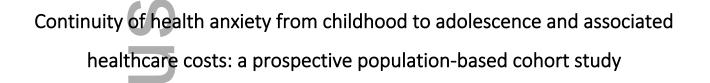


## MR. MARTIN K. RIMVALL (Orcid ID : 0000-0003-2627-5523)

Article type : Original Article



## Running head: Health anxiety in youth and associated healthcare costs

Martin K. Rimvall,<sup>1,2</sup> Pia Jeppesen,<sup>1,2</sup> Anne Mette Skovgaard,<sup>3</sup> Frank Verhulst,<sup>1,2,4</sup> Else Marie Olsen,<sup>5,6</sup> and Charlotte Ulrikka Rask<sup>7,8</sup>

<sup>1</sup>Child and Adolescent Mental Health Center, Mental Health Services, Capital Region of Denmark, Denmark; <sup>2</sup>Department of Clinical Medicine, Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark; <sup>3</sup>National Institute of Public Health, University of Southern Denmark, Odense, Denmark; <sup>4</sup>Department of Child Psychiatry/Psychology, Erasmus University Medical Center, Rotterdam, Netherlands; <sup>5</sup>Department of Public Health, Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark; <sup>6</sup>Center for Clinical Research and Prevention, Capital Region of Denmark, Denmark; <sup>7</sup>Department of Child and Adolescent Psychiatry, Research Unit, Aarhus University Hospital, Aarhus, Denmark; <sup>8</sup>Department of Clinical Medicine, Aarhus University, Aarhus, Denmark

## Conflict of interest statement: See Acknowledgements for full disclosures.

This is the author manuscript accepted for publication and has undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the <u>Version of Record</u>. Please cite this article as <u>doi:</u> 10.1111/JCPP.13286

Background: Severe health anxiety (HA) is characterized by excessive and impairing worry and preoccupation with health issues and can cause increased and unnecessary medical examinations. HA in childhood and adolescence is scarcely explored, hindering the potential for prevention and early intervention. **Methods:** HA was assessed in 1278 children/youths at two time points at ages 11 and 16 years in a general population-based birth cohort. Register-based data on costs related to non-hospital-based primary and secondary somatic health services were obtained over the follow-up-period. Presence of functional somatic symptoms, emotional disorders and chronic somatic illness at baseline were included as covariates. Results: High HA (top 10% score) at age 11 predicted high HA at age 16 (relative risk [RR] 2.03, 95%CI 1.26-3.31). The group with persistent HA was small (n=17, 1.3%), resulting in broad confidence-intervals. The statistical effect of HA at age 11 on HA at age 16 was heavily reduced after adjustment for sex and all covariates (RR 1.49, 95%CI 0.85-2.60). In the adjusted model, somatic illness at age 11 (RR 1.91, 95%CI 1.22-2.98) and female sex (RR 3.33, 95%CI 2.01-5.50) were independently associated with HA at age 16. Persistent HA was associated with approximately doubled healthcare costs compared to the group with consistently low HA. Incident HA at age 16 was associated with increased costs over follow-up. The increased costs were not explained by chronic somatic illness. **Conclusions:** A small subgroup of children had persistent high levels of HA from late childhood to adolescence and displayed increased healthcare costs. Female sex and chronic somatic disorders at age 11 were independent risk factors of HA at age 16. These findings provide potential means of early identification and of therapeutic levers. Further intervention development and evaluation are needed. Keywords: Health anxiety; healthcare costs; longitudinal cohort; childhood and adolescence.

## Introduction

Severe health anxiety (HA) is characterized by excessive worry and preoccupation with health issues that affect everyday life (Asmundson, Abramowitz, Richter, & Whedon, 2010). A recent study suggests that HA might be on the rise in the general population, due to increasing focus on health-related issues in the media landscape, and easily accessible information on the internet that might induce or maintain and/or worsen HA (Tyrer, Cooper, Tyrer, Wang, & Bassett, 2019). HA symptoms are common and exist on a continuum in the general population, but for some individuals it can take a chronic and debilitating course. The diagnosis of hypochondriasis has historically encompassed the extreme clinical end point of HA, and has been regarded as part of somatoform disorders (Hiller, Rief, & Fichter, 2002). However, the diagnosis of hypochondriasis has recently been overturned in the DSM-5 as part of the somatic symptom and related disorders chapter and replaced by illness anxiety disorder, dominated by cognitive anxiety symptoms

concerning harbouring illness, and somatic symptom disorder, which is used if somatic symptoms are also present (American Psychiatric Association, 2013). Still, in the upcoming ICD-11, health anxiety will be categorized as hypochondriasis, but now under the section of obsessive-compulsive related disorders (Tyrer & Tyrer, 2019). Notably, suffering from HA does not preclude having medically well-explained somatic illness.

