Jeeze' and a couple of times I went … thought shall I put a patch on but I no I've got to persevere because if I put a patch on I know it will stop but I am back to square one so no I've got to persevere … I've got to persevere and I did and I carried on and that's it … eventually it disbursed and … great so I've never touched the patches since … it's really great I'm chuffed … 05* *… using the principles of the IWOTCH study was to get up and do something that … that … well my brain was interested in and allowed me to forget about all the other issues that were going on … so I had four and a half thousand stamps to put in numerical order from the catalogue and … mmm … and I spent hours and hours going through that … until it was complete and that's what I used to do when … when I woke up angry because I found … I realised it wasn't fair to my wife that I'm banging and throwing stuff about … mmm … so I'd get up and start this cataloguing and I used this cataloguing as … as my … as my crutch if you like through that bad period! 09*
Support from group or nurse	N/A	*…and that's what was good about the course with the support and the support network … but it's that conversation amongst yourselves because you all know you're in the same boat you know what I mean and a lot of ya will have … would've had similar experiences and similar thoughts and whatever it be … err … it's … it's that which I think motivates ya … 22* *… as I say I felt guilty that I hadn't dropped down more … mmm … but I was told not to feel guilty … mmm … and other things do come in on your life that can affect it. 07*
Theme 4: Living without opioids		
N/A	*[S]o within about two months in all I'd completely come off the opiates so … 08* *'I'm pleased that I came off them …'* 019	*…because me body was getting itself put right if you understand where I'm at … and in my mind I know I'm not abusing my body any more than what just for Paracetamols and everything I'm on now … 10* *…there's negative points of coming off them but I feel the plus side is that these tablets … these opioids are not doing any harm to me body anymore … 31* *… because of the course you know the few weeks that we were on that was a great help to me it just urged me to get off you know … wean myself off them which I did! 25*

N/A, not applicable.

Source

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TABLE 29 Barriers to the process of tapering

Pre tapering		
Subthemes	**Control – exemplar quotes**	**Intervention – exemplar quotes**
No intention: • Not receptive • 'I'm not addicted' • Not motivated	*…after I've had them I feel a lot better but I don't have any side effects … just keep them as low as I can. … I just know I just can't cope without something … 28* *… I am grateful for them because they are managing my pain and allowing me to function. Sometimes not very well but they are helping with the pain so I can you know do little bits and get about and you know have a sort of a normal life with it if that's possible as long as I can … 27*	*… I think I'd be in a bad place if I couldn't take them … I certainly don't think I'm addicted to opioids 16* *… but there again I had already made my decision that I only use the opioids as I need to … 14*
No choice, no alternatives	*The only way I can sort of logically get out of pain or reduce it is by taking tablets.'. 06* *but I am like still adamant that at the end of that day if I can get other medication that will work for me then I will be stopping it totally.12* *… if your pain levels are such you don't need it then you don't take it but if you get to the point and you think this really is … I'm waking up at night that's … that's why you use it…. 23*	*… scared to come off them but I'd love to try but I need the back-up!26* *… I really don't want to be on them that's my wish but … mmm … it's taught me that I cannot be without them which is unfortunate….25*
Not the right time: • Other health priorities • Won't fit in with life (holidays) • Awaiting procedures which may help or affect their pain, for example knee operation/ operative pain	*'I don't want to do it yet … I knew I needed to wait until the hip was done cos the pain was so bad.'. 08* *…unfortunately this study came at the wrong time for me … [on a higher dosage due to an operation with complications]. 11* *'… I personally would like to cut it down but I don't see how that's physically going to be possible at the moment … I'd had quite a good summer … winter's tend to be harder for me … Difficulty tapering over Christmas. 37* *… recently in the last month or so I've had a knee operation so I've had a partial knee operation on one leg so my pain is now diminished on that leg so it's for walking I've still got the pain on the other leg which I'm on a waiting list to get that done so when that's complete I can't see that I will have any need for any painkillers at all so … 17*	*…but I couldn't reduce my Morphine because I was going into hospital to have some work done and I knew that … mmm … as a result of that work I would be paralysed for three months down my right-hand side so I knew that there was no way I was going to be able to cope by reducing my meds at the time … 34* *I haven't tried to drop anymore 'cause there's just been that much going on … mmm … 07* *… we decided that we'd do nothing at all with the pain medication because we knew that when I went into hospital the … the surgeons in the hospital would look what I was on with pain medication and say 'that's not enough we wanna' and they would load it up so that I could get through that bad period so we decided to delay that until after the operation … 09* *… I'd not even considered that at all until … until I have the … my hip replaced and then that knee's done that hip's done me eyes are done then we can see … start tapering off maybe having one … one a day instead of two a day. 16*
Fear of: • Increased pain • Decreased function • Not coping • Opioids being stopped • Having no future access to opioids	*'That was the biggest fear on doing it that if I reduce it I'm gonna be in agony.'. 04* *… I just know I just can't cope without something and … err … and I've got my husband to look after and I've got my mother-in-law to look after and you know between the two of them and I also have my own interests and hobbies that I like to do and I can't do those either without something to … to help the pain!28*	*… as I say I had no intentions of reducing but I thought I would try it and I would go further but I'm scared of the consequences I mean if my neck or back … that gets much worse I'd been in a bloody wheelchair … 26* *'I remember thinking 'I'll be in so much pain and I'll be … I'll be even more angry with myself' so I was thinking, 'I really … I can't … I can't do this …' it was you know to see it on paper alone it was a lot … 21* *…what worried a lot of people was the thought of once their prescription's been stopped … what if they need it … 22* *… if I come off it and I still need it … what does that mean you know … can I go back on it again … 29*

TABLE 29 Barriers to the process of tapering (*continued*)

Pre tapering		
Subthemes	**Control – exemplar quotes**	**Intervention – exemplar quotes**
Resistance to group intervention messages: • Anger at GPs- (affecting GP–patient relationship) • Scepticism • Suspicious of trial motives and future recommendations • Credibility of facilitators (nurse non-expert/lay not the same as them)	N/A	*… but I'm quite annoyed that a GP who's prescribing more and more and more and should ought to … jolly well ought to know the research background so … and there was a lot of anger in the room that I was in about that … 29* *but I was a little pessimistic … mmm … because of knowing how much pain I've been in … in the past and nothing else has worked … 07* *…so for some people it was like they were using it as their 'reason not to' you know what I'm trying to say … 'oh she don't <u>really</u> know' you know 'if she'd been on them for as long as us' … 22*
During tapering		
Subthemes	**Control – exemplar quotes**	**Intervention – exemplar quotes**
Increased pain	*Because I can't move first thing in the morning when I've laid in bed … 15* *'I've dropped down from 100 to 50mg now and the pain level's gone up …'06*	*I think I was wrong to come off them believe it or not … and I really want to get off them because that make one very constipated and I just wanted to be free of them but I couldn't manage it … Saturday and Sunday were dreadful days I was in such pain! 25* *I'm now down to eight in the morning … eight at night and I know that I can't get any lower … my body is now saying … I'm not saying that it won't do down in the future but at the moment I've … I've got to leave alone because I'm a lot more problems with my joints … I have total body pain and my knees are really causing me a lot of pain … mmm … it wakes me up at night … mmm … whereas before the pain was at a level that I could cope with I'm now barely coping but I'm still persevering on the eight … 34* *…but I did reduce them to 40 … 20 in the morning and 20 at night but I'm VERY reluctant … if they could give me something and say … mmm … well try it but if it goes wrong get this into you quick … I would. 26* *… 'Oh that's going to be good I can come off these altogether!' … but then suddenly the pain increases again so at that stage I thought … well you know what can you do … suddenly sit here all day with your feet up or take one Tramadol and do a little bit … 30*
Unpleasant withdrawal symptoms	*Wasn't easy to come off … it's just a feeling of being unwell all the time … it took quite a while to come off them … 19*	*… but I'd say the symptoms were far worse when I reduced the second half … cramps in my legs and the … oh the hot sweats and cold sweats they went on for a long time that was horrible … 01* *… I mean it was bad enough coming off them gradually because there time … there times you just felt as if you … you'd got a craving and you … for example if you came off them from … I don't know five a day down to four a day or something like that and you'd try to skip and go to three a day then it was really … you'd get a craving and think … cor … the hot sweats and feeling achy and pains. So it was … I was really very bad tempered over the period withdrawal … 30* *… and I've been on it ever since until I started on this course and I eventually weaned myself off them as I was told to but the last bit was 'poor' it was crazy 'cause I couldn't sleep properly I was jumping up and down … I was running round … I was literally running round that … the lounge all the time pulling my hair and … real cold turkey effect and … mmm … when that had sort of got out of my system I was ok and now I'm on completely 'zero' painkillers … 05*

continued

TABLE 29 Barriers to the process of tapering (*continued*)

During tapering		
Subthemes	**Control – exemplar quotes**	**Intervention – exemplar quotes**
Tapering too fast	N/A	*… it's a shame that there wasn't another way or to have changed the patches in some way to have come down at a slower rate and perhaps then I may have had more success I think with coming down 25% because this particular patch that I'm on … the Butec one … it only comes in 5's … 07* *… I just wanted to see how … see how it goes … well maybe to stop all like the cold turkey effect at the end maybe I should've kept it on for maybe another couple of weeks you know done it that way … I don't know but I just done what I was told and that was it but then I got there … I got there! 05* *The tapering I thought was a good idea but I already knew that I wouldn't be able to follow it on a weekly basis I knew that it wouldn't work for me that and as long as I could do it in my time frame and not a 12 week or whatever week pattern then that was fine and there was no right or wrong answer to that and it was a case of … for me I was doing this for me not for the group study for me … for it to work for me it had to be done at my pace and if my pace was a reduction of 2mgs every month then that's albeit what it had to be I knew I couldn't follow a strict pattern than that … if it was that strict then I wouldn't've be able to do it and I would've left the study! 34*
GP unsupportive of the process or poor access	*[GP stated][You] Can't come off them we've tried all sorts 15* *… to get to see my GP it's an absolute nightmare … you've got 10 minutes and if you've got a health issue you need to talk about you haven't got time to talk about the study so I've not had any conversations about it with the doctor at all … 04* *… getting help really it's very difficult and getting an appointment up here is very difficult! 20*	*… there was no … mmm … impetus to … mmm … or indication or approach to me to talk about coming off the … mmm … Fentanyl …. but the prescribers would just … there had been no question as … or no 'would you like to talk about it could we look at a different … would it be helpful … would it …' absolutely nothing! 29* *…cos the doctor actually … err … didn't seem at all conversant with the idea … 32* *so I went to see her and I was absolutely gob smacked when she just said 'there's nothing we can give ya' and I said 'well' and she said 'just take Paracetamol' and I said 'well can you give us a prescription for Paracetamol' and she said 'well no just go and buy them' didn't want to know and I just thought … well why bother … I just thought why bother coming to see you if that's your attitude you're going to have … 30*
Relatives worried not supportive of process	N/A	*… even my brother noticed he said 'you know it's been really rough for you coming off … 07* *How it worked out was when I was in hospital I took and when I came here … I think I took it two times as well as my daughter said 'mummy you are in too much pain' 38*
Missing trial support	N/A	*I know that I couldn't have done it without going into a group to begin with to have that information if someone had just sat me down and said 'you're doing to reduce this by this and this' I would be screaming I think … no, no I can't you know yeah.21* *…when I was doing the IWOTCH course cos you've got the support … err … it think it's like quitting smoking or anything else as in if you've got that little group round ya it's helpful but sadly once you come away from it that support networks gone isn't it so I think you lose … I can only speak for myself … I think you lose incentive to a degree … 22*
After stopping opioids		
Subthemes	**Control – exemplar quotes**	**Intervention – exemplar quotes**
New or returned pain	*'… so eventually I went back on to them because the pain was just getting too great and winter was coming … 35*	*… I came completely off the opioids while I was doing the course … completely off them … erm … stopped them all … err … sadly I fell over in December … it caused me a load of problems I slipped a disc and whatever and hurt me left hip … err … so I went back on them to deal with the initial pain and if I'm completely honest with myself the pain's now bearable again but I've gone to that what I call my traditional crutch that I rely on … 22*

TABLE 29 Barriers to the process of tapering (*continued*)

After stopping opioids		
Subthemes	**Control – exemplar quotes**	**Intervention – exemplar quotes**
HCPs advocating opioids for postoperative pain	*I know at the hospital they want to give me Morphine and everything and even the Paramedics were and I said 'no I'm coming down off it I don't wanna go back up on it' and the doctor was saying 'oh it'll just be for a couple of days' and I'm thinking you don't realise how hard it is to come down and I didn't want any interference of like going back up again to have to wean myself off again so I refused all pain relief in the hospital … 12*	*So since the study I … I went for months you know sort of just saying … 'No!' until I had … mmm … an accident in March where it affect my arm now I'm in a plate now from here to here and then I think for about a week I was taking Tramadol … 38*
GP re-prescribing for pain when there are no alternatives	N/A	*'right you know we think you're ready to come off the painkillers if you want to come off the painkillers … I mean my doctor's still quite willing to put me back on Tramadol if I want it! 09*

N/A, not applicable.

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Control participant interviews (*n* = 20)

Control participants were given the My Opioid Manager self-learning manual and a relaxation CD with instructions for use.

'My Opioid Manager' manual

Fourteen reported My Opioid Manager was either interesting or informative. Some spoke about it '*making you think*' which had the potential to trigger wanting to decrease their opioids.

> *… to make you think about what you're taking and why you're taking it …*
>
> *08*

> *It just makes you think about you are taking a drug that's addictive.*
>
> *12*

Most valued the information, found it easy to read and could relate to it either to give expanded or new knowledge about opioid medication.

> *… not a guide book but as an information giver … I thought that summarised something that's really very complicated in an understandable format …*
>
> *23*

> *I found this actually quite useful and I'm gonna keep this … to keep looking over …*
>
> *11*

Some found some of the information about possible side effects or risks interesting and sometimes quite shocking

> *… I was never told about the constipation problems that it would cause and obviously you read about the side-effects in the little leaflets and then it's put away!*
>
> *20*

> *[S]leep apnoea … that was a bit scary.*
>
> *23*

Relaxation CD

Most (10) listened to the CD once or twice and did not find it useful. Another four who used it more than once or twice said that ultimately it was not useful for them. However, five participants used it to good effect over the trial period, some on a regular basis and others 'as and when' they felt they needed it.

Intervention participant interviews (*n* = 20)

We present the findings of the intervention interviews under the following themes:

- Being in a group (seven subthemes).
- Nurse one-to-one consultations.
- Group sessions of interest.
- Acceptability the intervention.

Being in a group (seven subthemes)

Some people talked about the groups in a general way.

> *Because you see other people's problems and you think … 'Well blimey I'm not on me own!' … and then you've got like a camaraderie you'd sort of help each other … 'Oh you've done really well this week you know … that's really good you've cut down' and then you get somebody who'd say 'oh well I've only done so much' and we'd say 'but well it doesn't matter you've done a little bit' so yeah it was … it was quite good and then you'd get somebody who'd perhaps be a bit despondent and say 'oh I don't think I'll ever be able to do it' and we'd try to spur them on and it just got quite … quite a close knit group really.* 31

Data about being in a group had seven subthemes: (1) shared experience, (2) social comparisons, (3) support, (4) being committed to something, (5) group numbers, (6) perceptions about group facilitators and (7) challenges to establishing group cohesion. Exemplar quotes are given in *Figure 7*.

1. Shared experience

Participants spoke of being with people who understood and valued listening to each other's stories surrounding their types of opioids, dosages, pain, the effect pain and opioids had on their lives, their doctor's involvement and how they coped.

On the whole, they appreciated having a lay facilitator who had experience of what they were going through.

2. Social comparisons

Some people reported that groups had a competitive feel, for example, my pain is worse than yours.

Some positioned themselves in relation to other group members as being 'like me' or not like me' which affected the personal relevance, for example type of opioids, causes of pain, pain experience or the effect on their lives.

3. Support

When talking about groups, participants often referred to support they received from the group.

4. Being committed to something

Some felt that commitment to the study group could be a motivation to taper.

5. Group Numbers

Group numbers varied between 2 and around 10. Small groups of three and below meant they heard fewer people's stories, but larger groups were sometimes problematic.

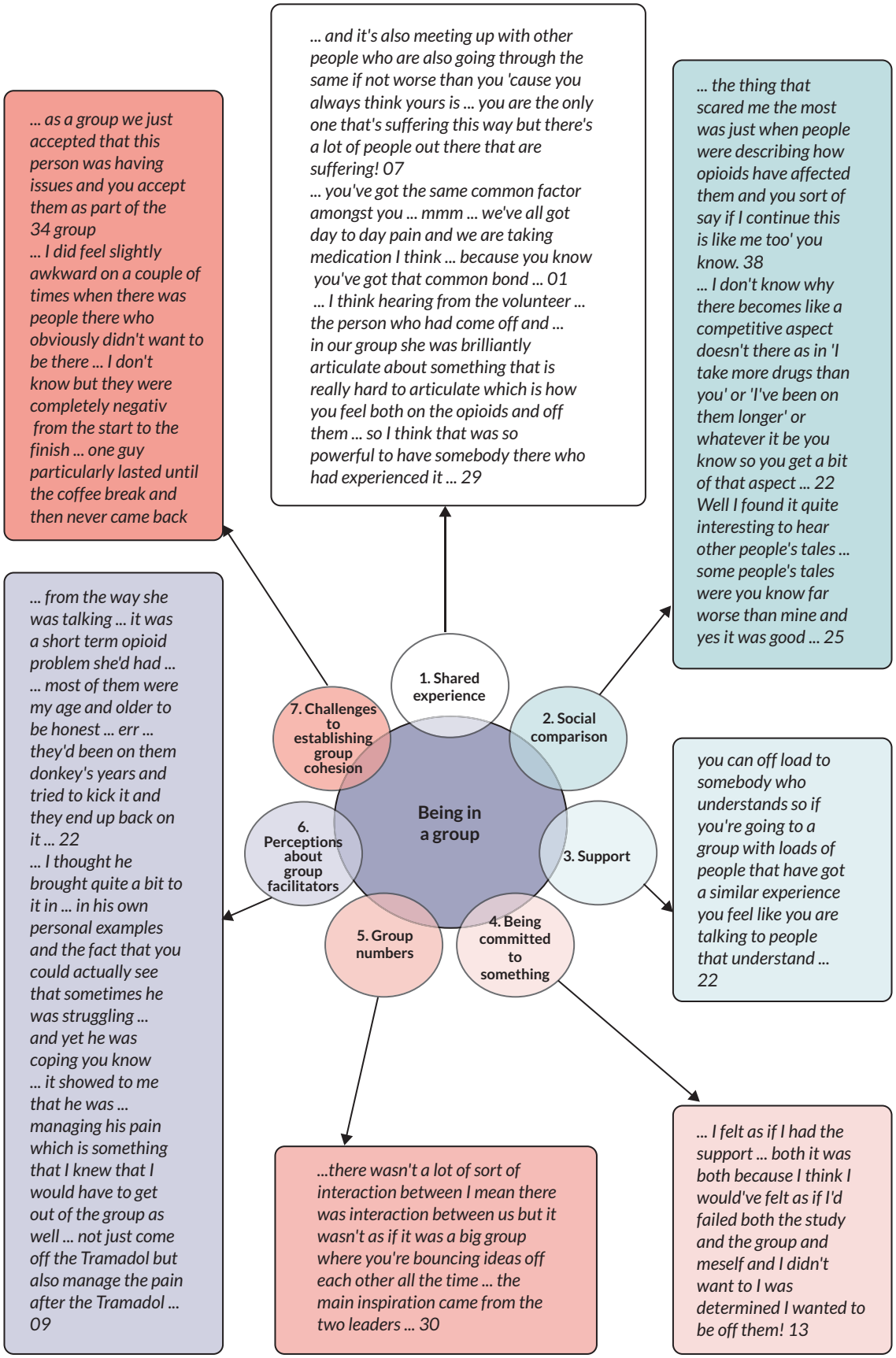

FIGURE 7 Group subthemes with exemplar quotes from intervention participants. Reproduced with permission from Nichols *et al.*[5] This is an Open Access article distributed in accordance with the terms of the Creative Commons Attribution (CC BY 4.0) licence, which permits others to distribute, remix, adapt and build upon this work, for commercial use, provided the original work is properly cited. See: https://creativecommons.org/licenses/by/4.0/. The figure includes minor additions and formatting changes to the original text.

6. Perceptions about group facilitators

Nine people in the intervention group felt the groups were well run. There were many examples of facilitators giving good information and the facilitators contributing to a positive group climate. There was evidence of good facilitation techniques which promoted individual disclosure and sharing within the group. Occasionally facilitation slipped into a more didactic teaching style. Nurses were more likely to be perceived as motivational if a good relationship was established but this was not always the case. Lay facilitators were generally extremely well received.

However, there were a few examples where the delivery was not helpful or that a resistant group felt that the lay person did not share their experience, for example, they had not been on opioids for as long as group members and so were not perceived to be facing the same problems.

7. Challenges to establishing group cohesion

There were some challenging issues within specific groups: for example, the information presented was questioned and the nurse was not able to provide satisfactory supplementary information. A couple of participants from different groups spoke about a disruptive member of the group affecting the group dynamics. In one case, the group tried to include them; in the other, the group tolerated them as 'other than the group'.

Both participants and staff mentioned they would like to know what had happened to everyone in the group. This was not possible in this study.

The next section explores what participants felt about being in a group.

Nurse one-to-one consultations: patient perspectives

Fourteen participants commented on these sessions. Three could not remember or did not comment directly. Thirteen described a good relationship with the nurse and that these sessions gave them a chance to explore the personal application of what they had learnt at the groups.

The interactions were mostly seen as supportive and encouraging.

> *… she was hopeful she said I had the determination to succeed in coming off the Tramadol … erm … so I felt positive with that … that I had like sort of the support with the words that I could actually do it … I just felt encouraged like that I could do it meself so I liked the support I suppose and the fact that they believed in me … yeah!*
>
> *13*

Group sessions of interest

Five particular intervention sessions were raised on multiple occasions.

1. Opioid information

The majority felt they had gained new knowledge about opioids and their possible side effects. Some also commented that sometimes they had not previously attributed certain effects to their opioids, so the new information changed their understanding of side effects. Some said that they had not realised the potential strength or dangers of opioids or how they were classified and spoke of being scared or frightened by their potential damage. A session on tapering was also mentioned as helpful by most people.

2. Anger irritability and frustration

Thirteen people commented on this session. They identified with this session which made them realise '*it's not only me!*' A good example of the value of social validation.

> *… when we did the angry and the irritability and the frustration it was quite like a light coming on I thought it was maybe me that had the problems but it was a realisation that it's almost part and parcel of the pain …*
>
> *09*

3. Relaxation

Most participants spoke about relaxation and enjoyed the practical session, although most people did not use the relaxation CD.

4. Mindfulness

Everyone commented on mindfulness (either the sessions or the CD). Some did not use it or were uncertain how it differed from relaxation or were unsure what it was. Most people did not find it helpful.

> *… and I'm still a little bit unsure exactly what it is to be truthful … erm … I know all it seems to me as if it's a bit of a buzz word that's been going around for a couple of years …*
>
> *30*

5. Distraction techniques

Most commented on this theme. They spoke about it being a new concept in terms of not realising they type of things they could try, such as changing activities or trying new activities. Some also realised that some activities they were already doing might be working in this way.

Acceptability of the intervention

When asked for suggestions about whether any changes were needed to the intervention, half felt it was fine as delivered. Suggested changes were more support, more group time, more contact during tapering, less didactic delivery and more local delivery.

One (dissonant voice) felt that study participants should have been reimbursed for travel and meals and concluded that the intervention aims were not clearly presented.

> *I don't think the study … the title or the way it's presented actually nominates what actually is doing because what you're doing is teaching people pain management by distraction…*
>
> *14*

All said they would recommend the I-WOTCH intervention to others but five felt it would not necessarily work for everyone stating that it needs to be the 'right person' who would be open and receptive to the approach.

Intervention delivery staff interviews

(*n* = 10 nurses, *n* = 6 lay facilitators and *n* = 2 other HCP)

We have presented the staff interview under these headings: Intervention delivery staff characteristics, Training, Venues, Facilitators, Suggestions for changing aspects of the group intervention, Group dynamics, One-to-one sessions, Factors affecting readiness to change across group sessions, Categories of change experience.

Intervention delivery staff characteristics

Nurse facilitators: 1 interviewed for pilot (not in this analysis) and 10 in main study

Lay facilitators: 1 interviewed for pilot (not in this analysis) and 6 main study

Healthcare professionals: 2 in main study (only took days 2 and 3, lay took day 1)

Training

All facilitators enjoyed delivering the intervention. They felt the training was adequate and thought the manual was comprehensive.

> *As I said I really enjoyed it I was really … really impressed with how you know the actual … the … the training and support that we had as a facilitator and actually the … mmm … you know the information that was given to participants as well…*
>
> *Nurse (N)05*

> *… actually that [the manual] was very good because it took you through every single section very, very clearly I mean from a personal point of view I would go through it obviously beforehand and you know and a lot of use of highlighter … a very good guide to the sessions … that was very good the facilitator manual … I think you know I would've been lost without it … it'd been much more difficult … very well written.*
>
> *N09*

The main challenge highlighted by almost all facilitators was that often there was a long time period between the training and delivery and, consequently, the updating training sessions were appreciated.

> *… she was more than happy to go through the sessions with us as a refresher which was great but because I actually went back and revisited my work book I think … mmm … it … a lot of stuff was still quite fresh in my mind and because it was … it's quite thorough and really, really detailed … err … it … that really, really helped.*
>
> *Lay (L)03*

This time lapse was also in part due to the difficulties of getting research passports. On the whole, people felt supported by the team with regards to tapering queries or the App not working. There were occasional issues with problems contacting the team, especially with remote sites.

A couple felt less confident about delivering sessions with which they were not familiar, for example, mindfulness or teaching posture to people who were physically disabled.

Some said that would have been helpful for their confidence if they had had the chance to practise delivering some content during the training.

Quality assurance which was usually carried out on day 1 was appreciated by all as a source of support, help with setting up at the venue, having someone to answer tricky questions and a reassurance that they were delivering as required which helped their confidence for subsequent groups.

> *I wanted that there was somebody there on the first day actually because it was quite good to find out how … whether I was actually doing it [correctly] … 'Am I hitting the mark? … Am I getting where I need to be? Is there anything I can improve on?' which was really good.*
>
> *L05*

Although everyone felt the training and support was good, all had put in a great deal of unpaid preparation time to enable them to facilitate the course. The nurses often read around the subjects they were taking, for example opioid medication and sleep.

> *I don't think I could've had more training I just needed more background knowledge that I could only get myself from further reading…*
>
> *N03*

Lay facilitators spent additional preparation time going over the manual to improve their confidence to deliver it effectively.

Venues

Venues varied greatly with groups and 1 : 1 sessions being held in a variety of community settings. Some had problems with being in isolated buildings and were sometimes asked to lock up. Lone worker policies were observed but phone signals and difficulties such as getting hold of the trial team were unforeseen and unsatisfactory in a few cases.

Sometimes equipment was not working, or the DVD did not play, but there were written backup scripts in the manual.

Facilitators

Most facilitators worked well together, but some would have preferred the continuity of the same person to work with which was not possible in a research setting. Differences of opinion centred around differences in delivery style or on disagreements about who should be taking which sessions. Some met prior to the group (again unpaid) so that they did not have to meet for the first time on day 1, but others did not or could not do this.

Facilitators felt that a nurse and lay person worked well together commenting that having a lay person was key and that it was less likely to work as well with two nurses.

> *…I think it's excellent I … do not remove the lay facilitators if you're going forward they have to be there…*
>
> *N02*

Nurses spoke about the days being 'quite full and on' having little down time from chatting to participants. N02

Some lay facilitators spoke about how tiring it could be, especially with the travelling to the venue and facilitating all day. (L02 and L06).

Suggestions for changing aspects of the group intervention

Suggestions were very variable and relatively minor and almost all felt that the package worked well 'as delivered'.

Group dynamics

Different groups behaved differently. The 'easier' groups from a facilitator's point of view those that contributed more easily and were receptive to the information and techniques provided. More challenging groups were those in which individuals (or more than one member) were actively resistant to the concepts or exhibited challenging behaviour such as interrupting or 'rubbishing' the content.

The groups who worked best seemed to 'gel' sometimes as early as day 1, sometimes it was on day 2 that clarification was reached *'Understanding where this was going' L05*, but definitely by day 3 where they had shared experiences and had formed supportive 'bonds' or 'trust' within the group. *'Became a little family' L05*.

One-to-one sessions

The tapering app seemed easy to use, but there were occasional technical glitches, for example no signal or drugs not listed which were overcome by contacting WCTU and writing plans.

Speed of tapering: Nurses and participants often wanted to go slower than the app, for example tramadol coming down in 50 mg doses, feeling unconfident doing it too fast or having withdrawal effects.

> *… a lot of the participants … mmm … didn't feel that they could taper at that speed and my sort of take on that is that it is a marathon not a sprint and you know if you can't taper at that speed then you know we'll go a bit further…*
>
> *N10*

Patient control, confidence and motivation were important. Nurses needed to deal with a lot of 'offloading' from participants but felt that participants needed the opportunity to talk.

> *[I]t gives them an opportunity to talk openly with me and perhaps mention thangs that they haven't been able to mention within the group.*
>
> *N10*

Some nurses noticed a change between the participants in the first and second face to face.

> *...people used phrases like they'd felt they'd 'come from behind a curtain'. And they didn't seem quite so dazed...*
>
> *N06*

Factors affecting readiness to change across the group sessions: facilitator perspective.
After day 1, some participants did not return; the facilitators felt this may have been due to prior expectations, practical difficulties or not being open to the idea of tapering.

> *It wasn't what they thought it would be.*
>
> *N03*

> *Some people seemed to have no intention of looking at other ways to deal with their pain 'Not ready'*
>
> *L04*

> *'Shutters down' straight away.*
>
> *L05*

On day 1, facilitators felt that a lot of participants were sceptical. (L04, L07) Some had a fear of coming off opioids and there tended to be a lot of negativity, and some were argumentative or rude.

