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INTEGRATIVE MEDICINE SECTION

A Systematic Review of Practiced-Based Research of Complementary and Integrative Health Therapies as Provided for Pain Management in Clinical Settings: Recommendations for the Future and a Call to Action

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Disclosure and conflicts of interest: Dr. Dusek is the Principal Investigator of BraveNet's PRIMIER study. Dr. Dusek is also the Chair of the Practice-based Research Scientific Interest Group of the Academic Consortium for Integrative Medicine and Health (the Consortium), and from April 2020 until May 2021 he served as the Research Working Group Chair of the Consortium.

Study registration: PROSPERO database (CRD42020159193).

Abstract

Objective. The goal of this systematic review was to evaluate practice-based, real-world research of individualized complementary and integrative health (CIH) therapies for pain as provided in CIH outpatient clinics. **Methods**. A systematic review was conducted on articles in PubMed, Ovid, Cochrane, Web of Science, Scopus, and Embase published through December 2020. The study was listed in the PROSPERO database (CRD42020159193). Major categories of variables extracted included study details and demographics, interventions, and outcomes. **Results**. The literature search yielded 3,316 records, with 264 assessed for full-text review. Of those, 23 studies (including ~8,464 patients) were specific to pain conditions as a main outcome. Studies included chiropractic, acupuncture, multimodal individualized intervention/programs, physiotherapy, and anthroposophic medicine therapy. Retention rates ranged from 53% to 91%, with studies offering monetary incentives showing the highest retention. The 0–10 numerical rating scale was the most common pain questionnaire (n = 10; 43% of studies), with an average percent improvement across all studies and time points of 32% (range: 18–60%). **Conclusions**. Findings from this systematic review of practice-based, real-word research indicate that CIH therapies exert positive effects on various pain outcomes. Although all studies reported beneficial impacts on one or more pain outcomes, the heterogeneous nature of the studies limits our overall understanding of CIH as provided in clinical settings. Accordingly, we present numerous recommendations to improve publication reporting and guide future research. Our call to action is that future practice-based CIH research is needed, but it should be more expansive and conducted in association with a CIH scientific society with academic and health care members.

Key words: Systematic Review; Complementary and Integrative Health; Integrative Medicine; Practice-Based Research; Chiropractic; Acupuncture

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Introduction

The predominant treatment for chronic and acute pain in the United States is the use of anti-inflammatory, anticonvulsant, and opioid analgesics [1]. However, these analgesic options are often ineffective and have several serious side effects, including the possibility of tolerance and dependency [2].

To mitigate the opioid crisis in the United States, nonpharmacological approaches are increasingly being used to treat pain and are recommended by many official bodies and experts in pain medicine [3]. Specifically, the Institute of Medicine [4], the military [5], the Centers for Disease Control and Prevention [6], the former U.S. Surgeon General [7], the National Academies of Sciences, Engineering, and Medicine [8], the Food and Drug Administration [9], the American College of Physicians [10], the Department of Defense and Veterans Affairs [11], and the National Institutes of Health (NIH) [12] acknowledge that the use of opioid medications has not successfully treated pain and has led to serious abuse, addiction, illness, and disability, and they call for evidence-based, comprehensive pain care that includes nonpharmacological complementary and integrative health (CIH). CIH is individualized care that takes into account the physical, emotional, mental, social, and spiritual characteristics and needs of the individual in its treatment plan [13,14].

Several CIH therapies, such as chiropractic, acupuncture, and massage, are already widely used for pain management [13,14], with an estimated 44% of opioid-prescribed patients with chronic pain using some form of CIH [15]. Furthermore, many CIH therapies are known to be safe, are accepted by patients, and have been used successfully for thousands of years [3]. Numerous systematic reviews and meta-analyses of randomized controlled trials (RCTs) of CIH therapies have reported efficacy for the treatment and management of pain and pain-related health conditions, including, but not limited to, chiropractic, massage, and acupuncture for chronic low back pain [16–20], neck pain [16,21,22], shoulder pain [16,22], arthritic pain [16,23], headaches [16,24,25], cancer-related pain [26–28], veterans with pain [29], and musculoskeletal-related pain [30,31]. Given the demonstrated efficacy under RCT conditions, evaluation of the effectiveness of CIH therapies for pain management within practice-based (or real-world) clinical practice is a logical next step, as outlined by the National Center of Complementary and Integrative Health (NCCIH) [32].

Whereas RCTs assess the efficacy of specific interventions for specific patient populations in "controlled settings," observational studies evaluate the effectiveness of treatments in the real world of clinical practice. The highly individualized nature of CIH interventions also can make the RCT model problematic, as CIH treatments often change over time on the basis of the individual's response to treatment. Although there is a growing body of RCTs that document the efficacy of CIH approaches for pain, this body of research does not accurately inform the real-world practice of CIH because of the controlled nature of the randomized clinical trial paradigm. Specifically, results from most RCT study designs are not sufficient for truly guiding future clinical practice [33]. Therefore, despite some inherent limitations, practice-based, observational effectiveness research presents a promising option for using information gleaned from real-world clinical practice to inform future clinical practice [34].

Despite the widespread use and efficacy of CIH for pain management [3], there are no systematic reviews summarizing scientific articles focused on practice-based effectiveness research of CIH therapies for pain management in CIH health care settings. Therefore, the goal of this systematic review was to evaluate the practice-based, real-world effectiveness of individualized CIH therapies (including but not limited to acupuncture, massage, traditional Chinese medicine, chiropractic, naturopathy, integrative medicine physician consultations, and osteopathic medicine) for pain management provided in CIH outpatient or speciality clinics. The focus was exclusively on published works of prospective or retrospective observational, cohort, or registry-based longitudinal studies, with RCTs as well as standardized treatment protocols being explicitly excluded.

Methods

A systematic review of practice-based research of CIH therapies was conducted on articles published through December 2020 in PubMed, OVID, Cochrane, Web of Science, Scopus, and Embase. The study was listed in the PROSPERO database (CRD42020159193), and PROSPERO guidelines were used. Search terms are noted in the Appendix. The following study inclusion criteria were used: individualized treatment (i.e., not standardized), longitudinal effectiveness design (i.e., two or more data collection points), patient-reported validated outcome measures, outpatient and speciality CIH clinics, participants more than 18 years of age, a sample size of at least 25, and full text available published in English. The systematic review focused exclusively on published works of prospective or retrospective observational, cohort, or registry-based longitudinal studies as a means to study the real-world use of CIH therapies as provided in CIH clinical settings. RCTs and standardized treatment protocols were excluded.

Our first step was the review of article titles and abstracts from the literature search and identification of studies that potentially met inclusion criteria for full-text review (authors JAD and JS and three others). All full-text pdfs were imported into a data platform to assist with review. Discrepancies were discussed between coders, and the senior author (JAD) made the final

determination. Next, five independent coders (NLD, JS, JAD, and two others) reviewed the full studies, with two coders reviewing each study. Variables extracted included study details and demographics (location, total number of participants, retention rate, incentives, gender, age, race/ethnicity, and socioeconomic status [SES]);), intervention characteristics (population type, setting, number of sites, time frame, design, intervention/program, and interventionists), and outcome characteristics (main outcome constructs, measures/instruments, main result, multivariate analysis, clinical response, and effect sizes). Discrepancies in the full-text extraction between coders were resolved by group discussion and by a determination of the lead author (NLD).

The results of the extraction were imported into the data platform Covidence (www.covidence.org; Covidence, Melbourne, Victoria, Australia), which is a commercial software platform that helps with organizing articles and streamlines the process of systematic, scoping, and general reviews.

Results

The literature search yielded 3,316 records, with 264 assessed for full-text review. Of those, 23 studies (including 8,464 patients) were specific to pain conditions or pain-related measures as a main outcome and had longitudinal assessments. Figure 1 depicts the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram indicating the number of studies identified, screened, determined to be eligible, and included. Main reasons for exclusion included: n = 60, standardized treatment; n = 50, wrong outcomes; n = 22, setting not in a CIH clinic; n = 14, included children; n = 16, wrong design; n = 11, abstracts only; n = 11, wrong intervention; n = 13, data unavailable; n = 9, too few participants; n = 7, clinical trial registration only; n = 5, could not retrieve article; n = 4, were duplicates; n = 3, not published in not English; and n = 2, hospitalized.

