Sexual quality of life in patients with axial spondyloarthritis

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Summary in English

Background

Research on the impact of health status on sexual activity and sexual quality of life (QOL) in patients with axial spondyloarthritis (axSpA) is scarce.

Aim

The overall aim of the studies was to examine the impact of health status on sexual activity and sexual QOL in male and female patients with axSpA.

Methods

Three hundred and seventy-nine consecutive patients with axSpA, aged 18–81 years, who visited the outpatient rheumatology clinics at two Norwegian hospitals were included. Data on demographic factors, disease, treatment, and lifestyle variables were collected by doctors and nurses from questionnaires, laboratory test results, direct interviews, and physical examinations, at the baseline and after 5 years. At the follow-up, 245 patients participated. A broad-spectrum data collection method was used to obtain data for demographics, patient-reported outcome measures (PROMS), and disease activity/damage. PROMS measures included the Health Assessment Questionnaire (HAQ), Bath Ankylosing Spondylitis Patients Global Score (BAS-G), Bath Ankylosing Spondylitis Functional Index (BASFI), Bath Ankylosing Spondylitis Activity Index (BASDAI), 15D Measure of Health-Related Quality of Life (15D), Health Survey Short-Form-36 items (SF-36), and Sexual Quality of Life–Female (SQOL-F). Data on disease activity and damage were obtained from the Bath Ankylosing Spondylitis Metrology Index (BASMI) and the Maastricht Ankylosing Spondylitis Enthesis Score (MASES).

Results

The mean age of the patients at the baseline was 45.6 years (standard deviation, SD ± 11.9) and the mean disease duration was 13.9 years (SD ± 11.4); 66.5% were men. Of the study cohort, 81.1% had a sexual partner and 76.3% were married or cohabiting. Biological disease-modifying antirheumatic drugs (bDMARDs) were used

by 22% of the patients, and the mean comorbidity rate was low (0.7 per patient). A large percentage of patients with axSpA were working (70.7%), and 55.7% had more than 13 years of education.

At the baseline, one of five patients reported that their health status had a negative impact on sexual activity. Most patients had low disease activity and low disability. A large negative impact on sexual activity was independently associated with being a woman, high body mass index (BMI kg/m^2)), current smoking, and a reduced health-related QOL (HRQOL) (Paper I).

In the adjusted analysis, sexual QOL was impaired in patients with active axSpA, and impaired sexual QOL was associated with elevated BAS-G score, C-reactive protein (CRP)level, and use of bDMARDs. Being a woman and increased BMI were also independently associated with a decreased sexual QOL (Paper II).

At the 5-year follow-up, significant increases were observed in the number of comorbidities and use of bDMARDs. The patients displayed better disease control (e.g., lower scores on the CRP, MASES, BASFI, and BAS-G) but no significant changes in sexual QOL. The frequencies of negative lifestyle factors such as smoking had decreased. In patients older than 65 years and in those who exercised <1 h/week, a decreased sexual QOL was reported (Paper III).

Conclusions

This cohort of outpatient patients with axSpA reported a low impact of health status on sexual activity and sexual QOL. Sexual QOL did not seem to worsen over time and remained stable through the 5-year follow-up despite an increase in the number of comorbidities. Effective disease control and changes in healthy lifestyle habits may help to improve the outcomes for these patients.

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Norsk sammendrag

Bakgrunn

Det finnes lite forskningen på hvilken innvirkning helsestatus har på seksuell aktivitet og seksuell livskvalitet hos pasienter med axSpA.

Hensikt

Det overordnede målet med studien var å undersøke hvilken påvirkning helsestatus har på seksuell aktivitet og seksuell livskvalitet hos mannlige og kvinnelige pasienter med axSpA.

Metode

Trehundre og syttini pasienter med axSpA i alderen 18–81 år ble fortløpende inkludert i studien ved besøk på polikliniske revmatologiske klinikker ved to norske sykehus. Data på demografiske faktorer, sykdom, behandling og livsstils variabler ble samlet inn av leger og sykepleiere ved å bruke spørreskjemaer, laboratorietester, direkte intervjuer og fysiske undersøkelser. Dette ble gjort ved baseline og etter 5 år. Ved oppfølgingen deltok tohundre og førtifem pasienter. Det ble samlet data på: demografi variabler, pasientrapporterte utfallsmål (PROMS) og sykdomsaktivitet/skade. PROMS som ble brukt var, HAQ, BAS-G, BASFI, BASDAI, 15D, SF-36 og SOQL-F. Data på sykdomsaktivitet og skade ble samlet ved å benytte spørreskjemaet BASMI og MASES.

Funn

Ved basseline hadde pasientene en gjennomsnittsalder på 45,6 år (standardavvik, SD ±11,9), med en gjennomsnittlig sykdomsvarighet på 13,9 år, (SD ±11,4), og 66,5 % var menn. Av studiekohorten hadde 81,1 % en seksuell partner og 76,3 % var gift eller samboer. Biologiske sykdomsmodifiserende antireumatiske legemidler (bDMARD) ble brukt av 22 % av pasientene, og det var få tilleggssykdommer (gjennomsnitt 0,7 per pasient). En stor andel av pasientene med axSpA var i arbeid (70,7 %) og 55,7 % hadde mer enn 13 års utdanning. Ved

baseline rapporterte én av fem pasienter at helsestatusen deres hadde en negativ innvirkning på seksuell aktivitet. De fleste pasientene hadde lav sykdomsaktivitet og rapporterte om god fysisk funksjon. En stor negativ innvirkning på seksuell aktivitet var uavhengig assosiert med kvinnelig kjønn, høy kroppsmasseindeks (BMI), røyking og redusert helserelatert livskvalitet (HRQOL) (artikkel I). I de justerte analysene var seksuell QOL redusert hos pasienter med aktiv axSpA, (målt ved hjelp av forhøyet BAS-G og CRP, og med bruk av bDMARDs). Kvinnelig kjønn og økt BMI var også uavhengig assosiert med redusert seksuell QOL (papir II). Ved 5-års oppfølgingen ble det funnet en signifikant økning i antall tilleggssykdommer, mer bruk av bDMARDs, bedre sykdomskontroll (vises ved lavere skår på CRP, MASES, BASFI og BAS-G), men ingen signifikante endringer i seksuell livskvalitet. Negative livsstilsfaktorer som røyking var redusert. Hos pasienter eldre enn 65 år og hos de som trente mindre enn 1 time/uke ble det rapportert en reduksjon i seksuell livskvalitet (artikkel III).

Konklusjon

Pasienter med axSpA i våre studier rapporterte en lav innvirkning av helsestatus på seksuell aktivitet og seksuell livskvalitet. Seksuell livskvalitet så ikke ut til å forverres over tid og forble stabil gjennom 5-års oppfølgingen til tross for en økning i antall tilleggssykdommer. Effektiv sykdomskontroll og endring til en sunnere livsstilsvaner kan ha bidratt til å forbedre resultatene for denne pasientgruppen.

Abbreviations

AS	Ankylosing spondylitis
ASAS	Assessment of SpondyloArthritis international Society
AxSpA	Axial SpondyloArthritis
BASDAI	Bath Ankylosing Spondylitis Activity Index
BASFI	Bath Ankylosing Spondylitis Functional Index
BASMI	Bath Ankylosing Spondylitis Metrology Index
BAS-G	Bath Ankylosing Spondylitis Patients Global Score
bDMARD	Biological disease-modifying antirheumatic drug
BMI	Body mass index
CRP	C-reactive protein
CsDMARD	Conventional synthetic disease-modifying antirheumatic drug
EULAR	European Alliance of Associations for Rheumatology
HAQ	Health Assessment Questionnaire
HLA-B27	Human leukocyte antigen – B27
HP	Health Personnel
HRQOL	Health-related quality of life
MASES	Maastricht Ankylosing Spondylitis Enthesitis Score
MHH	Martina Hansen's Hospital
MRI	Magnetic resonance imaging
Nr-axSpA	Non-radiographic axial spondyloarthritis
NSAID	Non-steroidal anti-inflammatory drug
PROMS	Patient-reported outcome measures

PsA	Psoriatic arthritis
QOL	Quality of life
RA	Rheumatoid arthritis
R-axSpA	Radiographic axial spondyloarthritis
Sexual QOL	Sexual quality of life
SF-36	Health Survey Short-Form-36 items
SpA	Spondyloarthritis
SQOL-F	Sexual quality of life – Female
SSHF	Sørlandet Hospital
TNF	Tumour necrosis factor
T2T	Treat-to-target
UIA	University of Agder
WHO	World Health Organization
15D	The 15D Measure of Health-Related Quality of Life

Innhold

List of figures and tables

List of papers

I. Berg, K.H., Rohde G, Prøven, A., Almås, E., Benestad, E.E.P., Østensen, M., Haugeberg, G. Exploring the relationship between demographic and disease-related variables and perceived effect of health status on sexual activity in patients with axial spondyloarthritis: associations found only with non-disease variables. *Scandinavian Journal of Rheumatology*, 2017; *46*(6), 461-467. doi:10.1080/03009742.2017.1279684

II. Berg, K.H., Rohde, G., Prøven, A., Benestad, E.E.P., Østensen, M., Haugeberg, G. Sexual Quality of Life in Patients with Axial Spondyloarthritis in the Biologic Treatment Era. *The Journal of rheumatology*, 2019; doi:10.3899/jrheum.180413

III. Berg, K.H., Rohde, G., Pripp, A., Prøven, A., Benestad, E.E.P., Østensen, M., Haugeberg, G. Increased proportion of comorbidities but no deterioration of sexual QOL during a 5-year follow-up in patients with axSpA in the biologic treatment era. *Rheumatology*, 2021; doi.org/10.1093/rheumatology/keaa887

1 Background

1.1 Introduction

In 2007, a prospective longitudinal observational study of axial inflammatory rheumatic disorders, including ankylosing spondylitis (AS), was designed, with the title: 'Inflammatory back pain and Bechterew's disease in Norway'. The project was designed by Professor Glenn Haugeberg at Sørlandet Hospital (SSHF). The overall aim of the study was to explore the epidemiology, demographics, disease presentation, morbidity, health-related quality of life (HRQOL), including sexual QOL, treatment, and health-care economics for these patients. For questions on sexuality, Professor Esben Ester Pirelli Benestad and Professor Elsa Almås at the University of Agder (UIA) were consulted. Although the study was planned as a multicentre study in Norway, only two clinics were able to participate. The two rheumatology outpatient clinics were located at SSHF in Kristiansand and Martina Hansen's Hospital (MHH) in Bærum. This thesis is part of the above-mentioned project, with a cross-sectional longitudinal design.

Through working in a rheumatology outpatient clinic as a nurse and team leader for over 25 years, I have developed a personal and professional interest in axSpA and the impact of axSpA on a patient's life, ability to work, social life, relationships, and sexual QOL. I have noted that patients with axSpA have stated that their disease has impacted their sexual QOL. During this time, my interest in research matured. In October 2010 I started to work at the Rheumatology Department at SSHF and was involved in data collection as one of the study nurses for this project, later taking on a leading role for all data collection. When I was given an opportunity to use part of the collected data focusing on the impact of health status on sexual activity and sexual QOL in male and female patients with axSpA over a 5-year period in the framework of a PhD funded by the University of Agder, I made the decision driven by curiosity to challenge myself and to move into the world of health-care research.

The disease burden for patients with axSpA has been reported to be extensive, in the past (Boonen et al., 2015; Garrido-Cumbrera et al., 2019; Sieper et al., 2016).

However, in the new millennium with new treatment strategies and improved patient management, disease outcomes have improved (Smolen et al., 2014; Smolen et al., 2018). The improvement has been driven by the introduction of biological disease-modifying antirheumatic drugs (bDMARDs) from around 2005. Furthermore, a treat-to-target (T2T) strategy, which has been documented to improve outcomes for patients with rheumatoid arthritis (RA) since 2012 (Smolen et al., 2010) has also been recommended for the follow-up of patients with axSpA (Smolen et al. (2014). The T2T strategy defines remission as the target and assesses patients' preferences in the decision-making process of treatment (Smolen et al., 2014; Smolen et al., 2018). In addition, programmes on self-management of the disease, focusing on its physical, emotional, and social consequences have proven to be beneficial for coping with axSpA (Molto et al., 2021). The emergence of both better and more powerful medications and the change to a patient-centred approach, as a partner in their own care and given the opportunity to be involved in decision-making, has given patients with axSpA the possibility of coping better in living with this chronic disease (Agrawal & Machado, 2020; Torre-Alonso, Queiro, Comellas, Lizán, & Blanch, 2018).

PROMs are important for obtaining the patients' perception of health, HRQOL, and sexual QOL in a clinical setting. PROMs include any reports that patients have given on their health condition (Cappelleri et al., 2014). PROMs are also recognized as important outcome tools to identify any disease activity and functional impairments (Khanna et al., 2011; Madsen, 2018). In a study by Rohde et al. on the same patient population as the current studies, patients having axSpA reported decreased HRQOL, including reduced physical functioning, compared with published norm-based data for the general population (Rohde, Berg, Prøven, & Haugeberg, 2017).

One of the key functions in human beings is sexual activity, which affects both quality of life (QOL) and sexual QOL (Gallinaro, Akagawa, Otuzi, Sampaio-Barros, & Gonçalves, 2012). However, in general, sexual QOL remains an unexplored area of research, including patients with axSpA. So far, the research focus has been on sexual activity, functioning, and dysfunction, which are all related to sexual QOL, but little

attention has been given to this topic (Akkurt et al., 2016; Christensen et al., 2011; Shen et al., 2013). Despite the importance of sexual QOL, sexual issues and sexual health among patients with rheumatic diseases, including axSpA, are often unaddressed or neglected by health personnel (HP) and are rarely raised in consultations with rheumatology specialists (Helland, Garratt, Kjeken, Kvien, & Dagfinrud, 2013; Josefsson & Gard, 2012). Therefore, in this thesis, the focus is on the significance of the patient's state of health on sexual activity and perception of sexual QOL in those with axSpA.

1.2 Axial spondyloarthritis

In this section, I will give a brief overview of axSpA in the context of spondyloarthritis (SpA) disorders, diagnosing and classification of axSpA with its different phenotypes of axial inflammatory disease, the epidemiology of axSpA, disease characteristics and course, its burden, and implications for the individual living with axSpA. Finally, the T2T strategy and medical treatment of patients with axSpA will be described.

1.2.1. Axial spondyloarthritis as part of the spondyloarthritis concept

In 1974, Moll et al. defined the SpA concept as a group of disorders with common features that may affect several organs including the spine, the sacroiliac joints, peripheral joints, and peri-articular structures (Moll, Haslock, Macrae, & Wright, 1974). This included the diagnosis of axial spondyloarthritis (AS) (previously also called Bechterew's disease), psoriatic arthritis (PsA), reactive arthritis, inflammatory bowel disease-related arthritis, and undifferentiated arthritis. It is important to emphasize that all these disorders can present with axial inflammatory involvement, but only for AS, axial skeleton involvement is mandatory.

1.2.2. Characteristics of axSpA and its disease course

From the axial skeleton involvement perspective in SpA, axSpA can be defined as a chronic, inflammatory rheumatic disease affecting the axial skeleton, causing severe pain, stiffness, and fatigue (Bal et al., 2011). AxSpA is divided into two sub-phenotypes: one characterized by signs of inflammation on radiographs (radiographic

axSpA), in patients and one with axial skeleton inflammation without signs of inflammation on radiographs (non-radiographic axSpA). During the disease course, patients with axSpA may suffer structural damage in their spine due to the development of osteophytes in the intervertebral joints which contributes to disease burden and disease severeness (Garg, van den Bosch, & Deodhar, 2014).

1.2.3. Epidemiology of axSpA

Obviously, the use of different criteria for axial inflammatory disease will also impact the epidemiology of axSpA (Bakland & Nossent, 2013). In a study from Northern Norway in a population with chronic back pain and with a high prevalence of human leucocyte antigen (HLA)-B27, 8.4% met the Assessment of SpondyloArthritis international Society (ASAS) classification criteria for axSpA, whereas only 2.4% met the modified New York criteria (Bakland & Nossent, 2013). The estimated prevalence of axSpA in Norway is 0.3% to 1.2% (Bakland & Nossent, 2013). Among the types of SpA, axSpA is the most common diagnosis found among 0.15% to 1.8% of people of European origin and is more frequent in populations with a high prevalence of human leukocyte antigen-B27 (HLA-B27), as seen in northern latitudes (Zochling & Smith, 2010).

1.2.4. Diagnosing and classification of axSpA in a historical context

Different criteria have been developed to diagnose AS (radiographic sacroiliitis) (van der Linden, Valkenburg, & Cats, 1984). For this phenotype of axSpA, the Rome criteria were developed in 1961, which were later modified and reformulated as the New York criteria in 1966 and in 1984 the modified New York criteria were developed. To fulfil these criteria, signs of sacroiliitis must be present on X-rays, termed radiographic axial spondyloarthritis (r-axSpA). With the introduction of magnetic resonance imaging (MRI), visualization of the axial inflammatory disease process before bone damage was visible on X-rays—defined as non-radiographic axial spondyloarthritis (nr-axSpA)—became possible (Bennett et al., 2008).

In 2009, the ASAS and the European Alliance of Associations for Rheumatology (EULAR) published new classification criteria for axSpA, (Rudwaleit et al., 2009b). These criteria were applied in the present study to select patients

according to their inclusion criteria Figure 1. The new ASAS criteria for axial inflammatory disease include both radiographic (sacroiliitis on X-rays) and non-radiographic axial inflammatory (sacroiliitis on MRI) phenotypes. They also included a non-imaging arm for patients with chronic back pain being HLA-B27 positive and with various SpA features as shown in Figure 1.

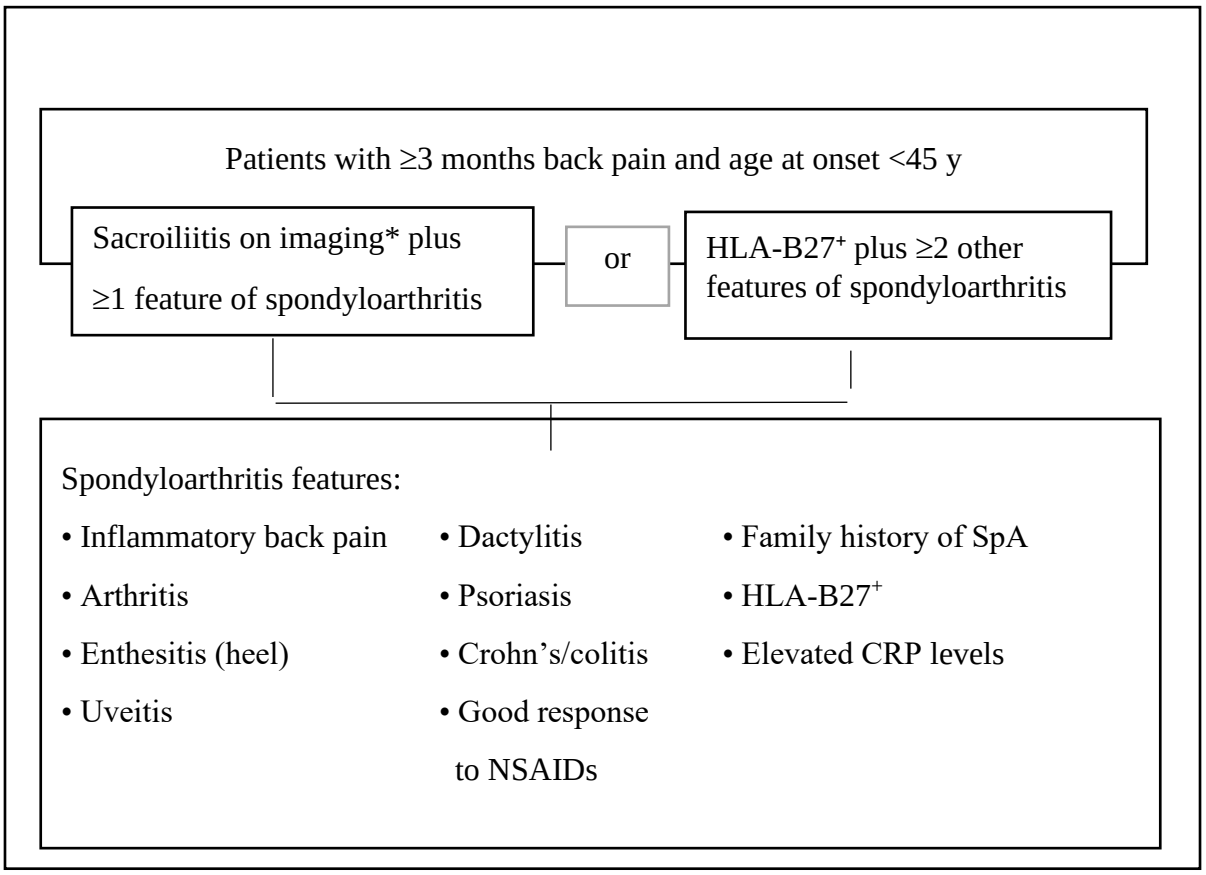

Figure 1. The ASAS classification criteria for axial spondyloarthritis

ASAS, Assessment of SpondyloArthritis international Society; CRP, C-reactive protein; NSAIDs, non-steroidal anti-inflammatory drugs; SpA, spondyloarthritis. *Sacroiliitis on imaging refers to definite radiographic sacroiliitis according to the modified New York criteria or sacroiliitis on MRI according to the ASAS consensus definition. Adapted from (Rudwaleit et al., 2009b).

The new ASAS criteria for axial inflammatory disease thus include patients at an earlier stage in the disease course as when sacroiliitis first was diagnosed after beeing visible on X-rays (Feldtkeller, Bruckel, & Khan, 2000).

Patients with nr-axSpA and r-axSpA share common clinical features such as uveitis, enthesitis, peripheral arthritis, psoriasis, irritable bowel disorder and dactylitis which all significantly impact HRQOL (Sieper & Poddubnyy, 2017; Strand & Singh, 2017; Taurog, Chhabra, & Colbert, 2016). However, there are differences. Risk factors for developing AS have been identified and include smoking, male gender, the HLA-B27^{+} genotype and sacroiliitis on MRI (Bakland, Nossent, & Gran, 2005; Bennett et al., 2008; Videm, Cortes, Thomas, & Brown, 2014).

Historically, axSpA has been considered a disease that predominantly affects men, and the ratio between men and women has varied from 2:1 to 4:1 (Bakland & Nossent, 2013; Zochling & Smith, 2010). However, better diagnostic procedures revealed that a significant proportion of women also suffer from axSpA. Using MRI and ASAS criteria for diagnosis has now narrowed the gap in the ratio between men and women (Baumberger & Khan, 2017; Rusman, van Vollenhoven, & van der Horst-Bruinsma, 2018). Although the time to diagnosis of axSpA has decreased for men over the years, women still experience a much longer diagnostic delay than men because of differences in the rate of disease manifestation (Rusman et al., 2018).

1.2.5. The impact of axSpA on the patient's daily life

AxSpA is a chronic disease and patients living with it can experience the disease in different ways. It typically starts in early adulthood (<40 y), which is a critical period of life when most people finish their education and move on to a career and might have started a family (Sieper et al., 2009). The inflammation may lead to structural damage in both the spine and the sacroiliac joints and lead to a great impact on patients' mobility, physical function, and ability to work as well as lifestyle (J. T. Rosenbaum, Pisenti, Park, & Howard, 2019). All the symptoms caused by axSpA might also lead to difficulties in relationships and have a negative impact on HRQOL, including sexual relationships and sexual QOL (Strand & Singh, 2017).

The persistence of inflammation in the sacroiliac joints and the spine causes pain, develops into chronic back pain, and may lead to postural changes. Severely reduced mobility of the spine causes stiffness and pain, and hampers performing daily activities, such as personal care, dressing, and housework, regardless of whether

patients have r-axSpA or nr-axSpA (Singh & Strand, 2009; Strand & Singh, 2017; Özdemir, 2011). Working ability can be affected, depending on the person's type of work. Heavy work may be more difficult than working in an office and living in rural areas is more difficult than in the cities. Difficulties with working might further affect a person's economic situation (Hollick et al., 2020; Nikiphorou & Ramiro, 2020). Furthermore, engaging in leisure activities can be difficult, and it might be necessary to change focus and find other types of leisure activities (Hamilton-West & Quine, 2009; Özdemir, 2011).

The impact of axSpA varies between patients and influences men and women in different ways (Hwang, Ridley, & Reveille, 2021; Landi et al., 2016). Women tend to report more negative impacts of the disease than men in physical, discomfort, emotional, and social areas (T. Y. Rosenbaum, 2010). Men are often diagnosed earlier in life and have more radiographic damage. However, women have longer delay in getting a diagnosis; they have a higher disease burden, higher disease activity, respond significantly less well to tumour necrosis factor (TNF) inhibitors, and do not have the same treatment responses as men (Hwang et al., 2021; Rusman et al., 2018).

Fatigue can also be a major problem caused by inflammatory processes in the body. Sleep disturbances, such as insomnia and waking several times during the night, can have major negative effects on patients' sleep quality and can lead to daytime fatigue, as well as influencing all other activities (Aissaoui et al., 2012; Kotsis, Voulgari, Drosos, Carvalho, & Hyphantis, 2014).

One additional problem is the unpredictability of disease activity and rapid change in the disease course, which makes it difficult to plan activities ahead. Some patients manage living well with the disease, even though the disease is active; they adapt positively and adjust how to manage their illness by using strategies to optimize their QOL. Some persons tend to 'deny' limitations caused by the disease (Essers et al., 2015; Sirgy, 2012), whereas others experience that high disease activity might harm the quality of sleep, increase pain, and reduce their QOL (Macfarlane, Rotariu, Jones, Pathan, & Dean, 2020). Because of the nature of axSpA, and possible implications for the patients with this disease, it is important to provide an early

diagnosis and start treatment without delay so that disease perception, loss of function, and impairment can be minimized (Garg et al., 2014; Shim, Jones, Pathan, & Macfarlane, 2018).

1.2.6. Treatment strategies and drugs used to treat patients with axSpA

To manage axSpA successfully, a combination of non-pharmacological and pharmacological treatments is required (Regel et al., 2017; Ward et al., 2019). Treatment should be individualized and based on the whole person; thus, not only the disease symptoms should be considered but also other aspects, such as comorbidities, QOL, and medication use (Smolen et al., 2018; van der Heijde et al., 2017). An important point is that patients need to participate in the decision process, so it is important to give information on a level that is understandable regardless of literacy ability and level of education (Wittink & Oosterhaven, 2018). The treatment goal for pharmacological treatment is to eliminate or reduce symptoms, achieve clinical remission, prevent worsening of the disease, and reduce damage (van der Heijde et al., 2017). Pharmacological treatment relies on the treatment recommendations of the 2016 ASAS-EULAR management for axSpA (van der Heijde et al., 2017). These include non-steroidal anti-inflammatory drugs (NSAIDs), local glucocorticoid injections, conventional synthetic disease-modifying antirheumatic drugs (csDMARDs), and bDMARDs (van der Heijde et al., 2017). The bDMARDs including antitumour necrosis factor agents are an effective option for patients with high disease activity where NSAIDs and exercise are not sufficient to reduce pain and inflammation. The most frequently used csDMARDs are methotrexate and Salazopyrin, they have been used for many years and mostly for patients who have peripheral arthritis (Caso et al., 2015).

Non-pharmacological treatments such as regular exercise aim to maintain physical functioning (Agrawal & Machado, 2020; Rausch Osthoff, Juhl, et al., 2018; Regel et al., 2017). Another important non-pharmacological treatment is a change in lifestyle: stopping smoking (Chung, Machado, van der Heijde, Agostino, & Dougados, 2012; Poddubnyy et al., 2012; Ramiro et al., 2015); losing weight (van der Heijde et al.,

2017); and education to understand better the disease and its management (Candelas et al., 2016; Zangi et al., 2015).

The concept of ‘T2T’, defined for axSpA and peripheral SpA in 2012 (Smolen et al., 2014; Smolen et al., 2018) and reviewed in 2017, aims at early clinical remission or achieving an inactive disease, with an improvement in the BASDAI of 50%, less pain, and better scores on the Bath Ankylosing Spondylitis Metrology Index (BASMI) and BASFI as well as normalization of CRP levels and of the erythrocyte sedimentation rate. The concept considers the patient’s treatment goals and individualizes the treatment to prevent structural damage (Smolen et al., 2018).

1.2.7. Previous research

A literature search was performed to obtain an overview of research on the impact of axSpA on sexual QOL in patients from the start of the study 2009 to 2022. For inclusion, papers in the English language was chosen. The search was performed with the following terms: words for Quality of life or well-being, and sexual*, and ‘ankylosing spondylos’ or ‘bechterew’ and free text terms and terms from the databases subject headings, in the following databases: CINAHL, MEDLINE (EBSCOhost) and APA PsycInfo (Ovid), up to 30th of March 2022 (Figure 2). In addition, hand searching was performed in reference list and cited by articles.

The literature search resulted in 23 papers and five research areas: sexual activity (n = 4), sexual QOL (n = 1), sexual relationships (n = 1), sexual satisfaction (n = 1), and sexual dysfunction and function (n = 16) (Appendix 4).

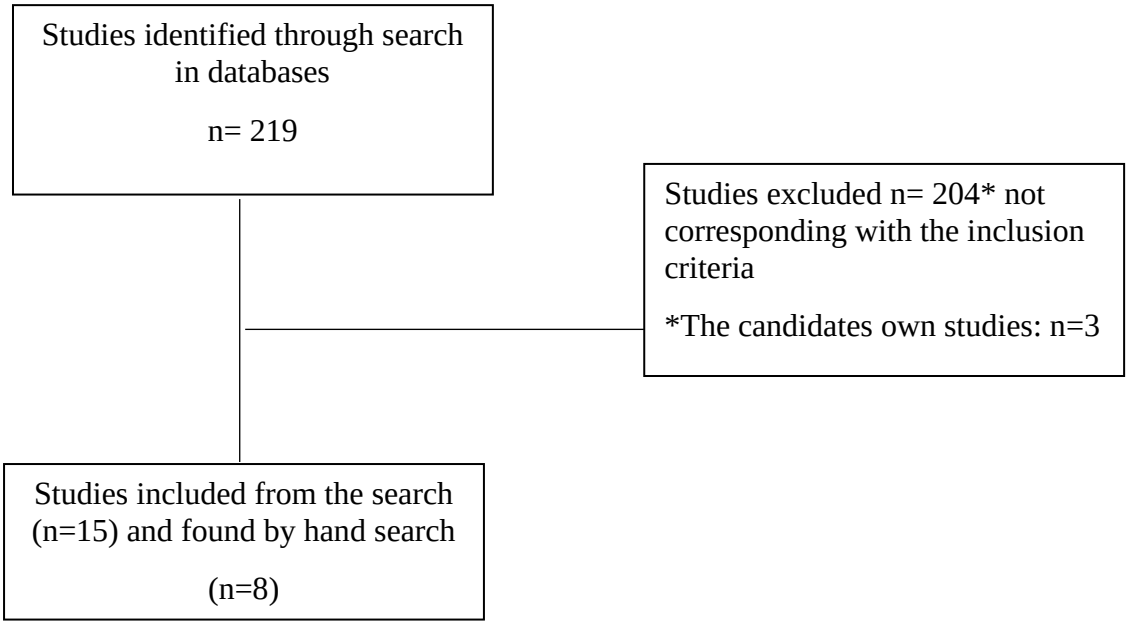

Figure 2. Search history for publications on sexual activity and sexual QOL

The search resulted in four papers on sexual activity, showing that AS, with its chronic nature and associated poor function, has a considerable influence on patients' sexual activity (Fu et al., 2018; Gallinaro et al., 2012; Rostom et al., 2013; Yao et al., 2016). As for the perceptions of sexual QOL among patients with axSpA, only one study was identified, showing that sexual QOL and disease activity improved after treatment with a bDMARD (Dong, Zheng, Shi, & Liu, 2015). One study was found on sexual relationships: it revealed a substantial impact, regarding physical outcomes and psychological state (Healey et al., 2009). Patients with axSpA reported that their sexual satisfaction declined after being diagnosed with axSpA (Akkuş, Nakas, & Kalyoncu, 2010). Studies on sexual dysfunction and function in patients with rheumatic diseases (including patients with axSpA) show impaired sexual function related to the functional status and disease activity including erectile dysfunction, decreased functionality, joint involvement, poor HRQOL, and depression with a negative impact on sexual intercourse (Dhakad et al., 2015; Erdem, Ortac, & Salabas, 2020; Fan et al., 2015; Oh et al., 2009; Rezvani, Ök, & Demir, 2012; Santana et al., 2017; Sariyildiz et al., 2013; Shen et al., 2013; Tristano, 2009; Özkorumak, Karkucak, Civil, Tiryaki, & Özden, 2011). Another study, (Bal et al., 2011) showed problems with satisfaction from intercourse, while Nisihara et al. (2021) reported worse sexual performance. In two other studies, sexual dysfunction was more common for women

with AS compared with the normal population and another study found that the impact seemed to be worse for men than for women with AS (Akkurt et al., 2016; Liu, Dong, Chen, Wang, & Tu, 2015). Increased smoking had a negative impact on sexual functioning in men with AS (Aykurt Karlıbel et al., 2019). No difference was found on sexual functioning and psychological burden between r-axSpA and nr-axSpA (Gözüküçük et al., 2021). For more details, see Appendix 4.

1.3 Theoretical framework

In this chapter, the theoretical framework of the thesis will be elaborated: the concepts of sexuality, sexual health, and sexual activity as an integrated part of health, HRQOL, QOL, and sexual QOL.

1.3.1 Sexuality

Sexuality is a person's ability to experience or express sexual feelings. It is unique to every person and does not exist alone: it is a part of the biopsychosocial perspective. Moreover, it is a broad term that affects a person in many ways and is affected by biological, physical, social, erotic, and spiritual dimensions (Graugaard, Giraldi, & Møhl, 2019). The motive for sexual activity is both complex and unpredictable. Sexuality is part of human life and has different purposes, such as reproduction, feelings of love, relief of tensions, intimacy, relations between people, and respect of people's own and other boundaries. Sexuality can also be used as a component of rehabilitation, recreation, and relaxation (Graugaard et al., 2019; J. S. Greenberg, Bruess, & Oswalt, 2016). Every person is a sexual being, but sexuality in terms of how it affects the body and intimacy has varied over time and has been influenced and affected by cultural and value systems. One of the key points in maintaining QOL, as defined by the World Health Organization (WHO), is sexuality, defined as:

> '… a central aspect of being human throughout life encompasses sex, gender identities and roles, sexual orientation, eroticism, pleasure, intimacy and reproduction. Sexuality is experienced and expressed in thoughts, fantasies, desires, beliefs, attitudes, values, behaviours, practices, roles and relationships. While sexuality can include all these dimensions, not all of them are always

> experienced or expressed. Sexuality is influenced by the interaction of biological, psychological, social, economic, political, cultural, legal, historical, religious and spiritual factors.' (WHO, 2006b)

Human sexuality encompasses a network of feelings that is unique for every person. This unique feeling is built by a person's individual experience and inherent properties. Sexuality is affected by biological, psychological, socio-cultural, moral, spiritual, and ethical and legal factors. How this network is composed on the individual level is unknown (Almås & Benestad, 2010; Graugaard et al., 2019; J. S. Greenberg et al., 2016).

The relationship between chronic disease and human sexuality has many aspects. Verschuren et al. propose a generic conceptual framework to present a conceptualization of chronic disease, where the chronic disease has implications on the physical condition (such as disease activity, treatment, and complications) and the psychological well-being (such as acceptance) which further influence sexual functioning and sexual well-being as a part of sexuality (Verschuren, Enzlin, Dijkstra, Geertzen, & Dekker, 2010). At the same time, it is important to consider different aspects such as the person's age and changing health conditions, and how the chronic disease progresses and which type of function or dysfunction the patients have that is linked to their sexuality (Carrillo-González, Sánchez-Herrera, & Chaparro-Díaz, 2013; Verschuren et al., 2010). Further, it might be important to consider that there is a difference between acute and chronic diseases. Whereas sudden progression of the disease requires immediate adaptation, progressive chronic disease requires continuous adaptation. The impact on these adaptations is affected by the person's place in life (Carrillo-González et al., 2013; Verschuren et al., 2010).

From an early age, we learn the socio-cultural meaning of gender, often being defined as either a boy or girl and our community will influence our perception of gender both psychologically, socially, and culturally (J. S. Greenberg et al., 2016). Gender differences in sexuality are pervasive and affect our thoughts and feelings, and is important to take into consideration for patients with axSpA (Graugaard et al., 2019; J. M. Greenberg, Smith, Kim, Naghdechi, & IsHak, 2017; Prairie, Scheier, Matthews,

Chang, & Hess, 2011). The effect of having a chronic disease—such as axSpA—can also lead to psychological distress, loss of self-esteem, fatigue, depression and grief, and affect sexual outcomes and further sexuality (Özkorumak et al., 2011). AxSpA can cause physical changes where activity can cause pain, leading to poor functional capacity; thus, it can interfere with sexual activity (Fu et al., 2018).

1.3.2 Sexual health

Sexual health is an important part of overall health, consisting of psychological (attention and communication), physiological (hormones, the impact of drug use, and medical problems), moral, and cultural aspects (J. S. Greenberg et al., 2016). Because all individuals are sexual beings and sexuality is part of the individual identity, sexual health concerns everyone (J. M. Greenberg et al., 2017; J. S. Greenberg et al., 2016). A definition of sexual health was given in 2006 by the WHO (WHO, 2006a).

