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Review Articles

Perspectives on Participation in Clinical Trials Among Individuals With Pain, Depression, and/or Anxiety: An ACTTION Scoping Review

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Abstract: **For individuals experiencing pain, the decision to engage in clinical trials may be influenced by a number of factors including current and past care, illness severity, physical functioning, financial stress, and caregiver support. Co-occurring depression and anxiety may add to these challenges. The aim of this scoping review was to describe perspectives about clinical trial participation, including recruitment and retention among individuals with pain and pain comorbidities, including depression and/or anxiety. We searched PubMed, CINAHL, PsycINFO, and Cochrane CENTRAL databases. Study features, sample demographics, perspectives, barriers and/or motivations were collected and described. A total of 35 assessments were included in this scoping review with 24 focused on individuals with pain (24/35, 68.6%), 9 on individuals with depression and/or anxiety (9/35, 25.7%), and 2 on individuals with pain and co-occurring depression/anxiety (2/35, 5.7%). Barriers among participants with pain and those with depression included: research team's communication of information, fear of interventional risks, distrust (only among respondents with pain), too many procedures, fear of inadequate treatment, disease-life stressors, and embarrassment with study procedures (more commonly reported in participants with depression). Facilitators in both groups included: altruism and supportive staff, better access to care, and the ability to have outcome feedback (more commonly among individuals with depression). Individuals with pain and depression experience challenges that affect trial recruitment and retention. Engaging individuals with pain within research planning may assist in addressing these barriers and the needs of individuals affected by pain and/or depression.**

Perspective: ***This review highlights the need to address barriers and facilitators to participation in clinical trials, including the need for an assessment of perspectives from underserved or marginalized populations.***

Keywords: *Review, pain, depression, research participation, patient engagement, clinical trials.*

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The ethical conduct of clinical trials is dependent on informed and voluntary participation from representative samples of persons likely to benefit from experimental interventions. For individuals experiencing pain, the decision to participate in clinical trials may be influenced by current and past clinical

care, severity of illness, physical functioning, financial stress, and caregiver support, among other factors.

Research outside the context of pain (eg, cancer, HIV, depression) has assessed barriers and facilitators that affect trial participation.[41] Personal benefit, altruism, and trust were found to be facilitating factors for study participation, regardless of research setting and trial design. Barriers were commonly reported and varied among different populations and severities of illness. Practical challenges were noted as well as barriers specific to trial-based research, with participants expressing concerns about randomization, treatment changes, and the inherent uncertainty of trials.[41] Identifying if these features are similar among individuals with pain can assist researchers with study design and recruitment and retention, and in turn, research efficiency and generalizability.

A qualitative synthesis of 15 studies assessed factors that impact trial recruitment among patients with depression. [25] Findings indicated that patients with depression are less likely to participate in research if it might exacerbate their condition. Additionally, concerns about cognitive capacity for consent and patient welfare, treatment preferences, and trial burden were all noted as barriers to participation. The symptoms and presentation of depression were a barrier noted among many studies. Although the assessment of trial-specific factors affecting recruitment has been completed among patients with depression, it has not been examined within the context of pain.

Pain and depression are conditions that often co-occur.[2] Observational research has suggested a bidirectional relationship among pain and mental illness, specifically depression and anxiety.[7] Signs and symptoms of depression (eg, loss of motivation and interest, fatigue, etc.) and anxiety likely influence willingness to participate and retention in clinical trials.[25] Addressing these factors may increase the efficiency of conducting trials and reduce the negative impact on recruitment and retention within clinical studies.

The purpose of this review is to describe perspectives about clinical trial participation, including barriers and facilitators for trial recruitment and retention among individuals with pain-related conditions, depression, and/or anxiety. A scoping review was deemed appropriate due to the broad nature of the topic, the heterogeneity and diversity of sample populations, and the varied methods (ie, qualitative and quantitative) to capture individual perspectives. This review did not aim to critically appraise evidence but instead describe perspectives as it relates to participation in clinical trials.[36] Because depression/anxiety and pain frequently co-occur, we hypothesized that there would be similar perspectives between these conditions but also reported any differences.

Methods

This scoping review was conducted according to the Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) Checklist (Appendix 1).[48,40] Given that the report represents a scoping review of the literature, registration was not permitted according to PROSPERO guidelines.

Eligibility Criteria

Studies were included if they assessed patient-specific preferences related to clinical trial participation, recruitment, or retention (barriers, facilitators, etc.) for the treatment of any pain condition, depression, and/or anxiety. Facilitators were characteristics that motivated trial participation and/or supported participation for individuals. Exclusion criteria were: assessments of treatment preferences or goals of therapy only, assessments of researcher preferences, studies that assessed mixed samples of patients and clinicians without separating the data, studies that only provided reasons for trial dropouts or attrition without any other data or qualitative component (ie, interview, survey or focus group), or abstracts without data if further information could not be obtained.

Although we did not specifically search for perspectives about treatment outcomes, upon review of full-texts, we decided to evaluate any that were within our search results. Much of that research has already been addressed by Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (IMMPACT).[49] For studies where pain, depression, and/or anxiety were secondary to another condition, the perspective assessment needed to address something relevant to one of those components. Although literature searches were focused on pain, depression, and/or anxiety, any psychiatric condition was included if it otherwise met criteria for inclusion.

Information Sources

PubMed, Cumulative Index to Nursing and Allied Health Literature (CINAHL), American Psychological Association PsycInfo and Cochrane CENTRAL were searched from inception through December 14, 2020 and February 5, 2021, respectively, using appropriate search terminology (Appendix 2). Authors of published abstracts were contacted for additional information. Reference lists of relevant articles were also reviewed for additional studies.

Data Review Process and Extraction

Title/abstract screening and full-text review were performed independently by at least 2 review authors (MF, EM, AK, KS). Disagreement between reviewers was resolved by discussion. When agreement could not be reached, a third author (MF, EM) adjudicated.

Four authors (MF, EM, AK, KS) performed data extraction. At least 2 authors independently extracted information from each article. A data extraction form was piloted prior to use (Appendix 3). In addition, a coding manual was developed to clarify entry and promote consistency in the evaluation of methodology.

Information related to study features, sample demographics, perspectives related to trial design and barriers and/or motivating factors to trial participation were collected (Appendix 3). As part of project planning, authors identified how other researchers (ie, O'Cathain 2013, Sheridan 2020, Cheung 2020) assigned perspectives into thematic categories. We approached the process in a similar fashion.[10,38,41] Where possible, we utilized coding/interpretations as they were presented by the original authors. When articles did not provide specific themes, we categorized perspectives without duplicating across categories. Comparisons of preferences between pain, depression, and anxiety were planned if the sample for each was large enough. Critical appraisal of evidence quality was not conducted. Descriptive statistics were used, where applicable. Perspectives related to study design were categorized by theme.

Results

Search results identified 660 de-duplicated records from the initial search across all databases. Of these, 604 (91.5%) were excluded due to lack of eligibility, based on title and abstract screening. A total of 61 full-text articles were reviewed with 27 excluded (Fig 1) for the following reasons: lack of data about preferences related to clinical trial design (6/27, 22.2%); abstract without data (4/27, 14.8%); no pain or psychiatric condition (4/27, 14.8%); focused on treatment preferences only (4/27, 14.8%); mixed sample without separation of participant perspectives (3/27, 11.1%); duplicate research (1/27, 3.7%); assessment unrelated to pain or psychiatric condition (1/27, 3.7%); or other reasons (4/27, 14.8%). One study performed 2 separate phases of data collection, so each phase was extracted separately.[49] This yielded a total of 35 extracted assessments across 34 articles (Table 1, Appendix 4). For all results, the N=35 unless otherwise noted.

