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Faculty of health sciences / Department of community medicine

Prevalence and predictors of fatigue among people living with HIV in Northern and Southern Norway

From the cross-sectional study of mental health and quality of life among people living with HIV in Northern and Southern Norway, 2014-2015

Ranveig Langseth

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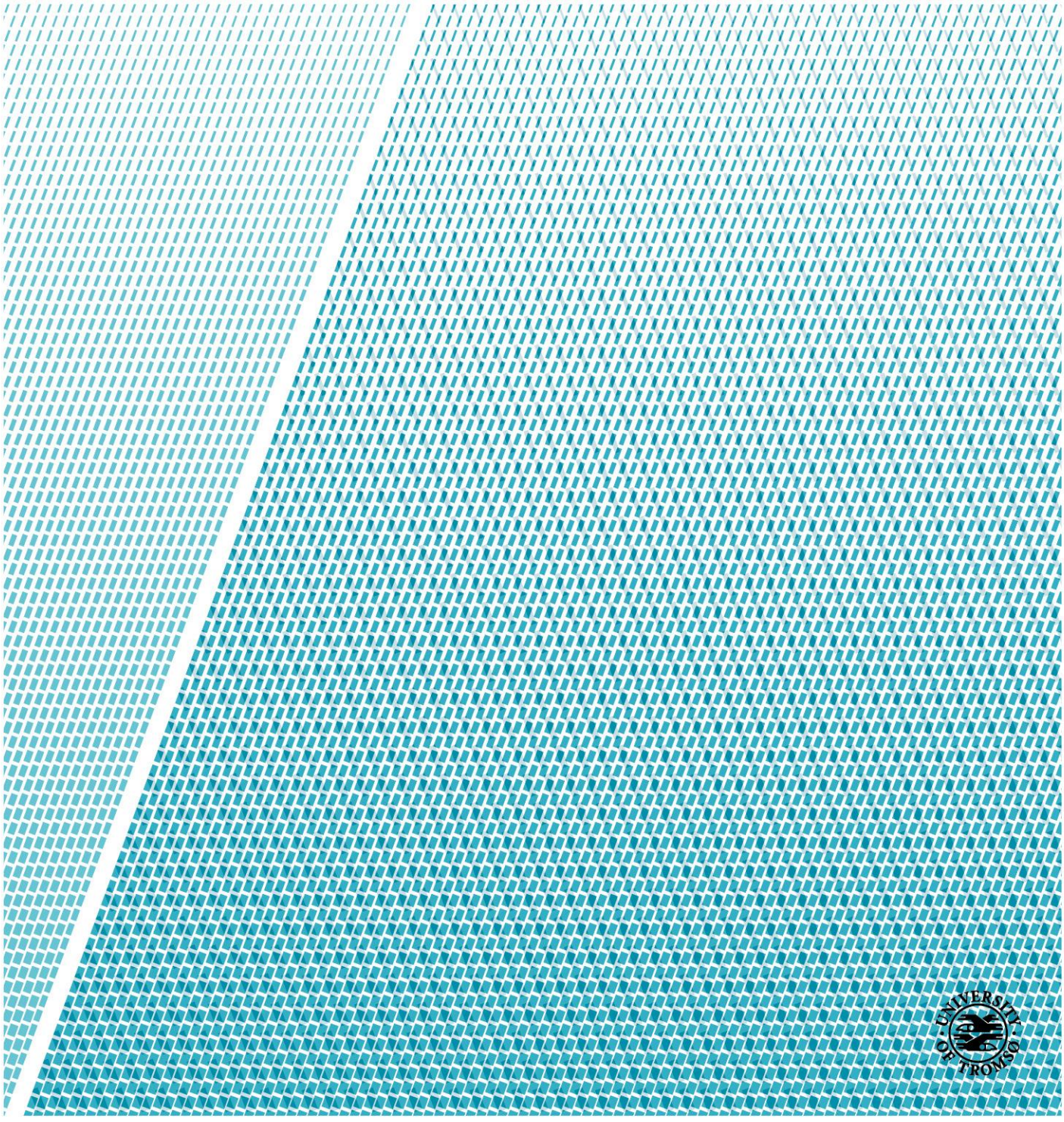
Main supervisor: Rigmor Berg
Co-supervisor: Marko Lukic



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When I agreed to work as a research nurse back in 2014, only one knew that I today would deliver a Master thesis on fatigue and HIV, and that was you Vegard. You had a plan and never doubted me. I am so grateful for your support, without you this would never have happened. Luckily, there is an army of health care workers in Kristiansand and Tromsø, who have just as much faith in you, and who have contributed in different ways to our survey. They are the best!

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Ranveig Langseth

Abstract

Background: Fatigue is described as a persisting sensation of tiredness and exhaustion that potentially interferes with daily life functioning. Since the first descriptions of AIDS, fatigue has been the most noted symptom, but to our knowledge, fatigue has never been investigated among people living with HIV (PLWH) in Norway.

Objectives: The aim is to investigate the prevalence and the predictors of fatigue among PLWH in Northern and Southern Norway.

Material and methods: A cross-sectional survey was conducted between December 2014 and September 2015 at two hospitals. The survey consisted of hospital records and a structured interview containing eight instruments. Fatigue was defined as a score of four points or more on the Chalder Fatigue Scale, and factors associated with fatigue were assessed with logistic regression analyses.

Results: 244 patients; 94 fatigued (38.5%) and 150 non-fatigued; were included in the analysis. The final regression model consisted of ten covariates; age, gender, men who have sex with men, CD4+ count, living alone, high education, multimorbidity, mental distress, bodily pain and trouble sleeping. The strongest predictors of fatigue were symptoms of anxiety and depression measured as presence of mental distress (aOR 8.98, 95% CI 3.81-21.15) and increased bodily pain on a scale from 0-10 (aOR 1.44, 95% CI 1.25-1.67). Other significant predictors were living alone (aOR 2.99, 95% CI 1.36-6.56), trouble sleeping (aOR 2.67, 95% CI 1.06-6.71) and multimorbidity (aOR 5.64, 95% CI 1.52-20.95).

Conclusion: The prevalence of fatigue among people living with HIV in Southern and Northern Norway is 38%, almost two times higher than the estimated prevalence in the Norwegian general population (22%). We identified mental distress, bodily pain, trouble sleeping, living alone and multimorbidity as predictors of fatigue. PLWH live longer due to highly effective antiretroviral therapy and improving their quality of life is important. If fatigue and its predictors, like mental distress and bodily pain, are identified and addressed, it may improve the quality of life for many. More research on prevention and treatment strategies for fatigued PLWH is needed, and should be implemented in the daily clinical routines.

Keywords

HIV, AIDS, PLWH, fatigue, chronic fatigue, Chalder Fatigue Scale, mental health, depression, anxiety, Norway

List of Abbreviations

AIDS	Acquired immune deficiency syndrome
ART	Antiretroviral therapy
AUDIT	Alcohol Use Disorder Identification Test
BDI-II	Beck's Depression Inventory version 2
CD4+	T–lymphocyte cell bearing CD4+ receptor
FQ	Chalder fatigue scale/Fatigue Questionnaire
DUDIT	Drug Use Disorder Identification Test
HIV	Human immunodeficiency virus
HSCL-25	Hopkins Symptom Checklist-25
MSIS	Norwegian Surveillance System of Communicable Diseases
MSM	Men who have sex with men
NIPH	Norwegian Institute of Public Health
NPR	National Patient Registry
PLWH	People living with HIV
PTSD	Post-traumatic stress disorder
PTSS-16	Post-traumatic stress scale-16
RNA	Ribonucleic acid
SF-36	Medical Outcomes Study 36-items Short-Form Health Survey
SSHF	Hospital of Southern Norway
SPSS	Statistical Package for Social Science
UiT	University of Tromsø, The Arctic University
UNN	University hospital of North Norway

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1 Introduction

The human immunodeficiency virus (HIV) was first described in 1984 as the cause of acquired immune deficiency syndrome (AIDS), and HIV/AIDS soon became a worldwide epidemic (Sepkowitz, 2001). Major improvements for people living with HIV (PLWH) came with access to antiretroviral therapy (ART), especially in the industrialized part of the world. Potent ART has transformed HIV from a death sentence to a chronic illness, and the goal of HIV-care has shifted from delaying death to achieving optimal health. Since the first descriptions of AIDS, fatigue has been the most noted symptom. Fatigue affects mental and physical functioning which in turn interfere with family, work and social life (Barroso et al., 2014). Understanding HIV-related fatigue in order to prevent or treat, can improve the quality of life for many. A review from 2010 identified mental health as the strongest predictor of fatigue along with comorbidity, sleeping difficulties, use of ART, unemployment and inadequate income (Jong et al., 2010). This study aims to find the prevalence and investigate the predictors of fatigue in PLWH in Northern and Southern Norway[1].

1.1 Objectives

Objectives:

1) Investigate the prevalence of fatigue among PLWH in Northern and Southern Norway.
2) Investigate the predictors of fatigue among mental health, socio-demographic, HIV- and other health related factors.

Hypotheses:

1) There is a high prevalence of fatigue among people living with HIV in Norway.
2) Depression is positively associated with fatigue and is the strongest predictor of fatigue.

[1] Norther Norway is here the counties Troms with Svaldbard, Finnmark and parts of Nordland. And Southern Norway is the two Agder counties (and must not be confused with South Norway).

2 Background

2.1 HIV epidemiology

UNAIDS estimated approximately 36.7 million people living with HIV in 2016. In a global perspective, the number of new HIV cases peaked in 1997, and AIDS related deaths have steadily decreased since 2006 due to better antiretroviral treatment (Trickey et al., 2017). In Norway 213 new cases of HIV were registered in 2017 through The Norwegian Surveillance System of Communicable Diseases (MSIS), and by the end of 2017 a total of 6277 people have tested positive for HIV since the registration started in 1984 (NIPH., 2018). Twice as many men (4260) than women (2017) have been registered. The MSIS registrations do not give a total number of people living with HIV in Norway today, since some are deceased or have moved abroad. The planned Norwegian quality register for HIV (NORHIV) estimates that 3425 people lived with HIV in 2015 (NORHIV, Bergersen, B.M., 2016) whereas 5843 were registered in MSIS the same year. The NORHIV number was based on National Patients Registry-codes (NPR-codes), a disease specific code sent electronically from the hospitals after all consultations. Norway has universal health care coverage, and PLWH receive consultations, medications and other HIV-related services without any personal cost at the public hospitals. The NPR codes, though probably slightly underestimated, offer a good estimate of the number of people living with HIV in Norway. The Norwegian population consisted in 2015 of 5.16 million inhabitants (SSB, 2015), and the estimated prevalence of HIV in Norway is then 66/100.000.

Most of the PLWH in Norway live in the capital; more than 46% are registered as patients at Oslo University Hospital (OUS). Of the remaining 18 hospitals, 9 follow up 100-300 patients each, and 9 follow up less than 90 patients each (NORHIV, Bergersen, B.M., 2016). Men infected with HIV through homosexual transmission are referred to as men who have sex with

men (MSM). MSM has a high prevalence of HIV on all continents (Beyrer et al., 2012), and there is an increased trend of HIV transmission among MSM in Norway (Jakopanec et al., 2013). In Norway 33% of all cases of HIV in MSIS were registered with homosexual transmission and the number for OUS is 47%. Many PLWH are not native Norwegians, but have migrated from high endemic countries. Africa is the dominating continent; 77% of those who got HIV from heterosexual transmission before arrival to Norway were born in Africa (NIPH., 2018). The Norwegian Institute of Public Health (NIPH) estimates that 1600-1800 immigrants with HIV lived in Norway in 2017.

