The relationship between cancer-related fatigue and the daily movement pattern among breast cancer patients

-A cross-sectional study

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Abstract

Aim
The aim of this study is to examine the relationship between cancer-related fatigue and the daily movement pattern in breast cancer patients. The purpose was driven by the research questions: Are there independent relationships between low and moderate-to-vigorous physical activity with cancer-related fatigue? Are there independent relationships between total sedentary behavior, breaks in sedentary and prolonged sedentary time with cancer-related fatigue?

Method
This is a cross-sectional study containing data from a larger, intervention study ("OptiTrain"), which included 240 breast cancer patients. 124 of those 240 were included in this study. Patients self-reported cancer-related fatigue and wore a GT3X+ accelerometer for seven days to measure physical activity as well as sedentary behavior. Data was analysed through binary correlation, one-way ANOVA, Bonferroni Post Hoc test and logistic regression modeling.

Results
A weak, positive correlation was found between cancer-related fatigue and both sedentary time ($r_s= .237$, $p = .008$) and sedentary bouts ($r_s= .177$, $p = .05$). A weak, negative correlation was found between cancer-related fatigue and low-intensity physical activity ($r_s= -.207$, $p = .021$). Statistically significant differences were found between fatigue groups and sedentary time ($p=.013$), low-intensity physical activity ($p=.002$) and sedentary breaks ($p=.040$). Higher tertile of percentage of daily wear time spent sedentary was associated with significantly higher odds ratio of moderate/severe cancer-related fatigue; Odds ratio=9.52 (95% CI 2.69-33.72) for high vs. low tertile, and odds ratio=6.12 (1.85-20.22) for medium vs. low tertiles, after adjustment for potential confounders. Also, high percentage of daily wear time spent in moderate-to-vigorous physical activity induced a higher odds ratio for moderate/severe cancer-related fatigue; 3.76
(1.05-13.43) compared to low. A borderline positive association was found between high number of prolonged sedentary bouts per day and cancer-related fatigue.

**Conclusion**

As survivorship increases, it is important for cancer patients to continue important daily habits in order to return to normal life after treatment. Increasing low-intensity physical activity and reducing total sedentary time as well as sedentary bouts may reduce cancer-related fatigue in breast cancer patients.
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1 Background

In 2014, over 64,000 cases of cancer were diagnosed in Sweden with 48% of the diagnoses being women. Breast cancer is the most common type of cancer among women. 31% of all female cancer diagnosis is breast cancer. In Sweden, over 9,000 women were diagnosed with breast cancer in the year 2014. Breast cancer has had an average annual increase of cases of 1.4% in the last 20 years with a 10-year survival rate of 83.5% (Socialstyrelsen 2014-12-26). Five-year survival rates have steadily increased over the past 40 years due to early detection as well as aggressive and successful treatments for each patient (Brown et al., 2012).

Treatment for breast cancer can include many different combinations, depending on the stage and type of the cancer. Local treatments include surgery and radiation therapy, which treat only the tumor and leave the rest of the body alone. These treatment types would be more suitable for a patient within an early stage of breast cancer. Systemic therapies can reach a cancer cell anywhere in the body and include chemotherapy, hormone therapy and targeted therapy and can be used for more advanced stages of breast cancer (American Cancer Society, 2017).

1.1 Cancer-related fatigue

Many side effects come with a breast cancer diagnosis and treatment. Side effects most reported during chemotherapy treatment include fatigue, nausea, joint and muscle pain, anxiety, depression and sleeping problems (Backman et al., 2016). Cancer-related fatigue (CRF) is considered to be the most common side-effect of cancer that negatively affects the quality of life of those diagnosed. One way to describe CRF is as a distressing, persistent, subjective sense of physical, emotional and/or cognitive tiredness or exhaustion related to cancer or cancer treatment that is not proportional to recent activity and interferes with usual functioning (Berger et al., 2015). The origins of CRF are not entirely understood but previous research points to many contributing factors (LaVoy et al., 2016). CRF is not a normal type of fatigue that can be fixed with sleep or rest. It is an ongoing, daily fatigue that is not able to be resolved by any solution and is reported to be a symptom before, during and after treatment (Berger et al., 2015). This
makes CRF a side-effect of treatment that lasts much longer than other symptoms (Bennett et al., 2007), with 70%-100% of the cancer patient population affected (Cramp and Byron Daniel, 2012).