> *Start off pessimistic*
>
> *L03*

This resistance to change sometimes changed around day 2 or 3

> *Became friends ... Reassurance that they're not alone ... Building Trust*
>
> *L07*

> *Wow that had blown their minds about that morning session [opioid information Day 2]!*
>
> *L04*

> *... I think by sort of early afternoon is when people started you know listening a bit more thinking, 'Oh ok maybe there is an alternative'.*
>
> *L07*

By day 3, facilitators described the general feeling that confidence was high.

Although one or two groups did not progress or gel well, especially if there were disruptive individuals or the group was not very interactive, by day 3 the majority of groups were working well together. Comments included:

> *Sometimes it took until Day 3 to realise they were stuck in a boom bust cycle.*
>
> *L05*

> *You were a nice cohesive force,*
>
> *L02*

People were really into it – plenty of interaction

L04

Now dealing with positive people looking and moving forward.

L04

Categories of change

Three categories of change experience are explained in *Figure 8*.

Turning points

Staff spoke about two turning points which came around the opioid information and side effects (*Table 30*).

Implementation of the I-WOTCH intervention: dose delivered, received and fidelity of delivery

Figure 9 discussses the implementation of the I-WOTCH group intervention in relation to dose delivered, received and fidelity of delivery.

Groups run (dose delivered)

Thirty-five groups were run which included two pilot groups. Fifteen were from areas in the NE and 20 from the Midlands. (See main trial information for specific areas.) Two groups were scheduled but did not gain enough numbers to run them. Participants were offered the next most local group.

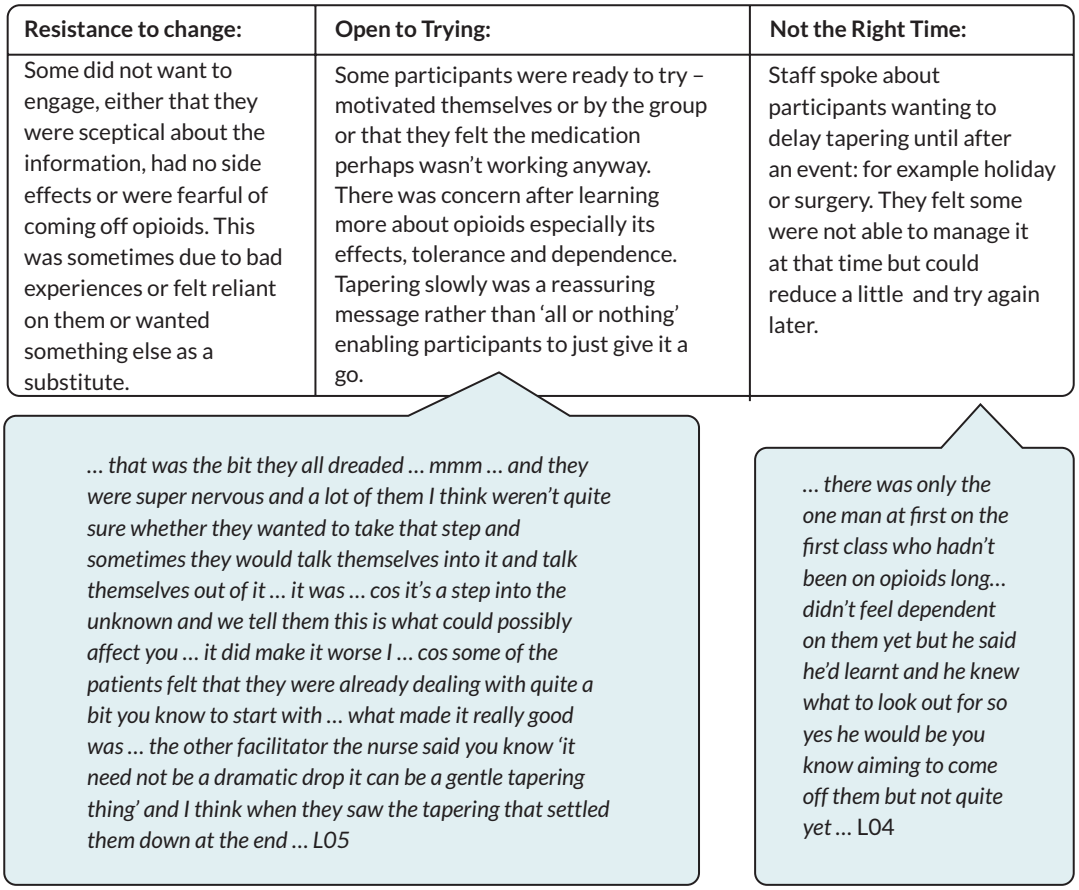

FIGURE 8 Three categories of change experience.

TABLE 30 Turning points identified by staff

(1)On the morning of day 1	(2) On the morning of day 2
Some were shocked and unaware of the issues and surprised to learn opioids are not helpful long term. *Bit of an eye opener N09* *I think they were surprised to learn that opioids aren't helpful long term … they were all … they would've been I think of the view that … err … I need to take this because if I don't take it I'll be in even more pain rather than this doesn't seem to be working cos I'm still in pain after 20 years! N11* *[Angry with Doctors] and I think they were quite cross that they were getting it and being giving it and the length of time they'd been given … mmm that didn't go down too well in any of the groups! L05*	When they started to think how they may start tapering and asked more questions. This was after the second session about opioids which covered withdrawal and John's tapering story which worked well. *… my opinion was that they really needed their hands holding if they were going to make the jump … H2* *… and then on day two pretty much you can tell who is more open to it and more … and it would be … it … you know most of the time it was the majority of the group you'd have the one or two that were still sceptical during day two still kind of like asking us questions … L03*

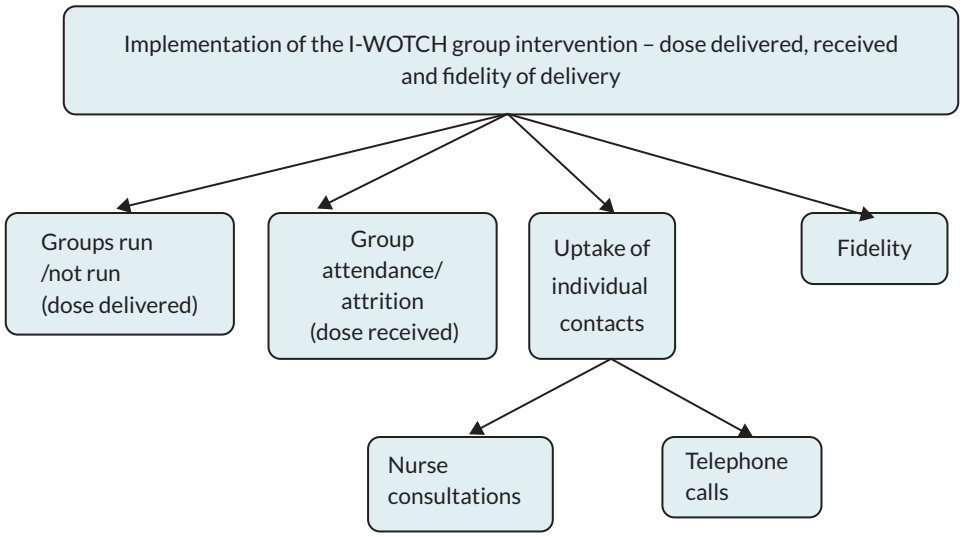

FIGURE 9 Dose delivered, received and fidelity of delivery. Reproduced with permission from Nichols *et al.*[5] This is an Open Access article distributed in accordance with the terms of the Creative Commons Attribution (CC BY 4.0) licence, which permits others to distribute, remix, adapt and build upon this work, for commercial use, provided the original work is properly cited. See: https://creativecommons.org/licenses/by/4.0/. The figure includes minor additions and formatting changes to the original text.

Groups delivered (dose received)

a. Uptake and attendance (dose received)

We ran 35 groups; 17.37 was the mean group size at randomisation, a mean of 8.7 allocated to each intervention group. The actual attendance mean group size was 6.24. Out of the 305 randomised to the intervention, 90 (30%) did not attend any sessions. One hundred and sixty-six (54%) attended all three group sessions. Thirteen participants attended day 1 only which resonates with some of the interview comments about participants sometimes leaving the group at this point. One hundred and ninety (62%) attended the first one-to-one consultation and 131 (43%) both the first and second. One hundred and sixty-seven (55%) had at least one telephone call.

b. Participant reasons for non-attendance throughout the study

The three main reasons given for not attending an intervention session were poor health, competing family interests and work commitments

Fidelity of intervention delivery

Full tables of adherence and competence scores are given in *Appendix 5*, *Tables 79* and *80*.

Each of the 33 (11 sessions from early, mid and late phases) group sessions checked were given percentage score and all were totalled; adherence = 83%, range 25–100 with a median of 88. Competence = 79%, range 0–100% with a median of 86%. Other sessions not rated all occurred except for a distraction session of day 2 (early phase) and overall summary of day 1 (mid phase) which were missing. This may have been that they were not recorded or did not occur.

We also listened and judged fidelity of 27 one-to-one consultations (around 14% of the total). The fidelity score total averages were 91% for adherence with a range of 61–100 and 93% for competence, with a range of 50–100%. A 10% check by a second researcher showed good agreement as *Tables 31* and *32* show.

Feedback forms

Thirty-one responses were received in total from the last 10 groups. (We have treated these data with caution as only a subset of group participants were approached.) We have presented the data for each question which suggests responders had high satisfaction across many different aspects of the course (*Table 33*).

Change mechanism questions

Change mechanism question results are given in the main results in *Table 5*. The credibility question – I feel that involvement in this study has helped me to reduce my opioid use: Not at all, by a little, by half, so I only use a little, so I use no opioids results, as the table below indicates, shows that those in the intervention group perceived that involvement in the study was effective in helping them to reduce opioid use by more than those in the control group at 8 and 12 months *Table 34*.

Contextual issues: following a thread using mixed methods

The main contextual issue was participants' state of readiness to taper. This sometimes was because of health issue such as operations, appointments or the time of year. Our two regions did not seem to show obvious differences in the interview data, all had long-term pain, many spoke about polypharmacy, and they often had multiple health problems to contend with which were often the reasons given for not engaging with interviews or withdrawing from the study. No gender issues were apparent. Decisions to taper were highly personal and seemed to be based upon people's readiness to change.

Revisiting our logic model

After our initial analysis, we revisited our logic model (see *Appendix 5*, *Table 72*), specifically our interim targets (*Table 35*).

TABLE 31 Fidelity check – adherence

Group	First rater	Second rater	Agreed
Day 1 session 2	25	25	25
Day 1 session 3	94	94	94
Day 2 session 13	88	90	89
Day 2 session 14	56	66	61

TABLE 32 Fidelity check – competence

Group	First rater	Second rater	Agreed
Day 1 session 2	0	0	0
Day 1 session 3	90	87	88
Day 2 session13	100	100	100
Day 2 session 14	58	43	50

TABLE 33 Participant feedback form findings

Q1: Were the aims of the course made clear?	**Out of 27 responses: 26 Yes 1 No**			
Q2: What were the three most useful things on this course?	Twenty-six responses (but not all filled in all three). Three most useful things (ranked)			
	Theme	First	Second	Third
	Appreciation of the information	8	7	3
	Being in a group – meeting and interacting	8	8	2
	Supported by facilitators	3	3	1
	Lay facilitator input	3	1	0
	Techniques taught in course which were helpful (all different)	3	3	0
	Motivational aspects	1	0	4
	Support of GP	0	0	3
Q3: What three things would you suggest to make this course better for future participants?	Out of 24 responses, 6 suggested to keep it as it is. The overall suggestions from the remainder were disparate. Some wanted more time for discussion (but one wanted shorter sessions due to comfort), more contacts with staff, more meetings, especially at end of entire course. Practical issues specific to venue, for example, closeness, parking, one toilet. Two suggested CDs should also be in MP3/4 format. Specific issues: One felt the App advice was unrealistic, one did not like the meditation, one did not like the My Opioid Manager manual, one had not used CDs.			
	Very confident	**Confident**	**Not very confident**	**Not confident at all**
Q4: How confident do you feel that the course content will help you personally?	14	11	1	4
Q5: How confident do you feel that you will be able to use this in the future?	16	10	0	1
	Very good	**Good**	**Satisfactory**	**Poor**
Q6: Overall were the facilitators?	23	4	1	0
Q7: Overall were the handouts?	15	12	1	0
	Very useful	**Useful**	**Not very useful**	**Not useful at all**
Q8: How did you find the face-to-face meeting with the nurse?	22	5	1	0
Q9: How did you find the telephone calls with the nurse?	18	9	1	0
Q10: Overall, how useful did you find the whole course?	22	5	0	1
Q11: Is there anything else you'd like to say?	Twenty-one responses to an open comments box. Fifteen positives, two negatives (course was a waste of time and that the approach had not worked for them) and three mixed. Indicative quotes: *'I am now completely off tramadol and despite still going through some nasty withdrawal symptoms I am so glad I had the opportunity to attend the course. I didn't realise how bad the drug is and how ineffective it is for long term chronic pain. I am looking forward to getting my life back'.* *'I would recommend this course to anyone who has a chance to attend it. It has helped me to come off one of my painkillers, to be more outgoing, to talk about my problems more and given me more confidence when in a group of people'.*			

TABLE 34 Involvement in study reducing opioid use at 4, 8 and 12 months after the intervention

I feel that involvement in this study has helped me to reduce my opioid use	Control 4/12 follow-up	Intervention 4/12 follow-up	Control 8/12 follow-up	Intervention 8/12 follow-up	Control 12/12 follow-up	Intervention 12/12 follow-up
N	159	192	149	181	160	188
Opioids reduced not at all/ by a little	125 (79%)	54 (28%)	109 (73%)	54 (30%)	112 (70%)	51 (26%)
Opioids reduced by half	10 (6%)	21 (11%)	16 (11%)	20 (11%)	17 (11%)	18 (10%)
Opioids reduced so I only use a little/so I use none	14 (9%)	112 (58%)	21 (14%)	102 (56%)	28 (18%)	116 (62%)
Missing	10 (6%)	5 (3%)	3 (2%)	5 (3%)	3 (2%)	3 (2%)

TABLE 35 Mapping findings against logic model

Interim targets	Findings
Staff training: To facilitate groups, deliver individual tapering consultations and telephone support in an inclusive and non-judgemental manner	Fidelity scores and participant data support that this target was achieved
Individual participant changes: **a Knowledge of:** opioids, withdrawal effects, chronic pain	Learning about opioids was a key motivator to taper. Staff data includes two turning points which were integral to motivation to taper. Participant data support that some participants at the start of the study were not aware of the effects of opioids.
Individual participant changes: **b Fostering change:** self-validation, legitimising pain, normalising expectations	The group environment promoted these aspects as evidenced by the fidelity data, staff and participant interviews.
Individual participant changes: **c Motivation to change by:** improved self-efficacy, effective tapering	Self-efficacy was a significant motivator evidenced in the self-efficacy change mechanism questions, staff interviews, participant interviews.
d Skills: General self-regulation Pain self-regulation Communication skills	Individual skills such as distraction and relaxation were said to be useful by some participants; the principles were taken on board and incorporated into their lives via hobbies and enjoyable activities. Feedback forms suggested some sessions were more useful than others for individuals, but no-one felt sessions should be removed. Mindfulness was the main session that some people did not 'get'. Although all sessions were prompted for at interviews, some couldn't remember much about each session, possibly due to length of time which had passed (interviewed at 12 months post randomisation).

Overarching themes

We now draw together the four overarching themes across all the process evaluation data: the right time to taper, the backdrop of life with chronic pain, needing support and the group effect (*Table 36*).

We identified four overarching themes across the data: the right time, the backdrop of life with chronic pain, needing support and the group effect (*Figure 10*).

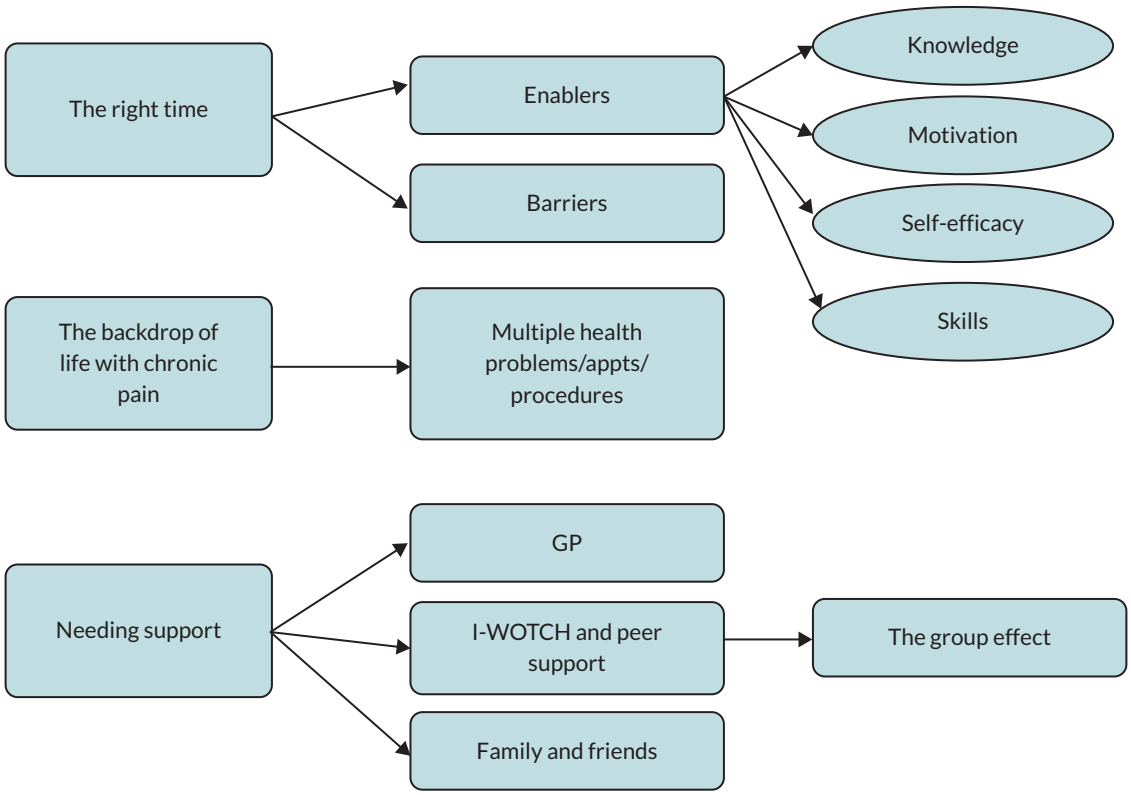

FIGURE 10 Overarching themes.

TABLE 36 Description of overarching themes

1 The right time to taper	
This is a decision only the participant can make, are they ready to start the tapering process? The I-WOTCH intervention appeared to be a strong motivator to attempt tapering alongside other motivators but there were also important barriers. Participants across both arms of the study exhibited three categories of 'readiness to taper'.	
A. Resistant to change/tapering	Even though all participants had enrolled on a research project to help people to taper opioids, some decided that they did not want to taper. Some were satisfied with their opioids and had no intention of coming off them. Some were fearful of stopping due to fear of returning to unmanageable pain or negative past experiences of decreasing the opioids. Intervention staff described a resistance or scepticism from some group members a few of these did not attend further after day 1. Sometimes their healthcare professionals were not supportive of decreasing their opioids which supported their beliefs that they should remain on them.
B. Open to trying to taper and moving forwards	Some trial participants had already decided to try tapering and a few had already started and wanted to continue. Their motivation was boosted by; not wanting to take medications, disliking opioid side effects, feeling the opioids may be ineffective and being encouraged by their GP or family members. Those who attended the I-WOTCH group sessions felt that the information given about opioids and the support given, both by the group and/or its facilitators, had helped them. Most valued the one-to-one nurse consultations, where flexible tapering plans were agreed. Staff spoke about the need for the patient to feel confident and be in control of their tapering plan.
C. Open to trying to taper but not the right time	Some people had taken on board the message but felt it was not the right time to start on a tapering programme. Reasons given were that they wanted to wait until after scheduled operations, or events such as holidays, some also felt the time of year was a factor to consider (winter being more challenging).
Motivators and barriers to tapering	We have identified multiple potential enablers and barriers to tapering
Knowledge, motivation, self-efficacy and skills	Three of the main components which lead to being motivated to taper were gaining knowledge about opioids, being supported and gaining new self-management skills (see *Figure 10*). Some control group participants were also motivated to taper using the 'My Opioid Manager' self-learning manual and relaxation CD with help from their GP.
2 The backdrop of life with chronic pain	
The most important contextual aspect of the data was that people with chronic pain often have a history of multiple health problems and polypharmacy. This makes life busy and challenging with health procedures, appointments and management of their pain to contend with alongside their day-to-day activities. They talk about how their mental, emotional and physical symptoms impact on their lives. Taking on board even the idea of tapering is a further challenge which some are unable or unwilling to consider	
3 Needing support	
This theme underscores the need for support from many different areas. A supportive GP who is knowledgeable about the tapering process can be integral to successful tapering (although some highly motivated individuals may be able to go it alone). GPs who patients feel are not interested or actively discourage tapering give a powerful reason not to try. Participants appreciated that it was their personal decision how and when to taper, some GPs actively encouraged this with good effect. Support from the I-WOTCH intervention staff helped people to explore their opioid use and agree a mutually acceptable plan with which they could talk to their GP about implementing. Lay intervention staff were appreciated by both the participants and the nurse facilitators as they brought their experiences to the table. Peer support from the groups was evident with people helping others to explore more about opioids and potentially to start on their tapering journey.	
4 The Group Effect	
Groups that participants felt went well spoke about group cohesion, vicarious learning from and with other group members and that the group gelled. Interpersonal relationships, trust and sharing gave a sense of a shared identity as the group bonded with some citing a social accountability to the group feeling they had a common purpose, that is to taper their opioids. These positive traits lead to a good group climate providing motivation and improved self-efficacy to taper. Conversely, when groups had issues like disruptive or dominant members, cohesion was more difficult. Facilitators could contribute to help the group to function well by addressing negative factors which would allow the group to 'gel' as early as the beginning of day 2. Once the group were working well (day 2 or 3), they worked well together at the tasks set.	

Chapter 7 Discussion

Twelve months after recruitment, the I-WOTCH intervention helped an additional 22% of participants to stop opioids, and a further 8% to reduce by at least 50%,with no adverse effect on pain-related disability or pain levels. Reductions in the numbers reporting opioid use were evident at each follow-up point. Additionally, at 4 months – where any immediate detrimental effects of opioid withdrawal were likely to be most evident – we found positive effects on both mental health and health utility. Importantly, tapering was achieved in this study largely through healthcare professional and peer group support and not opioid substitution.

The I-WOTCH intervention was specifically designed to address barriers to opioid tapering including health beliefs and fear of withdrawal and enhance confidence and motivation through group and one-to-one support. Monitoring and slow tapering were key components. In line with guidelines, we have found careful monitoring, using a multimodal approach, developing a therapeutic alliance with the patient, enhancing this relationship through effective communication and motivational interviewing, and slow and gradual individualised tapering to reduce adverse effects including withdrawal symptoms.[85]

The framework of I-WOTCH including behavioural activation, behaviour change, self-management of pain, physical and psychological dependence, stigma and cognitive behavioural techniques specifically targeted at opioid use further supports the use of non-pharmacological techniques in opioid reduction.[86,87]

Having support and a shared experience in a group emerged as important to people tapering their strong opioids. I-WOTCH gave people a forum in which to learn about the current thinking about opioid usage and its effects. It also gave them examples of how feasible or personally relevant coming off them might be. For some, this was a step they had considered; others wanted to put 'a toe in the water' before trying. Some people did not want or see the need to taper. Even those who decided not to taper were made aware of the issues and most seemed to want to keep dosages low. If it was not the right time to taper, some said they were aware of the process should they decide to taper at a later date.

From our process evaluation, we found the intervention was delivered as intended. Fidelity assessments show that there was good adherence to delivering the intervention as intended, and that those delivering the intervention were in the main competent. On the whole, participants and staff felt the intervention 'package' worked well as conceived. Key enablers and barriers to opioid tapering were identified and an overarching model devised.

The minimum threshold in the trial for participants having an adequate 'dose' of the intervention was at least one of the 3 day's education sessions and at least one 1 : 1 session with a nurse. So even though staff might be delivering the intervention across the 3 days and the 1 : 1s adhering to the manual and delivering it competently, not all participants attend all sessions, and only 54% attended all three interventions days. Practical issues such as venue parking and comfort and lay input were key factors in both participant and staff data.

In addition, staff interviews indicated that for those people who were initially sceptical or resistant found that there were two information turning points when (1) the advantages of decreasing opioids started to outweigh the disadvantages. This was also strengthened by (2) having a lay facilitator who had 'been there and done it' providing a social comparison as well as support for the group. The turning points may also show a change in the social norm of initially being happy to take opioids versus new information suggesting that this may not be desirable.

Data from the change mechanism questions suggest that some people had high expectations of the study helping them to taper and some were well motivated and confident as seen in the baseline demographic data. The intervention arm also showed an increase in motivation and study credibility as opposed to the control participants (see *Table 34*).

The Information–Motivation–Behavioural Skills model[82] is a useful lens through which to view the process evaluation findings. Participants gained information and knowledge about the behaviour (tapering of opioids), the study and the

group provided the motivation for this behavioural change for some patients and provided detailed information on how to taper so participants had the necessary behavioural skills to perform this tapering behaviour.

To the best of our knowledge, this is the first economic evaluation study of a self-management intervention (i.e. I-WOTCH) to motivate and support opioid tapering in individuals with chronic non-malignant pain. The CCA shows that in the base-case results (ITT population) the I-WOTCH programme is more expensive strategy for supporting strong opioid tapering in individuals with chronic non-malignant pain compared to best usual care. However, using the CEM to extrapolate costs and benefits associated with I-WOTCH and best usual care showed that I-WOTCH is more effective (+ 0.314 QALYs) and costlier (+£9277) than best usual care using the inputs described in *Chapter 5*. This results in a deterministic ICER of £29,543 (and a probabilistic ICER of £34.614 with a 49.6% probability of being cost-effective at a WTP threshold of £30,000 per QALY). The lack of convergence between the deterministic ICER and probabilistic ICER suggests large uncertainty in the model parameters. The value of conducting further primary research to reduce the current level of uncertainty associated with the decision to consider I-WOTCH cost-effectiveness was £61,455 per person. This suggests that it would be worthwhile investing in a confirmatory study.

Extensive sensitivity analysis demonstrated the robustness of our findings and the significant decision uncertainty associated with our results. Value of information analysis, however, indicated that it would be worthwhile to conduct further long-term research to improve estimation of the long-term effectiveness and cost-effectiveness of the I-WOTCH intervention.

The scale of the opioid crisis in the UK is not as severe as in the USA or Canada. However, this is an ongoing issue in the UK with recent studies reporting opiates as a frequent cause of death due to drug poisoning.[88,89] Observed patterns of opioid use reported in the I-WOTCH trial indicate that over time individuals who receive the I-WOTCH intervention are more likely to self-regulate their consumption of opioids. Extrapolating this effect beyond the 12-month horizon of the trial (assuming that the ability to self-regulate will reduce over time in line with the waning rate observed in the I-WOTCH trial over its 12-month follow-up) indicates that individuals who are able to self-regulate their use of strong opioids also achieve a reduction in their exposure to the excess mortality rate associated with long-term consumption of strong opioids. The results from the deterministic base-case analysis of the long-term cost-effectiveness model indicate that, adopting a lifetime horizon, the I-WOTCH intervention is cost-effective compared to best usual care at a £30,000 per QALY threshold. The uncertainty associated with the probabilistic results, however, suggests that additional primary research may be worthwhile to confirm these findings.

Further evidence emerged regarding opioid tapering interventions during the conduct of our study including two systematic reviews. The first examining the role of pain management programs (PMP) conducted outside the primary care setting on opioid cessation. Two RCTs (n = 238) reported a 30% complete opioid withdrawal in the intervention group (PMP) versus 12% in the usual-care group [risk ratio 2.15 (95%CI 1.02 to 4.53)].[21] The second systematic review of primary care-based opioid reduction interventions in chronic non-malignant pain patients reported on four RCTs using mindfulness and meditation–cognitive–behavioural approaches. None showed a statistically significant between-group difference. However, opioid tapering was not an explicitly stated goal in any of the RCTs.[22]

Limitations

Participants in the I-WOTCH study volunteered to take part in the study and, therefore, at the outset may have been committed to exploring a reduction, if not a complete cessation, of opioid use. Our findings therefore may not be generalisable to people not convinced of the benefits of opioid cessation. Although only 47% of participants had full adherence, the similar effect sizes observed in our complier-average casual effect analysis give reassurance that our conclusions are robust. Our follow-up rate of 72% was disappointing, but is in keeping with other studies of complex intervention for chronic pain, and compares favourably with follow-up in another recent study (63% at 9 months).[90]

Our findings may be limited to populations using lower opioid doses, as 33% of our participants used < 30 MED per day. Our participants were largely drawn from a community setting with very few recruited from secondary care, possibly limiting applicability in a specialist setting where patients may present on higher opioid doses and seek substitution of

their opioids with other drugs or devices. We have not been able to assess the long-term benefits/harms from opioid cessation beyond the 1-year follow-up of this trial.

Another trial (*N* = 250), published after our analyses were complete, reported that 16% of people receiving supportive group therapy and 35% of people offered 'mindfulness orientated recovery enhancement' reduced opioid use by ≥ 50% ($p = 0.009$) at 9 months. Positive effects were also reported on opioid misuse, opioid use, pain severity and pain-related functional interference over 9 months.[90] Taken with our findings, these data indicate that behavioural and support interventions can produce substantial and sustained reductions in opioid use.

There may be an element of recall bias in our interviews which were undertaken at 12 months after the intervention. There is also evidence that people transform their experiences over time.[91] The participant feedback forms were completed post group sessions but only for the last 10 groups. We are thus treating these feedback form findings with great care and present them as tentative suggestions. It is also possible that participant recall might also be affected by being on opioids. Often specific sessions were not recalled in detail, and this is reflected in our overarching themes. It seems likely that the aspects which were most helpful may be remembered.

