

Behavior Problems in Children and Adolescents With Chronic Physical Illness: A Meta-Analysis

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Objective To examine the risk of emotional and behavioral problems among children with a chronic physical illness. **Methods** Random-effects meta-analysis was computed to integrate the results of 569 studies that used the Child Behavior Checklist, Youth Self Report, and the Teacher Report Form. **Results** Young people with a chronic physical illness have higher levels of internalizing ($g = .47$ standard mean difference), externalizing ($g = .22$) and total behavior problems ($g = .42$) than healthy peers. The largest differences were found in parental ratings and the weakest differences in adolescent self-ratings. Strongest elevations of internalizing problems were found for chronic fatigue syndrome and strongest elevations of externalizing problems were observed for epilepsy and migraine/tension-type headache. Effects also varied by country and, in part, by age, gender, year of publication, and study design. **Conclusions** The results call for regular screens for psychological distress and referrals for mental health services, when needed.

Key words Achenbach System of Empirically Based Assessment; Child Behavior Checklist; chronic illness; externalizing problems; internalizing problems; meta-analysis.

Epidemiological studies have shown that about 15% of children and adolescents, on average, have a chronic physical health condition (van der Lee, Mokkink, Grootenhuis, Heymans, & Offringa, 2007). These conditions are risk factors for behavior problems (e.g., Barlow & Ellard, 2006). Analyzing the prevalence of behavior problems of children with chronic physical illness and identifying related risk factors is of theoretical and practical relevance. First, it helps to understand psychosocial consequences of chronic physical diseases. Second, it provides valuable information for clinicians regarding who should be screened for which kind of problems. Third, it provides important information about the need for preventing these problems as part of an integrated treatment. Since many chronic diseases cannot be cured, a main goal is to reduce the consequences of the diseases on the lives of children and adolescents.

Multivariate approaches to child psychopathology often distinguish between externalizing and internalizing problems and disorders (Achenbach, 1991). Externalizing

problems include delinquent and aggressive behaviors, and internalizing problems include somatic complaints, anxiety, depression, and social withdrawal.

Elevated levels of internalizing as well as externalizing problems may be observed in children with chronic physical illness (Barlow & Ellard, 2006; Lavigne & Faier-Routman, 1992). Sources of elevated internalizing problems in children with a chronic physical illness may be the perceived lack of control over the illness and its symptoms or progression (e.g., in epilepsy or sickle cell disease), frightening symptoms (e.g., in the case of asthma or epilepsy), restrictions in positive activities (e.g., due to hospitalization), peer rejection (e.g., in the case of visible abnormalities, such as cleft lip and palate), as well as side effects of therapy (e.g., in the case of radiation and chemotherapy of cancer patients). In addition, symptoms of the physical illness, such as pain, may lead to elevated scores of somatic complaints that are part of internalizing problem clusters (Achenbach, 1991).

Externalizing problems may be elevated when the physical illness affects brain function and the associated behavioral regulation (e.g., in the case of epilepsy). In addition, externalizing problems may be a response to illness-related frustrations, such as being teased by peers (Reijntjes et al., 2010). However, some sources of internalizing problems (restrictions of positive activities, low control over symptoms or the course of the disease, overlap with somatic symptoms of the disease) are probably more widespread than the sources of externalizing problems, possibly leading to greater effects of chronic illness on internalizing problems. Up to now, five meta-analyses have assessed internalizing and externalizing problems of children with chronic illness. A meta-analysis of 87 studies by Lavigne and Faier-Routman (1992) found stronger elevations of internalizing ($d = .55$ SD units) than of externalizing problems ($d = .26$) in children with chronic physical illness. Young people with sensory and neurological disorders showed the highest elevation of overall symptoms, but the authors did not compare specific chronic illnesses with regard to externalizing and internalizing problems. More recently, McQuaid, Kopel, and Nassau (2001), and Rodenburg, Stam, Meijer, Aldenkamp, and Deković (2005) observed elevated levels of internalizing ($d = 0.73$ – 1.38) and externalizing problems ($d = 0.35$ – 0.81) in children with asthma and epilepsy, respectively. Furthermore, Karsdorp, Everaerd, King, and Mulder (2007) observed elevated levels of total behavior problems ($d = .47$), and of internalizing ($d = .47$) and externalizing problems ($d = .19$) in children with congenital heart disease. Finally, a meta-analysis of LeBovidge, Lavigne, Donenberg, and Miller (2005) observed only elevated levels of internalizing problems ($d = .47$) but not of externalizing problems ($d = .04$) in young people with arthritis.

These meta-analyses have limited test power for the search of moderating effects of study characteristics. Thus, the goal of the present meta-analysis was to compare the levels behavior problems of children and adolescents with different chronic physical illnesses to those of their healthy peers and to identify moderating effects of study characteristics. Since available measures of behavior problems differ with regard to the assessed dimensions, we focused on the instruments that have been most widely used with young people with chronic illness—the Child Behavior Checklist (CBCL—a parent report) as well as the parallel Youth Self Report (YSR which is used in 11- to 18-year-olds) and the Teacher Report Form (TRF; Achenbach, 1991).

Influences of Study Characteristics

Specific expectations about effects of nine study characteristics could be stated.

Internalizing Versus Externalizing Problems

In line with previous meta-analyses (Karsdorp et al., 2007; Lavigne & Faier-Routman, 1992; LeBovidge et al., 2005; McQuaid et al., 2001; Rodenburg et al., 2005), we expected to find higher levels of internalizing than of externalizing problems. Since the content of the Somatic Complaints subscale overlaps with illness-specific somatic symptoms (Perrin, Stein, & Drotar, 1991), we also expected to find the strongest effect size in this scale.

Informant

Studies on depression in children with chronic illness have found higher between-group differences in parent-rated symptoms than in self-rated symptoms of their children (Bennett, 1994; Pinquart & Shen, in press). However, Lavigne and Faier-Routman (1992) and Rodenburg et al. (2005) did not find significant differences between child, parent, and teacher reports of behavior problems, possibly due to lack of statistical power. Based on a larger number of studies, we wanted to test whether young people with chronic illness show stronger elevations of parent-rated behavior problems than of self-rated behavior problems.