We briefly review the results of the studies below, grouped by study details and demographics (Table 1), intervention characteristics (Table 2), and outcome characteristics (Table 3). Within each table, studies are ordered in reverse chronological order and grouped by type of intervention: chiropractic (n = 13), acupuncture (n = 5), multimodal individualized intervention/programs (n = 4), a physiotherapy intervention (n = 1), and an anthroposophic medicine (AM) therapy intervention (n = 1).

Results of Study Characteristics

Publication Year

Figure 2 displays the number of publications per year of all 23 studies included.

Location of Study

Most studies were conducted in the United States (n = 18, 78%), followed by the UK (n = 1, 4%), Germany (n = 1, 4%), Singapore (n = 1, 4%), Sweden (n = 1, 4%), and Switzerland (n = 1, 4%) (see Table 1).

Sample Size

At baseline, half of the studies had a sample size of fewer than 100 participants (n = 11, 48%) (see Table 1). More than a quarter of studies had between 101 and 500 participants (n = 8, 35%), one study (4%) had between 501 and 1,000 participants, and three studies (13%) had more than 1,000 participants.

The total number of participants across all studies was at least 8,464, with 6,696 from chiropractic studies, 800 from acupuncture studies, 799 from multimodal studies, 94 from the physiotherapy study, and 75 from the AM therapy study. The total sample is reported as "at least" because three studies did not report the number of subjects at baseline, so the number analyzed was used instead in these cases (see Table 1).

Incentives and Retention

Retention rates ranged from 53% to 91%, although the time frame by which retention was defined varied from study to study (e.g., 1 month, 12 months) (see Table 1). Only two studies (9%) reported that they offered participants monetary incentives, with both studies offering cash ranging from $5 to $50 per research step (e.g., enrollment or survey completion). Studies with participant incentives showed retention rates of 90% [35] and 91% [36], which were the highest retention rates across all studies. Both studies that included incentives were NIH-funded studies, highlighting the need for the budget to remunerate participants for high retention. One study also offered compensation to physicians but not patients, with a retention rate of 88% [37].

Demographics

The percentage of females enrolled ranged across studies from 7.6% to 100%, with most studies (77%) enrolling more female participants than male participants (see Table 1). Participants' mean age ranged across studies from 28.5 to 50.9 years; however, most studies (78%) had a mean age between 40 and 50 years. Only seven studies (35%) reported socioeconomic status (e.g., income or education), and only 11 studies (48%) reported race or ethnicity. Most studies that reported race/ethnicity consisted largely of White/Caucasian, non-Hispanic participants, with the exception of Miller and colleagues [38] and Niemtzow and colleagues [39], who enrolled 44% and 31% Black/African American participants, respectively.

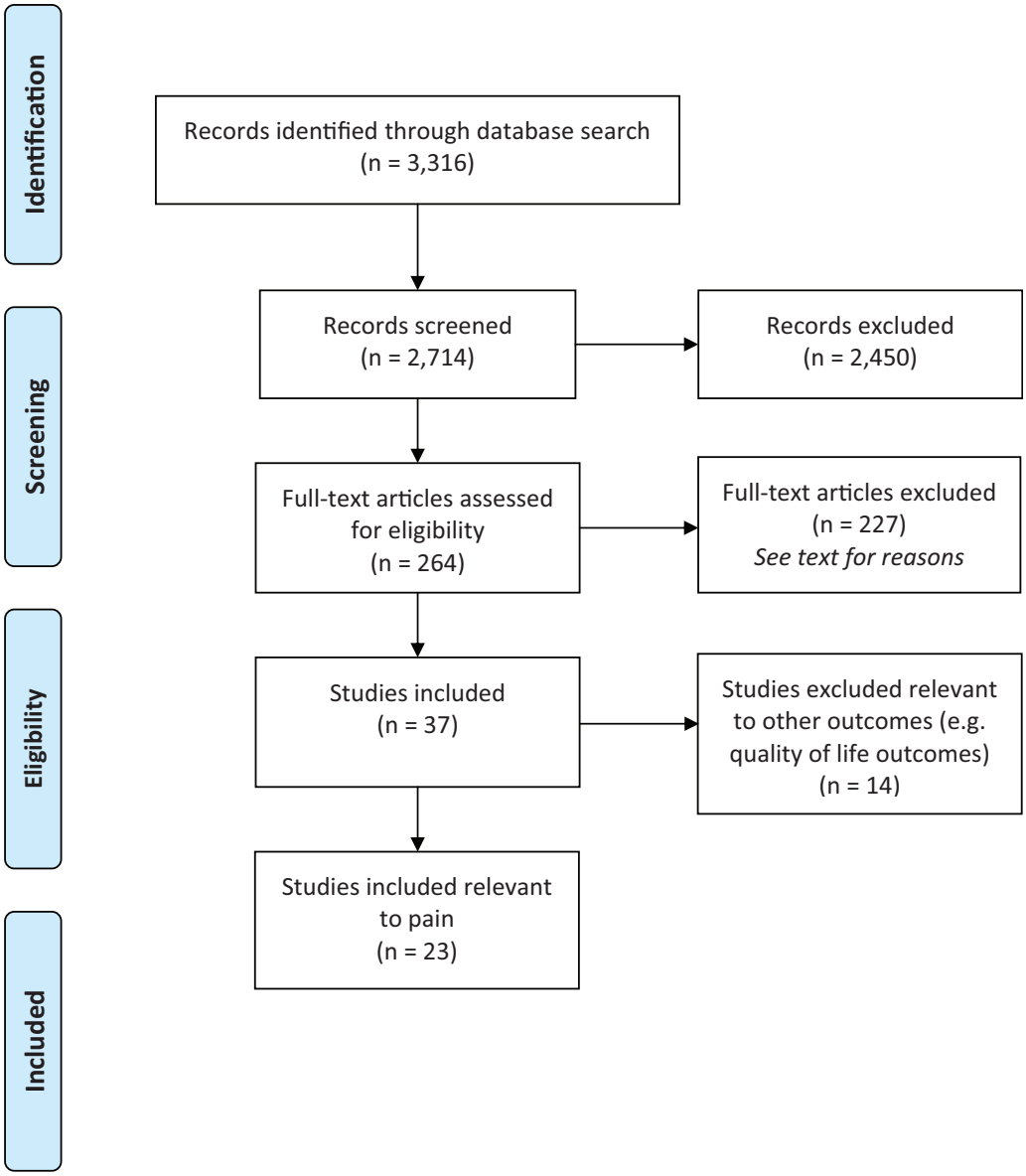

Figure 1. PRISMA flow diagram.

Patient Population

Most studies enrolled patients with chronic or acute pain (n = 16, 70%), with most enrolling patients with low back pain (n = 9), followed by patients with neck pain (n = 3), general pain (n = 3), and either low back or neck pain (n = 1).

In addition to patients with chronic or acute pain in general, studies enrolled veteran patients (n = 4, 17%), oncology patients (n = 2, 9%), general clinic patients (n = 1, 4%), patients with a musculoskeletal disorder of the spine (n = 1, 4%), and patients with a herniated disk (n = 1, 4%) (see Table 2).

Number of Sites

A majority of the articles included evaluation at one clinical site (15 studies; 68%). Eight studies (35%), of which most were chiropractic studies, assessed effectiveness of the intervention at multiple sites (see Table 2).

Design

The majority of studies were prospective (n = 14, 61%), and the remaining studies were retrospective (n = 9, 39%) (see Table 2).

Intervention Type

The review includes the following intervention types: 13 chiropractic (56%), five acupuncture (22%), four multimodal (17%), one physiotherapy (4%), and one AM therapy (4%). The treatments were individualized for all studies as part of inclusion criteria; however, some studies indicated only the average duration and/or frequency of treatment (see Table 2).

