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REVIEW ARTICLE

The Impact of Individualized Complementary and Integrative Health Interventions Provided in Clinical Settings on Quality of Life: A Systematic Review of Practice-Based Research

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Abstract

Background: The goal of this systematic review was to evaluate the impact of individualized complementary and integrative health (CIH) interventions on quality-of-life outcomes as collected in CIH outpatient clinics.

Methods: A systematic review was conducted using PubMed, OVID, Cochrane, Web of Science, Scopus, and Embase through December 2020. Inclusion criteria were as follows: individualized CIH treatment, longitudinal effectiveness design, patient-reported outcomes, outpatient CIH clinic setting, participants aged ≥18 years, sample size of ≥25, and English full text. The study was listed in the PROSPERO database (CRD42020159193), and PRISMA guidelines were used. The variables extracted from articles focused on study details/demographics, CIH intervention characteristics, and outcome characteristics.

Results: The literature search yielded 3316 records with 264 assessed for full-text review. Of these, 19 studies (including ∼14,002 patients) were specific to quality of life (or well-being) as a main outcome. Most studies included were multidisciplinary studies ($n=12$), followed by acupuncture ($n=4$), chiropractic ($n=3$), and massage or reflexology ($n=1$). The short-form group of questionnaires (SF-12, SF-36, SF-8) were the most used quality-of-life/well-being questionnaire, comprising 37% of studies ($n=7$), and the Patient Reported Outcomes Measurement Information System (PROMIS) measures comprised 21% ($n=4$). Both questionnaires are normed to U.S. population, allowing for comparison. The average improvement across the comparable SF and PROMIS measures for Physical Health was 6% (range 2%–20%) and for Mental Health was 5% (range 1%–11%), demonstrating clinical significance. Improvements in the observational studies are comparable to improvements reported from randomized controlled trials.

Conclusions: Results from this systematic review indicate that CIH therapies largely have positive effects on health-related quality of life and well-being for various patient populations seen in CIH clinical settings. Direct comparisons across studies were limited due to the variability in study design and incomplete reporting in some of the publications. Suggestions for improving the design and reporting for future practice-based research are provided.

Keywords: systematic review, complementary and integrative health, integrative medicine, practice-based research, quality of life, well-being, cancer, pain

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Introduction

The World Health Organization (WHO) defines quality of life as a health-related construct related to ''an individual's perception of their position in life in the context of culture and value systems, as well as their goals, expectations, standards and concerns.''[1] Therefore, quality of life is a multidimensional construct,[2,3] widely recognized as health-related, with the WHO definition of health being not only the absence of disease but also complete mental, social, and physical well-being.[3] The construct of quality of life shares common components and highly significant correlations with the construct of well-being.[4] As such, these terms are sometimes used interchangeably[4] and will be for the purpose of the current review.

While biomedical outcomes have traditionally served as the endpoints in health and medical research, it is also important to assess patient-reported outcomes of quality of life and well-being to fully encompass the clinical benefit of health interventions.[5] Information revealed by such outcomes captures patient perspectives and perceived satisfaction, allowing for a holistic assessment of the effects of treatment on patients' lives, even after the completion of a treatment course.[6] Moreover, quality-of-life assessment carries prognostic significance,[7] as it has shown to be a predictor of treatment success and patient survival. Studies also show that utilizing patient-reported outcomes, such as in quality of life and well-being, results in improved communication between patients and providers[8] and better symptom control.[9]

In the case of chronic and/or terminal illness where no effective cure is available, or may only modestly prolong life, treatment emphasis is often placed on improving health-related quality of life.[10] For instance, cancer clinical trials have increasingly adopted patient-reported outcomes as important endpoints,[11] with standardized implementation.[12] Indeed, measures of quality of life and well-being are vital in conditions as cancer and chronic pain, as well as other chronic condition, where the effects of illness on patients' lives transcend the objective to include subjective functional measures.[13]

Complementary and integrative health (CIH) utilizes evidence-based conventional and alternative medical approaches that focus on the health of the whole person, including emotional, mental, physical, social, and spiritual health. As such, CIH is ideally suited as an individualized rather than standardized approach to health care that considers different aspects of the patient's characteristics and life circumstances in the treatment plan. CIH therapies, such as acupuncture, chiropractic, and massage, are widely used by U.S. adults for therapeutic purposes, including improving well-being and quality of life.[14,15] The use of CIH therapies has risen in recent decades, at both individual and institutional levels. According to the 2007 National Health Interview Survey, it was estimated that there were $\sim$354 million visits to CIH practitioners in 2007.[15] Increases were seen from 2012 to 2017 in the use of specific complementary health approaches among U.S. adults.[16] At the institutional level, the availability of CIH services offered in U.S. hospitals increased from 37% in 2007 to 42% in 2010.[17]

Both patients and practitioners in primary care settings acknowledge that a health care approach, which includes CIH therapies, can fill gaps in treatment effectiveness for people with complex chronic conditions.[18] Indeed, meta-analyses and systematic reviews of randomized controlled trials (RCTs) have reported efficacy of CIH for improving quality of life in many patient populations, including cancer patients,[19–22] veterans,[23] and chronic pain patients.[24–27] Given their exhibited efficacy under RCT conditions, evaluation of the pragmatic effectiveness of CIH therapies for improving quality of life within clinical practice settings is the logical next step in the progression of research, as delineated by the National Center of Complementary and Integrative Health (NCCIH).[28] Indeed, pragmatic effectiveness trials allow for the assessment of the effectiveness of interventions in routine clinical practice settings, thereby providing a more realistic understanding of the risks and benefits of intervention, which can support patient and clinician decisions.[29]

Despite the widespread use and efficacy of CIH therapies for quality of life and well-being,[30] there are no systematic reviews summarizing scientific articles focused on the pragmatic effectiveness (or practice-based research) of CIH therapies for quality of life in health care settings. Previously, our team published a systematic review of practice-based research of CIH practices as provided for pain relief in clinical settings.[31] In the context of that systematic review, we discovered an average percent improvement across studies and time points of 32%.

Accordingly, the goal of the current systematic review was to use the same methodology to evaluate the effectiveness of individualized CIH programs and therapies (including but not limited to acupuncture, chiropractic, Traditional Chinese Medicine, integrative medicine physician consultations, naturopathy, and osteopathic medicine) provided in outpatient CIH clinics on quality-of-life outcomes. While a standardized treatment can still be part of ''real-world'' care, individualized treatments are ideal within the CIH model and, accordingly, are the focus of this review. To ensure generalizability to clinical patients, the focus of this review was solely on published prospective or retrospective observational, cohort, or registry-based longitudinal studies, with the exclusion of RCTs.

Methods

Eligibility criteria

The following study inclusion criteria were used: individualized treatment (i.e., not standardized length or number of sessions), longitudinal effectiveness design (i.e., two or more data collection points), patient-reported validated outcome measures for health-related quality of life and well-being, taking place in an outpatient CIH clinic, having participants older than 18 years, comprising a sample size of at least 25, and availability of full text published in English. This systematic review focused exclusively on published works of prospective or retrospective observational, cohort, or registry-based longitudinal studies (i.e., pragmatic effectiveness) to study the use of CIH therapies provided in CIH clinical settings. Controlled observational studies were included, but only the experimental group outcomes were included in this review. RCTs were excluded.

