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Health anxiety as a continuous construct in the general population

Measuring the distribution of health anxiety and the associations with healthcare use, physical disease and cardiovascular risk factors

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Coming from a family where we speak English and Norwegian every other sentence, it seems fitting to take this next part in Norwegian: Kjære pappa, Lise, Sandra og “ho mamma” her også, takk for at dere er verdens beste heiagjeng! Takk for at dere vet når jeg trenger en pause, på telefon, på hytta eller i Salangen, og for at dere av og til minner meg på at livet er mer enn en doktorgrad (av og til må bare bacheloren bli prioritert). Det er så godt å ha en stødig base “i bunn”, som alltid støtter meg i å prøve det jeg har lyst til, og som stiller opp, uansett.

And back to English: It is extremely easy to get carried away, as I am lucky to have so many wonderful people around me. But André made me promise that this would not go over one page, as it will destroy the layout (André has helped me with the formatting). Thank you to my friends who have given me dinner, a break when I needed it, and who have also understood when this thesis had to be my top priority. I am back!

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Abstract

Background: Health anxiety (HA) has most commonly been examined in people with severe HA, with a similar symptom burden as people diagnosed with hypochondriasis. However, some have proposed that HA is better conceptualised as a continuous construct, with levels ranging from low to severe. Severe HA is associated with high healthcare use and reduced quality of life. At present, there is little knowledge on the distribution of HA, as a continuous construct, in the general population. In addition, healthcare use is increasing globally, as is the prevalence of people living with physical disease and cardiovascular risk factors; therefore the association between all levels of HA and these aspects are important to examine.

Aim: The aim of this thesis was to study the distribution of HA as a continuous construct in the general population, to examine sociodemographic and social network factors associated with HA, as well as to examine the relationship between HA and healthcare use and physical disease and cardiovascular risk factors.

Methods: This thesis used cross-sectional data from 21 083 participants aged 40 years and older from the seventh survey of the Tromsø study (Tromsø7), a large multipurpose health-survey in Norway, conducted in 2015-2016. HA was measured with two 6-itemed Whiteley Index scales (the WI-6 and the WI-6-R); responses were given on a 5-point Likert scale, with a range of possible total scores from 0 to 24. Sociodemographic and social network factors included age, gender, education, household income, friendship, and participation in organised activities. Participants reported their healthcare use as attendance to, and number of consultations with three types of healthcare services (primary, somatic specialist, and mental specialist healthcare), in the last 12 months. They also reported on the absence, current or previous presence of 13 physical diseases, as well as cardiovascular risk factors.

Results: HA was highly skewed in our sample of the general adult population, with an exponential distribution. Of all the sociodemographic and social network variables, friendship showed the strongest association with HA level. HA as a continuous construct was associated with an increased level of use of all types of healthcare services. HA was consistently higher in the population that reported current or previous physical disease and cardiovascular risk factors than in the healthy reference group.

Conclusion: Our results from Tromsø7 support conceptualising HA as a continuous construct. Mean HA in the study sample was low, but all levels of HA were associated with increased healthcare use. Having physical disease and cardiovascular risk factors were consistently associated with increased HA. I believe that these results indicate that investigating HA as a continuous construct reveals that all levels of HA, including lower levels, deserve attention, both in future research and clinical practice.

Sammendrag

Bakgrunn: Forskning på temaet helseangst (HA) har i stor grad fokusert på alvorlig helseangst; personer som har symptombyrde likt de med hypokondri. HA er samtidig foreslått som et kontinuerlig fenomen, med alvorlighetsgrader som varierer fra lite til alvorlig. Alvorlig, eller høy grad av HA, er assosiert med høyt helsetjenesteforbruk og redusert livskvalitet. HA som et kontinuerlig fenomen har vi lite kunnskap om, heller ikke hvordan dette fordeler seg i den generelle befolkningen. I Norge og i verden er helsetjenesteforbruk økende, sammen med økende forekomst av fysisk sykdom og kardiovaskulære risikofaktorer. Sammenhengen mellom HA som et kontinuerlig fenomen og disse faktorene er derfor viktig å undersøke.

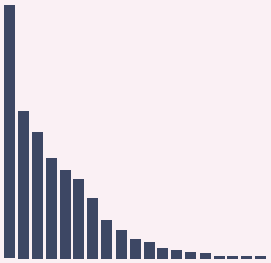
Formål: Formålet med denne doktorgraden var å undersøke fordelingen av HA som et kontinuerlig fenomen i en voksen, generell befolkning, samt undersøke hvordan ulike faktorer var assosiert med HA; sosiodemografiske og sosiale faktorer, ulike typer helsetjenesteforbruk, fysisk sykdom og kardiovaskulære risikofaktorer.

Metode: Doktorgraden brukte spørreskjemadata fra 21 083 personer som var 40 år eller eldre, som deltok på Tromsøundersøkelsen (Tromsø7) i 2015-2016, og hadde et tverrsnittdesign. HA ble målt med to versjoner av måleverktøyet Whiteley Index (WI-6 og WI-6-R), med en totalscore 0 til 24 der høyere score indikerer høyere HA. Sosiodemografiske faktorer inkluderte alder, kjønn, utdanning, husholdningsinntekt, vennskap og deltakelse i organisert aktivitet. Helsetjenesteforbruk inkluderte bruk av primærhelsetjenesten, somatisk spesialisthelsetjeneste og psykiatrisk spesialisthelsetjeneste de siste 12 måneder. Deltakerne rapporterte også om de hadde ulike somatiske sykdommer, nå eller tidligere, og om de hadde kardiovaskulære risikofaktorer.

Resultat: HA var skjevfordelt i den generelle voksne befolkningen og hadde en eksponentiell fordeling. Av de sosiodemografiske variablene var vennskap den variabelen som var sterkest assosiert med HA. Alle grader av HA var assosiert med alle typer helsetjenesteforbruk. Grad av HA var gjennomgående høyere hos deltakere med fysisk sykdom sammenlignet med deltakere uten sykdom. Dette gjaldt både personer med nåværende og tidligere sykdom, samt de med kardiovaskulære risikofaktorer.

Konklusjon: Våre resultater, med utgangspunkt i Tromsø7, viser HA som et kontinuerlig fenomen. Selv om gjennomsnittsscoren av HA var lav, var alle grader av HA assosiert med helsetjenesteforbruk. Sammenhengen mellom HA og fysisk sykdom var også konsekvent. Jeg mener våre funn indikerer at alle grader av HA er viktig og fortjener økt oppmerksomhet, både i fremtidig forskning og klinisk praksis.

Thesis at a glance



PAPER 1

Research question: To study the distribution of health anxiety in a general adult population and the association of health anxiety and sociodemographic factors

Study sample: 21 083 participants from the Tromsø7 survey

Exposure: Age, gender, education, household income, friendship, and participation in organized activities

Outcome: Health anxiety, measured with the six-item Whiteley Index (WI-6)

PAPER 2

Research question: To examine the association between health anxiety and primary, somatic specialist and mental specialist healthcare use and the association by different levels of use

Study sample: 18 499, 18 311 and 18 158 participants from the Tromsø7 survey gave self-reported information on primary, somatic specialist and mental healthcare use, respectively

Exposure: Health anxiety, measured with the six-item Whiteley Index (WI-6)

Outcome: Primary healthcare use, somatic specialist healthcare use, and mental specialist healthcare use the last 12 months

PAPER 3

Research question: To examine the association between health anxiety and number of diseases, different disease categories and cardiovascular risk factors in a large sample of the general population

Study sample: 18 432 participants from the Tromsø7 survey

Exposure: Number of physical diseases, different disease categories and cardiovascular risk factors

Outcome: Health anxiety, measured with the revised six item Whiteley Index (WI-6-R)

Illustrations: Mostphotos.com

List of papers

This thesis is based on the following papers:

Paper 1

Norbye AD, Abelsen B, Førde OH, Ringberg U.
Distribution of health anxiety in a general population and associations with demographic and social network characteristics.
Psychological Medicine, 2020:1-8. doi:10.1017/ S0033291720004122

Paper 2

Norbye AD, Abelsen B, Førde OH, Ringberg U.
Health anxiety is an important driver of healthcare use.
BMC Health Services Research, 2022;22(1):138. doi: 10.1186/s12913-022-07529-x

Paper 3

Norbye AD, Abelsen B, Førde OH, Ringberg U.
The association between health anxiety, physical disease and cardiovascular risk factors in the general population – a cross-sectional analysis from the Tromsø study: Tromsø 7.
BMC Primary Care, 2022;23(1):140, doi: 10.1186/s12875-022-01749-0

Abbreviations

HA	Health anxiety
ICD	International classification of diseases
DSM	Diagnostic and Statistical Manual of Mental Disorders
WI-6	Six-item Whiteley Index
WI-6-R	Whiteley Index-6 including illness rumination
Exp.B	Exponentiated Beta
OR	Odds ratio
GP	General practitioner
NOK	Norwegian krone
HADS	Hospital Anxiety and Depression Scale
REK	Regional Committees for Medical and Health Research Ethics

Preface

It has been my privilege to spend the last 4 years on the study of health anxiety (HA) and the field of psychology and epidemiology. As a physiotherapist, I spent 8 years working at a hospital, both at the clinic for chronic back pain and in the neurology department, and completed my MSc in neurological physiotherapy. Working with patients at the hospital showed me that there were aspects of illness that needed to be addressed, outside of examinations and rehabilitation, such as pain and fear. At the neurology department, I worked with patients who had both chronic and fluctuating diseases, such as multiple sclerosis, as well as patients with functional disorders. My experience was that we, as healthcare personnel, came up short in meeting the patients' worry that accompanied their illness. I therefore felt very fortunate when UiT The Arctic University of Norway announced a PhD position on the topic of HA. The data collected from the seventh survey of the Tromsø study (Tromsø7) some years previously allowed me to delve into a field that was totally new to me and required knowledge of both psychology and epidemiology – fields that felt quite different from my daily work as a physiotherapist.

This thesis is based on three articles, all of which use data from Tromsø7. Paper 1 aimed to describe the distribution of HA as a continuous construct in the general population and to explore aspects associated with HA score. The results indicated that HA in the general population was low. Most studies have only explored the category of severe HA; there is little knowledge on the aspects associated with HA as a continuous construct. I wanted to investigate if HA, along the whole continuum, could be of interest. Therefore, Paper 2 examined whether HA was associated with healthcare use. A growing body of research has indicated that HA can accompany physical disease, but most of this research has been conducted in patient populations. In Paper 3, I wanted to explore whether HA was associated with different diseases, including current and previous disease, and risk factors.

I believe that this thesis contributes to the understanding of HA as a continuous construct, and my findings imply that HA is important in the general population. Although mean HA was low in this study sample, HA along the whole continuum was associated with increased healthcare use and a wide range of physical diseases. I believe these results indicate that HA should be assessed and addressed, even when it cannot be categorised as severe.

1 Introduction

Health anxiety (HA) concerns worry of disease (1), and in this thesis, HA is perceived as a continuous construct ranging from mild worry to excessive anxiety. I will start by introducing how HA is conceptualised in research; as a diagnosis, a category, and as a wider continuum, to provide a context for how HA is viewed in this PhD project. Most research, including that cited in this thesis, has used HA as a diagnosis or a category, and there is a knowledge gap of the concept of HA as a continuous construct.

Next, I will give an overview of how HA can manifest and where it is placed with other disorders, and how it can be treated. Then I will introduce how HA is measured in research, and lastly, I will present the three topics investigated in this thesis; the distribution of HA and associated aspects; sociodemographic and social network factors, healthcare use, physical disease and cardiovascular risk factors.

1.1 From diagnosis to graded presence

1.1.1 Health anxiety as a diagnosis

Some researchers use HA as a synonym for hypochondriasis (2-6). The diagnosis of hypochondriasis is defined as "a persistent preoccupation with the possibility of having one or more serious physical disorders and a persistent preoccupation with…physical appearance. Normal or commonplace sensations and appearances are often interpreted by patients as abnormal and distressing" in the International Classification of Diseases, 10th revision (ICD-10) (7), where it is classified under the diagnostic category somatoform disorders. In the 11th revision of the ICD (ICD-11) (8), hypochondriasis has shifted from the diagnostic category somatoform disorders to obsessive-compulsive or related disorders (9, 10). ICD-11 was developed in 2019 and came into effect January 2022 (8), but has not yet been implemented in Norway.

The definition of hypochondriasis in the Diagnostic and Statistical Manual of Mental Disorders (DSM), developed by the American Psychiatric Association, has seen several revisions, and have included aspects as absence of physical disease, duration of symptoms and disease conviction (11). However, in the recent fifth revision of the DSM (DSM-V) (12), hypochondriasis (as named in DSM-IV) was divided into two new diagnoses: Illness anxiety

disorder, where symptoms of anxiety are dominant, and somatic symptom disorder, where physical symptoms dominate the clinical picture (13). Following this change, it is believed that 75% of patients who would have been diagnosed with hypochondriasis prior to the DSM-V now fall into the category of somatic symptom disorder and the remaining 25% into that of illness anxiety disorder (12). These new diagnoses have been met with some criticism. Bailer et al. (13) claim that the DSM-V separation is unrealistic, as their study showed that these patients had similar levels of HA and thus should be seen as one patient group. Their findings gave reason to believe that the diagnostic separation seemed to be based on quantitative (symptom burden) rather than qualitative (different characteristics) differences (13).

The alterations of the hypochondriasis diagnostic criteria over the years in both ICD and DSM seem to indicate that it is not a well-established diagnosis, easily applicable for clinical work. As most research on patients with an ICD or DSM diagnosis have used the ICD-10 (7) or previous DSM-IV (14) diagnostic manuals, I will apply the name "hypochondriasis" to encompass all the ICD and DSM diagnoses of hypochondriasis, illness anxiety disorder and symptom somatic disorder when describing research classifying HA as a diagnosis.

Whereas hypochondriasis in the general population is relatively rare with a prevalence below 1 % (15), the prevalence of the extended condition of severe HA is considered to be much higher.

1.1.2 Health anxiety as a category

Several studies have claimed that hypochondriasis as a diagnosis is too restrictive (5, 15, 16), and different authors have therefore used the term health anxiety as a less restricted category, including some but not all of the diagnostic criteria, or by the use of measurement tools to define a cut-off. These "subthreshold conditions" have been introduced in recent years, using different terminology; subthreshold hypochondriasis (17), abridged hypochondriasis (15), illness worry (17), illness anxiety (18) and severe HA (5).

Studies conducted in the general population have found a point prevalence and 12 month prevalence of severe HA of 3.4-13.1% (19-22) and 2.12-4.2%, respectively (17, 21, 23), with values as high as 20-60% in patients with somatic disease (24-30).

In this thesis, I will apply “severe HA” to encompass all of the terms that is used to describe HA in the severe end of the continuous scale, including research classifying HA as a category or the beforementioned subthreshold conditions.

1.1.3 Health anxiety as a continuum

HA was first described as a continuous construct in 1986, where Salkovskis and Warwick described “anxiety about health” in people who did meet the diagnostic criteria for hypochondriasis, but who were “very common in non-psychiatric clinics and constitute a major drain on time and resources” (1, p. 597). The wider definition of HA can thus include the whole continuum, from low levels of HA to the DSM and ICD diagnoses (Figure 1, inspired by the figure from Lebel et al. (31)).

Today, there is little consensus on what HA includes, including whether HA should be assessed as a taxonomic (categorical) construct, indicating that people with HA have distinct qualities different to those without HA, or as a dimensional (continuous) construct, where people have different levels of HA that are determined based on quantitative rather than qualitative characteristics (32). In this discussion, I consider the work of Ferguson (33) to be important. This taxonomy analysis, examining the latent structure of the construct of HA, supported the notion of HA as a continuous construct, where severe HA and hypochondriasis are included at the very end of the scale and there are quantitative differences between different scores along the whole continuum (33). This changes HA from a categorical condition to something that all people have, just to a greater or lesser extent. This notion was supported by Longley et al. (32), who replicated the analyses in a larger sample of young adults using several measurement tools to capture different indicators of HA. Both Ferguson (33) and Longley et al. (32) underlined the fact that most research had been conducted with extreme-group comparisons, thus losing the continuity of the HA construct. When capturing HA as a continuous construct, Ferguson (33) highlights the importance of examining its distribution in a large, unselected sample.

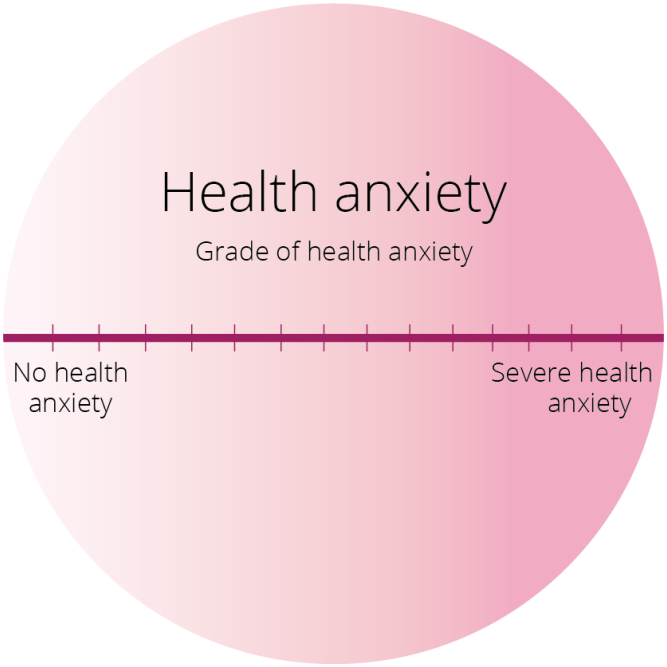


***Figure 1**: Illustration of health anxiety as a continuous construct.*

In line with Ferguson (33) and Longley et al. (32), I believe that HA can, and should, be assessed as a continuous construct in the general population. Moreover, use of cut-off to define severe HA or hypochondriasis can lead to an underestimation of associations related to people who do not meet these cut-offs, and the use of such strict categorisation to define severe HA might also be unnecessary if the goal is not to identify patients with hypochondriasis as defined in today's diagnostic systems. In this thesis, I will use the term continuous to describe the dimensional construct of HA, as described by Ferguson (33) and Longley et al. (32).

When assessing HA as a continuous construct, the prevalence becomes less important, but the distribution of HA as well as associated aspects along the whole continuum becomes of interest.

1.2 Manifestation and similarities with other anxiety disorders

HA is shortly described as worry of and preoccupation about having a disease (1), and the continuity of the construct indicate that also the symptoms of HA can range from mild and fluctuating to severe and persistent. Symptoms of severe HA/hypochondriasis includes dysfunctional assumptions about illness, including overestimation of disease (34, 35), and an increased sensitivity to physical symptoms (34, 36). Illness rumination is also believed to be a core characteristic (35, 37), which is also common in other mental disorders (35).

Indeed, severe HA/hypochondriasis share similarities with other anxiety disorders and can appear in combination with other disorders such as anxiety and depression (35, 38). The lack of agreement in diagnostic manuals as to whether severe HA itself is a somatoform disorder (ICD-10 and DSM-V) or an obsessive-compulsive disorder (ICD-11) illustrates the lack of consensus among both researchers and clinicians.

People with generalised anxiety disorder often also have HA (39). However, whereas persons with generalised anxiety disorder often have worries in several domains, people with severe HA are specifically worried about health, and often specific diseases (13). In addition, people with generalised anxiety disorder have a lower tendency to exhibit the reassurance seeking behaviour of contacting healthcare services (40). Also similar to people with severe HA, those with panic anxiety often misinterpret bodily signals as potentially harmful (40). However, whereas people with panic anxiety focus on the acute consequences of symptoms, people with severe HA are mostly concerned about diseases that can be prevented or cured if diagnosed early (34). Obsessive-compulsive disorders and severe HA share safety-seeking behaviours and body checking as a way to reduce anxiety, but with the important difference that people with HA experience more anxiety related to bodily signals (40).

Treatment for severe HA and hypochondriasis includes pharmacological and psychological interventions (2). Pharmacological treatment most commonly includes antidepressants (2), but patients with severe HA/hypochondriasis tend to prefer psychological treatment over pharmaceutical interventions (41). The recommended psychological treatment for severe HA is cognitive behavioural therapy (36), and there is increasing evidence that the more severe the level of HA, the more effective the treatment (42), thus confirming that HA is a treatable condition.

1.3 No consensus on the measurement of health anxiety in research

The diverse definitions of HA employed in research makes comparison between studies difficult, and reported prevalence varies widely between different studies and different countries.

Several measurement tools have been developed to assess HA and hypochondriasis; the most common are the Whiteley Index (43), the Illness Attitude Scale (44) and the Health Anxiety Inventory (45). All of these measurement tools have shown satisfactory psychometric properties (2, 3), indicating good validity and reliability. Both the Health Anxiety Inventory and Whiteley Index have several shorter versions (45, 46). Shorter versions of the Whiteley Index have been recommended, especially for screening purposes (15), due to their simplicity, and today, these versions are the most commonly used measurement tools (36).

The original Whiteley Index, developed by Pilowsky in 1967, included 14 questions with dichotomous response options, which consisted of three factors identified in the original factor analysis: 1) bodily preoccupation, 2) disease phobia and 3) disease conviction (originally called "Conviction of the presence of disease with non-response to reassurance") (43). Since then, numerous versions of the Whiteley Index have been proposed (46). Today, this measurement tool is recommended as a single-factor structure (47), and it has several versions, some with dichotomous (3, 48, 49) and some with Likert scale response options (37, 47, 50-52). Although the original Whiteley Index (43) had dichotomised response options (yes/no), the Likert scale is believed to better differentiate the responses (46) and to better reflect the continuum of HA (47). Likert scale response options are in general preferred by respondents and also show higher reliability (53).

Some researchers have designed their own questions to capture severe HA in a general population. One large survey in Australia used the question "Have you ever worried a lot about serious illness despite reassurance from a doctor?", which was thought to capture the diagnostic construct of hypochondriasis (21). Respondents who replied "yes" to this question further reported if this worry lasted for 12 months, 6 months, at present, or during their lifetime (21). Two other studies defined HA as a positive answer to the question "In the past 12 months, have you had a period of 6 months or more when you worried about having a serious physical illness most of the time?" (54) or "In the past 12 months, have you had a period of 1 month or more when you worried about having a serious physical illness most of

the time?" (22). These surveys severe HA, likening HA to hypochondriasis but with an emphasis on the duration of worry.

1.4 Health anxiety and associated factors

As previously mentioned, due to the use of different measurement tools, cut-offs, and definitions of HA, comparisons between studies are difficult. Most studies in the general population have explored the prevalence of severe HA and hypochondriasis. Others have defined severe HA in the general population using percentile cut-offs. Knudsen et al. (55), Berge et al. (52) and Mykletun et al. (56) used the highest 5 or 10% percentile to examine the prospective consequences of severe HA in Norway. They reported that severe HA was associated with increased risk of future disability pensions (56), ischaemic heart disease (52) and cancer incidence in men (55).

Previous research has shown inconsistent associations between HA and sociodemographic factors. HA can manifest at any age, but it most commonly develops in early adulthood (36). One study found that children aged 8-15 years have a low prevalence of severe HA (6), but it defined HA as the ICD-10 diagnosis of hypochondriasis, so it is not known whether these children experienced lower levels of HA. Older age has been found to be associated with lower HA (21), higher HA (19), and some studies showed non-significant associations (17, 20). Similar inconsistencies have been shown for the association between HA and gender, with some studies reporting no significant association (17, 20, 21) and others finding a higher level of HA in women than in men (19). The same applies for education (17, 20, 21) and income (19, 20) although a newly published meta-analysis reported overall lower HA by higher socioeconomic status (57), and having a partner or spouse (17, 20, 21). All the aforementioned studies used different cut-offs and definitions of HA, which might contribute to the observed associations.

To the best of my knowledge, no one has yet examined the distribution of the wider construct of HA in in the general population, although some studies have reported a low mean HA (58-60). Studies from patient populations and primary healthcare settings have reported that HA, as a continuous construct, is skewed and has a low mean score (28, 50, 61, 62). Therefore, there is a need for studies that examine HA as a continuous construct, and that explore its distribution in the general population.

1.4.1 Health anxiety and healthcare use

Severe HA is associated with higher sick-leave (5) and increased risk of disability pension (56). Both outcomes suggest frequent contact with healthcare services. In addition, several studies have reported that people with frequent healthcare use, especially primary healthcare use, have increased HA (63, 64), and one study report HA to be a predictor of future primary healthcare use (50).

A much-sited article from Barsky et al. (65) found that patients with severe HA had significantly higher healthcare use compared to patients below the uppermost 14% percentile cut-off, both the year before and after baseline measurement of HA. Similarly, Fink et al. (4) prospectively examined healthcare use among patients with hypochondriasis, severe HA and mild HA, all categorised by their own suggested diagnostic criteria (16), compared with patients with a well-defined medical condition. They reported that patients attending primary healthcare with severe HA had significantly higher healthcare use and lower self-rated physical health up to 2 years after baseline measurement, compared with the other groups. Interestingly, patients with mild HA did not have worse self-reported health nor increased healthcare use during the follow-up time. In contrast, Hansen et al. (61) found a dose-response association between the continuous measure of HA and hospital admissions. Conroy et al. (62) also measured HA continuously and reported a significant association between lower HA and primary healthcare use. The authors state: “In general, studies of HA have been concentrated on the pathological end of the spectrum” (62, p. 49). Over 20 years later, this is still the case.

Too little is known about how HA as a continuous construct relates to healthcare use. Few studies have examined the association between HA and healthcare use beyond primary healthcare, and especially whether any association is apparent below the defined cut-off levels of severe HA or diagnosis of hypochondriasis. As many people with HA perceive their symptoms as a somatic condition rather than psychological (66), this may hinder appropriate treatment. As Taylor and Brooks (67) point out: “Convincing a patient with HA to see a psychotherapist is difficult, as patients will view their referral as dismissing their “real” medical concerns” (67, p. 62) . In Norway, 14% of primary healthcare consultations lead to referrals to specialist healthcare (68), and physicians report that patient pressure is an important factor when deciding to refer a patient (69). It is therefore important to investigate

whether HA at any level of the continuum may be an important factor in referrals to specialist healthcare.

A recent review (70) of healthcare use in different anxiety disorders expressed the need for epidemiological studies on HA and healthcare use in the general population, as healthcare avoidance cannot be assessed in studies conducted in healthcare settings.

1.4.2 Health anxiety, physical disease and cardiovascular risk factors

Horenstein and Heimberg (70) speculated that the relationship between HA and healthcare use can, at least in part, be explained by physical disease. HA is characterised by increased anxiety or fear of illness, independent of whether the feared condition is present or not. There is growing evidence that HA is prevalent in people with physical diseases (31), indeed, several recent studies in medical settings have shown that HA is not uncommon alongside physical diseases (24, 25, 27, 28), thus the association between HA and physical disease merits closer attention.

Different disease-specific anxiety measures have been examined in different patient groups and the most common are fear of cancer recurrence (71) and cardiac anxiety (72). Also more general measures such as fear of progression have also been speculated to include the same illness-related fears (73). It has been suggested that the wider construct of HA includes these more disease-specific measures of worry and anxiety (31).

HA in the presence of disease is perhaps more understandable than in a healthy population, and indeed, one population survey showed that many people with severe HA had a physical disease (17). However, people with physical disease and severe HA report reduced quality of life (29, 74), reduced daily function (31) and show unfortunate coping strategies (72). It is therefore important to assess whether HA is particularly relevant in specific diseases, or if having any physical disease is associated with HA. Furthermore, it is now known whether having experienced previous disease, as well as risk factors for disease, are important for HA score on a population level.

Most recent research has examined the topic of HA and physical disease in specific patient populations (29, 75-77) and within the healthcare system (25-27). The relationship between HA, physical disease and risk factors for disease becomes more and more relevant as

populations age and the prevalence of chronic non-communicable diseases increases, and these associations are well-suited to examine in a large general population.

2 Rationale and aims of the thesis

Research on HA has mostly focused on patient populations and those with severe HA. There is a lack of knowledge on the distribution and associations of the HA continuum from a population perspective. The seventh survey of the Tromsø study (Tromsø7), offers a unique opportunity to fill these knowledge gaps, and to examine HA as a continuous construct with a validated measurement tool in a general population. Using data from the Tromsø7, the main aim of this thesis was to study the distribution of HA as a continuous construct in a general population, and to examine different aspects associated with HA. This was separated into three specific aims:

1. To explore the distribution of HA as a continuous construct and investigate its associated factors
2. To examine associations between HA and primary, somatic specialist and mental specialist healthcare use
3. To examine associations between HA and physical disease and cardiovascular risk factors

3 Material and methods

This thesis has a cross-sectional design, and the study sample consisted of the 21 083 Tromsø7 participants aged 40 years or older who answered two different questionnaires in the Tromsø7 survey.