2.2 HIV-related fatigue

Fatigue is one of the most prevalent and bothersome symptoms of HIV, and has a strong impact on people's quality of life as it affects mental and physical functioning, which in turn interfere with family, work and social life (Barroso et al., 2014; Wilson et al., 2016). In international studies the reported prevalence of fatigue varies from 33-88% in PLWH (Henderson et al., 2005; Jong et al., 2010), and from 7-42% in the general population (Finsterer and Mahjoub, 2014; Lewis and Wessely, 1992). The prevalence of fatigue in the general Norwegian population is estimated to be 22% (Loge et al., 1998). In healthy individuals fatigue after physical activity is expected, but in people suffering from various diseases, fatigue may endure after rest and is described as an overwhelming sense of tiredness, lack of energy, inertia or fragility that increase with activity and reduce the person's normal capacities (Barroso and Voss, 2013; Davis and Walsh, 2010)

In general, long time stress or disease are related to fatigue, and fatigue is furthermore influenced by age, gender, personality type, life experience, physical activity and nutrition (Finsterer and Mahjoub, 2014). In healthy working individuals disturbed sleep is found to be the strongest predictor of fatigue along with high work demands, low social support, being female and having high age (Akerstedt et al., 2004). Fatigue is a known symptom in chronic

diseases such as cardiopulmonary, endocrine, metabolic, hematologic, neoplastic, infectious, rheumatologic, psychological and neurological conditions (UpToDate, Chirelli, C., 2018), and HIV-related fatigue intensity increases with the number of comorbidities (Corless et al., 2008). Explanatory factors are high stress level from loss of social position and social support, disease labeling, coping patterns, reduced physical activity and chronic inflammation (Kurien et al., 2013, Jong et al., 2010). In addition, misuse of alcohol and drugs is associated with fatigue (UpToDate, Fosnocht, K.F., 2018). The causal patterns of fatigue are complex and involve mechanisms within muscle fibers, metabolic accumulation, proinflammatory cytokines and inadequate function in the motor cortex (Dantzer et al., 2008; Abd-Elfattah et al., 2015; Finsterer and Mahjoub, 2014). The mechanisms of fatigue will not be discussed further in this study.

A 2010 review of 42 studies found that the strongest predictors of HIV-related fatigue were psychological factors like depression and anxiety. Significant associations were also established for the socio-demographic variables unemployment and inadequate income, and the physiological factors sleep disturbance, comorbidity and ART-use (Jong et al., 2010). Conflicting results exist with regard to the association of fatigue with variables such as gender, age, ethnicity, having children or partner, education level, sexual orientation, time since diagnose, CD4+ count and virus load has been observed in some studies, but not found significant in other (Barroso et al., 2010; Henderson et al., 2005; Millikin et al., 2003; Jong et al., 2010).

An overview of fatigue symptom management from 2017 divided associations of HIV-related fatigue into three dimensions; physiological, psychological and behavioral (Perazzo et al., 2017). The main psychological factors in this overview are depression, anxiety, traumatic events and social isolation. Psychological factors are anemia, chronic inflammation, endocrine dysfunction and side effects of ART, while behavioral factors are physical inactivity and poor

sleep hygiene. The association of ART and fatigue is often related to disturbance in sleep (Gakhar et al., 2013), and sound sleeping habits are important for optimal functioning since sleep and fatigue correlate to cognitive impairment (Byun et al., 2016).

The strong correlation of fatigue with psychological factors like depression, is acknowledged (Millikin et al., 2003; Slot et al., 2015; Perazzo et al., 2017; Voss et al., 2007; Jong et al., 2010). Depression is the most common mental disorder among PLWH, affecting twice as many as in the general population, but is often under-diagnosed and poorly met by the health care services (Whetten et al., 2008; Noh et al., 2012; Rodkjaer et al., 2010). There is an association between depression and poor ART-adherence (Huynh et al., 2013; Ingersoll and Cohen, 2008; Corless et al., 2013), and there are indications that fatigue is negatively related to ART-adherence (Gay et al., 2011; Al-Dakkak et al., 2013). The high depression rate is explained by stigma experience, emotional reactions after HIV diagnosis, effects of HIV on the brain, side effects of ART and of opportunistic infection treatments (Chandra et al., 2005) and is associated with reduced quality of life (Whetten et al., 2008; Corless et al., 2013). There is also a direct association between fatigue and reduced quality of life (Voss et al. 2006) and overall, PLWH report lower quality of life than the general public despite good adherence, viral suppression and a stable immune system (Miners et al., 2014).

As PLWH life expectancy rises with improved treatment, new questions arise about their quality of life and how it may be improved. Therefore, data on fatigue is requested for the well treated Norwegian PLWH. A 2008 study on fatigue and comorbidity used data from five countries including Norway, but the results were not presented by country (Corless et al., 2008). Thus, to our knowledge, this will be the first study on prevalence and predictors of fatigue among PLWH in Norway.

3 Materials and Methods

3.1 Material

The data collection was performed between 2014 and 2015 as part of the *Mental health and quality of life among PLWH in Northern and Southern Norway Survey*. The study has a cross-sectional design. In Norway, the care for PLWH is organized by the secondary health care service, and all medication must be prescribed by a specialist in infectious diseases. This study is a collaboration between two hospitals, the Southern Hospital of Norway (SSHF) and the University hospital of North Norway (UNN). The two hospitals follow up patients in the northern and southern counties in Norway, and the counties include both rural and urban areas. Together they follow up 8% of all PLWH in Norway (NORHIV., 2016).

3.1.1 Pilot-study

A pilot-study was performed in 2012, to test the feasibility of the study and to estimate the time required to conduct the survey. The pilot-study identified a high prevalence of depression and anxiety among PLWH. The study, which was completed with the help of a medical student, took two hours, and some instruments were replaced in order to reduce the time spent. In addition, variables about comorbidity and socio-demographics were added.

3.1.2 Ethical considerations

The study is approved by REK NORD, Regional ethics committee in Northern Norway, (ref 2011/1925). Participating in the study was voluntary, and all patients were informed about the study orally and in writing, and had to sign a written consent form before inclusion. All information from the survey is kept confidential. Patients were offered extra consultations at the outpatient clinics after the interview if anything came up that had to be addressed concerning their mental health.

3.1.3 Organizing and funding

The Project group consisted of Vegard Skogen, M.D., Ph.D., specialist in clinical microbiology and infectious diseases, UNN and University of Tromsø, The Arctic University (UiT), Tore Sørlie, M.D., Ph.D., specialist in psychiatry, UNN and UiT, Ole Rysstad, M.D., specialist in pulmonary diseases, SSHF, and Birgit Lie, M.D., Ph.D., specialist in community medicine and General Practitioner, SSHF.

All data was collected at the outpatient clinics at the hospitals. The study was mostly funded through the regular budget, and external funding was obtained from the Norwegian Directorate of Health and was used as salary for a research nurse at UNN.

3.1.4 Study Population

All HIV-positive patients above 18 years, registered at the HIV outpatient clinics at SSHF and UNN were eligible to participate in the study. The patients were asked to participate regardless of language and literacy. Patients with a severe mental disorder or cognitive impairment that would make them incapable of answering the questions, were excluded.

3.1.5 Inclusion period

The HIV-positive patients have regular visits at least one to four times a year at the outpatient clinics. The survey was conducted as a formalized interview following the regular consultation. The interview consisted of eight instruments with a total of 147 questions. A nurse performed the interviews in Norwegian, English or French, and professional pre-informed interpreters were used when needed (n=13). The interview lasted from 30 to 60 minutes, and all interviews were conducted between December 2014 and September 2015. Data on medications, comorbidities and blood test results were extracted from the medical records.

3.1.6 Data management

Paper schemes were used during the structured interview at UNN. At SSHF, the answers were typed directly into the journal system, DiaGraphIT GoTreatIT® Infection, and only a few paper schemes were used. All the paper schemes were punched into the journal system and later double checked by two nurses. The data were extracted from GoTreatIT® through Windows Excel to IBM Statistical Package for Social Science version 24 (SPSS). The study data are saved according to local procedures in a secured research database at UNN.

3.2 Methods

3.2.1 Dependent variable

Fatigue was measured with the Chalder Fatigue Scale, also known as the Fatigue Questionnaire (FQ), a validated scale of mental and physical fatigue (Jackson, 2015; Chalder et al., 1993). The 11 questions in FQ were answered "less than usually", "as usually", "more than usually" or "much more than usually". A bimodal score grades the answers 0-0-1-1, with total score between 0 and 11, where fatigue is defined as a score of four points or more. This definition of fatigue was used as the dependent variable in the analysis. Non-fatigued and fatigued participants are presented as **fatigued** 0=no, 1=yes. The FQ also contains two extra questions about duration of fatigue, this information was used to identify the chronically fatigued**.** In **chronic fatigue**, symptoms of fatigue must have persisted for more than 6 months.

3.2.2 Independent variables

The independent variables were selected based on results from Jong's systematic review (Jong et al., 2010), Barroso's articles (Barroso et al., 2010; Barroso et al., 2016; Barroso et al., 2014), a literature search from 2017 (Loades and Kagee, 2017), and information on chronic diseases and substance abuse related to fatigue (Perazzo et al., 2017; UpToDate, Fosnocht, K.F., 2018, Guaraldi et al., 2014). Jong and colleagues (2010) identified the strongest predictors of fatigue

to be unemployment, inadequate income, use of ART, comorbidity, sleeping difficulty, depression and anxiety; Barraso and colleagues (2010, 2014, 2016) list unemployment, ART, time since diagnosis, stressful life events, and psychological distress as important variables; and Loades and Kagee (2017) identified functional sleep, viral load, CD4+ count, age, gender, transmission route, adherence to ART, pain and social-, educational- and occupational functioning as factors to be assessed in future research.. This survey did not contain information on income, but other socio-demographic variables (education, native country and cohabitation) were added.

3.2.2.1 Socio-demographic variables

Socio-demographic variables are age, gender, hospital, education, cohabitation, employment and native country.

- **Age** was measured in years and used as a continuous variable.
- **Gender** was coded female=0, male=1.
- The variable **hospital** represents the hospital where the participants performed the survey, University Hospital of North Norway or Hospital of Southern Norway.
- **Education** was registered in number of years in school and presented as 0=low education (≤12 years) and 1=high education (>12 years).
- **Work status** was answered with 13 different alternatives, the four largest groups (full-time job, unemployed, disabled pensioner and student) were kept unaltered, and the remaining groups were collapsed into "other". The group "student" includes settled immigrants participating in the Norwegian introductory course. The original grouping is displayed in appendix Table 6.
- **Cohabitation** was calculated based on marital status and whether the participants lived with a partner or not. The variable is presented as living together=0 and living alone=1.

- N**ative country** is the country where the participant was born. The 50 different countries listed, except for Norway, were merged into four continents; Europe, Asia, South-America and Africa. Native Norwegians were kept as reference group.

3.2.2.2 HIV and health related variables

The HIV-related variables are time since diagnosis, transmission route, virus suppression, CD4+ count, ART, and treatment failure. The other health related variables are hepatitis C, bodily pain, anaemia, comorbidity/multimorbidity and trouble sleeping.

