

# The Predictive Value of Health Anxiety for Cancer Incidence and All-Cause Mortality: A 44-Year Observational Population Study of Women

Robert Sigström, PhD<sup>1,3</sup>, Tore Hällström, PhD<sup>1</sup>, Margda Waern, PhD<sup>1,2</sup>, Ingmar Skoog, PhD<sup>1,3</sup>

<sup>1</sup>Department of Psychiatry and Neurochemistry, Institute of Neuroscience and Physiology, Sahlgrenska Academy, University of Gothenburg, Sweden

<sup>2</sup>Region Västra Götaland, Sahlgrenska University Hospital, Psychosis Department, Gothenburg, Sweden.

<sup>3</sup>Region Västra Götaland, Sahlgrenska University Hospital, Department of Cognition and Old age psychiatry, Gothenburg, Sweden

## Corresponding author:

Robert Sigström

Postal address:

University of Gothenburg,

Institute of Neuroscience and Physiology

Wallinsgatan 6

SE 431 41 Mölndal, Sweden.

E-mail: robert.sigstrom@gu.se

Fax: +46 31 776 04 03

Tel: +46 31 342 70 02

## Conflicts of Interest and Source of Funding

None of the authors declare a conflict of interest. This work was supported by grants from the Swedish state under the agreement between the Swedish government and the county councils, the ALF-agreement (MW, grant number ALF715841), (IS, grant number ALF716681); the Swedish Research Council (MW, grant numbers 2013-2699, 2016-01590), (IS, grant numbers

11267, 2005-8460, 2007-7462, 2012-5041, 2015-02830, 2019-01096, 2013-8717, NEAR 2017-00639); the Swedish Research Council for Health; Working Life and Welfare (MW, 2012-1138, 2016-07097), (IS, grant numbers 2001-2646, 2003-0234, 2004-0145, 2004-0150, 2006-0020, 2006-0596, 2008-1111, 2008-1229, 2010-0870, 2012-1138, 2013-1202, 2013-2496, AGECAP 2013-2300, 2018-00471), Stena Foundation, Konung Gustaf V:s och Drottning Victorias Frimurarestiftelse, Hjärnfonden (FO2014-0207, FO2016-0214, FO2018-0214, FO2019-0163), Alzheimerfonden, Eivind och Elsa K:son Sylvans stiftelse, The Alzheimer's Association Zenith Award (ZEN-01-3151), The Alzheimer's Association Stephanie B. Overstreet Scholars (IIRG-00-2159), The Bank of Sweden Tercentenary Foundation, Stiftelsen Söderström-Königska Sjukhemmet, Stiftelsen för Gamla Tjänarinnor, Handlanden Hjalmar Svenssons Forskningsfond and The Göteborg Medical Society.

## **Abstract**

**Objective:** Long-term data concerning mortality and serious illness as a function of health anxiety are scarce. We aimed to study health anxiety in relation to long-term mortality and cancer morbidity among women.

**Methods:** A Swedish population sample of women (N=770, ages 38-54 years) took part in a general medical and psychiatric examination in 1968-69 and were followed until 2013 in national Swedish registries for all-cause mortality and first diagnosis of cancer. A modified version of the Whiteley index questionnaire (maximum score=12) was employed to measure health anxiety. Scores were trichotomized based on quartiles as no (score 0, lowest quartile), mild-moderate (score 1-2, middle quartiles) and high (score  $\geq 3$ , highest quartile) health anxiety. Risks of death and cancer were evaluated with Cox regression models.

**Results:** Compared to women with mild-moderate health anxiety levels, women with no health anxiety had a higher risk of death (age-adjusted hazard ratio [HR] 1.22, 95% confidence interval [CI] 1.00-1.49; fully adjusted for baseline sociodemographic, mental and physical health variables HR 1.44, 95% CI 1.17-1.76). Women with high health anxiety levels had a greater risk of death in age-adjusted analysis (HR 1.26, 95% CI 1.04-1.54; fully adjusted HR 1.21, 95% CI 0.98-1.49). For both groups, the mortality risk was time-dependent and declined during follow-up. We observed no between-group differences in risk of cancer.

**Conclusions:** In this population-based cohort of midlife women, health anxiety was moderately associated with mortality in a u-shaped fashion. Absence of health anxiety entailed the greatest risk when other factors were taken into account.