3.1 The Tromsø study

The Tromsø study is a large, population-based health survey that has been conducted intermittently since 1974 (78). It was initially conducted to explore the high prevalence of cardiovascular diseases in Northern Norway, but has since expanded into a large, multipurpose health survey that includes both questionnaire data and a wide range of clinical examinations (78). Tromsø7 was conducted in 2015-2016; all adults aged 40 years or older living in Tromsø (n=32 591) received a 4-page questionnaire (Q1) along with an invitation to participate (79). Two reminders were sent if necessary. Those who accepted to participate were also invited to a clinical examination (covering height and weight, blood samples, blood pressure, etc.) and asked to complete a second, 47-page questionnaire (Q2), which covered a wide range of health-related topics and included a food frequency questionnaire (79). A selected sample were invited to a second clinical examination, which will not be addressed in this thesis. Tromsø7 was conducted before this PhD project; therefore I was not involved in data collection. Of the 32 591 invited, 21 083 (63%) answered Q1 (Appendix C) and Q2 (Appendix E) and attended the clinical examination.

Participation in Tromsø7 was highest among those born in Norway, those who had attended previous surveys and those aged 50-79 years old (79). For non-participants, only information regarding age and gender is publicly available. An overview of the Tromsø7 study participation showed that non-participation was not random. Participation was higher in younger age groups; among invitees aged 80 years and older, fewer women than men participated. (Table 1, retrieved from Hopstock et al. (79)).

Table 1. *Participation in Tromsø7 by age and gender.*

Age, years	Women			Men			Total		
	Invited	Participated	%	Invited	Participated	%	Invited	Participated	%
40-49	5 195	3 378	65.0	5 562	3 054	54.9	10 757	6 432	59.8
50-59	4 534	3 245	71.6	4 327	2 790	64.5	8 861	6 035	68.1
60-69	3 586	2 677	74.7	3 543	2 502	70.6	7 129	5 179	72.6
70-79	2 001	1 361	68.0	1 897	1 315	69.3	3 898	2 676	68.7
80-89	981	389	39.7	639	325	50.9	1 620	714	44.1
90-104	242	24	9.9	84	23	27.4	326	47	14.4
Total	16 539	11 073	67.0	16 052	10 009	62.4	32 591	21 083	64.7

3.2 Measurement of health anxiety

HA was measured in Tromsø7 using the Whiteley Index, which was included in Q1 and consisted of seven questions (Table 2). Responses were given on a 5-point Likert scale (from "not at all" to "a great deal").

***Table 2**. Questions included in Tromsø7 with questions included in the WI-6 and the WI-6-R.*

Item	Text	Questions included in WI-6	Questions included in WI-6-R
1	Do you think there is something seriously wrong with your body?	x	x
2	Do you worry a lot about your health?	x	x
3	Is it hard for you to believe the doctor when he/she tells you there is nothing to worry about?	x	x
4	Do you often worry about the possibility that you have a serious illness?	x	x
5	If a disease is brought to your attention (e.g., via TV, radio, internet, newspapers or by someone you know), do you worry about getting it yourself?	x	x
6	Do you find that you are bothered by many different symptoms?	x	
7	Do you have recurrent thoughts about being ill that are difficult to get off your mind?		x

WI-6: Whiteley Index-6, WI-6-R: Whiteley Index-6 including illness rumination

During the planning of Tromsø7, a research team located at the Research Clinic for Functional Disorders and Psychosomatics at Aarhus University Hospital in Denmark proposed a revised Whiteley Index, which substituted the question "Are you bothered by different pains and aches" from the original Whiteley Index (43), with a new question on illness rumination: "Do you have recurrent thoughts about being ill that are difficult to get off your mind?" (question 7, Table 2). This new question was believed to capture the "core" feature of rumination in severe HA and hypochondriasis, whereas the previous question on

symptoms had too much overlap with chronic pain conditions. The revised questionnaire was sent to the project group for inclusion in Tromsø7 (personal communication) (80).

However, when starting this PhD project, question 7 had not yet been published or validated. There are numerous versions of the Whiteley Index, and it has been used with different factor structures, identified through confirmatory factor analytic results (3). However, one paper examined the psychometric properties of 11 different versions and recommended the Whiteley Index-6 (WI-6) as a single-factor model (47). Therefore, for Papers 1 and 2, we used the first six questions for the WI-6 (Table 2); question 7 was not considered. Prior to analysing Paper 3, however, a validation study was published which recommended substituting question 7 in place of question 6 (Table 2) (37). This revised WI-6 (WI-6-R) (37) was a good fit for Paper 3, which covered chronic disease, as question 6 could capture physical symptoms of disease rather than worries about disease. In this thesis, I will use the full term "Whiteley Index" when discussing this measurement tool in general, and WI-6 and WI-6-R, respectively, when talking about the two different versions used in Papers 1-3.

3.2.1 Analyses of the Whiteley Index

The original Whiteley Index has shown high internal consistency, stability, and convergent validity in both patients in contact with healthcare services and the general population (81). We chose to use the WI-6 as a single-factor model with 5-point Likert scale response options, as recommended in Veddegjærde et al. (47). Later, the study by Carstensen et al. (37), confirmed the good model fit of WI-6, but recommended the WI-6-R.

We conducted a confirmatory factor analysis for the WI-6 prior to Paper 1, and for the WI-6-R prior to Paper 3. The rationale was to confirm that these measurement tools had structural validity and internal consistency in our Tromsø7 study sample.

Confirmatory factor analysis is a common way to assess construct validity (82), and to confirm the structural model of a measurement tool (83). The goodness of fit, correlation and variable contribution confirmed that both the WI-6 and the WI-6-R had a common explained variance. We also tested internal consistency by Cronbach's alpha using these two sets of 6 questions (Table 2) graded on a Likert scale (0-4); a single-factor solution showed a score of 0.83 for the WI-6 and 0.84 for the WI-6-R, which is considered a very good measure of

internal consistency (83). We therefore chose to use the one-dimensional Whiteley Index to measure HA.

We also chose to sum the individual scores for each of the six questions into a total score, with equal weighting for each question (0-4). Thus total HA scores ranged from 0-24, in order to capture the continuity of the score, in line with several other studies (49-52, 84, 85). To my knowledge, no studies using the one-dimensional Whiteley Index have chosen to give different weights to the different questions included in the measurement tool.

3.3 Measurement of healthcare use

Healthcare use set as the outcome variable in Paper 2, and was measured in Q1 using the following question; “Have you, due to your own health, consulted the following healthcare services: general practitioner (GP), emergency room, psychologist or psychiatrist, another medical specialist other than a GP or a psychologist or psychiatrist (not at hospital) during the last 12 months?” Participants responded “yes” or “no”, and those who responded yes also gave the number of consultations. They also reported whether they had been admitted to a hospital, a psychiatric out-patient hospital service, or a somatic out-patient hospital service in the last 12 months, and if so, how many times. We categorised these consultations by type of healthcare service: Primary healthcare (consultations with GP and emergency room visits), somatic specialist healthcare (hospital admissions, consultations with a somatic out-patient hospital service and medical specialists in private practice) and mental specialist healthcare (consultations with a psychiatric out-patient hospital service and psychologist/psychiatrist in private practice).

These responses were then categorized into three types of healthcare services (Table 3).

Table 3. *Overview of the three different healthcare services and included healthcare providers, and frequency distribution of the different levels of use for each healthcare service (primary, somatic specialist and mental specialist healthcare).*

Healthcare services	Included consultations with:	Categories	Levels of use (consultations)	Percent
Primary healthcare	GP	Non-use		20%
	Emergency room	Quartiles of use	1st level (1)	21%
			2nd level (2)	19%
			3rd level (3-4)	20%
			4th level (5-89)	20%
Somatic specialist healthcare	Admissions to hospital	Non-use		60%
	Somatic out-patient hospital service	Quartiles of use	1st level (1)	16%
			2nd level (2)	10%
			3rd level (3)	5%
	Medical specialists in private practice		4th level (4-170)	9%
Mental specialist healthcare	Psychiatric out-patient hospital service	Non-use		96%
	Psychologist/psychiatrist in private practice	Quartiles of use	1st level (1-3)	1%
			2nd level (4-6)	1%
			3rd level (7-12)	1%
			4th level (13-130)	1%

The range in number of consultations by type of healthcare services was large, with the largest range in somatic specialist healthcare (Table 3). As the ends of this range included plausible responses (mean of 3 consultations/week over a period of 12 months), we did not exclude such extreme variables. However, to minimise the adjustment of the mean if measuring healthcare use as a continuous variable, we chose to divide healthcare use into levels for each healthcare service; non-use and quartiles of use (number of consultations in quartiles) 5 categories in total.

Non-use was registered as the reference category and coded if participants answered "no" to all questions regarding healthcare use within each healthcare service. The highest range in the number of consultations was observed in the highest quartile of use. Most participants reported 1 or 2 consultations in the lower quartiles of use, whereas the highest quartiles of use may be considered frequent users (including a range of 4-170 consultations). The exception here was mental healthcare, which had more consultations in the lower quartiles (Table 3).

The questions regarding healthcare use in general and specific number of consultations were independent in the Tromsø7 dataset, which led to some inconsistencies. Many people who

answered “no” to healthcare use for a specific healthcare provider were coded as having missing information on the number of consultations. I dealt with this problem by recoding responses prior to analyses, as follows (by the example of GP):

- For participants who reported no consultations with a GP and had missing information on number of consultations, the number of consultations was recoded as 0.
- For participants with missing information on consultations with a GP but a response of 0 for number of consultations, healthcare use was recoded as “no”.

In addition, some participants had implausible responses to the questions on healthcare use and number of consultations. Exemplified by GP, participants were excluded if they:

- Had missing information on consultations with a GP and the number of consultations
- Answered “no” to consultations with a GP but answered more than 0 for number of consultations with a GP
- Answered “yes” to consultations with a GP but answered 0 for number of consultations.

Many people had thorough reporting for some, but not all the types of healthcare services. We therefore used three different datasets: one for each type of healthcare service. However, the re-coding and exclusion criteria remained the same. After exclusions, the final analyses included 18 499 participants in the dataset for primary healthcare use, 18 311 for somatic specialist healthcare use, and 18 158 for mental specialist healthcare use.

3.4 Measurement of physical disease and cardiovascular risk factors

For Paper 3, physical diseases were included as exposure variables and HA was set as the outcome variable in the analyses. In Q1, participants were asked to report whether they had the following chronic conditions: high blood pressure, previous myocardial infarction, heart failure, atrial fibrillation, angina pectoris, previous cerebral stroke, diabetes, chronic renal disease, chronic bronchitis/emphysema/chronic obstructive pulmonary disease, asthma, cancer, rheumatoid arthritis, osteoarthritis and/or migraine. Participants also reported whether they used blood pressure or cholesterol lowering medication. Response options were “no”, “yes, now” or “yes, previously”.

The included chronic conditions represent some of the most common non-communicable diseases (86), and we used these variables in two ways. First, we created a variable called "number of physical diseases" (0, 1, 2, 3 or 4 or more). This number included all conditions except high blood pressure, which was classified as a risk factor, not a disease. "Number of physical diseases" for each participant was counted as the total number of chronic conditions for which they replied either "yes now" or "yes, previously". The number of self-reported diseases ranged from 0-13.

We also wanted to look at the association between HA and specific disease categories, while removing the influence of other diseases. To this end, we created several disease categories (cardiovascular diseases, diabetes or kidney disease, cancer, respiratory disease, rheumatic diseases and migraine) (Table 4). To be included in one category, e.g., cancer, participants had to have answered "no" to all diseases in the other diseases categories. Participants with diseases in more than one disease category were excluded. Participants who answered "yes, previously" for one disease and "yes, now" for another within the same disease category, were categorised as "yes, now".

Table 4. *List of diseases included in the different disease categories*

Disease category	Included diseases
No disease	None of the below mentioned
Cancer	Cancer
Cardiovascular disease	Heart failure, atrial fibrillation, angina pectoris, myocardial infarction, cerebral stroke
Diabetes or kidney disease	Diabetes, kidney disease
Respiratory disease	Asthma, chronic bronchitis/emphysema/chronic obstructive pulmonary disease
Rheumatism	Rheumatoid arthritis, osteoarthritis
Migraine	Migraine
Cardiovascular risk factors	High blood pressure, use of blood pressure or cholesterol lowering medication

Finally, we created one category called “cardiovascular risk factors”, which included those who reported having high blood pressure and/or the use of blood pressure or cholesterol lowering medication (Table 4). This category was dichotomous, with the response options; “yes” or “no”.

The reference group for all analyses were participants who reported no current physical disease, no previous physical disease and no cardiovascular risk factors (healthy reference group).

3.5 Confounders

3.5.1 Papers 1-3

Suspected confounders included demographic variables (age and gender), indicators of socioeconomic position (education and household income), and social network variables.

Age on 31.12.2015 was recorded as a continuous variable and gender was registered as male or female. There are conflicting results regarding the association between HA and age (17, 19, 21) and gender (19, 21), so we believed that these were important factors to explore.

Socioeconomic variables have been found to be associated with HA (57) and are known to be associated both with healthcare use (87) and physical disease (88). Education was determined by the question “What is the highest level of education you have completed?”, with the response options: primary education up to 10 years of schooling, vocational/upper secondary education (minimum 3 years), college/university fewer than 4 years or college/university minimum of 4 years. Household income was registered as “the household’s total taxable income last year” with eight response options: <150 000 NOK, 150 000-250 000 NOK, 251 000-350 000 NOK, 351 000-450 000 NOK, 451 000-550 000 NOK, 551 000-750 000 NOK, 751 000-1 000 000 NOK and more than 1 000 000 NOK. These categories were merged into: low (<451 000), lower middle (451 000-750 000), upper middle (751 000- 1 000 000) or high (>1 000 000 NOK) in all three papers, in order to get equal sized groups.

There is some evidence that social variables are associated with other anxiety disorders (89, 90), as well as physical disease (91) and healthcare use (92), although the association between social network characteristics and primary healthcare use seems more conflicting.

Originally, we included five questions on social network characteristics:

- "Do you live with a spouse/partner?" (yes/no)
- "How many children do you have?" (including biological children, adopted children, stepchildren and foster children)
- Two questions regarding friendship: "Do you have enough friends you can talk confidentially with?" (yes/no) and "Do you have enough friends who can give you help and support when you need it?" (yes/no)
- Participation in organised activities was exemplified as sports, leisure activities, voluntary work and the like, and we used the original response options "never, or just a few times a year", "1-2 times a month", "approximately once a week" or "more than once a week".

When conducting the analyses in Paper 1, number of children was not associated with HA when used as a dichotomous or continuous variable, nor when differentiating by the different original variables. Living with a spouse/partner was significant in the univariate analyses in Paper 1, and was therefore included in the analyses of Papers 1 and 2.

Questions about friendship were included as confounders in all three papers. We merged the questions on friendship as they were highly correlated, into one variable called "close friends". Participants were categorised as "no" if they answered no to both questions, "to some extent" if they answered "no" to one of the questions and "yes" if they answered yes to both original questions. In Papers 2 and 3, this variable was called "quality of friendship and "friendship", respectively. The naming of this variable was somewhat inconsistent, as we gradually realised that we did not want to infer closeness or quality of friendship from the participants' original responses.

3.5.2 Paper 2

In Paper 2, we included physical and mental illness in addition to the confounders above when adjusting for the association between HA and healthcare use, as both were hypothesised to increase HA and are known to adjust the association between severe HA and healthcare use (21, 23, 50). The self-reported diseases reported in Q1 (table 4), including high blood pressure, were merged into one variable called "physical illness" if registered as "yes, now", for these analyses. This variable was categorized as none, one, or two or more.

We used two questions to measure mental illness. When analysing the association between HA and primary- and somatic specialist healthcare use, we used the question from Q1: "Have you ever had, or do you currently have, psychological problems for which you have sought help?" The response options included "no", "yes, now" and "yes, previously". However, there was a multicollinearity when examining mental specialist healthcare use, where we asked participants if they had attended a psychiatric out-patient hospital service or had consultations with a psychologist or psychiatrist in private practice the past 12 months. Therefore, for this analysis, we used the Hospital Anxiety and Depression Scale (HADS) (93), a well-used and validated measurement tool that renders a total score (HADS-T) ranging from 0-42 (94) (Appendix D). We chose to use the HADS total score (HADS-T) to indicate mental illness and to use it as a confounder to distinguish between HA and other mental health issues in the association between HA and mental healthcare use. Although it is most commonly used to measure anxiety and depression separately (95), the HADS-T has shown satisfying internal consistency (94). However, there is less consensus on the appropriate cut-off to apply for mental illness when using the HADS-T, with suggested cut-offs ranging between 8 and 15 (94). I chose to use the cut-off score of 15, the same cut-off score as a Norwegian study (96) who stated this as recommended by the authors designing the HADS (93).

3.5.3 Paper 3

In Paper 3 I chose to use the HADS-T as a continuous measure when including it as a confounder, due to the lack of consensus regarding cut-offs (94, 95), except for descriptive purposes.

In Paper 3, we also included the confounder "disease in first-degree relatives" when examining the association between HA and physical disease, as many of the diseases can be hereditary, and we speculated that it could adjust the association. The participants were asked whether their first-degree relatives (mother, father, children, siblings) had any of the following: myocardial infarction before the age of 60, angina pectoris, cerebral stroke, asthma, diabetes, breast cancer, prostate cancer or colon cancer. Participants were categorised as "yes" if they reported that their first-degree relatives had one or more of these diseases, and "no" if they had none of them. We analysed these diseases both as one group and as separate variables to comply with the different disease categories, but as these analyses yielded the same results, we chose to include disease in first-degree relatives as one collective variable.

3.6 Statistical analyses

Whereas Paper 1 was more descriptive in character, Papers 2 and 3 were based on prior hypotheses. In the chapters below, the focuses of Papers 1 (HA distribution), 2 (healthcare use) and 3 (physical disease) will be described separately.

All main analyses were performed with STATA (STATA Corp LP, College Station, Texas, USA), version 15.1 and 16.1. The confirmatory factor analyses used prior to Paper 1 and 3, as well as the simple univariate figure using summary plot for Paper 2, were conducted using IBM SPSS Statistics for Windows (IBM Corp. in Armonk, NY), version 26.0 and 27.0. The summary plot presents mean healthcare use by HA score, with 95% confidence intervals. The level of statistical significance (p-level) for all analyses was set at 0.05.

Descriptive analyses included calculation of central tendencies (mean, median) and measures of variance (range, quartiles, percentiles, standard deviation) for continuous variables, and frequency distribution for categorical variables.

In the exploratory and descriptive Paper 1, we tested several hypothesised associated variables, but only the statistically significant variables were included in the final regression analysis. For Papers 2 and 3, we did not carry out a hierarchical stepwise model, but all variables theoretically hypothesised to influence the associations were included. In Papers 2 and 3, the regression analysis presented includes both the unadjusted associations and the associations after adjusting for confounders. In Paper 2, the HADS-T was included as a dichotomous variable. In Paper 3, the HADS-T was included both with and without a quadratic term, which yielded very similar results, so we used the HADS-T without a quadratic term in the regression analysis.

3.6.1 The exponential regression model

As has been reported in other populations (47, 49), we observed a highly skewed distribution of Whiteley Index in our study sample. Indeed, we saw scores that spanned the whole scale of 0-24, but 75% of the participants had a score of 5 points or less on the WI-6, which presents certain analytical challenges. Most researchers have chosen to analyse the Whiteley Index using either a chosen cut-off (17, 19, 20), quartiles (49, 52) or percentiles (52, 55, 56, 65). However, we wanted to keep the continuity of the measurement and avoid categorising the scale. The most common way to analyse a continuous scale is by using linear regression.

However, in this case the assumption of a normal distribution was not met. We initially tried to log transform the data, but as so many participants had a WI-6 score of 0, this did not result in a normal distribution of the residuals.

We looked to generalised linear models as a solution, as they extend the ordinary least-squares regression to a model that is appropriate for a variety of response distributions (97). By log transforming the model itself, rather than the original variables, we reached a normal distribution of residuals. When modelling a generalised linear model regression analysis, one specifies the family, link, and scale function.

First, we decided to use the gamma family. It is most commonly used for modelling continuous outcome, but it can also be used with count data where the response can only be greater than or equal to zero, and where the results relate to a gamma distribution (97).

Secondly, we had to specify the link function. The log-linked gamma represents the log-rate of the response. This model specification is identical to the exponential regression analysis commonly used in survival analyses, and is recommended for data with an exponential decline (97). Finally, the set scale mimics the distribution of the model, and we found that for our data, the distribution fitted best a scale of 1 (figure 2). As modelled in Papers 1 and 3, the coefficients were presented with the exponentiated beta (exp(b)), which describes the percentage difference in the Whiteley Index score (e.g., an exp(b) of 1.42 indicated a 42 % increase in HA score).

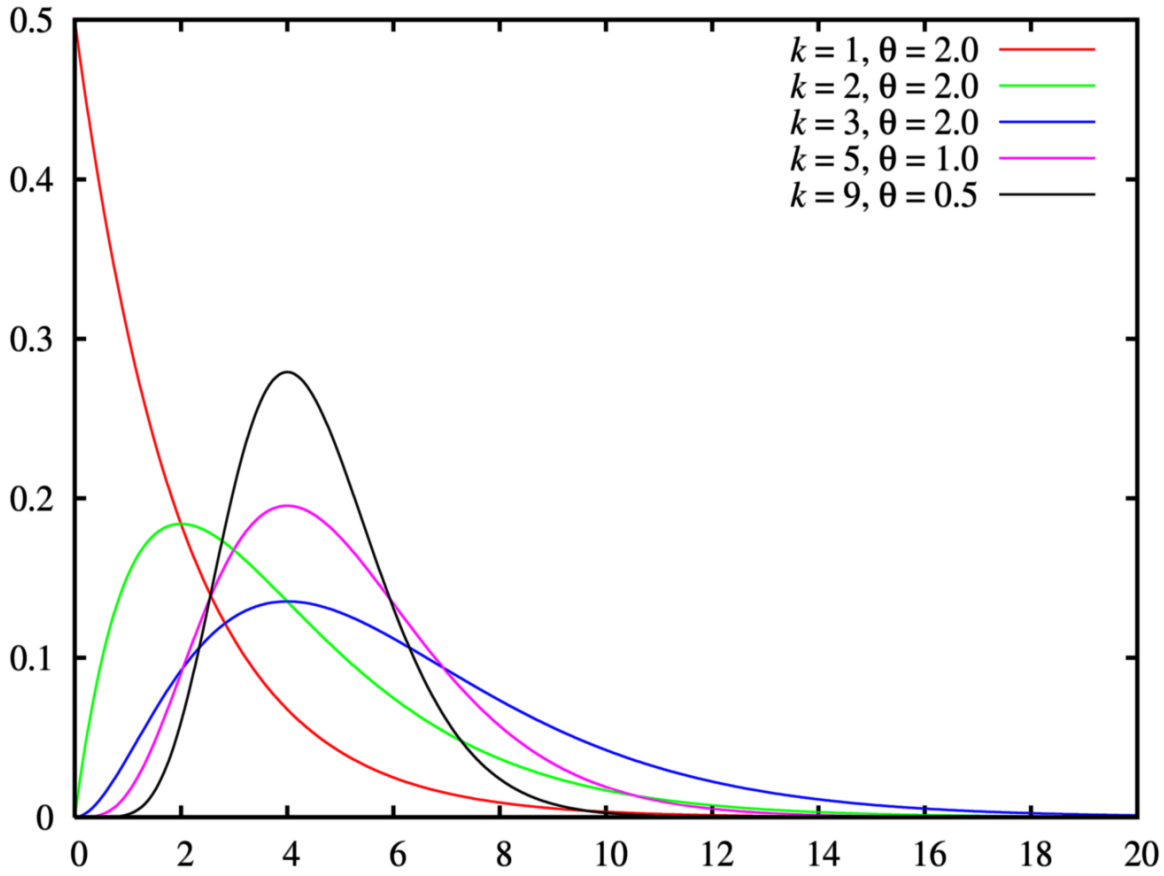


Figure 2. *Different gamma distributions. Cburnett, CC BY-SA 3.0, via Wikimedia Commons*

Another possible generalised linear model was the negative binomial regression analysis, which is recommended for count data (97). However, exponential regression analysis gave the best fit when testing posthoc analyses using the Akaike information criterion and the Bayesian information criterion (97, p. 56-58), and we therefore chose to use exponential regression for our analyses where HA was the outcome variable, namely in Papers 1 and 3.

3.6.2 The unconstrained continuation-ratio regression model

As described in chapter 3.3, participants reported their use of different types of healthcare services, and the number of consultations for each service. We chose to categorise the number of consultations instead of treating it as a continuous measure, due to the concentration to low numbers of consultations combined with a large range in number of consultations (Table 3).

Secondly, we chose to categorise the number of consultations into ordered categories rather than dichotomised categories, as we wanted to examine whether HA was associated with

increasing levels of use. Category 0 represented non-use, and quartiles of use as level of use 1-4. Thus, for Paper 2, we used a regression analysis for ordinal responses.

The most common ordinal regression analysis is the proportional odds model, in which the association between HA and level of healthcare use is independent of the different categories (98). In other words, the odds ratio (OR) of the association between HA and different levels of healthcare use will be similar, independent of which categories are compared. However, the proportional odds assumption was not met, indicating that the association between HA and healthcare use differed across levels of use.

We therefore had to consider other ordinal regression models that did not require proportional odds. When the probability of being in one category is conditional on the probability of being in another category (98), which we suspected in Paper 2, a continuation-ratio model can be appropriate (98). The constrained continuation-ratio logistic regression model compares each response category with all lower categories, and assumes that the effect of the exposure variable is similar across categories (99). However, we did not assume that the HA score would have the same association across the different levels of healthcare use. Therefore, we chose to use the unconstrained continuation-ratio regression model to analyse the association. The unconstrained continuation-ratio regression model is similar to the constrained model, where each level of use is compared with all lower levels (99), but in contrast to the constrained continuation-ratio regression model, the OR is specific for each comparison. The ORs can therefore be interpreted as threshold-specific exposure effects (100).

When conducting posthoc analyses using the Akaike information criterion and the Bayesian information criterion (97), the values were similar between the constrained- and unconstrained continuation-ratio regression analyses. However, the confidence intervals in the chosen unconstrained regression analyses did not overlap to any large degree, indicating that the association between HA and level of healthcare use was not similar across categories, and justified the choice of the unconstrained continuation-ratio regression model as suitable for our analyses.

3.6.3 Interaction analyses

For all three papers, we checked for possible interactions based on a theoretical approach, and we chose to present significant interactions by stratified analyses. The theoretical assumptions are presented for each paper below:

Paper 1: In the main analyses, we found that HA decreased with increasing age, but at the same time, higher household income was associated with lower HA. As our study sample included participants aged 40 years or older, we suspected that the association between HA and household income could depend on age. In Norway, transition to retirement provokes a percentage-reduction in income. We did not have information on work status, but as most people retire at age 67, we considered people aged 67 years or older to be retired. We found a significant interaction between age and household income and therefore chose to repeat stratified analyses using two categories: working-age participants (aged <67 years) and retirement-age participants (aged ≥ 67 years).

Paper 2: When analysing healthcare use, we suspected that the association between HA and primary and somatic specialist healthcare use would depend on the presence of physical disease. Indeed, regular check-ups with a GP are recommended for many diseases, and are not necessarily an indication of HA. Although we adjusted for physical disease, we also wanted to examine whether the association between HA and primary and somatic specialist healthcare use would be different in the subpopulations with and without physical disease. Likewise, we hypothesised that the association between HA and mental specialist healthcare use could differ based on the HADS-T. Therefore, we explored interactions between healthcare use and morbidity (physical disease in primary and somatic specialist healthcare and mental illness symptom load for mental specialist healthcare). We found significant interactions both for physical disease in primary healthcare and HADS-T in mental specialist healthcare and did stratified analyses to show the different associations. No significant interactions were evident for HA and physical diseases in somatic specialist healthcare.

Paper 3: Similarly, in Paper 3, we suspected two possible interactions in the associations between HA and physical disease. We suspected that the association between physical disease and HA would depend on education, and similarly, a possible interaction of age. However, no interactions were evident.

3.6.4 Missing data

Of the 21 083 study participants, 817 had missing information in the WI-6 used in Papers 1 and 2. In Paper 3, 811 participants had one or more missing values in the WI-6-R. In Paper 1, all 817 participants were excluded prior to the analyses. For Papers 2 and 3, we chose to exclude participants with missing to either the exposure or the outcome variables prior to analyses. We chose not to exclude participants with missing responses for confounders prior to the analyses, but participants with missing values in confounders were consecutively excluded when included in the model, ending in a complete-case analysis.

When analysing the association between HA and physical disease in Paper 3, participants with diseases in two different categories (e.g., cancer and angina pectoris) were excluded. However, participants were not excluded if they had cardiovascular risk factors in addition to a specific disease category (e.g., high blood pressure and cancer). Participants could state several diseases within each disease category (e.g., angina pectoris and heart failure).

There were some differences in missing values between questionnaires, with considerably fewer missing values observed in Q1 than Q2. Most of the questions considered in this thesis were from Q1; however, Q2 contained the HADS, which had considerably more missing responses (n=1951) compared to the item with the highest number of missing values in Q1: household income, 898 missing.

