

Research paper

Interactive group-based orientation sessions: A method to improve adherence and retention in pragmatic clinical trials

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ABSTRACT

Background: Intervention adherence and trial retention are challenging for clinical trials testing intensive behavioral interventions. Operational constraints or trial designs may preclude using effective retention strategies such as financial incentives. We examined whether implementing pre-enrollment orientation sessions was associated with higher intervention adherence and retention in a pragmatic clinical trial.

Methods: The trial tested an intensive behavioral intervention for patients with chronic pain on long-term opioids. Orientation sessions were implemented two years into trial recruitment at one site. Held before informed consent and randomization, these mandatory, group-based orientation sessions provided trial specifics, explained research methods principles, and leveraged motivational interviewing techniques. Using a pre-post design and multivariate models, we assessed adherence (number of intervention meetings attended) and retention (completed quarterly pain assessments over 12 months) before (04/2014–12/2015; n = 209) and after (01/2016–02/2017; n = 258) implementation. Also, we evaluated whether session implementation affected the proportion and characteristics of enrolled patients.

Results: After implementing orientation sessions, patients had higher intervention adherence than before (M = 7.6, SD = 3.8 vs. M = 5.6, SD = 4.5, respectively; mean difference = 2.0, 95% CI [0.9, 3.2], p = .001), and 2.8 times greater odds of completing quarterly assessments (95% CI [1.3, 5.8], p = .007). Fewer patients enrolled after implementing sessions than before (38.1% vs. 70.8%, 95% CI [26.4, 39.1], p < .001), with no differences in patient characteristics.

Conclusions: Implementing orientation sessions during recruitment may be useful for promoting trial adherence and retention. To ensure enrollment goals are met, target population size and barriers affecting patients' ability to attend orientation sessions should be considered, especially for patients with complex medical conditions.

Clinical trials registration number: NCT02113592.

1. Introduction

Clinical trials often face challenges with intervention adherence and trial retention, especially trials that require substantial patient commitment and test intensive behavioral interventions [1]. Frequently, researchers grapple with differential retention between study arms or among certain subpopulations. In a recent meta-analysis of health behavior trials, intervention participants had lower retention than control participants, posing threats to internal validity [2]. Fur-

ther, participants' experiences in either trial arm could affect retention both positively and negatively. Intervention participants might feel obligated to complete a trial because they received free treatment, or they may drop out due to frustration with poor outcomes. Control participants may drop out if they are minimally committed to the trial given low involvement in activities. Without successful engagement and retention of all research participants, the effectiveness and generalizability of an intervention cannot be determined and resources are potentially wasted [3,4].

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Effective strategies to address adherence and retention, such as providing financial incentives, using study databases to track participants, and helping participants overcome participation barriers by offering transportation vouchers may not always be feasible [5,6]. Rather, pragmatic clinical trials take place within real-world clinical settings so incentives are rarely used, data collection is often limited to electronic health records, and assistance generally mimics that of clinical practice [7]. Thus, adherence and retention strategies are critically needed for pragmatic trials, and could also inform clinical practice.

One potential strategy is conducting pre-enrollment orientation sessions during trial recruitment, used to date in behavioral weight-management efficacy trials and a chronic disease self-management program [8,9]. In the Fresh Start weight-management trial [10], interactive, group-based orientation sessions, originally developed by Goldberg and Kiernan [8], were held prior to obtaining informed consent. The sessions provided trial specifics, explained key research methods, and leveraged motivational interviewing techniques to diffuse potential participant ambivalence about participation. As trial retention was 93% at 18 months [10], pre-enrollment orientation sessions show promise for promoting retention. However, retention data were observational as there was no control group and all trial participants attended an orientation session. In the widely-implemented Chronic Disease Self-Management Program in which more than 100,000 U.S. adults participated, "Session Zero" information sessions were held prior to the program's six workshops at some community sites. Workshop attendance was higher at sites when Session Zero was offered than when it was not [9]. However, the direct effect of Session Zero on participant adherence could not be determined because attendance was not tracked at the participant level [9].

Pain Program for Active Coping and Training (PPACT) was a pragmatic clinical trial that evaluated an intensive behavioral intervention for patients with chronic pain on long-term opioids. To address initially low rates of adherence and retention, PPACT introduced interactive, group-based pre-enrollment orientation sessions approximately two years into the trial. The delayed implementation of the orientation sessions offered the opportunity to assess whether these sessions were associated with higher intervention adherence and trial retention. Additionally, we evaluated whether implementation affected the proportion of eligible patients who enrolled and explored whether their demographic and clinical characteristics differed from the target population.

2. Methods

2.1. Data source and study population

The data source is the PPACT pragmatic clinical trial, described above. The core of the PPACT intervention is 12 weekly group meetings, which participants were expected to attend. The intervention group meetings provided training on how to adopt evidence-based pain coping skills and increase physical activity (described elsewhere [11]). Patients were enrolled (i.e., consented and randomized) in the pragmatic trial for 12 months. Quarterly assessments consisted of the PEG [12,13], a validated 3-item measure derived from the short form of the Brief Pain Inventory (BPI-SF) [14,15]. The PEG assessments were collected via three different mechanisms to take advantage of automated options and increase scalability for this pragmatic trial, including the patient electronic health record web portal (kp.org), Kaiser's interactive voice response phone system, and via phone with a live person [16].