**Keywords:** health anxiety, epidemiology, mortality, cancer, population studies

**Abbreviations:** PPSW: Prospective Population Study of Women; HAM-D: Hamilton Depression Rating Scale; SCR: Swedish Cancer Registry

## Introduction

Health anxiety is characterized by exaggerated worry and fear that bodily symptoms might represent serious disease (1). Health anxiety has been related to health service utilization, poor self-rated health and disability (2, 3) and is amenable to psychotherapeutic intervention (4). While of obvious interest to those affected, little research has examined risk of serious illness and death in persons with health anxiety. Health anxiety could have numerous effects on health-related behaviors, which in turn could influence both morbidity and mortality. Worry about cancer has been associated with preventive behaviors, such as attending breast cancer screening (5) and sunscreen use (6), indicating possible protective effects on general health. Conversely, previous population-based studies found an association between health anxiety and ischemic heart disease among both men and women (7) and higher incidence of cancer among men but not among women (8). One study found an association between diagnostic-level hypochondriasis and all-cause mortality (9). However, there are several possible sources of confounding to such associations. Worrying about serious disease may be related to having a chronic health condition (10), which may increase the risk for future serious disease. Furthermore, the effect of health anxiety is difficult to disentangle from that of co-existing psychiatric conditions. The above-cited increased risk of ischemic heart disease was halved and no longer statistically significant after adjustment for a measure of general anxiety (7). Finally, elevated risk for non-fatal disease in individuals with health anxiety may partly reflect a higher detection rate as a consequence of greater health care consumption. Inversely, assuming that low levels of health anxiety may be associated with less health care utilization, elevated risk of fatal conditions among such persons could be obscured if only non-fatal disease is studied. To better understand the relationship between health anxiety and physical health outcomes, it is necessary to study not only people with high levels of health anxiety,

but also those with lower levels. It is also important to investigate both non-fatal and fatal disease-related outcomes.

### *Aims*

Our primary aim was to investigate the relationship between level of health anxiety and all-cause mortality. The secondary aim was to examine risk of cancer in relation to level of health anxiety.

## **Sample**

This study is based on the multidisciplinary Prospective Population Study of Women in Gothenburg, Sweden (PPSW) (11). The original aim of the study was to examine the physical and mental health of middle-aged women in the community, as such epidemiological studies were few at the time. To yield a sample representative of the background population, women were systematically sampled from the Revenue Office Register based on their birth date. At baseline in 1968, 899 women born in 1914, 1918, 1922 and 1930 were invited to take part in a psychiatric examination and 800 (89%) accepted. The interview was performed by a psychiatrist (T.H.) and usually took place within three weeks of the PPSW general health examination (12). We excluded 16 women who did not return the health anxiety questionnaire, 12 with missing data on other variables and two who could not be tracked for vital status during follow-up, leaving 770 women for inclusion. Written informed consent was obtained from all participants at baseline, in accordance with the Helsinki Declaration. The study was approved by the regional ethical review board in Gothenburg.

## **Methods**

### *Main exposure*

All women were asked to fill out a Swedish translation of a screening questionnaire for health anxiety, the Whiteley index (13). Its original version includes 14 yes-or-no questions. Questions “G” and “I” were excluded from the version administered in the present study, since these were perceived to be of less importance, as reflected by the relatively low frequency of endorsement in individuals with health anxiety, as compared to other psychiatric patients, in the original study of the Whiteley index (13). Thus, the Whiteley index contained 12 questions (Table S1, Supplemental Digital Content), yielding a maximum score of 12 points. The instrument has no established cut-point for defining health anxiety, although a

score  $\geq 5$  on the 14-point version has been suggested as optimal for identification of severe health anxiety (14). The distribution of scores in the present sample is displayed in Figure S1 (Supplemental Digital Content). We divided the sample into three groups based on quartiles: the lowest (0 points, no health anxiety); middle two (1-2 points, mild-moderate health anxiety levels); and highest ( $\geq 3$  points, high health anxiety levels).

#### *Other baseline variables*

Household income was self-reported, calculated as the sum of the yearly incomes of the participant and her partner (if any). Self-reported education was dichotomized into mandatory (6-7 years depending on year of birth) or beyond mandatory. Marital status was dichotomized as married and/or cohabiting versus single. Waist/hip ratio and systolic blood pressure were measured during the physical examination, when blood for analysis of serum-triglycerides was also collected. Smoking status was classified as current versus former or never.

Frequency of alcohol consumption was operationalized as intake of beer, wine or spirits more than once per week versus less. Leisure time physical activity was assessed with the Saltin-Grimby Physical Activity Level Scale (15), a four point scale, dichotomized into almost no physical activity versus all other groups.

