Systematic Review on Intensive Interdisciplinary Pain Treatment of Children With Chronic Pain

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abstract

BACKGROUND AND OBJECTIVE: Pediatric debilitating chronic pain is a severe health problem, often requiring complex interventions such as intensive interdisciplinary pain treatment (IIPT). Research is lacking regarding the effectiveness of IIPT for children. The objective was to systematically review studies evaluating the effects of IIPT.

METHODS: Cochrane, Medline/Ovid, PsycInfo/OVID, PubMed, PubPsych, and Web of Science were searched. Studies were included if (1) treatment was coordinated by ≥ 3 health professionals, (2) treatment occurred within an inpatient/day hospital setting, (3) patients were <22 years, (4) patients experienced debilitating chronic pain, (5) the study was published in English, and (6) the study had ≥ 10 participants at posttreatment. The child's pain condition, characteristics of the IIPT, and 5 outcome domains (pain intensity, disability, school functioning, anxiety, depressive symptoms) were extracted at baseline, posttreatment, and follow-up.

RESULTS: One randomized controlled trial and 9 nonrandomized treatment studies were identified and a meta-analysis was conducted separately on pain intensity, disability, and depressive symptoms revealing positive treatment effects. At posttreatment, there were large improvements for disability, and small to moderate improvements for pain intensity and depressive symptoms. The positive effects were maintained at short-term follow-up. Findings demonstrated extreme heterogeneity.

CONCLUSIONS: Effects in nonrandomized treatment studies cannot be attributed to IIPT alone. Because of substantial heterogeneity in measures for school functioning and anxiety, meta-analyses could not be computed. There is preliminary evidence for positive treatment effects of IIPT, but the small number of studies and their methodological weaknesses suggest a need for more research on IIPTs for children.

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REVIEW ARTICLE

Pediatric chronic pain that results in significant distress and disability is a serious health problem. There is an increasing number of children who present to hospitals for treatment of chronic pain.[1] The most common chronic pain conditions include headache, functional abdominal pain, and musculoskeletal pain, including back pain.[2,3] Many of these children are severely impaired in their daily activities; they are unable to attend school regularly, and often suffer from severe emotional distress.[1,4] Children and their families exact high costs on the health care system, estimated to be $19.5 billion annually in the United States.[5]

Today, there is consensus regarding the complexity of pediatric chronic pain that results in significant distress and disability, and regarding the interaction among biological, social, and psychological factors accounting for and exacerbating pediatric chronic pain.[6,7] This complex health problem often requires a comprehensive treatment approach that focuses on medical and physiologic aspects and on the child's physical functioning, and emotional impairment. Collaboration among multiple disciplines is thus recommended to assess and develop a treatment plan.[8] Intensive interdisciplinary pain treatment (IIPT) has gained increased support as a treatment of choice for these children.[8,9] IIPT involves coordinated interventions among at least 3 disciplines (eg, pediatricians, clinical child psychologists, and physiotherapists) working together in the same facility in an integrated way.[10,11] Furthermore, IIPT implies that treatment is provided in an inpatient[9] or day hospital setting,[12] with participants typically receiving an average of 8 hours of treatment per day over a 1- to 3-week period. The collaborative goal is to improve functioning and reengagement in age-specific activities, such as regular school attendance.[8] The target populations for such programs are typically youths who are unable to make progress in an outpatient treatment setting or present with severe pain-related disability.

Although there is a plethora of research into the effectiveness of IIPT in adult patients[10] and into the mechanisms that account for the positive outcomes,[13] there is a dearth of research into the effectiveness of IIPT for children and adolescents. Previous reviews highlight the effectiveness of psychological therapies for the treatment of chronic pain in youth,[14,15] but no reviews have examined the benefits of IIPT, despite the growing need for and interest in this particular form of treatment. In addition, although we know the components of IIPT programs for youth with chronic pain are diverse, no previous studies have systematically examined the programs and described the treatments.

Therefore, in the current study we systematically reviewed the literature to identify studies investigating the effects of IIPT. Our aims were twofold. First, we aimed to describe the nature of the IIPT used to treat pediatric chronic pain that results in significant distress and disability and to provide details on treatment components. Second, we conducted a meta-analysis of randomized controlled trials (RCTs) and nonrandomized treatment studies (NRSs) separately, focusing on 5 outcome domains (pain intensity, disability, school absence, anxiety, depressive symptoms) to evaluate the effectiveness of IIPT at immediate posttreatment and follow-up.

METHOD

The review was registered with PROSPERO (http://www.crd.york.ac.uk/PROSPERO/) and the detailed study protocol can be accessed under the registration number CRD42014010719.

Criteria for Inclusion and Exclusion

RCTs and NRSs were considered eligible for inclusion in the present review. NRSs were defined as quantitative studies estimating the effectiveness of the IIPT that did not use randomization.[16] Even though potential biases, such as selection bias, may be greater in NRSs, we decided to include NRSs because randomization of severely affected children with chronic pain is extremely difficult. Furthermore, studies were included if (1) the intervention was coordinated by ≥3 different health professionals, (2) treatment occurred within an inpatient or day hospital treatment setting, (3) the target population was children and adolescents (<22 years old), (4) children enrolled were experiencing severe and disabling chronic pain as defined by individual study criteria (eg, patients had to be struggling with chronic pain, and chronic pain was interfering with functioning[17]), (5) studies were published in English, and (6) studies had ≥10 participants at posttreatment. Studies were excluded if pain was associated with life-threatening malignant disease, or if they were reviews or case studies.

