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

Tanja Hechler, PhD, MSc, Marie Kanstrup, MSc, Amy Lewandowski Holley, PhD, MSc, Laura E. Simons, PhD, MSc, Rikard Wicksell, PhD, MSc, Gerrit Hirschfeld, PhD, MSc, Boris Zernikow, MD, PhD

**abstract**

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

**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 IIP, 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 IIP 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 IIP, but the small number of studies and their methodological weaknesses suggest a need for more research on IIPs for children.

This trial has been registered with PROSPERO (http://www.crd.york.ac.uk/PROSPERO/) (identifier CRD42014010719).

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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. The most common chronic pain conditions include headache, functional abdominal pain, and musculoskeletal pain, including back pain. 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. Children and their families exact high costs on the health care system, estimated to be $19.5 billion annually in the United States. 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. 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. Intensive interdisciplinary pain treatment (I IPT) has gained increased support as a treatment of choice for these children. IPT 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. Furthermore, IPT implies that treatment is provided in an inpatient or day hospital setting, 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. 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 IPT in adult patients and into the mechanisms that account for the positive outcomes, there is a dearth of research into the effectiveness of IPT for children and adolescents. Previous reviews highlight the effectiveness of psychological therapies for the treatment of chronic pain in youth, but no reviews have examined the benefits of IPT, despite the growing need for and interest in this particular form of treatment. In addition, although we know the components of IPT 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 IPT. Our aims were twofold. First, we aimed to describe the nature of the IPT 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 IPT at immediate posttreatment and follow-up. 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 IPT that did not use randomization. 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), (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

METHOD
The review was registered with PROSPERO and the detailed study protocol can be accessed under the registration number CRD42014010719.
<table>
<thead>
<tr>
<th>Author</th>
<th>Treatment Setting</th>
<th>Study Design</th>
<th>Pain Location/ Diagnosis*</th>
<th>Treatment Duration, in Weekdays</th>
<th>Baseline, n</th>
<th>Post, n</th>
<th>FU1, n</th>
<th>FU2, n</th>
<th>Outcome Domains Assessments After IIPT, mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chalkiadis et al24</td>
<td>Inpatient</td>
<td>NRS: Cross-sectional</td>
<td>51% comorbid medical condition 30% no clear etiology for pain 19% organic precipitant</td>
<td>5</td>
<td>207</td>
<td>207</td>
<td>No. of children with school absence</td>
<td>Not specified</td>
<td></td>
</tr>
<tr>
<td>Eccleston et al25</td>
<td>Day hospital</td>
<td>NRS: Case series</td>
<td>CRPS 28.4% 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%</td>
<td>18</td>
<td>57</td>
<td>56</td>
<td>43</td>
<td>Pain Post</td>
<td></td>
</tr>
<tr>
<td>Gauntlett-Gilbert et al26</td>
<td>Day hospital</td>
<td>NRS: Case series</td>
<td>CRPS 27%</td>
<td>27% 15 98 94 73</td>
<td>Pain Post</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hechler et al27b</td>
<td>Inpatient</td>
<td>NRS: Case series</td>
<td>Headache 30% Diffuse idiopathic 21% Abdominal pain 18% Localized idiopathic 12% Back pain 6% CRPS 6% Disease related 3% Fibromyalgia 3%</td>
<td>15</td>
<td>33</td>
<td>26</td>
<td>31</td>
<td>Pain 3</td>
<td></td>
</tr>
<tr>
<td>Hechler et al27b</td>
<td>Inpatient</td>
<td>RCT</td>
<td>Headache 79% Musculoskeletal pain diagnosis 54% Abdominal pain diagnosis 28% Other pain diagnosis 8%</td>
<td>15</td>
<td>IG = 61</td>
<td>IG = 52</td>
<td>IG = 50</td>
<td>IG = 44</td>
<td>Pain 6</td>
</tr>
<tr>
<td>Hirschfeld et al28</td>
<td>Inpatient</td>
<td>NRS: Case series</td>
<td>Headache 50% Abdominal pain 13% Back pain 10% Diffuse idiopathic 9% Disease related 7% Fibromyalgia 9% Localized idiopathic 4% CRPS 3%</td>
<td>15</td>
<td>167</td>
<td>141</td>
<td>136</td>
<td>Pain 3</td>
<td></td>
</tr>
<tr>
<td>Logan et al29</td>
<td>Day hospital</td>
<td>NRS: Case series</td>
<td>CRPS 84.3%, 33.7% neuropathic pain (not meeting full criteria for CRPS)</td>
<td>15</td>
<td>56</td>
<td>55</td>
<td>30</td>
<td>Pain 2-24</td>
<td></td>
</tr>
</tbody>
</table>