3.6.5 Weighted analyses

We chose to conduct survey weighting analyses for Paper 1 in order to adjust for non-response. Participants younger than 70 years of age were weighted lower, and men were weighted lower than women. However, as the weighted and unweighted analyses gave identical results, the results in all papers are from the unweighted analyses.

3.7 Ethics

The Tromsø study and Tromsø7 were approved by Regional Committees for Medical and Health Research Ethics (REK North, reference REK 2014/940) (Appendix A). This thesis was approved by the REK North in November 2016 (reference REK 2016/1793) (Appendix B). This study was conducted in accordance with the Helsinki declaration and all participants gave written informed consent before participation (Appendix E).

4 Results

4.1 Participant characteristics

Participant characteristics were similar for all three studies. Mean age among the 21 083 study participants from Tromsø7 was 56 years (standard deviation 11, range: 40-95 years). 52.5% were women, and the gender distribution was similar across all age groups. There were some gender differences: women were significantly more educated than men, whereas men reported significantly higher household income than women.

The WI-6 was highly skewed in an exponential distribution and the three different study samples were close to identical with regards to the distribution of Whiteley Index (Figure 3).

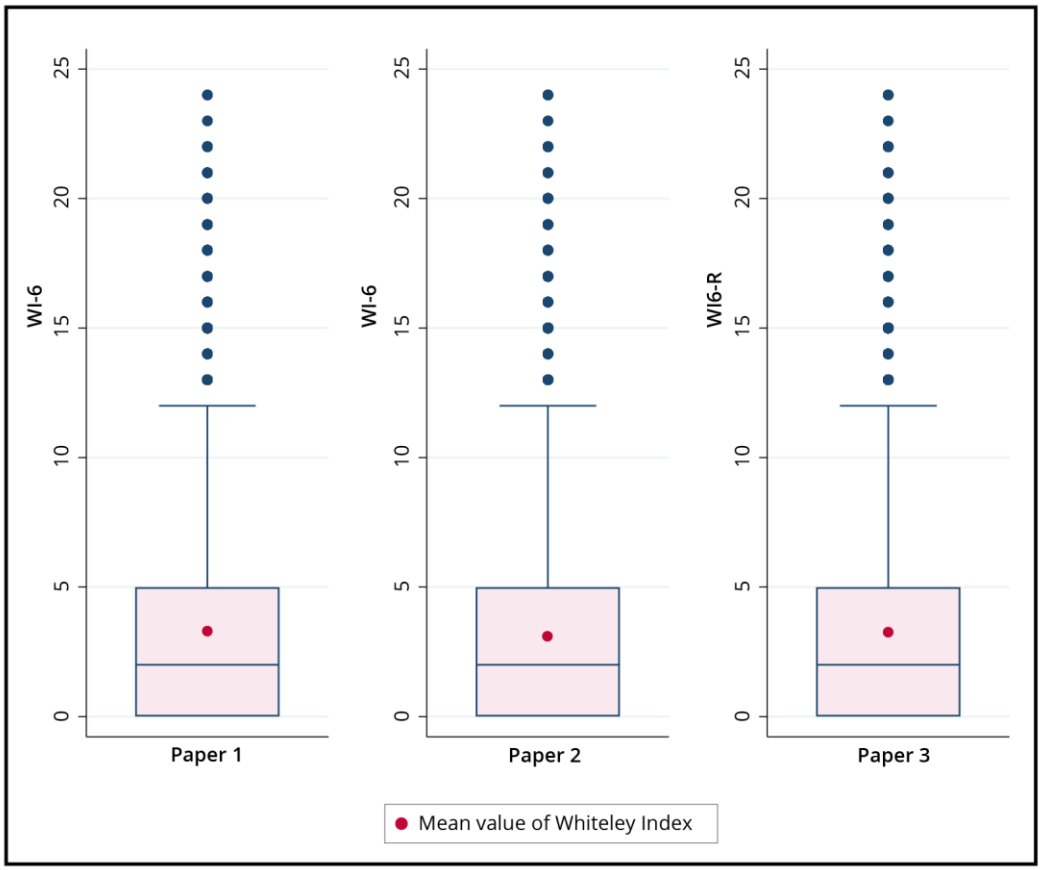


Figure 3. *Participant characteristics of Whiteley Index score by box-and-whiskers plot. Box outlined by upper and lower quartile, with median and mean values. Whiskers defined by 1.5 interquartile range and outliers indicated as blue dots.*

Approximately 4 % of the total study sample had missing values on the WI-6 and the WI-6-R. There were some differences between those with complete and missing responses to the Whiteley Index; participants with missing values were more often women and were older (mean age 64) than those with complete results. People with missing information also had lower socioeconomic status, as measured by education and household income.

4.2 Main results

4.2.1 Paper 1

The aim of Paper 1 was to study the distribution of HA in a general population and to explore the association between HA and demographic variables, socioeconomic position, and social network variables. 20 266 participants had no missing information on the WI-6 and were included in the analysis. In total, 75% of participants had a total HA score of 5 points or less, 5% had a HA score above 10 points, and 1% had a score of more than 14 points.

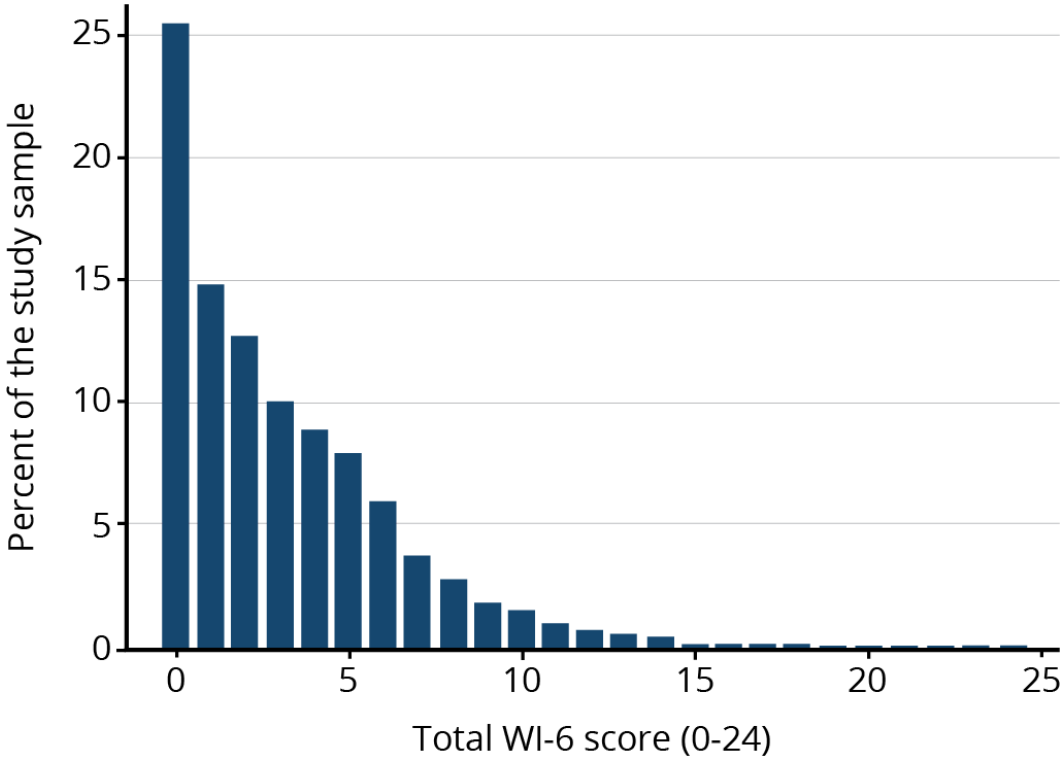


Figure 4. *Distribution of health anxiety in Tromsø7 study participants as measured by the Whiteley Index (WI-6).*

Age, education, household income, quality of friendship and participation in organized activities were significantly associated with HA, whereas gender and living with a spouse/partner were not. The variable quality of friendship demonstrated the strongest association with HA; participants who reported “no” regarding friendship had 61% higher levels of HA than those who reported “yes”. We found no clear cut-offs to describe people with higher or lower HA and no step-wise manner in which to define different levels of HA. We therefore concluded that HA is appropriately measured as a continuous construct.

4.2.2 Paper 2

The aim of Paper 2 was to determine how HA was associated with primary, somatic specialist and mental specialist healthcare use and to examine any differences in the potential association by level of healthcare use. HA was measured with the WI-6, and 18 499, 18 311 and 18 158 participants reported on primary healthcare, somatic specialist healthcare and mental specialist healthcare use, respectively, during the previous 12 months. There was large variation in use across these categories; 80% reported primary healthcare use, 40% reported somatic specialist healthcare use and 4% reported mental specialist healthcare use.

An increased WI-6 score was positively associated with significantly increased use of all three types of healthcare services (figure 5). These results remained significant after adjustment for confounders, which resulted in only marginally reduced OR. A 1-point increase in the WI-6 score was significantly associated with progressively increased OR of higher levels of use, compared to all lower levels, in primary (OR 1.06-1.15) and somatic specialist healthcare (OR 1.05-1.14). The findings from mental specialist healthcare showed that a 1-point increase of WI-6 score was significantly associated with a more gradual increase in mental specialist healthcare use, with an OR of 1.06-1.08.

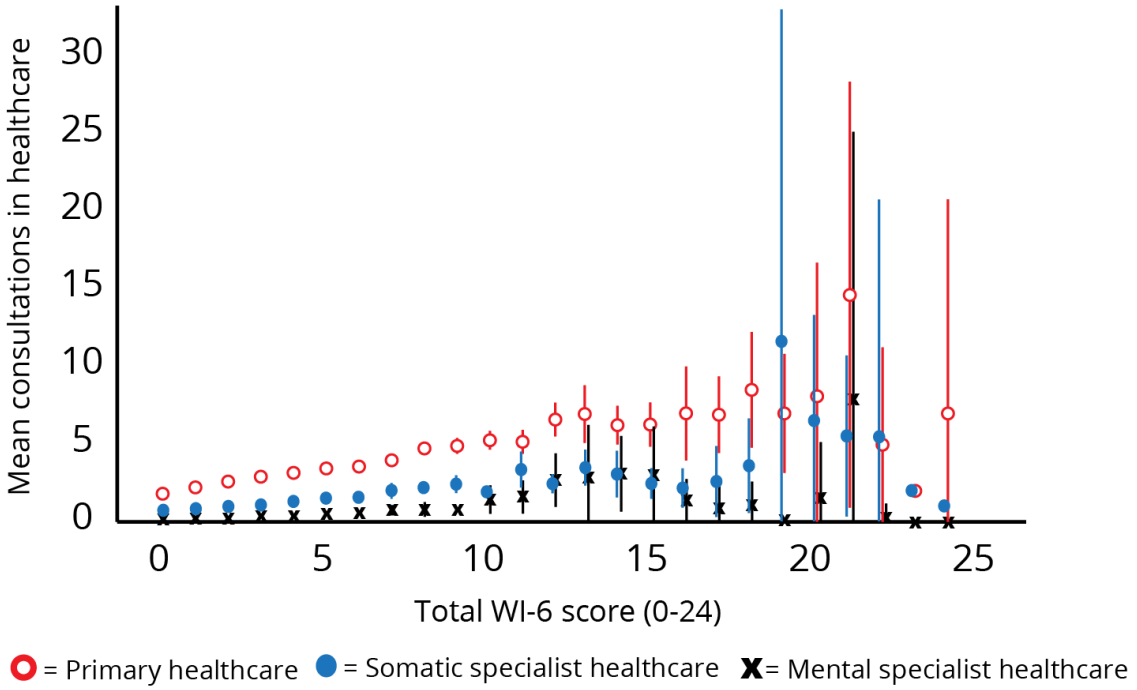


Figure 5. *Association between health anxiety and healthcare use for the outcome variables a) primary healthcare, b) somatic specialist healthcare and c) mental specialist healthcare, indicating mean healthcare use with 95% confidence intervals for each 1-point increase in the Whiteley Index 6 (WI-6) score.*

4.2.3 Paper 3

The aim of Paper 3 was to examine the association between the outcome variable HA and the exposure variables 1) number of diseases, 2) different disease categories and 3) cardiovascular risk factors. A total of 18 432 participants had complete information on the WI-6-R, a wide range of non-communicable diseases, and cardiovascular risk factors and were included in the analyses. HA was consistently and significantly associated with number of physical diseases, different disease categories and cardiovascular risk factors. Participants reporting one disease had 31% higher HA scores than the healthy reference group, whereas participants reporting four or more diseases had a more than two-fold increase in HA scores compared to the healthy reference group. Participants in most disease categories also had a significant increase in HA scores compared to the healthy reference group. People with cancer, diabetes and cardiovascular disease had the highest increase in HA scores (increase of 122%, 61% and 53%, respectively), considerably higher than participants with other diseases such as respiratory disease (30%). Most previous diseases and cardiovascular risk factors were also significantly associated with increased HA score. We concluded that HA should be assessed alongside both current and previous physical diseases, as well as cardiovascular risk factors.

5 Discussion

5.1 Main results

The aim of this thesis was to study the distribution of HA as a continuous construct, and to examine the different aspects associated with HA. We found that, while the level of HA was low in the general population, participants had scores that spanned the whole Whiteley Index scale (0-24). We also found that social network characteristics were important for the level of HA. We demonstrated that all levels of HA were significantly associated with healthcare use, both in primary and specialist healthcare. Finally, we found that HA was higher in a general population with physical disease and cardiovascular risk factors, which strengthens the argument that HA is important and can present alongside disease.

As in all research, this thesis made several methodological considerations, which will be discussed before a more general discussion of the results.

5.2 Methodological considerations

In this chapter, I will present considerations concerning the PhD project itself, and discuss different types of bias and their implications.

5.2.1 Study design

All three studies included in this thesis were based on data from Tromsø7, which was the first survey in the Tromsø study to include a measure of HA. The cross-sectional analyses from my thesis give a "snapshot" of the population at a single time point (101), and the analyses can be classified as explorative/descriptive and analytical; in this thesis, Paper 1 had an explorative and descriptive focus, while Papers 2 and 3 had a more analytical and hypothesis-driven approach.

5.2.2 Which came first; the chicken or the egg – the curse of the cross-sectional design

A cross sectional study is particularly vulnerable to temporal bias, which occurs when the assumptions about the direction of associations are incorrect (101). While cross-sectional studies can explore associations; they do not allow the researcher to assess their direction. In Paper 2, I hypothesised that HA was a driver of healthcare use and defined HA as the

exposure. Symptoms such as reassurance-seeking and safety behaviour in people with severe HA is recognized as key characteristics and associated with healthcare use (66), and HA is recognized as a predictor for future primary healthcare use (50, 84). However, it is possible that higher HA is a consequence of higher healthcare use. Similarly, in Paper 3, I chose to state physical disease as the exposure, hypothesizing that the disease predicted the HA score. A study of participants defined "at risk" for developing breast cancer, found no difference in HA levels compared to participants with average risk (102), indicating that any difference in HA did not occur prior to disease. On the other hand, a review report some evidence that fear of cancer prior to screening is associated with higher attendance (103), although the evidence is not conclusive. If HA prior to screening and examination determine the probability of attendance, this can affect who are being diagnosed. In this PhD project, however, I do not know whether physical disease increased HA, whether the presence of HA increased the probability of being diagnosed with a physical disease or whether HA is itself a risk factor for disease. Due to the study design, I cannot draw conclusions regarding the direction of the association.

5.2.3 Selection bias

Selection bias occurs when there are systematic differences between the study sample and the population it seeks to represent (104, p. 258). As participants were not purposefully selected prior to Tromsø7 (all residents aged 40 years or older were invited), possible selection bias may have occurred as a result of differences between participants and non-participants. For example, people with mental illness are less likely to participate in population surveys (105). If this is also true for Tromsø7, participants with anxiety and depression may be underrepresented in the study sample. One can hypothesise that this also applies to those with higher levels of HA. However, although it has never been examined, some have speculated that people with higher levels of HA are more likely to attend health-related surveys as these often are promoted as "health check-ups" (56). If people with higher HA are more likely to attend, this could result in higher a population mean in my sample.

Studies have also found that participation in health surveys is associated with higher healthcare use (106), which may impact the results of Paper 2. If the assumption between HA and healthcare use shows the true relationship, I do not expect any shift in the results, as people with higher HA use healthcare services more whereas non-participants with lower HA and those who use the healthcare system less, will be similar to the association found in my

study. However, if non-participants with no HA have a similar distribution of healthcare use similar to that of participants with higher HA, this may lead to an overestimation of the associations, or even a false positive association. Similarly, people with a serious disease are less likely to participate in population surveys (105). If this is also true for Tromsø7, the study sample will be somewhat healthier than the general population, which could lead to bias towards the null, and an underestimation in my results.

Although response rates in surveys are declining (106), the response rate in the Tromsø study has been quite high (78) compared to other population-based studies (105), with a participation rate in Tromsø7 of 65% (79). The gender distribution in this rate was fairly equal (62.4% of invited men and 67% of invited women participated), which reduces the risk of biased results due to differences in gender. However, there was a slightly skewed distribution of participants by age group, which might introduce selection bias, especially when looking for tendencies in the older age groups. Indeed, the participation rate was between 52.7% and 75% in the age group 40-79 years, but there was a sharp decline in response rate for participants over 80 years old, although men aged 80-85 years had a high participation rate. Among the older participants, men had a higher response rate than women, which is different from most epidemiological studies (107). One can speculate that participants those in the oldest age groups who did participate in Tromsø7 had better health and function than non-participants, as has been found in another Norwegian study (105).

Other variables related to non-participation can be controlled for by including the selection variable as a confounder. For example, lower education has been related to non-participation (105, 106, 108), meaning that participants often have higher mean education compared to the general population. The confounders responsible for the bias can be controlled for in the analyses by adjusting for education, thereby removing the impact of selection bias (109). However, if those with low education have higher HA, as found in Paper 1, this adjustment can lead to an underestimation of the strength of the association between HA and education, as presented in Paper 1.

5.2.4 Information bias and recall bias

Information- and recall bias are a form of misclassification bias, which may lead to imprecise or erroneous measurements (101). These biases must be considered when using self-reported measurements, especially when asking about past events, and is a “systematic error due to

differences in accuracy and completeness of recall to memory of past events or experiences" (104, p. 149). In Paper 2, respondents answered questions about their healthcare use in the previous past 12 months. Although Langhammer et al. (105) found that self-reported healthcare use is fairly similar to register information, the number of consultations may be vulnerable to recall bias. This especially concerns those with increased healthcare use, and older age (110).

The aim of Paper 2 was to have an "overall perspective". I wanted to examine different healthcare services rather than different healthcare providers, so I chose to merge providers in similar healthcare services to create types of healthcare services (primary, somatic specialist and mental specialist healthcare services) and set healthcare use for each of these types as a main outcome. One of the main strengths of this categorisation is that it minimised the risk of recall bias- or information bias across different types of healthcare providers. These outcomes of healthcare use require that participants have some knowledge of the healthcare system (e.g., consultations with a medical specialist in private practice versus somatic out-patient hospital services), and differentiating between the different healthcare providers outlined in this survey may be vulnerable to misclassification bias. However, I chose to merge the different healthcare services to more general healthcare services (e.g., both consultations with a medical specialist in private practice and hospital out-patient services were classified as somatic specialist healthcare), in the hope of minimising the effect of any misclassification errors and successive information bias.

In Tromsø7, there was only one question regarding hospital admission, and the question did not distinguish between admissions due to somatic and mental health. I chose to include this question as a part of somatic healthcare use. A national report from the Norwegian Health Directorate reported that close to 40% of the Norwegian population had been in contact with somatic hospital services in 2016 (111), whereas only 4.7 % of the adult population were in contact with mental specialist healthcare overall, nationally (112). During the last decade, consultations at out-patient clinics have increased dramatically whereas admissions have decreased in the mental specialist healthcare (112). However, I cannot rule out that some admissions to a psychiatric hospital were misclassified as somatic specialist healthcare use, but this will probably not apply to many individuals, and is therefore not likely to have affected the results considerably.

5.2.5 The measurement of health anxiety

Both the WI-6 (47) and the WI-6-R (37) have shown good psychometric properties, for which *validity* and *reliability* are key measures. Reliability is the capability to provide consistent results, while validity examines if the measurement tool measures what it is meant to measure (83). Reliability of self-reported health measurements is often tested by internal consistency (113), and Cronbach's alpha is the recommended test for measuring covariance and correlation between items (83). An alpha coefficient above 0.60 is usually considered acceptable, and a coefficient above 0.70 is considered good (83). As part of testing for reliability and consistency using the WI-6 and the WI-6-R in this study sample, I got a Cronbach's alpha of 0.83 and 0.84, respectively, indicating that the different questions measured the same, one-dimensional construct and could be summarised to a total score. A confirmatory factor analysis is recommended to test construct validity, as well as to confirm the structural model of an instrument (83). Therefore, I conducted a confirmatory factor analysis to investigate if different variables measured the same dimension by assessing the goodness of fit, correlation and contribution from each variable, and concluded that the questions included in the WI-6 and WI-6-R had a common explained variance.

5.2.6 Measuring health anxiety without a time frame

Unfortunately, an error in the Tromsø7 questionnaire led to some missing information in the Whiteley Index. The original Whiteley Index asked "have you in the past 12 months…", but this was not included in the questionnaire sent out to the invited participants. The wording of the question may have had an impact on how participants answered, as all questions were formulated in the present tense. The findings could therefore be considered to be applicable to a recent time frame, implying that the HA score was representative of the point at which respondents answered the questionnaire (e.g., do you think, do you often), although I cannot conclude that this is the case. Further interpretations would be speculations.

5.2.7 Other considerations

In Paper 2, I chose to separate the continuous healthcare use variable "number of consultations" of healthcare use into five levels of use. This was done because the distribution of consultations was skewed, with the majority of participants using each type of healthcare service just a few times a year. Due to some very high values, employing healthcare use as a continuous variable would have resulted in a shift of the mean. At the same time, I did not want to exclude these high values, because they were plausible and would contribute to

understanding the association between HA and healthcare use. However, the application of levels of use can mask the trend in the 4th quartile, in which healthcare use ranged between 5-89, 4-170 and 13-130 consultations, in each type of healthcare service, respectively. In primary healthcare, «frequent users» can be defined as people who have more than 30 consultations a year (64), and our choice of categorizing the users into quartiles might have masked any specific trends for this subsample compared to the lower levels of this 4th quartile.

In Paper 3, I chose to investigate the relationship between HA and the different disease categories exclusively, to ensure that the association between HA and each disease category was not confounded by other disease categories. However, by excluding people with diseases in different disease categories, I cannot say anything about the burden of different disease combinations. For example, coronary heart disease is a common complication of diabetes (114), and participants with these combinations was excluded from the analyses. However, these combinations could to some degree be captured in the number of diseases analysis. The World Health Organization defines multimorbidity as the "coexistence of two or more chronic conditions in the same individual" (115, p. 3). I chose to categorise the number of diseases, current or previous, into five categories (0, 1, 2, 3, 4 or more), as we had enough participants to analyse such subpopulations, and as four or more diseases which may indicate a different disease burden than the common classification of two or more. Indeed, the results from Paper 3 shows that the level of HA was increased with each increase in number of diseases.

I also chose to merge some variables. I initially speculated whether the association differed between those with acute and chronic cardiovascular diseases, so I divided these into acute events (myocardial infarction and stroke) and chronic conditions (heart failure, atrial fibrillation, angina pectoris). However, as this yielded only small changes in the results, I chose to present cardiovascular diseases as one disease category.

5.2.8 Confounding and interactions

There are several types of variables that should be assessed and accounted for when examining the association between an exposure and an outcome: interactions, confounders, mediators and colliders. In this thesis, I defined age, gender, education, household income, social network characteristics, mental illness, physical disease and illness in first-degree relatives as confounders. All these variables were chosen based on what I believe would

affect HA based on previous research, and were mainly considered confounders or possible interaction variables.

A confounder is a third component that is associated with, or is believed to affect, both the exposure and the outcome (104, p. 55). In the three articles, I considered social network characteristics, such as "friendship" and "participation in organised activities" as confounders (Figure 6), i.e. a factor that would affect HA, healthcare use (92) and physical disease (91):

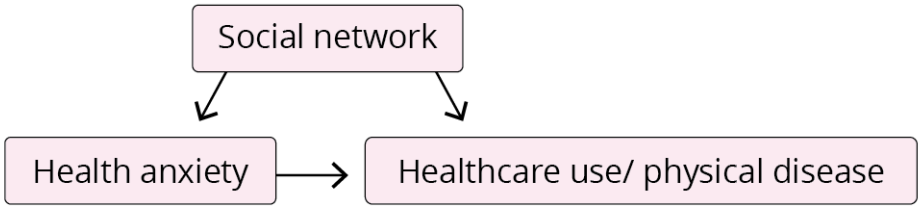


Figure 6. *Illustration of social network characteristics as confounding variables to the association between health anxiety and healthcare use/physical disease*

However, it may also be that HA and healthcare use/physical disease affect social network characteristics (Figure 7), which could introduce collider bias into the model.

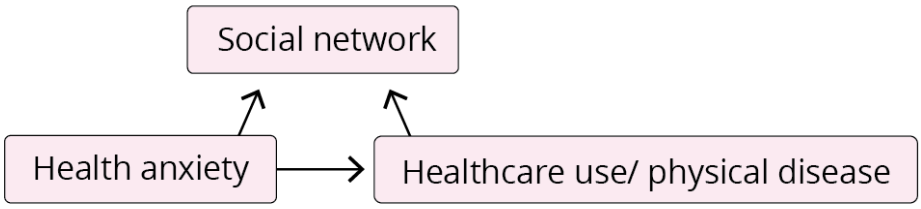


Figure 7*. Illustration of social network characteristics as collider variables to the association between health anxiety and healthcare use/physical disease*

A collider is "a variable that is the common effect of an exposure and an outcome" (104, p. 50), and should not be included in the model. Morbidity can lead to social isolation and challenges to participation in social activities (116). In addition, the diagnosis of hypochondriasis is often accompanied by stigma and negative reactions from healthcare providers (117). It can therefore be speculated that this stigma is also associated with negative

reactions/feelings in other domains. Adjusting for social network characteristics as a collider could have introduced a noncausal association (104, p. 50).

Even if the chosen confounders were defined correctly as confounders, all the analyses in Papers 2 and 3 may be vulnerable to residual confounding, i.e. confounding that is still evident after adjustment for suspected confounders (104, p. 248). This may be due to incorrect measurement of confounders, or to the presence of confounders that were not measured or included in the model (104). Reports of subjective health complaints could have been included in the study and would have been relevant for both Papers 2 and 3. Research has shown that musculoskeletal pain predicts increased healthcare use both in primary and somatic specialist healthcare (118), and one article has also found higher HA in people not diagnosed with cardiovascular disease, compared to those who received a diagnosis (119). Therefore, the results from Paper 2 could be vulnerable to residual confounding, as they were only adjusted for only physical diagnoses. However, a newly published longitudinal study found no additional influence of HA on the association of musculoskeletal pain and future healthcare use (85), and was therefore not a clear suspected confounder in our study.

Similarly, during the planning phase, subjective health complaints and health-related quality of life were decided to be outside the scope of Paper 3 as outcomes, but I could have considered them as confounders when adjusting the association between HA and physical diseases. Subjective health complaints and health-related quality of life could also have given an indication of severity and function, information we did not get from the specific questions on diagnoses.

Interaction occurs when the effect of the exposure on the outcome is dependent on a third variable (107, p. 149). Possible interaction analyses should only be carried out based on a priory assumptions (101). In Paper 1, I suspected that the association between HA and household income was dependent on age. This was not an a priory assumption, but based on my interpretation of the results. In Paper 2, my a priory assumptions were that the association between HA and primary healthcare use would depend on physical disease, and similarly, that the HADS-T would modify the association between HA and mental specialist healthcare use. In Paper 3, I suspected that the association between HA and physical disease would depend on age, and that an interaction would exist between age and education in the association between HA and physical diseases.