Search Strategy

Studies for this review were identified by searches of the following databases conducted by a research librarian (Karolinska Institutet University Library): Cochrane, Medline/PubMed, PsycInfo/OVID, PubMed, PubPsych, and Web of Science. The search used 3 groups of keywords. The first group defined the intervention (ie, keywords such as "interdisciplinary" were included). The second group defined the target population (ie, children and adolescents). The third group defined the clinical condition (ie, chronic pain). Main terms were Pain or Chronic Pain combined with terms to express

HECHLER et al

TABLE 1 Characteristics of Included Studies

Author	Study Design	Treatment Setting	Pain Location/ Diagnosis[a]	Treatment Duration, in Weekdays	Baseline, n	Post, n	FU1, n	FU2, n	Outcome Domains	Assessments After IIPT, mo
Chalkiadis et al[24]	NRS: Cross-sectional	Inpatient	51% comorbid medical condition 30% no clear etiology for pain 19% organic precipitant	5	207	207			No. of children with school absence	Not specified
Eccleston et al[25]	NRS: Case series	Day hospital	CRPS 26.4% Diffuse idiopathic 24.6% Fibromyalgia 15.8% Disease related 14.0% Localized idiopathic 12.3% RAP 3.5% Headache 1.7% Renal pain 1.7%	18	57	56	43		Pain Disability School sessions attended Anxiety (general) Depressive symptoms	Post 3
Gauntlett-Gilbert et al[26]	NRS: Case series	Day hospital	Diffuse/ localized idiopathic 27% CRPS 20% Back pain 19% Abdominal pain 13% Pain associated with hypermobility 11% Other (eg, headache) 10%	15	98	94	73		Pain Disability School sessions missed Anxiety (pain-specific) Depressive symptoms	Post 3
Hechler et al[27b]	NRS: Case series	Inpatient	Headache 30% Diffuse idiopathic 21% Abdominal pain 18% Localized idiopathic 12% Back pain 6% CRPS 6% Disease related 3% Fibromyalgia 3%	15	33		26	31	Pain Disability School days missed	3 12
Hechler et al[9]	RCT	Inpatient	Headache 79% Musculoskeletal pain diagnosis 54% Abdominal pain diagnosis 23% Other pain diagnosis 8%	15	IG = 61 CG = 59	IG = 52 CG = 56	IG = 50 CG = 50	IG = 44 CG = 42	Pain Disability School days missed Anxiety (pain-specific) Depressive symptoms	Post 6 12
Hirschfeld et al[28]	NRS: Case series	Inpatient	Headache 50% Abdominal pain 13% Back pain 10% Diffuse idiopathic 9% Disease related 7% Fibromyalgia 5% Localized idiopathic 4% CRPS 3%	15	167		141	136	Pain Disability School days missed Anxiety (general) Depressive symptoms	3 12
Logan et al[29]	NRS: Case series	Day hospital	CRPS 64.3%, 35.7% neuropathic pain (not meeting full criteria for CRPS)	15	56	55	30		Pain Disability School functioning Anxiety (general) Depressive symptoms	Post 2–24

TABLE 1 Continued

Author	Treatment Setting	Study Design	Pain Location/ Diagnosis[a]	Treatment Duration, in Weekdays	Baseline, n	Post, n	FU1, n	FU2, n	Outcome Domains	Assessments After IIPT, mo
Maynard et al[30]	Rehabilitation	NRS: retrospective chart review	CRPS 46% Headache 22% Abdominal pain 20% Functional gait disorder and traumatic brain injuries 10% Postconcussive syndrome, developmental delays, Ehlers-Danlos syndrome 7.3% Additional comorbid medical diagnosis 61%	27	41	41	19		Disability No. of children with school absence	Post 3
Simons et al[12]	Day hospital	NRS: Case series	Neuropathic pain 93% Musculoskeletal pain 7%	15	145	141	125		Pain Disability Anxiety (pain-specific) Depressive symptoms	Post 2
Weiss et al[17]	Rehabilitation	NRS: Case series	Abdominal pain 30% Headache 26% Generalized 25% Back/neck pain 8% Extremities 7% Pelvic area 2%	15	112	112			Pain Disability Anxiety (pain-specific) Depressive symptoms	Post

Some cells were intentionally left blank as no data were collected at that time point. CG, control group; CRPS, Complex Regional Pain Syndrome; FU, follow-up; IG, intervention group; Post, assessment at immediate posttreatment; RAP, Recurrent Abdominal Pain.

[a] As reported in the studies.

[b] Due to overlapping samples, only data from children aged 7 to 10 y were included from Hechler et al.[27]

interdisciplinary or multiprofessional teams, in the context of children and adolescents. The complete search strategy is available in Supplemental Appendix 1. All databases were searched from database inception up to February 17, 2014. Abstracts were screened for eligibility by 2 independent researchers (TH, MK). Discrepancies were resolved by discussion with 2 additional independent researchers (AH, LS) until consensus was reached. Articles that met the inclusion criteria were reviewed in full-text by independent researchers (TH, MK, AH) and evaluated by 3 additional independent researchers (BZ, RW, LS). Discrepancies were resolved by discussion.