*Pain Location/ Diagnosis: In patients with comorbid medical conditions, pain is described in the context of associated medical conditions. In patients without comorbid medical conditions, pain is described as idiopathic or specific to the area of pain.
interdisciplinary or multiprofessional
team(s), 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. 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 most commonly used in the other
studies. Pain intensity outcomes were
assessed by using a numerical rating
scale (NRS) or a visual analog scale. The
disability outcomes were assessed by
two independent researchers
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.

### TABLE 1

<table>
<thead>
<tr>
<th>Author</th>
<th>Treatment Setting</th>
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<th>Treatment Duration, in Weekdays</th>
<th>Baseline, n</th>
<th>Post, n</th>
<th>FU1, n</th>
<th>FU2, n</th>
<th>Outcome Domains</th>
<th>Assessments After IAPT, mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maynard et al</td>
<td>Rehabilitation</td>
<td>NRS: retrospective chart review</td>
<td>CRPS 48% 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%</td>
<td>27</td>
<td>41</td>
<td>41</td>
<td>19</td>
<td>Disability No. of children with school absence</td>
<td>Post 3</td>
<td></td>
</tr>
<tr>
<td>Simons et al</td>
<td>Day hospital</td>
<td>NRS: Case series</td>
<td>Neuropathic pain 93% Musculoskeletal pain 7%</td>
<td>15</td>
<td>145</td>
<td>141</td>
<td>125</td>
<td>Pain Disability Anxiety (pain-specific) Depressive symptoms</td>
<td>Post 2</td>
<td></td>
</tr>
<tr>
<td>Weiss et al</td>
<td>Rehabilitation</td>
<td>NRS: Case series</td>
<td>Abdominal pain 30% Headache 28% Generalized 25% Back/neck pain 8% Extremities 7% Pelvic area 2%</td>
<td>15</td>
<td>112</td>
<td>112</td>
<td></td>
<td>Pain Disability Anxiety (pain-specific) Depressive symptoms</td>
<td>Post</td>
<td></td>
</tr>
</tbody>
</table>

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.

As reported in the studies.

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

The outcomes used in each trial for the respective domains are shown in Table 1.
**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. 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. By use of the first, randomization bias, allocation bias, blinding bias, incomplete outcome data, and selective reporting bias in the RCT were assessed. 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**

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

FIGURE 1

PRISMA flow diagram.
The Quality Appraisal Tool for case series\textsuperscript{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.\textsuperscript{32} The items were used for a detailed description of the included NRSs (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,\textsuperscript{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,\textsuperscript{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\textsuperscript{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

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Post</th>
<th>Effect Size [95%CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M  SD</td>
<td>M  SD</td>
<td>Total</td>
</tr>
<tr>
<td>ECLESTON2003</td>
<td>6.69 2.04</td>
<td>6.91 2.01</td>
<td>43</td>
</tr>
<tr>
<td>GAUNTLETTGILBERT2013</td>
<td>7.8 1.3</td>
<td>7.7 1.4</td>
<td>94</td>
</tr>
<tr>
<td>LOGAN2012</td>
<td>6.5 2.5</td>
<td>4.7 3.1</td>
<td>50</td>
</tr>
<tr>
<td>SIMONS2012</td>
<td>6.42 2.15</td>
<td>5.16 2.75</td>
<td>141</td>
</tr>
</tbody>
</table>