- The continuous variable **time since diagnosis** was computed in years from the date of study inclusion minus the date of first consultation or positive HIV-test.
- **Transmission route** was coded into four categories: 1=heterosexual, 2=MSM (homosexual), 3=other (blood transfusion, mother to child or infected syringes) and 4=unknown. In addition, transmission was dichotomized as **MSM,** coded 0=no, 1=yes,
- CD4+ count was measured as absolute count of CD4+ T Lymphocyte cells ($x10^9$/L) in the blood (**CD4+ ($x10^9$/L)**), and was kept without alterations as a continuous variable.
- Virus suppression was defined as less than 50 ribonucleic acid copies (RNA) per ml blood, and presented as **virus suppressed** 0=no, 1=yes.
- Antiretroviral therapy (ART) are participants who used HIV-medication, presented as **ART** 0=no and 1=yes. Participants who started medication on the same day as they were included in the study were set as 0.
- **Treatment failure** was defined as not virus suppressed after 6 months of treatment, (>50 HIV RNA/ART >6 months) and presented as treatment failure 0=no, 1=yes. Participants who started ART less than 6 months before the inclusion date were kept out of the equation.

- **Hepatitis C antibody** was extracted from the blood samples and presented as positive hepatitis C antibody test 0=no, 1=yes.
- **Anaemia** was calculated from haemoglobin blood levels. The reference values from the UNN laboratory were used as cut off points for anaemia; <11.5 (g/dl) for women and <13.0 (g/dl) for men (0=no, 1=yes).
- **Comorbidity** was categorized with 2 or 3 groups. The variable with three groups consisted of no comorbidity=0, comorbidity=1 and multimorbidity=2. In the binary variable no comorbidity and comorbidity were collapsed into one group presenting **multimorbidity** as 0=no and 1=yes. No comorbidity was defined as the absence of the following diagnoses: renal failure, thyroid disease, diabetes, cardiovascular disease, osteoporosis, arthritis, physical impairment, cancer, stroke, asthma or chronic obstructive pulmonary disease**.** Comorbidity was defined as the presence of one of the diagnoses, and multimorbidity was the presence of two or more diagnoses (Guaraldi et al., 2014).
- **Bodily pain** was computed from the pain dimension score of the Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36). Question 21 and 22 in the SF-36 measure physical pain during the last week on a scale from 0-100, where 100 is no pain. The scores were inverted and divided by ten. Bodily pain was used as a continuous variable on a scale from 0-10 were 0 is no pain.
- **Trouble sleeping** is the question: "Do you have trouble falling or staying asleep the last week?" Answered "not at all", "a little bit", "quite a bit" and "almost always", and scored 1 to 4 respectively. The answers were recoded 1=0, 2=0, 3=1, 4=1, and presented as trouble sleeping 0=no and 1=yes.

3.2.2.3 Mental health variables

The mental health variables are based on the Hopkins symptom checklist-25 (HSCL-25), the Beck's Depression Inventory version 2 (BDI-II), the Post Traumatic Stress Scale-16 (PTSS-16), Alcohol Use Disorder Identification Test (AUDIT) and the Drug Use Disorder Identification Test (DUDIT). The instruments were used to identify mental distress, depression, anxiety, post-traumatic stress disorder and alcohol and drug abuse.

- **HSCL-25** measures mental health based on presence of depression and anxiety symptoms during the last four weeks (Derogatis et al., 1974). The symptoms were answered "not at all", "a little", "quite a bit" and "extremely" and rated 1 to 4 respectively. The **total score** is the mean value of all 25 questions. Separate scores were also calculated for anxiety and depression. The **anxiety score** is the mean value of the first 10 questions, and the **depression score** is the mean value of the 15 last questions. All HSCL-25 scores are presented as a number between 1 and 4, where 1 is no symptoms. A total score of 1.75 or more is defined as having mental distress (Mattisson, 2013, Nettelbladt et al., 1993), and presented as **mental distress** 0=no, 1=yes.
- All participants with a HSCL-25 total score ≥1.75 were scored again for depression with the **BDI-II**. The BDI-II consists of 21 questions and is a diagnostic tool for severity of depression. BDI-II divides the participants into four categories: minimal depression=1, mild depression=2, moderate depression=3 and severe depression=4, with cut points <14, 14-19, 20-29 and >29 respectively. The participants who scored <1.75 on the HSCL-25 were coded 0 and used as a reference group labelled "not depressed".
- **Post-traumatic stress disorder** (PTSD) was calculated from PTSS-16. The PTSS-16 consists of 16 questions about the frequency of symptoms after stressful life experiences were present the last week. The answers were given as "not at all", "a little bit", "quite

a bit" and "almost always", scored 1-4 respectively. A total mean score above 2.5 was defined as PTSD (Raphael et al, 1989) and presented 0=no, 1=yes.

- The values **Alcohol abuse risk** and **Drug abuse risk** are the outcome of the Alcohol Use Disorder Identification Test (AUDIT) (10 questions) and the Drug Use Disorder Identification Test (DUDIT) (11 questions). Drugs include all kinds of substances, illegal or legal, that are not prescribed from a doctor. The tests calculate the risk of abuse the last year based on gender. The risk is given as a number between 1 to 4, where 1 is no risk of abuse. The variable was recoded 1=0, 2-4=1, collapsing the three risk categories into one group. Alcohol abuse risk and the drug abuse risk variables are presented as 0=no, 1=yes.

3.2.1 Statistical analysis

The statistics is performed in SPSS. The demographic variables were computed with crosstabulations and descriptive analysis. The variables are presented in Tables 1-3 as means (M) with standard deviation (SD) or total numbers with percentages.

The Odd Ratios (OR) were calculated using logistic regression. The crude ORs were calculated with univariate analysis entering the independent variables separately against the dependent variable. For the adjusted OR (aOR), all the covariates were entered into the regression model at the same time.

To identify the regression model with the best model fit, all the potential variables were added as covariates and run in a backward model with 0.10 percent probability of stepwise removal. Five covariates (living alone, high education, bodily pain, multimorbidity and mental distress) became significant at a 5% level and were kept in the analysis. Then the other variables were re-entered and removed several times while checking for changes in the model summary and the Hosmer and Lemeshow test, ending up with ten covariates representing the socio-

demographic, mental health, HIV and other health related characteristics. In the final regression model, the dependent variable fatigue is binary, three independent variables are continuous; age, CD4+ count and bodily pain, and seven are dichotomous; gender, living alone, high education, MSM, multimorbidity, mental distress and trouble sleeping.

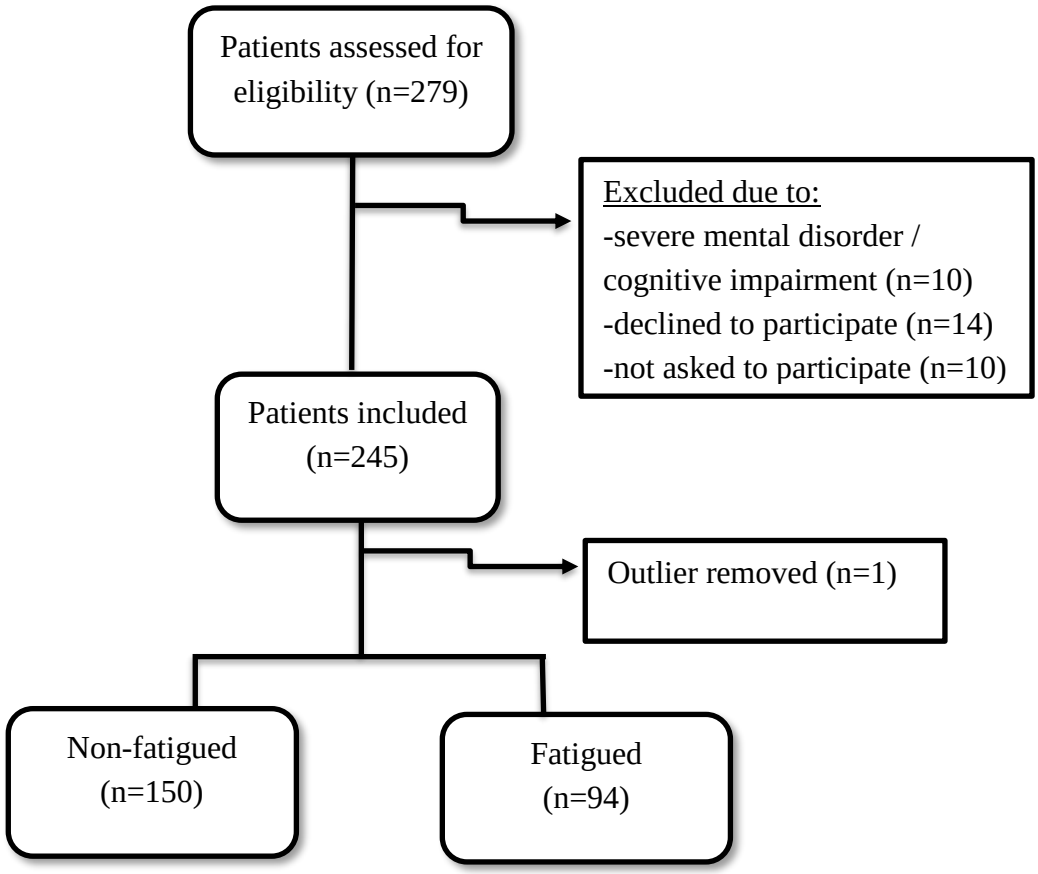
The ORs and the aORs are presented with 95% Confidence Intervals (CI) and p-values. All significance levels are set at <0.05. Correlations were checked for in the correlation matrix and in the collinearity statistics. The number of residuals above 2 were less than 5%. Cook's influence statistics showed one outlier with levels higher than 1, and a closer look displayed large discrepancies in the answers and the outlier was removed from the analysis.

3.2.2 Missing data

Four participants did not give information about the duration of fatigue. In Table 1, the variable work status has two missing, and in Table 3, PTSD has one missing and BDI-II has two missing. All the missing variables were from fatigued participants. Variables with missing data in Tables 1 and 3 are marked with a *. The final regression model does not contain any missing data.

4 Results

Figure 1. Flowchart of included participants



As shown in Figure 1, a total of 121 patients from the Hospital of Southern Norway (SSHF) and 158 patients from the University Hospital of North Norway (UNN) were registered at the out-patient clinics between December 2014 and September 2015 (n=279). 10 patients were excluded due to severe mental disorders or cognitive impairment. 14 declined to participate for various reasons and 10 people were not asked to participate or did not have contact with the hospital during the recruitment period. Of the 279 patients registered at the hospitals, 245 completed the survey, which gives a response rate of 87.8%. One outlier was later removed and a total of 244 patients were included in the analysis.

4.1 Prevalence and demographic characteristics

The prevalence of fatigue among the participants was 38.5%, as 94 out of 244 of the participants scored 4 or more on the FQ. Chronic fatigue was seen in 44 of the fatigued cases (18% of all participants, 4 missing). Increased time since onset of fatigue symptoms was related to fatigue intensity; as all mean FQ total bimodal scores increased with time. The chronic fatigued participants had the highest FQ total score with a mean of 7.36 (SD=2.06). (Appendix Table 5).

The socio-demographic characteristics are presented in Table 1 and display similar distribution of age, gender and native countries between the two hospitals, but some differences were seen in work status, education, cohabitation and fatigue.

The participants were between 18 and 77 years old, had a mean age of 43.7 years (SD=11.7) and the average time since diagnose was 9.36 years (SD=7.39). 46.7% of the participants were women and 53.3% were men. Only 32.8% of the participants were born in Norway, the other were immigrants. The largest immigrant group was from Africa (n=100), and four countries had more than ten immigrants each; Eritrea, Ethiopia, Somalia and Thailand.