Type of Illness

We put our focus for analyzing further moderators on studies based on parental reports, as they comprise approximately 80% of the reported effect sizes. We expected the strongest effect sizes for internalizing problems to be found for those illnesses that are associated with a higher number of stressors (such as activity restrictions, frightening symptoms, and lack of control over symptoms). The strongest levels of externalizing problems were expected for illnesses that affect brain function (epilepsy, headache, and spina bifida).

Age

Karsdorp et al. (2007) only found elevated levels of behavior problems of children with congenital heart disease in older patients. We tested whether this result could be replicated in the present meta-analysis.

Gender

In general, male adolescents show higher levels of externalizing problems than their female peers, whereas the reverse is found for internalizing problems (Steinberg, 2008).

If behavior problems are gender-specific responses to illness-related stressors, these gender differences may be accentuated in young people with chronic illnesses.

Country

On average, better medical and psychosocial services may be available in industrial countries than in developing or threshold countries. Therefore, we expected to find smaller effect sizes in studies from industrialized countries.

Publication Status

As nonsignificant results may be less likely to be published (Lipsey & Wilson, 2001), we wanted to test whether unpublished studies (e.g., dissertations) would report lower effect sizes than published studies.

Year of Publication

We expected to find lower between-group differences in more recent studies because of progress in the treatment of many diseases (e.g., Bleyer, 2002) and the development of psychosocial services for young people with chronic illness.

Study Quality

Some clinical samples may over-represent highly distressed young people seeking treatment for their chronic disease, which is why we expected stronger between-group differences in clinical (convenience) samples than in random community-based samples.

Exploratory Analysis of Other Moderators

Moderating effects of duration of illness, race/ethnicity, target of comparison (test norms vs. healthy control group), and sociodemographic matching of the patient and control group were assessed exploratively, because no theory-based expectations could be stated and/or because results from previous meta-analyses are contradictory.

Methods

Sample

Studies were identified through electronic databases (PSYCINFO, MEDLINE, Google Scholar, and PSYINDEX [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 chronic fatigue syndrome or cleft or cystic fibrosis or deaf or diabetes or epilepsy or headache or heart disease or hearing impairment or HIV or inflammatory bowel disease or kidney disease or liver disease or migraine or rheumatism or sickle cell or spina bifida or visual impairment] and

[Child Behavior Checklist or Youth Self Report or Teacher Report Form or Achenbach System of Empirically Based Assessment]) and cross-referencing. Criteria for inclusion of studies in the present meta-analysis were:

- (a) they used the CBCL (CBCL 4–18, CBCL 1½–5), YSR or TRF;
- (b) the studies were published since the development of the scales and before May, 2011;
- (c) they compared levels of behavior problems between young people with chronic physical illnesses and healthy peers or test norms, or they provided sufficient information for a comparison with established normative data (e.g., by reporting standardized *T*-scores, raw score, and percentage of respondents above defined cut-offs);
- (d) mean age of participants was ≤ 18 years; and
- (e) standardized between-group differences in behavior problems were reported or could be computed.

Documentation of a physician's diagnosis within each study was not a requirement because of the need to include broad-based survey studies for which medical documentation might not have been available. In order to include studies from different regions of the world, we also did not limit the included studies to those written in English. Studies published in Chinese, Dutch, English, German, Korean, Portuguese, Spanish, and Turkish were included. Available unpublished studies (e.g., dissertations) were also included. Studies were excluded if the samples of children were identified because they had "clinical" levels of behavior problems.

We identified 693 studies. After screening and assessing for eligibility, we were able to include 569 studies in the meta-analysis. A flow chart of the search for studies is provided in Appendix A1, and the studies included are listed in the Appendix A2 (see Supplementary Data). Most of the studies were done in industrialized countries. However, we were able to include studies from Brazil, China, the Dominican Republic, India, Egypt, Malaysia, Thailand, and Turkey. Information from the World Bank (2010) was used for coding countries as developed or developing/threshold countries.

We entered the number of patients and control group members, mean age, percentage of girls and percentage of members of ethnic minorities, country of data collection, year of publication, type of illness, duration of illness, the sampling procedure (1 = probability samples, 0 = convenience samples), use of a control group (0 = yes, 1 = comparison with test norms), equivalence of patient and control group (1 = yes, 2 = not tested, 3 = no), the rater of behavior

problems (1 = adolescent, 2 = parent, 3 = teacher), and the standardized size of between-group differences in total problems, internalizing problems, externalizing problems, withdrawn behavior, somatic complaints, anxiety/depression, delinquent behavior, aggressive behavior, social problems, thought problems, and attention problems. 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. All studies were coded by the first author, and one-third of them also by the second author. A mean inter-rater reliability of 94% (range 89–100%) was established. Differences were resolved by discussion.

Statistical Integration of the Findings

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

1. We computed effect sizes d for each study as the difference in behavior problems between the sample with chronic illnesses and the control sample divided by the pooled SD . If the authors only provided test scores for children and adolescents with chronic illness, we used the norms from the test manuals for comparison. If separate CBCL scores were reported for mothers and fathers, we averaged both scores. Outliers that were more than 2 SD from the mean of the effect sizes were recoded to the value at 2 SD , based on Lipsey and Wilson (2001).
2. Using Hedges' g , effect size estimates were adjusted for bias due to overestimation of the population effect size in small samples. Hedges' g leads to smaller estimations of the effect size than Cohen's d , but the difference declines with increasing sample size and is less than 1% for sample sizes of 80 and larger.
3. Weighted mean effect sizes and 95% confidence intervals (CIs) were computed. The significance of the mean was tested by dividing the weighted mean effect size by the standard error of the mean. To interpret the practical significance of the results, we used Cohen's criteria (Cohen, 1988): Differences of $g = 0.20$ – 0.49 are small, of $g = 0.50$ – 0.79 medium, and of $g \geq 0.8$ large.

4. Homogeneity of effect sizes was computed by use of the Q -statistic.
5. In order to test the influence of moderator variables, we used an analogue of an analysis of variance and weighted ordinary least squares regression analyses. In univariate analyses, a significant Q_b -score indicates heterogeneity of the effect sizes between the compared conditions. Which conditions differ is tested by comparing the 95% CIs. Differences between two conditions are significant if CI of two effect sizes do not overlap (Lipsey & Wilson, 2001). Statistical power analysis was computed based on Hedges and Pigott (2001).