*Effect size $= \overline{\text{Post}} - \overline{\text{Baseline}} / \text{SD Baseline}*$

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

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Follow-up</th>
<th>Effect Size [95%CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M  SD</td>
<td>M  SD</td>
<td>Total</td>
</tr>
<tr>
<td>ECLESTON2003</td>
<td>6.69 2.04</td>
<td>6.51 2.25</td>
<td>43</td>
</tr>
<tr>
<td>GAUNTLETTGILBERT2013</td>
<td>7.8 1.3</td>
<td>7.2 2</td>
<td>73</td>
</tr>
<tr>
<td>HECHLER2010-children</td>
<td>6.5 1.6</td>
<td>2.3 2.9</td>
<td>33</td>
</tr>
<tr>
<td>HIRSCHFELD2013</td>
<td>6.83 1.78</td>
<td>2.83 2.66</td>
<td>120</td>
</tr>
<tr>
<td>SIMONS2012</td>
<td>6.42 2.15</td>
<td>3.54 3</td>
<td>122</td>
</tr>
</tbody>
</table>

*Effect size $= \overline{\text{Follow-up}} - \overline{\text{Baseline}} / \text{SD Baseline}*$

**FIGURE 2**
Effect sizes ($d$) for changes in pain intensity from baseline to immediate posttreatment and to 3-month follow-up.
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 RCT9 and 9 NRSs12,17,24–30 (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.

Changes in disability from baseline to immediate post-treatment

<table>
<thead>
<tr>
<th></th>
<th>Baseline M</th>
<th>SD</th>
<th>Post M</th>
<th>SD</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>ECLESTON2003</td>
<td>34.25</td>
<td>6.94</td>
<td>30.27</td>
<td>12.08</td>
<td>43</td>
</tr>
<tr>
<td>GAUNTLTTGILBERT2013</td>
<td>18.4</td>
<td>6.5</td>
<td>16.1</td>
<td>6.5</td>
<td>94</td>
</tr>
<tr>
<td>LOGAN2012</td>
<td>29 10</td>
<td>9</td>
<td>7</td>
<td>48</td>
<td>-0.57</td>
</tr>
<tr>
<td>MAYNARD2010</td>
<td>19.5 14.8</td>
<td>10.6</td>
<td>9.5</td>
<td>41</td>
<td>-0.60</td>
</tr>
<tr>
<td>SIMONS2012</td>
<td>32 10.3</td>
<td>9.76</td>
<td>8.29</td>
<td>115</td>
<td>2.16</td>
</tr>
<tr>
<td>WEISS2013</td>
<td>23.84</td>
<td>11.57</td>
<td>12.79</td>
<td>11.05</td>
<td>-0.96</td>
</tr>
</tbody>
</table>

Re Model
Heterogeneity = 96%
-4.00 -1.50 1.00
Decrease Increase

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

<table>
<thead>
<tr>
<th></th>
<th>Baseline M</th>
<th>SD</th>
<th>Follow-up M</th>
<th>SD</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>ECLESTON2003</td>
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<td>6.94</td>
<td>29.32</td>
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<td>43</td>
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<td>6.5</td>
<td>15.1</td>
<td>7.6</td>
<td>73</td>
</tr>
<tr>
<td>HIRSCHFELD2013</td>
<td>35.2</td>
<td>8.1</td>
<td>28.1</td>
<td>12.6</td>
<td>31</td>
</tr>
<tr>
<td>LOGAN2012</td>
<td>39.19 18.5</td>
<td>22.82</td>
<td>9.06</td>
<td>109</td>
<td>-1.92</td>
</tr>
<tr>
<td>MAYNARD2010</td>
<td>29 10</td>
<td>8.2</td>
<td>8.5</td>
<td>41</td>
<td>-2.08</td>
</tr>
<tr>
<td>SIMONS2012</td>
<td>19.5 14.8</td>
<td>4.5</td>
<td>5.2</td>
<td>19</td>
<td>-1.01</td>
</tr>
<tr>
<td>WEISS2013</td>
<td>32 10.3</td>
<td>7.69</td>
<td>9.22</td>
<td>97</td>
<td>-2.36</td>
</tr>
</tbody>
</table>