Study Features

Perspectives were obtained from individuals with pain (24/35, 68.6%); depression, and/or anxiety (9/35, 25.7%); or pain with some having co-occurring anxiety/depression (2/35, 5.7%). Within assessments only reporting pain (N=24), pain was primarily chronic in nature and included: juvenile arthritis (3/24, 12.5%); osteoarthritis (3/24, 12.5%); pelvic pain (3/24, 12.5%); mixed chronic pain (2/24, 8.3%); headache (2/24, 8.3%); chronic pain not otherwise specified (2/24, 8.3%); back and/or joint pain not otherwise specified (1/24, 4.2%); chest pain post-acute coronary syndrome (1/24, 4.2%), cancer-related pain (1/24, 4.2%), Duchenne muscular dystrophy (1/24, 4.2%), rheumatoid arthritis (1/24, 4.2%), sickle cell disease (1/24, 4.2%), gout (1/24, 4.2%), spinal stenosis (1/24, 4.2%), and end-of-life pain (1/24, 4.2%).

Nine assessments obtained perspectives from individuals with both pain and with depression and/or anxiety, 7/9 (77.8%) focused entirely on depression, while 2/9 (22.2%) focused on depression and anxiety. One of the 2 assessments focusing on depression and anxiety noted the coexistence of anxiety without stating how many patients also had anxiety[12]; the other obtained

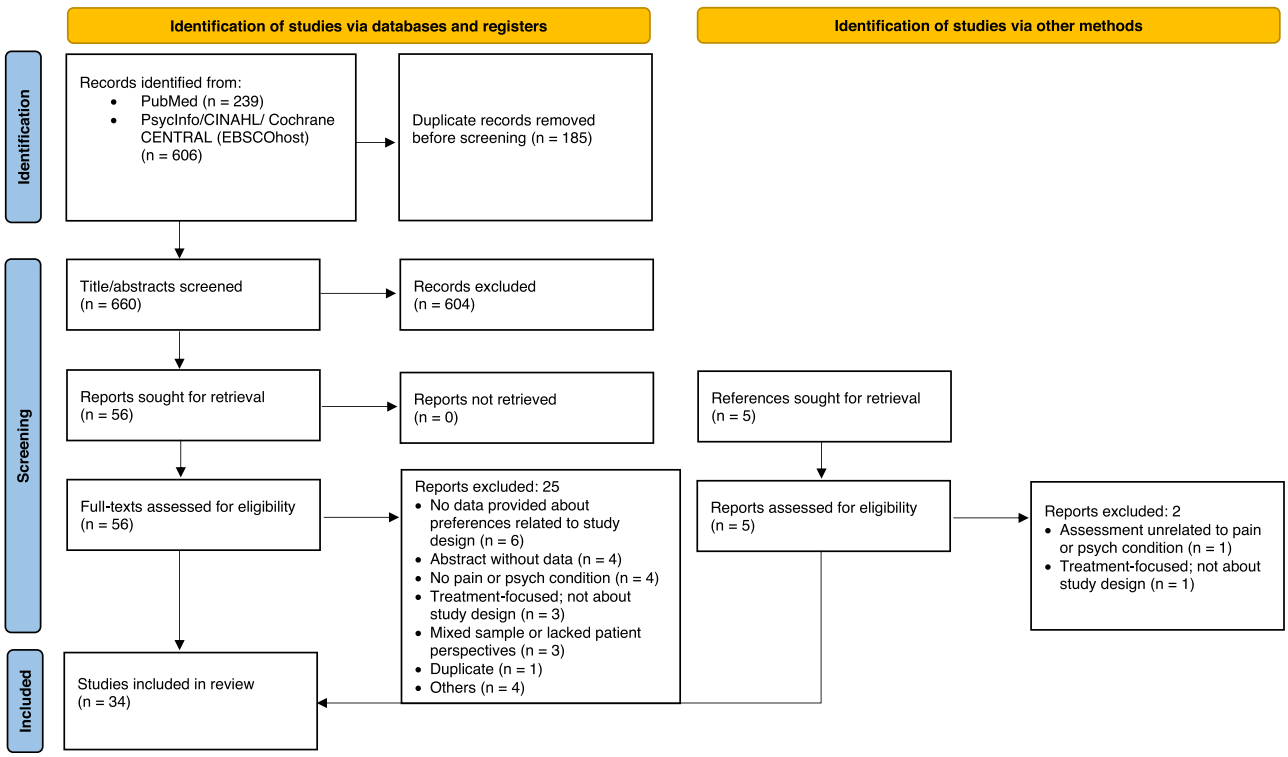

Figure 1. PRISMA flow diagram (Color).
From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71. For more information, visit: http://www.prisma-statement.org/

Table 1. Characteristics of Included Assessments of Perspectives Related to Study Design.

Reference	*Sample*	*Sample Country*	*Pain and Psychological Features*	*Sample Size Providing Perspectives*	*Data Collection Method*
Ackerman 2013[1]	Adult	Australia	Pain only (100% osteoarthritis)	258 patients	Individual interview
Barnes 2012[3]	Adult	England, Scotland	Depression only (100%)	25 patients	Interview & survey
Bennett 2017[5]	Adult	England	Pain only (end-of-life)	19 total: 15 patients; 4 caregivers	Interview & survey
Bove 2018[8]	Adult	USA	Pain only (100% spinal stenosis)	50 participants	Focus group
Cheung 2020[10]	Adult	USA	Pain/depression: 177 (35%) back pain; 215 (43%) joint pain; 210 (42%) depression	501 participants	Survey
Cramer 2011[12]	Adult	England	Depression/anxiety: (100% depression; anxiety noted but not quantified)	73 mix of patients and participants	Individual interview
DasMahapatra 2017[13]	Adult	Global	Pain/depression: 241 (15%) fibromyalgia; 125 (8%) rheumatoid arthritis; 91 (5%) depression	1621 participants	Survey
Dennin 2020[14]	Adult	USA	Depression/anxiety associated with Parkinson's disease	16 total: 14 participants; 2 care-partners	Individual interview & focus group
Denny 2018[15]	Adult	England, Scotland	Pain only (100% pelvic pain, including endometriosis)	14 patients	Individual interview & focus group
Dowrick 2007[16]	Adult	England	Depression only (100%)	5 patients	Individual interview
Gaudiano 2013[20]	Adult	USA	Depression only (100%)	55 patients	Other*
Gaudiano 2016[19]	Adult	USA	Depression only (100%)	615 participants	Survey
Hislop Lennie 2013[21]	Adult	England	Pain only (100% osteoarthritis)	51 participants	Survey
Hissink Muller 2018[22]	Mixed	Netherlands	Pain only (100% juvenile arthritis)	Phase I: 15 parents, 7 patients; Phase II: 23 parents, 7 patients	Survey (Phase 1) & interview (Phase 2)
James 2019[26]	Not stated; assumed adult	USA	Pain only (100% chronic pain not otherwise specified)	190 survey respondents (mix of patients and participants): 94 on opioids in last 6 mo; 96 had no opioids in last 6 mo	Survey
Leinisch-Dahlke 2004[28]	Adult	Germany	Pain only (100% headache, including migraine)	486 patients	Survey
Lenguerrand 2020[29]	Adult	England	Pain only (100% osteoarthritis)	142 patients	Individual interview
Lenze 2017[30]	Adult	USA	Depression only (100%)	20 patients	Focus group & survey
Middleton 2017[32]	Mixed	England	Pain only (100% endometriosis)	14 patients	Focus group (N=4) & interviews (N=10)
Midgley 2016[33]	Pediatric	England	Depression only	76 adolescent patients	Individual interview
Morgan 2019[35]	Mixed	Austria, Italy, USA	Pain only (100% juvenile arthritis)	83 participants/parents	Survey
Nelson 2013[37]	Not stated; assumed adult	England, Wales	Pain only (100% cancer)	42 participants	Individual interview
Paterson 2008[39]	Adult	Australia	Pain only (100% headache, including migraine)	10 participants	Individual interview
Sherratt 2017[42]	Mixed	England	Pain only (100% juvenile arthritis)	28 patients and parents	Individual interview