We implemented the orientation sessions in Kaiser Permanente Northwest (KPNW) (Fig. 1), which was one of three trial sites. Here, using a pre-post study design and multivariate models, we assessed intervention adherence (number of intervention group meetings at-

tended) and retention (completion of quarterly pain assessments over 12 months) before (April 2014–December 2015; n = 209) or after (January 2016–February 2017; n = 258) the PPACT trial implemented orientation sessions at KPNW. The KPNW Institutional Review Board provided oversight for all study activities.

2.2. Rationale for implementing orientation sessions

The rationale for implementing the orientation sessions was twofold. First, approximately two years into the PPACT trial, intervention adherence at the KPNW site was low as almost 25% never attended a single intervention group meeting and on average, only 85% of PPACT trial participants completed the low-burden 3-item pain assessment across all four follow-up time points. Interviews with participants who had only attended a few intervention group meetings revealed they were confused about the intervention and trial requirements, which affected their ability to fulfill trial commitments.

Second, due to an aggressive Kaiser Permanente health care system-wide effort to taper opioids among patients with chronic pain on high doses of the medication, which accompanied the April 2016 release of the Centers for Disease Control (CDC) Guideline for Prescribing Opioids for Chronic Pain [17], many individuals in the PPACT trial target population were receiving letters alerting them to changes in their pain medication while they were being approached about trial participation. Numerous patients whom we contacted expressed concern about the anticipated changes in their pain medication and misperceived the opportunity to participate in the PPACT trial as being linked to or driven by the opioid prescription changes. Therefore, orientation sessions were also developed and implemented as part of the recruitment process to try to address potential misperceptions.

2.3. Recruitment protocols before and after implementing orientation sessions

Patients with evidence of a pain condition on long-term opioid treatment, based on electronic health records (EHR) data, were potentially eligible for the PPACT trial (described elsewhere [11]). Throughout the trial, potentially eligible patients were first mailed an informational letter and then contacted by phone; during the calls, research staff provided an overview of the trial, conducted eligibility screening, and addressed questions. Before implementing the orientation sessions, if patients were eligible and interested in the trial, follow-up phone calls were scheduled for two to three days later to conduct the informed consent. However, after implementation, patients who were eligible and interested were invited to attend an in-person, hour-long orientation session at their primary care clinic before deciding to participate. Typically, patients were offered three dates and times for an orientation session over the following month and chose one to attend. They were sent a confirmatory email and received a reminder phone call the day before. If patients attended the orientation session, they were contacted by phone in the following week to determine whether they wanted to enroll in the trial and, if appropriate, move forward with the informed consent process.

2.4. Orientation session overview

Modeled after Goldberg and Kiernan [8], the hour-long orientation sessions were designed for approximately 15 attendees to easily interact and ask questions and were led by KPNW PPACT senior research staff. PPACT trial specifics included outlining the rationale for the pragmatic study design; describing the two trial arms (PPACT intervention and usual care), individual PPACT behavioral intervention components and the trial's primary outcome measure; and independence of trial eligibility and participation from the KPNW system-wide opioid tapering initiative. Research methods principles included