Half of all the Norwegians and South-Americans were fatigued, whereas 1 in 3 of the Europeans, Asians and Africans were fatigued. Overall, the gender distribution differed among the native countries; there were more women from Asia and Africa and more men from Norway, Europe and South-America. The prevalence of fatigue was higher among the 130 males (43.1%) than the 114 females (33.3%), and 58% of the MSM were fatigued (n=31). MSM were more likely to be Norwegian (71%), highly educated (74%), living alone (80%) and mentally distressed (52%) compared to the mean distribution, whereas women were more likely to be immigrants (68%), have low education (70%), cohabitate (56%) and not mentally distressed (73%). Fatigued participants were older than the non-fatigued (M=45.2, SD=11.9 vs

M=42.8, SD=11.6), were more likely to live alone (69.1% vs 41.3%) and to have high education (48.9% vs 37.5%). The participants were asked about their work status; 35.1% reported working full time, 11.6% reported unemployment and 11.6% were disabled pensioners, 11.1% were students or participants in the Norwegian introduction course (the other categories are displayed in Appendix Table 6). The disabled pensioners (64%) and the unemployed (40%) were more fatigued than the full-time employed (28%) and the students (22%). Attempts were made to regroup the work status variables in the preliminary analysis (data not shown), but none of the work status categories were kept in the regression model. The distribution of immigrants and education level differed between the work status groups, especially between the two groups with high level of fatigue; the unemployed had 93% with low education and 93% immigrants, and the disabled pensioners had 54% with low education and 32% immigrants.

Table 1. Sociodemographic characteristics of the study sample (N=244)

Mental health and quality of life among people living with HIV in Northern and Southern Norway, 2014-2015

Characteristics		Chalder Fatigue Scale		Hospital		Gender	
	Total	Non-fatigued	Fatigued	UNN	SSHF	Female	Male
Participants, N (%)	244	150 (61.5)	94 (38.5)	135 (55.3)	109 (44.7)	114 (46.7)	130 (53.3)
Age (y), mean (SD)	43.7 (11.7)	42.8 (11.6)	45.2 (11.9)	44.3 (11.9)	43.1 (11.5)	41.7 (10.7)	45.5 (12.3)
Hospital N (%)							
UNN	135 (55.3)	89 (59.3)	46 (48.9)			63 (55.3)	72 (55.3)
SSHF	109 (44.7)	61 (40.7)	48 (51.1)			51 (44.7)	58 (44.7)
Gender, N %							
Female	114 (46.7)	76 (50.7)	38 (40.4)	63 (46.7)	51 (46.7)		
Male	130 (53.3)	74 (49.3)	56 (59.6)	72 (53.3)	58 (53.2)		
Cohabitation, N (%)							
Living together	117 (48)	88 (58.7)	29 (30.9)	72 (52.6)	45 (41.3)	64 (65.1)	53 (40.8)
Living alone	127 (52.0)	62 (41.3)	65 (69.1)	63 (47.4)	64 (58.7)	50 (43.9)	77 (59.2)
Education, N (%)							
Low education	142 (58.2)	94 (62.7)	48 (51.1)	71 (52.6)	71 (65.1)	80 (70.2)	62 (47.7)
High education	102 (41.8)	56 (37.5)	46 (48.9)	64 (47.4)	38 (34.9)	34 (29.8)	68 (52.3)
Work status, N* (%)							
Working full time	85 (35.1)	61 (40.7)	24 (26.1)	56 (41.5)	29 (27.1)	36 (32.1)	49 (37.7)
Unemployed	28 (11.6)	17 (11.3)	11 (12.0)	13 (9.6)	15 (14.0)	16 (14.3)	12 (9.2)
Disable pensioner	28 (11.6)	10 (6.7)	18 (19.6)	11 (8.1)	17 (15.9)	11 (9.8)	17 (13.1)
Student	27 (11.2)	21 (14)	6 (6.5)	17 (12.6)	10 (9.4)	15 (13.4)	12 (9.2)
Other	74 (30.6)	41 (27.3)	33 (35.9)	38 (28.2)	36 (33.6)	34 (30.4)	40 (30.8)
Native country, N (%)							
Norway	80 (32.8)	40 (26.7)	40 (42.6)	46 (34.1)	34 (31.2)	16 (14.0)	64 (49.2)
Europe	16 (6.6)	11 (7.3)	5 (5.3)	8 (5.9)	8 (7.3)	6 (5.3)	10 (7.7)
South-America	10 (4.1)	5 (3.3)	5 (5.3)	5 (3.7)	5 (4.6)	1 (0.9)	9 (6.9)
Asia	38 (15.6)	25 (16.7)	13 (13.8)	22 (16.3)	16 (14.7)	29 (25.4)	9 (6.9)
Africa	100 (41.0)	69 (46.0)	31 (33.0)	54 (40.0)	46 (42.2)	62 (54.4)	38 (29.2)

SD: standard deviation
UNN: University hospital of North Norway
SSHF: Hospital of Southern Norway
*N=242, 2 missing fatigued female cases from SSHF

As seen in Table 2, the participants were well treated with 93% on ART, 94% were virus supressed after 6 months of treatment and mean levels of CD4+ T Lymphocytes at 0.50 ($x10^9$/L) (SD=0.26). There was a small difference between fatigued and non-fatigued cases regarding treatment failure with 6% versus 5.5% respectively. A large proportion (43.9%) reported "unknown" as transmission route, and not knowing the route of transmission was more frequent among females (51%) than males (37%). Only one participant reported needle sharing as transmission route (Appendix Table 7). Overall 7.4% were at risk of drug abuse, but the number of intravenous drug users or previous users were not established. Both alcohol abuse risk (18.1% vs 12.0%) and drug abuse risk (13.8% vs 3.3%) were higher among the fatigued than the non-fatigued. Alcohol risk abuse did not contribute to the regression model, whereas drug risk abuse had an impact. Having risk of drug abuse increased the risk of fatigue, but was left out of the final regression model due to poorer fit than the variable trouble sleeping. Trouble sleeping was present in 25% of all participants and 50% of the fatigued. There were more participants with multimorbidity among the fatigued (13.8%) than the non-fatigued (5.3%), but having only one comorbidity showed the opposite relationship (11.7% vs 14%). Hepatitis C antibody (13.8%) and anaemia (10.6%) were more frequent among the fatigued than the non-fatigued (10% and 8.7%, respectively). Hepatitis C and anaemia were added in the comorbidity variable at one point, but later removed as it did not contribute to the model. The fatigued experienced more pain than the non-fatigued; on a scale from 0-10, in which 0 indicates no pain, the non-fatigued had a mean score of 1.69 (SD=2.21) and the fatigued had a mean score of 4.90 (SD=5.50).

Table 2. HIV and health related characteristics of the study sample (N=244)
Mental health and quality of life among people living with HIV in Northern and Southern Norway, 2014-2015

Characteristics	Chalder Fatigue Scale		
	Total N=244	Non-fatigued N=150	Fatigued N=94
Time since diagnose, mean (SD)	9.36 (7.39)	9.15 (6.85)	9.7 (8.22)
Transmission route, N (%)			
Heterosexual	97 (39.8)	62 (41.3)	35 (37.2)
Men who have sex with men	31 (12.7)	13 (8.7)	18 (19.1)
Other	9 (3.7)	5 (3.3)	4 (4.3)
Unknown	107 (43.8)	70 (46.7)	37 (39.4)
Antiretroviral therapy, N (%)	227 (93.0)	138 (92.0)	88 (93.6)
Virus suppressed, N (%)	211 (86.5)	130 (86.7)	81 (86.2)
Treatment failure, N* (%)	12 (5.7)	7 (5.5)	5 (6.0)
CD4+ ($x10^9$/L), mean (SD)	0.53 (0.26)	0.54 (0.29)	0.52 (0.22)
Hepatitis C antibody, N	28 (11.5)	15 (10.0)	13 (13.8)
Anemia, N (%)	23 (9.4)	13 (8.7)	10 (10.6)
Comorbidity, N (%)			
No comorbidity	191 (78.3)	121 (80.7)	70 (74.5)
Comorbidity	32 (13.1)	21 (14.0)	11 (11.7)
Multimorbidity	21 (8.6)	8 (5.3)	13 (13.8)
Bodily pain, mean (SD)	2.93 (2.96)	1.69 (2.21)	4.90 (5.50)
Trouble sleeping, N (%)	63 (25.8)	16 (10.7)	47 (50.0)

SD: standard deviation; CD4+: T–lymphocyte cell bearing CD4+ receptor
*participants on antiretroviral treatment >6 months (N=212)

The mental health characteristics presented in Table 3 display a clear link between mental health and fatigue; 64.9% of the fatigued participants and only 10.6% of the non-fatigued participants had mental distress. All the three HSCL-25 mean scores (scale 1-4) were higher among the fatigued than the non-fatigued, which indicates higher levels of both anxiety (M=1.9, SD=10.32 vs M=1.29, SD=0.60) and depression (M=2.21, SD=0.67 vs M=1.40, SD=0.36) among the fatigued. The association between depression and fatigue was seen for all BDI-II-scores and none of the non-fatigued were severely depressed. All participants with PTSD (n=15) were severely depressed (N=19). Due to the strong relationship between PTSD and severe depression, PTSD was left out of the regression model. The analysis was at one point run without the severely depressed participants, but the main results remained unchanged and the severely depressed were kept in the equation (data not shown).

Table 3: Mental health characteristics of the study sample (N=244)

Mental health and quality of life among people living with HIV in Northern and Southern Norway, 2014-2015

Characteristics	Chalder Fatigue Scale		
	Total N=244	Non-fatigued N=150	Fatigued N=94
Hopkins Symptoms Checklist-25, mean (SD)			
Total Score	1.64 (.58)	1.35 (.32)	2.09 (.60)
Anxiety score	1.53 (.54)	1.29 (.32)	1.91 (.60)
Depression score	1.71 (.64)	1.40 (.36)	2.21 (.67)
Mental distress, N (%)	77 (31.5)	16 (10.6)	61 (64.9)
Beck's Depression Inventory, N* (%)			
Not depressed	167 (69.0)	134 (89.3)	33 (35.9)
Minimal depression	16 (6.6)	5 (3.3)	11 (12.0)
Mild depression	25 (10.3)	7 (4.7)	18 (19.5)
Moderate depression	15 (6.2)	4 (2.7)	11 (12.0)
Severe depression	19 (7.9)	0 (0)	19 (20.6)
Post-Traumatic Stress Disorder, N* (%)	15 (6.1)	0 (0)	15 (16.1)
Drug abuse risk, N (%)	18 (7.4)	5 (3.3)	13 (13.8)
Alcohol abuse risk, N (%)	35 (14.3)	18 (12.0)	17 (18.1)

SD: standard deviation
*BDI-II: N=242, 2 missing fatigued cases
*PTSD: N=243, 1 missing fatigued case

4.2 Predictors of fatigue

The results from unadjusted and adjusted analyses are presented in Table 4. All ten variables (age, gender, cohabitation, high education, MSM, CD4+ count, multimorbidity, bodily pain, mental distress and trouble sleeping) independently contributed to the regression model as predictors or confounders. The model performed well with sig .953 for The Hosmer and Lemeshow Test and Omnibus Test of model Coefficients Chi-square of 144.045 (χ^2 (10, N=244) = 114.045, p < .000). The model summary implied that between 44.8% and 60.9% of the variability is explained by the model.

Five out of ten covariates in the final regression model were significantly associated with fatigue. Mental distress had an aOR of 8.98 (aOR 8.98, 95% CI 3.81-21.15), indicating that patients with a HSCL total score above 1.75 were almost nine times more likely to report symptoms of fatigue than those not fatigued. Mental distress had the highest aOR among the dichotomous variables. A significant result was also seen when the HSCL-25 total score was used as a continuous variable (OR, 45.44, 95% CI 16.89-122.22) (range 1-4), but the variable had a large confidence interval due to high impact on the model from the severely depressed, and the binary variable was preferred in the model. Having bodily pain was associated with fatigue with an aOR of 1.44 per increase in pain score (range 0 to 10) (aOR 1.44, 95% CI 1.25-1.67), indicating that the likelihood of fatigue increases with the severity of pain. Bodily pain (Wald 24.99) and mental distress (Wald 25.21) contributed most to the predictive ability of the model as they both had three times as high Wald statistics than the third highest covariate living alone (Wald 7.43). Bodily pain and mental distress had p-values less than .001 in both the crude and the adjusted analysis.