Results

Data from 51,422 children and adolescents with chronic illnesses were included. The largest subgroup had asthma ($n = 13,793$), followed by epilepsy ($n = 6,815$), cancer ($n = 3,936$), heart diseases ($n = 2,692$), diabetes ($n = 2,136$), hearing impairments ($n = 2,136$), sickle cell disease ($n = 1,897$), cleft lip and palate ($n = 1,817$), arthritis ($n = 1,746$), migraine/tension headache ($n = 1,188$), kidney/liver disease ($n = 937$), HIV-infection ($n = 771$), spina bifida ($n = 700$), cystic fibrosis ($n = 674$), inflammatory bowel disease ($n = 579$), chronic fatigue syndrome ($n = 289$), and visual impairment ($n = 186$). The participants had a mean age of 10.6 years ($SD = 6.8$ years); 45.9% of them were girls and 43.7% were members of ethnic minorities.

Power analysis indicates that the probability was .8 that the study will detect a small effect sizes of $d = .20$.

Levels of Internalizing, Externalizing, and Total Problems

When summing up all effect sizes, we observe higher levels of total problem behavior in children with chronic illness as compared to healthy peers or test norms ($g = .42$, 95% CI 0.38–0.45, $Z = 24.93$, $p < .001$). Similarly, levels of internalizing problems ($g = .47$, CI 0.44–0.50, $Z = 29.73$, $p < .001$) and externalizing problems ($g = .22$, CI .19–.25, $Z = 14.76$, $p < .001$) were elevated in children with chronic illness.

According to Cohen's criteria for interpreting effect sizes (Cohen, 1988), effects were small to moderate when using parental and teacher ratings. In studies using adolescent ratings, effects on total problems and internalizing problems were small, and no significant effect size was found for externalizing problems (Table 1).

Table 1. Behavior Problems in Children With Chronic Illness: Variations by Source of Information

Differences between raters	Parent reports				Teacher reports				Adolescent reports							
	Q_b	k	g	95%-CI	Q_w	k_0	k	g	95%-CI	Q_w	k_0	k	g	95%-CI	Q_w	k_0
Total problems	29.69***	559	.46***	.42 .49	576.27	333,069	60	.37***	.27 .48	55.55	2,470	73	.17***	.07 .27	82.59	720
Internalizing problems	26.51***	618	.51***	.47 .54	642.86	454,638	71	.38***	.27 .48	41.59	5,724	88	.27***	.18 .36	109.38	45,447
Withdrawn	12.76**	258	.57***	.52 .62	252.03	104,432	26	.50***	.34 .66	23.95	717	46	.34***	.22 .45	55.09	953
Somatic complaints	7.20*	298	.72***	.66 .78	295.44	205,813	22	.56***	.33 .78	13.72	590	47	.53***	.38 .67	66.03*	1,037
Anxious/depressed	19.132**	252	.53***	.48 .57	252.57	81,840	25	.47***	.31 .63	16.83	580	46	.25***	.14 .37	55.40	588
Externalizing problems	28.57***	596	.24***	.21 .27	605.20	99,375	73	.27***	.18 .37	77.11	1,691	72	-.01	-.10 .08	64.86	0
Delinquent	11.50**	248	.33***	.28 .39	247.60	34,343	20	.39***	.21 .58	19.81	184	41	.10	-.06 .26	48.68	0
Aggressive	20.19***	287	.40***	.35 .45	306.06	66,732	25	.44***	.27 .62	27.05	490	44	.10	-.02 .22	40.26	0
Other problems																
Social problems	22.43***	215	.60***	.54 .66	237.35	78,944	25	.67***	.49 .86	20.52	1,329	45	.26***	.12 .39	41.72	661
Thought problems	19.32***	221	.48***	.43 .53	210.72	57,668	21	.58***	.40 .76	20.42	588	41	.21***	.09 .32	56.01	376
Attention problems	27.18***	244	.66***	.60 .72	266.57	125,992	26	.71***	.52 .90	19.60	1,291	43	.25***	.11 .39	29.97	593

Note. k = number of studies; g = effect size; 95% CI = lower and upper limits of 95% CI; Q_b = test for homogeneity of effect sizes between conditions (Q_b) and within conditions (Q_w); k_0 = fail-safe N . * $p < .05$, ** $p < .01$, *** $p < .001$.

As shown by the Q_b -statistics, the effect sizes of total problems differed between raters (parent rating: $g_P = .46$, teacher rating: $g_T = .37$, child/adolescent rating: $g_C = .17$; Table 1). Effect sizes for internalizing problems ($g_P = .51$, $g_T = .38$, $g_C = .27$) and externalizing problems ($g_P = .24$, $g_T = .27$, $g_C = -.01$) also differed between raters. The nonoverlap of the CI indicates that elevations of internalizing ($g_P = .51$ vs. $g_C = .27$) and externalizing problems ($g_P = .24$, $g_C = -.01$) as well as total problems ($g_P = .46$, $g_C = .17$) in children with chronic illnesses were more pronounced in studies that used parental reports than in studies using child self-reports. In addition, the non-overlap of the CI indicates that effect sizes for total symptoms ($g_T = .37$ vs. $g_C = .17$) as well as externalizing problems ($g_T = .27$ vs. $g_C = -.01$) were larger if teacher reports rather than child self-reports were used.

Significant rater effects were also observed for most subscales. Effect sizes of withdrawn behavior ($g_P = .57$ vs. $g_C = .34$), anxiety/depression ($g_P = .53$ vs. $g_C = .25$), delinquent behavior ($g_P = .33$ vs. $g_C = .10$), aggressive behavior ($g_P = .40$ vs. $g_C = .10$), social problems ($g_P = .60$ vs. $g_C = .26$), thought problems ($g_P = .48$ vs. $g_C = .21$), and attention problems ($g_P = .66$ vs. $g_C = .25$) were larger for parental reports than for adolescent reports. Effect sizes for aggressive behavior ($g_T = .44$ vs. $g_C = .10$), social problems ($g_T = .67$ vs. $g_C = .26$), thought problems ($g_T = .58$ vs. $g_C = .21$), and attention problems ($g_T = .71$ vs. $g_C = .25$) were also significantly larger for teacher reports than for adolescent reports (Table 1).

