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SPECIAL ISSUE: META-ANALYSES AND REVIEWS

Effective Interventions for Idiopathic Chronic Pelvic Pain: A Systematic Review

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Abstract

Background Chronic pelvic pain (CPP) in women is a debilitating condition with symptoms that affect both medical and psychological systems, yet for those with idiopathic CPP (i.e., those without a known physiologic cause), no consensus for intervention exists.

Aim A systematic review was conducted to identify the effectiveness of current biomedical, psychosocial, and integrative interventions for idiopathic CPP (ICPP).

Method Five databases (PubMed, CINAHL, Cochrane, PsycInfo, Web of Science) were systematically searched with multiple keywords for publications from 2008–2022. Articles were coded for sample characteristics, research design, type of intervention, and intervention outcomes.

Results Nineteen studies met criteria. The majority of the interventions (14 studies) were biomedical, either invasive (e.g., injections), or non-invasive (e.g., medications). Five studies evaluated integrative interventions that combined biomedical and psychosocial components (e.g., a multimodal pain treatment center). Invasive biomedical interventions were better at relieving short-term pain and non-invasive biomedical interventions were superior for long-term pain; integrated interventions reduced both short-term and long-term pain. Integrative interventions also improved mental health, sexual health, and QOL.

Conclusion Although most interventions for ICPP have been biomedical, integrative interventions showed greater outcome effectiveness, suggesting a focus on integrative interventions in the future.

Keywords Systematic review · Intervention · Chronic pelvic pain · Women's health · Pain · Mental health · Sexual health · Quality of life

Introduction

Chronic pelvic pain (CPP) in women is comprised of an assortment of gynecological, urological, gastrointestinal, and musculoskeletal symptoms, including vaginal discharge, difficulty with urination, constipation, and pelvic muscle tenderness [1, 2]. Although there is no international definition for CPP, it is usually agreed that these symptoms must be noncyclical and last for at least six months [3, 4]. CPP is a physically and mentally debilitating condition, with women describing the pain as interfering with sexual interactions, fertility, household tasks, and work [5]. CPP in contexts such as these is often called situational CPP, when the pain is brought on by specific activities (e.g., during sex), or at specific times (e.g., during menstrual periods). However, CPP also can manifest as a continual condition, interfering with tasks as basic as standing and exercising [6]. When there is no observable physiological cause for chronic pelvic pain, it is labelled as *idiopathic chronic pelvic pain* (ICPP). Only half of women who report symptoms of chronic pelvic pain receive a diagnosis, and for those that do, the diagnosis may take multiple years to be received [7, 8]. Given that approximately 14% of women in the United States are diagnosed with any form of CPP [9], this implies that approximately 7% of the US female population experiences ICPP.

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The Psychological Experience of ICPP

While CPP conditions can be diagnosed across both sexes, ICPP can be a uniquely gendered experience, particularly for women [10]. Many women describe the experience of chronic pelvic pain as causing depression, irritability, and other negative emotional states [11]. These negative emotions are often intensified when others respond that their pain is not real or exaggerated, which is frequently described in women's pain literature [12]. One woman described feeling as though her medical team was telling her to "just get on with it and live with it" [13, pg. 449]. Elevated levels of anxiety may be a result of concerns that the pain is due to an undiagnosed medical condition [3, 14]. Increased levels of depression may stem from the inability to carry on one's daily life such as missing work or pleasurable social activities because of the intrusive and unrelenting pain [3, 15].

For women with ICPP, these negative emotions may be exacerbated by interactions with healthcare providers. For example, when medical professionals are unable to identify a physiological cause for the pain, differential diagnosis may shift toward psychological causes, resulting in self-blame, and magnifying distress [16, 17]. A large proportion of women with chronic pelvic pain (60–80%) are given a diagnosis of somatoform disorder, which means that the pain cannot be attributed to any physiological problem, yet is causing significant emotional distress [4, 18]. With this diagnosis, providers often refer women to psychiatrists, thus treating ICPP as a psychological disorder, rather than a medical one.

Presently, there is no consensus for treatment of ICPP [19, 20] which can exacerbate psychological distress [21, 22]. In order to understand what "best practices" for treatment of ICPP might be, we conducted a systematic review of intervention research studies for women with ICPP, with the aim of identifying which interventions most effectively reduce symptoms and distress. Specifically, we examine the efficacy of interventions on multiple outcomes: pain reduction, mental health, quality of life, and sexual health.

Methods

Study Selection

The review follows the PRISMA guidelines [23], but was not pre-registered. Inclusion criteria targeted studies that (1) recruited a sample that was composed of exclusively of women, aged 18 years or older, at least some of whom had ICPP; (2) original empirical research studies that examined the efficacy of an intervention for CPP (vs. simply describing it); and (3) were written in English. An intervention study was defined as a research study that assessed how a treatment or program affected one or more medical and/or psychological outcomes. Exclusion criteria were: (1) reviews, commentaries, or case studies; (2) studies where the entire sample had CPP caused by a diagnosable condition (e.g., endometriosis, cancer); (3) studies that focused exclusively on situational pain (e.g., dyspareunia or dysmenorrhea); and (4) studies where sexual abuse and/or trauma was the primary antecedent of CPP. These exclusion criteria were based on our interest in distinguishing idiopathic CPP from CPP with a known determinant. Notably, many women's health diagnoses (e.g., endometriosis) average multiple years to reach diagnosis [8]; for the purpose of this review, as long as some of the women in the sample were not yet diagnosed with a CPP condition, they met eligibility criteria.

