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The prospective association between health anxiety and cancer detection: A cohort study linking the Hordaland Health Study (HUSK) with the Norwegian Cancer Registry

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ABSTRACT

Objective: Health anxiety is associated with distress and disability, and overutilization of health services, but it is not known whether high levels of health anxiety may lead to increased detection of severe diseases such as cancer. By linking a large population based health study with the national cancer registry, the aim of the study was to investigate a potential prospective association between health anxiety in men and women and later cancer detection and tumour metastasis at the time of diagnosis.

Method: A longitudinal study with a 13.2 year follow-up linking the population-based Hordaland Health Study (HUSK) and the Cancer Registry of Norway (CRN) was conducted. Health anxiety was measured with the Whiteley Index. Associations were examined through gender stratified Cox regression analyses adjusted for relevant covariates.

Results: No association was found between baseline health anxiety and cancer detection for women (adjusted HR: 1.21, 95% CI: 0.42–3.50), but a positive association was found between health anxiety at baseline and cancer detection for men (adjusted HR: 1.76, 95% CI: 1.06–2.91). No statistically significant association was demonstrated between health anxiety and cancer metastasis for either gender.

Conclusion: An increased level of health anxiety in men may be advantageous, as it may motivate to self-examination and healthcare seeking when disturbing symptoms arise. Research is needed to investigate whether health anxiety has a protective effect on cancer metastasis at the time of detection, or whether health anxiety increases the risk of over-diagnosis and overtreatment.

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Introduction

Health anxiety is characterised by a persistent preoccupation of having or being in the process of developing a serious medical condition or disease [1,2]. Levels of health anxiety extend from mild to severe forms, and include defined mental disorders such as illness phobia and hypochondriasis. Persons with high levels of health anxiety are intensively worried about their health, are preoccupied with bodily symptoms, and are actively seeking reassurance despite beliefs that their symptoms are not taken seriously by others. The lifetime prevalence of health anxiety in the general population has been found to be around 6%, while the point prevalence is 3.4% [3]. The prevalence seems to peak in middle age [3]. Health anxiety is considered to be a long-lasting condition [4], and patients with health anxiety often report poorer mental and physical functioning than patients with a well-defined medical condition [4]. Health anxiety also increases the risk for adverse functional outcomes such as early retirement or departure from the paid workforce [5]. As the core symptom is fear of presence or development of a serious and potential life-threatening medical condition, persons with high levels of health anxiety are excessive users of health care services, with increased use of primary care, specialist health care and laboratory tests [4,6–8].

Fear of death is an integral part of health anxiety, and the preoccupation with potential presence of a serious disease may be an expression of this fear [9]. Personal experience with serious illness, either one's own or the illness of a close friend or relative, is a vulnerability factor for developing health anxiety [7,8]. Several cross-sectional studies have found more physical illness among individuals with high levels

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compared with individuals with lower levels of health anxiety [3,8,10]. However, the causal direction of this relationship cannot be established in cross-sectional studies, and high health anxiety may indeed be the result of direct experience with illness and disease. To the best of our knowledge, no study has examined whether the direction may go the other way, thus, or whether individuals with health anxiety have increased risk of developing and detecting a serious medical condition in the future.

As one of the leading causes of mortality in the western world, cancer is frequently a specific subject of health anxiety [10]. Cancer is strongly associated with increasing age, but some cancer diseases, in particular those that affect women (such as breast, ovary and cervix cancer), may also develop in relatively young age [11]. Fear of cancer may lead to increased health care visits to check and test for bodily signals suspected by the person to be symptoms of malignant tumours. This in turn may lead to detection of cancer tumours that may otherwise go unnoticed, or to detection of tumours before metastasis develops. By linking a large population based health study in Western Norway with the national cancer registry, we aimed to investigate whether there may be a prospective association between health anxiety and detection and medical diagnosis of a cancer tumour. More specifically, we wanted to examine whether men and women with high levels of health anxiety compared with the general male and female population have i) higher prevalence of a subsequent incident cancer diagnosis, and ii) lower risk of tumour metastasis at the time of diagnosis.

