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Reducing Opioid Use for Chronic Pain With a Group-Based Intervention
A Randomized Clinical Trial

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IMPORTANCE Opioid use for chronic nonmalignant pain can be harmful.

OBJECTIVE To test whether a multicomponent, group-based, self-management intervention reduced opioid use and improved pain-related disability compared with usual care.

DESIGN, SETTING, AND PARTICIPANTS Multicentered, randomized clinical trial of 608 adults taking strong opioids (buprenorphine, dipipanone, morphine, diamorphine, fentanyl, hydromorphone, methadone, oxycodone, papaveretum, pentazocine, pethidine, tapentadol, and tramadol) to treat chronic nonmalignant pain. The study was conducted in 191 primary care centers in England between May 17, 2017, and January 30, 2019. Final follow-up occurred March 18, 2020.

INTERVENTION Participants were randomized 1:1 to either usual care or 3-day–long group sessions that emphasized skill-based learning and education, supplemented by 1-on-1 support delivered by a nurse and lay person for 12 months.

MAIN OUTCOMES AND MEASURES The 2 primary outcomes were Patient-Reported Outcomes Measurement Information System Pain Interference Short Form 8a (PROMIS-PI-SF-8a) score (T-score range, 40.7-77; 77 indicates worst pain interference; minimal clinically important difference, 3.5) and the proportion of participants who discontinued opioids at 12 months, measured by self-report.

RESULTS Of 608 participants randomized (mean age, 61 years; 362 female [60%]; median daily morphine equivalent dose, 46 mg [IQR, 25 to 79]), 440 (72%) completed 12-month follow-up. There was no statistically significant difference in PROMIS-PI-SF-8a scores between the 2 groups at 12-month follow-up (−4.1 in the intervention and −3.17 in the usual care groups; between-group difference: mean difference, −0.52 [95% CI, −1.94 to 0.89]; $P = .15$). At 12 months, opioid discontinuation occurred in 65 of 225 participants (29%) in the intervention group and 15 of 208 participants (7%) in the usual care group (odds ratio, 5.55 [95% CI, 2.80 to 10.99]; absolute difference, 21.7% [95% CI, 14.8% to 28.6%]; $P < .001$). Serious adverse events occurred in 8% (25/305) of the participants in the intervention group and 5% (16/303) of the participants in the usual care group. The most common serious adverse events were gastrointestinal (2% in the intervention group and 0% in the usual care group) and locomotor/musculoskeletal (2% in the intervention group and 1% in the usual care group). Four people (1%) in the intervention group received additional medical care for possible or probable symptoms of opioid withdrawal (shortness of breath, hot flushes, fever and pain, small intestinal bleed, and an overdose suicide attempt).

CONCLUSIONS AND RELEVANCE In people with chronic pain due to nonmalignant causes, compared with usual care, a group-based educational intervention that included group and individual support and skill-based learning significantly reduced patient-reported use of opioids, but had no effect on perceived pain interference with daily life activities.

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Opioids are widely used to treat chronic nonmalignant pain.[1] In 2022, an Agency for Healthcare Research and Quality report concluded that opioids may have small beneficial effects for chronic nonmalignant causes of pain, but are not superior to nonopioid therapy and are associated with increased risk of short- and long-term harms.[2] In 2020, more than 142 million opioid prescriptions were dispensed in the US.[3]

Optimal methods for reducing opioid use remain unclear. Tapering opioids quickly without providing alternatives for pain management has potential to cause harm, including suicide, or mental health crisis.[4,5] However, prior studies that used pain self-management, complementary medicine, pharmacological and biomedical intervention, and opioid replacement to reduce chronic opioid use were limited by poor study methodology or lack of evidence of safety.[6]

Multimodal treatment approaches that include nonpharmacologic strategies may prevent harm due to rapid tapering while facilitating effective treatment of chronic pain.[7] The I-WOTCH (Improving the Wellbeing of People With Opioid Treated Chronic Pain) randomized clinical trial (RCT) was conducted within the UK National Health Service to test whether a multimodal approach that facilitated opioid tapering in people with chronic nonmalignant pain could reduce opioid use and improve pain control among people using opioids to treat chronic pain from nonmalignant causes.

Key Points

Question Among patients with chronic pain, does a multicomponent intervention consisting of group meetings, education, individual support, and skill-based learning reduce opioid use and improve pain interference with daily activities compared with usual care?

Findings In this multicentered, randomized clinical trial that included 608 participants with chronic pain due to nonmalignant causes from primary care settings in the UK, at 12-month follow-up, 29% of people in the intervention group, compared with 7% in the usual care group, discontinued opioids, but there were no statistically significant differences in pain interference with daily life activities between the 2 groups at 12 months.

Meaning Among patients with chronic pain due to nonmalignant causes, a group-based educational intervention significantly reduced opioid use had no effect on perceived pain compared with usual care.

Methods

Trial Design and Oversight

The trial protocol was approved by the Yorkshire & The Humber–South Yorkshire Research Ethics Committee and was overseen by an independent trial steering committee, with an independent data monitoring and ethics committee. Written informed consent was obtained from participants by mail.

The trial protocol is available in Supplement 1. The initial protocol was developed on September 9, 2016, and finalized on February 10, 2021, before any data were evaluated. The initial statistical analysis plan was completed on May 8, 2018, and finalized on January 29, 2019, before any data were analyzed.

The clinical trial was designed as a pragmatic, multicenter, 1:1 RCT to test the superiority of an intervention, compared with usual care, for improving outcomes in people with chronic nonmalignant pain. Enrollment began May 17, 2017, and ended January 30, 2019. Final follow-up occurred March 18, 2020.

Participants

Participants were 18 years or older and using strong opioids as defined by the British National Formulary (buprenorphine, dipipanone, morphine, diamorphine, fentanyl, hydromorphone, methadone, oxycodone, papaveretum, pentazocine, pethidine, tapentadol, and tramadol) for at least 3 months on most days in the preceding month for chronic nonmalignant pain[8] (eTable 2 in Supplement 2). Race and ethnicity data were collected using self-report, and participants selected from fixed UK Census categories. Data on race and ethnicity were collected to evaluate the generalizability of results in the UK.

Potential participants with multiple prior prescriptions of strong opioids were identified from the electronic records of general (family) practices in the midlands and northeast geographic areas of England (**Figure 1**). People living in chronic care facilities (care homes) or unable to leave their home without assistance and those using methadone that was not prescribed for chronic pain were excluded. Posters advertising the study were placed in clinics to identify potential volunteers. Eligibility was determined by telephone.

Participants completed baseline questionnaires by mail (**Table 1**). Medication use at baseline and informed consent were confirmed by telephone.