Five databases (PubMed, CINAHL, Cochrane, PsycInfo, and Web of Science) were searched for articles published between January 1, 2008–December 31, 2022. This timeframe was chosen given increased calls for multidisciplinary treatments for CPP that began in 2008 [24]; the last search of these databases occurred on January 4, 2023. Titles and abstracts were searched for the keywords "chronic pelvic pain" AND "intervention" AND "women". Of the titles and abstracts returned, duplicates were removed, and the full text of each publication was reviewed to ensure that all inclusion criteria were met.

Article Coding

Rayyan software was used for coding [25]. Articles that met inclusion criteria were coded by the first author across three domains: type of intervention; research design; and intervention outcomes. A random sample of 10% of the articles were coded for interrater reliability by the fourth author (95.6% agreement).

Type of Intervention Eligible articles were initially coded as including one of three types of intervention: biomedical, psychosocial, or integrative. *Biomedical interventions* could be non-invasive (exclusively using medications) or invasive (e.g., surgery or nerve stimulation), or a combination of the two. *Psychosocial* (behavioral) interventions exclusively used non-biomedical interventions, such as psychotherapy or yoga. *Integrative* interventions combined both biomedical and psychosocial elements.

Sample Characteristics Sample characteristics included the number or proportion of participants with ICPP, sample size, age of participants (mean and/or range), race and ethnicity, socioeconomic status (education, income), and marital

status. These variables were included to assess variables that may impact stated outcomes.

Research Design Studies were coded for whether they met each of the three design components of a randomized clinical trial: 1) inclusion of both intervention and control/ comparison groups; 2) random assignment to condition; and 3) pre- and post-test assessments. The Quality Index [26], designed for both randomized and non-randomized intervention research, was used to code each article for strengths and weaknesses, and adds an overall assessment of study rigor. Each study was rated on four metrics – the quality of reporting, external validity, internal validity, and statistical power – summed into an overall score indicating the quality of a study, ranging from 0 to 31.

Intervention Outcomes Four categories of intervention outcomes were examined (1) pain, (2) mental health (e.g., anxiety, depression, alexithymia, and distress), (3) quality of life, and (4) sexual health (e.g., sexual functioning and sexual impairment). These categories were chosen based on prior literature identifying them as potential effects of living with chronic pelvic pain [5, 21, 22]. Note that the measurement of these outcomes varied across studies, with some using standardized scales and others using visual or verbal analogue scales (see Electronic Supplementary Material, Table 1).

Results

Figure 1 describes the selection of studies using the PRISMA flowchart. A total of 1,617 articles were retrieved and 26 duplicates were removed. After screening the titles and abstracts for inclusion criteria, another 1,520 articles were removed, and after full-text screening of the 71 remaining articles, only 19 articles remained in the review. Reasons for exclusion can be found in Fig. 1; two-thirds of the articles submitted to full-text screening were excluded because their samples did not include women with ICPP. One study appeared eligible [27], but after review by the authors, it was deemed to present identical data to another article in the review [28] and was excluded.

Characteristics of Studies Included in the Review

The 19 articles that met inclusion criteria were all quantitative intervention studies, although slightly less than half (nine; 47.4%) were randomized clinical trials (RCTs) [28–36]. Studies were conducted in the United Kingdom (n = 4), Brazil (n = 4), India (n = 3), United States (n = 2), Egypt (n = 2), Germany (n = 1), Poland (n = 1), Canada (n = 1), and Norway (n = 1).

Fourteen studies (73.7%) evaluated biomedical interventions and the remaining five studies (26.3%) used an integrative intervention, combining biomedical and psychosocial elements. No studies were classified as solely psychosocial. Sample characteristics of the 19 studies are presented in Table 1, research designs in Table 2, and intervention outcome in Tables 3, with the top half of each table describing the biomedical interventions and the bottom half the integrative interventions. Outcomes will be reported first for the biomedical interventions and then for the integrative interventions.

Biomedical Interventions

As shown in Table 1, nearly two-thirds (64.3%) of the biomedical intervention studies recruited samples that were comprised entirely of women with ICPP. An additional 21.4% recruited samples that were comprised of women with ICPP or CPP, but analyzed the two conditions separately, thus allowing us to make conclusions about women with ICPP. Two studies (14.3%) included subsamples of women with ICPP and CPP, but combined them for analyses, which limits conclusions about the intervention effectiveness for women with ICPP.

It should be noted that the biomedical intervention studies varied widely regarding the degree to which sociodemographic variables were reported, including age and ethnicity of participants. The mean age across the studies that reported age was 31.80 ($SD = 8.5$). The three studies that reported race or ethnicity were largely White [28, 31, 36] and only five studies described the socioeconomic status of the sample, finding fairly high levels of education [28, 31, 32] and employment [36, 37].