Methods

The Hordaland Health Study (HUSK)

HUSK was an epidemiological, population based health study with data collection conducted between 1997 and 1999 in the Hordaland County of Western Norway. All individuals born between 1953 and 1957 who lived in Hordaland at the time (N = 29,400) received a personal invitation to participate in the health study. A total of 18,565 persons (63.1% of the invited) agreed to participate. Data was collected through physical examinations and a battery of self-report instruments distributed in two questionnaires. Questionnaire 1 was included with the invitation to the health study, and was collected at the physical examination. Questionnaire 2 consisted of two different versions that each was randomly given to 50% of the participants at the physical examination. These were returned by mail.

Exposure: health anxiety measured with Whiteley Index (WI)

Health anxiety was measured with the Whiteley Index (WI) in version 1 of Questionnaire 2. WI was developed by Pilowsky and colleagues in the mid-1960s [12]. It is considered a classic scale for measuring health anxiety and hypochondriasis, and is widely used. The scale consists of 14 items, aiming to assess three dimensions of health anxiety, namely disease phobia, somatic symptoms and disease conviction. The participants are asked to rate how much each statement describes their health worries on a 5-point scale labelled as 1 “not at all”, 2 “to some extent”, 3 “moderately”, 4 “to a considerable extent” and 5 “to a great extent”. Studies have differed in the number of WI items that they have included, and the cut-off that they have used [12–14]. In the present study, we decided on the 90th percentile as the cut-off, in an attempt to separate men and women with scores that differed substantially from the common responses, and thus were considered likely to have higher levels of health anxiety than the general population. Responses were missing on some of the items among the participants. For participants who had replied to 9 or more of the 14 items (n = 809) the sum score was imputed as mean score * 14.

Outcome: cancer detection and metastasis

The main outcome in the present study was cancer detection, defined as incident cancer diagnosis 0.5 to 13.2 years after HUSK participation. Presence of metastasis at the time of cancer diagnosis was also included as an outcome. Information on cancer incidence and metastasis was taken from the Cancer Registry of Norway (CRN) [15]. The cancer registry was established in 1951, and all hospitals and pathology laboratories in Norway are legally required to report neoplasms to CRN. The registry is thus close to complete for the Norwegian population [16]. The CRN discriminates between pre-malignant and malignant tumours, and classifies the diagnoses according to the ICD-7 system [17]. The stage of metastasis at time of diagnosis is classified as local (within the organ), regional (spread outside the organ, but within the bodily region), distant (spread outside the bodily region) or unknown. HUSK participants were linked to CRN through their personal identification number.

In the present study, cancer detection was operationalized as the first date of cancer diagnosis in CRN after HUSK participation. Cancer metastasis was coded as a binary variable: local versus regional/distant. Cases with unknown cancer metastasis (n = 54) were excluded from the metastasis analysis.

Covariates

Due to the generally higher incidence of cancer among women compared to men in this age group [11], we wanted to examine a potential association between health anxiety and cancer within each gender separately. We thus conducted the analyses stratified by gender. Several covariates that were assessed in HUSK were included in the analyses. Self-reported *marital status* was categorized as “married/partner”, “unmarried”, “widow/widower”, “divorced” and “separated”, while the highest achieved *educational level* was for the purpose of the present study categorized as: “higher education (college/university)”, “high school” and “compulsory school only”. We also included information about health related behaviour in terms of *physical activity*, *alcohol consumption* and *smoking*. Physical activity was coded according to mean hours per week with physical activity, giving a continuous variable ranging from no physical activity to more than 3 h a week with hard physical activity (involving sweating and being out of breath). The measure of alcohol consumption was based on gender specific percentiles: 0) abstainer, i) low consumption (0–33 percentile), ii) moderate consumption (34 to 66 percentile) and iii) high consumption (67–100 percentile). Individuals who reported daily use of cigarettes, cigars or pipe were defined as *daily smokers*. Some physical measures were also included, namely body mass index (BMI) and gender specific waist–hip ratio (WHR). The participants were also asked about the presence of the following somatic conditions: heart attack, diabetes, stroke, multiple sclerosis, angina pectoris or asthma (yes/no). Finally we include self-reported information regarding the number of 1st degree relatives (mother, father, sister, brother, child) previously or currently diagnosed with cancer.