(*continued on next page*)

Table 1. Continued

Reference	Sample	Sample Country	Pain and Psychological Features	Sample Size Providing Perspectives	Data Collection Method
Smith 2016[43]	Adult	USA	Pain only (low back pain 63, 42%; musculoskeletal not specified as low back or osteoarthritis pain 26, 17%; neuropathic pain 20, 13%; osteoarthritis 9, 6%; fibromyalgia 7, 5%; multiple conditions 7, 5%; chronic regional pain syndrome 5, 3%; other 13, 9%)	150 participants	Other*
Stamuli 2017[44]	Adult	UK	Pain only (100% rheumatoid arthritis)	100 participants	Survey
Tallon 2011[45]	Adult	England	Depression only (100%)	252 patients	Survey
Taylor 2013[46]	Adult	New Zealand	Pain only (100% gout)	21 patients	Other*
Turk 2008 Phase 1[49]	Adult	USA	Pain only (100% chronic pain not otherwise specified)	31 patients	Focus group
Turk 2008 Phase 2[49]	Adult	USA	Pain only (migraine or other chronic headache 216, 22%: rheumatoid arthritis 50, 5%; osteoarthritis 184, 19%; pain related to cancer 8, 1%; low back pain 523, 55%; neck or shoulder pain 441, 46%; fibromyalgia 269, 28% painful diabetic neuropathy 26, 3%; other neuropathic pain 352, 37%; other 201, 21%)	959 participants	Survey
van den Berg 2017[6]	Adult	England	Pain only (100% chest pain post-acute coronary syndrome)	10 patients	Individual interview
Vercellini 2015[50]	Adult	Italy	Pain only (100% pelvic pain, including endometriosis)	500 patients	Survey
Verhaart 2019[51]	Pediatric	Australia, Canada, France, Italy, Netherlands, UK, USA	Pain only (100% Duchenne muscular dystrophy)	78 participants and caregivers	Survey
Voice of the Patient 2014[47]	Mixed	USA	Pain only (100% sickle cell disease)	Unclear	Interview & survey
Wu 2016[53]	Adult	China	Pain only (100% back or joint pain not otherwise specified)	441 patients	Survey

*Single study with two data collection periods evaluated independently that utilized interviews and conjoint decision-making survey methods

perspectives of mental health outcomes, including depression and anxiety, in patients with Parkinson's disease.[14]

Within the 2 assessments that focused on pain with some of the sample also reporting depression, 1 assessment reported perspectives from 1,621 participants with 9 different primary conditions, including: rheumatoid arthritis (125/1621, 8%), fibromyalgia (241/1621, 15%), and depression (91/1621, 5%), among others unrelated to pain or depression/anxiety.[13] The other study obtained perspectives from 501 patients with more than 2 chronic conditions, with participants able to select multiple chronic conditions. Of the 501 participants in the sample with at least 2 chronic conditions, 177/501 (35%) were noted to have back pain, 215/501 (43%) had joint pain, and 210/501 (42%) had depression.[10] Our sample was not sufficiently large nor descriptive enough to allow us to make comprehensive

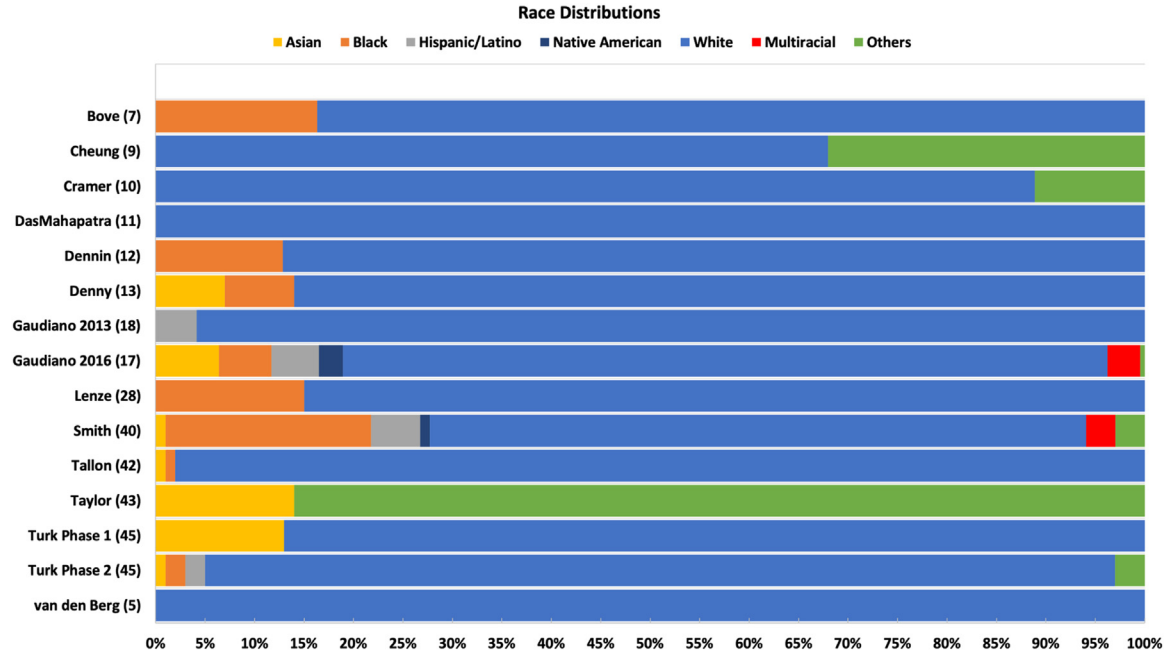

Figure 2. Race distributions of participants providing perspectives, N=15 (Color).

comparisons of perspectives between individuals with pain versus depression versus anxiety or any combination of these, but we have presented findings separately for the assessments among individuals with pain versus pain and depression/anxiety versus depression/anxiety only and noted differences where data were available.

Perspectives were gathered from individuals with pain using survey-based methods (13/35, 37%), individual interviews (9/35, 25.7%), mixed methods (ie, survey and individual interviews, 8/35, 23%), and focus groups (2/35, 5.7%). Three studies (3/35, 8.6%) (Table 1) utilized alternative methods. Of the studies using alternative methods, 2 studies captured perspectives via a conjoint decision-making exercise, and the other by having participants read 3 brief vignettes followed by questions on the Credibility and Expectancy Scale.[20,43,46]

Most studies obtained patient or caregiver perspectives as a primary objective (23/35, 65.7%), or were embedded within pilot/feasibility studies (12/35, 34.3%). Studies utilized mostly active and direct recruitment (23/35, 65.7%), largely from clinics, registries, mailed invitation, and practitioner referral. Studies also utilized passive recruitment (3/35, 8.5%) (eg, indirect strategies such as advertisements or flyers), mixed recruitment strategies (5/25, 14.2%), or were not described (4/35, 11.4%). A total of 17/35 (49%) of studies included participants with current and/or past participation in clinical research studies. Twelve included current participation (100% of the sample) within pilot/feasibility studies, and 5 studies reported some (but not all) past trial participation. Within these, the number within the sample ranged from 12% to 75%.

Study sites were located in metropolitan areas (22/35, 62.8%), listed as rural/urban/semi-urban[35] (1/35, 2.8%) or as location not described/other (12/35 34.2%). Other locations included no physical study site (ie, participants were assessed via an online survey and/or by a mailed-in survey). Locations of participants included respondents only within the U.S. (11/35, 31.4%), outside the U.S. (21/35, 60%) and mixed geographic locations (3/35, 8.5%).

