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Functional somatic symptoms in adolescence and young adulthood

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Chapter 1| general introduction

Functional somatic symptoms: a problem?

Functional somatic symptoms (FSS) are symptoms for which no underlying medical condition can be identified. Somatic symptoms which are in fact due to a well-defined medical disease but are more severe, more impairing, or persist longer than expected based on the underlying medical findings are also considered functional. The term FSS encompasses several pain symptoms such as musculoskeletal pains and headache, but also other somatic complaints such as abdominal symptoms and fatigue. FSS are very common in the general pediatric population with 25-35% of all children and adolescents experiencing FSS (1-3). FSS are often transient in nature and might thus be considered normal rather than a health problem (1-3). Yet, FSS can become highly persistent in some young people (3-9), and prevalence rates of most functional pains and fatigue increase with increasing age (4,5). Around 10% of all adolescents and young adults experience daily or high intensity pains which last longer than three months (4,5). These ongoing FSS can lead to problems such as impaired daily physical and social activities, parental distress, and school absenteeism (4,5,10,11). In addition, FSS in late adolescence increase the risk of severe and persistent FSS in adulthood, and other health problems later in life (6,8,12-15).

Of all children, adolescents and young adults with FSS, around one third visits primary health care for these symptoms (16,17). Health care professionals are thus frequently consulted by pediatric and young adult patients with FSS (18-20). In addition to the influence of FSS on children's and young adult's health care consumption, FSS also affect the economic productivity of young adults (21,22). Considering the prevalence, impact and costs of FSS, it is undeniable that, although medically not well explained, FSS are a major medical problem.

Etiology: Diathesis-stress model

The etiology of FSS in young people is largely unclear. FSS are believed to be the result of a multifactorial process in which physiological, psychological and social factors all play an important role (23,24). To understand the contribution of different potential risk factors in the development of FSS, experiencing symptoms can be conceptualized as the result of an interaction between personal vulnerabilities or diathesis for FSS and external factors triggering FSS.

How vulnerable young people are for the development of FSS may depend on how they respond to external triggers such as psychosocial stressors or infections. Vulnerabilities may predispose young people for non-adaptive or prolonged psychological and physiological stress-responses. These responses are thought to cause and perpetuate FSS by increasing bodily signals (e.g. palpitations, dysfunctional breathing) or alter the awareness of bodily signals (e.g. sensitization, preoccupation). In addition, both vulnerability for non-adaptive stress responses and external triggers

may influence cognitions, emotions and behavior to bodily signals (23). Psychosocial stressors, for example, can induce a depressed mood, catastrophizing, or avoidance behavior (25-28). One can imagine that once someone is depressed, learned an avoidant coping style, or becomes inactive, his/her vulnerability for non-adaptive responses towards external triggers further increases. The continuous interaction between personal vulnerabilities and external triggers may thus create a negative spiral, resulting in ongoing FSS. In other words, chronic FSS may develop when the burden of external triggers, including psychosocial stressors, exceeds the capacity of a person to psychologically and physiologically cope with these triggers over time.