Statistical procedures

The population eligible for inclusion in the present study includes all of those who received WI in version 1 of Questionnaire 2 in HUSK (N = 9472), which were randomly distributed to half of the HUSK participants. The other half of the HUSK participants, who received version 2 of Questionnaire 2, were thus excluded from all analyses in the present study. In order to avoid increased health anxiety levels due to previously diagnosed cancer, we excluded all persons diagnosed in CRN with cancer before HUSK (n = 130). We also excluded all individuals diagnosed with cancer during the first 6 months after HUSK participation (n = 5) to avoid possible

heightened levels of health anxiety due to realistic suspicion of cancer presence at the time of health survey participation. Further, we excluded 2294 persons who did not complete the WI, and 26 individuals with missing data on 9 or more items. There was no increased cancer incidence among non-responders or those with missing data on WI items ($P = .787$). Finally, we excluded 10 participants diagnosed with benign tumours. Registration of benign tumours in CRN was not related to health anxiety ($P = .811$). The final sample consisted of 7007 individuals, 74.0% of those who were given version 1 of HUSK Questionnaire 2. These persons were followed until the first date of cancer diagnosis in CRN, or until 31st December 2010, giving a follow-up time ranging from 6 months to 13.2 years.

Gender stratified associations between health anxiety at baseline and subsequent cancer incidence and metastasis were examined with Cox proportional regression models in two blocks: i) unadjusted and ii) adjusted for all covariates. The association estimates are presented as hazard ratios (HR) with 95% confidence intervals (CI) and *P*-values. In the multivariate analyses, listwise deletion was employed for cases with missing information (between 0.1% and 2.4% of the total sample, see Table 1). The cumulative hazard of cancer diagnoses by year after HUSK participation for men and women with scores under and above the 90th percentile on the Whiteley Index was also plotted in a Nelson–Aalen survival plot. All analyses were conducted in Stata version 12.

Ethics

The present study was approved by the Regional Ethics Committee of Western Norway (REK). The linkage between HUSK and the Norwegian Cancer Registry was approved by REK and the Norwegian Data Inspectorate. All HUSK participants gave their written informed consent for linkage with health registries at the time of participation.

Results

Descriptive characteristics of the men and women participating in the HUSK study are given in Table 1. Both cancer incidence and regional/distal metastasis were more common among women compared with men (Table 1). During follow-up, 124 (3.4%) of the men and 187 (5.6%) of the women were diagnosed with incident cancer. Of these, 36 (29.0%) male and 79 (42.2%) female cancer cases had regional or distant metastasis at the time of diagnosis (Table 1). There was no difference in mean score and standard deviation between men and women above the 90th percentile cut-off on WI.

As described in Table 2, health anxiety was significantly associated with subsequent incident cancer in both the unadjusted ($P = .009$) and adjusted ($P = .028$) models for men. Thus, men with high levels of health anxiety at HUSK participation were found to have around 80% increased risk for later cancer detection than men with lower levels of health anxiety. No association between health anxiety and cancer detection was found for women (unadjusted: $P = .951$, adjusted: $P = .651$). The yearly cumulative hazard for cancer diagnosis for men and women with scores under and above the 90th percentile cut-off on WI is shown in Fig. 1. In terms of regional and distal metastasis, no significant association with health anxiety was found for any of the genders (Table 2). However, small numbers in these analyses may have obscured the associations of interest.

Table 1
Descriptive characteristics of male and female HUSK participants. Total N = 7007 and follow-up: 6 months to 13.2 years.

