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## Developing e-health applications to promote a patient-centered approach to medically unexplained symptoms

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*Document Version*

Publisher's PDF, also known as Version of record

*Publication date:*

2019

[Link to publication in University of Groningen/UMCG research database](#)

*Citation for published version (APA):*

van Gils, A. (2019). *Developing e-health applications to promote a patient-centered approach to medically unexplained symptoms*. [Thesis fully internal (DIV), University of Groningen]. Rijksuniversiteit Groningen.

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# CHAPTER 8



**Sexual abuse predicts  
functional somatic symptoms:  
an adolescent population study.**

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**ABSTRACT**

**Background:** The main aim of this study was to investigate the effect of childhood sexual abuse on medically not well explained or functional somatic symptoms (FSS) in adolescents. We hypothesized that sexual abuse predicts higher levels of FSS and that anxiety and depression contribute to this relationship. In addition, we hypothesized that more severe abuse is associated with higher levels of FSS and that sexual abuse is related to gastrointestinal FSS in particular.

**Methods:** This study was part of the Tracking Adolescents' Individual Lives Survey (TRAILS): a general population cohort which started in 2001 (N = 2230; 50.8% girls, mean age 11.1 years). The current study uses data of 1680 participants over four assessment waves (75% of baseline, mean duration of follow-up: 8 years). FSS were measured by the Somatic Complaints subscale of the Youth Self-Report at all waves. Sexual abuse before the age of sixteen was assessed retrospectively with a questionnaire at T4. To test the hypotheses linear mixed models were used adjusted for age, sex, socioeconomic status, anxiety and depression.

**Results:** Sexual abuse predicted higher levels of FSS after adjustment for age sex and socioeconomic status (B=.06) and after additional adjustment for anxiety and depression (B=.03). While sexual abuse involving physical contact significantly predicted the level of FSS (assault; B=.08, rape; B=.05), non-contact sexual abuse was not significantly associated with FSS (B=.04). Sexual abuse was not a stronger predictor of gastrointestinal FSS (B=.06) than of all FSS.

**Conclusions:** Sexual abuse predicts FSS in adolescents. Further research is needed to clarify possible mechanisms underlying relationship between sexual abuse and FSS.

## INTRODUCTION

Functional somatic symptoms (FSS), or symptoms that are not well explained by an underlying pathology, are common in adolescence and can be very persistent and impairing (1, 2). In children and adolescents gastrointestinal complaints, pain, and fatigue are the most common symptoms (2-4). The etiology of FSS is not well understood, but several social, psychological and biological risk factors have already been identified (5-7). One of these potential risk factors for FSS is sexual abuse (8-12). Yet, previous studies that investigated the effect of sexual abuse on FSS mostly relied on cross-sectional analyses of recalled sexual abuse and current FSS (8, 9). This may have introduced biases. For example; people who suffer from anxiety, depression, or FSS may more easily recall negative events that triggered the same mood or resulted in the same symptoms (13). In addition, often the effect of sexual abuse on one specific type of FSS in female clinical populations was studied (8, 9). Thus, it remains unclear if the recall of sexual abuse predicts a spectrum of prospectively assessed FSS in the general adolescent population. Further, most studies did not adjust for concurrent symptoms of anxiety and depression or chronic stressors. Yet, symptoms of anxiety and depression may (partly) explain the association between sexual abuse and FSS (6, 14). Indeed, in the two studies in adolescents that adjusted for symptoms of anxiety and/or depression, the association between sexual abuse and FSS was reduced or no longer significant (11, 12). Furthermore, the effect of sexual abuse on FSS might depend on the type of abuse that was experienced, such as abuse involving contact versus abuse without bodily contact, but not much has been written on this topic (9, 15, 16). Finally, a meta-analysis found that sexual abuse and gastrointestinal complaints, but not headache or fibromyalgia, were related in adults (9). This raises the question whether sexual abuse might be a risk factor for gastrointestinal FSS in particular.

This study investigates the relation between sexual abuse and a spectrum of prospectively assessed FSS in a large population-based cohort of Dutch adolescents. It was hypothesized that 1) Sexual abuse predicts higher levels of FSS; 2) Symptoms of anxiety and depression explain at least part of this relationship; 3) Sexual abuse involving contact predicts a higher level of FSS than sexual abuse not involving contact. In addition, this study explored if sexual abuse is related to gastrointestinal symptoms in particular.