Information sources

A systematic review of practice-based research of CIH therapies was conducted using PubMed, Cochrane, Web of Science, OVID, Embase, and Scopus from inception through December 2020.

Search strategy

The study was listed in the PROSPERO database (CRD42020159193; protocol submitted November 20, 2019, and approved April 28, 2020) and to which PRISMA guidelines were adhered. Specific search terms are noted in Supplementary Material S1.

Selection process

The results of the extraction were imported into Covidence, a commercial software platform that assists in organizing articles and streamlines the process of systematic, scoping, and general reviews (www.covidence.org). Authors J.A.D. and J.S., as well as three others, first reviewed article abstracts from the literature search and identified studies that potentially met the inclusion criteria for full-text review. All full-text articles were imported into Covidence to assist with review. Any discrepancies were then discussed between coders, and the senior author (J.A.D.) made the final determination of inclusion.

Data collection process

Next, four independent coders (N.L.D., J.S., A.A., J.A.D.) reviewed the full texts of the studies, with two coders reviewing each study. Discrepancies in the full-text extractions between coders were resolved by discussion and by determination of the senior author (J.A.D.).

Data items

Variables extracted included study details and demographics (location, total number of participants, retention rate, incentives, gender, age, race/ethnicity, socioeconomic status [SES]), intervention characteristics (population type, setting, number of sites, time frame, design, intervention/program, interventionists), and outcome characteristics (main outcome constructs, measures/instruments, main result, multivariate analysis, clinical response, and effect sizes).

Study risk of bias in individual studies

To assess risk of bias within studies, we evaluated whether there was any reporting bias in terms of selective outcome reporting or attrition bias within each study based on the Cochrane Risk of Bias Assessment Tool.[32] Two reviewers (N.L.D. and J.A.D.) independently assessed each study, and any discrepancies were resolved by consensus.

Results

Study selection

The literature search yielded 3316 records with 264 assessed for full-text review. Of those, 19 studies (including $\sim$14,002 patients) were specific to quality-of-life-related or well-being-related measures as a main outcome. There were 18 studies specific to pain or other outcomes that were not included. A recently published systematic review addressed the articles with pain outcomes.[31] There were five studies that were included in both reviews as they reported both quality-of-life and pain outcomes.

Figure 1 depicts the PRISMA flow diagram indicating the number of studies identified, screened, determined to be eligible, and included. Main reasons for exclusion include: $n=60$ standardized treatment, $n=53$ wrong outcomes, $n=22$ setting not 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 with no published results, $n=5$ could not retrieve article, $n=4$ were duplicates, $n=3$ were not published in a language other than English, and $n=2$ hospitalized patients.

Study characteristics

Study results are briefly reviewed below, grouped by study details and demographics (Table 1), intervention characteristics (Table 2), and outcome characteristics (Table 3). Within each table, studies are listed in reverse chronological order and grouped by type of intervention: multidisciplinary ($n=12$), acupuncture ($n=4$), chiropractic ($n=3$), massage, aromatherapy, or reflexology intervention ($n=1$). One study, Secor et al.,[33] is represented twice, as the intervention was either acupuncture or chiropractic; as such, it is listed under both categories in the tables.

Publication year. Figure 2 shows the years of publications of all 19 studies included in this article.

Location of study. Most studies were carried out in the United States (74%, $n=14$), followed by the United Kingdom (10.5%, $n=2$), Canada (10.5%, $n=2$), and Sweden (5%, $n=1$).

Sample size. At baseline, 3 studies (21%, $n=4$) had participants fewer than 100, less than half of the studies had between 101 and 500 participants (37%, $n=7$), and 1 study (5%, $n=1$) had participants totaling more than 500 but fewer than 1000. There were 5 studies (26%, $n=5$) that had more than 1000 participants. One study did not specify its number of participants.

The total number of participants across all studies was at least 14,002, among which 10,694 were from multidisciplinary studies, 209 were from acupuncture studies, 2270 were from chiropractic studies, and 829 participants were from the massage, aromatherapy, or reflexology study. One study did not report the number of participants at baseline; therefore, the term ''at least'' has been used to show the total sample size at baseline (Table 1).

Incentives and retention. The retention rate ranged from 26% to 91%, although what defined retention varied from study to study (Table 3). Three studies did not report the retention rate. The time point for the retention rate varied across the studies and, where indicated, ranged from 4 weeks to 12 months, although one study measured participants up to 1446 days of follow-up (Table 3).

Five studies reported offering incentives to participants in form of gift cards or no cost services (26% of studies). Three of these studies offered participants gift cards ranging from $10 to $90 in value, one study offered 10-pounds sterling toward the cost of therapies, and one study did not charge a fee for therapies. Studies offering incentives did not always show high retention rates; however, the study with the highest retention rate (91%) offered up to $80 in gift cards. This suggests that budget allocation for participant incentives in such studies may help in increasing the retention rate of participants.

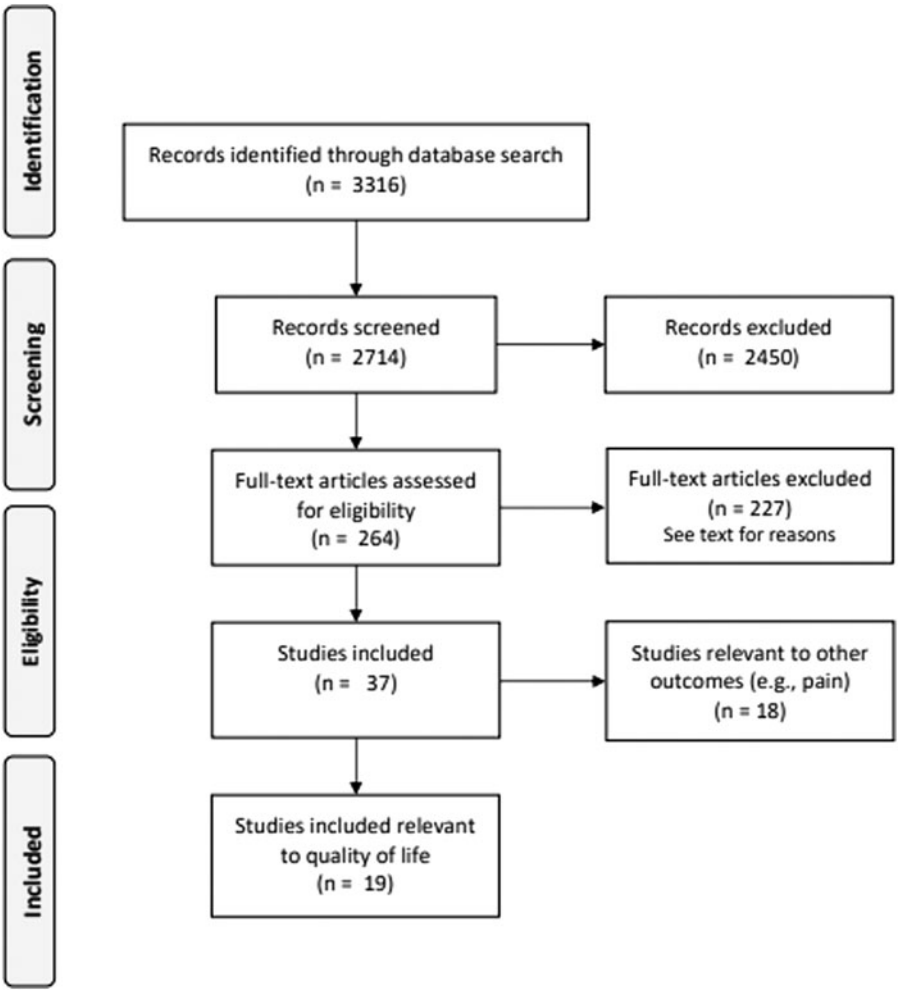

FIG. 1. PRISMA flow diagram.