There are some limitations specific to the economic evaluation. The COVID-19 pandemic hindered access to GP records from all patients participating in the I-WOTCH trial. This meant we were unable to extract data on opioid prescribing to support our overall clinical findings, and other health service activity data. In consultation with the study's TSC/DMC, the I-WOTCH team decided to estimate transition probabilities to the different I-WOTCH model health states based on IPD from the I-WOTCH trial. The I-WOTCH team does not have any evidence indicating that these types of biases are likely to affect one study group more than other. Third, the I-WOTCH study follow-up was 12 months. As a result, significant but plausible clinical assumptions had to be made to extrapolate the observed 12-month data over a lifetime horizon. A longer-term follow-up in future studies will help add evidence to the assumptions of the economic model.

Chapter 8 Equality, diversity and inclusion

Ninety-seven per cent of participants in the I-WOTCH trial were White British, which could limit the generalisability of our findings. Participants in the I-WOTCH study volunteered to take part, gaps in current knowledge and best practice to increase recruitment of diverse populations remain.[92] In the original design, we had planned to recruit across a geographical spread representing varied opioid prescribing and ethnic diverse populations. Unfortunately, due to logistic reasons we were unable to recruit in London, the most ethnically diverse part of the UK. We were however able to recruit in The North East of England and Midlands a geographical spread representing varied opioid prescribing. We recruited from 120 sites in the West Midlands and 71 sites in South Tees.

Research team and wider involvement

The Chief Investigator (HS) and Co-chief Investigator (SE) are from ethnic minority groups. The I-WOTCH coinvestigators and wider study team also included members from minority ethnic backgrounds. Sixty per cent of co-applicants (9/15) and 60% (6/10) named authors of this report were female. We put together a diverse team with experience/expertise in pain medicine, primary care, statistics, psychology, health economics, process evaluation and clinical trial management.

Junior members of the team were supported through appropriate line management and mentorship, with opportunities to progress to senior roles. We recognise the importance of collaboration and interdisciplinary working, providing both formal and informal openings to raise awareness of the diversity of teams, research activities and opportunities and for knowledge exchange. Ensuring that such initiatives are clearly communicated is central to the research culture activities at the University. During the study, there were several successful professorial promotions, part of which was supported by the I-WOTCH study.

There was substantial PPI involvement throughout the I-WOTCH study which benefited the design, delivery and dissemination of results. Two lay advisors were recruited via the Universities/User Teaching and Research Action Partnership, and gave considerable input. In addition, PPI meetings were held. The James Cook University Hospital (South Tees Hospitals NHS Foundation Trust) allowed opportunity for volunteer participants (people with chronic pain and experience of opioid therapy and/or opioid tapering) and opportunity to input to intervention development/content and structure. This was particularly beneficial in understanding the potential barriers and facilitators to opioid tapering and what could help people engage with the intervention.

Chapter 9 Implications for decision-makers

To our knowledge, with 608 participants this is the largest trial of supported opioid tapering using a multicomponent intervention aimed for patients. Quality assurance of intervention delivery and participant interviews have given us an understanding of what mechanisms the I-WOTCH programme are engaging for the behaviour change and the opioid reduction while implementing self-management of pain strategies. We have developed a robust training programme and a manualised tapering programme which is deliverable in the community by trained I-WOTCH nurses and lay people. The involvement of patient partners and piloting was crucial in the development of the I-WOTCH programme. The control intervention, although labelled usual care, was chosen to represent the best available medical care internationally at the time.

We provide four recommendations to inform future implementation.

1. The intervention of three group days and two face-to-face contacts with telephone calls was acceptable to participants. Minor changes are needed to the training and delivery to enhance facilitators' confidence and facilitation skills.
2. Triaging people to assess their expectations, motivations, confidence, their 'readiness to taper' and their preference for tapering with the aid of a My Opioid Manager plus the aid of their GP or in a group is likely to decrease attrition rates, ensuring that those ready to change attended the groups. There is some limited evidence that some of those ready and confident in the control group did taper with the tapering plan and My Opioid Manager. Those who feel they would like to try the group need an open mind. Prior discussions would help patients make the decision whether or not to engage at that time.
3. GPs need to be conversant with the aims and delivery of the group intervention, so they can support patients to undertake tapering.
4. Group processes were found to be important in this study, providing support and motivation.

Chapter 10 Research recommendations

Future research includes testing the I-WOTCH intervention in other healthcare settings (secondary care) and with different populations. In addition to testing the incorporation of innovation and digital technologies to further advance the applicability of I-WOTCH, we propose the following research areas based on the I-WOTCH clinical trial:

1. Can the I-WOTCH intervention be replicated in different populations and settings?
2. Can the I-WOTCH intervention be adapted for use in people who do not speak English?
3. Can the I-WOTCH intervention be adapted for on-line delivery?
4. How does the I-WOTCH intervention compare with alternative opioid tapering interventions in head-to-head comparisons?

Chapter 11 Conclusions

At 12 months, the group-based I-WOTCH intervention helped an additional 22% of participants to stop opioids, and a further 8% to reduce by at least 50%, with no adverse effect on pain-related disability or pain levels. The I-WOTCH intervention to manage NMCP is likely to generate similar health benefits and have a similar cost to management with strong opioids. In other words, I-WOTCH might represent good value for the NHS. The process evaluation highlighted the importance of having support and sharing experiences for those trying to taper. The intervention has high acceptability and started many on a tapering journey.

Additional information

CRediT contribution statement

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WCTU Programming Team: Software.

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Patient data statement

This work uses data provided by patients and collected by the NHS as part of their care and support. Using patient data is vital to improve health and care for everyone. There is huge potential to make better use of information from people's patient records, to understand more about disease, develop new treatments, monitor safety and plan NHS services. Patient data should be kept safe and secure, to protect everyone's privacy, and it is important that there are safeguards to make sure that they are stored and used responsibly. Everyone should be able to find out about how patient data are used. #datasaveslives You can find out more about the background to this citation here: https://understandingpatientdata.org.uk/data-citation

Data-sharing statement

All data requests should be submitted to the Warwick Clinical Trials Unit, Data Sharing Committee, contact e-mail: WCTUDataAccess@warwick.ac.uk. Access to anonymised data may be granted following review.

Ethics statement

The research study was conducted in accordance with the World Medical Association Declaration of Helsinki and applicable research governance standards. The study was reviewed, and granted favourable opinion on 13 September 2016, by the Yorkshire and The Humber – South Yorkshire Research Ethics Committee, Reference 16/YH/0325.

Information governance statement

University of Warwick is committed to handling all personal information in line with the UK Data Protection Act (2018) and the General Data Protection Regulation (EU GDPR) 2016/679. Under the Data Protection legislation, University of Warwick is the Data Controller, and you can find out more about how we handle personal data, including how to exercise your individual rights and the contact details for our Data Protection Officer here (https://warwick.ac.uk/services/legalandcomplianceservices/dataprotection/).

Disclosure of interests

Full disclosure of interests: Completed ICMJE forms for all authors, including all related interests, are available in the toolkit on the NIHR Journals Library report publication page at https://doi.org/10.3310/GJHS2715.

Primary conflicts of interest: **Harbinder K Sandhu** reported receiving grants from the National Institute for Health and Care Research (NIHR) and serving as director of Health Psychology Services Ltd, providing psychological services for a range of health-related conditions. **Andrea D Furlan** is author of My Opioid Manager book and app, distributed in iTunes and Google Play for healthcare professionals and owned by University Health Network, the hospital where she works. Both book and app are free of charge. Andrea D Furlan has a monetised YouTube (YouTube, LLC, San Bruno, CA, USA) channel since January 2021 that contains some videos about opioids and opioid tapering. Since April 2021, Andrea D Furlan has an unrestricted educational grant to maintain an online self-assessment opioid course for health care professionals in Canada. The funding is provided by the Canadian Generics Pharmaceutical Association. **Stephanie JC Taylor** reported being chief investigator [13/146/02, RP-PG-0609-10181] or coinvestigator on multiple previous and current research grants from the NIHR and was appointed as an NIHR Senior Investigator (Primary Health Care) in 2023. She also leads the Wellcome doctoral training programme, and is Institute Lead for Barts Charity grant for Academic Centre for Healthy Ageing. **Andrea Manca** has received consultancy fees for participating in Pharmaceutical and Medical Device Industry Advisory Boards in the area of musculoskeletal pain. Andrea Manca is a member of the NICE Technology Appraisal Committee. Prof Iglesias Urrutia is a former member of the NICE Medical Technologies Advisory Committee. **Anisur Rahman** reported receiving support from the National Institute for Health and Care Research

University College London Hospital Biomedical Research Centre (NIHR UCLH BRC). **Kate Seers** reported receiving grants from NIHR during the conduct of the study and being a member of a different NIHR funding board (HS&DR) 2010–8. **Nicole KY Tang** reported receiving grants from NIHR Health Technology Assessment and UK Research and Innovation Medical Research Council and being chief investigator [PB-PG-0213-30121] or coinvestigator of other chronic pain–related projects funded by the NIHR, Medical Research Council, and Warwick-Wellcome Translational Partnership. **Sam Eldabe** reported receiving grants from the NIHR [14/224/04] during the conduct of the study and personal fees from Medtronic, Boston Scientific, Mainstay Medical, and Saluda Medical and grants from Medtronic and NIHR outside the submitted work; and being chair of the NHS England Clinical Reference Group for Specialised Pain. **Martin Underwood** reported being chief investigator [NIHR202614, RP-PG-1212-20018] or coinvestigator on multiple previous and current research grants from the NIHR, Arthritis Research UK, and coinvestigator on grants funded by the Australian National Health and Medical Research Council; being an NIHR senior investigator until March 2021; receiving travel expenses for speaking at conferences from the professional organisations hosting the conferences; serving as director and shareholder of Clinvivo Ltd; being part of an academic partnership with Serco Ltd, funded by the European Social Fund, related to return-to-work initiatives; receiving some salary support from University Hospitals Coventry and Warwickshire; being a coinvestigator on three NIHR-funded studies receiving additional support from Stryker Ltd; receiving honoraria for teaching/lecturing from the Consortium for Advanced Research Training in Africa; and receiving grants from the Research Council of Norway. Until March 2020, he was an editor of the NIHR journal series and a member of the NIHR Journal Editors Group, for which he received a fee. He was a member of the Health Technology Assessment Commissioning Committee 1 September 2010–1 August 2014. **Dawn Carnes** reported receiving grant funding from the Chartered Society for Physiotherapists, National Council for Osteopathic Research, Osteopathic Foundation, General Osteopathic Council and University College of Osteopathy. She is the Chairperson for the Strategy Committee of the Council for Allied Health Professions in Research. No other disclosures were reported.

Disclaimer

Publications

Scientific publications

Nichols VP, Abraham C, Eldabe S, Sandhu HK, Underwood M, Seers K; I-WOTCH team. Process evaluation protocol for the I-WOTCH study: an opioid tapering support programme for people with chronic non-malignant pain. *BMJ Open* 2019;**9**:e028998. https://doi.org/10.1136/bmjopen-2019-028998.

Sandhu HK, Abraham C, Alleyne S, Balasubramanian S, Betteley L, Booth K, *et al.* Testing a support programme for opioid reduction for people with chronic non-malignant pain: the I-WOTCH randomised controlled trial protocol. *BMJ Open* 2019;**9**:e028937. https://doi.org/10.1136/bmjopen-2019-028937.

Manchira Krishnan S, Gc VS, Sandhu HK, Underwood M, Eldabe S, Manca A, Iglesias Urrutia CP; I-WOTCH team, *et al.* Protocol for an economic analysis of the randomised controlled trial of Improving the Well-being of people with Opioid Treated CHronic pain: I-WOTCH Study. *BMJ Open* 2020;**10**:e037243. https://doi.org/10.1136/bmjopen-2020-037243

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Sandhu HK, Booth K, Furlan AD, Shaw J, Carnes D, Taylor SJC, *et al.* Reducing opioid use for chronic pain with a group-based intervention: a randomized clinical trial. *JAMA* 2023;**329**:1745–56. https://doi.org/10.1001/jama.2023.6454.

Peer review editorial

Sandhu H, Underwood M, Furlan AD, Noyes J, Eldabe S. What interventions are effective to taper opioids in patients with chronic pain? Editorial. *BMJ* 2018;**362**:k2990. https://doi.org/10.1136/bmj.k2990.

Peer-reviewed comment and responses

Sandhu HK, Eldabe S, Underwood M. A group-based intervention to reduce opioid use for chronic pain – reply. *JAMA* 2023;**330**:1193–4. https://doi.org/10.1001/jama.2023.13782

Media features

Output type	Title	Forum	Location	Date	Contributor/author
Radio	Discussing I-WOTCH trial and opioids for chronic pain	Touch FM	Coventry and Warwickshire region, UK	26 January 2018	Harbinder Sandhu
Radio	Discussing I-WOTCH trial and opioids for chronic pain	BBC Coventry and Warwickshire	Coventry and Warwickshire region, UK	23 January 2018	Harbinder Sandhu
Radio	Discussing I-WOTCH trial and opioids for chronic pain	BBC West Midlands	West Midlands region, UK	23 January 2018	Harbinder Sandhu
Radio	Discussing I-WOTCH trial and opioids for chronic pain	BBC Radio Four Today	National, UK	1 March 2019	Harbinder Sandhu
Radio	Discussing I-WOTCH trial and opioids for chronic pain	BBC Radio Four Inside Health	National, UK	6 March 2019	Harbinder Sandhu
TV	Discussing I-WOTCH trial and opioids for chronic pain	Central News	West Midlands region, UK	23 January 2018	Harbinder Sandhu/Martin Underwood/Colin Tysall
TV	Discussing I-WOTCH trial and opioids for chronic pain	ITV News	National, UK	26 January 2018	Harbinder Sandhu
TV	Discussing I-WOTCH trial and opioids for chronic pain	BBC Breakfast News	National, UK	16 March 2018	Harbinder Sandhu
BMJ Podcast	Discussing I-WOTCH trial and opioids for chronic pain	BMJ	National and International	11 October 2020	Harbinder Sandhu/Andrea Furlan/Colin Tysall
TV	Discussing I-WOTCH trial and opioids for chronic pain	BBC Midlands Today	West Midlands region, UK	9 September 2020	Harbinder Sandhu
Radio	Discussing I-WOTCH trial and opioids for chronic pain	Capital FM	West Midlands region, UK	6 August 2021	Harbinder Sandhu
Radio	Discussing I-WOTCH trial Results and opioids for chronic pain	BBC Midlands Today	West Midlands region, UK	30 May 2023	Harbinder Sandhu/Colin Tysall
Radio	Discussing I-WOTCH trial Results and opioids for chronic pain	BBC Coventry and Warwickshire	West Midlands region, UK	31 May 2023	Harbinder Sandhu
Radio	Discussing I-WOTCH trial Results and opioids for chronic pain	BBC Radio Newcastle	Northeast region UK	31 May 2025	Harbinder Sandhu

Other media outputs

National Institute for Health and Care Research. Evidence: Group-based Intervention Reduced Opioid Use among People with Long-term Pain, 10 December 2024. https://doi.org/10.3310/nihrevidence_65161; https://evidence.nihr.ac.uk/alert/group-based-intervention-reduced-opioid-use-among-people-with-long-term-pain/

YouTube Video I-WOTCH Trial Results: Unveiling the results of Opioid Tapering, Dr Andrea Furlan, www.youtube.com/watch?v=nNGYpG-ClMVU, YouTube Social Media Platform – International/US and Canada, July 2023

Five minutes with … Dr Harbinder Sandhu, *The Psychologist Magazine*, *British Psychological Society*, 15 November 2018. www.bps.org.uk/psychologist/five-minutes-dr-harbinder-sandhu

Conference presentations

Date	Conference/scientific meeting	Title of presentation	Format of presentation	Authors/contributors *(*presenting author)*
12–14 March 2025	United Kingdom Spine Societies Board (UKSSB), Brit Spine, Manchester, UK	Managing Opioid Use and its reduction	Invited speaker	***Harbinder Sandhu** on behalf of the I-WOTCH study team
4–7 September 2024	41st The European Society of Regional Anaesthesia and Pain Therapy (ESRA) Annual Congress, Prague	Improving the wellbeing of people with opioid treated chronic pain (I-WOTCH): results of a UK randomized clinical trial *Acceptance of Best Paper Award*	Oral (virtual)	***Harbinder Sandhu** on behalf of the I-WOTCH study team
5–9 August 2024	International Association for the Study of Pain (IASP) World Congress on Pain, Amsterdam, the Netherlands	How patients with chronic non-malignant pain experience opioid tapering: a process evaluation.	Poster	***Kate Seers**, Vivien Nicholls, Charles Abraham, Martin Underwood, Sam Eldabe, Harbinder Sandhu on behalf of I-WOTCH study team
20 July 2024	Algesiologikum Summer Symposium on Pain Medicine, Munich, Germany	*Pain therapy with opioids: does it still have a future?* *What interventions are effective to taper opioids in patients with chronic pain?*	Invited speaker	***Sam Eldabe**
28 June 2024	Continuous Professional Development Conference, University of Birmingham and Pain-Train UK, Birmingham, UK	IWOTCH research study; Improving the wellbeing of people with opioid treated chronic pain	Invited speaker	***Martin Underwood**
15–19 June 2024	Health Technology Assessment international (HTAi), Annual Scientific Meeting, Seville, Spain	Addressing Global Health Priorities: Cost-Effectiveness of I-WOTCH vs. Best Usual Care for Opioid Reduction in Non-Malignant Chronic Pain	Oral	***Cynthia Iglesias Urrutia**
7 November 2023	Wessex Academic Health Sciences Network (AHSN) Lead Opioid Prescribing Group, Wessex, UK	I-WOTCH Trial and Results Update – AHSN Lead Opioid Prescribing Group (Wessex)	Oral	***Cathy Price**
18–20 July 2023	51st Annual Scientific Meeting of Society for Academic Primary Care (SAPC)	Improving the wellbeing of people with opioid treated chronic pain (I-WOTCH): results of a UK randomized clinical trial	Oral	**Harbinder Sandhu** on behalf of the I-WOTCH study team

Date	Conference/scientific meeting	Title of presentation	Format of presentation	Authors/contributors *(*presenting author)*
9–11 May 2023	British Pain Society 56th Annual Scientific Meeting, Glasgow, UK	Supported Opioid Tapering – Emerging Evidence from UK Research Improving the wellbeing of people with opioid treated chronic pain, findings from a RCT Can being a lay facilitator support people in opioid tapering? Experience of the I-WOTCH Intervention	Oral workshop	***Harbinder Sandhu** ***Colin Tysall** ***Sarah Harrisson**
9–11 May 2023	British Pain Society 56th Annual Scientific Meeting, Glasgow, UK	The importance of being in a group for people with chronic non-malignant pain when tapering strong opioids: a process evaluation	Poster	***Kate Seers,** Vivien Nicholls, Charles Abraham, Martin Underwood, Sam Eldabe, Harbinder Sandhu on behalf of I-WOTCH study team
27 September 2022	University of Toronto Rehabilitation Institute – Rehab Pain Service Rounds	Psychological interventions for opioid tapering in pain. The I-WOTCH randomized controlled trial	Oral (virtual)	***Harbinder Sandhu**
19–23 September 2022	International Association for the Study of Pain (IASP) World Congress on Pain, Toronto, Canada	Clinical aspects of tapering opioids for chronic non-cancer pain. Presentation of research results from UK, US and Canada	Topical Workshop	***Andrea Furlan, *Harbinder Sandhu** and ***Mark Sullivan**
14–15 November 2019	The 12th Royal Marsden opioids, cannabinoids and gabapentinoids conference, London, UK	Interventions for tapering opioids	Invited speaker (oral presentation)	***Harbinder Sandhu**
11 November 2019	Royal college of Physicians. Avoiding harm from over prescribing. How to reduce waste and dependence on prescription drugs, London, UK	Tackling the opioid epidemic – is there a way forward for patients in chronic pain?	Invited Speaker	***Harbinder Sandhu**
19–23 September 2022	International Association for the Study of Pain (IASP) World Congress on Pain, Toronto, Canada	Process Evaluation of the Improving the Wellbeing of people with Opioid Treated CHronic Pain (I-WOTCH) Study: an Opioid Tapering Support Programme for People with Chronic Non-malignant Pain	Poster	***Vivien Nicholls**, Kate Seers, Martin Charles Abraham, Underwood, Sam Eldabe, Harbinder Sandhu on behalf of I-WOTCH study team
6–9 October 2019	International Clinical Trials Methodology Conference, Brighton, UK	Telephone interviews versus postal questionnaires in Rehabilitation and Clinical care trials	Poster	***Katie Booth**, Dongquan Bi, Ranjit Lall
4–7 September 2019	The 11th Congress of the European Pain Federation EFIC, Valencia, Spain	The role of self-management in the treatment of musculoskeletal disorders: current evidence and practical recommendations A multimodal intervention programme for opioid reduction for people with chronic non-malignant pain (The I-WOTCH study) – design, delivery and lessons learnt.	Workshop	***Harbinder Sandhu** ***Nicola Walsh** ***Nathan Hutting**
3–6 July 2019	International Forum for Back and Neck Pain Research in Primary Care, Quebec, Canada	Opioid management for people with chronic non-malignant pain: interventions, guidelines and lessons learnt – where do we go from here?	Workshop	***Andrea Furlan** ***Harbinder Sandhu** ***Sam Eldabe**
3–6 July 2019	International Forum for Back and Neck Pain Research in Primary Care, Quebec, Canada	Testing a support programme for opioid reduction for people with chronic non-malignant pain: The I-WOTCH study	Poster	***Harbinder Sandhu *et al.*** on behalf of the I-WOTCH study team

Date	Conference/scientific meeting	Title of presentation	Format of presentation	Authors/contributors *(*presenting author)*
3–6 July 2019	International Forum for Back and Neck Pain Research in Primary Care, Quebec, Canada	A complex multimodal support programme for opioid reduction for people with chronic non-malignant pain Theoretical Framework and Application	Poster	***Harbinder Sandhu** *et al.* on behalf of the I-WOTCH study team
1 July 2019	West Midlands Pain study day, Birmingham, UK	A multimodal intervention programme for opioid reduction – design, delivery and lessons learnt so far	Oral	***Harbinder Sandhu**
9–11 June 2019	International conference on opioids, Boston, UK	A multimodal intervention programme for opioid reduction – design, delivery and lessons learnt so far	Oral	***Harbinder Sandhu** on behalf of the I-WOTCH study team
15 May 2019	Primary Care Showcase day, London, UK	Opioids and Gabapentinoids for Chronic Non-Malignant Pain	Oral	***Martin Underwood**
29 November 2018	Rotary Club, Coventry UK	Improving the Wellbeing of People with Opioid Treated Chronic Pain- The I-WOTCH study	Invited Speaker	***Harbinder Sandhu**
12–16 September 2018	International Association of the Study of Pain (IASP) 17th World Congress on Pain	Improving the Wellbeing of people with Opioid Treated CHronic pain – The I-WOTCH Study – recruitment so far and lessons learned	Poster	***Harbinder Sandhu** *et al.* on behalf of the I-WOTCH study team
12–16 September 2018	International Association of the Study of Pain (IASP) 17th World Congress on Pain	A complex multimodal self-management behaviour change intervention for the tapering of opioids: theories, processes and application	Poster	***Harbinder Sandhu** *et al.* on behalf of the I-WOTCH study team
10 August 2018	Australian Psychological Society, College of Health Psychologists, Melbourne, Australia	Using small group interventions to reduce opioid use among people with long term pain	Oral	***Charles Abraham**, Harbinder Sandhu on behalf of the I-WOTCH study team
10–12 July 2018	Society for Academic Primary Care (SAPC) ASM, London, UK	Title: Improving the Wellbeing of people with Opioid Treated CHronic pain – The I-WOTCH Study – recruitment so far and lessons learned	Poster	***Harbinder Sandhu** *et al.* on behalf of the I-WOTCH study team
12–14 July 2017	Society for Academic Primary Care (SAPC) ASM, University of Warwick, Coventry, UK	Improving the Wellbeing of people with Opioid Treated CHronic pain – The I-WOTCH Study	Poster	***Harbinder Sandhu** *et al.* on behalf of the I-WOTCH study team
12–14 July 2017	Society for Academic Primary Care (SAPC) ASM, University of Warwick, Coventry, UK	Developing a complex multimodal self-management behaviour change intervention for Improving the Wellbeing of people with Opioid-Treated CHronic pain: which theories, processes and materials are required?	Poster	***Alison Hipwell,** Harbinder Sandhu, Martin Underwood, Colin Tysall, Sally Brown, Dawn Carnes, Stephanie Taylor, Sam Eldabe on behalf of the I-WOTCH study team
3–5 May 2017	British Pain Society Annual Scientific Meeting, Birmingham, UK	Improving the Wellbeing of people with Opioid Treated CHronic pain – The I-WOTCH Study	Poster	***Harbinder Sandhu**, Alison Hipwell, Martin Underwood, Sally Brown, Colin Tysall, Sam Eldabe on behalf of the I-WOTCH study team
3–5 May 2017	British Pain Society Annual Scientific Meeting, Birmingham, UK	Developing a complex multimodal self-management behaviour change intervention: theories, processes and materials.	Poster	***Alison Hipwell,** Harbinder Sandhu, Martin Underwood, Colin Tysall, Sally Brown, Dawn Carnes, Stephanie Taylor, Sam Eldabe on behalf of the I-WOTCH study team

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Appendix 1 Severe adverse event causality relationship

TABLE 37 Severe adverse event causality relationship

Relationship to trial treatment	Description
Unrelated	There is no evidence of any causal relationship
Unlikely to be related	There is little evidence to suggest there is a causal relationship (e.g. the event did not occur within a reasonable time after administration of the trial medication or device). There is another reasonable explanation for the event (e.g. the participant's clinical condition, other concomitant treatment).
Possible relationship	There is some evidence to suggest a causal relationship (e.g. because the event occurs within a reasonable time after administration of the trial medication or device). However, the influence of other factors may have contributed to the event (e.g. the participant's clinical condition, other concomitant treatments).
Probable relationship	There is evidence to suggest a causal relationship, and the influence of other factors is unlikely.
Definitely related	There is clear evidence to suggest a causal relationship, and other possible contributing factors can be ruled out.

Taken from I-WOTCH Trial Protocol.

Appendix 2 Morphine equivalent dose calculation

Medications taken were reported in four formats at each time point; pain killer **tablets** taken regularly over the last 4 weeks, pain killer **patches** used over the last 4 weeks, pain killer **liquid** medication used over the last 4 weeks, and pain killers taken '**as and when needed**' in an average week.

The calculations for each format are listed below, using the morphine conversion factors and frequency factors given in the tables below. For each participant, the MED calculated for each format was then summed together to give the MED taken at that time point.

Tablets daily MED = (morphine conversion factor) × (strength of medication (mg)) × (how many taken) × (frequency factor)

Patches daily MED = (morphine conversion factor) × (strength of medication (mcg)) × (how many used)

Liquids daily MED = (morphine conversion factor) × (strength of medication(mg/ml)) × (bottle size(ml)/number of days the last bottle of this size lasted)

For 'as and when needed' drugs, use same calculations as above, but for tablets also multiply by (number of days taken/7).

Morphine conversion factor

TABLE 38 Opioid equivalences for final analyses

	UK RCOA FPM	UK BNF	Australia ANZCA	US CDC	US CMS	Canada IMPS/National Pain Center	Mid-point Canada range	Mode	Conversion value agreed	Minimum	Maximum
Tablets											
Buprenorphine sublingual			40		30			35	**35**	30	40
Codeine	0.1	0.1	0.13	0.15	0.15	0.1–0.2	0.15	0.15	**0.15**	0.1	0.2
Dihydrocodeine	0.1	0.1			0.25			0.1	**0.1**	0.1	0.25
Hydromorphone	7.5	5	5	4	4	5		5	**5**	4	7.5
Morphine	1	1	1	1	1	1		1	**1**	1	1
Oxycodone	2	1.5	1.5	1.5	1.5	1.5		1.5	**1.5**	1.5	2
Pethidine			0.12					0.12	**0.12**	0.12	0.12
Tapentalol	0.4		0.3	0.4	0.4	0.3–0.4		0.4	**0.4**	0.3	0.4
Tramadol	0.15	0.1	0.2		0.1	0.1–0.2	0.15	0.1,0.15	**0.125**	0.1	0.2
Liquids											
Morphine	1	1	1		1			1	**1**	1	1
Oxycodone	2	1.5	1.5	1.5	1.5	1.5		0.5	**1.5**	1.5	2
Patches											
Buprenorphine 5	12	12	10		9			12			
Buprenorphine 10	24	24	20		18						
Buprenorphine 20	48	48	40		36						
Buprenorphine mcg/hour	2.4	2.4	2		1.8			2.4	**1 mcg/ hour = 2.4 mg/ day**	1.8	2.4
Fentanyl 12	45	30	37.5	30	30			30			
Fentanyl 25	90	60	75	60	60	60–134	97	60			
Fentanyl 37	135	90	112.5	90	90	135–179	157	90			
Fentanyl 50	180	120	150	120	120	180–224	202	120			
Fentanyl 62	225	150	187.5	150	150	225–269	247	150			
Fentanyl 75	270	180	225	180	180	270–314	292	180			

continued

TABLE 38 Opioid equivalences for final analyses (*continued*)

	UK RCOA FPM	UK BNF	Australia ANZCA	US CDC	US CMS	Canada IMPS/National Pain Center	Mid-point Canada range	Mode	Conversion value agreed	Minimum	Maximum
Fentanyl 87	315	210	262.5	210	210	315–359	337	210			
Fentanyl 100	360	240	300	240	240	360–404	382	240			
Fentanyl 300	1120	720	900	720	720			720			
Fentanyl mcg/hour	3.6	2.4	3	2.4	2.4	3.43	3.43	2.4	**1 mcg/hour = 2.4 mg/day**	2.4	3.6

Notes
1 mcg/hour buprenorphine or fentanyl equivalent to 2.4 mg morphine= 2.4 mg/day.
Range of midpoints of Canadian conversion for buprenorphine according to dose 2.82–4.04. Midpoint of midpoints = 3.43.