The three other significant predictors of fatigue were living alone (aOR 2.99, 95% CI 1.36-6.56), trouble sleeping (aOR 2.67, 95% CI 1.06-6.71) and multimorbidity (aOR 5.13, 95% CI 1.25-21.15). High education was significantly related to increased fatigue in the backward

analysis (data not shown), but the relationship was neither significant in the unadjusted (OR 1.58, 95% CI 0.94-2.66) nor the adjusted analysis (aOR 2.15, 95% CI 0.95-4.87).

Age, gender and MSM were re-entered in the regression model as confounding factors as they contributed positively to the model fit. Being male shifted from increased risk (OR 1.45, 95% CI 0.89-2.51) to decreased risk of fatigue after adjustment (aOR 0.82, 95% CI 0.35-1.95). The relationship between gender and fatigue remained non-significant. The variable MSM had significant crude OR (OR 2.51, 95% CI 1.17-5.41), but it became non-significant after adjustment (aOR 1.43, 95% CI 0.38-5.23).

None of the HIV-related variables were significantly associated with fatigue, only CD4+ count contributed enough to the final regression model to be selected. Low CD4+ count was negatively associated with presence of fatigue, and got a narrower CI after adjustment (aOR 0.90 95% CI 0.78-1.04), but the association remained non-significant.

Table 4. Logistic regression of factors associated with fatigue (N=244)

Mental health and quality of life among people living with HIV in Northern and Southern Norway, 2014-2015

	crude Odds Ratio			adjusted Odds Ratio		
	OR	95% CI	*p*	aOR	95% CI	*p*
Age	1.02	(0.99 - 1.04)	.120	1.01	(0.98 - 1.05)	.515
Male gender	1.49	(0.89 - 2.51)	.131	0.82	(0.35 – 1.94)	.654
Living alone	3.18	(1.84 - 5.49)	.000*	2.99	(1.36 - 6.56)	.006*
High education	1.58	(0.94 – 2.66)	.085	2.15	(0.95 – 4.87)	.068
MSM	2.51	(1.17 - 5.41)	.018*	1.43	(0.39 - 5.23)	.586
CD4+ ($x10^9$/L)	0.97	(0.88 – 1.07)	.514	0.90	(0.78 - 1.04)	.179
Multimorbidity	2.85	(1.13 – 7.16)	.026*	5.13	(1.40 - 18.73)	.013*
Bodily pain	1.54	(1.37 - 1.73)	.000*	1.44	(1.25 - 1.67)	.000*
Mental distress	15.48	(7.93 - 30.24)	.000*	8.98	(3.81 - 21.15)	.000*
Trouble sleeping	8.38	(4.34 – 16.16)	.000*	2.67	(1.06 - 6.71)	.037*

aOR: all scores in logistic regression with 10 covariates (age, gender, cohabitation, high education, MSM, CD4+ count, multimorbidity, bodily pain, mental distress and trouble sleeping) are shown in this table.
Age: OR per 1year increase (scale 18-77); CD4+ ($x10^9$/L): OR per 0.10 increase (scale 0.01-1.83); bodily pain: OR per 1-unit increase (scale 0-10).
OR: crude Odds Ratio; aOR: adjusted Odds Ratio; CI: Confidence Interval; MSM: men who has sex with men; CD4+: T–lymphocyte cell bearing CD4+ receptor
*Significant at 5% level

5 Discussion

This is to our knowledge the first Norwegian study on HIV-related fatigue. Using FQ, the prevalence of fatigue among PLWH in Northern and Southern Norway is 38.5%. The strongest predictors of fatigue are mental distress and bodily pain. Other significant predictors are living alone, trouble sleeping and multimorbidity.

5.1 Prevalence of fatigue

A fatigue prevalence of 38.5% among PLWH is in the low range of previously reported study findings (Jong et al., 2010). This may be explained by free access to high quality health care services and other social support systems in Norway. In addition, this study was not performed by self-referral as all the participants were recruited trough the hospitals, and a high response rate indicated that both the fatigued and the non-fatigued were included. It is expected that those excluded have a higher fatigue rate than the included since one of the exclusion criteria was severe mental disorders which are associated with fatigue. Only ten patients were excluded due to severe mental disorders or cognitive impairment and would therefore not make a large contribution to the fatigue prevalence if included. There is no indication that those who declined or otherwise did not participate were more fatigued than the included participants.

Fatigue is described as persisting in the literature (Pence et al., 2009), and a longitudinal study from 2014 showed little variability among the fatigued; those who entered the study most fatigued remain fatigued during the 3-year follow-up (Barroso et al., 2014). Long standing fatigue symptoms are also seen in our study as chronic fatigue was seen in 44% of all fatigued cases. The chronic fatigued had higher fatigue intensity than those fatigued less than six months; the CFS mean values increased with the duration of fatigue. This indicates a higher intensity of fatigue with time, which is consistent with previous findings (Barroso et al., 2014; Pence et al., 2009). Loge and colleagues (1998) assessed fatigue in the general Norwegian population in

1997, with the use of the same instrument as in our study (FQ) which makes it easier to compare the two studies. They found that 22% scored 4 or more on the FQ and 11% were chronically fatigued (n=2287), which is nearly half of what was found in our study (38.5% and 18%, respectively). Both the Norwegian general population and the Norwegian PLWH have fatigue prevalence in the low range of international studies, but fatigue among PLWH should still be recognised as a common and persisting symptom.

5.2 Demographic findings and predictors of fatigue

This study identified five significant predictors of fatigue; mental distress, bodily pain, living alone, trouble sleeping, and multimorbidity. The strongest predictors are mental distress due to high aOR compared with the other dichotomous variables, and bodily pain with a dose response for each increase in pain score. ORs obtained for continuous and dichotomous variables cannot be directly compared. However, due to the observed consistency throughout all the preliminary analyses, high ORs and the large impact on the final regression model, we recognise mental distress and bodily pain to be the strongest predictors of fatigue among PLWH.

Mental distress is depression and anxiety symptoms measured with the HSCL-25. Higher mean scores were seen for both the anxiety and the depression values in Table 2. The mean depression value was higher than the mean anxiety value, but it is not possible to say whether it is anxiety or depression that is most related to fatigue since the two symptoms often are present in the same individual. A strong relationship between mental distress and fatigue is in accordance with previous findings (Barroso et al., 2010; Jong et al., 2010; Barroso and Voss, 2013). Mental distress is a common symptom as nearly 1/3 of all participants and 2/3 of the fatigued participants had symptoms of anxiety and depression. However, higher depression rates have been found in international studies (Noh et al., 2012; Whetten, 2008; Rodkjaer et al., 2010). A Danish study found that 38% had BDI-II score >14 (n=207) (Rodkjaer et. al., 2010). Our study found that 24% had a BDI-II score >14. This lower depression prevalence mirrors the lower

fatigue prevalence which already is discussed. PLWH have often experienced traumatic events (Corless et al., 2013; Whetten, 2008). In our study all participants identified with PTSD had severe depression and fatigue, so there is a clear link between the three variables. It is not possible to establish any causality between fatigue and depression due to the cross-sectional study design. Fatigue can be both a cause and a symptom of depression at the same time. Barroso and colleagues (2010) demonstrated that changes in depression indicated changes in fatigue during a one-year follow-up, and that providing coping strategies for depression, better sleep hygiene and increased physical activity led to a decrease in fatigue intensity among PLWH (Barroso et al., 2010; Barroso et al., 2016). Identifying and treating depression are important when assessing fatigue treatment strategies.

Pain as a predictor for HIV-related fatigue has been less investigated than depression, and was one of the factors warranted for further research by Loades and Kagee (2017). Wilson (2016) identified muscle aches/joint pain (and sleep difficulty), as the most prevalent and most bothersome symptoms among PLWH, whereas abdominal pain and numbness/pain in the feet were less prevalent, but bothersome. The underlying causes for the experienced pain were not assessed in our study. Still, the association between fatigue and pain was so strong that pain should be used as a variable in future research on fatigue.

In our study, trouble sleeping was identified as a predictor of fatigue. The variable was based on one question, which gives little information about the type of difficulty the participants experienced, whether it was insomnia and/or sleep insufficient from reduced quantity or quality of sleep. There are many causes and consequences of sleep disturbances, associations to psychiatric disorders, use of ART, pain and several medical conditions are known (UptoDate, Chirelli, C., 2018). Future research with a validated instrument which assesses different aspects of sleep disturbance might give more information about the relationship between fatigue and type of sleep disturbance.

Multimorbidity was seen in only 13 fatigued cases. This is reflected in a large confidence interval, but the variable had an independent impact on the regression model and a lower p-value after adjustment. There are some uncertainties about this variable. The definitions of comorbidity and multimorbidity could have been done differently, but entering hepatitis and anaemia into comorbidity in the preliminary analysis did not change the result. Our study found that participants diagnosed with one other chronic disease were less fatigued, but two or more diseases were associated with fatigue. Corless and colleagues (2008) showed a relationship between the number of comorbidities and fatigue severity, but they included hepatitis and depression as comorbidities. Since depression is such a strong predictor of fatigue, including depression in the comorbidity variable, like in the previously mentioned study, would have changed the results of the comorbidity/multimorbidity variable in our study. The comorbidities chosen in our study are based on a review from Guaraldi and colleges (2014) on multimorbidity. They list anaemia as a comorbidity, but not hepatitis and depression. There is a large ongoing study in Denmark on HIV and comorbidities (Ronit et al., 2016) that might contribute to a standardisation of the comorbidity definitions in PLWH in the future.

Females are found to be more fatigued than men in the healthy population (Akerstedt et al., 2004; Engberg et al., 2017). In our study, males are more fatigued before adjustment, but after adjustment female predicted fatigue, although the results were non-significant. Gender differences were seen; males were older, more likely to have high education, live alone and be born in Norway. These are variables with high numbers of fatigued participants in the sociodemographic table. The prevalence of fatigue among MSM was high, and reporting MSM was significantly associated with fatigue in the univariate analysis. After adjusting for the other covariates, MSM was no longer significant. The MSMs were more likely to live alone, have high education and have mental distress than the mean, which all were adjusted for in the multivariate analysis. There are uncertainties about the number of MSM measured in this study,

and the number of MSM was low compared to the registered MSMs in MSIS. On one hand the Norwegian surveillance system reported a higher percentage of MSM, so it is likely that there are MSMs among the participants reporting "unknown" as transmission route and this could affect the prevalence of fatigued MSM in our study. On the other hand, the number of "unknown" was higher among the females than the males, indicating that many people do not know how they got HIV (or are reluctant to tell), not only the MSM. A question like: "Did you have sex with someone of your own sex, in the period of assumed HIV-transmission?" might have been a better measurement of MSM. Being MSM and HIV-positive is characterised as living with a double stigma; first that of being gay and then that of being HIV-positive (Gibbie et al., 2012). This double burden might explain the high prevalence of mental distress and fatigue displayed.

Low CD4+ counts are associated with high risk of opportunistic infections since the immune system is weakened. The relationship between CD4+ count and fatigue in our study goes toward a lower fatigue among those with high CD4+ count in the adjusted analysis, but the result was not significant. We did not establish any significant associations between any of the HIV-related factors and fatigue. International literature describe conflicting results concerning the associations between fatigue and time since diagnosis, CD4+ count and virus suppression (Jong et al., 2010).