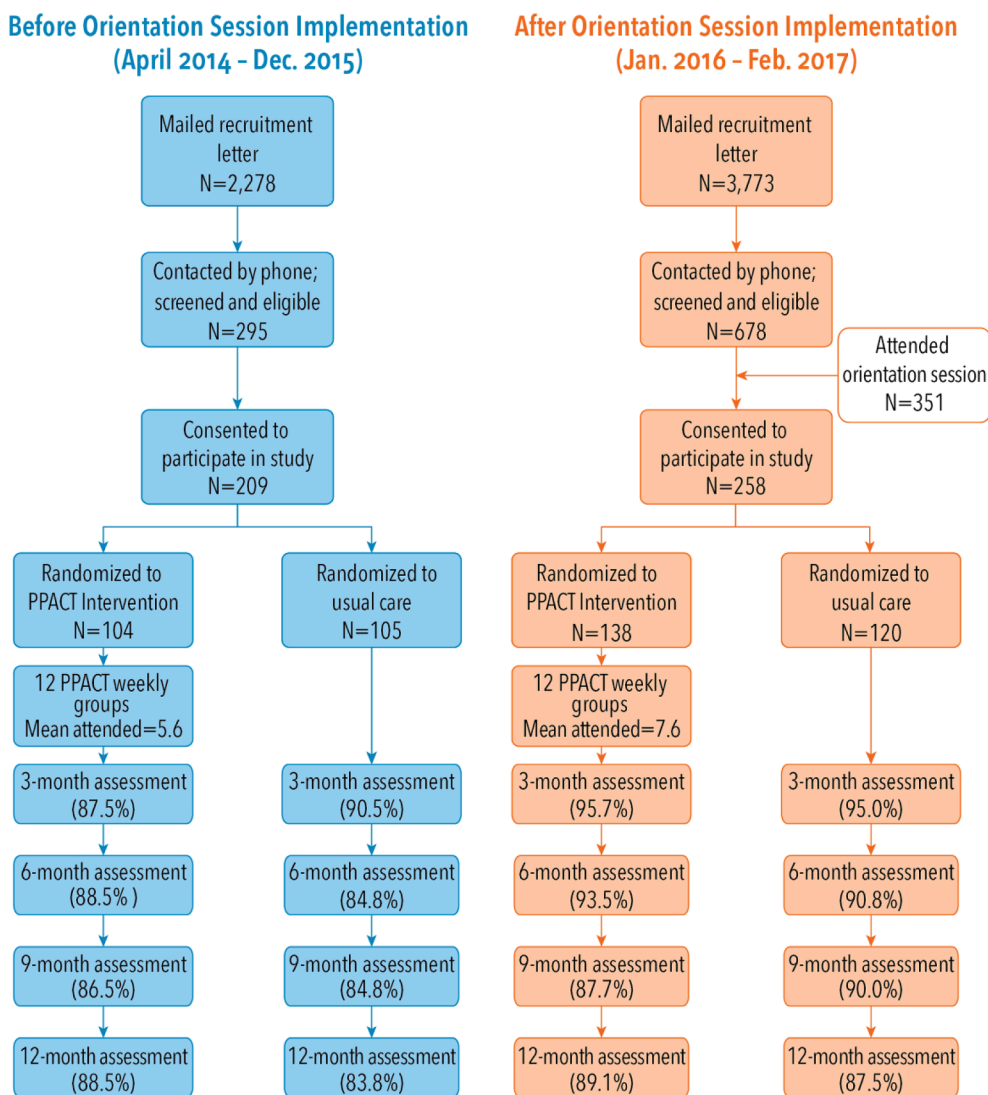


Fig. 1. PPACT recruitment and study activities at KPNW site.

explaining the rationale for randomization and the methodological impact of poor retention on trial conclusions. Motivational interviewing techniques addressed potential participant ambivalence about trial participation and behavior change [8]. To promote similar retention by trial arm, the orientation sessions emphasized the equal importance of data completion by participants in both arms. To support participants in making an informed decision as to whether to participate in a pragmatic clinical trial, the presenter divided the attendees into small groups of three to four people to discuss the pros and cons of being or not being in the trial, and then left the room so attendees would feel free to discuss their opinions. Upon the presenter's return, each small group shared their pros and cons with the larger group, and the presenter recorded all pros and cons on a flip chart or whiteboard, engaged in reflective listening, and remained neutral regarding trial participation [8]. Fig. 2 summarizes common pros and cons that emerged from these discussions.

2.5. Outcomes for this pre-post study design

Primary Outcomes. We assessed two primary outcomes: intervention adherence (number of PPACT intervention group meetings attended out of 12) and trial retention (participant completion of a pain assessment at each quarterly time point over 12 months).

	BEING IN THE STUDY	NOT BEING IN THE STUDY
PROS	<ul style="list-style-type: none"> • New knowledge • Support & validation • Hope for improvement • Impact on research & clinical practice 	<ul style="list-style-type: none"> • Cost savings (Time & money) • No pressure to change • Discomfort avoided • Hassle-free
CONS	<ul style="list-style-type: none"> • Randomization process • Expectations • Time commitment • Accountability 	<ul style="list-style-type: none"> • Missed opportunity • Status quo/No change • No contribution • Health care management challenges

Fig. 2. Pros and cons of participating in a research study.

Secondary Outcome. To assess whether implementing orientation sessions prior to randomization affected the proportion of eligible patients who enrolled in the PPACT trial, we tracked the number of patients at three enrollment stages before and after implementing orientation sessions: those mailed a recruitment letter, those eligible and interested in the trial after the initial phone call, and those who enrolled (i.e., provided verbal consent and were randomized).

Exploratory Outcomes. In post-hoc analyses, we explored whether implementing orientation sessions affected the sample characteristics

of eligible KPNW patients who enrolled in the PPACT trial relative to the characteristics of the eligible KPNW target population who were approached before and after implementing the orientation sessions. Characteristics included the 19 demographic and clinical characteristics assessed in the main PPACT pragmatic trial that could have potentially influenced the PPACT trial's primary outcome (pain impact). Thus, not all characteristics may be relevant to the primary outcomes of interest here (adherence and retention) but provided a framework for exploration.