Source

Frequency factor

TABLE 39 Medication frequency factor

Medication frequency	Frequency factor
Once a day	1
Twice a day	2
Three times a day	3
Four times a day	4
Five times a day	5
Six times a day	6
Seven times a day	7
Eight times a day	8
Nine times a day	9
Ten times a day	10
Once every 2 days	0.5
Once every 3 days	0.33
Once every 4 days	0.25
Once every 5 days	0.2
Once every 6 days	0.17
Once a week	0.14
Twice a week	0.29
Thrice a week	0.43
Four times a day	0.57
Not stated	0

Appendix 3 Statistics supplementary materials 1

TABLE 40 Screening of potential participants summarised by practice/clinic/office name

Region	Practice number	Practice population	Number identified by search	Total number excluded	Total number mail-out	Total number replied	Total number interested	Total number not interested	Total number eligible	Total number ineligible	Total number randomised
South Tees											
South Tees	1	8000	231	95	136	10	9	1	7	0	3
South Tees	2	6000			147	5	5	0	2	0	1
South Tees	3	23,000	256	64	192	30	29	1	21	3	9
South Tees	4	10,000			137	11	10	1	3	1	2
South Tees	5	9000	230	8	222	19	14	5	5	1	3
South Tees	6	14,000	404	200	204	17	14	3	8	1	1
South Tees	7	10,000			103	12	12	0	6	1	1
South Tees	8	9000	264	101	163	16	15	1	7	3	5
South Tees	9	10,000	401	346	55	8	6	2	2	0	1
South Tees	10	5000	109	1	108	11	8	3	2	2	1
South Tees	11	6000			151	17	13	4	6	5	2
South Tees	12	16,000	294	35	259	29	23	6	13	4	8
South Tees	13	3000			61	3	3	0	1	1	0
South Tees	14	7000			122	15	14	1	6	3	4
South Tees	15	3000			71	6	6	0	5	1	1
South Tees	16	15,000			175	14	12	2	5	4	4
South Tees	17	9000	71	17	54	0	0	0	0	0	0
South Tees	18	3000			61	10	5	5	2	2	2
South Tees	19	9000			153	13	13	0	7	2	3
South Tees	20	13,000			356	30	28	2	10	3	5
South Tees	21	6000			157	17	16	1	4	0	1
South Tees	22	9000	226	41	185	28	28	0	7	5	2
South Tees	23	19,000			99	8	8	0	5	2	2
South Tees	24	15,000			261	20	20	0	11	1	8

continued

TABLE 40 Screening of potential participants summarised by practice/clinic/office name (*continued*)

Region	Practice number	Practice population	Number identified by search	Total number excluded	Total number mail-out	Total number replied	Total number interested	Total number not interested	Total number eligible	Total number ineligible	Total number randomised
South Tees	25	14,000	159	18	141	30	27	3	12	7	7
South Tees	26	3000	159	14	145	17	16	1	8	4	6
South Tees	27	12,000	287	97	190	15	13	2	0	0	0
South Tees	28	4000	82	8	74	7	7	0	1	2	1
South Tees	29	25,000	82	25	57	5	5	0	4	1	3
South Tees	30	20,000	526	102	424	39	32	7	16	13	9
South Tees	31	6000	141	20	121	14	13	1	6	6	3
South Tees	32	5000	174	5	167	30	26	4	12	9	9
South Tees	33	4000	51	4	47	8	6	2	4	0	1
South Tees	34	6000	138	4	134	19	18	1	9	4	6
South Tees	35	10,000	159	64	95	13	11	2	6	1	5
South Tees	36	8000			217	17	17	0	0	0	0
South Tees	37	9000	191	20	171	23	20	3	12	6	8
South Tees	38	11,000	305	9	295	15	14	1	0	0	0
South Tees	39	9000	331	70	261	23	21	2	9	6	6
South Tees	40	7000	347	326	21	1	1	0	0	0	0
South Tees	41	12,000	364	118	246	13	12	1	8	4	1
South Tees	42	2000	38	2	36	3	3	0	3	0	1
South Tees	43	6000	182	23	159	11	11	0	4	4	3
South Tees	44	18,000	259	35	224	38	38	0	19	9	11
South Tees	45	4000	224	175	49	6	6	0	3	2	1
South Tees	46	2000	17	2	15	9	6	3	2	1	1
South Tees	47	2000	37	3	34	5	5	0	4	0	2
South Tees	48	7000	96	32	64	7	7	0	1	0	1
South Tees	49	9000			121	13	13	0	7	2	1
South Tees	50	3000	38	1	37	3	3	0	1	1	1

TABLE 40 Screening of potential participants summarised by practice/clinic/office name (*continued*)

Region	Practice number	Practice population	Number identified by search	Total number excluded	Total number mail-out	Total number replied	Total number interested	Total number not interested	Total number eligible	Total number ineligible	Total number randomised
South Tees	51	6000	65	16	49	5	4	1	0	0	0
South Tees	52	10,000	246	55	191	10	9	1	3	3	2
South Tees	53	18,000	0	0	0	1	1	0	0	0	0
South Tees	54	11,000			165	19	18	1	10	5	7
South Tees	55	5000	65	17	48	16	13	3	7	4	2
South Tees	56	5000	101	16	85	9	9	0	4	1	2
South Tees	57	11,000	254	48	206	23	23	0	12	1	7
South Tees	58	15,000	67	34	261	23	22	1	12	5	7
South Tees	59	5000	93	15	78	6	4	2	2	1	0
South Tees	60	6000	131	29	92	16	15	1	10	5	5
South Tees	61	6000	113	8	105	14	12	2	5	3	2
South Tees	62	14,000	193	166	174	15	14	1	4	8	2
South Tees	63	8000			160	12	11	1	5	3	3
South Tees	64	10,000	300	37	263	28	21	7	10	7	5
South Tees	65	9000			30	4	4	0	1	0	0
South Tees	66	19,000	473	199	274	14	12	2	6	4	2
South Tees	67	7000	150	72	78	12	10	2	7	3	4
South Tees	68	8000			165	15	13	2	2	3	0
South Tees	69	8000	130	80	50	8	7	1	7	0	5
South Tees	70	6000	170	28	142	15	12	3	11	1	8
South Tees	71	11,000	214	69	145	27	24	3	18	3	9
West Midlands											
West Midlands	Self referral					9	9	0	7	2	2
West Midlands	72	5000	91	30	61	4	4	0	1	1	0
West Midlands	73	3000	19	0	19	1	1	0	0	1	0

continued

TABLE 40 Screening of potential participants summarised by practice/clinic/office name (*continued*)

Region	Practice number	Practice population	Number identified by search	Total number excluded	Total number mail-out	Total number replied	Total number interested	Total number not interested	Total number eligible	Total number ineligible	Total number randomised
West Midlands	74	10,000	66	0	66	6	6	0	3	2	2
West Midlands	75	18,000	172	45	127	17	17	0	12	3	6
West Midlands	76	12,000	92	16	76	6	6	0	5	1	2
West Midlands	77	14,000	140	31	109	14	14	0	6	4	3
West Midlands	78	13,000	113	0	113	17	17	0	9	4	6
West Midlands	79	49,000			400	41	40	1	23	8	8
West Midlands	80	9000	102	40	62	3	3	0	2	1	1
West Midlands	81	5000	59	47	12	0	0	0	0	0	0
West Midlands	82	10,000	113	37	76	8	8	0	5	1	4
West Midlands	83	3000	34	10	24	3	3	0	1	0	1
West Midlands	84	13,000	248	42	206	29	26	3	16	5	11
West Midlands	85	7000	86	23	63	10	9	1	5	2	4
West Midlands	86 (Hospital)					3	3	0	2	1	1
West Midlands	87	5000	0	0	91	6	6	0	3	3	2
West Midlands	88	5000	83	17	66	12	11	1	6	5	2
West Midlands	89	16,000	230	43	187	20	20	0	12	6	11
West Midlands	90	11,000	132	12	120	15	15	0	13	2	9
West Midlands	91	4000	57	0	57	6	6	0	3	1	2
West Midlands	92	3000	46	3	43	2	2	0	1	1	0
West Midlands	93	7000	184	8	176	7	7	0	0	0	0
West Midlands	94	7000			105	4	4	0	0	0	0
West Midlands	95	4000	29	1	28	0	0	0	0	0	0
West Midlands	96	8000	178	134	44	8	8	0	0	0	0
West Midlands	97	2000	19	2	17	0	0	0	0	0	0

TABLE 40 Screening of potential participants summarised by practice/clinic/office name (*continued*)

Region	Practice number	Practice population	Number identified by search	Total number excluded	Total number mail-out	Total number replied	Total number interested	Total number not interested	Total number eligible	Total number ineligible	Total number randomised
West Midlands	98	4000	55	9	46	4	4	0	1	2	1
West Midlands	99	7000	109	32	77	7	7	0	6	0	5
West Midlands	100	15,000	94	13	81	6	6	0	4	2	2
West Midlands	101	17,000			64	2	2	0	0	1	0
West Midlands	102	9000	145	50	195	18	18	0	14	2	9
West Midlands	103	10,000	124	28	96	5	5	0	3	1	1
West Midlands	104	8000	51	2	49	6	3	3	1	2	1
West Midlands	105	6000	63	6	56	16	15	1	8	7	6
West Midlands	106	14,000	209	38	171	25	22	3	12	7	8
West Midlands	107	7000	89	11	78	9	8	1	1	7	0
West Midlands	108	10,000	135	4	131	11	11	0	5	3	2
West Midlands	109	6000	62	12	50	5	5	0	4	1	2
West Midlands	110	3000	74	20	50	11	9	2	1	8	1
West Midlands	111	9000	95	10	85	18	18	0	3	7	3
West Midlands	112	5000	32	11	21	7	7	0	1	3	1
West Midlands	113	12,000	99	40	59	11	11	0	4	3	4
West Midlands	114	5000	59	10	49	10	9	1	2	2	2
West Midlands	115	10,000	113	32	81	17	17	0	5	4	5
West Midlands	116	4000	41	14	27	4	4	0	1	1	1
West Midlands	117 (Hospital)					1	1	0	1	0	1
West Midlands	118 (Hospital)					1	1	0	0	0	0
West Midlands	119	11,000	67	48	19	2	2	0	1	0	0
West Midlands	120	12,000	125	11	114	13	13	0	3	7	2
West Midlands	121	7000	106	26	80	8	8	0	2	1	1

continued

TABLE 40 Screening of potential participants summarised by practice/clinic/office name (*continued*)

Region	Practice number	Practice population	Number identified by search	Total number excluded	Total number mail-out	Total number replied	Total number interested	Total number not interested	Total number eligible	Total number ineligible	Total number randomised
West Midlands	122	9000	52	14	38	4	4	0	2	2	0
West Midlands	123	18,000	316	107	207	15	15	0	10	5	5
West Midlands	124	9000	32	9	23	3	3	0	3	0	1
West Midlands	125	5000	44	0	44	5	5	0	1	2	0
West Midlands	126	16,000	365	56	312	9	9	0	6	2	2
West Midlands	127	20,000	430	19	411	19	19	0	12	7	9
West Midlands	128	6000	109	13	96	6	6	0	4	2	4
West Midlands	129	12,000	197	47	150	3	3	0	2	1	0
West Midlands	130	10,000	220	102	118	2	2	0	1	1	0
West Midlands	131	9000	215	41	174	4	4	0	3	1	2
West Midlands	132	3000	68	7	61	2	2	0	1	1	0
West Midlands	133	9000			29	4	4	0	1	1	1
West Midlands	134	13,000	177	29	148	23	23	0	11	8	7
West Midlands	135	13,000	103	30	73	8	8	0	3	3	3
West Midlands	136	12,000	44	3	41	12	12	0	8	4	6
West Midlands	137	21,000	180	49	130	22	22	0	15	6	4
West Midlands	138	16,000				1	1	0	1	0	0
West Midlands	139	10,000	20	1	19	3	3	0	2	0	2
West Midlands	140	9000	123	11	112	16	16	0	7	5	3
West Midlands	141	13,000	208	5	203	21	20	1	13	3	5
West Midlands	142	9000	228	10	218	24	24	0	16	5	8
West Midlands	143	7000	104	13	91	17	17	0	8	9	5
West Midlands	144	9000	192	25	167	12	12	0	8	4	5
West Midlands	145	7000	73	16	57	4	4	0	2	1	1
West Midlands	146	8000	117	33	84	13	13	0	11	2	9
West Midlands	147	15,000	61	32	29	6	6	0	3	1	1

TABLE 40 Screening of potential participants summarised by practice/clinic/office name (*continued*)

Region	Practice number	Practice population	Number identified by search	Total number excluded	Total number mail-out	Total number replied	Total number interested	Total number not interested	Total number eligible	Total number ineligible	Total number randomised
West Midlands	148	7000	32	19	13	2	2	0	1	1	1
West Midlands	149	14,000	159	25	134	17	17	0	8	8	4
West Midlands	150	16,000	66	4	62	7	7	0	2	3	2
West Midlands	151	7000			69	2	2	0	0	2	0
West Midlands	152	9000	52	15	37	3	3	0	2	1	2
West Midlands	153	16,000			88	8	8	0	3	1	3
West Midlands	154	4000	19	4	15	4	4	0	0	2	0
West Midlands	155	16,000	74	50	24	8	6	2	4	2	3
West Midlands	156	8000	90	39	51	2	2	0	1	1	1
West Midlands	157	7000	21	3	18	0	0	0	0	0	0
West Midlands	158	2000			17	3	3	0	2	0	1
West Midlands	159	9000	89	24	65	4	4	0	3	0	0
West Midlands	160	5000			33	6	6	0	1	0	1
West Midlands	161	9000			141	32	32	0	21	7	11
West Midlands	162	13,000			52	11	11	0	5	0	3
West Midlands	163	4000			49	5	5	0	1	1	1
West Midlands	164	11,000			180	29	29	0	17	8	10
West Midlands	165	7000			33	1	1	0	1	0	0
West Midlands	166	16,000	131	130	243	26	26	0	16	7	9
West Midlands	167	8000	124	20	104	13	13	0	7	5	5
West Midlands	168	4000	43	12	31	4	4	0	2	2	2
West Midlands	169	5000	54	4	48	4	4	0	1	2	0
West Midlands	170	7000	83	35	48	10	8	2	4	2	1
West Midlands	171	11,000	167	29	138	27	25	2	18	5	13
West Midlands	172	4000	101	29	72	9	9	0	6	1	4

continued

TABLE 40 Screening of potential participants summarised by practice/clinic/office name (*continued*)

Region	Practice number	Practice population	Number identified by search	Total number excluded	Total number mail-out	Total number replied	Total number interested	Total number not interested	Total number eligible	Total number ineligible	Total number randomised
West Midlands	173	4000	98	37	61	5	5	0	4	1	3
West Midlands	174	5000	114	44	70	2	2	0	1	0	1
West Midlands	175	29,000	287	41	248	27	27	0	18	5	14
West Midlands	176	6000	78	1	77	10	10	0	6	0	5
West Midlands	177	14,000	179	44	135	8	8	0	1	1	1
West Midlands	178	11,000	102	12	90	19	18	1	11	3	10
West Midlands	179	17,000	207	35	172	32	30	2	9	4	8
West Midlands	180	10,000	129	11	118	15	15	0	10	2	7
West Midlands	181	14,000			54	7	7	0	3	3	2
West Midlands	182	15,000	186	23	163	17	16	1	6	7	3
West Midlands	183	17,000	193	107	86	4	4	0	3	1	2
West Midlands	184	12,000	83	66	109	12	12	0	6	0	5
West Midlands	185	5000	51	6	45	7	7	0	3	1	2
West Midlands	186	12,000	189	0	189	14	14	0	7	5	3
West Midlands	187	10,000	89	52	94	1	1	0	1	0	1
West Midlands	188	16,000	129	20	109	5	5	0	2	2	0
West Midlands	189	13,000	140	13	127	13	13	0	5	1	2
West Midlands	190	12,000	114	31	83	17	17	0	14	1	11
West Midlands	191	11,000	124	19	105	16	16	0	10	4	5
Unknown	Unknown					1	1	0	0	1	0
TOTAL		**1,819,694**	**21,353**	**5618**	**20,900**	**2220**	**2087**	**133**	**1050**	**491**	**608**

TABLE 41 Randomised participants by group and treatment

	Standard care	Self-management	Total
Group 1: Stratford	10	9	19
Group 2: Kenilworth	8	9	17
Group 3: Rugby	11	11	22
Group 4: Coventry 1	12	13	25
Group 5: East Staffs 1	8	9	17
Group 6: Sedgefield 1	5	5	10
Group 7: Middlesbrough 1	10	9	19
Group 8: South East Staffs	11	10	21
Group 9: Witney	5	6	11
Group 10: Middlesbrough 2	5	5	10
Group 11: North Durham 1	6	5	11
Group 12: Abingdon	9	9	18
Group 13: Coventry 2	12	12	24
Group 14: Oxford City	9	10	19
Group 15: Corby	5	4	9
Group 16: Northampton 1	8	11	19
Group 17: North Warwickshire	13	12	25
Group 18: Dudley	9	10	19
Group 19: Nottingham City 1	13	11	24
Group 20: Nottingham City 2	6	6	12
Group 21: Sedgefield 2	3	4	7
Group 22: North Tyneside 1	5	5	10
Group 23: HAST 1	9	8	17
Group 24: North Durham 2	12	12	24
Group 25: Leicester City 1	7	5	12
Group 26: North Tyneside 2	10	9	19
Group 27: North Durham 3	12	13	25
Group 28: Redcar	4	4	8
Group 29: Worcester	10	11	21
Group 30: Redditch	13	12	25
Group 31: Redditch 2	10	11	21
Group 32: Northumberland 1	9	9	18
Group 33: Northumberland 2	11	12	23
Group 34: HAST 2	7	9	16
Group 35: DDES 3	6	5	11
TOTAL	303	305	608

TABLE 42 Overall summary of withdrawals by treatment arm[a]

	Standard care *N* = 303	Self-management *N* = 305	TOTAL *N* = 608
Participant discontinued intervention package only and will be followed up	N/A	8 (3%)	8 (1%)
Participant withdrew from study completely and will not be followed up	53 (17%)	46 (15%)	99 (16%)
Participant withdrew consent for receiving text messages in relation to study	52 (17%)	47 (15%)	99 (16%)
Participant withdrew consent for taking part in the interview study	46 (15%)	45 (15%)	91 (15%)

N/A, not applicable.
a Summary of total number of withdrawal requests, that is participants may have more than one request.

Source
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TABLE 43 Follow-up rates throughout trial[a]

			Not followed up			Follow-up outcome		
Treatment group	Time point	Total to reach time point	Deceased	Withdrawn completely	Follow-up due	Completed[b]	Non-responder	Total completed[c]
Standard care	Baseline	303	0 (0%)	0 (0%)	303	303 (100%)	0 (0%)	303 (100%)
	4 months	303	0 (0%)	5 (2%)	298	202 (68%)	96 (32%)	202 (67%)
	8 months	298	1 (< 1%)	32 (11%)	265	166 (63%)	99 (37%)	166 (55%)
	12 months	265	0 (0%)	8 (3%)	257	211 (82%)	46 (18%)	211 (70%)
Self-management	Baseline	305	0 (0%)	0 (0%)	305	305 (100%)	0 (0%)	305 (100%)
	4 months	305	2 (1%)	8 (3%)	295	228 (77%)	67 (23%)	228 (75%)
	8 months	295	0 (0%)	26 (9%)	269	199 (74%)	70 (26%)	199 (65%)
	12 months	269	2 (1%)	9 (3%)	258	229 (89%)	29 (11%)	229 (75%)

a Empty questionnaires that were returned have been classed as non-responder.
b % out of follow-up due.
c % out of total randomised.

Source
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TABLE 44 Timing of complete withdrawals throughout the trial

	Standard care *N* = 303	Self-management *N* = 305	TOTAL *N* = 608
Post randomisation to 4-month follow-up	5	8	13
4–8 months follow-up	32	26	58
8–12 months follow-up	16	12	28
Overall	53	46	99

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TABLE 45 Summary of intervention data

	Self-management *N* = 305
Time from randomisation to first group session (days)	
Mean (SD)	19.9 (24.8) (*n* = 296)
Median (IQR)	12 (6–23) (*n* = 296)
Didn't attend first group session	85/296 (29%)
Time from randomisation to first one-to-one consultation (days)	
Mean (SD)	28.0 (20.5) (*n* = 269)
Median (IQR)	22 (16–33) (*n* = 269)
Didn't attend first one-to-one	98/269 (36%)
Time from first group session to final one-to-one consultation (course duration) (days)	
N	305
Mean (SD)	33.4 (28.7) (*n* = 273)
Median (IQR)	44 (9–58) (*n* = 273)
Didn't attend final one-to-one	107/273 (39%)
Group session attendance[2,3]	
Number randomised to intervention	305
Attended day 1 only	13/305 (4%)
Attended day 1 and 2 only	17/305 (6%)
Attended day 1 and 3 only	10/305 (3%)
Attended day 1, 2 and 3	166/305 (54%)
Attended no days	90/305 (30%)
Missing	9/305 (3%)
Group size at randomisation (participants) – intervention group only	
Number of groups	35
Mean (SD)	8.71 (2.9) (*n* = 35)
Median (IQR)	9 (5–11) (*n* = 35)
Group size at session 1 (participants)[a]	
Number of groups	35
Mean (SD)	6.24 (2.82) (*n* = 35)
Median (IQR)	7 (3–8) (*n* = 35)
Missing groups	2/35 (6%)
Face-to-face interviews	
Attended first F2F interview	190/290 (66%)
Attended both F2F interviews	131/290 (45%)

continued

TABLE 45 Summary of intervention data (*continued*)

	Self-management *N* = 305
Telephone interviews	
Attended first telephone session	167/271 (62%)
Attended both telephone sessions	152/271 (56%)
Compliance	
Number of participants who had full compliance	144/305 (47%)
Number of participants who had minimal compliance	190/305 (62%)
Number who had less than minimal compliance	115/305 (38%)

a Six participants who attended day 1 attended groups they were not *randomised* too. This has been summarised by groups they attended, not randomised too.

TABLE 46 Pre-specified subgroup analyses of the 12-month PROMIS-8A outcome

Subgroups	Standard care *N*; mean (95% CI)	Self-management *N*; mean (95% CI)	Unadjusted effect estimate (95% CI)	Interaction effect; *p*-value[a]
Anxiety				
< 9	93; 63.3 (61.8 to 64.8)	114; 62.6 (61.1 to 64.1)	−0.71 (−2.84 to 1.43)	$p = 0.15$
≥ 9	115; 65.7 (64.3 to 67.0)	113; 65.7 (64.4 to 67.0)	0.04 (−1.81 to 1.90)	
Depression				
< 9	100; 62.3 (60.8 to 63.7)	109; 61.7 (60.2 to 63.1)	−0.60 (−2.66 to 1.46)	$p = 0.25$
≥ 9	105; 66.7 (65.5 to 68.0)	119; 66.4 (65.1 to 67.7)	0.35 (−2.14 to 1.45)	

a Based on a heteroscedastic partially nested mixed-effect model with corrected degrees of freedom, adjusted for age, gender, baseline pain intensity, geographical location, baseline opioid band, baseline PROMIS-8A T-score and interaction term. The education support group was used as the cluster variable for the education and support intervention arm, with individual clusters of size 1 used for each participant in usual care.

TABLE 47 Pre-specified subgroup analyses of the 12-month opioid use outcome

Subgroups		Standard care *N* (%)	Self-management *N* (%)	Unadjusted effect estimate (95% CI)[a]	Interaction effect; *p*-value[b]
Anxiety < 9	MED = 0	8/92 (9%)	32/110 (29%)	4.31 (1.87 to 9.92)	$p = 0.31$
	MED > 0	84/92 (91%)	78/110 (71%)		
≥ 9	MED = 0	6/114 (5%)	33/113 (29%)	7.42 (2.97 to 18.57)	
	MED > 0	108/114 (95%)	80/113 (71%)		

TABLE 47 Pre-specified subgroup analyses of the 12-month opioid use outcome (*continued*)

Subgroups		Standard care *N* (%)	Self-management *N* (%)	Unadjusted effect estimate (95% CI)[a]	Interaction effect; *p*-value[b]
Depression < 9	MED = 0	8/99 (8%)	29/106 (27%)	4.28 (1.85 to 9.92)	*p* = 0.46
	MED > 0	91/99 (92%)	77/106 (73%)		
≥ 9	MED = 0	6 (6%)	36/118 (31%)	7.17 (2.88 to 17.86)	
	MED > 0	98 (94%)	82/118 (69%)		

a OR (95% CI) reported.
b Based on partially nested mixed-effect logistic model adjusted for age, gender, baseline pain intensity, geographical location, baseline opioid band and interaction term. The education support group was used as the cluster variable for the education and support intervention arm, with individual clusters of size 1 used for each participant in usual care. OR and 95% CI reported.

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TABLE 48 Pre-specified sensitivity analysis – treatment effectiveness estimate based on the primary outcomes having excluded those participants included in the process evaluation interviews

	Standard care *N* = 192	Self-management *N* = 208	Unadjusted estimate (95% CI); *p*-value	Adjusted estimate (95% CI); *p*-value
PROMIS-8A			−0.68 (−2.19 to 0.82); *p* = 0.37	−1.04 (−2.33 to 0.26); *p* = 0.12[a]
N	191	208		
Mean (SD)	64.6 (7.5)	63.9 (7.8)		
Median (IQR)	64.9 (59.8–69.4)	64.4 (58.8–69.2)		
Missing	1	0		
Opioid use			5.87 (3.10 to 11.10); ***p* < 0.001**[b]	6.12 (2.95 to 12.71); ***p* < 0.001**[c]
N	189	205		
Taking non-opioids only (MED = 0)	13 (7%)	62 (30%)		
Taking opioids (MED > 0)	176 (93%)	143 (70%)		
Missing	3	3		

a Based on a heteroscedastic partially nested mixed-effect model with corrected degrees of freedom, adjusted for age, gender, baseline pain intensity, geographical location, baseline opioid band and baseline PROMIS-8A T-score. The education support group was used as the cluster variable included as a random effect to account for partial clustering in one arm.
b ORs (95% CI) and *p*-value reported.
c Based on partially nested mixed-effect logistic model adjusted for age, gender, baseline intensity, geographical location and baseline opioid band. The education support group was used as the cluster variable for the education and support intervention arm, with individual clusters of size 1 used for each participant in usual care. OR and 95% CI reported.

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TABLE 49 Pre-specified sensitivity analysis – treatment effectiveness estimate based on the primary outcome having adjusted for any imbalance in death rates across both treatment arms

	Standard care *N* = 303	Self-management *N* = 305	Adjusted estimate (95% CI); *p*-value
PROMIS-8A			−0.90 (−2.09 to 0.30); *p* = 0.14[a]
N	210	229	
Mean (SD)	64.7 (7.3)	64.2 (7.7)	
Median (IQR)	65.1 (59.8–69.2)	65 (59–69.2)	
Missing	93	76	
Opioid use			5.55 (2.80 to 10.99); ***p* < 0.001**[b]
N	208	225	
Taking non-opioids only (MED = 0)	15 (7%)	65 (29%)	
Taking opioids (MED > 0)	193 (93%)	160 (71%)	
Missing	95	80	

a Based on a heteroscedastic partially nested mixed-effect model with corrected degrees of freedom, adjusted for age, gender, baseline pain intensity, geographical location, baseline opioid band, baseline PROMIS-8A T-Score and death. The education support group was used as the cluster variable for the education and support intervention arm, with individual clusters of size 1 used for each participant in usual care.
b Based on partially nested mixed-effects logistic model adjusted for age, gender, baseline pain intensity, geographical location, baseline opioid use (MED) and death. The education support group was used as the cluster variable for the education and support intervention arm, with individual clusters of size 1 used for each participant in usual care. OR (95% CI) and *p*-value reported.

TABLE 50 Pre-specified treatment effectiveness estimates based on the primary outcome for people with different pain disorders

Primary outcome	Pain disorder[a]	Standard care	Self-management	Adjusted estimate (95% CI); *p*-value
PROMIS-8A	***Lower back pain***			
	Mean (SD)	64.7 (7.1) (*n* = 175)	64.4 (7.7) (*n* = 178)	−0.83 (−2.24 to 0.57); *p* = 0.24[b]
	Chronic widespread pain			
	Mean (SD)	66.0 (6.5) (*n* = 103)	66.0 (7.1) (*n* = 103)	−0.52 (−2.33 to 1.30); *p* = 0.57[b]
	Multisite pain			
	Mean (SD)	64.7 (7.3) (*n* = 183)	64.7 (7.5) (*n* = 207)	−0.41 (−1.70 to 0.88); *p* = 0.53[b]
Opioid use	***Back pain***			
	Taking non-opioids only (MED = 0)	9/173 (5%)	52/174 (30%)	7.66 (3.38 to 17.35); ***p* < 0.001**[c]
	Taking opioids (MED > 0)	164/173 (95%)	122/174 (70%)	
	Chronic widespread pain			
	Taking non-opioids only (MED = 0)	7/101 (7%)	31/101 (31%)	5.38 (1.73 to 16.71); ***p* < 0.004**[c]
	Taking opioids (MED> 0)	94/101 (93%)	70/101 (69%)	

TABLE 50 Pre-specified treatment effectiveness estimates based on the primary outcome for people with different pain disorders (*continued*)

Primary outcome	Pain disorder[a]	Standard care	Self-management	Adjusted estimate (95% CI); *p*-value
	Multisite pain			
	Taking non-opioids only (MED = 0)	13/181 (7%)	59/205 (29%)	5.15 (2.52 to 10.52); ***p* < 0.001**[c]
	Taking opioids (MED > 0)	168/181 (93%)	146/205 (71%)	

a Four hundred and eighty-two participants were classed under multiple pain categories. Thirty-four participants did not fall into any of the pain categories.
b Based on a heteroscedastic partially nested mixed-effect model with corrected degrees of freedom, adjusted for age, gender, baseline pain intensity, geographical location, baseline opioid band and baseline PROMIS-8A T-score. The education support group was used as the cluster variable for the education and support intervention arm, with individual clusters of size 1 used for each participant in usual care.
c Based on partially nested mixed-effect logistic model adjusted for age, gender, baseline pain intensity, geographical location and baseline MED. The education support group was used as the cluster variable for the education and support intervention arm, with individual clusters of size 1 used for each participant in usual care. OR and 95% CI reported.

