# Depressive Symptoms in Children and Adolescents with Chronic Physical Illness: An Updated Meta-Analysis

Martin Pinquart, PhD, and Yuhui Shen, Cand Psych
*Department of Psychology, Philipps University*

All correspondence concerning this article should be addressed to Martin Pinquart, PHD, Department of Psychology, Philipps University, D-35032 Marburg, Germany. E-mail: pinquart@staff.uni-marburg.de

Received July 8, 2010; revisions received and accepted October 20, 2010

**Objective** To integrate results of available studies that compared levels of depressive symptoms of children and adolescents with chronic physical illness to healthy peers or test norms. **Methods** Random-effects meta-analysis was computed with 340 studies and 450 subsamples. **Results** Children and adolescents with chronic illness have, on average, higher levels of depressive symptoms than their healthy peers ($d = .19$ *SD* units). Differences are strongest for chronic fatigue syndrome ($d = .94$), fibromyalgia ($d = .59$), cleft lip and palate ($d = .54$), migraine/tension head ache ($d = .51$), and epilepsy ($d = .39$). Larger effect sizes were found in studies with higher proportion of girls, with a healthy control group, from developing countries, published before 1990, and that used parent rating or clinician ratings rather than child ratings. **Conclusions** Pediatricians and others working with children with chronic illnesses should screen children with chronic physical illness for symptoms of psychological distress and make appropriate referrals for mental health services, when needed.

**Key words** chronic illness; depression; meta-analysis; psychological functioning; psychological health.

In the United States, the number of children and adolescents with chronic health conditions has increased dramatically in the past four decades (Perrin, Bloom, & Gortmaker, 2007). Although results from epidemiological studies differ considerably, an overview of articles found that, on average, 15% of children and adolescents have a chronic health condition (van der Lee, Mokkink, Grootenhuis, Heymans, & Offringa, 2007).

Chronic illness is a risk factor for psychological problems, such as depressive symptoms (e.g., Bennett, 1994). For example, the presence of physical symptoms, such as pain and fatigue, combined with the need for disease management regimes, are likely to interfere with many aspects of daily life, such as regular school attendance and maintaining peer relations, and may cause frustration (e.g., Suris, Michaud, & Viner, 2004). Children with chronic illness may feel different from his peers and experience peer rejection, which may have detrimental effects on their self-concept (e.g., Sandstrom & Schanberg, 2004). In addition, chronic illnesses may foster inappropriate parental attitudes and behaviors, ranging from overprotection to rejection, which may impair psychological well-being (e.g., Holmbeck et al., 2002). In some cases, poor prognosis may cause feelings of helplessness and hopelessness. Finally, side effects of treatments may cause psychological distress (e.g., Miller et al., 2008).

A meta-analysis by Bennett (1994) on 60 statistical effects from 46 studies found that children and adolescents with chronic medical problems have elevated levels of depressive symptoms, but differences with test norms or healthy control groups were small (mean $d = .27$ *SD* units). Because (a) the number of studies has increased considerably since this meta-analysis, (b) the effects of chronic illness on depressive symptoms may have changed over time, and (c) the previous meta-analysis could not test for moderating effects of many study characteristics, the

*Journal of Pediatric Psychology* 36(4) pp. 375–384, 2011
doi:10.1093/jpepsy/jsq104
Advance Access publication November 18, 2010
*Journal of Pediatric Psychology* vol. 36 no. 4 © The Author 2010. Published by Oxford University Press on behalf of the Society of Pediatric Psychology.
All rights reserved. For permissions, please e-mail: journals.permissions@oup.com

Downloaded from https://academic.oup.com/jpepsy/article/36/4/375/926006 by U.S. Department of Justice user on 16 August 2022

goal of the present study was to provide an updated meta-analysis on the association between chronic physical illness and depressive symptoms in children and adolescents.

Depressive symptoms have to be distinguished from a depressive disorder, such as major depression. Rating scales assess depressive symptoms as a continuous variable, and scores above defined cutoffs on valid scales would imply a depressive disorder. However, depression diagnosis is based on a clinical interview, and a number of symptoms have to be present during a specified time period (Emslie & Mayers, 1999). Because about 90% of the available studies with chronically ill children used depression rating scales rather than clinical diagnoses, the present meta-analysis focuses on depressive symptoms.

## Research Questions

In the first research question we ask whether children and adolescents with chronic physical illnesses have elevated levels of depressive symptoms, and whether this would differ between illnesses. Some authors have argued that the nature of the child's disorder is not important in determining its psychological consequences, because children with chronic physical disorders face common life experiences and problems based on generic dimensions of their conditions, rather than on idiosyncratic characteristics of any specific disease entity (e.g., Stein & Jessop, 1982). Other authors have suggested that certain illness characteristics or parameters may be more related to depressive symptoms, such as neurologically related illnesses (e.g., epilepsy; Plioplys, 2003), characteristics of illnesses that have social implications (e.g., cosmetic effects, e.g., cleft lip; De Sousa, Devare, & Ghanshani, 2009), and chronic pain (Eccleston, Crombez, Scotford, Clinch, & Connell, 2004). Bennett (1994) reported moderate effect sizes for asthma ($d = .54$) and sickle cell disease ($d = .48$), a small effect size for diabetes ($d = .22$), and no elevated levels of depressive symptoms in young people with cancer ($d = .00$) and cystic fibrosis ($d = -.04$). However, due to the small number of studies per type of illness ($N = 4$–13), effect sizes were not tested to see if they differed significantly from zero or if illnesses differed from one another.