Table 1. Study details and demographics for all studies

Author(s)	Publication Year	Country	Total Number at Baseline	Maximum Number Analyzed for Any Outcome	Retention	Incentives	Gender (% Female)	Age (Mean and Standard Deviation or Range)	Race/Ethnicity	SES
Chiropractic studies										
Gedin et al.	2019	Sweden	Acute: 149; Chronic: 97	Acute: 81; Chronic: 57	54% acute and 59% chronic completed follow-up	Not specified	Acute: 39.5%; Chronic: 63.2%	Acute: 49.3 (12.9); Chronic: 46.3 (14.7)	Not specified	Not specified
Hays et al.	2019	USA	2024	1,835	90.7% completed follow-up	Up to $80 in gift cards for participating	74%	49, range 21–95	Caucasian (88%), Asian (3%), African American (2%), American Indian/Pacific Islander/Other (2%)	Income: 32% ≥$100,000, 56% college degree or higher
Wirth et al.	2019	Switzerland	Not specified	67	Not specified	Not specified	53.7%	46.8 (17.6)	Not specified	Not specified
Corcoran et al.	2017	USA	117	70	60% completed discharge measures	Not specified	100%	44.8 (13.5)	Caucasian (86%), African Americans (10%), unknown (4%); no Hispanic/Latino	Not specified
Burke	2014	USA	34	25	73.5% completed post-assessment	Not specified	56%	40.5 (16.4)	Not specified	Not specified
Dunn et al.	2011a	USA	78	54	69.2% completed a minimum of 2 treatments and consults	Not specified	13%	50.9, range 22–84	Not specified	Not specified
Dunn et al.	2011b	USA	253	171	67.6% completed discharge	Not specified	7.6%	53.3 (CI 50.8–55.9)	Predominantly White	Not specified
Lisi	2010	USA	Not specified	31	Not specified	Not specified	19%	28.5, range 19–47	Not specified	Not specified
Newell & Field	2007	UK	788	622 (calculated)	79% completed 4-week follow-up	Not specified	52.00%	Not specified	Not specified	Not specified
Haas et al.	2005	USA	2,872	2,780	66% completed 3-month follow-up	Not specified	Chronic: 55.4%; Acute: 47.7%	Chronic: 42.2 (14.4); Acute: 42.1 (12.9)	White non-Hispanic Chronic: 91.8%; Acute: 91.6%	College degree: chronic DC, 28.5; acute DC, 33.8% Income: <$12,000 (%) chronic Doctor of Chiropractic (DC), 9.5%; acute DC, 7.1%
Secor et al.	2004	USA	Not specified	54	Not specified	Not specified	72.2%	45.0, range 21–84	Caucasian (94.4%), Hispanic (5.6%)	Not specified
Schliesser et al.	2003	USA	39	22		Not specified	Not specified	Not specified	Not specified	Not specified

(continued)

Author(s)	Publication Year	Country	Total Number at Baseline	Maximum Number Analyzed for Any Outcome	Retention	Incentives	Gender (% Female)	Age (Mean and Standard Deviation or Range)	Race/Ethnicity	SES
					56% completed measures within 6 months					
Nyiendo et al.	2000	USA	93	49	53% completed 1-month follow-up	Not specified	48.40%	40.4 (13.4)	Black 2.2%, White non-Hispanic 85.9%, Native American 9.8%, All other 2.2%	37.7% college degree or higher
Acupuncture studies										
Miller et al.	2019	USA	Not specified	68	Not specified	Not specified	54.0%	Median 55, range 31–89	Caucasian 50%, African American 44%, other 6%	Not specified
Thompson et al.	2015	USA	90	65	72% completed at least two acupuncture sessions	Not specified	69.0%	52.0, range 20–74	89% non-Hispanic and 82% White	Not specified
Maiers et al.	2008	USA	485	416	86% completed 4-week follow-up	Not specified	67.0%	36.0, range 18–82	White 92%, Asian 2.1%, Black 2.5%, American Indian 1.2%, Hispanic 1.4%, other 1.7%	61.2% college degree or higher
Niemtzow et al.	2008	USA	119	105	88% completed 4-week follow-up	Not specified	50.8%	Range 21–85	Alaska Native/ American Indian 6%; Asian 3%; Black 31%; Hispanic 2.5%; White 63%; Other 4%	65% college degree or higher
Secor et al.	2004	USA	Not specified	38	Not specified	Not specified	67.9%	45.0, range 21–84	Caucasian (100%)	Not specified
Multimodal studies										
Gibson et al.	2020	USA	174	99	56.9% completed follow-up and at least 3 visits	Not specified	16%	60.0 (13.0)	Caucasian/white 61.6%; Black or African American 15.2%; Hispanic or Latino 9.1%; Other 14.1%	82.8% had some college or more
Wayne et al.	2018	USA	156	141	90.4% completed 12-month follow-up	$50 per assessment	67.30%	50.2 (16.5)	White 86.8%; African American	84.0% college degree or higher

(continued)

Author(s)	Publication Year	Country	Total Number at Baseline	Maximum Number Analyzed for Any Outcome	Retention	Incentives	Gender (% Female)	Age (Mean and Standard Deviation or Range)	Race/Ethnicity	SES
Abrams et al.	2013	USA	409	252	62% completed all 4 visits	Not specified	74.10%	48.6 (15.2)	7.9%; Asian 2.6%; other 2.6% ~81% White	Not specified
Murphy et al.	2009	USA	60	46	76.7% completed end-of-treatment measure	Not specified	Not specified	47.8 (14.0), range 22–80	Not specified	Not specified
Physiotherapy										
Goh et al.	2010	Singapore	94	55	58.5% with complete documentation	Not specified	50%	42.4 (13.7), range 21–79	Not specified	Not specified
AM therapy										
Hamre et al.	2009	Germany	75	66	88% completed at least one follow-up	Physicians were compensated €40 per patient; patients received no compensation	85%	49.0 (12.0), range 20–74	Not specified	35% highly educated (level 3), 81% income more than 900€ per month

Note: Secor et al. (2004) had two separate cohorts: one chiropractic and one acupuncture.

Main Outcome Constructs and Measures

All studies measured at least one pain or pain-related outcome (see Table 3). The most common pain questionnaire used was a single-item 0–10 numerical rating scale (NRS) (n = 10 studies, 43%; pain intensity), followed by Bournemouth Questionnaires (Bournemouth Questionnaire [BQ], Back Bournemouth Questionnaire [BBQ], Neck Bournemouth Questionnaire [NBQ], and Bournemouth Disability Questionnaire [BDQ]) (n = 6, 26%; multidimensional pain: intensity, interference, disability, fear avoidance), a single-item visual analog scale (VAS) (n = 3, 13%; pain intensity), Patient-Reported Outcomes Measurement Information System (PROMIS) measures (n = 2, 9%; intensity and interference), the BBQ (n = 2, 9%; multidimensional pain), and the Revised Oswestry Low-Back Pain Questionnaire (RODQ) (n = 2, 9%; disability). All other questionnaires were used in only one article.

Duration of Assessments

Because of the heterogeneous inclusion of different time points across studies, we elected to report only one main time point per study, which was the longest follow-up time point of each study. With respect to shorter-term outcomes, four studies assessed participants at 4 weeks (~1 month). Eight studies reported main assessments at end of treatment or discharge. Two studies assessed participants at 3 months and one within 3 months. One study reported a mean follow-up of 109 days (approximately 3 and a half months).

With respect to longer-term assessment (6 months or later), six studies (26%) included long-term follow-ups as main assessment points, with two studies assessing changes at 6 months, two studies at 12 months, one study at a mean of 14.5 months, and one study at 24 months (see Table 3).

Main Outcome Results

All pain-related measures were significantly improved for the 15 studies in which significance (*P* values) was reported (see Table 3). For the seven studies in which significance was not reported, the participants showed marked mean improvement in all pain-related measures [35,40–45], either by meeting the minimal clinically important difference (MCID) when specified [35,40,41,44] or through NRS or VAS improvement when the MCID was not specified [42,43,45].