Demographics. Overall, there were more female participants than male participants, with the percentage of female participants ranging from 28% to 100% across all studies (Table 1). When reported, participants' mean age throughout studies ranged from 39.3 to 59.8 years. Only 4 of 19 studies (21%) reported SES (e.g., either in terms of income and/or education), and 13 (68%) studies reported race and/or ethnicity. Most of these studies had a large percentage of White/Caucasian (50%–100%) population, except for Miller et al.[34] and Niemtzow et al.,[35] who enrolled 44% and 31% Black/African American participants, respectively.

Patient population. Most studies enrolled clinic patients with any health concern (37%, $n=7$), followed by patients with cancer (32%, $n=6$), chronic pain or acute pain (21%, $n=4$), and veteran or military (11%, $n=2$).

Number of sites. Thirteen of 19 studies (68%) included 1 clinical site for evaluation. The remaining 6 studies (32%) were conducted at multiple sites (ranging from 2 to 125 sites); most of these were chiropractic studies (Table 2).

Design. Most studies were prospective (68%, $n=13$), and the rest were retrospective (32%, $n=6$) (Table 2).

Intervention type. The review includes 12 multidisciplinary intervention studies (63%), 4 acupuncture (21%), 3 chiropractic (16%), and 1 massage, aromatherapy, or reflexology study (5%). This review selected studies that provided individualized treatment as part of their inclusion criteria.

Main outcome constructs and measures. Health-related quality of life was the most reported outcome construct (79%, $n=15$), followed by well-being (21%, $n=2$) and cancer-related well-being (10.5%, $n=2$). Studies included in the review used different sets of questionnaires to assess outcomes. The most common questionnaire used was any version of the short-form (SF) survey (37%, $n=7$): SF-12 ($n=4$), SF-36 ($n=2$), SF-8 ($n=1$). The second most common measure was any Patient Reported Outcomes Measurement Information System (PROMIS) measure (21%, $n=4$): PROMIS-10 ($n=2$), PROMIS-29 ($n=1$), PROMIS-28 ($n=1$), followed by the Edmonton Symptom Assessment System (ESAS), 10.5% ($n=2$); Measure Yourself Concerns and Wellbeing (MYCaW), 10.5% ($n=2$); Functional Assessment of Cancer Therapy–General (FACT-G), 5% ($n=1$); World Health Organization Well-Being Index (WHO-5), 5% ($n=1$); Numerical Rating Scale (11-point NRS), 5% ($n=1$); EQ-5D, vertical visual analogue scale (EQ-VAS), 5% ($n=1$); and Measure Yourself Medical Outcome Profile (MYMOP2), 5% ($n=1$).

Table 1. Study Details and Demographics for All Included Studies

Authors	*Publication year*	*Country*	*Total No. at baseline*	*Maximum No. analyzed for any outcome*	*Retention*	*Incentives*	*Gender (% female)*	*Age, M (SD) or (range)*	*Race/ethnicity*	*SES*
Multidisciplinary studies										
Elwy et al.[38]	2020	United States	394	119	30.2% completed all time points	Total of $90 in gift cards if all 5 surveys were completed.	28	59.3 years (range 29–85 years)	Not specified	Not specified
Crocker et al.[40] Herman et al.[63] (for extra info)	2019 2014	United States	253	177	70% completed 2 visits	$10 gift card per time point	70	52 (10.8)	American Indian/ Native American/Alaska Native (1.1%); Asian or Asian American (0.6%); Black/ African American (4.5%); Hispanic/Latino (4.5%); White (86.4%); Others (2.3%); missing (0.6%)	11.3% < $50,000; 27% income ≥ $150,000; 87% 4-year college graduate or more
Beidelschies et al.[41]	2019	United States	398 (propensity-matched pairs)	220	55.3% completed follow-up	Not specified	75.9	52.70 (13.54)	White (91.2%)	Median income $62,776 ($42,244 to $76,831)
Dusek et al.[36]	2018	United States	3473	1541	44.4% completed at least 2 PROMIS-10 measures	Not specified	85	59.8 (14.3)	White (93%); Hispanic (1%)	Not specified
Lopez et al.[44]	2017	United States	2474	642	25.9% completed follow-up	Not specified	71.1	57.2 (12.2)	White (73.2%); Black (8.2%); Hispanic (10.8%); Other (7.9%)	Not specified
Abrams et al.[47]	2013	United States	409	252	62% completed all 4 visits	Not specified	74.1	48.6 (15.18)	White (∼81%)	Not specified

(*continued*)

TABLE 1. (CONTINUED)

Authors	*Publication year*	*Country*	*Total No. at baseline*	*Maximum No. analyzed for any outcome*	*Retention*	*Incentives*	*Gender (% female)*	*Age, M (SD) or (range)*	*Race/ethnicity*	*SES*
Harrington et al.[45]	2012	United Kingdom	1527	402	27% completed follow-up	No fee for therapies	100	30%–51% younger than 50 years, and 45%–63% aged 50–69 years	White (83%–98%)	Not specified
Frenkel et al.[46]	2010	United States	229	73	31.8% completed follow-up	Not specified	60	56.0 (range 21–90 years)	Not specified	Not specified
Brazier et al.[39]	2008	Canada	46	34	73.9% completed follow-up	Not specified	61	Range 30–89 years	Not specified	Not specified
Greeson et al.[37]	2008	United States	763	370	48.5% completed follow-up	Not specified	66.3	49.4 (15.5) (range 14–93 years)	White (75.2%); African American (7.2%); Asian (0.9%); Hispanic (0.7%); Native American (0.4%); Other (0.7%); unknown/not reported (14.9%)	Not specified
Myklebust et al.[42]	2008	United States	274	85	31% completed follow-up	Not specified	87.1	51.2 (10.2) (range 23–82 years)	White (91%); Black (1%); Asian (1%)	Not specified
Mulkins et al.[43]	2003	Canada	320	212	66.3% completed follow-up	Not specified	67	45.0 (14.9)	Not specified	Not specified

(*continued*)

Table 1. (Continued)