Perceived psychological stress was assessed with an open question on whether the participant had been sleepless, irritable, nervous, anxious, fearful or anxiety-ridden in relation to social factors during at least one month at any time during the last five years, dichotomized to often-all the time versus never-sometimes. Depressive symptoms were assessed during the

psychiatric interview using the 17-item Hamilton Depression Rating Scale (HAM-D) (16).

Phobic anxiety was assessed in a two-stage process. First, participants self-rated their fear of 26 different phobic stimuli on a four-point scale (0-3) (Table S2, Supplemental Digital

Content). All fears with scores 2-3 were evaluated during the psychiatric interview, with



assessment (some-moderate-severe) of fear intensity and avoidance behaviour. We defined phobia as a fear of at least moderate intensity with at least moderate avoidance behaviour. We summed the number of phobias (range 0-18) as a measure of phobic anxiety.

Information on prevalent disease was collected during the general medical examination. Twenty-five participants had a history of cancer, one had a history of stroke, four had diagnosed diabetes, and none had a history of myocardial infarction. In 1968, not every inhabitant in Sweden was listed with a primary care doctor. The women were asked if they regularly consulted a specific doctor, and this was employed as a baseline marker of health care utilization. A further marker was a history of hospitalization at any time (childbirth excluded).

## **Outcome measures**

All persons living in Sweden are given a unique personal identification number, enabling linkage to national registers.

### *All-cause mortality*

We continuously monitored survival of participants using the Swedish Population Register. Follow-up time was calculated by subtracting the date of the psychiatric interview from the date of death recorded in the register or January 1<sup>st</sup>, 2013, whichever came first.

### *Incident cancer*

We retrieved information on first incident cancer from the Swedish Cancer Register (SCR) (17). Since 1958, Swedish doctors are required by law to report cancer diagnoses (except basal cell carcinoma of the skin) to this register. Among participants with no history of cancer at baseline (N=748), 268 (35.9%) had at least one entry in the SCR during the observation period. Follow-up time was calculated by subtracting the date of the psychiatric interview

from the date of first cancer diagnosis in the SCR, the date of death or January 1<sup>st</sup>, 2013, whichever came first.

### **Statistical analysis**

Differences in baseline characteristics between women with no, mild-moderate and high health anxiety levels were tested for statistical significance with Pearson Chi-square test for categorical variables and with one-way analysis of variance (ANOVA) for continuous variables. We used Cox regression models to estimate the effect of different levels of health anxiety on mortality and incidence of cancer. Results are presented as hazard ratios (HR:s) with 95% confidence intervals (CI:s). We fitted five models for each exposure (Tables 2 & 3): (i) an age-adjusted model, (ii) a model including age and other mental health variables, (iii) a model including age and sociodemographic variables, (iv) a model including age, physical health indices and health behaviours and (v) all variables included in models (i) to (iv). We did not include known disease at baseline in any model due to low prevalence. Potential time-dependence of the effects was estimated via the interaction between time and health anxiety. Analyses were made with IBM SPSS Statistics version 24.

## Results

Table 1 shows baseline characteristics of the sample according to health anxiety level.

Compared to women with mild-moderate health anxiety, women with no health anxiety had lower serum-triglycerides, a lower HAM-D score and were less likely to report psychosocial stress. Compared to women with mild-moderate health anxiety, women with high health anxiety had lower household income, a higher mean HAM-D score, a greater number of phobias and were more likely to report psychosocial stress. Further, they were more likely to have a specified doctor, and to have been hospitalized.

### *All-cause mortality*

Median follow-up was 37.0 years (inter-quartile range 28.2-43.6 years). Table 2 shows the results of all models of all-cause mortality. The reference group was women with mild-moderate health anxiety levels. In the age-adjusted model, the risk of death was elevated for those with no health anxiety (HR 1.22, 95% CI 1.00-1.49,  $p=0.047$ ), and for those with high levels of health anxiety (HR 1.26, 95% CI 1.04-1.54,  $p=0.021$ ). In a model including also mental health factors, the risk of death was elevated for women with no health anxiety (HR 1.27, 95% CI 1.04-1.55,  $p=0.018$ ) but not for women with high health anxiety (HR 1.13, 95% CI 0.92-1.39,  $p=0.26$ ). Adjusted for physical health variables and health behaviours, both no health anxiety (HR 1.40, 95% CI 1.15-1.72,  $p=0.001$ ) and high levels of health anxiety (HR 1.32, 95% CI 1.08-1.62,  $p=0.006$ ) were associated with mortality. Finally, in a model adjusted for all potential confounders and mediators, the HR:s were 1.44 (95% CI 1.17-1.76,  $p<0.001$ ) and 1.21 (95% CI 0.98-1.49,  $p=0.076$ ), respectively.