Chiropractic. Chiropractic studies (see Table 3) included improvements in pain intensity for low back pain patients at 4 weeks / 1 month [44,46,47], 3 months [48], 6 months [49], 12 months [48,49], and end of care/treatment or discharge [50,51]. Pain intensity was also improved at end of care/treatment or discharge (mean = 33 days) for patients with a musculoskeletal disorder of the spine [41], within 3 months of initial treatment for patients with pain [52], within 6 months and at

Table 2. Intervention and design characteristics for all studies

Author(s)	Publication Year	Study Population	Study Setting	Nubmer of Sites	Study Time Frame	Prospective or Retrospective	Intervention or Interventionists	Duration or Length
Chiropractic studies								
Gedin et al.	2019	Patients with acute or chronic low back pain	Chiropractic clinics	23	October 2012 to January 2013	Prospective	Chiropractic	Not specified
Hays et al.	2019	Patients with chronic low back or neck pain	Chiropractic clinics	125	The study lasted 3 months, and according to clinicaltrials.gov, the date of the last participant's research activity was December 31, 2018	Prospective	Chiropractic	Not specified
Wirth et al.	2019	Patients with low back pain from spine surgery division	Chiropractic teaching clinic	1	June 2014 to October 2016	Prospective	Chiropractic	Median of the number of consultations was 8, most completed care within 6 months
Corcoran et al.	2017	Female veterans with low back pain	Chiropractic clinic at Veterans Health Administration health care system	1	January 1, 2009, to December 31, 2015	Retrospective	Chiropractic	Mean number of treatments was 7.9, range 3–19
Burke	2014	Patients with a musculoskeletal disorder of the spine	Academic health centers of chiropractic college	1	December 2012 to September 2013	Prospective	Chiropractic care and ConnecTX Therapy	Median number of treatments was 6
Dunn et al.	2011	Veterans with neck pain	Veterans Health Administration medical center chiropractic clinic	1	January 1, 2009, to December 31, 2009	Retrospective	Chiropractic	Mean number of treatments was 8.7, range 2–26
Dunn et al.	2011	Veterans with low back pain	Veterans Health Administration medical center chiropractic clinic	1	January 1, 2009, to December 31, 2009	Retrospective	Chiropractic	Mean number of treatments per case was 8.7, range 2–26
Lisi	2010	Veteran patients with pain	Veteran chiropractic clinic	1	November 1, 2007, to April 30, 2008	Retrospective	Chiropractic	Mean number of treatments was 6.1
Newell & Field	2007	Patients with low back pain	Large private chiropractic clinic	1	January 2006 to September 2006	Prospective	Chiropractic	Mean number of treatments was 6.1
Haas et al.	2005	Patients with acute or chronic low back pain	Chiropractic clinics	51	1994 to 1996	Prospective	Chiropractic (n = 60)	Not specified
Secor et al.	2004	Patients with pain having 3 treatments within 3 months	Hospital-affiliated outpatient clinic	1	October 1, 2002, to December 31, 2002	Prospective	Chiropractic	At least 3 treatments within 3 months of initial session, average treatment duration of 35.1 (21.9) days
Schliesser et al.	2003	Patients with neck pain and radiating pain into upper extremities	Private chiropractic office	1	1998 to 2001	Retrospective	Chiropractic	Mean number of treatments was 13.2 (8.2), range 6 to 37

(continued)

Author(s)	Publication Year	Study Population	Study Setting	Nubmer of Sites	Study Time Frame	Prospective or Retrospective	Intervention or Interventionists	Duration or Length
Nyiendo et al.	2000	Patients with chronic low back pain	Chiropractic clinics	40	3 months in late 1992	Prospective	Chiropractic and family medicine physicians	Mean number of visits was 4
Acupuncture studies								
Miller et al.	2019	Oncology patients with pain	Palliative medicine clinic	1	May 1, 2013, to December 31, 2015	Retrospective	Palliative medicine physician certified in medical acupuncture	Median number of acupuncture treatments was 2, range 1–13
Thompson et al.	2015	Oncology patients with pain and other symptoms	Integrative oncology clinic	1	September 2010 to October 2012	Retrospective	Internal medicine physician provider trained in acupuncture	72% of patients received at least two sessions, range 1–23. Sessions were between 30 and 60 minutes.
Maiers et al.	2008	Clinic patients where pain was the most common issue	Acupuncture and Oriental medicine teaching clinic	1	January 2005 to February 2006	Prospective	Acupuncture and Traditional Chinese Medicine from third-year acupuncture students	Not specified
Niemtzow et al.	2008	Active-duty military members, dependents, and retirees with acute and chronic pain	Air Force base medical center, acupuncture clinic	1	October 2003 to September 2005	Prospective	Traditional medical acupuncturist electroacupuncture, auriculotherapy, and electroauriculotherapy	Not specified
Secor et al.	2004	Patients with pain having 3 treatments within 3 months	Hospital-affiliated outpatient clinic	1	October 1, 2002, to December 31, 2002	Prospective	Acupuncture	At least 3 treatments within 3 months of initial session, average treatment duration of 35.1 (21.9) days
Multimodal studies								
Gibson et al.	2020	Veterans with chronic pain	Large Veterans Affairs health care system and outpatient campuses	6	November 2015 to February 2018	Retrospective	Interdisciplinary chronic pain care; medical provider, psychologist, pharmacist, cognitive behavioral therapist, acupuncturist, physical therapist, chiropractor, massage therapist, mind-body therapist, yoga provider	Average of 3–4 IPT appointments over 2–3 months

(continued)

Author(s)	Publication Year	Study Population	Study Setting	Nubmer of Sites	Study Time Frame	Prospective or Retrospective	Intervention or Interventionists	Duration or Length
Wayne et al.	2018	Patients with chronic or intermittent low back pain	CIH clinic	1	February 2012 to November 2014	Prospective	Nonstandardized, individual approach of CIH; acupuncturist, chiropractic physician, craniosacral therapist, dietician and nutritionist, CIH physician, health coach, massage therapist, movement therapist, psychiatrist	7.3 visits on average over 13 weeks
Abrams et al.	2013	Patients with chronic pain	CIH clinics	9	June 2009 to November 2010	Prospective	Nonstandardized, individual approach to CIH; CIH physician consults, various therapists in Traditional Chinese Medicine, manipulation therapy, exercise, yoga, mind/body therapies, and other alternative medical systems	Not specified
Murphy et al.	2009	Patients diagnosed with lumbar radiculopathy secondary to herniated disk	CIH clinic	1	March 8, 2004, to December 4, 2006	Prospective	Nonstandardized, individual approach to CIH; chiropractic physician and physical therapist team	11 treatments on average
Physiotherapy								
Goh et al.	2010	Patients presenting primarily with low back pain	Musculoskeletal physiotherapy clinic	1	January 2009 to June 2009	Retrospective	Physiotherapy; tailored manual therapy techniques, specific exercises and education	Average of 3.6 sessions
AM therapy								
Hamre et al.	2009	Patients with low back pain	Office-based practice or outpatient clinic	41	January 1, 1999, to December 31, 2005	Prospective	AM therapy (n = 41)	Median therapy duration was 98 days (range: 70–146 days), median number of therapy sessions was 12 (range: 10–12)

Note: Secor et al. (2004) had two separate cohorts: one of chiropractic and one of acupuncture.