In the second research question we analyze whether the effect sizes would differ by other study characteristics.

### *Age*

On the one hand, depressive symptoms are more common in adolescence than in childhood, and adolescents may be confronted with more illness-related stressors than children (e.g., when chronic illnesses hinder the development of peer groups and intimate relationships; Suris et al., 2004). On the other hand, adolescents might also have better coping abilities (e.g., because of higher cognitive abilities; Skinner & Zimmer-Gembeck, 2007). Thus, average age differences in the association between chronic illness and depressive symptoms are probably small. Bennett (1994) reported that age was generally unrelated to depressive symptoms, but he did not provide results from a statistical test of age differences.

### *Gender*

On average, female adolescents are more likely than males to react to stressors with depressive symptoms (Piccinelli & Wilkinson, 2000), which could lead to stronger effects of chronic illness on depressive symptoms. Bennett (1994) reported that the results of individual studies were inconsistent but he did not formally test for gender differences.

### *Race/Ethnicity*

Because it is less clear whether race/ethnicity would moderate the size of between-group differences, we did not state a hypothesis.

### *Country*

Because young people from industrialized, developed countries may have better access to health care than their peers from developing countries, we expected finding lower between-group differences in depressive symptoms in developed countries.

### *Year of Publication*

Progress in the treatment of many diseases (e.g., Bleyer, 2002) and the development of services for young people with chronic illness may lead to lower between-group differences in more recent studies.

### *Rater and Assessment Methods*

Bennett (1994) found higher between-group differences in parent-rated depressive symptoms ($d = 0.58$) than in self-rated depressive symptoms ($d = 0.02$), which may either indicate that young patients tend to underreport their psychological symptoms or that parents underestimate their children's ability to adapt to their illness. Differences between raters were also expected to lead to higher levels of depressive symptoms in young people with chronic illnesses in studies that used parent ratings as a measure of depressive symptoms (e.g., the Affective Problems scale of the Child Behavior Checklist (CBCL);

Downloaded from https://academic.oup.com/jpepsy/article/36/4/375/926006 by U.S. Department of Justice user on 16 August 2022

Achenbach, Dumenci, & Rescorla, 2003) than in studies that used self-reports of the child.

### *Duration of Illness*

A longer duration of the disease gives more time for psychological adaptation, but may also lead to an accumulation of negative illness-related consequences, such as the effect of repeated school absence on grades. Thus, we did not state a specific hypothesis.

### *Study Quality*

Associations of chronic illness with depressive symptoms may be stronger in clinical convenience samples than in representative community-based samples, because clinical samples may overrepresent highly distressed young people seeking treatment for their chronic disease. Similarly, the size of between-group differences in depressive symptoms may vary between studies that used groups matched on sociodemographic variables and studies that did not control for these between-group differences, because the lack of control for demographic variables may cause unsystematic bias rather than a general overestimation or underestimation of between-group differences in depressive symptoms.

### *Target of Comparison*

Finally, between-group differences may be larger in studies that compared children with chronic illnesses to healthy peers than in studies that compared depressive symptoms of chronically ill children to test norms, because the norm population probably includes some children with chronic illnesses. In fact, Bennett (1994) found such a difference ($d = 0.67$ vs. $d = 0.02$).

## Methods

### *Sample*

Studies were identified from the literature through electronic databases [PSYCINFO, MEDLINE, Google Scholar, PSNYDEX (an electronic data base of psychological literature from German-speaking countries)—search terms: (chronic illness or disability or aids or arthritis or asthma or cancer or cleft or chronic fatigue syndrome or cystic fibrosis or diabetes or fibromyalgia or hemophilia or hearing impairment or HIV or epilepsy or inflammatory bowel disease or migraine or rheumatism or sickle cell or spina bifida or visual impairment) and (children or adolescents or adolescence) and (depression or depressive or mental health or psychological health)], and cross-referencing. Criteria for inclusion of studies in the present meta-analysis were:

(a) the studies have been published before September, 2010,
(b) they compared the levels of depressive symptoms or the frequency of depression diagnoses between children and adolescents with chronic physical illness and their healthy peers or test norms, or they provided sufficient information for a comparison with established normative data (e.g., by reporting standardized *T*-scores),
(c) mean age of participants ≤18 years, and
(d) standardized between-group differences in depressive symptoms were reported or could be computed.

Documentation of physician diagnosis within each study was not a requirement, because of the need to include broad-based survey studies for which medical documentation might not be available. However, studies were excluded if they focused on young people with chronic illnesses that have been referred to psychological services due to depressive symptoms, or if sufficient information for computing effect sizes was not reported. In order to include studies from different regions around the world, we also did not limit the included studies to those written in English. Available unpublished studies were also included.

Approximately 25% of the total number of studies surveyed were eliminated, mainly because they did not assess depressive symptoms or depression diagnosis (14%), provided insufficient information about the effect sizes (4%), did not exclusively focus on children and adolescents with chronic physical illnesses (3%), had an average age of participants >18 years (1%), duplicated results of previously published studies (1%), or were not available via interlibrary loan (1%). After the exclusion of such studies, we were able to include 340 studies in the meta-analysis that provided results for 450 subsamples. The studies included are listed in the Appendix S1 (see the Supplementary Data).