Authors	Publication year	Country	Total No. at baseline	Maximum No. analyzed for any outcome	Retention	Incentives	Gender (% female)	Age, M (SD) or (range)	Race/ethnicity	SES
Acupuncture studies										
Miller et al.[34]	2019	United States	68	Not specified	Not specified	Not specified	54	Median 55 (range 31–89 years)	Caucasian (50%); African American (44%); Other (6%)	Not specified
Thompson et al.[48]	2015	United States	90	65	72% completed at least 2 acupuncture sessions	Not specified	69.0	52.0 (range 20–74 years)	Non-Hispanic (89%); White (82%)	Not specified
Niemtzow et al.[35]	2008	United States	119	105	88.2% completed follow-up	Not specified	50.8	Range 21–85 years	Alaska Native/ American Indian (6%); Asian (3%); Black (31%); Hispanic (2.5%); White (63%); other (4%)	65% college degree or higher
Secor et al.[33]	2004	United States	Not specified	38	Not specified	Not specified	67.9	45.0 (range 21–84 years)	Caucasian (100%)	Not specified
Chiropractic studies										
Gedin et al.[49]	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

(*continued*)

Table 1. (Continued)

Authors	*Publication year*	*Country*	*Total No. at baseline*	*Maximum No. analyzed for any outcome*	*Retention*	*Incentives*	*Gender (% female)*	*Age, M (SD) or (range)*	*Race/ethnicity*	*SES*
Hays et al.[50]	2019	United States	2024	1835	90.7% completed follow-up	Up to $80 in gift cards for participating	74	49 (range 21–95 years)	Caucasian (88%); Asian (3%); African American (2%); American Indian/Pacific Islander/Other (2%)	32% ≥ $100,000; 30% $60,000 to $99,999; 36% $10,000 to $59,999; 2% < $10,000; 93% some college or higher
Secor et al.[33]	2004	United States	Not specified	54	Not specified	Not specified	72.2	45.0 (range 21–84 years)	Caucasian (94.4%); Hispanic (5.6%)	Not specified
Massage, aromatherapy, or reflexology										
Harris et al.[51]	2010	United Kingdom	66	57	86.4% completed follow-up	10 pounds sterling toward the cost of the patient's treatment	73	39.3 (range 19–75 years)	Not specified	Not specified

Secor et al.[33] is one study split by cohort.
M, mean; SD, standard deviation; SES, socioeconomic status.

Table 2. Intervention and Design Characteristics for All Studies

Authors	*Publication year*	*Study population*	*Study setting*	*No. of sites*	*Study time frame*	*Prospective or retrospective*	*Intervention and/or interventionist*	*Intervention duration*
Multidisciplinary studies								
Elwy et al.[23]	2020	Veterans participating in any CIH	VA medical center	2	Not specified	Prospective	Multimodal CIH program; most common practices used were yoga, meditation, acupuncture, Tai Chi, and healing touch.	Average of 1.52 types of CIH treatment
Crocker et al.[40] Herman et al.[63] (for extra info)	2019 2014	Clinic patients with any health concern	Integrative Medicine primary care clinic	1	Not specified	Prospective	Nonstandardized individual approach to IM delivered by primary care MDs, acupuncturist, chiropractor, behavioral health clinician, dietician, health coach, and nurse.	The median number of acupuncture treatments was 2 (range: 1–13); 81% had 1–3 and 19% had ≥4
Beidelschies et al.[41]	2019	New clinic patients with any health concern	Functional medicine outpatient clinic	1	April 1, 2015, to March 1, 2017	Retrospective	Nonstandardized individual approach to functional medicine delivered by functional medicine physicians, dietician, health coach, and behavioral health therapist.	Not specified
Dusek et al.[36]	2018	Patients with any health concern who completed at least 1 PROMIS-10	IM clinic	3	November 2013 to October 2016	Retrospective	Nonstandardized individual approach to IM delivered by IM physician, advance practice nurse, and psychologist.	Not specified
Lopez et al.[44]	2017	Cancer patients presenting for an IO physician encounter	IM clinic at cancer center	1	September 2009 to December 2013	Retrospective	IM physician consult + possible other IM interventions (acupuncture, diet, massage, meditation, music therapy, physical therapy).	Initial consultation and follow-up visit. Mean time to first follow-up was 99.1 days (SD 146.6, range 1–1446)

(*continued*)

TABLE 2. (CONTINUED)

Authors	*Publication year*	*Study population*	*Study setting*	*No. of sites*	*Study time frame*	*Prospective or retrospective*	*Intervention and/or interventionist*	*Intervention duration*
Abrams et al.[47]	2013	Patients with chronic pain	IM clinics in PBRN	9	June 2009 to November 2010	Prospective	Nonstandardized individual approach to IM including IM consults, acupuncture, TCM, manipulation therapy, exercise, yoga, mind–body therapies, and other alternative medical systems.	Not specified
Harrington et al.[45]	2012	Breast cancer patients	Center providing IM programming	3	April 2007 to September 2009	Prospective	Multimodal oncology support program including acupuncture, nutrition, massage, aromatherapy, shiatsu, counseling, and hypnotherapy and reflexology delivered by specialist nurses and therapists.	Not specified
Frenkel et al.[46]	2010	Cancer patients	IM oncology clinic	1	January 20007 to December 2008	Retrospective	IM physician consultation.	Single IM consultation
Brazier et al.[39]	2008	Cancer patients who signed up for an introductory IM program	IM oncology clinic	1	May 2004 to September 2004	Prospective	Integrative cancer care delivered by physicians and complementary practitioners (nutritionist, massage therapist, a naturopath, a doctor of Traditional Chinese Medicine, and music therapists).	Two days of seminars and experiential sessions and two 90-min initial consultations followed by additional 30-min follow-up visits with the physicians on an individualized basis

(*continued*)

TABLE 2. (CONTINUED)

Authors	*Publication year*	*Study population*	*Study setting*	*No. of sites*	*Study time frame*	*Prospective or retrospective*	*Intervention and/or interventionist*	*Intervention duration*
Greeson et al.[37]	2008	Clinic patients with diverse medical condition	IM clinic at a university	1	September 1998 and June 2001	Prospective	Anthroposophical medicine, nutritional medicine, Western herbs, homeopathy, nutritional counseling, and acupuncture.	Not specified
Myklebust et al.[42]	2008	Clinic patients with any health concern	IM clinic	1	May 2003 to February 2006	Prospective	Nonstandardized individual approach to IM delivered by IM family physicians with additional training in alternative therapies.	Not specified
Mulkins et al.[43]	2003	Clinic patients with any health concern	IM clinic	1	January 1, 2001, to December 31, 2001	Prospective	Nonstandardized individual approach of IM delivered by physicians, multiple therapists including acupuncturists, massage therapists, and naturopaths.	The average number of visits per person was 10.7 (range 1–32)
Acupuncture studies								
Miller et al.[34]	2019	Cancer patients	Palliative medicine clinic	1	May 01, 2013, to December 31, 2015	Retrospective	Acupuncture delivered by palliative medicine physician certified in medical acupuncture.	Median number of acupuncture treatments was 2 (range 1–13)
Thompson et al.[48]	2015	Cancer patients	IM oncology clinic	1	September 2010 to October 2012	Retrospective	Western medical acupuncture delivered by internal medicine physician provider trained in acupuncture at a Western medical school.	72% of patients received at least 2 sessions (range 1–23) Sessions were between 30 and 60 min

(*continued*)