Measurement Domains

Five outcome domains (pain intensity, disability, school functioning, anxiety, depressive symptoms) were selected as dependent variables, according to recommended outcome domains for clinical trials in pediatric chronic pain research.[18] If multiple measures were used for a single outcome domain within 1 study, we chose the measure with the most empirical support and/or the measure that was most commonly used in the other studies. Pain-intensity outcomes were most commonly reported as self-report rating on a numerical rating scale or visual analog scale. The disability outcome was assessed by using measures of functional disability (eg, the Functional Disability Inventory).[19] School functioning was assessed in various ways (eg, number of children who attended school, or number of days absent from school). Anxiety was assessed with general and pain-specific anxiety measures by using, for example, the Anxiety Scale for Pupils,[20] the Fear of Pain Questionnaire,[21] or the Pain-Related Cognition Questionnaire.[22] Depressive symptoms were assessed by the Child Depression Inventory.[23] The outcomes used in each trial for the respective domains are shown in Table 1.
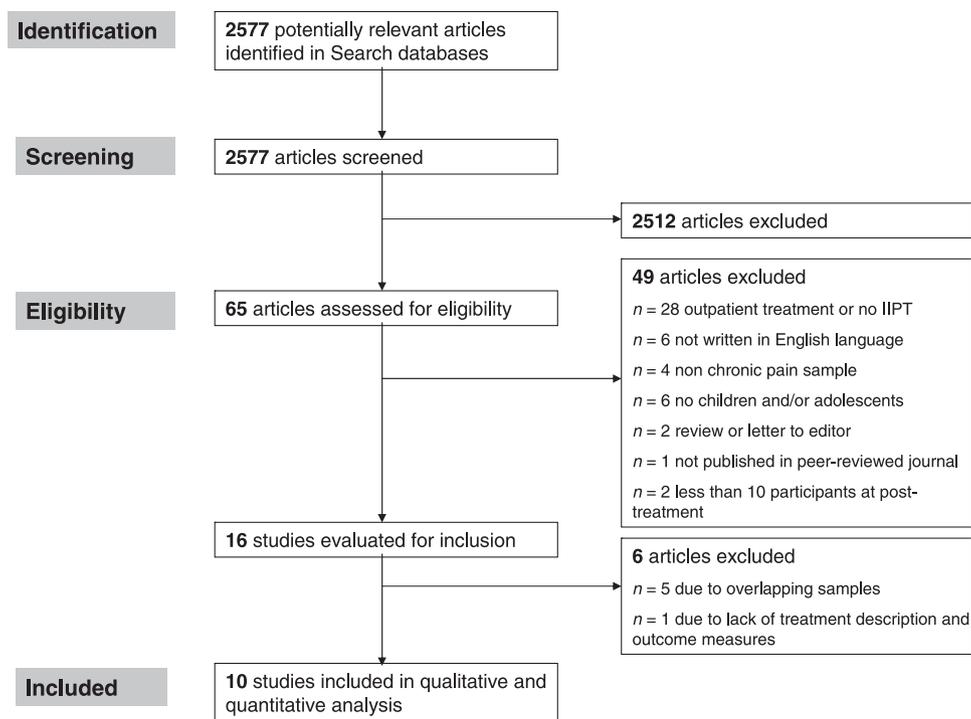
FIGURE 1
PRISMA flow diagram.

Data Extraction

For data extraction, the included articles were randomly assigned to 3 teams of 2 reviewers (TH, BZ; MK, RW; AH, LS). The 2 reviewers then conducted data extraction for the respective articles. Discrepancies were resolved by discussion. Two reviewers verified the entire data extraction of all studies. For the included articles, information regarding the design of the study, the child's pain condition, demographics, characteristics of the IIPT and treatment components, and outcome measurement tools were extracted. Raw data for the 5 outcome domains from each study was used to conduct a meta-analysis of treatment effects at each relevant time point (baseline, immediately posttreatment, and follow-up).

Quality Ratings

Quality ratings were extracted by use of the Cochrane Collaboration Risk of Bias Tool for RCTs and by use of the Quality Appraisal Tool for NRS.[31,32] By use of the first, randomization bias, allocation bias, blinding bias, incomplete outcome data, and selective reporting bias in the RCT were assessed.[33] Summary assessments of quality ratings of RCTs were obtained by use of defined criteria for classification of "low," "unclear," or "high" risk of bias.

TABLE 2 Examples of Included Treatment Components Per Health Discipline

Discipline	Treatment Component
Physician	Appropriate pain medication
	Evaluation and treatment of ongoing medical issues
	Diagnostic evaluation
Clinical psychology	Teach pain-coping strategies
	Address negative thinking
	Teach stress-coping strategies
	Education
	Biofeedback
	Exposure-based interventions
	Sleep hygiene
	Relaxation
	Reinforcement of functional behavior
	Treat comorbid psychological disorders
	ACT strategies
Physiotherapy	Increase activity
	Graded exposure
	Improve strength
	Improve flexibility
	Improve fitness
Nurses	Address acute medical issues
	Daily evaluation
	Support school attendance
Occupational therapy	Maximize independence in self care
	Individualized sensory reduction program

ACT, acceptance and commitment therapy.

The Quality Appraisal Tool for case series[31,32] has the advantage that it provides 2 sets of items in line with the objectives of the present systematic review: (1) a set of items for hypothesis testing (including items such as "study conducted prospectively," "outcomes measured before/after intervention"), and (2) a set of items describing study/intervention characteristics (eg, "inclusion/exclusion criteria," "intervention clearly defined") (Supplemental Appendix 2). The 2-factor structure of the tool was revealed in a recent study including 6 researchers who rated 35 studies each.[32] The items were used for a detailed description of the included NRS (Supplemental Appendix 3). No summary assessment was made. The link between the Quality Appraisal Tool and the assessment of risk of bias is unclear.

Data Analysis

The results of the searches are presented using a PRISMA flowchart. Participant characteristics and treatment characteristics are presented for each study. Quality ratings of the studies are summarized descriptively.

Meta-analysis of the 5 Outcome Domains

The quantitative analysis examined the 5 outcome domains at 2 time points, immediately after treatment and at short-term follow-up. Because of the limited number of studies ($n = 3$) that presented long-term follow-up data, results could not be computed. Because only 1 RCT was identified during the literature search, we present pooled estimates for the NRSs and present the RCT separately. Continuous data for the 5 outcome domains were used to analyze the overall estimate of effect size of IIPT. Cohen d effect size (ie, the difference between posttreatment and baseline divided by the SD at baseline) was computed. Effect sizes for short-term follow-up were computed by using the

same formula. According to Cohen,[34] effect sizes of 0.2, 0.5, and 0.8 were defined as small, medium, and large. Larger effect sizes are associated with greater improvement in the respective outcome domain.

Because correlations between repeated assessments were not provided,[33] sensitivity analyses were performed. This analysis substituted different correlation coefficients (ranging between $r = 0.10$ and $r = 0.90$), and yielded significant overall effects across the studied range of correlation coefficients. Random-effects analyses were used to pool data on the outcomes due to differing measurement instruments. The I^2-statistic as a measure of heterogeneity was reported for each meta-analysis. The outcomes showed substantial heterogeneity

($I^2 > 50\%$). A random-effects model takes into account measurement error beyond subject sampling error that is randomly distributed. We used an inverse variance method to weigh assessments of outcome, meaning larger studies were given more weight in comparison with smaller studies. Confidence intervals were calculated. Confidence intervals not including zero were considered statistically significant. Because the measures for anxiety and school functioning were too dissimilar, we computed effect sizes only for the separate measures without pooling these estimates.