## METHODS

### Participants

This study was part of the Tracking Adolescents' Individual Lives Survey (TRAILS), a prospective population based cohort recruited from five municipalities in the North of the Netherlands (de Winter et al., 2005). In total 3483 potential participants from 135 primary

schools were identified based on their date of birth. Schools, parents and children were informed and all had to agree to participate for inclusion. Children incapable of participating due to mental retardation, serious physical illness or handicap were excluded from the study, as were children with no Dutch, Turkish or Moroccan speaking parent or guardian. At baseline in 2001, 2230 children were included (mean age 11.1 years [ $SD = 0.6$ ]). Extensive recruitment efforts were made to increase the representativeness of the cohort. No differences were found between responders and non-responders in sociodemographic factors and health outcomes (de Winter et al., 2005). Data from four assessment waves were used for this study (T1-T4, T2: mean time to follow up 2.5 years, mean age 13.6 years [ $SD = 0.5$ ]; T3: mean time to follow up 5.2 years, mean age 16.3 years [ $SD = 0.7$ ]; T4: mean time to follow up 8.0 years, mean age 19.1 years [ $SD = 0.6$ ]). Data on sexual abuse were collected for 1680 participants at T4 (Table 1). Attrition over the four waves was associated with being male, a low socioeconomic status, peer problems, substance use and externalizing problems (Nederhof et al., 2012). A more detailed description of the recruitment efforts, population characteristics and non-response bias can be found elsewhere (17-19). Approval by the Dutch Central Committee on Research Involving Human Subjects was obtained. Written informed consent was given by parents at T1 and by adolescents at T2, T3 and T4.

## Measures

*Functional Somatic Symptoms.* FSS were assessed with nine items of the Somatic Complaints subscale of the Youth Self-report (YSR) at T1-T4 (20). The YSR has been shown to have a good cross-cultural validity (21). The items refer to somatic symptoms without a known medical cause or without an obvious reason in the past six months; pain, headache, stomachache, nausea, vomiting, eye problems, skin problems, dizziness, and fatigue. Participants indicated whether they experienced these complaints *never* (0), *sometimes or a bit* (1) or *often or a lot* (2). Factor analyses showed that the items 'eye problems' and 'skin problems' had low factor loadings at all assessment waves (7), suggesting that these items do not accurately represent the underlying construct of FSS. Therefore, these items were excluded. The remaining seven items at T1-T4 showed good internal consistency with Cronbach's alpha T1: 0.76, T2: 0.77, T3: 0.75, T4: 0.79. The average score of these 7 items was used as a continuous outcome measure (range 0-2).

In the YSR questionnaire at T4, there was a difference between the online and the paper-and-pencil questionnaire presented to participants (22). In the online version, the somatic complaints subscale was preceded by a screening question referring to somatic symptoms without a known cause or obvious reason in the past 6 months. For the participants who filled in they had *never* experienced those somatic symptoms, five items (pain, headache, stomachache, nausea and vomiting) of the YSR somatic symptom scale were not shown and all automatically set to *never*. The two items dizziness and fatigue were assessed apart from this screening question, and were therefore assessed similarly in the online and the paper-

and-pencil questionnaire. Because of this additional screening question in the online version, participants who filled in the online questionnaire ( $N = 1395$ , 82%) scored substantially lower on FSS than participants using the paper-and-pencil questionnaire (independent t-test: difference = 0.11,  $p < .01$ ). To correct for the difference in method, 'type of questionnaire' was included as a covariate in all analyses.