Randomization

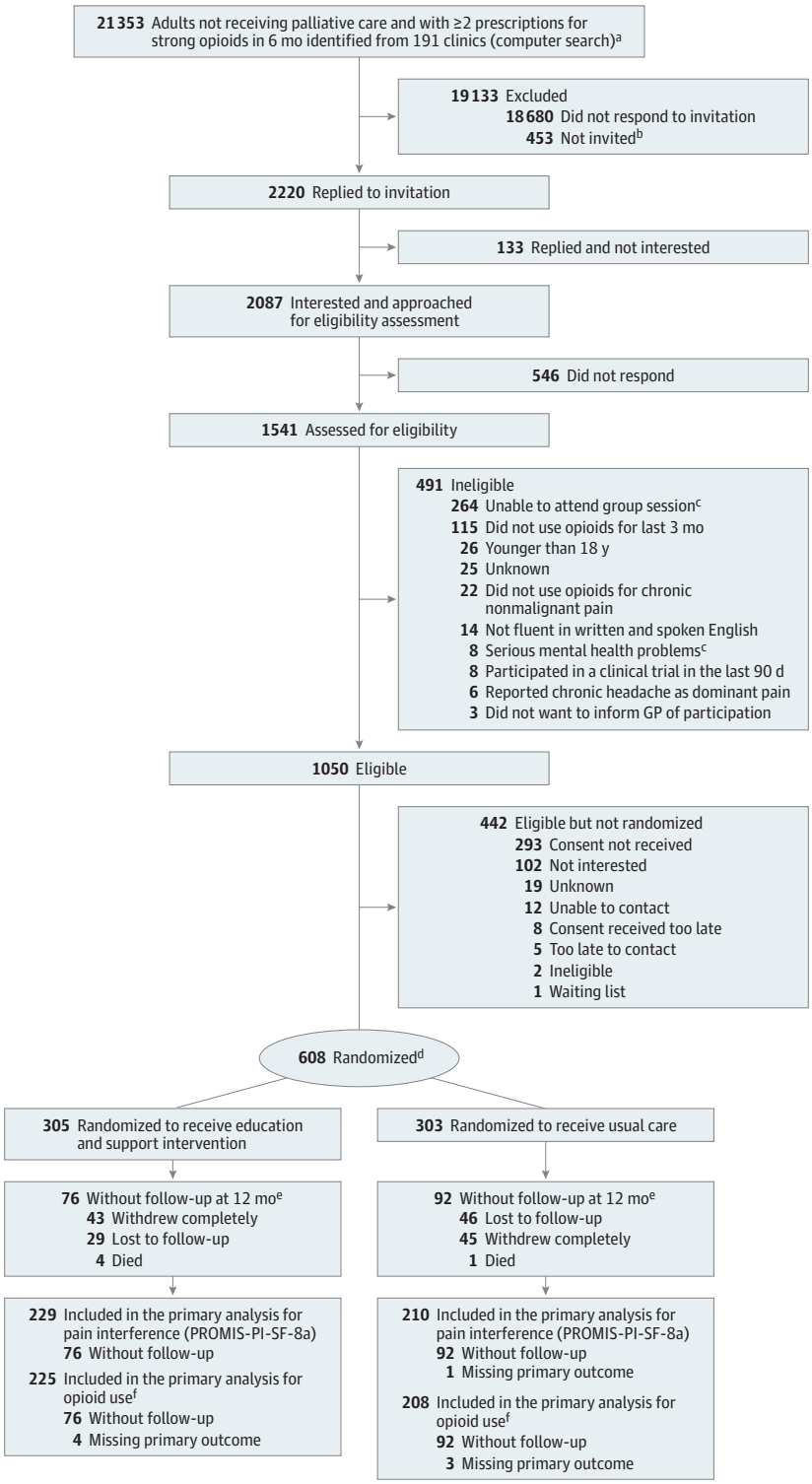
Participants were randomized in a 1:1 ratio using a minimization program stratified by geographic locality (midlands/northeast of England), baseline score for pain intensity (low intensity ≤8 and high intensity ≥9), and baseline morphine equivalent dose of opioids (0-29, 30-59, 60-89, 90-119, 120-149, and ≥150 mg).

Randomization was performed by the Warwick Clinical Trials Unit programming team using Structured Query Language. Randomization was performed when at least 16 participants had completed baseline testing because 16 participants was sufficient to begin an intervention group. Participants were not blind to group assignment.

Interventions

Both groups received enhanced usual care, consisting of *My Opioid Manager* based on the 2010 Canadian Opioid Guideline,[10] a self-help booklet containing information about pain, opioids, and opioid tapering, as well as a relaxation CD. In addition, the intervention group was offered a group-based educational intervention designed to encourage opioid cessation with a mutually agreeable decision plan between the participant and nurse. The intervention also increased

Figure 1. Participant Selection, Randomization, and Follow-up in the I-WOTCH Trial



GP indicates general practitioner; I-WOTCH, Improving the Wellbeing of People With Opioid Treated Chronic Pain; and PROMIS-PI-SF-8a, Patient-Reported Outcomes Measurement Information System Pain Interference Short Form 8a.

[a] Nine self-referrals and 5 secondary care referrals.

[b] General practitioner practice felt it inappropriate to approach. Reasons included malignant pain, short life expectancy, care home resident/housebound, severe mental illness, and active cancer causing pain.

[c] One person listed both reasons.

[d] Randomization stratified by geographic locality, baseline pain severity (low/high), and baseline morphine equivalent dose of opioids. Two self-referrals and 2 secondary care referrals.

[e] See eTable 11 in Supplement 2 for follow-up rates and availability of secondary outcomes at 4 and 8 months. See eTables 10 and 12 through 14 in Supplement 2 for information on withdrawals.