Study Quality. Study design varied widely (Table 2). Half of the biomedical interventions were randomized control trials (RCTs) [28, 30–34, 36] and all used a placebo for the control group. Only nine of the studies (including five of the RCTs) were registered on www.clinicaltrials.gov or preregistered. All studies clearly stated hypotheses, aims, and results, with interventions that were clearly described, and used appropriate statistical tests as described in the study quality checklist [26]. Only two studies recruited representative samples [28, 38], with most of the remaining being convenience samples. The average study quality was 23.4 (out of a possible 31) on the Quality Index, which is considered to be in the "good" range [39].

Invasive Biomedical Interventions. Of the 14 biomedical interventions, slightly over half (57.1%) examined the effects of invasive biomedical treatments [30, 33, 34, 37, 38, 40–42]. Amongst all invasive biomedical interventions,

Table 1 Sample Characteristics

Citation #	Authors (date)	% of sample with ICPP	Sample Size	Age *M (SD)* Range	Race/ Ethnicity[b]	Socioeconomic Status	Marital Status
	Biomedical Intervention Studies						
[30]	Daniels et al. (2009)	54%[a]	487	30.6 (7.5)	--	--	--
[34]	de Bernardes et al. (2010)	100%	26	40 (12.3) 34-49	--	--	--
[40]	Carrico and Peters (2011)	4.8%	60	40[c] 22-61	--	--	--
[37]	Amin et al. (2015)	100%	117	34.1 (5.95)	--	Employment: Employed: 71.8%	--
[33]	da Rosa et al. (2015)	57.7%	26	51.5 (15.5)	--	--	--
[38]	Montenegro et al. (2015)	100%	30	37.7 (3.1)	--	--	--
[41]	Sokal et al. (2015)	11.1% [a]	9	Med = 57 41-77	--	--	--
[31]	Lewis et al. (2016)	100%	47	26.9 (6.7) 18-43	Caucasian: 100%	Education: Secondary: 25.5% University: 74.5% Deprivation score: Affluent: 17.1% Intermediate: 44.7% Deprived: 19.1% Very deprived: 17.0%	Married: 25.6% Single: 61.7% Separated: 2.1% Divorced: 10.6%
[45]	Priya et al. (2016)	100%	60	32.6 (5.9) 20-45	--	--	--
[42]	Sillem et al. (2016)	50% [a]	28	--	--	--	--
[44]	Sharma et al. (2017)	100%	122	48[c] 18-60	--	--	--
[32]	AbdelHafeez et al. (2019)	100%	64	31.5 (5.2)	--	Education: Illiterate: 3.3% Primary: 28.3% Secondary: 63.3% University: 5%	
[28]	Hewitt et al. (2020)	100%	306	30.3 (8.15)	White: 97.4% Black: 0.3% Asian: 2.0% Mixed: 0.3%	Education: Primary: 2.9% Secondary: 30.4% Tertiary: 66.0%	--
[36]	Flynn et al. (2021)	100%	12	37.7 (7.9)	White: 75% South Asian: 8.3% Metis[d]: 8.3% Other: 8.3%	Employment: Unemployed: 16.7% Employed, F-T: 41.7% Employed, P-T: 16.7% Student: 25%	Married: 50% Relationship: 1.3% Single: 41.7%
	Integrative Intervention Studies						
[49]	Haugstad et al. (2018)	100%	40	--	--	--	--
[48]	Aboussouan et al. (2020)	34.5%	116	42.7 (12.8) 18-70	Non-Hispanic White: 88.8% African American: 7.8%	Education: High school or less: 18.1% Associate/Tech/ Some college: 37.1% Bachelors: 28.5% Postgraduate: 15.5%	Married: 54.3% Single: 19.0% Divorced: 12.1%

Table 1 (continued)

	Integrative Intervention Studies						
[47]	Ferreira Guiran et al. (2016)	8%	58	43.3 (11)	--	Education: < Elementary: 34% Elementary: 16% Some high school: 3% High school: 38% Some college: 3% College graduate: 5%	Married: 71% Single: 29%
[46]	Saxena et al. (2017)	100%	60	31.8 (6.1)	--	--	--
[35]	Chong et al. (2018)	30%	30	33.2 (9.0) 21-51	Caucasian: 96.7% Mexican and Scottish: 3.3%	Education: Secondary: 16.7% Tertiary: 83.3% Employment: Unemployed: 66.7% Employed: 33.3% Deprivation Score: Affluent: 13.3% Intermediate: 53.3% Deprived: 16.7% Very deprived: 16.7%	--

Dashes indicate that data were not reported

[a]ICPP subsample was analyzed separately from the rest of the sample

[b]Terms for racial/ethnic groups are taken verbatim from article

[c]Studies did not report standard deviations

[d]The word *métis*, which means "mixed" in French, can be used for any aboriginal person of mixed descent [59]

the only outcome measured was self-reported pain. There is some evidence of improvement in reported short-term pain for a variety of invasive biomedical interventions, however the evidence for long-term benefit is more limited. Comparisons between studies is challenging due to design and intervention differences, however this short-term benefit of intervention is a common thread.