1.1.1 Methods to measure cancer-related fatigue
CRF can be difficult to measure because there is no agreed upon conceptual framework for which it can be measured and assessed universally (Berger et al. 2012). CRF is a symptom that is best subjectively measured. Physicians rely on patients to assess their own CRF using self-reports, considered to be the most accurate measure but can still pose a problem due to varying ideas of fatigue (Berger et al., 2015). Although there is no universal definition of CRF, most insinuate the multidimensional condition of fatigue. A self-report that questions all aspects of this symptom is therefore best for assessing. There are many assessments out there that differ by the number of questions, the way they are constructed and in the type of scale used (Wang and Woodruff, 2015). The Piper Fatigue Scale is a subjective questionnaire that uses four dimensions to assess fatigue. This scale has been constructed from the theoretical framework, The Integrated Fatigue Model, and uses both objective and subjective factors to assess fatigue (Jakobsson et al., 2013). The Revised Piper Fatigue Scale was constructed to shorten down the amount of questions of the original questionnaire. This scale has also been used previously with breast cancer patients and has found to be both reliable and valid (Battaglini et al., 2014; Canário et al., 2016; Jakobsson et al., 2013).

1.2 The daily movement pattern
The daily movement pattern of an individual consists of sedentary (SED) behaviors as well as physical activity (PA) of different intensities, often defined as low-intensity physical activity (LIPA) and moderate-to-vigorous physical activity (MVPA). Research in the recent years has found that SED behavior can still be dangerous for active people who meet the PA recommendations (Lee & Shiroma, 2014), showing that both ends of the movement spectrum need to be independently analysed (Broderick et al., 2013).
1.2.1 Physical Activity
PA can be defined as any bodily movement done by skeletal muscles that produces energy expenditure (Shephard & Balady, 1999). These can be done while you are working, at your home, during your commute or during planned exercise (Mattsson et al., 2014). All of these movements or lack of, add up to the total daily movement pattern. The energy cost and intensity of these movement patterns are expressed and defined using the unit, metabolic equivalents (METs). LIPA is defined as less than 3 METs. Moderate activity is defined between 3-6 METS while vigorous activity is greater than 6 METs (Ainsworth et al., 1993). After diagnosis, cancer patients tend to decrease the amount of daily PA. Irwin and colleagues (2003) found a decrease of 2 hours a week of total PA from pre- to post- diagnosis in breast cancer patients.

1.2.2 Methods to measure physical activity
Previous research has chosen to use both subjective and objective methods to measure daily movement. Self-reports such as questionnaires or logbooks have been the most common form of measurement. These may be convenient but have shown that cancer patients tend to overestimate the amount of PA completed. It has been found that the outcome from objective measurements cannot be used interchangeably with the outcome from subjective measurements (Mazzoni et al., 2017; Hagstromer et al. 2010). Due to the cognitive impairments that can occur in cancer patients, self-reporting may not be the best way to measure PA (Wefel et al., 2004). Objective methods such as accelerometers therefore have become widely used to measure PA. Accelerometers measure acceleration of the body, with some of the newer models able to obtain triaxial data. The ActiGraph G3TX+ is a commonly used accelerometer that also contains an inclinometer (Troiano et al., 2008). The ActiGraph takes acceleration measurements from three different axes, X-, Y- and Z-, in three different planes- horizontal, vertical and lateral.

1.2.3 Sedentary Behavior
SED behavior is also an important pattern that should be analysed, defined as less than 1.5 METs. Cancer patients have been found to be SED for 70% of their day up to two weeks after treatments, even after the seven-day period when acute side effects of chemotherapy disappear
(Tonosaki and Ishikawa, 2014). Previous research shows that a SED lifestyle can have negative effects on quality of life in cancer survivors as well (George et al., 2014, Lynch 2010).

Total SED time is not the only SED behavior that should be analysed for cancer patients and survivors. The amount of breaks from sitting have been shown to have a positive influence on metabolic health (Healy et al., 2011). Prolonged sitting, analysed as SED bouts that occur (> 20 minutes of continuous sitting), has been shown to negatively influence quality of life in breast cancer survivors (Hartman et al., 2017) and different metabolic aspects in healthy adults (Ekblom et al., 2015).