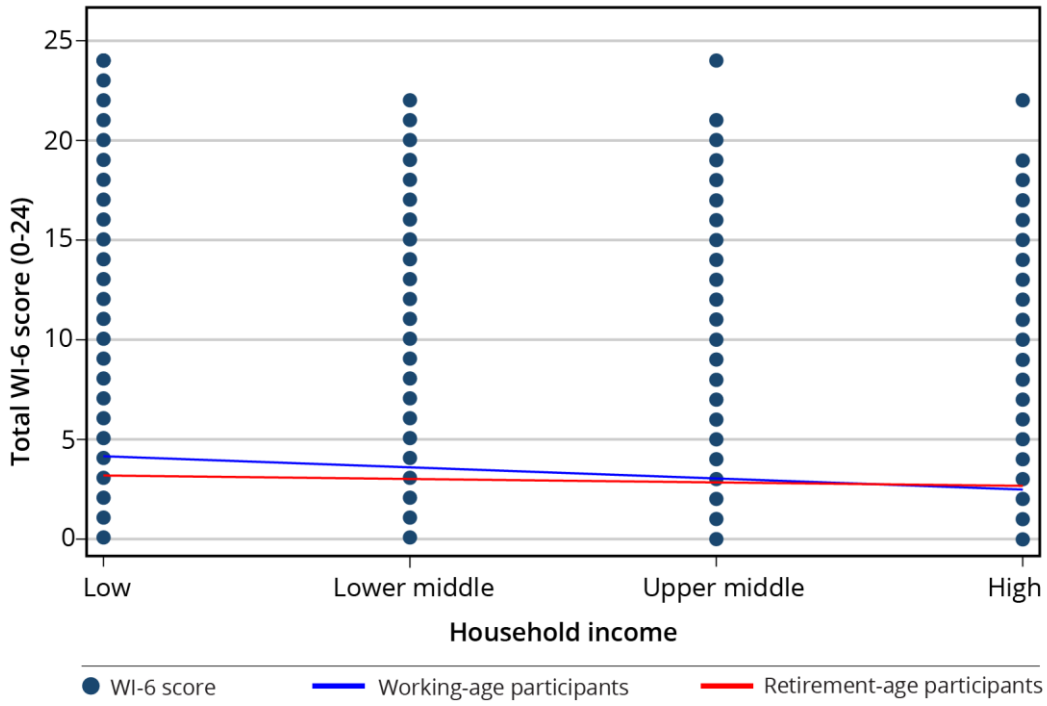


Figure 8*. The association between household income and health anxiety (WI-6) by age; Working-age participants and retirement-age participants.*

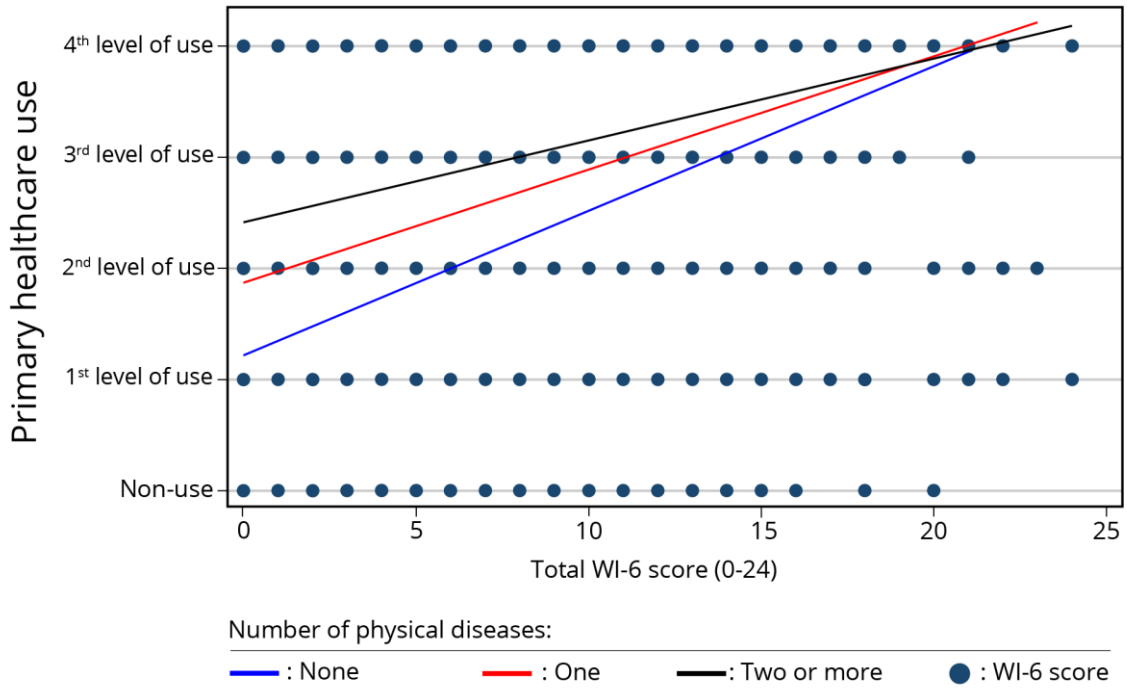


Figure 9. *The association between health anxiety (WI-6) and primary healthcare use by number of physical diseases; None, one, two or more.*

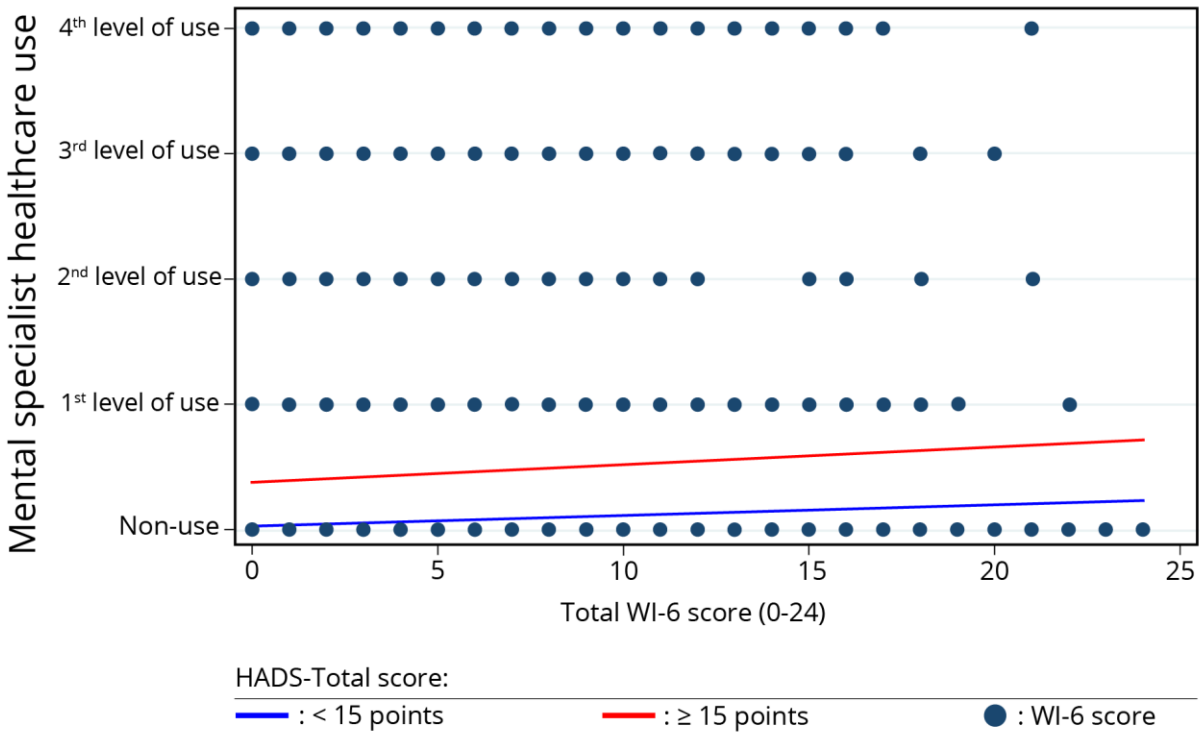


Figure 10. *The association between health anxiety (WI-6) and mental specialist healthcare use by HADS- Total score; < 15 points, ≥ 15 points.*

An interaction can be evident in two ways. A quantitative interaction is evident if the effect sizes are different within the different strata (101). A qualitative difference, however, indicates that the association between the exposure and the outcome behaves differently within the strata, such as they cancel each other out if testing for interaction is not performed (101, p. 209-252, 120). As seen in Figures 8 and 9, there was evidence of an interaction with qualitative differences, supporting the decision to use stratified analyses to present the results. The interaction between HA and the HADS-T on mental specialist healthcare use (Figure 10), however, seems more quantitative in character, and it can be discussed whether showing stratified analysis in addition to the primary analysis was necessary.

5.2.9 Statistical considerations – the choice of complete-case analyses

I chose to exclude participants with missing exposure (Paper 1) and outcome values (Papers 2 and 3) prior to analyses. However, in Stata, all regression models exclude all missing values by default. As a result, all analyses are classified as complete-case-analyses. In the univariate analyses, the percentage of excluded participants due to missing variables was between 12 and14%, but in the fully-adjusted analyses, this percentage was successively higher when

including the confounding variables to the model. The number of participants included in each of the fully-adjusted analyses are presented in each article. I chose to not exclude participants with missing values for confounders in doing the descriptive- and univariate analyses only, because I wanted to include as much information on the exposure and outcome as possible. Although complete-case analyses are common in medical research (121), this approach is vulnerable to biased results, and multiple imputation should perhaps have been considered. However, an assumption for multiple imputation is that values are "missing at random" (122), and I was reluctant to make that assumption. I therefore considered using complete-case analyses a safe option. However, the writing of this thesis made me realise that a more conscious approach to missing data may have changed my decision to use complete-case analyses.

5.2.10 Generalisability

This thesis presents results from an adult, general population aged 40 years or older. Previous studies have shown that levels of HA have a peak prevalence in middle age (mid-30s to mid-50s) (21), and my study sample was therefore suitable to answer my research questions. However, one article comparing HA in young and old age groups reported that young adults (aged 18-30 years) have higher HA than older adults (aged ≥60 years) (123). On the other hand, a recent study examining HA in a general population (aged 18-72 years) during the COVID-19 pandemic (59) reported a mean HA similar to that in my study sample, indicating that the results from this thesis are comparable to findings from other populations. However, to allow for further generalisations, e.g. to examined wither whether the age span in Tromsø7 mask some important association regarding aspects of behaviour between different generations, replication in other populations with a larger age span than Tromsø7 is needed.

Most of the research concerning HA in the general population has been conducted in middle- to high income countries (United States, Australia, United Kingdom, Germany), and one can speculate that HA is more relevant for people in these countries than in low-income countries. Although it did not examine HA as a continuous construct, one important World Health Organization collaborative study gave a rare opportunity to examine the prevalence of severe HA/hypochondriasis from 14 countries with different income categories (124). Based on results from primary care clinics, they found that between-country variations in the prevalence of severe HA were relatively small (124), and that variations could not be easily explained by cultural differences (125). Nevertheless, this study explored severe HA and

hypochondriasis, and it is unclear if the distribution or associated factors are generalisable across cultures and countries. In general, differences in HA across cultures and global regions are to a large degree unknown.

In this thesis, the proportion of participants who reported primary healthcare use (80%), somatic specialist healthcare use (40%) and mental specialist healthcare use (4%) in Paper 2 is in line with reports of national healthcare use (126, 127), indicating that the study participants are representative of the Norwegian population. However, there are organisational and financial differences in healthcare systems that may affect the generalisation of the results from Paper 2 to other countries. All inhabitants in Norway are covered by the public insurance system, and the majority of the cost of primary and specialist healthcare is covered by governmental block grants and tax funds (128). Therefore, it is possible that the association between HA and healthcare use, including use at lower levels of HA, observed in Paper 2 is due to the relatively small individual costs related to this use. Indeed, out-of-pocket costs for individuals is less in Norway compared to other countries, and this economic factor might alter this association in other countries.

The low individual healthcare costs may also increase the probability of acquiring an early diagnosis, which may in turn affect morbidity and reduce mortality. The life expectancy in Norway is higher than the European average (128), and although mortality due to non-communicable diseases is decreasing (128), the prevalence of chronic non-communicable diseases is increasing both in Norway and other middle- to high- income countries (129). Therefore, the association between HA, physical diseases and cardiovascular risk factors observed in Paper 3 should also be of relevance to other countries.

5.3 Discussion - results revisited

The results from each paper are discussed in detail in each manuscript, whereas in this chapter I will present an overview of what this thesis adds to the knowledge in this field, as well as the further research and clinical implications of this work.

In my thesis, I measured HA as a continuous construct in the general population. The results present the distribution of HA, and I have demonstrated that HA is associated with social network characteristics, healthcare use, physical disease and cardiovascular risk factors. The

overview of this field is particularly challenging, as there is no consensus on the definition of HA, and most previous research has been based on the DSM-IV or ICD-10 diagnosis of hypochondriasis. There are challenges when studying something that has no clear distinction between what is healthy and "normal", what is illness or disease, and a suspected large grey are in between. The results from this thesis imply that, from a population perspective, all levels of HA are important.

5.3.1 Distribution of health anxiety in the general population and associated factors

In this thesis, I examined the distribution of HA in a general population and found that, although the mean HA score is low, participants scores were spread over the entire range of our HA measurement tool. Latent structure analyses in recent years support the notion of HA as a dimensional and continuous construct (32, 33), both in young and healthy student populations (32) and in working-age populations (mean age 43), both with and without physical illness (33). My contribution is to present HA as such in a large, general population. The continuous perspective has several implications and suggestions. In line with Ferguson (33) and Longley et al. (32), I believe that the comparisons between the few participants with severe HA and the majority with lower HA may mask important associations that could identify risk factors for increased HA, consequences of different levels of HA and perhaps fluctuations in these levels, and may not capture the complexity of the phenomenon of HA. Especially in large population studies, distribution of HA and mean HA may identify important trends, and more knowledge is needed on those at the lower ends of the HA spectrum, which is also relevant to healthcare services.

Previous research has presented inconsistent results on which associated factors are important, both in the general population (15) and in patient populations (15, 31). The diverse use of cut-offs and definitions of HA might be decisive to the associations observed in different studies. However, this thesis highlights that other aspects can also be important for the level of HA, namely social network characteristics.

5.3.2 Why are social relationships so important?

In Paper 1, I found friendship to be the single most important factor associated with HA score, where those stating "no" to the question on friendship had 61% higher HA scores; participation in organised activities more than once a week was also significantly associated

with lower HA scores when compared to not participating in organised activities. This is a novel finding in the research field of HA. Although they have never been examined in relation to HA, several studies have looked at social relationships and their association with mental health and other anxiety disorders. Participation in organised or cultural activities is associated with increased survival (130), as well as increased well-being and lower HADS-T, with a dose-response indication (89). A study of mental health in adolescents found that those participating in team sports had better mental health than those doing individual sports (131), indicating that social belonging might be more important to mental health than physical activity alone. The results from Paper 1 can indicate that a sense of belonging, independent of the type of organised activity, may be important for health in general and also for HA levels. Similarly, friendship was the most important factor associated with the level of HA of the variables explored in Paper 1. This contrasts the findings of Flensborg-Madsen et al. (90), who found that neither qualitative or quantitative considerations of friendship were associated with the risk for an anxiety disorder. However, loneliness was a strong predictor. Our questions, although thought to measure the quality of friendship, could capture some psychological components of loneliness, which could explain the strong association found in Tromsø7.

5.3.3 Health anxiety and healthcare use – lower levels should also be recognised

In this PhD project, I found consistent evidence that HA as a continuous construct was associated with healthcare use as well as current and previous disease and cardiovascular risk factors. One key implication of this thesis is the discussion of clinical importance of HA in those without severe HA – we do not know *how low* on the spectrum HA becomes important, and at which level HA becomes clinically relevant outside diagnostic criteria. Several authors have tried to define clinically relevant HA (3, 51), but have used the diagnostic criteria of hypochondriasis to identify people with severe HA. I would advocate that, especially within the healthcare system, there should be a discussion of what clinically relevant HA is, and on the other hand, at what HA score requires diagnosis and targeting treatment. In Paper 2, I found associations between HA and healthcare use in a progressively increasing manner, especially in primary and somatic specialist healthcare. The increasing HA I observed with increased use of specialist healthcare services may elevate the risk of overdiagnosis, overtreatment, and inappropriate healthcare use. This is perhaps especially relevant in somatic healthcare, as it is the service with which most people with HA have contact (66). The results

from Paper 2 indicate that increased focus should also be placed on lower levels of HA in patient treatment and consultations, and that HA should be assessed according to its relevance even if it is not elevated enough to require a primary diagnosis. One review recommended routine use of the Whiteley Index as a screening tool in medical settings to optimise treatment and ensure unnecessary impairment and healthcare utilisation (15).

Interestingly, and in contrast to the findings of HA as a continuous construct, Asmundson and colleagues (132) found a distinctive difference between those with no HA and those on the rest of the HA scale in a student population. In their evaluation of the latent structure of HA, they found indications that, although the majority of people (81%) have levels of HA that span the continuum, those stating no HA (19% of the sample) had distinctly different characteristics. The authors proposed that stating "no HA" may have negative consequences, such as health negligence, and recommend that further studies examine the continuity of the anxious majority. My aim in Paper 2 did not include examining those with an HA score of 0 specifically; therefore I cannot conclude whether no HA indicated health negligence. However, for the "anxious majority", there was a consistent trend of healthcare use with increasing HA score, especially in primary healthcare. When considering healthcare services combined, this adds up to a large number of consultations each year.

5.3.4 Can health anxiety be beneficial?

Because of the cross-sectional research design, I cannot know whether HA is important in acquiring a diagnosis, or whether HA arose in response to disease. Indeed, HA is associated with increased healthcare use, and the tendency of bodily vigilance alongside healthcare use can increase the probability of being diagnosed with a physical disease. As proposed by Asmundson et al. (132), one could speculate that HA would be beneficial and lead to reduced mortality or disease severity, if detected early. Some prospective studies have addressed this hypothesis. In 2021, Sigstrom et al. (49) published a cohort study with 44 years of follow-up, examining the relationship between HA, cancer incidence and all-cause mortality in women. They found no association between HA and cancer incidence, but found a U-shaped increased all-cause mortality among participants with no HA and those with severe HA, compared to participants with mild- to moderate HA. In a Norwegian cohort (55), there was an association between severe HA and cancer incidence in men, but not cancer severity. The authors speculated that the lack of association in women could be explained by the Norwegian cancer screening program, which mainly targets women, and may reduce the importance of HA as a

factor for cancer detection. Both studies concluded that some degree of HA can be beneficial for the detection of disease and for mortality. In contrast, severe HA has been associated with an increased risk of ischaemic heart disease, even after adjusting for cardiovascular risk factors (52). Although the highest risk was found in those who had HA scores in the 90th percentile, the association followed a dose-response pattern. Similarly, one study found that after a cardiac event, HA was found to be an independent risk factor for new a major adverse cardiac event, also after adjusting for cardiac severity (72). However, to examine whether the association with HA changes for different diseases, whether different HA scores are associated with different risks of disease or other long-term consequences, or importantly, to examine whether some level of HA is beneficial, longitudinal studies are needed.

Although studies indicate the potential benefits of HA, there is consistent evidence that HA in populations with physical disease is associated with reduced quality of life (29, 74), reduced daily function higher health impairment (31), unfortunate coping strategies (72, 133), increased reassurance-seeking behaviour (71), and patients report a decreased sense of ability to deal with the disease (29, 133, 134). In Paper 3, I found that people with different current diseases had 13-119% higher HA than healthy participants, and that increasing number of physical diseases was associated with progressively increased HA. This shows the importance of the increased burden HA can place on populations with physical disease and cardiovascular risk factors, and that the consequences of this burden deserve more attention.

5.3.5 Previous disease also deserves attention

Paper 3 investigated the association between HA and previous disease, and although the coefficients were lower than for current disease, the results were consistent and mostly showed a significant association. To-date, there are no studies that explore previous disease with respect to the general concept of HA. I therefore looked to disease-specific measurements, such as fear of cancer recurrence, for comparison. Indeed, fear of cancer recurrence is important, as the measurement implies that the cancer is in remission. A review by Simard et al. (71) showed that the majority of cancer survivors had low to moderate fear of cancer recurrence, but a considerable number did worry about the cancer recurring. A high score of fear of cancer recurrence was associated with increased reassurance-seeking behaviour, several psychological reactions and reduced quality of life (71). This corresponds well with my results, which indicated that, although a disease disappears or is medically well-treated, the experience of being ill can cause HA to linger. The proportion of the population

with previous disease is growing, due to the increased prevalence of physical disease (129, 135) and reduced mortality, especially for the two largest groups of non-communicable diseases: cancer and cardiovascular disease (86, 129), which makes the relationship between HA and previous diseases relevant.

5.3.6 Is population health anxiety increasing?

In contrast to my hypothesis, I found no interaction between age and physical disease in Paper 3, indicating that disease status does not affect the association with HA in younger adults differently compared to older age groups. Some reports have indicated that HA is increasing, both in student populations (60) and medical clinics (24). In Tromsø7, increasing age was associated with lower HA, with no interaction of physical disease. Due to the cross-sectional design of this thesis, I do now know whether HA declines with age, or if there is a cohort effect indicating that the todays young have higher HA scores than previous generations of young people. If the results indeed indicate a cohort effect, the population mean of HA can be expected to rise. There are some hypotheses for why this may be. Increased knowledge about the risk factors and causal pathways for disease has led to a shift, from a societal focus to an individual focus on health, disease, and successive responsibility (60). In addition, there is a barrage of news stories and social media posts that give health advice (eat this to avoid dementia) (136) and recount horror stories (had a headache, found cancer) (137). If we recognise one's responsibility to maintain good health, does it then become one's own responsibility to avoid illness?

If the population mean of HA is increasing, the results from my thesis are particularly important, given the consistent associations between HA and healthcare use, as well as between HA in the general population and physical disease and cardiovascular risk factors.

6 Conclusions

In this thesis, I aimed to examine the distribution of HA, as a continuous construct, and associated aspects in an adult sample of the general population.

My results support findings from previous studies that conceptualise HA as a continuous construct ranging from mild to excessive. The distribution I observed in the general population was highly skewed. Although the mean HA score was low, scores in the study sample spanned the entire scale of Whiteley Index. Social network characteristics were highly associated with HA. Further, I found that HA was associated with both primary, somatic specialist and mental specialist healthcare use, and that increasing healthcare use was associated with progressively increasing HA. Lastly, I presented an overview of the association between HA, physical diseases and cardiovascular risk factors, indicating that HA is increased in those with physical disease. The findings from this thesis indicate that HA merits closer attention even when it cannot be categorised as severe.

7 Implications and further research

The exploration of HA as a continuous construct is a relatively new field of research, and there is still much work to be done. This thesis had a population-based approach, and is therefore not easily transferred to the clinical setting. However, I believe that this thesis contributes to the knowledge on the distribution of, and associated aspects of HA as a continuous construct, and shows that also people with lower HA, i.e., those without an ICD-10 or DSM-V diagnosis, deserve attention.

In Paper 1, I found that social network characteristics were important factors associated with HA score. Although I also looked at the epidemiological factors age, gender, education, and household income, previous research has shown conflicting evidence regarding the importance and directions of associations between HA and these factors, although a recent review, summarizing the total impact of socioeconomic factors, found indication of social inequality associated with higher HA (57). Although this is in accordance also with our findings, the estimates in our results can indicate that we should also be exploring other aspects that are important in HA, and social relationships may be more important than where you come from and what you do. Social belonging is important for both mental (90) and physical (91) health, and my results showed that it is also important for the level of HA and may also be important in the reduction and management of HA.

In Paper 2, I found significant associations between HA and primary and specialist healthcare use. All levels of HA were significantly associated with healthcare use. Although this has been found in other studies (61, 62) as well, much important research is yet to be done. A natural next step would be to examine the causal relationship between these two aspects: can HA predict future healthcare use, or is healthcare use itself a cause of HA? At what level is HA associated with overuse, and how can healthcare personnel optimally address HA in patients who do not require targeted treatment? Both qualitative and quantitative research will be important to delve into this topic further and understand this relationship.

Finally, the results from Paper 3 should be seen as an “overview” on the association between HA and a wide range of physical diseases and cardiovascular risk factors, which affects a large proportion of the population. The vast majority of people with HA and physical disease have been open with healthcare providers about their worries (22), which gives healthcare

personnel an opportunity to address the possible aggravated burden that HA may place on persons with physical disease, even when the HA is not severe enough to require targeted treatment. Future research should examine the causality in this relationship: does HA precede disease, or is HA a reaction to a diagnosis? We also need to learn more about whether HA is an independent risk factor for worse outcomes, as may be the case for cardiovascular disease (52, 72), or if HA may be beneficial to disease detection. On the other end of the scale, it would be interesting and important to further explore the work of Asmundson and colleagues (132), who asked if "no HA" may result in health negligence.

It was not within the scope of this thesis to examine the relationship between HA and conditions related to self-reported symptoms. Previous research has found that severe HA is prevalent in patients with pain disorders (28, 138), and this association should be assessed further. In Norway, musculoskeletal disorders are common and a large reason for absence from work (128), and some results indicate that HA can play a part in how patients experience their pain (139). And what about those who do not receive a diagnosis? Some studies have found that those with non-cardiac chest pain and respiratory symptoms (119, 140) are more anxious than those who receive a diagnosis, i.e., who get "an answer" to explain their worry. In a healthcare system organised to diagnose or exclude somatic disease, we do not know enough about how patients experience getting a "negative" result.

Finally, I want to share some of my personal reflections. Our view of health is shifting, from something that we experience but do not control, to something that is our own responsibility. With the rise of non-communicable diseases (135) and more knowledge on how to prevent them, it is important for public health authorities to communicate what individuals can do to stay healthy. But what are the "side effects" of this public health message? Initial research indicates that the mean HA in the population is increasing (60). Although this might not lead to an increase in those receiving ICD-10 and DSM-V diagnoses of hypochondriasis, illness anxiety disorder and somatic symptom disorder, the results reported in this this thesis lead me to believe that some of the consequences may still be undesirable.

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Paper 1

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Distribution of health anxiety in a general adult population and associations with demographic and social network characteristics

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Abstract

Background. Health anxiety (HA) is associated with increased risk of disability, increased health care utilization and reduced quality of life. However, there is no consensus on which factors are important for the level of HA. The aim of this study was to explore the distribution of HA in a general adult population and to investigate whether demographic and social factors were associated with HA.

Methods. This study used cross-sectional data from the seventh Tromsø study. A total of 18 064 participants aged 40 years or older were included in the analysis. The six-item Whiteley Index (WI-6) with a 5-point Likert scale was used to measure HA. Sociodemographic factors included age, sex, education, household income, quality of friendship and participation in an organized activity.

Results. HA showed an exponential distribution among the participants with a median score of 2 points out of 24 points. In total, 75% had a total score of 5 points or less, whereas 1% had a score >14 points. Education, household income, quality of friendship and participation in organized activity were significantly associated with HA. The variable quality of friendship demonstrated the strongest association with HA.

Conclusion. Our study showed an exponential distribution of HA in a general adult population. There was no evident cut-off point to distinguish participants with severe HA based on their WI-6 score, indicating the importance of analysing HA as a complex, continuous construct. HA demonstrated strong associations with quality of friendship and participation in an organized activity.

Introduction

Being concerned about one's own health serves an important adaptive function – it increases survival. Dealing with symptoms of illness in a timely manner is beneficial. However, some individuals become overly health anxious and develop worries that range from mild to extreme concerns (Rachman, 2012). This is called health anxiety (HA). Severe HA has been found to increase health care use (Barsky, Ettner, Horsky, & Bates, 2001; Bobevski, Clarke, & Meadows, 2016) and the risk of long-term sick leave (Eilenberg, Frostholm, Schroder, Jensen, & Fink, 2015) and is a persistent condition if left untreated (Fink, Ornbol, & Christensen, 2010). HA is often associated with other anxiety disorders, such as panic disorder and generalized anxiety disorder (Sunderland, Newby, & Andrews, 2013). Despite growing evidence of the consequences of HA, we know little about the distribution of HA in the general population. One reason is that most research on HA has been performed with patient populations (Bilani et al., 2019; Seivewright et al., 2004; Tyrer et al., 2011).

Measurement of HA

The three most frequently used self-report measures to assess HA, all originally developed for screening purposes for the diagnosis of hypochondriasis, are the Short Health Anxiety Inventory (SHAI) (Salkovskis, Rimes, Warwick, & Clark, 2002), the Illness Attitude Scale (IAS) (Kellner, Abbott, Winslow, & Pathak, 1987) and the Whiteley Index (WI) (Pilowsky, 1967). The WI is a self-rated instrument developed in 1967 as a diagnostic tool for hypochondriasis but later began to be used to screen for HA. The use of diverse self-report measures makes comparisons between screening studies difficult.

Distribution of HA

There is no consensus on the appropriate cut-off points to define HA with different versions of WI, although most studies have chosen to set a cut-off point. Hedman et al. (2015) have

recommended a cut-off point of 5 with a WI with 14 questions and dichotomous response options. However, no other studies have reported this threshold in population studies. The lack of criteria to define HA through the different self-report measures is a challenge within this field of research. This affects the reliability and validity of assessments of HA prevalence, which has been reported to be between 2.7% and 13%. A study based on the IAS estimated a point prevalence of 6% in a German population (Bleichhardt & Hiller, 2007), but the representativeness of the sample was dubious because most participants in the sample had low education levels. Martin and Jacobi (2006), however, found an overall 12-month prevalence of 2.75%, using diagnostic interviews for screening purposes. In New Zealand, a convenience sample of elderly individuals over 65 years found a prevalence of 7% with the SHAI (Boston & Merrick, 2010). Sunderland et al. (2013) observed a point prevalence of 3.4% and a 12-month prevalence of 4.2% based on an Australian national survey. However, their assessment was restricted by the use of only one single question: 'Have you ever worried a lot about serious illness despite reassurance from a doctor?' Furthermore, two articles from Canada and the USA reported a prevalence of illness worry (Looper & Kirmayer, 2001; Noyes, Carney, Hillis, Jones, & Langbehn, 2005) of 6% and 13%, respectively. These authors assessed illness worry based on the same question but asked the respondents to report based on different time periods: 'In the past 12 months, have you had a period of 6 months (Looper & Kirmayer, 2001) or 1 month (Noyes et al., 2005) or more when you worried about having a serious physical illness most of the time?'