An RCT assessing inferior hypogastric plexus blockade vs. acupuncture found decreased between-group pain scores as well as a significant difference in those experiencing no change in their pain relief among those receiving acupuncture, compared to the blockade, at 12-week follow-up [37]. Another RCT assessed the effect of paraspinal anesthetic block injections and found significantly decreased within-group, but non-significant between-group, pain scores at end-of treatment; however, these effects were not significant after one week [33]. A third RCT, using a crossover design found that intravaginal electrical stimulation was more likely to reduce pain score than a placebo at end-of-treatment, but longitudinal analyses were not completed [34]. A one-group pre-post design assessing sacral roots stimulation found significantly decreased within-group pain scores at end of treatment and six-month follow-up, but failed to find results at the 1-year follow-up [41]. A study comparing anesthetic injection with ischemic compression with 1-, 4- and 12-week follow-ups found that those receiving the anesthetic injection reported significantly decreased pain scores only at 12-week follow-up and also had significantly less pain than the compression intervention at 4- and 12-week follow-ups [38]. This study also demonstrated clinical significance, with participants experiencing such a strong response to the local anesthetic (nearly

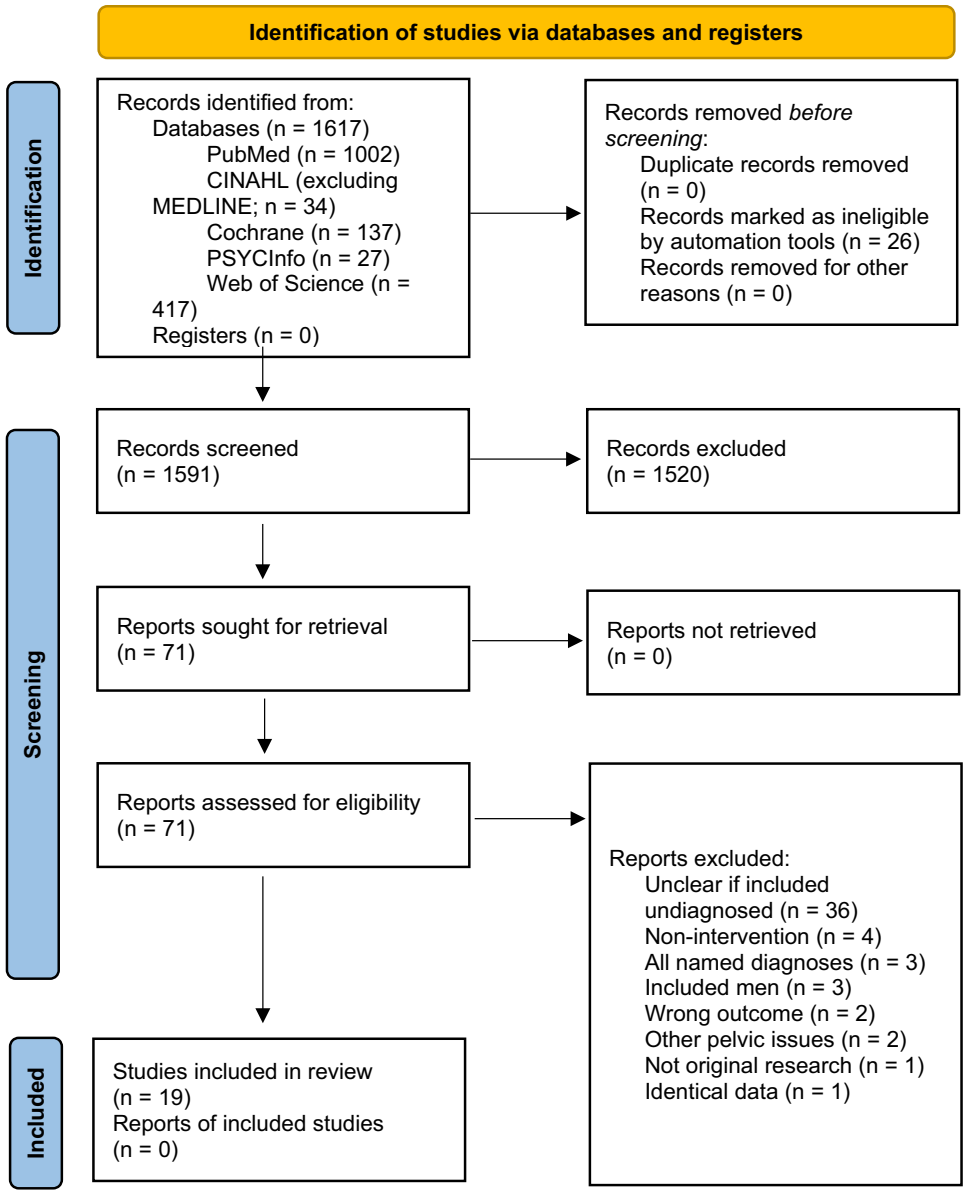

Fig. 1 PRISMA 2020 flow diagram for new systematic reviews which included searches of databases and registers only. From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. https://doi.org/10.1136/bmj.n71. For more information, visit: http://www.prisma-statement.org/

four times that of compression) that the trial was terminated early. A study assessing vaginal diazepam (which did not use a control group or random assignment) found "significantly decreased" pain levels at end of treatment; however, statistical significance of the pre-post difference was not tested [40, pg. 283]. Similarly, a study assessing the effect of osteopathic physical therapy (a form of physical therapy in which a physician's fingers are inserted into the vaginal canal for muscular release) reported that half of the women with ICPP reported improved pain, but the authors did not include analyses of significance nor explicitly state when the post-test assessments were administered [42]. An RCT assessing laparoscopic uterosacral nerve ablation compared to laparoscopy without ablation reported no significant findings [30].