Re Model
Heterogeneity = 94%
-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.
(5 studies), reinforcement of the child’s functional behavior (6 studies), and strategies to reduce parental attention on the child’s pain (3 studies).

**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 effect of IIPT in the RCT \((d = -1.19\); 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 effect sizes 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 4 Descriptive Data on Assessment and Effect Sizes for Separate Measures of Anxiety

<table>
<thead>
<tr>
<th>Author and Year</th>
<th>Study Design</th>
<th>Component of Anxiety</th>
<th>Measure</th>
<th>Changes in Anxiety From Baseline to Immediate Posttreatment</th>
<th>95% CI</th>
<th>Changes in Anxiety From Baseline to Short-term Follow-up</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>ECCLESTON2003</td>
<td>NRS: Case series</td>
<td>General</td>
<td>Spence Children’s Anxiety Scale</td>
<td>Effect Size d</td>
<td>−0.06</td>
<td>−0.36 to 0.24</td>
<td>−0.58</td>
</tr>
<tr>
<td>HIRSCHFELD2013</td>
<td>NRS: Case series</td>
<td>Pain-specific</td>
<td>Anxiety Questionnaire for Pupils</td>
<td>Effect Size d</td>
<td>−0.38</td>
<td>0.69 to −0.07</td>
<td>−0.07 to 0.25</td>
</tr>
<tr>
<td>LOGAN2012</td>
<td>NRS: Case series</td>
<td>Pain-specific</td>
<td>Multidimensional Anxiety Scale</td>
<td>Effect Size d</td>
<td>−1.25 to −0.59</td>
<td>−0.07</td>
<td></td>
</tr>
<tr>
<td>GAUNTLETTGilbert2013</td>
<td>NRS: Case series</td>
<td>Pain-specific</td>
<td>Pain Catastrophizing Scale for Children</td>
<td>Effect Size d</td>
<td>0.50</td>
<td>0.74 to −0.25</td>
<td>0.85</td>
</tr>
<tr>
<td>SHEPPARD2012</td>
<td>NRS: Case series</td>
<td>Pain-specific</td>
<td>Pain Catastrophizing Scale for Children</td>
<td>Effect Size d</td>
<td>1.02</td>
<td>1.39 to −0.66</td>
<td>1.02</td>
</tr>
<tr>
<td>SIMONS2012</td>
<td>NRS: Case series</td>
<td>Pain-specific</td>
<td>Fear of Pain Questionnaire for Children</td>
<td>Effect Size d</td>
<td>−1.14</td>
<td>1.06 to −0.63</td>
<td>−1.57</td>
</tr>
</tbody>
</table>

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

The aim of the present review was to evaluate the effectiveness of IIPT for children with chronic pain 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 pain, and no improvement was observed for disability posttreatment (d = 0.39) and no effect in the NRSs but large effects in both RCT and NRS at short-term follow-up (d = 1.33). In conclusion, IIPT may elicit rapid improvements in disabled children with chronic pain who have received interventions for previous treatment effects of IIPT on depressive symptoms and of psychological therapies on pain intensity. This needs to be confirmed in future well-designed trials.