	Men (n = 3659) n (%)	Women (n = 3348) n (%)	Missing n (%)
Cancer incidence	124 (3.4)	187 (5.6)	–
Cancer metastasis[a]	36 (29.0)	79 (42.2)	–
Mean score WI cut-off (SD)[b]	37.8 (0.3)	38.0 (0.3)	–
Marital status (not married)	986 (27.0)	830 (24.8)	–
Education level (higher education)	1377 (37.9)	1143 (34.5)	56 (0.8)
Physical activity (none)	151 (4.1)	83 (2.5)	–
Alcohol consumption (high)	1080 (30.0)	829 (25.6)	169 (2.4)
Smoking (yes)	1274 (34.8)	1191 (35.6)	–
Obese (yes)[c]	442 (12.1)	359 (10.8)	7 (0.1)
Abdominal obesity (yes)[d]	1907 (52.1)	534 (16.0)	–
Other somatic conditions (1 or more)[e]	292 (8.0)	284 (8.5)	15 (0.2)
Cancer in family (yes)[f]	1118 (30.6)	1170 (35.0)	–

[a] Regional or distal cancer metastasis at time of diagnosis.
[b] ≥90th percentile score on Whiteley Index.
[c] BMI > 30.
[d] WHR > 0.85 for women and WHR > 0.90 for men.
[e] Confirmation of one or more of the following conditions: heart attack, angina pectoris, stroke, diabetes, asthma, and multiple sclerosis.
[f] Confirmation of cancer among one or more of 1st degree relatives: mother, father, brother, sister, and child.

Discussion

The present study was based on a sample from the general population linked with a complete, national cancer registry. No association was found between baseline health anxiety and cancer incidence for women, but a positive association was found between health anxiety at baseline and cancer incidence for men. We believe that it is unlikely that a real difference in cancer incidence between men with and without high levels of health anxiety exists. The results may therefore indicate that men with high levels of health anxiety are more likely to detect a malignant tumour than men with lower levels of health anxiety.

The gender difference in the association between high levels of health anxiety and incident cancer in our sample is interesting, and may perhaps be explained by general gender differences in health care utilization and cancer detection strategies. Early detection of cancer increases the chance of survival and curative treatment [18,19]. According to the World Health Organization, population-based strategies for early detection of cancer consist of two components: i) public education on how to detect warning signs of cancer and engage in adequate and prompt action, and ii) mass population screening [20]. Since 1995–96, Norway has run two nationwide screening programmes for the most common types of cancer among women. In the breast cancer screening programme, all Norwegian women aged 50 to 69 are invited to a mammography examination every second year [21], while all women between ages 25 and 69 are invited to cytology and HPV testing every third year in the cervical cancer screening programme [22]. In our sample, 57% of incident cancers among women were either breast or cervix cancer. Exclusion of these cases did not change the results for women in a sensitivity analysis (data not shown). Thus, the general invitation to cancer screening may reduce the importance of health anxiety as a driver for individual cancer detection strategies among Norwegian women.

In contrast, similar screening programmes for the most common types of male cancers do not exist to date in Norway. Norwegian men may thus be left more to themselves in order to detect and report warning signs of cancer. In general, men consult health care services less often than women [23], and there is also evidence suggesting that men tend to engage in less frequent self-examination and delay reporting of cancer symptoms to their doctors [24]. Therefore, men with higher levels of health anxiety, who hence are more likely to have both increased awareness of bodily symptoms and to call upon their doctors when they discover such symptoms, may be more likely to detect incident cancer. As such, higher levels of health anxiety may motivate men to engage in adequate and prompt actions when they detect unusual and disturbing symptoms.

An obvious continuation of the hypothesis that increased health anxiety among men leads to improved cancer detection would be to explore whether increased levels of health anxiety also resulted in less metastasis at the time of cancer detection. We attempted to examine this in the present study, but small numbers (only 36 men in our sample were diagnosed with regional/distal cancer metastasis at the time of diagnosis) precluded any real investigation and interpretation of this issue. The association between health anxiety and cancer metastasis at the time of detection is thus an interesting topic for future studies.