Non-invasive Interventions. All non-invasive interventions included in this review were comprised exclusively of women with ICPP, allowing us to make stronger conclusions. Of the six studies, three RCTs [28, 31, 32] examined the effects of gabapentin, an anticonvulsant used to control nerve pain [43], compared to a placebo; the other three compared oxytocin nasal spray to a nasal spray placebo [36], transcutaneous electrical nerve stimulation to a placebo [44], and birth control compared to vaginal ring (an intervention which, for the purposes of our analyses, we consider "combined", as it compared an invasive and non-invasive intervention) [45]. Moreover, they assessed mental health outcomes in addition to pain.

Pain. Two gabapentin trials found significantly decreased between-group pain scores, at approximately

Table 2 Research Designs

Citation #		Elements of an RCT			Type of intervention	Type of Design	Quality Index
		Control group	Random assignment	Pre- and post-assessments			
	Biomedical Intervention Studies						
[30]	Daniels et al. (2009)	X	X	X	Invasive	RCT	25
[34]	de Bernardes et al. (2010)	X[a]	X	X	Invasive	RCT	24
[40]	Carrico and Peters (2011)			X	Invasive	One group	13
[37]	Amin et al. (2015)		X	X	Invasive	Two group	21
[33]	da Rosa et al. (2015)	X	X	X	Invasive	RCT	28
[38]	Montenegro et al. (2015)		X	X	Invasive	Two group	28
[41]	Sokal et al. (2015)			X	Invasive	One group	21
[31]	Lewis et al. (2016)	X	X	X	Non-invasive	RCT	30
[45]	Priya et al. (2016)		X	X	Combined	Two group	24
[42]	Sillem et al. (2016)				Invasive	One group	13
[44]	Sharma et al. (2017)	X[b]		X	Non-invasive	Comparison	24
[32]	AbdelHafeez et al. (2019)	X	X	X	Non-invasive	RCT	25
[28]	Hewitt et al. (2020)	X	X	X	Non-invasive	RCT	31
[36]	Flynn et al. (2021)	X[a]	X	X	Non-invasive	RCT	21
	Integrative Intervention Studies						
[49]	Haugstad et al. (2008)	X	X	X	-	RCT	21
[47]	Ferreira Guiran et al. (2016)			X	-	One group	17
[46]	Saxena et al. (2017)		X	X	-	Two group	20
[35]	Chong et al. (2018)	X	X	X	-	RCT	23
[48]	Aboussouan et al. (2020)	X[b]		X	-	Comparison	20

[a]Crossover design

[b]Comparison group

[c]Combined intervention has both invasive and non-invasive elements

three- and six-month "follow-up"; notably, the participants were still taking gabapentin at follow-up [31, 32]. One of these trials found decreased *within-group* pain scores for those taking gabapentin at three- and six-month follow-up [32]; the other did not test within-group differences [31]. The third gabapentin RCT failed to find any significant decreases in pain [28].

The remaining non-invasive interventions were mixed in their findings. One RCT found that oxytocin better reduced pain severity compared to a placebo at end of treatment [36]. An intervention without random assignment found that the group receiving transcutaneous electrical nerve stimulation had decreased within-group pain scores at four week follow-up [44]. The study comparing an a non-invasive intervention (birth control pill) with an invasive treatment (vaginal ring) found decreased within-group pain scores for both groups at the end of the first month of treatment and at the end of treatment (84 days of continuous treatment). Additionally, no women with ICPP were considered to be in "severe" pain at the end of treatment, a statistically-significant difference from the pre-test [45].

Mental Health. One gabapentin RCT [31] found a significant between-group decrease in anxiety at six-month follow-up, but not at three-month follow-up, and not for depressive symptoms at either time point. Another gabapentin RCT [25] did not produce a significant change in a measure of psychological distress. Again, it should be noted that participants were still taking gabapentin during the follow-ups.

Quality of Life. Half of non-invasive biomedical interventions studies, all RCTs, included quality of life outcomes; however, none produced significant results [28, 30, 31].

Sexual Health. Two studies, a gabapentin RCT [28] and one comparing the effects of the pill vs. the vaginal ring [45] examined sexual health, but neither produced significant between-group differences.