Sample Demographics

Studies obtained adult perspectives (26/35, 74.2%), pediatric perspectives (2/35, 5.7%), both adult and pediatric perspectives (5/35,14.2%), or were not described (2/35, 5.7%). In the 2 studies that focused on pediatric perspectives, 1 was in childrenaffected by Duchenne muscular dystrophy and the other assessed adolescents affected by depression. [33,51] In the 5 studies with mixed samples, all perspectives were obtained from participants with pain.[22,32,35,42,47] In the 2 studies that did not describe the age of the study sample, participants were assumed to be adults based on the disease state assessed.[26,37] Five studies (14.2%) included mostly older patients based on the average age of the sample, 3 of which were in patients with pain, 1 in patients with depression and 1 in patients with mental health impacted by Parkinson's disease.[5,8,14,21,30]

Among studies reporting gender (27/35, 77.1%), 14 studies noted the sample was represented by >70% female participants. Eight studies (22.8%) did not report gender or sex assigned at birth for the sample, and no studies reported other gender identities. Eleven assessments (31.4%) required English literacy as part of study inclusion. One study (2.8%) purposefully sampled women experiencing economic hardship living with depression from divested areas in England.[12]

Racial/ethnic identity (Fig 2) was reported for the sample in only 15/35 (42.9%) studies. Within studies that collected information on racial/ethnic identity, the number of studies with participants identifying as one of following races/ethnicities included: White (14/15, 93.3%), Black (9/15, 60%), Asian (8/15, 53.3%), Native-American

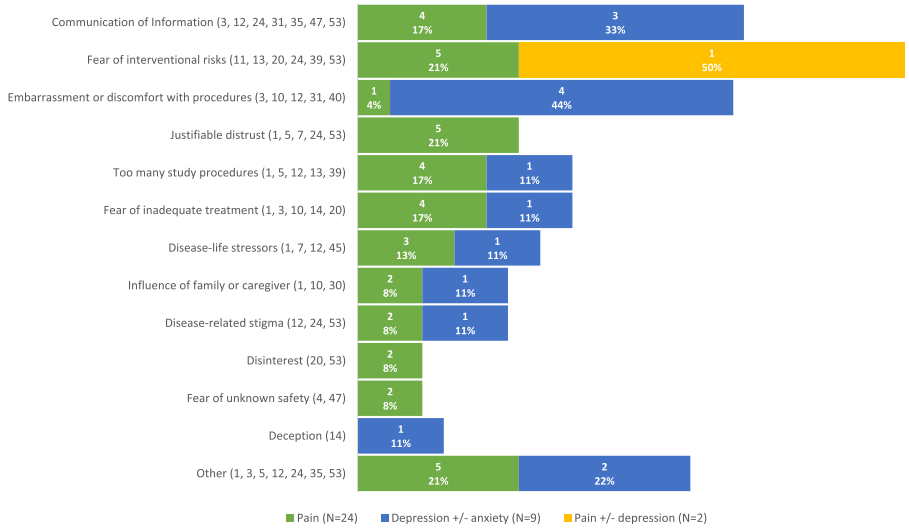

Figure 3. Percentage and number of studies reporting barriers to clinical trial participation (Color).

(6/15, 40%), Hispanic/Latino (4/17, 23.5%), and multiracial (3/15, 20%). Where reported, racial/ethnic percentages ranged from: 67 to 100% for White; 0 to 21% for Black; 0 to13% for Asian; 0 to 5% for Hispanic/Latino; 0 to 2.6% Native-American; and 0 to 3.5% for multiracial.

Other study features were infrequently and inconsistently reported among studies, including level of education (12/35, 34.2%); participants living with someone else in the household (10/35, 28.6%); employment status (10/35, 28.6%); insurance status (1/35, 2.8%); and disease duration (7/35, 20%) and severity (12/35, 34.2%).

Barriers to Trial Participation

Studies that reported barriers to clinical trial participation are noted within Fig 3 and separated by individuals with pain, depression, and mixed illness. Seven studies identified concerns related to the research team's communication of information as barriers to participation, 4 of which were among individuals with pain and 3 among individuals with depression and/or anxiety. Fear of interventional risks, distrust of healthcare providers, concerns about too many study procedures, fear of inadequate treatment, and disease-life stressors were more frequently noted as a barrier among patients with pain. In 1 study that purposefully recruited participants from divested areas among individuals experiencing economic hardship, some of the patients who declined to participate stated that they would not be able to attend any groups because of family commitments such as lack of regular childcare.[12]

Embarrassment with study procedures was mostly noted among participants with depression. These concerns were expressed as feeling self-conscious, the intrusive nature of the questions asked, embarrassment with bringing up the past, and symptoms of illness that created anxiety and embarrassment.[3,12,14,33]

Distrust of providers was noted as feelings of skepticism with clinical research.[1,8] This barrier was exclusively reported in the studies of pain. One study noted the importance of cultural sensitivity and awareness of the challenges faced by individuals affected by the presence of sickle cell disease.[47]

Among patients with chronic pain, disease-related stigma was noted as fear of labeling or judgment based upon past opioid use.[26] For patients with sickle cell disease, this was described as being "relegated to the status of only a Black disease".[47] For patients with mental health impacted by Parkinson's disease, disease-related stigma was related to changes in bowel movements, sexual activity, and mood.[14]

Motivations for Trial Participation

Fig 4 depicts studies that addressed motivating factors to clinical trial participation. Fifteen studies noted that a desire to help others is a motivation to participate in clinical trials. Additionally, rapport of research staff is motivating; notably staff that were empathetic, attentive listeners, trustworthy, and sociodemographically representative of people normally affected by the condition. Better access to care was described more often among patients with pain whereas receipt of outcome feedback, such as sharing data relevant to progress or improvement with participants was a motivator more commonly noted among patients with depression.

Perspectives Related to Trial Design That Affect Willingness to Participate

Recruitment, Randomization, and Blinding

Personal referral from the patient's primary care provider was noted in 2 studies, both of which included individuals with depression, as an influencing factor in willingness to participate.[12,13] Four studies among individuals with pain, depression, and mixed samples noted concerns with blinding and reported that people with pain would not agree to participate in studies if they were blinded.[10,13,28,50] Randomization was a source of concern, discomfort, and at times, confusion for participants. Three studies noted that an element of choice within the

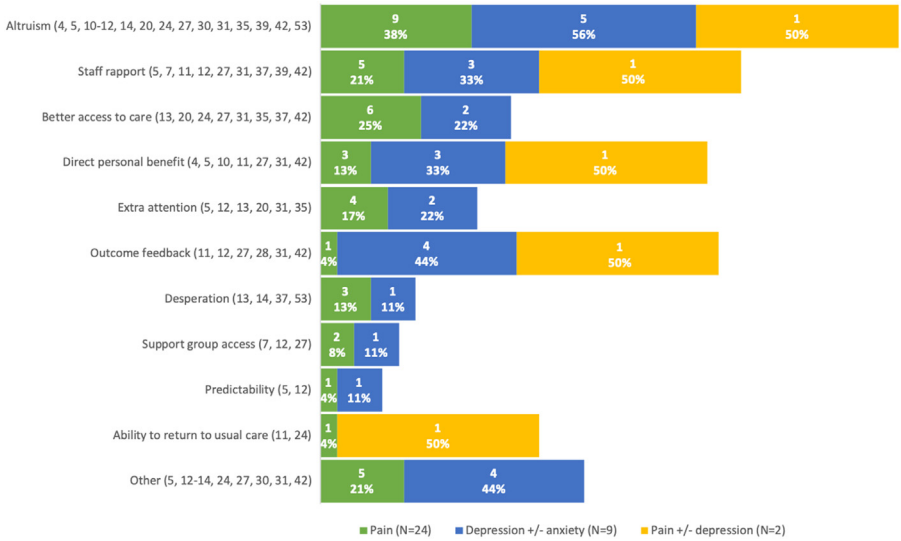

Figure 4. Percentage and number of studies reporting facilitators to clinical trial participation (Color).

randomization process would enhance willingness to participate.[15,32,50] Detailed communication of information about trial details, safety, and expectations of participation was noted among many studies as a factor affecting willingness to participate.[3,14,26,33,37,47,51]