1.2.4 Methods to measure sedentary behavior

Subjective methods such as logbooks and questionnaires have been the most common way to measure SED behavior. Mazzoni and colleagues (2017) have found that cancer patients tend to underestimate the amount of SED behavior making subjective measurements not as reliable as objective measurements and that the outcomes from these two methods of measurement cannot be used interchangeably for SED behavior. The ActiGraph G3TX+ is the most commonly used accelerometer to measure SED behavior in studies with older adults (Van Cauwenberg et al., 2014).

1.3 Earlier research

Supervised exercise interventions have shown to reduce CRF in breast cancer survivors (Speck et al., 2010; Berger et al., 2012; Backman et al., 2016; Meneses-Echavez et al., 2015) as well as for breast cancer patients (Baruth et al., 2015; Battaglini et al., 2014; Backman et al., 2016).

However, there have been studies contradicting these findings. A meta-analysis consisting of 56 studies with both cancer patients and survivors found that aerobic exercise but not resistance exercise, significantly reduced fatigue (Cramp and Byron Daniel, 2012) while Courneya and colleagues, (2007) found no statistical significance between either aerobic or resistance exercise and CRF in a randomized control trial with breast cancer patients. Johnsson and colleagues (2016), found strong evidence in previous research that supports using supervised aerobic and resistance training to provide relief for CRF. They found a recommended amount of 150 minutes
a week of moderate intensity aerobic exercise or 75 minutes of high intensity aerobic exercise a week are recommended for adult patients with a cancer diagnosis as well as strength training 2-3 times per week.

In a cross-sectional study that measured breast cancer patients 2-10 weeks post-surgery, patients that reported more MVPA had less fatigue interference than those that reported less MVPA (Stagl et al., 2014). Woo-kyoung and colleagues (2017) found that 231 breast cancer survivors who were in the highest PA group in their cross-sectional study, had lower fatigue scores than the lowest PA group. Similar results were found by Canário and colleagues (2016) measuring breast cancer patients using a subjective PA measurement as well as the Piper Fatigue Scale to assess CRF.

Less is known about the association between SED behavior and CRF. Some studies have found that total SED time is associated with fatigue (Phillips et al., 2015; Rogers et al., 2011) while George and colleagues (2013) found that when measuring SED behavior via self-report, no association was found.

Since there is not an exact dose or intensity recommendation of PA to reduce CRF, further investigation must continue. This study contributes to the previous and future research by examining different PA intensities and their independent relationship with CRF. This study also explores different aspects of sedentary behavior including total time as well as bouts and breaks in hopes of creating a better understanding of these variables and their independent relationship with CRF.
2 Purpose

The purpose of this study is to examine the relationship between CRF and the daily movement pattern in breast cancer patients. This will be explored using the following research questions:

2.1 Research Questions

- Are there independent relationships between low and moderate-to-vigorous physical activity with cancer-related fatigue?
- Are there independent relationships between total sedentary behavior, breaks in sedentary and prolonged sedentary time with cancer-related fatigue?

3 Methods

3.1 Study design

This cross-sectional study uses baseline data from a larger, intervention study called OptiTrain. This study is an ongoing, randomised controlled exercise trial. OptiTrain consists of a 16-week training intervention that follows breast cancer patients over 5 years as they continue their own fitness journey when the intervention is over.

The study centre is located at Karolinska University Hospital and Karolinska Institutet, Stockholm, Sweden. Analyzation of data was performed at The Swedish School of Sport and Health Sciences, Stockholm, Sweden.

3.2 Participants

Recruitment for this study began in March 2013 with recruitment complete in 2016. 240 women with a breast cancer diagnosis and who would be receiving chemotherapy were recruited from the Department of Oncology Breast and Sarcoma units at Radiumhemmet and Södersjukhuset,
Karolinska University Hospital in Stockholm, Sweden. After agreeing to participate in this study, the women then completed a cardiovascular health questionnaire and performed an echocardiogram. Subjects were informed by research nurses at The Clinical Trials Unit at Radiumhemmet of eligibility. Inclusion for the study included women between the ages of 18-70 years old with Stage I-IIIa (non-advanced) breast cancer and about to begin adjuvant chemotherapy (Wengström et al. 2017). Exclusion criteria included subjects with advanced disease, subjects that were advised not to participate in PA for safety reasons, bone or brain metastases, cognitive dysfunction or were unable to speak or understand the Swedish language.