We entered the number of patients and control group members, mean age, percentage of girls and of members of ethnic minorities, the country of data collection, year of publication, type of illness, duration of illness, the sampling procedure (1 = probability samples, 0 = convenience samples), the use of a control group (0 = yes, 1 = comparison with test norms), equivalence of patients and control group (1 = yes, 2 = not tested, 3 = no), the rater of depressive symptoms (1 = child, 2 = parent, 3 = teacher, 4 = clinician), the measurement of the variables, and the standardized size of between-group differences in

Downloaded from https://academic.oup.com/jpepsy/article/36/4/375/926006 by U.S. Department of Justice user on 16 August 2022

depressive symptoms. If between-group differences were provided for several subgroups within the same publication (e.g., for different illnesses), we entered them separately in our analysis instead of entering the global association. If data from more than one rater were collected, we entered the effect sizes separately because we were interested in whether the effect size would vary by the source of information. However, in order to avoid a disproportional weight of these studies, we adjusted the weights of the individual effect sizes so that the sum of the weights of the effect sizes was equal to the weight of the study if only one effect size had been reported (Lipsey & Wilson, 2001). Based on one third of the coded studies, a mean inter-rater reliability of 93% (range 86–100%) was established.

### *Measures*

Depressive symptoms were most often assessed with the Child Depression Inventory (CDI; Kovacs, 1992; 203 samples), structured clinical interviews (46 samples), the Beck Depression Inventory/Beck Youth Inventory (Beck, Beck, & Jolly, 2001; 41 samples), the Behavior Assessment System for Children (Reynolds & Kamphaus, 2004; 39 samples), the Affective Problems scale of the CBCL (13 samples), and the depression scale of the Minnesota Multiphasic Personality Inventory (MMPI) (Tellegen et al., 2003; 10 samples).

Information from the World Bank (2010) was used for coding countries as developed or developing/threshold countries.

### *Statistical Integration of the Findings*

Calculations for the meta-analysis were performed in six steps, using random-effects models and the method of moments (for computations, see Lipsey & Wilson, 2001).

1. We computed effect sizes *d* for each study as the difference in depressive symptoms between the sample with chronic illness and the control sample divided by the pooled *SD*. If the authors provided only test scores for children and adolescents with chronic illness, we used the norms from the test manual for comparison. However, because Twenge and Nolen-Hoeksema (2002) provided norms for the CDI based on a much larger sample than the original manual (Kovacs, 1992), we used the norms by Twenge and Nolen-Hoeksema (2002). Outliers that were more than two *SD* from the mean of the effect sizes were recoded to the value at two *SD* (Lipsey & Wilson, 2001).
2. Effect size estimates were adjusted for bias due to overestimation of the population effect size in small samples.
3. Weighted mean effect sizes and 95% confidence intervals (95% CIs) were computed. The significance of the mean was tested by dividing the weighted mean effect size by the SE of the mean. To interpret the practical significance of the results, we used the Binomial Effect Size Display (BESD; Rosenthal & Rubin, 1982) and Cohen's criteria (Cohen, 1988). According to Cohen, differences of $d \geq .8$ are interpreted as large, of $d = .50–.79$ as medium, and of $d = .20–.49$ as small.
4. For testing whether the results may be influenced by publication bias (a trend for nonsignificant results not being published), we used the ''trim and fill'' algorithm (Duval & Tweedie, 2000), which estimates an adjusted effect size in the presence of publication bias.
5. Homogeneity of effect sizes was computed by use of the *Q* statistic.
6. In order to test the influence of moderator variables, we used an analogue of analysis of variance and weighted ordinary least squares regression analyses.

## Results

Data from 33,047 children and adolescents with chronic illnesses were included. The largest subgroups had asthma ($N = 9{,}274$), diabetes ($N = 4{,}058$), cancer ($N = 3{,}400$), migraine or tension-type head ache ($N = 2{,}300$), and epilepsy ($N = 2{,}096$). The participants had a mean age of 12.6 years ($SD = 2.6$ years); 50.2% of them were girls and 32.5% were members of ethnic minorities.

On average, children and adolescents with chronic physical illnesses had higher levels of depressive symptoms than their healthy peers—a small to very small effect (Table I). According to the BESD, 54.8% of children with chronic illnesses and 45.2% of their healthy peers would show depressive symptoms above the median. The trim-and-fill algorithm did not find any evidence for a file-drawer problem, and the original effect size remained unchanged after applying this procedure.

We computed separate effects in cases where at least five studies were available for a particular chronic disease. Separate effect sizes could be computed for 16 illnesses. Strongest between-group differences were found for chronic fatigue syndrome, fibromyalgia, migraine/tension

Downloaded from https://academic.oup.com/jpepsy/article/36/4/375/926006 by U.S. Department of Justice user on 16 August 2022