Compensation, Time, and Transportation

The ability to continue treatment after study completion was noted in 1 study, particularly as it related to patient payment for therapy and rehabilitation services.[8] Another study noted that coverage for study-related injury was a factor that affected willingness to participate.[13] Other studies indicated that providing enough compensation was important[10,14,26] and 1 study suggested weekly compensation for time and travel was preferred.[43]

Concerns related to transportation were noted among 5 studies[1,8,13,14,29], 2 of which were in older populations.[8,14] The ability to drive, access transportation, and fears about the distance to study visits were noted in the study of patients with mental health affected by Parkinson's disease.[14]

A lack of time for study visits, and the duration and frequency of study visits were concerns noted within several studies. All concerns but one were reported by individuals impacted by pain.[1,5,8,10,15,32,43] Comments related to too many study sessions, interference with work or family, and suggestions to reduce the number and duration of follow-up visits were described. Conversely, for assessments in women with pelvic pain, a longer study duration (3-year) was widely noted as acceptable by patients to allow time for extra monitoring and time for "the body to adjust" and have breaks between adjustments.[15,32]

Interventions and Access to Current and/or Past Treatments

Willingness to participate based upon factors related to the interventions administered was affected by many factors. Fears of interventional risks were expressed as concerns about side effects and return of symptoms.[13,15,22,26,42,47] For studies involving patients with pain, the decision to participate was heavily influenced by past experiences with treatment. Also, route of administration was noted as a factor, particularly among parents, and within assessments of parenteral therapies.[15,42] The inconvenience of administration of injections and impact on the ability to go to school and work was noted.[15] In 1 study, patients who took opioids were generally willing to participate in an opioid tapering study.[26] For participants with headache, most surveyed would agree to take part in a placebo-controlled study and would not find it unpleasant to learn if their symptoms responded to placebo.[28] Drugs with longer durations of action and the ability to decide when to treat acute attacks were preferred among individuals with headache.[28]

Assessments of individuals with depression noted a preference for psychotherapy[19,20], and 1 study indicated that patients were not interested in counseling.[3] In an assessment of a small cohort of patients with depression, all agreed they would not be willing to participate in authorized deceptive design, in which individuals are told in advance about a temporary deceptive element in the trial. Nor willing to participate in post-hoc deceptive design, when a participant is notified after the trial is over that deception occurred.[16] In addition, patients indicated that the possibility of placebo or inadequate treatment alternatives impacted their willingness to participate.[13,16] In individual interviews of 76 adolescents with depression, 50% noted it was difficult to remember the differences among the 3 arms of psychological therapy, and "few" had a clear understanding of the differences among each arm.[33]

The desire to access past treatments was noted within fears of inadequate treatment and the ability to take current medications.[1,3,15,22,26,30,42,40] All of these assessments, except for one[30], were in patients with pain. Fears related to withdrawal or unfair drug

discontinuation without other effective options for the management of chronic pain[26] or the desire to avoid past treatments that were ineffective[1,3,15,22,42] were noted. Among patients with depression, 1 study described preference to tailor treatments based on past experience, symptoms, and side effects.[30]

Outcomes and Data Collection

Five studies focused entirely on outcome preferences within clinical trials among individuals with pain.[35,44,46,49,53] Outcome prioritization mostly focused on pain relief, functional improvement, and quality of life. In one study among patients with depression[30], preferred outcomes were psychological well-being and symptomatic improvement as well as safety (ie, avoidance of fall-related injury) associated with antidepressants.

In terms of data collection methods, four studies noted that in-home visits offered convenience, flexibility and/or supported rapport with research staff.[5,33,37,45] One study noted that electronic tablet-based assessments for self-reported psychological well-being were largely acceptable among participants.[30] Study participants preferred fewer study procedures including reduced number of assessments; less frequent assessments; and procedures that require less time.[1,5,6,10,13–16,29,42,43,43,45] One study among patients with depression noted that questionnaires were lengthy, repetitive, and difficult to understand.[45]

Less invasive outcome assessments and forms of data collection are preferred.[6,43,45,51] One study noted that patients thought that trials that included more invasive measures (eg, biopsy and cold water sensory testing) warranted higher compensation.[43]

No studies provided participant perspectives related to parallel vs crossover or pragmatic vs efficacy designs. In addition, no studies assessed whether source of funding affects trial participation.

Discussion

Our findings largely noted preferences among individuals affected by pain and to a lesser extent preferences among individuals with depression. We did not identify any assessments solely focused on individuals with anxiety. Only 2 assessments noted anxiety co-occurring with depression and 2 assessments noted pain co-occurring with depression in proportion of the overall sample. Despite this, it is more than likely that some proportion of individuals in the "pain only" assessments also had co-occurring, but not reported, depression or anxiety and vice versa for the assessments of individuals with depression only.

Outside of altruism and staff rapport, facilitators for trial participation largely reflect individuals with pain who may not be satisfied with current outcomes and/or seek alternative treatment options, which aligns with who is generally recruited into clinical trials.[4] The burden of illness can affect trial participation, including the need for enhanced social support and transportation if mobility is impacted or if distance from clinical study sites is perceived as inconvenient. The impact of disease-related stigma and concerns related to privacy may also deter participation. For some populations with children, declining participation and dropouts are due to lack of childcare.[12] Among individuals with chronic pain, research has shown that a shift to telehealth may offer solutions to some of the barriers we identified. Telehealth may offer greater flexibility as it relates to ease of access and convenience, while also promoting empowerment via self-knowledge and self-efficacy. However, the delivery of telehealth presents its own barriers, including the impersonal aspects of delivery, challenges with technology, and the need for digital literacy.[17,18]

Direct referral by a provider may also facilitate participation in clinical trials.[12,13] Although it may be argued that added attention by providers may augment placebo effects or be a source of bias, advocating for an individualized approach should be the priority with patient care and research alike. Increasing healthcare provider knowledge of research opportunities and disease-related stigma, along with recruiting via use of social media and community networks were noted as important.[47]

Most studies did not report additional comorbidities of the sample population, and as previously mentioned, it was likely that pain, depression, anxiety, and other mental health disorders coexisted among the study populations.[2] Post-hoc analysis of exclusion criteria from the 24 studies that assessed 'pain only' revealed that none of these studies explicitly excluded participants with mental health comorbidities. In fact, many formally or informally assessed the effect of pain on mood. Many assessments lacked consistent reporting of features that may be relevant for consideration in the context of patient or caregiver perspective. Population features such as education, caregiver support, employment and/or disability, and pain severity were infrequently or inconsistently reported.

There are several notable gaps to the literature. One notable gap was the lack of assessment from underserved or marginalized populations. Only 1 study described recruitment strategies that deliberately involved reaching out to individuals experiencing economic hardship.[12] In addition, methodology within of some of the assessments, such as the requirement for internet access or for multiple onsite visits, may have reduced the ability or willingness of some populations to engage. Where demographic data were presented, a lack of diverse representation appeared to be confirmed. For example, for studies that reported demographics related to gender, most were heavily represented by female views. For those that reported race, the participants were overwhelmingly white and were disproportionately so in studies conducted in the United States. And, more than a third of studies (31%) required English literacy as part of participation. Based on a lack of reporting, we could not determine whether individuals living in rural settings, those without routine access to healthcare, those with lower education levels

Table 2. Clinical Trial Design Considerations for Recruitment and Retention.

Recruitment Considerations[11,23,24,27,31,47]

- Direct and strategic recruitment to underserved and understudied patient populations is needed. Consider the use of patient partners to develop recruitment strategies.
- Education of the public via press, internet, or social media regarding the importance of clinical trials and how to access research opportunities.
- Providers may need education about how to connect patients with research opportunities.