HA in adults often goes unnoticed for years, resulting in patients undergoing unavailing medical investigations for prolonged periods of time, without alleviating potentially disabling symptoms of HA (Fink, Ørnbøl, & Christensen, 2010; Tyrer, Eilenberg, Fink, Hedman, & Tyrer, 2016). Furthermore, clinically impairing HA is associated with increased rates of all other types of mood and anxiety disorders (Sunderland, Newby, & Andrews, 2013). In adults, recent review found cognitive behavioural therapy to be an effective intervention for HA (Cooper, Gregory, Walker, Lambe, & Salkovskis, 2017). Thus, apart from the treatment effect on HA symptoms that can improve well-being of individuals, interventions for HA may have important societal value, as HA is associated with increased health service use (Bobevski, Clarke, & Meadows, 2016), and consequently increased healthcare costs (Fink et al., 2010). There is evidence of poorer outcomes of treatment for HA in severe and chronic cases (olde Hartman et al., 2009), and retrospective reports indicate that many adults with HA first experience difficulties in childhood (Noyes et al., 2002). This indicates that there might be an untapped potential for recognition, prevention, and early intervention directed at HA already in childhood and adolescence.

Despite this, research on the subject in childhood and adolescence is scarce. During the past decades, specific measures for measuring HA in childhood have been developed, such as the Childhood Illness Attitude Scales (CIAS) (Wright & Asmundson, 2003), demonstrating that symptoms of HA indeed occur in childhood and adolescence. Cross-sectional studies of young people has also found associations between HA and other psychopathology, such as other anxiety disorder symptoms including obsessive-compulsive disorder symptoms (Wright, Lebell, & Carleton, 2016), subclinical psychotic experiences (Rimvall et al., 2019), functional somatic symptoms (FSS) (Rask, Elberling, Skovgaard, Thomsen, & Fink, 2012), and depression (Sirri, Garotti, Grandi, & Tossani, 2015), as well as somatic conditions such as congenital heart disease (Oliver et al., 2018). A longitudinal study of the Copenhagen Child Cohort 2000 (CCC2000) found increased healthcare costs among individuals with high HA scores at age 11, and showed some continuity of parent reported child HA at age 6 years and child self-reported HA at age 11 (Rask et al., 2016).

To our knowledge, no studies have previously examined the continuity of HA from childhood to adolescence. We aim to extend on previous findings from the CCC2000 prospective general population

birth cohort and investigate potential continuity of HA symptoms from age 11 years until age 16 and associated healthcare costs. Based on the current literature, we hypothesized that persistent HA would be associated with continuously high healthcare costs over time, whereas remitting and increasing HA from age 11 to 16 would show decreasing and increasing costs over time, respectively.

## Methods

## Study population

The prospective birth cohort study, CCC2000, encompasses 6090 children born in Copenhagen County, Denmark, in year 2000. The current study utilizes longitudinal questionnaire data from two follow-ups at ages 11 and 16 years, collected from May 2011 to October 2012 and August 2016 to November 2017 respectively. All eligible children/youths were invited by postal letters at age 11 and by governmental email systems at age 16. Participants for the current study with baseline data at age 11 were characterized by fewer perinatal adversities and came from families with fewer sociodemographic adversities compared to non-participants (Rask et al., 2016). Further details regarding the cohort can be found elsewhere (Olsen et

al., 2019).



At age 11, HA was measured using the CIAS (Wright & Asmundson, 2003), which is a developmentally modified version of the adult measure, the Illness Attitude Scales (Kellner, 1986). We used a 21 items version of the CIAS in the current study, encompassing three factors: fears, help-seeking behaviour, and impact of symptoms (Thorisdottir et al., 2017). All items were scored on a 3-point Likert scale (1 = none of the time, 2 = sometimes, 3 = a lot of the time), resulting in potential scores from 21-63, Cronbach's alpha 0.81 in the current study. HA at age 16 was measured using the Whiteley-8, which corresponds to the well validated Whiteley-7 (Fink et al., 1999) with an added question on presence of illness-related ruminations, that is regarded as an important feature of health anxiety (Fink et al., 2004). All eight items are scored on a 1-5 (1 = not at all, 5 = a lot) resulting in a score of 8-40, Cronbach's alpha 0.92 in the current study. The Whiteley Index was chosen for the assessment at age 16 to secure comparable data with a large Danish cohort study of adults for future collaborations, the Danish Study of Functional Disorders, Dan Fund (Dantoft et al., 2017). Also, the measure is likely developmentally suitable as the youths approach adulthood.

FSS, emotional ICD-10 psychiatric disorders, and chronic somatic illness at age 11 were included as potential explanatory factors for both persistence of HA and the association between HA and healthcare costs. FSS were measured by self-report using the Children's Somatization Inventory 24 (Walker, Beck, Garber, & Lambert, 2009), Cronbach's alpha 0.83 in the current study. Chronic somatic illness was reported by parents using a pre-defined list of chronic somatic conditions (e.g. epilepsy, diabetes), which had been diagnosed by a medical doctor. Emotional disorders were assessed using the Development and Well-Being Assessment synthesizing information from parents, the children themselves, and in some cases teachers (Goodman, Ford, Richards, Gatward, & Meltzer, 2000). Final diagnoses were made by trained child and adolescent psychiatrists, integrating information from both structured questions and open-ended descriptions from all available informants. Interrater reliability for any diagnosis was good (Kappa=0.81), as previously reported in detail (Jeppesen et al., 2015).