[f] Opioid use calculated as morphine equivalent dose per day in the four weeks prior to 12-month follow-up.

participants' self-efficacy (confidence), implemented self-management strategies for pain, and improved well-being.[11]

The intervention included 3-day-long group meetings held once weekly and led by a trained intervention nurse and by a lay person with chronic nonmalignant pain and experience with opioid tapering. Group topics for discussion included education about opioids and withdrawal and skills-based learning for self-management of pain. Case studies illustrating successful opioid tapering and challenges were discussed. Participants also received an educational DVD,

Table 1. Baseline Demographic Characteristics and Outcome Measures of All Randomized Participants by Treatment Group

Characteristic	No. (%)	
	Education and support intervention (n = 305)	Usual care (n = 303)
Age, mean (SD), y	62.1 (11.9)	60.4 (13.8)
Gender[a]		
No.	304	301
Male	125 (41)	117 (39)
Female	178 (59)	184 (61)
Other	1 (<1)	0
Race and ethnicity/ancestry[b]		
No.	304	301
Black African	1 (<1)	0
Black Caribbean	3 (1)	3 (1)
Black Other	1 (<1)	0
Indian	2 (1)	4 (1)
Pakistani	1 (<1)	0
White	295 (97)	290 (96)
Other	1 (<1)	3 (1)
Prefer not to say	0	1 (<1)
Employment status		
No.	304	301
Employed	67 (22)	65 (22)
Unable to work due to long-term sickness	78 (26)	76 (25)
Retired from paid work	134 (44)	136 (45)
Other[c]	25 (8)	24 (8)
Age at time of leaving full-time education, y[d]		
No.	304	301
≤16	174 (57)	172 (57)
≥17	125 (41)	123 (41)
Other	5 (2)	6 (2)
Length of time experiencing pain, y		
No.	304	301
≤5	52 (17)	53 (18)
>5	252 (83)	248 (82)
Time taking opioids, y		
No.	304	301
≤5	115 (38)	125 (42)
>5	189 (62)	176 (58)
Type of pain disorder[e]		
No.	299	300
Multisite pain	277 (93)	264 (88)
Lower back pain	241 (81)	249 (83)
Chronic widespread pain	154 (52)	137 (46)
Daily opioid use, morphine equivalent dose/d[f]		
0-29.9	103 (34)	98 (32)
30-59.9	95 (31)	103 (34)
60-89.9	42 (14)	44 (15)
90-119.9	18 (6)	17 (6)
120-149.9	10 (3)	12 (4)
≥150	37 (12)	29 (10)
Median (IQR), mg	49 (25-81) [n = 305]	44 (25-75) [n = 303]

(continued)

Table 1. Baseline Demographic Characteristics and Outcome Measures of All Randomized Participants by Treatment Group (continued)

Characteristic	No. (%)	
	Education and support intervention (n = 305)	Usual care (n = 303)
Baseline scale scores, mean (SD)		
Pain interference (PROMIS-PI-SF-8a)[g]	68.5 (6.0) [n = 304]	68.2 (6.2) [n = 301]
Pain intensity (PROMIS-PI-SF-3a)[h]	69.3 (6.8) [n = 305]	68.8 (7.1) [n = 303]
SF-12[i]		
Mental component score	41 (10.8) [n = 304]	41 (11.4) [n = 301]
Physical component score	32 (8.1) [n = 304]	32 (8.1) [n = 301]
Pittsburgh Sleep Quality Index[j]	12 (4.3) [n = 278]	12 (4.1) [n = 285]
HADS[k]		
Anxiety	9 (5.1) [n = 303]	9 (5.1) [n = 298]
Depression	9 (4.6) [n = 304]	9 (4.6) [n = 298]
Pain Self-Efficacy Questionnaire[l]	24 (12.7) [n = 301]	25 (13.6) [n = 300]
EQ-5D-5L[m]		
Utility	0.3 (0.3) [n = 304]	0.4 (0.3) [n = 301]
VAS	47 (21.4) [n = 304]	49 (21.3) [n = 301]
SHOWS[n]	11 (5.5) [n = 303]	11 (5.0) [n = 301]

Abbreviations: EQ-5D-5L, EuroQol 5-dimension 5-level; HADS, Hospital Anxiety and Depression Scale; PROMIS-PI-SF-3a, PROMIS Scale v1.0–Pain Intensity Short Form 3a; PROMIS-PI-SF-8a, Patient-Reported Outcomes Measurement Information System Pain Interference Short Form 8a; SF, Short Form; SHOWS, Short Opiate Withdrawal Scale; VAS, visual analog scale.

[a] Categories from which participants could choose included male, female, prefer not to answer, and other.

[b] Ethnicity was self-reported using the listed options, with participants only able to select 1 option. There were no participants who reported Chinese or Bangladeshi ethnicity. "Other" was included as a category from which participants could choose.

[c] Other employment status includes participants who were still receiving part-time or full-time education, caring for home/family, unemployed, or other.

[d] Leaving education at age 17 years or older includes participants who left education aged 17 to 19 years, 20 years or older, or participants still in education. "Other" most often referred to those who returned to education later in life.

[e] Participants self-reported sources of pain and were able to report more than 1.

[f] For opioid types by region, see eTable 2 in Supplement 2.

[g] PROMIS-PI-SF-8a uses 8 self-reported items from the prior 7 days to determine how much pain interferes with daily life. Reported as standardized T scores and calculated using the recommended HealthMeasures Scoring Service, higher scores indicate greater interference. Scores 40.7 to 60 are considered average, while scores 60 to 77 indicate high interference.[9] Indicative minimal clinically important difference (MCID), 3.5 (eTable 33 in Supplement 2).

[h] PROMIS-PI-SF-3a uses 3 self-reported items from the prior 7 days to determine how much pain interferes with daily life. Reported as standardized T scores and calculated using the recommended HealthMeasures Scoring Service, higher scores indicate greater pain intensity. Scores 36.3 to 60 are considered average, while scores 60 to 81.8 indicate high pain intensity.[9] MCID, 3.5 (eTable 37 in Supplement 2).

[i] The 12-item Short Form Health Survey compiles 8 domains of daily living to assess quality of life. Scores range from 0 to 100, with higher scores reflecting better physical and mental functioning. Mental MCID, 3.3; physical MCID, 3.8 (eTable 34 in Supplement 2).

[j] Pittsburgh Sleep Quality Index scores range from 0 to 21, with higher scores indicating worse sleep quality. The 19 self-reported questions are combined to create 7 component scores. The score is calculated by summing the 7 component scores (range, 0-3) to create a global score ranging from 0 to 21. This global score has been reported. MCID, 3.0 (eTable 37 in Supplement 2).

[k] HADS anxiety and depression scores range from 0 to 21, with higher scores indicating worse anxiety and depression. Each of the 7 questions measuring anxiety has a score ranging from 0 to 3. These 7 scores are summated to create the reported anxiety score. The same method applies to depression score. Anxiety MCID, 1.7; depression MCID, 1.7 (eTable 35 in Supplement 2).

[l] Pain Self-Efficacy Questionnaire scores range from 0 to 60, with higher scores indicating stronger self-efficacy beliefs. The questionnaire consists of 10 questions, each having a score ranging from 0 to 6. The score is calculated by summing these 10 scores to create the reported score. MCID, 7.0 (eTable 37 in Supplement 2).

[m] EQ-5D-5L utility score ranges from less than 0 to 1, with higher scores indicating better quality of life. EQ-5D-5L VAS score ranges from 0 to 100, with scores of 100 indicating "best health you can imagine" and 0 indicating "worst health you can imagine." These scores ranging from 0 to 100 were self-reported by participants and that self-reported score is reported. Utility MCID, 0.07; VAS MCID, 7.0 (eTable 36 in Supplement 2).