*Sexual Abuse.* At T4 a traumatic youth experience questionnaire was filled out by the participants. In line with the Dutch definition of childhood sexual abuse, the questionnaire refers to sexual abuse before the age of 16. The questionnaire contains five items referring to sexual abuse by an adult family member, acquaintance of the family, or stranger (items listed in Table 2). Each question could be answered with *never*, *happened once*, or *happened more than once*. All questions were followed by the question 'At what age did this happen?'. In agreement with previous literature (9, 15, 16, 23, 24), a hierarchic scale consisting of *never experienced any form of sexual abuse* (0), *only experienced non-contact sexual abuse* (1), *experienced at least one form of contact abuse but no rape* (2) and *experienced rape* (3) was constructed. Because of the known age of the participants at each assessment wave and the retrospectively self-reported age of abuse, it could be reconstructed before which wave(s) the abuse took place. In some cases, the age of the participant at the time of the sexual abuse experience was similar to the age of the participant at a certain wave (T1: 9 participants, T2: 17 participants, T3: 16 participants). In these cases it remained unclear whether this type of sexual abuse took place before or after the participant filled in the somatic complaints questionnaire for that wave. Therefore, the score on the sexual abuse scale was reported as unknown (missing) for that particular wave and the higher scores on the sexual abuse scale were reported only at the following waves.

*Anxiety and Depression.* Symptoms of anxiety and depression in the past six months were assessed with the YSR DSM-IV Anxiety (six items) and Depression (thirteen items) subscales at T1-T4 (Achenbach et al., 2003; Ferdinand, 2008). The item 'overtiredness' was excluded from the Depression scale to prevent overlap with the Somatic Complaints subscale.

*Socioeconomic Status.* Sexual abuse often occurs in the context of other stressors (25, 26). One way of taking other ongoing stressors into account is adjustment for socioeconomic status (SES) (27). In line with previous research (28), SES was assessed using data on household income, educational level of both parents and occupational level of both parents using the International Standard of Classification of Occupations (29). These five indicators were documented at baseline and at T4. They were combined into one SES measure at T1, used at T1-T3, and one SES measure at T4, used at T4.

### Statistical Analysis

Analyses were performed using SPSS 20.0. Linear mixed models (LMMs) were used to study the influence of sexual abuse on the level of FSS during adolescence (30). Outcome variables were mean FSS scores at T1-T4. Sexual abuse, age, sex, SES and type of questionnaire were entered as fixed factors. A random intercept was included. To study the contribution of symptoms of anxiety and depression to the relationship between sexual abuse and FSS, anxiety and depression were added to the model as fixed factors. The Bayesian information criterion was used to define the best fitting model. To study the relationship between sexual abuse and FSS over time, the interaction term 'age\*sexual abuse' was added. Before doing this age was centred at the mean age of all four assessment waves (14.78) in order to make useful interpretations of possible outcomes. The effect of the type of abuse on the level of FSS was studied by entering the categories of the hierarchic sexual abuse scale as separate dummies in the model. To examine the effect of sexual abuse on the level of gastrointestinal FSS the mean gastrointestinal FSS item scores were studied as outcome variables. All predictors were included simultaneously in the LMMs analyses. The unstandardized estimates, *B* values, are displayed to describe the associations of the predictors with the main outcome variable FSS. P-values < .05 were considered statistically significant. Because the FSS mean item scores at T4 and gastrointestinal FSS mean item scores on all waves were skewed in the sample, bootstrapping was used to verify the estimates of *B*s and their confidence intervals for the parameters in the LMMs (31). Ten thousand bootstrap samples were performed per analysis.

## RESULTS

### Sample Characteristics

The characteristics of the sample of 1680 participants are shown in Table 1. The mean FSS score declined over time. The drop of mean FSS scores between T3 and T4 is partly due to the change in format of the questionnaire described in the method section. In this sample, 154 participants experienced some form of sexual abuse before the age of 16. Thirty participants experienced sexual abuse before T1, 18 were sexually abused between T1-T2, 80 between T2-T3, and 16 participants between T3 and T4. Please note that most participants were already 16 at T3 which might explain the low number of new cases of sexual abuse between T3-T4. Age of onset of sexual abuse ranged between 2 and 15 years old ( $M = 12.4$  years,  $SD = 3.2$ ) with a peak incidence in 14 and 15 year olds ( $n = 83, 54\%$ ).