2.6. Analyses

Primary outcomes. To examine whether implementing orientation sessions was associated with higher intervention adherence (number of PPACT intervention group meetings attended during the study period), we used a two-level hierarchical linear model (also known as multilevel regression, mixed model, or random coefficients regression [18–20]) with one independent variable—orientation session (before/after) and modeled the clustering of patients within their primary care provider as a random effect. The random effect accounts for the intra-class correlation of patients nested within providers, consistent with the overall PPACT trial cluster randomization. In a second model, we controlled for average daily dose of opioid medication (≥ 90 morphine milligram equivalents daily/or less) by adding it as an independent variable. Because the distribution of this count variable did not follow a negative binomial distribution that is typical of count variables, we used an identity link and Gaussian distribution (i.e., standard linear mixed model).

$$\begin{aligned} \text{Level 1 Model: Adherence}_{ij} &= B_{0j} + B_{1j}\text{Orientation Sessions}_{ij} + r_{ij} \\ \text{Level 2 Model : } B_{0j} &= \gamma_{00} + u_{0j} \\ &B_{1j} = \gamma_{10} \end{aligned}$$

Where Adherence_{ij} is the measure for the i th person nested within the j th provider, $\text{Orientation Sessions}$ is coded 0 for before, 1 for after for the i th person nested within the j th provider, B_{0j} is the intercept for the j th provider, B_{1j} is the coefficient associated with $\text{Orientation Sessions}$ for the j th provider, r_{ij} is the random error associated with the i th person nested within the j th provider, γ_{00} is the overall mean intercept, u_{0j} is the random effect on the intercept of the j th provider, γ_{10} is the overall mean slope.

To examine whether implementing orientation sessions was associated with higher trial retention (participant completion of pain assessment at each quarterly time point over 12 months), we used three-level hierarchical generalized linear models using a log link and binomial distribution (also known as multilevel logistic regression) that accounted for the nesting of repeated observations (quarterly assessments) within patients within providers. We evaluated four models. All four models included three independent predictors—time (linear effect; Level 1), orientation session (before/after; Level 2), and trial arm (control/intervention; Level 3)—as well as Level 2 (i.e., person level) random effects for the Level 1 intercepts and slope for time, and Level 3 (i.e., provider level) random effects for the Level 2 intercept. The second model also included the interaction of time and orientation session; the third model included the interaction of time and trial arm; and the fourth model included average daily dose of opioid medication.

$$\begin{aligned} \eta &= \ln(\text{Probability of Retention}_{ijk}/(1 - \text{Probability of Retention}_{ijk})) \\ \text{Level 1 Model: } \eta &= \pi_{0jk} + \pi_{1jk}\text{Time}_{ij} + e_{ijk} \\ \text{Level 2 Model : } \pi_{0jk} &= B_{00k} + B_{01k} \text{ Orientation Sessions}_{jk} + r_{0jk} \\ &\pi_{1jk} = B_{10k} + r_{1jk} \\ \text{Level 3 Model : } B_{00k} &= \gamma_{000} + \gamma_{001}\text{Arm}_k + u_{00k} \\ &B_{10k} = \gamma_{100} \\ &B_{01k} = \gamma_{010} \end{aligned}$$

Where η is the log of the odds of Retention for the i th observation nested within the j th person nested within the k th provider, π_{0jk} is the intercept for the j th person nested within the k th provider, π_{1jk} is the coefficient associated with time for the j th person nested within the k th provider, Time is the assessment period for the i th observation nested within the j th person nested within the k th provider, e_{ijk} is the random error associated with the for the i th observation nested within the j th person nested within the k th provider, B_{00k} is the mean intercept for the k th provider after adjusting for Orientation Sessions, $B_{01k} = \gamma_{010}$ is the coefficient associated with Orientation Sessions (0 = before, 1 = after) for the j th person nested within the k th provider, r_{0jk} is the random effect on the intercept for the j th person nested within the k th provider, $B_{10k} = \gamma_{100}$ is the mean slope of time for the j th person nested within the k th provider, r_{1jk} is the random effect on the slope of time for the j th person nested within the k th provider, γ_{000} is the overall mean intercept after adjusting for arm, γ_{001} is the coefficient associated with Arm (0 = control, 1 = intervention) for the k th provider, u_{00k} is the random effect for the intercept of the k th provider, γ_{100} is the overall mean slope of time.

Secondary outcome. To evaluate whether implementing orientation sessions affected the proportion of eligible patients who enrolled in the trial, we conducted a Chi-squared test to compare the proportion of potentially eligible patients who enrolled (i.e., provided verbal consent and were randomized) before and after implementing orientation sessions.

Exploratory outcomes. To explore whether implementing orientation sessions affected the demographic and clinical characteristics of the patient sample who enrolled in the trial relative to the characteristics of the target population of potentially eligible KPNW patients during the same time periods (before and after implementing orientation sessions), we conducted a 2X2 ANOVA (for continuous characteristics) or logistic regression (for categorical characteristics) with two independent predictors—trial enrollment (yes/no) and orientation session (no/yes, i.e., before/after)—and the interaction between the two predictors. A significant interaction term would suggest that the orientation sessions themselves contributed to differences in demographic or clinical characteristics of patients who enrolled before and after implementation, rather than changes in the target potentially eligible population over time. All analyses were evaluated using a two-tailed alpha level of 0.05 and 95% confidence intervals.