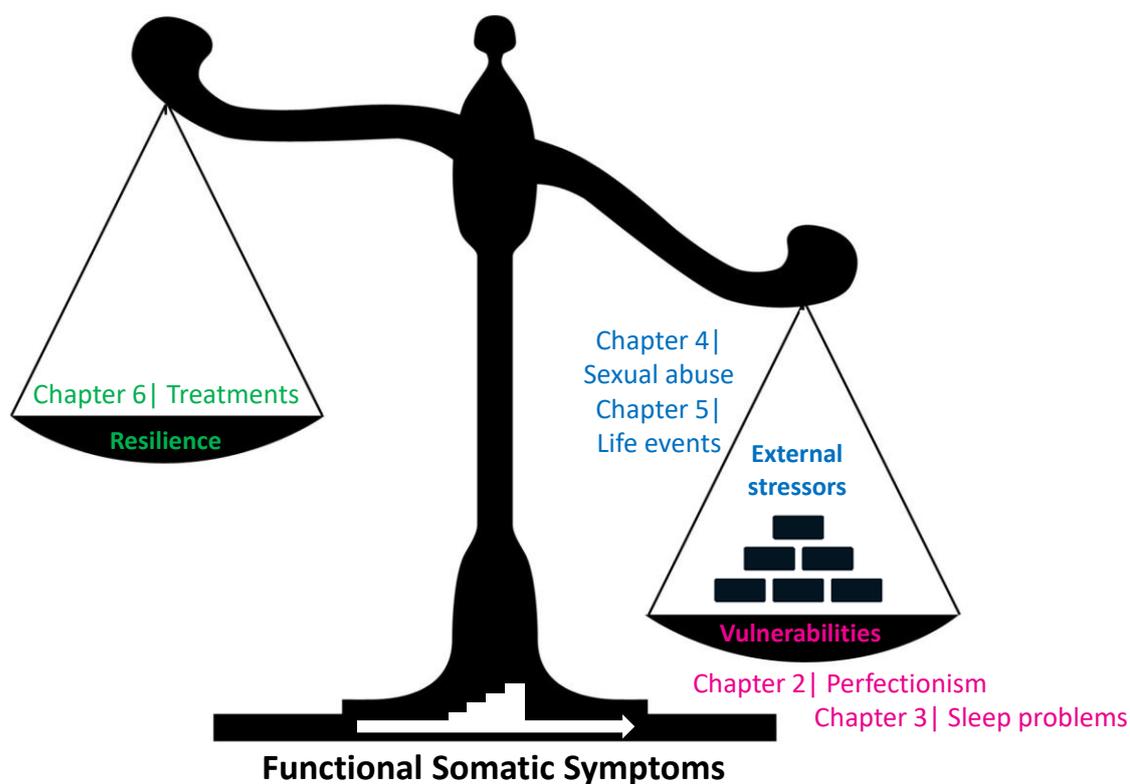
Older adolescence and young adulthood as window of vulnerability

FSS are believed to be the result of various interacting physiological, psychological and social risk factors (24,29). Potential risk factors for FSS should thus be studied in a developmental period wherein the exposure to these factors is relatively high or thought to be of relatively great influence. Older adolescence and emerging adulthood (i.e. 16-25 years) are characterized by profound psychosocial changes. Adolescents finish high school and gradually the dependency of childhood is replaced by the potentially demanding responsibilities of adulthood. Different possibilities in work, love, social environment and personal beliefs are explored. Because of these new and increasing responsibilities and the exploration of life options, many older adolescents and young adults face various, and potentially stressful, life events (30). Increasing external demands and life events are thought to play an important role in the development of FSS (2,24,31). During the same time period, personality characteristics are shaped, and activities and sleep behavior change (32,33). Certain personality characteristics such as neuroticism and inactivity or lack of sleep may sensitize young people for FSS later in life (34). Taken the above together, late adolescence and young adulthood could be considered a unique and important period to study the role of the above mentioned personal vulnerability factors and external stressors in the development of FSS.

This thesis

In this thesis I have investigated the roles of the personal vulnerability factors perfectionism and sleep problems, and the role of life events, in the development of FSS. In addition, the content and effectiveness of psychological treatments for FSS in children was systematically reviewed and analyzed. The outline of this thesis can be visualized within the diathesis-stress model of FSS as shown in Figure 1.

Figure 1.1. Diathesis-stress model.



Note. FSS can be conceptualized as an interaction between personal vulnerabilities to develop FSS (e.g. perfectionism and sleep problems) and external factors, including psychosocial stressors, triggering FSS (e.g. sexual abuse, life events).

Personal vulnerability factors or diathesis

As described above, FSS can be conceptualized as a mismatch between burdens or demands and an individual's capacity to deal with these external triggers. A risk factor of potential importance is a 'vulnerable personality'. In particular the trait neuroticism has been theorized to cause FSS (2,24,29,31,35). In adults, it has been shown that this trait increases the incidence of negative life events and heightens reactivity to external stressors. Neuroticism has further been associated with poor mental and physical health including FSS in both children and adults (34,36-39). Maladaptive perfectionism, characterized by self-criticism, is assumed to be closely related to neuroticism (40,41), but received less attention in the research field of FSS. So far, perfectionistic characteristics have only been investigated in adults with chronic fatigue syndrome (42-44). It therefore remains unclear if perfectionism is a typical feature of adult patients with chronic fatigue syndrome or indeed predictive of various FSS in later adolescence.