Depression and sleep disturbance are associated with treatment failure (Huynh et al., 2013). Gay and colleagues (2011) list treatment of fatigue as a strategy to improve ART-adherence, and a systematic review from 2014 found a relationship between low ART-adherence and presence of fatigue. We found only a small difference in treatment failure in the fatigued group (5.5%) compared to the non-fatigued (6.0%), and we cannot conclude that fatigue is associated with poor ART-adherence. Possible explanations might be that our study population is well treated due to close follow-up by the health care system, combined with improvements in ART

the last years, such as less side-effects and easier complacence due to one tablet regimes. It is possible that fatigued patients would have had poorer adherence if they had to make a larger effort to access the medications.

Other studies have identified unemployment as a risk factor for fatigue. Disabled pensioners and unemployed were more fatigued than students and those who work full-time, but work status did not contribute to the regression model and our study was not able to establish any significant relationship between fatigue and any of the work status answers. The disabled pensioners were most fatigued, which can be explained by the same reason they became disabled, but these reasons are not known. There are social support systems in Norway for the unemployed and for disabled pensioners, but the amount of received payment is set based on previous income. Inadequate income has been associated with fatigue (Jong et al., 2010), but there was no information about income in this study, and such information might have contributed to a relationship between income, work status and fatigue. Work status was also linked to education. Only two participants with high education were unemployed. High education was associated with fatigue, but the association was not statistically significant. The opposite result was found in a study of the general Swedish population, where high education was associated with low fatigue intensity (Engberg et al., 2017). The correlation between high education, work status, native country and gender might influence the results for high education, especially since there was no adjustment for native country and work status in the multivariate analysis.

5.3 Strengths and limitations

The study had a cross-sectional design and it is therefore impossible to establish any causality between the presented predictors and the dependent variable. There were limitations to the number of variables which could be entered into the final regression model, as we had only 244 participants. Some estimates have large confidence intervals due to a small sample size. With

more participants and greater power, some variables, such as high education and drug abuse, might have become significant. To limit the risk of confounding, all the variables in the final regression model were adjusted for, and the variables were based on previous known confounders and predictors. Drug-abuse was the last variable to be removed from the final regression model and is therefore not adjusted for, but the removal did not change the result of the other predictors. Another potential confounder is physical activity, a variable associated with reduced fatigue (Webel et al., 2016; Barroso et al., 2016), but our survey did not include information about this variable.

The survey's strengths include the high response rate, few excluded participants and no missing variables in the regression. The inclusion of non-speaking Norwegians and people with poor reading and writing skills improves the external validity as the study sample is close to the target population. To avoid bias in translation for the non-Norwegian/English speaking participants, the interpreters had received the survey via mail in advance, and the same interpreters were used in both hospitals. The interviews were standardized, and the three nurses who performed the interviews were instructed to respond in the same manner if the participants wanted further explanations about the questions. Validated instruments were used when possible to increase the reliability and the possibility to compare the findings with existing literature. Questionnaires always introduce a risk of recall bias. Our questions were about events and symptoms in the last week, last month or last year. Most of them were about the last week, a relative short time period to remember. The only question related to events from more than a year ago was transmission route. The question yielded several answers in the category unknown.

The socio-demographic variables differed little between the two hospitals, and it is likely that the demographics reflect the situation in medium sized hospitals in Norway. The group of PLWH followed up in OUS has a larger percentage of MSM and injecting drug users than the

rest of Norway, and therefore the fatigue prevalence might be somewhat higher in that geographic area. However, the predictors should be similar in all parts of Norway since the symptoms that explain fatigue are the same. There are some uncertainties about the validity of the background prevalence, since the study was performed 20 years ago.

The results in this study are relevant to health care providers. Fatigue is a common symptom which is rarely addressed in the clinical daily routine. If fatigue and its predictors, like mental distress and bodily pain, are identified and addressed, it may improve the quality of life for the individual patient. More research on prevention and treatment strategies for fatigued PLWH is needed, and should be implemented in the daily clinical routines. Hopefully, the present study can improve the situation for this vulnerable patient group, which is subject to considerable international attention, but less research and focus in Norway.

6 Conclusion

Symptoms of fatigue are common among PLWH in Northern and Southern Norway. The prevalence of 38% is almost two times higher than the estimated prevalence in the general Norwegian population (22%). Fatigue intensity increases over time and is the most pronounced in the chronically fatigued. Since chronic fatigue is seen in 44% of the fatigued PLWH, fatigue must be recognised as a persisting symptom. In our study, mental distress, such as anxiety and depression, and bodily pain were identified as the strongest predictors of fatigue. Other significant predictors were trouble sleeping, living alone and multimorbidity. None of the HIV-related factors assessed were associated with fatigue, and we did not find poorer ART-adherence among fatigued participants. PLWH live longer due to highly effective ART, and improving their quality of life is important. If fatigue and its predictors, like mental distress and bodily pain, are identified and addressed, it may improve the quality of life for many. More research on prevention and treatment strategies for fatigued PLWH is needed, and should be implemented in the daily clinical routines.

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8 Appendix

Table 5: Duration of fatigue vs intensity of fatigue (N=244)

Duration of fatigue	Chalder fatigue scale bimodal score		
		Mean (SD)	Median
	N=244	3.17 (3.38)	2
0	150	0.78 (1.06)	0
<1 week	7	6.14 (1.86)	5
<3 months	25	6.68 (2.29)	6
3-6 months	14	7.07 (1.77)	7
>6 months	44	7.36 (1.99)	8
Missing	4	5.75 (2.06)	5.5

SD: standard deviation

Table 6: Work status vs fatigue and education (N=242)

		Chalder fatigue scale		Education	
Work status	**Total N=242**	**Non-fatigued N=150**	**Fatigued N=92**	**Low education N=142**	**High education N=102**
Full-time job	85	61	24	39	46
Student	27	21	6	15	12
Pensioner	15	9	6	6	9
Part-time job	10	8	2	8	2
Part-time job / Sick leave	3	3	0	2	1
Part-time job / Unemployed	10	4	6	7	3
Part-time job / Disabled pensioner	6	5	1	5	1
Sick leave	10	5	5	6	4
Unemployed	28	17	11	26	2
Medical rehabilitation	1	1	0	1	0
Occupational rehabilitation	17	5	12	9	8
Disabled pensioner	28	10	18	15	13
Maternity leave	2	1	1	1	1

Table 7: Transmission route by gender vs fatigue (N=244)

			Chalder fatigue scale	
Gender	**Transmission route**	**Total N=244**	**Non-fatigued N=150**	**Fatigued N=94**
Male	Heterosexual	44	30	14
	MSM	31	13	18
	Blood transfusion	5	3	3
	Needle sharing	1	0	1
	Unknown	49	28	21
	Total	**130**	**74**	**56**
Female	Heterosexual	53	32	21
	Blood transfusion	2	1	1
	Perinatal	1	1	0
	Unknown	58	42	16
	Total	**114**	**76**	**38**

Forespørsel om deltakelse i forskningsprosjektet:

"Psykisk helse og livskvalitet hos HIV positive i Norge og nordvest Russland"

Bakgrunn og hensikt
Dette er et spørsmål til deg om å delta i en forskningsstudie for å undersøke psykisk helse og livskvalitet blant HIV positive pasienter ved infeksjonsmedisinsk poliklinikk ved Sørlandet Sykehus (SSHF), Universitetssykehuset i Nord Norge (UNN), HIV sentrene i Murmansk og Arkhangelsk. Man vet lite om hvordan dette er blant HIV positive i Norge og nordvest Russland. Dette vil være et supplement til de undersøkelser du allerede får. Vi ønsker å undersøke dette for å bidra til at de som trenger ekstra oppfølging vil få dette.

Hva innebærer studien?
Du vil i tillegg til de vanlige undersøkelser som er rutine ved HIV poliklinikken, bli intervjuet av en av de faste helsearbeiderene ved poliklinikken. Det er en kartlegging som består av intervju ved bruk av flere kartleggingsskjema som vil gi informasjon om din psykiske helse og forhold knyttet til denne. Dersom vi finner at det er behov for ekstra oppfølging vil det bli tatt initiativ til dette. Du vil få dette i tillegg til den vanlige medisinske behandling ved poliklinikken som vil fortsette som ellers.

Mulige fordeler og ulemper
Vi håper du vil oppleve kartleggingen som en mulighet til økt oppmerksomhet. Du vil hvis det avdekkes behov for oppfølging få henvisning til mer helsehjelp enn tilfellet er i dag.

Hva skjer med informasjonen om deg?
Informasjonen vil være en del av din journal så du kan få rett behandling og vil være omfattet av samme taushetsplikt som annen journalinformasjon. Videre tiltak utløst av funn vil kun bli gjort med din tillatelse i tilfelle behov for viderehenvisning.

Informasjonen som registreres om deg skal brukes slik som beskrevet i hensikten med studien.
Det vil ikke være mulig å identifisere deg i resultatene av studien når disse publiseres.

Alle opplysningene fra din journal som blir benyttet til forskning, vil bli behandlet uten navn og fødselsnummer eller andre direkte gjenkjennende opplysninger. En kode knytter deg til dine opplysninger og prøver gjennom en navneliste. Det er kun autorisert personell knyttet til prosjektet som har adgang til navnelisten og som kan finne tilbake til deg.

Frivillig deltakelse
Det er frivillig å delta i studien. Du kan når som helst og uten å oppgi noen grunn trekke ditt samtykke til å delta i studien. Dette vil ikke få konsekvenser for din videre behandling. Dersom du ønsker å delta, undertegner du samtykkeerklæringen på siste side. Om du nå sier ja til å delta, kan du senere trekke tilbake ditt samtykke uten at det påvirker din øvrige behandling. Dersom du senere ønsker å trekke deg eller har spørsmål til studien, kan du kontakte Seksjonsoverlege Vegard Skogen UNN 77669022 / 07766, Avdelingsoverlege Ole Gunnar Rysstad SSHF 38073000, sjefslege Vjavheslav Zinevich HIV senteret i Murmansk eller sjefslege Jelena Popova HIV senteret i Arkhangelsk

Ytterligere informasjon om studien finnes i kapittel *A* – *utdypende forklaring av hva studien innebærer.*
Ytterligere informasjon om biobank, personvern og forsikring finnes i kapittel B – *Personvern, økonomi og forsikring.*

Samtykkeerklæring følger etter kapittel B.

Kapittel A- utdypende forklaring av hva studien innebærer

- Kriterier for deltakelse:
  Alle HIV positive pasienter over 18 år som følges ved SSHF, UNN og HIV sentrene i Murmansk og Arkhangelsk blir invitert inn i studien
- Bakgrunnsinformasjon om studien:
  Det er liten kunnskap om psykisk helse og livskvalitet blant HIV positive pasienter i Norge. Nyere internasjonal forskning har pekt på behov for økt oppmerksomhet om dette for å bidra til bedre oppfølging og behandling av pasientene.
- Undersøkelser, blodprøver og annet den inkluderte må gjennom:
  Kartlegging i løpet av en konsultasjon hvor det brukes internasjonalt anerkjente kartleggingsskjemaer
- Tidsskjema – hva skjer og når skjer det?
  Kartlegging vil skje parallelt med de oppsatte konsultasjoner for HIV sykdommen.
- Mulige fordeler:
  Behov for oppfølging vil bli avdekket gjennom kartleggingen og tiltak iverksatt som følge av dette
- Mulige bivirkninger:
  Ingen
- Mulige ubehag/ulemper:
  Ingen
- Pasientens/studiedeltakerens ansvar:
  Ingen utover å møte avtalte kontroller
- Pasienten/studiedeltakeren vil bli fortløpende oppdatert om funn og orientert om evt. behov for oppfølgning

Kapittel B - Personvern, biobank, økonomi og forsikring

Personvern
Opplysninger som registreres om deg er del av din vanlige journal ved ditt sykehus. Ved UNN vil de aktuelle data også lagres i en allerede etablert og godkjent forskningdatabase. Dataene er der anonymisert. Ved SSHF vil kun de data som brukes til forskning være anonymisert.
Alle som får innsyn har taushetsplikt.