All data analyses were conducted by using R and the metafor package[35] and the SPSS software version 21.0 (IBM SPSS Statistics, IBM Corporation, Chicago, IL).
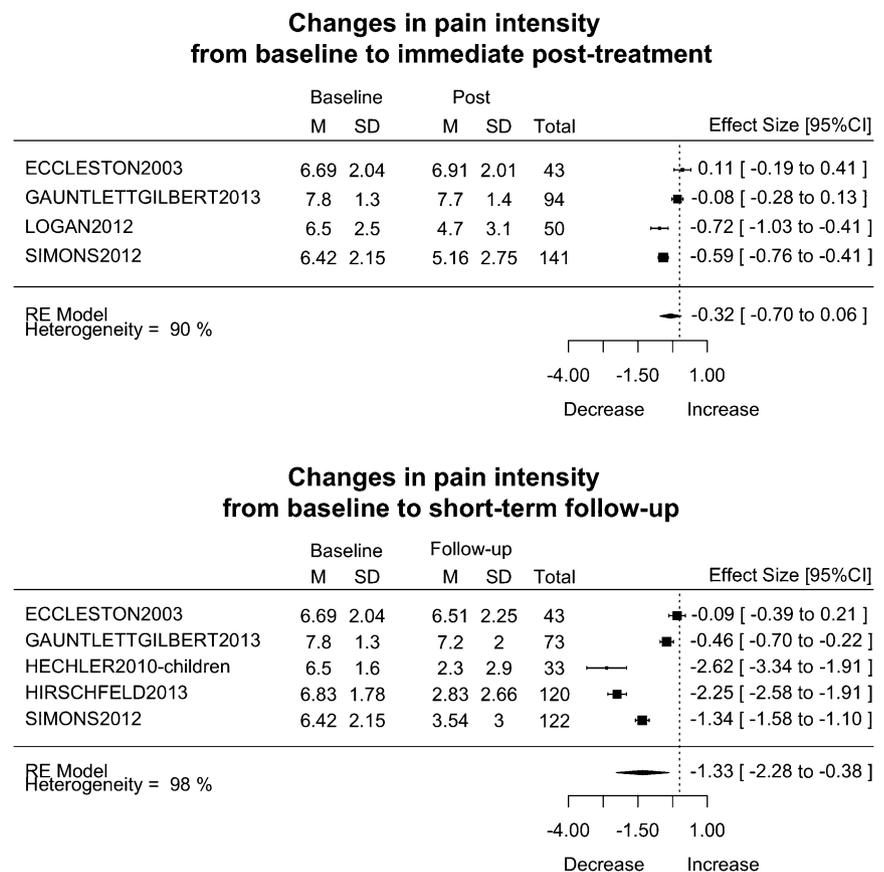

Changes in pain intensity from baseline to immediate post-treatment

	Baseline		Post			Effect Size [95%CI]
	M	SD	M	SD	Total	
ECCLESTON2003	6.69	2.04	6.91	2.01	43	0.11 [-0.19 to 0.41]
GAUNTLETTGILBERT2013	7.8	1.3	7.7	1.4	94	-0.08 [-0.28 to 0.13]
LOGAN2012	6.5	2.5	4.7	3.1	50	-0.72 [-1.03 to -0.41]
SIMONS2012	6.42	2.15	5.16	2.75	141	-0.59 [-0.76 to -0.41]

RE Model
Heterogeneity = 90 %   -0.32 [-0.70 to 0.06]

-4.00 -1.50 1.00
Decrease   Increase

Changes in pain intensity from baseline to short-term follow-up

	Baseline		Follow-up			Effect Size [95%CI]
	M	SD	M	SD	Total	
ECCLESTON2003	6.69	2.04	6.51	2.25	43	-0.09 [-0.39 to 0.21]
GAUNTLETTGILBERT2013	7.8	1.3	7.2	2	73	-0.46 [-0.70 to -0.22]
HECHLER2010-children	6.5	1.6	2.3	2.9	33	-2.62 [-3.34 to -1.91]
HIRSCHFELD2013	6.83	1.78	2.83	2.66	120	-2.25 [-2.58 to -1.91]
SIMONS2012	6.42	2.15	3.54	3	122	-1.34 [-1.58 to -1.10]

RE Model
Heterogeneity = 98 %   -1.33 [-2.28 to -0.38]

-4.00 -1.50 1.00
Decrease   Increase

FIGURE 2
Effect sizes (d) for changes in pain intensity from baseline to immediate posttreatment and to 3-month follow-up.

HECHLER et al

RESULTS

Results of Search

The initial search yielded 2577 abstracts. Of these, 65 articles met the initial inclusion criteria. The final set of 16 studies was reviewed by 3 pairs of researchers to extract data. At this stage, 5 studies that reported on overlapping samples were identified.[36–40] We decided to include articles that first presented results on the respective samples, or articles that presented new aspects (eg, assessment of additional outcomes) into the present review. An additional article with lack of treatment description and outcome data also was excluded.[41] Data from 10 studies were extracted (Fig 1).

The 10 studies were 1 RCT[9] and 9 NRSs[12,17,24–30] (1 cross-sectional study, 7 case series, and 1 retrospective chart review) (Table 1). The studies were conducted between 2001 and 2014, with 8 published between 2010 and 2014, in North America (4), Europe (5), and Australia (1).