## Healthcare costs

Healthcare costs were obtained from the Danish National Health Service Register (Sahl Andersen, De Fine Olivarius, & Krasnik, 2011). We included all expenses related to consultations, examinations and tests performed by, or in relation to, general practitioners and other medical specialties outside of hospital settings, but still part of the tax-funded medical system available for all citizens in Denmark. Costs incurred by visits to psychologists and psychiatrists were not included, since we sought to examine potentially unnecessary, and thereby preventable, medical health expenses in the HA group. In order to estimate if high/low healthcare costs were linked to the approximate time-period around which high/low HA symptoms levels were reported, we calculated the expenses for all individuals for the years 2011-2012 (around the 1<sup>st</sup> HA measurement), 2013-2014 (interim period), and 2015-2016 (around the 2<sup>nd</sup> HA measurement), respectively. Costs for the whole period were adjusted to 2016 prices available from Statistics Denmark and converted to euros (<u>https://dst.dk/da/Statistik/emner/priser-ogforbrug/forbrugerpriser/forbrugerprisindeks</u>).

## Family and perinatal characteristics

We obtained register data on family sociodemographic and perinatal characteristics of the participants from the Integrated Data Base for Labour Market Research and the Medical Birth Register and used these for attrition analyses. We used information on birth weight, singleton/twin birth, maternal age at birth, maternal education by 2010, family constitution at birth, changes in family composition, parental mental disorder, and ethnic minority status.

## Ethics

The CCC2000 study was approved by the Danish Data Protection Agency (CSU-FCFS-2016-004, I-Suite 04544), and the Committee on Health Research Ethics in the Capital Region of Denmark has evaluated the project (protocol 16023242). Rules and recommendations according to the Helsinki Declaration regarding the use and anonymization of personal data were followed, and the data is only to be used for research purposes. Participants gave informed consent.

## Statistical analyses

For attrition analyses, youths who provided follow-up data at age 16 years were compared with those who only participated at age 11 regarding background characteristics using Chi-square analyses.

For the analyses on HA continuity from age 11 to age 16 years, HA symptoms at both ages were dichotomized into high (top 10%) and low (bottom 90%) scores based on the entire population participating at the respective follow-ups, thus including individuals for whom longitudinal data was not available. This approach was in line with previous studies of the CCC2000 11-year follow-up (Rask et al., 2016; Rimvall et al., 2019). We categorized HA symptoms from age 11 to 16 into four groups based on continuity of symptoms: a) persistent (high score at both follow-ups), remitting (high at age 11, low at age 16), incident (low at age 11, high at age 16), and consistently low HA (low at both follow-ups). The distribution of the covariates sex, chronic somatic illness, emotional disorders and FSS were assessed for the four groups. The relative risk for persistent high score was calculated by binary regression analyses using a log-link function. Multiple linear regression was used to assess the continuity of HA measured on continuous scales at both ages 11 and 16.

Differences in annual healthcare costs measured in euros (€) between the consistently low HA group and the three other groups were assessed pairwise using linear regression at baseline in 2011-2012, in the interim period in 2013-2014 and at follow-up in 2015-2016.

Using a linear mixed model with a random intercept, we assessed the changes in healthcare costs over the follow-up period for the 4 different HA groups.

All analyses were adjusted stepwise for sex and chronic somatic illness (present vs. not present), emotional disorders (present vs. not present) and FSS (measured on a continuous scale), all three variables assessed at baseline.

All statistical analyses were performed using STATA 15, and 95% CI were used. Underlying assumptions for the linear regression and mixed model were assessed by inspection of residual plots. Due to the expected left-skewing of the residuals (owing to the general population sample) we used a non-parametric bootstrap method, with 5000 repetitions, to estimate 95% bias corrected and accelerated bootstrap confidence intervals.

For post-hoc sensitivity analyses we a) applied top 15% and 20% cut-off scores for the HA measures at both ages, instead of the a priori determined top 10% scores and b) redefined the top 10% HA-score at age 11 by excluding items on children's help seeking from parents in the CIAS.

## USIU

Results

# At baseline, 1884 children (31% of live sample) participated in self-reports of HA at age 11. These children were characterized by fewer perinatal and sociodemographic adversities compared to the total population as detailed in previous work (Rask et al., 2016). Follow-up data at age 16 was obtained for 1278 (68%) of those participants. Children with data from both assessments were more often female, had older mothers with higher levels of education at baseline, and came less often from immigrant families compared to those lost to follow-up, see Table S1 for details.

Persistently high HA was found in 17 individuals (1.3%), whereas 104 (8.1%) had remitting HA, 80 (6.3%) had incident HA, and 1077 (84.3%) consistently scored within the bottom 90% HA scores (Table 1). The distribution of the covariates sex, chronic somatic illness, emotional disorders and FSS across the four HA groups are also shown in Table 1.

-Table 1-

Table 2 shows the continuity of HA from age 11 to 16. A top 10% score at age 11 was associated with a top 10% score at age 16 (RR 2.03 95%CI 1.26-3.31). This estimated association was reduced after adjustment for sex and chronic somatic illness (RR 1.70 95%CI 1.03-2.79) and further reduced after full adjustment (RR 1.49 95%CI 0.85-2.60). The covariates sex and chronic somatic illness at age 11 had an independent effect on age 16 HA in the final model, whereas emotional disorders and FSS at age 11 did not stand out as independent predictors. HA viewed on a continuous scale at both ages also showed

continuity from age 11 to 16:  $\beta$ =0.20 (95%Cl 0.13-0.28). This association was somewhat reduced after full adjustment for the above covariates:  $\beta$ =0.15 (95%Cl 0.08-0.22).