**Table 1.** Characteristics of the Study Sample.

Characteristic	T1	T2	T3	T4
Subjects, <i>N</i> (% T4)	1658 (99%)	1642 (98%)	1466 (87%)	1680 (100%)
Female subjects, <i>n</i> (%) <sup>a</sup>	912 (55.0%)	898 (54.7%)	812 (55.4%)	921 (54.8%)
Age, mean years (SD)	11.1 (0.6)	13.5 (0.5)	16.2 (0.7)	19.1 (0.6)
FSS, mean (SD)	0.47 (0.35)	0.40 (0.36)	0.35 (0.34)	0.20 (0.31)
Sexually abused, <i>N</i> (%) <sup>a</sup>	30 (1.8%)	58 (3.4%)	138 (8.3%)	154 (9.2%)
FSS sexually abused, mean (SD)	0.61 (.36)	0.58 (.48)	0.53 (.41)	0.32 (0.41)
Sexually abused females, <i>n</i> (%) <sup>b</sup>	23 (2.5%)	46 (5.0%)	108 (11.7%)	120 (13.0%)
Sexually abused males, <i>n</i> (%) <sup>b</sup>	7 (0.9%)	12 (1.6%)	30 (4.0%)	34 (4.5%)

Note. T1-T4 represent the four assessment waves. FSS = functional somatic symptoms. <sup>a</sup>Percentages based on the total number of participants who attended the corresponding wave. <sup>b</sup>Percentages based on the total number of females/males who attended the corresponding wave.

The incidence of the five different forms of sexual abuse is shown in Table 2. When participants were divided in the three groups used for the hierarchic scale, 35 participants (23%) experienced non-contact sexual abuse only, 65 participants (42%) experienced at least one form of sexual abuse involving assault but no rape and 54 participants (35%) experienced rape. In total, 51% of all abused participants reported to have experienced at least one specific form of sexual abuse more than once.

**Table 2.** Incidence of the five forms of sexual abuse.

	Valid <i>N</i>	T1 <i>n</i> (%)	T2 <i>n</i> (%)	T3 <i>n</i> (%)	T4 <i>n</i> (%)
Non-contact	1645	21 (1.3)	38 (2.3)	86 (5.2)	98 (6.0)
Being touched	1645	22 (1.3)	40 (2.4)	87 (5.3)	96 (5.8)
Forced to touch	1646	15 (0.9)	24 (1.5)	42 (2.6)	50 (3.0)
Attempted rape	1679	10 (0.6)	18 (1.1)	51 (3.0)	62 (3.7)
Rape	1680	7 (0.4)	13 (0.8)	43 (2.6)	54 (3.2)

Note. T1-T4 represent the four assessment waves.

### Sexual Abuse and FSS during Adolescence

To assess the influence of sexual abuse on FSS during adolescence, LMMs with FSS (T1-T4) as outcomes were used. Sexual abuse significantly predicted an higher level of FSS during adolescence when adjusted for age, type of questionnaire, sex and SES (Table 3). The interaction term 'age\*sexual abuse' did not significantly predict FSS, meaning that the effect of sexual abuse did not change over time. When symptoms of anxiety and depression were

also taken into account, the strength of the relationship between sexual abuse and FSS was affected but remained significant ( $B = .03$ , 95% CI [.02, .05],  $p < .001$ ). Bootstrapping yielded similar results.

**Table 3.** Linear mixed models: The association of sexual abuse with functional somatic symptoms.

Predictors	<i>B</i>	95% CI	<i>p</i>
Intercept	.19	[.17, .22]	.001
Sex: Female	.13	[.10, .15]	.001
Age	-.03	[-.03, -.02]	.001
SES	-.02	[-.04, -.01]	.002
Sexual abuse	.06	[.04, .08]	<.001

*Note.* Linear mixed models are adjusted for type of questionnaire. Age is centered at 14.78. SES = socioeconomic status.

### Type of Sexual Abuse and FSS

In order to test the effect of the type of abuse on FSS the hierarchic scale in the form of dummies as separate predictors was entered in the LMMs. Having experienced assault or (also) rape predicted a higher level of FSS, while having experienced non-contact sexual abuse was not significantly related to FSS (Table 4). Bootstrapping yielded similar results.