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TABLE 51 Summary of opioid use using inverse probability weights

	Education and support intervention	Control	Total	Adjusted estimate (95% CI)[a]; *p*-value
Opioid use: total MED of all opioid pain killers taken over the last 4 weeks (daily MED) IF taking opioids at 12 months				4.61 (2.09 to 10.13); ***p* < 0.001**
N	225	208	433	
Taking non-opioids only (MED = 0)	65 (29%)	15 (7%)	80 (18%)	
Taking opioids (MED > 0)	160 (71%)	193 (93%)	353 (82%)	

a Based on partially nested mixed-effect logistic model adjusted for age, gender, baseline pain intensity, geographical location and baseline opioid band, with inverse probability weights. The education support group was used as the cluster variable for the education and support intervention arm, with individual clusters of size 1 used for each participant in usual care. OR and 95% CI reported.

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TABLE 52 Adverse events and SAEs summarised by treatment group[a]

	Standard care *N* = 303	Self-management *N* = 305
AEs		
Number of AEs reported	11	25
Number of participants reporting AE	8/303 (3%)	22/305 (7%)
SAEs		
Number of SAEs reported	20	32

continued

TABLE 52 Adverse events and SAEs summarised by treatment group (*continued*)

	Standard care *N* = 303	Self-management *N* = 305
Number of participants reporting SAE	16/303 (5%)	25/305 (8%)
Reason SAE deemed serious		
Death[b]	1/303 (< 1%)	4/305 (1%)
Life-threatening	2/303 (1%)	1/305 (< 1%)
Hospitalisation or prolongation of existing hospitalisation	17/303 (6%)	25/305 (8%)
Persistent or significant disability or incapacity	0/303 (0%)	1/305 (< 1%)
Congenital anomaly/birth defect	0/303 (0%)	0/305 (0%)
Other	1/303 (< 1%)	2/305 (1%)
SAE severity assessment		
Mild	1/303 (< 1%)	0/305 (0%)
Moderate	5/303 (2%)	9/305 (3%)
Severe	13/303 (4%)	19/305 (6%)
Fatal/life-threatening	1/303 (< 1%)	4/305 (1%)

a % out of total randomised; however, some participants have reported multiple SAEs.
b All five deaths were classed as unrelated.

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TABLE 53 Assessment of SAEs summarised by treatment group[a]

Assessment of SAEs	Standard care *N* = 303	Self-management *N* = 305	TOTAL *N* = 608
SAE related to trial intervention			
Definitely	0/303 (0%)	0/305 (0%)	0 (0%)
Probably	0/303 (0%)	1/305 (< 1%)	1 (0%)
Possibly	1/303 (< 1%)	3/305 (1%)	4 (1%)
Unlikely	7/303 (2%)	4/305 (1%)	11 (2%)
Unrelated	12/303 (4%)	24/305 (8%)	36 (6%)
Expectedness of SAE[b]			
Expected	1 (< 1%)	2 (1%)	3 (0.5%)
Unexpected	0 (0%)	2 (1%)	2 (< 1%)

a % out of total randomised.
b Only applicable if relation to trial is definitely, probably or possibly.

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TABLE 54 Exploratory opioid use at 12 months (continuous outcome)

	I-WOTCH intervention	Control	Total	Adjusted estimate (95% CI)[a]; *p*-value
Opioid use: total MED of all opioid pain killers taken over the last 4 weeks (daily MED) at 12 months				−17.1 (−25.38 to −8.84); $p < 0.001$
Median (IQR)	18 (0–50) (*n* = 225)	29 (14–53) (*n* = 208)	25 (6–50) (*n* = 433)	

a Based on a heteroscedastic partially nested mixed-effect model with corrected degrees of freedom, adjusted for age, gender, baseline pain intensity, geographical location and baseline MED. The education support group was used as the cluster variable for the education and support intervention arm, with clusters of size 1 used for each participant in usual care.

Source

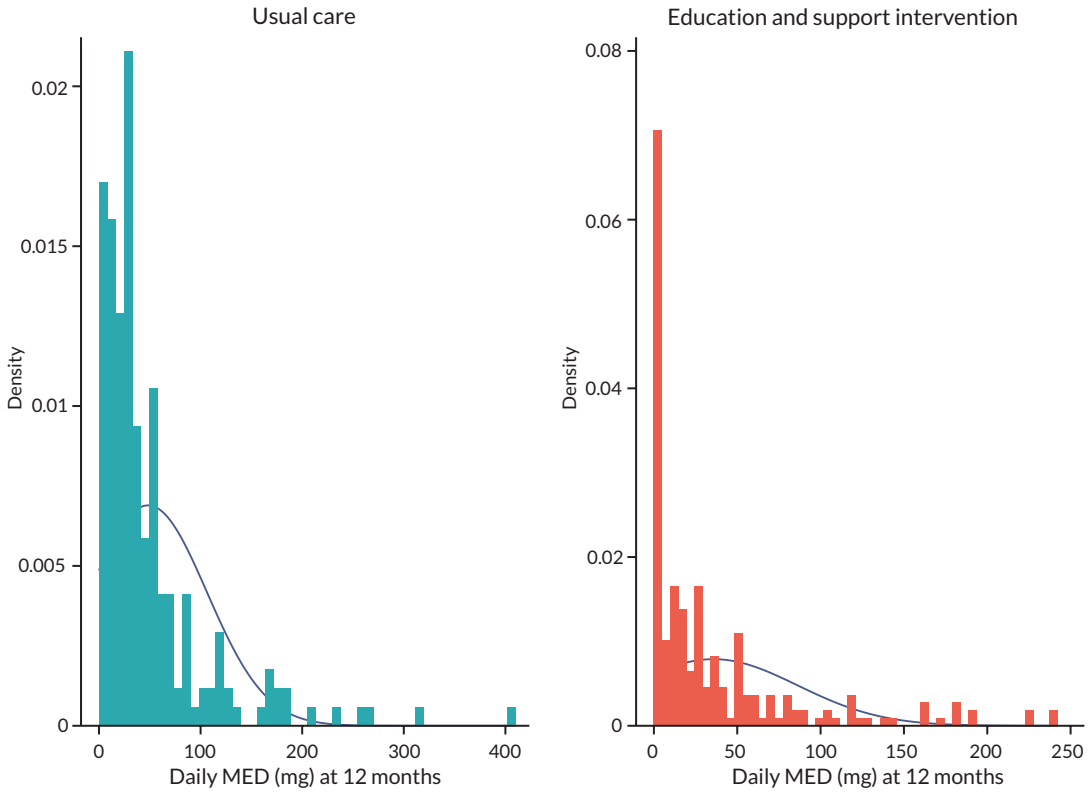

FIGURE 11 Histogram of daily MED at 12 months by treatment group. Green line shows normal distribution for reference. Reproduced with permission from Sandhu *et al.*[1] This is an Open Access article distributed under the terms of the Creative Commons Attribution Licence, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited. See: https://creativecommons.org/licenses/by/4.0/. The figure includes minor additions and formatting changes to the original text.

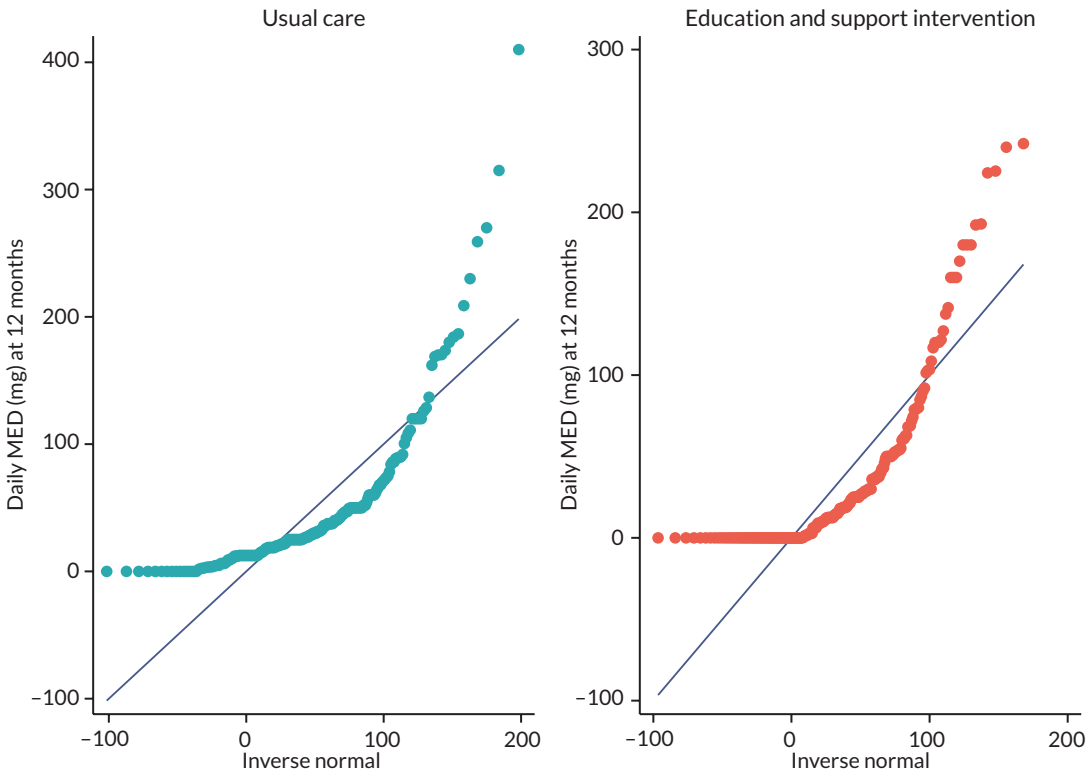

FIGURE 12 Q–Q plot of daily MED at 12 months by treatment group. Blue line shows normal distribution for reference. Reproduced with permission from Sandhu *et al.*[1] This is an Open Access article distributed under the terms of the Creative Commons Attribution Licence, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited. See: https://creativecommons.org/licenses/by/4.0/. The figure includes minor additions and formatting changes to the original text.

Appendix 4 Health economics supplementary materials

TABLE 55 Data collection strategy for I-WOTCH's economic analyses

Data collected	Source	Follow-up points
Baseline data		
Age	PtQ	Baseline
Gender	PtQ	Baseline
Ethnic group	PtQ	Baseline
Current work status	PtQ	Baseline
Age at leaving full-time education	PtQ	Baseline
Pain duration	PtQ	Baseline
Opioid intake duration	PtQ	Baseline
Pain conditions	PtQ	Baseline
Pain severity stratification group	PtQ	Baseline
Measures of health benefit		
ADLs (PROMIS PI-SF-8A)	PtQ	Baseline, 4, 8 and 12 months
ShOWS	PtQ	Baseline, 4, 8 and 12 months
	PtD	Weekly over first 4 months

continued

TABLE 55 Data collection strategy for I-WOTCH's economic analyses (*continued*)

Data collected	Source	Follow-up points
Generic health-related quality of life (EQ-5D-5L)	PtQ	Baseline, 4, 8 and 12 months
	PtD	Weekly over first 4 months
Healthcare utilisation (volume, admissions, consultations, attendances and/or contacts)		
Medications	PtQ	Baseline, 4, 8 and 12 months
Hospital care		
Inpatient	PtQ	Baseline, 4, 8 and 12 months
Outpatient	PtQ	Baseline, 4, 8 and 12 months
Community health and social care		
GP surgery	PtQ	Baseline, 4, 8 and 12 months
GP home	PtQ	Baseline, 4, 8 and 12 months
Practice nurse	PtQ	Baseline, 4, 8 and 12 months
District nurse (i.e. at home)	PtQ	Baseline, 4, 8 and 12 months
Occupational therapist	PtQ	Baseline, 4, 8 and 12 months
Counsellor	PtQ	Baseline, 4, 8 and 12 months
Psychologist	PtQ	Baseline, 4, 8 and 12 months
Social worker	PtQ	Baseline, 4, 8 and 12 months
Physiotherapist	PtQ	Baseline, 4, 8 and 12 months
Other	PtQ	Baseline, 4, 8 and 12 months

PtD, patient diaries; PtQ, patient questionnaire.

TABLE 56 Micro-costing I-WOTCH intervention for intervention arm

Delivery		Training	
Number of participants		Number of facilitators	34
Target attendance	305	Training cost	£26,327
Minimum attendance (attended all 3 days)	164	Refresher training cost	£459.66
Maximum attendance (attended at least first day)	204	Training travel cost	£378.60
Number of days of intervention	93	Training expenses	£106.80
		Number of training days	81
Total venue cost	£ 9078.81	Total cost of training	£27,272.06
Facilitation cost per day, mean (range)	£97.62 (0–788.52)	Cost of training per day	£336.69
Cost of consumables for per participant (pp)		*Cost of consumables per facilitator(pf)*	
Handout	£3.28		
Opioid manager	£2.60	Opioid manager	£2.60
Compact disk (CD)	£1.50	CD	£1.50
Total consumables (pp)	£7.38	Total consumables (pf)	£4.10

TABLE 56 Micro-costing I-WOTCH intervention for intervention arm (*continued*)

Delivery		Training	
Total facilitation cost	£29,121.06		
Total venue cost	£9078.81		
Total consumables cost	£2268.7	Total consumables cost	£143.5
Total delivery	£40,468.57	Total cost of training	£27,415.56
Total cost of I-WOTCH intervention			
Total I-WOTCH cost (total delivery + training)	£67,884.13		
Average cost of I-WOTCH intervention			
Target attendance	£222.57		
Minimum attendance	£413.93		
Maximum attendance	£332.77		

TABLE 57 Micro-costing I-WOTCH intervention for control arm

Cost of consumables for participants (per participant)				Total
Opioid manager	£2.60	CD	£1.50	£4.10

TABLE 58 Unit costs of pain killer medications considered

Drug	Brand	Form	Preparation	Strength	Size	Volume	Rate (GBP)
Buprenorphine	Temgesic	Ampoule	300 µg/1 ml	0.3 mg/ml	5		2.46
Tramadol	Tramadol	Ampoule	100 mg/2 ml	50 mg/ml	5		4.9
Tramadol	Tramadol	Ampoule	100 mg/2 ml	50 mg/ml	10		10
Tramadol	Zamadol	Ampoule	100 mg/2 ml	50 mg/ml	5		5.49
Oxycodone	Lynlor	Capsule		5 mg	56		11.43
Oxycodone	Lynlor	Capsule		10 mg	56		22.86
Oxycodone	Lynlor	Capsule		20 mg	56		45.71
Morphine	MXL	Capsule		30 mg	28		10.91
Morphine	MXL	Capsule		60 mg	28		14.95
Morphine	MXL	Capsule		90 mg	28		22.04
Morphine	MXL	Capsule		120 mg	28		29.15
Morphine	MXL	Capsule		150 mg	28		36.43
Morphine	MXL	Capsule		200 mg	28		46.15
Oxycodone	OxyNorm	Capsule		5 mg	56		11.43
Oxycodone	OxyNorm	Capsule		10 mg	56		22.86
Oxycodone	OxyNorm	Capsule		20 mg	56		45.71
Oxycodone	Shortec	Capsule		5 mg	56		11.43

continued

TABLE 58 Unit costs of pain killer medications considered (*continued*)

Drug	Brand	Form	Preparation	Strength	Size	Volume	Rate (GBP)
Oxycodone	Shortec	Capsule		10 mg	56		22.86
Oxycodone	Shortec	Capsule		20 mg	56		45.71
Tramadol	Tramadol hydrochloride	Capsule		50 mg	30		0.76
Tramadol	Tramadol hydrochloride	Capsule		50 mg	100		2.53
Tramadol	Zamadol	Capsule		50 mg	100		2.53
Morphine	Zomorph	Capsule		10 mg	60		3.47
Morphine	Zomorph	Capsule		30 mg	60		8.3
Morphine	Zomorph	Capsule		60 mg	60		16.2
Morphine	Zomorph	Capsule		100 mg	60		21.8
Morphine	Zomorph	Capsule		200 mg	60		43.6
Tramadol	Zydol	Capsule		50 mg	30		0.76
Tramadol	Zydol	Capsule		50 mg	100		2.53
Cocodamol	Cocodamol	Effervescent tablet		30 mg/500 mg	32		2.34
Cocodamol	Cocodamol	Effervescent tablet		30 mg/500 mg	100		7.31
Cocodamol	Cocodamol	Effervescent tablet		8 mg/500 mg	100		6.66
Cocodamol	Codipar	Effervescent tablet		15 mg/500 mg	100		8.25
Cocodamol	Paracodol	Effervescent tablet		8 mg/500 mg	32		2.13
Cocodamol	Solpadol	Effervescent tablet		30 mg/500 mg	32		2.34
Cocodamol	Solpadol	Effervescent tablet		30 mg/500 mg	100		7.31
Codeine phosphate	Codeine phosphate	Injection	60 mg/ml	60 mg/ml	10		24.38
Dihydrocodeine	Dihydrocodeine tartrate	Injection	50 mg/ml	50 mg/ml	10		105.27
Fentanyl	Fentanyl	Injection	100 µg/2 ml	50 µg/ml	10		14.17
Fentanyl	Fentanyl	Injection	500 µg/10 ml	50 µg/ml	10		14.325
Fentanyl	Fentanyl	Injection	2.5 mg/50 ml	50 µg/ml	1		5
Meptazinol	Meptid	Injection	100 mg/ml	100 mg/ml	10		19.21
Methadone	Methadone hydrochloride	Injection	35 mg/3.5 ml	10 mg/ml	10		12.87
Methadone	Methadone hydrochloride	Injection	50 mg/1 ml	50 mg/ml	10		17.72
Morphine	Morphine	Injection	10 mg/10 ml	1 mg/ml	10		14.25
Morphine	Morphine	Injection	10 mg/1 ml	10 mg/ml	10		9.36
Morphine	Morphine	Injection	15 mg/ml	15 mg/ml	10		10.74
Morphine	Morphine	Injection	1 mg/ml	1 mg/ml	10		28.7
Morphine	Morphine	Injection	20 mg/ml	20 mg/ml	10		59.7
Morphine	Morphine	Injection	30 mg/ml	30 mg/ml	10		11.49
Morphine	Morphine	Injection	5 mg/5 ml	1 mg/ml	10		39.6
Morphine	Morphine	Injection	60 mg/2 ml	30 mg/ml	5		10.07
Morphine	Morphine infusion	Injection	100 mg/50 ml	2 mg/ml	1		6.48

TABLE 58 Unit costs of pain killer medications considered (*continued*)

Drug	Brand	Form	Preparation	Strength	Size	Volume	Rate (GBP)
Morphine	Morphine infusion	Injection	100 mg/50 ml	2 mg/ml	10		64.8
Morphine	Morphine infusion	Injection	50 mg/50 ml	1 mg/ml	1		5.78
Morphine	Morphine infusion	Injection	50 mg/50 ml	1 mg/ml	10		38.7
Oxycodone	Oxycodone	Injection	10 mg/1 ml	10 mg/ml	5		8
Oxycodone	Oxycodone	Injection	10 mg/1 ml	10 mg/ml	10		15
Oxycodone	Oxycodone	Injection	20 mg/2 ml	10 mg/ml	5		16
Oxycodone	Oxycodone	Injection	20 mg/2 ml	10 mg/ml	10		30
Oxycodone	Oxycodone	Injection	50 mg/1 ml	50 mg/ml	5		70.1
Oxycodone	Oxycodone	Injection	50 mg/1 ml	50 mg/ml	10		135
Oxycodone	OxyNorm	Injection	10 mg/1 ml	10 mg/ml	5		8
Oxycodone	OxyNorm	Injection	20 mg/2 ml	10 mg/ml	5		16
Oxycodone	OxyNorm	Injection	50 mg/1 ml	50 mg/ml	5		70.1
Pethidine	Pethidine	Injection	100 mg/2 ml	50 mg/ml	10		4.66
Pethidine	Pethidine	Injection	50 mg/1 ml	50 mg/ml	10		5.11
Pethidine	Pethidine	Injection	50 mg/5 ml	10 mg/ml	10		52.91
Methadone	Physeptone	Injection	10 mg/1 ml	10 mg/ml	10		7.63
Methadone	Physeptone	Injection	10 mg/1 ml	10 mg/ml	100		73.05
Methadone	Physeptone	Injection	20 mg/2 ml	10 mg/ml	10		13.15
Methadone	Physeptone	Injection	35 mg/3.5 ml	10 mg/ml	10		12.87
Methadone	Physeptone	Injection	50 mg/1 ml	50 mg/ml	10		17.72
Methadone	Physeptone	Injection	50 mg/2 ml	25 mg/ml	10		17.72
Methadone	Physeptone	Injection	50 mg/5 ml	10 mg/ml	10		16.33
Oxycodone	Shortec	Injection	10 mg/1 ml	10 mg/ml	5		8
Oxycodone	Shortec	Injection	20 mg/2 ml	10 mg/ml	5		16
Oxycodone	Shortec	Injection	50 mg/1 ml	50 mg/ml	5		70.1
Fentanyl	Sublimaze	Injection	500 µg/10 ml	50 µg/ml	5		6.53
Tramadol	Zydol	Injection	100 mg/2 ml	50 mg/ml	5		4
Codeine phosphate	Codeine phosphate	Liquid	15 mg/5 ml	3 mg/ml	1	200 ml	1.62
Codeine phosphate	Codeine phosphate	Liquid	15 mg/5 ml	3 mg/ml	1	200 ml	1.9
Codeine phosphate	Codeine phosphate	Liquid	15 mg/5 ml	3 mg/ml	1	2000 ml	16.2
Codeine phosphate	Codeine phosphate	Liquid	25 mg/5 ml	5 mg/l	1	500 ml	6.64
Dihydrocodeine	Dihydrocodeine tartrate	Liquid	2 mg/ml	2 mg/ml	1	150 ml	9.23
Codeine phosphate	Galcodine	Liquid	15 mg/5 ml	3 mg/ml	1	2000 ml	9.9

continued

TABLE 58 Unit costs of pain killer medications considered (*continued*)

Drug	Brand	Form	Preparation	Strength	Size	Volume	Rate (GBP)
Methadone	Methadone hydrochloride	Liquid	10 mg/ml	10 mg/ml	1	150 ml	12.01
Methadone	Methadone hydrochloride	Liquid	1 mg/ml	1 mg/ml	1	50 ml	1
Methadone	Methadone hydrochloride	Liquid	1 mg/ml	1 mg/ml	1	100 ml	0.82
Methadone	Methadone hydrochloride	Liquid	1 mg/ml	1 mg/ml	1	100 ml	0.8
Methadone	Methadone hydrochloride	Liquid	1 mg/ml	1 mg/ml	1	100 ml	0.8
Methadone	Methadone hydrochloride	Liquid	1 mg/ml	1 mg/ml	1	100 ml	0.82
Methadone	Methadone hydrochloride	Liquid	1 mg/ml	1 mg/ml	1	500 ml	4.1
Methadone	Methadone hydrochloride	Liquid	1 mg/ml	1 mg/ml	1	500 ml	4
Methadone	Methadone hydrochloride	Liquid	1 mg/ml	1 mg/ml	1	500 ml	4
Methadone	Methadone hydrochloride	Liquid	1 mg/ml	1 mg/ml	1	500 ml	4
Methadone	Methadone hydrochloride	Liquid	1 mg/ml	1 mg/ml	1	500 ml	4.1
Methadone	Methadone hydrochloride	Liquid	1 mg/ml	1 mg/ml	1	2500 ml	26.925
Methadone	Methadone hydrochloride	Liquid	1 mg/ml	1 mg/ml	1	2500 ml	27
Methadone	Methadone hydrochloride	Liquid	1 mg/ml	1 mg/ml	1	2500 ml	32.1
Methadone	Methadone hydrochloride	Liquid	1 mg/ml	1 mg/ml	1	2500 ml	32.1
Methadone	Methadone hydrochloride	Liquid	20 mg/ml	20 mg/ml	1	150 ml	24.02
Morphine	Morphine	Liquid	10 mg/5 ml	2 mg/ml	1	100 ml	1.84
Morphine	Morphine	Liquid	10 mg/5 ml	2 mg/ml	1	300 ml	5.29
Morphine	Morphine	Liquid	10 mg/5 ml	2 mg/ml	1	500 ml	8.55
Morphine	Oramorph	Liquid	10 mg/5 ml	2 mg/ml	1	100 ml	1.89
Morphine	Oramorph	Liquid	10 mg/5 ml	2 mg/ml	1	300 ml	5.29
Morphine	Oramorph	Liquid	10 mg/5 ml	2 mg/ml	1	500 ml	8.5
Morphine	Oramorph	Liquid	20 mg/ml	20 mg/ml	1	30 ml	4.98
Morphine	Oramorph	Liquid	20 mg/ml	20 mg/ml	1	120 ml	19.5
Oxycodone	Oxycodone	Liquid	10 mg/ml	9 mg/ml	1	120 ml	46.63
Oxycodone	Oxycodone	Liquid	5 mg/5 ml	1 mg/ml	1	250 ml	9.71
Oxycodone	OxyNorm	Liquid	10 mg/ml	10 mg/ml	1	120 ml	46.63
Oxycodone	OxyNorm	Liquid	5 mg/5 ml	1 mg/ml	1	250 ml	9.71
Tapentadol	Palexia	Liquid	20 mg/ml	20 mg/ml	1	100 ml	17.8
Tapentadol	Palexia	Liquid	20 mg/ml	20 mg/ml	1	200 ml	35.6
Oxycodone	Shortec	Liquid	10 mg/ml	9 mg/ml	1	120 ml	46.63
Oxycodone	Shortec	Liquid	5 mg/5 ml	1 mg/ml	1	250 ml	9.71
Tramadol	Teamadol	Liquid	100 mg/ml	100 mg/ml	1	10 ml	3.5
Tramadol	Maxitram SR	Modified release Capsule		50 mg	60		7.24
Tramadol	Maxitram SR	Modified release		100 mg	60		14.47

TABLE 58 Unit costs of pain killer medications considered (*continued*)

Drug	Brand	Form	Preparation	Strength	Size	Volume	Rate (GBP)
Tramadol	Maxitram SR	Modified release Capsule		150 mg	60		21.71
Tramadol	Maxitram SR	Modified release Capsule		200 mg	60		28.93
Tramadol	Tramquel SR	Modified release Capsule		50 mg	60		7.24
Tramadol	Tramquel SR	Modified release Capsule		100 mg	60		14.47
Tramadol	Tramquel SR	Modified release Capsule		150 mg	60		21.71
Tramadol	Tramquel SR	Modified release Capsule		200 mg	60		28.93
Tramadol	Zamadol SR	Modified release Capsule		50 mg	60		7.24
Tramadol	Zamadol SR	Modified release Capsule		100 mg	60		14.47
Tramadol	Zamadol SR	Modified release Capsule		150 mg	60		21.71
Tramadol	Zamadol SR	Modified release Capsule		200 mg	60		28.93
Tramadol	Zamadol Melt	Orodispersible Tablet		50 mg	50		7.12
Buprenorphine	Bupeaze	Patch		35 µg/hour	4		15.8
Buprenorphine	Bupeaze	Patch		52.5 µg/hour	4		23.71
Buprenorphine	Bupeaze	Patch		70 µg/hour	4		31.6
Buprenorphine	Buplast	Patch		35 µg/hour	4		15.8
Buprenorphine	Buplast	Patch		52.5 µg/hour	4		23.71
Buprenorphine	Buplast	Patch		70 µg/hour	4		31.6
Buprenorphine	Bupramyl	Patch		5 µg/hour	4		17.6
Buprenorphine	Bupramyl	Patch		10 µg/hour	4		31.55
Buprenorphine	Bupramyl	Patch		20 µg/hour	4		57.46
Buprenorphine	Butec	Patch		5 µg/hour	4		17.6
Buprenorphine	Butec	Patch		10 µg/hour	4		31.55
Buprenorphine	Butec	Patch		15 µg/hour	4		49.15
Buprenorphine	Butec	Patch		20 µg/hour	4		57.46
Buprenorphine	BuTrans	Patch		10 µg/hour	4		31.55
Buprenorphine	BuTrans	Patch		5 µg/hour	4		17.6
Buprenorphine	BuTrans	Patch		15 µg/hour	4		49.15
Buprenorphine	BuTrans	Patch		20 µg/hour	4		57.46
Fentanyl	Durogesic DTrans	Patch		12 µg/hour	5		12.59

continued

TABLE 58 Unit costs of pain killer medications considered (*continued*)

Drug	Brand	Form	Preparation	Strength	Size	Volume	Rate (GBP)
Fentanyl	Durogesic DTrans	Patch		25 µg/hour	5		17.99
Fentanyl	Durogesic DTrans	Patch		50 µg/hour	5		33.66
Fentanyl	Durogesic DTrans	Patch		75 µg/hour	5		46.99
Fentanyl	Durogesic DTrans	Patch		100 µg/hour	5		57.86
Fentanyl	Fencino	Patch		12 µg/hour	5		12.59
Fentanyl	Fencino	Patch		25 µg/hour	5		17.99
Fentanyl	Fencino	Patch		50 µg/hour	5		33.66
Fentanyl	Fencino	Patch		75 µg/hour	5		46.99
Fentanyl	Fencino	Patch		100 µg/hour	5		57.86
Fentanyl	Fentalis	Patch		25 µg/hour	5		17.99
Fentanyl	Fentalis	Patch		50 µg/hour	5		33.66
Fentanyl	Fentalis	Patch		75 µg/hour	5		46.99
Fentanyl	Fentalis	Patch		100 µg/hour	5		57.86
Buprenorphine	Hapoctasin	Patch		35 µg/hour	4		15.8
Buprenorphine	Hapoctasin	Patch		52.5 µg/hour	4		23.71
Buprenorphine	Hapoctasin	Patch		70 µg/hour	4		31.6
Fentanyl	Matrifen	Patch		12 µg/hour	5		12.59
Fentanyl	Matrifen	Patch		25 µg/hour	5		17.99
Fentanyl	Matrifen	Patch		50 µg/hour	5		33.66
Fentanyl	Matrifen	Patch		75 µg/hour	5		46.99
Fentanyl	Matrifen	Patch		100 µg/hour	5		57.86
Fentanyl	Mezolar Matrix	Patch		12 µg/hour	5		12.59
Fentanyl	Mezolar Matrix	Patch		25 µg/hour	5		17.99
Fentanyl	Mezolar Matrix	Patch		37.5 µg/hour	5		15.46
Fentanyl	Mezolar Matrix	Patch		50 µg/hour	5		33.66
Fentanyl	Mezolar Matrix	Patch		75 µg/hour	5		46.99
Fentanyl	Mezolar Matrix	Patch		100 µg/hour	5		57.86
Fentanyl	Opiodur	Patch		12 µg/hour	5		12.59
Fentanyl	Opiodur	Patch		25 µg/hour	5		17.99
Fentanyl	Opiodur	Patch		50 µg/hour	5		33.66
Fentanyl	Opiodur	Patch		75 µg/hour	5		46.99
Fentanyl	Opiodur	Patch		100 µg/hour	5		57.86
Fentanyl	Osmanil	Patch		12 µg/hour	5		12.59
Fentanyl	Osmanil	Patch		25 µg/hour	5		17.99
Fentanyl	Osmanil	Patch		50 µg/hour	5		33.66
Fentanyl	Osmanil	Patch		75 µg/hour	5		46.99