## -Table 2-

Figure 1 shows the mean annual healthcare costs for the four groups from 2011 to 2016. Persistent HA was associated with approximately 2-fold higher costs compared to the group with consistently low HA around baseline in 2011-2012 (246€ [95%CI 151-510] vs 124€ [95%CI 113-140]) and follow-up in 2015-2016 (191€ [95%CI 135-341] vs 115€ [95%CI 106-133]). Incident HA was associated with higher costs compared to consistently low HA around follow-up (207€ [95%CI 172-254] vs 115€ [95%CI 106-133]). Virtually no differences were found between remitting HA and consistently low HA at any timepoint.

-Figure 1-

Detailed differences in annual costs between the groups with remitting, incident and persistent HA symptoms compared to consistently low HA are shown in Table S2. The higher costs were only slightly explained by the covariates sex, chronic somatic illness, and emotional disorders, whereas FSS explained somewhat more of the costs in the final models. Mixed model analyses of the development of healthcare costs over the follow-up period found strong evidence that the costs in the incident group rose markedly over the follow-up period (76€ [95%CI 26-126]), whereas there was little to no evidence that the costs within the groups with consistently low, remitting and persistent HA- changed between follow-ups, see Table S3 for details. Notably, adjustment did not change the estimated development in costs.

Sensitivity analyses using alternative cut-offs for HA (15% and 20% respectively instead of the a priori defined 10% cut-off) produced no changes in the overall findings regarding neither persistence of HA nor healthcare costs. When we redefined the top 10% HA-score by excluding items on children's help seeking from parents at age 11, costs at age 11 were reduced in 2011-2014 for the new persistent group, but still had higher costs in 2015-2016. Healthcare costs for the groups with consistently low, remitting and incident groups remained largely unchanged, as did the estimated continuity of HA.

## Discussion

## Main findings

There was strong evidence of continuity of HA scores from age 11 to 16 when viewing HA-symptoms on a continuous scale at both ages. However, only a small group of children expressed high levels of HA at both

follow-ups at age 11 and 16 (persistent HA). In the final adjusted model (adjusted for sex, chronic somatic illness, emotional disorder and FSS), the evidence of an independent effect of high HA at age 11 on high HA at age 16 was markedly reduced, whereas chronic somatic illness at age 11 and female sex stood out as independent predictors of HA at age 16. As hypothesized, the group that had high HA levels at both follow-ups had approximately twice as high healthcare costs over follow-up compared to youths with consistently low HA levels. Also, the group with increasing/emerging high HA levels over follow-up displayed increased healthcare costs over follow-up, as hypothesized. The costs remained higher even after adjustment for chronic somatic illness. However, our hypothesis that the group with remitting HA had decreasing healthcare costs was dismissed, as the group had consistently low costs.

## Methodological considerations

The strengths of the study include the longitudinal design, the large sample size, and the additionally collected information on the children's mental and somatic health at baseline, that allowed relevant adjustments to the analyses. Furthermore, detailed register data on healthcare costs were obtained independently and unbiased of the participants' own health perceptions. All healthcare costs presented were based on public health services available to all participants, limiting bias due to socioeconomic characteristics of the participants. However, the findings should also be interpreted in the light of some important limitations. First, even though the sample size was large, namely the persistent HA group was small, contributing to broad confidence intervals. Second, due to the 5-year period between data-points, the data presented cannot simply be regarded as continuous. Multiple examinations of the youths between the long follow-up period would have been advantageous to describe more sophisticated and appropriate trajectories of HA, as HA is expected to often exhibit fluctuating courses in line with other types of anxiety (Pine & Klein, 2015). Third, participants in the current study were characterized by fewer psychosocial adversities compared to the general population. This likely resulted in less variation in the data than would be expected in the general population. Fourth, different measures of HA were utilized at ages 11 and 16. Although this can be regarded as a limitation, it also underscores some continuity of the concept of HA over time in the current study, rather than merely a psychometric continuity. Also, the top 10% cut-off utilized is arbitrary, but sensitivity analyses indicated robustness of the findings, as the overall findings did not change markedly when alternative cut-offs were applied. Fifth, no information on parental HA was collected, which might be an important factor, as the parents' HA and health related behaviours may affect the healthcare costs of the children (Thorgaard, Frostholm, Walker, Stengaard-Pedersen, et al., 2017). Finally, we lack a measure of adverse childhood events at age 11, which can also affect the course and development of HA (Reiser, McMillan, Wright, & Asmundson, 2014).

### Interpretation

We have previously found that parent reported HA at ages 5-7 was associated with child self-reported HA at age 11 (Rask et al., 2016). Together with the current findings and retrospective reports suggesting that adult HA is often preceded by similar symptoms in childhood and adolescence (Noyes et al., 2002), the overall evidence suggests continuity of HA across the lifespan.

As outlined in the introduction, important findings from cross-sectional studies on children and adolescents have shown that HA is associated with a broad array of other types of psychopathology (Oliver et al., 2018; Rask et al., 2016; Rimvall et al., 2019; Sirri et al., 2015; Wright et al., 2016). Crucially, even in the adjusted analyses, there was still evidence of an independent effect of high HA at age 11 on the risk of high HA at age 16, since the findings were only partially explained by chronic somatic illness. However, the effect of age 11 HA was markedly reduced after further adjustment for emotional disorders, and particularly FSS. Furthermore, it can be argued that we over-adjusted our analyses when adjusting for FSS and emotional disorders, as these variables and HA have overlapping features and are likely to have bidirectional influences.