Another potential risk factor predisposing individuals for FSS, is having troubles with sleeping. Sleep habits change in young adults, and suffering from sleep problems

is a common phenomenon at these ages (45). FSS and sleep are thought to influence each other from day to day (46). Problems with sleeping have also been shown to precede pain symptoms over long time periods (i.e. years) (47), and thus the question arises if sleep problems can actually perpetuate pain and increase the level of experienced pain on the long term. Suggested mechanisms for this potential effect are general deconditioning of the body which increases the level of bodily signals, impaired filtering mechanisms by central sensitization, or depletion of coping resources due to increased emotional disturbances (48,49).

External stressors

External stressors are postulated to play a major role in the etiology of FSS (2,24,31). As mentioned earlier, life events have been hypothesized to trigger a cascade of stress-responses which increase bodily signaling, decrease the filtering of these signals, and/or influence emotions, cognitions and behavior towards stressors and bodily signals (23). Altered psychological stress-responses and FSS may create even more daily distress or increase personal vulnerability for FSS. However, empirical evidence confirming the role of stressors in the development of FSS chiefly relies on retrospective studies in adult populations suffering from specific functional somatic disorders (50-53). Findings from retrospective studies in clinical samples of adults are not well generalizable, and may be influenced by selection and recall bias. Prospective research on this topic is scarce (3,54-56) and it remains largely unknown to what extent life events influence FSS in young people (2,24,31). Therefore, prospective research in adolescent populations is needed to identify the role of life events in the development of FSS during this life-phase.

Another yet unanswered question is if some types of external stressors are particularly important for the development of specific FSS. The relation of a sexual abuse history with abdominal FSS, for example, has far more often been investigated than the relation of sexual abuse with other types of FSS (53). It remains unclear if sexual abuse has indeed a particular influence on abdominal FSS. It has also been suggested that especially illness-related events, more than other types of events, are important for the development of FSS (57,58), possibly by increasing attention or anxiety for bodily signals (59). However, whether illness-related events are more strongly related to FSSs than non-illness-related events has not been studied yet. One could also wonder if negative life events are still important in the context of more chronic stressors such as a low socio-economic status. Low socio-economic status has been related to both the experience of more life events and the development of FSS and might thus account for the relation between life events and FSS (60,61). Further, it would be informative for treatment purposes to investigate if early life stressors make young people more vulnerable for the effects of subsequent stressors. Childhood disadvantages, for example, may be seen as triggering factors but may also sensitize

individuals for the effects of distress later in life (31). Likewise, adolescents who grew up in poorly functioning households or who suffer from anxiety or depression may be more sensitive to the effects of recent life events. Revealing unfortunate combinations of vulnerabilities and later stressors could lead to a better identification of the individuals most susceptible to FSS.

Targets for psychological treatments

Based on the diathesis-stress model there are two ways to intervene with the development and course of FSS; decreasing the vulnerability of young people for further development of FSS and increasing resources to cope with external triggers. With regard to the potential vulnerability factor perfectionism, treatments with specific treatment elements and forms aimed at perfectionistic emotions, cognitions and behaviors may be effective to treat FSS. Sleep hygiene education could be an effective intervention to reduce sleep problems and their role in the development of FSS. If external stressors do indeed play a prominent role in the development of FSS, coping skills training or cognitive behavioral treatment (CBT) specifically aimed at cognitions and behaviors towards external stressors could also be promising.