[n] SHOWS score ranges from 0 to 30, with higher scores indicating more severe symptoms. The scale consists of 10 questions, each with a score of 0 to 3, which are summed to give the reported score. MCID, 3 (eTable 37 in Supplement 2).

relaxation CD, mindfulness CD, and distraction techniques. Additionally, participants had an individual, 1-hour consultation (based on motivational interviewing) with a nurse, 2 monitoring telephone calls (30 minutes each), and a face-to-face consultation (1 hour).[12] Nurses used a tapering app specifically designed for this trial that computed a standard opioid tapering plan consisting of a reduction of 10% of the baseline dose each week until 30% of the baseline dose was reached, then a reduction of 10% of the remaining dose per week (eTable 3 in Supplement 2). The tapering program was individualized according to opioid preparation and individual circumstances. Audio recordings of a 10% subset of intervention activities were analyzed by the process evaluation team (C.A., V.N., K.S.) to assess intervention fidelity and the extent to which the intervention was delivered according to the manual of procedures.[13,14] The total time required for each group and individual session was 17 hours over an 8- to 10-week period.

Primary Outcomes

There were 2 primary outcomes measured at 12-month follow-up: the Patient-Reported Outcomes Measurement Information System (PROMIS) Pain Interference Short Form 8a (PROMIS-PI-SF-8A) score (T-score range, 40.7-77; 77 indicates worst pain interference; minimal clinically important difference [MCID], 3.5; eTable 33 in Supplement 2) and the proportion of participants reporting no opioid use over the previous 4 weeks at 12-month follow-up[15] (eTable 2 in Supplement 2). Results for both primary outcomes were from patient report, obtained by mailed questionnaire. Patients who did not return a mailed questionnaire for the primary outcomes were telephoned. In addition, self-reported opioid use data were confirmed in a subsequent telephone call.

Validated MCID values specific to this intervention were not available for any outcome measures. MCID values were, therefore, based on existing literature (eTables 33-37 in Supplement 2).

Investigators originally planned to report opioid use as daily morphine equivalent dose (MED) during the 4 weeks prior to 12-month follow-up.[16] However, the final opioid use data did not satisfy the normality assumption of the linear regression, due to a large number of zero values and data were positively skewed (eTables 30-32 and eFigures 1-2 in Supplement 2). Therefore, the primary outcome for opioid use was changed to the proportion of participants reporting no opioid use. This decision was made after looking at the blind distribution of data.

Secondary Outcomes

Secondary outcomes were pain intensity (PROMIS Scale v1.0-Pain Intensity Short Form 3a; T-score range, 36.3-81.8; 81.8 indicates worst pain intensity; MCID, 3.5 [eTable 37 in Supplement 2])[17,18]; severity of opioid withdrawal symptoms (Short Opiate Withdrawal Scale [SHOWS]; score range, 0-30; 30 indicates worst symptoms; MCID, 3.0 [eTable 37 in Supplement 2])[19]; health-related quality of life (SF-12v2 health survey and EuroQol 5-dimension 5-level [EQ-5D-5L]; SF-12 mental and physical component scores range, 0-100, 100 indicates best functioning; mental MCID, 3.3; physical MCID, 3.8 [eTable 34 in Supplement 2] and EQ-5D-5L utility score range: <0-1, 1 indicates best quality of life; EQ-5D-5L visual analog scale range, 0-100, 100 indicates best health; utility MCID, 0.07; visual analog scale MCID, 7.0 [eTable 36 in Supplement 2])[20,21]; sleep quality (Pittsburgh Sleep Quality Index; score range, 0-21, 21 indicates worst sleep quality; MCID, 3.0 [Supplement 2])[22]; emotional well-being (Hospital Anxiety and Depression Scale; score range, 0-21, 21 indicates worst anxiety or depression; anxiety MCID, 1.7; depression MCID, 1.7 [eTable 35 in Supplement 2])[23]; self-efficacy (Pain Self-Efficacy Questionnaire; score range, 0-60, 60 indicates strongest self-belief; MCID, 7.0 [eTable 37 in Supplement 2])[24]; and the proportion of participants who reduced opioids by 50% from baseline. Secondary outcomes were measured at baseline and 4, 8, and 12 months.

Additional secondary measures were the proportion of participants who reduced opioids by 50% from baseline, measured at 4, 8, and 12 months, and PROMIS-PI-SF-8a scores and the proportion of participants reporting no opioid use over the previous 4 weeks, measured at 4 and 8 months. Follow-up questionnaires were mailed at 4, 8, and 12 months. When questionnaires were not returned by mail, participants were called by telephone to collect PROMIS-PI-SF-8a, opioid use, and EQ-5D-5L.[21] Prescribed opioid medication from clinician records and use of health care resources were not reported. While the intent was to blind outcome assessors, some participants revealed treatment allocation during these calls, thus complete blinding was not achieved.

Adverse Events

Participants were asked if they experienced any adverse events (AEs) during their taper of opioids in each individual session by the nurse. The principal investigator and clinical members of the study team assessed and confirmed each adverse event. All AEs and serious adverse events (SAEs) were reported to the trial management group for review and oversight.

Statistical Analysis

The original sample size calculation used the PROMIS-PI-SF-8a as the primary outcome.[15] To attain a meaningful difference of 3.5 points on PROMIS-PI-SF-8a, equivalent to a standardized mean difference of 0.35, assuming a usual care group mean of 50, an SD of 10, at 5% significance with 90% power (intraclass correlation coefficient of 0.01, mean group size of 10 participants), and allowing for 20% attrition required 468 randomized participants. Adjusting the significance level to 2.5% for 2 primary outcomes and adjusting the design effect for clustering to reflect actual group sizes gave a revised sample size of 542.

The original protocol, dated September 9, 2016, had a single primary outcome of pain interference. The target sample size of 468 was achieved on October 24, 2018, and on this date additional potential participants had provided informed consent and were available for randomization. Therefore, the protocol was revised on December 19, 2018, to increase the sample size to 542 and add the primary outcome of opioid use. The independent trial steering committee, data monitoring committee, funders, and ethics committee all supported a decision to continue recruitment and include a secondary primary outcome. Independent trial steering committee approval was given on October 12, 2018 (section 1 of Supplement 2). Neither the study team nor the independent trial steering committee reviewed any data prior to this decision. The analysis plan and protocol were finalized before data collection was complete. No decisions on outcome selection were made after data were available.

The main analyses were according to treatment allocation at the time of randomization. Primary outcomes used 2-sided tests at the 2.5% significance level. All other statistical tests were 2-sided at the 5% significance level. The estimates, 95% CIs, and *P* values were reported for each statistical test.