Trial Design Considerations[38]

- The research team should be diverse and empathetic. Rapport with study participants may improve retention.
- Researchers may consider adding an element of choice into trial design (e.g., the ability to opt out of a non-preferred treatment).
- Researchers may consider the addition of a qualitative component within clinical trials to assess engagement, perspectives related to design and preferences, and reasons for declining participation and dropouts.
- Researchers may consider reporting reasons for and demographics of those declining participation as a way to better understand individual needs, particularly those of marginalized communities.

Trial Conduct Considerations

- Researchers should utilize multiple strategies and modalities for communication to deliver study-related information (e.g., written handouts, regular newsletter updates, videos, etc.).
- Engage participants, patient partners, or both to ensure appropriate compensation of time and travel and consider enabling access to treatment after completion of the trial.

or those not currently being paid for work were adequately represented. In addition, 17/35 (49%) of studies included participants with current and/or past participation in clinical research studies, 12/35 (34.3%) of which were part within pilot/feasibility studies. Therefore, the perspectives within this review lack diversity and representation and may not reflect the opinions of individuals who do not actively seek treatment.

Given this, community-based recruitment efforts to address barriers and facilitators among individuals with pain outside the healthcare system are needed. Focusing on marginalized communities and rebuilding trust are necessary to more broadly reflect true community needs. Collecting reasons for declining participation may be helpful in these efforts as well as efforts to differentiate perspectives among individuals with past/current trial participation versus those without. We were unable to make comparisons that need to be systematically addressed in future research.

Although few studies in our review reported comorbid diagnoses, it is very likely that individuals with chronic pain have coexisting illnesses. The barriers and facilitators identified in this review among individuals with pain and/or depression align with other research.[41] A systematic review of 26 different systematic reviews examined facilitators and barriers to research participation for any medical condition. Personal benefit and extra attention along with access to new therapies was noted most commonly as a facilitator followed by altruism, rapport, burden and convenience, and financial benefit. Barriers to participation noted within that review included fears related to safety; followed by practical difficulties with time; transportation and cost; distrust; aversion to randomization; specific treatment preferences; stigma; uncertainty; and desire for choice. Some barriers were noted within specific populations. For example, distrust was reported as a barrier within minoritized and marginalized groups and stigma was a barrier to recruitment for trials in HIV or mental health.[41] Our findings about distrust were among individuals with pain, 1 study was in patients with sickle cell disease and 2 studies had a population average age over 70 years.[1,6,8,26,47] The lived experiences of patients who have experienced racialized discrimination adds context for this distrust and underscores the need for antiracism practices in study design and dissemination of findings.[34] Within our findings, embarrassment with study procedures was more commonly noted among studies that included individuals with psychological illness, including adults and adolescents with depression.[3,12,14,33] Table 2 provides some considerations for engaging patients affected by pain and depression into clinical trials.[11,23,24,27,31,47]

A qualitative synthesis of 15 studies assessed factors that affect trial recruitment of patients with depression.[25] Many of these studies included mixed samples of patient and researcher perspectives, which was outside the scope of our review. However, four studies from this analysis were included in our review.[3,12,16,45] Our findings indicated that among individuals with depression, recruitment into trials was found to be affected by symptoms of depression, the risk of the study to mental health[3,16], stigma[45], and participant welfare and vulnerability[16]. Studies from the larger analysis also noted difficulties in recruiting due to the burden and inconvenience of trial procedures, treatment preferences, and the challenges with presenting research opportunities to individuals with depression.[3,16,25,45]

Rapport of the research team is a key component to retention in clinical trials. Also, the research team should be representative of the targeted population. Training and educating the team on cultural sensitivity, disease burden, and stigma may benefit recruitment and retention within clinical trials. Some individuals who participate in clinical trials perceive themselves as volunteers, and as such are hesitant to discuss other relevant medical issues due to it perhaps conflicting with the research agenda. One study captured these feelings in quotes such as "volunteer of my time, my body" and "we're here for their research not my research".[39]

Concerns with randomization, blinding, and access to effective treatment were noted among individuals with pain and depression. Partially randomized study designs have been utilized to incorporate an element of participant preference into the randomization process. In an assessment of treatment options for patients with endometriosis, Middleton et al utilized a flexible-entry, adaptive design model with a first-phase feasibility

assessment to gauge willingness to core design features (randomization, control, etc.) followed by clinician and participant discussion about which drug within a class of options would be preferred.[32] Partially randomized designs assign those who were willing to be randomized as usual, and those not willing to be randomized are assigned to treatment based on preferences, although these design strategies are not very common among individuals with chronic pain.[52] In our findings, one study which evaluated a mixed sample of patients with back and joint pain, 42% of which also had depression, suggested that the average patient prefers personalized trials that are less burdensome in terms of cost and time commitment, but that patient preference in personalized trials is highly variable, suggesting that individual differences must be accounted for when recruiting participants.[10] Another recruitment consideration may be to offer an open-label extension to all participants who complete the blinded phase of a study.

Input by individuals with pain adds value to clinical research. Such partners can assist with many aspects of trial design including recruitment considerations and strategies; adequate compensation for time and travel; modes and format of data collection; patient-oriented outcome measures; review and formatting of communication of study information; and results dissemination.[9] Incorporating a qualitative component into study methods at the pretrial stage as part of a pilot or feasibility study should be considered. If engagement of potential participants is not feasible before research is commenced, strategies can be implemented within ongoing trials or upon conclusion of participation.[38] The Patient Centered Outcomes Research Initiative (PCORI) in the U. S., Canada's Strategy for Patient-Oriented Research (SPOR), and Patient and Public Involvement (PPI) within the United Kingdom highlight just a few of the international efforts to engage patients as partners in clinical trials.[23] Building research relationships with individuals with pain as life-long partners can benefit all stakeholders.

This scoping review provides the first overview, to our knowledge, of patient and participant perspectives as they relate to study participation, recruitment and retention in trials among patients with pain and depression. A lack of information was found related to individuals with anxiety. We performed a broad search across multiple databases and included any painful condition across any age group. Limitations related to the perspectives collected within this review have been noted. We employed identical search strategies for each of the disease states of interest (pain, depression, and anxiety), yet it is likely some relevant literature was not found given the scope of vocabulary for this topic. In addition, our review lacked formal evaluation of included studies with respect to study quality and bias. Data collection methods (eg, open-ended questions, targeted questions, etc.) could bias the findings. We also extracted and included data, such as insurance coverage (although not commonly noted), that may not be relevant to individuals outside of the U.S.

Conclusions

This review identified patient preferences that affect willingness to participate in clinical trials among individuals with pain and depression. Despite including anxiety within our search, we did not find sufficient data about perspectives in the setting of anxiety. Although altruism and the rapport of the research team are motivating reasons for participation among many individuals with pain, it is also important to recognize that chronic pain and depression can present challenges to recruitment and retention within clinical trials. The assessment of perspectives, barriers, and facilitators in underserved populations is needed, as the current evidence lacks diverse representation. Engaging individuals with pain in the research planning process may assist in addressing the barriers and the needs of individuals affected by pain and/or depression.

Disclosures

RHD: has received in the past 5 years research grants and contracts from the US Food and Drug Administration and the US National Institutes of Health, and compensation for serving on advisory boards or consulting on clinical trial methods from Abide, Acadia, Adynxx, Analgesic Solutions, Aptinyx, Aquinox, Asahi Kasei, Astellas, Biogen, Biohaven, Biosplice, Boston Scientific, Braeburn, Cardialen, Celgene, Centrexion, Chiesi, Chromocell, Clexio, Collegium, Concert, Confo, Decibel, Editas, Eli Lilly, Endo, Ethismos (equity), Eupraxia, Exicure, Glenmark, Gloriana, Grace, Hope, Lotus, Mainstay, Merck, Mind Medicine (also equity), Neumentum, Neurana, NeuroBo, Novaremed, Novartis, OliPass, Pfizer, Q-State, Reckitt Benckiser, Regenacy (also equity), Sangamo, Sanifit, Scilex, Semnur, SIMR Biotech, Sinfonia, SK Biopharmaceuticals, Sollis, SPRIM, Teva, Theranexus, Toray, Vertex, Vizuri, and WCG.