Quality Ratings of Included Trials

All 10 studies provided a clear and sufficiently detailed description of the treatment and participant characteristics. Notably, several consistent methodological limitations were seen. Primarily, only 1 study was an RCT. This RCT was scored as low risk of bias for selection bias and allocation concealment. There was an unclear risk of bias for blinding of outcome assessment, incomplete outcome data, and selective reporting. Given that only 1 RCT was included, risk of bias was not used in the data synthesis. All 9 NRSs did not include a control group. Only 3 studies reported recruitment rates, with the mean recruitment rate being 89.6%. Eight studies reported response rate at posttreatment with a mean response rate of 97.1%. Eight studies also reported response rates at follow-up with a mean of 74.5%. Quality ratings of the 9 NRSs are summarized in Supplemental Appendix 3.

Included Participants Characteristics

The 10 studies included a total of 1020 participants (757 girls, 263 boys) at baseline. The mean number of participants per study was 92. Eight studies included an immediate posttreatment assessment with a total of 810 participants. Eight studies included a short-term follow-up (2 to 6 months) with a total of 557 participants, and 3 studies included a long-term follow-up (12 months) with a total of 253 participants. The average age of the children entering the study was 13.9 years (SD 1.5). The mean duration of pain (reported in 7 studies) was 2.95 years (SD 2.8). Pain diagnoses/locations of the children are depicted in Table 1.

Characteristics of the IIPTs

More than half of the treatments included 5 disciplines (7 studies). Most frequently, the treatments included medical (9 studies), psychological (10 studies), and physical interventions (10 studies). Mean treatment duration was 16 days (SD 5.3; range: 5–27 days). Table 2 presents examples of the reported treatment components per health discipline across all included studies.

Three studies provided details on the children's pain medication at baseline and its change over the course of the treatment. Only 1 study[24] reported on intensive medical interventions, such as nerve blocks and epidural catheters. In this study, 29 children (14%) underwent nerve blocks.

Most studies included parental interventions (8 studies), with the most common being education
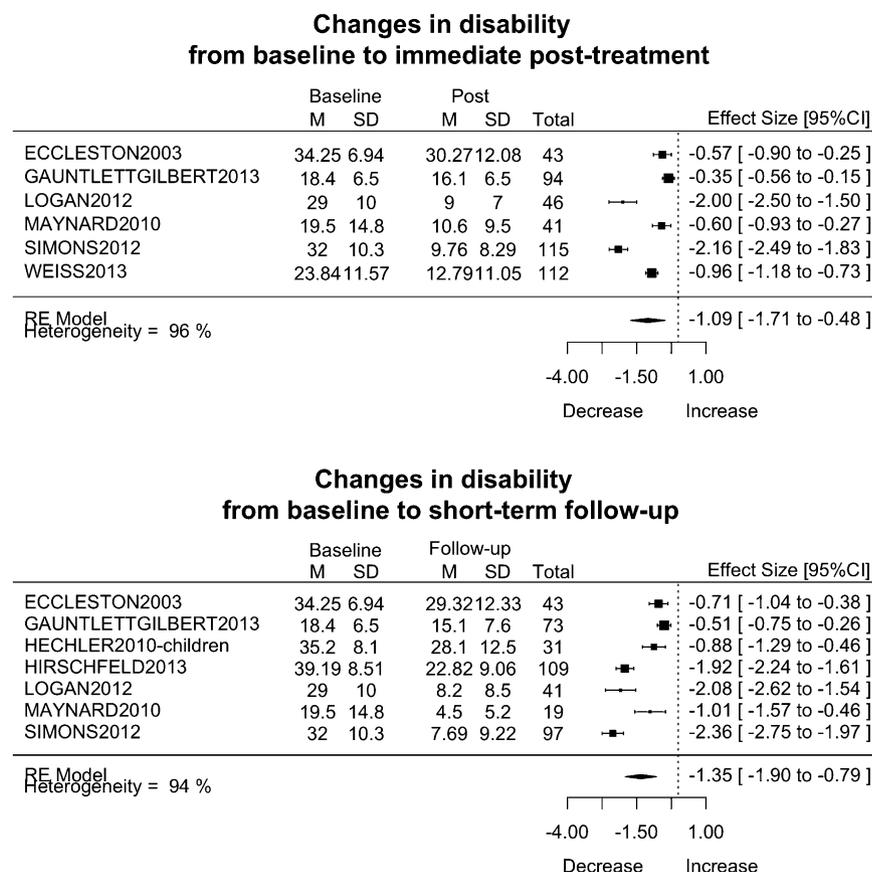
Changes in disability from baseline to immediate post-treatment

	Baseline M SD	Post M SD	Total	Effect Size [95%CI]
ECCLESTON2003	34.25 6.94	30.27 12.08	43	-0.57 [-0.90 to -0.25]
GAUNTLETTGILBERT2013	18.4 6.5	16.1 6.5	94	-0.35 [-0.56 to -0.15]
LOGAN2012	29 10	9 7	46	-2.00 [-2.50 to -1.50]
MAYNARD2010	19.5 14.8	10.6 9.5	41	-0.60 [-0.93 to -0.27]
SIMONS2012	32 10.3	9.76 8.29	115	-2.16 [-2.49 to -1.83]
WEISS2013	23.84 11.57	12.79 11.05	112	-0.96 [-1.18 to -0.73]
RE Model Heterogeneity = 96 %				-1.09 [-1.71 to -0.48]

-4.00   -1.50   1.00

Decrease   Increase

Changes in disability from baseline to short-term follow-up

	Baseline M SD	Follow-up M SD	Total	Effect Size [95%CI]
ECCLESTON2003	34.25 6.94	29.32 12.33	43	-0.71 [-1.04 to -0.38]
GAUNTLETTGILBERT2013	18.4 6.5	15.1 7.6	73	-0.51 [-0.75 to -0.26]
HECHLER2010-children	35.2 8.1	28.1 12.5	31	-0.88 [-1.29 to -0.46]
HIRSCHFELD2013	39.19 8.51	22.82 9.06	109	-1.92 [-2.24 to -1.61]
LOGAN2012	29 10	8.2 8.5	41	-2.08 [-2.62 to -1.54]
MAYNARD2010	19.5 14.8	4.5 5.2	19	-1.01 [-1.57 to -0.46]
SIMONS2012	32 10.3	7.69 9.22	97	-2.36 [-2.75 to -1.97]
RE Model Heterogeneity = 94 %				-1.35 [-1.90 to -0.79]

-4.00   -1.50   1.00

Decrease   Increase

FIGURE 3

Effect sizes (*d*) for changes in disability from baseline to posttreatment and to 3-month follow-up.