In line with Ferguson (2009), we assume that HA is more accurately represented as a dimensional rather than a categorical construct. To the best of our knowledge, there have been no studies exploring the distribution of HA in a general population, despite the belief that HA is experienced on a continuum ranging from mild concerns to severe anxiety (Ferguson, 2009). The Tromsø study: Tromsø 7, a health survey that included all adult inhabitants in the municipality of Tromsø, Norway, has given us a rare opportunity to describe the different degrees of HA in a general population. The aim of this article is to study the distribution of a self-report HA measure in a general adult population and the association of HA with sociodemographic variables. In the available data set, HA was measured with the six-item WI (WI-6).

Method

Study design and population

This study used cross-sectional, self-reported data from the Tromsø study: Tromsø 7. The Tromsø study is a large Norwegian population-based health survey that includes the collection of self-reported data, interviews, physical examinations and the collection of biological material. Seven surveys have been conducted since 1974 with different birth cohorts. The Tromsø study is described in detail elsewhere (Jacobsen, Eggen, Mathiesen, Wilsgaard, & Njolstad, 2012). The current Tromsø study, Tromsø 7, was conducted in 2015–2016. All inhabitants in the municipality of Tromsø aged 40 years or older were invited, for a total of 32 591 men and women. A questionnaire was included in the invitation, which the participants brought with them in a filled-out form to the clinical examination. At the examination, participants provided additional self-reported information on a wide range of topics, including sociodemographic and health-related information. The invited participants received one reminder if they did not attend their examination. By the end of 2016, 21 083 participants had taken part in Tromsø 7, representing an attendance rate of 65%. A total of 67% of the invited women and 62.5% of the invited men participated in the study. However, the participation rates were lower among participants 80 years or older, with an attendance rate of 34% for women and 48% for men.

Variables

Dependent variable

We measured HA using the one-factor, WI-6. The WI originally consisted of 14 questions, each to be answered with a false/true response. Today, versions of the WI are available with 14, 13, 11, 10, 8, 7 and 6 items with both true/false and 5-point Likert scale response options (Welch, Carleton, & Asmundson, 2009). The 5-point Likert scale version is considered beneficial for use in a general population (Welch et al., 2009) as it is easier for respondents to use (Preston & Colman, 2000) and captures the continuity of a phenomenon (Ferguson, 2009).

Table 1 provides an overview of the WI-6 questions. All respondents answered each question with one of the following response options: 'not at all', 'to some extent', 'moderately', 'to a considerable extent' or 'to a great extent'. Item scores were transformed into values from 0 to 4 (0 representing 'not at all' and 4 representing 'to a great extent'), and the item scores were summed to a total score (Y) ranging from 0 to 24, where $Y = 0$ represented no HA and $Y = 24$ represented the highest possible measurement of HA. In the questionnaire, the introduction ('In the past 12 months, have you…') was omitted, which limited our knowledge of which time frame the participants used as a reference.

Demographic and social variables

Since the existing literature has reported inconsistent findings on the background demographic characteristics associated with HA, we chose to include both demographic and social variables. Age on 31 December 2015 was reported and was included both as a continuous variable and in 10-year age groups. As only 16 participants were over 90 years of age, the two oldest age groups were merged into '80 years or older'. Education was reported as 'the highest level of education you have completed', with four categories: primary education up to 10 years of schooling, vocational/upper secondary education (minimum 3 years), college/university (< 4 years) or college/university (≥ 4 years). The wording of the household income question was as follows: 'What was the household's total taxable income last year?', with eight categories ranging from 'less than 150 000 Norwegian kroner (NOK)' (approximately 12 000 British pound Stirling (GBP) to 'more than 1 million NOK' (80 000 GBP). The household income categories were merged into four categories: low (less than NOK 451 000), lower middle (NOK 451– 750 000), upper middle (NOK 751 000–1 million) or high (more than NOK 1 million). The national average value (data from Statistics Norway) was set as the reference value in the regression analysis for both the education and household income variables.

Participants were asked two questions concerning their family life: 'Do you live with a spouse/partner?' and 'How many children do you have?' Participants reported their biological children, adopted children, stepchildren and foster children. We merged these alternatives into one dichotomized variable named 'Children', where 0 indicated 'no' responses to all of the

Table 1. Questions included in the WI-6

Question	Text
1	Do you think there is something seriously wrong with your body?
2	Do you worry a lot about your health?
3	Is it hard for you to believe the doctor when he tells you there is nothing to worry about?
4	Do you often worry about the possibility that you have a serious illness?
5	If a disease is brought to your attention (e.g. via TV, radio, internet, newspapers or someone you know), do you worry about getting it yourself?
6	Do you find that you are bothered by many different symptoms?

alternatives and 1 indicated a 'yes' response to one or more of the alternatives.

We also included two questions about the quality of friendship: 'Do you have enough friends who can give you help and support when you need it?' and 'Do you have enough friends you can talk confidentially with?' These two variables were highly correlated and were merged into one variable named 'Close friends'. This new variable included three categories: 'No', for those who answered 'no' to both original questions; 'To some extent', for those who answered 'yes' to only one original question; and 'Yes', for those who answered 'yes' to both original questions. Finally, the participants rated their participation in the organized activity with the following options: 'never or just a few times a year', '1–2 times a month', 'approximately once a week' or 'more than once a week'.

Statistical analysis

All analyses were performed with STATA version 15.1 (STATA Corp LP, College Station, Texas, USA). Participants with missing values for the dependent variable (HA) were excluded prior to the analyses. In the descriptive analyses, the means were calculated for continuous variables, and the frequency distributions were calculated for the categorical variables. Due to the non-normal distribution of the dependent variable (HA), we considered both a negative binomial distribution and a decreasing exponential distribution to model any association between HA (Y) and the relevant covariables (X_i). Exponential regression gave the best fit when tested with the Akaike information criterion (AIC) and Bayes information criterion (BIC). We, therefore, used a multivariate exponential regression model in both the bivariate and multivariate analyses:

$$Y = \alpha \cdot e^{-(\beta i \cdot X_i)}$$

$i = 1,\ldots,n$; n = number of covariables

The covariables age and gender were included in all analyses. Only statistically significant covariables were included in the final multivariate model. The level of statistical significance (p value) was set at 0.05. We also conducted survey weighting analyses to adjust for non-response, which gave identical results as the unweighted analyses. The presented results are from the unweighted analyses.

The dependent variable (HA) in the estimated model is presented with the exponential beta [exp(b)], where exp(b) describes the percentage difference in the WI-6 score relative to the reference category for the different covariables with all else held constant. We found a significant interaction between age and household income and performed an additional analysis with age-stratified groups: we categorized those under 67 as 'working-age participants' and those 67 years or older as 'retirement-age participants'.

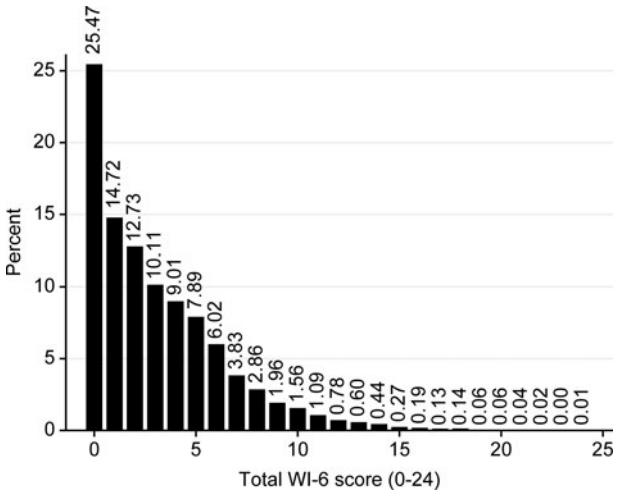

Fig. 1. The distribution of HA in the population as measured by the WI-6. $N = 20\,266$ persons.

Ethics

The study was approved by the Regional Committee for Medical and Health Research Ethics (ID 2016/1793). All participants gave written informed consent before admission.

Results

Participant characteristics and the distribution of HA in the study population

A total of 21 083 persons between 40 and 99 years old participated in this study; 52.5% were women, and the mean age was 56 (S.D. 11) years. A total of 817 participants had one or more missing items on the WI-6 and were excluded from the analysis.

The distribution of HA was highly skewed with exponential distribution (Fig. 1). The mean and median scores of the WI-6 were 3.3 and 2 points, respectively. In total, 75% of the participants had a total score of 5 points or less, 5% had a score above 10 points and 1% had a total score of more than 14 points. The study population's demographic and social characteristics, including the mean WI-6 scores in the participant subgroups, are listed in Table 2. The WI-6 scores ranged from 0 to 20–24 in all subgroups categorized according to the demographic and social variables.

Associations between HA and sociodemographic factors

In the bivariate exponential regression analyses, all variables except gender were significantly associated with HA (results not shown). In the multivariate analysis, the variables concerning family life ('Do you have a spouse/partner' and 'Do you have children') were non-significant and were excluded from the final

Table 2. Demographic and social factors of the respondents, including the mean HA value as measured by the WI-6, by respondent characteristics

Variable	Categories	*N*	Percent	Mean HA value indicated by the WI-6	Percent with 5 points or above, WI-6	Percent with 10 points or more, WI-6
Age	40–49 years	6 432	31	3.2	28	6
	50–59 years	6 035	29	3.2	28	6
	60–69 years	5 179	25	3.0	27	5
	70–79 years	2 676	13	3.0	26	4
	80 years or older	761	4	3.3	27	4
	Total	21 083				
Gender	Female	11 074	53	3.1	27	5
	Male	10 009	47	3.1	27	5
	Total	21 083				
Educational level	Primary education	4 796	23	3.5	28	7
	Vocational/Upper secondary ed.	5 756	28	3.2	28	5
	College/University <4 years	4 008	19	3.2	23	5
	College/University ⩾4 years	6 145	30	2.8	27	4
	Total	20 705				
Household income	Low (less than NOK 451 000)	4 545	20	3.8	34	8
	Lower middle (NOK 451–750 000)	5 884	29	3.3	29	5
	Upper middle (NOK 751 000–1 million)	4 741	25	3.1	27	5
	High (more than NOK 1 million)	5 015	27	2.5	20	3
	Total	20 185				
Do you live with a spouse/ partner?	No	4 609	22	3.5	31	7
	Yes	15 283	77	3.0	26	5
	Total	19 892				
Do you have children?	No	1 711	8	3.1	30	7
	Yes	18 705	92	3.9	27	5
	Total	20 416				
Do you have friends you can get support from and talk confidentially with? ('Close friends')	No	1 621	8	4.9	46	14
	To some extent	1 774	9	4.2	38	10
	Yes	17 117	83	2.9	24	4
	Total	20 512				
Organized activity	Never or just a few times a year	11 310	55	3.3	29	6
	1-2 times a month	4 981	24	3.0	26	5
	Approximately once a week	2 587	13	2.9	25	4
	More than once a week	1 856	9	2.7	23	4
	Total	20 744				

model. Table 3 shows the final model including the demographic and statistically significant social factors.

Respondents who did not have friends to get support from and talk confidentially with had significantly higher HA than those who did have such friends (Table 3). Answering 'no' to the 'Close friends' questions was associated with a 61% higher WI-6 score while answering 'to some extent' was associated with a 41% higher WI-6 score compared to that of the reference category (answering 'yes'). Similarly, regarding the frequency of participation in organized activity, participating in an organized activity

Table 3. Associations between HA, as measured by the WI-6, and relevant sociodemographic factors according to the multivariate exponential regression

Variable		Exp(b)	95% CI[a]
Age, by 10-year age groups		0.93[c]	0.92–0.95
Gender	Female	1	
	Male	1.01	0.98–1.04
Education	Primary education	1.04[b]	1.00–1.09
	Vocational/Upper secondary ed.	1	
	College/University <4 years	1.03	0.99–1.08
	College/University ⩾4 years	0.95[c]	0.91–0.98
Household income	Low (less than 451 000 NOK)	1.17[c]	1.12–1.21
	Lower middle (451–750 000 NOK)	1	
	Higher middle (751 000–1 million NOK)	0.93[c]	0.89–0.96
	High (>1 million NOK)	0.78[c]	0.75–0.81
Do you have friends you can get support from and talk confidentially with? ('Close friends')	Yes	1	
	To some extent	1.42[c]	1.34–1.49
	No	1.61[c]	1.53–1.70
Organized activity	Never or just a few times a year	1	
_	1–2 times a month	0.97	0.94–1.01
	Once a week	0.95[b]	0.91–0.99
	More than once a week	0.88[c]	0.83–0.92
Constant		4.5	4.13–4-94

[a]95% CI = 95% confidence interval.
[b]Significant below 0.05 level.
[c]Significant below 0.01 level.
N = 18 984 persons

once a week or more was associated with significantly lower HA than the other categories. Household income showed a negative association with HA. Gender was not significantly associated with HA.

We found age to be negatively associated with WI-6 scores. In addition, there was a significant interaction between age and household income. A stratified analysis for age was therefore performed, with the participants divided into working-age participants and retirement-age participants, as shown in Table 4. The mean HA value was similar in both groups. The stratified analysis showed that HA decreased with increasing age among working-age participants but showed no association with age among retirement-age participants. The quality of friendship remained strongly negatively associated with HA in both strata. Participation in organized activity was significantly negatively associated with HA among retirement-age participants who reported participating weekly, but this relationship was non-significant among working-age participants. In addition, the associations of HA with both education and household income were non-significant in the retirement-age participant group.

Discussion

Distribution of HA

In the present study, HA in the population is explored as a continuous rather than a dichotomous characteristic. We found an exponential distribution of HA on the WI-6 scale ranging from 0 to 24. There was no evident cut-off point to distinguish participants with severe HA based on their WI-6 scores, indicating the importance of analyzing HA as a complex, continuous construct. To the best of our knowledge, this is the first study to report HA as a continuous phenomenon in a general population. Although the mean HA level was low, there was great variation within all participant subpopulations. This finding illustrates the continuity of HA. We found no difference in the level or presence of HA related to gender, which is in concordance with other epidemiological studies on HA (Boston & Merrick, 2010; Martin & Jacobi, 2006; Sunderland et al., 2013). Although women are reported to have a higher prevalence of other anxiety disorders than men (Bekker & van Mens-Verhulst, 2007; Flensborg-Madsen, Tolstrup, Sorensen, & Mortensen, 2012), this does not appear to be the case with HA. In light of our results, we think it is relevant to also explore the consequences of HA-related health care use, disability and comorbidity for slight and moderate as well as severe HA.

Because we used a representative sample rather than a convenience sample, our results show a valid distribution of HA in a general adult population. In addition, by using a validated measurement tool rather than one question, we were able to better capture the complex nature of HA. Finally, most of the research on the prevalence of HA was published before 2010 (Bleichhardt & Hiller, 2007; Looper & Kirmayer, 2001; Martin & Jacobi, 2006; Noyes et al., 2005). Therefore, our research is important to provide updated knowledge of the occurrence of HA in a general population.

Table 4. Associations between HA, as measured by the WI-6, and relevant sociodemographic factors, stratified by age

		<67 years N = 15 132		≥67	N = 3 852
Variable		Exp(b)	[a]95% CI	Exp(b)	95% CI[a]
Age, by 10-year age groups		0.94[c]	0.92–0.96	1.00	0.94–1.07
Gender	Female	1		1	
	Male	1.01	0.98–1.05	1.00	0.93–1.06
Education	Primary education	1.04	1.00–1.09	1.10[b]	1.01–1.19
	Vocational/Upper secondary ed.	1		1	
	College/University <4 years	1.02	0.99–1.08	1.08	0.97–1.19
	College/University ⩾4 years	0.93[c]	0.91–0.98	1.06	0.96–1.18
Household income	Low (less than 451 000 NOK)	1.24[c]	1.18–1.31	1.04	0.97–1.12
	Lower middle (451–750 000 NOK)	1		1	
	Higher middle (751 000–1 million NOK)	0.93[c]	0.89–0.97	0.93	0.83–1.04
	High (>1 million NOK)	0.78c[c]	0.74–0.81	0.97	0.84–1.12
Do you have friends you can get support from and talk confidentially with? ('Close friends')	Yes	1		1	
	To some extent	1.41[c]	1.33–1.49	1.42[c]	1.28–1.58
	No	1.61[c]	1.52–1.71	1.60[c]	1.42–1.80
Organized activity	Never or just a few times a year	1		1	
	1–2 times a month	0.98	0.94–1.02	0.96	0.88–1.04
	Once a week	0.97	0.92–1.02	0.89[b]	0.80–0.98
	More than once a week	0.87[c]	0.82–0.92	0.89	0.79–1.00
Constant		4.29	3.79–4.85	2.63	1.67–4.14

[a]95% CI = 95% confidence interval.
[b]Significant below 0.05 level.
[c]Significant below 0.01 level.

The quality of friendship and participation in organized activity

To the best of our knowledge, this is the first report showing that the quality of friendship is highly associated with HA. Our results show that 17% of the population indicated that they had no or little perceived support and confidentiality from friends. Interestingly, our model estimated that compared to those who answered yes to both 'Close friends' questions, participants who did not report such high quality of friendship had 42–61% higher HA. As there is some overlap between the different anxiety disorders (Zimmermann, Chong, Vechiu, & Papa, 2020), it is relevant to examine the association of friendship with other anxiety disorders. One prospective study found that the quality and quantity of social networks were non-significant for the development of anxiety disorders, whereas perceived loneliness was a significant predictor of anxiety (Flensborg-Madsen et al., 2012). The questions in our study related to the quality of friendship might be interpreted similarly to questions about perceived loneliness. In our study, reduced perceived quality of friendship was the single most important factor associated with the level of HA.

Perceived loneliness may also play a part in the negative association between HA and participation in organized activity. In our study, we did not differentiate participation in physical or other social activities, as both types of activities are thought to be overall beneficial for health (Bygren, Konlaan, & Johansson, 1996; Dore, O'Loughlin, Beauchamp, Martineau, & Fournier, 2016). Participation in organized activity may increase survival (Bygren et al., 1996), and it is associated with higher life satisfaction and lower anxiety and depression (Cuypers et al., 2012). In a review paper on anxiety disorders, exercise was found to be a protective factor for the development of anxiety disorders (Zimmermann et al., 2020). This might be in concordance with our cross-sectional results, which showed that participation in an organized activity once a week or more was significantly associated with low levels of HA.

Interaction between age and household income on HA

In the stratified analyses, we found that while household income was highly associated with the level of HA in the working-age group, this factor was not significantly associated with HA for the retirement-age group. This finding may suggest that factors other than household income are associated with HA in older participants. The difference in significant associations may also indicate differences between the two groups. Most of the participants aged 67 years or older were retired, which would have reduced the differences in their income, as most retired participants would have a percentage-wise reduction in income. We also identified descriptive differences between the two groups related to education, with higher education being more common among younger participants. However, in the retirement-age group, we also found a large variation in maximum HA, ranging from 14 to 22 points out of 24 points.

Interestingly, we found age to be negatively associated with HA up to the age of 67, indicating a decline in HA in the retirement-age groups. This association is in accordance with the results of Sunderland et al. (2013) on a population aged 15–85 years. They found that the prevalence of HA was lowest in the youngest and oldest participants, with a peak in middle age. A similar trend was observed in our study among participants 40 years and older. Interestingly, the negative association of age with HA was non-significant among retirement-age participants. The findings of Boston and Merrick (2010), who found no association between HA and age in a population over 65 years, are also in accordance with our results. We cannot conclude whether an age or cohort effect can explain this finding. If it is an age effect, we would expect similar findings in future research. If our HA research illustrates a cohort effect, we can expect an increasing number of people with HA in the years to come.

Strength and limitations

A strength of our study is the large study sample and high participation rate compared to other population-based studies (Langhammer, Krokstad, Romundstad, Heggland, & Holmen, 2012). In addition, we chose to use the recommended 5-point Likert scale, which has been found to have better psychometric properties than dichotomous options (Welch et al., 2009). Previous studies using different versions of the WI have mostly used dichotomous response options. The WI is recommended for use as a screening tool for HA (Weck, Richtberg, & Neng, 2014) and is beneficial for use in population health surveys because of its relatively limited number of questions compared to the SHAI (14 or 18 questions) or the IAS (29 questions). We hope that the use of a recommended measurement tool for a general population will motivate other studies to include this relatively short measurement of HA in future health surveys. More studies are needed to further explore the usefulness of this procedure.

Despite the representative sample in our study, a Norwegian study found that people with mental illness were less likely than those without mental illness to participate in population surveys (Langhammer et al., 2012). However, the Tromsø study is marketed as a health check in addition to a health survey. In contrast to other anxiety disorders, HA is characterized by the seeking of reassurance for bodily stress and fears (Mykletun et al., 2009). We therefore do not believe that HA-related avoidance has affected participation in the Tromsø study.

In the questionnaire, the introduction ('In the past 12 months, have you…') was omitted. Unfortunately, this limited our knowledge of which time frame the participants used as a reference. There is a lack of knowledge of the variation in low and moderate HA over time. However, severe HA is persistently present, with little variation over time periods (Fink et al., 2010).

When the participants gave self-reported information regarding HA, they answered the seventh question: 'Do you have recurring thoughts about having a disease that is difficult to be rid of?' We decided to not include this question in our study in line with the recommended use of the WI-6 (Veddegjaerde, Sivertsen, Wilhelmsen, & Skogen, 2014). This seventh question was not validated for use in a general population. All analyses with both versions of the questionnaire gave identical results. Therefore, we do not believe that excluding the seventh question influenced our results.

Conclusion

In conclusion, our study demonstrates the continuity that is believed to characterize HA. Future studies should explore the impacts of this continuum. The findings indicate that social factors of friendship and participation in an organized activity may be decisive for HA levels.

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Conflict of interest. None declared.

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Paper 2

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Health anxiety is an important driver of healthcare use.

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RESEARCH

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Health anxiety is an important driver of healthcare use

Anja Davis Norbye*, Birgit Abelsen, Olav Helge Førde and Unni Ringberg

Abstract

Background: Healthcare use is increasing, and health anxiety (HA) is recognized as an important associated factor. Previous research on the association between HA and healthcare use has mostly explored HA as a dichotomous construct, which contrasts the understanding of HA as a continuous construct, and compared healthcare use to non-use. There is a need for studies that examine the association between healthcare use and the continuum of HA in a general population.

Aim: To explore the association between HA and primary, somatic specialist and mental specialist healthcare use and any differences in the association by level of healthcare use.

Methods: This study used cross-sectional data from the seventh Tromsø study. Eighteen thousand nine hundred sixty-seven participants aged 40 years or older self-reported their primary, somatic specialist and mental specialist healthcare use over the past 12 months. Each health service was categorized into 5 groups according to the level of use. The Whiteley Index-6 (WI-6) was used to measure HA on a 5-point Likert scale, with a total score range of 0–24. Analyses were conducted using unconstrained continuation-ratio logistic regression, in which each level of healthcare use was compared with all lower levels. Morbidity, demographics and social variables were included as confounders.

Results: HA was positively associated with increased utilization of primary, somatic specialist and mental specialist healthcare. Adjusting for confounders, including physical and mental morbidity, did not alter the significant association. For primary and somatic specialist healthcare, each one-point increase in WI-6 score yielded a progressively increased odds ratio (OR) of a higher level of use compared to all lower levels. The ORs ranged from 1.06 to 1.15 and 1.05 to 1.14 for primary and somatic specialist healthcare, respectively. For mental specialist healthcare use, the OR was more constant across levels of use, ranging between 1.06 and 1.08.

Conclusions: In an adult general population, HA, as a continuous construct, was significantly and positively associated with primary, somatic specialist and mental healthcare use. A small increase in HA was associated with progressively increased healthcare use across the three health services, indicating that the impact of HA is more prominent with higher healthcare use.

Keywords: Healthcare use, Health anxiety, Whiteley index, Epidemiology

Background

Internationally, healthcare use is increasing. The main reasons for healthcare use are symptoms of illness and disease. However, there is a growing concern about the trend in over-diagnosis and over-treatment [1]. There are several reasons for this trend, but both patient preference and patient wishes for reassurance account for a

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considerable number of referrals [2, 3]. In Norway, general practitioners (GPs) are gatekeepers for treatment in both somatic and psychiatric specialist healthcare. Thus, patients must be referred, mainly by GPs, to be entitled to care in specialist health services. Approximately 14% of all consultations in primary healthcare in Norway lead to referrals for specialist healthcare [4].

Fear and anxiety may have an impact on perceived illness and therefore on the need for contact with health services, known as health anxiety (HA). Although there is no consensus for a definition of HA [5], it was first suggested as a milder form for hypochondriasis commonly assessed in a non-psychiatric setting [6]. At present, HA is seen both as conceptually different than hypochondriasis [5, 7], and as a milder form of the diagnosis of hypochondriasis, describing the continuum of worry and anxiety [6] and also the diagnosis of hypochondriasis is being evaluated with alterations both in the diagnostic manuals DSM-V [8] and ICD-11 [9]. In concordance with other authors [10, 11], we conceptualize health anxiety as a condition including hypochondriasis in its most serious form, but which is not limited to the diagnostic criteria.

Although HA is thought to be a continuous construct [11], most studies have studied HA as a categorical construct, dichotomizing HA into severe HA or no/little HA. The prevalence of severe HA in the general population varies from 2 to 10% [12] but has been reported to be as high as 78% in patient populations [13], and one review reported that the prevalence of severe HA is increasing in student populations [14]. There are several negative consequences of HA. Previous research has found associations between HA and higher levels of health impairment [15] and shown that HA increases the risk of long-term sick leave [16]. Severe HA is also an independent risk factor for disability pensions [15]. In a large Norwegian cohort, HA increased the risk of ischaemic heart disease by 70% after cardiovascular risk factors were accounted for [17].

The association between health anxiety and healthcare use

Severe HA is recognized as an important driver of increased healthcare use due to reassurance-seeking behaviour [18]. Frequent attenders in both primary and specialist care have higher HA scores [19–22], and HA commonly is observed alongside physical and mental morbidity [23]. However, one study found no association between healthcare use and increasing HA severity [24], while another found that people with mild HA used primary care significantly less often than people with a medical condition [13]. To explore the association between different levels of HA and healthcare use, studies must be performed in a general population.

The knowledge gap and our aim

A common feature of the existing literature is the dichotomization of HA, healthcare use [25–28] or both [23, 29, 30]. In addition, few studies have explored how HA is associated with the use of different healthcare services. Two studies explored different health services but reported overall healthcare use without differentiating between the services [25, 29]. Sunderland et al. [23] reported information on both consultation with GPs and mental health professionals; however, the reason for attendance was reported as "due to a mental problem". This might lead to an underestimation of the association, as people with HA often perceive their symptoms to be somatic rather than psychological in character [12].

Only Bobevski et al. [28] reported the association between HA and the use of primary healthcare, psychiatrist or psychologist healthcare and medical specialist healthcare; however, they still reported HA as a dichotomous construct. To our knowledge, only Tomenson et al. [31] explored the level of HA and different levels of use in a general population and found that HA was a predictor of increased healthcare use; however, they examined only primary care.

We therefore aimed to determine how HA, as a continuous construct, was associated with primary, somatic specialist and mental specialist healthcare use and to explore any differences in the potential association by level of healthcare use. We hypothesized that HA and primary healthcare use would be most strongly associated due to self-initiated consultations, whereas somatic and mental specialist healthcare use would be less affected by increasing HA due to the gatekeeper function of primary healthcare.

Methods

Study design and population

This study used cross-sectional, self-reported data from the Tromsø study: Tromsø 7, which was conducted in 2015–2016. The Tromsø study is a large Norwegian population-based health survey; see information about the Tromsø study and the data collection described elsewhere [32, 33]. In Tromsø 7, all inhabitants in the municipality of Tromsø aged 40 years or older were invited to participate, for a total of 32,591 men and women. By the end of 2016, 21,083 participants had taken part in Tromsø 7, resulting in a response rate of 65%.

Variables

Outcome variables

The respondents answered questions related to healthcare use by reporting whether they had consultations with different health services or admissions to hospital

during the past 12 months and the number of consultations. Healthcare use was divided into three main categories. Primary healthcare use included consultations with a GP or an emergency ward. Somatic specialist healthcare use included admissions to hospital, consultations with a somatic outpatient hospital service or medical specialist in private practice. Mental specialist healthcare included consultations with a psychiatric outpatient hospital service or consultations with a psychologist or psychiatrist in private practice.

Each of the three outcome variables was divided into five categories, where 0 represented non-use and 1–4 represented quartile levels of successively increasing numbers of consultations among users.

Exposure variable

We measured HA using the six-item Whiteley Index-6 (WI-6), which has shown satisfactory psychometric properties [34]. This index has 5-point Likert scale response options, and the item scores are summed to a total score ranging from 0 to 24.