> '… a state of physical, emotional, mental and social well-being in relation to sexuality; it is not merely the absence of disease, dysfunction or infirmity. Sexual health requires a positive and respectful approach to sexuality and sexual relationships, as well as the possibility of having pleasurable and safe sexual experiences, free of coercion, discrimination, and violence. For sexual health to be attained and maintained, the sexual rights of all persons must be respected, protected and fulfilled.'

Sexual health is a relatively new concept and was first taken into the International Statistical Classification of Disease and Related Health Problems in 2019 (Epstein, 2021).

Good sexual health is a resource and can promote one's QOL and how a person copes with a disease (J. M. Greenberg et al., 2017). Education on sexuality and sexual health given by HPs is an important source for obtaining sexual health because it also implies respect for the person's sexual rights (Ministry of Health and Care Services, 2016; Starrs et al., 2018). Sexual health issues are one of many areas for HP to address in consultations (Ministry of Health and Care Services, 2016). Helland et al. (2013) found that HP accepted sexual health as an important issue for patients and relevant for health care in the field of rheumatology. At the same time, they identified some barriers to addressing sexual health, such as the feeling of being uncomfortable with the topic and lack of knowledge and education on how to address sexual health issues

(Helland et al., 2013). Areskoug-Josefsson et al. also identified barriers among Swedish social work students who considered themselves uncomfortable and not prepared sufficiently for dealing with patients' sexual health (Areskoug-Josefsson, Rolander, & Bülow, 2019).

1.3.3. Sexual activity

Sexual activity is part of good sexual health and QOL and an aspect of life affected by personal characteristics, interpersonal relationships, family circumstances, socio-cultural conditions, environment, and records of sexual activity of the couple, and one's own physical and mental health and hormonal status (J. M. Greenberg et al., 2017). Physical difficulties (Fu et al., 2018; Gallinaro et al., 2012; Yao et al., 2016), fatigue, and sleep disturbance (Rostom et al., 2013), can reduce sexual activity. Furthermore, the frequencies of sexual activity and level of intimacy might also change in different phases of life and be affected by a person's view of their body image, having a partner, culture, society, and health (Graugaard et al., 2019; J. S. Greenberg et al., 2016).

1.3.4. Health

Different definitions of health have been promoted during the last decades and the meaning has changed over the years (Larson, 1999; Leonardi, 2018). How we define health might have implications for clinical practice, policy making, and health-care services (Leonardi, 2018). The medical model has been used widely in the USA, the WHO model has gained popularity and newer models such as the wellness model and the environmental model have added new meaning to the definition of health (Larson, 1999).

The 'medical model' has a view of the body as a machine that is possible to fix: also referred to as the 'old medical model'. Georg Engel proposed in a series of papers from 1960 to 1980 to add the psychosocial dimension to broaden the biomedical approach calling it the 'biopsychosocial model' also referred to as the 'the new medical model' (Farre & Rapley, 2017). The intention is to give HP the opportunity to evaluate all factors that could contribute to illness, not the biological factors alone (Farre & Rapley, 2017; Larson, 1999).

The ‘holistic model’, with a broader perspective than the medical model, introduced positive health as an idea. This was exemplified by the WHO definition of health as, ‘…a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity’ (WHO, 1948). The definition has been criticized for stating that health and disease cannot coexist, even though some studies report that people with severe chronic diseases have reported their QOL as being equal or superior to people with no chronic disease (Wahl, Rustoen, Hanestad, Gjengedal, & Moum, 2005). The holistic model has the advantage of allowing for discrimination of people at the higher end of functioning; it focuses on mental as well as physical health, and on broader issues of active participation in life (World Health Organization, 1984). Therefore, in 1984, a WHO discussion document proposed moving away from viewing health as a state, towards a dynamic model that presented it as a process or a force. The new suggestion was:

> ‘The extent to which an individual or group is able to realize aspirations and satisfy needs, and to change or cope with the environment. Health is a resource for everyday life, not the objective of living; it is a positive concept, emphasizing social and personal resources, as well as physical capacities.’ (World Health Organization, 1984)

This definition of health is a resource for living and incorporates both social and personal resources as well as physical capacities (World Health Organization, 1984). This definition has been chosen in this thesis even though it has met some criticisms as not meeting the challenges in today’s health-care systems and for not meeting needs in clinical and scientific fields. The definition is in line with the approach and philosophy of care as T2T in patients with axSpA. So far, no new attempts for a definition have reached consensus (Leonardi, 2018).

1.3.5. QOL in a health context

As for health, many definitions of QOL have been suggested and it can mean different things for different people (Fayers & Machin, 2016, p. 4; Post, 2014). However, there is agreement that QOL is a multidimensional concept, which in different contexts may comprise different characteristics, meanings, and perspectives, including multiple aspects of people’s lives, such as good health, comfort in

relationships, material comfort, and safety. Other aspects of QOL are the opportunity to learn, creative expression, the opportunity to help and encourage others, and socializing in all stages of life (Fayers & Machin, 2007; Spilker, 1996). The WHO definition of QOL from 1997 is chosen in this thesis, it encompasses a personal assessment of the person, their physical health status (e.g. daily physical functioning), and their psychological and social status (e.g. mood, companionship, and recreational activities), and is defined as:

> 'An individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns.' (WHO, 1997)

QOL may be viewed at several levels. Spilker divides QOL into three levels (Spilker, 1996) (Figure 3). The top level is global QOL and contains overall well-being and satisfaction with life. HRQOL might be defined as health status, components placed in the middle level, and single aspects of HRQOL are defined as the level of specific parts of QOL in the pyramid's lowest level. We have included measures of concepts on levels one and two of Spilker's model.

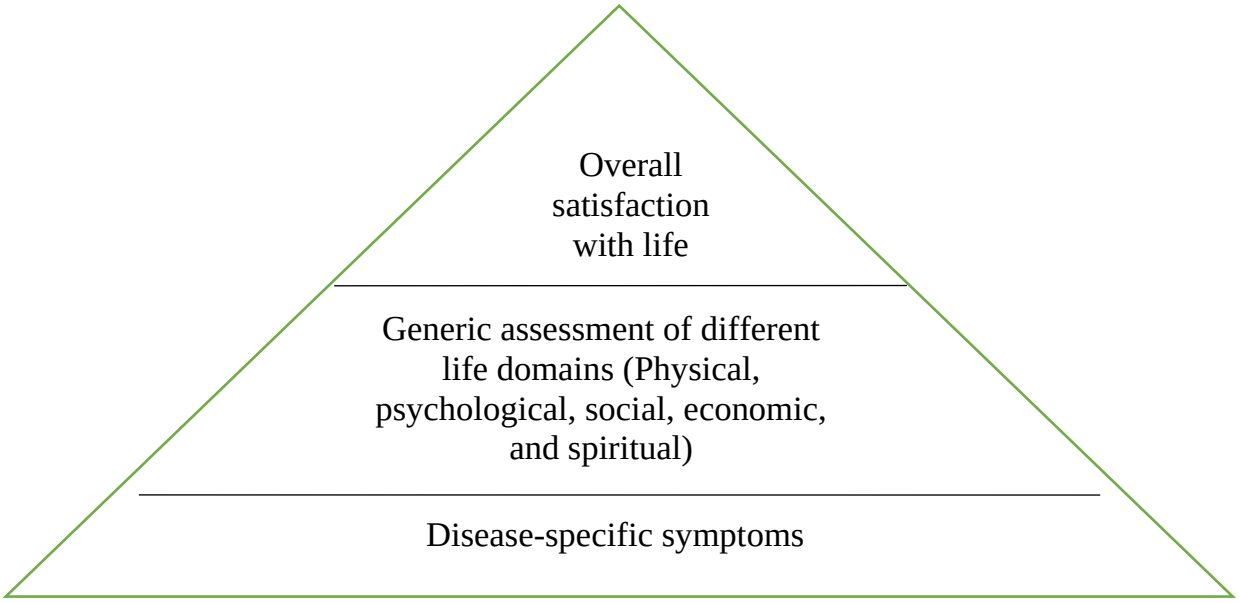

Figure 3. Spilker's model combining measurements of the overall, generic, and disease-related aspects of QOL (Spilker, 1996)

The levels are not mutually exclusive: one level might affect another and can also impact domains within the same level (Ferrans, 1990; Ferrans, Zerwic, Wilbur, & Larson, 2005; Spilker, 1996). Sirgy has suggested that the different domains both within and between the three levels of QOL often affect each other in a positive way (Sirgy, 2012). QOL and HRQOL are recognized and well-accepted among researchers. These concepts have also been used for many years to estimate both positive and negative aspects in terms of the impact of specific diseases. The two terms have also been used to measure the efficacy of interventions in clinical trials and have become valid indicators in assessing whether a particular treatment benefits patients (Spilker, 1996). Furthermore, QOL and HRQOL have been incorporated into strategic documents nationally and internationally. Nationally, the Norwegian Ministry of Health has used the terms to make national plans and uses QOL as an important goal (Ministry of Health and Care Services, 2016).

1.3.6. Health-related quality of life (HRQOL)

Both Ferrans (1990) and Spilker (1996) note that the terms QOL and HRQOL have been used interchangeably. In addition, for HRQOL there is no consensus on the definition (Ferrans, 1990; Karimi & Brazier, 2016; Spilker, 1996). We use the definition of HRQOL proposed by Cappelleri et al., who define HRQOL as a concept with multiple domains representing a person's general perception of the effect of illness and treatment on the physical, psychological, and social aspects of life (Cappelleri et al., 2014). HRQOL is recognized as an important issue in understanding the impact of a disease on a person's life (Ferrans et al., 2005). Because QOL has been used to describe many different aspects over time such as physical functioning, health status, symptoms, psychosocial adjustment, well-being, happiness, and life satisfaction, HRQOL was introduced 'to narrow the focus on the effect of health, illness and treatment on QOL' (Ferrans et al., 2005). The theoretical framework of HRQOL is based on a multidimensional perspective of health, as it covers the patient's own experiences. HRQOL focuses on a person's level of ability, daily functioning, and ability to experience a fulfilling life (Spilker, 1996).

1.3.7. Linking objective variables with HRQOL

The model of linking objective variables with HRQOL by Wilson and Cleary (1995)—later revised by Ferrans et al. (2005)—includes a taxonomy of variables that has a connection with and influences HRQOL. The revised model will be used as a framework for this study (Ferrans et al., 2005; Wilson & Cleary, 1995). The model divides the health outcomes on a continuum with five types of measures, each measuring patient outcomes. The five boxes in the middle of the model, describe biological factors, symptoms, functional status, general health perceptions, and overall HRQOL (Figure 4).

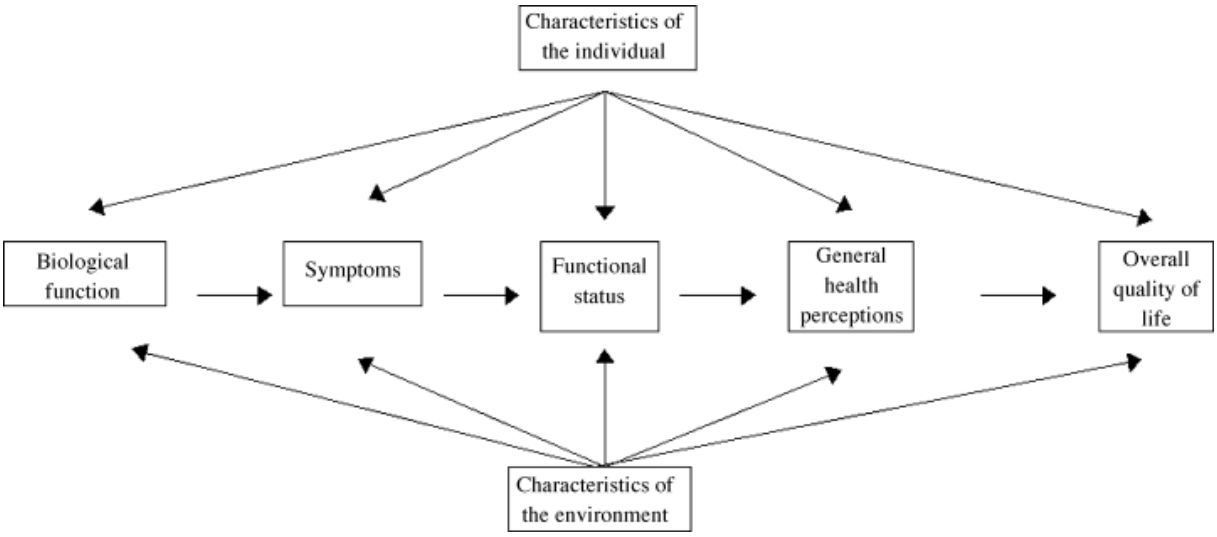

Figure 4. Conceptual framework of HRQOL (Ferrans et al., 2005)
(Used with permission from John Wiley & Sons, Inc.)

The first box in Wilson and Cleary's model is 'biological function'; originally called biological and physiological variables, with pathological function at one end and optimal function at the other. It includes the dynamic processes that support life and the whole organism, including molecular and cellular processes. In the revised model, both individual and environmental characteristics are considered to affect biological function (Ferrans et al., 2005). Individuals have genetic characteristics and compositions that predispose them to develop diseases such as axSpA. How people act, and their knowledge, lifestyle, and attitudes serve as psychological characteristics affecting biological functioning. In the model, 'symptoms' focus on the entire organism, related to the individual's physical, psychological, and psychophysical aspects rather than on the cellular and organism levels (Ferrans et al., 2005).

The functional status comprises four domains of functions: physical function, social function, role function, and psychological function. The fourth box, 'general health perception' integrates all the aspects of health described earlier in the model and at the same time evaluates all aspects of health. These causal pathways in this model are important for clinical practice and can be used in clinical treatment and care of patients with axSpA. Here, objective, and subjective health outcomes and factors were included to identify causal pathways in patients with axSpA, by collecting data on

demographic and clinical variables, functional status, damage, comorbidity, HRQOL, and the disease's impact on sexual activity and sexual QOL. The fifth box in the middle of the model, overall QOL, described as subjective well-being, is how happy and satisfied a person is with life overall. It is a synthesis of experiences and feelings that people have (Ferrans et al., 2005). Overall QOL was not measured in the present study. Often included in QOL studies are several characteristics identified as determinants or associates of QOL, such as educational level, personality, coping mechanisms, and marital status, which also are included in this study (Loge, Kaasa, Hjermstad, & Kvien, 1998).

1.3.8. Sexual quality of life

Sexual QOL is defined as the status that describes the individual's subjective evaluation of the positive and negative aspects of one's sexual relationship, and his/her subsequent affective response to this evaluation (Koh & Sewell, 2015). Sexual QOL includes both sexual health and sexuality involving communication, culture, ethical, and global areas (Graugaard et al., 2019; J. S. Greenberg et al., 2016). To have a fulfilling sex life is important for sexual QOL at all ages. Forbes et al. found that being older was a negative factor for sexual QOL, but learned strategies—also called sexual wisdom—together with a positive relationship with a partner was positive for sexual QOL (Forbes, Eaton, & Krueger, 2017). Therefore, measuring sexual QOL is an important issue for assessing short- and long-term outcomes of disease, especially when having a disease that can cause sexual problems (Hwang et al., 2021; Symonds, Boolell, & Quirk, 2005). To have good sexual QOL and satisfactory HRQOL, it is important to focus on both subjective and objective perspectives associated with axSpA, such as demographic and clinical variables, functional status, damage, comorbidity, the disease impact on sexual activity and sexual QOL. In this thesis, HRQOL and sexual QOL refer to Spilker's second level for patients with axSpA (Spilker, 1996).

1.3.9. Psychology of QOL and 'response shift'

The psychology of QOL includes mechanisms of how patients tend to adjust and manage their illness and how they use strategies to optimize all aspects of their

QOL (Sirgy, 2012). One of these strategies is ‘response shift’, defined as a change in internal standards and values and a redefinition of what is important in the patient’s life in relation to their QOL (Schwartz et al., 2006; Sirgy, 2012). The response shift has been described as recalibrating (by changes in internal standards of measurements), reprioritizing (by changes in the priority of components of the target construct), and reconceptualizing (by redefinition of the target construct) (Sprangers & Schwartz, 1999; Yang et al., 2016).

Developing a chronic disease such as axSpA requires recalibration of the perceived QOL. There can be differences in how a person can or cannot shift focus. Some patients are ‘decliners’ of the response shift, and some are ‘improvers’. A decliner does not adapt to the situation, whereas an improver achieves a response shift with or without help from others, and decliners might use a strategy of somatization or hypochondriasis, leading to a lack of response shift (Wilson, 1999; Yang et al., 2016). The process might be influenced by a person’s social and structural context, which can promote or inhibit changes (Yang et al., 2016). For example, affective understanding and practical support from family and friends can promote changes, which can help the person to achieve new goals and thereby improve QOL and sexual QOL (Sirgy, 2012).

2 Aims of the study

The overall aim of this thesis was to examine the impact of health status on sexual activity and sexual QOL in male and female patients with axSpA. The specific aims were:

In Paper I (a cross-sectional study) the aim was to explore the relationship between demographic and disease-related variables and the perceived effect of health status on sexual activity in patients with axSpA and answer the following specific research questions:

In Paper II (a cross-sectional study) the aim was to examine the relationship between demographics, disease-related variables, treatment, and sexual QOL in men and women with axSpA and to answer the following specific research questions:

In Paper III (a prospective cohort study with a 5-year follow-up) the aim was to explore whether a follow-up would reveal long-term changes in perception of sexual QOL in male and female patients with axSpA and to answer the following specific research questions:

3 Materials and methods

In this chapter, ethical considerations will be elaborated, followed by study description, study design, patient recruitment, data collection, PROMs, and finally a presentation of the statistical analyses used in the three sub-studies.

3.1 Ethics

The aim of the Norwegian Health Research Act is to 'promote good and ethically sound medical and health research' (The Health Research Act, 2008). To achieve this, people who are willing to participate in research are needed. The research should be of some benefit for the participants and possible factors of risk and harm should be calculated. Further, respect for human dignity as self-determination and justice includes fair treatment and the right to anonymity (Polit & Beck, 2008). To be able to fulfil these all patients received written information about the study (Appendix 7) together with a letter with the time for the consultation appointment. When the patients were coming to the consultation, the were given oral information and informed consent was obtained from all patients. When given their consent to participating, all data set was given a number with connection to a master list. All procedures performed were done in accordance with the ethical standards set by the Declaration of Helsinki (World Medical Association, 2013).

A research protocol was sent to the Regional Committee for Medical Research Ethics of South-East Norway and approved under the number IRB 4.2007.2152).

3.1.1. Collecting sensitive data

Collecting data on sexual activity and sexual QOL in patients with axSpA is sensitive and closely related to 'vulnerable groups'. Furthermore, Liamputtong (2007) defines several groups as being vulnerable, including chronically ill people, who were the target of our research (Liamputtong, 2007). On the other hand, patients with axSpA might be considered not to be especially vulnerable, but the issue of sexual activity and sexual QOL can be sensitive for patients and has to be taken into onsideration (Liamputtong, 2007).

To be both clinician and researcher at the same time, like me in the current study, can present some challenges and causes ethical considerations, and involves all three principles in the Belmont Report 1979: first, respect for the person's autonomy; second, beneficence (protecting the patients from harm); third, justice providing the same fairness for all participants (HHS, 1979). Loyalty to and trust in the researcher can lead to the patient agreeing to participate in research without being fully aware of all the implications of the project. In the present study, the nurses were both clinicians and researchers, which could put the patients in a conflict between loyalty to the health-care providers and their own wishes. Patients should be aware of the type of data they are agreeing to provide, especially concerning sensitive data such as data on sexual health. To accommodate the three principles in the Belmont Report, the patients were given written and oral information about the study, the type of data collected, how the data were stored and made anonymous as soon as they were collected (HHS, 1979; Lovdata, 2017). They were also informed about how the data would be used for research and publications and their right to withdraw from the study at any time (World Medical Association, 2013).

3.2 Study description and study design

The present study was a prospective cohort study that comprised three sub-studies presenting objective and self-reported data of patients with axSpA (Table 1). In Papers I and II, a cross-sectional study design was used (Polit & Beck, 2008). In Paper III, a prospective cohort study with a 5-year follow-up design was used, where data were collected at two time points, which allowed us to make comparisons over time and to determine whether changes had occurred (Polit & Beck, 2008). In the last paper, the patients were followed over a period of 5-years. Papers I and II include baseline data on the same sample of patients with axSpA, whereas Paper III includes patients with data available at both the baseline and at the 5-year follow-up. Across the different sub-studies in Papers I–III, sample size, study design, dependent and independent variables, and analyses varied. Table 1 gives an overview.

Table 1. Study design, dependent and independent variables, and analyses used in Papers I–III

	Paper I	**Paper II**	**Paper III**
Sample (n)	n = 379	n = 360	n = 245*
Study	Cross-sectional	Cross-sectional	Prospective cohort with 5-year follow-up
Dependent variable	15D (question 15)	SQOL-F	SQOL-F
Independent variables: **Demographics** **Health status** Clinical measures Damage Self-reported HRQOL Treatment	 Age, gender BMI (kg/m^2), Smoker, employment Exercise CRP, 68 tender joints, 66 swollen joints, BASDAI, MASES BASMI BASFI, HAQ, BAS-G SF-36 NSAID, csDMARD, bDMARD	 Age, gender BMI (kg/m^2), Smoker, employment Exercise CRP, 68 tender joints, 66 swollen joints, BASDAI, MASES BASMI BASFI, HAQ, BAS-G SF-36 NSAID, csDMARD, bDMARD	 Age, gender BMI (kg/m^2), Smoker, employment Exercise CRP, 68 tender joints, 66 swollen joints, BASDAI, MASES BASMI BASFI, HAQ, BAS-G SF-36 NSAID, csDMARD, bDMARD
Analyses	Chi-squared Independent *t* tests Univariate and multivariate logistic regression Nagelkerke R^2	Chi-squared Independent *t* tests Linear regression (GLM) Cronbach's α Pearson correlation Nagelkerke R^2	McNemar's tests Paired-samples *t* tests Univariable and multivariable regression (GLM) Cohen's effect size Nagelkerke R^2

* Not all patients from MHH were invited for the 5-year follow-up because of a lack of financial resources. 15D, a generic, comprehensive, 15-dimensional, standardized, self-administered measure of HRQOL; SF-36, Health Survey Short-Form-36 items; GLM, General Linear Model; SQOL-F, Sexual Quality of Life – Female; BASFI, Bath Ankylosing Spondylitis Functional Index; HAQ, Health Assessment Questionnaire; BAS-G, Bath Ankylosing Spondylitis Patients Global Score; BASDAI, Bath Ankylosing Spondylitis Activity Index; MASES, Maastricht Ankylosing Spondylitis Enthesitis Score; BMI, body mass index; BASMI, Bath Ankylosing Spondylitis Metrology Index; csDMARD, synthetic disease-modifying antirheumatic drug; bDMARD; biological disease-modifying antirheumatic drug.

3.3 Patient recruitment and data collecting

Patients with axSpA were recruited from the outpatient clinics at two hospitals in Norway: SSHF and MHH. Patients had to be aged ≥18 years with no upper limit. In addition, they had to speak and understand Norwegian and be in a physical and mental condition suitable to give informed consent. When the study was designed, the modified New York criteria were applied (van der Linden et al., 1984). The ASAS classification criteria for axSpA published in 2009 (Rudwaleit et al., 2009a; Rudwaleit et al., 2009b) including both patients with radiographic axSpA (AS) and non-radiographic axSpA was not available. After inclusion of patients in the present study, all patients were checked that they fulfilled these criteria (Rudwaleit et al., 2009a; Rudwaleit et al., 2009b).

The patients were identified by the study nurses, who used the list for planned patient interviews at the outpatient rheumatology clinics. The patients were contacted by telephone before the appointment and informed about the study, invited to participate, and were then included consecutively. During the baseline consultation, the patients were informed that they would get an invitation to a 5-year follow-up. Baseline data collection was performed from 2008 to 2011 and after five years from 2013 to 2016, which enabled the exploration of data related to health and disease-related issues over time. At the beginning of the data collection, no power calculation of size was done. The aim was to recruit all patients with axSpA visiting the outpatient clinics, fulfilling the inclusion criteria, who were scheduled for control appointments in a timeframe from 2008 to 2011. In total, 397 patients with axSpA were invited to participate. Eight patients declined the invitation without giving any reason, which led to data collection from 389 patients (Figure 5). In the middle of the process of inviting patients for the 5-year follow-up, the inclusion of patients at MHH was stopped because of a lack of financial resources. This meant that 109 patients were not invited to participate in the follow-up. In total, 280 patients at the two hospitals were invited to the follow-up, 35 did not accept the invitation, 31 had moved and four had died.

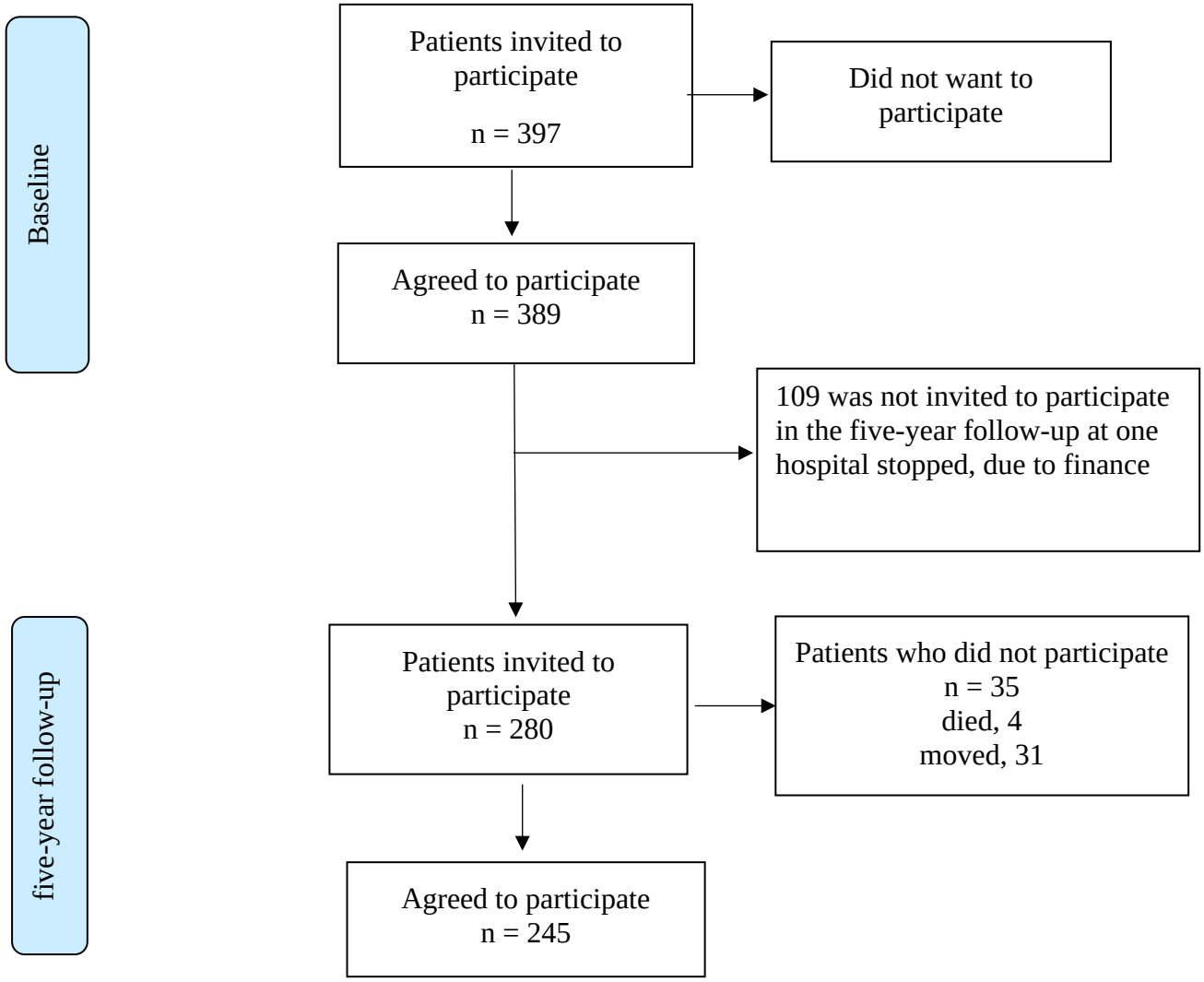

Figure 5: Flow chart describing the sample of patients with axSpA included at baseline and five-year follow-up.

3.4 Demographic variables, medication, and physical examinations

Doctors and nurses assigned to the project obtained demographic data from patients such as age, weight, employment, education, married or cohabiting, and if they had a partner with whom to have sex. We also collected data on exercise, alcohol use, smoking, sex (categorized as man or woman), weight in kg and height in centimetres to calculate the body mass index (BMI kg/m^2). Data on educational level

were organized into three groups: <10, 11–13, and >13 years. Employment was categorized as working, on sick leave, on disability benefits, or as retired. This was recoded into working or unemployed (on sick leave, disability benefits, and retired) in the analyses. Exercise was organized into >3 h/week, 1–3 h/week, <1 h/week, seldom or never, these were further recoded to >1 h/week and <1 h/week in the analyses.

Data on alcohol use were collected by asking how often the patient had drunk alcohol during the last 30 days, organized into five groups: never, 2–6 glasses/week, 7–14 glasses/week, 14–21 glasses/week, and more than 21 glasses/week. For statistical purposes, these groups were recoded to never, 1–6 glasses/week and ≥7 glasses/week. Smoking status was organized as non-smoker, previous smoker, and current smoker, and for statistical purposes recoded to smoker and non-smoker (non-smoker and previous smoker). In addition, disease duration was calculated as the time from when the ASAS criteria were fulfilled until the date of inclusion. Information regarding current medication was collected by asking the patients and checking patients' hospital files. The doctors and nurses assigned to the project obtaining data also performed physical examinations such as the MASES Score, which is an examination of tender points, showing inflammation in the tendons (Heuft-Dorenbosch et al., 2003). Further, the BASMI, which is a test of function and an expression for disease damage (Jenkinson et al., 1994), and examination of tenderness and swelling in 68/66 joints were performed (Duarte-García et al., 2019). Objective measures such as the CRP level was obtained from laboratory tests (Table 2).

Table 2. An overview of the measures of disease activity and damage

Measures	Reported by	Description	Papers
MASES	Physician/nurse	Disease activity	I, II, and III
CRP	Laboratory	Disease activity	I, II, and III
68 tender and 66 swollen joints counts	Physician/nurse	Disease activity	I, II, and III
BASMI	Physician/nurse	Damage	I, II, and III

MASES, Maastricht Ankylosing Spondylitis Enthesitis Score; CRP, C-reactive protein level; BASMI, Bath Ankylosing Spondylitis Metrology Index.

3.5 Patient-reported outcome measures (PROMs) used in the study

PROMs measure a patient's perceptions of health, sickness, and effect of treatment, and encompass measures of symptoms, functions, health, and QOL (Fayers & Machin, 2016). The PROMS used in this thesis were HAQ, BAS-G, BASFI, BASDAI, 15D, SF-36, and SQOL-F (Table 3).

Table 3. Patient-reported outcome measures used in this study

Measures	Reported by:	Description	Paper
HAQ	Patients ≥18 years	Physical ability	I, II, and III
BAS-G	Patients ≥18 years	Effect of AS on patients' well-being	I, II, and III
BASFI	Patients ≥18 years	Daily activity	I, II, and III
BASDAI	Patients ≥18 years	Disease activity	I, II, and III
15D	Patients ≥18 years	QOL	I
SF-36	Patients ≥18 years	HRQOL	I and II
SQOL-F	Patients ≥18 years	Sexual QOL	II and III

HAQ, Health Assessment Questionnaire; BAS-G, Bath Ankylosing Spondylitis Patients Global Score; BASFI, Bath Ankylosing Spondylitis Functional Index; BASDAI, Bath Ankylosing Spondylitis Activity Index; 15D, A generic, comprehensive, 15-dimensional, standardized, self-administered measure of HRQOL; SF-36, Health Survey Short-Form-36 items; SQOL-F, Sexual Quality of Life – Female.

3.5.1. The Health Assessment Questionnaire (HAQ)

This tool was used to measure physical disability. The questionnaire comprises 20 questions about the performance of physical activity over the last week and covers eight areas: dressing and getting ready, arising, eating, walking, personal hygiene, reach, grip, and common daily activity. Each item has a four-level response scale from 0 to 3, where 0 is no difficulty, 1 is some difficulty, 2 is much difficulty, and 3 indicates inability to do the activity (Fries, Spitz, Kraines, & Holman, 1980). HAQs

are used frequently to measure physical disability in patient groups. The questionnaire has established validity and reliability, internationally and in Norway (Bruce & Fries, 2003; Uhlig, Haavardsholm, & Kvien, 2005).

3.5.2. The Bath Ankylosing Spondylitis Patients Global Score (BAS-G)

This tool was used to measure the effect of axSpA on a patient's well-being during the last week and in the last 6 months (Jones, Steiner, Garrett, & Calin, 1996). Each question has a numerical rating scale range of 0–10, where 0 is the most positive and 10 the most negative. It was tested for reliability, validity, and sensibility in the original and Swedish versions (Jones et al., 1996; Waldner, H., & C.H., 1999). It was translated and validated into Norwegian by the medical company MSD-Norway, using standardized translation procedures according to an international cross-cultural translation manual (Fayers & Machin, 2016). However, the translation procedure has not been published.

3.5.3. Bath Ankylosing Spondylitis Functional Index (BASFI)

This questionnaire comprises 10 questions about how the patient has managed daily activity over the last week and focuses on axial pain, peripheral joint pain, fatigue/tiredness, enthesitis, and morning stiffness. Each question has a visual analogue scale of 0 to 10, with 0 being the most positive and 10 the most negative score. It has been found to be a valid and appropriate composite to define disease activity in patients with AS (Calin et al., 1994). The questionnaire was translated into Norwegian by the medical company MSD-Norway (see above), using standardized translation procedures according to an international cross-cultural translation manual (Fayers & Machin, 2016). However, the translation procedure has not been published.

3.5.4. Bath Ankylosing Spondylitis Activity Index (BASDAI)

This was used to measure disease activity. It is a self-reported questionnaire measuring disease activity with six questions about how the patient has felt over the last week concerning tiredness, pain, and morning stiffness. Each question has a score from 0 (nothing to report) to 10 (the most negative answer) in the other end, this is a numerical ranking scale. The patient chooses the number suitable for their situation: a

lower number shows lower disease activity. The BASDAI was developed and validated by Garrett et al., with established validity and reliability (Garrett et al., 1994). It has been translated into Norwegian and validated by MSD-Norway (see above), using standardized translation procedures according to an international cross-cultural translation manual (Fayers & Machin, 2016). However, the translation procedure has not been published.

3.5.5. Measure of Health-Related Quality of Life (15D)

This was used to measure the impact of health status on sexual activity. It is a generic, multidimensional, standardized tool for evaluating HRQOL and is primarily used as a single-index measure but can be used as a profile utility measure. The questionnaire captures the health status by assessing 15 dimensions: mobility, vision, hearing, breathing, sleeping, eating, speech, elimination, usual activities, mental function, discomfort and symptoms, depression, distress, vitality, and sexual activity. Each dimension is assessed by one question using five response categories with the following response options for sexual activity: no adverse effect, has a slight effect, has a considerable effect, makes it almost impossible, and makes it impossible.

In the current study, we used only question 15 in the 15D questionnaire and for analysis, the five response options were dichotomized as follows: no adverse effect/slight effect to ‘no/little effect’, and considerable effect/almost impossible/sexual activity impossible to ‘large effect’.

The self-administered questionnaire was independently translated into Norwegian from an English version by the physicians, who discussed the translations and agreed on a consensus version. The Norwegian version had also been compared with the original Finnish version (Stavem, 1999). The 15D instrument has been used in different patient groups when the focus is on HRQOL (Helland, Dagfinrud, & Kvien, 2008; Rohde, Berg, Pripp, Prøven, & Haugeberg, 2019; Rohde et al., 2017) and has favourable validity and reliability (Sintonen, 2001; Saarni et al., 2006).

3.5.6. Health Survey Short-Form-36 items (SF-36)

This was used to measure HRQOL. The SF-36 is a self-reported generic health status questionnaire (Ware & Kosinski, 2005). It is widely used internationally and is not specific to age, treatment, or disease group. It comprises 36 questions and eight

domains: general health, bodily pain, physical function, role limitations (physical), mental health, vitality, social function, and role limitations (emotional). The eight domains can be combined into a Physical Component Summary score (PCS) and a Mental Component Summary score (MCS) measuring distinct components of health, physical, and mental health. The PCS and MCS scales were used in this study (Ware & Kosinski, 2005). The SF-36 was scored according to published procedures. Each question has a response range of 0–100 with 100 representing excellent health. Imputation for missing data was included in scoring, in accordance with the original guidelines (Ware & Kosinski, 2005). Reliability and validity in the SF-36 are satisfactory, as indicated in earlier Norwegian studies (Loge et al., 1998).