Results of Meta-analysis

Pain Intensity

Five studies with a total of 379 participants were included in the analysis to investigate whether IIPT improved pain intensity after treatment. The RCT showed a significant small effect ($d = -0.38$; 95% confidence interval [CI] −0.67 to −0.10]). The meta-analysis of the 4 NRSs showed a small and nonsignificant effect ($d = -0.32$, 95% CI −0.70 to 0.06, $z = -1.64$, $P = .101$, $I^2 = 90\%$).

At short-term follow-up, 6 studies with a total of 440 participants were included. The RCT reported a large and significant effect ($d = -1.19$; 95% CI −1.56 to −0.82]). Within the 5 NRSs there was also a large and significant effect ($d = -1.33$, 95% CI −2.28 to −0.38, $z = -2.74$, $P = .01$, $I^2 = 98\%$). Forest plots are presented in Fig 2.

Disability

Seven studies with a total of 498 participants were included in the analysis to investigate whether IIPT improved disability after treatment. We found evidence for a large effect of IIPT in the RCT ($d = -0.80$; 95% CI −1.13 to −0.47) and across 6 NRSs ($d = -1.09$, 95% CI −1.71 to −0.48, $z = -3.47$, $P < .001$, $I^2 = 96\%$).

At short-term follow-up, 8 studies with a total of 463 participants were included. There was a large effect of IIPT in the RCT ($d = -1.47$; 95% CI −1.87 to −1.07) and across 7 NRSs ($d = -1.35$, 95% CI −1.90 to −0.79, $z = -4.73$, $P < .001$, $I^2 = 94\%$). Forest plots are presented in Fig 3.

School Functioning

Because of substantial heterogeneity in how school functioning was assessed, we computed effect sizes only for the separate measures but did not pool these estimates (Table 3). The RCT and 1 NRS revealed large effects on school functioning at posttreatment. The RCT and 4 NRSs revealed moderate to large effects on school functioning at short-term follow-up with effect sizes ranging between 0.53 (school sessions attended) and −1.0 (school days missed).

Anxiety

Because of substantial heterogeneity in how anxiety was assessed, we computed effect sizes only for the separate measures without pooling these estimates (Table 4). Within the RCT, no beneficial effect of IIPT on measures of anxiety at posttreatment was observed. Four of 6 NRSs found evidence for beneficial effects of IIPT on measures of anxiety with large effect sizes ranging from −0.82 (Pain Catastrophizing Scale for Children) to −1.14 (Fear of Pain Questionnaire for Children).

At short-term follow-up, the RCT and 4 NRSs found positive effects of IIPT on the anxiety measures with effects ranging from moderate (−0.38, general anxiety) to large effect sizes (−1.57, pain-specific anxiety).

Depressive Symptoms

Six studies with a total of 458 participants were included in the analysis to investigate if IIPT decreased depressive symptoms. Within the RCT, no beneficial effect of IIPT on depressive symptoms was observed ($d = -0.22$, 95% CI −0.51 to 0.07]). Across 5 NRSs, we found a small beneficial effect ($d = -0.37$, 95% CI −0.64 to −0.11], $z = -2.81$, $P < .001$, $I^2 = 84\%$).

At short-term follow-up, 5 studies with a total of 325 participants were included. There was a moderate effect within the RCT ($d = -0.59$, 95% CI −0.93 to −0.26) and a small effect of IIPT in the 4 NRSs ($d = -0.40$, 95% CI −0.68 to −0.12], $z = -2.77$, $P = .001$, $I^2 = 81\%$). Forest plots are presented in Fig 4.

TABLE 3 Descriptive Data on Assessment and Effect Sizes for Separate Measures of School Functioning

| Author and Year | Study Design | Measure | Changes in School Functioning From Baseline to Immediate Posttreatment | | Changes in School Functioning From Baseline to Short-term Follow-up | |
			Effect Size d	95% CI	Effect Size d	95% CI
CHALKIADIS2001	NRS: Cross-sectional	No. of children with school absence				
ECCLESTON2003	NRS: Case series	School sessions attended			0.53	0.21 to 0.85
GAUNTLETTGILBERT2013	NRS: Case series	School sessions missed			−0.63	−0.88 to −0.38
HECHLER2010	NRS: Case series	School days missed			−0.82	−1.22 to −0.43
HECHLER2014	RCT	School days missed	−0.88	−1.21 to −0.54	−1.00	−1.36 to −0.64
HIRSCHFELD2013	NRS: Case series	School days missed			−0.96	−1.18 to −0.74
LOGAN2012	NRS: Case series	School functioning	−0.94	−1.28 to −0.61	−0.94	−1.30 to −0.58
MAYNARD2010	NRS: Case series	No. of children with school absence				

Some cells were intentionally left blank as no data were collected at that time point.

TABLE 4 Descriptive Data on Assessment and Effect Sizes for Separate Measures of Anxiety

Author and Year	Study Design	Component of Anxiety	Measure	Changes in Anxiety From Baseline to Immediate Posttreatment		Changes in Anxiety From Baseline to Short-term Follow-up	
				Effect Size d	95% CI	Effect Size d	95% CI
		General					
ECCLESTON2003	NRS: Case series		Spence Children's Anxiety Scale	−0.06	−0.36 to 0.24	−0.38	−0.69 to −0.07
HIRSCHFELD2013	NRS: Case series		Anxiety Questionnaire for Pupils			−0.50	−0.74 to −0.25
LOGAN2012	NRS: Case series		Multidimensional Anxiety Scale	−0.92	−1.25 to −0.59		
		Pain-specific					
GAUNTLETTGILBERT2013	NRS: Case series		Pain Catastrophizing Scale for Children	−0.82	−1.06 to −0.59	−0.85	−1.12 to −0.59
HECHLER2014	RCT		Pain Catastrophizing Scale for Children	0.00	−0.28 to 0.28	−1.02	−1.39 to −0.66
WEISS2013	NRS: Case series		Pain Catastrophizing Scale for Children	−0.85	−1.06 to −0.63		
SIMONS2012	NRS: Case series		Fear of Pain Questionnaire for Children	−1.14	−1.38 to −0.91	−1.57	−1.87 to −1.27

Some cells were intentionally left blank as no data were collected at that time point.