**Table 4.** Linear mixed models: The effect of the severity of sexual abuse on functional somatic symptoms.

Predictors	<i>B</i>	95% CI	<i>p</i>
Intercept	.20	[.17, .22]	.001
Sexual abuse 'non-contact'	.04	[-.05, .12]	.39
Sexual abuse 'assault'	.08	[.05, .12]	<.001
Sexual abuse 'rape'	.05	[.03, .08]	<.001

*Note.* Results of linear mixed models adjusted for: Age, gender, socioeconomic status and type of questionnaire.

### Sexual Abuse and Gastrointestinal FSS

To study the influence of sexual abuse on gastrointestinal FSS in particular, LMMs with gastrointestinal FSS as outcome variables were used. Sexual abuse significantly predicted the level of gastrointestinal symptoms during adolescence ( $B = .06$ , 95% CI [.04, .08],  $p < .001$ ). However, the size of this effect was similar to the effect of sexual abuse on the broader spectrum of FSS as shown in Table 3. Bootstrapped analyses gave essentially the same results.

## DISCUSSION

This study suggests that sexual abuse predicts higher levels of FSS during adolescence when adjusting for age, sex and SES. Additional adjustment for symptoms of anxiety and depression affected the strength of this relationship. When the effect of abuse type on the level of FSS was studied, contact sexual abuse predicted a higher level of FSS while no significant association of non-contact sexual abuse with FSS was found. Finally, the effect of sexual abuse was not more prominent in gastrointestinal FSS than in a broader spectrum of FSS.

This study has several strengths. First, the large population-based cohort makes it credible that the findings are generalizable to the population. The prevalence of FSS found in this study was largely similar to previous studies in the general adolescent population, which further strengthens this assumption (2-4). In addition, the variable FSS was composed of a spectrum of FSS and the hierarchic sexual abuse scale used in this study reduced the loss of information. This probably reflects both variables more accurately than labelling them as absent or present. Third, FSS were prospectively assessed which reduced the chance of report bias. Finally, the analyses were adjusted for SES and symptoms of anxiety and depression.

When interpreting the results the following limitations should be taken into account. First, FSS were measured with a questionnaire and asked for symptoms 'without an obvious reason' or 'without a known medical cause'. Hence, it cannot be ruled out that some FSS were actually medically explained symptoms. Second, sexual abuse was assessed retrospectively, an inevitable problem because the ethics committee did not approve confronting children with these types of questions before the age of 16. This has probably led to a small underestimation of the prevalence of sexual abuse (32), and may have caused some inaccurate answers with regard to the age of the participant at the time that the sexual abuse occurred. The use of records of child protective services (CPS) would have solved the inaccuracy, but CPS substantially underestimate the prevalence of sexual abuse (32), and might introduce selection bias. However, imprecise recollection of the age of onset of the abuse would probably only have weakened the association between sexual abuse and FSS. Third, there was no information about possible non-response or drop-out rates of abused children or children with severe FSS. Though, if sexually abused participants or participants with severe somatic complaints would be more prone to drop-out, this would again probably only have weakened the found association. Moreover, the prevalence of sexual abuse found in the sample of this study was only in the lower range of what previous studies reported, and would probably have been higher if sexual abuse before the age of 18 instead of the age of 16 was assessed in this study (23). Finally, when interpreting the findings of this study it should be acknowledged that detailed information about the sexual abuse, such as

frequency, duration or perceived psychological impact, was not available. Therefore, the hierarchic scale may reflect more underlying characteristics of sexual abuse than severity in terms of the type of sexual abuse alone. Furthermore, the found associations of sexual abuse with FSS were not adjusted for other types of childhood abuse. This may have led to some overestimation of the associations between sexual abuse and FSS.

To the best of our knowledge, no previous studies have investigated the effect of sexual abuse on a spectrum of FSS in the general adolescent population. Two previous studies found that multiple unfavourable household circumstances and adversities, including sexual abuse, were associated with the occurrence of FSS in adolescents (33, 34). Several other studies found that sexual abuse was associated with specific types of FSS in adolescents (12, 15, 35-37). In addition, a history of sexual abuse was found to be associated with a spectrum of FSS in children placed in a high care foster home (11). Only one study additionally adjusted the effect of sexual abuse on gastrointestinal FSS for symptoms of anxiety and depression, and found that these symptoms fully explained the effect (12). Thus, it seems that the effect of sexual abuse on FSS is at least partly explained by symptoms of anxiety and depression. It could be that the mediating role of symptoms of anxiety and depression is greater for some particular FSS such as gastrointestinal FSS.