TABLE 2. (CONTINUED)

Authors	*Publication year*	*Study population*	*Study setting*	*No. of sites*	*Study time frame*	*Prospective or retrospective*	*Intervention and/or interventionist*	*Intervention duration*
Niemtzow et al.[35]	2008	Active duty military members, dependents, and retirees with acute or chronic pain	Air force base medical center, acupuncture clinic	1	October 2003 to September 2005	Prospective	Traditional acupuncture, electroacupuncture, auriculotherapy, and electroauriculotherapy delivered by a trained medical acupuncturist.	Not specified
Secor et al.[33]	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 39.6 (22.7) days
Chiropractic studies								
Gedin et al.[49]	2019	Patients with acute or chronic back pain	Chiropractic clinics	23	October 2012 to January 2013	Prospective	Chiropractic delivered by a chiropractor.	Not specified
Hays et al.[50]	2019	Patients with chronic low-back pain 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 delivered by a chiropractor.	Not specified

(*continued*)

TABLE 2. (CONTINUED)

Authors	*Publication year*	*Study population*	*Study setting*	*No. of sites*	*Study time frame*	*Prospective or retrospective*	*Intervention and/or interventionist*	*Intervention duration*
Secor et al.[33]	2004	Patients with pain having 3 treatments within 3 months	Hospital affiliated outpatient clinic	1	October 1, 2002, to December 31, 2002	Prospective	Chiropractic delivered by a chiropractor.	At least 3 treatments within 3 months of initial session, average treatment duration of 33.9 (21.5) days
Massage, aromatherapy, or reflexology								
Harris et al.[51]	2010	Clients seeking complementary therapy session	IM clinic at a university	1	October 2007 to December 2007 and January 2008 to March 2008	Prospective	Massage, aromatherapy or reflexology delivered by 13 students in their final year of a BSc Complementary Therapies degree, qualified practitioners in aromatherapy, massage, and reflexology.	An average of 2.7 visits to the clinic: the majority ($n=27$) visited once only during the 16-week period; 39 clients made more than 1 visit; and 1 client made a total of 13 visits

Secor et al.[33] is one study split by cohort.
CIH, complementary and integrative health; IM, Integrative Medicine; TCM, Traditional Chinese Medicine.

Table 3. Outcome Characteristics and Results for All Studies

Authors	*Publication year*	*Main outcome constructs*	*Main outcome measure*	*Main time point*	*Main result, M (SD), and (% improvement)*	*Clinical response definition*	*Clinical response*
Multidisciplinary studies							
Elwy et al.[23]	2020	Health-related quality of life	PROMIS-28	12 months	Overall score: 72.3 (21.39) to 72.9 (ns) (1%) [different ns]	Not specified	Not specified
Crocker et al.[40] Herman et al.[63] (for extra info)	2019 2014	Health-related quality of life	SF-12, WHO-5	12 months	General Health: 63.9 to 69.9** (9%) Physical Health: 45.4 to 47.6** (5%) Mental Health: 47.2 to 50.3*** (7%) WHO-5: 55.6 to 62.2** (12%)	Not specified	Clinically meaningful improvement in 45% of patients after all treatments
Beidelschies et al.[41]	2019	Health-related quality of life	PROMIS-10	12 months	Physical Health: 45.9 (8.33) to 47.5 (8.49)*** (4%) Mental Health: 46.7 (9.21) to 47.2 (9.33) (ns) (1%)	At least a 5-point increase	Not reported at 12 months
Dusek et al.[36]	2018	Health-related quality of life	PROMIS-10	1–30 days: 16% 31–60 days: 30% 61–90 days: 17% 90+ days: 37%	Physical Health: 43.1 (8.2) to 44.3 (8.8) (3%) Mental Health: 44.0 (8.9) to 45.0 (9.4) (2%) [*p*-values not reported]	At least a 5-point increase (individually)	Mental Health: 23.5% Physical Health: 24.2%
Lopez et al.[44]	2017	Cancer-related well-being	ESAS	Average of 99.1 days (146.6), range 1–1446 days	Well-being: 3.8 (2.6) to 3.5 (2.5)** (8%)	Not specified	Not specified
Abrams et al.[47]	2013	Health-related quality of life	SF-12	24 weeks (6 months)	Physical Health: 37.7 to 41.5*** (10%) Mental Health: 43.5 to 46.5*** (7%)	Not specified	Not specified

(*continued*)

TABLE 3. (CONTINUED)

Authors	*Publication year*	*Main outcome constructs*	*Main outcome measure*	*Main time point*	*Main result, M (SD), and (% improvement)*	*Clinical response definition*	*Clinical response*
Harrington et al.[45]	2012	Well-being	MYCaW	3–12 months	Well-being: 3.30 (1.41) to 2.63 (1.28)**** (20%)	Not specified	Not specified
Frenkel et al.[46]	2010	Well-being	MYCaW	6–12 weeks	Well-being: 2.50 (1.4) to 1.87 (1.64)*** (25%)	A decrease of at least 2 points (overall)	Patients did not experience a 2-point improvement
Brazier et al.[39]	2008	Health-related quality of life	FACT-G	5 months	Physical Health: 22 to 22 (ns) (0%) Emotional Health: 18 to 19 (ns) (6%) Overall Health: 81 to 84 (ns) (4%)	Not specified	Not specified
Greeson et al.[37]	2008	Health-related quality of life	SF-36	3 months	Physical Health: 40.7 (12.29) to 43.0 (12.39) (6%) Mental Health: 43.6 (11.69) to 47.8 (11.29) (10%) [*p*-values not reported]	Not specified	Not specified
Myklebust et al.[42]	2008	Health-related quality of life	SF-12	2–36 months	Physical Health: 45.6 (13.4) to 49.7 (11.5)** (9%) Mental Health: 40.2 (7.9) to 41.6 (7.0) (ns) (3%)	Not specified	Not specified
Mulkins et al.[43]	2003	Health-related quality of life	SF-36	6 months	General Health: 54.8 (22.3) to 60.5 (22.6)** (10%) Physical Health: 43.4 (9.1) to 45.2 (8.6)* (4%) Mental Health: 40.2 (10.5) to 44.5 (10.6)** (11%)	Not specified	Not specified

(*continued*)

TABLE 3. (CONTINUED)