3.5.7. Sexual quality of life-Female questionnaire

The Sexual quality of life-Female questionnaire (SQOL-F) was chosen to measure sexual QOL. In 2005, Symonds, Boolell, and Quirk developed the SQOL-F, based on the work of Abraham and co-workers, which again was based on Spitzer's QOL measure. The SQOL-F is a generic self-reporting questionnaire for assessing the relationship between female sexual dysfunction and QOL (Symonds et al., 2005). It comprises 18 positive and negative items, rated on a 6-point response: completely agree, moderately agree, slightly agree, slightly disagree, moderately disagree, and completely disagree. The response categories are scored 1–6, giving a total score range of 18–108. A higher score indicates better sexual QOL (Symonds et al., 2005). The questionnaire has shown good psychometric properties according to convergent validity, discriminant validity, and test–retest validity (Symonds et al., 2012; Symonds et al., 2005). SQOl-F has not been validated in a Norwegian population. The questionnaire was translated into Norwegian by the MAPI Research Institute in 2006 for use in clinical trials (Downey, CA, USA; not published). To our knowledge, no other studies has used SQOL-F in patients with axSpA but used other questionnaire on SQOL (Dong et al., 2015).

Maasoumi et al. (2013) translated SQOL-F into Persian and identified four categories: psychosexual feelings (range 7–42), sexual and relationship satisfaction (range 5–30), self-worthlessness (range 3–18), and sexual repression (range 3–18). These reflect various aspects or dimensions of sexual QOL and showed good

psychometric properties in the Iranian population. These categories were also used in this study. We applied Cronbach's α test for evaluating the reliability of the questionnaire and its subcategories. The results were 0.77 for total sexual QOL, 0.91 for psychosexual feelings, 0.81 for sexual and relationship satisfaction, 0.84 for self-worthlessness, and 0.87 for sexual repression, which were considered as acceptable reliability for the patients in the current study (Fayers & Machin, 2007).

3.6 Analyses

For statistical analysis, IBM SPSS Statistics v. 22.0 was used in Paper I; v. 24.0 in Paper II, and v. 25.0 in Paper III (IBM Corp., Armonk, NY, USA). In all three papers, descriptive statistics were used to describe the samples, which are presented as the mean and standard deviation (±SD) for continuous variables and as number and percentage (%) for categorical variables. In Papers I and II, comparisons between groups were applied using chi-squared tests for categorical variables and independent-sample Student's *t* tests for continuous variables. In Paper III, the comparison between baseline and 5-year follow-up, McNemar's test was used for categorical variables and paired-samples Student's *t* tests for continuous variables (Table 1) (Altman, 2006).

To explore the relationship between demographic and disease-related variables and the perceived effect of health status on sexual activity in patients with axSpA (question 15 in Paper I) the 15D questionnaire was dichotomized into no/little or a large effect of health status on sexual activity in patients with axSpA. To identify associations with the dependent variable (question 15 in the 15D questionnaire), we included demographic variables and variables on disease activity, health status, damage, comorbidity, and treatment centre, in univariate and multivariate logistic regression analyses (enter procedure). Variables with $p < 0.20$ tested in the univariate analysis were included in the multivariate model, and a backward procedure was used to test for robustness (Table 1).

In Paper II, to examine the adjusted association between demographic, disease-related variables and sexual QOL, for both the total score and for the four categories, a

general linear model (GLM) was used in SPSS. The independent variables in the multiple analyses were chosen based on $p < 0.1$ in the univariate analyses and adjusted for age and gender. In the final multivariate model, we included the impact of demographic variables and variables on disease activity, health status, damage, comorbidity, and treatment centre. To explore the reliability of the SQOL-F questionnaire with its total score and sub-scores, we used Cronbach's α test (Table 1).

In Paper III, changes in the sexual QOL score were calculated by subtracting the baseline score from the score at the 5-year follow-up. The effect size was calculated by subtracting the mean sexual QOL score (and its categories) at baseline from the mean score at the 5-year follow-up and divided by the SD at baseline within the groups. Cohen's effect size index was used to interpret and estimate the proportion of patients with clinically significant changes in sexual QOL over the studied period (Fayers & Machin, 2007; Polit & Beck, 2008, 2018). Multivariable regression (GLM) analyses were used to identify associations between demographic variables and variables on disease activity, health status, damage, comorbidity, and treatment centre at baseline and at the 5-year changes in sexual QOL sum score and its sub-scores (Fayers & Machin, 2007). The level of significance was set to $p < 0.05$.

4 Main findings

This section gives a summary of the findings in papers I–III. More detailed information can be found in the original paper attached at the end of this thesis.

4.1 Papers I and II

4.1.1 Demographic data at baseline

In all, 397 patients with axSpA were invited to participate in the study, of whom 389 completed the questionnaires (Figure 5). The participants had a mean age of 45.6 years, SD ±11.9), 66.5% were men, and 55.7% reported having more than 13 years of education. Their mean disease duration was 13.9 years, SD (±11.4) and the patients reported to have few other co-morbidities (mean = 0.7; SD ±0.9). A high proportion of the patients were married, or cohabiting (76.3%) and the majority (81.1%) said that they had a partner with whom to have sex. Most of the patients (84.8%) exercised for >1 h/week.

4.1.2. Paper I

Most of the 379 patients with axSpA answered the question of how their state of health had an impact on their sexual activity (15D). The 10 patients who did not answer the question had a mean age of 52.2 years, vs. 46.6 years in the group who answered the question ($p = 0.09$). In addition, those who did not answer the question had a longer disease duration: 28.8 years vs. 13.9 years ($p = 0.016$). Most (82.3%) of the patients who answered the question, reported that their health status had little or no impact on their sexual activity. There were some differences between genders, where more women than men reported their health status to have had a large impact on sexual activity (23.6% vs. 14.7% ($p = 0.031$)). Furthermore, there were some additional differences between men and women: men had higher BMI (27.6 kg/m^2 vs. 25.6 kg/m^2; $p = 0.001$), higher alcohol consumption (1–6 glasses per week 73.5% vs. 65.9%, more than 7 glasses per week 11.6% vs. 7.1%; $p = 0.012$), higher employment rate (76.6% vs. 66.9%, $p = 0.048$), reported lower disease activity (BASDAI score 3.03 SD ±2.10 vs. 3.5 SD ±2.1; $p = 0.037$) and lower health status (HAQ 0.52 SD ±0.47 vs. 0.65 SD ±0.54; $p = 0.012$) than women. Physical examinations revealed that

men had lower inflammation in the tendons (by MASES), but more damage on the skeleton (by BASMI), than women.

In the adjusted analyses, the characteristics that were significantly associated with a large negative effect on health status on sexual activity were being a woman, having a high BMI, being a current smoker, and reduced HRQOL (measured by SF-36, PCS, and MCS).

4.1.3. Paper II

Here, 360 out of the 389 patients responded to questions on sexual QOL. The responders reported to have a higher consumption of alcohol (82.0% vs. 62.1%; p = 0.033), higher employment rate (72.2% vs. 48.3%; p = 0.003), exercised more (86.6% vs. 72.4%; p = 0.038), and more were cohabitant (78.6% vs. 37.9%; $p < 0.001$) than non-responders to the questionnaire. Some differences between gender were identified for sexual QOL; men reported better on total sexual QOL (78, SD ±10.9 vs. 75, SD ±11.9; p = 0.026), and on the subgroup, sexual repression (16, SD ±3.4 vs. 14, SD ±4.1; p = 0.005). Furthermore, women had lower BMI, more inflammation in the tendons, and lower physical function than men. In the adjusted analyses, low BAS-G and CRP scores and use of bDMARDs were associated with higher sexual QOL, whereas female gender and increased BMI were independently associated with lower sexual QOL.

4.1.4 Paper III

In all, 280 patients with axSpA were invited to participate at 5-year follow-up; 245 agreed to take part, and 221 completed the questionnaires on sexual QOL both at baseline and at the 5-year follow-up (Figure 5).

The 221 patients with axSpA who answered the question on sexual QOL were significantly younger (mean 45.4 years, SD ±10.8) vs. 50.9, SD ±10.8; p = 0.025) and more were married or cohabiting (81% vs. 42%; $p < 0.001$) than the non-responders. Among the responders fewer reported smoking (26% vs. 46%; p = 0.046), and they exercised more (89% vs. 75%; p = 0.046) than those who did not answer the questionnaire. Over the 5-year period, no significant changes in sexual QOL were revealed. However, the patients used more bDMARDs and there was a significant

increase in the incidence of comorbidities from 0.58 to 0.95. In the multivariate analysis, a decrease in sexual QOL after 5 years was observed in patients exercising <1 h/week at baseline (p = 0.048) and in patients aged >65 years.

5 Discussion

In this section, the main findings will be discussed across the three papers according to the following topics: significance of the state of health for sexual activity, sexual quality in life in patients with axSpA, differences between men and women related to sexual activity and sexual quality of life and sexual quality of life in a social context, followed by methodological considerations.

5.1 Significance of the state of health for sexual activity

Sexual activity is an important part of being a person and has multiple purposes, such as pleasure, bonding to a partner, showing love and affection, and reproduction (Graugaard et al., 2019). Health status has been reported to have a negative impact on sexual activity in patients with axSpA (Helland et al., 2008). Although few studies have examined the impact of health status on sexual activity in men and women with axSpA, health status has been reported to have a negative impact on sexual activity in patients with AS (Fu et al., 2018; Gallinaro et al., 2012; Rostom et al., 2013; Yao et al., 2016). However, it is difficult to compare our studies with these earlier studies because of differences in the settings, measurements, and timing: for example, for data collected before and after surgery (Fu et al., 2018; Gallinaro et al., 2012; Rostom et al., 2013; Yao et al., 2016).

In the thesis study population of patients with axSpA, with a mean age of 46 years and 33% as women, about 18% reported their health status to have a large impact on sexual activity. A Norwegian study of outpatients with PsA, a prototype of peripheral SpA, with a mean age of 52 years and 49% as women that used the 15D questionnaire, a similar percentage (18%) reported that their health status had a large impact on sexual activity (Haugeberg, Michelsen, Østensen, & Kavanaugh, 2020). In another Norwegian study that used the same questionnaire in patients with RA, 31% reported that their health status had a considerable influence on their sexual activity (Helland et al., 2008). The study by Helland et al. (2008) included a higher percentage of women (74%) with a mean age of 58 years (Helland et al., 2008). By contrast, slightly different results were reported in a Norwegian study of 181 patients with wrist fracture, aged 50 years and

older (mean age 65 years, 84% women), in which only 13% reported that their health status had a large negative impact on sexual activity (Rohde, Berg, & Haugeberg, 2014).

From the studies mentioned above, it seems that a lower percentage of patients with inflammatory joint disorders, including axSpA, perceive that their health status has a more negative impact on sexual activity than that seen in the Norwegian background population (Haugeberg, Michelsen, & Kavanaugh, 2020; Helland et al., 2008; Rohde et al., 2014). The reason why fewer patients with axSpA report that their disease has a large impact on sexual activity may reflect the influence of various factors. Patients reporting little or no impact in the studies presented here may differ on lifestyle factors. For example, fewer patients in this cohort smoked, more exercised regularly, 78% were married or cohabiting, and their disease activity was low, as indicated by less inflammation in the tendons and better self-reported health status.

5.1.1. Lifestyle factors important for health status

Both smoking and obesity are important lifestyle factors related to health status (Bindesbøll, Garrido-Cumbrera, Bakland, & Dagfinrud, 2020; Zhao et al., 2019). These factors as well as physical activity are important for patients with axSpA because they have a strong impact on health status, which may be even stronger than that of the disease itself (Chimenti et al., 2021). Obesity in patients with axSpA can increase the disease activity (Bindesbøll et al., 2020), and obesity (BMI >30 kg/m^2) is more common in patients with axSpA than in the general population (Maas et al., 2016). The findings of the present studies are to some degree consistent with those described above. For example, in Paper I, overweight patients (BMI 28.5 kg/m^2) reported that their health status negatively impacted their sexual activity; these patients also had lower scores for well-being (BAS-G), physical disability (HAQ), and HRQOL (measured by the SF-36; PCS, and MCS), and more problems managing daily activities (BASFI).

Smoking and obesity can interfere with and lead to poorer responses to treatment. In a large study from England of 758 participants (66% men, mean age 45 years), smoking was associated with worse disease severity but had no impact on discontinuation of anti-TNF therapy (Zhao et al., 2019). In the current cohort, smoking

and obesity has been reported to reduce patients' HRQOL and impact their sexual activity (Berg et al., 2017). A review article from Spain found that, in two studies, smokers had a negative response to anti-TNF therapy but that four other studies identified no differences in the clinical response to such treatment (Zurita Prada, Urrego Laurín, Guillén Astete, Kanaffo Caltelblanco, & Navarro-Compán, 2021). In the same review, five of six studies found that obesity had a negative impact on the response to anti-TNF therapy (Zurita Prada et al., 2021). In the present studies, no disease- or treatment-related variables were independently associated with a negative impact of health status on sexual activity.

5.1.2 Disease activity in patients with axSpA

Patients who reported that health status had a large impact on sexual activity reported higher disease activity, lower physical HRQOL and less exercise, were more likely to be unemployed, used more alcohol, smoked more, had a higher BMI, and had more comorbidities (Berg et al., 2017). High disease activity along with inflammation in the axial skeleton leads to pain and restrictions in mobility, which can impair sexual activity, limit physical activity, and impair physical HRQOL (Agrawal & Machado, 2020; Rausch Osthoff, Niedermann, et al., 2018; Regel et al., 2017).

Health status is also influenced by physical activity and lifestyle (Regel et al., 2017). Exercise is important for managing daily activities and for disease control, general well-being, and preventing other diseases, and is an essential part of the non-pharmacological treatment in patients with axSpA. (Agrawal & Machado, 2020; Regel et al., 2017). The National Norwegian (2014) recommendation for daily physical activity is 150 min/week for adults. In the studies presented here, 84.8% of patients exercised more than 1 hour/week. In previous studies, smoking was negatively associated with disease activity, functional status, and HRQOL (Chung et al., 2012; Mattey, Dawson, Healey, & Packham, 2011). In our studies, current smoking also had a negative impact on sexual activity (Paper I).

In general, the disease activity in the current study cohort was low, and the long disease duration (mean disease duration 13.9 years) probably reflects that most of the patients were middle-aged (mean age 46.6 years). Different results may have been

obtained from a cohort with a younger mean age and shorter disease duration. Young patients tend to report more pain and have had less time to adjust to the disease because axSpA often occurs in early adulthood (Sieper et al., 2009). For example, in a study of a large group of patients with early axSpA, those with high disease activity had worse physical HRQOL but not mental HRQOL (van Lunteren et al., 2018). Low disease activity in the current cohort most likely reflects good disease control because a higher percentage (23%) of patients used bDMARDs at the baseline and 40% used these drugs at the 5-year follow-up. High disease activity and damage, as assessed by the BASMI, are associated with worse physical and mental HRQOL (Rohde et al., 2017). Studies of men with axSpA have found that high disease activity and disease manifestations, such as damage to the hip joints and spine, can negatively interfere with sexual activity (Fu et al., 2018; Gallinaro et al., 2012; Yao et al., 2016).

In addition to lifestyle factors and pathophysiological processes, health status is also influenced by psychosocial factors, as discussed below. Some patients manage to live well with the disease, even when it is active, because they adapt positively and adjust their strategies to optimize their HRQOL as a way to manage their illness (Sirgy, 2012).

5.1.3 Psychosocial and environmental factors

Social influences of a partner, family, friends, and HPs are important environmental factors to HRQOL and sexual QOL (Ferrans et al., 2005; Graugaard et al., 2019). Living with a partner can provide social and psychological support, although feedback from a partner can increase awareness of the influences of axSpA on sexual activity (Starrs et al., 2018). In our studies, high percentages of patients reported having a partner to have sex with (81.1%) and being married or cohabiting (76.3%). Living in a social context with a close partner may be important for managing living with axSpA as a lifelong condition (Raybone, Family, Sengupta, & Jordan, 2019). This may partly explain why as high as 80% of the patients in our studies reported that their health status had little or no impact on their sexual activity. After living with the disease for many years, the patients had probably adapted and developed strategies to make sexual activity satisfactory, possibly through

recalibration of their mindset to optimize their sex life (Sprangers & Schwartz, 1999; Yang et al., 2016).

5.2 Sexual quality of life in patients with axSpA

At the baseline in these studies, impaired sexual QOL was independently associated with being a woman, high BMI, high disease activity, and use of bDMARDs (Paper II). The same associations with being a woman and BMI were observed in the study of the impact of health status on sexual activity, as discussed above (Paper I). By contrast, markers of inflammation were associated with impaired sexual QOL but not with health status and had no impact on sexual activity (Berg et al., 2017). Interestingly, the current use of bDMARDs was associated with impaired sexual QOL. Use of bDMARDs may be considered to be a surrogate marker for disease activity, and these drugs are prescribed for patients with more severe disease, high disease activity, insufficient exercise, and poor response to NSAIDs (van der Heijde et al., 2017).

The treatment of patients with axSpA has changed during the last 20 years. The main change in treatment appeared around 2000 with the introduction of TNF inhibitors (i.e., bDMARDs) (Agrawal & Machado, 2020). Previously, patients with axSpA experienced greater impairment, especially functionally, because the treatments were less effective in controlling the disease. Medications such as bDMARDs improve disease outcomes significantly and bring more patients with axSpA into remission (Agrawal & Machado, 2020). A study from China of 42 male patients with AS found that sexual QOL and sexual activity improved when patients used a TNF-α inhibitor (Dong et al., 2015). This is consistent with the 5-year data in our studies, in which the disease activity was lower and bDMARDs were used more frequently than at the baseline, which may indicate better disease control. Good disease control improves disease activity and, by reducing pain and inflammation, has a positive effect on sexual QOL (Dong et al., 2015). However, our studies are the only ones to use the SQOL-F in patients with axSpA. The only previous study of sexual QOL from China, found that sexual QOL improved in men when using bDMARDs (Dong et al., 2015).

Comorbidities can be experienced as an additional burden for patients with axSpA. In general, our patients reported few comorbidities, but the number of comorbidities increased from the baseline to the 5-year follow-up, although there was no significant change in sexual QOL. Good disease control, low disease activity, and better physical functioning may explain the lack of changes in these other variables. Our findings contrast with recent studies in which overall comorbidity was associated with worse outcomes of disease severity, work production, mortality, and QOL (Nikiphorou et al., 2018; Zhao et al., 2020).

The current cohort of patients with axSpA had a large age range (18–81 years). Most of the patients were aged between 31 and 65 years, and few of the patients were younger than 30 years. The mean disease duration of the cohort was about 14 years. Younger patients with early and active disease can experience greater impairment of sexual function, which leads to lower sexual QOL (van Lunteren et al., 2018). We compared sexual QOL in those over and under 30 years of age in this cohort. The 23 patients aged <30 years showed few differences, and had lower scores on the BASMI scale (damage), shorter disease duration, higher scores for sexual repression (loss of joy with sexual activity, being embarrassed, and avoiding sexual activity), and lower scores on comorbidity than the patients >30 years.

The research on axSpA and sexual QOL is scarce, and minimal data are available for comparison with studies from other countries. The only other study is from China and involved 42 AS patients with mean age of 32 ± 7 years and shorter disease duration (7.8 ± 8.0 years)(Dong et al., 2015). In that study, sexual QOL improved while the men used bDMARDs. The Chinese health-care system, social and economic systems are different from those in Norway. No longitudinal data on healthy controls are available for comparison with our findings. In another study of the present cohort, comparison of HRQOL between patients and the normal population showed lower HRQOL among patients with axSpA (Rohde et al., 2017). However, during the 5-year follow-up of the present cohort, improvements in the physical dimension of HRQOL were observed, and these changes indicated better physical function (Rohde et al., 2019).

Sexual QOL is not routinely discussed with patients in rheumatology outpatient clinics in Norway (Helland et al., 2013) or in Sweden (Areskoug-Josefsson et al., 2019). Addressing sexual concerns is important to sexual QOL. One useful method is to implement a model for communication such as the Permission, Limited Information, Specific Suggestions, and Intensive Therapy model (PLISSIT). When asking patients to participate in a study of sexual activity and sexual QOL, HPs need to give patients the permission to talk about such topics. Giving permission is the first step in the PLISSIT model (Annon, 1976; de Almeida, Britto, Figueiredo, Moreira, & de Carvalho, 2019), which was not used explicitly in the current study. However, by inviting patients to participate in a study, HPs acknowledge that sexual activity and sexual QOL are important subjects to address. Giving patients the opportunity to express their concerns about and thoughts on their sexual activity and sexual QOL is part of the recognition of the patient as a whole person and not just a person with a disease. As seen in a Norwegian study, HPs in rheumatology with more knowledge and education about sexuality addressed sexual issues more frequently (Helland et al., 2013). The PLISSIT is a good tool for structuring patient–HP conversations and may render HPs more confident in discussing sexual activity and sexual QOL, which may be a sensitive area for both people.

The goal for medical treatment for patients with axSpA is to reduce disease activity, obtain remission, and improve and maintain flexibility in the spine to produce a normal posture and reduce functional limitations (Strand & Singh, 2017). Combining treatment strategies, implementing management programmes, and including patients in the decision-making may help to reduce disability and improve HRQOL (Smolen et al., 2018; van der Heijde et al., 2017). Maintaining the ability to work and reducing other complications related to the disease, such as comorbidities, are also important (Nikiphorou & Ramiro, 2020). These factors all influence the overarching goal of supporting QOL, including HRQOL and sexual QOL, as identified in our studies.

5.3 Differences in disease perceptions between men and women related to sexual activity and sexual QOL

Although both men and women tend to receive their diagnosis of axSpA earlier now than just a few years ago, the time from the onset to diagnosis is still longer for women (8.8 years) than for men (6.5 years), and more men than women are diagnosed with axSpA, which is consistent with the current study where 67% of the patients with axSpA were men (Baumberger & Khan, 2017; Jovaní, Blasco-Blasco, Ruiz-Cantero, & Pascual, 2017). This is in contrast with a study by Landi et al. (2017) that found that men reported a longer diagnostic delay than women (Landi et al., 2016). Such a delay in diagnosis may create a greater disease burden for women and may delay the onset of treatment (Rusman et al., 2018). The delay in diagnosis may reflect the greater disease severity in men, as seen as radiological damage and progression (Baraliakos, Listing, von der Recke, & Braun, 2011; Landi et al., 2016; Roussou & Sultana, 2011; Rusman et al., 2018; Östlund et al., 2014). Radiological damage and progression in our studies could not be explored because radiographs and MRI scans were not available. In a study by Rusman et al. (2018), women reported greater disease burden, as shown by a delay in diagnosis, higher disease activity, and lower response to TNF inhibitors. Our studies found similar trends; that is, the female patients had higher self-reported disease activity, worse health status, less ability to manage their daily activities, and greater inflammation in the tendons than did male patients.

Sexuality is a crucial part of a person's identity and sexual identity, and has a psychological, physiological, moral, and cultural/social context. People's perception of their place in a social context and other aspects of life, including their disease, affects their QOL and HRQOL (Cappelleri et al., 2014; Ferrans et al., 2005). A higher percentage of female than male patients in our studies reported that their health status had a negative impact on sexual activity. This finding contrasts with the findings of another study that found no gender differences regarding the impact of health status on sexual activity in patients with PsA (Haugeberg, Michelsen, & Kavanaugh, 2020). Men with RA report a greater impact of health status on sexual activity than women with the disease (Helland et al., 2008). The differences between earlier studies and our studies may be explained by the inclusion of different patient groups—patients with axSpA,

PsA, and RA. It is known that women exhibit greater inflammation in tendons, which may elicit greater pain and worsen physical function and self-reported disease activity (Landi et al., 2016). It is also known that increased pain leads to difficulties in sexual activity and that pain and discomfort caused by disease activity affect both physical and psychosocial relationships and may further impact sexual activity. Pain that impairs sexual activity may have a negative impact on sexual QOL (T. Y. Rosenbaum, 2010).

Disease activity, as measured by the BASDAI at the baseline in our studies, was lower for men than for women, and men had less enthesitis than women. This is consistent with findings from a study of Ibero-American men and women, which found that men had lower disease activity (BASDAI), were younger, had higher work disability rates, more structural damage, lower disease activity, and better QOL than women (Landi et al., 2016). For HRQOL, men in the present cohort reported better scores on vitality, bodily pain, and physical role limitations than women but had lower HRQOL (SF-36) scores than the norm-based SF-36 score in another study from Norway (Rohde et al., 2017). One explanation may be differences in how men and women respond to the questions asked. In general, women tend to encourage more conversation than men and to disclose more information about themselves. Simultaneously, women tend to equalize their status, whereas men tend to assert differences (Schneider & Stone, 2014). These differences can influence patients' responses both when completing PROMS and when reporting to doctors and nurses. How patients evaluate their health and communicate health problems is connected to emotions and the influence of cultural gender differences. Women and men express emotions differently; women tend to report both positive and negative affect more intensively but not more often than men (Schneider & Stone, 2014). These differences may also have affected the findings of the present studies.

5.4 The impact of employment on sexual QOL

There is a close connection between education and employment because higher educational achievement provides opportunities for a larger range of work (Shim et al., 2018). Employment can influence health habits and may also be important for sexual

QOL. Employment is important in the social context because participating in working life is important both economically and socially, and it can positively affect a person's psychological health (Bryngelson, 2009; Ramonda et al., 2016). Employment generates groups and networks that can influence health habits; it also generates income and increases the ability to perform disease prevention behaviours (Shim et al., 2018). The state of health is important for sexual activity and sexual QOL.

The employment rate in our studies was high (71%). A positive influence of being in paid work has also been reported in a previous study showing significant improvements in work productivity in patients with axSpA using bDMARDs (Shim et al., 2018). In our studies, we had no data on work productivity, which could have been useful for providing a broader picture about the differences between patients who work and do not work. Even if patients with axSpA are well treated, having a chronic long-term disease increases the risk of withdrawal from the labour force (Boonen, Boone, Albert, & Mielants, 2018). Low disease activity and use of bDMARDs, as observed in the current cohort, were associated with the high employment rate in a study from Italy that found that high disease activity correlated with decreased work productivity (de Hooge et al., 2016). Hagelund et al. suggested that impaired functioning outside work is likely to also cause problems at work. However, these data were from 2003 to 2007, when bDMARDs were not prescribed widely (Haglund, Petersson, Bremander, & Bergman, 2015).

5.5 Methodological considerations

In this section I will discuss methodological considerations related to study design and, psychometric properties of the questionnaire, external validity, and statistical considerations.

5.5.1 Study design

To address the overall aim of the studies, a cross-sectional design was applied in Papers I and II, and a prospective cohort study with a 5-year follow-up in Paper III (Polit & Beck, 2018). A major limitation of cross-sectional studies is that they do not permit causal interpretation but can only identify associations between dependent and

independent variables (Polit & Beck, 2008). The rationale for choosing these designs for the present studies was that we wanted to describe relationships between phenomena at a fixed point in time (Polit & Beck, 2018) to examine the impact of health status on sexual activity and sexual QOL (Table 1) .

The advantage of using a follow-up design, as in Paper III, is that it allows the researcher to follow a group of people over time, to identify the predictors of changes, and to explore the effects of changes on the outcomes measured. It is also important because no other follow-up studies have been reported for patients with axSpA after introduction of a new treatment such as bDMARDs. Here, the interval between the baseline and follow-up was 5 years. There are challenges if the intervals between the data collecting time points are too long because there is a risk of attrition, such as loss of patients, which can reduce the representativeness of the results (Polit & Beck, 2018). Only data from patients who had participated at the baseline and at the 5-year follow-up were included in these analyses. Among the 289 patients invited to the follow-up, only 35 were lost to follow-up. There were minor differences between those who were invited and those who were not: fewer of the patients without 5-year data were cohabiting, were not current users of bDMARDs, and exercised for less than 1 h/week, which could indicate that their disease was less active.

5.5.2 Psychometric properties of the questionnaires

Most of the outcome measures used in these studies are used widely in studies of axSpA and were recommended by the ASAS working group (Che et al., 2015; Sieper et al., 2009), and all have been tested psychometrically. In addition, the PROMS information provided by the patients, and questionnaires collected by doctors and nurses have been used in previous studies and been shown to have satisfactory reliability and validity (Kiltz, Gossec, Baraliakos, & Braun, 2016). The PROMS used in these studies is part of the daily routine in the outpatient clinic at the two hospitals. A more detailed discussion of the specific PROMS used as the main outcome measures in the three sub-studies is given below.

The 15D instrument is considered to be suitable both as a profile and single-index score measure. Its psychometric properties are satisfactory and, when used as a single

index, represents the overall HRQOL (Sintonen, 2001). Here, we used one question, number 15, of the entire questionnaire. The completion rate of the 15D questionnaire and question number 15 in particular in our studies was high (97%) compared with the 75% completion rate for question 15 in a previous study of patients with RA (Helland et al., 2008). Discrepancies can occur when the measures are clustered around a high score (ceiling) or a low score (floor) (question 15 in 15D) and can further reduce the validity and reliability (Polit & Beck, 2008; Polit & Yang, 2016).

The SQOL-F questionnaire is a validated instrument shown to have good psychometric properties (Symonds et al., 2005). We also used the sub-scores introduced and validated by Maasoumi et al. (2013), which have been shown to have good psychometric properties in the Iranian population. It is a limitation that no other studies were available for comparison for the responses to this questionnaire and for a specific disease such as axSpA or other rheumatological diseases. Another limitation is the lack of data for comparison with the Norwegian population. However, as a part of these studies, we performed factor analysis and confirmed the sub-scores identified by Maasoumi et al. We calculated Cronbach's α for the total score and sub-scores as a part of the reliability testing.

In the present study, we chose to use the SQOL-F in men and women although, to our knowledge, it has not been used on men in scientific studies (Symonds et al., 2005). Given the gender differences in the perception of sexual matters, we changed question 4 from "women" to "men and women". This decision was based on the suggestion of the developer of the questionnaire that "the questionnaire can also be used on partners and on male partners with minor modifications" (Symonds et al., 2005). Abraham et al. (2008) stated that the items of the SQOL-F are also applicable to men with only a small change needed to question 4, "When I think about my sexual life, I feel less of a man" (Abraham, Symonds, & Morris, 2008), as we did in the current study.

5.5.3 External validity

External validity pertains to the generalization of research results where findings from one setting can be transferred to other populations and settings (Polit & Beck, 2018). The patients who participated in the present studies were referred and

recruited from the outpatient clinics in two hospitals. This may have led to sample bias because patients referred to hospital clinics tend to have more severe disease than a population-based cohort, such as patients treated by general practitioners. Another threat to external validity is the differences in age and use of bDMARDs between participants, which may have influenced the results for other variables. However, these characteristics of the patient cohort reflect the real-life population of the patients attending the hospital outpatient clinics.

Data were collected by both doctors and nurses at the two hospitals, and this is both a strength and a weakness. The data collection from two hospitals could be considered as a strength, and the involvement of different people to collect data could be considered as a weakness. However, these patterns reflected the real-life situation in the clinics, although we do not know to what extent these differences impacted the results. Loss of data may have hindered generalization (Polit & Beck, 2018) ; for example, in Paper III, only patients with data at both the baseline and the 5-year follow-up were included in the analyses.

Because of funding restrictions at one of the hospitals (MHH), not all patients from the baseline were invited to the 5-year assessment. In a follow-up study, loss of patients who leave during the study can be a challenge, and attrition can be a threat to internal validity (Polit & Beck, 2018). A high drop-out rate could influence the representativeness of the results if those who drop out differ from those who continue being part of the study. However, in the present studies, the drop-out rate after 5 years was only 35 of 280 (12.5%), and it was random and caused by death (n = 4) or moving to another place (n = 31; Figure 5). None of the participants decided to leave the study after 5 years for other reasons, possibly because talking about sexual QOL in relation to their disease may have met a need in these patients.

5.5.4 Statistical considerations

In our studies, we chose to present scores on instruments such as the HAQ, BASFI, MASES, CRP, and BASDAI as the mean ± SD instead of the median and interquartile range, although some of the scores are somewhat skewed with an excess of zeros. However, the dependent and independent variables do not need to be

normally distributed in a regression model. The assumption about normal distribution in linear regression analyses relates to the residuals, and we assessed the distribution of the residuals. Linear regression models tend to be robust for moderate deviations from the assumptions of a normal distribution and especially with a high number of observations. Transformation of variables or use of statistical models with other distributional assumptions can address these issues, but their interpretation is more difficult and not commonly used. In our experience, the overall results and conclusions tend to be similar between such approaches and the findings of linear regression analyses in a large sample. For statistical modelling in the multiple analysis, we used a clinically driven approach to select the relevant independent variables and performed further comparisons using multiple analysis.

Throughout the study each patients had to answer nearly 100 questions (Table 3), this may be seen as a burden for the patients and hamper validity of the data(Polit & Beck, 2008). At the same time answering many questions is routine in every consultation at these outpatients' clinics. There was a high response rate on answering questions in the study.

More patients did not answer some of the questionnaire items in Paper II (n = 29) than in Paper I (n = 10) at the baseline. The patients who did not answer some of the questions in Paper I were older and had been ill for a longer time than the responders. For the non-responders on the SQOL-F, fewer were married, and they worked and exercised less. The non-responders in Paper III were older, tended not to be married or cohabiting, smoked more, and exercised less. It is possible that answering questions about how axSpA affects sexual activity may have been easier than answering questions about sexual QOL.

Data on comorbidity were collected by interviewing the patients and from the patients' files. The data were collected as specific entities and were further aggregated into groups of related diseases using the following categories: cardiovascular, pulmonary, neurological, endocrine, haematological, gastrointestinal, urogenital, malignant, mental disorders, and other. A summary score was calculated (Sarfati, 2016). This coding could have been more thoroughly described or used in other ways. For

example, the Charlson Comorbidity Index (Charlson, Pompei, Ales, & MacKenzie, 1987) could have been used as a prognostic tool for assessing the risk of mortality in our patients.

6 Conclusions

A chronic disease, such as axSpA, can impair HRQOL, including sexual activity and sexual QOL. Sexual QOL, which is part of HRQOL but reflects a broader concept than sexual activity, includes both psychological and social dimensions. Only a small percentage of the patients with axSpA in our studies (~20%) reported that their health status had a large negative effect on their sexual activity. Women reported a larger effect of health status on sexual activity than men. In these studies, gender and lifestyle factors, but not disease-related variables, negatively influenced sexual activity. Only being a woman, high BMI, current smoking, and poor HRQOL were associated with the impact of health status on sexual activity. This is promising because lifestyle factors such as smoking and BMI are modifiable. In the adjusted analyses, being a woman, high BMI, disease activity measured by the BAS-G and CRP, and the use of bDMARDs were negatively associated with sexual QOL. Compared with men, women reported better sexual QOL on the sub-score sexual repression. Sexual repression includes factors such as losing the pleasure of sexual activity and feeling uncomfortable and embarrassed, which lead to avoiding sexual activity.

Sexual QOL in our patients with axSpA remained stable through a 5-year follow-up despite an increase in the number of comorbidities. Simultaneously, intensification of medical treatment (e.g., use of bDMARDs) led to better disease control and reduction in some of the negative lifestyle factors such as smoking habits. Patients who exercised less and were aged >65 years reported lower psychosexual feelings of being frustrated, depressed, worried about their partner's rejection, and feelings. Women had a lower BMI and BASMI score, and higher MASES and HAQ scores than men.

These encouraging findings indicate that both effective control of disease activity and changes initiated by patients with axSpA, such as a reduction in smoking, weight loss, and more exercise, might contribute to improved sexual QOL. In addition, these findings raise awareness of the need to focus on comorbidities in daily practice because these can hamper achieving the target of remission of axSpA.

In the clinical context, the word “burden” is often used. The words chosen to describe the implications of having axSpA can affect patients and their spouse and family. The characterization of axSpA can affect how HPs communicate with the patients and how patients look upon themselves. Because there are few studies on sexual QOL, it is important to move the focus from burden to sexual QOL and to focus on how to live well in a social context when having axSpA.

6.1 Implications for clinical practice

- Knowing about the patient’s experience of having axSpA and its effect on sexual activity and sexual QOL is important to the ability of HPs in clinical practice to meet the patient and be better prepared to answer questions on these topics.
- The findings from these studies add valuable information about the impact of health status on sexual activity and sexual QOL because earlier research on these topics is scarce.
- The results of these studies will be of interest to HPs working with patients with axSpA by enabling them to become more aware of the influence axSpA can have on sexual activity and sexual QOL.
- This knowledge should be significant in patient-centred care according to the T2T strategy.
- A holistic approach to disease activity and the implications of having axSpA should be adopted and should include a focus on lifestyle factors, treatment, and comorbidities.
- When discussing sexual QOL, it is important to regard each patient as an individual and to understand the spectra of diseases and challenges in sexual activity and the implications for sexual QOL.

6.2 Further research

- Including partners in research when exploring the impact of health status on sexual activity and sexual QOL will added valuable information for HPs.
- Interviewing the patients and their partners will provide additional information about how they perceive axSpA and what types of relationships are important to them. Because many of the patients in this cohort were cohabiting, we know little about those who were not married or cohabiting. Interviewing such patients will provide important information on what is important to them.