We observed an interaction with time for both no ( $p=0.040$ ) and high ( $p=0.002$ ) health anxiety levels. For both conditions, the hazard ratio for all-cause mortality declined over time relative to those with mild-moderate health anxiety levels. This is displayed in Table 3 and Figure 1.

*Risk of cancer*

Among women without a history of cancer at baseline, slightly over one third in each health anxiety group were registered with at least one cancer diagnosis during the observation period. None of the tested models showed associations between health anxiety level and cancer risk (Table 4).

## Discussion

In this observational prospective population study, we found that women without health anxiety had an increased mortality risk compared to those with mild-moderate levels of health anxiety. This risk became more pronounced when taking physical health-related variables into account. High levels of health anxiety were also associated with mortality, but this risk was attenuated when taking other mental health variables into account. Excess mortality risks for both no health anxiety and high level of health anxiety declined with follow-up time, and thus with increasing number of deaths. There was no effect of health anxiety on risk of cancer.

Taking a range of mental and physical health indicators into account, no health anxiety was associated with elevated mortality risk when compared to mild-moderate levels. The observational design of our study requires consideration of whether this is a causal relationship. Residual confounding is unlikely since the estimated effect increased when other measured factors were taken into account. Women with no health anxiety had lower serum-triglycerides and lower levels of depressive symptoms and psychosocial stress than those with mild-moderate health anxiety. This indicates, if anything, better observed health at the beginning of the study. However, as in any study of this kind, we cannot exclude the possibility of unmeasured confounding factors. While we are not aware of any previous research on mortality in relation to low levels of health anxiety, our results are in line with a study in which all-cause mortality was elevated in adults with low general anxiety as measured by the Hospital Anxiety and Depression Scale (HADS) (18). However, one previous study reported that although low trait anxiety in adolescence was associated with accident-related mortality before age 25, it was associated with a reduced risk of non-accidental death up to age 50 (19). Our findings may not reflect a specific causal effect of low *health* anxiety, but rather an effect of low *general* anxiety. Further, the relation between low anxiety levels and mortality may vary across the lifespan.

Assuming causality, we suggest two possible explanations to our findings, which may be subject to further study. First, low health anxiety may result in lower motivation to adhere to treatment, monitor illness and risk factors and to change hazardous health behaviours. Second, having no health anxiety may entail lower awareness of bodily symptoms, including those of serious disease, and this could result in delayed diagnosis and treatment. In support of this, a population-based study of people diagnosed with cancer found that anxiety as measured by the HADS was associated with lower likelihood of beyond local extent of disease at diagnosis (20). Delay might be more common in midlife compared to late life, when serious illness is more likely to occur. This could explain in part the observed time-dependent elevated mortality risk, with higher risk early during follow-up.

Also high health anxiety levels, as compared to mild-moderate levels, were related to mortality. The baseline characteristics of women with high levels health anxiety differed from those with mild-moderate health anxiety. They had higher levels of depressive symptoms, phobic anxiety and psychosocial stress, which is in alignment with previous population-based studies of health anxiety (7, 21, 22). Also, they were more likely to have regular contact with a specific doctor and to have been previously hospitalized. Their excess mortality risk was markedly attenuated when other mental health factors were taken into account. Mental disorders, such as depression, have been consistently associated with mortality (23) and we acknowledge the possibility of residual confounding. Our study differs from a previous study among men, in which increasing scores on the “hypochondriasis” sub-scale of the Minnesota Multiphasic Personality Inventory (MMPI) was associated with mortality (24). One reason for this difference may be that the effect of health anxiety on mortality differs between men and women. This would be in line with, for example, studies of the association between *phobic* anxiety and cardiovascular mortality, which seems to be stronger among men than among women (25, 26). Another explanation is that the Whiteley index and the MMPI

hypochondriasis scale measure different phenomena. The latter almost exclusively includes various physical symptoms, which may or may not correspond to actual serious disease, while the Whiteley index focuses on affective and cognitive aspects of health anxiety (13). Another population study found diagnostic-level hypochondriasis to be strongly associated with mortality (hazard ratio 5.73), even when other mental disorders were taken into account (9). However, that study included a small number of cases and had no information on participants' physical health. Of note, previous findings on the relationship between other forms of anxiety and mortality in middle aged and older individuals are disparate, including protective (27), null (28), positive (29, 30) or U-shaped (18) associations. Divergent findings may in part be explained by differential effects on mortality, depending on the type of anxiety identified by the various instruments employed in these studies.