Partially nested mixed-effects regression (linear and logistic) models to estimate the treatment effects for both primary and secondary outcomes were used (**Tables 2** and **3**). Age, gender, site location, baseline pain intensity, baseline opioid band (for linear model only), and the baseline value of the

Table 2. Daily Opioid Use and PROMIS-PI-SF-8a Scores at 12 Months (Primary Outcome) and 4 Months and 8 Months (Secondary Outcomes)

	No./total (%)				
	Education and support intervention	Usual care	Absolute difference, % (95% CI)	Adjusted effect estimate (95% CI)	*P* value
Primary outcome[a]					
Fully tapered off opioids at 12 mo (MED = 0)[b]	65/225 (29)	15/208 (7)	21.7 (14.8 to 28.6)	OR, 5.55 (2.80 to 10.99)[c]	<.001
PROMIS-PI-SF-8a at 12 mo, mean (SD)[d]	64.2 (7.7) [n = 229]	64.7 (7.3) [n = 210]	MD, −0.52 (−1.94 to 0.89)	−0.89 (−2.12 to 0.33)[e]	.15
Secondary outcomes					
Fully tapered off opioids (MED = 0)[b]					
At 4 mo	58/224 (26)	7/201 (3)	22.4 (16.1 to 28.7)	OR, 11.61 (5.06 to 26.63)[c]	<.001
At 8 mo	57/193 (30)	11/163 (7)	22.8 (15.3 to 30.3)	OR, 7.25 (3.46 to 15.18)[c]	<.001
≥50% MED reduction from baseline					
At 4 mo	112/224 (50)	31/201 (15)	34.6 (26.3 to 42.8)	OR, 6.12 (3.77 to 9.92)[f]	<.001
At 8 mo	110/193 (57)	38/163 (23)	33.7 (24.1 to 43.2)	OR, 4.94 (3.04 to 8.03)[f]	<.001
At 12 mo	129/225 (57)	57/208 (27)	29.9 (21.1 to 38.8)	OR, 3.76 (2.47 to 5.71)[f]	<.001
PROMIS-PI-SF-8a score, mean (SD)[d]					
At 4 mo	64.5 (7.5) [n = 227]	64.6 (7.2) [n = 202]	MD, −0.09 (−1.48 to 1.31)	−0.73 (−1.93 to 0.48)[e]	.24
At 8 mo	64.5 (7.3) [n = 199]	64.9 (7.5) [n = 166]	MD, −0.39 (−1.93 to 1.14)	−0.75 (−2.10 to 0.59)[e]	.27

Abbreviations: OR, odds ratio; MD, mean difference; MED, morphine equivalent dose; PROMIS-PI-SF-8a, Patient-Reported Outcomes Measurement Information System Pain Interference Short Form 8a.

[a] A total of 433 (71.2%) of the 608 randomized participants had opioid use primary outcome data reported. A total of 439 (72.2%) of the 608 randomized participants had pain interference (PROMIS-PI-SF-8a) primary outcome data reported.

[b] Daily MED over previous 4 weeks. Reported are those who fully tapered off opioids (MED = 0 mg). See eTable 1 in Supplement 2 for equivalences used. See eTable 18 in Supplement 2 for opioid tapering by baseline MED band.

[c] Based on partially nested mixed-effect logistic model adjusted for age, gender, baseline pain intensity, geographic location, and baseline MED. 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 reported.

[d] PROMIS-PI-SF-8a T score reported. Refer to footnote a of Table 1 on PROMIS-PI-SF-8a scoring and calculation. Indicative minimal clinically important difference (MCID), 3.5 (eTable 33 in Supplement 2).

[e] 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 PROMIS-PI-SF-8a T score. 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.

[f] 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.

dependent variable were covariates in the fixed-effects model. The education support group was the cluster variable for the intervention group, with individual clusters of size 1 used for each participant in usual care, to account for the partial clustering.[25,26] Model assumptions were assessed as appropriate.

In a sensitivity analysis, an instrumental variable analysis to adjust for nonadherence was performed on 2 levels of adherence: (1) minimal adherence (attending day 1 of the intervention plus the first 1-on-1 session) and (2) full adherence (attending 3 days, the first 1-on-1 session, and ≥1 telephone calls).[27] In addition to the usual assumptions for this analysis, monotonicity was required. An inverse probability weighting analysis was conducted as a sensitivity analysis to assess whether the missing data affected conclusions.[28]

A prespecified subgroup analysis for the primary outcomes, testing for an interaction for baseline anxiety, depression, and opioid use, defined using their median values was completed. Prespecified sensitivity analyses for the primary outcome, excluding participants included in process evaluation interviews, adjusting for the imbalance of death, and split by baseline pain disorders were also completed (eTables 23-25 in Supplement 2). Because of the potential for type I error due to multiple comparisons, findings for analyses of secondary end points should be interpreted as exploratory. Statistical analyses were conducted using Stata version 16.1 (StataCorp).[29]

Results

Recruitment

Of 20 900 people approached in 191 general practices, 2220 potential participants expressed interest in study participation and 9 people self-referred (eTables 5-6 in Supplement 2). Of these, 1541 (69%) were reached by telephone and assessed for eligibility. Of these, 608 people (39%) were randomized (mean [SD] age, 61 [12.9] years; 362 [60%] were female; and 585 [96%] reported their ethnicity as White British and 8 as Black [1.3%]) (Figure 1; Table 1; eTables 7-9 in Supplement 2). At baseline, 34% (103/305) in the intervention group and 32% (98/303) in the usual care group were in the lowest opioid category (0-29.9 MED per day), with 12% (37/305) and 10% (29/303) in the highest opioid category (≥150 MED per day) in the intervention and usual care groups, respectively (Table 1).