Even though the data on healthcare costs presented in the current study have large confidence intervals, persistently high HA was consistently associated with increased healthcare costs in the primary healthcare services compared to the group with consistently low HA, over and above chronic somatic illness. This could indeed suggest that maladaptive healthcare seeking at age 11 is indicative of persistence of HA and a potential target for identification of severe courses.

Noteworthily, in the fully adjusted models, female sex and chronic somatic illness at age 11 stood out as robust risk factors of later high levels of HA at age 16 – more so than high HA levels at age 11. Absence of somatic illness is not required to have HA, and somatic symptom burden has also previously been found to be associated with higher levels of HA (Lee, Creed, Ma, & Leung, 2015). These individuals require the same, or perhaps even more critically, intervention directed at HA as individuals without somatic illness (Oliver et al., 2018). This emphasizes the need for identification of children that are likely to develop impairing HA in the settings of primary healthcare and paediatrics. Although some individuals might already require specialized interventions in childhood, our findings also suggest that most individuals that reported high HA at age 16 did not report HA within the highest 10% at age 11. Intolerance of uncertainty, i.e. difficulties coping with uncertainty and fear of the unknown, has been suggested to be important in the development of HA, particularly in youth with anxiety sensitivity (Wright et al., 2016). As youths with chronic somatic illness are inherently prone to uncertainty due to their condition, it is likely

that accommodation to fears and worries related to having a chronic somatic disorder might delay or prevent the development of HA. Thus, attempts to reduce uncertainties, e.g, by thorough education and information to the families about the child's somatic disorder, may constitute a viable target for preventive intervention in non-psychiatric settings. This might particularly be important among girls as they are at higher risk of developing HA in later adolescence and early adulthood (Sunderland et al., 2013), as well as other emotional disorders (Pine & Klein, 2015). Furthermore, prior findings suggest that parental (maternal) HA and maladaptive help-seeking on behalf of their children might impact the illness behaviours of the child itself (Thorgaard, Frostholm, Walker, Jensen, et al., 2017). This notion supports future investigation of family-based interventions directed towards families with high levels of anxiety/worries and health care seeking, since family based preventive interventions directed at children of parents with other anxiety disorders have shown promising results (Lawrence, Rooke, & Creswell, 2017). Furthermore, more specific interventions for HA in childhood and adolescence need to be developed and tested (Frostholm & Rask, 2019), although treatment with primarily cognitive behavioural therapy in adults overall have shown positive and potent results (Cooper et al., 2017).

Future observational studies could beneficially study the applicability of diagnostic criteria of HA-related disorders (hypochondriasis in ICD-10 and illness anxiety disorder/somatic symptom disorder in DSM-5) in children and adolescents, which the current study could not provide. Also, in depth studies of HA trajectories and risk factors of persistence would be very interesting, especially in clinical paediatric samples, since they likely constitute an at-risk group. Even though some individuals who show persistent HA across development might require specialized treatment, evidence points at HA as a common phenomenon in the community. Many individuals might benefit from more generalist treatment options that could include treatment for HA related problems alongside treatment of other psychopathology and somatic illness, which commonly co-occur with HA. Knowledge among clinicians in paediatric settings, that chronic somatic illness and female sex are important predictors of development of health anxiety, might improve timely identification, prevention and/or treatment. Important personal, as well as societal, gains might be achieved by identifying and intervening towards HA in youth.

## **Supporting information**

Additional supporting information may be found online in the Supporting Information section at the end of the article:

## Table S1. Attrition analyses.

 Table S2. Differences in annual healthcare costs between health anxiety symptom groups.

**Table S3.** Changes in healthcare costs from 2011 to 2016 by health anxiety symptom group.



## Acknowledgements

The authors thank the funding sources of the study: TrygFonden (J. nr. 7-10-0189, 7-11-0341 and 109903), Lundbeckfonden (J. nr. R54-A5843), and Øster-Jørgensen og Rønhild Andersen Fonden. M.K.R. was funded by a PhD grant from the Mental Health Services of the Capital Region of Denmark. The authors also thank Jens Søndergaard Jensen (Msc) for contributing to the statistical analyses and Anja Munkholm (PhD), Lars Clemmensen (PhD), Anne Dorothee Müller (MbSc), Maja Gregersen (MSc), and Kia Elten (Msc) for contributions to the data collection. F.V. publishes the Dutch translations of ASEBA materials from which he receives remuneration. The remaining authors have declared that they have no competing or potential conflicts of interest.

## Correspondence

Martin K. Rimvall, Child and Adolescent Mental Health Center, Mental Health Service, Kildegaardsvej 28, 3A, 1st floor, 2900 Hellerup, Denmark; Email: <u>martin.rimvall@regionh.dk</u>

Autho

## Key points:

- Health anxiety, characterized by ruminations and excessive fears of severe somatic illness, is poorly described in childhood and adolescence.
- We examined continuity of health anxiety from age 11 to 16 years in a prospective, populationbased cohort.
- Health anxiety displayed some continuity over time, but persistent health anxiety was rare, yet associated with continually increased healthcare costs, independently of somatic illness.
- Symptoms of health anxiety were commonly reported in both childhood and adolescence in cross section.
- Female sex and somatic illness were additional predictors of health anxiety. Timely
  identification by clinicians working with children is important, as anxiety is highly tractable.
  However, studies on specific interventions for health anxiety in youths are lacking.