It could be expected that health anxiety would be associated with increased risk of cancer, due not only to the association with mortality, but also to the possibility of higher detection rates as a result of greater health care consumption. However, this was not the case. Our findings are in agreement with a previous, larger population study of middle-aged adults, with shorter follow-up (13 years), which found no association between health anxiety and cancer risk in women (8). That study, however, found an association among men, again suggesting that health anxiety may have different outcomes in men and women.

There may be several explanations for our finding that high health anxiety levels was, if anything, associated with mortality but not with risk of cancer. Our data on cancer was limited to crude incidence. Potential behavioral effects of health anxiety might rather influence stage at presentation or survival after diagnosis, as discussed above with reference to previous research (20). High levels of health anxiety may result in various avoidance behaviors related to phobia of illness or hospitals (31), resulting in irrational behavior in the event of symptoms of serious disease (32). For example, while worry or fear about cancer may prompt help-

seeking when reassurance from health care professionals is anticipated, they may result in avoidance when life-threatening conditions are suspected (33). The result would be patient's delay in detection and treatment. Third, patients with high health anxiety levels are reported to be more likely than others to be disappointed with health care services (34), which may, with time, reduce help-seeking, resulting in negative effects on health. Finally, people with high health anxiety levels may more often than others be considered "difficult" by health care providers (34), which may reduce diagnostic accuracy and thus timely treatment of serious disease.

### *Strengths and limitations*

The strengths of this study include the well-characterized sample, the long follow-up and the dimensional measure of health anxiety, as opposed to a dichotomous diagnostic variable. This made it possible to study different levels of health anxiety across the sample. Limitations include, first, that we used a slightly modified version of the Whiteley Index, which has not been examined for validity and reliability. Since the removed items were least often endorsed by individuals with health anxiety in the contemporary original study of the index (13), we believe that this modification had negligible influence on our results. Second, the sample was relatively small, resulting in imprecise estimates and limiting our statistical power for further analyses of for example survival after cancer diagnosis. Third, since the initiation of the study in 1968, there has been considerable progress in the understanding of etiology, prevention and treatment of serious diseases, resulting in improved prognosis and reduced overall mortality rates. Public awareness of these improvements may also have changed the phenomenon of health anxiety in itself. This may have implications for generalizability of our study to present conditions.



## **Conclusion**

Clinicians should be aware of that among women, both low and high levels of health anxiety are associated with higher mortality risk from mid-life to old age, especially in early late-life when mortality rates are still relatively low. Further research is needed in order to test associations in more recent-born cohorts of women and men, and to understand the mechanisms behind the associations in order to elucidate whether interventions may be warranted.

## References

1. Tyrer P. Recent Advances in the Understanding and Treatment of Health Anxiety. *Curr Psychiatry Rep.* 2018;20:49.
2. Fink P, Ørnbøl E, Christensen KS. The outcome of health anxiety in primary care. A two-year follow-up study on health care costs and self-rated health. *PLoS One.* 2010;5:e9873.
3. Bobevski I, Clarke DM, Meadows G. Health anxiety and its relationship to disability and service use: findings from a large epidemiological survey. *Psychosomatic medicine.* 2016;78:13-25.
4. Tyrer P, Cooper S, Salkovskis P, Tyrer H, Crawford M, Byford S, Dupont S, Finnis S, Green J, McLaren E. Clinical and cost-effectiveness of cognitive behaviour therapy for health anxiety in medical patients: a multicentre randomised controlled trial. *The Lancet.* 2014;383:219-25.
5. Hay JL, McCaul KD, Magnan RE. Does worry about breast cancer predict screening behaviors? A meta-analysis of the prospective evidence. *Preventive medicine.* 2006;42:401-8.
6. Kiviniemi MT, Ellis EM. Worry about skin cancer mediates the relation of perceived cancer risk and sunscreen use. *Journal of behavioral medicine.* 2014;37:1069-74.
7. Berge LI, Skogen JC, Sulo G, Igland J, Wilhelmsen I, Vollset SE, Tell GS, Knudsen AK. Health anxiety and risk of ischaemic heart disease: a prospective cohort study linking the Hordaland Health Study (HUSK) with the Cardiovascular Diseases in Norway (CVDNOR) project. *BMJ open.* 2016;6:e012914.
8. Knudsen AK, Berge LI, Skogen JC, Veddegjaerde KE, Wilhelmsen I. The prospective association between health anxiety and cancer detection: A cohort study linking the Hordaland Health Study (HUSK) with the Norwegian Cancer Registry. *J Psychosom Res.* 2015;79:148-52.
9. John U, Rumpf H-J, Hanke M, Meyer C. Mental disorders and total mortality after 20 years in an adult general population sample. *European Psychiatry.* 2020:1-22.
10. Looper KJ, Kirmayer LJ. Hypochondriacal concerns in a community population. *Psychological Medicine.* 2001;31:577-84.
11. Bengtsson C, Blohme G, Hallberg L, Hallstrom T, Isaksson B, Korsan-Bengtzen K, Rybo G, Tibblin E, Tibblin G, Westerberg H. The study of women in Gothenburg 1968-1969--a population study. General design, purpose and sampling results. *Acta Medica Scandinavica.* 1973;193:311-8.