SSHF og UNN ved administrerende direktør er databehandlingsansvarlig. Data lagres etter gjeldende regler i Russland.

Rett til innsyn og sletting av opplysninger om deg og sletting av prøver
Hvis du sier ja til å delta i studien, har du rett til å få innsyn i hvilke opplysninger som er registrert om deg. Du har videre rett til å få korrigert eventuelle feil i de opplysningene vi har registrert. Dersom du trekker deg fra studien, kan du kreve å få slettet de anonymiserte data om innsamlede prøver og opplysninger, med mindre opplysningene allerede er inngått i analyser eller brukt i vitenskapelige publikasjoner.

Økonomi
Studien vil være ledd i en vanlig klinisk oppfølgning av HIV positive pasienter ved UNN, SSHF og HIV sentrene i Murmansk og Arkhangelsk.
Databehandling og bearbeiding vil bli søkt finansiert gjennom forskningsmidler fra Helsedirektorat, Helse Nord, Helse Sør Øst, HOD og andre tilsvarende finanseiringskilder.

Forsikring

Ingen annen forsikring utover det som er omfattet i pasientrettighetene er nødvendig.

Informasjon om utfallet av studien
Deltakerne har rett til å få informasjon om utfallet/resultatet av studien.

Samtykke til deltakelse i studien

Jeg er villig til å delta i studien

(Signert av prosjektdeltaker, dato)

Jeg bekrefter å ha gitt informasjon om studien

(Signert, rolle i studien, dato)

Sjekkliste studievariabler

Dato:

		Svar
Nummer		
Kjønn		
Fedreland		
Statsborgerskap		
	Asylsøker	
	Flyktning med opphold	
	Innvandrer -ikke vestlig	
	Innvandrer -vestlig	
	Statsborgerskap	
Sivilstand		
	Enslig	
	Gift	
	Samboer	
	Skilt	
	Enke(mann)	
Utdannelse	Antall år	
Arbeidsforhold		
	Jobb; fulltid -deltid	
	Sykemeldt	
	Medisinsk rehabilitert	
	Arbeidavklaringspenger	
	Arbeidsledig	
	Uføretrygdet	
	Pensjonert	
	Student	
	Fødselspermisjon	
	Pappapermisjon	
	Jobb deltid -sykemeldt	
	Jobb deltid -arbeidsledig	
	Jobb deltid -uføretrygdet	

Mentalhelse og mestring		
Henvist til psykiatrisk behandling	JA	NEI
Har/har hatt psykiatrisk behandling	JA	NEI
Har læring- og mestringskurs	JA	NEI
Har individuellplan	JA	NEI
Har barn	JA	NEI
Hvis ja_Bor med egne barn	JA	NEI
Informert sine nærmeste om diagnosen	JA	NEI
Åpen om sin diagnose	JA	NEI
Røyker	ja	nei

Smittemåte _____

Heteroseksuell	
Homoseksuell/MSM	
Sprøytemisbruk	
Blodtransfusjon	
Medfødt	
Ukjent	

Hentes fra DIPS

T4
HIV-RNA
Hb
Na
K
Ca
PTH
kreatinin
vit-D 25-OH
ASAT
ALAT
T8-celler
hepatitt C antistoff
hepatitt B surface antigen

Nåværende med.

Startdato

Tidligere med

Resistens	**Kryss**
Anivirale komb	
Proteasehemmere	
NRTI	
NNRTI	
Andre antivirale midler	
Integrasehemmere	
Ingen resistens påvist	

CDC

Kategori A
Kategori B
Kategori C

Komorbiditet

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 rundt aktuelt tall for hver plage/hvert symptom.

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

HSCL-25

- Derogatis LR, Lipman RS, Rickels K, Uhlenhuth EH, Covi L. The Hopkins Symptom Checklist (HSCL): a self-report symptom inventory. Behav Sci. 1974 Jan;19(1):1-15.

Forskningsenhet for kontrollerte kliniske forsøk i nasjonalt ryggnettverk

PTSS-16

De følgende spørsmålene handler om symptomer som folk kan ha etter skremmende og voldsomme begivenheter. Nå stiller vi deg noen spørsmål om slike symptomer. Kan du si hvor mye du selv har vært plaget av slike symptomer i den siste uken?

	Aldri	Av og til	Ofte	Alltid/for det meste
1. Tilbakevendende tanker eller minner om de skremmende og voldsomme hendelsene?	0	1	2	3
2. Følt som om du opplever hendelsen igjen?	0	1	2	3
3. Tilbakevendende mareritt om begivenhetene?	0	1	2	3
4. Føler deg isolert fra andre mennesker?	0	1	2	3
5. Er ute av stand til å føle noe ordentlig?	0	1	2	3
6. Blir lett forskrekket, spesielt skvetten?	0	1	2	3
7. Har vanskeligheter med å konsentrere deg	0	1	2	3
8. Har søvnproblemer?	0	1	2	3
9. Føler at du er på vakt?	0	1	2	3
10. Føler deg irritabel eller blir fort sint?	0	1	2	3
11. Unngår aktiviteter som minner deg om de ubehagelige og voldsomme hendelsene?	0	1	2	3
12. Vært ute av stand til å huske deler av de voldsomme hendelsene?	0	1	2	3
13. Vært mindre interessert I dagligdagse aktiviteter?	0	1	2	3
14. Føler som om du ikke har noen fremtid?	0	1	2	3
15. Unngår tanker og følelser som er forbundet med de ubehagelige og voldsomme hendelsene?	0	1	2	3
16. Hatt plutselige følelsesmessige eller kroppslige reaksjoner når du blir minnet om det som skjedde?	0	1	2	3

Raphael B, Lundin T, Weisaeth L. A research method for the study of psychological and psychiatric aspects of disaster. Acta Psychiatr Scand Suppl 1989; 353: 1 – 75.

Tretthet (Fatigue)

Vi vil gjerne vite om du har følt deg sliten, svak eller i mangel av overskudd den siste måneden. Vennligst besvar ALLE spørsmålene ved å krysse av for det svaret du synes passer best for deg. Vi ønsker at du besvarer alle spørsmålene selv om du ikke har hatt slike problemer. Vi spør om hvordan du har følt deg i det siste og ikke om hvordan du følte deg for lenge siden. Hvis du har følt deg sliten lenge, ber vi om at du sammenlikner deg med hvordan du følte deg sist du var bra. (Ett kryss for hver linje)

1. Har du problemer med at du føler deg sliten?
☐ Mindre enn vanlig ☐ Ikke mer enn vanlig ☐ Mer enn vanlig ☐ Mye mer enn vanlig

2. Trenger du mer hvile?
☐ Nei, mindre enn vanlig ☐ Ikke mer enn vanlig ☐ Mer enn vanlig ☐ Mye mer enn vanlig

3. Føler du deg søvnig eller døsig?
☐ Mindre enn vanlig ☐ Ikke mer enn vanlig ☐ Mer enn vanlig ☐ Mye mer enn vanlig

4. Har du problemer med å komme i gang med ting?
☐ Mindre enn vanlig ☐ Ikke mer enn vanlig ☐ Mer enn vanlig ☐ Mye mer enn vanlig

5. Mangler du overskudd?
☐ Ikke i det hele tatt ☐ Ikke mer enn vanlig ☐ Mer enn vanlig ☐ Mye mer enn vanlig

6. Har du redusert styrke i musklene dine?
☐ Ikke i det hele tatt ☐ Ikke mer enn vanlig ☐ Mer enn vanlig ☐ Mye mer enn vanlig

7. Føler du deg svak?
☐ Mindre enn vanlig ☐ Som vanlig ☐ Mer enn vanlig ☐ Mye mer enn vanlig

8. Har du vansker med å konsentrere deg?
☐ Mindre enn vanlig ☐ Som vanlig ☐ Mer enn vanlig ☐ Mye mer enn vanlig

9. Forsnakker du deg i samtaler?
☐ Mindre enn vanlig ☐ Ikke mer enn vanlig ☐ Mer enn vanlig ☐ Mye mer enn vanlig

10. Er det vanskeligere å finne det rette ordet?
☐ Mindre enn vanlig ☐ Ikke mer enn vanlig ☐ Mer enn vanlig ☐ Mye mer enn vanlig

11. Hvordan er hukommelsen din?
☐ Bedre enn vanlig ☐ Ikke verre enn vanlig ☐ Verre enn vanlig ☐ Mye verre enn vanlig

12. Hvis du føler deg sliten for tiden, omtrent hvor lenge har det vart? (Ett kryss)
☐ Mindre enn en uke
☐ Mindre enn tre måneder
☐ Mellom tre og seks måneder
☐ Seks måneder eller mer

13. Hvis du føler deg sliten for tiden, omtrent hvor mye av tiden kjenner du det? (Ett kryss)
☐ 25 % av tiden
☐ 50 % av tiden
☐ 75 % av tiden
☐ Hele tiden

T. Chalder, G. Berelowitz, T. Pawlikowska, L. Watts, S. Wessely, D. Wright, and E. P. Wallace. Development of a fatigue scale. J.Psychosom.Res. 37 (2):147-153, 1993.

SF-36

INSTRUKSJON: Dette sporreskjemaet handler 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 gjennomfore dine daglige gjoremål.

Hvert sporsmål skal besvares ved å sette en ring rundt det tallet 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 din helse er:

(sett ring rundt ett tall)

Utmerket	1
Meget god	2
God	3
Nokså god	4
Dårlig	5

2. Sammenliknet med for ett år siden, hvordan vil du si at din helse stort sett er nå?

(sett ring rundt ett tall)

Mye bedre nå enn for ett år siden	1
Litt bedre nå enn for ett år siden	2
Omtrent den samme som for ett år siden	3
Litt dårligere nå enn for ett år siden	4
Mye dårligere nå enn for ett år siden	5

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

(sett ring rundt ett tall på hver linje)

AKTIVITETER	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 en 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 dine daglige gjøremål på grunn av din fysiske helse?

(sett ring rundt ett tall på hver linje)

	JA	NEI
a. Du har måttet **redusere tiden** du har brukt på arbeid eller på andre gjøremål	1	2
b. Du har **utrettet mindre** enn du hadde ønsket	1	2
c. Du har vært hindret i å utføre **visse typer** arbeid eller gjøremål	1	2
d. Du har hatt **problemer** med å gjennomføre arbeidet eller andre gjøremål (for eksempel fordi det krevde ekstra anstrengelser)	1	2

5. I løpet av de siste 4 ukene, har du hatt noen av følgende problemer i ditt arbeid eller i andre dine daglige gjøremål på grunn av følelsesmessige problemer (som for eksempel å være deprimert eller engstelig)?

(sett ring rundt ett tall på hver linje)

	JA	NEI
a. Du har måttet **redusere tiden** du har brukt på arbeid eller på andre gjøremål	1	2
b. Du har **utrettet mindre** enn du hadde ønsket	1	2
c. Du har utført arbeidet eller andre gjøremål **mindre grundig** enn vanlig	1	2

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

(sett ring rundt ett tall)

Ikke i det hele tatt	1
Litt	2
En del	3
Mye	4
Svært mye	5

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

(sett ring rundt ett tall)

Ingen	1
Meget svake	2
Svake	3
Moderate	4
Sterke	5
Meget sterke	6

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

(sett ring rundt ett tall)

Ikke i det hele tatt	1
Litt	2
En del	3
Mye	4
Svært mye	5

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:

(sett ring rundt ett tall på hver linje)

	Hele tiden	Nesten 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.)?