The non-overlap of the 95% CIs indicates that elevations of internalizing problems were more pronounced than elevations of externalizing problems, although these differences were only significant for parent ratings ($g_P = .51$ vs. $g_C = .24$) and adolescent self-ratings ($g_C = .27$ vs. $-.01$).

In order to address the potential for a file drawer problem a fail-safe n calculation was conducted, based on Rosenthal (1991). Results revealed that 34,343–454,638 studies with null results would be required to negate the range of effect sizes for the CBCL observed (Table 1).

The use of the CBCL in patients with chronic illness has been criticized because the somatic complaints scale may assess, at least in part, illness-specific symptoms which would cause an overestimation of total and internalizing problems (Perrin et al., 1991). In fact, the non-overlap of the CI shows that the effect size for parental ratings of somatic complaints ($g_P = .72$) is significantly higher than for the other subscales of internalizing problems (withdrawal: $g_P = .57$, anxiety/depression: $g_P = .53$; Table 1). No such differences were found for adolescent and teacher ratings. In order to estimate whether the results would differ when excluding the somatic complaints

subscale, we computed a modified total problems score of the CBCL by averaging the effect sizes of all subscales except somatic complaints. Similarly, we computed a modified Internalizing Problems score by averaging the effect size of the withdrawn behavior and anxiety/depression. This procedure was possible for about 50% of the available studies. As indicated in the Supplementary Appendix 3, the modified scales showed moderate effects for total problems ($g_p = .51$) and internalizing problems ($g_p = .53$), and their CI overlapped with the CIs of the original scales in Table I. Thus, the results were quite similar for the original and modified scales.

Comparison of Illnesses

The next analysis focused on the comparison of the different kinds of illnesses. Separate effect sizes were reported if at least five studies were available for a particular illness. Since studies on vision loss and hearing loss did not report separate effect sizes for the associated different diseases, we used only sum categories of vision and hearing loss. The following analyses are based on parental reports of their children's behavior.

As indicated by the *Q*-statistics (Table II, first line), the effect sizes for internalizing, externalizing, and total problems varied between diseases. Statistically significantly elevated levels of total behavior problems were observed for all assessed diseases except for cleft lip and palate and HIV infection. Elevated levels of internalizing problems were found for all diseases except cleft lip and palate. With regard to total problems, moderate effect sizes were found for migraine/tension-type headache ($g_p = .75$), kidney/liver disease ($g_p = .70$), epilepsy ($g_p = .63$), chronic fatigue syndrome ($g_p = .62$), asthma ($g_p = .61$), hearing impairment ($g_p = .56$), and spina bifida ($g_p = .50$). According to Cohen's (1988) criteria, elevations of internalizing problems were large in children with chronic fatigue syndrome ($g_p = 1.42$). In addition, moderate elevations were observed with regard to migraine/tension headache ($g_p = .77$), epilepsy ($g_p = .66$), chronic kidney/liver disease ($g_p = .67$), asthma ($g_p = .63$), inflammatory bowel disease ($g_p = .60$), and spina bifida ($g_p = .59$). Small effect sizes are listed in Table II.

Elevated levels of externalizing problems in children with chronic illness were only observed for 10 out of 17 diseases/disabilities (Table II). Interestingly, a negative effect size was observed for externalizing problems of children with cleft lip and palate ($g_p = -.24$): Parents of these children reported fewer symptoms than parents of healthy children.

The effect sizes for most illness groups were homogeneous. However, heterogeneity beyond sampling error was observed with regard to the levels of total problems in

young people with epilepsy and kidney/liver diseases, levels of internalizing problems in children with arthritis, heart diseases, and kidney/liver diseases, as well as levels of externalizing problems of young patients with chronic fatigue syndrome, kidney/liver diseases, and the sum category of other illnesses.

Scores on the CBCL subscales for the individual diseases are reported in Table III. Effect sizes for all subscales varied between disease groups. According to Cohen's criteria (1988), large effect sizes were found for spina bifida (attention problems: $g_p = 1.00$, social problems: $g_p = .94$, withdrawal: $g_p = .93$), epilepsy (attention problems: $g_p = 1.07$, social problems: $g_p = .88$), chronic fatigue syndrome (anxious-depressiveness: $g_p = .99$, somatic complaints: $g_p = 1.35$), HIV-infection/AIDS (withdrawal: $g_p = 1.44$, delinquency: $g_p = .84$), inflammatory bowel disease (withdrawal: $g_p = .84$, somatic complaints, $g_p = 1.47$), kidney/liver disease (somatic complaints: $g_p = .88$, attention problems: $g_p = .86$), asthma (somatic complaints: $g_p = 1.02$), arthritis/rheumatism (somatic complaints: $g_p = .92$), and sickle cell disease (somatic complaints: $g_p = .84$).

Moderator Effects of Sociodemographic Characteristics

In order to compare our results on age differences with the study by Karsdorp et al. (2007), we divided the sample into the same age groups. The *Q*-statistics indicates significant age differences for the three problem scales. The non-overlap of the CI indicates that effect sizes were smaller in children under the age of 6 years than in the other age groups for total problems ($g_p = .19$ vs. $g_p = .48$), internalizing ($g_p = .18$ vs. $g_p = .48-.55$), and externalizing problems ($g_p = .06$ vs. $g_p = .25-.28$; Table II). The effect sizes within each age group were homogeneous, except the total score and the internalizing score in the youngest group.

In order to explore moderating effects of gender, we trisected the sample according to the percentage of female participants. Significant gender differences were observed with regard to total and externalizing problems. The non-overlap of the CI indicates that the levels of total ($g_p = .58$) and externalizing problems ($g_p = .38$) showed significantly higher elevations if the samples were comprised of two-thirds or more male participants.

Furthermore, we observed significant differences between children from developing and developed countries for all three problem scales. Stronger elevations of problems were found in children with chronic illnesses living in developing/threshold countries ($g_p = .47-.65$) than in developed countries ($g_p = .22-.49$). However, no significant moderating effects were found for ethnicity and duration of illness.