3.3 Ethical considerations

Ethical permissions (with numbers 2012/1347-31/1, 2013/632-32 and 2014/408-32) have been obtained from the Regional Ethical Review Board in Stockholm. All participants will provide informed written consent prior to their entry into the study. In the case that changes in the protocol are necessary, relevant amendments will be made and submitted to the relevant ethics trial registration authorities. (Wengström et al. 2017)

3.4 Measurement of the daily movement pattern

The daily movement pattern was objectively measured via tri-axial accelerometer (ActiGraph model GT3X+, ActiGraph LCC, Pensacola, FL, USA) that subjects were asked to wear on their hip for seven consecutive days. The belt was to be worn at all times except when bathing or participating in water activities. The subjects were given the accelerometer at the hospital after agreeing to partake in the study. They were asked to wear the device for the following 7 days. The device recorded daily PA as well as SED behavior patterns using subject’s accelerations in movement. The accelerometer was initialized and downloaded using the ActiLife v.6.10.1 software. Raw data sampling frequency was set to 30 Hz, and extracted as 60-s epoch with low frequency extension filter for the present analyses. Patients mailed back accelerometers after the 7 days.
3.5 Accelerometer data processing

Minimum requirement for inclusion of accelerometer data was 4 days with at least 600 minutes of valid daily monitor wearing. Counts per minute (cpm) is the unit that raw accelerometer data is expressed in, and were based on 60 second epochs. Wear time was calculated by subtracting non-wear time from 24 hours. At least 60 continuous minutes of no movement (0 cpm) was defined as non-wear time, allowing for a maximum of 2 minutes of cpm between 0-200. The sampled acceleration from all three axes in the 60-s data were compiled the vector magnitude. Time was considered SED when spent between intensities of 0-199 cpm (Aguilar-Farias et al., 2014). LIPA was considered between 200-2689 cpm and MVPA from 2690 cpm (Sasaki et al., 2011). The daily movement pattern is presented as 1) percentage of wear time spent in the three intensity-specific categories: SED, LIPA and MVPA, 2) time spent in prolonged SED bouts: the number of bouts consisting of 20 consecutive minutes below the SED threshold of 199 cpm (SED bouts) and 3) the number of breaks in SED per day (SED breaks).

3.6 Measurement of cancer-related fatigue

CRF was assessed using a Swedish Version of the Revised Piper Fatigue Scale. This is a 22-questions survey divided into four different dimensions of subjective fatigue. They are cognitive/mood, behavioral/severity, sensory, and affective meaning (Piper et al., 1998). Subjects answer the questions based on how they felt when answering or the day or answering. The scale begins at the number 0 and ends at 10. These questions are used to calculate the subscales and overall total fatigue score of the subject. For this study, all 22 questions were added together and then divided the number by 22 to achieve the average score, keeping it within 0-10. According to the scoring scale, a score of 0 means no fatigue, 1-3 means mild fatigue, 4-6 moderate fatigue and 7-10 severe fatigue (Piper et al., 1998). These four categories of CRF have also been recommended from the National Comprehensive Cancer Network (Berger et al., 2017). This scale has proven dependable with psychometric properties for gauging individual dimensions of fatigue found among patients of cancer in the Swedish populations (Jakobsson et al. 2013).
3.7 Other measurements
Baseline testing was performed 7 weeks after surgery and 2 weeks after chemotherapy had begun. Height and weight were measured and BMI (kg·m\(^{-2}\)) subsequently calculated at baseline testing. From self-administered questionnaires, education was dichotomized into university degree or not, smoking habits were dichotomized into regular daily smoker or not, comorbidities (hypertension, arthritis, heart disease) were dichotomized into none, one or more than two, menopausal status was dichotomized into menopausal or none, civil status was dichotomized into living with partner or none and on sick leave at baseline was dichotomized into on sick leave or none.

3.8 Data Analysis
Accelerometer data and Piper Fatigue Scale data were taken during the same week, 7 weeks after the patients have had surgery and 2 weeks after the first chemotherapy treatment. To be included in the present analysis, valid accelerometer, fatigue as well as confounding variable data had to be provided by the subject. Out of the 240 women that agreed to participate in the study, 124 women had complete data to be included in the present analyses (figure 1).
3.9 Statistical Analysis

All data was analysed using the IBM SPSS (Statistical Package for the Social Sciences) 24 statistical package for Windows (SPSS, Chicago, IL, USA). Significance levels were set at $p < .05$.