Table I. *Differences in Depression between Children with and without Chronic Illness: Univariate Analysis of Moderator Variables*

| | *k* | *d* | 95% CI | *Z* | $Q_w$ |
|---|---|---|---|---|---|
| Total difference | 450 | .19 | 0.15 to 0.23 | 9.28*** | 577.72*** |
| Kind of illness | | | | $Q_B(15,433) = 114.31$*** | |
| Arthritis/rheumatism | 24 | −.08 | −0.26 to 0.10 | −0.89 | 27.25 |
| Asthma | 56 | .12 | 0.01 to 0.23 | 2.21* | 66.52 |
| Cancer | 62 | −.07 | −0.18 to 0.04 | −1.21 | 53.65 |
| Chronic fatigue syndrome | 14 | .94 | 0.67 to 1.213 | 6.90*** | 13.62 |
| Chronic migraine/tension-type head ache | 22 | .51 | 0.32 to 0.70 | 5.25*** | 15.32 |
| Cleft lip and palate | 7 | .54 | 0.21 to 0.86 | 3.23** | 11.78 |
| Cystic fibrosis | 15 | −.05 | −0.27 to 0.18 | −0.41 | 6.96 |
| Diabetes | 57 | .09 | −0.02 to 0.20 | 1.55 | 65.51 |
| Epilepsy | 32 | .39 | 0.24 to 0.54 | 5.09*** | 35.86 |
| Fibromyalgia | 10 | .59 | 0.30 to 0.87 | 4.06*** | 10.50 |
| HIV infection/AIDS | 9 | −.02 | −0.30 to 0.26 | −0.15 | 2.61 |
| Heart disease | 5 | .23 | −0.15 to 0.62 | 1.19 | 3.90 |
| Inflammatory bowel disease | 14 | .18 | −0.05 to 0.42 | 1.52 | 22.24 |
| Sensory impairment | 9 | .31 | 0.03 to 0.58 | 2.17* | 5.48 |
| Sickle cell disease | 24 | .04 | −0.14 to 0.22 | 0.40 | 19.94 |
| Spina bifida | 9 | .30 | 0.03 to 0.58 | 2.14* | 2.84 |
| Other illnesses/mixed samples | 83 | .34 | 0.25 to 0.44 | 7.00*** | 97.00 |
| Mean age | | | | $Q_B(1,443) = 0.67$ | |
| ≤12 years | 175 | .16 | 0.09 to 0.24 | 4.45*** | 196.70 |
| >12 years | 270 | .20 | 0.15 to 0.26 | 6.89*** | 260.66 |
| Percentage of girls | | | | $Q_B(2,392) = 8.97$* | |
| <33.3% | 48 | .16 | 0.03 to 0.30 | 2.33* | 46.66 |
| 33.3–66.6% | 290 | .15 | 0.10 to 0.21 | 5.47*** | 282.44 |
| >66.6% | 57 | .36 | 0.24 to 0.49 | 5.65*** | 75.98 |
| Percentage of members of ethnic minorities | | | | $Q_B(1,175) = 2.63$ | |
| <Mean | 83 | .14 | 0.03 to 0.24 | 2.55** | 104.90* |
| >Mean | 94 | .19 | 0.07 to 0.32 | 3.63*** | 65.09 |
| Country | | | | $Q_B(1,449) = 8.12$* | |
| Developing/threshold countries | 41 | .40 | 0.25 to 0.54 | 5.33*** | 32.30 |
| Developed countries | 410 | .17 | 0.13 to 0.22 | 7.20*** | 431.40 |
| Year of publication | | | | $Q_B(2,448) = 9.81$** | |
| <1990 | 55 | .29 | 0.16 to 0.42 | 4.29*** | 55.84 |
| 1990–1999 | 128 | .08 | −0.00 to 0.17 | 1.86 | 138.37 |
| 2000–2010 | 268 | .23 | 0.17 to 0.29 | 7.75*** | 268.26 |
| Rater of depressive symptoms | | | | $Q_B(3,444) = 38.32$*** | |
| Child/adolescent | 336 | .12 | 0.07 to 0.17 | 4.67*** | 381.33* |
| Parent | 60 | .50 | 0.38 to 0.62 | 8.24*** | 44.79 |
| Teacher | 7 | .15 | −0.19 to 0.49 | 0.89 | 3.33 |
| Clinician | 47 | .34 | 0.21 to 0.48 | 5.05*** | 34.50 |
| Assessment of depression | | | | $Q_B(7,439) = 67.18$*** | |
| Beck Depression Inventory/Beck Youth Inventory | 41 | .24 | 0.10 to 0.38 | 3.34*** | 43.22 |
| Behavior Assessment System for Children | 39 | .17 | 0.03 to 0.31 | 2.38* | 23.61 |
| CBCL: Affective problems | 13 | .69 | 0.45 to 0.94 | 5.52*** | 13.37 |
| Child Depression Inventory | 203 | .03 | −0.04 to 0.09 | 0.83 | 228.03 |
| Depression scale of the MMPI | 10 | .60 | 0.28 to 0.92 | 3.74*** | 4.90 |
| Revised Child Anxiety and Depression Scale | 6 | .06 | −0.30 to 0.41 | 0.31 | 4.07 |
| Structured clinical interview | 46 | .33 | 0.20 to 0.46 | 5.11*** | 36.37 |
| Other measures | 89 | .36 | 0.26 to 0.45 | 7.40*** | 105.25 |

(continued)

Downloaded from https://academic.oup.com/jpepsy/article/36/4/375/926006 by U.S. Department of Justice user on 16 August 2022