DISCUSSION

The aim of the present review was to evaluate the effectiveness of IIPT for children with chronic pain that results in significant distress and disability. Effectiveness was evaluated in terms of improvement in 5 relevant outcome domains. Our review provided evidence for positive treatment effects using both RCT and NRS designs. Large improvements were observed for disability, small improvements were observed for pain intensity and symptoms of depression. That said, the paucity of studies and their methodological weaknesses are notable, as we identified only 1 published RCT and 9 NRSs. Findings also demonstrated extreme heterogeneity, and because of this, the results of these analyses should be interpreted with caution. Clearly while interest in IIPT is increasing (as reflected by 8 of the 10 identified studies being published within the past 4 years) there is a need for more studies with more vigorous study designs to promote further developments of effective treatments.[42]
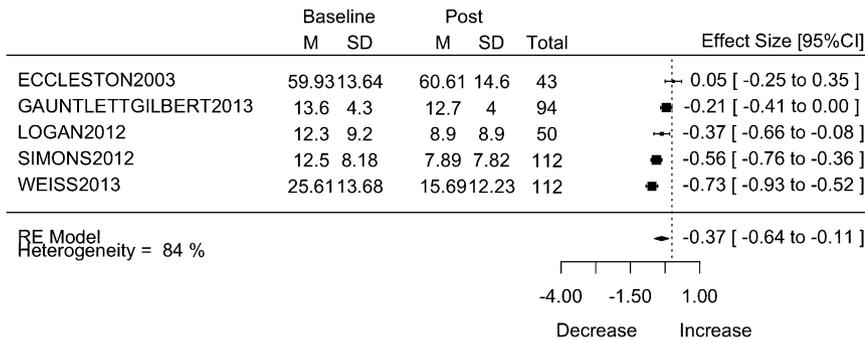
The preliminary evidence for positive treatment effects of the IIPT show particular promise when compared with the following: (1) treatment effects of psychological interventions for children with chronic pain,[43] for the present review, we compared the present treatment effects with treatment effects of psychological interventions for non–headache pain only,[43] as this sample included children with various pain conditions; (2) benchmarks of treatment effects of psychological treatments for adults with chronic pain[44]; and (3) treatment effects of IIPT for adults with chronic low back pain.[13] Comparing psychological interventions for children ($SMD_{psychological\_children} = -0.45$) with benchmarks for adult psychological treatment ($d_{benchmark} = 0.37$) and with IIPT for adults (median effect size$_{IIPT\_adults} = 0.54$), we observed

larger effects for reductions in disability for IIPT posttreatment ($d_{IIPT:\ NRS} = -1.09$; $d_{IIPT:\ RCT} = -0.80$). Results need to be interpreted with caution because of the lack of RCTs and the study weaknesses of the NRSs. However, they suggest that the collaborative treatment goal to improve functioning despite ongoing pain may be achieved immediately in children and maintained at short-term follow-up. This is important given that the affected children suffer for an average of 3 years before initiating IIPT.[4]

In this review, IIPT had only small immediate effects in the RCT on reducing pain intensity ($d_{IIPT:\ RCT} = -0.38$) and no effect in the NRSs but large effects in both, RCT and NRS, at short-term follow-up ($d_{IIPT:\ RCT} = -1.19$; $d_{IIPT:\ NRS} = -1.33$). In comparison, there is evidence of moderate beneficial effects of psychological therapies on pain reduction posttreatment ($SMD_{psychological\_children} = -0.57$) and of no beneficial effects at follow-up.[43] In accordance with clinical experience and recent research,[45] results suggest that IIPT may elicit rapid improvements in disability independent of changes in pain intensity. This needs to be confirmed in future well-designed trials.

In line with treatment effects of cognitive-behavioral therapy for adolescent depression, which yields moderate treatment effects ($d_{depression} = 0.53$),[46] the single RCT found moderate effects at short-term follow-up ($d_{IIPT:\ RCT} = -0.59$). The NRSs found small effects ($d_{IIPT:\ NRS} = -0.40$) and psychological interventions for children with chronic pain yielded no effect.[43] These potentially positive findings of the IIPT on depressive symptoms warrant replication in future well-designed RCTs. High rates of emotional distress in children with highly disabling chronic pain[4] and high rates of comorbidity with full-blown diagnosis of psychological

Changes in depressive symptoms from baseline to immediate post-treatment

	Baseline		Post				Effect Size [95%CI]
	M	SD	M	SD	Total		
ECCLESTON2003	59.93	13.64	60.61	14.6	43		0.05 [-0.25 to 0.35]
GAUNTLETTGILBERT2013	13.6	4.3	12.7	4	94		-0.21 [-0.41 to 0.00]
LOGAN2012	12.3	9.2	8.9	8.9	50		-0.37 [-0.66 to -0.08]
SIMONS2012	12.5	8.18	7.89	7.82	112		-0.56 [-0.76 to -0.36]
WEISS2013	25.61	13.68	15.69	12.23	112		-0.73 [-0.93 to -0.52]
RE Model Heterogeneity = 84 %							-0.37 [-0.64 to -0.11]

```
        -4.00   -1.50   1.00
         Decrease      Increase
```