- It will be useful to examine the different education programmes and to what extent sexual education is a part of education programmes for patients and partners. Qualitative research is needed to examine how patients understand all the information given (i.e., their health literacy).
- It will be useful to conduct further follow-up studies of patients with axSpA on sexual activity and sexual QOL, to illuminate this topic further.
- It will be important to continue to focus on exercise and lifestyle factors such as obesity as comorbidities because these can increase disease activity and impair sexual QOL.
- Other measures that could be used in further research include a questionnaire on depression, a measure of pain using scales such as the visual analogue scale, and a standardized assessment of fibromyalgia tender points to address pain in a wider context.

Further research would also benefit from having X-rays of all patients, which would allow the differentiation between non-radiographic and radiographic axSpA.

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Appendices

1. Paper I
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Paper I

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Exploring the relationship between demographic and disease-related variables and perceived effect of health status on sexual activity in patients with axial spondyloarthritis: associations found only with non-disease variables

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Exploring the relationship between demographic and disease-related variables and perceived effect of health status on sexual activity in patients with axial spondyloarthritis: associations found only with non-disease variables

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Objective: To explore the relationship between demographic and disease-related variables and the perceived effect of health status on sexual activity in patients with axial spondyloarthritis (ax-SpA).

Method: The study assessed 379 ax-SpA patients consecutively recruited from two rheumatology outpatient clinics. Data collection included information on demographics, markers and measures of ax-SpA disease, treatment, comorbidity, and health-related quality of life (HRQoL) using the Short Form-36. The perceived effect of health status on sexual activity was assessed using question 15 in the HRQoL instrument 15D.

Results: The mean age of the patients was 45.6 years, 66.5% were men, 87.3% were human leucocyte antigenB27 positive, and mean disease duration was 13.9 years. A total of 312 patients (82.3%) reported their health status to have no/little effect and 17.7% patients reported their health status to have a large negative effect on their sexual activity. In univariate analysis, increased body mass index (BMI), smoking, alcohol consumption, unemployed status, low physical activity, comorbidities, and higher disease activity (Bath Ankylosing Spondylitis Questionnaire), impaired body movement and lower HRQoL were associated with a large effect on sexual activity. In adjusted analyses, only female gender, high BMI, current smoking, and low HRQoL showed significant associations.

Conclusion: Approximately 20% of ax-SpA patients reported a large negative effect on their sexual activity. Female gender, high BMI, current smoking, and reduced HRQoL were associated with health status having a large effect on sexual activity, whereas no measures reflecting ax-SpA disease showed an independent association.

Axial spondyloarthritis (ax-SpA) is a chronic, systemic inflammatory rheumatic disease affecting the axial skeleton, which may also involve peripheral joints, entheses, and other organs (1). The disease, which most often presents in early adulthood, may cause significant pain, fatigue, stiffness, and loss of physical function, thus having a major impact on quality of life (QoL) even at a young age (2–5). QoL is a subjective and multidimensional concept with physical, psychological, social, and spiritual dimensions (6). Sexual activity and enjoyment are considered to be components of QoL, particularly the physical and psychological dimensions. According to the World Health Organization, sexual health is defined as a state of physical, emotional, mental, and social well-being in relation to sexuality (7). The physical and psychological consequences of a chronic disease may also thus influence the QoL, including sexual function and sexual perception, from a lifelong perspective.

Despite the importance of sexual health as part of a person's QoL (8, 9), limited data are available on sexuality in patients with rheumatic disease including ax-SpA (10). In the present study, we aimed to explore the relationship between demographic and diseaserelated variables and the perceived effect of health status on sexual activity in patients with ax-SpA.

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Method Patient recruitment

The ax-SpA patients included in this study were consecutively recruited when visiting the outpatient rheumatology clinics at Martina Hansens Hospital (MHH) and Sørlandet Hospital (SSHF), Norway. To be included, the patients had to be 18 years or older and fulfil the Assessment of SpondyloArthritis international Society (ASAS) criteria for ax-SpA (11). Data collection at the two centres was carried out at the same time, between October 2008 and May 2011.

Data collection

Demographic characteristics, disease features, therapy, and QoL data were systematically collected by patient questionnaires, interviews, physical examination, and laboratory tests. Demographic data included age, gender, body mass index (BMI), smoking, alcohol consumption, education, work status, physical exercise, and QoL. Disease duration was defined as the time between the date fulfilling the ASAS criteria for ax-SpA and the date for inclusion in the study. Human leucocyte antigen (HLA)B27 status was registered, and the Bath Ankylosing Spondylitis Metrology Index (BASMI) was registered. Data on comorbidities (cardiovascular, pulmonary, neurological, endocrine, haematological, gastrointestinal, urogenital, malignant, and mental disorders, as well as peripheral arthritis) were collected, and a summary score to reflect comorbidity was calculated.

Disease activity was assessed by the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), 68 tender and 66 swollen joint count, the Bath Ankylosing Spondylitis Patients Global Score (BAS-G) and morning stiffness, the Maastricht Ankylosing Spondylitis Enthesitis Score (MASES), and C-reactive protein (CRP) levels. Physical function was assessed by the Bath Ankylosing Spondylitis Functional Index (BASFI) and the Health Assessment Questionnaire (HAQ). Information regarding current medication, including non-steroidal anti-inflammatory drugs (NSAIDs), synthetic disease-modifying anti-rheumatic drugs (sDMARDs), and biological disease-modifying anti-rheumatic drugs (bDMARDs), was registered.

Health-related quality of life (HRQoL) was assessed by the 36-item Short Form Health Survey (SF-36), which is a self-reported and generic questionnaire assessing eight domains: general health, bodily pain, physical function, role limitations (physical), mental health, vitality, social function, and role limitations (emotional). The eight domains can be combined into a physical and mental sum scale that reflects physical and mental health. The physical component summary (PCS) and the mental

component summary (MCS) scales were used in this study (12). To examine the effect of health status on sexual activity, we used item 15 in the 15D questionnaire (13).

The 15D questionnaire is a generic, multidimensional, standardized tool for evaluating HRQoL, which is used primarily as a single index measure but can also be used as a profile utility measure. The 15D questionnaire captures the health status by assessing 15 dimensions: mobility, vision, hearing, breathing, sleeping, eating, speech, elimination, usual activities, mental function, discomfort and symptoms, depression, distress, vitality, and sexual activity (13). Each dimension is assessed by one question using five response categories. Item 15 addresses the effect of health on sexual activity with the following response options.

My state of health:

1. has no adverse effect on my sexual activity
2. has a slight effect on my sexual activity
3. has a considerable effect on my sexual activity 4. makes sexual activity almost impossible
5. makes sexual activity impossible.

The 15D instrument has been used in different patient groups when the focus is HRQoL (2, 14), and has shown favourable clinometric performance (13, 15).

Statistical analyses

Statistical analyses were performed using SPSS for Windows (version 22). Continuous variables are presented as mean with standard deviation (sd) and categorical variables as numbers and percentages (%). Comparisons between two groups were analysed using the chi-squared test for categorical variables and independent samples t-test for continuous variables.

For analytical purposes, the five response categories in item 15 in the 15D instrument were dichotomized. The responses 'no effect' and 'slight effect' were defined as 'no/little' effect, and the categories 'considerable effect', 'sexual activity almost impossible' and 'sexual activity impossible' were categorized as 'large effect'.

Associates with the dependent variable no/little or large effect of health status on sexual activity in patients with ax-SpA were explored in univariate and multivariate logistic regression analysis (enter procedure). In the multivariate model, we included variables tested in univariate analysis with a p value < 0.20. The multivariate model was also tested for its robustness by applying forward and backward procedures, and analyses of the hospital cohorts separately. The level of significance was set at $p < 0.05$.

The R square was assessed by Nagelkerke R square.

Ethical and legal aspects

The study was approved by the Regional Committee for Medical Research Ethics in Norway (REK no. 4.2007.2152). All patients gave written informed consent before inclusion.

Results Participants

In total, 389 ax-SpA patients were consecutively recruited at the two participating rheumatology outpatient clinics. Among them, 10 patients (four MHH and six SSHF patients) did not answer question 15 on sexuality in the 15D questionnaire. These patients were older than those answering the question (52.2 vs 45.6 years, p = 0.09) and had longer disease duration (22.8 vs 13.9 years, p = 0.016).

Table 1 shows data for all the 379 included patients and separately for patients reporting their health status to have no/little (n = 312) and large effect (n = 67) on sexual activity. The mean age for all patients was 45.6 (11.9) years, ranging from 18 to 81 years, and 66.5% of the patients were men. The mean disease duration was 13.9 (11.4) years; 87.3% of the patients were HLA-B27 positive. Among the participants, 81.1% reported having a partner with whom they currently had sex and 76.3% being married or cohabitant. Current treatment included NSAIDs in 43.8%, sDMARDs in 4.9%, and bDMARDs in 22%. The comorbidity summary score was 0.7 per patient. In the study population, 11% of patients had less than 10 years' education, 32.7% had 11–13 years' education, and 55.7% had more than 13 years of education. There was no significant difference between the subgroups with regard to these data.

For the demographic variables listed in Table 1, a statistically significant difference between participants from SSHF (n = 127) and MHH (n = 252) was found only for education (> 13 years, 48.1% vs 59.5% p = 0.011). MHH patients had better disease outcome than SSHF patients for BASDAI [2.9 (2.1) vs (3.7 (2.1), p = 0.001], BASFI [2.6 (2.2) vs 3.1 (2.2), p = 0.042], BAS-G [3.6 (2.5) vs 4.4 (2.6), p = 0.008], and MASES [2.4 (2.9) vs 4.9 (4.7), p < 0.001]. For HRQoL measured by SF-36, a statistically significant better PCS score was found among MHH patients than among SSHF patients [40.6 (9.1) vs 37.7 (10.0), p = 0.006], whereas no significant difference was found for the MCS [48.4 (10.6) vs 48.0 (9.5), p = 0.78]. For the separate domains in SF-36, a statistically significant difference between MHH and SSHF patients was found only for vitality [49.5 (20.2) vs 44.1 (19.8), p = 0.012], bodily pain [50.9 (20.1) vs 43.6 (20.2), p = 0.001], and physical role limitation [46.7 (41.8) vs 34.9 (39.5), p = 0.008]. More MHH patients were treated with bDMARDs (29.7% vs 9.0%, p < 0.001). For the other variables listed in Table 1, including item 15 in the 15D questionnaire, no significant differences were seen between the two centres. Thus, for the present analysis, the results are presented as pooled

data from both hospitals. In multivariate analysis, we adjusted for centre.

For perceived effect of health status on sexual activity, 36.4% reported no effect on sexual activity while 45.9% reported little effect, 15.6% reported considerable effect, 1.3% reported that sexual activity was almost impossible, and 0.8% reported that sexual activity was impossible. The percentage of patients with no and little impact was 82.3%.

A statistically significant difference between men and women for variables listed in Table 1 was found for BMI [27.6 kg/m^2 (4.6) vs 25.6 (4.7), p = 0.001], alcohol consumption [1–6 glasses per week (73.5% vs 65.9%), more than 7 glasses per week (11.6% vs 7.1%) p = 0.012], employed/self-employed status (76.6% vs 66.9%, p = 0.048), BASDAI [3.03 (2.10) vs 3.5 (2.1), p = 0.037], MASES [2.5 (3.5) vs 4.4 (3.8), p < 0.001], BASMI [2.6 (2.2) vs 2.0 (1.6), p = 0.015], BASFI [2.7 (2.2) vs 2.8 (2.3) p = 0.602], and HAQ [0.52 (0.47) vs 0.65 (0.54), p = 0.012]. For the eight domains in SF-36, a statistically significant difference between men and women was found for vitality [49.2 (19.9) vs 44.8 (20.9), p = 0.046], bodily pain [50.4 (20.6) vs 44.9 (20.0), p = 0.015], and physical role limitation [46.6 (41.7) vs 36.4 (39.9), p = 0.024].

Figure 1 shows the proportion of men and women reporting the extent of impact that their disease had on sexual activity. The difference between the genders was statistically significant (p = 0.024). Significantly more women than men reported their health status to have a large impact on their sexual activity (23.6% vs 14.7%, p = 0.031).

For the other variables listed in Table 1, patients reporting a large negative effect of health status on sexual activity had significantly higher BMI, were smokers, had higher alcohol consumption, were unemployed, exercised less, and had more comorbidities, higher disease activity (BASDAI, BAS-G, MASES, morning stiffness), lower physical function (BASFI, HAQ), more disease damage (BASMI), and lower HRQoL (PCS and MCS).

In Table 2, the associations between the independent variables and the dependent variable tested in both univariate and multivariate analyses are shown. The following variables were found to be independently associated with a large negative effect of health status on sexual activity: female gender [odds ratio (OR) = 2.30, 95% confidence interval (CI) 1.00–5.26], increased BMI (OR = 1.12, 95% CI 1.02–1.22), current smoking (OR = 3.55, 95% CI 1.55–8.09), low SF-36 PCS (OR = 0.88, 95% CI 0.82–0.94), and low SF-36 MCS (OR = 0.95, 95% CI 0.91–0.99). The same patterns were seen using forward and backward procedures, and when applying the multiple analyses separately for each hospital cohort. Furthermore, when removing SF-36, MCS and PCS as independent variables in the final multiple model (Table 2), the disease and treatement variables were not found to be associated with health status to have an effect on sexual activity.

Table 1. Characteristics of all axial spondyloarthritis patients and of the subgroups reporting health status to have no/little effect and a large effect on their sexual activity.

	All (n = 379)	No/little effect (n = 312)	Large effect (n = 67)	p
Demographic				
Age (years)	45.6 (11.9)	45.2 (11.9)	47.8 (11.9)	0.098
Female	127 (33.5%)	97 (31.1%)	30 (44.8%)	0.031
BMI (kg/m^2)	27 (4.7)	26.07 (4.24)	28.49 (6.21)	0.007
Current smoker	102 (26.9%)	77 (24.8%)	25 (37.9%)	0.029
Employed/self-employed	268 (70.7%)	235 (77.6%)	33 (53.2%)	< 0.001
Exercise > 1 h/week	330 (84.8%)	273 (88.3%)	48 (71.6%)	0.001
Clinical measures CRP				
(mg/dL)	8.59 (11.96)	8.50 (11.77)	9.01 (12.86)	0.76
68 tender joint count	0.42 (1.76)	0.42 (1.79)	0.45 (1.31)	0.76
66 swollen joint count	0.12 (0.62)	0.11 (0.57)	0.16 (0.80)	0.49
BASDAI	3.19 (2.1)	2.86 (1.96)	4.73 (2.02)	< 0.001
MASES	3.16 (3.73)	2.82 (3.55)	4.72 (4.14)	< 0.001
Damage				
BASMI	2.40 (2.04)	2.27 (1.98)	3.00 (2.18)	0.008
Self-reported health status BASFI				<
	2.73 (2.23)	2.34 (1.99)	4.53 (2.39)	0.001
BAS-G	3.88 (2.57)	3.45 (2.42)	5.91 (2.31)	< 0.001
HAQ	0.56 (0.49)	0.48 (0.45)	0.95 (0.54)	< 0.001
HRQoL SF-36*				<
PCS (0–100)	39.7 (9.51)	41.4 (9.02)	32.2 (7.97)	0.001
MCS (0–100)	48.3 (10.29)	49.5 (9.49)	42.9 (12.10)	< 0.001
Current treatment				
NSAID	166 (43.8%)	136 (81.9%)	30 (18.1%)	0.859
sDMARD	19.5 (4.9%)	67 (21.5%)	18 (26.9%)	0.337
bDMARD	85 (22.4%)	67 (21.5%)	18 (26.9%)	0.337

Continuous variables are expressed as mean (standard deviation); categorical variables are expressed as number (percentage). In the group comparisons, the independent samples t-test was used for continuous variables and the chi-squared test for categorical variables.

*Range: 0–100, where 100 indicates a high health-related quality of life (HRQoL).

BMI, body mass index; CRP, C-reactive protein; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; MASES, Maastricht Ankylosing Spondylitis Enthesitis Score; BASMI, Bath Ankylosing Spondylitis Metrology Index; BASFI, Bath Ankylosing Spondylitis Functional Index; BAS-G, Bath Ankylosing Spondylitis Patients Global Score; HAQ, Health Assessment Questionnaire; SF-36, 36item Short Form Health Survey; PCS, physical component summary; MCS, mental component summary; NSAID, non-steroidal antiinflammatory drug; sDMARD, synthetic disease-modifying anti-rheumatic drug; bDMARD, biological disease-modifying anti-rheumatic drug.

Discussion

The main findings in this study were that approximately one out of five ax-SpA outpatient clinic patients reported their perceived health status to have a large negative effect on their sexual activity. Non-disease-related patient characteristics (female gender, high BMI, and being a current smoker, scoring low on SF-36 PCS and MCS) were mainly found to be independently associated with a large effect of perceived health status on sexual activity. Only in unadjusted analysis was a statistically significant association observed between sexual activity in ax-SpA patients and measures of increased disease activity (e.g. BASDAI, MASES), such as pain, stiffness, impaired physical function (BASDAI, HAQ), and increased skeletal damage (BASMI).

Our data may indicate that the disease burden has only a minor influence on sexuality, which may reflect the major advances in medical treatment and general care for

ax-SpA patients in the past decade. More effective medications are available and early aggressive treatment strategies have been more commonly adopted, including the treat-to-target strategy for ax-SpA (16). Better outcomes improve health statusandQoLandwillinfluencehowpatientsarereporting the effect of the disease on sexual activity. In general, our patients had mean low disease activity and only a few patients had problems with their joints. Peripheral arthritis canhaveasignificantimpactduringsexualactivityandmay influence a patient's answers (17).

In contrast to the expected results, lifestyle-related factors (e.g. high BMI and smoking), not disease-related factors, had the greatest impact on sexual activity. In our study, high BMI had a negative impact on sexual activity. High BMI can influence HRQoL and may impair sexual QoL because of a negative body image, especially in women (18, 19). Previous studies have also reported a significant association between low BMI and regular sexual activity, or satisfaction with sexual activity (20, 21). Smoking was also associated

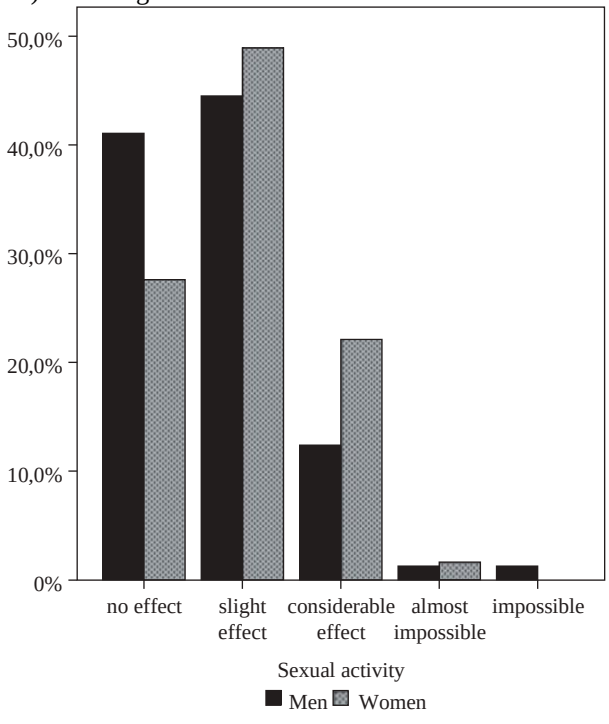

Figure 1. Proportion of self-reported effect of perceived health status on sexual activity in 252 men and 127 women with axial spondyloarthritis. Comparison between genders was made using the independent samples t-test (p = 0.024).

with a large effect on sexual activity in our study. Nicotine, one of the major components in tobacco, is a complex drug with multiple pharmacological effects that can modulate the experience of pain (22, 23).

In our study, more female than male ax-SpA patients reported a large negative effect of ankylosing spondylitis (AS) on sexual activity. Several reports have observed female AS patients to report a more severe disease status in patient-reported outcomes (8, 24). Moreover, in the general population and in people with rheumatoid arthritis (RA), sexual problems are reported more frequently in women than in men (25, 26).

Impairment of sexual function involves both physical and psychological components. In a large study of 612 AS patients (men 72%) with a mean age of 51 years, 38% reported that their sexual relationships were affected 'moderately', 'quite a bit', or 'extremely' by their AS (3). Sexual problems in AS have been reported to be associated with physical impairment/pain (3, 27), disease activity (28), morning stiffness (29), limited joint mobility (30), anxiety and depression (30, 31), impaired HRQoL (14, 24), and sexual relationship/intercourse (3, 32). Previous studies have shown that urogenital disorders may affect sexual function in males (33); however, few patients in our cohort reported urogenital disorders, and none of the male patients reported a varicocele.

Compared to RA patients, fewer patients with ax-SpA patients in our study reported a large negative effect on sexuality. In the study by Helland and colleagues, 31% of the RA patients (mean age 58.5 years) reported their health status to have a large negative impact on their sexual activity. In that study, male gender, younger age, fatigue, mental distress, impaired physical function, and low efficacy regarding symptoms were found to be independently associated with reporting perceived problems with sexual activity (2).

We found that impairment of both the physical and the mental HRQoL components of the SF-36 measure were independently associated with reporting health status to have a negative effect on sexual activity. A similar association has been reported in other studies recruiting individuals from the general population (26, 34).

Exercise had a positive influence on QoL and indirectly also on sexual functioning. However, the ability to perform exercise may reflect a general better health status, with a positive effect on sexual functioning. In our study, the patients had a low rate of comorbidities and high relationship stability, as 81% had a partner to have sex with and 76% were married or cohabiting.

In several randomized studies, treatment with bDMARDs has been shown to reduce symptoms (e.g. pain, morning stiffness) and disease activity, and to improve physical function (35). In our study, the proportion of ax-SpA patients using bDMARDs was 22%, whereas it was 11.6% in a study by Healey and colleagues (3), and disease scores on BASDAI and BASFI were lower in our study than in the studies by Healey and Shen et al (3, 36). This may partly explain why none of the disease variables was significantly and independently associated in the multivariate analyses.

Table 2. Association between demographic and disease-related variables and perception of health status having a large effect on sexual activity in axial spondyloarthritis patients, tested in unadjusted and adjusted logistic regression analyses.

	Unadjusted		Adjusted model	
	OR (95% CI)	p	OR (95% CI)	p
Demographic				
Age (years)	1.02 (1.00–1.04)	0.099	1.01 (0.98–1.05)	0.429
Female	1.80 (1.05–3.08)	0.033	2.30 (1.00–5.26)	0.048
BMI (kg/m^2)	1.08 (1.02–1.14)	0.008	1.12 (1.02–1.22)	0.014
Current smoker	0.54 (0.31–0.95)	0.031	3.55 (1.55–8.09)	0.003
Employed/self-employed	3.04 (1.72–5.36)	< 0.001	0.98 (0.42–2.32)	0.967
Exercise > 1 h/week	3.00 (1.59–5.66)	0.001	0.56 (0.22–1.40)	0.213
Clinical measures				
BASDAI	1.55 (1.35–1.78)	< 0.001	1.09 (0.80–1.48)	0.587
MASES	1.13 (1.06–1.21)	< 0.001	1.02 (0.92–1.13)	0.728
Damage				
BASMI	1.18 (1.04–1.33)	0.009	1.04 (0.84–1.28)	0.730
Self-reported health status				
BASFI	1.54 (1.36–1.76)	< 0.001	0.97 (0.71–1.32)	0.822
HRQoL SF-36*				<
PCS	0.88 (0.86–0.92)	< 0.001	0.88 (0.82–0.94)	0.001
MCS	0.95 (0.92–0.97)	< 0.001	0.95 (0.91–0.99)	0.013
Current treatment				
NSAID	1.05 (0.62–1.78)	0.86		
sDMARD	1.26 (0.40–3.91)	0.69		
bDMARD	1.34 (0.41–1.36)	0.34		
R_2			0.396	

The adjusted model included all the selected variables using the enter procedure.

Range: 0–100, where 100 indicates a high health-related quality of life (HRQoL).

OR, odds ratio; CI, confidence interval; BMI, body mass index; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; MASES, Maastricht Ankylosing Spondylitis Enthesitis Score; BASMI, Bath Ankylosing Spondylitis Metrology Index; BASFI, Bath Ankylosing Spondylitis Functional Index; BAS-G, Bath Ankylosing Spondylitis Patients Global Score; HAQ, Health Assessment Questionnaire; SF-36, 36-item Short Form Health Survey; PCS, physical component summary; MCS, mental component summary; NSAID, nonsteroidal anti-inflammatory drug; sDMARD, synthetic disease-modifying anti-rheumatic drug; bDMARD, biological disease-modifying anti-rheumatic drug.

Strengths and weaknesses

A strength of our study was that a large proportion of the patients (97%) answered the questions addressing sexual problems, a rate higher than that reported in other articles, where 20–25% did not answer questions addressing sexual problems (2, 14). Patients of both genders were consecutively recruited, and there were few exclusion criteria. The patients included reflect the number of men and women in the cohort of AS patients from both hospitals.

Data were collected at two centres, which can be considered as both a strength and a weakness: the strength is that this provided internal validity, while the weakness is that data were collected by different people; however, this also reflectedthe actual scenario inthe clinics. Furthermore, the external validity may be hampered by the differences between the groups, especially related to age and the use of bDMARDs. The difference in the proportion of patients treated with bDMARDs between the two hospitals (MHH 29% and SSHF 9%) may potentially influence the results of the other variables. We have adjusted for both the hospital and treatment with bDMARDs in the multivariate analysis.

The study is a cross-sectional study that did not permit any causal interpretation; thus, we can only establish associations between dependent and independent variables. The patients were recruited in a hospital setting and may therefore have more severe disease than a community-based cohort. The cohort was not compared with healthy controls. As we only used a single-item question to determine the effect of health status on sexual activity, we have no knowledge about other non-disease-related problems that could have influenced the answer (3). Sexual activity and enjoyment are complex

phenomena, which should ideally be measured using several items to capture various aspects (26).

Conclusion

Adjusted analysis showed female gender, high BMI, current smoking, and reduced HRQoL, but not disease-related factors, to be associated with a large effect on sexual activity in ax-SpA patients. Patients with a perceived negative effect of their health status on sexual activity should be informed that a healthy lifestyle may also have a positive effect on their sex life. The role of new treatment strategies such as biologics which improve the symptoms of AS should be investigated in prospective studies.

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Paper II

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Sexual Quality of Life in Patients with Axial Spondyloarthritis in the Biologic Treatment Era

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Sexual Quality of Life in Patients with Axial Spondyloarthritis in the Biologic Treatment Era

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ABSTRACT. ***Objective.*** To examine the relationship between demographics, disease-related variables, treatment, and sexual quality of life (SQOL) in men and women with axial spondyloarthritis (axSpA).

Methods. AxSpA patients were consecutively recruited from 2 rheumatology outpatient clinics in southern Norway. A broad spectrum of demographics, disease, treatment, and QOL data were systematically collected. SQOL was assessed using the SQOL-Female (SQOL-F) questionnaire (score range 18–108). Appropriate statistical tests were applied for group comparison, and the association between independent variables and SQOL-F was examined using multiple linear regression analysis.

Results. A total of 360 (240 men, 120 women) axSpA patients with mean age 45.5 years and disease duration 13.9 years were included. Seventy-eight percent were married/cohabiting, 26.7% were current smokers, 71.0% were employed, 86.0% performed > 1-h exercise per week, and 88.0% were HLA-B27–positive. Mean (SD) values for disease measures were C-reactive protein (CRP) 8.5 (12.1) mg/l, Bath Ankylosing Spondylitis Disease Activity Index 3.1 (2.1), Bath Ankylosing Spondylitis Global Score (BAS-G) 3.8 (2.5), Bath Ankylosing Spondylitis Functional Index 2.7 (2.2), and Health Assessment Questionnaire 0.6 (0.5). The proportion of patients using nonsteroidal antiinflammatory drugs was 44.0%, synthetic disease-modifying antirheumatic drugs (DMARD) 5.0%, and biologic DMARD 24.0%. Mean (SD) total sum score for SQOL was 76.6 (11.3). In multivariate analysis, female sex, increased body mass index, measures reflecting disease activity (BAS-G and CRP), and current biologic treatment were independently associated with a lower SQOL.

Conclusion. Our data suggest that inflammation in patients with axSpA even in the biologic treatment era reduces SQOL. (First Release April 1 2019; J Rheumatol 2019;46:1075–83; doi:10.3899/jrheum.180413)

Key Indexing Terms:
AXIAL SPONDYLOARTHRITIS
BIOLOGICAL DMARD
SEXUAL QUALITY OF LIFE
DISEASE ACTIVITY

Axial spondyloarthritis (axSpA) is a chronic, systemic inflammatory rheumatic disease affecting the axial skeleton[1]. AxSpA most often has its onset in early adulthood, which is an important time in life when most people start relationships and prepare for and start their career[2]. The characteristics of the disease may affect quality of life (QOL)[3]. QOL is a broad concept that is both subjective and multidimensional, and has psychological, social, and spiritual dimensions[4]. The physical and psychological consequences of a chronic disease such as axSpA may influence all dimensions of QOL, including sexual function and sexual perception, in a lifelong perspective. Sexual QOL (SQOL) is not clearly defined in the literature; however, it includes the relationship between sexual dysfunction and QOL[3,5]. Sexual activity and enjoyment are components of the physical and psychological dimensions of QOL. Further, sexual activity as part of reproduction is considered one of the key functions of human beings, with its effect on QOL. According to the World Health Organization, sexual health is defined as a state of physical, emotional, mental, and social well-being in relation to sexuality[6].

The literature has focused mainly on dysfunction or sexual problems[7,8,9]. In the present study, we aimed to focus on the quality and patients' perception of SQOL, investi-

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gating the relationship between SQOL and demographics, disease-related variables, and treatment in men and women with axSpA.

MATERIALS AND METHODS

Patient recruitment. The patients with axSpA included in this cross-sectional study were consecutively recruited when visiting the outpatient rheumatology clinics at Martina Hansens Hospital (MHH) and Sorlandet Hospital (SSHF), Norway. To be included, the patients had to be 18 years or older and fulfill the Assessment of Spondyloarthritis international Society (ASAS) criteria for axSpA[10]. Patients had to be in a physical and mental condition in which they were capable to give confirmed consent, and understand written and vocal Norwegian language.

Data collection. A broad range of demographic characteristics, disease, treatment, and QOL data were systematically collected, partly by using patient questionnaires, direct interviews, physical examination, and laboratory tests. Demographic data included age, sex, body mass index (BMI), smoking status (current smoker, previous smoker, and nonsmoker), alcohol consumption (never, 1–6 glasses, ≥ 7 glasses/week), education (education < 10 yrs, 11–13 yrs, and > 13 yrs), work status (employed and unemployed), and physical exercise (< 1 h/week and > 1 h/week). Previous smokers were considered as nonsmokers. Disease duration was defined as the time between the date fulfilling the ASAS criteria for axSpA and the date for inclusion in the study. HLA-B27 status was registered. Data on comorbidities were recorded by nurse interview and by reviewing medical records and included the following: cardiovascular diseases, pulmonary diseases, neurological disorders, endocrine disorders, hematological disorders, gastrointestinal disorders, urogenital disorders, peripheral arthritis, cancer, and mental disorders; these data were integrated into a sum score to reflect comorbidity.

Disease activity was assessed by the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), 68 tender and 66 swollen joint counts, Maastricht Ankylosing Spondylitis Enthesitis Score (MASES), and C-reactive protein (CRP). Physical function was assessed by Bath Ankylosing Spondylitis Functional Index (BASFI) and the Health Assessment Questionnaire (HAQ). To measure damage, the Bath Ankylosing Spondylitis Metrology Index (BASMI) was used. Data on Bath Ankylosing Spondylitis Global Score (BAS-G) and morning stiffness were also collected. Current medication was registered, including nonsteroidal antiinflammatory drugs (NSAID), synthetic disease-modifying antirheumatic drugs (sDMARD), and biologic DMARD (bDMARD).

Health-related QOL (HRQOL) was assessed by the Medical Outcomes Study Short Form-36 (SF-36), a self-reported and generic questionnaire assessing 8 domains: general health, bodily pain, physical function, role limitations (physical), mental health, vitality, social function, and role limitations (emotional). The 8 domains can be combined into a physical and mental sum scale that reflects physical and mental health. The physical component summary (PCS) and the mental component summary (MCS) scales were used in this study[11].

SQOL was assessed using the generic SQOL-Female (SQOL-F) questionnaire developed to study the relationship between female patients and SQOL[5]. A modified version of SQOL-F was also used for men[12]. SQOL-F can also be used on partners, with minor modifications[5]. In our study, we changed the fourth question to "When I think about my sex life, I feel less of a woman/man." The questionnaire was translated into Norwegian by Mapi Research Trust in 2006. SQOL consists of 18 items, rated on a 6-point response scale: completely agree, moderately agree, slightly agree, slightly disagree, moderately disagree, completely disagree. The response categories are scored 1–6, giving a total score range of 18–108. A higher score indicates better SQOL[5]. In this paper we also have used subscores, identified and validated by Maasoumi, *et al*[3] based on the Symonds SQOL-F questionnaire, which reflects various aspects or dimensions of SQOL as shown in Table 1. All data were collected on the same day for each patient.

Statistical analyses. Statistical analyses were performed using IBM SPSS Statistics (version 24; IBM). Continuous variables are presented as the mean with SD and categorical variables as numbers and percentages. For group comparison we used chi-square for categorical variables, and independent t test and Pearson correlation for continuous variables.

Linear regression analysis (general linear model) in SPSS was used to examine the univariate/unadjusted and adjusted association between demographic- and disease-related variables, and for SQOL (SQOL-F) total score and subscores. The independent variables in the multiple analyses were chosen based on $p < 0.1$ in the univariate analyses (demographic, comorbidity, disease activity measures, health status, and current treatment in Table 2), and also adjusted for age and sex. Analyses were also performed with and without the HRQOL SF-36 measures in the model.

In the final multivariate model, we included demographic variables, disease activity (assessed by BASDAI and MASES scores), health status (assessed by HAQ, BASFI, and BAS-G scores), damage (assessed by BASMI score), comorbidity, and treatment center. For robustness, we also tested the multiple regression models by using forward and backward procedure. Cronbach's alpha test was used to examine the reliability of the SQOL-F questionnaire with its total score and its subscores. The level of significance was set at $p < 0.05$.

Ethical and legal aspects. The study was approved by the Regional Committee for Medical Research Ethics in Norway (REK no.: 4.2007.2152). All patients gave written informed consent before inclusion.

RESULTS

Demographic and disease-related characteristics. A total of 389 patients with axSpA were consecutively recruited at the 2 participating rheumatology outpatient clinics. Among them, 29 patients (MHH 10 and SSHF 19 patients) did not answer the SQOL-F questionnaire. The significant differences between responders and nonresponders on SQOL were that responders had a higher consumption of alcohol ($p = 0.033$), were more often employed ($p = 0.003$), exercised more ($p = 0.038$), and were more often cohabitant ($p < 0.001$).

Cronbach's alphas in our study expressing reliability of the test were 0.75 for the SQOL-F total score, 0.91 (excellent) for psychosexual feelings, 0.82 (good) for sexual and relationship satisfaction, 0.82 (good) for self-worthlessness, and 0.60 (questionable) for sexual repression.

Statistically significant differences for mean (SD) between patients at MHH (n = 246) and SSHF (n = 114) were found for BASDAI [2.9 (2.0) vs 3.6 (2.0), $p = 0.02$], BAS-G [3.6 (2.5) vs 4.3 (2.6), $p = 0.015$], MASES [2.4 (2.9) vs 4.9 (4.76), $p < 0.001$], and the sum score of comorbidities [0.8 (1.0) vs 0.4 (0.7), $p < 0.001$]. Further, more MHH patients than SSHF patients were treated with bDMARD (29.7% vs 9.0%, $p < 0.001$). For HRQOL, measured by SF-36, a statistically significant better PCS was found among MHH patients compared to SSHF patients [40.7 (9.1) vs 37.9 (9.8), $p = 0.011$]. For the other variables listed in Table 2, no significant differences were seen between the 2 centers. For the present analysis, the results are presented as pooled data from both hospitals and adjusted for center in multivariable analyses.

In Table 2, data are shown for all patients with axSpA (n = 360) included in the SQOL analyses and for men (n = 240) and women (n = 120) separately. The mean age for

Table 1. Subcategories in the Sexual Quality of Life–Female (SQOL-F) questionnaire[3].

Category	SQOL-F Questions (Question No.)	Range	High Score Indicates Positive/Negative Direction
Psychosexual feelings	Frustrated (2) Depressed (3) Anxious (7) Angry (8) Worry (10) Worry of partner's hurt or rejection (16) Feeling like losing something (17)	7–42	Positive
Sexual and relationship satisfaction	Enjoy (1) Good feeling about oneself (5) Closeness to partner (9) Talk to partner about sexual matters (13) Satisfaction with frequency of sexual activity (18)	5–30	Negative
Self-worthlessness	Feeling like less of a woman/man (4) Losing confidence (6) Feeling of guilt (15)	3–18	Positive
Sexual repression	Loss of pleasure (11) Embarrassed (12) Avoiding (14)	3–18	Positive

all patients was 45.5 years (11.9); 67.0% were men and 33.0% women, 78.0% were married or cohabiting, and 86.0% reported exercising > 1 h per week. Mean (SD) values for disease measures were as follows: BASDAI 3.1 (2.06), MASES 3.2 (3.67), BASFI 2.7 (2.21), BAS-G 3.8 (2.53), and HAQ 0.6 (0.49). Among patients, 88.0% were HLA-B27–positive; current users of NSAID were 44.0%, of sDMARD 5.0%, and of bDMARD 24.0%. Only 3 patients treated were concomitantly treated with bDMARD and sDMARD. When comparing men and women with axSpA (Table 2), women had a significantly lower BMI [25.4 (4.4) vs 27.5 (4.5) kg/m^2, $p < 0.001$]. Women had higher MASES scores [4.5 (3.8) vs 2.5 (3.4), $p < 0.001$], lower BASMI [2.0 (1.6) vs 2.6 (2.2), $p = 0.005$], and higher HAQ [0.6 (0.5) vs 0.5 (0.5), $p = 0.025$]. For the other variables listed in Table 2, no statistically significant differences were found between men and women, including HRQOL measures.