Authors	*Publication year*	*Main outcome constructs*	*Main outcome measure*	*Main time point*	*Main result, M (SD), and (% improvement)*	*Clinical response definition*	*Clinical response*
Acupuncture studies							
Miller et al.[34]	2019	Cancer-related well-being	ESAS	End of treatment	Well-being: 3.5 (2.5) to 2.5 (1.8)*** (29%)	A decrease of at least 2 points (individually)	Clinically meaningful improvement was reported in 51% after the first and in 45% after all treatments
Thompson et al.[48]	2015	Quality of life	11-point NRS	Post last acupuncture session	NRS: 4.12 (2.52) to 3.14 (2.27)**** (24%)	A decrease of at least 2 points (individually)	Rates of MCID after the last session exceeded 41%
Niemtzow et al.[35]	2008	Health-related quality of life	SF-8	4 weeks	Physical Health: 34.1 (8.44) to 41.1 (8.71)*** (20%) Mental Health: 49.4 (10.21) to 52.4 (8.63)** (6%)	Not specified	Not specified
Secor et al.[33]	2004	Health-related quality of life	SF-12	Within 3 months	Physical Health: 44.8 (9.8) to 46.9 (8.2)** (5%) Mental Health: 48.8 (9.8) to 49.8 (9.5) (ns) (2%) General Health: 3.53 (1.0) to 3.75 (0.8)** (6%)	Not specified	Not specified
Chiropractic studies							
Gedin et al.[49]	2019	Health-related quality of life, overall health	EQ-5D, EQ-VAS	4 weeks	Acute pain EQ-5D: 0.65 (0.26) to 0.86 (0.14)** (32%) EQ-VAS: 68.47 (17.4) to 78.1 (20.62)** (14%). Chronic pain EQ-5D: 0.69 (0.19) to 0.73 (0.20)* (6%) EQ-VAS: 68.11 (20.08) to 71.88 (20.38) (ns) (6%)	MCID for EQ-5D index is a change of at least 0.07 (overall)	EQ-5D index was of MCID for acute but not chronic back pain

(*continued*)

TABLE 3. (CONTINUED)

Authors	*Publication year*	*Main outcome constructs*	*Main outcome measure*	*Main time point*	*Main result, M (SD), and (% improvement)*	*Clinical response definition*	*Clinical response*
Hays et al.[50]	2019	Health-related quality of life	PROMIS-29	3 months	Physical Health: 46 (7) to 47 (8)**** (2%) Mental Health: 48 (7) to 50 (7)**** (4%)	An effect size of at least 0.20 (individually)	Physical Health: 14% met MCID Mental Health: 30% met MCID
Secor et al.[33]	2004	Health-related quality of life	SF-12	Within 3 months	Physical Health: 46.5 (8.6) to 48.0 (6.9)* (3%) Mental Health: 48.7 (9.5) to 50.0 (8.9) (ns) (3%) General Health: 3.61 (0.9) to 3.83 (0.8)** (6%)	Not specified	Not specified
Massage, aromatherapy, or reflexology							
Harris et al.[51]	2010	Health-related quality of life	MYMOP2	3 months	Activity: 3.5 (1.2) to 2.8 (1.8)** (20%) Well-being: 2.8 (1.4) to 2.6 (1.5) (ns) (7%) Profile score: 3.3 (1.0) to 2.7 (1.2)** (18%)	Not specified	Not specified

Secor et al.[33] is one study split by cohort.

*$p<0.05$, **$p<0.01$, ***$p<0.001$, ****$p<0.0001$.

EQ-VAS, EuroQol visual analogue scale; ESAS, Edmonton Symptom Assessment System; FACT-G, Functional Assessment of Cancer Therapy–General; MCID, minimal clinically important difference; MyCaW, Measure Yourself Concerns and Wellbeing; MYMOP2, Measure Yourself Medical Outcome Profile; NRS, Numerical Rating Scale; PROMIS-29, Patient-Reported Outcomes Information System; SF-12 (8, 36), short-form health survey; WHO-5, World Health Organization Well-Being Index.

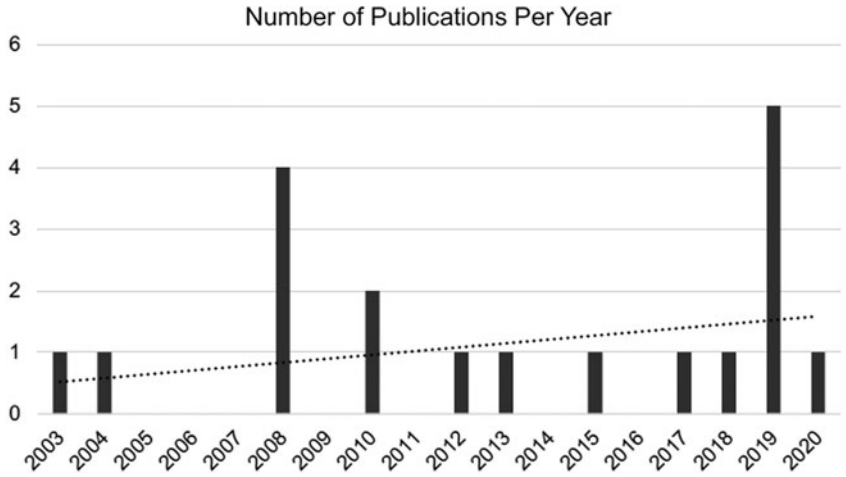

FIG. 2. Number of publications per year included in the systematic review.

Duration of assessments. In this review, we report only one main time point from each study (the longest follow-up time point), due to the variation in the number of time points across studies. With respect to shorter term outcomes, two studies reported main assessment at 4 weeks. Two studies did not provide a specific time period but noted that outcomes were assessed at the end of treatment course and after last acupuncture session respectively. Additionally, four studies conducted the follow-up at 3 months, and two studies assessed participants at 6 months. With respect to longer term assessment (6 months or later), three studies assessed changes at 12 months.

The remainder of the studies included different time points for participant follow-up. One study included the percentage of participants at each stage of the follow-up (1–30 days: 16%, 31–60 days: 30%, 61–90 days: 17%, 90+ days: 37%). One other study included the mean follow-up time (first follow-up visit, average of 99.1 days [146.6], range 1–1446 days). Four studies reported follow-up ranging from 6 weeks to 36 months (Table 3).

Main outcome results. Health-related quality-of-life measures (physical, mental, well-being) were significantly improved in most of the studies where significance (p-value) was reported (Table 3). However, in four studies, either significance (p-value) was not reported,[36,37] or the results were not significant[38,39]; however, one of these studies did report clinically significant improvements on both PROMIS-10 Physical Health and Mental Health for a proportion of study subjects.[36]

The comparable SF and PROMIS measures were the most common questionnaires used ($n = 11$, 58% of studies). Baseline values for Physical Health ranged from 43.1 to 46.5 for PROMIS measures and from 37.7 to 45.6 for SF measures, both of which are half of a standard deviation below the national normed score of 50. Baseline values for Mental Health ranged from 44.0 to 48.0 for PROMIS measures and from 40.2 to 49.4 for SF measures, which are also half of a standard deviation below the national normed score of 50. The average percent improvement across all studies and time points was 6% for Physical Health (range 2%–20%) and 5% for Mental Health (range 1%–11%). We further describe the overall results by intervention type.

Multidisciplinary. Of the multidisciplinary studies, six studies enrolled clinic patients with any health concern,[36,37,40–43] four studies included cancer patients,[39,44–46] one study included chronic pain patients,[47] and one study included veterans.[38]

In general, there were significant improvements in Mental Health, Physical Health, and General Health on the SF-12 and quality of life on the WHO-5,[40] and significant improvements in Physical Health but not Mental Health on the PROMIS-10[41] at 12 months following multidisciplinary CIH treatment for CIH clinic patients. In another study, patients with any health concern significantly improved in Physical Health but not Mental Health on the SF-12 2–36 months,[42] and improved in Physical Health, Mental Health, and General Health on the SF-26 6 months following multidisciplinary treatment.[43] In another study, while statistical significance was not reported, 24% of clinic patients achieved clinically meaningful improvements in health-related quality of life on the PROMIS-10 between 1 and 90+ days following multidisciplinary treatment.[36] In Greeson et al.,[37] clinic patients improved in Mental Health and Physical Health on the SF-36 at 3 months, but statistical significance was not reported (Table 3).