Table II. Association of Study Characteristics With Elevated Levels of CBCL Behavior Problems in Children With Chronic Illness

Kind of illness/disability	Total problems				Internalizing problems				Externalizing problems				
	k	g	95%-CI	Q	k	g	95%-CI	Q	k	g	95%-CI	Q	
Arthritis/Rheumatism	27	.20*	.04	36	31.31 ^b	33	.48***	.34	.62	31	.13	-.01	.26
Asthma	55	.61***	.51	.72	50.43 ^b	64	.63***	.53	.72	58	.29***	.20	.36
Cancer	59	.29***	.19	.39	39.24 ^b	69	.34***	.25	.43	64	.06	-.03	.15
Chronic fatigue syndrome (CFS)	10	.62***	.34	.91	11.46 ^b	9	1.42***	1.11	1.73	7	.09	-.23	.40
Cleft lip and palate	27	.04	-.11	.19	43.32 ^b	28	-.05	-.20	.09	26	-.24***	-.38	-.10
Cystic fibrosis	18	.27**	.07	.46	15.49 ^b	15	.37***	.16	.58	15	.14	-.06	.34
Diabetes	33	.30***	.16	.43	27.61 ^b	41	.40***	.27	.52	41	.26***	.14	.38
Epilepsy	74	.63***	.54	.72	100.93** ^b	71	.66***	.57	.75	68	.37***	.29	.46
Hearing impairment	16	.56***	.27	.65	13.69 ^b	17	.31**	.13	.49	18	.34***	.18	.51
Heart disease	37	.42***	.30	.55	32.15 ^b	31	.44***	.31	.58	29	.24***	.10	.37
HIV infection/AIDS	9	.19	-.06	.45	7.82 ^b	11	.27*	.04	.50	10	.19	-.04	.41
Inflammatory bowel disease (IBD)	10	.30*	.05	.56	7.43 ^b	13	.60***	.38	.82	10	.04	-.19	.29
Kidney/liver disease	22	.70***	.52	.88	41.29** ^b	24	.67***	.50	.85	21	.34**	.16	.51
Migraine/tension-type headache	17	.75***	.56	.95	8.48 ^b	25	.77***	.62	.93	21	.36***	.20	.52
Sickle cell disease	10	.38***	.16	.61	4.39 ^b	16	.48***	.29	.67	20	.26**	.09	.42
Spina bifida	7	.50*	.16	.84	1.53 ^b	10	.59***	.33	.84	11	.32**	.09	.55
Visual impairment	6	.48*	.14	.82	2.88 ^b	6	.33	.00	.67	6	.33*	.00	.65
Other illnesses/ mixed samples ^c	122	.51***	.44	.59	133.17 ^b	135	.54***	.47	.61	137	.32***	.25	.38
Duration of illness					1.53 ^a								
<Mean (5.7 years)	129	.49***	.42	.57	170.58** ^b	134	.59***	.51	.67	127	.30	.23	.37
>Mean	125	.43***	.35	.50	87.87 ^b	134	.49***	.41	.57	127	.19	.12	.27
Mean age					17.68*** ^a								
<6 years	43	.19**	.06	.32	60.83 ^b	43	.18*	.05	.30	42	.06	-.06	.18
6-10 years	169	.48***	.41	.54	153.46 ^b	178	.48***	.42	.54	178	.28	.22	.34
>10 years	321	.48***	.43	.53	335.19 ^b	372	.55***	.51	.60	352	.25	.20	.29
Percentage of girls					8.11** ^a								
<33.3%	103	.58***	.49	.66	93.98 ^b	115	.56***	.47	.64	115	.38***	.30	.46
33.3-66.6%	330	.43***	.38	.48	348.79 ^b	359	.50***	.46	.55	347	.22***	.18	.26
>66.6%	70	.44***	.33	.55	71.34 ^b	87	.55***	.45	.65	80	.20***	.10	.29
Percentage of members of ethnic minorities					0.27 ^a								
<Mean	74	.42***	.33	.51	84.01 ^b	97	.52***	.44	.60	85	.18***	.11	.26
>Mean	66	.45***	.36	.55	64.38 ^b	88	.41***	.33	.49	87	.18***	.11	.26

(continued)

Table III. Comparison of Subscales by Kind of Illness

	Withdrawn ($Q_b = 58.81^{***}$)			Somatic complaints ($Q_b = 70.13^{***}$)			Anxious/depressed ($Q_b = 42.45^{***}$)			Delinquent ($Q_b = 47.30^{***}$)		
	<i>k</i>	<i>g</i>	95%-CI	<i>k</i>	<i>g</i>	95%-CI	<i>k</i>	<i>g</i>	95%-CI	<i>k</i>	<i>g</i>	95%-CI
Arthritis/rheumatism	10	.56***	.31 .80	11	.92***	.63 1.21	7	.49***	.21 .77	7	.10	-.19 .39
Asthma	9	.46***	.20 .72	15	1.02***	.76 1.28	14	.64***	.46 .82	14	.44***	.22 .66
Cancer	25	.50***	.35 .66	30	.77***	.60 .94	20	.47***	.31 .64	23	.13	-.03 .29
Chronic fatigue syndrome	9	.77***	.49 1.05	10	1.35***	1.02 1.68	7	.99***	.67 1.31	8	-.03	-.32 .25
Kidney/liver disease	18	.76***	.58 .94	17	.88***	.65 1.11	19	.68***	.51 .85	13	.31**	.09 .52
Cleft lip and palate	22	.41***	.26 .56	22	.45***	.25 .64	23	.32***	.18 .47	16	.31***	.14 .48
Cystic fibrosis	4	-.06	-.49 .37	6	.67***	.26 1.09	3	.18	-.35 .70	6	.68***	.34 1.03
Diabetes	12	.40***	.20 .61	13	.65***	.40 .91	13	.43***	.24 .63	14	.21*	.02 .40
Epilepsy	35	.74***	.63 .86	38	.78***	.63 .92	36	.63***	.51 .74	35	.48***	.37 .59
Hearing impairment	8	.38***	.16 .60	9	.29*	.01 .57	8	.36**	.14 .59	7	.34**	.11 .57
Heart disease	8	.32**	.10 .54	7	.40*	.09 .71	8	.21	-.01 .43	4	.10	-.21 .41
HIV infection/AIDS	1	1.44***	.64 2.24	4	.06	-.43 .55	3	.62**	.17 1.06	2	.84**	.27 1.40
IBD	5	.84***	.52 1.15	5	1.47***	1.06 1.88	4	.60***	.27 .93	3	.20	-.17 .57
Kidney/liver disease	18	.76***	.58 .94	17	.88***	.65 1.11	19	.68***	.51 .85	13	.31**	.09 .52
Migraine	12	.39***	.20 .59	17	.78***	.56 1.00	10	.51***	.30 .72	11	.07	-.13 .27
Sickle cell disease	7	.46**	.15 .75	10	.84***	.53 1.14	3	.22	-.16 .59	5	.26	-.06 .59
Spina bifida	4	.93***	.55 1.31	3	.59*	.06 1.12	1	.30	-.33 .94	3	.31	-.11 .73
Visual impairment	3	.26	-.22 .75	5	.28	-.19 .75	2	.14	-.47 .75	5	.14	-.24 .51
Other illnesses	66	.61***	.52 .70	76	.64***	.54 .75	71	.57***	.48 .66	72	.43***	.34 .52