3. Results

3.1. Primary outcomes

Intervention adherence. After implementing orientation sessions, PPACT participants had higher intervention adherence at the 12 PPACT group meetings than before implementing orientation sessions ($M = 7.6$, $SD = 3.8$ vs. $M = 5.6$, $SD = 4.5$, respectively; mean difference = 2.0, 95% CI [0.9, 3.2], $p = .001$). Controlling for average daily dose of opioid medication did not change results. In addition, after implementing the orientation sessions, the percentage of enrolled PPACT participants who never attended any of the 12 PPACT group meetings at the KPNW site was lower than the percentage of enrolled PPACT participants who never attended any group meetings before implementing sessions, 9.4%–23.1%, respectively; difference = 13.7% (95% CI for the difference in these two proportions [4.2, 23.1], $p = .004$) (Fig. 3).

Trial retention. Table 1 presents the unadjusted rates for completing the quarterly pain assessments by assessment time point. As there was an ICC of 0.65 for the person level and a near-zero ICC for the provider level ($< 1.0 \times 10^{-30}$), we conducted both the originally specified three-level multilevel logistic regression model as well as a more parsimonious two-level model that excluded the random effect of provider. Given the unsurprising identical results for regression coeffi-

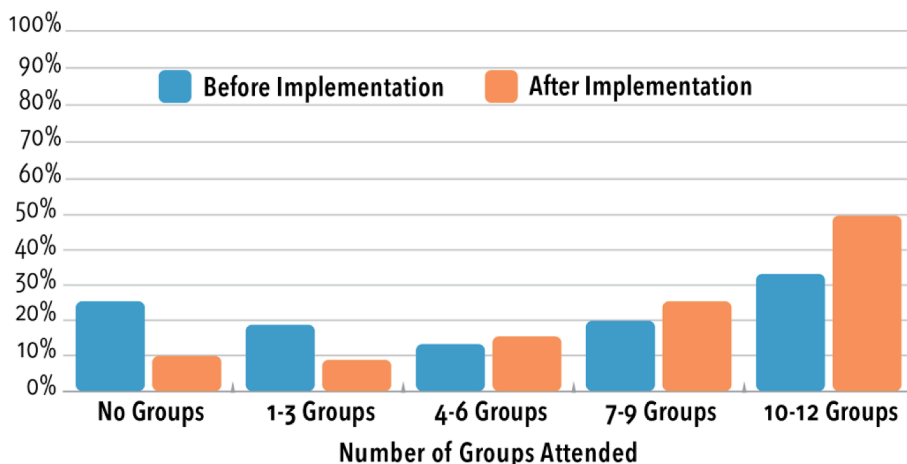


Fig. 3. Intervention groups attended pre- & post-implementation of orientation sessions.

Table 1

Unadjusted retention rates before and after implementing orientation sessions by PPACT trial arm.

Time Point	Before Implementing Orientation Sessions			After Implementing Orientation Sessions			Difference After-Before
	Intervention (N = 104)	Usual Care (N = 105)	Total (N = 209)	Intervention (N = 138)	Usual Care (N = 120)	Total (N = 258)	
3-month	87.5%	90.5%	89.0%	95.7%	95.0%	95.4%	6.4%
6-month	88.5%	84.8%	86.6%	93.5%	90.8%	92.3%	5.7%
9-month	86.5%	84.8%	85.7%	87.7%	90.0%	88.8%	3.1%
12-month	88.5%	83.8%	86.1%	89.1%	87.5%	88.4%	2.3%

clients and associated inferential tests between the three- and two-level models, we report the more parsimonious two-level results. After implementing orientation sessions, PPACT participants had 2.8 higher odds of completing quarterly pain assessments than before implementing the orientation sessions (95% CI [1.3, 5.8], $p = .007$). In the three remaining models, there were no effects for time by orientation ($p = .10$), time by trial arm ($p = .50$) or average daily dose of opioid medication ≥ 90 MME ($p = .92$).

3.2. Secondary outcome

After implementing orientation sessions, the proportion of patients who enrolled in the PPACT trial was lower than before implementing the sessions, 38.1% ($n = 258/678$) vs. 70.8% ($n = 209/295$), respectively (difference = 32.7%, 95% CI [26.4, 39.1], $p < .001$).

3.3. Exploratory outcomes

In post-hoc analyses, all but one of the 19 interactions for patient demographic and clinical characteristics were not significant, indicating that any differences observed before and after implementing the orientation sessions may have been representative of overall changing trends in the potentially eligible KPNW target population approached during the two time periods, rather than the orientation sessions (Table 2). Only the interaction term for race was significant, suggesting that after implementing the orientation sessions, a lower proportion of patients who reported a non-White race (Black, African American or Other) enrolled in the trial than before, 5.4% vs. 8.6% respectively (interaction OR = 1.24, 95% CI [1.03, 1.51], $p = .02$). Clinical significance of this interaction should be interpreted in an exploratory context in which a large number of tests were conducted and that the interaction would not be statistically significant with appropriate correction for multiple comparisons.