Further research is needed to identify mechanisms, next to symptoms of anxiety and depression, underlying the relationship between sexual abuse and FSS. One such potential mechanism could be that the chronic stress caused by sexual abuse results in alterations in hypothalamic-pituitary-adrenal axis functioning. These alterations can cause low cortisol stress-responses (38). A low cortisol level is thought to be an underlying factor of some FSS (39, 40).

In some previous studies it was suggested that the effect of sexual abuse on FSS might depend on the type of the abuse (15, 16), but this study could not fully confirm these findings. In this study, contact sexual abuse was indeed related to FSS while non-contact sexual abuse was not (16). However, assault not involving rape had the strongest association with FSS. There are several possible reasons why especially sexual abuse involving contact was related to FSS. For example, it could be that abuse involving contact triggers physical distress while abuse without contact does not.

The results of this study indicate that the effect of sexual abuse on gastrointestinal FSS is similar to the effect of sexual abuse on a broader spectrum of FSS. In contrast, a previous meta-analysis found a significant relationship of sexual abuse with chronic gastrointestinal complaints but not with fibromyalgia and headache in adults (9). However, the few studies investigating sexual abuse in relation to FSS may have lacked the power to show a significant

association in this meta-analysis. On the other hand, in the current study the effect of sexual abuse on FSS was not adjusted for other types of abuse, which may have reduced the power to detect a specific effect of sexual abuse on gastrointestinal symptoms. Previous studies in adolescents mainly focused on gastrointestinal FSS and could therefore not make this comparison (11, 12, 15, 35, 36).

The findings of this study suggest that sexual abuse is associated with higher levels of FSS in adolescents. Symptoms of anxiety and depression explained part of the effect of sexual abuse on FSS. In addition, findings indicate that sexual abuse is related to a broad spectrum of FSS and not only to particular symptoms. If these findings are replicated, FSS might be seen as a supplementary signal when childhood sexual abuse is suspected. However, it is important to keep in mind that sexual abuse explains only a small part of the variance in FSS and most adolescents with FSS were not sexually abused (in this sample the positive predictive value of experiencing at least one FSS often, or two FSS sometimes, was 14% at T4). Further research is needed to investigate to what extent sexual abuse in adolescence predicts clinically relevant FSS (e.g. functional impairment and health care visits), and how FSS are related to other types of abuse.