Table I. *Continued*

| | *k* | *d* | 95% CI | *Z* | $Q_w$ |
|---|---|---|---|---|---|
| Total difference | 450 | .19 | 0.15 to 0.23 | 9.28*** | 577.72*** |
| Duration of illness | | | | $Q_B(1,179) = 0.97$ | |
| <Median (4.7 years) | 91 | .21 | 0.11 to 0.32 | 3.97*** | 99.55 |
| >Median | 90 | .14 | 0.03 to 0.24 | 2.57* | 84.86 |
| Representativeness of the sample | | | | $Q_B(1,449) = 8.04$* | |
| Convenience sample (clinical sample) | 412 | .17 | 0.13 to 0.22 | 7.19*** | 426.11 |
| Random sample/community sample | 39 | .39 | 0.25 to 0.54 | 5.33*** | 38.38 |
| Basis of comparison | | | | $Q_B(2,446) = 45.39$*** | |
| Control group | 241 | .33 | 0.27 to 0.39 | 10.89*** | 236.95 |
| Test norms | 207 | .03 | −0.03 to 0.10 | 1.00 | 223.25 |
| Equivalence of patients and control group | | | | $Q_B(2,234) = 0.13$ | |
| No | 31 | .33 | 0.17 to 0.49 | 4.09*** | 25.63 |
| Yes | 109 | .32 | 0.23 to 0.40 | 7.04*** | 122.14 |
| Not tested | 97 | .34 | 0.25 to 0.43 | 7.22*** | 94.60 |

*Note*. $k$ = number of studies; $d$ = effect size; $Z$ = test for significance of $d$. 95% CI = lower and upper limits of 95% confidence interval; $Q_w/Q_b$ = test for homogeneity of effect sizes within (w) and between (b) groups. *$p < .05$, **$p < .01$, ***$p < .001$.

type headache, epilepsy, and spina bifida. However, no significant between-group differences were found for arthritis/rheumatism, cancer, cystic fibrosis, diabetes, heart diseases, HIV infection/AIDS, inflammatory bowel disease, and sickle cell disease. Health status explained between 0% (sickle cell disease) and 18.1% (chronic fatigue syndrome) of the variance of depressive symptoms. According to the BESD, 71.3% of children with chronic fatigue syndrome show depressive symptoms above the median, as compared to 28.7% in healthy controls. In addition, 64.1% of children with fibromyalgia show depressive symptoms above the median, but only 35.9% of their healthy peers. As indicated by the non-overlap of the 95% CIs, between-group differences were stronger for chronic fatigue syndrome than for arthritis, asthma, cancer, cystic fibrosis, diabetes, epilepsy, heart disease, HIV infection, inflammatory bowel disease, sensory impairment, sickle cell disease, and spina bifida. Differences were also stronger for fibromyalgia and migraine/tension-type head ache than for arthritis, asthma, cancer, cystic fibrosis, diabetes, HIV infection, and sickle cell disease. In addition, differences were stronger for epilepsy than for arthritis, cancer, cystic fibrosis, diabetes, and sickle cell disease. Furthermore, differences were stronger for cleft lip and palate than for arthritis, cancer, cystic fibrosis, and diabetes.

The size of between-group differences did not vary by age and race/ethnic minority status. We also checked whether the results would differ between studies that included some young adults and studies that exclusively focused on adolescents, and found no significant differences [$Q(1,256) = 0.21$, NS]. However, larger between-group differences were found in samples with higher percentages of girls. Larger differences were also found in studies from developing countries than from developed countries and for studies published before 1990 than in studies that were published in the 1990s. In line with our expectations, between-group differences were stronger in studies that used parent ratings of depressive symptoms than in studies that used child reports. In addition, differences were stronger when clinician-ratings rather than child ratings were used. Regarding measures used, between-group differences were stronger in studies that used the Affective Problems scale of the CBCL than in other studies. Between-group differences were also stronger when using the Beck Depression Inventory/Beck Youth Inventory, the depression scale of the MMPI, or structured clinical interviews than when using the CDI.

Because the lack of significant effect size on the CDI may indicate that this measure might not be sensitive for depressive symptoms of young people with chronic illnesses, we also checked whether the results would be consistent in studies that compared children with chronic illness to test norms and to healthy control groups. Children with chronic physical illness reported higher CDI scores than healthy members of the control group ($d = .29$, 95% CIs .19–.39, $Z = 5.69$, $p < .001$). However, the reverse was true when comparing them to test norms ($d = -.20$, CI –0.26 to –0.14, $Z = -5.84$, $p < .001$). These results indicate that the CDI norms reported by Twenge and Nolen-Hoeksema (2002) may overestimate the prevalence of depressive symptoms in general populations, and researchers should collect data from a healthy control group. We also checked whether our results would change if we use the test norms by Kovacs (1992) but our results remained unchanged.

Downloaded from https://academic.oup.com/jpepsy/article/36/4/375/926006 by U.S. Department of Justice user on 16 August 2022

Table II. *Multivariate Test for Moderating Effects (weighted multiple linear regression analysis)*

| Variable | *B* | β | *Z* | *p* |
|---|---|---|---|---|
| Percentage girls (1 = 66% and higher, 0 = others) | .16 | .15 | 3.50 | .001 |
| Publication before 1990 (1 = yes, 0 = no) | .13 | .10 | 2.31 | .03 |
| Developed county (1 = yes, 0 = no) | −.09 | −.11 | −2.50 | .02 |
| Child rating (1 = yes, 0 = no) | −.14 | −.13 | −2.61 | .01 |
| CDI (1 = yes, 0 = no) | −.18 | −.18 | −3.83 | .001 |
| Comparison with test norm (1 = yes, 0 = no) | −.23 | −.23 | −5.23 | .001 |
| Representativeness of the sample | .05 | .03 | 0.74 | .46 |
| Constant | 1.17 | | 7.20 | .001 |
| $R^2$ | .21 | | | |
| *N* | 436 | | | |

*Note*. *B* (β) = (un-)standardized regression coefficient. $R^2$ = explained variance.