Cancer patients reported an improvement in well-being on the ESAS at follow-up (mean 99.1 days)[44] and on the MyCaW at 3–12 months[45] and 6–12 weeks.[46] There were no significant improvements in quality of life on the FACT-G at 5 months, although there were significant improvements in emotional health at 6 weeks (Table 3).[39]

Chronic pain patients showed significant improvements in health-related quality of life with regard to Mental Health and Physical Health at 24 weeks/6 months on the SF-12 across nine CIH clinics (Table 3).[47]

The singular study included with a veteran patient population did not show significant overall improvement in quality of life at 12 months; however, participants who specifically used meditation, Tai Chi, and yoga improved in different aspects of the PROMIS-28.[38] This study only reported results by these three groups seemingly *post hoc*, rather than overall; as such, the overall results were obtained through electronic correspondence with the senior author (Table 3).

Acupuncture. Acupuncture studies with cancer patients reported improvement in cancer-related well-being on the ESAS,[34] and quality of life on an NRS[48] at the end of treatment. In another acupuncture study, active-duty military members, dependents, and retirees with acute or chronic pain showed improvement in health-related quality of life at 4 weeks following treatment using the SF-8, specifically the Physical Health and Mental Health components.[35] Another study reported improvements in health-related quality of life in chronic pain patients within 3 months of acupuncture treatment using the SF-12, particularly in General Health and Physical Health (Table 3).[33]

Chiropractic. Chiropractic studies reported improvements in health-related quality of life in patients with back pain within 3 months of chiropractic treatment using the EQ-5D-EL and EQ-VAS,[49] in patients with chronic low-back pain or neck pain at 4 weeks using the PROMIS-29 with specific regard to Physical Health and Mental Health,[50] and pain patients at 3 months using the SF-12, particularly in General Health and Physical Health (Table 3).[33]

Massage, aromatherapy, or reflexology. There were significant improvements in the profile (summary) quality of life score and activity score, but not well-being, from the MYMOP2 in general clinical patients 3 months following massage, aromatherapy, or reflexology (Table 3).[51]

Minimal clinically important difference. Eight of 19 studies (42%) reported clinically meaningful results: 4 multidisciplinary, 2 acupuncture, and 2 chiropractic. Seven of these eight studies reported a clinically significant improvement threshold, but one did not specify the threshold. Clinically meaningful response definition varied from study to study: a five-point improvement on the PROMIS-10,[36,41] a two-point improvement on MYCaW,[46] NRS,[48] and ESAS[34]; a change score of 0.07 on the EQ-5D index,[49] and an effect size of at least 0.20 on the PROMIS-29 scores.[50] One study did not specify the definition of the minimal clinically important difference (MCID).[40] All these studies but one[46] reported clinically significant results.

Multivariate analysis. There was only one study in which the multivariate analysis was reported,[36] and as such, these are not represented in the table. In this study, logistical regression found that single or divorced patients showed less improvement in both Mental Health and Physical Health over time. In addition, a younger group was associated with less improvement in Mental Health over time, whereas Black patients and patients with Medicaid insurance coverage were associated with less improvement in Physical Health over time.[36]

Effect sizes. We did not include effect sizes in the tables as they were only available for three studies (16%). Effect sizes ranged from small to medium (0.10–0.38), with 0.38 for SF-36 Mental Health and 0.28 for SF-36 Physical Health following 3 months of multidisciplinary treatment for clinic patients[37]; 0.29 for PROMIS-29 Mental Health, 0.24 for Physical Health, 0.17 for General Health, and 0.34 for WHO-5 12 months following multidisciplinary treatment for clinic patients[40]; and 0.16 for PROMIS-29 Emotional Health and 0.10 for Physical Health 3 months following chiropractic care for patients with chronic low-back pain or neck pain.[50]

Risk of bias assessment. With respect to attrition bias, one study did not report baseline sample size[33] and one study did not report sample size at follow-up[34]; therefore, the retention rate for these studies is unknown. With respect to reporting bias, two studies met qualification for high risk of bias. One study did not report overall results, but only reported results by grouped by yoga, Tai Chi, or meditation, which seemed to be *a posteriori* decision. We obtained the overall means from the authors, which did not significantly differ.[38] We conclude that this was a study with a high risk of reporting bias. One study did not report statistical significance but did report clinical significance.[36] We were unable to obtain the *p*-values, despite potential significance, making this study a low–medium risk of bias. While one other study did not report significance, we determine this to be a low risk of bias, as the changes appear to be significant based on other similar results with the same magnitude of changes.[37]

Discussion

To the best of our knowledge, this is the first review of practice-based research of CIH therapies provided in CIH outpatient clinics for quality of life or well-being. Findings from this systematic review reveal that CIH therapies have beneficial effects on quality-of-life and well-being outcomes. All 18 included studies reported beneficial impact on one or more quality-of-life- or well-being-related outcomes. Overall, we report that there is evidence for improvements in quality of life and well-being following CIH therapies in CIH outpatient clinics, including multidisciplinary Integrative Medicine programs, chiropractic, acupuncture, and massage and reflexology.

Multidisciplinary, individualized CIH interventions are exemplary of the practice of CIH, in which the use of multiple evidence-based conventional and CIH therapies is encouraged. However, some CIH clinics offer only one or two CIH therapies, such as acupuncture or chiropractic treatment. The majority of studies in our review focused on multidisciplinary CIH programs, followed by acupuncture and chiropractic. Taken together, evidence from the observation studies in the current systematic review supports the use of individualized CIH therapies in an outpatient setting, particularly the use of multidisciplinary CIH programs and/or acupuncture for the improvement of quality of life for various patient populations. In contrast, a previous systematic review of observational studies of individualized CIH for pain showed that chiropractic was more studied treatment approach than multidisciplinary.[31]

As mentioned previously, research in primary health care settings supports that both patients and practitioners understand that a multidisciplinary health care approach, which includes CIH therapies, fills gaps in treatment effectiveness for patients with complex chronic conditions.[18] Therefore, practice-based research is the next logical step to determine CIH effectiveness within the real-world clinical setting where care is delivered, instead of in a less ecologically valid RCT.[52] Indeed, in a recent commentary written by the

NCCIH leadership[53] begins by stating that the NCCIH supports the ''continuum of the biomedical research pipeline, whereby a complementary health intervention moves from basic and mechanistic research, through efficacy trials, through dissemination and implementation.'' Not explicitly mentioned in the NCCIH commentary is the evaluation of pragmatic effectiveness research in real-world clinical settings after the efficacy research has been conducted.[54] Our systematic review focuses on summarizing the effectiveness of such data.