Summary of Biomedical Intervention Studies. The majority of biomedical interventions produced significant changes in self-reported pain. Intervention effects on mental health, quality of life, and sexual health were seldom assessed, and when they were, were for the most part non-significant. This conclusion, however, must be qualified by the research design and study quality. Half of the biomedical intervention studies were randomized clinical trials and, notably, those

Table 3 Intervention Outcomes

Citation #		Outcome: Pain	Other Outcomes
	Biomedical Intervention Studies		
[30]	Daniels et al. (2009)	– (nerve ablation)	
[34]	de Bernardes et al. (2010)	EOT: Decreased between-group pain score (electrical stimulation vs. placebo)	
[40]	Carrico and Peters (2011)	EOT: "Significantly decreased"[a] within-group pain score (vaginal diazepam)	
[37]	Amin et al. (2015)	EOT, 2-weeks, 6-weeks, & 12-weeks: Decreased between-group pain scores (blockade vs. acupuncture) 3-month: Change in pain relief (blockade vs. acupuncture)	
[33]	da Rosa et al. (2015)	EOT: Decreased within-group pain scores (sacral roots stimulation)	
[38]	Montenegro et al. (2015)	4- & 12-weeks: Decreased between-group pain scores (injection vs. compression) 12-weeks: Decreased within-group pain scores (injection) Terminated early; injection 4 × stronger than compression	
[41]	Sokal et al. (2015)	EOT & 6-months: Decreased within-group pain scores (sacral roots stimulation)	
[31]	Lewis et al. (2016)	3- & 6-months: Decreased between-group pain scores (gabapentin vs. placebo)	6-month: Decreased between-group anxiety (gabapentin vs. placebo)
[45]	Priya et al. (2016)	1 month of treatment & EOT: Decreased within-group pain scores (both vaginal ring and pill) EOT: Decreased number of women in "severe pain" category	
[42]	Sillem et al. (2016)	"A few weeks"[a]: "Improved"[a] within-group pain scores (osteopathic physical therapy)	
[44]	Sharma et al. (2017)	4-weeks: Decreased within-group pain scores (electrical nerve stimulation)	
[32]	AbdelHafeez et al. (2019)	12- & 24-weeks: Decreased between-group pain scores (gabapentin vs. placebo) 3- & 6-months: Decreased within-group pain scores (gabapentin)	
[28]	Hewitt et al. (2020)	– (gabapentin)	
[36]	Flynn et al. (2021)	EOT: Decreased between-group pain severity (oxytocin vs. placebo)	
	Integrative Intervention Studies		
[49]	Haugstad et al. (2008)	1-year: Decreased within-group pain scores (gynecologic and somatocognitive treatments)	1-year: Decreased between-group anxiety score 1-year: Decreased between-group depression score 1-year: Decreased between-group coping score 1-year: Decreased within-group anxiety score 1-year: Decreased within-group coping score
[47]	Ferreira Guiran et al. (2016)	6-months: Decreased within-group pain score (integrated pain clinic)	6-months: Decreased within-group depression score 6-months: Decreased within-group anxiety score
[46]	Saxena et al. (2017)	8-weeks: Decreased between-group pain scores (anti-inflammatories plus yoga vs. anti-inflammatories) 8-weeks: Decreased within-group pain score (anti-inflammatories plus yoga)	8-weeks: Increased between-group quality of life scores (anti-inflammatories plus yoga vs. anti-inflammatories) 8-weeks: Increased within-group quality of life (anti-inflammatories plus yoga)

Table 3 (continued)

Citation #		Outcome: Pain	Other Outcomes
[35]	Chong et al. (2018)	EOT and 4-weeks: Decreased between-group pain score (consultation and acupuncture vs. consultation vs. standard of care)	EOT: Decreased within-group anxiety (consultation and acupuncture) 4- and 8-weeks: Increased within-group anxiety (standard of care)
[48]	Aboussouan et al. (2020)	– (integrated pain clinic)	EOT: Decreased between-group depression (women with CPP vs. women without CPP) EOT: Decreased within-group alexithymia (women with CPP) EOT: Increased between-group sexual functioning impairment (women with CPP vs. women without CPP) EOT: Increased within-group sexual functioning (women with CPP)

EOT = end of treatment; with the exception of footnoted articles, all results shown in Table 3 are statistically or clinically significant results. Analyses that were not significant are noted in the Results section

[a]The authors did not include statistical analyses of results; the language included is pulled from their article

studies were *not* predictive of intervention success. Two clear patterns emerged: first, the non-invasive intervention studies were better designed and found more significant effects across time and outcome domain, and second, gabapentin produced significant changes in more than just pain reduction.

Integrative Interventions

Five studies tested integrative interventions combine biomedical and psychosocial treatment strategies; study designs and sample sizes varied widely (Table 3) and no two interventions were alike: Moreover, only two of these samples were composed entirely of women with ICPP [29, 46] while the others combined women with CPP and ICPP in analyses [35, 47, 48]. As with the biomedical intervention studies, few of the integrative intervention studies reported or analyzed sociodemographic data (Table 1).

Two of the integrative intervention studies were RCTs, one comparing an integrative treatment to a biomedical treatment [29], and one a three-arm design that compared traditional Chinese medicine health consultation to the consultation plus balance method electro-acupuncture to a control condition of standard care [35]. This three-arm study was the only one that was pre-registered. Mirroring the biomedical interventions, study quality was considered "good" (20.2 out of a possible 31 on the Quality Index) [39].

Pain. All five integrative intervention studies included some self-report measure of pain, and four found that pain decreased significantly after the intervention, measured at different time intervals from immediately post-intervention to one year post-intervention [35, 46–48].