	Aggressive ($Q_b = 51.87^{***}$)			Social problems ($Q_b = 99.19^{***}$)			Attention problems ($Q_b = 89.33^{***}$)			Thought problems ($Q_b = 55.81^{***}$)		
	<i>k</i>	<i>g</i>	95%-CI	<i>k</i>	<i>g</i>	95%-CI	<i>k</i>	<i>g</i>	95%-CI	<i>k</i>	<i>g</i>	95%-CI
Arthritis/rheumatism	6	.45**	.12 .77	6	.11	-.19 .41	7	.16	-.16 .49	8	.33*	.06 .60
Asthma	19	.29**	.09 .49	10	.05	-.19 .29	15	.26*	.02 .50	12	.28*	.06 .49
Cancer	26	.24**	.08 .40	20	.58***	.40 .76	19	.44***	.24 .64	18	.27***	.11 .43
Chronic fatigue syndrome	8	-.11	-.42 .19	6	.21	-.15 .57	5	.54*	.13 .95	5	.41*	.06 .75
Cleft lip and palate	20	.25**	.08 .42	17	.51***	.34 .69	15	.50***	.29 .71	15	.47***	.30 .63
Cystic fibrosis	6	.47*	.11 .83	3	.31	-.23 .86	4	.74**	.25 1.23	6	.33*	.02 .65
Diabetes	14	.28**	.08 .49	13	.24*	.03 .44	13	.41***	.18 .65	14	.23**	.06 .40
Epilepsy	39	.62***	.50 .74	35	.88***	.76 1.00	42	1.07***	.94 1.19	38	.74***	.64 .84
Hearing impairment	9	.41***	.18 .64	7	.55***	.28 .81	10	.62***	.38 .86	7	.55***	.44 .77
Heart disease	7	.14	-.11 .40	6	.49***	.21 .76	8	.48**	.22 .75	3	.41**	.10 .73
HIV infection/AIDS	3	.10	-.37 .57	3	.28	-.16 .72	3	.62*	.11 1.13	2	.53*	.01 1.05
IBD	4	.42*	.04 .80	2	.25	-.24 .73	1	.00	-.71 .71	2	.43*	.04 .83
Kidney/liver disease	18	.70***	.50 .89	14	.64***	.43 .86	16	.86***	.64 1.08	13	.40***	.20 .59
Migraine	11	.27*	.05 .49	11	.40***	.19 .61	10	.41***	.16 .66	11	.31***	.13 .49
Sickle cell disease	9	.30*	.01 .58	5	.19	-.13 .52	6	.33	-.08 .74	5	.33*	.01 .65
Spina bifida	4	.56**	.16 .97	3	.94***	.52 1.36	4	1.00***	.56 1.43	2	.40	-.05 .84
Visual impairment	5	.40*	.01 .80	2	.42	-.23 1.08	5	.53*	.09 .97	3	.36	-.09 .81
Other illnesses	79	.44***	.35 .52	52	.83***	.72 .93	63	.70***	.60 .81	58	.54***	.46 .63

Note. *k* = number of studies; *g* = effect size; 95% CI = lower and upper limits of 95% CI; Q_b = test for homogeneity of effect sizes across the different diseases.
p* < .05, *p* < .01, ****p* < .001.

Moderator Effects of Characteristics of the Publication

The Q_b -statistics indicates that published and unpublished studies did not differ in effect size. As the CBCL was introduced 30 years ago, we compared results from these

three decades. The Q_b -statistics indicates that the effect size for externalizing problems, but not for internalizing and total problems, differ by year of publication. As shown by the nonoverlap of the CI, elevations of externalizing problems of children with chronic illness were

stronger in studies that were published before 1990 ($g_p = .47$) than in later studies ($g_p = .19-.25$).

Furthermore, the Q_b -statistics indicates that levels of externalizing, but not of internalizing and total problems, vary by the target of comparison. Significantly stronger between-group differences in externalizing problems were observed in studies that used a healthy control group ($g_p = .30$) than in studies that compared behavior problems of children with chronic illnesses to test norms ($g_p = .20$). The effect size of the latter group was heterogeneous.

Finally, effect sizes for externalizing problems varied by the sociodemographic equivalence of the patient group and control group. The nonoverlap of the CI indicates that significantly weaker effect sizes were observed in studies with nonequivalent control groups ($g_p = .10$) than in other studies ($g_p = .20-.28$). However, the effect sizes did not vary by the representativeness of the samples. Most effect sizes of the subgroups were homogeneous. Nonetheless, the test for heterogeneity was significant for the levels of total problems in random samples.

We also ran all analyses with the modified total problems and internalizing problems scale (Appendix A3). The results were very similar to the findings with the original scales (e.g., mean difference for total problems $g_p = .51$, internalizing problems: $g_p = .53$). Only the moderating effect of age on the level of internalizing problems was not replicated in that analysis.

Because some moderator variables may be correlated, we concluded our investigation by testing whether the univariate moderator effects could be replicated in multivariate analysis. Only those moderators that were significant in at least one univariate analysis were included. In order to

compare the diseases with the largest univariate effect sizes (asthma, chronic fatigue syndrome, epilepsy, kidney/liver disease, or migraine/tension-type headache) against the other chronic conditions, a dummy variable was created for the type of illness. As shown in Table IV, all univariate moderator effects remained significant.