The content and effectiveness of investigated psychological treatments for children suffering from FSS has never been systematically reviewed (62-64). It thus remains largely unclear if predisposing factors, such as perfectionism and sleep problems, and potential triggers such as external stressors, are currently treated, how this is done, and whether this approach is effective. Illness characteristics such as the type of FSS, symptom severity, comorbidities and age of the patient could also influence the effectiveness of therapies (65). The effect of these illness characteristics on outcomes have not yet been described or analyzed in children and adolescents with FSS (62-64). To guide future research and clinical care, it would be helpful to systematically explore what perpetuating factors are already targeted in psychological treatments, how this is done, and for who this is most effective.

Outline of this thesis

In this thesis we aimed to reveal the effects of perfectionism, sleep problems and life events on FSS in adolescents and young adults. To provide an overview of what risk factors are already targeted in the treatment of FSS, how these risk factors are targeted, and how effective these approaches are, the literature was systematically reviewed on the content and effectiveness of psychological treatments for FSS in children and adolescents.

In *chapter 2* we investigated whether perfectionism was associated with higher levels of FSS, and predicted an increase in FSS over years. The long-term bidirectional relations between sleep problems and three pain types, abdominal pain, headaches, and musculoskeletal pain, are described in *chapter 3*. In *chapter 4* we have studied the

association between childhood sexual abuse and FSS during adolescence. In *chapter 5* we investigated the effects of negative life events on FSS in older adolescents. In *chapter 3* and *chapter 5* interactions between vulnerability factors and stressors on the level and type of FSS are explored. Finally, a systematic review and meta-analyses of psychological treatments and their effectiveness for the treatment of children suffering from FSS is provided in *chapter 6*.

The potential risk factors addressed in the first four chapters are all investigated with data from the Tracking Adolescents' Individual Lives Survey (TRAILS), a general population cohort of adolescents and emerging adults from the North of the Netherlands. The main objective of TRAILS is to investigate the etiology, underlying mechanisms, and course of mental and physical health during adolescence and young adulthood (66). At baseline in 2001, 2230 children and their parents were included in this cohort. To date, TRAILS participants have been assessed five times, every 2-3 years, from the age of 11 until the age of 22. Extensive recruitment efforts ensured that of the all adolescents enrolled at baseline, 96% participated at the second wave, 81% participated at the third wave, 84% participated at the fourth wave, and 80% participated at the fifth wave (67,68).