Although health anxiety may have a positive consequence in that tumours are detected early with an increased probability of successful treatment, increased cancer detection may also have important

Table 2
Association between ≥90th percentile score on Whiteley Index at baseline and i) cancer incidence and ii) regional or distant cancer metastasis at time of diagnosis 0.5 to 13.2 years after HUSK participation, stratified by gender (Cox regression analysis).

Men				
	Cancer incidence		Regional or distal cancer metastasis[a]	
	Predicting 124 (3.4%) cases among 3659 participants		Predicting 36 (1.0%) cases among 3628 participants	
	HR (95% CI)	*P*-value	HR (95% CI)	*P*-value
Unadjusted	1.89 (1.17–3.05)	$P = .009$	1.59 (0.62–4.08)	$P = .338$
Fully adjusted	1.76 (1.06–2.91)	$P = .028$	1.21 (0.42–3.50)	$P = .728$
Women				
	Cancer incidence		Regional or distal cancer metastasis[a]	
	Predicting 187 (5.6%) cases among 3348 participants		Predicting 79 (2.4%) cases among 3326 participants	
	HR (95% CI)	*P*-value	HR (95% CI)	*P*-value
Unadjusted	1.02 (0.63–1.63)	$P = .951$	0.48 (0.18–1.31)	$P = .152$
Fully adjusted	1.12 (0.69–1.81)	$P = .651$	0.50 (0.18–1.39)	$P = .184$

[a] Cases with unknown metastasis (n = 53) excluded from analysis.

adverse side effects. Lessons from several decades of cancer screening programmes have showed that screening for cancers (in particular breast and prostate cancer) may result in overdiagnosis and overtreatment [25]. Besides allocating resources away from more useful areas, overtreatment also exposes the individual to unnecessary harmful effects of the cancer-treatment itself, such as urinary, bowel and sexual dysfunction in prostate cancer treatment [26], side effects of chemotherapy [27] and complications of colorectal surgery [28]. Future research should therefore examine whether health anxiety is associated with overdiagnosis and overtreatment in cancer.

Limitations

The present study examined the prospective association between health anxiety and cancer in a general population sample in linkage with a comprehensive national register of objective and quality assured cancer diagnoses, enabling a follow-up of more than 13 years. Despite these strengths, the present study also has some important limitations.

Firstly, health anxiety was assessed through self-report with a screening instrument, and not validated by a health professional. The ability of WI to separate between "real" and "imagined" illnesses is not known. It is likely that the experience of "real" and disturbing bodily symptoms may increase the scores on WI. We tried to reduce this threat to the external validity of WI by excluding all cases with incident cancer diagnosed the first six months after HUSK participation, and by adjusting for the most common somatic illnesses in this age-group in the analyses. Further, the structural validity of WI has been examined in a range of studies, with mixed findings (for an overview of some of these studies, see Table 1 in Veddegjaerde et al. [29]). In a recent published confirmatory factor (CFA) analysis and item response theory (IRT) analysis on the HUSK population, it was indicated that the use of the full and original 14-item WI did not yield a satisfactory CFA fit [29]. Neither did any of 10 other previously suggested models that were investigated [29]. Based on IRT and CFA analyses, the use of a 6 item one factor approach was suggested [29]. In the present study, we did an ad-hoc examination of the analyses using the 6-item short