Discussion

The present study found elevated levels of behavior problems in children and adolescents with chronic physical illnesses. On average, elevations of internalizing problems, social problems, attention problems, and thought problems were larger than elevations of externalizing problems. The effect sizes varied between the types of illnesses as well as raters of behavior problems, country and, in part, by age, gender, year of publication, study design, and equivalence of patient and control group. The discussion will be organized according to the order of the research questions.

Levels of Internalizing, Externalizing, and Total Problems

We observed stronger elevations of internalizing problems than of externalizing problems of children and adolescents with chronic physical illness. This difference cannot be explained by the fact that the internalizing score includes somatic complaints which may reflect illness-specific somatic symptoms (Perrin et al., 1991). First, our meta-analysis showed that the main results remain unchanged when excluding the somatic complaints subscale. Note that other correcting procedures of individual studies, such as deleting other ambiguous items, led to similar results

Table IV. Multivariate Analysis of Moderating Effects of Study Characteristics (Multiple Linear Regression Analysis)

	Total problems			Internalizing problems			Externalizing problems		
	B	β	Z	B	β	Z	B	β	Z
Kind of illness (2 = asthma/CFS/epilepsy/migraine/tension-type headache, 1 = others)	.17	.22	10.11***	.25	.26	6.46***	.14	.15	3.70***
Mean age (1 = lower than 6 years, 2 = others)	.36	.22	10.88***	.31	.18	4.53***	.17	.11	2.64**
Percentage girls (2 = larger 33%, 1 = others)	-.11	-.09	-4.28***	-.09	-.08	-1.99*	-.16	-.15	-3.76***
Country (2 = developed country, 1 = developing/threshold country)	-.04	-.05	-2.56*	-.11	-.13	-3.35***	-.13	-.17	-4.13***
Year of publication (1 = before 1990, 2 = others)	-.13	-.08	-3.80***	-.04	-.02	-0.58	-.23	-.17	-4.13***
Target of comparison (2 = test norms, 1 = healthy control group)	-.02	-.03	-1.22	.00	.00	0.07	-.09	-.11	-2.55*
Equivalence of patients and control condition (1 = no, 2 = yes/not tested)	.07	.03	1.37	.14	.06	1.53	.20	.10	2.32*
(Constant)	-.04		-0.29	-.16		-0.56	.57		2.14*
R^2	.12			.13			.14		
n	493			548			528		

Note. * $p < .05$, ** $p < .01$, *** $p < .001$.

(e.g., Gleissner et al., 2008). Second, similar differences are found when comparing levels of anxiety/depression and withdrawn behavior with delinquent and aggressive behavior. The difference indicates that sources of internalizing problems (e.g., restrictions of positive activities) may be more widespread and/or may have stronger effects on children with chronic physical illness than sources of externalizing problems.

The analysis of the CBCL subscales indicated that, in addition to somatic problems, children with chronic illness are particularly at increased risk for attention and social problems. Attention problems are, in part, consequences of physical diseases, as in the case of epilepsy and chronic headache (Hernandez, Sauerwein, Jambaqué, de Guise, Lussier, & Lortie, 2003). In addition, thinking or worrying about ones' illness may impair their attention. Social problems refer to being too dependent upon others, not getting along with peers or getting teased (Achenbach, 1991). Elevations of these symptoms indicate that chronic illnesses often impair peer relations and that they may also impair the development of autonomy.

The present meta-analysis showed that adolescents do not only report fewer behavior problems than their parents, but also that similar differences exist when comparing teacher and adolescent reports. As externalizing problems can often be easily observed by parents or teachers, adult reports on externalizing behaviors may, therefore, be regarded as quite objective (Frick, Barry, & Kamphaus, 2009). Our results may indicate that children with chronic illness tend to underreport their symptoms, for example, because they want to present themselves as healthy functioning individuals (Huberty, Austin, Harezlak, Dunn, & Ambrosius, 2000). Alternatively, parents and teachers may underestimate the ability of the children to adapt toward their illness. For example, caring for a child with chronic illness causes parental distress (e.g., Ashkani, Dehbozorgi, & Tahamtan, 2004) which could lead to biased estimations of child problems (Youngstrom, Loeber, & Stouthamer-Loeber, 2000).

Because the YSR—in contrast to the CBCL—was only used with 11-year-olds and older adolescents, differences between studies with the CBCL/TRF and the YSR might also reflect different age ranges studied. However, as the total, internalizing and externalizing CBCL scores of 11-year-olds and older adolescents were significantly higher than the YSR scores, the diverging age ranges of both instruments cannot explain the observed rater differences.

Comparison of Illnesses

Our results indicate that elevated levels of internalizing problems are observed in children with most chronic

physical illnesses whereas elevations of externalizing problems are rather illness-specific. Most illnesses with the strongest elevations of externalizing problems, i.e. epilepsy, migraine/tension-type headache, and hearing impairment, are always or often associated with impaired brain function. Neuroimaging studies have identified frontal lobe brain abnormalities in patients with epilepsy and migraine (e.g., Herrman et al., 2002; Schmitz et al., 2010). These abnormalities are associated with executive function deficits, which could affect the inhibition of externalizing problems. Side effects of medications, such as corticosteroids, may in part explain elevated externalizing problems among children with kidney and liver diseases (Soliday, Grey, & Lande, 1999). The observed lower level of externalizing problems in children with cleft lip and palate as compared to healthy controls or test norms are difficult to interpret because the subscales of delinquent and aggressive behaviors showed elevated scores. More research is needed before definite conclusions can be drawn.

Differences between illnesses in the levels of internalizing problems were impressive. The largest effect size was observed for chronic fatigue syndrome which may, in part, be based on a symptom overlap of tiredness, unspecific pain, sleep problems, and other somatic symptoms. However, large elevations of internalizing problems persisted after eliminating the somatic complaints subscale (Appendix 3). Fatigue is also likely to interfere with many positive aspects of daily life which may cause internalizing problems, such as withdrawal or depressed symptoms. Interestingly, young people with chronic fatigue syndrome did not show elevated levels of externalizing problems, possibly because being tired inhibits such behaviors.