TABLE 58 Unit costs of pain killer medications considered (*continued*)

Drug	Brand	Form	Preparation	Strength	Size	Volume	Rate (GBP)
Fentanyl	Osmanil	Patch		100 µg/hour	5		57.86
Buprenorphine	Panitaz	Patch		20 µg/hour	4		57.46
Buprenorphine	Panitaz	Patch		5 µg/hour	4		17.6
Buprenorphine	Panitaz	Patch		10 µg/hour	4		31.55
Buprenorphine	Reletrans	Patch		5 µg/hour	4		17.6
Buprenorphine	Reletrans	Patch		10 µg/hour	4		31.55
Buprenorphine	Reletrans	Patch		15 µg/hour	4		49.15
Buprenorphine	Reletrans	Patch		20 µg/hour	4		57.46
Buprenorphine	Relevtec	Patch		35 µg/hour	4		15.8
Buprenorphine	Relevtec	Patch		52.5 µg/hour	4		23.71
Buprenorphine	Relevtec	Patch		70 µg/hour	4		31.6
Buprenorphine	Sevodyne	Patch		10 µg/hour	4		31.55
Buprenorphine	Sevodyne	Patch		20 µg/hour	4		57.46
Buprenorphine	Sevodyne	Patch		5 µg/hour	4		17.6
Buprenorphine	Transtec	Patch		35 µg/hour	4		15.8
Buprenorphine	Transtec	Patch		52.5 µg/hour	4		23.71
Buprenorphine	Transtec	Patch		70 µg/hour	4		31.6
Fentanyl	Victanyl	Patch		12 µg/hour	5		12.59
Fentanyl	Victanyl	Patch		25 µg/hour	5		17.99
Fentanyl	Victanyl	Patch		50 µg/hour	5		33.66
Fentanyl	Victanyl	Patch		75 µg/hour	5		46.99
Fentanyl	Victanyl	Patch		100 µg/hour	5		57.86
Fentanyl	Yemex	Patch		12 µg/hour	5		12.59
Fentanyl	Yemex	Patch		25 µg/hour	5		17.99
Fentanyl	Yemex	Patch		50 µg/hour	5		33.66
Fentanyl	Yemex	Patch		75 µg/hour	5		46.99
Fentanyl	Yemex	Patch		100 µg/hour	5		57.86
Tramadol	Zydol	Soluble tablet sugar free		50 mg	20		2.79
Tramadol	Zydol	Soluble tablet sugar free		50 mg	100		13.33
Fentanyl	Abstral	Tablet		100 µg	10		49.99
Fentanyl	Abstral	Tablet		100 µg	30		149.7
Fentanyl	Abstral	Tablet		200 µg	10		49.99
Fentanyl	Abstral	Tablet		200 µg	30		149.7
Fentanyl	Abstral	Tablet		300 µg	10		49.99

continued

TABLE 58 Unit costs of pain killer medications considered (*continued*)

Drug	Brand	Form	Preparation	Strength	Size	Volume	Rate (GBP)
Fentanyl	Abstral	Tablet		300 µg	30		149.7
Fentanyl	Abstral	Tablet		400 µg	10		49.99
Fentanyl	Abstral	Tablet		400 µg	30		149.7
Fentanyl	Abstral	Tablet		600 µg	30		149.7
Fentanyl	Abstral	Tablet		800 µg	30		149.7
Oxycodone	Abtard	Tablet		5 mg	28		12.52
Oxycodone	Abtard	Tablet		10 mg	56		25.04
Oxycodone	Abtard	Tablet		15 mg	56		38.12
Oxycodone	Abtard	Tablet		20 mg	56		50.08
Oxycodone	Abtard	Tablet		30 mg	56		76.23
Oxycodone	Abtard	Tablet		40 mg	56		100.19
Oxycodone	Abtard	Tablet		60 mg	56		152.49
Oxycodone	Abtard	Tablet		80 mg	56		200.39
Tramadol	Brimisal PR	Tablet		100 mg	60		18
Buprenorphine	Buprenorphine	Tablet		2 mg	7		0.88
Buprenorphine	Buprenorphine	Tablet		8 mg	7		1.92
Buprenorphine	Buprenorphine	Tablet		400 µg	50		10.07
Buprenorphine	Buprenorphine	Tablet		400 µg	7		1.6
Oxycodone	Carexil	Tablet		5 mg	28		12.52
Oxycodone	Carexil	Tablet		10 mg	56		25.04
Oxycodone	Carexil	Tablet		20 mg	56		50.08
Oxycodone	Carexil	Tablet		40 mg	56		100.19
Oxycodone	Carexil	Tablet		80 mg	56		200.39
Cocodamol	Cocodamol	Tablet		15 mg/500 mg	100		3.56
Cocodamol	Cocodamol	Tablet		30 mg/500 mg	100		3.27
Cocodamol	Cocodamol	Tablet		30 mg/500 mg	30		0.98
Cocodamol	Cocodamol	Tablet		30 mg/500 mg	100		3.27
Cocodamol	Cocodamol	Tablet		60 mg/1000 mg	100		11.85
Cocodamol	Cocodamol	Tablet		8 mg/500 mg	100		2.47
Cocodamol	Cocodamol	Tablet		8 mg/500 mg	500		13.15
Cocodamol	Cocodamol	Tablet		8 mg/500 mg	1000		26.3
Cocodamol	Cocodamol	Tablet		8 mg/500 mg	32		0.895
Codeine Phosphate	Codeine Phosphate	Tablet		15 mg	28		0.74
Codeine Phosphate	Codeine Phosphate	Tablet		15 mg	100		2.64

TABLE 58 Unit costs of pain killer medications considered (*continued*)

Drug	Brand	Form	Preparation	Strength	Size	Volume	Rate (GBP)
Codeine Phosphate	Codeine Phosphate	Tablet		30 mg	28		0.87
Codeine Phosphate	Codeine Phosphate	Tablet		30 mg	100		3.11
Codeine Phosphate	Codeine Phosphate	Tablet		60 mg	28		1.48
Cocodamol	Codipar	Tablet		15 mg/500 mg	100		3.56
Dihydrocodeine	DF118	Tablet		40 mg	100		11.51
Dihydrocodeine	DHC continus MR	Tablet		60 mg	56		5.2
Dihydrocodeine	DHC continus MR	Tablet		90 mg	56		8.66
Dihydrocodeine	DHC continus MR	Tablet		120 mg	56		10.95
Dihydrocodeine	Dihydrocodeine	Tablet		30 mg	28		0.86
Dihydrocodeine	Dihydrocodeine tartrate	Tablet		30 mg	500		16.6
Dihydrocodeine	Dihydrocodeine tartrate	Tablet		30 mg	30		1.28
Dihydrocodeine	Dihydrocodeine tartrate	Tablet		30 mg	100		3.07
Codydramol	Dihyrdrocodeine with Paracetamol	Tablet		10 mg/500 mg	30		0.71
Codydramol	Dihyrdrocodeine with Paracetamol	Tablet		10 mg/500 mg	100		2.37
Codydramol	Dihyrdrocodeine with Paracetamol	Tablet		10 mg/500 mg	500		12.5
Codydramol	Dihyrdrocodeine with Paracetamol	Tablet		20 mg/500 mg	56		5.72
Codydramol	Dihyrdrocodeine with Paracetamol	Tablet		20 mg/500 mg	112		11.13
Codydramol	Dihyrdrocodeine with Paracetamol	Tablet		30 mg/500 mg	56		6.82
Fentanyl	Effentora	Tablet		100 µg	4		19.96
Fentanyl	Effentora	Tablet		100 µg	28		139.72
Fentanyl	Effentora	Tablet		200 µg	4		19.96
Fentanyl	Effentora	Tablet		200 µg	28		139.72
Fentanyl	Effentora	Tablet		400 µg	4		19.96
Fentanyl	Effentora	Tablet		400 µg	28		139.72
Fentanyl	Effentora	Tablet		600 µg	4		19.96
Fentanyl	Effentora	Tablet		600 µg	28		139.72
Fentanyl	Effentora	Tablet		800 µg	4		19.96
Fentanyl	Effentora	Tablet		800 µg	28		139.72
Codydramol	Eroset	Tablet		10 mg/500 mg	30		0.71
Codydramol	Eroset	Tablet		10 mg/500 mg	100		2.37

continued

TABLE 58 Unit costs of pain killer medications considered (*continued*)

Drug	Brand	Form	Preparation	Strength	Size	Volume	Rate (GBP)
Buprenorphine	Espranor	Tablet		2 mg	7		0.88
Buprenorphine	Espranor	Tablet		8 mg	7		1.92
Tramadol	Invodol	Tablet		100 mg	60		5.55
Tramadol	Invodol	Tablet		150 mg	60		8.31
Tramadol	Invodol	Tablet		200 mg	60		11.35
Cocodamol	Kapake	Tablet		30 mg/500 mg	100		3.27
Oxycodone	Leveraxo	Tablet		5 mg	28		12.52
Oxycodone	Leveraxo	Tablet		10 mg	56		25.04
Oxycodone	Leveraxo	Tablet		20 mg	56		50.08
Oxycodone	Leveraxo	Tablet		30 mg	56		76.23
Oxycodone	Leveraxo	Tablet		40 mg	56		100.19
Oxycodone	Leveraxo	Tablet		60 mg	56		152.49
Oxycodone	Leveraxo	Tablet		80 mg	56		200.39
Oxycodone	Longtec	Tablet		5 mg	28		12.52
Oxycodone	Longtec	Tablet		10 mg	56		25.04
Oxycodone	Longtec	Tablet		15 mg	56		38.12
Oxycodone	Longtec	Tablet		20 mg	56		50.08
Oxycodone	Longtec	Tablet		30 mg	56		76.23
Oxycodone	Longtec	Tablet		40 mg	56		100.19
Oxycodone	Longtec	Tablet		60 mg	56		152.49
Oxycodone	Longtec	Tablet		80 mg	56		200.39
Oxycodone	Longtec	Tablet		120 mg	56		305.02
Tramadol	Mabron	Tablet		100 mg	60		15.52
Tramadol	Mabron	Tablet		150 mg	60		23.28
Tramadol	Mabron	Tablet		200 mg	60		31.04
Paracetamol	Mandanol	Tablet		500 mg	100		1.53
Tramadol	Maneo	Tablet		100 mg	60		6.95
Tramadol	Maneo	Tablet		150 mg	60		10.4
Tramadol	Maneo	Tablet		200 mg	60		14.2
Tramadol	Marol	Tablet		100 mg	60		6.94
Tramadol	Marol	Tablet		150 mg	60		10.39
Tramadol	Marol	Tablet		200 mg	60		14.19
Meptazinol	Meptid	Tablet		200 mg	112		22.11
Cocodamol	Migraleve Yellow	Tablet		8 mg/500 mg	16		0
Morphine	Morphgesic	Tablet		30 mg	60		12.47

TABLE 58 Unit costs of pain killer medications considered (*continued*)

Drug	Brand	Form	Preparation	Strength	Size	Volume	Rate (GBP)
Morphine	Morphgesic	Tablet		60 mg	60		18.04
Morphine	Morphgesic	Tablet		100 mg	60		38.5
Morphine	Morphgesic	Tablet		10 mg	60		5.2
Morphine	MST Continus	Tablet		5 mg	60		3.29
Morphine	MST Continus	Tablet		10 mg	60		5.2
Morphine	MST Continus	Tablet		15 mg	60		9.1
Morphine	MST Continus	Tablet		30 mg	60		12.47
Morphine	MST Continus	Tablet		60 mg	60		24.32
Morphine	MST Continus	Tablet		100 mg	60		38.5
Morphine	MST Continus	Tablet		200 mg	60		81.34
Buprenorphine	Natzon	Tablet		2 mg	7		0.88
Buprenorphine	Natzon	Tablet		8 mg	7		1.92
Buprenorphine	Natzon	Tablet		400 µg	7		1.6
Oxycodone	Onexila	Tablet		10 mg	28		12.52
Oxycodone	Onexila	Tablet		20 mg	28		12.52
Oxycodone	Onexila	Tablet		40 mg	28		25.04
Oxycodone	Onexila	Tablet		80 mg	28		50.09
Oxycodone	Oxeltra	Tablet		5 mg	28		12.52
Oxycodone	Oxeltra	Tablet		10 mg	56		25.04
Oxycodone	Oxeltra	Tablet		15 mg	56		38.12
Oxycodone	Oxeltra	Tablet		20 mg	56		50.08
Oxycodone	Oxeltra	Tablet		30 mg	56		76.23
Oxycodone	Oxeltra	Tablet		40 mg	56		100.19
Oxycodone	Oxeltra	Tablet		60 mg	56		152.49
Oxycodone	Oxeltra	Tablet		80 mg	56		200.39
Oxycodone	OxyContin	Tablet		5 mg	28		12.52
Oxycodone	OxyContin	Tablet		10 mg	56		25.04
Oxycodone	OxyContin	Tablet		15 mg	56		38.12
Oxycodone	OxyContin	Tablet		20 mg	56		50.08
Oxycodone	OxyContin	Tablet		30 mg	56		76.23
Oxycodone	OxyContin	Tablet		40 mg	56		100.19
Oxycodone	OxyContin	Tablet		60 mg	56		152.49
Oxycodone	OxyContin	Tablet		80 mg	56		200.39
Oxycodone	OxyContin	Tablet		120 mg	56		305.02
Oxycodone	Oxylan	Tablet		5 mg	28		12.52
Oxycodone	Oxylan	Tablet		10 mg	56		25.04

continued

TABLE 58 Unit costs of pain killer medications considered (*continued*)

Drug	Brand	Form	Preparation	Strength	Size	Volume	Rate (GBP)
Oxycodone	Oxylan	Tablet		20 mg	56		50.08
Oxycodone	Oxylan	Tablet		40 mg	56		100.19
Oxycodone	Oxylan	Tablet		80 mg	56		200.39
Tapentadol	Palexia	Tablet		50 mg	28		12.46
Tapentadol	Palexia	Tablet		50 mg	56		24.91
Tapentadol	Palexia	Tablet		75 mg	28		18.68
Tapentadol	Palexia	Tablet		75 mg	56		37.37
Tapentadol	Palexia SR	Tablet		50 mg	28		12.46
Tapentadol	Palexia SR	Tablet		50 mg	56		24.91
Tapentadol	Palexia SR	Tablet		100 mg	56		49.82
Tapentadol	Palexia SR	Tablet		150 mg	56		74.73
Tapentadol	Palexia SR	Tablet		200 mg	56		99.64
Tapentadol	Palexia SR	Tablet		250 mg	56		124.55
Hydromorphone	Palladone	Tablet		1.3 mg	56		8.82
Hydromorphone	Palladone	Tablet		2.6 mg	56		17.64
Hydromorphone	Palladone SR	Tablet		2 mg	56		20.98
Hydromorphone	Palladone SR	Tablet		4 mg	56		28.75
Hydromorphone	Palladone SR	Tablet		8 mg	56		56.08
Hydromorphone	Palladone SR	Tablet		16 mg	56		106.53
Hydromorphone	Palladone SR	Tablet		24 mg	56		159.82
Cocodamol	Panadol Ultra	Tablet		12.8 mg/500 mg	20		3.61
Paracetamol	Paracetamol	Tablet		500 mg	100		1.53
Paracetamol	Paracetamol	Tablet		500 mg	100		1.5
Paracetamol	Paracetamol	Tablet		500 mg	1000		15.63
Paracetamol	Paracetamol	Tablet		1 g	100		2.5
Paracetamol	Paravict	Tablet		500 mg	100		1.53
Pethidine	Pethidine	Tablet		50 mg	50		49.92
Methadone	Physeptone	Tablet		5 mg	50		2.84
Buprenorphine	Prefibin	Tablet		2 mg	7		0.88
Buprenorphine	Prefibin	Tablet		8 mg	7		1.92
Buprenorphine	Prefibin	Tablet		400 µg	7		1.6
Oxycodone	Reltebon	Tablet		5 mg	28		12.52
Oxycodone	Reltebon	Tablet		10 mg	56		25.04
Oxycodone	Reltebon	Tablet		15 mg	56		38.12
Oxycodone	Reltebon	Tablet		20 mg	56		50.08
Oxycodone	Reltebon	Tablet		30 mg	56		76.23

TABLE 58 Unit costs of pain killer medications considered (*continued*)

Drug	Brand	Form	Preparation	Strength	Size	Volume	Rate (GBP)
Oxycodone	Reltebon	Tablet		40 mg	56		100.19
Oxycodone	Reltebon	Tablet		60 mg	56		152.49
Oxycodone	Reltebon	Tablet		80 mg	56		200.39
Codydramol	Remedeine	Tablet		20 mg/500 mg	56		5.87
Codydramol	Remedeine	Tablet		20 mg/500 mg	112		11.13
Codydramol	Remedeine	Tablet		30 mg/500 mg	56		6.82
Morphine	Sevredol	Tablet		10 mg	56		5.31
Morphine	Sevredol	Tablet		20 mg	56		10.61
Morphine	Sevredol	Tablet		50 mg	56		28.02
Cocodamol	Solpadeine Max	Tablet		12.8 mg/500 mg	20		3.61
Cocodamol	Solpadeine Max	Tablet		12.8 mg/500 mg	30		4.65
Cocodamol	Solpadol	Tablet		30 mg/500 mg	30		0.98
Cocodamol	Solpadol	Tablet		30 mg/500 mg	100		3.27
Buprenorphine	Subutex	Tablet		2 mg	7		0.88
Buprenorphine	Subutex	Tablet		8 mg	7		1.92
Buprenorphine	Subutex	Tablet		400 µg	7		1.6
Buprenorphine	Te mgesic	Tablet		200 µg	50		5.04
Buprenorphine	Te mgesic	Tablet		400 µg	50		10.07
Buprenorphine	Tephine	Tablet		200 µg	50		5.04
Buprenorphine	Tephine	Tablet		400 µg	50		10.07
Tramadol	Tilodol	Tablet		100 mg	60		15.52
Tramadol	Tilodol	Tablet		150 mg	60		23.28
Tramadol	Tilodol	Tablet		200 mg	60		31.04
Tramadol	Tradorec XL	Tablet		100 mg	30		14.1
Tramadol	Tradorec XL	Tablet		200 mg	30		14.98
Tramadol	Tradorec XL	Tablet		300 mg	30		22.47
Tramadol	Tramulief	Tablet		100 mg	60		6.98
Tramadol	Tramulief	Tablet		150 mg	60		10.48
Tramadol	Tramulief	Tablet		200 mg	60		14.28
Tramadol	Zamadol	Tablet		150 mg	28		10.7
Tramadol	Zamadol	Tablet		200 mg	28		14.26
Tramadol	Zamadol	Tablet		300 mg	28		21.39
Tramadol	Zamadol	Tablet		400 mg	28		28.51
Cocodamol	Zapain	Tablet		30 mg/500 mg	100		3.27
Tramadol	Zeridame	Tablet		100 mg	60		17.21

continued

TABLE 58 Unit costs of pain killer medications considered (*continued*)

Drug	Brand	Form	Preparation	Strength	Size	Volume	Rate (GBP)
Tramadol	Zeridame	Tablet		150 mg	60		25.82
Tramadol	Zeridame	Tablet		200 mg	60		34.43
Oxycodone	Zomestine	Tablet		5 mg	28		12.52
Oxycodone	Zomestine	Tablet		20 mg	56		50.08
Oxycodone	Zomestine	Tablet		40 mg	56		100.19
Oxycodone	Zomestine	Tablet		80 mg	56		200.39
Tramadol	Zydol	Tablet		50 mg	60		4.6
Tramadol	Zydol	Tablet		50 mg	20		2.79
Tramadol	Zydol	Tablet		50 mg	100		13.33
Tramadol	Zydol	Tablet		100 mg	60		17.22
Tramadol	Zydol	Tablet		150 mg	60		25.83
Tramadol	Zydol	Tablet		200 mg	60		34.4
Tramadol	Zydol XL	Tablet		150 mg	30		12.18
Tramadol	Zydol XL	Tablet		200 mg	30		17.58
Tramadol	Zydol XL	Tablet		300 mg	30		24.94
Tramadol	Zydol XL	Tablet		400 mg	30		32.47
Tramadol	Zytram	Tablet		75 mg	60		5.15
Tramadol	Zytram	Tablet		100 mg	60		6.94
Tramadol	Zytram	Tablet		150 mg	60		10.39
Tramadol	Zytram	Tablet		200 mg	60		14.19

Note
µg is microgram.

TABLE 59 Unit costs for categories of resource use considered

Resource	Cost of contact (£)	Unit used	Section and page number	Assumption and reference
Counsellor	44.33	Per contact	Section 9 Page 113	Average cost per hour of contact of band 5, 6, and 7 including qualification (PSSRU 2019)
Day care admission	752.00	Per admission	Sheet Index	National Reference Cost (2019)
District nurse home visit	53.20	Per visit	Page 117	Duration of contact 30 minutes, consultation time 30 minutes and travel time 12 minutes for 56 *p* per mile with average 5 miles (PSSRU 2015). Average unit cost per hour of patient-related work for nurse including qualifications from band 5 and 6 (PSSRU 2019)
District nurse surgery visit	36.00	Per visit	Page 117	Duration of contact 30 minutes and consultation time 30 minutes. Average unit cost per hour of patient-related work, nurse including qualifications from band 5 and 6 (PSSRU 2019)
GP home visit	89.60	Per contact	Section 10.3b Page 120 PSSRU 2019, travel time from Section 10.8a Page 176 PSSRU 2015	23.4 minutes of contact including 11.4 minutes of contact (PSSRU 2019) and 12 minutes of travel. Travel is costed for 56 *p* per mile with an average 5 miles (PSSRU 2015).

TABLE 59 Unit costs for categories of resource use considered (*continued*)

Resource	Cost of contact (£)	Unit used	Section and page number	Assumption and reference
GP telephone	15.32	Per contact	Section 10.5 Page 123	GP lead telephone consultation including training. Average time per intervention 4 minutes (PSSRU 2019)
GP surgery visit	34.20	Per contact	Section 10.3b Page 120	For 9.22 minutes of contact excluding direct care costs (PSSRU 2019)
Inpatient hospital admissions	3477.36	Per admission	Sheet Index	Weighted average cost of elective and non-elective inpatient admissions (National Reference Cost 2019)
Occupational therapist	24.00	Per contact	Section 11.4 Page 133	Duration of contact for 30 minutes (PSSRU 2019)
Physiotherapy	31.50	Per contact	Page 113	Duration of contact 35 minutes. Unit cost per hour including qualifications for band 7 (PSSRU 2019)
Practice nurse	14.47	Per contact	Section 10.2 page 118 PSSRU 2019, contact time from Section 10.6 Page 174 PSSRU2015	Duration of contact 15.5 minutes (PSSRU 2015). Unit cost per hour face-to-face contact including qualifications (PSSRU 2019)
Psychologist	92.60	Per contact	Section 9 Page 113	Duration of contact 1 hour. Per hour including qualifications band 7, 8a–b, 8c–d, 8d–9 (PSSRU 2019)
Social worker	51.00	Per contact	Section 11.1 Page 130	Per hour of contact (PSSRU 2019)

Note
Unit used is per contact/visit/admission.

TABLE 60 Missing outcome data

	Complete cases across variables		Complete cases per variable		Full cases (imputation)*	
	Usual care	I-WOTCH	Usual care	I-WOTCH	Usual care	I-WOTCH
ADL	102 (33.66)	133 (43.60)	146 (48.18)	182 (59.67)	303 (100)	305 (100)
EQ-5D-5L	102 (33.66)	133 (43.60)	146 (48.18)	180 (59.02)	303 (100)	305 (100)
ShOWS	102 (33.66)	133 (43.60)	113 (37.29)	147 (48.20)	303 (100)	305 (100)
Medication use	102 (33.66)	133 (43.60)	143 (47.19)	174 (57.05)	303 (100)	305 (100)
Inpatient admission	102 (33.66)	133 (43.60)	112 (36.96)	149 (48.85)	303 (100)	305 (100)
Day case admission	102 (33.66)	133 (43.60)	113 (37.29)	147 (48.20)	303 (100)	305 (100)
Social care contacts	102 (33.66)	133 (43.60)	119 (39.27)	158 (51.80)	303 (100)	305 (100)

* Multiple imputation carried out using predictive mean matching.

TABLE 61 Generalised linear mixed-model coefficients for measure of health benefit for ITT population; Other gender treated as 'Other'

	ADL			ShOWS			EQ-5D-3L		
Parameter	Coefficient (log scale)	SE	*p*-value	Coefficient (log scale)	SE	*p*-value	Coefficient (logit scale)	SE	*p*-value
Intercept	62.321 (4.132)	2.298	≤ 0.001	13.685 (2.616)	3.220	≤ 0.001	0.682 (0.763)	0.056	0.010
Intervention (I-WOTCH)	1.003 (0.003)	0.007	0.706	1.009 (0.009)	0.035	0.784	0.497 (−0.012)	0.013	0.803
Follow-up time	0.984 (−0.016)	0.002	≤ 0.001	0.957 (−0.044)	0.023	0.119	0.508 (0.032)	0.003	0.003
Age	0.999 (−0.001)	0.000	≤ 0.001	0.988 (−0.012)	0.001	≤ 0.001	0.502 (0.008)	0.001	≤ 0.001
Gender (male)	0.988 (−0.012)	0.007	0.086	0.967 (−0.034)	0.031	0.277	0.513 (0.052)	0.014	0.342
Gender (other)	0.874 (−0.135)	0.070	0.069	0.437 (−0.828)	0.266	0.039	0.731 (1.000)	0.088	0.113
Pain duration (1–5 years)	1.069 (0.067)	0.035	0.037	1.087 (0.084)	0.204	0.600	0.411 (−0.360)	0.067	0.186
Pain duration (more than 5 years)	1.073 (0.070)	0.036	0.031	1.165 (0.152)	0.218	0.339	0.412 (−0.356)	0.067	0.190
Opioid intake duration (1–5 years)	0.983 (−0.017)	0.021	0.427	0.902 (−0.103)	0.083	0.223	0.556 (0.225)	0.037	0.142
Opioid intake duration (more than 5 years)	0.983 (−0.017)	0.021	0.413	0.941 (−0.061)	0.086	0.471	0.524 (0.096)	0.038	0.540
Opioid use band (30–59 mg)	1.037 (0.036)	0.010	≤ 0.001	1.043 (0.042)	0.053	0.388	0.426 (−0.298)	0.018	≤ 0.001
Opioid use band (60–89 mg)	1.046 (0.045)	0.012	≤ 0.001	1.025 (0.025)	0.063	0.667	0.420 (−0.323)	0.023	0.001
Opioid use band (90–119 mg)	1.047 (0.046)	0.015	0.001	1.077 (0.075)	0.084	0.309	0.408 (−0.372)	0.028	0.001
Opioid use band (120–149 mg)	1.050 (0.049)	0.016	0.001	1.083 (0.079)	0.090	0.305	0.397 (−0.418)	0.029	≤ 0.001
Opioid use band (≥ 150 mg)	1.057 (0.056)	0.011	≤ 0.001	1.163 (0.151)	0.064	0.004	0.364 (−0.558)	0.021	≤ 0.001
Pain severity (high)	1.096 (0.091)	0.015	≤ 0.001	1.409 (0.343)	0.099	≤ 0.001	0.348 (−0.628)	0.023	≤ 0.001

Note
Coefficients and SEs for the EQ-5D regression are displayed on the original scale (probability). Coefficients are also presented on their back transformed scale. Both the ADL and ShOWs models provide estimates on the log scale which are additive on this scale (multiplicative on the back-transformed scale). Therefore, for ADL and ShOWs if a coefficient is > 1 the parameter increases health benefit, where as if the coefficient is < 1 the parameter decreases health benefit. For the EQ-5D-3L statistical model, which provides estimates on the logit scale, if the coefficient is > 0.5, the parameter increases health benefit. If the coefficient is < 0.5, the parameter decreases health benefit. The following reference categories were used for the categorical variables: intervention, best standard of care; gender, female; pain duration, < 1 year; opioid intake duration, < 1 year; opioid use band, 0–29 mg; pain severity, low.

Example calculation using coefficient values

The coefficients on the Logit scale are used in the equation (2) outlined on page 36 of the main report in order to calculate logOdds. The example below is to calculate EQ-5D-3L for a patient with the following characteristics (see *Table 62*):

- Is randomised to the I-WOTCH arm.
- Record is taken at the 12th follow-up visit.
- 65 years old.

- Male.
- Pain duration less than a year.
- Opioid intake duration (1–5 years).
- Opioid use band (120–149 mg).
- High pain severity.