Table 1 provides an overview of the WI-6 questions. All respondents answered each question with one of the following response options: "not at all", "to some extent", "moderately", "to a considerable extent" or "to a great extent". The item scores were accordingly transformed into values from 0 to 4 and summed to a total score. The WI-6 score is also presented as a 5-category variable, where 0 = not at all and 1–4 denote quartiles 1–4.

Confounders: morbidity, demographic and social variables

We included three groups of possible confounders in the analyses, as they were believed to be associated with both the level of HA and healthcare use.

Morbidity Both mental and physical illnesses are the main reasons for healthcare use and have previously been found to confound the association between severe HA and healthcare use [23, 28, 31]. We used one variable for physical illness and two for mental illness. The participants reported whether they had any of the following conditions: high blood pressure, heart failure, atrial fibrillation, angina pectoris, diabetes, kidney disease, chronic bronchitis/emphysema/chronic obstructive pulmonary disease, asthma, cancer, rheumatoid arthritis, arthrosis, migraine and previous myocardial infarction or stroke. These self-reported diseases were merged into one variable called "physical illness" and categorized as none, one, or two or more, independent of the type of illness, in line with Tomenson et al. [31].

Mental illness was reported in two different ways. For analyses regarding primary healthcare and somatic specialist healthcare use, we included the question "Have you ever had, or do you currently have, psychological problems for which you have sought help?" The response options included "no", "yes, now" and "yes, previously". Due to multicollinearity between this question and the use of mental healthcare, the measurement tool Hospital Anxiety and Depression Scale (HADS) [35] was included as an indicator of mental illness in the analyses of mental healthcare use. The HADS is a questionnaire based on participants' responses to 14 questions concerning symptoms of anxiety or depression the past week. The HADS cut-off was set at 15 points out of 42 [35].

Socioeconomic variables Both education and income have been found to be associated with both HA and healthcare use, but with different trends for different types of health services [36]. The participants were asked to report their education as "the highest level of education you have completed", with four categories: primary education up to 10 years of schooling, vocational/upper secondary education (minimum 3 years), college/university (< 4 years) or college/university (≥ 4 years). Household income was reported according to four categories: low (less than NOK 451000, approximately 12,000 British pound sterling (GBP), lower middle (NOK 451–750,000), upper middle (NOK 751000–1 million) or high (more than NOK 1 million, approximately 80,000 GBP).

Table 1 Questions included in the WI-6

Question	Text
1	Do you think there is something seriously wrong with your body?
2	Do you worry a lot about your health?
3	Is it hard for you to believe the doctor when he tells you there is nothing to worry about?
4	Do you often worry about the possibility that you have a serious illness?
5	If a disease is brought to your attention (e.g., via TV, radio, internet, newspapers or someone you know), do you worry about getting it yourself?
6	Do you find that you are bothered by many different symptoms?

Previous research [23, 26, 32] has found social factors to be related to the level of HA. "Do you live with a spouse/partner?" was reported as "yes" or "no". Due to their large correlation, two questions about the quality of friendship ("Do you have enough friends who can give you help and support when you need it?" and "Do you have enough friends you can talk confidentially with?") were merged into a variable named "Quality of friendship", which included three categories: no, for those who answered "no" to both original questions; to some extent, for those who answered "yes" to only one original question; and yes, for those who answered "yes" to both original questions. Finally, the participants reported their participation in organized activity with the following options: "never or just a few times a year", "1-2 times a month", "approximately once a week" or "more than once a week".

Demographic variables The demographic variables included gender and age as of 31.12.2015.

Statistical analysis

All analyses were performed with STATA version 16.1 (STATA Corp LP, College Station, Texas, USA). Participants were excluded if they had missing or invalid responses to the outcome variables or the exposure variable. As a sensitivity analysis, we repeated all analyses for participants who also had complete responses to all confounders. Since there were no changes in the results, we include participants with complete responses to the exposure (HA) and outcome variables in the results section.

In the descriptive analyses, means (medians) were calculated for the continuous variables, and frequency distributions were calculated for the categorical variables. The associations between HA and different levels of healthcare use are presented as summary plots. HA was included as an exposure variable in all regression analyses and supplemented with relevant confounders. The analyses were conducted in a stepwise manner; we first presented an unadjusted model, then a model adjusted for morbidity, and finally a third model adjusted for all relevant confounders. The level of statistical significance (p-value) was set at 0.05.

As the proportional odds assumption was not met for the ordinal regression for either outcome variable, we used unconstrained continuation-ratio regression analysis [37] to model healthcare use. The unconstrained continuation-ratio model compared each level of healthcare use with all lower response levels and allowed the odds ratio (OR) to vary for each comparison [37]. The ORs were thus interpreted as threshold-specific exposure effects [38], where the effect of exposure (X) depended on the category (Y).

We explored possible interactions between morbidity and healthcare use by adding an interaction term in the regression model and performed stratified analyses where applicable.

Ethics

The study was conducted in accordance with the Declaration of Helsinki and was approved by the Regional Committee for Medical and Health Research Ethics (ID 2016/1793). All participants gave written informed consent before admission.

Results

Participant characteristics and descriptive statistics of healthcare use in the study population

A total of 21,083 persons aged between 40 and 99 years participated in this study; 52.5% were women, and the mean age was 56 (SD 11) years. After excluding participants with missing or invalid responses for the outcome or exposure variables, 18,499, 18,311 and 18,158 participants reported whether they had used primary healthcare, somatic specialist healthcare and mental healthcare, respectively, during the last 12 months. The distribution of users was different across the three healthcare services; 80% reported having consultations in primary healthcare the past 12 months, whereas 40% reported having consultations in somatic specialist healthcare, and 4% reported having consultations in mental specialist healthcare. The frequency distribution of participants and number of consultations are presented in Table 2.

Among the users of either healthcare service, the median numbers of consultations were 2 consultations for primary and somatic specialist healthcare and 6 consultations for mental healthcare in the past 12 months. The mean (median) WI-6 score for all participants was 3.1 (2) out of 24 points, with a mode of 0. The mean (median) numbers of contacts with primary healthcare, somatic specialist healthcare and mental specialist healthcare in the last year by HA, social and demographic variables and somatic and mental morbidity are outlined in Table 3. In categorizing HA according to the quartiles of the WI-6 score, we found that healthcare use increased with increasing HA, especially in primary and somatic specialist healthcare.

The association between health anxiety and healthcare use

Healthcare use increased with increasing HA for both primary healthcare (Fig. 1a) and somatic healthcare (Fig. 1b). However, there was more uncertainty regarding the association between HA and mental specialist healthcare use (Fig. 1c) due to the few users of this health

Table 2 Frequency distribution of healthcare utilisation (primary, somatic specialist and mental specialist healthcare use), and associated health anxiety measured by WI-6, mean(median) values

Variable	Categories	Levels of use	N	Percent	HA by WI-6, mean(median)
Primary healthcare (PHC)	Non-use		3753	20%	1.9 (1)
	PHC users:	1st level (1 consultation)	3904	21%	2.3 (1)
		2nd level (2 consultations)	3558	19%	2.9 (2)
		3rd level (3–4 consultations)	3706	20%	3.6 (3)
		4th level (5–89 consultations)	3578	20%	4.9 (4)
	Total		18,499	100%	
Somatic specialist healthcare (SSHC)	Non-use		11,050	60%	2.6 (2)
	SSHC users:	1st level (1 consultation)	2902	16%	3.1 (2)
		2nd level (2 consultations)	1841	10%	3.7 (3)
		3rd level (3 consultations)	828	5%	4.0 (4)
		4th level (4–170 consultations)	1690	9%	4.9 (4)
	Total		18,311	100%	
Mental specialist healthcare (MSHC)	Non-use		17,517	96%	2.9 (2)
	MHC users:	1st level (1–3 consultations)	202	1%	5.1 (4)
		2nd level (4–6 consultations)	146	1%	4.7 (4)
		3rd level (7–12 consultations)	148	1%	5.1 (5)
		4th level (13–130 consultations)	145	1%	6.2 (6)
	Total		18,158	100%	

service. Table 4 presents the results of the regression analyses, presented as the ORs associated with each one-unit change in the WI-6 score.

An increased WI-6 score was positively associated with increased utilization of all three health services (Table 4). When we adjusted for confounders, including physical and mental morbidity, the association remained significant, and the OR was only marginally reduced.

The impact of health anxiety was larger with higher healthcare use

In primary and somatic specialist healthcare, the odds of increased use increased progressively with each one-point increase in the WI-6 score, indicating that the impact of HA was more prominent with higher healthcare use.

In the fully adjusted model, a one-point increase in the WI-6 score resulted in a 7% increased odds of the lowest level of use of primary healthcare compared to non-use. Furthermore, with a one-point increase in the WI-6 score, the OR of the highest level of use compared to all lower levels increased to 1.15.

In somatic specialist healthcare, a one-point increase in the WI-6 score resulted in a 5% increased odds of the lowest level of use compared to non-use. Similar to primary healthcare use, we found a progressive pattern in the OR of somatic specialist healthcare use, with a one-point increase in the WI-6 score increasing the OR of the highest level of use compared to all lower levels to 1.14.

Only 4% of the participants reported using mental specialist healthcare in the past 12 months. A one-point increase in the WI-6 score resulted in a 7% increased odds of use compared to non-use and a significant increase in the OR of a higher level of use compared to all lower levels. The association between HA and mental specialist healthcare use did not show the progressive pattern seen in primary and somatic specialist healthcare.

Adjusting for confounders, especially physical and mental morbidity, hardly affected the association between health anxiety and healthcare use

The association between HA and primary healthcare use and somatic specialist healthcare use remained nearly unchanged for the first level of use compared to that for non-use after adjustment for the confounders; after adjustment, the OR remained at 1.07 in primary care and changed from 1.06 to 1.05 in somatic specialist healthcare.

For higher levels of use, adjustment for the confounding variables only slightly reduced the effect measure for the OR for both primary and somatic specialist care use and was largest for primary healthcare use; the OR changed from 1.20 to 1.15 for the fourth level of use compared to

Table 3 Mean (median) number of consultations last year in primary healthcare (PHC), somatic specialist healthcare (SSHC) and mental specialist healthcare(MSHC) according to health anxiety, social and demographic variables and somatic and mental morbidity

Variable				PHC use, mean (median)	SSHC use, mean (median)	MSHC use, mean (median)
	Categories	N	Percent			
WI-6 score of HA	0 points	5162	26%	1.8 (1)	0.7 (0)	0.2 (0)
	1. quartile (1–2 points)	5564	28%	2.4 (2)	0.9 (0)	0.2 (0)
	2. quartile (3 points)	2048	10%	2.9 (2)	1.1 (0)	0.3 (0)
	3. quartile (4–6 points)	4645	23%	3.4 (2)	1.4 (0)	0.4 (0)
	4. quartile (7–24 points)	2847	15%	5.0 (4)	2.4 (1)	1.1 (0)
		20,266				
Age	40–49 years	6432	32%	2.7 (2)	1.1 (0)	0.6 (0)
	50–59 years	6035	30%	2.8(2)	1.1 (0)	0.4 (0)
	60–69 years	5179	24%	2.9 (2)	1.2 (0)	0.2 (0)
	70–79 years	2676	11%	3.4 (2)	1.4 (0)	0.04 (0)
	80 years or older	761	3%	4.3 (3)	2.0 (0)	0.1 (0)
	Total	21,083				
Gender	Female	11,074	51%	3.2 (2)	1.3 (0)	0.5 (0)
	Male	10,009	49%	2.5 (2)	1.0 (0)	0.2 (0)
	Total	21,083				
Educational level	Primary/partly secondary education	4796	23%	3.5 (2)	1.1 (0)	0.3 (0)
	Upper secondary education	5756	28%	3.0 (2)	1.2 (0)	0.3 (0)
	Tertiary education, short	4008	19%	2.9 (2)	1.2 (0)	0.4 (0)
	Tertiary education, long	6145	30%	2.4 (2)	1.2 (0)	0.5 (0)
	Total	20,705				
Household income	Low (less than NOK 451.000)	4545	23%	3.7 (2)	1.5 (0)	0.6 (0)
	Lower middle (NOK 451–750.000)	5884	29%	3.1 (2)	1.3 (0)	0.4 (0)
	Upper middle (NOK 751–1 million)	4741	23%	2.7 (2)	1.1 (0)	0.3 (0)
	High (More than NOK 1 million)	5015	25%	2.1 (1)	1.0 (0)	0.2 (0)
	Total	20,185				
Physical illness	None	10,924	52%	2.0 (1)	0.8 (0)	0.3 (0)
	One	6171	29%	3.3 (2)	1.4 (0)	0.4 (0)
	Two or more	3987	19%	4.8 (4)	2.2 (1)	0.4 (0)
	Total	21,082				
Mental illness	No	17,660	87%	2.6 (2)	1.1 (0)	N/A
	Yes, now	898	4%	6.0 (5)	1.9 (0)	
	Yes, previously	1826	9%	3.6 (3)	1.5 (0)	
		20,384				
HADS	Under 15 points	17,864	93%	N/A	N/A	0.2 (0)
	15 points or more	1268	7%			2.5 (0)
	Total	19,132				
Living with a spouse/partner	No	4609	23%	3.2 (2)	1.3 (0)	0.6 (0)
	Yes	15,283	77%	2.7 (2)	1.2 (0)	0.3 (0)
	Total	19,892				
Do you have friends you can get support from and talk confidentially with? ("Quality of friendship")	No	1621	8%	3.7 (2)	1.4 (0)	1.2 (0)
	To some extent	1774	9%	3.2 (2)	1.3 (0)	0.5 (0)
	Yes	17,117	83%	2.7 (2)	1.2 (0)	0.3 (0)
	Total	20,512				

Table 3 (continued)

Variable	Categories	N	Percent	PHC use, mean (median)	SSHC use, mean (median)	MSHC use, mean (median)
Participating in organised activity	Never, or just a few times a year	11,310	5%	3.0 (2)	1.2 (0)	0.4 (0)
	1–2 times a month	4981	24%	2.9 (2)	1.3 (0)	0.3 (0)
	Approximately once a week	2597	13%	2.7 (2)	1.2 (0)	0.3 (0)
	More than once a week	1856	9%	2.5 (2)	1.0 (0)	0.4 (0)
	Total	20,744				

all lower levels for primary care, whereas the OR changed from 1.16 to 1.14 for somatic specialist healthcare. The association between mental specialist healthcare use and HA was more affected by adjustment for the confounding variables; however, these results should be interpreted with caution due to few participants in the user groups compared to non-users.

Interaction between the WI-6 score and morbidity

We found a significant interaction between HA and physical illness regarding primary healthcare use, and stratified analyses are presented in Supplementary Table 1. For the participants reporting multimorbidity, the WI-6 score was not associated with the lower levels of use of primary healthcare (1–2 consultations), but a one-point increase in the WI-6 score resulted in a significant increase in the odds of a higher level of use compared to all lower levels.

There was also a significant interaction between the WI-6 and HADS scores that affected the use of mental specialist healthcare (Supplementary Table 2). Due to the few participants with HADS scores $\geq$15 points ($N=193$) distributed in the different levels of mental specialist healthcare use, only an unadjusted analysis was performed. In the unadjusted model, the WI-6 score was significantly associated with the first level of use compared to non-use for those with HADS scores $\geq$15 but was not significantly associated with increased levels of use.

Discussion

Main findings

In our study, we found that HA was independently and positively associated with the utilization of primary, somatic specialist and mental specialist healthcare. This significant association remained after we adjusted for confounders, including physical and mental morbidity. For all three health services, a one-point increase in the WI-6 score significantly increased the odds of a higher level of use compared to all lower levels. Although the magnitudes are relatively small, the estimates show how even a very small increase in health anxiety is associated with increased level all healthcare use. To our knowledge, we are the first to report that HA, as a continuous construct, in a general population is significantly associated with increasing levels of use of different healthcare services. This finding implies that lower levels of HA should also be recognized. Interestingly, the trends in these associations were similar across all health services, in contrast to our hypothesis.

Primary and somatic specialist healthcare use

Primary healthcare use largely occurs through self-initiated contact, and we found that increased levels of HA were associated with increasing levels of consultations. In accordance with other studies [20, 23, 28], this association was not altered by adjustment for mental or physical illness. However, we found a significant interaction between HA and the number of illnesses (Supplementary Table 1). For the participants with two or more present chronic illnesses, the association between HA and primary care use was not significant for infrequent users (1 or 2 consultations per year). Many patients with multimorbidity often have one or two consultations a year as an arrangement with their GPs and not as self-initiated contact, and their use may therefore not be triggered by HA.

The demand for service in specialist healthcare in Norway is predominantly driven by referrals from primary care, and it was therefore surprising that we found such a strong association between HA and all levels of somatic specialist healthcare use. The association between HA and somatic specialist healthcare use has been previously documented in patients [21, 22], but there have been few population studies. Bobevski et al. [28] reported that people with severe HA were more likely to use specialist medical services (OR 1.7) and to be frequent attenders in somatic specialist healthcare (OR 2.4). However, our results shown in Table 4 demonstrate that lower levels of

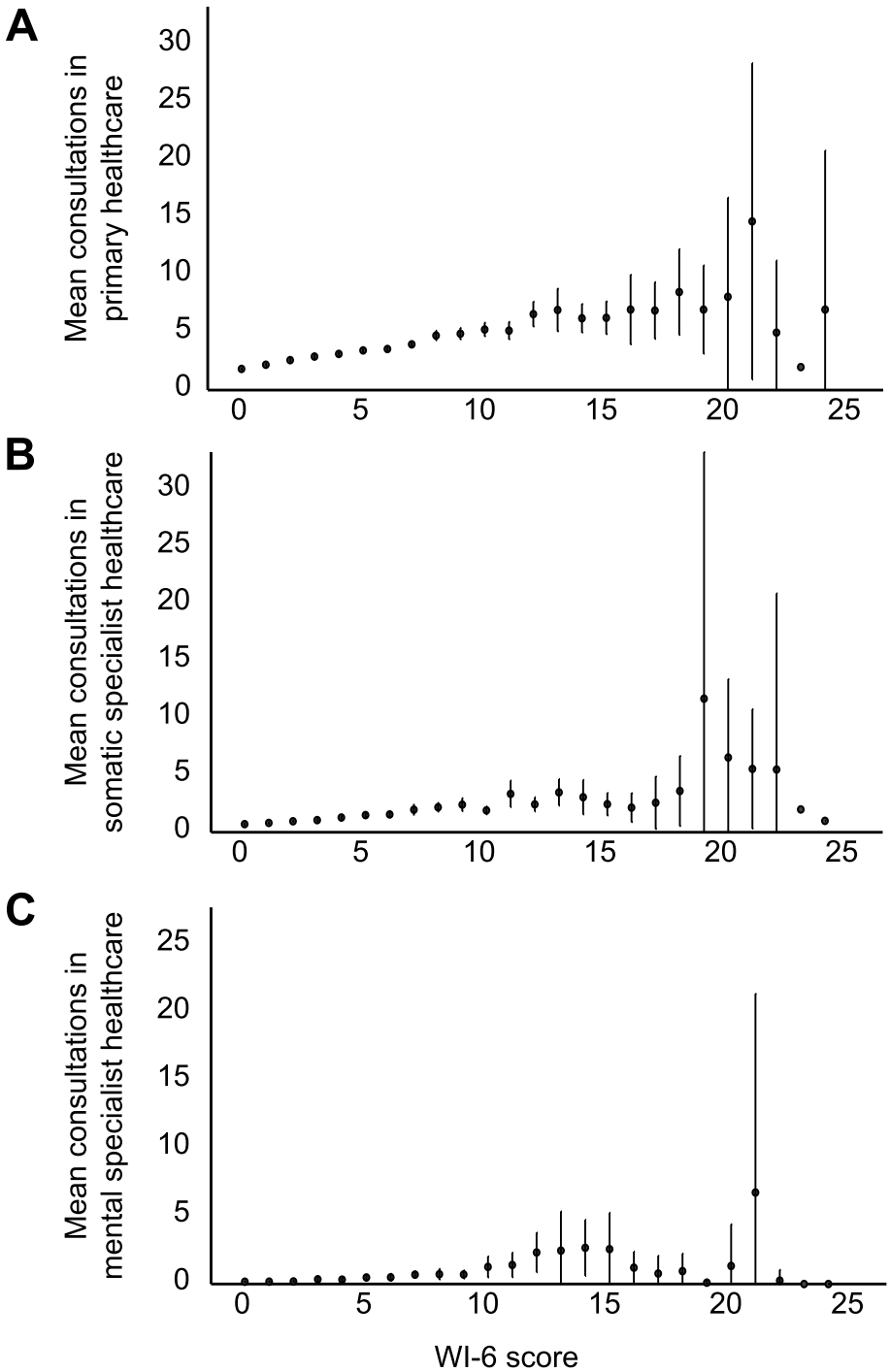

Fig. 1 The association between the exposure variable HA and healthcare use for the outcome variables primary healthcare (**a**), somatic specialist healthcare (**b**) and mental specialist healthcare (**c**), indicating mean healthcare use with 95% confidence intervals (Y axis) for each unit increase in the WI-6 score (X axis)

HA were also positively associated with somatic specialist healthcare use. This finding is supported by Hansen et al. [39], who found a dose-response association of HA and healthcare use in patients recruited from a hospital setting. Studies conducted in somatic specialist healthcare have reported a prevalence of severe HA among patients

Table 4 Unconstrained-continuation ratio regression models for healthcare utilisation (primary, somatic specialist and mental specialist healthcare). Odds ratio (OR) and 95% confidence interval (CI) shown for the exposure variable health anxiety

Outcome variable		OR (95% CI) represents:	Unadjusted model		Adjusted for physical and mental[a] morbidity		Fully adjusted model[b]	
			OR	95% CI	OR	95% CI	OR	95% CI
Primary healthcare, N: Unadjusted: *n* = 18,499, Adj. morbidity: *n* = 18,249 Fully adjusted: *n* = 16,603	Non-use		–		–		–	
	1st level of use	*1st* vs *non-use*	1.07**	1.05–1.08	1.05**	1.03–1.07	1.07**	1.05–1.09
	2nd level of use	*2nd* vs *1st level or lower*	1.10**	1.08–1.11	1.07**	1.06–1.09	1.08**	1.06–1.10
	3rd level of use	*3rd* vs *2nd level or lower*	1.14**	1.12–1.15	1.10**	1.09–1.12	1.11**	1.09–1.13
	4th level of use	*4th* vs *3rd level or lower*	1.20**	1.18–1.21	1.15**	1.14–1.16	1.15**	1.14–1.17
Somatic specialist healthcare, N: Unadjusted: *n* = 18,311, Adj. morbidity: *n* = 18,073 Fully adjusted: *n* = 16,389	Non-use		–		–		–	
	1st level of use	*1st* vs *non-use*	1.06**	1.04–1.07	1.04**	1.03–1.06	1.05**	1.03–1.06
	2nd level of use	*2nd* vs *1st level or lower*	1.09**	1.08–1.11	1.07**	1.06–1.09	1.09**	1.07–1.10
	3rd level of use	*3rd* vs *2nd level or lower*	1.10**	1.08–1.12	1.07**	1.05–1.09	1.08**	1.06–1.11
	4th level of use	*4th* vs *3rd level or lower*	1.16**	1.14–1.17	1.13**	1.11–1.14	1.14**	1.12–1.16
Mental specialist healthcare, N: Unadjusted: *n* = 18,158, Adj. morbidity: *n* = 16,636 Fully adjusted: *n* = 15,142	Non-use		–		–		–	
	1st level of use	*1st* vs *non-use*	1.15**	1.12–1.19	1.10**	1.06–1.14	1.07**	1.03–1.12
	2nd level of use	*2nd* vs *1st level or lower*	1.13**	1.08–1.17	1.06*	1.02–1.12	1.06*	1.01–1.11
	3rd level of use	*3rd* vs *2nd level or lower*	1.15**	1.11–1.19	1.07*	1.02–1.12	1.05*	1.01–1.11
	4th level of use	*4th* vs *3rd level or lower*	1.20**	1.16–1.24	1.09**	1.05–1.14	1.07*	1.02–1.13

* Significant below 0.05 level

** Significant below 0.01 level

[a] mental illness is registered with the question "have you had mental illness for which you have sought help?" when analysing primary and somatic specialist healthcare use, and with HADS for mental healthcare use

[b] Included adjustment variables: Age, gender, education, household income, physical and mental morbidity, living with a spouse/partner, quality of friendship and participation in organised activity

as high as 20–60% [22, 40], indicating that among those who use health services, HA is common.

Mental specialist healthcare

The association between HA and mental specialist healthcare use has been less examined. However, an Australian survey with 8841 participants aged 16–85 included questions concerning mental healthcare use. Based on this survey, Sunderland et al. [23] reported healthcare use due to a mental health problem, and Bobevski et al. [28] assessed whether HA was associated with healthcare use and explored high-frequency use of mental health services. Both studies reported that people with current HA, as a dichotomous construct, used mental healthcare more than those without HA. Bobevski et al. [28] found that HA was associated with increased odds of mental healthcare use but not with a higher frequency of use. We found significantly increased odds of higher use with even a small increase in HA. Our results should be interpreted as preliminary findings due to the relatively small proportion of participants who had used mental health services; however, we are the first to highlight that HA may also be an important factor for the frequency of consultations in mental specialist healthcare.

Strengths and limitations

One major strength of this study is the large representative sample, which enabled us to include users of different health services and non-users. The large study sample made it possible to explore different levels of healthcare use and examine HA as a continuous construct and therefore to assess healthcare use with increasing HA. The magnitude of healthcare use reported in our study is close to reports of national healthcare use [41, 42], indicating that the study participants are representative of the Norwegian population.

In the survey, the introduction to the HA questionnaire ("In the past 12 months, have you…") was omitted. This limited our knowledge of the time frame that the participants used as a reference. For people with established severe HA, HA shows little or no variation over time [13], but there is insufficient knowledge about the time variation in lower levels of HA.

All our results are based on self-reports, which are prone to recall bias. A Norwegian survey [43] found overall close agreement between self-reports regarding morbidity and medical records, with a tendency for under-reporting in self-report measures. Additionally, healthcare utilization has been found to be

under-reported in self-reports, especially with increased healthcare use and in older age [44]. If under-reporting was a factor in this study, the strength of the observed association may have been under-estimated.

Because of our cross-sectional design, we cannot conclude whether HA is the cause of increased healthcare use or a consequence of use. However, prospective studies have found that HA is an independent predictor of future healthcare utilization, independent of morbidity [31, 39]. As there is an increase in healthcare use even with low levels of HA (Fig. 1) and independent of morbidity, the association can hardly be explained by experiences of the healthcare system. We therefore believe that HA was a driver of healthcare use in our study.

Impact of HA on healthcare utilization

Most people with severe HA contact their GPs rather than other health personnel [18]; however, HA is often unrecognized since the patient's somatic complaints dominate the clinical encounter. Severe HA is a persistent condition if left untreated, and misguided treatment, screening and reassurance from somatic healthcare might not reduce or might even trigger underlying anxiety rather than treat it [18]. The mean level of HA in our population was 3.1 with a mode of 0, indicating that the majority of participants had low levels of HA. This may be interpreted as a normal attitude towards own health. However, even the lower HA scores were associated with increased healthcare use. All questions included in the WI-6 indicates a negative value, and there is no evidence that a lower score indicate health negligence. When background illness is accounted for, all use initiated by health anxiety can be considered overuse. For healthcare services overall, this association contributes to a large number of consultations per year.

Only a small proportion of the participants in our study were frequent users of specialist health services. However, 25% of the participants had 1–2 consultations with somatic specialist healthcare (Table 2). HA seems to be an important driver of these consultations. Although GPs maintain that medical reasons are the main reason for referrals, a significant number of referrals are provided to reassure the patient [2]. This finding is in accordance with our results, indicating that HA is an independent driver of healthcare use in specialist health services. The increased use of specialized healthcare with increasing HA may raise the risk for over-diagnosis and over-treatment and inappropriate use of healthcare, especially in somatic specialist care. Optimally, lower levels of HA in patients should be recognized and dealt with in primary healthcare. If HA assessment fails and patients are referred, the consequences for both patient and specialist care may be large. This study indicates that also lower levels of HA should therefore be of increased focus in patient consultations.

This study makes an important contribution to the research field of HA, in which most studies have explored HA as a dichotomous condition that is either severe or non-existent. Our results support previous research showing a dose-response association between HA and healthcare use [39] and suggest that not only severe HA is severe.

Conclusions

Our study demonstrates that HA, as a continuous construct, was significantly and positively associated with the utilization of primary, somatic specialist and mental specialist healthcare in an adult general population. One small increase in HA was associated with progressively increased healthcare use across the three health services, indicating that the impact of HA is more prominent for higher healthcare use.

Abbreviations

HA: Health anxiety; WI-6: Whiteley Index-6; GP: General practitioner; OR: Odds ratio; PHC: Primary healthcare; SSHC: Somatic specialist healthcare; MSHC: Mental specialist healthcare; HADS: Hospital Anxiety and Depression Scale; GBP: British pound sterling; NOK: Norwegian kroner.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12913-022-07529-x.

Additional file 1.

Additional file 2.