References

- (1) Berntsson LT, Kohler L, Gustafsson JE. Psychosomatic complaints in schoolchildren: a Nordic comparison. *Scand J Public Health* 2001 Mar;29(1):44-54.
- (2) Eminson DM. Medically unexplained symptoms in children and adolescents. *Clin Psychol Rev* 2007 Oct;27(7):855-871.
- (3) 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.
- (4) Hoftun GB, Romundstad PR, Zwart JA, Rygg M. Chronic idiopathic pain in adolescence--high prevalence and disability: the young HUNT Study 2008. *Pain* 2011 Oct;152(10):2259-2266.
- (5) Mallen C, Peat G, Thomas E, Croft P. Severely disabling chronic pain in young adults: prevalence from a population-based postal survey in North Staffordshire. *BMC Musculoskelet Disord* 2005 Jul 21;6:42.
- (6) Lamers F, Hickie I, Merikangas KR. Prevalence and correlates of prolonged fatigue in a U.S. sample of adolescents. *Am J Psychiatry* 2013 May;170(5):502-510.
- (7) El-Metwally A, Salminen JJ, Auvinen A, Kautiainen H, Mikkelsen M. Prognosis of non-specific musculoskeletal pain in preadolescents: a prospective 4-year follow-up study till adolescence. *Pain* 2004 Aug;110(3):550-559.
- (8) Kashikar-Zuck S, Parkins IS, Ting TV, Verkamp E, Lynch-Jordan A, Passo M, et al. Controlled follow-up study of physical and psychosocial functioning of adolescents with juvenile primary fibromyalgia syndrome. *Rheumatology (Oxford)* 2010 Nov;49(11):2204-2209.
- (9) Huguet A, Miro J. The severity of chronic pediatric pain: an epidemiological study. *J Pain* 2008 Mar;9(3):226-236.
- (10) Roth-Isigkeit A, Thyen U, Stoven H, Schwarzenberger J, Schmucker P. Pain among children and adolescents: restrictions in daily living and triggering factors. *Pediatrics* 2005 Feb;115(2):e152-62.
- (11) Janssens KA, Oldehinkel AJ, Dijkstra JK, Veenstra R, Rosmalen JG. School absenteeism as a perpetuating factor of functional somatic symptoms in adolescents: the TRAILS study. *J Pediatr* 2011 Dec;159(6):988-93.e1.
- (12) Bohman H, Jonsson U, Paaren A, von Knorring L, Olsson G, von Knorring AL. Prognostic significance of functional somatic symptoms in adolescence: a 15-year community-based follow-up study of adolescents with depression compared with healthy peers. *BMC Psychiatry* 2012 Jul 27;12:90-244X-12-90.
- (13) Thornton GC, Goldacre MJ, Goldacre R, Howarth LJ. Diagnostic outcomes following childhood non-specific abdominal pain: a record-linkage study. *Arch Dis Child* 2015 Jul 28.
- (14) Walker LS, Sherman AL, Bruehl S, Garber J, Smith CA. Functional abdominal pain patient subtypes in childhood predict functional gastrointestinal disorders with chronic pain and psychiatric comorbidities in adolescence and adulthood. *Pain* 2012 Sep;153(9):1798-1806.
- (15) Brattberg G. Do pain problems in young school children persist into early adulthood? A 13-year follow-up. *Eur J Pain* 2004 Jun;8(3):187-199.
- (16) Rask CU, Ornbol E, Fink PK, Skovgaard AM. Functional somatic symptoms and consultation patterns in 5- to 7-year-olds. *Pediatrics* 2013 Aug;132(2):e459-67.
- (17) Perquin CW, Hunfeld JA, Hazebroek-Kampschreur AA, van Suijlekom-Smit LW, Passchier J, Koes BW, et al. Insights in the use of health care services in chronic benign pain in childhood and adolescence. *Pain* 2001 Nov;94(2):205-213.
- (18) Verhaak PF, Meijer SA, Visser AP, Wolters G. Persistent presentation of medically unexplained symptoms in general practice. *Fam Pract* 2006 Aug;23(4):414-420.
- (19) Nimnuan C, Hotopf M, Wessely S. Medically unexplained symptoms: an epidemiological study in seven specialities. *J Psychosom Res* 2001 Jul;51(1):361-367.
- (20) Starfield B, Gross E, Wood M, Pantell R, Allen C, Gordon IB, et al. Psychosocial and psychosomatic diagnoses in primary care of children. *Pediatrics* 1980 Aug;66(2):159-167.
- (21) Sleed M, Eccleston C, Beecham J, Knapp M, Jordan A. The economic impact of chronic pain in adolescence: methodological considerations and a preliminary costs-of-illness study. *Pain* 2005 Dec 15;119(1-3):183-190.
- (22) Zonneveld LN, Sprangers MA, Kooiman CG, van 't Spijker A, Busschbach JJ. Patients with unexplained physical symptoms have poorer quality of life and higher costs than other patient groups: a cross-sectional study on burden. *BMC Health Serv Res* 2013 Dec 17;13:520-6963-13-520.