Illness duration did not moderate the size of between-group differences, but this information was available only for about one third of the included studies. Similarly, the equivalence of patient group and control group had no significant moderating effect. However, effect sizes varied by the representativeness of the sample and by target of comparison. Stronger between-group differences were found in studies with representative samples than in those with convenience samples, and in studies that compared young people with chronic illnesses against a healthy control group.

Finally, because the moderator variables may not be independent from each other, we checked whether the observed bivariate moderator effects would persist in multivariate analysis. We included study characteristics with significant univariate moderating effects. Because of the large number of types of illnesses that were compared, we could not include this variable in the multivariate analysis. As shown in Table II, the effects of gender, year of publication, rater, CDI, country, and target of comparison remained significant in multivariate analysis. However, the effect of representativeness of the sample was no longer significant in multivariate analysis.

## Discussion

The present meta-analysis shows that young people with chronic physical illnesses have, on average, higher levels of depressive symptoms than their healthy peers. However, this difference varies by the kind of illness, country, gender, rater of depressive symptoms, method of assessing depressive symptoms, year of publication, and target of comparison. This study goes beyond previous meta-analysis and narrative reviews by testing whether the levels of depressive symptoms differ between types of illness and whether the effect size is influenced by a large number of study characteristics.

When comparing different kinds of illness, we found that the effect sizes were quite divergent and impressive for some of these illnesses. Depressive symptoms were highest in chronic fatigue syndrome, diseases characterized by chronic pain (fibromyalgia, migraine/tension-type headache), cleft lip and palate, and epilepsy diseases that were not analyzed in the previous meta-analysis.

There has been a debate about whether the visibility and social consequences of a disease, restrictions of positive activities, brain dysfunction associated with some kinds of illnesses, side effects of treatments, or specific symptoms of illnesses, such as pain, have the strongest effect on psychological health. Although these factors are difficult to compare across illnesses and patient samples, our results indicate that the strongest effect sizes are found if more than one of these factors occur simultaneously. Chronic fatigue syndrome is associated with tiredness and restrictions of positive activities, alterations in brain physiology and associated cognitive difficulties, and often with headaches and muscle aches (Afari & Buchwald, 2003). In addition, symptom overlap of chronic fatigue syndrome and depression may play a role because the CDI (Kovacs, 1992) contains items on fatigue and decreased school performance.

Fibromyalgia showed the second highest effect size, and is characterized by chronic widespread pain as well as associated restrictions of positive activities. In addition, neurophysiological changes and cognitive dysfunction are found, as indicated by impaired concentration and memory problems (e.g., Glass, 2006). Similarly, migraine and tension-type headache are a significant detriment to daily functioning and productivity (Roth-Isigkeit et al., 2006).

Whereas the co-occurrence of more than one factor could be suggested for explaining the elevated depressive symptoms in four out of five chronic illnesses with the highest effect sizes (chronic fatigue syndrome,

Downloaded from https://academic.oup.com/jpepsy/article/36/4/375/926006 by U.S. Department of Justice user on 16 August 2022

fibromyalgia, migraine/tension-type headache, epilepsy), there seems to be only one main explanation for elevated levels of depressive symptoms in young people with cleft lip and palate. Their symptoms probably reflect concerns about appearance and negative social consequences (such as being teased or rejected because of visible deformities and speech abnormalities; e.g., De Sousa et al., 2009). In fact, many adolescents with congenital and acquired facial differences report stigma experiences, such as being teased about how their face looks (Strauss et al., 2007).

In addition to explanations for above average effect sizes, is has to be explained why young people with arthritis, cancer, cystic fibrosis, diabetes, HIV infection, and sickle cell disease did not show higher levels of depressive symptoms than their healthy peers. The lack of elevated average levels of depressive symptoms in some kinds of illness may be based on the fact that many young patients experience few or even no symptoms of their disease. For example, many participants of studies on HIV infection and AIDS were HIV positive without experiencing symptoms of AIDS. Similarly, many children and adolescents with sickle cell disease are free of painful episodes and other severe symptoms for longer time intervals (Telfer et al., 2007). In addition, many children with juvenile arthritis experience prolonged periods of low levels of disease activity or even complete remission due to the development of new therapeutic agents (Ravelli & Martini, 2006).

The lack of elevated levels of depressive symptoms in patients with cancer and cystic fibrosis replicates previous findings (Bennett, 1994). Because both kinds of illness are life-threatening, patients may respond with denial in order to protect their psychological well-being. Nonetheless, Phipps, Steele, Hall, and Leigh (2001) did not find differences in the levels of defensiveness of cancer patients and children with other chronic illnesses. Another explanation may be that a larger number of studies focused on cancer survivors who have already successfully completed their therapy and may, therefore, no longer show elevated levels of distress. In fact, Jorngarden, Mattsson, and von Essen (2007) reported that adolescent cancer patients had higher levels of depressive symptoms than healthy peers 6 months after being diagnosed but lower levels at the 18-month follow-up. Unfortunately, we could not include the time since completion of therapy in our meta-analysis, because too few studies provided this information.