Bivariate correlation between demographic and clinical background variables showed a strong correlation ($r = > 0.5$) between age and disease duration ($p < 0.001$), morning stiffness and BASDAI ($p < 0.001$), morning stiffness and MASES ($p = 0.045$), BASFI and BASDAI ($p < 0.001$), BASDAI and BAS-G, HAQ, PCS, and MCS ($p < 0.001$), BASFI and BAS-G, HAQ, PCS, and MCS ($p < 0.001$), BAS-G and MASES ($p < 0.001$), and HAQ and MASES ($p < 0.001$).

Further, we identified moderate correlation ($r = 0.3$–0.5) between age and sum comorbidity ($p < 0.001$), work and sum comorbidity ($p < 0.001$), work and BASFI ($p < 0.001$), HAQ and PCS ($p < 0.001$), work and sum comorbidity ($p < 0.001$), work and BASFI ($p < 0.001$), BASMI and disease duration ($p < 0.001$), BASMI and BASFI ($p < 0.001$), BASFI and morning stiffness ($p < 0.001$), and BASDAI and MCS ($p < 0.001$). Weak and negligible correlations are not shown.

SQOL data. Total SQOL score and subscores for domains for all patients and for men and women separately are shown in Table 3. When comparing SQOL between MHH and SSHF, patients from MHH reported lower subscores for psychosexual feelings [32.6 (8.7) vs 34.7 (7.4), $p = 0.019$], self-worthlessness [15.3 (3.6) vs 16.2 (2.8), $p = 0.005$], and sexual repression [14.9 (3.8) vs 16.0 (3.3), $p = 0.004$], and higher scores for sexual and relationship satisfaction [13.4 (6.2) vs 10.8 (4.4), $p < 0.001$].

As shown in Table 3, compared to men, women reported a significantly lower SQOL sum score [74.7 (11.9) vs 77.6 (10.9), $p = 0.026$] and a lower score for sexual repression [14.4 (4.1) vs 15.6 (3.4), $p = 0.005$; higher score is positive], whereas for the other sub-domains in SQOL, no significant differences were found between sexes.

Unadjusted association between demographic- and disease-related variables and SQOL. In Table 4 univariate/unadjusted associations are shown for SQOL-F sum score and for SQOL-F subscores. As shown, employment status, increased comorbidity score, BASDAI, BASMI, morning stiffness, BASFI, BAS-G, HAQ, CRP, and bDMARD were associated with a reduced SQOL-F score, whereas male sex and the SF-36 PCS and MCS were associated with a higher SQOL score.

Adjusted associations between demographic- and disease-related variables and SQOL. In the multivariate analyses presented in Table 5 (without SF-36 measure in the model), these were independently associated with a higher SQOL total score: male sex (B = 4.2, $p = 0.014$), low BMI

Table 2. Demographic data, disease markers, disease activity measures, damage, health status, treatment, and comorbidity in 360 patients with axial spondyloarthritis.

Characteristics	All, n = 360	Women, n = 120	Men, n = 240	p
Demographics				
Age, yrs	45.5 (11.9)	45.0 (12.0)	46.0 (12.0)	0.797
Living alone, n (%)	282 (78)	91 (76)	191 (80)	0.374
BMI, kg/m^2	26.9 (4.6)	25.4 (4.4)	27.5 (4.5)	< 0.001
Current smoker, yrs, n (%)	96 (27)	32 (27)	64 (27)	0.966
Alcohol, n (%)				0.051
Never	64 (18)	29 (24)	35 (15)	
1–6 glasses	254 (71)	81 (68)	173 (73)	
≥ 7 glasses	38 (11)	9 (8)	29 (12)	
Education, yrs, n (%)				0.644
< 10	38 (11)	13 (11)	25 (11)	
11–13	116 (32)	35 (29)	81 (34)	
> 13	204 (57)	72 (60)	132 (56)	
Employed/self-employed, n (%)	256 (71)	78 (68)	178 (77)	0.090
Exercise > 1 h/week, n (%)	309 (86)	105 (88)	204 (86)	0.510
Disease duration, yrs	14.0 (11.3)	12.6 (11.0)	14.8 (11.0)	0.082
Comorbidity, total score (range 0–10)	0.7 (0.9)	0.8 (0.9)	0.7 (0.9)	0.525
Disease marker				
HLA-B27–positive (n = 349), n (%)	316 (88)	100 (86)	216 (93)	0.051
Disease activity measures				
CRP, mg/l	8.5 (12.1)	7.7 (13.0)	8.9 (11.0)	0.424
68 tender joint count	0.39 (1.7)	0.33 (1.0)	0.22 (2.0)	0.398
66 swollen joint count	0.10 (0.6)	0.06 (0.3)	0.12 (0.7)	0.254
BASDAI (0–10)	3.1 (2.1)	3.4 (2.0)	3.0 (2.0)	0.080
MASES enthesitis score	3.2 (3.7)	4.5 (3.8)	2.5 (3.4)	< 0.001
Damage				
BASMI (0–10)	2.4 (2.0)	2.0 (1.6)	2.6 (2.2)	0.005
Health status				
Morning stiffness, min, n (%)				
< 30	215 (61)	69 (60)	146 (62)	0.667
> 31	137 (39)	47 (40)	90 (38)	
BASFI (0–10)	2.7 (2.2)	2.7 (2.2)	2.7 (2.2)	0.754
BAS-G (0–10)	3.8 (2.5)	4.0 (2.4)	3.8 (2.6)	0.539
HAQ (0–3)	0.6 (0.5)	0.6 (0.5)	0.5 (0.5)	0.025
Health-related QOL				
SF-36 PCS	39.8 (9.4)	38.8 (9.1)	40.3 (9.6)	0.163
SF-36 MCS	48.4 (10.4)	47.9 (10.3)	48.6 (10.4)	0.569
Current treatment, n (%)				
NSAID	159 (44)	57 (48)	102 (43)	0.368
Synthetic DMARD	17 (5)	7 (6)	10 (4)	0.482
Biologic DMARD	85 (24)	22 (18)	63 (26)	0.095

Continuous variables are presented as mean (SD) and categorical variables as n (%). Chi-square was used to compare categorical data and independent t tests for continuous variables. BMI: body mass index; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; MASES: Maastricht Ankylosing Spondylitis Enthesitis Score; CRP: C-reactive protein; BASFI: Bath Ankylosing Spondylitis Functional Index; BASMI: Bath Ankylosing Spondylitis Metrology Index; HAQ: Health Assessment Questionnaire; QOL: quality of life; BAS-G: Bath Ankylosing Spondylitis Global Score; SF-36 PCS: Medical Outcomes Study Short Form-36 physical component summary; MCS: mental component summary; NSAID: nonsteroidal antiinflammatory drugs; DMARD: disease-modifying antirheumatic drugs.

(B = –0.4, p = 0.034), low CRP (B = –0.15, p = 0.026), low BAS-G (B = –1.7, p = 0.002), and nonuse of bDMARD (B = 6.4 , p < 0.001). Male sex (B = 2.44, p = 0.045), low BMI (B = –0.29, p = 0.015), low BAS-G (B = –1.36, p < 0.001), and nonuse of bDMARD (B = 3.91, p = 0.003) were independently associated with high scores in psychosexual feelings. Living alone (B = 3.11, p = 0.001) and high BAS-G (B = 0.65, p = 0.016) were independently associated with high scores in sexual relationship satisfaction. Male sex (B = 1.11, p = 0.027), low BMI (B = –0.11, p = 0.021), low CRP (B = –0.05, p = 0.015), low BAS-G (B = –0.49, p = 0.002), and non-use of bDMARD (B = 1.89, p < 0.001) were independently associated with a high score on self-worthlessness. These variables were independently associated with high sexual repression: young age (B = –0.05, p = 0.014), male sex (B = 1.37, p = 0.012), low CRP (B = –0.05, p = 0.017), low BAS-G (B = –0.42, p = 0.013), and nonuse of bDMARD (B = 1.17, p = 0.044). The

Table 3. Sexual quality of life (SQOL) assessed by the SQOL questionnaire in 360 patients with axial spondyloarthritis.

Variables	All, n = 360	Women, n = 120	Men, n = 240	p
SQOL sum score (range 18–108)	76.6 (11.3)	74.7 (11.9)	77.6 (10.9)	0.026
Psychosexual feelings (range 7–42)	33.3 (8.3)	32.2 (8.9)	33.8 (8.0)	0.087
Sexual and relationship satisfaction(range 5–30)	12.5 (5.8)	12.9 (6.2)	12.3 (5.6)	0.361
Self-worthlessness (range 3–18)	15.6 (3.4)	15.1 (3.5)	15.7 (3.3)	0.112
Sexual repression (range 3–18)	15.2 (3.7)	14.4 (4.1)	15.6 (3.4)	0.005

Data presented as SQOL sum score and SQOL subscores, for all and for men and women separately. Independent t tests were used when comparing the groups. Continuous variables are expressed as mean (SD).

demographic- and disease-related variables included in the multiple analyses explained 16.5% of the variance in SQOL-F sum, 16.7% in psychosexual feelings, 9.7% in sexual relationship satisfaction, 16.9% in self-worthlessness, and 16.3% in sexual repression. The same pattern of associations was seen when the multivariate model was performed with the forward and backward procedure (data not shown). Further, only minor differences in the results were seen when SF-36 measures were included in the model (data not shown).

DISCUSSION

The main finding of our study is that SQOL is impaired in patients with active axSpA, as indicated by association with elevated BAS-G and CRP. Further use of bDMARD was also associated with impaired SQOL. Among demographic variables, we found that female sex and increased BMI were independently associated with impaired SQOL.

Minor differences between sexes were identified, with men reporting about a 3% higher total score on SQOL than women. Except for a higher score for sexual repression in men, no significant differences between the sexes were found for the other subcategories. As in other studies, men are more likely to report feeling positive about their sexual life, self-confidence in their ability to perform well in a sexual relationship, and having value as a sexual partner[3,5].

Depression analysis was not performed in our study, but the SF-36 summary scales (MCS and PCS) show no significant differences in MCS between men and women. Several factors may contribute to lower SQOL in women, one being lower self-confidence. An increased BMI can lead to low self-confidence[13]; women experience increased BMI more often than men[14]. Differences between the sexes in the clinical presentation of axSpA, such as more fatigue and enthesitis in women, may also account for SQOL differences[15,16]. In our study, women reported more enthesitis than men and may have had more pain from enthesitis, resulting in reduced SQOL. Studies in patients with SpA[17] and RA have also found a greater effect of disease symptoms on sexual activity in female patients[16]. Further, women and men are different in how they present their health status and communicate their health problems[18]. This may influence the way they answer questionnaires. In contrast to our results, van Berlo, *et al* observed in a study with rheumatoid arthritis patients a stronger correlation between sexual problems, physical health, and disease activity in men than in women, but there were no sex differences regarding sexual satisfaction[19]. Differences observed between studies may partly be explained by various levels of disease activity, which in general were low in our study.

An increased level of CRP reflecting inflammatory activity was negatively associated with total SQOL and with 2 of 4 subscales: self-worthlessness and sexual repression. BAS-G was the only self-reported disease variable significantly associated with SQOL, indicating that axSpA may markedly reduce well-being and SQOL. High disease activity may make the patient lose confidence as a sexual partner and feel less attractive as a woman or man. Grief and shame over being disabled may raise feelings of guilt or resentment, which could also strain the relationship[5,16]. However, in our study, BASMI, mainly reflecting damage to the spine, was significantly higher in men than in women (2.6 vs 2.0, respectively), indicating a higher damage score in men compared with women.

In our study, current use of bDMARD was independently associated with a negative total SQOL-F score and the SQOL-F subscale scores, except in sexual relationship satisfaction. Good disease control achieved by bDMARD has been reported to improve physical and psychological outcomes in both ankylosing spondylitis (AS) and axSpA patients[20,21,22]. In our study, bDMARD were used by 24% of the patients but only by 11.6% in the study by Healey, *et al*[20]. In our study, fewer female than male patients used bDMARD (18% in women and 26% in men). One explanation may be that the indication for prescribing anti-tumor necrosis factor (anti-TNF) treatment was first approved for patients with radiological axSpA and AS, diseases with male predominance. Later on, the indication for anti-TNF treatment also included patients diagnosed with nonradiographic axSpA, which has a more equal sex distribution than AS[23,24]. In our study, current use of bDMARD was independently associated with a negative total SQOL-F and the SQOL-F subscales, except for sexual relationship satisfaction. This is most likely explained by the cross-sectional study design, which did not allow for drawing conclusions about causality. In the present study, the use of bDMARD might be a marker of disease activity that does not reflect a causal negative effect of bDMARD on SQOL.

Table 4. Univariate associations between demographic data, disease markers, disease activity measures, damage, health status, treatment, comorbidity, and SQOL (measured by SQOL questionnaire) total score and subscores examined in 360 patients with axial spondyloarthritis.

Variables	SQOL-F Sum, range 18–108, B (95% CI)	p	Psychosexual, range 7–42, B (95% CI)	p	Sexual and Relationship Satisfaction, range 5–30, B (95% CI)	p	Self–worthlessness, range 3–18, B (95% CI)	p	Sexual Repression, range 3–18, B (95% CI)	p
Age, yrs	–0.49 (–0.15 to 0.05)	0.328	–0.01 (–0.08 to 0.06)	0.795	0.038 (–0.01 to 0.09)	0.142	–0.02 (–0.05 to 0.01)	0.148	–0.06 (–0.09 to –0.02)	< 0.001
Male	3.04 (0.56–5.51)	0.017	1.76 (–0.07 to 3.59)	0.059	–0.66 (–1.95 to 0.62)	0.310	0.64 (–0.10 to 1.39)	0.088	0.128 (0.48–2.08)	0.002
Living alone	0.49 (–2.38 to 3.36)	0.736	–1.18 (–3.28 to 0.93)	0.273	2.77 (1.32–4.21)	< 0.001	–0.57 (–1.42 to 0.28)	0.188	–0.52 (–1.45 to 0.42)	0.275
BMI, kg/m^2	–0.27 (–0.57 to 0.02)	0.071	–0.17 (–0.38 to 0.04)	0.108	0.06 (–0.09 to 0.20)	0.443	–0.09 (–0.18–0.01)	0.035	–0.06 (–0.16 to 0.03)	0.207
Nonsmoker	–0.12 (–2.79 to 2.55)	0.929	–0.38 (–2.34 to 1.59)	0.706	–0.46 (–1.82 to 0.90)	0.505	0.47 (–0.33 to 1.26)	0.249	–0.25 (–0.62 to 1.11)	0.580
Alcohol, per week										
Never	–0.58 (–5.13 to 3.98)	0.803	0.95 (–2.40 to 5.95)	0.576	–1.25 (–3.58 to 1.07)	0.290	0.36 (–0.98 to 1.70)	0.599	–0.53 (–2.00 to 0.94)	0.480
1–6 glasses	2.46 (–1.41 to 6.33)	0.212	3.10 (0.26–5.95)	0.033	–2.69 (–4.67 to –0.72)	0.008	1.43 (0.29–2.57)	0.014	0.62 (–0.63 to 1.87)	0.329
≥ 7 glasses	Ref.		Ref.		Ref.		Ref.		Ref.	
Education, yrs										
< 10	–2.51 (6.45–1.43)	0.211	–0.31 (–3.22 to 2.59)	0.832	0.21 (–1.82 to 2.24)	0.840	–1.25 (–2.42 to –0.08)	0.037	–1.15 (–2.42 to 0.13)	0.079
11–13	0.52 (–2.08 to 3.11)	0.696	0.86 (1.05–2.77)	0.377	–0.16 (–1.50 to 1.17)	0.811	–0.15 (–0.92 to 0.62)	0.710	–0.02 (–0.87 to 0.82)	0.956
> 13	Ref.		Ref.		Ref.		Ref.		Ref.	
Unemployed/self-employed	–3.64 (–6.4 to 9.4)	0.008	–3.64 (–6.34 to –0.94)	0.008	0.98 (–0.40 to 2.36)	0.162	–0.80 (–1.62 to 0.01)	0.053	–1.41 (–2.29 to –0.54)	0.002
Exercise < 1 h/week	–3.12 (–6.58 to 0.33)	0.076	–1.90 (–4.44 to 0.64)	0.143	0.63 (1.15–2.41)	0.487	–0.66 (–1.69 to 0.37)	0.209	–1.19 (–2.31 to –0.06)	0.038
Disease duration, yrs	–0.01 (–0.11 to 0.10)	0.918	0.02 (–0.06 to 0.10)	0.612	0.04 (–0.02 to 0.09)	0.161	–0.02 (–0.05 to 0.01)	0.160	–0.04 (–0.08 to –0.01)	0.019
Comorbidity, total score (range 0–10)	–1.96 (–3.12 to –0.70)	0.002	–1.29 (–2.22 to –0.36)	0.007	0.85 (0.21–1.50)	0.010	–0.59 (–0.96 to –0.22)	0.002	–0.92 (–1.32 to –0.52)	< 0.001
Disease marker										
HLA-B27–positive, n = 349	2.15 (–1.96 to 6.27)	0.304	1.93 (–1.09 to 4.96)	0.210	–0.22 (–2.31 to 1.88)	0.839	–0.04 (–1.24 to 1.17)	0.953	0.54 (–0.78 to 1.86)	0.423
Disease activity measures										
CRP (mg/l)	–0.06 (–0.16 to 0.04)	0.264	–0.05 (–0.12 to 0.03)	0.201	0.05 (–0.01 to 0.10)	0.077	–0.03 (–0.06 to 0.00)	0.091	–0.03 (–0.06 to 0.00)	0.069
68 tender joint count	–3.2 (–1.01 to 0.36)	0.354	–0.14 (–0.64 to 0.37)	0.596	–0.94 (–0.55 to 0.16)	0.279	–0.02 (–0.23 to 0.18)	0.829	0.03 (–0.19 to 0.25)	0.791
66 swollen joint count	–1.65 (–3.58 to 0.29)	0.095	–0.59 (–2.02 to 0.84)	0.418	–0.43 (–1.43 to 0.56)	0.392	–0.38 (–0.96 to 0.20)	0.198	–0.24 (–0.88 to 0.39)	0.450
BASDAI (0–10)	–1.36 (–1.92 to –0.80)	< 0.001	–1.08 (–1.48 to –0.67)	< 0.001	0.37 (0.08–0.66)	0.012	–0.31 (–0.47 to –0.14)	< 0.001	–0.35 (–0.54 to –0.17)	< 0.001
MASES enthesitis score	–0.27 (–0.59 to 0.05)	0.100	–0.183 (–0.42 to 0.05)	< 0.001	–0.06 (–0.23 to 0.10)	0.443	–0.03 (–0.13 to 0.07)	0.550	0.01 (–0.10 to 0.11)	0.889
Damage										
BASMI (0–10)	–0.76 (–1.34 to –0.17)	0.011	–0.42 (–0.85 to 0.01)	0.058	0.19 (–0.11 to 0.49)	0.223	–0.27 (–0.44 to –0.10)	0.002	–0.26 (–0.45 to –0.07)	0.009
Health status										
Morning stiffness, min										
< 30	3.01 (0.57–5.45)	0.016	2.46 (0.66–4.25)	0.007	–0.62 (–1.87 to 0.64)	0.335	0.46 (0.27–1.16)	0.219	0.73 (–0.06 to 1.53)	0.071
> 31	Ref.		Ref.		Ref.		Ref.		Ref.	
BASFI (0–10)	–1.27 (–1.79 to –0.76)	< 0.001	–0.91 (–1.29 to –0.53)	< 0.001	0.36 (0.09–0.63)	0.010	–0.36 (–0.52 to –0.21)	< 0.001	–0.36 (–0.53 to –0.19)	< 0.001
BAS-G (0–10)	–1.28 (–1.73 to –0.03)	< 0.001	–1.00 (–1.33 to –0.67)	< 0.001	0.38 (0.14–0.61)	0.002	–0.32 (–0.45 to –0.18)	< 0.001	–0.34 (–0.49 to –0.20)	< 0.001
HAQ (0–3)	–4.32 (–6.69 to –1.95)	< 0.001	–3.42 (–5.26 to –1.68)	< 0.001	1.67 (0.44–2.90)	0.008	–1.14 (–1.85 to –0.43)	0.002	–1.44 (–2.22 to –0.67)	< 0.001
Health-related QOL										
SF-36 PCS	0.20 (0.07–0.32)	0.002	0.16 (0.07– 0.25)	0.001	–0.05 (–0.11 to 0.02)	0.164	0.04 (0.00–0.08)	0.035	0.05 (0.00–0.09)	0.030
SF-36 MCS	0.34 (0.23–0.45)	< 0.001	0.29 (0.21–0.37)	< 0.001	–0.17 (–0.23 to –0.11)	< 0.001	0.10 (0.07–0.14)	< 0.001	0.12 (0.08–0.15)	< 0.002
Current treatment										
NSAID last 10 days	0.23 (–2.16 to 2.60)	0.847	0.09 (–1.65 to 1.84)	0.916	0.15 (–1.06 to 1.37)	0.804	0.06 (–0.64 to 0.77)	0.859	–0.09 (–0.86 to 0.68)	0.817
Synthetic DMARD	2.18 (–3.35 to 7.72)	0.438	1.58 (–2.50 to 5.65)	0.448	–0.99 (–3.83 to 1.86)	0.497	1.02 (–0.62 to 2.67)	0.223	0.56 (–1.24 to 2.37)	0.539
Biologic DMARD	3.46 (0.72–6.20)	0.014	2.19 (0.16– 4.22)	0.034	–0.77 (–2.19 to 0.65)	0.289	1.35 (0.54–2.16)	0.001	0.68 (–0.22 to 1.58)	0.139

Univariate associations were performed using general linear model B (95% CI). SQOL: sexual quality of life; SQOL-F: SQOL-Female questionnaire; BMI: body mass index; CRP: C-reactive protein; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; MASES: Maastricht Ankylosing Spondylitis Enthesitis Score; BASFI: Bath Ankylosing Spondylitis Functional Index; BAS-G: Bath Ankylosing Spondylitis Global Score; BASMI: Bath Ankylosing Spondylitis Metrology Index; HAQ: Health Assessment Questionnaire; SF-36 PCS: Medical Outcomes Study Short Form-36 physical component summary; MCS: mental component summary; NSAID: nonsteroidal antiinflammatory drugs; DMARD: disease-modifying antirheumatic drugs.

Table 5. Independent associations between demographic data, disease markers, disease activity measures, damage, health status, treatment, comorbidity, and sexual quality of life (measured by SQOL questionnaire) explored in 360 patients with axial spondyloarthritis.

Variables	SQOL-F Sum, range 18–108, Adj B (95% CI)	p	Psychosexual, range 7–42, Adj B (95% CI)	p	Sexual and Relationship Satisfaction, range 5–30, Adj B (95% CI)	p	Self–worthlessness, range 3–18, Adj B (95% CI)	p	Sexual Repression, range 3–18, Adj B (95% CI)	p
Demographics										
Age, yrs	–0.04 (–0.18 to 0.09)	0.521	0.02 (–0.12 to 0.08)	0.689	0.06 (0.01–0.13)	0.099	–0.03 (0.07–0.01)	0.189	–0.05 (–0.10 to 0.01)	0.014
Male	4.22 (0.85–7.59)	0.014	2.44 (0.06–4.83)	0.045	–0.86 (–2.57 to 0.84)	0.319	1.11 (0.13–2.10)	0.027	1.37 (0.30–2.43)	0.012
Living alone	1.47 (–2.18 to 5.13)	0.428	–0.95 (–3.54 to 1.64)	0.471	3.11 (1.26–4.95)	0.001	–0.19 (–1.25 to 0.087)	0.722	–0.23 (–1.37 to 0.92)	0.694
Employed/ self-employed	–0.45 (–4.04 to 3.15)	0.807	–0.01 (–2.55 to 2.54)	0.997	–0.81 (–2.63 to 1.01)	0.379	0.16 (0.89–1.22	0.764	–0.04 (–1.18 to 1.10)	0.946
Education, yrs										
< 10	–2.51 (–7.61 to 2.60)	0.334	–1.23 (–4.84 to 2.39)	0.054	1.01 (–1.57 to 3.59)	0.440	–1.06 (–2.53 to 0.042)	0.160	–0.86 (–2.47 to 0.34)	0.289
11–13	1.21 (–1.99 to 4.42)	0.458	0.97 (–1.31 to 3.24)	0.403	–0.08 (–1.70 to 1.54)	0.926	–0 to 42 (–0.98 to 0.90)	0.930	0.34 (–0.68 to 1.36)	0.511
> 13	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Exercise < 1 h/week	–3.79 (–7.93 to 0.35)	0.072	–1.93 (–4.86 to 1.00)	0.196	0.05 (–2.02 to 2.14)	0.961	–0.54 (–1.75 to 0.07)	0.377	–1.17 (–2.48 to 0.14)	0.080
Current smoker	–1 to 33 (–4.63 to 1.97)	0.427	–1.48 (–3.81 to 0.87)	0.218	0.11 (–1.57 to 1.78)	0.901	–0.05 (–1.01 to 0.92)	0.924	0.12 (–0.93 to 1.17)	0.821
Alcohol, per week										
Never	–0.34 (–6.15 to 5.47)	0.908	–1.02 (–5.13 to 3.10)	0.626	1.54 (–1.39 to 4.48)	0.302	–0.31 (–2.01 to 1 to 38)	0.717	–0.40 (–2.24 to 1.44)	0.667
1–6 glasses	2.23 (–2.64 to 7.11)	0.367	1.24 (–2.21 to 4.69)	0.480	–0.51 (–2.97 to 1.95)	0.683	0.93 (–0.51 to 2.36)	0.204	0.60 (–0.96 to 2.15)	0.451
≥ 7 glasses	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
BMI (kg/m^2)	–0.36 (–0.69 to –0.03)	0.034	–0.29 (–0.52 to 0.06)	0.015	0.15 (–0.2 to 0.32)	0.075	–0.11 (–0.21 to 0.02)	0.021	–0.09 (–0.20 to 0.01)	0.088
Disease activity measures										
BASDAI (range 0–10)	–0.14 (–1.42 to 1.14)	0.829	–0.35 (–1.25 to 0.56)	0.455	0.17 (–0.48 to 0.82)	0.601	0.04 (–0.34 to 0.42)	0.840	0.02 (–0.40 to 0.42)	0.967
MASES (range 0–13)	0.11 (–0.34 to 0.55)	0.639	0.03 (–0.29 to 0.34)	0.863	–0.10 (–0.33 to 0.12)	0.367	0.07 (–0.06 to 0.20)	0.291	0.10 (–0.06 to 0.24)	0.182
CRP, mg/dl	–0.15 (–0.29 to –0.02)	0.026	–0.9 (–0.19 to 0.003)	0.059	0.04 (–0.03 to 0.11)	0.224	–0.05 (–0.09 to –0.01)	0.015	–0.05 (–0.19 to –0.01)	0.017
Health status										
BASFI (range 0–10)	0.14 (–1.41 to 1.69)	0.857	0.52 (–0.57 to 1.62)	0.348	–0.56 (–1.34 to 0.23)	0.162	0.07 (–0.38 to 0.53)	0.748	0.02 (–0.47 to 0.52)	0.924
BAS-G (range 0–10)	–1.70 (–2.74 to –0.66)	0.002	–1.36 (–2.10 to 0.63)	< 0.001	0.65 (0.12–1.18)	0.016	–0.49 (–0.80 to 0.19)	0.002	–0.42 (–0.75 to 0.09)	0.013
HAQ (range 0–3)	2.45 (–2.72 to 7.62)	0.351	0.55 (–3.11 to 4.21)	0.766	0.89 (–1.72 to 3.50)	0.503	0.59 (–0.93 to 2.11)	0.443	0.25 (–1.40 to 1.90)	0.767
Damage										
BASMI (range 0–10)	0.18 (–6.69 to 1.05)	0.667	0.21 (0.41–0.82)	0.507	–0.18 (–0.62 to 0.26)	0.412	0.04 (–0.21 to 0.30)	0.752	0.10 (–0.17 to 0.38)	0.463
Comorbidity, mean total score range 0–10	–1.65 (–3.55 to 0.25)	0.088	–0.75 (–2.10 to 0.60)	0.275	0.30 (–0.66 to 1.26)	0.542	–0.55 (–1.11 to 0.00)	0.052	–0.56 (–1.16 to 0.46)	0.070
Current treatment										
NSAID	–0.002 (–3.03 to 3.03)	0.999	–0.37 (–2.52 to 1.77)	0.733	0.31 (–1.23 to 1.83)	0.695	0.23 (–0.66 to 1.12)	0.616	–0.01 (–0.97 to 0.96)	0.986
Synthetic DMARD	2.61 (–4.23 to 9.47)	0.454	1.00 (–2.86 to 6.86)	0.419	–1.02 (–4.49 to 2.45)	0.564	0.92 (–1.10 to 2.94)	0.373	0.69 (–1.51 to 2.88)	0.538
Biologic DMARD	6.43 (2.85–10.01)	< 0.001	3.91 (1.38–6.45)	0.003	–0.68 (–2.49 to 1.13)	0.459	1.89 (0.84–2.93)	< 0.001	1.17 (0.03–2.30)	0.044
Center, SSHF (N/Y)	1.66 (–1.88 to 5.22)	0.357	2.31 (–0.21 to 4.82)	0.072	–2.18 (–3.97 to 0.38)	0.018	0.65 (–0.40 to 1.69)	0.224	0.80 (–0.33 to 1.04)	0.165
R^2, %	16.5		16.7		9.7		16.9		16.3	

Adjusted analyses were performed using multiple regression analyses and applying a general linear model using SPSS Statistics. Adj: adjusted unstandardized regression coefficients with 95% CI and p values. SQOL: sexual quality of life; BMI: body mass index; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; MASES: Maastricht Ankylosing Spondylitis Enthesitis Score; CRP: C-reactive protein; BASFI: Bath Ankylosing Spondylitis Functional Index; BAS-G: Bath Ankylosing Spondylitis Global Score; BASMI: Bath Ankylosing Spondylitis Metrology Index; HAQ: Health Assessment Questionnaire; NSAID: nonsteroidal antiinflammatory drugs; DMARD: disease-modifying antirheumatic drugs; SSHF: Sorlandet Hospital, Norway.

Our patient population differed from those of other studies regarding disease activity and comorbidities such as cardiovascular diseases, diabetes mellitus, osteoporosis, and depressive disorders[25]. In a previous study of the perceived effect of health status on sexual activity in our axSpA cohort, the majority of patients (82%) reported that their health status had no or insignificant effects on their sexual life[26], reflecting low disease activity and low burden of comorbidities (< 1 per patient) in our patients.

In our study, high BMI was independently associated with a low total SQOL score and with the subdomains "psychosexual feelings" and "self-worthlessness." Our study is in line with previous studies reporting higher BMI as negatively associated with several aspects of QOL in patients with AS[13]. A high BMI may induce a negative body image, reducing sexual activity and impairing SQOL, particularly in women[13,14,27]. In a recent report we found that female sex, high BMI, current smoking, and reduced HRQOL were independently associated with health status and a large negative effect on sexual activity[26]. As expected, living alone was negatively associated with sexual and relationship satisfaction. Our results indicate that both physical (e.g., BMI) and social factors (e.g., living alone) exert an influence on SQOL when combined with disease characteristics such as the presence of inflammation.

The strength of our study was the high response rate (97% of surveyed) to answering questions addressing SQOL, exceeding the rate in other studies[28]. Patients of both sexes were consecutively recruited, and there were few exclusion criteria, which indicates good internal validity of the study. At one outpatient clinic (SSHF), we have previously reported minor differences between the included and not included patients with axSpA examined for both demographics and disease measures[26].

Data were collected at 2 hospitals, which can be considered both a strength and a weakness. A strength is that both hospitals follow the treat-to-target strategy, aiming to reach low disease activity or remission[29]. Our study used a cross-sectional design and did not permit any causal interpretation; therefore, we can establish associations only between dependent and independent variables. The patients were recruited in a hospital setting and may therefore have had more severe diseases than a community-based sample. A major limitation is that the patient cohort was not compared with healthy controls. Sexual activity and enjoyment are complex phenomena, which ideally should be measured using several items to record various aspects of SQOL[30]. Further, lack of data on radiological damage, hip involvement and replacements, and standardized assessment of fibromyalgia tender points might be considered limitations.

Our study indicates that SQOL is lower in females and in axSpA patients with active disease shown by elevated BAS-G and CRP. The use of bDMARD was also independently associated with a lower SQOL score, possibly reflecting bDMARD treatment in this cross-sectional study as a marker of axSpA disease activity and not causality between bDMARD use and impaired SQOL. Thus, we believe that our data indicate that good disease control suppressing inflammation may improve SQOL in patients with axSpA. The association between increased BMI and low SQOL should encourage patients to change their lifestyle, which then may improve SQOL. It is also to be emphasized that our goal in clinical practice is not only to treat inflammation but to take care of the whole patient and address patient needs, including SQOL. Longterm observational followup studies of patients with axSpA that examine the effects of disease on SQOL are needed to investigate changes over time.

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Paper III

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Original article

Increased proportion of comorbidities but no deterioration of sexual quality of life during a 5-year follow-up in patients with axial spondyloarthritis in the biologic treatment era

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Abstract

Objective. To explore patient perception of sexual quality of life (SQOL), an important category of QOL, in male and female patients with axial SpA (axSpA) after a 5 year follow-up.

Methods. A broad spectrum of demographic, disease-related, treatment and SQOL data was collected at baseline and at the 5 year follow-up. SQOL was assessed by the SQOL-Female (SQOL-F) questionnaire. For statistical analysis, McNemar's tests, paired *t*-tests and multiple regression analyses were applied.

Results. A total of 245 axSpA patients (168 men and 77 women) from outpatient clinics were examined (mean age 46 years, mean disease duration 11.9 years at baseline). Compared with baseline, the patients had lower CRP, lower Maastricht Ankylosing Spondylitis Enthesitis Scores, lower BASFI scores, less use of smoking and significantly more patients were treated with biologic DMARDs at the 5 year follow-up. Patient perception of SQOL was basically unchanged at the 5 year follow-up despite a significantly increased proportion of comorbidities, including cardiovascular, endocrine and gastrointestinal disease. A decrease in SQOL after 5 years was observed only in patients exercising <1 h/week at baseline ($P = 0.048$) and in patients >65 years old.

Conclusion. In our axSpA patients, no statistically significant changes in SQOL were observed over 5 years, despite a significant increase in comorbidities. Overall disease symptoms decreased, indicating better disease control. Increased use of biologic drugs at the 5 year follow-up may have contributed to this favourable outcome.

Key words: Key words: axial spondyloarthritis, bDMARD, SQOL (sexual quality of life), follow-up, disease control, lifestyle

CLINICAL SCIENCE

Rheumatology key messages

- There was a significant increase in comorbidities but no significant changes in sexual quality of life (SQOL) over a 5 year period.
- Exercise <1 h/week was associated with a deterioration in total SQOL score over the 5 year period.
- SQOL in patients with axSpA benefits from good disease control and a healthy lifestyle.

Introduction

Axial SpA (axSpA) is a chronic, systemic inflammatory rheumatic disease affecting the axial skeleton [1]. AxSpA can be divided into two subgroups, radiographic axSpA (r-axSpA) and non-radiographic axSpA (nr-axSpA), which also may cause peripheral arthritis and increase the risk of comorbidities [2]. The onset of axSpA is predominantly in early adulthood, which is an important time in life when most people start

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relationships and prepare for or start their careers [3]. In recent years, major improvements in clinical outcomes have been achieved in patients with axSpA. This has been attributed to biologic DMARDs (bDMARDs) and the treat-to-target (T2T) treatment strategy [4].

Despite improvements in clinical outcomes, the physical and psychological consequences of axSpA may still influence all dimensions of quality of life (QOL), including sexual function and sexual perception. The understanding of sexual QOL (SQOL) includes the relationship between sexual function, intimate relationships and QOL [5, 6]. In general, limited data are available on sexuality and SQOL in patients with rheumatic diseases, including axSpA [7].

In previous studies, the impact of axSpA on sexuality has mainly explored sexual dysfunction or sexual problems in cross-sectional studies [8–11], whereas axSpA patients' perceptions of SQOL have rarely been investigated. In a recent cross-sectional study of the present cohort, we found female sex, increased BMI, measures reflecting disease activity and current use of bDMARDs to be independently associated with impaired SQOL [12].

To our knowledge, long-term changes of SQOL in axSpA patients have not been examined previously. Thus the aim of this study was to explore whether a follow-up after 5 years would reveal long-term changes in perception of SQOL in male and female axSpA patients. Furthermore, we wanted to explore which baseline demographic, disease-related or lifestyle variables were associated with changes in SQOL.