Table 3. Outcome characteristics and results for all studies

Author(s)	Publication Year	Main Outcome Construct(s)	Main Outcome Measures(s)	Main Time Point(s)	Main Result(s) Mean and Standard Deviation (% Change)	Multivariate Statistics	Clinical Response Definition	Clinical Response
Chiropractic studies								
Gedin et al.	2019	Pain intensity, disability	11-point NRS, ODI	4 weeks (~1 month)	Acute: NRS Pain: 4.81 (2.05) to 1.83 (1.72)*** (38%); ODI 23.96 (14.97) to 10.38 (10.96)*** (56.7%) Chronic: NRS Pain: 4.59 (2.44) to 3.69 (2.24)** (19.6%); ODI: 19.61 (11.66) to 16.73 (12.26)** (14.7%)	N/A	MCID for NRS is 2-point reduction, MCID for ODI is 10.5-point reduction	Acute back pain: NRS and ODI were all of MCID Chronic back pain: none of the observed changes were of MCID
Hays et al.	2019	Health-related quality of life, including pain interference	PROMIS-29	3 months	PROMIS-29: Pain Interference: 56 (7) to 54 (8)**** (3.6%)	N/A	An effect size of at least 0.20	Pain effect size = 0.20, met MCID
Wirth et al.	2019	Pain intensity, multidimensional pain	11-point NRS, BQ	12 months	NRS Pain: 5.43 (2.37) to 4.05 (2.87)** (25.4%); BQ total: 39.80 (15.16) to 29.00 (17.90)**** (27.1%)	N/A	Not specified	Not specified
Corcoran et al.	2017	Multidimensional low back pain	BBQ	End of care or discharge	BBQ: 43.1 to 30.7*** (27.3%)	N/A	MCID of 30% for BBQ and NRS	27.3% average score improvement, did not meet MCID
Burke	2014	Pain intensity, pain behavior, and pain interference	PROMIS	End of care; 33 ± 22.5 days	PROMIS Pain Intensity: 49.5 (4.86) to 40.5 (6.93) (18.2%) Pain Behavior: 55.5 (2.85) to 48.4 (9.15) (12.8%) Pain Interference: 57.7 (7.13) to 48.4 (7.88) (16.1%)	N/A	T score at baseline that was greater than 50 and showing a pre–post decrease in the T score	48% met clinical significance for pain intensity, 84% for pain behavior and interference
Dunn et al.	2011a	Pain intensity, multidimensional pain	11-point NRS, NBQ	At discharge or last available collected measures	NRS Pain: 5.7 to 3.1**** (45.6%); NBQ: 35.6 to 21.7**** (39.0%)	N/A	30% change from baseline for both the NRS and NBQ	67% patients met or exceeded the MCID for both measures
Dunn et al.	2011b	Pain intensity, multidimensional low back pain	11-point NRS, BBQ	End of care or discharge	NRS Pain: 5.9 to 3.7 (37.4%)*** BBQ: 40.3 to 26.6 (34.6%)***	N/A	MCID of 30% improvement in NRS and BBQ	60.2% met or exceeded MCID for NRS, and 53.8% met or exceeded MCID for BBQ
Lisi	2010	Pain intensity	11-point NRS	Last visit/end of treatment, within 6 months	NRS Pain: 6.5 (range 4 to 9) to 3.7 (range 0 to 9) (no P values) (43.1%)	N/A	MCID of 2 points on NRS	61% reported a decrease of 2 or more points on the NRS, meeting criteria

(continued)

Author(s)	Publication Year	Main Outcome Construct(s)	Main Outcome Measures(s)	Main Time Point(s)	Main Result(s) Mean and Standard Deviation (% Change)	Multivariate Statistics	Clinical Response Definition	Clinical Response
Newell & Field	2007	Multidimensional low back pain	BQ	12 weeks (~3 months)	BQ Total: to 7 (1, 17) (80.6%); Pain: to 1 (0, 3)* (83.3%), Disability ADL: to 0 (0, 2)* (100%), Disability SOC: to 0 (0, 2)* (100%)	Duration of pain was a strong predictor of the 12-week outcome, with patients with duration of >4 weeks faring significantly worse than those with a more acute duration.	Not specified	A clinically significant drop of 27 points on the BQ at 4 weeks
Haas et al.	2005	Pain intensity, functional disability	VAS, RODQ	12 months	VAS Pain: Chronic: to 23.9 (27)** (50%), Acute: to 40.9** (21.3%); Disability: Chronic: to 16.1 (17.1)** (58.2%), Acute: to 29.4 (20.6)** (29.7%)	Results published elsewhere	Not specified	Adjusted mean differences were clinically important for chronic patients at 3 months
Secor et al.	2004	Pain intensity	11-point NRS	Within 3 months	NRS Pain: 4.2 to 2.0**** (52.4%)	N/A	Not specified	Not specified
Schliesser et al.	2003	Pain intensity	VAS	Within 6 months of first assessment	VAS Pain: 50.1 (19.2) to 8.7 (14.4)* (82.6%)	N/A	Not specified	Not specified
Nyiendo et al.	2000	Pain intensity, disability, sensory and affective pain quality	VAS, RODQ, MPQ	1 month	VAS Pain: 42.5 (21.4) to 29.4 (23.8) (30.8%); RODQ: 38.9 (13.8) to 27.6 (18.6) (29%); MPQ Sensory: 7.3 (5.0) to 5.0 (5.6) (31.5%); MPQ Affective: 2.3 (2.7) to 1.0 (1.8) (no P values) (56.5%)	N/A	Not specified	Not specified
Acupuncture studies								
Miller et al.	2019	Cancer-related pain intensity	ESAS	End of treatment or discharge	ESAS Pain: 4.5 (2.5) to 2.8 (2.3)**** (37.8%)	N/A	Clinically meaningful improvement is at least 2-point decrease in scores	Clinically meaningful improvement was reported in 35 (51%) after the first and in 77 (45%) after all treatments

(continued)

Author(s)	Publication Year	Main Outcome Construct(s)	Main Outcome Measures(s)	Main Time Point(s)	Main Result(s) Mean and Standard Deviation (% Change)	Multivariate Statistics	Clinical Response Definition	Clinical Response
Thompson et al.	2015	Pain intensity	11-point NRS	End of treatment or discharge	NRS Pain: 4.21 (2.50) to 2.70 (1.84)**** (35.9%)	N/A	Decrease of at least 2 points on NRS	Clinically meaningful improvement in 41% of patients
Maiers et al.	2008	Pain intensity	11-point NRS	4 weeks (~1 month)	NRS Pain: 5.20 (2.63) to 4.26 (2.42) (18.1%) (no P values)	N/A	Not specified	Not specified
Niemtzow et al.	2008	Pain intensity	11-point NRS	4 weeks (~1 month)	NRS Pain: 5.5 to 3*** (45.5%)	N/A	Not specified	Not specified
Secor et al.	2004	Pain intensity	11-point NRS	Within 3 months	NRS Pain: 5.0 to 3.3** (34%)	N/A	Not specified	Not specified
Multimodal studies								
Gibson et al.	2020	Pain intensity and interference	BPI	Mean = 109 (63) days	BPI Severity: 23.5 (7.0) to 22.4 (7.6) (NS, P = 0.11); BPI Pain Interference: 46.0 (15.9) to 40.5 (16.2)****	N/A	Not specified	Not specified
Wayne et al.	2018	Disability and bothersomeness of pain	RDQ and BOP	6 months	RDQ: 12.0 (5.8) to 9.0 (6.2) (25%); BOP: 6.3 (2.3) to 4.3 (2.7) (31.7%); (no P values)	N/A	30% improvement	BOP: from baseline to 3 months: 36.1%, 6 months: 37.6%, 12 months: 42.7 %
Abrams et al.	2013	Pain intensity and interference	BPI	24 weeks (~6 months)	BPI Pain Severity: 4.7 to 3.62*** (23%) BPI Pain Interference: 4.7 to 3.3*** (29.8%)	Multivariate logistic regression found that patients with higher baseline pain, non-Hispanic populations, and patients with fewer years of chronic pain were more likely to have a clinical meaningful response on BPI	At least 20% decrease in BPI pain interference	Mean BPI pain interference scores dropped 28%

(continued)

Author(s)	Publication Year	Main Outcome Construct(s)	Main Outcome Measures(s)	Main Time Point(s)	Main Result(s) Mean and Standard Deviation (% Change)	Multivariate Statistics	Clinical Response Definition	Clinical Response
Murphy et al.	2009	Disability, pain intensity, fear belief avoidance	BDQ, 11-point NRS, FABQ-Act	Long-term follow-up (mean of 14.5 months after end of treatment)	BDQ: improved by 31.0 (90) (67.4%); NRS Pain: 7.1 to 3.0 (57.7%); FABQ-Act 20.0. to 15.4 (23%) (no P values)	N/A	Threshold of 47% improvement for BDQ; 2-point improvement on NRS	Clinically meaningful improvements in pain and disability were seen in 79% and 70% of patients, respectively; at follow-up, clinically meaningful improvements in pain and disability were seen in 79% and 73% of patients, respectively.
Physiotherapy								
Goh et al.	2010	Functional status/ disability	PSFS	End of treatment	PSFS: 4.0 to 9.1 (no SDs or P values) (56%)	N/A	Not specified	Not specified
AM therapy								
Hamre et al.	2009	Pain intensity, functional status/disability	LBPRS, HFAQ	24 months	LBPRS: 34.99 (15.10) to 26.28 (16.91)*** (24.9%); HFAQ: 61.63 (19.77) to 72.68 (21.45)*** (15.2%)	N/A	Not specified	Most improvements were clinically relevant (effect size of 0.59 for both measures)

Note. Secor et al. (2004) had two separate cohorts: one of chiropractic and one of acupuncture.
FABQ = Fear Avoidance Belief Questionnaire; MPQ = McGill Pain Questionnaire.
*$P < 0.05$, **$P < 0.01$, ***$P < 0.001$, ****$P < 0.0001$.