12. Hällström T. Mental disorders and sexuality in the climacteric: a study in psychiatric epidemiology. Gothenburg: Scandinavian University Books; 1973.
13. Pilowsky I. Dimensions of hypochondriasis. *The British Journal of Psychiatry*. 1967;113:89-93.
14. Hedman E, Lekander M, Ljótsson B, Lindefors N, Rück C, Andersson G, Andersson E. Optimal Cut-Off Points on the Health Anxiety Inventory, Illness Attitude Scales and Whiteley Index to Identify Severe Health Anxiety. *PLoS One*. 2015;10:e0123412.
15. Saltin B, Grimby G. Physiological analysis of middle-aged and old former athletes. Comparison with still active athletes of the same ages. *Circulation*. 1968;38:1104-15.
16. Hamilton M. A rating scale for depression. *Journal of neurology, neurosurgery, and psychiatry*. 1960;23:56.
17. Barlow L, Westergren K, Holmberg L, Talbäck M. The completeness of the Swedish Cancer Register—a sample survey for year 1998. *Acta oncologica*. 2009;48:27-33.
18. Mykletun A, Bjerkeset O, Øverland S, Prince M, Dewey M, Stewart R. Levels of anxiety and depression as predictors of mortality: the HUNT study. *The British Journal of Psychiatry*. 2009;195:118-25.
19. Lee W, Wadsworth M, Hotopf M. The protective role of trait anxiety: a longitudinal cohort study. *Psychological medicine*. 2006;36:345-51.
20. Stewart R, Fosså SD, Hotopf M, Mykletun A. Extent of disease at first cancer presentation and previous anxiety and depressive symptoms: the HUNT study. *Br J Psychiatry*. 2020;217:427-33.
21. Sunderland M, Newby JM, Andrews G. Health anxiety in Australia: prevalence, comorbidity, disability and service use. *The British Journal of Psychiatry*. 2013;202:56-61.
22. Creed F, Barsky A. A systematic review of the epidemiology of somatisation disorder and hypochondriasis. *Journal of psychosomatic research*. 2004;56:391-408.
23. Cuijpers P, Vogelzangs N, Twisk J, Kleiboer A, Li J, Penninx BW. Differential mortality rates in major and subthreshold depression: meta-analysis of studies that measured both. *The British Journal of Psychiatry*. 2013;202:22-7.
24. Tolmunen T, Lehto SM, Julkunen J, Hintikka J, Kauhanen J. Trait anxiety and somatic concerns associate with increased mortality risk: a 23-year follow-up in aging men. *Annals of epidemiology*. 2014;24:463-8.

25. Kawachi I, Colditz GA, Ascherio A, Rimm EB, Giovannucci E, Stampfer MJ, Willett WC. Prospective study of phobic anxiety and risk of coronary heart disease in men. *Circulation*. 1994;89:1992-7.
26. Albert CM, Chae CU, Rexrode KM, Manson JE, Kawachi I. Phobic anxiety and risk of coronary heart disease and sudden cardiac death among women. *Circulation*. 2005;111:480-7.
27. Wedegaertner F, Arnhold-Kerri S, Sittaro N-A, Bleich S, Geyer S, Lee WE. Depression-and anxiety-related sick leave and the risk of permanent disability and mortality in the working population in Germany: a cohort study. *BMC Public Health*. 2013;13:145.
28. Saeed Mirza S, Arfan Ikram M, Hofman A, Tiemeier H. Anxiety does not predict mortality. A population-based study. *World Psychiatry*. 2015;14:103-4.
29. Roest AM, Martens EJ, de Jonge P, Denollet J. Anxiety and Risk of Incident Coronary Heart Disease A Meta-Analysis. *Journal of the American College of Cardiology*. 2010;56:38-46.
30. Denollet J, Maas K, Knottnerus A, Keyzer JJ, Pop VJ. Anxiety predicted premature all-cause and cardiovascular death in a 10-year follow-up of middle-aged women. *Journal of clinical epidemiology*. 2009;62:452-6.
31. Noyes R, Jr., Carney CP, Langbehn DR. Specific phobia of illness: search for a new subtype. *J Anxiety Disord*. 2004;18:531-45.
32. Tyrer P, Eilenberg T, Fink P, Hedman E, Tyrer H. Health anxiety: the silent, disabling epidemic. *BMJ*. 2016;353:i2250.
33. Persoskie A, Ferrer RA, Klein WM. Association of cancer worry and perceived risk with doctor avoidance: an analysis of information avoidance in a nationally representative US sample. *J Behav Med*. 2014;37:977-87.
34. Barsky AJ, Wyshak G, Latham KS, Klerman GL. Hypochondriacal patients, their physicians, and their medical care. *Journal of general internal medicine*. 1991;6:413-9.