Because the moderator effects of gender, country, year of publication, and target of comparison were in line with our expectations, they do not need not be discussed here. In addition to comparisons of child ratings and parent ratings (Bennett, 1994), we added an analysis of clinician ratings and teacher ratings. Because the effect sizes were lower for child ratings than for parent and clinician ratings, our results may support the suggestion that children with chronic illness underreport depressive symptoms or that parents and clinicians overreport depressive symptoms. However, because different measures were used for child, parent, and clinician ratings, we cannot rule out the possibility that the different effect sizes were caused by different methods of assessment.

Because the univariate effect of the representativeness of the sample was lost in multivariate analysis, we conclude that this effect was based on a confounding variable (the use of control groups rather than test norms in community-based studies with representative samples).

## Limitations and Conclusions

Some limitations of the present meta-analysis need to be mentioned. First, too few studies were available for separately analyzing depressive symptoms in some kinds of chronic illness, such as renal failure or congenital heart disease. Second, we analyzed cross-sectional data that did not allow for causal interpretation. The observed associations between chronic illness and depressive symptoms may indicate that chronic illness is a risk factor for depressive symptoms, but that depression may also affect the course of chronic illness (e.g., Helgeland, Sandvik, Mathiesen, & Kristensen, 2010), for example as mediated by a delay of seeking medical help and low compliance with medical procedures. In addition, third variables, such as living in poverty, may increase the risk for both chronic illness and depressive symptoms. Third, we could not test for some moderators, such as time since last treatment (because this information was rarely reported) or severity of the disease (which would be difficult to compare across different kinds of illness). Fourth, we could not analyze the processes that link chronic illness with depressive symptoms, such as metabolic changes, changes in activity patterns, or social stigmatization. Fifth, we focused on depressive symptoms rather than on depression diagnosis because too few studies were available that provided comparative data on the frequency of clinical depression. Finally, we assessed only one outcome variable. Effects on other variables (such as externalizing problem behaviors) have to be analyzed in future meta-analyses.

Nonetheless, some important conclusions can be drawn from the present meta-analysis. First, the small average differences between the levels of depressive symptoms in children with and without chronic illness indicate that many young people with chronic physical illnesses are well-adapted and resilient. Although average differences

Downloaded from https://academic.oup.com/jpepsy/article/36/4/375/926006 by U.S. Department of Justice user on 16 August 2022

between depressive symptoms of children with and without chronic physical illnesses are small to very small in a statistical sense, most effect sizes are practically meaningful when using Cohen's criteria for interpreting effect sizes or the BESD. Second, we conclude from the comparisons of levels of depressive symptoms across different kinds of illnesses that there are not only common effects of chronic illnesses (which would cause similar levels of depressive symptoms irrespective of the kind of chronic illness), but also illness-specific effects.

Third, we conclude that children with chronic fatigue syndrome, fibromyalgia, migraine or tension-type headache, cleft lip and palate, and epilepsy are at highest risk for developing depressive symptoms. Thus, pediatricians and others who work with these children should be aware of symptoms of psychological distress and make appropriate referrals for mental health services when needed. Fourth, because children and adolescents reported lower levels of depressive symptoms than their parents and clinicians, we recommend not to exclusively rely on child ratings. We also recommend using healthy peers as control group when working with the CDI.

With regard to future research, more research is needed that specifies the conditions under which children with chronic illnesses show elevated levels of psychological distress and that provides empirically supported explanations as to why some kinds of illness seem not to cause elevated levels of depressive symptoms. Similarly, more longitudinal studies are needed that analyze the extent to which chronic illness affects the course of depressive symptoms and depressive symptoms affect the course of the chronic illness. Furthermore, more studies are recommended on depressive symptoms in those chronic illnesses that could not be compared in our meta-analysis.

## Supplementary Data

Supplementary data can be found at: http://www.jpepsy.oxfordjournals.org/.

*Conflicts of interest*: None declared.

## References


Achenbach, T. M. (1991). *Manual for the child behavior checklist/4-18 and 1991 profile*. Burlington, VT: University of Vermont.

Achenbach, T. M., Dumenci, L., & Rescorla, L. A. (2003). *DSM*-oriented and empirically based approaches to constructing scales from the same item pools. *Journal of Clinical Child and Adolescent Psychology, 32*, 328–340.

Afari, N., & Buchwald, D. (2003). Chronic fatigue syndrome: A review. *American Journal of Psychiatry, 160*, 221–236.

Beck, J. S., Beck, A. T., & Jolly, J. (2001). *Manual for the Beck Youth Inventories of Emotional and Social Impairment*. San Antonio, TX: Psychological Corporation.

Bennett, D. S. (1994). Depression among children with chronic medical problems: A meta-analysis. *Journal of Pediatric Psychology, 19*, 149–169.

Bleyer, W. A. (2002). Cancer in older adolescents and young adults. *Medical and Pediatric Oncology, 38*, 1–10.

Cohen, J. (1988). *Statistical power analysis for the behavioral sciences*. Hillsdale: Erlbaum.

De Sousa, A., Devare, S., & Ghanshani, J. (2009). Psychological issues in cleft lip and cleft palate. *Journal of Indian Association of Pediatric Surgeons, 14*, 55–58.

Duval, S. J., & Tweedie, R. L. (2000). Trim and fill: A simple funnel plot-based method of testing and adjusting for publication bias in meta-analysis. *Biometrics, 56*, 455–463.

Eccleston, C., Crombez, G., Scotford, A., Clinch, J., & Connell, H. (2004). Adolescent chronic pain: Patterns and predictors of emotional distress in adolescents with chronic pain and their parents. *Pain, 108*, 221–229.