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Authors' contributions

All authors contributed to designing the study, interpreting results and revising the manuscript. ADN conducted the data analyses and wrote the manuscript with the assistance of BA, OHF and UR. All authors have read and approved the final manuscript.

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Availability of data and materials

All data are available by applying to the Tromsø Study: https://uit.no/research/tromsoundersokelsen

Declarations

Ethics approval and consent to participate

The study was conducted in accordance with the Declaration of Helsinki and was approved by the Regional Committee for Medical and Health Research Ethics (ID 2016/1793). All participants gave written informed consent before admission.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

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Publisher's Note

Supplementary Table 1: Associations between health anxiety and primary healthcare use, stratified by the presence of present physical illness

		If physical illness: None				**If physical illness: One**				**If physical illness: Two or more**			
		Unadjusted		**Fully adjusted model[b]**		**Unadjusted**		**Fully adjusted model[b]**		**Unadjusted**		**Fully adj. model [b]**	
Outcome variable		OR	†95 % CI			OR	†95 % CI					OR	†95 % CI
Primary healthcare	Non-use	-		-		-		-		-		-	
	1st level of use	1.07**	1.05 - 1.09	1.07**	1.04 - 1.10	1.04*	1.00 – 1.08	1.05**	1.02 - 1.10	1.02	0.96 - 1.08	1.04	0.97 - 1.10
	2nd level of use	1.10**	1.08 - 1.12	1.11**	1.08 - 1.13	1.07**	1.05 – 1.10	1.08**	1.04 - 1.11	1.02	0.98 - 1.05	1.03	0.98 - 1.07
	3rd level of use	1.15**	1.13 - 1.16	1.14**	1.12 - 1.17	1.09**	1.07 – 1.12	1.10**	1.07 - 1.13	1.09**	1.06 - 1.12	1.09**	1.05 - 1.12
	4th level of use	1.22**	1.20 – 1.24	1.20**	1.17 - 1.23	1.16**	1.14 – 1.18	1.15**	1.13 - 1.18	1.11**	1.08 - 1.14	1.10**	1.07 - 1.13

* Significant below 0.05 level

** Significant below 0.01 level

[b] Included adjustment variables: Age, gender, education, household income, physical and mental morbidity, living with a spouse/partner, quality of friendship and participation in organised activity

Supplementary Table 2: Unadjusted association between health anxiety and mental specialist healthcare use, stratified by HADS score

		If HADS score below 15 points		**If HADS score ≥15 points**	
		Unadjusted model		**Unadjusted model**	
Outcome variable		OR	†95 % CI	OR	†95 % CI
Mental specialist healthcare	Non-use	-		-	
	1st level of use	1.12**	1.07 - 1.17	1.08*	1.02 – 1.15
	2nd level of use	1.10**	1.04 - 1.17	1.01	0.94 – 1.08
	3rd level of use	1.11**	1.05 - 1.18	1.01	0.95 – 1.08
	4th level of use	1.15**	1.08 – 1.22	1.04	0.98 - 1.10

* Significant below 0.05 level

** Significant below 0.01 level

Paper 3

Norbye AD, Abelsen B, Førde OH, Ringberg U.

The association between health anxiety, physical disease and cardiovascular risk factors in the general population – a cross-sectional analysis from the Tromsø study: Tromsø 7.

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RESEARCH Open Access

The association between health anxiety, physical disease and cardiovascular risk factors in the general population – a cross-sectional analysis from the Tromsø study: Tromsø 7

Anja Davis Norbye*, Birgit Abelsen, Olav Helge Førde and Unni Ringberg

Abstract

Background: Health anxiety (HA) is defined as a worry of disease. An association between HA and mental illness has been reported, but few have looked at the association between HA and physical disease.

Objective: To examine the association between HA and number of diseases, different disease categories and cardiovascular risk factors in a large sample of the general population.

Methods: This study used cross-sectional data from 18,432 participants aged 40 years or older in the seventh survey of the Tromsø study. HA was measured using a revised version of the Whiteley Index-6 (WI-6-R). Participants reported previous and current status regarding a variety of different diseases. We performed exponential regression analyses looking at the independent variables 1) number of diseases, 2) disease category (cancer, cardiovascular disease, diabetes or kidney disease, respiratory disease, rheumatism, and migraine), and 3) cardiovascular risk factors (high blood pressure or use of cholesterol- or blood pressure lowering medication).

Results: Compared to the healthy reference group, number of diseases, different disease categories, and cardiovascular risk factors were consistently associated with higher HA scores. Most previous diseases were also significantly associated with increased HA score. People with current cancer, cardiovascular disease, and diabetes or kidney disease had the highest HA scores, being 109, 50, and 60% higher than the reference group, respectively.

Conclusion: In our general adult population, we found consistent associations between HA, as a continuous measure, and physical disease, all disease categories measured and cardiovascular risk factors.

Keywords: Health anxiety, Whiteley index, Epidemiology, Chronic diseases, Cardiovascular risk factors

Background

Health anxiety (HA) is defined as a worry of disease ranging from mild worry to excessive anxiety [1–3], although previous research has most commonly employed cut-offs to define high HA. HA is associated with both increased healthcare use [4] and disability benefits [5]. In a general population, people with a history of HA are substantially more likely to experience at least one physical or mental health disorder [6]. The prevalence of people living with a physical disease is growing due to an aging population and improvements in diagnostics and treatment [7, 8]. Further, primary prophylactic treatment of cardiovascular risk factors is increasing due to routine screening [9] and a decline in the cut-off used to define people at risk. Although screening for cardiovascular risk factors has not led

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to an increase in mental distress [10], we have little knowledge about the association with HA. Therefore, the association between HA and physical disease and cardiovascular risk factors deserves increased attention and relevance in clinical work.

The association between HA and physical disease has mostly been explored within specific patient groups. High HA has been reported in several patient populations with different physical diseases, such as cancer [11], cardiovascular disease [12, 13], diabetes [14], and kidney disease [15]. In addition, different studies have examined disease-specific anxiety such as fear of cancer recurrence [16], fear of hypoglycaemia [17], and cardiac anxiety [18]. However, a recent review [19] proposed that these are dimensions of the broader HA concept, and pointed out that disease-specific measurements in disease-specific populations make comparison between different diseases difficult.

The association between HA and physical disease and risk factors for disease has been less explored in the general population; only three studies on the topic have been published, with inconsistent results [6, 20, 21]. To our knowledge, only one study, published by Noyes and colleagues in 2000, has examined the association between HA and various diseases in a general adult (aged 40-65 years) population [22]. They found that high blood pressure, stroke, and chronic lung disease were associated with high HA. All of these studies used a single cut-off to dichotomise high and low HA, and to-date, no one has looked at this association while measuring HA as a continuous construct. HA is reported to be unequally distributed in the population [2], with no clear cut-offs to define high HA. In accordance with Rachman [1] and Ferguson [3], we support the idea that HA in the general population should be assessed as a continuous construct.

The aim of the present paper was to examine the association between HA and 1) number of diseases, 2) different disease categories, and 3) cardiovascular risk factors in a large sample of the general population.

Methods

Study design and population

The Tromsø study is a large Norwegian population-based health survey, where inhabitants of the municipality of Tromsø have been invited to seven different surveys (Tromsø 1-7) since in 1974 [23]. The present paper used cross-sectional, self-reported data from Tromsø 7, which was conducted in 2015-2016. All inhabitants aged 40 years or older (n = 32,591) were invited by post and received two reminders to participate. Informed consent was given upon attendance, where both self-reported and clinical measures were collected. This study only utilized self-reported measurements. Of the invited participants to the Tromsø 7, 21,083 gave informed consent and participated in this study (response rate of 65%). Only information concerning age and gender of non-participants were collected.

Variables

Dependent variable

We measured HA using a validated and modified one-factor, six-item Whiteley Index-6 (WI-6-R) (Table 1), which was included in the Tromsø 7 questionnaire. The WI-6-R has satisfactory psychometric properties [24] in a general population. Respondents answered each item on a 5-point Likert scale (0="not at all", 1="to some extent", 2="moderately", 3="to a considerable extent", 4="to a great extent"). Item scores were then summed to create a HA score ranging from 0 to 24, with higher scores indicating higher HA.

Independent variables

Participants gave information on the following diseases: heart failure, atrial fibrillation, angina pectoris, myocardial infarction, stroke, diabetes, kidney disease, chronic bronchitis/emphysema/chronic obstructive pulmonary disease, asthma, cancer, rheumatoid arthritis, osteoarthritis, and/or migraine. Response options were "no", "yes, now", or "previously, not now" for each disease except myocardial infarction and stroke, where only "no" and "previously, not now" were possible. Participants also

Table 1 Questions included in the Whiteley Index-6-R

Item	Text
1	Do you think there is something seriously wrong with your body?
2	Do you worry a lot about your health?
3	Is it hard for you to believe the doctor when he tells you there is nothing to worry about?
4	Do you often worry about the possibility that you have a serious illness?
5	If a disease is brought to your attention (e.g., via TV, radio, internet, newspapers or someone you know), do you worry about getting it yourself?
6	Do you have recurring thoughts about being ill that are difficult to get off your mind?

reported cardiovascular risk factors (high blood pressure, use of blood pressure lowering medication, or use of cholesterol lowering medication), now or previously.

When examining the association between HA score and number of diseases (number of diseases analysis), participants were categorised according to number of diseases (0, 1, 2, 3, >4), past or current, and cardiovascular risk factors were not counted as diseases. When examining the association between HA score and disease category (disease category analysis), we grouped the different diseases into eight disease categories, and cardiovascular risk factors were included as a separate category (Table 2).

Confounders

We included four groups of possible confounders in the analyses: disease-related variables, socioeconomic, social network, and demographic variables, all of which were taken from the Tromsø 7 questionnaire. The disease-related variables included disease in first-degree relatives and self-reported mental illness by the Hospital Anxiety and Depression Scale (HADS). Participants were asked if their first-degree relatives had any of the following: angina pectoris, stroke, asthma, diabetes, breast cancer, prostate cancer, colon cancer, or myocardial infarction before the age of 60. Participants were categorised as "yes" if they reported that their first-degree relatives had one or more of these diseases, and "no" if they had none of them. Disease in first-degree relatives was chosen as a confounder as we hypothesised that HA may be affected by disease in close family [1], and since many of the diseases can be hereditary. Mental illness is associated with HA [6] and physical disease [25–27]. We therefore included the measurement tool HADS [28] as a confounder. HADS is a questionnaire based on participants' responses to 14 questions concerning symptoms of anxiety and depression in the last week, with a total range of 0-42. Due to the diverse use of cut-offs for HADS total score [29], we used HADS as a continuous measure, except for descriptive purposes.

Socioeconomic variables were considered confounders based on associations with both HA [2] and physical disease [30]. Participants reported highest level of completed education (primary education up to 10 years of schooling, vocational/upper secondary education ≥3 years, college/university <4 years, or college/university ≥4 years) and annual household income, which was categorised as low (NOK <451,000), lower middle (NOK 451-750,000), upper middle (NOK 751000-1 million), or high (NOK >1 million). There were two social network variables: participation in organised activities and friendship. Both are associated with HA [2] and physical disease [31]. Response options for participation in organised activities were "never or just a few times a year", "1-2 times a month", "approximately once a week", or "more than once a week". The friendship variables included two questions: "Do you have enough friends who can give you help and support when you need it?" and "Do you have enough friends with whom you can talk confidentially?" Response options were "yes" and "no", and these were merged and coded as "no", for those who answered "no" to both questions; "to some extent", for those who answered "yes" to only one question; and "yes", for those who answered "yes" to both questions. Finally, demographic variables included gender and age as of 31 December 2015.

Statistical analyses

No participants were excluded prior to the analyses, but missing values were consequently excluded in the analyses and all results are therefore presented as complete-case. In the disease category analysis, disease categories were exclusive, thus participants with diseases in two different categories (e.g. cancer and angina pectoris) were excluded. However, participants were not excluded if they had cardiovascular risk factors in addition to a specific disease category, e.g. high blood pressure in addition

Table 2 Overview of disease categories and respective included diseases from the Tromsø study: Tromsø 7 (2015-2016)

Disease category	Included diseases
No disease	None of the below mentioned
Cancer	Cancer
Cardiovascular disease	Heart failure, atrial fibrillation, angina pectoris, myocardial infarction, stroke
Diabetes or kidney disease	Diabetes, kidney disease
Respiratory disease	Asthma, chronic bronchitis/emphysema/chronic obstructive pulmonary disease
Rheumatism	Rheumatoid arthritis, osteoarthritis
Migraine	Migraine
Cardiovascular risk factors	High blood pressure, use of blood pressure or cholesterol lowering medication

to cancer. Participants could state several diseases within each disease category, e.g. angina pectoris and heart failure. If they answered "previously, not now" for one disease and "yes, now" for another within the same disease category, they were categorised as "yes, now". We set the reference group for all analyses as participants who reported both no current or previous physical disease and no cardiovascular risk factors (healthy reference group).

In the descriptive analyses, frequency distributions are presented for categorical variables, and mean (Standard deviation, SD) median [quartiles 1, 3] for continuous variables. All analyses were performed with STATA version 16.1 (STATA Corp LP, College Station, Texas, USA).

Due to the non-normal and highly skewed distribution of the dependent variable HA, we used bivariate and multivariate exponential regression analyses to detect associations. The regression coefficients in the estimated models are presented with the exponentiated beta [exp(b)], where exp.(b) describes the percentage change in the WI-6-R score relative to the reference category for the different other categories.

The unadjusted regression model included the disease category independent variable, and the adjusted model adjusted for all specified confounders. We tested for two possible interactions: physical diseases and education and physical diseases and age, with the hypotheses that people with a higher education level would have more resources to handle disease, and that younger and older participants would deal with illness differently. However, no interactions were evident.

Ethics

The study was conducted in accordance with the Declaration of Helsinki and was approved by the Regional Committee for Medical and Health Research Ethics (REC North) in Norway (ID 2016/1793). All participants gave written informed consent before admission.

Results

Participant characteristics

Of the 21,083 Tromsø 7 participants (age range: 40-99 years; mean 56, SD 11), 52.5% were women. Supplementary Table 1 shows participant characteristics of the confounders. In total, 18,432 participants had complete information on the number of diseases and cardiovascular risk factors. Of these, 17,997 had completed the WI-6-R. The mean (SD) median [quartiles] HA score was 3.26 (3.39), 2[1,5] out of 24 points in the population, and HA scores increased with increasing number of diseases (Table 3).

For all the investigated disease variables, having no disease was the most common, with increased HA observed among those with one or more diseases, those who fell into any disease category, and those with cardiovascular risk factors. For most diseases, the mean HA score was higher among those with current disease compared to those with previous disease.

Association between health anxiety, physical disease, and cardiovascular risk factors

There was a significant, positive association between HA score and number of diseases, and between HA score and disease categories (Table 4). In the fully adjusted model, participants reporting one physical disease had 29% higher HA scores than the healthy reference group, and participants with four or more physical diseases had a two-fold increase in HA scores compared to the healthy reference group. HA was consistently associated with all disease categories, with higher HA scores in all disease categories compared to the healthy reference group.

For all disease categories, current disease was associated with higher HA scores than previous disease. Moreover, in most disease categories except previous diabetes or kidney disease and previous rheumatism, those with previous disease had higher HA scores than the healthy reference group. Participants with current cancer had the highest HA scores; twice as high as in the healthy reference group. Participants with current cardiovascular disease and current diabetes or kidney disease had an increase in HA scores of 50 and 60%, respectively, compared to the healthy reference group. Participants with cardiovascular risk factors also had a significant, 24% increase in HA scores compared to the healthy reference group.

Discussion

The aim of our study was to explore the association between HA and physical disease. We found several important and consistent results: Increasing number of diseases was associated with significantly higher HA scores. Both people reporting current and previous disease had higher HA scores compared to the healthy reference group. Cancer, cardiovascular diseases, and diabetes or kidney disease showed the strongest association with HA. Finally, participants with cardiovascular risk factors had significantly higher HA scores than the healthy reference group. To our knowledge, this is the first paper to demonstrate how HA is associated with both number of physical diseases, different disease categories, current and previous disease, and cardiovascular risk factors in the general population.

The HA scores we observed among those with four or more diseases were twice as high as scores among those with no diseases, and we believe this to be a novel finding. Although some studies have found an association

Table 3 Mean (SD) and median [quartiles 1, 3] health anxiety (HA) score according to number of physical diseases, disease category, and cardiovascular risk factors. Data from The Tromsø study: Tromsø 7 (2015-2016)

		N	Percent	Mean (SD), median [quartiles] HA score as indicated by the Whiteley Index-6-R
Number of physical diseases, 5 categories	None	7231	43%	2.28 (2.83), 1 [0-4]
	One disease	5801	35%	2.92 (3.14), 2 [0-4]
	Two diseases	2342	14%	3.54 (3.53), 3 [1-5]
	Three diseases	818	5%	4.23 (3.73), 3 [1-6]
	Four or more diseases	389	2%	4.80 (4.24), 4 [2-7]
	Total	16,581		
Disease category				
Cancer	No	7231	93%	2.28 (2.83), 1 [0-4]
	Previously, not now	450	6%	2.84 (3.14), 2 [0-4]
	Yes, now	127	2%	4.59 (4.09), 4 [1-6]
	Total	7808		
Cardiovascular disease	No	7231	88%	2.28 (2.83), 1 [0-4]
	Previously, not now	694	8%	2.95 (3.05), 2 [0-5]
	Yes, now	295	4%	3.51 (3.66), 2 [1-5]
	Total	8220		
Diabetes or kidney disease	No	7231	93%	2.28 (2.83), 1 [0-4]
	Previously, not now	154	2%	2.70 (2.76), 2 [1-4]
	Yes, now	371	5%	3.65 (3.62), 3 [1-5]
	Total	7756		
Respiratory disease	No	7231	87%	2.28 (2.83), 1 [0-4]
	Previously, not now	355	4%	2.66 (2.72), 2 [0-4]
	Yes, now	724	9%	3.02 (3.28), 2 [1-4]
	Total	8310		
Rheumatism	No	7231	81%	2.28 (2.83), 1 [0-4]
	Previously, not now	130	1%	2.12 (2.90), 1 [0-4]
	Yes, now	1620	18%	2.97 (3.15), 2 [1-5]
	Total	8981		
Migraine	No	7231	84%	2.28 (2.83), 1 [0-4]
	Previously, not now	629	7%	2.67 (2.84), 2 [0-4]
	Yes, now	779	9%	2.86 (3.17), 2 [0-5]
	Total	8639		
Cardiovascular risk factors	No	7231	78%	2.28 (2.83), 1 [0-4]
	Yes	2096	22%	2.65 (2.86), 2 [0-4]
	Total	9327		

between high HA and having a disease [6, 20], only one previous study has examined the association between HA and the number of physical diseases [21]. In contrast to our study, they did not find any significant association between HA and increasing number of diseases. However, they used a cut-off to dichotomise high and low HA, which might have obscured a significant trend. Unlike previous studies that used different cut-offs to measure HA [6, 21, 22], we utilised HA as a continuum, which may better represent the phenomenon of HA.

As this is a cross-sectional study, it cannot determine causality. We speculate that the observed association may be explained by the presence of disease increasing the risk of having higher HA score [19]. However, high HA is also associated with high healthcare use [4], which may increase the probability of acquiring a diagnosis. In addition, we do not know if HA is itself is a risk factor for future disease. High levels of HA has been found associated with increased risk for ischaemic heart disease [32], whereas Knudsen and colleagues [33] found that

Table 4 Association between health anxiety score and number of diseases, and between health anxiety score and disease category, presented with exponential regression coefficients. Data from The Tromsø study: Tromsø 7 (2015-2016)

		Unadjusted model		Adjusted model[a]	
		Exp(b)	95% CI	Exp(b)	95% CI
Number of diseases, 5 categories	None	1		1	
Unadjusted model, *N* = 16,169	One disease	1.28[c]	1.23 – 1.32	1.29[c]	1.24 – 1.34
Adjusted model, *N* = 13,971	Two diseases	1.55[c]	1.48 – 1.63	1.53[c]	1.45 – 1.61
	Three diseases	1.85[c]	1.72 – 2.00	1.89[c]	1.74 – 2.05
	Four or more diseases	2.11[c]	1.90 – 2.34	2.09[c]	1.85 – 2.36
Disease category					
Cancer	No	1		1	
Unadjusted model, *N* = 7655	Previously, not now	1.24[c]	1.13 – 1.37	1.32[c]	1.18 – 1.46
Adjusted model, *N* = 6761	Yes, now	2.01[c]	1.68 – 2.41	2.19[c]	1.80 – 2.69
Cardiovascular disease	No	1		1	
Unadjusted model, *N* = 8047	Previously, not now	1.30[c]	1.19 – 1.43	1.29[c]	1.17 – 1.40
Adjusted model, *N* = 7076	Yes, now	1.44[c]	1.31 – 1.59	1.50[c]	1.31 – 1.72
Diabetes or kidney disease	No	1		1	
Unadjusted model, *N* = 7597	Previously, not now	1.18[b]	1.01 – 1.39	1.13	0.95 – 1.34
Adjusted model, *N* = 6702	Yes, now	1.60[c]	1.43 – 1.78	1.60[c]	1.42 - 1.81
Respiratory disease	No	1		1	
Unadjusted model, *N* = 8149	Previously, not now	1.17[b]	1.05 – 1.30	1.13[b]	1.01 – 1.26
Adjusted model, *N* = 7208	Yes, now	1.32[c]	1.23 – 1.43	1.36[c]	1.25 – 1.48
Rheumatism	No	1		1	
Unadjusted model, *N* = 8776	Previously, not now	0.93	0.78 – 1.11	1.05	0.87 – 1.27
Adjusted model, *N* = 7694	Yes, now	1.30[c]	1.23 – 1.38	1.38[c]	1.29 – 1.47
Migraine	No	1		1	
Unadjusted model, *N* = 8478	Previously, not now	1.17[c]	1.08 – 1.27	1.12[b]	1.03 – 1.21
Adjusted model, *N* = 7551	Yes, now	1.26[c]	1.17 – 1.35	1.13[c]	1.03 – 1.23
Cardiovascular risk factors	No	1		1	
Unadjusted model, *N* = 9132	Yes	1.16[c]	1.10 – 1.23	1.24[c]	1.17 – 1.31
Adjusted model, *N* = 8014					

[a] Confounders included: age, sex, education, household income, disease in first-degree relatives, HADS score, friendship, and participation in organised activity. [b] Significant below 0.05 level. [c] Significant below 0.01 level. *CI* Confidence interval

high HA was associated with increased cancer incidence in men. Further, no association was found between HA and cancer incidence in a cohort of women, but high HA was associated with increased all-cause mortality [34]. To better examine and understand causal directionality in the relationship between HA and different diseases, and to investigate if gender influences the role of HA, a cohort study design is warranted.

The association between HA and different diseases

We found significant associations between HA scores and all disease categories investigated in this study, which included the most common non-communicable chronic diseases. Our results are in accordance with previous findings of high HA in patient populations [11, 14, 15, 18, 35]. Current cancer, cardiovascular diseases, and diabetes or kidney disease was associated with the highest HA scores. Fear of cancer and cardiovascular disease is common in people with HA [1, 36]. Having current diabetes or kidney disease was also highly associated with HA scores in this study. Diabetes control requires strict adherence and bodily monitoring. Fear of complications was strongly associated with HA in a previous population of patients with diabetes [14], and may explain the high association between HA and this disease category in our study. Assuming that the diseases occurred prior to the HA, it could be reasonable to suggest that the bodily monitoring and fear of the fatal outcome may explain the high associations in this general population.

Another consistent finding was that those reporting previous disease had lower HA scores than those with current disease, but they had still higher scores than the healthy reference group. Although most of the diseases included in our study are considered chronic, their symptoms can be reduced by proper treatment. We therefore speculate that some of our participants may have

some disease, but proper management of that disease decreased both their symptom burden and HA.

Interestingly, we found a significant association between HA and cardiovascular risk factors, with a coefficient similar to coefficients for migraine and respiratory disease. The impact of a 24% increase in HA score in otherwise healthy persons indicates a potential health burden on a population level. In Norway, the proportion of 70-74-year-olds taking blood pressure- or cholesterol lowering medication is increasing [37]; and was as high as 57% in 2016 [38]. Primary healthcare in Norway is well-functioning [39]. It is reasonable to assume that those who report a cardiovascular risk factor receive treatment, and thereby are at lowered risk for future cardiovascular disease. It is therefore interesting that we observed such a pronounced association between cardiovascular risk factors and HA. This significant association is important in the discussion of adverse effects in identifying people "at risk".

Possible cohort effect

Older age is associated with lower HA [40], and as physical diseases are more prevalent in older individuals, we hypothesised that the association between HA and disease may differ by age. However, we did not find any significant interaction, indicating that having a disease is not associated with higher HA in younger (40 years) compared to older age groups. Moreover, mean HA has increased in student populations in the past three decades [41], and if there is, in fact, a cohort effect, it is likely that today's youth may experience an even higher HA later in life due to the increased prevalence of disease in older age groups.

Methodological considerations

As this study uses a cross-sectional study design, we cannot determine whether HA occurs prior to the disease or in response to the disease, and caution should be taken when making assumptions of the directions of associations. Nevertheless, we believe that this study shows novel findings of associations in a general population, which may lay the foundation for future prospective studies.

A strength of this study is the large, representative sample from the general population, which enabled us to examine the association between HA and different diseases. We chose to use a validated measurement tool, which is a strength in the research field of HA, and used a revised version that distinguished the cognitive construct of illness worry from the presence of physical symptoms [24]. Comparisons between studies are difficult due to the use of different HA measurement tools [19] as well as reporting of different diseases [7]. Although our results align with studies in other countries [6, 22] and patient populations [11, 12, 14, 15], our sample is exclusively from inhabitants in a specific geographic region in Norway, and replication in other populations would allow for further generalisation of the results.

All our data on the occurrence of disease was self-reported, and any misclassification may be due to recall bias. If the reporting of disease is related to HA, e.g. if those with low HA under-report disease more than those with higher HA, this could bias our results. However, a Norwegian study examining consistency among self-reported diagnoses and clinical registries found good overall consistency [42].

In our study, we asked about current or previous disease, not duration of disease. One article examining HA in cancer patients found that HA was consistent over time after diagnosis and also during remission [43], and high HA has also been described as stable over time [44]. However, one study carried out in a sample of patients with diabetes found that high HA was most highly associated with a recent diagnosis [14]. Another factor concerning morbidity is severity of disease (risk of fatal outcome, the need for disease monitoring, chronic disability, etc.), as most of the diseases in our disease categories may have a wide range of severity. Interestingly, Tu et al. [15] found that increased HA was independent of kidney disease severity. However, as disease severity and duration may have influenced participants' responses, the lack of this information may increase any heterogeneity of the associations presented.

The introduction to the questionnaire, stating the timeframe of the past 12 months, was omitted in the survey. This limits our knowledge of the timeframe during which the participants answered. Although severe HA has been found to be stable over time [44], this is unknown for people with lower HA scores.

As in all survey research, selection bias may occur. Unfortunately, we have no information on factors related to non-response in the Tromsø 7, other than age and gender. However, a similar survey found that chronic diseases, e.g. diabetes, was related to non-attendance [42], indicating that survey populations may be healthier than non-respondents. Although not previously examined, it has been hypothesised that, in contrast to other mental illnesses, people with HA attend studies that are advertised as a "health check-up" [5], which was done in Tromsø 7. If the participants in the Tromsø 7 were healthier, whilst having higher HA, our results may be biased towards the null.

As Lebel et al. [19] pointed out, there is an overlap between disease-specific measures and HA. Although disease-specific HA may be more precise than the more

general concept of HA, we believe that HA should be used in a larger and comparative perspective.

Clinical implications

Our study demonstrates a consistent trend in the association between HA and physical disease which confirms knowledge from clinical practice and highlights the importance of assessing and addressing HA in patients with either current or previous disease. Past research has shown associations between HA and a wide range of diseases in patient populations. In line with those results, we suggest that while the proportion of HA may not vary considerably between diseases, the mere presence of disease is associated with higher HA. This association is relevant from a clinical perspective, as over 50% of our study sample had one or more diseases (Table 3). Severe HA is associated with a wide range of negative consequences, such as functional impairment, activity limitations, psychological distress [6], and increased healthcare use and work disability [4, 5, 45], and should be managed through targeted treatment to reduce associated negative consequences. However, as we have found in this study, increasing number of diseases is associated with higher HA, but overall, HA remains low. However, some studies found an association between lower HA score and higher healthcare use [46, 47] and therefore we do not know how low HA is relevant from a clinical perspective. From a healthcare systems perspective, it is important to account for HA in the management of disease, particularly in those with increased number of physical diseases. Even when HA is not severe enough to require diagnosis and targeted treatment, we believe it important that healthcare personnel acknowledge and address the additional burden that HA may place on persons with current or previous physical disease and those with cardiovascular risk factors.

Conclusion

In our general adult population, we found consistent associations between HA and physical disease and cardiovascular risk factors. The highest HA scores were found among those with four or more diseases and participants with current cancer, but the positive association was consistent in all disease categories and cardiovascular risk factors. Previous disease was also associated with increased HA. Our results indicate that HA should merit closer attention in future research on populations with physical disease and risk factors for disease.