## REFERENCES

1. Hunfeld JA, Perquin CW, Duivenvoorden HJ, Hazebroek-Kampschreur AA, Passchier J, van Suijlekom-Smit LW, et al. Chronic pain and its impact on quality of life in adolescents and their families. *J Pediatr Psychol*. 2001 Apr-May;26(3):145-53.
2. Perquin CW, Hunfeld JA, Hazebroek-Kampschreur AA, van Suijlekom-Smit LW, Passchier J, Koes BW, et al. The natural course of chronic benign pain in childhood and adolescence: a two-year population-based follow-up study. *Eur J Pain*. 2003;7(6):551-9.
3. Saps M, Seshadri R, Sztainberg M, Schaffer G, Marshall BM, Di Lorenzo C. A prospective school-based study of abdominal pain and other common somatic complaints in children. *J Pediatr*. 2009 Mar;154(3):322-6.
4. ter Wolbeek M, van Doornen LJ, Kavelaars A, Heijnen CJ. Severe fatigue in adolescents: a common phenomenon? *Pediatrics*. 2006 Jun;117(6):e1078-86.
5. Beck JE. A developmental perspective on functional somatic symptoms. *J Pediatr Psychol*. 2008 Jun;33(5):547-62.
6. Janssens KA, Rosmalen JG, Ormel J, van Oort FV, Oldehinkel AJ. Anxiety and depression are risk factors rather than consequences of functional somatic symptoms in a general population of adolescents: the TRAILS study. *J Child Psychol Psychiatry*. 2010 Mar;51(3):304-12.
7. Janssens KA, Klis S, Kingma EM, Oldehinkel AJ, Rosmalen JG. Predictors for persistence of functional somatic symptoms in adolescents. *J Pediatr*. 2014 Apr;164(4):900,905.e2.
8. Afari N, Ahumada SM, Wright LJ, Mostoufi S, Golnari G, Reis V, et al. Psychological trauma and functional somatic syndromes: a systematic review and meta-analysis. *Psychosom Med*. 2014 Jan;76(1):2-11.
9. Paras ML, Murad MH, Chen LP, Goranson EN, Sattler AL, Colbenson KM, et al. Sexual abuse and lifetime diagnosis of somatic disorders: a systematic review and meta-analysis. *JAMA*. 2009 Aug 5;302(5):550-61.
10. Davis DA, Luecken LJ, Zautra AJ. Are reports of childhood abuse related to the experience of chronic pain in adulthood? A meta-analytic review of the literature. *Clin J Pain*. 2005 Sep-Oct;21(5):398-405.
11. Kugler BB, Bloom M, Kaercher LB, Truax TV, Storch EA. Somatic symptoms in traumatized children and adolescents. *Child Psychiatry Hum Dev*. 2012 Oct;43(5):661-73.
12. van Tilburg MA, Runyan DK, Zolotor AJ, Graham JC, Dubowitz H, Litrownik AJ, et al. Unexplained gastrointestinal symptoms after abuse in a prospective study of children at risk for abuse and neglect. *Ann Fam Med*. 2010 Mar-Apr;8(2):134-40.
13. Blaney PH. Affect and memory: a review. *Psychol Bull*. 1986 Mar;99(2):229-46.
14. Chen LP, Murad MH, Paras ML, Colbenson KM, Sattler AL, Goranson EN, et al. Sexual abuse and lifetime diagnosis of psychiatric disorders: systematic review and meta-analysis. *Mayo Clin Proc*. 2010 Jul;85(7):618-29.
15. Bendixen M, Muus KM, Schei B. The impact of child sexual abuse—a study of a random sample of Norwegian students. *Child Abuse Negl*. 1994 Oct;18(10):837-47.
16. Leserman J, Drossman DA, Li Z, Toomey TC, Nachman G, Glogau L. Sexual and physical abuse history in gastroenterology practice: how types of abuse impact health status. *Psychosom Med*. 1996 Jan-Feb;58(1):4-15.
17. de Winter AF, Oldehinkel AJ, Veenstra R, Brunnekreef JA, Verhulst FC, Ormel J. Evaluation of non-response bias in mental health determinants and outcomes in a large sample of pre-adolescents. *Eur J Epidemiol*. 2005;20(2):173-81.
18. Huisman M, Oldehinkel AJ, de Winter A, Minderaa RB, de Bildt A, Huizink AC, et al. Cohort profile: the Dutch 'TRacking Adolescents' Individual Lives' Survey'; TRAILS. *Int J Epidemiol*. 2008 Dec;37(6):1227-35.
19. Nederhof E, Jorg F, Raven D, Veenstra R, Verhulst FC, Ormel J, et al. Benefits of extensive recruitment effort persist during follow-ups and are consistent across age group and survey method. The TRAILS study. *BMC Med Res Methodol*. 2012 Jul 2;12:93,2288-12-93.
20. Achenbach TM, Dumenci L, Rescorla LA. DSM-oriented and empirically based approaches to constructing scales from the same item pools. *J Clin Child Adolesc Psychol*. 2003 Sep;32(3):328-40.
21. de Groot A, Koot HM, Verhulst FC. Cross-cultural generalizability of the Youth Self-Report and Teacher's Report Form cross-informant syndromes. *J Abnorm Child Psychol*. 1996 Oct;24(5):651-64.
22. Janssens KA, Oldehinkel AJ, Bonvanie IJ, Rosmalen JG. An inactive lifestyle and low physical fitness are associated with functional somatic symptoms in adolescents. The TRAILS study. *J Psychosom Res*. 2014 Jun;76(6):454-7.
23. Barth J, Bermetz L, Heim E, Trelle S, Tonia T. The current prevalence of child sexual abuse worldwide: a systematic review and meta-analysis. *Int J Public Health*. 2012 Nov 21.
24. Zink T, Klesges L, Stevens S, Decker P. The development of a sexual abuse severity score: characteristics of childhood sexual abuse associated with trauma symptomatology, somatization, and alcohol abuse. *J Interpers Violence*. 2009 Mar;24(3):537-46.
25. MacMillan HL, Tanaka M, Duku E, Vaillancourt T, Boyle MH. Child physical and sexual abuse in a community sample of young adults: results from the Ontario Child Health Study. *Child Abuse Negl*. 2013 Jan;37(1):14-21.
26. Mills R, Scott J, Alati R, O'Callaghan M, Najman JM, Strathearn L. Child maltreatment and adolescent