**Table 1. Baseline characteristics of the sample according to level of health anxiety (N=770)**

	Level of health anxiety according to the Whiteley index						p-value		
	No		Mild-moderate		High		Mild-moderate vs. no	Mild-moderate vs. high	No vs. high
Total number, %	226	29.4%	317	41.2%	227	29.5%			
	<i>Mean</i>	<i>SD</i>	<i>Mean</i>	<i>SD</i>	<i>Mean</i>	<i>SD</i>			
Points on Whiteley questionnaire (max 12 points)	0.0	0.0	1.4	0.5	4.6	1.8			
Waist/hip ratio	0.74	0.05	0.74	0.05	0.74	0.06	0.95	0.31	0.31
Serum-triglycerides (mmol/l)	1.14	0.45	1.23	0.54	1.31	0.60	0.038	0.093	0.001
Systolic blood pressure (mmHg)	131.4	19.2	134.2	21.7	134.3	23.4	0.13	0.92	0.15
Total yearly household income (Thousand Swedish kronor)	41.8	20.5	41.0	24.0	35.9	16.7	0.66	0.006	0.001
Hamilton Depression Rating Scale (0-50)	1.2	3.4	2.0	4.5	4.9	7.0	0.029	<0.001	<0.001
Number of phobias (0-26)	1.2	1.9	1.4	2.0	3.0	3.5	0.18	<0.001	<0.001
	<i>N</i>	<i>%</i>	<i>N</i>	<i>%</i>	<i>N</i>	<i>%</i>			
Age (years)									
38	28	12.4%	45	14.2%	34	15.0%			
46	85	37.6%	122	38.5%	91	40.1%			
50	91	40.3%	115	36.3%	73	32.2%	0.77	0.77	0.29
54	22	9.7%	35	11.0%	29	12.8%			
Married	180	79.6%	262	82.6%	177	78.0%	0.38	0.17	0.66
Education beyond mandatory	62	27.4%	84	26.5%	45	19.8%	0.81	0.071	0.057
Low physical activity last year	34	15.0%	56	17.7%	42	18.5%	0.42	0.80	0.33
Current smoker	90	39.8%	130	41.0%	94	41.4%	0.78	0.93	0.73
Alcohol consumption more than once weekly	61	27.0%	98	30.9%	76	33.5%	0.32	0.53	0.13
Has a named doctor	125	55.3%	154	48.6%	145	63.9%	0.12	<0.001	0.063
Previous life-time hospitalization (excl. childbirth)	176	77.9%	242	76.3%	197	86.8%	0.68	0.002	0.013
Psychosocial stress	23	10.2%	51	16.1%	67	29.5%	0.048	<0.001	<0.001
Known serious disease prior to baseline*	6	2.7%	11	3.5%	13	5.7%	0.59	0.21	0.10

p-value: from one-way ANOVA for continuous variables and Pearson Chi-square for categorical variables

\*Cancer, diabetes, stroke, myocardial infarction

Level of health anxiety: Whiteley index score 0 = No health anxiety, scores 1-2= mild-moderate, scores  $\geq 3$ =high

**Table 2. All-cause mortality by level of health anxiety in a population-based sample of women (N=770)**

	Level of health anxiety according to the Whiteley index								
	No (N=226)			Mild-moderate (N=317)			High (N=227)		
Number (%) with event	175 (77.4)			233 (73.5)			172 (75.8)		
Person-years of follow-up	7565			11346			7514		
	HR	95% CI	p	HR	95% CI		HR	95% CI	p
Model 1	1.22	1.00-1.49	0.047	Reference category			1.26	1.04-1.54	0.021
Model 2	1.27	1.04-1.55	0.018	Reference category			1.13	0.92-1.39	0.26
Model 3	1.22	1.00-1.48	0.049	Reference category			1.23	1.00-1.49	0.046
Model 4	1.40	1.15-1.72	0.001	Reference category			1.32	1.08-1.62	0.006
Model 5	1.44	1.17-1.76	<0.001	Reference category			1.21	0.98-1.49	0.076