Changes in depressive symptoms from baseline to short-term follow-up

	Baseline		Follow-up				Effect Size [95%CI]
	M	SD	M	SD	Total		
ECCLESTON2003	59.93	13.64	58.8	13.87	43		-0.08 [-0.38 to 0.22]
GAUNTLETTGILBERT2013	13.6	4.3	12.7	5.2	73		-0.21 [-0.44 to 0.02]
HIRSCHFELD2013	13.19	7.89	8.59	6.92	73		-0.58 [-0.83 to -0.33]
SIMONS2012	12.5	8.18	6.88	7.81	96		-0.69 [-0.91 to -0.46]
RE Model Heterogeneity = 81 %							-0.40 [-0.68 to -0.12]

```
        -4.00   -1.50   1.00
         Decrease      Increase
```

FIGURE 4
Effect sizes (*d*) for changes in symptoms of depression from baseline to posttreatment and 3-month follow-up.

disorders[47] call for adequate interventions to decrease both pain and emotional distress. Future research on the effects of IIPT needs to clarify if the IIPT constitutes such an intervention.

Although the results show promise, previous studies have illustrated that pediatric chronic pain that results in significant distress and disability is sustained or even aggravated when not treated adequately.[36,48] To effectively address this concern, increasing the numbers of IIPTs for children and adolescents may be important. Recent studies showing the costs of complex pediatric pain[5] and studies into the efficiency of IIPT[9] may support the efforts of both increasing these programs and insurance coverage. The dissemination of IIPT protocols may facilitate the initiation of new programs and support more

clinical trials. Recent treatment manuals,[49] and characteristics of existing IIPTs provided in this review, may be valuable sources of information.

Several major limitations should be noted when interpreting the results of the present review. With the exception of the RCT, the NRSs were all lacking a control group, which hampers any causal interpretation of the positive findings and any weighing up the merits of the IIPT against alternative interventions. Clearly, the implementation of a control group constitutes a challenge, especially when testing interventions with severely affected children. There are at least 2 solutions at hand. First, NRS interventions could include a comparison group (eg, inpatient versus outpatient treatment). Two previous studies support this,

showing that children who participated in IIPT outperformed children in outpatient treatment in reductions in disability.[36,50] Second, assessment of effectiveness can be made by using benchmarks of expected treatment effects, as recently provided for treatment effects of psychological treatments for adults with chronic pain.[44]

We also found that none of the NRSs reported any sample-size or sensitivity analysis. This makes it very hard to assess the potential number of missed true effects and spurious findings. Furthermore, the pooled effect estimates for the NRSs exhibited considerable heterogeneity that may be related to differences in study design.

Because of substantial heterogeneity, especially for measures for school functioning and symptoms of anxiety, meta-analyses could not be computed. Even though the summary of separate effect sizes for the measures suggested positive treatment effects, recommendations for standardized assessments are warranted and need to be implemented in future clinical trials so that data can be pooled for future meta-analyses.

Although many IIPT programs focus on medical and physiologic aspects, the present review did not allow summarizing explicit effects of pain medication on pain intensity or functional outcomes because of a lack of data. An additional limitation is that the age range for the target population was wide (8–22 years), which also can limit conclusions regarding the effectiveness of IIPT for particular age groups. In addition, although all studies except 2[26,30] included children and adolescents exclusively aged between 8 and 18 years, the 2 studies with older participants did not discuss how they addressed the use of measures validated for children. This is clearly a focus for future research that warrants a more developmental focus

HECHLER et al

and a greater understanding of age differences in treatment response.[51]

CONCLUSIONS

The present review suggests that IIPT may be effective in immediately reducing disability and in maintaining this reduction. These effects seem to be independent of changes in pain intensity. IIPT yields small to moderate effects for symptoms of depression. Because of the paucity of studies into the effectiveness and efficacy of IIPT, and the weaknesses of the included NRSs, results need to be interpreted with caution. Combined efforts of health care sponsors, health care providers, and clinical researchers are needed to increase the number of IIPTs worldwide, to increase the number of clinical trials with standardized assessment of relevant outcome domains, and with more vigorous study designs that enable an assessment of IIPT efficacy and effectiveness. These efforts may result in appropriate health care structures for highly disabled children and may prevent long-term aggravation of pediatric chronic pain that results in significant distress and disability.

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ABBREVIATIONS

CI: confidence interval
IIPT: intensive interdisciplinary pain treatment
NRS: nonrandomized treatment study
RCT: randomized controlled trial
SMD: Standardised Mean Difference

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BOARDING ALL ROWS: *I recently had a very long overseas trip that involved multiple airlines and stopovers. At each stopover I was instructed to be at the departure gate more than 30 minutes before boarding time. Beyond that, however, each airline had their own approach to boarding passengers. Some loaded back to front while others boarded those in window seats first. I always thought the mathematics of unloading and boarding passengers fascinating (if seemingly imprecise). However, the logistics of boarding a plane, even a jumbo jet, pale beside the logistics of boarding a cruise ship.*

As reported in The New York Times *(Business Day: March 21, 2015), large cruise ships need to unload up to 6,000 arriving passengers and load 6,000 departing passengers all in less than 12 hours. Additionally, all the cabins need to be cleaned, the luggage must be sorted, and enough fresh provisions for a small city must be stored. Cruise ships have much larger crews than airlines (around 2,000 or more), but nonetheless, the amount that needs to be done in such a short time is incredible. Each step is elaborately choreographed to save time and avoid costly bottlenecks. Efficiency experts have conducted time and motion studies on the workers to improve efficiency. Design teams make exquisitely detailed recommendations. For example, the first task of the housekeepers is to separate and remove the bedding and linens to be cleaned from each cabin and store them in the hallway, which saves time later in the cleaning and sorting process. The housekeepers work independently until making the beds, at which time they team up. Such efficiencies allow a staff of less than 200 to clean more than 2,700 rooms in just a few hours.*

I do not cruise, so I cannot speak directly to the experience. While I do find the airline boarding process cumbersome, maybe one reason the cruise ships seem to do so well is that they do not have to deal with passengers trying to put oversize bags into overhead compartments.

Noted by WVR, MD

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