- mental health problems in a large birth cohort. *Child Abuse Negl.* 2013 May;37(5):292-302.
27. Sedlak AJ, Mettenberg J, Basena M, Petta I, McPherson K, Greene A, et al. 5.2 Differences in the incidence of maltreatment related to socioeconomic status (SES). In: *Fourth National Incidence Study of Child Abuse and Neglect (NIS-4): Report to Congress*; Washington, DC: U.S. Department of Health and Human Services, Administration for Children and Families.; 2010. p. 5-10.
28. Oakes JM, Rossi PH. The measurement of SES in health research: current practice and steps toward a new approach. *Social science & medicine.* 2003;56:769-84.
29. Ganzeboom HBG, Treiman DJ. Internationally Comparable Measures of Occupational Status for the 1988 International Standard Classification of Occupations. *Social Science Research.* 1996;25:201-39.
30. Brady T, West MA. Analyzing longitudinal data with the linear mixed models procedure in SPSS. *Evaluation & the Health Professions.* 2009;32(3):207-28.
31. Wright DB, London K, Field AP. Using bootstrap estimation and the PLug-in Principle for clinical psychology data. *Journal of Experimental Psychopathology.* 2011;2(2):252-70.
32. Everson MD, Smith JB, Hussey JM, English D, Litrownik AJ, Dubowitz H, et al. Concordance between adolescent reports of childhood abuse and Child Protective Service determinations in an at-risk sample of young adolescents. *Child Maltreat.* 2008 Feb;13(1):14-26.
33. Flaherty EG, Thompson R, Litrownik AJ, Zolotor AJ, Dubowitz H, Runyan DK, et al. Adverse childhood exposures and reported child health at age 12. *Acad Pediatr.* 2009 May-Jun;9(3):150-6.
34. Flaherty EG, Thompson R, Dubowitz H, Harvey EM, English DJ, Proctor LJ, et al. Adverse childhood experiences and child health in early adolescence. *JAMA Pediatr.* 2013 Jul;167(7):622-9.
35. Devanarayana NM, Rajindrajith S, Perera MS, Nishanthanie SW, Karunanayake A, Benninga MA. Association Between Functional Gastrointestinal Diseases and Exposure to Abuse in Teenagers. *J Trop Pediatr.* 2014 Jul 23.
36. Holmberg LI, Hellberg D. Sexually abused children. Characterization of these girls when adolescents. *Int J Adolesc Med Health.* 2010 Apr-Jun;22(2):291-300.
37. Zafar M, Kashikar-Zuck SM, Slater SK, Allen JR, Barnett KA, Lecates SL, et al. Childhood abuse in pediatric patients with chronic daily headache. *Clin Pediatr (Phila).* 2012 Jun;51(6):590-3.
38. Heim C, Nater UM, Maloney E, Boneva R, Jones JF, Reeves WC. Childhood trauma and risk for chronic fatigue syndrome: association with neuroendocrine dysfunction. *Arch Gen Psychiatry.* 2009 Jan;66(1):72-80.
39. Janssens KA, Oldehinkel AJ, Verhulst FC, Hunfeld JA, Ormel J, Rosmalen JG. Symptom-specific associations between low cortisol responses and functional somatic symptoms: the TRAILS study. *Psychoneuroendocrinology.* 2012 Mar;37(3):332-40.
40. Tak LM, Cleare AJ, Ormel J, Manoharan A, Kok IC, Wessely S, et al. Meta-analysis and meta-regression of hypothalamic-pituitary-adrenal axis activity in functional somatic disorders. *Biol Psychol.* 2011 May;87(2):183-94.