## References

- American Psychiatric Association. (2013). Diagnostic and statistical manual of mental disorders (5th ed.). In
   Washinton, DC: American Psychiatric Association.
   https://doi.org/10.1176/appi.books.9780890425596.744053
- Asmundson, G. J. G., Abramowitz, J. S., Richter, A. A., & Whedon, M. (2010). Health anxiety: Current perspectives and future directions. *Curr Psychiatry Rep*, *12*(4), 306–312. https://doi.org/10.1007/s11920-010-0123-9
- Bobevski, I., Clarke, D. M., & Meadows, G. (2016). Health Anxiety and Its Relationship to Disability and Service Use. *Psychosomatic Medicine*, *78*(1), 13–25. https://doi.org/10.1097/psy.0000000000252
- Cooper, K., Gregory, J. D., Walker, I., Lambe, S., & Salkovskis, P. M. (2017). Cognitive Behaviour Therapy for Health Anxiety: A Systematic Review and Meta-Analysis. *Behavioural and Cognitive Psychotherapy*, 45(2), 110–123. https://doi.org/10.1017/s1352465816000527

- Dantoft, T. M., Ebstrup, J. F., Linneberg, A., Skovbjerg, S., Madsen, A. L., Brinth, L., ... Jørgensen, T. (2017). Cohort description: The Danish study of Functional Disorders. *Clinical Epidemiology*, *9*, 127–139.
- Fink, P., Ewald, H., Jensen, J., Sørensen, L., Engberg, M., Holm, M., & Munk-Jørgensen, P. (1999). Screening for somatization and hypochondriasis in primary care and neurological in-patients: A seven-item scale for hypochondriasis and somatization. *Journal of Psychosomatic Research*, 46(3), 261–273. https://doi.org/10.1016/S0022-3999(98)00092-0
- Fink, P., Ørnbøl, E., & Christensen, K. S. (2010). The outcome of Health anxiety in primary care. a two-year follow-up study on health care costs and self-rated health. *PLoS ONE*, 5(3). https://doi.org/10.1371/journal.pone.0009873
- Fink, P., Ørnbøl, E., Toft, T., Sparle, K. C., Frostholm, L., & Olesen, F. (2004). A new, empirically established hypochondriasis diagnosis. *American Journal of Psychiatry*, 161(9), 1680–1691. https://doi.org/10.1176/appi.ajp.161.9.1680
- Frostholm, L., & Rask, C. U. (2019). Third Wave Treatments for Functional Somatic Syndromes and Health Anxiety Across the Age Span: A Narrative Review. *Clinical Psychology in Europe*, 1(1), e32217.
- Goodman, R., Ford, T., Richards, H., Gatward, R., & Meltzer, H. (2000). The Development and Well-Being Assessment: Description and Initial Validation of an Integrated Assessment of Child and Adolescent Psychopathology. *Journal of Child Psychology and Psychiatry*, *41*(5), 645–655. https://doi.org/10.1177/017084068800900203
- Hiller, W., Rief, W., & Fichter, M. (2002). Dimensional and categorical approaches to hypochondriasis. *Psychological Medicine*, *32*(4), 707–718. https://doi.org/10.1017/S0033291702005524
- Jeppesen, P., Clemmensen, L., Munkholm, A., Rimvall, M. K., Rask, C. U., Jørgensen, T., ... Skovgaard, A. M. (2015). Psychotic experiences co-occur with sleep problems, negative affect and mental disorders in preadolescence. *Journal of Child Psychology and Psychiatry*, 56(5), 558–565. https://doi.org/10.1111/jcpp.12319
- Kellner, R. (1986). Somatization and hypochondriasis. Network: Praeger.
- Lawrence, P. J., Rooke, S. M., & Creswell, C. (2017). Review: Prevention of anxiety among at-risk children and adolescents – a systematic review and meta-analysis. *Child and Adolescent Mental Health*, 22(3), 118–130. https://doi.org/10.1111/camh.12226

Lee, S., Creed, F. H., Ma, Y. L., & Leung, C. M. C. (2015). Somatic symptom burden and health anxiety in the

population and their correlates. *Journal of Psychosomatic Research*, 78(1), 71–76. https://doi.org/10.1016/j.jpsychores.2014.11.012