Table 3. Secondary Outcomes

	Mean (SD)				
	Education and support intervention	Usual care	Mean difference (95% CI)	Adjusted effect estimate (95% CI)[a]	*P* value[a]
Pain intensity (PROMIS-PI-SF-3a)[a]					
4 mo	65.0 (8.1) [n = 189]	65.9 (7.7) [n = 151]	−0.96 (−2.66 to 0.75)	−1.42 (−3.08 to 0.23)	.09
8 mo	65.0 (8.7) [n = 182]	65.9 (7.3) [n = 147]	−0.92 (−2.69 to 0.85)	−1.47 (−3.03 to 0.09)	.06
12 mo	64.7 (8.6) [n = 187]	65.6 (7.7) [n = 159]	−0.91 (−2.64 to 0.83)	−1.31 (−2.88 to 0.26)	.10
SF-12 mental component score[b]					
4 mo	45.8 (11.6) [n = 189]	44.4 (12.1) [n = 151]	1.38 (−1.16 to 3.92)	2.29 (0.30 to 4.27)	.02
8 mo	43.9 (11.7) [n = 181]	44.3 (12.0) [n = 146]	−0.39 (−2.98 to 2.20)	0.28 (−1.79 to 2.35)	.79
12 mo	43.4 (11.8) [n = 185]	44.1 (11.2) [n = 160]	−0.67 (−3.12 to 1.77)	0.41 (−1.59 to 2.42)	.68
SF-12 physical component score[b]					
4 mo	33.9 (10.0) [n = 189]	33.2 (9.3) [n = 151]	0.67 (−1.41 to 2.75)	0.87 (−0.62 to 2.36)	.25
8 mo	34.2 (9.2) [n = 181]	33.2 (9.4) [n = 146]	0.97 (−1.07 to 3.01)	1.06 (−0.52 to 2.65)	.19
12 mo	33.6 (8.8) [n = 185]	33.8 (9.3) [n = 160]	−0.24 (−2.15 to 1.66)	−0.02 (−1.49 to 1.44)	.98
Pittsburgh Sleep Quality Index[b]					
4 mo	11.2 (4.4) [n = 177]	12.1 (4.2) [n = 141]	−0.94 (−1.90 to 0.01)	−0.65 (−1.38 to 0.08)	.08
8 mo	10.8 (4.5) [n = 170]	11.8 (4.2) [n = 140]	−0.97 (−1.96 to 0.02)	−0.72 (−1.46 to 0.02)	.06
12 mo	11.3 (4.3) [n = 175]	11.6 (4.4) [n = 150]	−0.33 (−1.29 to 0.62)	−0.10 (−0.82 to 0.63)	.80
HADS anxiety score[b]					
4 mo	8.1 (4.8) [n = 187]	8.3 (5.3) [n = 149]	−0.16 (−1.25 to 0.93)	−0.59 (−1.30 to 0.12)	.10
8 mo	8.3 (5.0) [n = 176]	7.7 (5.0) [n = 146]	0.59 (−0.51 to 1.69)	0.27 (−0.44 to 0.99)	.44
12 mo	8.3 (5.0) [n = 182]	7.8 (5.3) [n = 157]	0.49 (−0.61 to 1.59)	0.11 (−0.67 to 0.89)	.78
HADS depression score[b]					
4 mo	7.6 (4.4) [n = 190]	8.1 (4.6) [n = 150]	−0.55 (−1.53 to 0.42)	−0.94 (−1.63 to −0.25)	.01
8 mo	7.9 (4.7) [n = 181]	8.1 (4.5) [n = 147]	−0.17 (−1.18 to 0.83)	−0.35 (−1.04 to 0.34)	.31
12 mo	8.3 (4.8) [n = 182]	7.7 (4.7) [n = 156]	0.58 (−0.45 to 1.60)	−0.02 (−0.77 to 0.73)	.95
Pain Self-Efficacy Questionnaire[b]					
4 mo	31.2 (14.6) [n = 189]	28.8 (14.7) [n = 147]	2.39 (−0.78 to 5.56)	4.19 (1.97 to 6.41)	<.001
8 mo	30.4 (14.8) [n = 180]	29.0 (14.4) [n = 146]	1.37 (−1.84 to 4.59)	2.05 (−0.18 to 4.28)	.07
12 mo	29.1 (15.2) [n = 185]	29.1 (13.5) [n = 159]	−0.01 (−3.08 to 3.06)	1.43 (−0.87 to 3.73)	.22
EQ-5D-5L utility[b]					
4 mo	0.43 (0.28) [n = 228]	0.40 (0.30) [n = 199]	0.03 (−0.03 to 0.08)	0.57 (0.01 to 0.10)	.02
8 mo	0.39 (0.28) [n = 197]	0.41 (0.29) [n = 166]	−0.02 (−0.08 to 0.04)	−0.001 (−0.05 to 0.05)	.96
12 mo	0.42 (0.28) [n = 227]	0.41 (0.29) [n = 209]	0.01 (−0.05 to 0.06)	0.02 (−0.02 to 0.06)	.32
EQ-5D-5L VAS[b]					
4 mo	53.3 (22.6) [n = 227]	51.6 (23.3) [n = 199]	1.66 (−2.72 to 6.04)	4.43 (0.70 to 8.16)	.02
8 mo	53.1 (23.2) [n = 197]	51.5 (23.7) [n = 165]	1.58 (−3.28 to 6.44)	3.88 (−0.24 to 7.99)	.06
12 mo	52.0 (24.0) [n = 228]	51.3 (23.7) [n = 209]	0.68 (−3.81 to 5.17)	2.35 (−1.62 to 6.32)	.24
Short Opiate Withdrawal Scale[b]					
4 mo	9.2 (5.1) [n = 190]	9.6 (6.0) [n = 150]	−0.4 (−1.59 to 0.79)	−0.65 (−1.61 to 0.31)	.18
8 mo	9.3 (5.4) [n = 181]	9.5 (5.2) [n = 146]	−0.20 (−1.36 to 0.97)	−0.29 (−1.20 to 0.61)	.52
12 mo	9.3 (5.4) [n = 183]	9.4 (5.5) [n = 156]	−0.11 (−1.27 to 1.06)	−0.35 (−1.34 to 0.65)	.49