While children with chronic fatigue syndrome had specific behavior problems, young people with migraine/chronic-tension type headache and epilepsy showed above-average levels of externalizing *and* internalizing problems. Above-average levels of internalizing problems in these illnesses may be based on restrictions of positive activities, lack of perceived control over symptoms, and changes of the brain. For example, epileptic activity in certain areas of the brain directly causes paroxysmal anxiety (Beyenburg, Mitchell, Schmidt, Elger, & Reuber, 2005).

Although the effect sizes of most diseases were homogeneous, they varied in particular between studies on kidney/liver disease. This heterogeneity is probably based on the fact that the specific illnesses within this group were quite heterogeneous, for example, when needing organ transplantation or showing a less severe disease.

In addition to the analysis of externalizing and internalizing problems, our study also analyzed problems in the fields of attention, thought, and social relations. Changes

in brain function could explain the observed high levels of attention problems in children with epilepsy and spina bifida. For example, Hernandez et al. (2003) observed that especially abnormalities of the frontal lobe of patients with epilepsy were associated with attention problems. Changes in the brain and the associated externalizing problems may also contribute to the high levels of social problems that were found in children with epilepsy. Observed high levels of social problems in children with spina bifida may be affected by the high levels of social withdrawal which inhibits the development of peer-relations.

Moderator Effects of Sociodemographic Characteristics

While in a meta-analysis on congenital heart disease Karsdorp et al. (2007) had found lower levels of behavior problems in children younger than 6 years than in those older than 10 years, our study found that the youngest group also differed from 6 to 10-year-olds. Below-average levels of behavior problems in younger children with chronic illness may indicate that some negative psychosocial consequences of their illness do not yet appear that early, such as being bullied by class mates.

Interestingly, we observed larger effect sizes for total and externalizing problems in studies with higher percentages of boys, whereas levels of internalizing problems did not increase significantly in the case of a higher percentage of girls. Thus, our results indicate that boys are more likely to react toward their illness with externalizing symptoms, possibly because this behavior is more consistent with the male gender role (Steinberg, 2008). Studies not specific to chronic physical illnesses have shown that gender differences in externalizing problems emerge, on average, earlier than gender differences in internalizing problems (Steinberg, 2008). This could lead to the observed lack of moderating effect of gender on the level of internalizing symptoms.

Characteristics of the Publication

The expected larger effect sizes of older studies were only observed with regard to externalizing behavior. This result may indicate that more progress has been made in the prevention or treatment of externalizing rather than internalizing problems. In fact, in the last two decades more studies on the prevention of externalizing problems have been published than on the prevention of internalizing problems (e.g., Röhrle, 2007). Alternatively, the effect of time of measurement might also be based on the use of different test norms. However, a supplementary analysis showed that larger elevations of externalizing problems are also found in older studies that compared children

with chronic illness with a healthy control group ($g_p = .60$ vs. $g_p = .21/g_p = .09$, $Q(2,327) = 53.11$, $p < .001$).

We only found weak evidence for the suggested higher effect sizes in studies that compared children with chronic illnesses to healthy peers rather than test norms. Probably children with severe chronic physical illnesses were underrepresented in the normative samples of the CBCL so that similarities between the normative samples and healthy control groups prevail.

Strengths and Limitations

Compared to previous meta-analyses on behavior problems with chronic illness, we were able to include a much larger data set. In order to collect a representative sample of studies, we also did not limit our analysis to studies published in English. This allowed for comparing a much larger number of chronic illnesses and for assessing a broader range of moderator variables.

Nonetheless, some limitations have to be mentioned. First, the available cross-sectional data did not allow for testing whether behavior problems were the consequences of the physical illness or whether some of these problems developed independently or even before the diagnosis of a chronic physical disease. However, we were able to show that children with chronic physical illness are at increased risk for these problems. Second, only a few studies were available for some kinds of illnesses, such as HIV-infection/AIDS and visual impairment. Third, due to space limitations, we did not include data on social competence that are also assessed with the CBCL. Fourth, we limited our analysis to the CBCL scales that have most often been used in studies on chronic illness. Too few studies were available for the DSM-oriented CBCL scales that were introduced by Achenbach, Dumenici, and Rescorla (2003). Fifth, in order to address the critique by Perrin et al. (1991) on the use of the somatic complaints subscale with people with chronic illness, we had to use a crude estimation of the corrected internalizing and total problems. Finally, we did not analyze whether similar results would be found when using other screening measures for behavior problems.

Conclusions

Despite these limitations, several conclusions can be drawn from this meta-analysis. First, we conclude that elevated levels of internalizing and total problems are observed in almost all chronic illnesses. However, the level and profile of behavior problems (e.g., whether internalizing and/or externalizing problems are elevated) varies between diseases. Second, the present meta-analysis highlights that

elevated levels of problems are also found in other areas, such as attention or social problems, whereas many studies focus exclusively on the internalizing and externalizing scores of the CBCL. Third, the inclusion of the somatic complaints subscale is unlikely to cause a serious bias when working with total problem scores and internalizing problem scores of children with chronic illness. Nonetheless, we agree with Perrin et al. (1991) that the results from somatic complaints scale would be difficult to interpret in this group of children. Fourth, due to the systematic differences between results from adolescent self-reports and parent/teacher reports, we recommend the use of different sources of information. If researchers or clinicians do not want to overlook patients with elevated levels of behavior problems, they should not rely exclusively on patient self-reports. Fifth, we conclude that boys and girls with chronic physical illness should routinely be screened for internalizing problems whereas boys would be the main target for screening for externalizing problems, given the observed gender differences. Sixth, the observed elevated levels of behavior problems call for a multidisciplinary team approach wherein medical and psychosocial personnel establish a collaborative treatment approach. In addition to treating the somatic disease, psychosocial interventions are needed for preventing and treating behavior problems. For example, Perrin, MacLean, Gortmarker, and Asher (1992) have shown that a stress management intervention reduced the level of behavior problems of young asthma patients. Seventh, given the higher levels of behavior problems among children with chronic physical illnesses from developing/threshold countries, more psychosocial services aimed at preventing or treating these problems are needed in these countries. Finally, future research should analyze the interplay of processes that mediate the effect of chronic physical illness on different forms of behavior problems. Such studies would be helpful for identifying starting points of interventions.

Supplementary Data

Supplementary data available at *JPEPSY* online.

Conflicts of interest: None declared.

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