4. Discussion

Implementing orientation sessions was associated with higher attendance at PPACT intervention group meetings as well as higher PPACT retention through the trial follow-up period as shown by higher patient completion of quarterly assessments. However, improvements in adherence and retention in this pragmatic clinical trial among patients with chronic pain came with a cost: overall enrollment rates dropped substantially – almost a third – once attending an orientation session became a required step in the trial enrollment process.

Our findings indicate that orientation sessions are an effective strategy for promoting adherence and retention to an intensive health behavior intervention through a one-year trial period. Used as the sole strategy to address these factors, as they were in the PPACT pragmatic trial because other strategies such as financial incentives were not feasible due to the pragmatic trial design, these orientation sessions resulted in retention rates of 88% or higher at each follow-up time point. This rate exceeds the average retention rate of 80% observed in similar behavior change trials [1]. Importantly, the effect of the orientation sessions did not appear to differ by trial arm, suggesting that holding these sessions prior to enrollment might be an effective strategy to prevent differential retention by arm, which is commonly observed in health behavior trials and significantly compromises the ability to assess an intervention's effectiveness [2]. The effect of the orientation sessions on PPACT group adherence was also positive. By implementing the orientation sessions, the PPACT trial achieved a PPACT intervention target goal, namely for patients to attend the majority of the 12 group meetings. Indeed, patients attended an average of 7.6 group meetings or 2 more meetings than patients who participated before implementing orientation sessions. In addition, the percentage of patients who never attended any group meetings was cut in half. After implementing the orientation sessions, fewer than 1 in 10 patients never attended any group meetings whereas 1 in 4 patients never attended any group meetings before implementing the orientation sessions.

Table 2
Characteristics of KPNW PPACT trial participants before and after implementing orientation sessions.

N (%) or Mean, (SD)	Before Implementation			After Implementation		
	Enrolled in Trial N = 209	Potentially Eligible N = 2277	Difference (Enrolled-Eligible)	Enrolled in Trial N = 258	Potentially Eligible N = 3773	Difference (Enrolled-Eligible)
Age, yrs.	58.3 (12.2)	57.2 (13.1)	1.1	62.0 (12.0)	58.8 (13.7)	3.2
Female	153 (73.2%)	1492 (65.5%)	7.7%	180 (69.8%)	2247 (59.6%)	10.2%
Race						
White	192 (91.9%)	2081 (91.4%)	0.5%	244 (94.6%)	3312 (87.8%)	6.8%
Black or African American and Other	17 (8.1%)	196 (8.6%)	-0.5%	14 (5.4%)	461 (12.2%)	-6.8%
Hispanic ethnicity	7 (3.4%)	64 (2.8%)	0.6%	3 (1.2%)	124 (3.3%)	-2.1%
Substance use						
Current smoking	48 (23.0%)	582 (25.6%)	-2.6%	40 (15.5%)	742 (19.7%)	-4.2%
Alcohol abuse	10 (4.8%)	58 (2.6%)	2.2%	12 (4.7%)	106 (2.8%)	1.9%
Drug abuse	11 (5.3%)	74 (3.3%)	2.0%	7 (2.7%)	116 (3.1%)	-0.4%
Chronic medical conditions						
Diabetes	51 (24.4%)	478 (21.0%)	3.4%	62 (24.0%)	773 (20.5%)	3.5%
Cardiovascular disorder	52 (24.9%)	388 (17.0%)	7.9%	58 (22.5%)	734 (19.5%)	3.0%
Hypertension	90 (43.1%)	847 (37.2%)	5.9%	97 (37.6%)	1207 (32.0%)	5.6%
Chronic pulmonary disease	48 (23.0%)	413 (18.1%)	4.9%	48 (18.6%)	668 (17.7%)	0.9%
Two or more of above chronic medical conditions	67 (32.1%)	595 (26.1%)	6.0%	78 (30.2%)	950 (25.2%)	5.0%
Mental health comorbidities						
Anxiety	49 (23.4%)	377 (16.6%)	6.8%	52 (20.2%)	668 (17.7%)	2.5%
Depression	90 (43.1%)	693 (30.4%)	12.7%	99 (38.4%)	920 (24.4%)	14.0%
Other mental health diagnoses	16 (7.7%)	63 (2.8%)	4.9%	15 (5.8%)	92 (2.4%)	3.4%
Chronic pain-related clinical characteristics						
Number of non-malignant chronic pain types, mean (SD)	3.2 (1.7)	2.5 (1.7)	0.7	2.6 (1.7)	2.3 (1.7)	0.3
Average daily morphine milligram equivalent (MME) dose ≥ 90	55 (26.3%)	468 (20.6%)	5.7%	36 (14.0%)	394 (10.4%)	3.6%
Benzodiazepine receipt	57 (27.3%)	623 (27.4%)	-0.1%	66 (25.6%)	839 (22.2%)	3.4%
High utilizer of primary care services	12 (5.7%)	81 (3.6%)	2.1%	10 (3.9%)	126 (3.3%)	0.6%