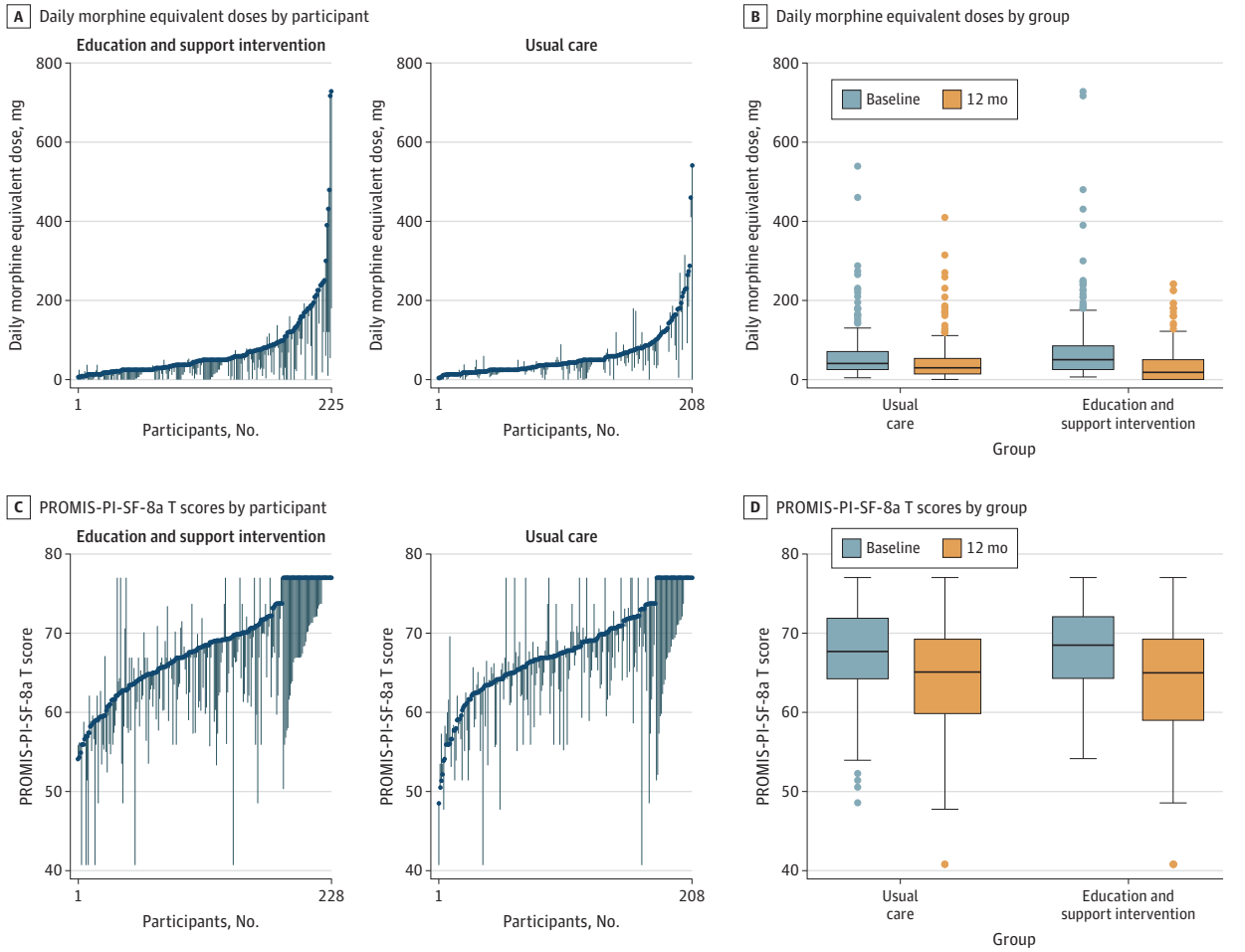
Abbreviations: EQ-5D-5L, EuroQol 5-dimension 5-level; HADS, Hospital Anxiety and Depression Scale; PROMIS-PI-SF-3a, PROMIS Scale v1.0–Pain Intensity Short Form 3a; SF, Short Form; VAS, visual analog scale.

[a] 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.

[b] See footnotes g through n in Table 1 for information on scoring, minimal clinically important differences, and calculations of each secondary outcome.

Thirty-five group interventions were delivered at 25 community locations (median group size, 9 [IQR, 5-11]); 206 of 305 participants (68%) attended the first session, 190 (62%) achieved minimum adherence of attending at least day 1 of the group sessions and a 1-on-1 session with the nurse, and 144 (47%) achieved full adherence to the program. The median time from randomization to the first group session was 12 days (IQR, 6-23) (eTable 15 in Supplement 2). Final follow-up was March 18, 2020, and the trial ended on November 11, 2021.

Figure 2. Pain Interference and Morphine Equivalent Dose Opioid Use Scores at Baseline and 12 Months



The parallel line plots (A and C) contain a line for each participant in the study with baseline and 12-month data available. Each line starts at the baseline value (circle) and extends along the line to the 12-month value. Panel C shows the Patient-Reported Outcomes Measurement Information System Pain Interference Short Form 8a (PROMIS-PI-SF-8a) standardized T score (range, 40.7-77), with higher scores signifying higher pain interference in daily life (see footnote g in Table 1 for information on PROMIS-PI-SF-8A scoring and ranges). Panel A shows the daily morphine equivalent dose (continuous value) used in the previous 4 weeks from the time point. Panels B and D show the corresponding box and whisker plots, with lines and boxes indicating medians and IQRs, whiskers indicating 1.5 × the IQR, and dots representing more extreme data.

Mean adherence (fidelity) to the course manual, defined as intervention delivery and adhering to the steps outlined in the manual, was 83% (range, 25%-100%, with a median of 88%) and competence of delivery as taught in the intervention training had a mean of 79% (range, 0%-100%, with a median of 86%). The 1-on-1 nurse consultation sample (n = 27) had an adherence to manual mean of 91% (range, 61%-100%) and competence mean of 93% (range, 50%-100%) (eTables 16-17 in Supplement 2).

Primary Outcomes

PROMIS-PI-SF-8a data were available for 439 of 608 participants (72%) and opioid use data were available for 433 of 608 participants (71%) at 12-month follow-up. PROMIS-PI-SF-8a scores improved in both groups over the 12-month trial: −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 (**Figure 2**).[9] There was no statistically significant between-group difference in PROMIS-PI-SF-8a scores (mean difference, −0.52 [95% CI, −1.94 to 0.89]; $P = .15$; Table 2). At 12 months, 65 of 225 participants (29%) in the intervention group and 15 of 208 (7%) in the usual care group had discontinued opioids (absolute difference, 21.7% [95% CI, 14.8% to 28.6%]; $P < .001$; odds ratio, 5.55 [95% CI, 2.80 to 10.99]; Table 2).

Secondary Outcomes

Of 10 secondary outcomes, collected over 3 points (ie, total of 30 secondary outcome measurements), 5 were statistically significant, favoring the intervention. At 12-month follow-up, the proportion of participants who reduced daily MED by 50% or more from baseline was 57% in the intervention group and 27% in the usual care group (absolute difference, 29.9% [95% CI, 21.1% to 38.8%]; odds ratio, 3.76 [95% CI, 2.47 to 5.71]; $P < .001$). The proportion of participants who reduced daily MED by 50%

or more at 4- and 8-month follow-up was also statistically significant (Table 2). At 4-month follow-up, participants randomized to the intervention had statistically significant improvement in mental health (SF-12 mental component score and Hospital Anxiety and Depression Scale depression subscale), pain self-efficacy (Pain Self-Efficacy Questionnaire), and health-related quality of life (EQ-5D-5L utility and visual analog scale scores) but not at any other points (Table 3). There were no statistically significant between-group differences in pain intensity (PROMIS Scale v1.0–Pain Intensity Short Form 3a), opioid withdrawal symptoms (SHOWS), or sleep quality measured by the Pittsburgh Sleep Quality Index at any point (Table 3).