- (23) Rief W, Barsky AJ. Psychobiological perspectives on somatoform disorders. *Psychoneuroendocrinology* 2005 Nov;30(10):996-1002.
- (24) Beck JE. A developmental perspective on functional somatic symptoms. *J Pediatr Psychol* 2008 Jun;33(5):547-562.
- (25) Lindert J, von Ehrenstein OS, Grashow R, Gal G, Braehler E, Weisskopf MG. Sexual and physical abuse in childhood is associated with depression and anxiety over the life course: systematic review and meta-analysis. *Int J Public Health* 2014 Apr;59(2):359-372.
- (26) Hasenbring MI, Verbunt JA. Fear-avoidance and endurance-related responses to pain: new models of behavior and their consequences for clinical practice. *Clin J Pain* 2010 Nov-Dec;26(9):747-753.
- (27) Witthoft M, Hiller W. Psychological approaches to origins and treatments of somatoform disorders. *Annu Rev Clin Psychol* 2010;6:257-283.
- (28) Andersen TE, Karstoft KI, Brink O, Elklit A. Pain-catastrophizing and fear-avoidance beliefs as mediators between post-traumatic stress symptoms and pain following whiplash injury - A prospective cohort study. *Eur J Pain* 2016 Feb 26.
- (29) Palermo TM, Valrie CR, Karlson CW. Family and parent influences on pediatric chronic pain: a developmental perspective. *Am Psychol* 2014 Feb-Mar;69(2):142-152.
- (30) Arnett JJ. Emerging adulthood. A theory of development from the late teens through the twenties. *Am Psychol* 2000 May;55(5):469-480.
- (31) Kozłowska K. Functional somatic symptoms in childhood and adolescence. *Curr Opin Psychiatry* 2013 Sep;26(5):485-492.
- (32) Maslowsky J, Ozer EJ. Developmental trends in sleep duration in adolescence and young adulthood: evidence from a national United States sample. *J Adolesc Health* 2014 Jun;54(6):691-697.
- (33) Aarnio M, Winter T, Peltonen J, Kujala UM, Kaprio J. Stability of leisure-time physical activity during adolescence--a longitudinal study among 16-, 17- and 18-year-old Finnish youth. *Scand J Med Sci Sports* 2002 Jun;12(3):179-185.
- (34) Deary V, Chalder T, Sharpe M. The cognitive behavioural model of medically unexplained symptoms: a theoretical and empirical review. *Clin Psychol Rev* 2007 Oct;27(7):781-797.
- (35) Lievesley K, Rimes KA, Chalder T. A review of the predisposing, precipitating and perpetuating factors in Chronic Fatigue Syndrome in children and adolescents. *Clin Psychol Rev* 2014 Apr;34(3):233-248.
- (36) Rosmalen JG, Neeleman J, Gans RO, de Jonge P. The association between neuroticism and self-reported common somatic symptoms in a population cohort. *J Psychosom Res* 2007 Mar;62(3):305-311.
- (37) Garralda ME. Somatisation in children. *J Child Psychol Psychiatry* 1996 Jan;37(1):13-33.
- (38) Kowal A, Pritchard D. Psychological characteristics of children who suffer from headache: a research note. *J Child Psychol Psychiatry* 1990 May;31(4):637-649.
- (39) Liebman WM. Recurrent abdominal pain in children: a retrospective survey of 119 patients. *Clin Pediatr (Phila)* 1978 Feb;17(2):149-153.
- (40) Enns MW, Cox BJ, Clara IP. Perfectionism and Neuroticism: A Longitudinal Study of Specific Vulnerability and Diathesis-Stress Models. *Cognitive Therapy and Research*. 2005;29(4):463-478.
- (41) Stairs AM, Smith GT, Zapolski TC, Combs JL, Settles RE. Clarifying the construct of perfectionism. *Assessment* 2012 Jun;19(2):146-166.
- (42) Dittner AJ, Rimes K, Thorpe S. Negative perfectionism increases the risk of fatigue following a period of stress. *Psychol Health* 2011 Mar;26(3):253-268.
- (43) Kempke S, Luyten P, Claes S, Goossens L, Bekaert P, Van Wambeke P, et al. Self-critical perfectionism and its relationship to fatigue and pain in the daily flow of life in patients with chronic fatigue syndrome. *Psychol Med* 2013 May;43(5):995-1002.
- (44) Kempke S, Van Houdenhove B, Luyten P, Goossens L, Bekaert P, Van Wambeke P. Unraveling the role of perfectionism in chronic fatigue syndrome: is there a distinction between adaptive and maladaptive perfectionism? *Psychiatry Res* 2011 Apr 30;186(2-3):373-377.
- (45) Ohayon MM, Roberts RE, Zulley J, Smirne S, Priest RG. Prevalence and patterns of problematic sleep among older adolescents. *J Am Acad Child Adolesc Psychiatry* 2000 Dec;39(12):1549-1556.
- (46) Valrie CR, Bromberg MH, Palermo T, Schanberg LE. A systematic review of sleep in pediatric pain populations. *J Dev Behav Pediatr* 2013 Feb;34(2):120-128.
- (47) Finan PH, Goodin BR, Smith MT. The association of sleep and pain: an update and a path forward. *J Pain* 2013 Dec;14(12):1539-1552.