- Noyes, R., Stuart, S., Langbehn, D. R., Happel, R. L., Longley, S. L., & Yagla, S. J. (2002). Childhood Antecedents Of Hypochondriasis. *Psychosomatics*, *43*(4), 282–289. https://doi.org/10.1176/appi.psy.43.4.282
- olde Hartman, T. C., Borghuis, M. S., Lucassen, P. L. B. J., van de Laar, F. A., Speckens, A. E., & van Weel, C. (2009). Medically unexplained symptoms, somatisation disorder and hypochondriasis: Course and prognosis. A systematic review. *Journal of Psychosomatic Research*, *66*(5), 363–377. https://doi.org/10.1016/j.jpsychores.2008.09.018
- Oliver, A. M., Wright, K. D., Kakadekar, A., Pharis, S., Pockett, C., Bradley, T. J., ... Erlandson, M. C. (2018). Health anxiety and associated constructs in children and adolescents with congenital heart disease: A CHAMPS cohort study. *Journal of Health Psychology*. https://doi.org/10.1177/1359105318755263
- Olsen, E. M., Rask, C. U., Elberling, H., Jeppesen, P., Clemmensen, L., Munkholm, A., ... Skovgaard, A. M. (2019). Cohort Profile: The Copenhagen Child Cohort Study (CCC2000) - design and cohort update from birth to adolescence. *International Journal of Epidemiology*, 1–14. https://doi.org/10.1093/ije/dyz256
- Pine, D. S., & Klein, R. G. (2015). Anxiety disorders. In *Rutter's Child and Adolescent Psychiatry* (pp. 822–840).
- Rask, C. U., Elberling, H., Skovgaard, A. M., Thomsen, P. H., & Fink, P. (2012). Parental-Reported Health Anxiety Symptoms in 5- to 7-Year-Old Children: The Copenhagen Child Cohort CCC 2000. *Psychosomatics*, 53(1), 58–67. https://doi.org/10.1016/j.psym.2011.05.006
- Rask, C. U., Munkholm, A., Clemmensen, L., Rimvall, M. K., Ørnbøl, E., Jeppesen, P., & Skovgaard, A. M.
  (2016). Health Anxiety in Preadolescence Associated Health Problems, Healthcare Expenditure, and Continuity in Childhood. *Journal of Abnormal Child Psychology*, 44, 823–832. https://doi.org/10.1007/s10802-015-0071-2
- Reiser, S. J., McMillan, K. A., Wright, K. D., & Asmundson, G. J. G. (2014). Adverse childhood experiences and health anxiety in adulthood. *Child Abuse and Neglect*, *38*(3), 407–413. https://doi.org/10.1016/j.chiabu.2013.08.007
- Rimvall, M. K., Jespersen, C. P., Clemmensen, L., Munkholm, A., Skovgaard, A. M., Verhulst, F., ... Jeppesen, P. (2019). Psychotic experiences are associated with health anxiety and functional somatic symptoms

in preadolescence. *Journal of Child Psychology and Psychiatry*, *60*(5), 524–532. https://doi.org/10.1111/jcpp.12986

- Sahl Andersen, J., De Fine Olivarius, N., & Krasnik, A. (2011). The Danish National Health Service Register. *Scandinavian Journal of Public Health*, *39*(7), 34–37. https://doi.org/10.1177/1403494810394718
- Sirri, Garotti, M. G. R., Grandi, S., & Tossani, E. (2015). Adolescents' hypochondriacal fears and beliefs: Relationship with demographic features, psychological distress, well-being and health-related behaviors. *Journal of Psychosomatic Research*, *79*(4), 259–264. Retrieved from www.elsevier.com/locate/jpsychores%5Cnhttp://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference &D=emed13&NEWS=N&AN=2015210662
- Sunderland, M., Newby, J. M., & Andrews, G. (2013). Health anxiety in Australia: Prevalence, comorbidity, disability and service use. *British Journal of Psychiatry*, 202(1), 56–61. https://doi.org/10.1192/bjp.bp.111.103960
- Thorgaard, M. V., Frostholm, L., Walker, L., Jensen, J. S., Morina, B., Lindegaard, H., ... Rask, C. U. (2017).
   Health anxiety by proxy in women with severe health anxiety: A case control study. *Journal of Anxiety Disorders*, 52(December 2016), 8–14. https://doi.org/10.1016/j.janxdis.2017.09.001
- Thorgaard, M. V., Frostholm, L., Walker, L. S., Stengaard-Pedersen, K., Karlsson, M. M., Jensen, J. S., ... Rask,
  C. U. (2017). Effects of maternal health anxiety on children's health complaints, emotional symptoms, and quality of life. *European Child and Adolescent Psychiatry*, 26(5), 591–601. https://doi.org/10.1007/s00787-016-0927-1
- Thorisdottir, A. S., Villadsen, A., LeBouthillier, D. M., Rask, C. U., Wright, K. D., Walker, J. R., ... Asmundson, G. J. G. (2017). Measurement invariance across Genders on the Childhood Illness Attitude Scales (CIAS). *Journal of Psychosomatic Research*, *98*(March), 34–39. https://doi.org/10.1016/j.jpsychores.2017.05.006
- Tyrer, P., Cooper, S., Tyrer, H., Wang, D., & Bassett, P. (2019). Increase in the prevalence of health anxiety in medical clinics: Possible cyberchondria. *International Journal of Social Psychiatry*, 65(7–8), 566–569. https://doi.org/10.1177/0020764019866231
- Tyrer, P., Eilenberg, T., Fink, P., Hedman, E., & Tyrer, H. (2016). Health anxiety: The silent, disabling epidemic. *BMJ (Online)*, *353*(April), 10–11. https://doi.org/10.1136/bmj.i2250
- Tyrer, P., & Tyrer, H. (2019). Etiology and Epidemiology of Health Anxiety. In *The Clinician's Guide to Treating Health Anxiety*. https://doi.org/10.1016/b978-0-12-811806-1.00003-2