Abbreviations

HA: Health Anxiety; WI-6-R: Whiteley Index 6-R; HADS: Hospital Anxiety and Depression Scale.

Supplementary Information

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Additional file 1: Supplementary Table 1. Population characteristics of participants in the Tromsø study: Tromsø 7 (2015-2016) by confounding variables.

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Authors' contributions

All authors contributed to designing the study, interpreting results and revising the manuscript. ADN conducted the data analyses and wrote the manuscript with the assistance of BA, OHF and UR. All authors have read and approved the final manuscript.

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Availability of data and materials

The data that support the findings of this study are available from the Tromsø study but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of the Tromsø study: https://uit.no/research/tromsoundersokelsen

Declarations

Ethics approval and consent to participate

The study was conducted in accordance with the Declaration of Helsinki and was approved by the Regional Committee for Medical and Health Research Ethics (REC North) in Norway (ID 2016/1793). All participants gave written informed consent before admission.

Consent for publication

Not applicable.

Competing interests

None declared.

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Publisher's Note

Supplementary table 1. Population characteristics by confounding variables

Variable	Categories	N	Percent
Age	40-49 years	6 432	31 %
	50-59 years	6 035	29 %
	60-69 years	5 179	25 %
	70-79 years	2 676	13 %
	80 years or older	761	4 %
	Total	21 083	
Gender	Female	11 074	53 %
	Male	10 009	47 %
	Total	21 083	
Educational level	Primary/partial secondary education	4 796	23 %
	Upper secondary education	5 756	28 %
	Tertiary education, short	4 008	19 %
	Tertiary education, long	6 145	30 %
	Total	20 705	
Household income	Low (less than NOK 451 000)	4 545	23 %
	Lower middle (NOK 451-750 000)	5 884	29 %
	Upper middle (NOK 751 000-1 million)	4 741	23 %
	High (More than NOK 1 million)	5 015	25 %
	Total	20 185	
Disease in first-degree relatives	No	15 894	78%
	Yes	4 505	22 %
	Total	19 892	
HADS total score	Below 11 points	15 895	83 %
	11 points or more	3 237	17 %
	Total	19 132	
Friendship	No	1 621	8 %
	To some extent	1 774	9 %
	Yes	17 117	83 %
	Total	20 512	
Organized activity	Never or just a few times a year	11 310	55 %
	1-2 times a month	4 981	24 %
	Approximately once a week	2 587	13 %
	More than once a week	1 856	9 %
	Total	20 744	

Appendices

A. Ethical approval for the Tromsø study: Tromsø7, by the Regional Committees for Medical and Health Research Ethics (REK North) [Norwegian]

B. Ethical approval for the study from the Regional Committees for Medical and Health Research Ethics (REK North) [Norwegian]

C. The first questionnaire (Q1) in the Tromsø study: Tromsø7 [Norwegian]

D. Extracted pages from the second questionnaire (Q2) in the Tromsø study: Tromsø7, including the Hospital Anxiety and Depression Scale (HADS) [Norwegian]

E. List of external links related to the Tromsø study: Tromsø7 [Norwegian]

Appendix A

Ethical approval for the Tromsø study: Tromsø7, by the Regional Committees for Medical and Health Research Ethics (REK North) [Norwegian]

REK
REGIONALE KOMITEER FOR MEDISINSK OG HELSEFAGLIG FORSKNINGSETIKK

Region:	Saksbehandler:	Telefon:	Vår dato:	Vår referanse:
REK nord	Veronica Sørensen	77620758	10.02.2015	2014/940/REK nord
			Deres dato:	**Deres referanse:**
			18.12.2014	

Vår referanse må oppgis ved alle henvendelser

Anne Elise Eggen
Institutt for samfunnsmedisin

2014/940 Den sjuende Tromsøundersøkelsen (Tromsø 7)

Forskningsansvarlig institusjon: Institutt for samfunnsmedisin
Prosjektleder: Anne Elise Eggen

Prosjektleders prosjektomtale
Tromsøundersøkelsen er en forskerinitiert epidemiologisk kohortstudie med mulighet for å studere forekomst, forebygging og behandling av kroniske sykdommer og plager, sammenhengen mellom psyke og soma, tannhelse, bruk av helsetjenester og hvordan kronisk plager påvirker livskvalitet. Tromsøundersøkelsen har fulgt befolkningen i Tromsø siden 1974, og brukes til forskning og til å følge risikofaktorer for sykdom i befolkningen. I Tromsø 7 vil det samles inn helseopplysninger via spørreskjemaer, biologiske materiale, målinger og kliniske undersøkelser. Alle aktuelle deltakere blir forespurt til å delta i en del 1 (basisundersøkelse), med videre forespørsel om å delta i del 2 (omfattende, kliniske undersøkelser) til deler av utvalget. Oppstart er planlagt primo 2015 med avslutning ved årsskiftet 2016/17. Undersøkelsen er planlagt for invitasjon av alle 40-79 år, tidligere deltakere i Tromsøundersøkelsen 80 år og eldre, og tidligere deltakere i ungdomskohorten 22-25 år.

Vurdering
Vi viser til utfylt søknadsskjema, vedlagt protokoll og øvrige vedlegg.

Prosjektet var oppe til vurdering på komiteens møte 12.06.2014. Prosjektgruppen, representert ved Anne Elise Eggen, Heidi Johansen og Inger Njølstad var invitert til komiteens møte og hadde en gjennomgang av Tromsø 7. Komiteen fikk muntlig svar på spørsmål de hadde, men komiteen ba også om en revidert protokoll og informasjonsskriv. I tillegg ble det bedt om tilbakemelding på følgende merknader: Om beredskap/sikkerhet/tilbakemeldinger til deltakere, spørreskjema samt en nærmere avklaring av hva ungdomsgruppen Fit Future skulle inviteres til.

Prosjektleder har gitt tilfredsstillende tilbakemeldinger. REK har således ingen innvendinger mot Tromsø 7.

Prosjektleder har også lagt frem siste versjon av informasjonsskrivet. På side 6 under overskriften «Personvern» andre avsnitt, siste setning «…..(REK nord) har vurdert testene og undersøkelsene som gjennomføres samt godkjent innsamling av prøver « utgår. Dette er for upresist og må endres til «…….. (REK nord) «har gjort en etisk og helsefaglig vurdering av undersøkelsene som gjennomføres, samt godkjent innsamlingen av prøver.»

Etter fullmakt er det fattet slikt vedtak:

Vedtak
REK har vurdert helseundersøkelsens medisinske og etiske forsvarlighet og har ingen innvendinger.

Sluttmelding og søknad om prosjektendring
Prosjektleder skal sende sluttmelding til REK nord på eget skjema senest 30.06.2017, jf. hfl. § 12. Prosjektleder skal sende søknad om prosjektendring til REK nord dersom det skal gjøres vesentlige endringer i forhold til de opplysninger som er gitt i søknaden, jf. hfl. § 11.

Klageadgang
Du kan klage på komiteens vedtak, jf. forvaltningsloven § 28 flg. Klagen sendes til REK nord. Klagefristen er tre uker fra du mottar dette brevet. Dersom vedtaket opprettholdes av REK nord, sendes klagen videre til Den nasjonale forskningsetiske komité for medisin og helsefag for endelig vurdering.

Med vennlig hilsen

May Britt Rossvoll
sekretariatsleder

Veronica Sørensen
rådgiver

Kopi til:magritt.brustad@uit.no

Appendix B

Ethical approval for the study from the Regional Committees for Medical and Health Research Ethics (REK North) [Norwegian]

REK
REGIONALE KOMITEER FOR MEDISINSK OG HELSEFAGLIG FORSKNINGSETIKK

Region:	Saksbehandler:	Telefon:	Vår dato:	Vår referanse:
REK nord			01.11.2016	2016/1793/REK nord
			Deres dato:	Deres referanse:
			20.09.2016	

Vår referanse må oppgis ved alle henvendelser

Unni Ringberg
Institutt for samfunnsmedisin

2016/1793 Helseangst - forekomst, pasientbelastning og helsetjenestebruk. Tromsøundersøkelsen: Tromsø 7

Forskningsansvarlig: UiT Norges arktiske universitet
Prosjektleder: Unni Ringberg

Vi viser til søknad om forhåndsgodkjenning av ovennevnte forskningsprosjekt. Søknaden ble behandlet av Regional komité for medisinsk og helsefaglig forskningsetikk (REK nord) i møtet 20.10.2016. Vurderingen er gjort med hjemmel i helseforskningsloven (hfl.) § 10, jf. forskningsetikkloven § 4.

Prosjektleders prosjektomtale
Personer med helseangst (HA) oppfatter forandringer i kroppens utseende eller funksjon som skadelig/alvorlige eller tom. dødelige. Internasjonale studier har vist at de har dårlig egen-vurdert helse og høyt forbruk av helsetjenester. Effektiv psykologisk behandling finnes, med ofte tilbys de ikke rådgiving eller behandling. Det er svært få befolknings-studier av HA, kun en i Norge. Studien er epidemiologisk med tverrsnittdesign (data fra den pågåendeTromsø-undersøkelsen nr7 (T7)). Helseopplysninger innhentes vha. spørreskjema, bl.a. helsetjenesteforbruk, egen-vurdert helse og kroniske sykdommer. Grad av HA skåres vha. syv validerte spørsmål, med fem nivå (Whiteley-7). Studien vil gi estimater av forekomst (prevalens) av HA i grupper av befolkningen. Vi vil undersøke sammenhenger (associations) mellom helsetjenesteforbruk og HA, samt mellom egen-vurdert helse / kroniske sykdommer og HA. Resultatene vil øke kunnskap om HA og bidra til at personer med HA får bedre omsorg og behandling.

Vurdering

Komiteen vurderte at Oddgeir Friborg var inhabil jf. forvaltningslovens § 6 og han fratrådte møtet under behandling av dette prosjektet

Data
Helseopplysninger innhentes ved hjelp av spørreskjema om blant annet helsetjenesteforbruk, egen-vurdert helse og kroniske sykdommer.

Vedlagte protokoll opplyser om at dette er avidentifiserbare data fra Tromsøundersøkelsen 7.

Forespørsel/informasjonsskriv/samtykkeskriv - Tromsøundersøkelsene
Det vises til allerede innhentet samtykke i forbindelse med helseundersøkelsen Tromsø 7

Komiteen vurderer at samtykket er dekkende.

Besøksadresse:
MH-bygget UiT Norges arktiske universitet 9037 Tromsø

Telefon: 77646140
E-post: rek-nord@asp.uit.no
Web: http://helseforskning.etikkom.no/

Vedtak

Med hjemmel i helseforskningsloven §§ 2 og 10 godkjennes prosjektet.

Sluttmelding og søknad om prosjektendring
Prosjektleder skal sende sluttmelding til REK nord på eget skjema senest 01.01.2024, jf. hfl. § 12. Prosjektleder skal sende søknad om prosjektendring til REK nord dersom det skal gjøres vesentlige endringer i forhold til de opplysninger som er gitt i søknaden, jf. hfl. § 11.

Klageadgang
Du kan klage på komiteens vedtak, jf. forvaltningsloven § 28 flg. Klagen sendes til REK nord. Klagefristen er tre uker fra du mottar dette brevet. Dersom vedtaket opprettholdes av REK nord, sendes klagen videre til Den nasjonale forskningsetiske komité for medisin og helsefag for endelig vurdering.

Med vennlig hilsen

May Britt Rossvoll
Sekretariatsleder

Kopi til: magritt.brustad@uit.no
postmottak@uit.no

Appendix C

The first questionnaire (Q1) in the Tromsø study: Tromsø7 [Norwegian]

Tromsø-undersøkelsen
2015–2016

KONFIDENSIELT

Skjemaet skal leses optisk. Vennligst bruk blå eller sort penn. Bruk blokkbokstaver. Du kan ikke bruke komma.

Dato for utfylling: ☐☐☐☐☐☐

HELSE OG SYKDOMMER

1.1 Hvordan vurderer du din egen helse sånn i alminnelighet?

Meget god	God	Verken god eller dårlig	Dårlig	Meget dårlig
☐	☐	☐	☐	☐

1.2 Hvordan synes du at helsen din er sammenlignet med andre på din alder?

Mye bedre	Litt bedre	Omtrent lik	Litt dårligere	Mye dårligere
☐	☐	☐	☐	☐

1.3 Har du eller har du hatt?
Sett ett kryss per linje.

	Nei	Ja nå	Før, ikke nå	Alder første gang
Høyt blodtrykk	☐	☐	☐	☐☐
Hjerteinfarkt	☐		☐	☐☐
Hjertesvikt	☐	☐	☐	☐☐
Atrieflimmer *(hjerteflimmer)*	☐	☐	☐	☐☐
Angina pectoris *(hjertekrampe)*	☐	☐	☐	☐☐
Hjerneslag/hjerneblødning	☐		☐	☐☐
Diabetes	☐	☐	☐	☐☐
Nyresykdom *(unntatt urinveisinfeksjon)*	☐	☐	☐	☐☐
Kronisk bronkitt/emfysem/KOLS	☐	☐	☐	☐☐
Astma	☐	☐	☐	☐☐
Kreft	☐	☐	☐	☐☐
Revmatoid artritt *(leddgikt)*	☐	☐	☐	☐☐
Artrose *(slitasjegikt)*	☐	☐	☐	☐☐
Migrene	☐	☐	☐	☐☐
Psykiske plager *(som du har søkt hjelp for)*	☐	☐	☐	☐☐

1.4 Har du langvarige eller stadig tilbakevendende smerter som har vart i 3 måneder eller mer?

☐ Nei ☐ Ja

TANNHELSE

2.1 Hvordan vurderer du din egen tannhelse?

	1	2	3	4	5	
Svært dårlig	☐	☐	☐	☐	☐	Svært god

2.2 Hvor fornøyd eller misfornøyd er du med tennene eller protesene dine?

	1	2	3	4	5	
Svært misfornøyd	☐	☐	☐	☐	☐	Svært fornøyd

BRUK AV HELSETJENESTER

3.1 Har du, grunnet egen helse, i løpet av de siste 12 måneder vært hos:

	Nei	Ja	Antall ganger
Fastlege/allmennlege	☐	☐	☐☐
Legevakt	☐	☐	☐☐
Psykiater/psykolog	☐	☐	☐☐
Legespesialist utenfor sykehus *(utenom fastlege/allmennlege/psykiater)*	☐	☐	☐☐
Tannlege/tannpleier	☐	☐	☐☐
Apotek *(for kjøp/råd om medisiner/behandling)*	☐	☐	☐☐
Fysioterapeut	☐	☐	☐☐
Kiropraktor	☐	☐	☐☐
Akupunktør	☐	☐	☐☐
Alternativ behandler *(homøopat, soneterapeut, healer etc)*	☐	☐	☐☐
Tradisjonell helbreder *(hjelper, «læser» etc)*	☐	☐	☐☐
Har du kommunisert via internett med noen av tjenestene over?	☐	☐	☐☐

3.2 Har du i løpet av de siste 12 måneder vært på sykehus?

	Nei	Ja	Antall ganger
Innlagt på sykehus	☐	☐	☐☐
Konsultasjon ved sykehus uten innleggelse:			
Ved psykiatrisk poliklinikk	☐	☐	☐☐
Ved annen sykehuspoliklinikk	☐	☐	☐☐

BRUK AV MEDISINER

4.1 Bruker du, eller har du brukt, noen av følgende medisiner? *Sett ett kryss per linje.*

	Aldri	Nå	Før, ikke nå	Alder første gang
Medisin mot høyt blodtrykk	☐	☐	☐	
Kolesterolsenkende medisin	☐	☐	☐	
Vanndrivende medisin	☐	☐	☐	
Annen medisin mot hjertesykdom *(f.eks. blodfortynnende, rytmestabiliserende, nitroglycerin)*	☐	☐	☐	
Insulin	☐	☐	☐	
Tabletter mot diabetes	☐	☐	☐	
Stoffskiftemedisin *(Levaxin/thyroxin)*	☐	☐	☐	

4.2 Hvor ofte har du i løpet av de siste 4 ukene brukt følgende medisiner? *Sett ett kryss per linje.*

	Ikke brukt siste 4 uker	Sjeldnere enn hver uke	Hver uke, men ikke daglig	Daglig
Smertestillende på resept	☐	☐	☐	☐
Smertestillende uten resept	☐	☐	☐	☐
Magesyrehemmende medisiner	☐	☐	☐	☐
Sovemidler	☐	☐	☐	☐
Beroligende medisiner	☐	☐	☐	☐
Medisin mot depresjon	☐	☐	☐	☐

4.3 Skriv alle medisiner (reseptfrie og reseptbelagte) du har brukt regelmessig siste 4 uker. *Ikke regn med reseptfrie vitamin-, mineral- og kosttilskudd, urter, naturmedisin etc.*

Får du ikke plass til alle medisinene, bruk eget ark.

KOSTHOLD

5.1 Spiser du vanligvis frokost hver dag?

☐ Nei ☐ Ja

5.2 Hvor mange porsjoner frukt og grønnsaker spiser du i gjennomsnitt per dag? *Med porsjon menes f.eks. et eple, en salatbolle.*

Antall porsjoner

5.3 Hvor ofte spiser du vanligvis disse matvarene? *Sett ett kryss per linje.*

	0–1 pr. mnd.	2–3 pr. mnd.	1–3 pr. uke	4–6 pr. uke	1 eller mer pr. dag
Rødt kjøtt *(alle produkter av storfe, får, svin)*	☐	☐	☐	☐	☐
Grønnsaker, frukt, bær	☐	☐	☐	☐	☐
Mager fisk *(torsk, sei)*	☐	☐	☐	☐	☐
Feit fisk *(laks, ørret, uer makrell, sild, kveite)*	☐	☐	☐	☐	☐

5.4 Hvor mange glass/beger drikker/spiser du vanligvis av følgende? *Sett ett kryss per linje.*

	Sjelden/ aldri	1–6 pr. uke	1 pr. dag	2–3 pr. dag	4 eller mer pr. dag
Melk/yoghurt tilsatt probiotika *(Biola, Cultura, Activia, Actimel, BioQ)*	☐	☐	☐	☐	☐
Fruktjuice	☐	☐	☐	☐	☐
Brus/leskedrikker:					
med sukker	☐	☐	☐	☐	☐
med kunstig søtning	☐	☐	☐	☐	☐

5.5 Hvor mange kopper kaffe og te drikker du daglig? *Sett 0 for de typene du ikke drikker daglig.*

	Antall kopper
Filterkaffe *(trakterkaffe)*	
Kokekaffe og/eller presskannekaffe	
Pulverkaffe	
Espressobasert kaffe *(fra kaffemaskin, kapsler etc)*	
Sort te *(f.eks. Earl Grey)*	
Grønn/hvit/oolong te	
Urtete *(f.eks. nype, kamille, Rooibos)*	

HELSEBEKYMRING

	Ikke i det hele tatt	Litt	Noe	En hel del	Svært mye
6.1 **Tror du at det er noe alvorlig galt med kroppen din?**	☐	☐	☐	☐	☐
6.2 **Er du svært bekymret over helsen din?**	☐	☐	☐	☐	☐
6.3 **Er det vanskelig for deg å tro på legen din dersom hun/han forteller deg at det ikke er noe å bekymre seg for?**	☐	☐	☐	☐	☐
6.4 **Er du ofte bekymret for muligheten for at du har en alvorlig sykdom?**	☐	☐	☐	☐	☐
6.5 **Hvis du blir gjort oppmerksom på en sykdom (f.eks. via TV, radio, internett, avis eller noen du kjenner), bekymrer du deg da for selv å få sykdommen?**	☐	☐	☐	☐	☐
6.6 **Opplever du at du plages av mange ulike symptomer?**	☐	☐	☐	☐	☐
6.7 **Har du tilbakevendende tanker (som er vanskelig å bli kvitt) om at du har en sykdom?**	☐	☐	☐	☐	☐

FYSISK AKTIVITET

7.1 **Hvis du er i lønnet eller ulønnet arbeid, hvordan vil du beskrive arbeidet ditt?** *Sett kryss i den ruta som passer best.*

- ☐ For det meste stillesittende arbeid *(f.eks. skrivebordsarbeid, montering)*
- ☐ Arbeid som krever at du går mye *(f.eks. ekspeditørarbeid, lett industriarbeid, undervisning)*
- ☐ Arbeid der du går og løfter mye *(f.eks. pleier, bygningsarbeider)*
- ☐ Tungt kroppsarbeid

7.2 **Angi bevegelse og kroppslig anstrengelse i din fritid det siste året.** *Hvis aktiviteten varierer gjennom året, ta et gjennomsnitt. Sett kryss i den ruta som passer best.*

- ☐ Leser, ser på TV / skjerm eller annen stillesittende aktivitet
- ☐ Spaserer, sykler eller beveger deg på annen måte minst 4 timer i uka *(inkludert gang eller sykling til arbeidsstedet, søndagsturer etc)*
- ☐ Driver mosjonsidrett, tyngre hagearbeid, snømåking etc minst 4 timer i uka
- ☐ Trener hardt eller driver konkurranseidrett regelmessig flere ganger i uka

7.3 **Siste uka, omtrent hvor lang tid tilbrakte du <u>sittende</u> på en typisk hverdag og fridag?** *F.eks. ved arbeidsbord, hos venner, mens du så på TV / skjerm.*

☐☐ timer sittende på en hverdag *(både jobb og fritid)*

☐☐ timer sittende på en fridag

ALKOHOL

8.1 **Hvor ofte drikker du alkohol?**

- ☐ Aldri
- ☐ Månedlig eller sjeldnere
- ☐ 2–4 ganger hver måned
- ☐ 2–3 ganger per uke
- ☐ 4 eller flere ganger per uke

8.2 **Hvor mange enheter alkohol (flaske øl, glass vin eller drink) tar du vanligvis når du drikker?**

1–2	3–4	5–6	7–9	10 eller flere
☐	☐	☐	☐	☐

8.3 **Hvor ofte drikker du 6 eller flere enheter alkohol ved en anledning?**

- ☐ Aldri
- ☐ Sjeldnere enn månedlig
- ☐ Månedlig
- ☐ Ukentlig
- ☐ Daglig eller nesten daglig

RØYK OG SNUS

9.1 **Har du røykt/røyker du daglig?**

☐ Aldri ☐ Ja, nå ☐ Ja, tidligere

9.2 **Har du brukt/bruker du snus eller skrå daglig?**

☐ Aldri ☐ Ja, nå ☐ Ja, tidligere

SPØRSMÅL OM KREFT

10.1 **Har du noen gang fått**

	Nei	Ja	**Hvis ja:** alder første gang	**Hvis ja:** alder siste gang
Utført mammografi	☐	☐		
Målt PSA (prostataspesifikt antigen)	☐	☐		
Utført tykktarmsundersøkelse (koloskopi, avføringsprøve)	☐	☐		

10.2 **Har noen i din nære biologiske familie hatt**

	Egne barn	Mor	Far	Mormor	Morfar	Farmor	Farfar	Tante	Onkel	Søsken
Brystkreft	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Prostatakreft	☐		☐		☐		☐		☐	☐
Tykktarmskreft	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

UTDANNING OG INNTEKT

11.1 **Hva er din høyeste fullførte utdanning?** *Sett ett kryss.*

- ☐ Grunnskole/framhaldsskole/folkehøyskole inntil 10 år
- ☐ Fagutdanning/realskole/videregående/gymnas minimum 3 år
- ☐ Høyskole/universitet mindre enn 4 år
- ☐ Høyskole/universitet 4 år eller mer

11.2 **Hva var din husstands samlede bruttoinntekt siste år?** *Ta med alle inntekter fra arbeid, trygder, sosialhjelp og lignende.*

- ☐ Under 150 000 kr
- ☐ 150 000–250 000 kr
- ☐ 251 000–350 000 kr
- ☐ 351 000–450 000 kr
- ☐ 451 000–550 000 kr
- ☐ 551 000–750 000 kr
- ☐ 751 000 –1 000 000 kr
- ☐ Over 1 000 000 kr

FAMILIE OG VENNER

12.1 **Hvem bor du sammen med?**

	Nei	Ja	Antall
Ektefelle/samboer	☐	☐	
Andre personer over 18 år	☐	☐	
Personer under 18 år	☐	☐	

12.2 **Har du nok venner som kan gi deg hjelp når du trenger det?**

☐ Ja ☐ Nei

12.3 **Har du nok venner som du kan snakke fortrolig med?**

☐ Ja ☐ Nei

12.4 **Hvor ofte deltar du vanligvis i foreningsvirksomhet som syklubb, idrettslag, politiske, religiøse eller andre foreninger?**

Aldri, eller noen få ganger i året	1–2 ganger i måneden	Omtrent 1 gang i uka	Mer enn 1 gang i uka
☐	☐	☐	☐

SPØRSMÅL TIL KVINNER

13.1 **Hvor gammel var du da du fikk menstruasjon første gang?**

Alder

13.2 **Er du gravid nå?**

☐ Nei ☐ Ja ☐ Usikker

13.3 **Hvor mange barn har du født?**

Antall barn

13.4 **Hvis du har født, fyll ut for hvert barn: fødselsår og vekt samt hvor mange måneder du ammet.** *Angi så godt du kan. Hvis flere barn, bruk ekstra ark.*

	Fødselsår	Fødselsvekt i gram	Ammet ant. mnd.
Barn 1			
Barn 2			
Barn 3			
Barn 4			
Barn 5			
Barn 6			

SPØRSMÅL TIL MENN

14.1 **Har du fått behandling for betennelse i prostata eller urinblæra?**

☐ Nei ☐ Ja

14.2 **Har du fått utført steriliseringsoperasjon?**

☐ Nei ☐ Ja **Hvis ja:** hvilket år

Tusen takk for ditt bidrag.

Appendix D

Extracted pages from the second questionnaire (Q2) in the Tromsø study: Tromsø7, including the Hospital Anxiety and Depression Scale (HADS) [Norwegian]

Her kommer noen spørsmål om hvorledes du føler deg. For hvert spørsmål setter du kryss for ett av de fire svarene som best beskriver dine følelser *den siste uken.* Ikke tenk for lenge på svaret – de spontane svarene er best.

28.11 Jeg føler meg nervøs og urolig

Mesteparten av tiden
Mye av tiden
Fra tid til annen
Ikke i det hele tatt

28.12 Jeg gleder meg fortsatt over tingene slik jeg pleide før

Avgjort like mye
Ikke fullt så mye
Bare lite grann
Ikke i det hele tatt

28.13 Jeg har en uroføIelse som om noe forferdelig vil skje

Ja, og noe svært ille
Ja, ikke så veldig ille
Litt, bekymrer meg lite
Ikke i det hele tatt

28.14 Jeg kan le og se det morsomme i situasjoner

Like mye nå som før
Ikke like mye nå som før
Avgjort ikke som før
Ikke i det hele tatt

28.15 Jeg har hodet fullt av bekymringer

Veldig ofte
Ganske ofte
Av og til
En gang i blant

28.16 Jeg er i godt humør

Aldri
Noen ganger
Ganske ofte
For det meste

28.17 Jeg kan sitte i fred og ro og kjenne meg avslappet

Ja, helt klart
Vanligvis
Ikke så ofte
Ikke i det hele tatt

28.18 Jeg føler meg som om alt går langsommere

Nesten hele tiden
Svært ofte
Fra tid til annen
Ikke i det hele tatt

28.19 Jeg føler meg urolig som om jeg har sommerfugler i magen

Ikke i det hele tatt
Fra tid til annen
Ganske ofte
Svært ofte

28.20 Jeg bryr meg ikke lenger om hvordan jeg ser ut

Ja, jeg har sluttet å bry meg
Ikke som jeg burde
Kan hende ikke nok
Bryr meg som før

28.21 Jeg er rastløs som om jeg stadig må være aktiv

Uten tvil svært mye
Ganske mye
Ikke så veldig mye
Ikke i det hele tatt

28.22 Jeg ser med glede frem til hendelser og ting

Like mye som før
Heller mindre enn før
Avgjort mindre enn før
Nesten ikke i det hele tatt

28.23 Jeg kan plutselig få en følelse av panikk

Uten tvil svært ofte
Ganske ofte
Ikke så veldig ofte
Ikke i det hele tatt

28.24 Jeg kan glede meg over gode bøker, radio og TV

Ofte
Fra tid til annen
Ikke så ofte
Svært sjelden

Appendix E

List of external links related to the Tromsø study: Tromsø7 [Norwegian]

The Tromsø study: Tromsø7

- Invitation to participate [Norwegian]: https://uit.no/Content/710341/cache=20203011123325/brosjyre.troms%C3%B87.pdf

- Consent form participants for participation in the Tromsø study: Tromsø7 [Norwegian]: https://uit.no/Content/575211/cache=20180805144729/Samtykke.den7.Tromsounderso kelsen.pdf

- The second questionnaire (Q2), including the Hospital Anxiety and Depression scale [Norwegian]: https://uit.no/Content/710352/cache=20203011124130/Q2%2BTroms%C3%B87.pdf