The impact of the orientation sessions on enrollment rates in the PPACT trial among patients with chronic pain was not trivial and may have been due to several factors. First, requiring attendance at the orientation session prior to enrollment created an extra step for eligible and interested patients to complete before deciding whether to participate, which could select for more motivated patients. Second, and perhaps more relevant, are factors specific to the population of chronic pain patients who were eligible for the PPACT trial, as these patients typically experience poor physical functioning which can affect their ability to travel to and attend in-person meetings outside their homes. Third, the major widespread changes in policy and practice to restrict or taper opioid prescriptions for patients with chronic pain that occurred nationally and within the KPNW health system in early 2016 when the orientation sessions were implemented could have undercut the target population's interest in engaging further with the KPNW health care system and their health care providers so as not to jeopardize or disrupt their current pain prescription levels. Therefore, future trials considering orientation sessions need to ensure that enrollment targets can be met even if only 35–40% of those who are eligible enroll. This includes considering the characteristics of the target population from which participants are to be recruited, especially for medically complex patients who face physical and social barriers when engaging with health care systems, as well as the size of the target population, as additional recruitment efforts and eligibility screening may be necessary.

Given that orientation sessions may be effective in promoting adherence in pragmatic clinical trials and require few resources, it is possible that they could be a useful tool to both engage patients and improve the delivery of behavioral interventions and programs in clinical settings. In fact, requiring orientation sessions prior to enrollment in or completion of a costly intervention is not uncommon in the delivery of clinical care [21,22].

Despite the strengths of our study, it also had limitations. Although our design enabled a comparison of those who enrolled before and after implementation of the orientation sessions, a stronger comparison would have been a simultaneous control group who were not required to attend the orientation sessions, and a randomized study design. In addition, as a result of widespread opioid prescription tapering, there were differences in the amount of opioids taken by patients who enrolled in the trial before and after implementation of the orientation sessions. However, we addressed this potential confounding by including average daily opioid dose as a covariate in our models. Lastly, the limited racial and ethnic diversity of the trial population at the KPNW site prevented us from being able to assess differences in adherence and retention among racial and ethnic subgroups. Importantly, recent reports suggest that those most impacted by chronic pain are more likely to be racial and ethnic minorities, as well as from limited financial means [23]. Hence, identifying whether orientation sessions impact participation and promote adherence and retention in trials among disadvantaged populations should be a focus of future work.

5. Conclusions

In summary, implementing orientation sessions when recruiting for an intensive behavior change trial or clinic-based intervention can be a useful strategy for improving adherence and retention, especially if other strategies such as financial incentives cannot be employed. If utilized, consideration of target population characteristics which may affect ability to attend an in-person session, such as physical and psychosocial barriers, should be explored to ensure enrollment targets can be met.

In addition, a large enough population may be needed to meet enrollment targets, as a smaller proportion of eligible participants may

choose to participate. Interactive group-based orientation sessions are a feasible and low resource approach to ensure participant engagement and retention.

Declaration of competing interest

The authors declare that they have no competing interests.

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List of Abbreviations

PPACT	Pain Program for Active Coping and Training pragmatic clinical trial
KPNW	Kaiser Permanente Northwest health care system
EHR	Electronic health records
CDC	Centers for Disease Control
PEG	A Three-Item Scale Assessing Pain Intensity and Interference
MME	Morphine milligram equivalents
ANOVA	Analysis of Variance
ICC	Intraclass correlation
CI	Confidence interval

Availability of data and material

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Authors' contributions

MM lead the overall design of the current study, directed the creation of datasets, contributed to the interpretation of results, and lead the writing of the manuscript. MCL and WMV developed the analytic plan and MCL conducted the final analyses; both were major contributors in writing the manuscript. LLD and MK were major contributors

to the overall design, contributed to the interpretation of results, and in writing the manuscript. All authors read and approved the final manuscript.