The results from this systematic review support the use of individualized CIH therapies for improving patient's quality of life. In addition to statistical significance, reporting clinical significance is essential to assign clinical meaning to the changes in patient-reported outcome measures. Most studies did not report MCIDs or clinical significance. Clinical significance ranged from 14% to 51% of patients meeting the criteria for MCID. However, previous thresholds for clinical significance for the PROMIS measures (five-point improvement or half a standard deviation) were higher than current threshold of a two- to three-point improvement.[55] Importantly, this change in clinical significance for the PROMIS measures aligns with the clinical significance threshold for SF measures, thereby allowing for crosswalk between the two.[55,56] As a result of the change in clinical significance for PROMIS, we contend that prior clinical significance levels were likely under reported in these studies.

Where comparisons were possible, meaning the same or similar intervention, outcome, and follow-up time point, the results of the observational studies from the current systematic review are comparable to results from RCTs. For example, evidence suggests that observational studies of CIH report similar improvements in health-related quality of life for patients with pain as reported in RCTs. A prospective observational study included in the current systematic review[33] and an RCT[57] found a 6% improvement in General Health on the SF-36 in patients with low-back pain following acupuncture.

Multidisciplinary CIH programs and acupuncture have been shown to improve cancer-related quality of life and well-being under observational and RCT conditions. For example, improvements in cancer-related well-being (MyCaW) were 25% at 6–12 weeks following a CIH consult from an observational study[46] compared with 50% improvement at 6 weeks following acupuncture from an RCT.[58] It would be preferable to compare observational studies of multidisciplinary interventions with RCTs of multidisciplinary interventions, but we did not find any in the literature.

Study weaknesses and limitations

Overall, all pragmatic effectiveness studies have several limitations, including selection bias, no blinding of subjects, and a neglect of causality and potential nonspecific effects.[29] Importantly, pragmatic effectiveness trials are a necessary step in understanding outcomes in more real-world clinical settings, as recommended by the NCCIH.[22] There were several study weaknesses that deserve discussion. First, most studies did not report participants' race, ethnicity, or SES, compromising the ability to determine whether the results are generalizable to different populations. For example, in one of the studies in this review, ethnicity was found as a predictor of improvement from multimodal CIH treatment.[36]

Therefore, given its role as a potential predictor variable, inclusion of race/ethnicity is important for reporting in future studies. Second, 47% of studies did not include the duration or average number of CIH treatments that patients received. Because of the nature of the review, CIH therapies and/or programs that were individualized on a patient-by-patient basis, there is natural variation in treatment duration and frequency. However, it is essential that the authors report the average treatment length and/or frequency to facilitate appropriate CIH care in clinical settings.

A third common study weakness was the lack of effect size reporting, comprising 84% of studies. While most studies usually report statistical significance, effect sizes provide an indication of the degree of improvement, and it is a recommended statistical outcome.[59,60] A fourth limitation is inconsistency with follow-up time points (e.g., 2–36 months), and while this may be more ecologically valid, it limits the ability to determine the temporal aspects of treatment guidelines. The final common study weakness was that only one study reported multivariate analyses for revealing potential predictor variables related to quality-of-life changes. Studies with smaller sample sizes are limited in conducting multivariate analysis; however, based on other researchers' recommendations,[61] a sample size of least 100 meets the criteria for multivariate analysis.

Therefore, we encourage the inclusion of multivariate analysis to identify if baseline characteristics (e.g., demographics, symptom severity) are independently associated with improvement in quality-of-life and well-being outcomes following different CIH interventions or if additional analytic approaches (e.g., effect modification) are needed to understand if any variables such as gender may influence the associations.

Limitations of systematic review

There were several limitations of the current review that are worth mentioning. First, the ability to make comparisons across studies and drawn conclusions was limited due to the variability in study design and incomplete reporting in some publications. Given these constraints, we made comparisons and syntheses where we deemed applicable. Second, we decided that the longest follow-up time would be the main time point to include (e.g., 6 and 12 months) in the tables when multiple time points were available. Therefore, this review is more focused on longitudinal (12 months) rather than shorter (immediately post) outcomes. Third, with an *a priori* focus exclusively on quality-of-life-related outcomes for this review, we were limited in the scope of findings, as we did not evaluate other outcome variables included in some of the studies, such as pain or stress.

Fourth, it is unknown how many studies with negative or null effects were conducted but not published (i.e., the file drawer problem). As such, we encourage publication of studies regardless of results, as all studies provide valuable information to assist in clinical guidelines. Finally, it is important to mention that there are a few studies which could have been included in this review; however, they did not report the outcome means, rendering the accuracy of the numbers extracted not guaranteed and comparisons between

studies limited. Some authors did not reply to our request for the mean values; therefore, those results were not included in this systematic review.

Suggestions for future research

Given the results of this systematic review, we have the following seven recommendations for authors in their future research publications focused on pragmatic effectiveness, practice-based research of CIH interventions. These recommendations are similar to recommendations made in a recently published systematic review for pain.[31] As such, the overlapping recommendations have been summarized in brief.

1. First, we recommend other authors to use the tables from this systematic review as a guide for comprehensive reporting of results. Use of this model will facilitate understanding best practices for the implementation of CIH interventions into clinical settings.
2. Second, at least half of the outcomes were measured within 6 months after the beginning of CIH treatment, we recommend that authors aim to also evaluate outcomes at greater than 6 months to assess whether the significant improvements in quality of life are sustained. Repeated measures across multiple time points will also enhance the ability to make proper CIH recommendations and expectations for patients across time.
3. Third, to allow for comparison across studies, we recommend studies to use PROMIS measures, which have been validated clinically in diverse populations[62] and financially supported by the National Institutes of Health.
4. Fourth, given that more than half of the studies did not report minimal clinically importance differences for determining the relevant clinical significance of the findings, we recommend researchers to include these metrics in their reports.
5. Fifth, given that reduced quality of life affects some minorities and SESs more than others,[30,36] enrolling more diverse populations would enable ascertaining the ideal approach to treat patients who may be at greater risk. Specifically, making efforts to include patients accurately reflect the demographics of the population.
6. Sixth, we noted that some of the highest participant retention rates were for studies in which monetary incentives were offered for participating. We recognize that including incentives is often contingent on available funding; however, if financially possible, we recommend providing incentives to improve participant retention, while also working to balance the pragmatic nature of the study.
7. Finally, we recommend that researchers conduct more pragmatic effectiveness trials with additional CIH therapies and programs that were absent from this review but are often sought in outpatient clinics, such as naturopathy, energy medicine, or acupressure.

Conclusions

Findings from this systematic review of pragmatic effectiveness studies in CIH outpatient clinics reveal that CIH therapies have beneficial effects on health-related quality of life, and well-being in various patient populations, including those with pain, cancer, and veterans. Most studies (90%) reported positive impacts on one or more quality-of-life-related outcomes; however, variability between some studies limited their comparability. Thus, based on this systematic review, we conclude that additional practice-based research in CIH is needed to help guide appropriate clinical practice.

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Authors' Contributions

J.A.D. designed the study. J.A.D. and J.S. identified included studies. J.S., J.A.D., N.L.D., R.S., and A.A. contributed to data extraction. N.L.D., J.A.D., and R.S. wrote the article. All authors read and approved the final article.

Author Disclosure Statement

No competing financial interests exist.

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Supplementary Material

Supplementary Material S1

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