TABLE 62 Example calculation using coefficient values

Parameter	Coefficient on logit scale	Input	Coefficient × Input
Intercept	0.762978275	1	0.762978275
Intervention (I-WOTCH)	−0.012000144	1	−0.012000144
Follow-up time	0.032002731	12	0.384032773
Age	0.008000043	65	0.520002773
Gender (male)	0.052011722	1	0.052011722
Gender (other)	0.99970208	0	0
Pain duration (1–5 years)	−0.359832969	0	0
Pain duration (more than 5 years)	−0.355703599	0	0
Opioid intake duration (1–5 years)	0.224943732	1	0.224943732
Opioid intake duration (more than 5 years)	0.09607383	0	0
Opioid use band (30–59 mg)	−0.29819005	0	0
Opioid use band (60–89 mg)	−0.322773392	0	0
Opioid use band (90–119 mg)	−0.37223946	0	0
Opioid use band (l20–149 mg)	−0.417980916	1	−0.417980916
Opioid use band (≥ 150 mg)	−0.558044696	0	0
Pain severity (high)	−0.627842082	0	0

TABLE 63 Generalised linear mixed-model coefficients for measure of health benefit for ITT population; other gender treated as 'Female'

	ADL			ShOWS			EQ-5D-3L		
Parameter	Coefficient (log scale)	SE	*p*-value	Coefficient (log scale)	SE	*p*-value	Coefficient (logit scale)	SE	*p*-value
Intercept	62.369 (4.133)	2.509	≤ 0.001	13.187 (2.579)	3.113	≤ 0.001	0.706 (0.876)	0.055	0.004
Intervention (I-WOTCH)	1.002 (0.002)	0.007	0.728	1.007 (0.007)	0.035	0.841	0.498 (−0.008)	0.013	0.849
Follow-up time	0.984 (−0.016)	0.002	≤ 0.001	0.957 (−0.044)	0.023	0.117	0.508 (0.032)	0.003	0.005
Age	0.999 (−0.001)	0.000	≤ 0.001	0.989 (−0.011)	0.001	≤ 0.001	0.502 (0.008)	0.001	≤ 0.001
Gender (male)	0.988 (−0.012)	0.006	0.047	0.966 (−0.035)	0.030	0.251	0.510 (0.040)	0.014	0.462
Pain duration (1–5 years)	1.056 (0.054)	0.035	0.098	1.125 (0.118)	0.229	0.492	0.400 (−0.405)	0.072	0.167
Pain duration (more than 5 years)	1.062 (0.060)	0.035	0.061	1.196 (0.179)	0.229	0.271	0.403 (−0.393)	0.070	0.164
Opioid intake duration (1–5 years)	0.991 (−0.009)	0.023	0.682	0.895 (−0.111)	0.086	0.209	0.553 (0.213)	0.036	0.161

continued

TABLE 63 Generalised linear mixed-model coefficients for measure of health benefit for ITT population; other gender treated as 'Female' (*continued*)

	ADL			ShOWS			EQ-5D-3L		
Parameter	Coefficient (log scale)	SE	*p*-value	Coefficient (log scale)	SE	*p*-value	Coefficient (logit scale)	SE	*p*-value
Opioid intake duration (more than 5 years)	0.992 (−0.008)	0.022	0.721	0.940 (−0.061)	0.087	0.468	0.517 (0.068)	0.038	0.660
Opioid use band (30–59 mg)	1.038 (0.037)	0.009	≤ 0.001	1.043 (0.042)	0.053	0.381	0.422 (−0.315)	0.019	≤ 0.001
Opioid use band (60–89 mg)	1.048 (0.047)	0.012	≤ 0.001	1.026 (0.025)	0.063	0.662	0.420 (−0.323)	0.023	0.001
Opioid use band (90–119 mg)	1.043 (0.042)	0.014	0.001	1.056 (0.054)	0.081	0.451	0.409 (−0.368)	0.029	0.002
Opioid use band (120–149 mg)	1.045 (0.044)	0.016	0.003	1.082 (0.079)	0.089	0.307	0.398 (−0.414)	0.030	0.001
Opioid use band (≥ 150 mg)	1.056 (0.054)	0.011	≤ 0.001	1.164 (0.152)	0.064	0.004	0.361 (−0.571)	0.021	≤ 0.001
Pain severity (high)	1.096 (0.092)	0.014	≤ 0.001	1.411 (0.344)	0.100	≤ 0.001	0.347 (−0.632)	0.024	≤ 0.001

Note
Coefficients and SEs are displayed on the original scale (probability). Coefficients are also presented on their back-transformed scale. Both the ADL and ShOWs models provide estimates on the log scale which are additive while multiplicative on the back-transformed scale. Therefore, for ADL and ShOWs if a coefficient is > 1 the parameter increases health benefit, where as if the coefficient is < 1 the parameter decreases health benefit. For the EQ-5D-3L statistical model, which provides estimates on the logit scale, if the coefficient is > 0.5, the parameter increases health benefit. If the coefficient is < 0.5, the parameter decreases health benefit. The following reference categories were used for the categorical variables: intervention, best standard of care; gender, female; pain duration, < 1 year; opioid intake duration, < 1 year; opioid use band, 0–29 mg; pain severity, low.

The sum of the logOdds (coefficient × input column) is 1.514. This is then converted to a score between 0 and 1 using the following formula:

$$\text{EQ} - \text{5D} - \text{3L} \quad \text{score} \quad = \frac{\exp(logOdds)}{1+\exp(logOdds)} = \quad \frac{\exp(1.514)}{1+\exp(1.514)} = 0.820$$

TABLE 64 Generalised linear mixed-model coefficients for measure of health benefit for ITT population; other gender treated as 'Male'

	ADL			ShOWS			EQ-5D-3L		
Parameter	Coefficient (log scale)	SE	*p*-value	Coefficient (log scale)	SE	*p*-value	Coefficient (logit scale)	SE	*p*-value
Intercept	62.598 (4.137)	2.492	≤ 0.001	13.357 (2.592)	3.117	≤ 0.001	0.693 (0.814)	0.055	0.006
Intervention (I-WOTCH)	1.001 (0.001)	0.006	0.827	1.006 (0.006)	0.035	0.849	0.497 (−0.012)	0.013	0.833
Follow-up time	0.984 (−0.016)	0.002	≤ 0.001	0.957 (−0.044)	0.023	0.117	0.508 (0.032)	0.003	0.004
Age	0.999 (−0.001)	0.000	0.001	0.989 (−0.011)	0.001	≤ 0.001	0.502 (0.008)	0.001	≤ 0.001
Gender (male)	0.986 (−0.014)	0.006	0.026	0.963 (−0.038)	0.031	0.224	0.511 (0.044)	0.013	0.430
Pain duration (1–5 years)	1.067 (0.065)	0.034	0.036	1.110 (0.104)	0.208	0.514	0.398 (−0.414)	0.070	0.146
Pain duration (more than 5 years)	1.070 (0.067)	0.033	0.026	1.170 (0.157)	0.211	0.310	0.404 (−0.389)	0.067	0.151
Opioid intake duration (1–5 years)	0.983 (−0.018)	0.018	0.342	0.900 (−0.105)	0.083	0.214	0.559 (0.237)	0.038	0.135
Opioid intake duration (more than 5 years)	0.983 (−0.017)	0.019	0.371	0.952 (−0.049)	0.086	0.555	0.525 (0.100)	0.038	0.518
Opioid use band (30–59 mg)	1.036 (0.035)	0.010	≤ 0.001	1.044 (0.043)	0.053	0.373	0.426 (−0.298)	0.018	≤ 0.001
Opioid use band (60–89 mg)	1.054 (0.053)	0.012	≤ 0.001	1.026 (0.025)	0.063	0.663	0.420 (−0.323)	0.023	0.001
Opioid use band (90–119 mg)	1.044 (0.043)	0.014	0.001	1.055 (0.054)	0.081	0.454	0.411 (−0.360)	0.027	0.001
Opioid use band (120–149 mg)	1.043 (0.042)	0.016	0.006	1.081 (0.078)	0.089	0.310	0.398 (−0.414)	0.029	0.001
Opioid use band (≥ 150 mg)	1.055 (0.053)	0.011	≤ 0.001	1.163 (0.151)	0.064	0.004	0.363 (−0.562)	0.022	≤ 0.001
Pain severity (high)	1.093 (0.089)	0.013	≤ 0.001	1.411 (0.344)	0.100	≤ 0.001	0.348 (−0.628)	0.024	≤ 0.001

Note
Coefficients and SEs are displayed on the original scale (probability). Coefficients are also presented on their back-transformed scale. Both the ADL and ShOWS models provide estimates on the log scale which are additive while multiplicative on the back-transformed scale. Therefore, for ADL and ShOWS if a coefficient is > 1 the parameter increases health benefit, where as if the coefficient is < 1 the parameter decreases health benefit. For the EQ-5D-3L statistical model, which provides estimates on the logit scale, if the coefficient is > 0.5, the parameter increases health benefit. If the coefficient is < 0.5, the parameter decreases health benefit. The following reference categories were used for the categorical variables: intervention, best standard of care; gender, female; pain duration, < 1 year; opioid intake duration, < 1 year; opioid use band, 0–29 mg; pain severity, low.

TABLE 65 Generalised linear mixed-model coefficients for measure of health benefit for PP population; other gender treated as 'Other'

	ADL			ShOWS			EQ-5D-3L		
Parameter	Coefficient (log scale)	SE	*p*-value	Coefficient (log scale)	SE	*p*-value	Coefficient (logit scale)	SE	*p*-value
Intercept	61.705 (4.122)	2.535	≤ 0.001	12.487 (2.525)	3.333	≤ 0.001	0.689 (0.795)	0.065	0.024
Intervention (I-WOTCH)	0.995 (−0.005)	0.008	0.553	0.955 (−0.046)	0.058	0.432	0.511 (0.044)	0.016	0.497
Follow-up time	0.983 (−0.017)	0.002	≤ 0.001	0.958 (−0.042)	0.039	0.331	0.508 (0.032)	0.003	0.006
Age	0.999 (−0.001)	0.000	0.001	0.989 (−0.011)	0.002	≤ 0.001	0.502 (0.008)	0.001	≤ 0.001

continued

TABLE 65 Generalised linear mixed-model coefficients for measure of health benefit for PP population; other gender treated as 'Other' (*continued*)

Parameter	ADL			ShOWS			EQ-5D-3L		
	Coefficient (log scale)	SE	*p*-value	Coefficient (log scale)	SE	*p*-value	Coefficient (logit scale)	SE	*p*-value
Gender (male)	0.993 (−0.007)	0.007	0.334	0.980 (−0.020)	0.038	0.590	0.502 (0.008)	0.016	0.920
Gender (other)	0.883 (−0.124)	0.070	0.093	0.460 (−0.776)	0.293	0.061	0.732 (1.005)	0.089	0.123
Pain duration (1–5 years)	1.084 (0.081)	0.042	0.030	1.149 (0.139)	0.274	0.480	0.401 (−0.401)	0.080	0.216
Pain duration (more than 5 years)	1.085 (0.082)	0.042	0.028	1.221 (0.199)	0.284	0.299	0.395 (−0.426)	0.079	0.183
Opioid intake duration (1–5 years)	0.971 (−0.029)	0.020	0.150	0.916 (−0.088)	0.116	0.438	0.563 (0.253)	0.040	0.136
Opioid intake duration (more than 5 years)	0.970 (−0.030)	0.020	0.125	0.971 (−0.029)	0.126	0.803	0.545 (0.180)	0.041	0.287
Opioid use band (30–59 mg)	1.041 (0.040)	0.011	≤ 0.001	1.051 (0.050)	0.059	0.351	0.426 (−0.298)	0.022	0.001
Opioid use band (60–89 mg)	1.053 (0.051)	0.013	≤ 0.001	1.001 (0.001)	0.073	0.989	0.422 (−0.315)	0.029	0.009
Opioid use band (90–119 mg)	1.046 (0.045)	0.016	0.004	1.117 (0.110)	0.101	0.189	0.395 (−0.426)	0.033	0.002
Opioid use band (120–149 mg)	1.048 (0.047)	0.019	0.009	1.117 (0.110)	0.108	0.211	0.402 (−0.397)	0.038	0.010
Opioid use band (≥ 150 mg)	1.060 (0.058)	0.012	≤ 0.001	1.141 (0.132)	0.069	0.021	0.358 (−0.584)	0.023	≤ 0.001
Pain severity (high)	1.106 (0.101)	0.016	≤ 0.001	1.409 (0.343)	0.133	≤ 0.001	0.350 (−0.619)	0.028	≤ 0.001

Note
Coefficients and SEs are displayed on the original scale (probability). Coefficients are also presented on their back-transformed scale. Both the ADL and ShOWS models provide estimates on the log scale which are additive while multiplicative on the back-transformed scale. Therefore, for ADL and ShOWS if a coefficient is > 1 the parameter increases health benefit, where as if the coefficient is < 1 the parameter decreases health benefit. For the EQ-5D-3L statistical model, which provides estimates on the logit scale, if the coefficient is > 0.5, the parameter increases health benefit. If the coefficient is < 0.5, the parameter decreases health benefit. The following reference categories were used for the categorical variables: intervention, best standard of care; gender, female; pain duration, < 1 year; Opioid intake duration, < 1 year; opioid use band, 0–29 mg; pain severity, low.

TABLE 66 Generalised linear model coefficients for total annual costs (ITT population)

	Total cost (other gender treated as 'Other')			Total cost (other gender treated as 'Female')			Total cost (other gender treated as 'Male')		
Parameter	Coefficient (log scale)	SE	*p*-value	Coefficient (log scale)	SE	*p*-value	Coefficient (log scale)	SE	*p*-value
Intercept	1204.133 (7.094)	2319.130	≤ 0.001	1188.165 (7.080)	2284.988	≤ 0.001	1191.625 (7.083)	2292.936	≤ 0.001
Intervention (I-WOTCH)	1.336 (0.289)	0.213	0.037	1.331 (0.287)	0.212	0.040	1.332 (0.287)	0.212	0.039
Age	1.003 (0.003)	0.006	0.548	1.004 (0.004)	0.006	0.521	1.004 (0.004)	0.006	0.518
Gender (male)	1.022 (0.021)	0.167	0.879	1.024 (0.023)	0.168	0.870	1.018 (0.017)	0.166	0.903
Gender (other)	0.219 (−1.518)	3.216	0.381	NA	NA	NA	NA	NA	NA
Pain duration (1–5 years)	0.771 (−0.260)	1.244	0.721	0.778 (−0.251)	1.255	0.730	0.774 (−0.256)	1.249	0.725
Pain duration (more than 5 years)	0.822 (−0.196)	1.281	0.783	0.822 (−0.196)	1.282	0.784	0.819 (−0.200)	1.277	0.780
Opioid intake duration (1–5 years)	1.194 (0.178)	0.701	0.650	1.188 (0.172)	0.698	0.659	1.191 (0.174)	0.699	0.655
Opioid intake duration (more than 5 years)	0.840 (−0.174)	0.495	0.657	0.842 (−0.171)	0.496	0.662	0.843 (−0.170)	0.497	0.664
Opioid use band (30–59 mg)	1.515 (0.415)	0.380	0.042	1.516 (0.416)	0.381	0.042	1.515 (0.416)	0.380	0.042
Opioid use band (60–89 mg)	1.524 (0.421)	0.498	0.096	1.526 (0.422)	0.498	0.095	1.524 (0.421)	0.498	0.096
Opioid use band (90–119 mg)	1.605 (0.473)	0.677	0.124	1.569 (0.451)	0.651	0.138	1.567 (0.449)	0.649	0.139
Opioid use band (120–149 mg)	1.300 (0.262)	0.592	0.421	1.299 (0.262)	0.592	0.421	1.299 (0.261)	0.592	0.422
Opioid use band (≥ 150 mg)	2.188 (0.783)	0.632	0.001	2.189 (0.784)	0.633	0.001	2.188 (0.783)	0.632	0.001
Pain severity (high)	1.196 (0.179)	0.428	0.511	1.195 (0.178)	0.428	0.512	1.195 (0.178)	0.428	0.511

Note
Coefficients and SEs are displayed on the original scale. Coefficients are also presented on their back-transformed scale. A one unit increase in the parameter will cause the total cost to increase or decrease by the coefficient value on the natural log scale (using the log scale coefficients). The following reference categories were used for the categorical variables: intervention, best standard of care; gender, female; pain duration, < 1 year; opioid intake duration, < 1 year; Opioid use band, 0–29 mg; pain severity, low.

TABLE 67 Generalised linear model coefficients for total annual costs (PP population)

Parameter	Total cost (other gender treated as 'Other')		
	Coefficient	SE	*p*-value
Intercept	921.416 (6.826)	2295.395	≤ 0.001
Intervention (I-WOTCH)	1.707 (0.535)	0.351	0.002
Age	1.003 (0.003)	0.007	0.688
Gender (male)	0.860 (−0.151)	0.167	0.360
Gender (other)	0.172 (−1.761)	2.494	0.308
Pain duration (1–5 years)	1.464 (0.381)	3.134	0.651
Pain duration (more than 5 years)	1.555 (0.441)	3.196	0.593
Opioid intake duration (1–5 years)	1.029 (0.028)	0.766	0.951
Opioid intake duration (more than 5 years)	0.669 (−0.402)	0.500	0.383
Opioid use band (30–59 mg)	1.546 (0.436)	0.466	0.067
Opioid use band (60–89 mg)	1.094 (0.090)	0.418	0.752
Opioid use band (90–119 mg)	1.371 (0.316)	0.704	0.375
Opioid use band (120–149 mg)	1.130 (0.122)	0.676	0.757
Opioid use band (≥ 150 mg)	2.022 (0.704)	0.675	0.006
Pain severity (high)	1.148 (0.138)	0.500	0.662

Note
Coefficients and SEs are displayed on the original scale. Coefficients are also presented on their back-transformed scale. A one unit increase in the parameter will cause the total cost to increase or decrease by the coefficient value on the natural log scale (using the log scale coefficients). The following reference categories were used for the categorical variables: intervention, best standard of care; gender, female; pain duration, < 1 year; opioid intake duration, < 1 year; opioid use band, 0–29 mg; pain severity, low.

TABLE 68 Annual probability of death by age for base-case population

Age	Probability for men	Probability for women	Source
0	0.004	0.004	Office for National Statistics. Deaths registered in England and Wales 2019 (Available from: www.ons.gov.uk/) peoplepopulationandcommunity/birthsdeathsandmarriages/deaths (accessed on 17 December 2019).
1	0.000	0.000	
2	0.000	0.000	
3	0.000	0.000	
4	0.000	0.000	
5	0.000	0.000	
6	0.000	0.000	
7	0.000	0.000	
8	0.000	0.000	
9	0.000	0.000	
10	0.000	0.000	
11	0.000	0.000	
12	0.000	0.000	

TABLE 68 Annual probability of death by age for base-case population (*continued*)

Age	Probability for men	Probability for women	Source
13	0.000	0.000	
14	0.000	0.000	
15	0.000	0.000	
16	0.000	0.000	
17	0.000	0.000	
18	0.000	0.000	
19	0.000	0.000	
20	0.001	0.000	
21	0.001	0.000	
22	0.001	0.000	
23	0.001	0.000	
24	0.001	0.000	
25	0.001	0.000	
26	0.001	0.000	
27	0.001	0.000	
28	0.001	0.000	
29	0.001	0.000	
30	0.001	0.000	
31	0.001	0.000	
32	0.001	0.000	
33	0.001	0.000	
34	0.001	0.001	
35	0.001	0.001	
36	0.001	0.001	
37	0.001	0.001	
38	0.001	0.001	
39	0.001	0.001	
40	0.002	0.001	
41	0.002	0.001	
42	0.002	0.001	
43	0.002	0.001	
44	0.002	0.001	
45	0.002	0.001	
46	0.002	0.002	
47	0.003	0.002	
48	0.003	0.002	

continued

TABLE 68 Annual probability of death by age for base-case population (*continued*)

Age	Probability for men	Probability for women	Source
49	0.003	0.002	
50	0.003	0.002	
51	0.004	0.002	
52	0.004	0.003	
53	0.004	0.003	
54	0.004	0.003	
55	0.005	0.003	
56	0.005	0.004	
57	0.006	0.004	
58	0.006	0.004	
59	0.007	0.005	
60	0.008	0.005	
61	0.008	0.005	
62	0.009	0.006	
63	0.010	0.007	
64	0.011	0.007	
65	0.012	0.008	
66	0.013	0.009	
67	0.014	0.009	
68	0.016	0.010	
69	0.017	0.011	
70	0.018	0.012	
71	0.020	0.013	
72	0.022	0.015	
73	0.026	0.017	
74	0.028	0.019	
75	0.031	0.021	
76	0.035	0.024	
77	0.039	0.027	
78	0.044	0.031	
79	0.048	0.034	
80	0.054	0.038	
81	0.060	0.044	
82	0.067	0.049	
83	0.075	0.056	
84	0.085	0.064	

TABLE 68 Annual probability of death by age for base-case population (*continued*)

Age	Probability for men	Probability for women	Source
85	0.095	0.072	
86	0.107	0.083	
87	0.119	0.093	
88	0.133	0.106	
89	0.150	0.119	
90	0.160	0.134	
91	0.179	0.151	
92	0.197	0.167	
93	0.215	0.184	
94	0.238	0.204	
95	0.261	0.228	
96	0.287	0.251	
97	0.304	0.267	
98	0.326	0.291	
99	0.370	0.310	
100	0.384	0.343	
101	1.000	1.000	

TABLE 69 Input parameters used in the state-transition model (PP scenario)

Input	Source	Description	Mean value (best usual care)	Mean value (I-WOTCH)
Transition probability (0–4 months)				
LTOT to IST	PtQ	Proportion of people engaged in IST	NA	0.563
LTOT to NIST	PtQ	Proportion of people engaged in NIST	0.571	0
LTOT to OF	PtQ	Proportion of people stopping any use of opioids	0.030	0.278
Remaining in LTOT	PtQ	Proportion of people who do not engage in IST and remain in LTOT	0.399	0.159
IST to LTOT	PtQ	Proportion of people withdrawing from IST	NA	0
IST to OF	PtQ	Proportion of people stopping any use of opioids	NA	0
Remaining in IST	PtQ	Proportion of people who remain engaging in IST	NA	1
NIST to LTOT	PtQ	Proportion of people withdrawing from NIST	0	NA
NIST to OF	PtQ	Proportion of people from NIST and stop any use of opioids	0	NA
Remaining in NIST	PtQ	Proportion of people who remain in NIST over time	1	NA
OF to LTOT	PtQ	Proportion of people who had remained OF but then restarted	0	0
Remaining in OF	PtQ	Proportion of people who remain OF	1	1

continued

TABLE 69 Input parameters used in the state-transition model (PP scenario) (*continued*)

Input	Source	Description	Mean value (best usual care)	Mean value (I-WOTCH)
Transition probability (5–8 months)				
LTOT to IST	PtQ	Proportion of people engaged in IST	NA	0.667
LTOT to NIST	PtQ	Proportion of people engaged in NIST	0.625	NA
LTOT to OF	PtQ	Proportion of people stopping any use of opioids	0.063	0.133
Remaining in LTOT	PtQ	Proportion of people who do not engage in IST and remain in LTOT	0.312	0.200
IST to LTOT	PtQ	Proportion of people withdrawing from IST	NA	0.185
IST to OF	PtQ	Proportion of people stopping any use of opioids	NA	0.099
Remaining in IST	PtQ	Proportion of people who remain engaging in IST	NA	0.716
NIST to LTOT	PtQ	Proportion of people withdrawing from NIST	0.283	NA
NIST to OF	PtQ	Proportion of people from NIST and stop any use of opioids	0.023	NA
Remaining in NIST	PtQ	Proportion of people who remain in NIST over time	0.694	NA
OF to LTOT	PtQ	Proportion of people who had remained OF but then restarted	0.444	0.200
Remaining in OF	PtQ	Proportion of people who remain OF	0.556	0.800
Transition probability (9–12 months)				
LTOT to IST	PtQ	Proportion of people engaged in IST	NA	0.115
LTOT to NIST	PtQ	Proportion of people engaged in NIST	0.534	0.192
LTOT to OF	PtQ	Proportion of people stopping any use of opioids	0.055	0.192
Remaining in LTOT	PtQ	Proportion of people who do not engage in IST and remain in LTOT	0.411	0.5
IST to LTOT	PtQ	Proportion of people withdrawing from IST	NA	0.235
IST to OF	PtQ	Proportion of people stopping any use of opioids	NA	0.074
Remaining in IST	PtQ	Proportion of people who remain engaging in IST	NA	0.691
NIST to LTOT	PtQ	Proportion of people withdrawing from NIST	0.262	NA
NIST to OF	PtQ	Proportion of people from NIST and stop any use of opioids	0.025	NA
Remaining in NIST	PtQ	Proportion of people who remain in NIST over time	0.694	NA
OF to LTOT	PtQ	Proportion of people who had remained OF but then restarted	0.385	0.119
Remaining in OF	PtQ	Proportion of people who remain OF	0.615	0.881
Transition probabilities to death				
All states to death	ONS	All-cause mortality rates from ONS[89]	Please see *Table 6*.A	
Utilities (4 months)				
LTOT	CCA		0.421	0.361
IST	CCA		NA	0.407
NIST	CCA		0.364	NA
OF	CCA		0.642	0.564

TABLE 69 Input parameters used in the state-transition model (PP scenario) (*continued*)

Input	Source	Description	Mean value (best usual care)	Mean value (I-WOTCH)
Utilities (8 months)				
LTOT	CCA		0.384	0.362
IST	CCA		NA	0.363
NIST	CCA		0.367	NA
OF	CCA		0.613	0.500
Utilities (12 months)				
LTOT	CCA		0.399	0.422
IST	CCA		NA	0.344
NIST	CCA		0.396	0.508
OF	CCA		0.465	0.506
Costs (4 months)				
LTOT	CCA		£1094.71	£2574.44
IST	CCA		NA	£1286.02
NIST	CCA		£1289.83	NA
OF	CCA		£541.80	£829.22
Costs (8 months)				
LTOT	CCA		£1184.32	£1372.74
IST	CCA		NA	£989.06
NIST	CCA		£1208.47	NA
OF	CCA		£473.80	£816.45
Costs (12 months)				
LTOT	CCA		£1335.17	£896.81
IST	CCA		NA	£1020.23
NIST	CCA		£1100.89	£220.92
OF	CCA		£1268.74	£552.83

PtQ, Patient questionnaire,

Note
Transition probabilities are obtained from the trial PtQ with no death considered. In the economic model, the cyclic dependent probabilities of death from life tables are incorporated.

TABLE 70 Baseline data for I-WOTCH economic evaluation (PP scenario)

Variable	Best usual care (%) *n* = 303	I-WOTCH (%) *n* = 144
Gender		
Female	184 (61.13)	85 (59.03)
Male	117 (38.87)	58 (40.28)
Other	0 (0.00)	1 (0.69)
Pain duration		
< 1 year	3 (1.00)	3 (2.08)
1–5 years	50 (16.61)	17 (11.81)
More than 5 years	248 (82.39)	124 (86.11)
Pain severity		
High	282 (93.07)	134 (93.06)
Low	21 (6.93)	10 (6.94)
Opioid use band		
0–29 mg	164 (54.13)	74 (51.39)
30–59 mg	45 (14.85)	20 (13.89)
60–89 mg	27 (8.91)	14 (9.72)
90–119 mg	17 (5.61)	9 (6.25)
120–149 mg	15 (4.95)	5 (3.47)
150 mg+	35 (11.55)	22 (15.28)
Opioid intake duration		
< 1 year	107 (35.55)	3 (2.08)
1–5 years	18 (5.98)	42 (29.17)
More than 5 years	176 (58.47)	99 (68.75)

Note
Values are counts (percentages) unless otherwise indicated.

TABLE 71 Baseline data for I-WOTCH's economic evaluation analysis (PP scenario)

	Best usual care *n* = 303			I-WOTCH *n* = 144		
Variable	**Mean**	**SD**	**Range**	**Mean**	**SD**	**Range**
Age	60.40	13.75	23–91	62.68	10.33	28–87
Measures of health benefit						
ADLs (PROMIS PI-SF-8A)	68.24	6.16	49–77	68.39	5.93	55–77
Severity of opioid withdrawal symptoms (ShOWS)	10.51	4.96	0–29	10.22	5.20	1–26
Generic health-related quality of life (EQ-5D-5L)	0.45	0.28	−0.29–1	0.44	0.28	−0.19–0.92
Healthcare utilisation						

TABLE 71 Baseline data for I-WOTCH's economic evaluation analysis (PP scenario) (*continued*)

Variable	Best usual care *n* = 303			I-WOTCH *n* = 144		
	Mean	SD	Range	Mean	SD	Range
Medications in MED	68.22	86.17	4.29–810	72.93	92.32	6.25–728.57
Hospital care (use)						
Inpatient stay (no of admissions)	0.14	0.47	0.00–3.00	0.08	0.30	0.00–2.00
Day case admissions	0.32	0.63	0.00–3.00	0.33	0.68	0.00–3.00
Community health and social care						
GP surgery (no. of visits/contacts)	2.82	2.93	0.00–24.00	2.96	2.51	0.00–15.00
GP home (no. of visits/contacts)	0.05	0.28	0.00–3.00	0.05	0.53	0.00–6.00
Practice nurse (no. of visits/contacts)	1.02	1.41	0.00–8.00	1.13	1.97	0.00–16.00
District nurse (i.e. at home) (no. of visits/contacts)	0.17	0.86	0.00–8.00	0.26	1.84	0.00–18.00
District nurse (i.e. at surgery) (no. of visits/contacts)	0.25	1.37	0.00–16.00	0.08	0.43	0.00–4.00
Occupational therapist (no. of visits/contacts)	0.36	2.16	0.00–30.00	0.17	0.50	0.00–2.00
Counsellor (no. of visits/contacts)	0.56	2.33	0.00–16.00	0.40	1.87	0.00–16.00
Psychologist (no. of visits/contacts)	0.28	1.69	0.00–18.00	0.29	1.69	0.00–16.00
Social worker (no. of visits/contacts)	0.21	1.66	0.00–20.00	0.02	0.13	0.00–1.00
Physiotherapist (no. of visits/contacts)	0.83	2.02	0.00–16.00	1.12	2.61	0.00–12.00

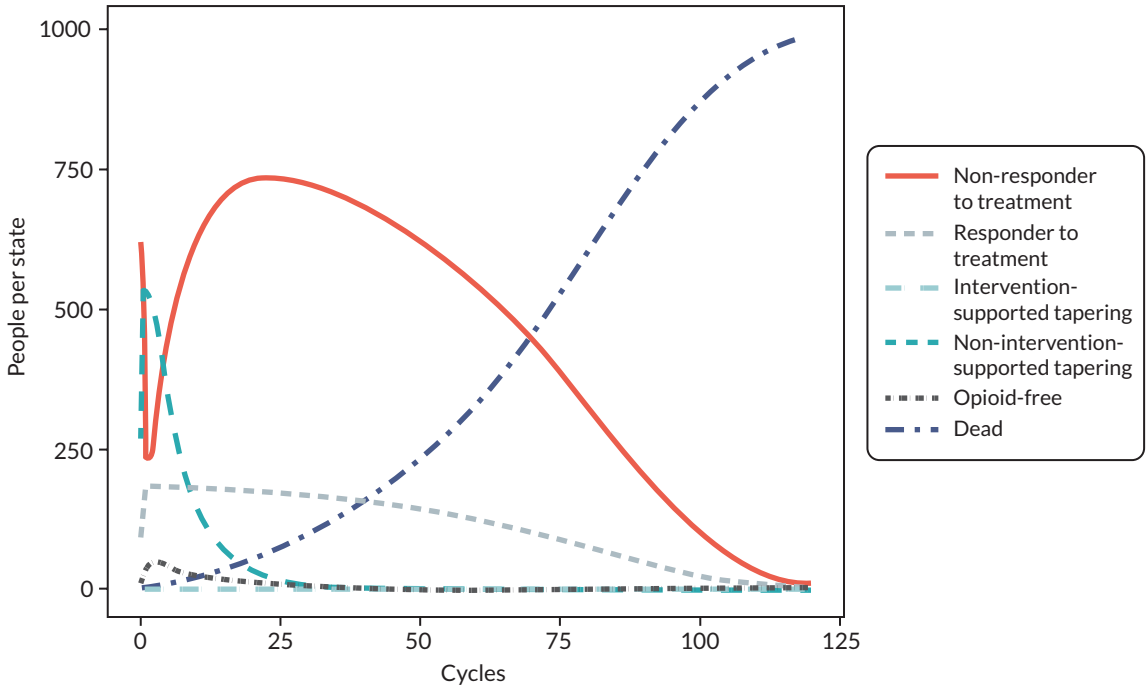

FIGURE 13 Proportion in state chart for baseline economic model (best usual care).