AK: During the last 36 months, BAK has received compensation for full-time work from ACTTION and the American Society of Addiction Medicine. She has also received compensation for freelance science writing and consulting from the health technology assessment company Hayes, Inc., the real-world evidence company, STATinMED, the government contractor, Palladian Associates, Filter Magazine, and the healthcare consulting company, PinneyAssociates. Her work for PinneyAssociates focused on regulatory submissions related to psychedelic drugs. None of her work, including work completed for PinneyAssociates, was supported by funding from the tobacco or e-cigarette industry.

MCF: During the last 36 months, MCF has received compensation for consultant work from ACTTION.

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Supplementary data

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REFERENCES

1. Ackerman IN, Buchbinder R, Osborne RH: Factors limiting participation in arthritis self-management programmes: an exploration of barriers and patient preferences within a randomized controlled trial. Rheumatol Oxf Engl England; 52:472-479, 2013

2. Bair MJ, Robinson RL, Katon W, Kroenke K: Depression and pain comorbidity: A literature review. Arch Intern Med 163:2433, 2003

3. Barnes M, Wiles N, Morrison J, Kessler D, Williams C, Kuyken W, Lewis G, Turner K: Exploring patients' reasons for declining contact in a cognitive behavioural therapy randomised controlled trial in primary care. Br J Gen Pract 62:e371-e377, 2012

4. Basics about clinical trials [Internet]: U.S. Food & Drug Administration. FDA, 2014. [cited 2022 Jan 7]. Available from: https://www.fda.gov/patients/clinical-trials-what-patients-need-know/basics-about-clinical-trials. Accessed November 14, 2022

5. Bennett MI, Mulvey MR, Campling N, Latter S, Richardson A, Bekker H, Blenkinsopp A, Carder P, Closs J, Farrin A, Flemming K, Gallagher J, Meads D, Morley S, O'Dwyer J, Wright-Hughes A, Hartley S: Self-management toolkit and delivery strategy for end-of-life pain: The mixed-methods feasibility study. Health Technol Assess Winch Engl 21:1-292, 2017

6. van den Berg P, Kendal S, Alderson HV, Body R: An exploration of patients' experiences of participation in a randomised controlled trial of the Manchester Acute Coronary Syndromes (MACS) decision rule. Emerg Med J BMJ Publishing Group; 34:593-598, 2017

7. Bondesson E, Larrosa Pardo F, Stigmar K, Ringqvist Å, Petersson IF, Jöud A, Schelin MEC: Comorbidity between pain and mental illness - Evidence of a bidirectional relationship. Eur J Pain 22:1304-1311, 2018

8. Bove AM, Lynch AD, Ammendolia C, Schneider M: Patients' experience with non-surgical treatment for lumbar spinal stenosis: A qualitative study. Spine J 18:639-647, 2017

9. Chambers CT: From evidence to influence: Dissemination and implementation of scientific knowledge for improved pain research and management. Pain 159:S56-S64, 2018

10. Cheung YK, Wood D, Zhang K, Ridenour TA, Derby L, St Onge T, Duan N, Duer-Hefele J, Davidson KW, Kronish I, Moise N: Personal preferences for personalised trials among patients with chronic diseases: an empirical Bayesian analysis of a conjoint survey. BMJ Open 10:e036056, 2020

11. Clinical Trials: The Heart and Soul of Science [Internet]. The Louisiana Community Engagement Alliance against COVID-19 Disparities (LA-CEAL) [cited 2022 Jun 15]. Available from: https://www.youtube.com/watch?v=5j8Ppc4Ti8w. Accessed November 14, 2022.

12. Cramer H, Salisbury C, Conrad J, Eldred J, Araya R: Group cognitive behavioural therapy for women with depression: Pilot and feasibility study for a randomised controlled trial using mixed methods. BMC Psychiatry 11:82, 2011

13. DasMahapatra P, Raja P, Gilbert J, Wicks P: Clinical trials from the patient perspective: Survey in an online patient community. BMC Health Serv Res 17:166, 2017

14. Dennin MD: Enhancing patient engagement in Parkinson's disease mental health research [Internet] ProQuest Information & Learning, 2020. Available from: https://login.libproxy.siue.edu/login?url=http://search.ebscohost.com/login.aspx?direct=true&db=psyh&AN=2020-04049-039&site=ehost-live&scope=site

15. Denny E, Weckesser A, Jones G, Bibila S, Daniels J, Bhattacharya S: Women's experiences of medical treatment for endometriosis and its impact on PRE-EMPT trial participation: a qualitative study. Pilot Feasibility Stud 4:168, 2018

16. Dowrick CF, Hughes JG, Hiscock JJ, Wigglesworth M, Walley TJ: Considering the case for an antidepressant drug trial involving temporary deception: A qualitative enquiry of potential participants. BMC Health Serv Res 7:64, 2007

17. Fernandes LG, Devan H, Fioratti I, Kamper SJ, Williams CM, Saragiotto BT: At my own pace, space, and place: A systematic review of qualitative studies of enablers and barriers to telehealth interventions for people with chronic pain. Pain 163:e165-e181, 2022

18. Fritz JM, Davis AF, Burgess DJ, Coleman B, Cook C, Farrokhi S, Goertz C, Heapy A, Lisi AJ, McGeary DD, Rhon DI, Taylor SL, Zeliadt S, Kerns RD: Pivoting to virtual delivery for managing chronic pain with nonpharmacological treatments: Implications for pragmatic research. Pain 162:1591-1596, 2021

19. Gaudiano BA, Ellenberg SR, Schofield CA, Rifkin LS: A randomized survey of the public's expectancies and willingness to participate in clinical trials of antidepressants versus psychotherapy for depression. Prim Care Companion CNS Disord 18, 2016. https://doi.org/10.4088/PCC.15m01879

20. Gaudiano BA, Hughes JA, Miller IW: Patients' treatment expectancies in clinical trials of antidepressants versus psychotherapy for depression: A study using hypothetical vignettes. Compr Psychiatry 54:28-33, 2013

21. Hislop Lennie K, Barbosa Boucas S, Adams J, Hutt Greenyer C: Patient and public involvement (PPI) in informing the osteoarthritis of the thumb therapy (OTTER) pilot trial: what matters most to people with thumb base osteoarthritis otter collaborations. Ann Rheum Dis [Internet] 72:778, 2013

22. Hissink Muller PCE, Yildiz B, Allaart CF, Brinkman DMC, van Rossum M, van Suijlekom-Smit LWA, van den Berg JM, Ten Cate R, de Vries MC: Participation in a single-blinded pediatric therapeutic strategy study for juvenile idiopathic arthritis: are parents and patient-participants in equipoise? BMC Med Ethics 19:96, 2018

23. Holzer KJ, Veasley C, Kerns RD, Edwards RR, Gewandter JS, Langford D, Yaeger L, McNicol E, Ferguson M, Turk DC, Dworkin RH, Haroutounian S: Partnering with patients in clinical trials of pain treatments: A narrative review. Pain 163:1862-1873, 2022

24. Hood AM, Booker SQ, Morais CA, Goodin BR, Letzen JE, Campbell LC, Merriwether EN, Aroke EN, Campbell CM, Mathur VA, Janevic MR: Confronting racism in all forms of pain research: A shared commitment for engagement, diversity, and dissemination. J Pain 23:913-928, 2022

25. Hughes-Morley A, Young B, Waheed W, Small N, Bower P: Factors affecting recruitment into depression trials: Systematic review, meta-synthesis and conceptual framework. J Affect Disord 172:274-290, 2015

26. James J, Lai B, Witt T: Patient engagement survey regarding future double-blinded, randomized controlled trial of tapering of chronic opioid therapy. J Prim Care Community Health 10, 2019. Thousand Oaks, California: Sage Publications Inc.N.PAG-N.PAG