Methods

Patient recruitment

At baseline, 379 adult axSpA patients were consecutively recruited and included in the study when visiting the outpatient rheumatology clinics at Martina Hansens Hospital (MHH; $n = 252$) and Sørlandet Hospital (SSHF; $n = 127$). Among these, 360 patients had responded to SQOL questions. All included patients were ≥18 years of age and fulfilled the Assessment of SpondyloArthritis international Society (ASAS) criteria for axSpA [13]. The study patients included at baseline have previously been described in detail [11, 12].

Data collection

The same data collection performed at baseline was also performed at the 5 year follow-up. Information on demographics, disease- and treatment-related variables and lifestyle were collected using questionnaires, laboratory tests, direct interviews and physical examination both at baseline and at the 5 year follow-up. Demographic data included age, gender, BMI (kg/m^2), current smoker status, alcohol consumption, work status and education. Education is presented as <10 years, 11–13 years and >13 years; this corresponds with the Norwegian education system where <10 years corresponds to lowest level of education, 11–13 years corresponds to high school and >13 years corresponds to college/university. Physical exercise was classified as >3 h/week, 1–3 h/week, <1 h/week and seldom or never. The four response categories were dichotomized. The response >3 h/week and 1–3 h/week were defined as >1 h/week and < 1 h/week and seldom or never were defined as <1 h/week. Disease duration was calculated from the date of diagnosis to the date of entry into the study. HLA-B27 status was registered. Data on comorbidities [cardiovascular diseases (CVDs), pulmonary diseases, neurological disorders, endocrine disorders, haematological disorders, gastrointestinal disorders, urogenital disorders, peripheral arthritis, cancer and mental disorders] were collected. We also computed a summed score to reflect comorbidity (range 0–10). This score has been used in other studies [11, 12, 14].

Disease activity was assessed by the BASDAI, 68 tender and 66 swollen joint counts, the Maastricht Ankylosing Spondylitis Enthesitis Score (MASES) and CRP. Physical function was assessed by the Bath Ankylosing Spondylitis Functional Index (BASFI) and the HAQ [15]. Data on the Bath Ankylosing Spondylitis Patient Global Score (BAS-G) and morning stiffness were also collected. Current medication, including NSAIDs, conventional synthetic DMARDs (csDMARDs) and bDMARDs was also recorded.

SQOL was assessed by the Sexual Quality of Life–Female (SQOL-F) questionnaire. The SQOL-F is a generic self-reported questionnaire that is used to assess the relationship between female sexual dysfunction and QOL [5]. The SQOL-F questionnaire was developed by Symonds *et al.* [16] based on Spitzer's Quality of Life Index. The questionnaire can also be used for partners and for male partners with minor modifications. In our study, we changed question 4 to 'When I think about my sexual life, I feel less of a woman/man' [16]. This is also supported in an article from Abraham *et al.* [17]: 'Discussion with experts, a review of the literature and interviews with men with either ED or PE suggested that the items of the SQOL-F were also applicable to men, with only small change needed to question QU 4: When I think about my sexual life I feel less of a man'. The questionnaire was translated into Norwegian by the Mapi Institute (Downey, CA, USA) in 2006. SQOL consists of 18 items, rated on a six-point scale: completely agree, moderately agree, slightly agree, slightly disagree, moderately disagree and completely disagree. A total score for SQOL and for the SQOL subcategories of psychosexual feelings, sexual and relationship satisfaction, self-worthlessness and sexual repression was calculated [18]. A higher score indicates better SQOL, except for sexual and relationship satisfaction, where a low score indicates better SQOL [12]. For the entire study population, Cronbach's α was 0.77 for total SQOL, 0.91 for psychosexual feelings, 0.81 for sexual and relationship satisfaction, 0.84 for self-worthlessness and 0.87 for sexual repression. The same pattern persisted when analysing women and men separately.

TABLE 1 Demographic data, disease markers, disease activity measures, damage, health status and comorbidity in 221 axSpA patients at baseline and the 5 year follow-up

Characteristics	Baseline	5 year follow-up	*P*-value
Demographics, *n* (%)			
Age, years, mean (S.D.)	46.0 (10.94)		
Married/cohabiting	179 (81)	185 (77)	0.405
Current smoker	57 (25.8)	38 (17)	< 0.001
Employed	162 (75.3)	153 (70.2)	0.073
Exercise >1 h/week	214 (87)	218 (89)	0.618
BMI, kg/m^2, mean (S.D.)	27.08 (4.4)	27.18 (4.5)	0.576
Education, *n* (%)			0.370
<10 years	25 (11)	20 (9)	
11–13 years	73 (33)	74 (34)	
>13 years	122 (56)	125 (57)	
Comorbidity			
Total score for comorbidity (range 0–10), mean (S.D.)	0.58 (0.82)	0.95 (1.13)	< 0.001
Disease activity measures, mean (S.D.)			
CRP (mg/dl)	8.25 (12.13)	5.34 (10.59)	< 0.001
BASDAI (range 1–10)	3.02 (2.05)	2.82 (2.16)	0.209
MASES (range 1–13)	3.19 (3.81)	1.30 (2.21)	< 0.001
Damage, mean (S.D.)			
BASMI	2.29 (1.92)	2.33 (2.07)	0.682
Health status, mean (S.D.)			
BASFI (range 0–10)	2.50 (2.09)	2.31 (2.12)	0.196
BAS-G (range 0–10)	3.67 (2.52)	3.03 (2.59)	0.003
HAQ (range 0–3)	0.51 (0.45)	0.45 (0.44)	0.075
Current treatment, *n* (%)			
NSAIDs	93 (43)	84 (39)	0.358
csDMARDs	14 (7)	14 (7)	0.688
bDMARDs	51 (23)	86 (40)	< 0.001

McNemar's tests were used to compare categorical data and paired-sample *t*-tests for continuous variables.

Statistical analyses

Statistical analyses were performed using SPSS Statistics version 25 (IBM, Armonk, NY, USA). Continuous variables are presented as mean (S.D.) and categorical variables as *n* (%). To compare data between baseline and the 5 year follow-up, we used McNemar's tests for categorical data and paired samples *t*-tests for continuous data. To calculate the SQOL change scores, we subtracted the baseline scores from the 5 year follow-up scores. We also calculated effect size by subtracting the mean SQOL score (and its subscores) at baseline from the mean score at the 5 year follow-up and then divided by the S.D. at baseline within the groups [19]. The effect size estimate was interpreted according to Cohen's effect size index: 0.2 as a small difference, 0.5 as moderate and ≥0.8 as large [19]. To estimate the proportion of patients with clinically significant changes in SQOL over the period, we identified patients with modest changes (5–9.99%), moderate changes (10–19.99%) and substantial changes (≥20%) [19].

Univariable and multivariable linear regression analyses [generalized linear model (GLM)] in SPSS were used to identify associations between demographic, clinical and treatment variables and 5 year changes in the SQOL sum score and its subcategories: demographic, comorbidity, measures of disease activity, damage, health status and treatment variables are listed in Table 1, with $P < 0.1$ tested in univariate analysis included in the linear multiple regression analysis. These factors also resonate with the wider theory within the field and clinical experience [20, 21].

Ethical and legal aspects

The study was approved by the Regional Committee for Medical Research Ethics in Norway (REK 4.2007.2152). All patients gave written informed consent before inclusion.

Patient involvement

After informed consent was obtained, the patients participated in the study by being interviewed and filling out questionnaires. There was no further patient involvement. The findings are provided in this publication.

Results

Of the 360 axSpA patients (MHH 246, SSHF 114) assessed at baseline with SQOL-F data available [12],

245 patients (MHH 138, SSHF 107) were assessed at the 5 year follow-up. Among the 245 patients assessed at the 5 year follow-up, 24 (MHH 12, SSHF 12) did not respond to the SQOL-F questionnaire, leaving 221 patients for the final analysis. Because of funding restrictions at MHH, not all included patients at baseline were invited for the 5 year assessment. This is reflected in the lower percentage of patients with follow-up data at MHH (56%) compared with SSHF (94%). Only minor differences in baseline characteristics were seen between patients with and without 5 year follow-up data. More patients without 5 year data were not cohabitating (32% *vs* 25%; $P = 0.023$), were not current users of bDMARDs (76% *vs* 64%; $P = 0.038$) and exercised <1 h/week (17% *vs* 7%; $P = 0.019$).

When comparing demographic and clinical characteristics between responders and non-responders, responders were significantly younger (mean 45.4 *vs* 50.9 years; $P = 0.025$), more were married or cohabitating (81% *vs* 42%; $P < 0.001$), fewer were smokers (26% *vs* 46%; $P = 0.037$) and more exercised longer (89% *vs* 75%; $P = 0.046$). For the other variables listed in Table 1, no significant differences were found.

Demographic data, disease activity measures, damage, health status and comorbidity at both baseline and the 5 year follow-up for the 221 patients are shown in Table 1. At the 5 year follow-up, the patients had more comorbidities (0.95 *vs* 0.58; $P \leq 0.001$), lower CRP (5.34 *vs* 8.25; $P < 0.001$), lower MASES (1.30 *vs* 3.19; $P < 0.001$), lower BAS-G scores (3.03 *vs* 3.67; $P = 0.003$), fewer were smokers (17% *vs* 26%; $P < 0.001$) and more were using bDMARDs (40% *vs* 23%; $P < 0.001$). We also compared baseline and 5 year follow-up data for each gender separately. In men, a significant change at the 5 year follow-up was found for the same variables as for the whole group. However, in women, the change between baseline and the 5 year follow-up was not found to be statistically significant for current smoking (28% *vs* 22%; $P = 0.180$), CRP [7.04 mg/dl (S.D. 13.6) *vs* 4.90 (9.56); $P = 0.147$] and BAS-G score [4.05 (S.D. 2.57) *vs* 3.41 (2.59); $P = 0.139$].

SQOL in patients with axSpA at baseline and the 5 year follow-up

As shown in Table 2, no statistically significant changes in the SQOL sum score and its subscore were found between baseline and the 5 year follow-up for all patients, as well as for men and women examined separately. The smallest change in SQOL was seen in self-worthlessness [−0.16 (S.D. 3.2)] and the largest in sexual and relationship satisfaction [0.51 (S.D. 5.2)]. The effect sizes for all were <0.2.

Although we did not find significant mean changes for SQOL in the whole cohort, over the 5 year period we identified some patients with clinically significant changes. Moderate/substantial improvement in SQOL was identified in 33 patients and deterioration in 33 patients. For psychosexual feelings, moderate/substantial improvement was identified in 55 patients and

Table 2 SQOL in axSpA patients with total score and subscores at baseline and the 5 year follow-up for all and for men and women separately

Characteristics	Baseline, mean (S.D.)	5 year, mean (S.D.)	*P*-value	Mean change (S.D.)	Baseline women, mean (S.D.)	5 year women, mean (S.D.)	*P*-value	Mean change (S.D.)	Baseline men, mean (S.D.)	5 year men, mean (S.D.)	*P*-value	Mean change (S.D.)
SQOL	76.5 (11.3)	79.0 (11.2)	0.633	0.32 (9.7)	73.4 (12.9)	75.3 (11.5)	0.194	1.9 (11.3)	77.8 (10.4)	77.5 (11.0)	0.647	−0.3 (8.9)
Psychosexual feelings	33.6 (8.3)	33.9 (8.3)	0.694	0.20 (7.4)	32.0 (9.7)	33.6 (7.9)	0.161	1.6 (8.7)	34.3 (7.6)	34.0 (8.5)	0.500	−0.4 (6.7)
Sexual and relationship satisfaction	11.8 (5.1)	12.3 (5.8)	0.161	0.5 (5.2)	12.1 (5.8)	12.6 (6.1)	0.555	0.4 (5.7)	11.7 (4.9)	12.1	0.193	0.5 (5.0)
Self-worthlessness	15.5 (3.5)	15.3 (3.2)	0.462	−0.16 (3.2)	14.8 (3.8)	14.8 (3.5)	0.961	−0.02 (3.7)	15.8 (3.3)	15.6 (3.2)	0.361	−0.2 (2.9)
Sexual repression	15.3 (3.6)	15.3 (3.5)	0.720	−0.08 (3.2)	14.3 (4.0)	14.4 (3.8)	0.898	0.1 (3.8)	15.8 (3.3)	15.6 (3.3)	0.557	−0.1 (2.8)

Paired-sample *t*-tests were used when comparing the groups psychosexual feelings (range 7–42), sexual and relationship satisfaction (range 5–30), self-worthlessness (range 3–18), sexual repression (range 3–18) and SQOL-F sum (range 18–108).

deterioration in 45 patients. Moderate/substantial improvement for sexual and relationship satisfaction was identified in 62 patients and deterioration in 47 patients. For self-worthlessness, moderate/substantial improvement was identified in 43 patients and deterioration in 50 patients. Finally, for sexual repression, moderate/substantial improvement was identified in 50 patients and deterioration in 43 patients. When comparing demographic and clinical data for patients with moderate/substantial deterioration with those patients with deterioration, we did not identify significant differences between the groups.

Baseline characteristics associated with 5 year changes in SQOL

Using multivariate analysis to identify baseline characteristics associated with 5 year changes in SQOL, we identified few significant associations. Exercise <1 h/week was associated with deterioration in total SQOL score [$\beta = -4.29$ (95% CI −8.55, −0.04); $P = 0.048$]) and age >65 years [$\beta = -0.12$ (95% CI −0.22, −0.01); $P = 0.028$] was associated with deterioration in the SQOL subscore of psychosexual feelings (Table 3).

Changes in comorbidity in patients with axSpA between baseline and the 5 year follow-up

The number of comorbidities increased significantly between the 5 year follow-up and baseline, with a total score of 0.95 (S.D. 1.13) *vs* 0.58 (S.D. 0.82) ($P < 0.001$). Within the type of comorbidity, significant deterioration at the 5 year follow-up was observed for gastrointestinal disorders (reflux and ulcus ventriculi; 18% *vs* 11%; $P < 0.001$), hypertension and hypercholesterolaemia (34% *vs* 21%; $P < 0.001$) and for endocrine disease (diabetes; 9% *vs* 5%; $P < 0.001$) (Table 4). As shown in Fig. 1, these differences were more prominent in men than in women.

Discussion

The main finding in this 5 year prospective study exploring axSpA patients recruited from two ordinary outpatient clinics revealed no deterioration in SQOL total score or its subscores during follow-up, although the number of comorbidities increased significantly.

At the same time, bDMARDs were used by a larger proportion of patients and a trend emerged towards better disease control, as reflected by reduced markers of disease activity, CRP, MASES and BASDAI, less pain and better functioning. Previous studies on health-related QOL (HRQOL) has shown significant clinical improvement using patient-reported outcome measures such as the HAQ, 36-item Short Form Health Survey (SF-36) and BASDAI and measurements of disease activity in both RA and AS [22–24]. The increased use of bDMARDs in our study may have contributed to lower disease activity, better functioning and less pain, thereby exerting a beneficial effect on SQOL.

Previous studies have shown that axSpA patients are at a higher risk of comorbidities than the general population [25, 26], which was also the case in our study. In general, comorbidities develop during the disease course, particularly CVD and depression [26–29], but they are often underdiagnosed in patients with AS [25]. From baseline to the 5 year follow-up, we found a significant increase in endocrine disease (predominantly diabetes), CVD and gastrointestinal symptoms, which was more marked in men than in women, in line with previous findings [2]. The increase in gastrointestinal symptoms included reflux and ulcers, possibly related to therapy with NSAIDs, which were used by 30–45% of our patients. The increase in cardiovascular comorbidities comprised mainly hypertension and hypercholesterolaemia. In a study using the same patient cohort, we found no increase in depression as assessed by either the SF-36 mental component summary score or self-reported depression (question 15) [14].

The lack of the expected deterioration in SQOL over a 5 year period despite the increased number of comorbidities might be partly explained by the psychology of QOL, whereby patients adjust and cope with their chronic illness [30]. Using various strategies, they tend to adjust their life goals, expectations and the way they want to live their life in accordance with the actual situation [31, 32]. Response shift is one such strategy and is defined as a change in internal standards and values and a redefinition of what is important in the patient's life [31, 32]. These findings are in line with a recent study from our group exploring HRQOL in the same cohort of axSpA patients [14]. In that study, no deterioration in HRQOL over the 5 year period occurred and the physical dimension in HRQOL (SF-36) improved [14].

There were few significant baseline characteristics associated with significant changes in SQOL. Exercise <1 h/week was associated with a decrease in SQOL. Other studies support the notion that exercise is positive in both patient-reported and physical outcomes in axSpA [33]. Exercise also helps prevent CVD and endocrine disease [34]. In addition to medical treatment, regular exercise is one of the core elements in the standard treatment of axSpA and has been shown to be important for both disease control and general well-being [35]. At both hospitals, disease-specific courses for patients with axSpA are routinely offered and information on lifestyle changes, such as quitting smoking and increasing regular exercise, is given.

Our study population had a considerable age range, from 18 to 81 years at baseline and at the 5 year follow-up. Older age at baseline was associated with a deterioration in the SQOL subscore of psychosexual feelings, but not with the total SQOL score. Increased age has been reported to reduce SQOL in healthy individuals [30], however, better disease control in our axSpA patients at 5 years compared with baseline might have compensated for the expected decrease in SQOL with increased age reported by others [36]. Ageing does not necessarily cause a lack of sexual desire, but may have

Table 3 Baseline predictors associated with 5 year changes in SQOL-F (ΔSQOL) sum score and SQOL subscores

Characteristics	SQOL-F sum (range 18–108), adj. β (95% CI)	*P*-value	Psychosexual feelings (range 7–42), adj. β (95% CI)	*P*-value	Sexual and relationship satisfaction (range 5–30), adj. β (95% CI)	*P*-value	Self-worthlessness (range 3–18), adj. β (95% CI)	*P*-value	Sexual repression (range 3–18), adj. β (95% CI)	*P*-value
Demographic factors										
Age (years)	−0.11 (−0.25, 0.02)	0.104	−0.12 (−0.22, −0.01)	0.028	0.07 (−0.01, 0.16)	0.087	−0.01 (−0.06, 0.03)	0.588	−0.45 (−0.10, 0.002)	0.059
Male	−0.37 (−4.29, 5.55)	0.357	−1.34 (−3.61, 0.94)	0.247	−0.69 (−2.43, 1.06)	0.437	0.46 (−0.48, 1.41)	0.337	0.33 (−0.67, 1.33)	0.511
Living alone	−3.02 (−6.88, 0.83)	0.123	−2.21 (−5.24, 0.82)	0.152	−0.87 (−3.24, 1.50)	0.471	−0.01 (−1.15, 0.56)	0.986	0.35 (−0.83, 1.54)	0.558
Education										
<10 years	4.20 (−0.23, 8.63)	0.063	3.26 (−0.24, 6.75)	0.067	−0.66 (−3.33, 2.02)	0.629	1.18 (−0.24, 2.60)	0.102	0.62 (0.88, 2.12)	0.415
11–13 years	2.27 (−0.58, 5.12)	0.118	1.08 (−1.14, 3.36)	0.332	−0.09 (−1.84, 1.67)	0.923	0.52 (−0.41, 1.44)	0.271	0.61 (−0.36, 1.58)	0.218
>13 years	Ref.		Ref.		Ref.		Ref.		Ref.	
Exercise <1 h/week	−4.29 (−8.55 to −0.04)	0.048	−3.29 (−6.64, 0.06)	0.054	0.62 (−1.95, 3.19)	0.634	0.78 (−2.1, 0.56)	0.249	−0.66 (−2.08, 0.75)	0.356
Exercise >1 h/week	Ref.		Ref.		Ref.		Ref.		Ref.	
BMI, kg/m^2	−0.18 (−0.49, 0.13)	0.245	−0.00 (−0.25, 0.24)	0.986	−0.03 (−0.22, 0.16)	0.724	−0.07 (−0.17, 0.03)	0.182	−0.04 (−1.15, 0.06)	0.432
Disease activity measures										
BASDAI (range 0–10)	−0.29 (−1.17, 0.59)	0.517	−0.20 (−0.89, 0.50)	0.623	0.03 (−0.49, 0.56)	0.898	0.02 (−031, 0.27)	0.895	−0.19 (0.50, 0.11)	0.213
CRP, mg/dl	0.09 (−0.03, 0.22)	0.125	0.01 (−0.09, 0.10)	0.846	0.04 (−0.03, 0.11)	0.283	0.02 (−0.2, 0.06)	0.265	0.04 (−0.00, 0.08)	0.055
Health status										
HAQ (range 0–3)	−1.59 (−5.46, 2.27)	0.417	−0.83 (−3.87, 2.22)	0.593	−0.73 (−3.09, 1.64)	0.544	0.02 (−1.25, 1.30)	0.970	0.25 (−1.09, 1.59)	0.712
Damage										
BASMI (range 0–10)	−0.19 (−0.90, 0.53)	0.611	−0.14 (−0.71, 0.42)	0.623	−0.01 (−0.45, 0.43)	0.967	−0.10 (−0.33, 0.14)	0.418	−0.01 (−0.25, 0.24)	0.961
Mean total score for comorbidity (range, 0–10)	−0.20 (−2.01, 1.62)	0.832	0.04 (−1.39, 1.47)	0.594	−0.32 (−1.43, 0.78)	0.564	0.20 (−0.39, 0.80)	0.500	−0.07 (−0.70, 0.56)	0.836
Current treatment										
NSAIDs	−0.84 (−1.87, 3.54)	0.541	−0.20 (−2.33, 1.94)	0.854	−0.51 (−2.17, 1.1)	0.544	−0.17 (−1.06, 0.72)	0.701	0.20 (−0.73, 1.14)	0.668
csDMARDs	1.62 (−7.13, 3.89)	0.562	0.08 (−4.28, 4.44)	0.972	0.00 (−3.39, 3.40)	0.998	0.78 (−1.06, 2.62)	0.403	0.56 (−1.39, 2.50)	0.571
bDMARDs	1.14 (−4.28, 2.00)	0.474	0.46 (−2.00, 2.92)	0.711	0.03 (−1.86, 1.93)	0.972	−0.21 (−1.25, 0.82)	0.688	0.59 (−0.49, 1.67)	0.285
SQOL at baseline										
SQOL baseline	−0.35 (−0.47, −0.24)	<0.001								
Psychosexual feelings			0.35 (−0.48, 0.22)	<0.001						
Sexual and relationship satisfaction					−0.32 (−0.47, −0.16)	<0.001				
Self-worthlessness							−0.42 (−0.53, 0.029)	<0.001		
Sexual repression									−0.37 (−0.50, −0.024)	<0.001
R^2, %		23.2		18		4.8		20.9		19.5

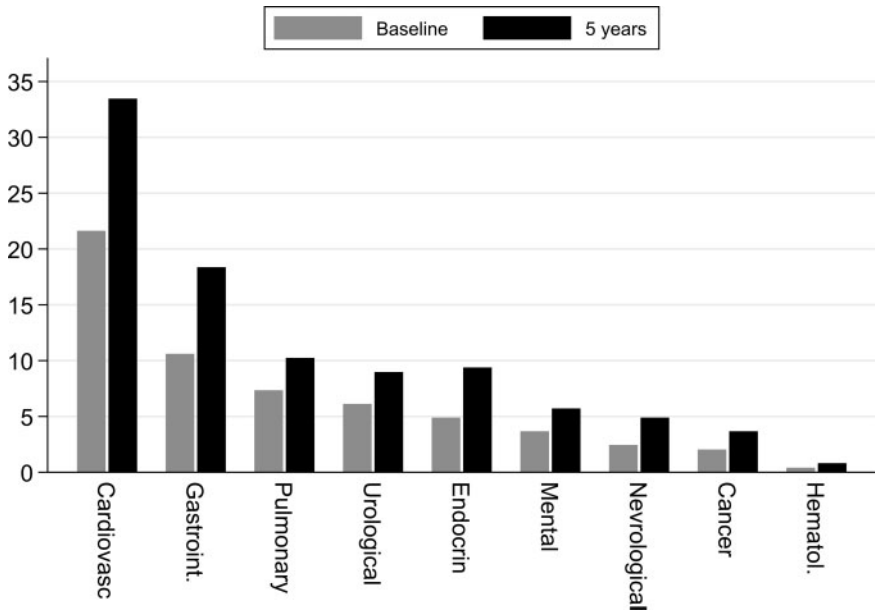
Baseline predictors associated with 5 year changes in SQOL-F (ΔSQOL) sum score and the SQOL subscores psychosexual feelings, sexual and relationship satisfaction, self-worthlessness and sexual repression in 221 patients with axSpA in outpatient clinics. The final model used linear regression analysis (GLM). adj.: adjusted unstandardized regression coefficients with 95% CI and *P* values. SQOL-F sum range 18–108. Reference values for statistical comparison.

Table 4 Comorbidities in axSpA patients at baseline and the 5 year follow-up for all patients and for men and women separately

Comorbidities	Baseline, *n*(%)	5 year, *n*(%)	*P*-value	Baseline, women (*n* = 77)	5 year, women (*n* = 77)	*P*-value	Baseline, men (*n* = 168)	5 year, men (*n* = 168)	*P*-value
Neurologic events/disease	6 (2)	12 (12)	0.031	2 (3)	3 (4)	1.000	4 (2)	9 (5)	0.063
Psychiatric diseases	9 (4)	14 (6)	0.063	2 (3)	4 (5)	0.500	7 (4)	10 (6)	0.250
Cancer	5 (2)	9 (4)	0.125	0	2 (3)		5 (3)	7 (4)	0.500
Endocrine disease	12 (5)	23 (9)	0.001	7 (9)	10 (13)	0.250	5 (3)	13 (8)	0.008
Haematological disease	1 (0.4)	2 (1)	1.000	0	1 (1)	1.000	1 (0.6)	1 (0.6)	1.000
Lung disease	18 (7)	25 (10)	0.039	4 (5)	6 (8)	0.500	14 (8)	19 (11)	0.125
Coronary heart disease	53 (21)	82 (34)	<0.001	19 (25)	30 (39)	0.001	34 (20)	52 (31)	<0.001
Gastrointestinal disease	26 (11)	45 (18)	<0.001	10 (13)	14 (18)	0.125	6 (10)	31 (19)	< 0.001
Urogenital disease	15 (6)	22 (9)	0.016	4 (5)	5 (6)	1.000	11 (6)	17 (10)	0.031

McNemar's tests were used to compare differences in categorical variables between baseline and the 5 year follow-up.

Fig. 1 Comorbidities (in %) at baseline and the 5 year follow-up in 245 axSpA patients



a strong influence on the quality of relationships and sexual functioning. The subcategory psychosexual feelings includes items such as frustration, depression, anxiety, anger, worrying about a partner's hurt or rejection, feeling like something is lost and becoming more aware of this as one gets older. Other studies suggest that the quality of sexuality is more important than quantity [30, 36]. Ageing may be associated with learned skills and strategies throughout a long life that can buffer age-related declines in SQOL, particularly in the context of a positive relationship; this is also called sexual wisdom [30]. Furthermore, with respect to the effect of age, younger patients have had their disease for a shorter time and are thus likely to be less affected by disease duration and resulting structural damage.

Strengths and limitations

A clear strength of our study is the long-term prospective follow-up of axSpA patients over a period of 5 years. Furthermore, the study comprised a relatively high number of patients followed during this period, and many variables (objective measures and generic and disease-specific patient-reported outcome measures) were included both at baseline and the 5 year follow-up. In Norway, rheumatology is a speciality on its own and

rheumatologists follow the T2T strategy to achieve optimal disease control in patients with axSpA. We believe that selection bias is probably limited because patients were consecutively collected from the daily outpatient clinic at the two hospitals. We also previously reported that patients recruited from the SSHF reflected the entire axSpA outpatient clinic cohort [11]. Thus the internal validity of the study is most likely good.

Some limitations of the study should be noted. Our patient population included patients ages 18–81 years and comprised all patients attending the outpatient clinic during a defined period. The age distribution of the patient population showed that only four patients were in the group 66–81 years and 23 patients were $\leq$30 years of age. The main proportion of the patients were between 31 and 65 years of age. The group of patients $<$30 years of age in our cohort is small. Younger patients with early and active disease may indeed suffer more impairment of sexual function resulting in less SQOL, but we have no subanalysis of the 21 patients $<$30 years of age.

Also, data collection using the SQOL-F in both genders was done with support from the literature, but it may be a limitation [16, 17].

Data were collected only twice over the 5 years. Thus, although we identified changes, it is unknown when the changes occurred, and another two or three time points for data collection would have been advantageous. In addition, there were some minor differences between patients who attended the follow-up and those who were lost to follow-up. From the data collected, we were unable to distinguish between radiographic axSpA and non-radiographic axSpA. Finally, interviewing the participants using qualitative methods could also have given us more in-depth information.

Conclusion

In our study over a 5 year period, we observed no deterioration in SQOL, despite an increase in age and the number of comorbidities. This finding is most likely explained by better disease control at 5 years compared with baseline due to more patients being treated with bDMARDs. Our findings add evidence to the importance of suppressing inflammation in axSpA patients to maintain and improve HRQOL, including SQOL.

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All authors contributed to the article.

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Data availability statement

Data are available upon request.

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Appendix 4

An overview of studies on sexual activity, sexual QOL, sexual relationships. Sexual satisfaction, and sexual dysfunction and function.

Table 1. An overview of studies on sexual activity, sexual QOL, sexual relationships, sexual satisfaction, and sexual dysfunction and function

	N	**Research question**	**Method and instruments**	**Main findings**
Sexual activity				
Gallinaro, A.L. et al. 2012 Brazil	32 patients 32 controls 28 mal2 4 women	Sexual activity in **AS**	Case-control HAQ-S, BASFI, BASDAI, VAS	The chronic nature of AS, associated with poor functional capacity and high activity, interferes with sexual intercourse. When sexual activity was possible, no difference was found between patients and controls.
Fu, J et al. 2019 China	31 male	Sexual activity in male AS patients before and after total hip arthroplasty (THA)	Longitudinal International Index of Erectile Function (IIEF)	Successful THA may improve sexual activity and better movement (flexion-extension range motion ROM, adduction-abduction ROM) improved sexual activity.
Yao, Z. et all. 2016 China	45 male	Assessment of changes in sexual activity after surgical treatment for AS-induced kyphosis	Retrospectively reviewed IIEF	Showed surgery may improve sexual functioning .

Rostom, s. et al. 2013 Marocco	110 male	The impact of AS on sexual activity	Modified New York criterias	2atigue and sleep disturbance was independently associated with perceived problems and sexual activity.
Sexual QOL				
Dong, X. et al. 2015 China	42 patients over 3 months	To investigate the therapeutic effect of a tumour necrosis factor-alpha (TNF-α) antagonist on the sexual quality of life of male patients with **AS**	Open label/longitudinal mSLQQ-QOL BASDAI	No significant differences in baseline data were found between the two groups. After treatment, disease activity and quality of life were improved in these two groups. Sexual quality of life and disease activity were improved after treatment with TNF-α antagonists in male patients with AS. The extent of improvement in sexual quality and disease activity are positively related.
Sexual relationships				
Healey, E. et al. 2009 United Kingdom	612 patients from 10 sites	To explore the impact of **AS** on sexual relationships in a large cohort of patients across the UK.	Multicenter cross-sectional HADS-d, BASFI, BASDAI ASES, VAS	AS substantially impacts patients' sexual relationships, both for physical outcomes and psychological state. 37.6% of males and 37.7% females reported that the disease impacts sexual relationships.
Sexual satisfaction				
Akkus, Y. 2010 Turkey	18 RA 15 AS 33 patients	Factors affecting the sexual satisfaction of patients with RA and **AS**	Descriptive DAS 28, HAQ, BASDAI, BASFI	Statistically significant difference in satisfaction before diagnosis compared to after. Sexual satisfaction was lower in RA patients; sexual satisfaction was negatively correlated with DAS 28 and HAQ. Nurses should be aware of sexual lifestyle and functioning.

Sexual dysfunction/function				
Erdem, IH. et al. 2020 Turkey	50 males 50 controls With AS patients	To investigate the incidence of erectile dysfunction (ED) in patients with AS with a control group and to investigate the risk factors for ED.	Case-control BASDAI, BASFI, ASOQOL	Erectile function scores slightly lower in the AS group than the control group. Risk of ED was shown as disease activity and psychological factors increased.
Rezvani, E.A. et al. 2012 Turkey	39 male AS 27 healthy controls	To investigate the impact of **AS** on sexual functions in male patients compared with the healthy controls. Identify the associations with disease-related variables.	Cross-sectional IIEF BDI ASQOL	Sexual dysfunction is common in male patients with AS. No statistically significant differences between AS and controls in terms of sexual functions. Sexual dysfunction is associated with an unfavorable psychological status.
Dhakad, U. et al. 2015 India	100 males and 100 controls with AS	To determine sexual dysfunctions and urinary symptoms in male **AS** patients and their association with various disease and patient factors	Case-control IIEF IPSS HADS BASFI. BASDAI	AS is associated with higher incidence of sexual dysfunction in male patients. ED is associated with anxiety, depression, longer duration of disease, higher BASFI score and higher age in AS patients.
Gözukücük, M. et al. 2021 Turkey	98 women (62 AS and 36 patients with nr.axSpA) 99 Healthy controls	Evaluate sexual functioning and disease related variables, physical and psychogenic states in female patients with nr-axSpA	Case-control FSFI, SF-36, HADS, Gynecological evaluation	No difference between AS and nr-axSpA related sexual functioning and psychological burden. Elderly women with axSpA disease duration and limitations in movement are more affected in genital arthropathy and sexual functioning.

Akkurt. HE, et al. 2016 Turkey		This study aimed to evaluate sexual function in females with **AS**, compare them with healthy controls, and demonstrate the effects of AS on female sexual functions.	Case-control FSFI VAS BASDAI	Sexual dysfunction was more common in female AS patients without marked impairment in body image and hip involvement when compared to normal population.
Nisihara, R. et al. 2021 Brazil	35 male patients with AS and 104 controls	To study erectile dysfunction in male patients and correlation to sexual hormonal profile and disease activity	Transversal observational, single center IIEF, FT, BT, SHBG, ASDAS,	Patients with AS had worse sexual performance than controls linked to disease activity, not to hormonal profile.
Sariyildiz, MA. et al. 2013 Turkey	37 females	To explore the impact of **AS** and the disease-related variables, psychological status, and the QOL on the female patients' sexual function	Cross-sectional FSFI	No significant correlation was observed with the disease duration, smoking status, depression, anxiety, pain, and ESR when the total scores and the scores from the domains of the FSFI were compared. The sexual function is impaired in female patients with AS. This impairment in the sexual function is especially related to the functional status and disease activity among the clinical and laboratory parameters.
Shen, B. et al. 2013 China	103 AS patients 78 males 25 females	A primary analysis of sexual problems in Chinese patients with **AS**	Single-center cross-sectional BIDQ SF-36 VAS HAQ	Both physical and psychological factors were shown to impact sexual relationship and function. Disease activity, physical function, and psychological well-being impact sexual health. To examine associations with demographic parameters, physical impairments, psychological problems.

Demir, S.E. et al. 2013 Turkey	23 AS patients 27 Controls	Assessment of sexual functions in female patients with **AS** compared with healthy controls	Case-control FSFI BDI Short-Form-36	Sexual problems in female patients with AS appear to be associated with higher depression levels, increased disease activity, decreased functionality, higher pain scores and decreased quality of life.
BAL, S. et al. 2011 Turkey	37 male patients 67 controls	Sexual functioning in **AS**	Case-control SF-36, disease duration, VAS, ESR, CRP, BASDAI, BASFI BASMI, BAS-G IIEF	Prevalence of ED like that for controls. AS patients have problems with satisfaction from intercourse.
Oh. JS, et al. 2009 Korea	22 males	The effect of antitumor necrosis factor agents on sexual dysfunction in male patients with **AS**: a pilot study	Open label without placebo BASDAI IIEF RAND-36	Anti-TNF therapy may improve sexual dysfunction in men with AS, in addition to reducing disease activity. Decreased ED. Only intercourse showed significant correlation with BASDAI..
Ôzkorumak. E, et al. 2011 Turkey	43 men recruited consecutively: matched control group	Sexual function in male patients with **AS**	Case-control Questionnaire on socio-demographic data BDI, GRSSS, BASDAI BASFI, BASMI, VAS	Sexual health of patients with AS appears to be based on two interrelated factors: psychological status (depression and anxiety) and disease activity.
Fan. D, et all. 2015 China	535 men with AS 430 male controls from 11 studies	TO drive a more precise estimation of the Sexual function and its clinical correlation in men with AS	Meta analysis	Sexual functioning is impaired in male patients with AS.

Santana. T, et al. 2017 Brasil	40 male patients with AS and 40 healthy controls	To study erectile dysfunction in ankylosing spondylitis patients	Case-control BASDAI, ASDAS, Sr, CRP, MASES, SPARCC, BASFI, HAQ, BASMI, IIEF.	High prevalence of erectile dysfunction among patients with AS, associated with disease activity measured with BASDAI.
Aykurt Karibel.I, 2019 Turky	67 mail patients with AS	Investigate the effect of smoking on sexual functioning	Prospective observational BASDAI, BASMI, BASFI, ASQoL, Fatigue and pain VAS scale, BDI, FTND, IIEF-5, Exh.CO	Sexual function in patients with AS is associated with, pain, fatigue, disease activity, functional status, QOL, depression and cumulative exposure to smoking. Sexual functioning tends to decline with increasing degree of smoking.
Liu. Y.F. 2015 China	484 cases from 5 studies	Investigate the impact of AS on sexual functioning, regardless of gender	Review, mata-analysis BASFI, BASDAI; ASQoL, IIEF, FSFI	AS has a certain impact on sexual functioning of male patients. And the impact seems to be greater for men than for women.