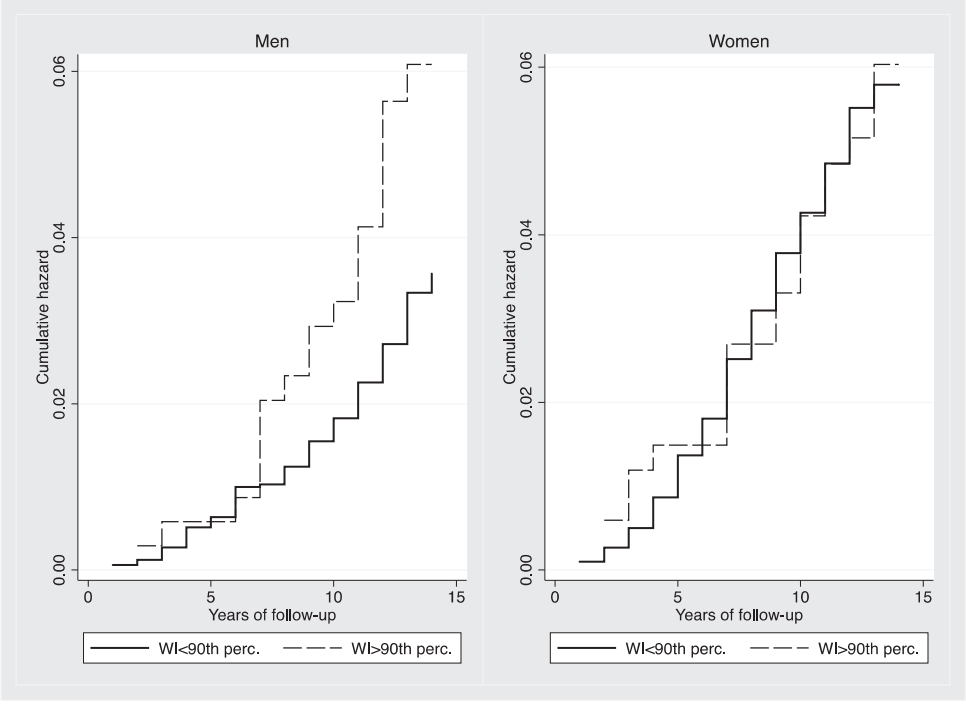

Fig. 1. Nelson–Aalen survival plots of the yearly cumulative hazard for cancer diagnosis for men and women with scores under and above the 90th percentile on Whiteley Index (WI).

version of WI. No substantial differences in the associations of interest when using the full compared to the abbreviated version of WI were found (data not shown). The cut-off based on scores above the 90th percentile was somewhat arbitrary, although this was chosen in order to identify men and women likely to have higher levels of health anxiety than the general population. Despite these limitations, WI is the most commonly used screening instrument for health anxiety assessments.

Secondly, self-selection and nonparticipation are always a challenge to epidemiological studies. A previous study of nonparticipants in the HUSK sample indicated more nonparticipation both among individuals with mental health problems and with cancer [30]. However, nonparticipation is likely to be a greater threat to studies assessing the prevalence of health conditions than to studies examining associations between variables. Nonparticipation is thus less likely to have any substantial impact on the results from the present study.

Thirdly, cancer is a heterogeneous group of diseases, with different characteristics and prognoses, and the inclusion of all cancer diagnoses in a single outcome may preclude important differences between the different types of cancer diseases. It would have been interesting to examine the association between health anxiety and different subtypes of cancer, but low numbers in each cancer category precluded the opportunity for a thorough examination of this issue in the present sample.

Finally, the results from the present study may not be generalized to other settings. For instance, health anxiety among women could be a more important contributor to cancer detection in countries that do not have mass screening programmes for breast and cervix cancer. Likewise, the results may not generalize to settings that have cancer-screening programmes for men. Furthermore, generalizations to other age-groups should be done with caution. In Norway, as in many other high income countries, the vast majority of cancer cases are diagnosed in persons aged 50 or more, and cancer is in general more common among men than women, except in the age-group 25 to 49 [31]. Thus, health anxiety may show different associations with cancer detection in age-groups where male cancer is more prevalent.

Conclusion

High levels of health anxiety in men were associated with subsequent detection of cancer. A certain level of health anxiety in men may thus be advantageous, as it may motivate them to engage in self-examination of cancer symptoms and healthcare seeking when such symptoms are discovered. However, health anxiety may also increase the risk of overdiagnosis and overtreatment in cancer. Research is needed to investigate whether health anxiety has a protective effect on cancer metastasis at the time of detection, whether the association between health anxiety and cancer differs between cancer diseases, and whether health anxiety is associated with overdiagnosis and overtreatment in cancer.

Conflict of interest

None of the authors have any conflicts of interest to declare.

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