Sensitivity Analyses

The instrumental variable analyses were not meaningfully different from the primary analysis (eTables 19-20 in Supplement 2). However, the analyses were limited by model assumptions, and the fact that the clinical trial was not blinded. The findings from the inverse probability weighting analysis showed no meaningful differences from the primary analysis (eTable 4 in Supplement 2). The tests for interaction in prespecified subgroup analyses were not statistically significant (eTables 21-22 in Supplement 2). Additional prespecified analyses also showed no change in conclusions (eTables 23-25 in Supplement 2).

Adverse Events

There were 52 serious adverse events (32 in the intervention and 20 in the usual care group) reported by 41 participants (25 in the intervention and 16 in the usual care group), including 5 deaths (4 in the intervention and 1 in the usual care group), metastatic prostate cancer, aortic dissection, lymphoma complication, subdural empyema secondary to otitis media, and unknown cause of death. In the usual care group, 1 SAE (arthritis flare-up, which resulted in a hospital admission) was possibly study related. In this participant, pain temporarily worsened by opioid withdrawal required hospital admission for pain control. In the intervention group, there was 1 expected SAE of moderate severity that was probably related to the study (hot flushes/shooting pains in limbs after tapering) and 3 possibly related SAEs (1 expected [hospitalization from joint/back pain] and 2 unexpected [surges in pain and hot sensations after tapering and small intestinal bleed, and an overdose suicide attempt]). Adverse events were reported by 22 of 305 participants (7%) and 8 of 303 participants (3%) in the intervention and usual care groups, respectively (eTables 26-29 in Supplement 2). The most common adverse events were psychological (eg, sleep disturbance, panic attack, suicidal thoughts, and low mood and suicidal ideation; 2% in the intervention group and 1% in the usual care group) and nervous system (eg, headache, muscle spasms, withdrawal symptoms, and vertigo; 2% in the intervention group and less than 1% in the usual care group).

Discussion

In this multicentered, randomized clinical trial, a group-based educational intervention that consisted of group and individual support as well as skill-based learning significantly reduced patient-reported use of opioids compared with usual care. However, there was no effect on perceived pain interference with daily life activities at 12-month follow-up.

Of 10 secondary outcome measures, collected over 3 points (a total of 30 secondary outcome measurements), only 5 of the measurements were statistically significant and improved in the intervention group compared with usual care. Tapering of opioids was achieved through health care professional and peer group support rather than prescribing additional medications. The intervention consisted of establishing a therapeutic alliance with the patient and gradual opioid tapering to reduce adverse effects including withdrawal symptoms.

A 2022 systematic review of opioid reduction interventions in primary care identified 4 RCTs (N = 231) of patient-centered interventions to reduce opioid use for chronic nonmalignant pain.[30] The interventions included mindfulness-oriented and meditation-cognitive behavioral approaches, but opioid tapering was not an explicit goal in these RCTs. None of these found a statistically significant between-group difference in opioid use.

In another 2022 systematic review that identified 2 RCTs (N = 238) of pain management programs not based in primary care reporting on opioid cessation, 30% of those in the intervention group and 12% in the usual care group stopped taking opioids (risk ratio, 2.15 [95% CI, 1.02 to 4.53]).[6] Similar to the current trial, the interventions included specific aims to reduce reliance on opioid through behavior change and incorporated a biopsychosocial framework.

A subsequent RCT of 250 participants published in 2022 reported that 16% of people receiving supportive group therapy and 35% of people offered mindfulness-oriented recovery enhancement reduced opioid use by 50% or more (P = .009) at 9 months, and no adverse events related to the intervention were reported.[31]

Limitations

This study had several limitations. First, opioid use among participants was measured using self-report on a mailed questionnaire, with participant-report verified in a telephone call from a member of the study team. Results for this primary outcome were not validated with blood or urine samples. Second, participants were not blind to group assignment. Third, study coordinators were regularly unblinded by study participants.

Fourth, individuals in this trial volunteered to participate and, therefore, were likely more committed to reduce use of opioid medications than people who did not participate. Fifth, only 47% of participants randomized to the intervention fully adhered to the intervention, defined as attending days 1 to 3 (group sessions), the first individual session with the nurse, and at least 1 further follow-up session. Sixth, the 12-month follow-up rate was 72%. Seventh, 33% of participants used an MED of less than 30 mg per day at baseline. Results may not be generalizable to people using higher doses of morphine at baseline.

Eighth, participants were recruited from a community setting. Results may not be applicable to other settings. Ninth, results may not be applicable to health care systems where opioid tapering requires shared prescribing between primary and secondary care. Tenth, the length of time needed to deliver the intervention and intensity may limit the generalizability in clinical practice. Eleventh, some AEs may have been missed if participants did not recall or report these.

Conclusions

A group-based educational intervention that included group and individual support and skill-based learning significantly reduced patient-reported use of opioids compared with usual care, but there was no effect on perceived pain interference with daily life activities.

ARTICLE INFORMATION

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Supervision: Sandhu, Furlan, Alleyne, Balasubramanian, Lall, Newton, Noyes, Rahman, Seers, Eldabe.
Other - health economics: Manca.
Other: Carnes.
Other - trial management: Tang.
Other - lead health economist: Iglesias-Urrutia.

Conflict of Interest Disclosures: Prof 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. Dr Furlan is author of *My Opioid Manager* book and app, distributed in iTunes and Google Play for health care professionals and owned by University Health Network, the hospital where she works. Both book and app are free of charge. Dr Furlan has a monetized YouTube channel since January 2021 that contains some videos about opioids and opioid tapering. Since April 2021, Dr 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. Prof Taylor reported being chief investigator or coinvestigator on multiple previous and current research grants from the NIHR. Dr Iglesias-Urrutia reported receiving grants from the NIHR during the conduct of the study; and for the past 10 years, she was a member of the Medical Technologies Advisory Committee at the National Institute for Health and Care Excellence. Prof Manca reported receiving nonfinancial support from the National Institute for Health and Care Excellence (having been a member of the institute's technology appraisal committee), personal fees from Pfizer, and grants from the NIHR outside the submitted work. Prof Rahman reported receiving grants from NIHR during the conduct of the study. Prof Seers reported receiving grants from NIHR during the conduct of the study and being a member of a different NIHR funding board (HS&DR). Prof Tang reported receiving grants from NIHR Health Technology Assessment and UK Research and Innovation Medical Research Council and being chief investigator or coinvestigator of other chronic pain–related projects funded by the NIHR, Medical Research Council, and Warwick-Wellcome Translational Partnership. Prof Eldabe reported receiving grants from the NIHR (project No. 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. Prof Underwood reported being chief investigator 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 organizations 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 3 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. No other disclosures were reported.

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