(sett ring rundt ett tall)

Hele tiden	1
Nesten hele tiden	2
En del av tiden	3
Litt av tiden	4
Ikke i det hele tatt	5

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

(sett ring rundt ett tall på hver linje)

	Helt riktig	Delvis riktig	Vet ikke	Delvis gal	Helt gal
a. Det viker som jeg blir syk litt lettere enn andre	1	2	3	4	5
b. Jeg er like frisk som de fleste jeg kjenner	1	2	3	4	5
c. Jeg tror at helsen min vil forverres	1	2	3	4	5
d. Jeg har utmerket helse	1	2	3	4	5

AUDIT

Alcohol Use Disorder Identification Test

Babor TF, Higgins-Biddle JC, Saunders JB, Monteiro MG. Audit. The Alcohol Use Disorder Identification Test. Guidelines for Use in Primary Care. World Health Organization, 2001.

Mann ○ Kvinne ○ Alder: _____ Dato: _____

1	Hvor ofte drikker du alkohol?	Aldri	1 gang i måneden eller sjeldnere	2-4 ganger i måneden	2-3 ganger i uken	4 ganger i uken eller mer
2	Hvor mange alkoholenheter tar du på en 'typisk' drikkedag?	1-2	3-4	5-6	7-9	10 eller flere
3	Hvor ofte drikker du seks alkoholenheter eller mer?	Aldri	Sjelden	Noen ganger i måneden	Noen ganger i uken	Nesten daglig
4	Hvor ofte i løpet av siste året var du ikke i stand til å stoppe å drikke etter at du hadde begynt?	Aldri	Sjelden	Noen ganger i måneden	Noen ganger i uken	Nesten daglig
5	Hvor ofte i løpet av siste året unnlot du å gjøre ting du skulle ha gjort pga. drikking?	Aldri	Sjelden	Noen ganger i måneden	Noen ganger i uken	Nesten daglig
6	Hvor ofte starter du dagen din med alkohol?	Aldri	Sjelden	Noen ganger i måneden	Noen ganger i uken	Nesten daglig
7	Hvor ofte i løpet av det siste året har du hatt skyldfølelse pga. drikking?	Aldri	Sjelden	Noen ganger i måneden	Noen ganger i uken	Nesten daglig
8	Hvor ofte i løpet av det siste året har det vært umulig å huske hva som hendte kvelden før pga drikking?	Aldri	Sjelden	Noen ganger i måneden	Noen ganger i uken	Nesten daglig
9	Har du eller andre blitt skadet som følge av at du har drukket?	Nei		Ja, men ikke i løpet av det siste året		Ja, i løpet av det siste året
10	Har en slektning, venn eller lege bekymret seg over drikkingen din, eller antydet at du bør redusere?	Nei		Ja, men ikke i løpet av det siste året		Ja, i løpet av det siste året

DUDIT

Drug Use Disorder Identification Test

2002 Anne H. Berman, Hans Bergman, Tom Palmstierna & Frans Schlyter V2.1

Mann ○ Kvinne ○ Alder: _____ Hovedrusmiddel: _____ Dato: _____

1 Hvor ofte bruker du andre rusmidler enn alkohol?	Aldri ○	1 gang i måneden eller sjeldnere ○	2-4 ganger i måneden ○	2-3 ganger i uken ○	4 ganger i uken eller mer ○
2 Bruker du flere enn ett rusmiddel ved ett og samme tilfelle?	Aldri ○	1 gang i måneden eller sjeldnere ○	2-4 ganger i måneden ○	2-3 ganger i uken ○	4 ganger i uken eller mer ○
3 Hvor mange ganger i løpet av en typisk dag tar du stoff/legemidler, når du tar rusmidler?	0 ○	1-2 ○	3-4 ○	5-6 ○	7 eller flere ○
4 Hvor ofte blir du kraftig påvirket av rusmidler?	Aldri ○	Sjeldnere enn en gang i måneden ○	Hver måned ○	Hver uke ○	Daglig eller nesten hver dag ○
5 Har du det siste året opplevd at lengselen etter rusmidler har vært så sterk at du ikke kunne stå imot?	Aldri ○	Sjeldnere enn en gang i måneden ○	Hver måned ○	Hver uke ○	Daglig eller nesten hver dag ○
6 Har det hendt at du i løpet av det siste året ikke kunne slutte å ta rusmidler når du først hadde begynt?	Aldri ○	Sjeldnere enn en gang i måneden ○	Hver måned ○	Hver uke ○	Daglig eller nesten hver dag ○
7 Hvor ofte i løpet av det siste året har du tatt rusmidler og så latt være å gjøre noe som du burde ha gjort?	Aldri ○	Sjeldnere enn en gang i måneden ○	Hver måned ○	Hver uke ○	Daglig eller nesten hver dag ○
8 Hvor ofte i løpet av det siste året har du hatt behov for å starte dagen med å ta rusmidler etter stort inntak dagen før?	Aldri ○	Sjeldnere enn en gang i måneden ○	Hver måned ○	Hver uke ○	Daglig eller nesten hver dag ○
9 Hvor ofte i løpet av det siste året har du hatt skyldfølelse eller dårlig samvittighet fordi du har brukt rusmidler?	Aldri ○	Sjeldnere enn en gang i måneden ○	Hver måned ○	Hver uke ○	Daglig eller nesten hver dag ○
10 Har du eller noen andre blitt skadet (psykisk eller fysisk) på grunn av din bruk av rusmidler?	Nei ○		Ja, men ikke i løpet av det siste året ○		Ja, i løpet av det siste året ○
11 Har en slektning eller venn, lege eller sykepleier, eller noen andre vært urolige for din bruk av rusmidler, eller sagt til deg at du bør slutte med rusmidler?	Nei ○		Ja, men ikke i løpet av det siste året ○		Ja, i løpet av det siste året ○

BDI-II

Velg det utsagnet i hver gruppe som best beskriver hvordan du har følt deg i løpet av de to siste ukene.

1.	0	Jeg føler meg ikke trist
	1	Jeg føler meg trist store deler av tiden
	2	Jeg føler meg trist hele tiden
	3	Jeg er så trist og ulykkelig at jeg ikke holder det ut
2.	0	Jeg er ikke motløs med tanke på fremtiden
	1	Jeg er mer motløs med tanke på fremtiden enn før
	2	Jeg forventer at ting ikke vil gå i orden for meg
	3	Jeg føler at fremtiden min er håpløs og at alt bare blir verre
3.	0	Jeg føler meg ikke mislykket
	1	Jeg har mislyktes mer enn jeg burde
	2	Når jeg ser tilbake ser jeg mange nederlag
	3	Jeg føler meg som en fullstendig mislykket person
4.	0	Jeg får like mye glede ut av ting jeg liker som før
	1	Jeg får ikke like mye glede ut av ting jeg liker som før
	2	Jeg får svært liten glede ut av de tingene som jeg pleide å like
	3	Jeg får ingen glede ut av de tingene jeg pleide å like
5.	0	Jeg føler ikke særlig mye skyld
	1	Jeg føler skyld for mange ting jeg har gjort eller burde gjøre
	2	Jeg føler skyld mesteparten av tiden
	3	Jeg føler skyld hele tiden
6.	0	Jeg føler ikke at jeg blir straffet
	1	Jeg føler det som om jeg kan bli straffet
	2	Jeg forventer å bli straffet
	3	Jeg føler det som om jeg blir straffet
7.	0	Mitt selvbilde er uforandret
	1	Jeg har fått mindre selvtillit
	2	Jeg er skuffet over meg selv
	3	Jeg misliker meg selv
8.	0	Jeg kritiserer eller bebreider ikke meg selv mer enn vanlig
	1	Jeg kritiserer meg selv mer enn jeg pleide
	2	Jeg kritiserer meg selv for alle mine feil
	3	Jeg klandrer meg selv alt leit som skjer
9.	0	Jeg har ingen tanker om å ta livet mitt
	1	Jeg har tanker om å ta livet mitt, men kommer ikke til å gjøre det
	2	Jeg ønsker å ta livet mitt
	3	Jeg ville tatt livet mitt hvis jeg fikk mulighet til det
10.	0	Jeg gråter ikke mer enn før
	1	Jeg gråter mer enn før
	2	Jeg gråter for hver minste ting
	3	Jeg ønsker å gråte men klarer det ikke
11.	0	Jeg er ikke mer urolig eller rastløs enn vanlig
	1	Jeg føler meg mer rastløs eller urolig enn vanlig
	2	Jeg er så urolig og rastløs at det er vanskelig å være i ro
	3	Jeg er så urolig og rastløs at jeg må bevege meg eller gjøre noe hele tiden

12.	0	Jeg har ikke mistet interessen for andre mennesker eller aktiviteter
	1	Jeg er mindre interessert i andre mennesker eller ting enn tidligere
	2	Jeg har mistet det meste av interesse for andre mennesker eller ting
	3	Det er vanskelig å bli interessert i noe som helst
13.	0	Jeg tar beslutninger like lett som før
	1	Jeg synes det er vanskeligere å ta beslutninger
	2	Jeg har mye større vanskeligheter med å ta beslutninger enn før
	3	Jeg har vanskeligheter med å ta enhver beslutning
14.	0	Jeg føler meg ikke verdiløs
	1	Jeg opplever meg ikke like verdifull og nyttig som før
	2	Jeg føler meg mer verdiløs enn andre mennesker
	3	Jeg føler meg fullstendig verdiløs
15.	0	Jeg har like mye energi som før
	1	Jeg har mindre energi enn jeg pleide
	2	Jeg har ikke nok energi til å gjøre særlig mye
	3	Jeg har ikke nok energi til å gjøre noe som helst
13.	A	Jeg har ikke merket noen endringer i søvnen min
	B	Jeg sover litt mer enn vanlig
	C	Jeg sover litt mindre enn vanlig
	D	Jeg sover mye mer enn vanlig
	E	Jeg sover mye mindre enn vanlig
	F	Jeg sover mesteparten av døgnet
	G	Jeg våkner 2 timer for tidlig og får ikke sove igjen
17.	0	Jeg er ikke mer irritabel enn vanlig
	1	Jeg er mer irritert enn vanlig
	2	Jeg er mye mer irritabel enn vanlig
	3	Jeg er irritabel hele tiden
18.	A	Jeg har ikke merket noen endringer i min matlyst
	B	Min matlyst er litt mindre enn vanlig
	C	Min matlyst er litt større enn vanlig
	D	Min matlyst er mye mindre enn vanlig
	E	Min matlyst er mye større enn vanlig
	F	Jeg har ingen matlyst i det hele tatt
	G	Jeg føler trang til å spise hele tiden
19.	0	Jeg kan konsentrere meg like bra som før
	1	Jeg kan ikke konsentrere meg like godt som før
	2	Jeg har vanskelig for å konsentrere meg
	3	Jeg merker at jeg ikke kan konsentrere meg om noe som helst
20.	0	Jeg er ikke mer trøtt eller utmattet enn tidligere
	1	Jeg blir fortere trøtt eller utmattet enn jeg pleier
	2	Jeg er for trøtt eller utmattet til å gjøre mange av de tingene jeg pleide å gjøre
	3	Jeg er for trøtt eller utmattet til å gjøre mesteparten av de tingene jeg pleide å gjøre
21.	0	Jeg har ikke merket noen endringer i min interesse for sex i det siste
	1	Jeg er mindre interessert i sex i det siste
	2	Jeg er mye mindre interessert i sex i det siste
	3	Jeg har mistet all interesse for sex