References

- [1] M. Coday, C. Boutin-Foster, T.G. Sher, J. Tennant, M.L. Greaney, S.D. Saunders, G. W. Somes, Strategies for retaining study participants in behavioral intervention trials: retention experiences of the nih behavior change consortium, *Ann. Behav. Med.* 29 (2) (2005) 55–65.
- [2] R. Crutzen, W. Viechtbauer, M. Spigt, D. Kotz, Differential attrition in health behaviour change trials: a systematic review and meta-analysis, *Psychol. Health* 30 (1) (2015) 122–134.
- [3] M.S. Fewtrell, K. Kennedy, A. Singhal, R.M. Martin, A. Ness, M. Hadders-Algra, B. Koletzko, A. Lucas, How much loss to follow-up is acceptable in long-term randomised trials and prospective studies?, *Arch. Dis. Child.* 93 (6) (2008) 458–461.
- [4] K.F. Schulz, D.A. Grimes, Sample size slippages in randomised trials: exclusions and the lost and wayward, *Lancet* 359 (9308) (2002) 781–785.
- [5] E.T. Warner, R.E. Glasgow, K.M. Emmons, G.G. Bennett, S. Askew, B. Rosner, G. A. Colditz, Recruitment and retention of participants in a pragmatic randomized intervention trial at three community health clinics: results and lessons learned, *BMC Publ. Health* 13 (2013) 192.
- [6] L.L. Davis, M.E. Broome, R.P. Cox, Maximizing retention in community-based clinical trials, *J. Nurs. Scholarsh.* 34 (1) (2002) 47–53.
- [7] K. Loudon, S. Treweek, F. Sullivan, P. Donnan, K.E. Thorpe, M. Zwarenstein, The PRECIS-2 tool: designing trials that are fit for purpose, *BMJ* 350 (2015) h2147.
- [8] J.H. Goldberg, M. Kiernan, Innovative techniques to address retention in a behavioral weight-loss trial, *Health Educ. Res.* 20 (4) (2005) 439–447.
- [9] L. Jiang, M.L. Smith, S. Chen, S. Ahn, K.P. Kulinski, K. Lorig, M.G. Ory, The role of session zero in successful completion of chronic disease self-management program workshops, *Front. Public Health* 2 (2014) 205.
- [10] M. Kiernan, S.D. Brown, D.E. Schoffman, K. Lee, A.C. King, C.B. Taylor, N.C. Schleicher, M.G. Perri, Promoting healthy weight with “stability skills first”: a randomized trial, *J. Consult. Clin. Psychol.* 81 (2) (2013) 336–346.
- [11] L. DeBar, L. Benes, A. Bonifay, R.A. Deyo, C.R. Elder, F.J. Keefe, M.C. Leo, C. McMullen, M. Mayhew, A. Owen-Smith, et al., Interdisciplinary team-based care for patients with chronic pain on long-term opioid treatment in primary care (PPACT) - protocol for a pragmatic cluster randomized trial, *Contemp. Clin. Trials* 67 (2018) 91–99.
- [12] C.S. Cleeland, K.M. Ryan, Pain assessment: global use of the brief pain inventory, *Ann. Acad. Med. Singapore* 23 (2) (1994) 129–138.
- [13] S. Keller, C.M. Bann, S.L. Dodd, J. Schein, T.R. Mendoza, C.S. Cleeland, Validity of the brief pain inventory for use in documenting the outcomes of patients with noncancer pain, *Clin. J. Pain* 20 (5) (2004) 309–318.
- [14] E.E. Krebs, M.J. Bair, T.M. Damush, W. Tu, J. Wu, K. Kroenke, Comparative responsiveness of pain outcome measures among primary care patients with musculoskeletal pain, *Med. Care* 48 (11) (2010) 1007–1014.
- [15] E.E. Krebs, K.A. Lorenz, M.J. Bair, T.M. Damush, J. Wu, J.M. Sutherland, S.M. Asch, K. Kroenke, Development and initial validation of the PEG, a three-item scale assessing pain intensity and interference, *J. Gen. Intern. Med.* 24 (6) (2009) 733–738.
- [16] A. Owen-Smith, M. Mayhew, M.C. Leo, A. Varga, L. Benes, A. Bonifay, L. DeBar, Automating collection of pain-related patient-reported outcomes to enhance clinical care and research, *J. Gen. Intern. Med.* 33 (Suppl 1) (2018) 31–37.
- [17] D. Dowell, T.M. Haegerich, R. Chou, CDC guideline for prescribing opioids for chronic pain—United States, 2016, *JAMA* 315 (15) (2016) 1624–1645.
- [18] J.J. Hox, *Multilevel Analysis: Techniques and Applications*, Routledge, 2010.
- [19] S.W. Raudenbush, A.S. Bryk, *Hierarchical Linear Models: Applications and Data Analysis Methods*, second ed., Sage Publications Inc, Thousand Oaks, CA, 2002.
- [20] T. Snijders, R. Bosker, *Multilevel Analysis: an Introduction to Basic and Advanced Multilevel Modeling*, Sage, Thousand Oaks, CA, 1999.
- [21] M.A. Kalarchian, M.D. Marcus, Psychosocial interventions pre and post bariatric surgery, *Eur. Eat Disord. Rev.* 23 (6) (2015) 457–462.
- [22] S. McDonald, S.E. Hetrick, S. Green, Pre-operative education for hip or knee replacement, *Cochrane Database Syst. Rev.* (1) (2004).
- [23] J. Dahlhamer, J. Lucas, C. Zelaya, R. Nahin, S. Mackey, L. DeBar, R. Kerns, M. Von Korff, L. Porter, C. Helmick, Prevalence of chronic pain and high-impact chronic pain among adults - United States, 2016, *MMWR (Morb. Mortal. Wkly. Rep.)* 67 (36) (2018) 1001–1006.