	Consistently low HA		Remitting HA		Incident HA		Persistent HA		Total sample	
	n = 1077		N=104		N=80		N=17		N=1278	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
N = 1278										
Sex (girl)	562	(52.2)	67	(64.4)	66	(82.5)	12	(70.6)	707	(55.3)
Chronic somatic illness	130	(12.6)	17	(17.4)	18	(23.4)	5	(25.0)	170	(13.9)
(55 missing)										
Emotional disorder	68	(6.3)	22	(21.2)	8	(10.0)	5	(29.4)	103	(8.1)
(2 missing)										
FSS (10% high score)	75	(7.0)	36	(34.6)	7	(8.8)	8	(47.1)	126	(9.9)

Walker, L. S., Beck, J. E., Garber, J., & Lambert, W. (2009). Children's somatization inventory: Psychometric

properties of the revised form (CSI-24). *Journal of Pediatric Psychology*, *34*(4), 430–440. https://doi.org/10.1093/jpepsy/jsn093

- Wright, K. D., Lebell, M. A. N. A., & Carleton, R. N. (2016). Intolerance of uncertainty, anxiety sensitivity, health anxiety, and anxiety disorder symptoms in youth. *Journal of Anxiety Disorders*, 41(2016), 35–42. https://doi.org/10.1016/j.janxdis.2016.04.011
- Wright, K. D., & Asmundson, G. J. G. (2003). Health anxiety in children: development and psychometric properties of the Childhood Illness Attitude Scales. *Cognitive Behaviour Therapy*, 32(April 2013), 194–202. https://doi.org/10.1080/16506070310014691

Table 1: Distribution of baseline covariates by health anxiety symptom group from age 11 to age 16.

Auth

HA = health anxiety FSS = functional somatic symptoms

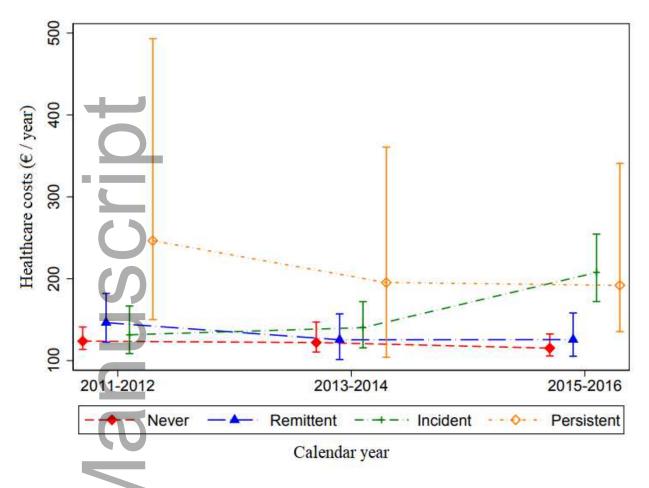
HA symptom groups were defined by top 10% HA scores at both ages: Consistently low HA = bottom 90% score at

both follow-ups, remitting HA = top 10% score only at age 11,

	RR	95% CI	p value	both follow-ups, remitting $\Pi A = 10^{-10}$ for $10^{-0}$ score only at age 11,
				incident HA = top 10% score only at age 16 and persistent HA = top
N=1278				10% score at both ages.
Unadjusted	$\bigcirc$	_		
Age 11 HA	2.03	1.26-3.31	0.005	
Model 1				Table 2. Delative wick of UA from age 11 to age 16
Age 11 HA	1.79	1.10-2.91	0.019	Table 2: Relative risk of HA from age 11 to age 16
Sex (female)	3.20	1.96-2.91	< 0.001	
Model 2 (55 missin	g)			
Age 11 HA	1.70	1.03-2.79	0.036	
Sex (female)	3.41	2.07-5.64	< 0.001	
Somatic illness	2.00	1.29-3.10	0.002	
Model 3 (56 missin	g)			
Age 11 HA	1.66	1.00-2.76	0.051	
Sex (female)	3.41	2.06-5.62	< 0.001	
Somatic illness	1.97	1.27-3.07	0.003	
Emotional disorder	r 1.13	0.62-2.07	0.684	
Model 4 (56 missin	g)			
Age 11 HA	1.49	0.85-2.60	0.163	
Sex (female)	3.33	2.01-5.50	< 0.001	
Somatic illness	1.91	1.22-2.98	0.004	
Emotional disorder	r 1.08	0.59-1.98	0.812	
FSS	1.02	0.99-1.05	0.274	HA = health anxiety FSS = functional somatic symptoms RR =
L				relative risk

HA scores were dichotomized at top 10% scores at both ages to indicate HA cases for the analyses. The effect of age 11 HA on age 16 HA was successively adjusted for sex (model 1), and further adjusted for age 11 chronic somatic illness (model 2), emotional disorders (model 3) and FSS (model 4).

## Figure 1: Health anxiety symptom groups and annual health care costs.



The graph shows unadjusted mean healthcare expenses with 95% bootstrapped and bias-corrected confidence intervals for the different health anxiety (HA) symptom groups over follow-up from around the time of the 11-year cohort assessment (year 2011-2012), between follow-ups (year 2013-2014) and around the time of follow-up (year 2015-2016).

Author