Emslie, G. J., & Mayes, T. L. (1999). Depression in children and adolescents: A guide to diagnosis and treatment. *CNS Drugs, 11*, 181–189.

Glass, J. M. (2006). Cognitive dysfunction in fibromyalgia and chronic fatigue syndrome: New trends and future directions. *Current Rheumatology Reports, 8*, 425–429.

Helgeland, H., Sandvik, L., Mathiesen, K. S., & Kristensen, H. (2010). Childhood predictors of recurrent abdominal pain in adolescence: A 13-year population-based prospective study. *Journal of Psychosomatic Research, 68*, 359–367.

Holmbeck, G. N., Johnson, S. Z., Wills, K. E., McKernon, W., Rose, B., Erklin, S., & Kemper, T. (2002). Observed and perceived parental overprotection in relation to psychosocial adjustment in preadolescents with a physical disability: The mediational role of behavioral autonomy. *Journal of Consulting and Clinical Psychology, 70*, 96–110.

Jorngarden, A., Mattsson, E., & von Essen, L. (2007). Health-related quality of life, anxiety and depression among adolescents and young adults with cancer: A


Downloaded from https://academic.oup.com/jpepsy/article/36/4/375/926006 by U.S. Department of Justice user on 16 August 2022

prospective longitudinal study. *European Journal of Cancer, 43*, 1952–1958.

Kovacs, M. (1992). *The Child Depression Inventory (CDI)*. New York: Multi-health Systems.

Lipsey, M. W., & Wilson, D. B. (2001). *Practical Meta-Analysis*. Thousand Oaks, CA: Sage.

Miller, J. M., Kustra, R. P., Vuong, A., Hammer, A. E., & Messenheimer, J. A. (2008). Depressive symptoms in epilepsy: prevalence, impact, aetiology, biological correlates and effect of treatment with antiepileptic drugs. *Drugs, 68*, 1493–1509.

Perrin, J. M., Bloom, S. R., & Gortmaker, S. L. (2007). Increasing childhood chronic conditions in the United States. *JAMA, 297*, 2755–2759.

Phipps, S., Steele, R. C., Hall, K., & Leigh, L. (2001). Repressive adaptation in children with cancer: A replication and extension. *Health Psychology, 6*, 445–451.

Piccinelli, M., & Wilkinson, G. (2000). Gender differences in depression. *British Journal of Psychiatry, 177*, 486–492.

Plioplys, S. (2003). Depression in children and adolescents with epilepsy. *Epilepsy and Behavior, 4*, S39–S45.

Reynolds, C. R., & Kamphaus, R. W. (2004). *Behavior Assessment System for Children* (2nd ed.). Circle Pines, MN: American Guidance Service.

Rosenthal, R., & Rubin, D. B. (1982). A simple, general purpose display of magnitude of experimental effect. *Journal of Educational Psychology, 74*, 166–169.

Roth-Isigkeit, A., Thyen, U., Stöven, H., Schwarzenberger, J., & Schmucker, P. (2005). Pain among children and adolescents: Restrictions in daily living and triggering factors. *Pediatrics, 115*, e152–e162.

Sandstrom, M. J., & Schanberg, L. E. (2004). Peer rejection, social behavior, and psychological adjustment in children with juvenile rheumatic disease. *Journal of Pediatric Psychology, 29*, 29–34.

Skinner, E. A., & Zimmer-Gembeck, M. J. (2007). The development of coping. *Annual Review of Psychology, 58*, 119–144.

Stein, R. E., & Jessop, D. J. (1982). A non-categorical approach to chronic childhood illness. *Public Health Reports, 97*, 354–362.

Strauss, R. P., Ramsey, B. L., Edwards, T. C., Topolski, T. D., Kapp-Simon, K. A., Thomas, C. F., … Patrick, D. L. (2007). Stigma experiences in youth with facial differences: A multi-site study of adolescents and their mothers. *Orthodontics & Craniofacial Research, 10*, 96–103.

Suris, J. C., Michaud, P. A., & Viner, R. (2004). The adolescent with a chronic condition. Part I: Developmental issues. *Archive of Diseases in Childhood, 89*, 938–942.

Telfer, P., Coen, P., Chakravorty, S., Wilkey, O., Evans, J., Newell, H., … Kirkham, F. (2007). Clinical outcomes in children with sickle cell disease. *Haematologica, 92*, 905–912.

Tellegen, A., Ben-Porath, Y. S., McNulty, J. L., Arbisi, P. A., Graham, J. R., & Kaemmer, B. (2003). *The MMPI-2 Restructured Clinical Scales: Development, Validation, and Interpretation*. Minneapolis, MN: University of Minnesota Press.

Twenge, J. M., & Nolen–Hoeksema, S. (2002). Age, gender, race, socioeconomic status, and birth cohort difference on the children's depression inventory: A meta-analysis. *Journal of Abnormal Psychology, 111*, 578–588.

van der Lee, J., Mokkink, L. B., Grootenhuis, M. A., Heymans, H. S., & Offringa, M. (2007). Definitions and measurement of chronic health conditions in childhood: A systematic review. *JAMA, 29*, 2741–2751.

World Bank (2010). *Country and Lending Groups*. Retrieved From http://data.worldbank.org/ about/ country-classifications/country-and-lending-groups.

Downloaded from https://academic.oup.com/jpepsy/article/36/4/375/926006 by U.S. Department of Justice user on 16 August 2022