BASFI - Bath Ankylosing Spondylitis Functional Index; BASDAI - Bath Ankylosing Spondylitis Activity Index; ESR – erythrocyte sedimentation rate; BAS-G - Bath Ankylosing Spondylitis Patients Global Score; BASMI - Bath Ankylosing Spondylitis Metrology Index; CRP - C-reactive protein ; ROM – range of motion; FSFI – Depression Inventory and Female Sexual Function Index; VAS – visual analogue scale for pain; IIEF – International Index of Erectile Function; IIEF-5 - International Index of Erectile Function classified into 5 categories; BDI – Beck Depression Inventory; ASES – Arthritis-Specific Self-Efficacy questionnaire; IPSS – International Prostate Symptom Score; HADS – Hospital Anxiety and Depression Scale; SD – Sexual Dysfunction; BIDQ – Body Image Disturbance Questionnaire; GRSSS – Glombok-Rust Sexual Satisfaction Scale; ROM – Range of Motion; AIMS2 – Arthritis Impact Measurement Scale; SF-12 – 12-Item Short-Form Health Survey; RAND- ; SF-36 – Medical Outcomes Short-Form-36 questionnaire; BMSFI – Brief Male Sexual Functioning Inventory; HADS-d – Hospital Anxiety and Depression Scale; mSLQQ-QOL – The Modified Sexual Life Quality Questionnaire; ASQoL – Ankylosing Spondylitis Quality of Life; VAS – visual analog scale; ASDAS – Ankylosing Spondylitis disease Activity Score; SPARCC – Spondyloarthritis Research Consortium of Canada; FTND – Fagerstrøm Test for Nicotine Dependence; Exh.CO – Carbon-monoxide in exhaled air;

Appendix 5

Approval Norwegian Center for Research Data

NTNU
Norges teknisk-naturvitenskapelige universitet

Det medisinske fakultet
Regional komite for medisinsk forskningsetikk
Helseregion Midt-Norge

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02.10.07	4.2007.2152		

Inflammatorisk ryggsykdom og etablert Bekhterevs sykdom i Norge. - En klinisk epidemiologisk studie av forekomst, sykelighet, klinisk presentasjon, livskvalitet seksualitet, og helseøkonomi og effekt av biologisk behandling.

Med hjemmel i lov om behandling av etikk og redelighet i forskning § 4 har Regional komité for medisinsk og helsefaglig forskningsetikk, Midt-Norge vurdert prosjektet i sitt møte 14. september 2007 med følgende vilkår og vurdering:

Hovedbegrunnelsen for å gjennomføre denne studien er at det er et stort behov for økt kunnskap om denne sykdommen (både tidlig og etablert stadium) baserte på populasjonsbasert studie design. Dette gjelder både klinisk epidemiologiske forhold, livskvalitet og helseøkonomi. Dataene fra denne studien vil således kunne bli en viktig kunnskaps kilde for leger og øke deres forståelse til hjelp i diagnostisering, behandling og oppfølging av pasienter med Bektherev sykdom. For helse byråkrater og helsepolitikere vil den studien gi viktig bakgrunnsinformasjon når beslutninger skal tas knyttet til bestemmelser om ressursbruk og rettigheter overfor denne pasientgruppen. Videre er det også et behov for å finne ut hvordan moderne og dyr behandling ("biologisk behandling") virker i den daglige bruk av disse medikamentene.

Metode:
Prospektiv klinisk epidemiologisk populasjonsbasert studie med et tverrsnitt og en longitudinel design. Pasienter med etablert Bektherevs sykdom vil bli identifisert ved hjelp av sykehusenes elektroniske diagnoseliste systemer. Det samme vil bli gjort ved å innhente diagnose lister fra deltagende privat praktiserende revmatologer og deltagende private Røntgensentra.
Allmennpraktikere vil i brevs form bli oppfordret til å henvise pasienter med Bekhterevs sykdom til undersøkelse ved de deltagende revmatologiske avdelinger. Pasientens diagnose vil bli verifisert og innkalt til undersøkelse og inklusjon i studien etter at pasienten har avgitt muntlig og skriftlig samtykke.
Pasienter som starter opp med biologisk behandling vil bli fulgt med objektive og subjektive effektmål.

For delstudien som omfatter undersøkelse av pasienter med tidlig Bektherev sykdom så vil denne basere seg på at primærleger vil bli oppfordret til å henvise pasienter med mistanke om Bektherev sykdom tidlig til revmatologisk avdeling for undersøkelse. Pasienter som har sagt seg villige til å delta i tverrsnittsstudien vil også bli forspurt om å ville delta i en prospektiv studie. Det vil ved hjelp av spørre skjema bli innhentet et bredt spekter av data knyttet til sosiodemografi, kliniske forhold, livskvalitet og helseøkonomi.

Komiteen har følgende merknader til prosjektet:

- Komiteen viser til prosjektprotokollen og det er uklart hvordan deltakerne skal inkluderes og hvordan dette finansieres. Komiteen stiller spørsmål om pasienter blir henvist for studiedeltakelsen, eller er det de som er henvist uavhengig av denne studien som skal inkluderes? Det kan være et forskningsetisk problem hvis henvisning er begrunnet i forskning og ikke begrunnet i vanlig klinisk praksis. Vil deltakere som eventuelt trekker seg fra studien underveis kunne fortsatte å gå til kontroller? Komiteen ber om tilbakemelding om dette.
- Det må utarbeides et informasjonsskriv som de aktuelle studiedeltakerne får før de blir henvist til senter for deltakelsen, slik at de som eventuelt henvises for studien og ikke for medisinsk vurdering og behandling kan få tatt standpunkt til dette på forhånd. Den første henvendelsen om deltakelse i studien må skje gjennom den som er klinisk ansvarlig overfor den konkrete pasienten, slik at taushetsplikt er bevart.
- Komiteen viser til informasjonsskrivet og det må utarbeides et totrinns skriv. Ett skriv må først informere om den overordnede studien og deretter må det utformes skriv som informerer direkte om understudier.
- Komiteen mener det er uheldig at det flere steder blir understreket at dette er dyre medisiner. Det bør være pasienten uvedkommende om dette er dyrt eller billig, dette aspektet bør ikke være noe om pasienten bør bekymre seg om.
- Det skal tas biologisk materiale. I henhold til Biobankloven må det søkes spesielt om dette, jf. § 4 i loven, og dette skal vurderes av Regional komité for medisinsk forskningsetikk før det meldes til Sosial- og helsedirektoratet. Komiteens sekretariat vil oversende meldingen til direktoratet så snart den er oversendt komiteen og vurdert. Komiteen må forelegges en punkt for punkt redegjørelse for de momentene som skal svares på etter lovens § 4. Det må opplyses i informasjonsskrivet til forsøkspersonene at det blir opprettet en biobank.
- Komiteens sekretariat vil oversende biobankmeldingen til direktoratet.

Komiteen ber om å få tilsendt artikkel/rapport når studien er fullført.

Vedtak:
"Komiteen godkjenner at prosjektet gjennomføres med de merknader som er gitt."

Vedtaket kan påklages og klagefristen er tre uker fra mottagelsen av dette brev, jf. fvl. §§ 28 og 29. Klageinstans er Den nasjonale forskningsetiske komité for medisin og helsefag (NEM), men en eventuell klage skal rettes til REK Midt-Norge. Avgjørelsen i NEM er endelig. Det følger av fvl. § 18

at en part har rett til å gjøre seg kjent med sakens dokumenter, med mindre annet følger av de unntak loven oppstiller i §§ 18 og 19.

Vi viser til dette.

Med hilsen

Arne Sandvik
Professor
Leder i komiteen

Arild Hals
Seniorrådgiver
Sekretær i komiteen

Appendix 6

Norwegian Social Science Data Service

Norsk samfunnsvitenskapelig datatjeneste AS
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Vår dato: 28.11.2007 Vår ref: 17602 / 3 / SF Deres dato: Deres ref:

TILRÅDING AV BEHANDLING AV PERSONOPPLYSNINGER

Vi viser til melding om behandling av personopplysninger, mottatt 01.10.2007. Meldingen gjelder prosjektet:

17602	*Inflammatorisk ryggsykdom og etablert Bekhterevs sykdom i Norge*
Behandlingsansvarlig	*Sørlandet sykehus HF, ved institusjonens øverste leder*
Daglig ansvarlig	*Glenn Haugeberg*

Personvernombudet har vurdert prosjektet, og finner at behandlingen av personopplysninger vil være regulert av § 7-27 i personopplysningsforskriften. Personvernombudet tilrår at prosjektet gjennomføres.

Personvernombudets tilråding forutsetter at prosjektet gjennomføres i tråd med opplysningene gitt i meldeskjemaet, korrespondanse med ombudet, eventuelle kommentarer samt personopplysningsloven/-helseregisterloven med forskrifter. Behandlingen av personopplysninger kan settes i gang.

Det gjøres oppmerksom på at det skal gis ny melding dersom behandlingen endres i forhold til de opplysninger som ligger til grunn for personvernombudets vurdering. Endringsmeldinger gis via et eget skjema, http://www.nsd.uib.no/personvern/melding/pvo_endringsskjema.cfm. Det skal også gis melding etter tre år dersom prosjektet fortsatt pågår. Meldinger skal skje skriftlig til ombudet.

Personvernombudet har lagt ut opplysninger om prosjektet i en offentlig database, http://www.nsd.uib.no/personvern/register/.

Personvernombudet vil ved prosjektets avslutning, 17.10.2008, rette en henvendelse angående status for behandlingen av personopplysninger.

Vennlig hilsen

Bjørn Henrichsen

Sølve Fauskevåg

Kontaktperson: Sølve Fauskevåg tlf: 55 58 25 83
Vedlegg: Prosjektvurdering

Appendix 7

Information and declaration of consent

Informasjonsskriv til pasienter med etablert Bekhterevs sykdom og ”tidlig Bekhterev” som ønsker å delta i en studien - Bekhterev i Norge

Forespørsel om å delta i forskningsprosjekt:

Om Bekhterevs sykdom:
Bekhterev sykdom er en kronisk systemisk leddbetennelsesykdom som hovedsakelig rammer små ledd i ryggen og som fører til smerte og stivhet. Over år kan sykdommen føre til tilstivning av ryggsøylen. Sykdommen kan også ramme andre organer i kroppen som f.eks tarmen, hjerte, skjelettet og øynene. Sykdommen er forbundet med stor sykelighet, redusert livskvalitet og fører ofte til redusert arbeidsevne og dermed økt risiko for tidlig uførhet. Sykdommen fører til store helsekostnader for både pasient og samfunn. Det er et stort behov for å øke vår kunnskap om denne sykdommen, blant annet fordi nye dyre medikamenter er tilgjengelige.
Diagnosen Bekhterevs sykdom er vanskelig å stille på et tidlig tidspunkt. Pasienter kan gå i flere år med plagene sine uten at riktig diagnose stilles. Dette fører ofte til stor frustrasjon hos pasienten og gir pasienten ofte en følelse av at han/hun ikke blir tatt på alvor. Vi ønsker derfor også å undersøke dem som har tidlig symptomer på Bekhterevs sykdom hvor sykdommen kan mistenkes, men hvor diagnosen ikke kan stilles helt sikkert. Dette er viktig fordi vi har som mål å komme tidlig i gang med behandling av sykdommen.

Denne studien:
Denne undersøkelsen som du har mulighet til å delta i, er planlagt som en førstegangsundersøkelse nå og så ny undersøkelse om 5 år dersom du har sikker sykdom og om 3 år dersom du har tidlig Bekhterev. Dersom du ønsker å delta, er det ingen forpliktelse om også å delta senere. Du kan når som helst trekke deg fra undersøkelsen.

Hva ønsker vi å oppnå med studien:
Undersøkelsen har som formål å undersøke hvordan pasienter med Bekhterevs sykdom har det og hvordan det går med dem. Vi ønsker blant annet å kartlegge hvor mange som har sykdommen, hvilke behandling som gis, sykdomsalvorlighet, grad av organskade, livskvalitet og kostnader. Videre ønsker vi å få oversikt over hvor mange pasienter som vil kunne være kandidater for annen behandling enn fysioterapi og betennelsesdempende (NSAID/COXIB).
Det er mangelfulle data på dette området og økt kunnskap trengs for om mulig å bedre tilbudet til denne pasientgruppen og kunne møte de utfordringer som vi i fremtiden står overfor for å kunne gi riktig behandling til riktig pasient.

Gjennomføring av undersøkelsen:
Pasienter med ”mistenkt/tidlig Bekhterev” og sikker Bekhterev sykdom som behandles/henvises revmatologiske avdelinger, privatpraktiserende revmatologer, eller som er blitt diagnostisert til å ha sykdommen ved Røntgenavdelingen eller private røntgensentre vil bli invitert til å ta del i undersøkelsen. Informasjon om studien gis både skriftlig og muntlig.
Det presiseres at det hele tiden er fullt mulig å gå ut av studien dersom man ikke ønsker videre deltagelse også uten å måtte angi grunn. Undersøkelsen vil inkludere utfylling av protokoll hvor man i hovedtrekk svarer på spørsmål, klinisk undersøkelse, røntgen undersøkelse, bentetthetsmåling med tanke på osteoporose og rutine blodprøver. Deltagelse i studien vil for deg ikke være forbundet med økte utgifter. Reisekostnader vil vi dessverre ikke kunne dekke dersom de ikke er en del av en rutinekontroll ved en Revmatologisk avdeling.

<u>Fordeler / ulemper for deg med å delta i undersøkelsen:</u>

Fordeler: Du vil bli grundigere undersøkt og fulgt opp enn det som er gjeldende ut fra dagens rutiner. Dette er ikke en sammenlignende undersøkelse av behandlingseffekt, det betyr at om du velger å delta eller ikke, vil du få samme type behandling som behandlende lege finner riktig å gi deg.
Ulemper: Du vil måtte bruke tid på utfylling av spørreskjema, klinisk undersøkelse, røntgenundersøkelser og blodprøver. Vi regner med at du vil måtte bruke ca 30-40 minutter ekstra på å besvare spørsmålene i spørreskjemaene som brukes. Du vil dersom du ønsker få full innsikt i helseopplysninger som registreres om deg ved å kontakte din lokale kontaktperson ved det sykehuset hvor du følges opp (se nedenfor). Opplysninger som er spesifikke for prosjktet vil bli lagret i prosjektmapper og lagret anonymt på datafiler. Medisinsk informasjon som er en del av rutine undersøkelsen vil bli lagret i din medisinske sykehusjournal og i din prosjektmappe.

Samtykkeerklæring:

Jeg har lest og fått utlevert et eksemplar av denne informasjonen, og i tillegg fått muntlig informasjon om forskningsprosjektet.
Jeg samtykker i å være med i forsøket, og er klar over at mitt samtykke ikke hindrer meg i når som helst å trekke meg fra forsøket uten å måtte oppgi grunn.

Jeg er informert om at alle opplysninger om meg vil behandles konfidensielt av forskningskvalifisert personale under ledelse av prosjektleder. Ved prosjektets slutt vil alle innsamlede opplysninger bli anonymisert. Det vil bli beholdt en navneliste separat som kan kobles til den anonymiserte databasen.
Jeg er informert om at jeg til enhver tid har mulighet til å se dataene som er lagret om meg.

Pasient / forsøksperson: _____

□ Sørlandet Sykehus
□ Revmatismesykehuset i Lillehammer
□ St.Olavs Hospital
□ Martina Hansen
□ Betanien Hospital
□ Andre deltagende sentra:_____

Med vennlig hilsen prosjektleder
professor dr.med Glenn Haugeberg
INM, DMF, NTNU, Trondheim
Overlege ved Revmatologisk avdeling, Sørlandet Sykehus HF

Appendix 8

Addition information to participants

Til deltagere i forskningsprojsektet – Bekhterev i Norge

Tilleggsinformasjon til deltagere i forskningsprosjektet – Bekhterev i Norge

Av NSD (Norsk samfunnsvitenskapelig datatjeneste AS Personvernombud for forskning) er vi gjort oppmerksom på at informasjonsbrevet som du fikk om studien også må inneholde konkret informasjon om hvilken institusjon som er ansvarlig for studien og hvem du skal kontakte dersom du ønsker å trekke deg fra studien. Dette gikk ikke tydelig frem i det informasjonsskrivet som du fikk da du ble med i studien. Denne studien er et sammarbeidsprosjekt mellom revmatologisk avdeling ved Sørlandet sykehus HF og revmatologisk avdeling ved Martina Hansens Hospital, der Sørlandet sykehus HF er databehandlingsansvarlig institusjon

Dersom du ønsker å trekke deg fra studien og også ønsker å få slettet data som er lagret må du kontakte følgende personer nedenfor:

- De som er inkludert i studien fra Sørlandet sykehus HF må kontakte Overlege Glenn Haugeberg (Tlf 38073142).
- De som er inkludert på Martina Hansens Hospital må kontakte Overlege Anne Prøven (Tlf 67521736).

Kontakperson for hele forskningsprosjektet er som tidligere anført i informasjonsskrivet: Professor dr.med. Glenn Haugeberg (Tlf 38073142).

Som du ble informert om har vi ønske om å gjøre en oppfølgingsstudie fem år etter at du ble med i denne studien. Til denne oppfølgingsundersøkelsen vil det bli sent ut en ny invitasjon. Selv om du nå er med i denne studien er det viktig å presisere at det er ingen forpliktelse i å delta senere.

I informasjonsskrivet brukte vi feilaktig begrepet anonymiserte data. Den riktige betegnelsen er avidentifiserte personopplysninger. Forskjellen er at så lenge prosjektet pågår så oppbevares det en koblingsnøkkel mellom persondata (som navn f.dato) og forskningsdatafilene.

Ved prosjektslutt vil datafilene bli anonymisert. Det vil si at koblingsnøkkelen mellom persondata og forskningsdatafilene vil bli slettet.

Prosjektslutt er satt til 01.01.2017.

Med vennlig hilsen

Prosjektleder
Professor dr.med. Glenn Haugeberg

Adresse:
Revmatologisk avdeling
Sørlandet sykehus HF
Serviceboks 416
4632 Kristiansand.S

Appendix 9

Patients` questionnaire

Protokoll - Inflammatorisk ryggsykdom og etablert Bekhterevs sykdom i Norge

Protokoll nr:_____ **Dato for utfylling av spørreskjema**: _____ **Sykehus**:_____

Navn:_____ **F.dato (pnr)**:_____

Adresse:_____

Postnr:_____ **Poststed**:_____ **Kommune**:_____

☐ **KONTROLL GRUPPE "MEKANISK RYGG".**

☐ **Klinisk Mistanke om Bekhterev (IBP): Enten IBP symptomer eller MR IS ledd positiv.**

☐ **Klinisk Bekhterev med røntgen funn tolkett som forenlig med AS.**

☐ **Etablert Bekhterev, d.v.s. oppfyller New York kriteriene.**

☐ **Bekhterevs sykdom – samtidig oppstart biologisk behandling ved inklusjon.**

IS-ledd billeddiagnostikk, rtg funn breskrevet i journalen:

☐ Rtg: Erosjoner J/N, sklerosering J/N
☐ MR: Inflammasjonstegn J/N (ødem J/N, synovitt J/N), Erosjoner J/N
☐ CT: Erosjoner J/N
☐ Skjelettscintigrafi: Sykdomsaktivitetstegn J/N

Kolumna:

☐ MR av kolumna. Inflammasjonstegn J/N

*New-York kriteriene for Bekhterev:

Symptom debut dato	Symptom ved debut	Klinisk diagnosedato	Diagnosedato
		(Mod. NY krit. ikke oppfylt)	(Mod. NY krit.

Modifiserte New York kriterier

Kliniske kriterier:

☐ 1. Karakteristiske lave ryggsmerter og stivhet > 3 mnd (Smerter som lindres ved bevegelse og ikke ved hvile)

☐ 2. Nedsatt bevegelse i nedre del av ryggsøyle i frontal og sideplan

☐ 3. Nedsatt thoraxbevegelse i forhold til normale verdier for samme alder og kjønn

Radiologisk kriterium:

☐ 4. Bilateral sakroilitt grad 2 eller mer ELLER unilateral grad 3 - 4

Sakroilittgradering

0: Normal 1: Mistenkelig (ingen entydig endring)
2: Minimal (minimal sakroilitt, definert ved begynnende uklarhet ved kanten av SI-leddene, noe juxtaartikulær sklerose, små begynnende erosjoner, og mulig leddspaltereduksjon)
3: Moderat (moderat sakroilitt, definert ved entydig sklerose på begge sider, uklare og utydelige kanter, og tydelige erosjoner med tap av leddspalte)
4: Alvorlig (fullstendig fusjon eller ankylose av leddene)

Diagnosegradering

Bekreftet AS hvis kriterium 4 OG minst en av kriteriene 1 - 3 er oppfylt
Sannsynlig AS hvis kriteriene 1, 2 og 3 ELLER bare kriterium 4 er oppfylt

HLA-B27 indikasjon

HLA-B27 tilstede? ○ Ja ○ Nei ◉ Ingen data Dato:

Inflammatorisk rygg plager siste uken:

IBP (inflammatory back pain) kriterier (kryss av):

- **Morgen stivhet:**
  a. Ingen morgenstivhet
  b. < 10 min
  c. 10-30 min
  d. 31-60 min
  e. >60 min
  f. >30 min
- Varighet av morgenstivhet: timer_____ minutter:_____
- **Ryggsmertene bedres ved:**
  a. Hvile
  b. Fysisk aktivitet
  c. Fysisk aktivitet men ikke med hvile
- **Rygg smertene forverres ved:**
  a. Hvile
  b. Fysisk aktivitet
  c. Fysisk aktivitet men ikke med hvile
- **Nattlig oppvåkning p.g.a. ryggsmerter:**
  a. Tidspunkt for oppvåkning om natten:____ Når legger du deg: Når står du opp:____
  b. Våkner når som helst på natten
  c. Bare i første halvdel av natten
  d. Bare i andre halvdel av natten
  e. I begge halvdeler av natten
- **Setesmerter:**
  a. Hatt en eller annen gang
  b. Ensidig
  c. Bilateral
  d. Vekslende
- Var det en forutgående hendelse som du husker før du fikk plagene?:
  a. Traume (ulykke, løfting, bæring etc....)
  b. Infeksjon
  c. Mentalt/emosjonelt stress
- Hvor lang tid tok det fra du fikk plagene og til du kontaktet en doktor: År:___, Måneder:____

Andre fenomener som hyppig ses ved Bekhterev (kryss av):

- Helsmerter (entesitt, akillestendinitt eller plantarfasciitt)
- Dactylitt ("pølsetå/finger")
- God respons på NSAID/COXIB

Demografiske data:

Kjønn: Mann: Kvinne:

Nåværende høyde: _____meter

Høyde som ung: _____ meter

Vekt:_____kg

Livvidde mål: _____ cm **BT**:_____ mmHg **Puls**:_____min

***Sivilstatus**: Enslig, gift/samboer, separert, skilt, enke/enkemann.

***Utdannelse**: <10år, 11-13, >13år,

***Arbeidsstatus:** Jobb :_____%, Sykemeldt: , Uføretrygdet: , Pensjonert:

Røyking: Aldri Røykte tidligere Røyker, Antall sigaretter pr dag:____.

Hvor ofte har du drukket alkohol de siste 30 dagene? Aldri, Ikke mer enn et glass per uke

2-6 glass per uke 7-14 glass per uke 14-21 glass per uke, Mer enn 21 glass per uke

***Noen i familien med Bekhterev sykdom? J/N, usikker, sannsynlig sikker**

Noen i familien med psoriasisleddgikt? J/N, usikker, sannsynlig sikker

Noen i familien med "IBD-relatert leddgikt" J/N, usikker, sannsynlig sikker

Andre revmatiske sykdommer i familien?: _____

Fysisk trening:

>3 timer/uke	o
1-3 timer/uke	o
mindre enn 1 time/uke	o
sjelden eller aldri	o

*Sykdomsaktivitet (selvrapportering) målt med:

*BASDAI (skala 0-10 for hvert spørsmål, 0 ingen problemer/plager)

Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)

I løpet av den siste uken, hvordan vil du beskrive

den generelle graden av utmattelse/tretthet du har erfart?

den generelle graden av smerter i nakke-, rygg eller hofter i forbindelse med Bekhterev sykdom?

det generelle nivået av smerte/hevelse du har hatt i ANDRE LEDD enn nakken-, ryggen eller hoftene?

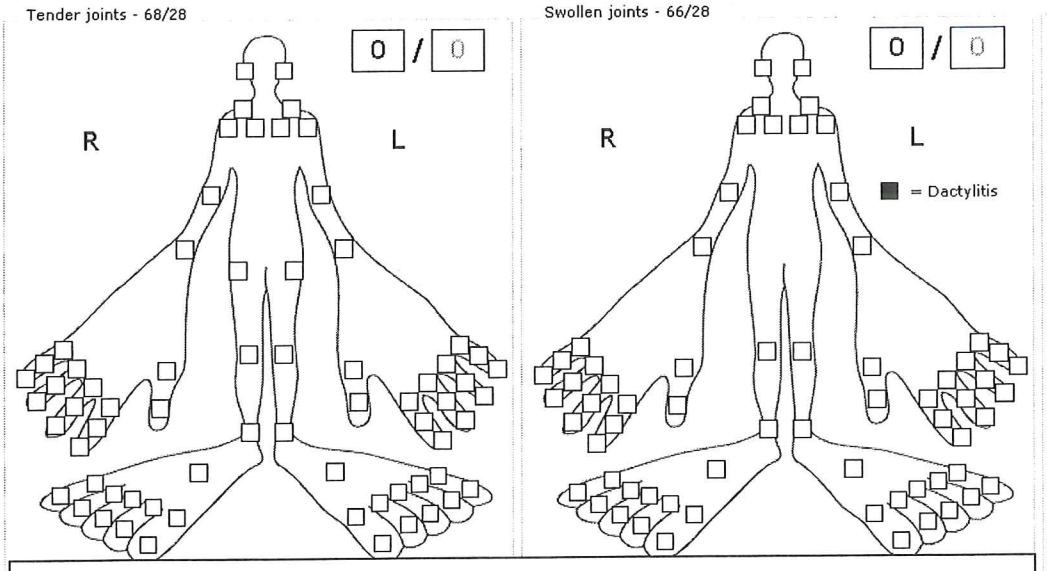
den generelle graden av ubehag du har hatt på eventuelle steder som gjør vondt ved berøring eller trykk?

den generelle graden av stivhet du har opplevd om morgenen fra det tidspunkt du våkner?

Hvor lenge varer morgenstivheten fra det tidspunktet du våkner?

BASDAI verdi:_____ Hentes fra selvrapportering i GTI!

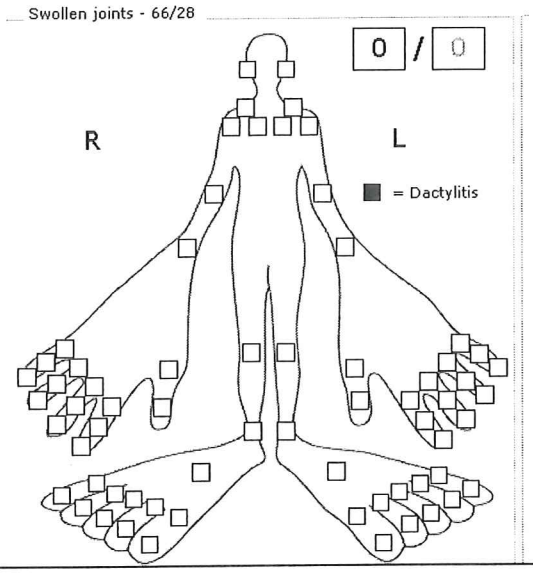
*Ømme og hovne perifere ledd ved aktuell u.s., (utføres av undersøker)



68 ømme ledd:_____ **66 hovne ledd:_____**

NB! registreres i GTI og på arket total sum føres opp!

Hovne perifere ledd (X) eller daktylitt (*) (historisk)?



66 hovne ledd:_____ registreres ikke i GTI kun her!
NB! sett kryss i figuren og merk event daktylitt! Total antall telles og føres opp.

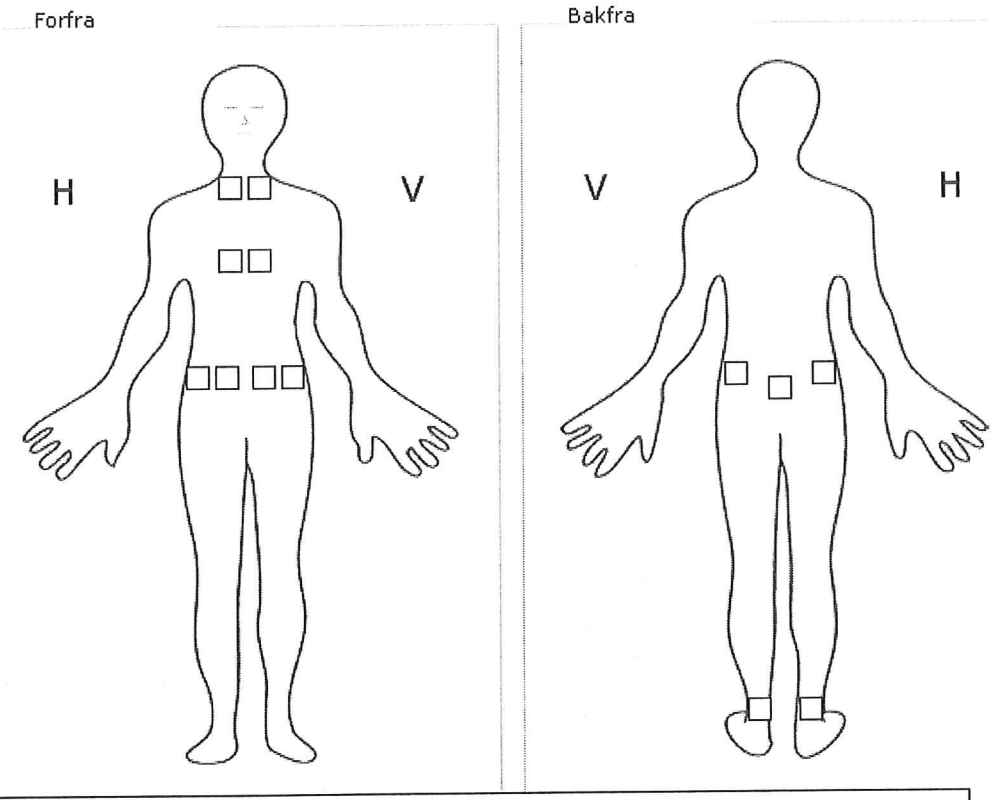
***Blodprøver:**
Følgende blodprøver tas også:

SR
CRP
Kolesterol
LDL
HDL
Triglyserider
HbA1C

BT systolisk
BT diastolisk

HLA-B27 (dersom det ikke er tatt!)

***Smerte i senefester (utføres av undersøker)**



Hjelpetekst kommer opp på GTI om du holder markør over u.s. stedet!
NB! registreres i GTI og på arket total sum føres opp!

Totalsum (0-13):_____

*Helsestatus (selvrapportering)

*Spørreskjema (HAQ, illustrasjon her er MHAQ)

I løpet av den siste uken, kunne du...	Uten problemer (0)	Med visse problemer (1)	Med store problemer (2)	Kunne ikke (3)
kle på deg selv, inkl. å knytte skolisser og å kneppe knapper?				
vaske håret?				
reise deg fra en stol m/rett rygg uten armlener?				
komme opp i og ut av sengen?				
skjære opp kjøtt?				
løfte en full kopp eller et fullt glass til munnen?				
åpne en ny melkekartong?				
gå utendørs på flat mark?				
gå opp 5 trappetrinn?				

HAQ verdi:_____ Hentes fra selvrapportering i GTI!

*Spørreskjema selvrapportering (skala 0-10 for hvert spørsmål, 0 ingen problemer/plager)

(BASFI)

BASFI Bath Ankylosing Spondylitis Functional Index

Siste uke hvordan klarte du å...

ta på strømper eller strømpebukser uten assistanse eller ved bruk av hjelpemiddel (for eksempel strømpe påtrekker)?

bøye deg forover fra midjen for å plukke opp en penn fra gulvet uten å bruke et hjelpemiddel?

nå opp til en høythengende hylle uten bruk av hjelpemidler (for eksempel gripetang)?

reise deg fra en spisebordsstol uten armlener eller annen hjelp?

reise deg opp fra liggende stilling på gulvet uten hjelp?

stå oppreist uten støtte i 10 min. uten å få ubehag?

gå opp 12-15 trappetrinn uten å bruke rekkverk eller gåstøtte (en fot på hvert trinn)?

se deg over skulderen uten å vri kroppen?

utføre fysisk krevende aktiviteter (for eksempel fysioterapiøvelser, hagearbeid eller sport)?

utføre en hel dags aktiviteter enten hjemme eller på arbeid?

BASFI verdi:_____
Hentes fra selvrapportering i GTI!

BAS-G Bath Ankylosing Spondylitis Global

Hvilken innvirkning har sykdommen hatt på ditt velbefinnende den siste uken?

Hvilken innvirkning har sykdommen hatt på ditt velbefinnen
månedene?

BAS-G verdi:_____
Hentes fra selvrapportering i GTI!

*Skade på skjelettet

***Funksjonsmål undersøkelse (trenet helsepersonell, registreres i GTI og her):**

Bath Ankylosing Spondylitis Metrology Index (BASMI)

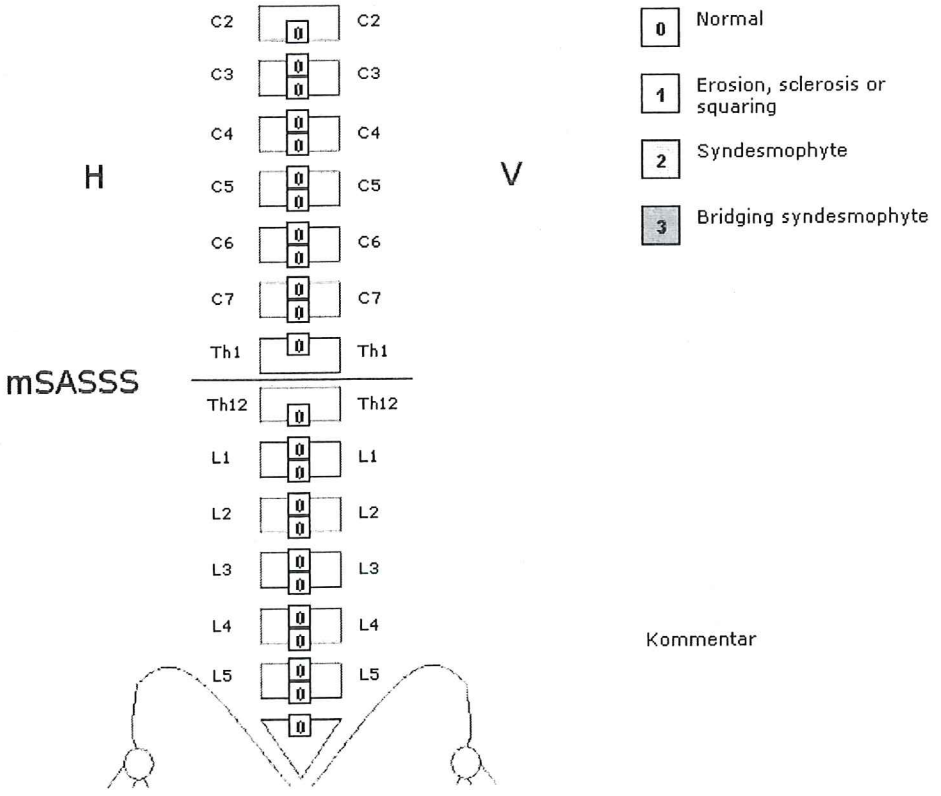
Cervical rotasjon:	°
Tragus (øregang) til vegg:	cm
Lumbal fleksjon (modifisert Schober's):	cm
Lumbal sidebøy:	cm
Intermalleolær avstand:	cm

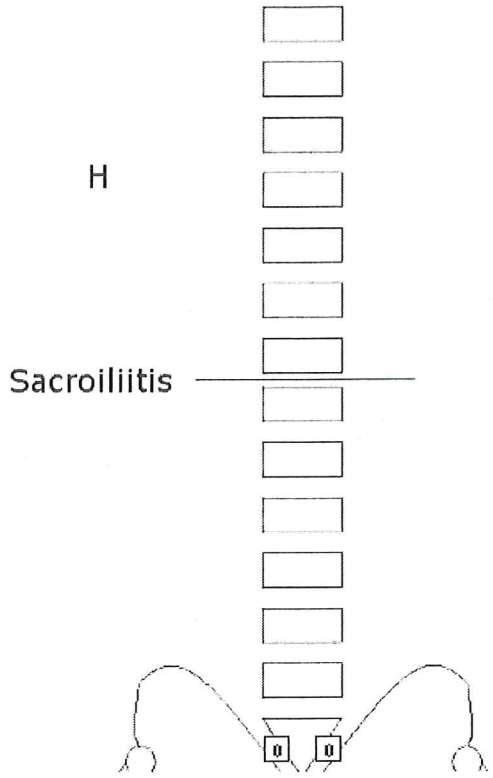
BASMI verdi:_____
Hentes fra selvrapportering i GTI!