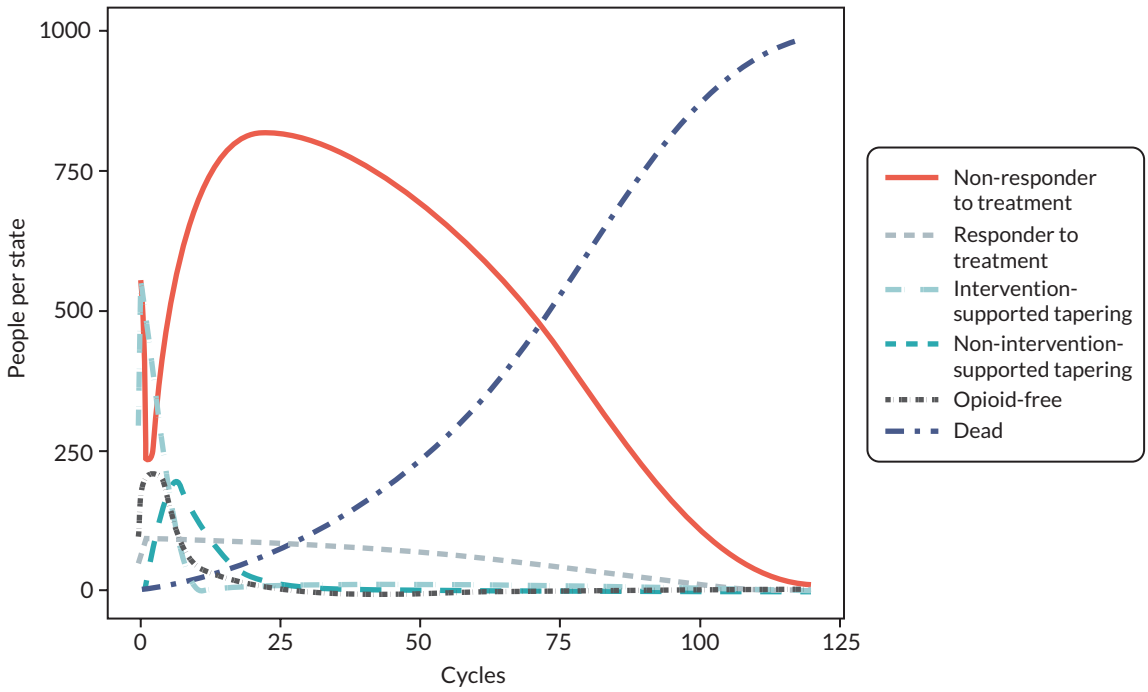

FIGURE 14 Proportion in state chart for baseline economic model (I-WOTCH).

Appendix 5 Process evaluation supplementary materials

TABLE 72 Logic model

The problem	Intervention aims	Intervention	Theory and guidance	Interim targets	Desired outcomes
People with chronic non-malignant pain are taking opioids, which have side effects and are not effective in the long term.	To test the effectiveness and cost effectiveness of a patient-centred multicomponent self-management intervention targeting withdrawal of strong opioids on ADLs for people living with chronic non-malignant pain	Manualised intervention delivery **Core pain management topics:** • Acute vs. Chronic pain • Acceptance • Attention control and distraction • the pain cycle • Posture and movement advice • Relaxation techniques • Stress busting for health action planning, problem solving, pacing, SMART goal setting • identifying and overcoming barriers to change • Mindfulness • Anger, irritability and frustration • Communication Skills **Core opioid-specific topics:** • The rationale of prescribing in chronic pain • Opioid induced tolerance and need for dose escalation • Evidence of usefulness of opioids short and long term • Side effects of opioids short term and long term • Case studies of successful discontinued opioid therapy • Opioid withdrawal symptoms • Advantages of slow supervised tapering • Symptom management during tapering • Pain control after opioids	Theory of Planned Behaviour Social Cognitive Theory Information Motivation and Behavioural (IMB model) skills Patient-Centred Communication Motivational Interviewing	Staff training To facilitate groups, deliver individual tapering consultations and telephone support in an inclusive and non-judgemental manner Individual participant changes: a Knowledge of: opioids, withdrawal effects, chronic pain b Fostering change: self-validation, legitimising pain, normalising expectations c Motivation to change by: Improved self-efficacy, effective tapering d Skills: • General self-regulation Psychological skills Identify reasons for negative emotions (anger/frustration/irritable) Identify problems and solutions, barriers to change Recognise errors in thinking/automatic thoughts Goal setting, goal review Physical skills Promote body awareness, posture Reduce muscle tension Body awareness and core strength Relaxation–contract relax • Pain self-regulation Understand that pain and mood are linked – when is pain bearable and when not bearable. Understanding of pain cycle, unhelpful emotions and behaviours Using mind to relieve pain does not mean pain in mind Distraction while relaxed Focus mind away from pain Mindfulness for pain Managing flare-ups Need for stretching • Communication skills How to communicate with GPs HCPs Listening skills – active and giving feedback in communication-reward for help.	Primary outcomes: PROMIS-PI-SF-8A Daily morphine equivalent opioid dose

SMART, specific, measurable, achievable, relevant, time-bound.

Day 1/Session 2/Title: pain information 30 minutes

Adherence: of the delivery as per protocol

Instructions:
When at all possible, please rate as 'Yes' or 'No'. If 'partially' then write reason in comments box

Questions need not be verbatim (unless specified) as long as content of session is covered.

TABLE 73 I-WOTCH fidelity day 1 session 2

Number	Item	Adherence	Comments
Intro	Did the facilitator(s) introduce the session?	Yes (2) Partially (1) No (0)	
Step 1	Did the facilitator(s) play the DVD of the biomedical explanation about acute and chronic pain?	Yes (2) Partially (1) No (0)	
	Did the facilitator(s) ask the group Q1 and discuss, 'What do you think about this explanation of pain? Is it missing anything?'	Yes (2) Partially (1) No (0)	
Step 2	Did the facilitator(s) present the bio-psycho-social explanation of pain?	Yes (2) Partially (1) No (0)	
	Did the facilitator(s) ask the group Q2 and discuss, 'What do you think about this explanation of pain?'	Yes (2) Partially (1) No (0)	
Step 3	Did the facilitator(s) play the DVD of Experiences of living with opioid-treated long-term pain?	Yes (2) Partially (1) No (0)	
	Did the facilitator(s) ask the group Q3 and discuss, 'What do you think about Caroline's description of living with opioid-treated long-term pain?'	Yes (2) Partially (1) No (0)	
Summary	Did the facilitator(s) consolidate/embed the group's learning at the end of the session? *For example, reading the summary, putting the session in context*	Yes (2) Partially (1) No (0)	
	Total adherence score (max 16)		
	Percentage adherence score (total adherence score */16 × 100)		

Comments: For use if sessions; go off track, include items which are not on checklist, contain surprising unforeseen aspects or the facilitation was not covered as intended. Also, if there was no opportunity to demonstrate the skill listed.

Day 1/Session 2/Title: pain information and opioid education

Competence of the quality of delivery or 'skill' of the facilitators

	Item	Competence measure	Comments (*use box below to expand*)
1	Did the facilitator(s) create opportunities for discussion, *for example did they; encourage individuals to participate, ask open questions, give enough time for the group to answer (rather than answer their own questions)*	Evident (2) Partially evident (1) Not evident (0) Did not happen in this session (N/A)	
2	Did the facilitator(s) encourage individual disclosure? *For example, did they ask different group members to comment or encourage the group to explore issues further (either individually or as a group)?*	Evident (2) Partially evident (1) Not evident (0) Did not happen in this session (N/A)	
3	Did the facilitator(s) validate participants' disclosures? *For example, do other people find this/think that? I know how you feel. Sometimes people may feel differently about things.*	Evident (2) Partially evident (1) Not evident (0) Did not happen in this session (N/A)	
4	Did the facilitator(s) give encouraging feedback on participants reported behaviours? *For example, did they give appraisal 'that's really good' or 'that's really good but I wonder if …'*	Evident (2) Partially evident (1) Not evident (0) Did not happen in this session (N/A)	
5	Did the facilitator(s) foster a positive group climate? For example, *did they use humour, say positive things about people 'that's a helpful comment' 'thank you for sharing that'*	Evident (2) Partially evident (1) Not evident (0) Did not happen in this session (N/A)	
6	Did the facilitator acknowledge and respond appropriately to admissions or statements of low self-efficacy? For example, *'yes this can be difficult but …' ideas or examples offered of how this may be done. Issues surrounding confidence.*	Evident (2) Partially evident (1) Not evident (0) Did not happen in this session (N/A)	
7	Did the facilitator respond appropriately to disclosures of negative events or barriers to progress?	Evident (2) Partially evident (1) Not evident (0) Did not happen in this session (N/A)	
	Total competence score (max 14)		
	Percentage competence score		

N/A, not applicable.
Comments: For use if sessions; go off track, include items which are not on checklist, contain surprising unforeseen aspects or the facilitation was not covered as intended. Also, if there was no opportunity to demonstrate the skill listed.

TABLE 74 Fidelity data collection checklist (sessions in bold assessed for fidelity)

	*Educational and/or self-management regarding pain or opioid use	Practical, reflection or summarising sessions (not assessed for fidelity, recorded if took place or not)
Day 1	**2, 3, 4, 7, 8**	1, 5, 6, 9, 10, 11
Day 2	**13, 14, 16**	12, 15, 17, 18, 19
Day 3	**21, 22, 23**	20, 22 part 2, 24, 25, 26, 27, 28

DAY 1
Session 1 Introduction
***Session 2 Pain information**
***Session 3 Painkiller information and opioid education**
***Session 4 Acceptance: John's story**
Session 5 Attention control and distraction
Session 6 Distraction activity – rose drawing
***Session 7 Good days, bad days when is pain bearable and when is it not?**
***Session 8 The pain cycle unhelpful emotions and behaviours**
Session 9 Posture
Session 10 Relaxation and breathing
Session 11 Summary of the day

DAY 2
Session 12 Reflections from day 1
***Session 13 Stress-busting – prioritising what's important, action planning, goal setting and pacing**
***Session 14 Withdrawal symptoms, case studies (Opioid Education 2)**
Session 15 Distraction activity- origami
***Session 16 Identifying and overcoming barriers to change Part 1 – recognising unhelpful thinking**
***Identifying and overcoming barriers to change Part 2– reframing negatives to positives**
Session 17 Mindful attention control
Session 18 Balance and introduction to stretch
Session 19 Summary of the day

DAY 3
Session 20 Reflections from day 2 and previous week
***Session 21 Anger, irritability and frustration**
***Session 22 Relationships Part 1 Getting the most from your healthcare team**
Session 22 Part 2 Relationships Part 2 Listening skills
***Session 23 Managing setbacks and non-drug management techniques**
Session 24 Distraction activity – mindfulness colouring
Session 25 Stretching muscles that commonly get tight
Session 26 Mindfulness of thoughts and senses
Session 27 Summary of day 3
Session 28 Summary of the course

TABLE 75 Fidelity first one-to-one nurse consultation

Item	Adherence	Score	Comments *(expand in box below)*
1	Was the participant asked about their thoughts/feelings on reducing their opioids?	Yes (2) Partially (1) No (0)	
2	Was the participant asked about their pain related medication usage?	Yes (2) Partially (1) No (0)	
3	Was the participant's pain discussed?	Yes (2) Partially (1) No (0)	
4	Was a tapering plan discussed/negotiated?	Yes (2) Partially (1) No (0) Not evident	
5	Were temporary withdrawal side effects mentioned?	Yes (2) Partially (1) No (0)	
6	Was a tapering plan summarised and a copy given to the participant?	Yes(2) Partially (1) No (0)	
7	Were barriers to implementing the tapering plan and setbacks discussed?	Yes (2) Partially (1) No (0) Not evident	
8	Did the nurse leave an opportunity for any questions?	Yes (2) Partially (1) No (0)	
9	Did the nurse ensure the participant knew to make an appointment with the GP?	Yes (2) Partially (1) No (0)	
	Total score out of 14 or 18 max		
	Percentage score total score/14 or 18 × 100		
Comments:			
Item	**Competence**	**Score**	**Comments *(expand in box below if nec.)***
1	Did the nurse allow participants to express their concerns/achievements?	Evident (2) Partially evident (1) Not evident (0)	
2	Did the nurse allow participants to discuss and/or explore their concerns/achievements?	Evident (2) Partially evident (1) Not evident (0)	
3	Did the nurse demonstrate empathy? For example, *did they show they understood the participant's feelings?*	Evident (2) Partially evident (1) Not evident (0)	
4	Did the nurse accept the participant's perspective? For example, *did they allow exploration of positive and negative feelings about pain and/or opioids, were they non-judgmental?*	Evident (2) Partially evident (1) Not evident (0)	
5	Did the nurse actively listen to the participant? For example, *did they use 'uhuu', 'oh' 'um' 'really' type of phrases to demonstrate they were listening*	Evident (2) Partially evident (1) Not evident (0)	

TABLE 75 Fidelity first one-to-one nurse consultation (*continued*)

Item	Adherence	Score	Comments *(expand in box below)*
6	Did they support self-efficacy? *For example, did they offer reassurance, suggest other techniques, congratulate them on any successes or small steps in the right direction.*	Evident (2) Partially evident (1) Not evident (0)	
	Total score out of 12 max		
	Percentage score total score/12 × 100		
Comments:			

TABLE 76 Interviewee characteristics and uptake for the interview study

Interviewee ID	Location cohort ID	Gender	Age decade	Opioid usage at 12 months compared to baseline: H = higher S = same L = lower 0 = no opioids	Opioid	Baseline morphine equivalent: 0–29 mg: 30–59 mg: 60–89mg: 90–119 mg 120–149 mg: 150 mg	Allocation Usual care/ intervention
3	1	F	30s	S	Tramadol MR	0–29	ITT
4	1	F	50s	L by half	Tramadol	0–29	UC
6	3	M	60s	H	Tramadol and cocodamol	0–29	UC
8	5 NE	F	60s	0	Zomorph(morphine)	30–59	UC
11	6	F	40s	S	Morphine SR and oromorph	150 +	UC
12	7 NE	F	50s	L	Oxycodone and liquid morphine	90–119	UC
18	8	F	80s	0	Morphine	0–29	UC
17	10	M	70s	S	Tramadol	0–29	UC
15	11	F	70s	H	Tramadol	0–29	UC
23	13	M	70s	H	Liquid morphine and codeine phosphate	0–29	UC
20	9 NE	M	60s	L	Morphine/codeine phosphate/ tramadol	60–89	UC
24	16	M	40/*50*	(S) Still on	Oxycodone changed to fentanyl unknown 12 m ME	90–119	UC
19	17 NE	M	60s	L sl.	Tapentadol/morphine/liquid morphine	60–89	UC
28	18 NE	F	70s	H	Morphine + liquid morphine	150 +	UC
27	19	F	50s	H	Fentanyl patches	150 +	UC
35	20	M	50s	sl L	Tramadol	30–59	UC
33	21	F	80s	Lower by 2/3	Buprenorphine patch	30–59	UC
37	26 NE	F	50s	S	Tramadol	60–89	UC
39	27	F	50s	L (or S)	Buprenorphine to morphine	30–59	UC
40	23 NE	F	60s	0 (or L)	Tramadol to codeine phosphate	0–29	UC
Total 20	7 NE 13 Midlands	7M 13F	Range 30s–80s	5H 5S 7L 30	Range of patches tables and liquid	8 0–29, 4 30–59, 3 60–89, 2 90–119,0 120–149, 3150 +	
Pilot 1	P1	F	70s	0	Dihydrocodeine/morphine	30–59	Int
5	2	M	60s	0	Buprenorphine patches	60–89	Int

TABLE 76 Interviewee characteristics and uptake for the interview study (*continued*)

Interviewee ID	Location cohort ID	Gender	Age decade	Opioid usage at 12 months compared to baseline: H = higher S = same L = lower 0 = no opioids	Opioid	Baseline morphine equivalent: 0–29 mg: 30–59 mg: 60–89mg: 90–119 mg 120–149 mg: 150 mg	Allocation Usual care/ intervention
7	3	F	50s	L sl	Buprenorphine patches	30–59	Int
9	5 NE	M	60s	0	Tramadol	0–29	Int
10	4 NE	F	50s	0	Fentanyl patches	30–59	Int
22	8	M	50s	H	Tramadol/morphine	60–89	Int
13	12 NE	F	50s	0	Tramadol	0–29	Int
14	9 NE	M	60s	S	Tramadol	0–29	Int
16	11	M	60s	H	Oxycodone	30–59	Int
26	13	M	70	L	Morphine	60–89	Int
21	15	F	60s	L sl	Morphine/liquid morphine	150 +	Int
25	16	F	80	L	Buprenorphine patches	30–59	Int
29	17 NE	F	50/60	L	Codeine phosphate and fentanyl patches	150 +	Int
30	22 NE	M	60/70	L	Tramadol	0–29	Int
31	20	F	60s	0	Fentanyl patches	90–119	Int
34	20	F	60s	H(S)	Hydromorphone	150 +	Int
32	21	F	80	L	Oxycodone	60–89	Int
38	24	F	70s	H sl	Tramadol	0–29	Int
36	26 NE	M	70s	L (or 0)	Oxycodone and liquid morphine	150 +	Int
41	29 NE	F	60s	L sl	Fentanyl patches andliquid morphine	30-59	Int
Total 20	8 NE 12 Midlands	8M 12F	Range 50s–80s	4H 1S 9L 60	Range of patches tables and liquid	5 0–29, 5 30–59, 4 60–89, 1 90–119, 0 120–149, 4150 +, 1 unknown	Int

TABLE 77 Baseline demographic characteristics of all randomised participants vs. interviewed participants

	Total *N* = 608	PE interviewees *N* = 40
Age (years)		
N	608	40
Mean (SD)	61.3 (12.9)	64.7 (11.9)
Median (IQR)	62.3 (53.0–70.7)	64.1 (58.5, 71.8)
Missing	0	0
Gender		
Male	242 (39.8%)	15 (37.5%)
Female	362 (59.5%)	25 (62.5%)
Other	1 (0.2%)	0 (0%)
Prefer not to say	0 (0.0%)	0 (0%)
Missing	3 (0.5%)	0 (0%)
Ethnicity		
White	585 (96.2%)	38 (95.0%)
Black Caribbean	6 (1.0%)	1 (2.5%)
Black African	1 (0.2%)	1 (2.5%)
Black Other	1 (0.2%)	0 (0.0%)
Indian	6 (1.0%)	0 (0.0%)
Pakistani	1 (0.2%)	0 (0.0%)
Bangladeshi	0 (0.0%)	0 (0.0%)
Chinese	0 (0.0%)	0 (0.0%)
Prefer not to say	1 (0.2%)	0 (0.0%)
Other	4 (0.7%)	0 (0.0%)
Missing	3 (0.5%)	0 (0.0%)
Employment status		
Employed	132 (21.7%)	6 (15.0%)
Unemployed	14 (2.3%)	0 (0.0%)
At school or full-time education	1 (0.2%)	0 (0.0%)
At school or part-time education	1 (0.2%)	0 (0.0%)
Unable to work due to long-term sickness	154 (25.3%)	13 (32.5%)
Looking after home/family	13 (2.1%)	0 (0.0%)
Retired from paid work	270 (44.4%)	21 (52.5%)
Other	20 (3.3%)	0 (0.0%)
Missing	3 (0.5%)	0 (0.0%)
Age left full-time education		
Did not receive formal education	2 (0.3%)	0 (0.0%)

TABLE 77 Baseline demographic characteristics of all randomised participants vs. interviewed participants (*continued*)

	Total *N* = 608	PE interviewees *N* = 40
Age 12 or less	1 (0.2%)	0 (0.0%)
Age 13–16	345 (56.7%)	21 (52.5%)
Age 17–19	135 (22.2%)	6 (15.0%)
Age 20 or over	109 (17.9%)	12 (30.0%)
Still in full-time education	4 (0.7%)	0 (0.0%)
Other	9 (1.5%)	1 (2.5%)
Missing	3 (0.5%)	0 (0.0%)
How long have you experience pain		
< 1 year	8 (1.3%)	0 (0.0%)
1–5 years	97 (16.0%)	9 (22.5%)
More than 5 years	500 (82.2%)	31 (77.5%)
Missing	3 (0.5%)	0 (0.0%)
How long have you been taking opioids for your chronic pain		
< 1 year	29 (4.8%)	0 (0.0%)
1–5 years	211 (34.7%)	20 (50.0%)
More than 5 years	365 (60.0%)	20 (50.0%)
Missing	3 (0.5%)	0 (0.0%)

TABLE 78 Reasons for declining interview

Reasons for declining interview	
Health – acute, for example operations, investigations, health appointments	7
'Not a good time'; work, trying something else, too busy	7
No reason given	2
Too depressing to go over it when no solution	1
Unable to contact	1

TABLE 79 Fidelity scores of group sessions

Fidelity scores in percentages								
Session	**Adherence** *(italics 10% check)*				**Competence**			
	Early	**Mid**	**Late**	**Total average/ range/median**	**Early**	**Mid**	**Late**	**Total average/ range/ median**
Day 1 session 2	100	81	25 *(25)*		92	64	0 *(0)*	
Day 1 session 3	94 *(94)*	100	44		90 *(87)* agreed 88	86	42	
Day 1 session 4	100	75	88		70	71	67	
Day1 session 7	72	89	83		80	75	90	
Day 1 session 8	100	88	81		100	60	75	
Day 2 session 13	77	88 *(90)* agreed 89	84		57	100*(100)*	100	
Day 2 session 14	56 *(66)* agreed 61	100	94		58*(43)* agreed 50	92	90	
Day 2 session 16	79	88	82		50	70	100	
Day 3 session 21	88	100	89		80	100	100	
Day 3 session 22pt 1	93	86	64		70	92	83	
Day3 session 23	90	73	91		100	100	100	
Average	**86.72**	**88.09**	**75.00**	**83.27%**	**76.09**	**82.73**	**77**	**78.61%**
Range	**61–100**	**73–100**	**25–94**	**25–100**	**50–100**	**60–100**	**0–100**	**0–100**
Median	**90**	**88**	**83**	**88**	**80**	**86**	**90**	**86**

TABLE 80 Fidelity scores of one-to-one nurse consultations

Time point	Fidelity group ID	Adherence score	Competence score
First	1	100%	100%
Second	2	93% *(93%)*	100% *(100%)*
First	3	61%	67%
Second	3	86%	83%
First	4 NE	100%	100%
Second	4 NE	100%	100%
First	5 NE	100%	100%
Second	5 NE	100%	100%
Second	6	100%	100%
First	7 NE	67%	100%
First	8	100%	100%
First	9 NE	83% *(94%)*94	100% *(83%)*92
Second	10	88%	83%

TABLE 80 Fidelity scores of one-to-one nurse consultations (*continued*)

Time point	Fidelity group ID	Adherence score	Competence score
Second	10	100%	100%
Early averages		**92.07%**	**94.64%**
Range		**61–100**	**67–100**
Time point	**Group ID**	**Adherence**	**Competence**
First	11	100%	100%
First	12 NE	94%	100%
Second	12 NE	100%	100%
First	13	89%	92%
First	14 NE	61% *(61%)*	50% *(50%)*
First	15	94%	100%
First	15	94%	100%
Second	20	71%	83%
Mid averages		**87.87%**	**90.63%**
Range		**61–100**	**50–100**
Time point	**Group ID**	**Adherence score**	**Competence score**
			Score
First	21	100%	92%
Second	21	93%	100%
First	24	94%	100%
Second	24	86% *(86%)*	100% *(100%)*
First	27	89%	83%
Late averages		**92.4%**	**95%**
Range		**86–100**	**83–100**
Total averages		**90.78%**	**93.42%**
Range		**61–100**	**50–100**

Source
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TABLE 81 Baseline confidence questions of all randomised participants by treatment group

	Control *N* = 303	Intervention *N* = 305	TOTAL *N* = 608
I want to reduce my opioid use			
Not at all	25 (8.3%)	21 (6.9%)	46 (7.6%)
By a little	45 (14.9%)	37 (12.1%)	82 (13.5%)
By Half	36 (11.9%)	44 (14.4%)	80 (13.2%)
So I only use a little	60 (19.8%)	95 (31.2%)	155 (25.5%)
So I use no opioids	133 (43.9%)	102 (33.4%)	235 (38.7%)
Missing	4 (1.3%)	6 (2.0%)	10 (1.6%)
I expect in 4 months' time, I will have reduced my opioid use			
Not at all	45 (14.9%)	43 (14.1%)	88 (14.5%)
By a little	78 (25.7%)	82 (26.9%)	160 (26.3%)
By half	56 (18.5%)	56 (18.4%)	112 (18.4%)
So I only use a little	67 (22.1%)	82 (26.9%)	149 (24.5%)
So I use no opioids	50 (16.5%)	37 (12.1%)	87 (14.3%)
Missing	7 (2.3%)	5 (1.6%)	12 (2.0%)
I am confident I could reduce my opioid use a lot over 4 months			
Not at all confident	90 (29.7%)	90 (29.5%)	180 (29.6%)
Somewhat confident	70 (23.1%)	77 (25.3%)	147 (24.2%)
Fairly confident	79 (26.1%)	79 (25.9%)	158 (26.0%)
Strongly confident	35 (11.6%)	40 (13.1%)	75 (12.3%)
Completely confident	22 (7.3%)	15 (4.9%)	37 (6.1%)
Missing	7 (2.3%)	4 (1.3%)	11 (1.8%)
I feel that involvement in this study can help me to reduce my opioid use			
Not at all	25 (8.3%)	22 (7.2%)	47 (7.7%)
By a little	76 (25.1%)	73 (23.9%)	149 (24.5%)
By half	38 (12.5%)	46 (15.1%)	84 (13.8%)
So I only use a little	68 (22.4%)	86 (28.2%)	154 (25.3%)
So I use no opioids	86 (28.4%)	69 (22.6%)	155 (25.5%)
Missing	10 (3.3%)	9 (3.0%)	19 (3.1%)

TABLE 82 Study outcomes at 4 months follow-up

	Standard care	Self-management
I want to reduce my opioid use (if still on opioids)		
Number still on opioids	194	166
Not at all	20 (10.3%)	18 (10.8%)
By a little	23 (11.9%)	11 (6.6%)
By half	32 (16.5%)	11 (6.6%)
So I only use a little	29 (14.9%)	31 (18.7%)
So I use no opioids	40 (20.6%)	57 (34.3%)
Missing	50 (25.8%)	38 (22.9%)
I feel that involvement in this study has helped me to reduce my opioid use		
N	159	192
Not at all	82 (51.6%)	30 (15.6%)
By a little	43 (27.0%)	24 (12.5%)
By half	10 (6.3%)	21 (10.9%)
So I only use a little	6 (3.8%)	33 (17.2%)
So I use no opioids	8 (5.0%)	79 (41.1%)
Missing	10 (6.3%)	5 (2.6%)

TABLE 83 Study outcomes at 8 months follow-up

	Standard care	Self-management
I want to reduce my opioid use (if still on opioids)		
Number still on opioids	152	136
Not at all	25 (16.4%)	20 (14.7%)
By a little	25 (16.4%)	16 (11.8%)
By half	24 (15.8%)	9 (6.6%)
So I only use a little	25 (16.4%)	26 (19.1%)
So I use no opioids	36 (23.7%)	45 (33.1%)
Missing	17 (11.2%)	20 (14.7%)
I feel that involvement in this study has helped me to reduce my opioid use		
N	149	181
Not at all	68 (45.6%)	27 (14.9%)
By a little	41 (27.5%)	27 (14.9%)
By half	16 (10.7%)	20 (11.0%)
So I only use a little	9 (6.0%)	28 (15.5%)
So I use no opioids	12 (8.1%)	74 (40.9%)
Missing	3 (2.0%)	5 (2.8%)

TABLE 84 Study outcomes at 12 months follow-up

	Standard care	Self-management
I want to reduce my opioid use (if still on opioids)		
Number still on opioids	193	160
Not at all	20 (10.4%)	18 (11.3%)
By a little	22 (11.4%)	10 (6.3%)
By half	27 (14.0%)	15 (9.4%)
So I only use a little	36 (18.7%)	32 (20.0%)
So I use no opioids	38 (19.7%)	49 (30.6%)
Missing	50 (25.9%)	36 (22.5%)
I feel that involvement in this study has helped me to reduce my opioid use		
N	160	188
Not at all	73 (45.6%)	26 (13.8%)
By a little	39 (24.4%)	25 (13.3%)
By half	17 (10.6%)	18 (9.6%)
So I only use a little	10 (6.3%)	44 (23.4%)
So I use no opioids	18 (11.3%)	72 (38.3%)
Missing	3 (1.9%)	3 (1.6%)

EME
HSDR
HTA
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