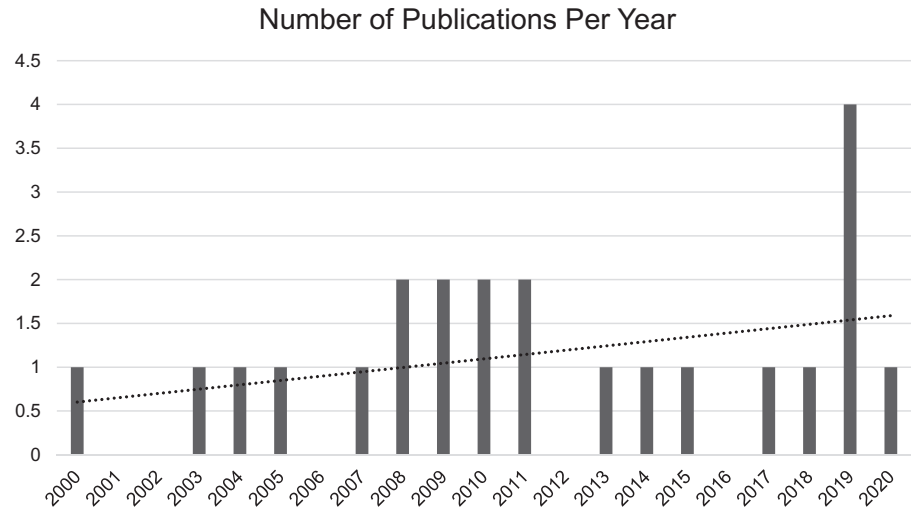

Figure 2. Number of publications per year included in the systematic review.

end of care for patients with neck pain [53,54], and 6 months after chiropractic care for veterans with pain [40].

Improvements were seen in pain interference and disability for patients with low back pain at 4 weeks/1 month [43,46], 3 months [36,48], and end of care [50,51]; improvements were seen in pain quality at 1 month [43]. Improvements in pain interference and disability were noted at end of care or discharge for patients with neck pain [53] and at end of care or discharge (mean = 33 days) for patients with a musculoskeletal disorder of the spine [41].

Acupuncture. Acupuncture studies (see Table 3) reported improvements in pain intensity at end of treatment or discharge for oncology patients with pain [38,55], 4 weeks after an initial acupuncture session for general clinic patients [42] and active-duty military members, dependents, and retirees with acute or chronic pain [39], and 3 months after initial treatment for patients with pain [52].

Multimodal. For multimodal CIH program studies (see Table 3), pain interference was improved at follow-up (mean = 109 days) for veterans with chronic pain [56], pain intensity and fear avoidance were improved at end of treatment or discharge and at follow-up for patients diagnosed with a herniated disk (mean-= 14.5 months after end of treatment or after discharge) [45], bothersomeness of pain and disability were improved at 12 months for patients with low back pain [35], and pain intensity and interference were improved at 24 weeks (~6 months) for patients with chronic pain [57].

Physiotherapy. Physiotherapy was associated with improvements in disability at end of treatment for patients with low back pain [45].

AM Therapy. AM therapy was associated with improvements in pain intensity and disability for patients with low back pain at a 24-month follow-up [37].

Multivariate Analysis

Only two studies (9%) conducted and reported a multivariate analysis to determine independent predictor variables: one chiropractic and one multimodal (see Table 3). In the chiropractic study for low back pain, duration of pain was a strong predictor of response on the BQ, with patients with pain of >4 weeks' duration faring significantly worse than those with a more acute duration [47]. In the multimodal CIH study, patients with higher baseline pain, non-Hispanic populations, and patients with fewer years of chronic pain were more likely to have a clinically meaningful response on the Brief Pain Inventory (BPI) [57].

Minimal Clinically Important Difference

The smallest benefit of value to patients is generally defined as the MCID [58]. In research, it is important to consider whether an observed change on a pain scale is meaningful to patients (or clinically significant), as opposed to a change that only reaches statistical significance [59]. To appropriately interpret the results from a pain scale, the MCID must be determined for the respective scale [58]; for example, the MCID on a 0–10 NRS in certain conditions is roughly 1.5 to 2.0 points [60].

Fifteen studies (65%) reported clinically meaningful results: nine chiropractic, two acupuncture, three multimodal, and one AM therapy (see Table 3). Specifically, a clinically meaningful response was defined as a two-point improvement on an NRS [40,44,46,55] or Edmonton Symptom Assessment Scale (ESAS) [38] or a particular percentage improvement in pain-related scores [44,50,51,54,57], or it was based on effect sizes [36,37]. Two studies reported results meeting a clinically significant improvement threshold, but the threshold was not defined [47,48]. Importantly, two of the 15 studies did not find clinically significant results. One study reported statistical significance on the BBQ after chiropractic

treatment for low back pain, but not clinical significance (27% improvement with 30% criteria) [51]. The other study found clinical significance on an NRS and on the Oswestry Disability Index (ODI) for acute but not chronic low back pain after chiropractic treatment [46].

Effect Sizes

We did not present effect sizes in the tables, as they were available for only five studies (22%) and ranged from medium to large (0.20–0.86): 0.20 for PROMIS-29 pain interference after 3 months of chiropractic treatment for low back or neck pain [36]; 0.20 for PROMIS pain interference, 0.38 for daily pain severity, and 0.36 for weekly pain severity (intensity) after 4 weeks of acupuncture treatment for patients with general pain [42]; 0.37 for BPI pain interference after multimodal treatment for veterans with chronic pain [56]; 0.59 on both the Low Back Pain Rating Scale (LBPRS) and Hanover Functional Ability Questionnaire (HFAQ) 24 months after AM therapy for low back pain [37]; and 0.86 on BBQ at the end of chiropractic treatment for low back pain [51].

Discussion

This is the first review of practice-based (or real-world) research of CIH therapies provided in outpatient or speciality CIH clinics for pain conditions or pain patients. Findings from this systematic review indicate that CIH therapies have positive effects on pain-related outcomes, including intensity, interference, disability, and fear avoidance of pain. All 22 included studies reported a beneficial impact on one or more pain-related outcomes. Overall, we report that there is evidence for improvements in pain-related measures (e.g., intensity, interference, disability) after CIH therapies in CIH outpatient clinics, including chiropractic [36,40,41,43,46–54], acupuncture [38,39,42,52,55], multimodal CIH programs [35,44,56,57], physiotherapy [45], and AM therapy [37].

The largest number of studies in our review focused on chiropractic care, followed by acupuncture and multimodal IM programs. Surprising, there were no studies that met the inclusion criteria for other CIH therapies that are commonly used in CIH outpatient clinics, such as massage, acupressure, physician consults, or energy medicine. This gap may be due to studies' failing to include longitudinal designs or studies' assessing the effectiveness of a standardized approach, which were two important inclusion criteria. Accordingly, there was a healing touch and massage study that was excluded from this review because it only had a single therapy session [61]. The gap could also be due to simply a lack of opportunity and interest to study other CIH modalities. As mentioned previously, research in primary health care settings supports that both patients and practitioners understand that a health care approach including CIH therapies "fills gaps in the treatment effectiveness" for people with complex, chronic conditions [31]. Hence, practice-based research is the logical approach for determining CIH effectiveness within the real-world clinical setting where care is delivered, rather than a less ecologically valid RCT [62].

Acute pain is pain that typically lasts less than 3 months, but may persist longer, and often has a clear connection to a physically identifiable source and resolves with tissue healing. However chronic pain is present for longer than 3 months and may or may not have a clear and current identifiable source [3]. In the largest review of its kind, Tick and colleagues [3] concluded that acupuncture, massage, and mind–body therapies have been recommended as evidence-based CIH treatments for acute pain, whereas chiropractic, acupuncture, osteopathic therapy, massage therapy, physical therapy, mind–body therapies, and cognitive behavioral therapy are recommended for chronic pain [3]. In the present systematic review, two multisite chiropractic studies investigated patients with chronic and acute low back pain as separate groups [46,48]. In one study, improvements in pain intensity and disability were larger for patients with acute pain than for patients with chronic pain, ranging from 38% to 57% improvement in pain and disability for acute pain and from 15% to 20% improvement in pain and disability for chronic pain at 4 weeks [46]. In the other study, the opposite was found: Improvements were larger for patients with chronic pain than for patients with acute pain, with improvements of 52% to 60% at 3 months and 50% to 58% at 12 months for patients with chronic pain and improvements of 23% to 32% at 3 months and 21% to 30% at 12 months for patients with acute pain [48]. Because neither study reported the average length or frequency of the intervention, we are limited in understanding reasons for these potential differences. Therefore, it is clear that future practice-based research is needed to understand an ideal or optimal CIH treatment regimen (dose and timing of treatments) for those patients presenting with acute and chronic pain.