- (48) Smith MT, Haythornthwaite JA. How do sleep disturbance and chronic pain inter-relate? Insights from the longitudinal and cognitive-behavioral clinical trials literature. *Sleep Med Rev* 2004 Apr;8(2):119-132.
- (49) Sivertsen B, Lallukka T, Petrie KJ, Steingrimsdottir OA, Stubhaug A, Nielsen CS. Sleep and Pain Sensitivity in Adults. *Pain* 2015 Feb 13.
- (50) Van Houdenhove B, Egle UT. Fibromyalgia: a stress disorder? Piecing the biopsychosocial puzzle together. *Psychother Psychosom* 2004 Sep-Oct;73(5):267-275.
- (51) Fukudo S. Stress and visceral pain: focusing on irritable bowel syndrome. *Pain* 2013 Dec;154 Suppl 1:S63-70.
- (52) 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.
- (53) 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):550-561.
- (54) King S, Chambers CT, Huguet A, MacNevin RC, McGrath PJ, Parker L, et al. The epidemiology of chronic pain in children and adolescents revisited: a systematic review. *Pain* 2011 Dec;152(12):2729-2738.
- (55) van Gils A, Janssens KA, Rosmalen JG. Family disruption increases functional somatic symptoms in late adolescence: the TRAILS study. *Health Psychol* 2014 Nov;33(11):1354-1361.
- (56) Gini G, Pozzoli T. Bullied children and psychosomatic problems: a meta-analysis. *Pediatrics* 2013 Oct;132(4):720-729.
- (57) Hotopf M. Childhood experience of illness as a risk factor for medically unexplained symptoms. *Scand J Psychol* 2002 Apr;43(2):139-146.
- (58) Schulte IE, Petermann F. Familial risk factors for the development of somatoform symptoms and disorders in children and adolescents: a systematic review. *Child Psychiatry Hum Dev* 2011 Oct;42(5):569-583.
- (59) van Tilburg MA, Levy RL, Walker LS, Von Korff M, Feld LD, Garner M, et al. Psychosocial mechanisms for the transmission of somatic symptoms from parents to children. *World J Gastroenterol* 2015 May 14;21(18):5532-5541.
- (60) Lacey RJ, Belcher J, Croft PR. Does life course socio-economic position influence chronic disabling pain in older adults? A general population study. *Eur J Public Health* 2013 Aug;23(4):534-540.
- (61) Brady SS, Matthews KA. The influence of socioeconomic status and ethnicity on adolescents' exposure to stressful life events. *J Pediatr Psychol* 2002 Oct-Nov;27(7):575-583.
- (62) Rutten JM, Korterink JJ, Venmans LM, Benninga MA, Tabbers MM. Nonpharmacologic treatment of functional abdominal pain disorders: a systematic review. *Pediatrics* 2015 Mar;135(3):522-535.
- (63) Eccleston C, Palermo TM, Williams AC, Lewandowski Holley A, Morley S, Fisher E, et al. Psychological therapies for the management of chronic and recurrent pain in children and adolescents. *Cochrane Database Syst Rev* 2014 May 5;5:CD003968.
- (64) Knight SJ, Scheinberg A, Harvey AR. Interventions in pediatric chronic fatigue syndrome/myalgic encephalomyelitis: a systematic review. *J Adolesc Health* 2013 Aug;53(2):154-165.
- (65) Schroder A, Sharpe M, Fink P. Medically unexplained symptom management. *Lancet Psychiatry* 2015 Jul;2(7):587-588.
- (66) 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):1227-1235.
- (67) 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):173-181.
- (68) 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.