Two studies were conducted in pain clinics that offered a wide menu of treatments. In one of the studies [47], treatment included tailored combinations of pain medications, laparoscopy, vaporization, hormonal treatment, gonadotropin-releasing hormones, physical therapy, bupivacaine injection, diet alterations, antispasmodics, transcutaneous electric nerve stimulation, amitriptyline, and individual and group psychotherapy. In the other [48], treatments included "medication management, individual, family and group psychotherapy, psychoeducation, physical and occupational therapy, occupational and physical therapy, individual and group psychotherapy, and weaning from habituating medications" (p. 3). Only one of these studies found significantly decreased within-group pain, six months into treatment [47]. However, neither of these studies used random assignment, systematically compared combinations of treatments, or analyzed women with CPP and ICPP separately, and only one [48] had a comparison group of women with non-pelvic chronic pain, limiting conclusions of what combinations of treatment components are most effective.

Two RCTs compared an integrative to a biomedical treatment. One compared standard gynecological treatment to gynecologic treatment plus somatocognitive therapy (i.e., cognitive factors are highlighted to encourage somatic/bodily awareness). Significantly decreased within-group pain scores were found at one-year follow-up [29]; the end of treatment data were published in a prior paper that falls outside the scope of this review [49]. The second study compared anti-inflammatory medication alone to ibuprofen plus yoga using random assignment, and found significantly reduced within- and between-group pain at eight weeks post-treatment for the combination condition [46].

The final integrative intervention was a three-group RCT that compared a traditional Chinese medicine health consultation to the consultation plus balance method electro-acupuncture to a control condition of standard care [35].

Clinically significant – but not statistically significant – decreases in pain were found at end of treatment and four weeks post-treatment among those in the combined consultation and acupuncture protocol compared to those who received consultation alone or standard care.

Mental Health. Four of the five integrative studies assessed mental health outcomes [29, 35, 47, 48], including both of the RCTs; all four showed positive changes at timepoints ranging from end of treatment to one year post-treatment. The studies of multimodal pain treatments found decreased depression at end of treatment, comparing women with CPP to women with non-pelvic chronic pain [48]. There was also decreased within-group alexithymia at the end of treatment among women with CPP [48] and lower within-group depression and anxiety at six-month follow-up [47]. The study comparing gynecological treatment alone to gynecological treatment with somatocognitive therapy found decreased between-group anxiety and depression at one-year follow-up (for the combined intervention compared to the gynecological treatment alone) and decreased within-group anxiety (for the combined intervention) [29]. Interestingly, coping *decreased* slightly, such that there was both decreased between- and within-group coping for those in the combined condition. Finally, the three-arm RCT found that individuals receiving the combined condition were less depressed and anxious at end of treatment, while individuals receiving the standard care condition were more depressed and anxious at four- and eight-week follow-up [35].

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Quality of life. Only one of two studies assessing this outcome found a significant finding: those who received anti-inflammatory medications combined with yoga had greater QoL than those taking the medications alone; there was also a within-group increase in quality of life at 8- week follow-up [43]. The study that involved Chinese traditional medicine [35] failed to find significant effects.

Sexual health. Only two studies examined the effects of an integrative treatment on sexual health. One of the studies that offered multiple treatment options, comparing women with various types of CPP to those with non-pelvic chronic pain [48], found a significant between-group difference in measured sexual impairment at end of treatment but not in the predicted direction: Women with CPP reported *greater* sexual impairment than those with non-pelvic chronic pain, but this result was not clinically significant. These women also reported *less* within-group sexual impairment. The RCT involving traditional Chinese medicine [35] failed to find significant effects.

Discussion

This systematic review examined the efficacy of current biomedical and integrative interventions for women with idiopathic chronic pelvic pain with the goal of informing "best practices". However, the interventions themselves were quite varied, and few examined outcomes other than short-term pain reduction. This, combined with poor research design, limits any recommendations about best practices.

However, a few suggestions for future work can be gleaned from the systematic review. Invasive biomedical interventions were better at relieving immediate pain, while non-invasive biomedical interventions were more effective at reducing pain long-term. This suggests that pairing pharmacological treatments with more invasive methods of pain reduction may foster pain reduction both in the immediate moment and in the long-term. When looking at integrative interventions, however, a second conclusion emerges: Not only were integrative interventions effective at reducing both short- *and* long-term pain, but they were also effective at improving mental health, quality of life, and/or sexual health at both end of treatment and in the long-term. Taken together, these findings suggest that a *multimodal* treatment regimen for women with ICPP might be most effective. This may mean that while some women will find a combined invasive and non-invasive biomedical treatment plan to reduce their pain (e.g., nerve stimulation and gabapentin), a psychosocial intervention should be used *in tandem* to target the distress that so many women with ICPP experience.

This distress gets to the core of the issue: While ICPP is a syndrome diagnosed by the experience of pain, it often

manifests with other symptoms. Thus, women presenting for treatment of ICPP should be asked what outcome(s) they would like to target. If they are bothered only by pain, perhaps a biomedical approach using the mechanism of interest (e.g., short- or long-term pain relief) should be used. If, however, there is any component of psychological distress involved, it would be beneficial for an integrative intervention to be used. Unfortunately, given the wide ranges of psychosocial and educational aspects of these interventions, it is difficult to provide advice on best practices. Notably, none of the integrative interventions used short-term cognitive-behavioral therapy nor pain-coping strategies, two interventions that have been successfully used with other pain conditions, including non-idiopathic chronic pelvic pain [50–52].