There was variability in the inclusion of different pain outcome measures, which limited our ability to compare changes in pain across studies. However, nearly half of the studies (n = 10) measured pain intensity with an 11-point 0–10 NRS (n = 10, 43% of studies), which allowed for some comparison across these studies. The average percent improvement in NRS across all studies and time points was 32%. The percent improvement ranged from 18% at 4 weeks with acupuncture treatment [42] to 58% at long-term follow-up (mean = 14.5 months) after multimodal treatment [44]. Over the short term, there was an average improvement of 30% at 4 weeks (~1 month), 40% at discharge or end of care (variable time), and 42% at 12 months. The improvements in pain intensity from the chiropractic studies (NRS range: 20–52%) are within the range of improvements of chiropractic treatment reported from RCTs, with 25% improvement in spinal pain after 2 weeks [63] and 24% improvement in

low back pain after 4 weeks [64]. Acupuncture studies reported a range of improvements in NRS pain intensity, from 18% to 46% after 4 weeks [39,42], and the percent improvement after acupuncture for cancer-related pain (ESAS) was 36–38% at end of treatment or discharge [38,55], which is higher than improvements reported from RCTs, with 20% at 5 days after initial treatment [65]. Taken together, this pattern suggests that the magnitude of improvement in pain intensity observed in practice-based outpatient clinical situations is somewhat comparable to improvements observed under RCT situations, with some indication that improvements may be greater in patients from practice-based effectiveness studies.

Study Weaknesses

There were a number of common study weaknesses that deserve discussion. One weakness was that numerous studies did not include participants' SES, race, or ethnicity, which undermines the ability to determine whether results are generalizable to a greater population. For example, in one of our reviewed studies, it was found that ethnicity was a predictor of response to multimodal CIH treatment [57]. Therefore, we advocate that race/ethnicity is an important demographic variable for future studies to include to allow for further examination of this variable as an important predictor of response.

Second, the average number of CIH treatments (or duration of treatment) was absent from 26% of the included studies. Because we focused our review on CIH therapies or programs that were individualized per patient, there is inherent variability in treatment duration. As such, we contend that it is essential for authors to report the average treatment length and frequency of treatments to enable comparison across studies to guide appropriate CIH care.

A third common study weakness was a lack of effect size reporting, with 78% of studies not providing that metric. Although most studies reported statistical significance, effect sizes provide a better indication of the degree of improvement, and their inclusion has been recommended as a part of standard results reporting in recent years [66,67].

A fourth common study limitation was the small sample size and limited number of clinics included in the studies. Specifically, the majority (83%) of studies included 500 or fewer patients, and 50% had a sample size of fewer than 100 patients. Furthermore, the majority (65%) of articles included evaluation at only one clinical site. To ensure that the results of studies are generalizable to clinical patients and clinicians, larger sample sizes and more clinical sites should be included, when possible, to better reflect the general patient and clinic population [68].

Lastly, most studies did not report multivariate analyses for uncovering potential predictor variables. We acknowledge that for studies with smaller sample sizes, conducting multivariate analysis would be statistically inappropriate. However, on the basis of others' recommendations [69], if the sample size of a study is at least 100, we advocate for inclusion of multivariate analysis to help identify how various baseline characteristics (e.g., pain intensity, duration of pain, demographics) are associated with responsiveness on pain outcomes after different CIH interventions.

Study Quality

Studies that we deemed "high quality" are those in which the largest number of our defined study elements were reported. One such study, Hays and colleagues [36], was an NCCIH-funded prospective chiropractic study for patients with low back or neck pain. We found the study to be of high quality because they included a very large sample (N = 2,024) with a high retention rate (91%) and also reported race/ethnicity and SES. Furthermore, the study included 125 clinical sites with geographic diversity and measured pain intensity with the PROMIS-29 at 3 months, with both statistical and clinical significance reported.

Another high-quality study was conducted by Haas and colleagues [48]. This was a prospective chiropractic study of patients with acute and chronic low back pain. We rated it as high quality because it included a large sample (N = 2,872), both race and ethnicity were reported, and it was a multisite study (n = 51 clinics). The authors measured both pain intensity and disability (VAS, RODQ) at 3 months and over the longer term, at 12 months. They also reported statistical and clinical significance, and they conducted a multivariate analysis, although those results were published in another article.

Wayne and colleagues [35] also conducted a high-quality study, which was an NCCIH-funded, prospective, single-site multimodal study of patients with low back pain. The study included a modest sample size (N = 156) but had a high retention rate (90%). The authors reported participants' race/ethnicity, SES, average number of visits, and duration of treatment and assessed disability (Roland Disability Questionnaire [RDQ]) and bothersomeness of pain (BOP) at 3, 6, and 12 months. In the publication, the authors did not report statistical significance, but clinical significance of the results was addressed.

Another high-quality study was a multimodal study of patients with chronic pain [57]. The study was conducted across the BraveNet Practice-Based Research Network of nine geographically diverse clinics with a clinical coordinating center [70]. The authors included a large sample size (N = 409), although the retention rate was not as high (62%) as other studies because of lack of participant remuneration. Strengths include a long-term assessment of pain with the BPI at 6, 12, and 24 weeks, as well as statistical significance and clinical significance reporting.

The multivariate analysis found that that higher baseline pain, non-Hispanic ethnicity, and fewer years of chronic pain were independent predictors of more improved BPI scores.

Lastly, a high-quality prospective study of AM therapy for low back pain [37] included 41 sites, had a decent sample size (N = 75) with high retention (88%), and reported SES but not ethnicity. Pain (LBPRS) and functional status (HFAQ) were measured at 24 months, the longest follow-up of all studies. The authors indicated the average length and frequency of the intervention and reported both statistical and clinical significance.

Limitations of the Review

There were a number of limitations of the present review that warrant mentioning. First, we were limited in our ability to make comparisons across studies and draw conclusions because of the heterogeneity in study design and incomplete reporting in the publications. Second, we elected not to include the outcomes for all time points and from every study in the tables, as some studies included more time points than space would allow [49,57]. In those instances, we included results from one main time point per study, which was the longest follow-up time point of each study.

Third, with an a priori focus solely on pain-related outcomes for this review, we did not assess all other variables included in some studies, such as quality of life, anxiety, or depression, and thus did not capture the entire scope of findings from these reports. Fourth, it is pertinent to also address a possible "file drawer problem," as it is unclear how many studies with null or negative effects might have been conducted but the results not published. As such, we encourage publication of studies with no positive effects or with negative effects, as these studies also provide valuable information to the research and clinical communities. Finally, it is important to note that there were several studies that would have been included in this review, but they either did not report the outcome means at all or reported them only in a figure, in which case the accuracy of the numbers extracted could not be guaranteed. Only one author responded to our request for additional information; studies from nonresponsive authors were unfortunately not included in this systematic review.

Suggestions for Future Research

The results of this systematic review highlight the heterogeneous state of the current research in CIH practice-based research, making it challenging to draw any firm conclusions. Therefore, we have the following recommendations for CIH researchers in their publications of practice-based research of CIH interventions, as well as in the design of future CIH practice-based research.

Reporting Recommendations

1. First, we recommend that authors use the tables in this review as a guide to ensure a more consistent and thorough reporting of their study results. Along with the study design recommendations, more complete reporting that is informed by this model will likely deepen our field's collective understanding of how to best implement CIH interventions in clinical settings.

2. Second, we recommend applying this systematic review methodology to future systematic reviews of other outcomes, including, but not limited to, quality-of-life outcomes in CIH outpatient clinics [71] and inpatient environments to assess the impact of CIH therapies on pain-related outcomes in hospitalized patients [72–75].