Compared to psychological interventions (SSM) of psychological treatments for adults (SSM = 0.45), we observed larger effects for reductions in disability for IIPT posttreatment (SSM = 0.53) for children with chronic pain yields positive effects on treatment effects of IIPT show particular promise when compared with the following: (1) treatment effects of psychological interventions for non-headache pain only; (2) benchmarks of treatment effects for adults with chronic pain, and (3) the preliminary evidence for positive effects of IIPT on depressive symptoms of children with the IIPT on depressive symptoms of children with chronic low back pain.13 These potentially positive findings of IIPT on depressive symptoms of children with chronic pain yielded to effect size = 0.51, with highly disabling chronic pain and high rates of comorbidity, suggest that IIPT may elicit rapid improvements in disabled children with chronic pain who have received previous treatment effects of IIPT on depressive symptoms and of psychological interventions on pain intensity. This needs to be confirmed in future well-designed trials.

In this review, IIPT had only small improvements in disability (d = 0.19) and no effect in the NRSs but large effects in both RCT and NRS at short-term follow-up (d = 1.33). In conclusion, IIPT may elicit rapid improvements in disabled children with chronic pain who have received previous treatment effects of IIPT on depressive symptoms and of psychological interventions on pain intensity. This needs to be confirmed in future well-designed trials.

In the follow-up (d = 0.53) of the single RCT found moderate effects for psychological interventions for children with chronic pain, and of psychological treatments for adults (SSM = 0.45), with highly disabling chronic pain and high rates of comorbidity, suggest that IIPT may elicit rapid improvements in disabled children with chronic pain who have received previous treatment effects of IIPT on depressive symptoms and of psychological interventions on pain intensity. This needs to be confirmed in future well-designed trials.

In conclusion, IIPT may elicit rapid improvements in disabled children with chronic pain who have received previous treatment effects of IIPT on depressive symptoms and of psychological interventions on pain intensity. This needs to be confirmed in future well-designed trials.
disorders 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. 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 and studies into the efficiency of IIPT may support the efforts of both increasing these programs and insurance coverage. The dissemination of IIP protocols may facilitate the initiation of new programs and support more clinical trials. Recent treatment manuals 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 (e.g., 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. 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.

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 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.

<table>
<thead>
<tr>
<th></th>
<th>Baseline M</th>
<th>SD</th>
<th>Post M</th>
<th>SD</th>
<th>Total</th>
<th>Effect Size [95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>ECCLESTON2003</td>
<td>59.93</td>
<td>13.64</td>
<td>60.61</td>
<td>14.6</td>
<td>43</td>
<td>0.05 [-0.25 to 0.35]</td>
</tr>
<tr>
<td>GAUNTLITTGILBERT2013</td>
<td>13.6</td>
<td>4.3</td>
<td>12.7</td>
<td>4</td>
<td>94</td>
<td>-0.21 [-0.41 to 0.00]</td>
</tr>
<tr>
<td>LOGAN2012</td>
<td>12.3</td>
<td>9.2</td>
<td>8.9</td>
<td>8.9</td>
<td>50</td>
<td>-0.37 [-0.66 to -0.08]</td>
</tr>
<tr>
<td>SIMONS2012</td>
<td>12.5</td>
<td>8.18</td>
<td>7.89</td>
<td>7.82</td>
<td>112</td>
<td>-0.56 [-0.76 to -0.36]</td>
</tr>
<tr>
<td>WEISS2013</td>
<td>25.6</td>
<td>11.38</td>
<td>15.69</td>
<td>12.23</td>
<td>112</td>
<td>-0.73 [-0.93 to -0.52]</td>
</tr>
</tbody>
</table>

Re Model Heterogeneity = 84%
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.

ACKNOWLEDGMENTS

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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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Hechler T, Wagner J, Zernikow B. Chronic pain treatment in children and adolescents: less is good, more is sometimes better. BMC Pediatr. 2014;14:262


**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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Tanja Hechler, Marie Kanstrup, Amy Lewandowski Holley, Laura E. Simons, Rikard Wicksell, Gerrit Hirschfeld and Boris Zernikow

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