Limitations

Overall, the eligible studies possessed weak research designs that provide less than conclusive evidence – less than half of the studies were RCTs, the gold standard in intervention research, and many had relatively small samples that limited statistical power. Similarly, outcome timepoint (and location of outcome assessment during course of intervention) varied widely. Some of the samples did not distinguish women with CPP (pain with a known cause) and ICPP (pain with an unknown cause). This is an important distinction, as coping and adjustment are more difficult when the symptoms do not have a disease label [53]. Additionally, it is possible that certain interventions for other types of chronic pain might have included women with ICPP, but were not included as part of this review because they were not focused on pain. This, in tandem with the overwhelmingly small samples in the studies included in this review, means that it is often difficult to disaggregate the samples to understand not only what worked, but also *for whom* and *at what times in the pain trajectory*. These methodological flaws are in sharp contrast to the "good" ratings most studies received on the quality index, which brings into relief how interventions should be designed and tested in order to produce translational findings. Given the large number of women with ICPP who endure daily pain and limitations on normal life activities, the paucity of well-designed research alone underlines the urgency of developing, testing, modifying, and disseminating effective interventions for this underserved population.

Blueprint for Future Research

Given renewed calls for multidisciplinary treatments for CPP that began 15 years ago [24], it is disappointing that the majority of interventions included in this review continue to be solely biomedical in nature. Slightly more than one-quarter of the studies reviewed had any psychosocial or behavioral component, despite the evidence that behavioral interventions work for many other types of pain, including non-idiopathic chronic pelvic pain [50, 52, 54, 55]. The unremitting pain of ICCP many face can lead to negative self-evaluative emotion (i.e., self-blame) given nonexistent pathology [16, 17]. Thus, behavioral medicine scientists should be encouraged to design interventions to address the interplay of pain and psychological distress, and to evaluate intervention effects using strong research designs. Given the findings of this systematic review, the following recommendations would strengthen future interventions studies focused on women with ICPP.

1. Combine psychosocial or behavioral treatments with a biomedical treatment plan, as integrative treatments were generally efficacious across multiple outcomes. Based on other chronic pain conditions, we might suggest adapting pain coping skills training, cognitive-behavioral therapy, or acceptance and commitment therapy. All are treatment modalities that have been successful with other types of pain [50, 51, 54–56]. Per our findings, we recommend that these not be tested individually (vs. a control condition), but in combination with biomedical treatments. We also recommend incorporating both invasive and non-invasive biomedical modalities into treatment planning, as invasive treatments might be more suited to immediate pain relief, while non-invasive treatments may be more suited to long-term pain relief.
2. Examine a more varied range of intervention outcomes besides pain. It is not surprising that most of the intervention studies reviewed had reduced pain as an outcome. Few studies, however, examined the effect of ICPP on mental health, quality of life, or sexual health. For example, pelvic pain has been shown to impede intimate relationships among women with endometriosis due to sexual avoidance and isolation [57]. Thus, future research should examine whether this finding extends to women with ICPP.
3. Address the sociodemographic context of the sample when designing and evaluating interventions. The current literature is based on samples that are largely White and heterosexual. Most of the studies reviewed did not report race/ethnicity (much less analyze it), and none reported sexual orientation or gender identity. These demographic variables not only determine the quality of health care, but may also affect attitudes toward pain and treatment, access to care, and type of treatment offered. In this same vein, research should examine how different cultural values for historically marginalized groups may affect attitudes toward ICPP and receptivity to treatment and ultimately, treatment success.

4. Test the feasibility and acceptability of behavioral and integrative treatments before conducting Phase III efficacy studies. For example, researchers need to know how ICCP patients from different cultural or sociodemographic groups, those who have tried many treatments vs. are starting their engagement with the medical profession feel about engaging in multiple treatments. Qualitative research would be beneficial to identify what outcomes, in addition to pain, are important to women with ICPP. This is a ripe arena for qualitative and mixed methods research among both patients with ICPP and their providers.
5. Turn the development of treatments for ICPP into an interdisciplinary endeavor. With the suggestion of pairing biomedical and behavioral treatments into a single intervention, medical and psychological professionals must work together in an integrative care model to deliver these treatments.

Conclusion

This review highlights the types and efficacy of interventions for women living with ICPP. Although there was not enough quality research to suggest best practices, the data point to an integrative treatment approach, mirroring the biopsychosocial model [58]. Future directions are to broaden the sociodemographic scope of this under-researched population, and to conduct formative research before embarking on well-designed clinical trials. Given the relative lack of research on treatments for women with ICPP, this review provides a first step toward improving the quality of care for women with ICPP.

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Declarations

Ethical Approval For this type of study, formal consent is not required.

Informed Consent As human subjects were not recruited for this review, informed consent was not obtained.

Research Involving Human Participants This article does not contain any studies with human participants performed by any of the authors.

Competing Interests The authors declare that they have no conflict of interest.

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