Study Design Recommendations and a Call to Action

1. First, as many studies enrolled patients with low back and neck pain, we recommend that clinical investigations of CIH for different pain populations be conducted, including headache-related pain and osteoarthritic pain, which, together with low back and neck pain, are the most common pain-related conditions in the United States [76].

2. Second, as most outcomes were assessed within 6 months after initiation of treatment (74%), we recommend that authors assess long-term outcomes (>6 months) to ascertain whether the significant improvements in pain-related outcomes are maintained over time.

3. Third, to improve comparison of results across studies, at a minimum we recommend that all researchers include an 11-point NRS for pain intensity. The NRS allows for pain assessment in case of time constraints or the need for rapid assessment, as it is a validated measure by itself and is also included in some larger measures, such as the PROMIS-29. Ideally, we encourage studies to include more comprehensive measures of pain, such as the PROMIS suite of measures, which includes 4-, 6-, and 8-item banks for assessing pain interference and has been clinically validated across diverse populations [77] and developed/recommended by the NIH. A recent article provides a cross-walk of NRS and PROMIS measures in patients with cancer [78]. We also recognize the benefit of the brief ESAS tool as an appropriate outcome for the cancer population.

4. Fourth, given that pain disproportionately affects certain minorities and SES groups [3], enrolling more diverse samples, including more Hispanic, African, and Asian Americans and lower-SES populations, would support identifying the best approach for treating pain in patients more at risk of pain conditions.

5. Fifth, we noted that the highest retention rates were for studies in which incentives were offered for patient participation.

We recognize that this is largely dependent on available funding, and the incentivized studies were funded by the NIH [35,36]. However, if fiscally possible, we recommend offering incentives to increase study retention to the highest possible levels.

6. Sixth, as only four different individual CIH therapies (chiropractic, acupuncture, physiotherapy, and AM therapy) were included in this review, we recommend that researchers conduct practice-based effectiveness trials with other CIH therapies (e.g., massage) and, most importantly, with individualized multimodal programs, which most strongly align with the principals of CIH.

7. Seventh, to increase the generalizability of results and advance the CIH field, we recommend that future CIH research would be most impactful by including multiple clinical entities and a large sample size. Two examples of CIH practice-based research that serve as a model for this proposal are from two recently completed projects: BraveNet Practice-Based Research Network (~5,000 patients enrolled over 17 sites) [79] and the Veterans Health Administration Office of Patient-Centered Care and Cultural Transformation (119 veterans enrolled at three Veterans Affairs sites) [80]. Although both of these efforts served as a first step, we propose that future CIH practice-based efforts must include a larger number of sites and more diverse participants with a common set of patient-reported pain outcomes. Thus, our call to action is that the most logical organization to galvanize support for multisite, CIH practice-based research would be the Academic Consortium for Integrative Health and Medicine (the Consortium). The Consortium is the organizational home of more than 70 major academic integrative health centers and health systems with integrative medicine foci (https://imconsortium.org/). Such a multicenter practice-based research effort could facilitate the development of benchmarks of success across CIH, as well as help guide clinicians toward evidence-based use of CIH to treat pain conditions.

If that were to happen, we envision a future state in which an individual seeking treatment at CIH clinics could be offered a choice of interventions that prior practice-based research has shown to be effective for that individual's clinical condition—given individuals' demographics and complete clinical presentation. The recommendation could include a "dose" or schedule of CIH services, which would foster development of optimized CIH pain interventions customized to individual patient needs and characteristics.

Conclusion

Findings from this systematic review of practice-based effectiveness studies in CIH outpatient clinics indicate that CIH therapies have positive effects on pain, including pain intensity, interference, and disability. All studies reported beneficial impacts on one or more pain-related outcome, but heterogeneity among studies limited their comparability. Therefore, on the basis of this review, we conclude that additional and future practice-based research in CIH is needed to help guide clinical practice, and our call to action is that the Consortium is the logical entity to galvanize support for this collaborative future research effort.

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Appendix

Search terms were: ((((((((((((acupuncture[mesh] OR acupuncture therapy[mesh] OR acupunctur*[title/abstract] OR medicine, Chinese traditional[mesh] OR traditional Chinese medicine[title/abstract] OR Chinese traditional medicine[title/abstract] OR Chinese medicine[title/abstract] OR massage[mesh] OR massage[title/abstract] OR naturopathy[mesh] OR naturopath*[title/abstract] OR chiropractic[mesh] OR manipulation, chiropractic[mesh] OR chiropractic*[title/abstract] OR osteopathic medicine[mesh] OR manipulation, osteopathic[mesh] OR osteopath*[title/abstract] OR yoga[mesh] OR yoga[title/abstract] OR (multidisciplinary[title/abstract] AND (integrative[title/abstract] OR complementary[title/abstract] OR alternative[title/abstract])) OR (consultation*[title/abstract] AND (integrative[title/abstract] OR complementary[title/abstract] OR alternative[title/abstract])) OR manual therap*[title/abstract] OR integrative medicine[mesh] OR integrative medicine[title/abstract] OR integrative oncology[title/abstract] OR integrative therapy[title/abstract] OR integrative therapies[title/abstract] OR integrative health[title/abstract] OR complementary medicine[title/abstract] OR complementary therapy[title/abstract] OR complementary therapies[title/abstract] OR complementary health approach*[title/abstract] OR complementary and alternative medicine[title/abstract] OR complementary and alternative therap*[title/abstract] OR alternative medicine[title/abstract] OR integrative approach*[title/abstract])))) AND ((Cohort Studies[mesh] OR Longitudinal Studies[mesh] OR Prospective Studies[mesh] OR Retrospective Studies[mesh] OR Case-Control Studies[mesh] OR cohort stud*[title/abstract] OR prospective[title/abstract] OR retrospective[title/abstract] OR registry stud*[title/abstract] OR registry-based stud*[title/abstract] OR observational stud*[title/abstract] OR longitudinal stud*[title/abstract] OR descriptive analysis[title/abstract] OR case-control*[title/abstract] OR historical stud*[title/abstract] OR long-term stud*[title/abstract] OR follow-up stud*[title/abstract] OR follow-up evaluat*[title/abstract] OR follow-up[title] OR effect*[title] OR outcome*[title]))))) NOT ((pediatric[title/abstract] OR fetal[title/abstract] OR child[title/abstract] OR children[title/abstract] OR baby[title/abstract] OR babies[title/abstract] OR infant*[title/abstract] OR newborn*[title/abstract] OR neonat*[title/abstract] OR adolescen*[title/abstract] OR teen*[title/abstract] OR teenager*[title/abstract])))) NOT ((animal*[title/abstract] OR mouse[title/abstract] OR mice[title/abstract] OR rats[title/abstract] OR dog[title/abstract] OR dogs[title/abstract] OR cat[title/abstract] OR cats[title/abstract] OR pig[title/abstract] OR pigs[title/abstract] OR canine[title/abstract] OR feline[title/abstract] OR porcine[title/abstract])))) NOT ((telemedicine[mesh] OR telemedicine[title/abstract] OR telehealth[title/abstract] OR teletherap*[title/abstract] OR telerehab*[title/abstract] OR mobile phone*[title/abstract] OR mobile app*[title/abstract])))) NOT ((Adaptive Clinical Trials as Topic[Mesh] OR Non-Randomized Controlled Trials as Topic[mesh] OR Clinical Trial Protocols as Topic[mesh] OR Controlled Clinical Trials as Topic[mesh] OR Clinical Trials as Topic[mesh] OR Pragmatic Clinical Trials as Topic[mesh] OR Randomized Controlled Trials as Topic[mesh] OR Adaptive Clinical Trial[Publication Type] OR Clinical Trial Protocol[Publication Type] OR Clinical Trial, Phase I[Publication Type] OR Clinical Trial, Phase II[Publication Type] OR Clinical Trial, Phase III[Publication Type] OR Clinical Trial, Phase IV[Publication Type] OR Pragmatic Clinical Trial[Publication Type] OR Controlled Clinical Trial[Publication Type] OR Randomized Controlled Trial[Publication Type] OR review*[title] OR protocol*[title] OR randomized[title] OR randomised[title] OR clinical trial*[title] OR case report*[title/abstract] OR cross-sectional[title/abstract] OR controlled trial*[title/abstract])))) AND english[lang].