27. Janevic MR, Mathur VA, Booker SQ, Morais C, Meints SM, Yeager KA, Meghani SH: Making pain research more inclusive: Why and how. J Pain 23:707-728, 2022

28. Leinisch-Dahlke E, Akova-Öztürk E, Bertheau U, Isberner I, Evers S, May A: Patient preference in clinical trials for headache medication: the patient's view. Cephalalgia 24:347-355, 2004

29. Lenguerrand E, Artz N, Marques E, Sanderson E, Lewis K, Murray J, Parwez T, Bertram W, Beswick AD, Burston A, Gooberman-Hill R, Blom AW, Wylde V: Effect of group-based outpatient physical therapy on function after total knee replacement: Results from a multicenter randomized controlled trial. Arthritis Care Res 72:768-777, 2020

30. Lenze SN, Potts MA: Brief Interpersonal Psychotherapy for depression during pregnancy in a low-income population: A randomized controlled trial. J Affect Disord 210:151-157, 2017

31. Letzen JE, Mathur VA, Janevic MR, Burton MD, Hood AM, Morais CA, Booker SQ, Campbell CM, Aroke EN, Goodin BR, Campbell LC, Merriwether EN: Confronting racism in all forms of pain research: Reframing study designs. J Pain 23:893-912, 2022

32. Middleton LJ, Daniels JP, Weckesser A, Bhattacharya S: PRE-EMPT trial collaborative group. Preventing recurrence of endometriosis by means of long-acting progestogen therapy (PRE-EMPT): report of an internal pilot, multi-arm, randomised controlled trial incorporating flexible entry design and adaption of design based on feasibility of recruitment. Trials 18:121, 2017

33. Midgley N, Isaacs D, Weitkamp K, Target M: The experience of adolescents participating in a randomised clinical trial in the field of mental health: a qualitative study. Trials 17:364, 2016

34. Morais CA, Aroke EN, Letzen JE, Campbell CM, Hood AM, Janevic MR, Mathur VA, Merriwether EN, Goodin BR, Booker SQ, Campbell LC: Confronting racism in pain research: A call to action. J Pain, 2022. S1526590022 000293

35. Morgan EM, Munro JE, Horonjeff J, Horgan B, Shea B, Feldman BM, Clairman H, Bingham CO 3rd, Thornhill S, Strand V, Alongi A, Magni-Manzoni S, van Rossum MAJ, Vesely R, Vojinovic J, Brunner HI, Harris JG, Horton DB, Lovell DJ, Mannion M, Rahimi H, Ravelli A, Ringold S, Ruperto N, Schrandt MS, Shenoi S, Shiff NJ, Toupin-April K, Tzaribachev N, Weiss P, Consolaro A: Establishing an updated core domain set for studies in juvenile idiopathic arthritis: A report from the OMERACT 2018 JIA workshop. J Rheumatol Canada; 46:1006-1013, 2019

36. Munn Z, Peters MDJ, Stern C, Tufanaru C, McArthur A, Aromataris E: Systematic review or scoping review? Guidance for authors when choosing between a systematic or scoping review approach. BMC Med Res Methodol 18:143, 2018

37. Nelson A, Fenlon D, Morris J, Sampson C, Harrop E, Murray N, Wheatley D, Hood K, Griffiths G, Barrett-Lee P: QUALZICE: A QUALitative exploration of the experiences of the participants from the ZICE clinical trial (metastatic breast cancer) receiving intravenous or oral bisphosphonates. Trials 14, 2013. 325–325

38. O'Cathain A, Thomas KJ, Drabble SJ, Rudolph A, Hewison J: What can qualitative research do for randomised controlled trials? A systematic mapping review. BMJ Open 3: e002889, 2013

39. Paterson C, Zheng Z, Xue C, Wang Y: Playing their parts": The experiences of participants in a randomized

sham-controlled acupuncture trial. J Altern Complement Med 14:199-208, 2008. New Rochelle, New York: Mary Ann Liebert, Inc.

40. Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) Checklist [Internet]. PRISMA, 2021. [cited 2021 Nov 2]. Available from: http://www.prisma-statement.org/Extensions/ScopingReviews. Accessed November 14, 2022

41. Sheridan R, Martin-Kerry J, Hudson J, Parker A, Bower P, Knapp P: Why do patients take part in research? An overview of systematic reviews of psychosocial barriers and facilitators. Trials 21:259, 2020

42. Sherratt FC, Roper L, Baildam E, Beresford MW, Stones SR, Ramanan A, Foster H, McErlane F, Rooney M, Peak M, Young B: Families' views on the feasibility of a corticosteroid trial in JIA: A qualitative study. Pediatr Rheumatol 15:132, 2017

43. Smith SM, Gewandter JS, Kitt RA, Markman JD, Vaughan JA, Cowan P, Kopecky EA, Malamut R, Sadosky A, Tive L, Turk DC, Dworkin RH: Participant preferences for pharmacologic chronic pain treatment trial characteristics: An ACTTION adaptive choice-based conjoint study. J Pain United States; 17:1198-1206, 2016

44. Stamuli E, Torgerson D, Northgraves M, Ronaldson S, Cherry L: Identifying the primary outcome for a randomised controlled trial in rheumatoid arthritis: the role of a discrete choice experiment. J Foot Ankle Res 10:57, 2017

45. Tallon D, Mulligan J, Wiles N, Thomas L, Peters TJ, Elgie R, Sharp D, Lewis G: Involving patients with depression in research: Survey of patients' attitudes to participation. Br J Gen Pract 61:e134-e141, 2011

46. Taylor WJ, Brown M, Aati O, Weatherall M, Dalbeth N: Do patient preferences for core outcome domains for chronic gout studies support the validity of composite response criteria? Arthritis Care Res United States 65:1259-1264, 2013

47. The Voice of the Patient. Sickle Cell Disease [Internet]: US Food and Drug Administration, Patient-Focused Drug Development Initiative. FDA, 2014 Oct. Available from: https://www.fda.gov/media/89898/download. Accessed November 14, 2022

48. Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, Moher D, Peters MDJ, Horsley T, Weeks L, Hempel S, Akl EA, Chang C, McGowan J, Stewart L, Hartling L, Aldcroft A, Wilson MG, Garritty C, Lewin S, Godfrey CM, Macdonald MT, Langlois EV, Soares-Weiser K, Moriarty J, Clifford T, Ö Tunçalp, Straus SE: PRISMA extension for scoping reviews (PRISMA-ScR): Checklist and explanation. Ann Intern Med 169:467-473, 2018

49. Turk DC, Dworkin RH, Revicki D, Harding G, Burke LB, Cella D, Cleeland CS, Cowan P, Farrar JT, Hertz S, Max MB, Rappaport BA: Identifying important outcome domains for chronic pain clinical trials: an IMMPACT survey of people with pain. Pain United States; 137:276-285, 2008

50. Vercellini P, Somigliana E, Cortinovis I, Bracco B, de Braud L, Dridi D, Milani S: "You can't always get what you want": from doctrine to practicability of study designs for clinical investigation in endometriosis. BMC Womens Health BioMed Central; 15:1-9, 2015

51. Verhaart IEC, Johnson A, Thakrar S, Vroom E, De Angelis F, Muntoni F, Aartsma-Rus AM, Niks EH: Muscle biopsies in clinical trials for Duchenne muscular dystrophy - Patients' and caregivers' perspective. Neuromuscul Disord NMD England; 29:576-584, 2019

52. Wasmann KA, Wijsman P, van Dieren S, Bemelman W, Buskens C: Partially randomised patient preference trials as an alternative design to randomised controlled trials: systematic review and meta-analyses. BMJ Open 9:e031151, 2019

53. Wu D: Patient preference of pain measurements: a cross-sectional study based on chronic low back pain population in china. J Altern Complement Med N Y N 22:A139, 2016