Spinal mobilitet

Brystkasseutvidelse	Bakhode-til-vegg avstand	Schober's test
cm	cm	cm

***Rtg undersøkelse av ryggsøyle (cervical, thoracal lumbal i sideplan) og ileosakralledd**





0 Normal

1 Suspicious (no definite change)

2 Minimal (minimal sacroiliitis, defined as the loss of definition at the edge of the SI joints, some juxtaarticular sclerosis, minimal erosions, and possible joint space narrowing)

3 Moderate (moderate sacroiliitis, defined as definite sclerosis on both sides, blurring and indistinct margins, and erosive changes, with loss of joint space)

4 Severe (complete fusion or ankylosis of the joints)

Kommentar

*Andre manifestasjoner (regsitreres både her og i GTI):

Hvor mange ganger hatt uveitt/iridocyklitt:_____ Subjektivt visustap: J/N

Tilstedeværelse

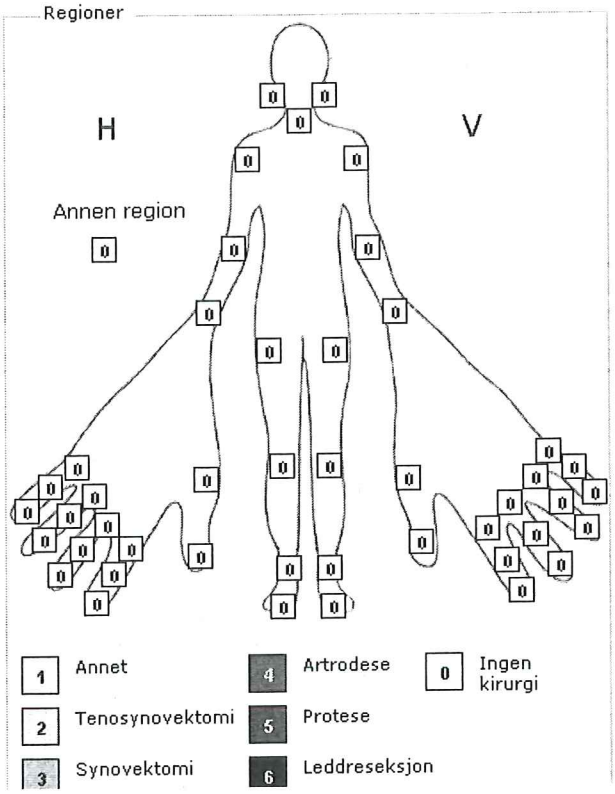
Ikke tilstede/ undersøkt 0

Mulig tilstede 1

Sikkert tilstede 2

Ak		Andre manifestasjoner	Kommentarer
0	0	Akutt fremre uveitt/iridocyclitt	
0	0	Aortitt/aortaklaffe insuffisiens	
0	0	Hjerterytmeforstyrrelse	
0	0	Inflammat. tarmsykdom (IBD)	
0	0	Psoriasis	
0	0	Lungefibrose/alveolitt	
0	0	Sekundær amyloidose	
0	0	Annet	

*Kirurgi status (regsitreres både her og i GTI)



Hvilke behandling har du fått for sykdommen (Oppdater også GTI!):

NSAID: Oppstart:_____ COXIB: Oppstart:_____ DMARD: Oppstart:_____

Biologiske medikamenter: Oppstart:_____ Omega-3 fettsyrer:

Paracet: Opiater: Fysioterapi: Egentrening: Varmtvannsbasseng trening:

Organisert gruppe fysioterapi i Norge: Behandlingsreiser i utlandet: Kiropraktikk:

Manuell terapi: Akupunktur: Homeopati: Annet: _____

Har du tilfredsstillende behandlingseffekt av NSAID/COXIB og eller fysioterapi: J/N

Synes du at du trenger bedre symptomlindrende effekt av behandlingen?: J/N

Hvor god symptomlindring gir NSAID/COXIB (0=ingen lindring, 10 komplett symptomlindring):__

Hvor god symptomlindring gir fysioterapi (0=ingen lindring, 10 komplett symptomlindring):__

Har du brukt eller bruker du noen av disse andre medikamentene:

o Folsyre oppstart:_____
o ACE hemmere oppstart:_____
o Statiner oppstart:_____
o Acetylsalicylsyre oppstart:_____
o Betablokker oppstart:_____
o Østrogener oppstart:_____

Hvilke medisiner har du brukt siste 10 dager?: _____

_____

_____

Annen sykdom (Komorbiditet, Oppdater også i GTI)

Angi hvilke av sykdommene nedenfor du har:

Hjertekarsykdom: Angina pectoris/bryst smerter: Diagnose når?:_____
Hjerteinfarkt: Antall:_____ Når:_____
Hjertesvikt
Arteriell hypertensjon: Når ble diagnosen stilt_____
Hyperkolesterolemi eller behandling for hyperkolesterolemi
Hjerteoperert, Dersom ja når (år):_____
Type operasjon:
Aortokoronar bypass, evt. antall operasjoner _____
PTCA/ Stenting, evt. antall ganger _____
Hjerteklaffoperasjon
Annet: :_____

Har du arvelighet for hjertekarsykdom? Angina pectoris, hjerteinfarkt eller akutt hjertedød hos

Kvinnelige 1. gradsslektninger <65 år
Mannlige 1. gradsslektninger < 50 år

Lungesykdom: Astma, KOLS, Annet:_____

Nevr. sykdom: Hjerneslag: Antall:_____ Når:_____
MS
Parkinson
Epilepsi
Annet:

Endokrin sykdom:
Stoffskiftesykdom: hypotyreose, hypertyreose
Diabetes mellitus: Når ble diagnosen stilt_____
Bruker insulin: ja o nei o

Hyperparathyreodisme
Annet:

Hemat. sykdom:_____

GI sykdommer:

Ulcus sykdom:
ulcus ventriculi, ulcus duodeni, ulcus duodeni og ventriculi
Inflamatorisk tarmsykdom: Mb.Crohn, Ulcerøs colitt)
Refluks sykdom
Annet:

Urogen sykdom: Nyresykdom, Annet: _____

Revm. sykdom: Inflam.leddsykdom:
RA, Bechterev, Psoriasis, Reaktiv, IBD, udiff.spondyl.
Andre: Collagenose Fibromylagi Urinsyregikt Artrose Annet ____

Kreftsykdom:
Første kreftdiagnose
Andre kreftdiagnose
Tredje kreftdiagnose

Mental lidelse:
Depresjon Manisk-depresiv Schizofreni Demens
Psyk. Utviklingshemmet
Annet:

Annet:
Alkoholisme
Synshemmet

Transplantasjon: _____

Osteoporose:

Arv

Har din mor hatt brudd etter 45-årsalderen? Ja Nei Ikke opplyst

Har din far hatt brudd etter 40-årsaldereren? Ja Nei Ikke opplyst

Hvor mange søsken har du? Antall: _____

Har en eller flere av dine søsken hatt brudd etter 40-årsalderen? Ja Nei Ikke opplyst

(Andre forhold?)

Spørsmål om kost

Hvor mye melk drikker du?:

Mer enn 0,5 liter daglig Mindre enn 0,5 liter daglig Sjeldent eller aldri

Ikke opplyst

Hvor ofte spiser du ost (antall høvlede osteskiver):

mer enn 3 skiver daglig , mindre enn 3 skiver daglig , sjeldent eller aldri □□, Ikke opplyst

Tar du vitamintilskudd Ja Nei Ikke opplyst

Tar du kalk Ja Nei Ikke opplyst □

Tar du D-vitaminer Ja Nei Ikke opplyst

Hormoner (Kun for kvinner)

Hvor gammel var du da du fikk din første menstruasjon? _____ år

Har du hatt uregelmessig menstruasjon? (manglende menstruasjon i lengre enn 3 måneder utenom graviditet) Ja Nei

Har du gjennomgått underlivsoperasjon? Ja □ Nei □

- I hvilken alder? _____ år

- Ble eggstokkene fjernet? Ja □ Nei □□□□□ vet ikke□□□□

Har du passert overgangsalderen? Ja, >6 måneder □ Ja, >12 måneder □□

□□□□□□Nei □□□□□□

□□Usikker□□

- Ved hvilken alder? _____ år

Har du tidligere hatt lavenergi brudd? Ja □ Nei □

Hva brakk du? Brudd 1:_____Alder:_____Brudd 2:_____Alder:_____

Brudd 3:_____Alder:_____Brudd 4:_____Alder:_____

Fall anamnese:
Antall fall siste år: □ Ingen, □ 1-3, □ 4 eller mer
Antall fall:_____

DEXA BMD målinger (Dato for u.s.:_____)

Lumbal kolumna (L2-4): _____g/cm2.T-score :_____ Z-score :_____
Lumbal kolumna (L1-4): _____g/cm2.T-score :_____ Z-score :_____
Venstre total hofte: _____g/cm2.T-score :_____ Z-score :_____
Høyre total hofte: _____g/cm2.T-score :_____ Z-score :_____

Rtg av ryggsøyle tatt □ (skores etter Genants semikvantitative metode)

Steroidebehandling

Har du brukt/bruker du steroider (mer enn 3 måneder):

Aldri Tidligere Nåværende Brukt siste året

Hvor lenge har du brukt Prednisolon? _____måneder

Høyeste dose som er brukt: _____mg

Vedlikeholdsdose:_____mg

Bruk av helsetjenester, ressurser:

Spørsmål knyttet blant annet til bosted og behov for helsetjenester:

Bosted siste året: Enebolig, Leilighet, Aldersbolig, Sykehjem, Pleie og omsorgs institusjon. Beskriv:_____

Bolig med: Trapper Heis

Hjelpebehov siste året (Helse ressursbruk):

Opphold i rehab. eller opptreningsinstitusjon: J / N, dager:_____

Almennpraktiserende lege: J / N: antall ganger:_____

Annen spesialist: J / N: antall ganger:_____Hvem:_____

Sykepleier på legekontor: J / N: antall ganger:_____

Fysioterapeut: J / N: antall enkelt behandlinger:_____

Ergoterapeut: J / N: antall enkelt ganger:_____

Sosionom: J / N: antall ganger:_____

Bassengtrening: J / N: antall enkelt ganger:_____

Trygghetsalarm: J / N

Sykehusinnleggelse siste år (telles ikke aktuell): J / N: ganger:____dager:____

Sykehjemsopphold siste år: J / N: antall dager:_____

Annen rehabiliterings institusjon J / N: antall dager:_____

Dagsenter: J / N: antall ganger pr uke :_____

Matombringing: J / N: antall ganger pr uke :_____

Blodprøver i løpet av siste år: J / N: antall:_____

Hjemmehjelp siste år: J / N: antall ganger pr uke :_____timer pr uke:_____

Hjemmesykepleier siste år: J / N: antall ganger pr uke :____timer pr uke:____

Hjelp av pårørende: J / N, Til hva:?_____

QUALITY OF LIFE

New 15D/Harri Sintonen

Pasient spørreskjema

Vennligst les gjennom alle svaralternativene til hvert spørsmål før du plasserer et kryss (x) for det alternativet som best beskriver din nåværende tilstand. Fortsett på samme måte for alle 15 spørsmålene. Gi bare ett svar på hvert spørsmål.

SPØRSMÅL 1. **BEVEGELIGHET**

1 ( ) Jeg er i stand til å gå normalt (uten vanskelighet) innendørs, utendørs og i trapper
2 ( ) Jeg er i stand til å gå uten vanskelighet innendørs, men utendørs og/eller i trapper har jeg litt problemer.
3 ( ) Jeg er i stand til å gå uten hjelp innendørs (med eller uten et hjelpemiddel), men utendørs og/eller i trapper bare med betydelig vanskelighet eller med hjelp fra andre.
4 ( ) Jeg er i stand til å gå innendørs kun med hjelp fra andre.
5 ( ) Jeg er fullstendig sengeliggende og ute av stand til å bevege meg omkring.

SPØRSMÅL 2. **SYN**

1 ( ) Jeg ser normalt, dvs. jeg kan lese aviser og tekst på TV uten vanskelighet (med eller uten briller).
2 ( ) Jeg kan lese aviser og/eller tekst på TV med litt vansker (med eller uten briller).
3 ( ) Jeg kan lese aviser og/eller tekst på TV med betydelige vansker (med eller uten briller).
4 ( ) Jeg kan ikke lese aviser eller tekst på TV hverken med briller eller uten, men jeg kan se godt nok til å gå omkring uten hjelp.
5 ( ) Jeg kan ikke se godt nok til å gå omkring uten en hjelper, dvs. jeg er nesten eller helt blind.

SPØRSMÅL 3. **HØRSEL**

1 ( ) Jeg hører normalt, dvs. normal tale (med eller uten et høreapparat).
2 ( ) Jeg hører normal tale med litt vansker.
3 ( ) Jeg hører normal tale med betydelige vansker; i samtaler må stemmer være høyere enn normalt.
4 ( ) Jeg hører selv sterke stemmer dårlig; jeg er nesten døv.
5 ( ) Jeg er helt døv.

SPØRSMÅL 4. **PUST**

1 ( ) Jeg er i stand til å puste normalt, dvs. uten å være kortpustet eller ha andre pustevansker.
2 ( ) Jeg er kortpustet under tungt arbeid eller sport, eller når jeg går raskt på flat mark eller i slak motbakke.
3 ( ) Jeg er kortpustet når jeg går på flat mark med samme tempo som andre på min alder.
4 ( ) Jeg blir kortpustet selv etter lett aktivitet, f.eks. når jeg vasker meg eller kler på meg.
5 ( ) Jeg har pustevansker nesten hele tiden, selv i hvile.

SPØRSMÅL 5. **SØVN**

1 ( ) Jeg er i stand til å sove normalt, dvs. jeg har ingen problemer med å sove.
2 ( ) Jeg har lette søvnproblemer, f.eks. vanskelig for å falle i søvn eller våkner av og til om natte
3 ( ) Jeg har moderate søvnproblemer, f.eks. forstyrret søvn eller føler jeg ikke har sovet nok.
4 ( ) Jeg har store søvnproblemer, f.eks. må bruke sovemedisiner ofte eller rutinemessig, eller våkner om natten og/eller for tidlig om morgenen.
5 ( ) Jeg lider av alvorlig søvnløshet, f.eks. er søvn nesten umulig selv med bruk av sovemedisiner, eller jeg forblir våken det meste av natten.

SPØRSMÅL 6. **SPISING**

1 ( ) Jeg er i stand til å spise normalt, dvs. uten hjelp fra andre.
2 ( ) Jeg er i stand til å spise selv med mindre vansker (f.eks. langsomt, kløhete, skjelvende, eller med spesielle hjelpemidler).
3 ( ) Jeg trenger noe hjelp fra en annen person for å spise.
4 ( ) Jeg er ute av stand til å spise selv i det hele tatt, slik at jeg må mates av en annen person.
5 ( ) Jeg er ute av stand til å spise i det hele tatt, slik at jeg mates enten med slange eller intravenøst.

SPØRSMÅL 7. **TALE**

1 ( ) Jeg er i stand til å snakke normalt, dvs. klart, hørbart og flytende.
2 ( ) Jeg har lette vansker med å snakke, f.eks. famler av og til etter ord, mumler eller endrer stemmeleiet.
3 ( ) Jeg kan gjøre meg forstått, men min tale er f.eks. oppstykket, nølende, stotrende eller stammende.
4 ( ) De fleste mennesker har store vansker med å forstå hva jeg sier.
5 ( ) Jeg kan bare gjøre meg forstått med fakter.

SPØRSMÅL 8. **VANNLATING/AVFØRING**

1 ( ) Min blære og tarm fungerer normalt og uten problemer.
2 ( ) Jeg har lette problemer med min blære- og/eller tarmfunksjon, f.eks. vansker med å urinere, eller løs eller hard avføring.
3 ( ) Jeg har betydelige problemer med min blære- og/eller tarmfunksjon, f.eks. "uhell" av og til, eller alvorlig forstoppelse eller diaré.
4 ( ) Jeg har alvorlige problemer med min blære- og/eller tarmfunksjon, f.eks. regelmessig "uhell", eller behov for kateterisering eller klyster.
5 ( ) Jeg har ikke kontroll over min blære- og/eller tarmfunksjon.

SPØRSMÅL 9. **VANLIGE AKTIVITETER**

1 ( ) Jeg er i stand til å utføre mine vanlige aktiviteter (f.eks. arbeid, studier, husarbeid, fritidsaktiviteter) uten vanskelighet.
2 ( ) Jeg er i stand til å utføre mine vanlige aktiviteter noe mindre effektivt eller med litt vanskelighet.
3 ( ) Jeg er i stand til å utføre mine vanlige aktiviteter mye mindre effektivt, med betydelig vanskelighet, eller ikke fullt ut.
4 ( ) Jeg kan bare klare en liten del av mine vanlige aktiviteter fra tidligere.
5 ( ) Jeg er ute av stand til å klare noen av mine vanlige aktiviteter fra tidligere.

SPØRSMÅL 10. **MENTAL FUNKSJON**

1 ( ) Jeg er i stand til å tenke klart og logisk, min hukommelse fungerer godt.
2 ( ) Jeg har litt vansker med å tenke klart og logisk, min hukommelse svikter meg av og til.
3 ( ) Jeg har merkbare vansker med å tenke klart og logisk, min hukommelse er noe redusert.
4 ( ) Jeg har store vansker med å tenke klart og logisk, min hukommelse er betydelig nedsatt.
5 ( ) Jeg er stadig forvirret og desorientert for sted og tid.

SPØRSMÅL 11. **UBEHAG OG SYMPTOMER**

1 ( ) Jeg har ikke fysisk ubehag eller plager, f.eks. smerte, verk, kvalme, kløe etc.
2 ( ) Jeg har lett fysisk ubehag eller plager, f.eks. smerte, verk, kvalme, kløe etc.
3 ( ) Jeg har tydelig fysisk ubehag eller plager, f.eks. smerte, verk, kvalme, kløe etc.
4 ( ) Jeg har alvorlig fysisk ubehag eller plager, f.eks. smerte, verk, kvalme, kløe etc.
5 ( ) Jeg har uholdbart fysisk ubehag eller plager, f.eks. smerte, verk, kvalme, kløe etc.

SPØRSMÅL 12. **DEPRESJON**

1 ( ) Jeg føler meg overhodet ikke trist, melankolsk eller deprimert.
2 ( ) Jeg føler meg litt trist, melankolsk eller deprimert.
3 ( ) Jeg føler meg middels trist, melankolsk eller deprimert.
4 ( ) Jeg føler meg svært trist, melankolsk eller deprimert.
5 ( ) Jeg føler meg ekstremt trist, melankolsk eller deprimert.

SPØRSMÅL 13. **STRESS**

1 ( ) Jeg føler meg overhodet ikke engstelig, stresset eller nervøs.
2 ( ) Jeg føler meg litt engstelig, stresset eller nervøs.
3 ( ) Jeg føler meg middels engstelig, stresset eller nervøs.
4 ( ) Jeg føler meg svært engstelig, stresset eller nervøs.
5 ( ) Jeg føler meg ekstremt engstelig, stresset eller nervøs.

SPØRSMÅL 14. **LIVSKRAFT**

1 ( ) Jeg føler meg frisk og energisk.
2 ( ) Jeg føler meg litt sliten, trett eller svak.
3 ( ) Jeg føler meg middels sliten, trett eller svak.
4 ( ) Jeg føler meg svært sliten, trett eller svak, nesten utslitt.
5 ( ) Jeg føler meg ekstremt sliten, trett eller svak, totalt utslitt.

SPØRSMÅL 15. **SEKSUELL AKTIVITET**

1 ( ) Min helsetilstand har ingen ugunstig virkning på min seksuelle aktivitet.
2 ( ) Min helsetilstand har en liten virkning på min seksuelle aktivitet.
3 ( ) Min helsetilstand har en betydelig virkning på min seksuelle aktivitet.
4 ( ) Min helsetilstand gjør seksuell aktivitet nesten umulig
5 ( ) Min helsetilstand gjør seksuell aktivitet umulig.

SF-36 SPØRRESKJEMA OM HELSE

INSTRUKSJON: Dette spørreskjemaet spør om hvordan du ser på din egen helse. Disse opplysningene vil hjelpe oss til å få vite hvordan du har det og hvordan du er i stand til å utføre dine daglige gjøremål.

Hvert spørsmål skal besvares ved å krysse av det alternativet som passer best for deg. Hvis du er usikker på hva du skal svare, vennligst svar så godt du kan.

1 Stort sett, vil du si helsen din er:

(Kryss av ett alternativ)
1 ☐ Utmerket
2 ☐ Meget god
3 ☐ God
4 ☐ Ganske god
5 ☐ Dårlig

2 Sammenlignet med for ett år siden, hvordan vil du si helsen din stort sett er nå?

(Kryss av ett alternativ)
1 ☐ Mye bedre nå enn for ett år siden
2 ☐ Litt bedre nå enn for ett år siden
3 ☐ Omtrent den samme som for ett år siden
4 ☐ Litt dårligere nå enn for ett år siden
5 ☐ Mye dårligere nå enn for ett år siden

3 De neste spørsmålene handler om aktiviteter som du kanskje utfører i løpet av en vanlig dag. Er helsen din slik at den begrenser deg i utførelsen av disse aktivitetene nå? Hvis ja, hvor mye?

	(Kryss av ett alternativ på hver linje) Ja, begrenser meg mye	Ja, begrenser meg litt	Nei, begrenser meg ikke i det hele tatt
a. Anstrengende aktiviteter som å løpe, løfte tunge gjenstander, delta i anstrengende idrett	1 ☐	2 ☐	3 ☐
b. Moderate aktiviteter som å flytte et bord, støvsuge, gå tur eller drive med hagearbeid	1 ☐	2 ☐	3 ☐
c. Løfte eller bære en handlekurv	1 ☐	2 ☐	3 ☐
d. Gå opp trappen flere etasjer	1 ☐	2 ☐	3 ☐
e. Gå opp trappen en etasje	1 ☐	2 ☐	3 ☐
f. Bøye deg eller sitte på huk	1 ☐	2 ☐	3 ☐
g. Gå mer enn to kilometer	1 ☐	2 ☐	3 ☐
h. Gå noen hundre meter	1 ☐	2 ☐	3 ☐
i. Gå hundre meter	1 ☐	2 ☐	3 ☐
j. Vaske deg eller kle på deg	1 ☐	2 ☐	3 ☐

4 I løpet av de siste 4 ukene, har du hatt noen av følgende problemer i ditt arbeid eller i andre av dine daglige gjøremål på grunn av din fysiske helse?

	(Kryss av ett alternativ på hver linje) JA	NEI
a. Har du redusert tiden du har brukt på arbeidet ditt eller andre aktiviteter	1 ☐	0 ☐
b. Har du utrettet mindre enn du hadde ønsket	1 ☐	0 ☐
c. Har du vært hindret i visse typer arbeid eller andre aktiviteter	1 ☐	0 ☐
d. Har du hatt vanskeligheter med å utføre arbeidet ditt eller andre aktiviteter (f.eks. fordi det krevde ekstra anstrengelser)	1 ☐	0 ☐

5 I løpet av de siste 4 ukene, har du hatt noen av følgende problemer i ditt arbeid eller i andre av dine daglige gjøremål på grunn av følelsesmessige problemer (f.eks. fordi du har følt deg deprimert eller engstelig)?

	(Kryss av ett alternativ på hver linje) JA	NEI
a. Har du redusert tiden du har brukt på arbeidet ditt eller andre aktiviteter	1 ☐	0 ☐
b. Har du utrettet mindre enn du hadde ønsket	1 ☐	0 ☐
c. Har ikke arbeidet eller utført andre aktiviteter like nøye som vanlig	1 ☐	0 ☐

6 I løpet av de siste 4 ukene, i hvilken grad har din fysiske helse eller følelsesmessige problemer hatt innvirkning på din vanlige sosiale omgang med familie, venner, naboer eller foreninger?

(Kryss av ett alternativ)
1 ☐ Ikke i det hele tatt
2 ☐ Litt
3 ☐ En del
4 ☐ Mye
5 ☐ Svært mye

7 Hvor sterke kroppslige smerter har du hatt i løpet av de siste 4 ukene?

(Kryss av ett alternativ)
1 ☐ Ingen
2 ☐ Meget svake
3 ☐ Svake
4 ☐ Moderate
5 ☐ Sterke
6 ☐ Meget sterke

8 I løpet av de siste 4 ukene, hvor mye har smerter påvirket ditt vanlige arbeid (gjelder både arbeid utenfor hjemmet og husarbeid)?

(Kryss av ett alternativ)
1 ☐ Ikke i det hele tatt
2 ☐ Litt
3 ☐ En del
4 ☐ Mye
5 ☐ Svært mye

9 De neste spørsmålene handler om hvordan du har følt deg og hvordan du har hatt det de siste 4 ukene. For hvert spørsmål, vennligst velg det svaralternativet som best beskriver hvordan du har hatt det. Hvor ofte i løpet av de siste 4 ukene har du:

(Kryss av ett alternativ på hver linje)

	Hele tiden	Nes-ten hele tiden	Mye av tiden	En del av tiden	Litt av tiden	Ikke i det hele tatt
a. Følt deg full av tiltakslyst?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐
b. Følt deg veldig nervøs?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐
c. Vært så langt nede at ingenting har kunnet muntre deg opp?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐
d. Følt deg rolig og harmonisk?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐
e. Hatt mye overskudd?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐
f. Følt deg nedfor og trist?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐
g. Følt deg sliten?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐
h. Følt deg glad?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐
i. Følt deg trett?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐

10 I løpet av de siste 4 ukene, hvor mye av tiden har din fysiske helse eller følelsesmessige problemer påvirket din sosiale omgang (som det å besøke venner, slektninger osv.)?

(Kryss av ett alternativ)
1 ☐ Hele tiden
2 ☐ Nesten hele tiden
3 ☐ En del av tiden
4 ☐ Litt av tiden
5 ☐ Ikke i det hele tatt

11 Hvor RIKTIG eller GAL er hver av de følgende påstander for deg?

(Kryss av ett alternativ på hver linje)

Påstander om din helse	Helt riktig	Delvis riktig	Vet ikke	Delvis gal	Helt gal
a. Det virker som om jeg blir lettere syk enn andre	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
b. Jeg er like frisk som de fleste jeg kjenner	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
c. Jeg forventer at helsen min vil bli dårligere	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
d. Helsen min er utmerket	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐

Spørsmål om seksualitet

Alle svarene dine vil bli behandlet strengt konfidensielt!

Hvor viktig eller uviktig er det å ha sex/seksualitet for at du skal være fornøyd med den daglige tilværelsen?

□ Meget viktig
□ Ganske viktig
□ Mindre viktig
□ Uten betydning

Har du større eller mindre glede av seksuallivet ditt nå enn tidligere, eller har du like stor glede av det?

□ Større
□ Mindre
□ Like stor glede
□ Tvil/vet ikke

Har du partner som du har sex med?

□ Nei □ Ja

Dersom du svarte Nei på spørsmålet "Har du partner som du har sex med?" vær så snill å svare på følgende spørsmål:
Jeg er ikke seksuelt aktiv for tiden av følgende grunner:
(sett kryss ved så mange svar som passer for deg)

□ Jeg har ingen partner for tiden
□ Jeg er for trett
□ Min partner er for trett
□ Jer er ikke interessert i sex
□ Min partner er ikke interessert i sex
□ Jeg har et fysisk problem som gjør seksuelle forhold vanskelig eller ubehagelig
□ Min partner har et fysisk problem som gjør seksuelle forhold vanskelig eller ubehagelig
□ Andre grunner

Dersom du svarte Ja på spørsmålet "Har du partner som du har sex med?" vær så snill å svare på følgende spørsmål:
Hvem tar vanligvis initiativet til og starter når du har seksuell kontakt/samleie?

□ Alltid jeg som gjør det
□ Som regel jeg
□ Like ofte jeg og den andre
□ Som regel den andre
□ Alltid den andre

Svar vennligst videre på spørsmålene nedenfor

Hvor mange ganger har du hatt seksuell kontakt/samleie de siste 4 uker?

□ Ingen ganger
□ 1 gang
□ 2-4 ganger
□ 5-10 ganger
□ 11 ganger eller flere

Synes du at du har seksuell kontakt samleie for ofte, passe eller for sjelden

□ For ofte
□ Passe
□ For sjelden

Alt i alt – hvor fornøyd er du med ditt seksualliv ?

□ Veldig fornøyd
□ Ganske fornøyd
□ Verken fornøyd eller misfornøyd
□ Litt misfornøyd
□ Misfornøyd

Hvor fornøyd er du med ditt seksualliv i dag med hvordan det var for fem år siden, er det da

□ Mye bedre
□ Noe bedre
□ Uforandret
□ Noe dårligere
□ Mye dårligere

Har du noen gang hatt seksuelle problemer som du har trengt hjelp til å løse **?**

□ Nei
□ Ja

Hva slags seksuelle problemer var det ? ***(sett så mange kryss du trenger)***

□ Manglende/lite lyst
□ Ogasmeproblemer
□ For tidlig utløsning
□ For sen utløsning
□ Smerter ved samleie
□ Reisnings-/potensproblemer
□ Tørrhet i skjeden
□ Følte med seksuelt avvikende
□ Manglende/liten seksuell interesse
□ Følelse av ikke å være attraktiv
□ Annet

Har du hatt noen av disse samme problemer den siste måneden, i så fall hvilke? ***(sett så mange kryss du trenger)***

□ Ingen problemer
□ Manglende/lite lyst
□ Orgasmeproblemer
□ For tidlig utløsning
□ For sen utløsning
□ Smerter ved samleie
□ Reisnings-/potensproblemer
□ Tørrhet i skjeden
□ Følte meg seksuelt avvikende
□ Manglende/liten seksuell interesse
□ Følelse av ikke å være attraktiv
□ Annet

Dersom du har/har hatt noen av problemene nevnt ovenfor, i hvilken grad vil du knytte dem til den sykdommen/tilstanden du har?

□ I meget stor grad
□ I noen grad
□ Ikke i det hele tatt.

Dersom du har/har hatt seksuelle problemer knyttet til sykdommen/tilstanden, skyldes de noe av det følgende (sett så mange kryss du trenger).

□ Tretthet
□ Stivhet
□ Smerter
□ Endring av kroppen
□ Endring i hvordan jeg føler andre oppfatter meg.
□ Bivirkning av medikamenter.

Spørreskjema om seksuell livskvalitet
(SQoL-F)

Dette spørreskjemaet består av en rekke utsagn som alle dreier seg om tanker og følelser som du kan ha om ditt seksualliv. Utsagnet kan dreie seg om enten positive eller negative sider ved seksuallivet ditt.

Du bes om å vurdere hvert utsagn etter hvor enig eller uenig du er i det ved å sette en ring rundt ett av seks svaralternativer.

Ved vurderingen av disse utsagnene, gjelder de følgende definisjoner:

Seksualliv: er både fysiske seksuelle aktiviteter og det følelsesmessige seksuelle forhold du har til din partner.

Seksuell aktivitet: omfatter enhver aktivitet som kan føre til seksuell stimulering eller seksuell nytelse, for eksempel samleie, kjærtegn, forspill, masturbasjon (dvs. at du selv masturberer eller at partneren masturberer deg) og munnsex (dvs. at din partner stimulerer dine kjønnsorganer med munnen).

Vanligvis er det første svaret som faller deg inn også det beste, så ikke bruk for lang tid på hvert spørsmål.

1. Når jeg tenker på seksuallivet mitt, er det en del av livet mitt generelt sett som jeg har glede av	*helt enig*	*ganske enig*	*litt enig*	*litt uenig*	*ganske uenig*	*helt uenig*
2. Når jeg tenker på seksuallivet mitt, føler jeg meg frustrert	*helt enig*	*ganske enig*	*litt enig*	*litt uenig*	*ganske uenig*	*helt uenig*
3. Når jeg tenker på seksuallivet mitt, føler jeg meg nedtrykt	*helt enig*	*ganske enig*	*litt enig*	*litt uenig*	*ganske uenig*	*helt uenig*
4. Når jeg tenker på seksuallivet mitt, føler jeg meg mindre verd som kvinne/mann	*helt enig*	*ganske enig*	*litt enig*	*litt uenig*	*ganske uenig*	*helt uenig*
5. Når jeg tenker på seksuallivet mitt, føler jeg meg fornøyd	*helt enig*	*ganske enig*	*litt enig*	*litt uenig*	*ganske uenig*	*helt uenig*
6. Jeg har mistet tiltroen til meg selv som en seksualpartner	*helt enig*	*ganske enig*	*litt enig*	*litt uenig*	*ganske uenig*	*helt uenig*
7. Når jeg tenker på seksuallivet mitt, føler jeg meg engstelig	*helt enig*	*ganske enig*	*litt enig*	*litt uenig*	*ganske uenig*	*helt uenig*
8. Når jeg tenker på seksuallivet mitt, føler jeg meg sint	*helt enig*	*ganske enig*	*litt enig*	*litt uenig*	*ganske uenig*	*helt uenig*
9. Når jeg tenker på seksuallivet mitt, føler jeg meg nær partneren min	*helt enig*	*ganske enig*	*litt enig*	*litt uenig*	*ganske uenig*	*helt uenig*
10. Jeg er bekymret for hvordan det skal gå med seksuallivet mitt i fremtiden	*helt enig*	*ganske enig*	*litt enig*	*litt uenig*	*ganske uenig*	*helt uenig*
11. Jeg har mistet gleden ved seksuell aktivitet	*helt enig*	*ganske enig*	*litt enig*	*litt uenig*	*ganske uenig*	*helt uenig*
12. Når jeg tenker på seksuallivet mitt, føler jeg meg utilpass	*helt enig*	*ganske enig*	*litt enig*	*litt uenig*	*ganske uenig*	*helt uenig*
13. Når jeg tenker på seksuallivet mitt, opplever jeg at jeg kan snakke med partneren min om ting som dreier seg om seksuallivet	*helt enig*	*ganske enig*	*litt enig*	*litt uenig*	*ganske uenig*	*helt uenig*
14. Jeg prøver å unngå seksuell aktivitet	*helt enig*	*ganske enig*	*litt enig*	*litt uenig*	*ganske uenig*	*helt uenig*
15. Når jeg tenker på seksuallivet mitt, føler jeg meg skyldig	*helt enig*	*ganske enig*	*litt enig*	*litt uenig*	*ganske uenig*	*helt uenig*

16. Når jeg tenker på seksuallivet mitt, er jeg bekymret for at partneren min føler seg såret eller avvist	*helt enig*	*ganske enig*	*litt enig*	*litt uenig*	*ganske uenig*	*helt uenig*
17. Når jeg tenker på seksuallivet mitt, opplever jeg det som om jeg har mistet noe	*helt enig*	*ganske enig*	*litt enig*	*litt uenig*	*ganske uenig*	*helt uenig*
18. Når jeg tenker på seksuallivet mitt, er jeg tilfreds med hyppigheten på seksuell aktivitet	*helt enig*	*ganske enig*	*litt enig*	*litt uenig*	*ganske uenig*	*helt uenig*

Hvordan har du det?

Når smerter og andre plager har vart en tid, blir en gjerne sliten og oppgitt. Dette gir ofte slike plager som nevnt nedenfor. Samlet blir disse her brukt som mål på at en er legemlig og psykisk presset.
Vurder hvor mye hvert symptom har vært til plage eller ulempe for deg de siste 14 dagene (til og med i dag).
Sett ring rundt tallet som passer best. Husk å sette *en ring utenfor hver plage/hvert symptom.*

(sett ring rundt tallet)	Ikke i det hele tatt	Litt	En god del	Svært mye
1. Anklager deg selv for ting.	1	2	3	4
2. Følelse av håpløshet m.h.t. fremtiden	1	2	3	4
3. Føler deg nedfor.	1	2	3	4
4. Føler deg ensom.	1	2	3	4
5. Har tanker om å ta ditt eget liv.	1	2	3	4
6. Følelse av å være fanget.	1	2	3	4
7. Bekymrer deg for mye.	1	2	3	4
8. Føler ikke interesse for noe.	1	2	3	4
9. Føler at du ikke er noe verd.	1	2	3	4
10. Plutselig skremt uten grunn.	1	2	3	4
11. Føler du deg engstelig.	1	2	3	4
12. Nervøs eller urolig.	1	2	3	4
13. Hjertebank.	1	2	3	4
14. Skjelving.	1	2	3	4
15. Føler deg anspent eller opphisset.	1	2	3	4
16. Anfall av redsel eller panikk.	1	2	3	4
17. Rastløshet, kan ikke sitte rolig.	1	2	3	4
18. Har lett for å gråte.	1	2	3	4
19. Føler du deg svimmel eller kraftløs.	1	2	3	4
20. Hodepine.	1	2	3	4
21. Føler deg slapp og uten energi.	1	2	3	4
22. Tap av seksuell interesse/opplevelse.	1	2	3	4
23. Dårlig appetitt.	1	2	3	4
24. Vanskelig for å sove.	1	2	3	4
25. Føler at alt krever stor anstrengelse.	1	2	3	4

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