HR: Hazard ratio, 95 CI: 95% Confidence interval, estimated from Cox proportional hazards models

Model 1: adjusted for age

Model 2: adjusted for age, Hamilton Depression Rating Scale score, psychosocial stress, number of phobias.

Model 3: adjusted for age, household income, marital status, educational level

Model 4: adjusted for age, waist/hip ratio, serum-triglycerides, systolic blood pressure, physical activity level, alcohol consumption, smoking status, having a named doctor, previous hospital admission.

Model 5: adjusted for all variables

Level of health anxiety: Whiteley index score 0 = No health anxiety, scores 1-2= mild-moderate, scores  $\geq 3$ =high

**Table 3. All-cause mortality according to level of health anxiety after different lengths of survival**

			Level of health anxiety according to the Whiteley index						
			No			Mild-moderate		High	
Survival	N	No. deaths	HR	95% CI	p		HR	95% CI	p
>5 years	764	574	1.46	1.19-1.79	<0.001	Reference category	1.22	0.99-1.51	0.068
>10 years	747	557	1.40	1.14-1.73	0.002	Reference category	1.20	0.97-1.49	0.096
>15 years	730	540	1.41	1.15-1.75	0.001	Reference category	1.19	0.96-1.48	0.121
>20 years	695	505	1.34	1.07-1.66	0.009	Reference category	1.11	0.89-1.40	0.35
>25 years	629	439	1.33	1.05-1.68	0.017	Reference category	1.05	0.82-1.34	0.69
>30 years	542	352	1.23	0.95-1.60	0.11	Reference category	0.94	0.71-1.24	0.67
>35 years	433	243	1.24	0.91-1.69	0.18	Reference category	0.82	0.58-1.15	0.25
>40 years	294	104	1.34	0.80-2.23	0.27	Reference category	1.09	0.66-1.81	0.74

HR: Hazard ratio, 95 CI: 95% Confidence interval, estimated from Cox proportional hazards models

Model adjusted for age, Hamilton Depression Rating Scale score, psychosocial stress, number of phobias, household income, marital status, educational level, waist/hip ratio, serum-triglycerides, systolic blood pressure, physical activity level, alcohol consumption, smoking status, having a named doctor, previous hospital admission.

Level of health anxiety: Whiteley index score 0 = No health anxiety, scores 1-2= mild-moderate, scores  $\geq 3$ =high

**Table 4. Risk of cancer according to level of health anxiety (N=748)**

	Level of health anxiety according to the Whiteley index							
	No (N=224)			Mild-moderate (N=307)		High (N=217)		
Number (%) with event	81 (36.2)			112 (36.5)		75 (34.6)		
Person-years of follow-up	6736			9920		6520		
	HR	95% CI	p			HR	95% CI	p
Model 1	1.10	0.83-1.47	0.51	Reference category		1.06	0.79-1.41	0.72
Model 2	1.12	0.84-1.49	0.45	Reference category		1.03	0.76-1.40	0.85
Model 3	1.11	0.83-1.47	0.49	Reference category		1.06	0.79-1.42	0.71
Model 4	1.07	0.80-1.43	0.65	Reference category		1.01	0.75-1.36	0.94
Model 5	1.08	0.80-1.45	0.62	Reference category		1.02	0.75-1.40	0.89

23 women had cancer before the study and were excluded from these analyses. One participant was censored before the first event.

HR: Hazard ratio, 95 CI: 95% Confidence interval, estimated from Cox proportional hazards models

Model 1: adjusted for age

Model 2: adjusted for age, Hamilton Depression Rating Scale score, psychosocial stress, number of phobias.

Model 3: adjusted for age, household income, marital status, educational level

Model 4: adjusted for age, waist/hip ratio, serum-triglycerides, systolic blood pressure, physical activity level, alcohol consumption, smoking status, having a named doctor, previous hospital admission.

Model 5: adjusted for all variables

Level of health anxiety: Whiteley index score 0 = No health anxiety, scores 1-2= mild-moderate, scores  $\geq 3$ =high



**Figure 1. Kaplan-Maier curve of survival according to health anxiety level**