Data was checked for normality using the Shapiro-Wilk test. Normally distributed quantitative variables are presented as mean with standard deviation, while skewed variables are presented as median with interquartile range (Q1-Q3).

Spearman rank correlation described the correlation between the Piper Fatigue Scale variable and the sub components of the daily movement pattern. Further, as the Piper Fatigue Scale variable was highly skewed (54.8% had the value zero), the variable is commonly split up and analysed in
in 4 groups; no fatigue (0), mild fatigue (1-3), moderate fatigue (4-6) and severe fatigue (≥7) (Berger et al., 2017). ANOVA (normally distributed activity variables) and Kruskal-Wallis test (non-normally distributed activity variables) was used to check for significant trends between the PFS grouped and activity variables. The Bonferroni Post Hoc test was used after to determine which of the groups differed from one another with no significant statistical difference found. No significant difference was found in wear time between groups (p=.100).

The Piper Fatigue Scale variable was further dichotomized to calculate the odds ratios (ORs) with 95% confidence interval (95% CI) for having any amount of fatigue (>0) vs. no fatigue (0) and having no/mild fatigue (<4) vs. moderate/severe fatigue (≥4), respectively, using binominal logistic regression (Berger et al., 2017). All daily movement pattern variables were arbitrarily divided into tertiles. Cut-offs were for SED (% of daily wear time) T1: ≤0.49, T2:0.49-0.57, T3: ≥0.57; LIPA (% of daily wear time) T1: ≤0.37, T2:0.37-0.43, T3: ≥0.43; MVPA (% of daily wear time) T1: ≤0.05, T2:0.05-0.08, T3: ≥0.08; SED bouts (no per day) T1: ≤4.14, T2:4.14-5.83, T3: ≥5.83; SED breaks (no per day) T1: ≤69.29, T2:69.29-79, T3: ≥79.

In raw analyses, each dichotomized fatigue variable was entered as dependent with each daily movement pattern variable (% of daily SED, % of daily LIPA, % of daily MVPA, no of SED bouts and no of SED breaks) as independent variable. In adjusted analysis, age, body mass index, education, smoking status, comorbidities, menopause status and civil status were added using the forward (conditional) stepwise method (p=0.05 for entry and p=0.10 for removal). SED was also additionally adjusted for MVPA, and MVPA was additionally adjusted for SED to investigate the independent importance of SED and MVPA, respectively. The bivariate correlation between these two variables was low (r_s = -0.46), well below the conservative limit of 0.6 that is commonly used for detection of intercorrelation between variables and possible introduction of multicollinearity in the model. No significant statistical differences were seen for any of the tertiles of the activity variables for the dichotomized dependent no fatigue vs. fatigue, and data was not presented.
4 Results

4.1 Descriptive statistics

The characteristics of the patients are presented in table 1.

<table>
<thead>
<tr>
<th>Table 1. Descriptive characteristics of patients (n=124)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
</tr>
<tr>
<td>Weight (kg)</td>
</tr>
<tr>
<td>Height (m)</td>
</tr>
<tr>
<td>BMI (kg·m⁻²)</td>
</tr>
<tr>
<td>High Education Level (University Degree)</td>
</tr>
<tr>
<td>BMI ≥ 25</td>
</tr>
<tr>
<td>Regular daily smoker</td>
</tr>
<tr>
<td>Comorbidities</td>
</tr>
<tr>
<td>0 comorbidities</td>
</tr>
<tr>
<td>1 comorbidity</td>
</tr>
<tr>
<td>≥ 2 comorbidities</td>
</tr>
<tr>
<td>Menopausal</td>
</tr>
<tr>
<td>Living with partner</td>
</tr>
<tr>
<td>On sick leave</td>
</tr>
<tr>
<td>SED (% of daily wear time)</td>
</tr>
<tr>
<td>LIPA (% of daily wear time)</td>
</tr>
<tr>
<td>MVPA (% of daily wear time)</td>
</tr>
<tr>
<td>Prolonged SED bouts (numbers per day)</td>
</tr>
<tr>
<td>Total SED breaks (numbers per day)</td>
</tr>
</tbody>
</table>

Data presented as median (Q1-Q3) or percentage

BMI = Body Mass Index
SED = Sedentary time
LIPA = Low intensity physical activity
MVPA = Moderate-to-vigorous physical activity
Piper scale total fatigue scores ranged from 0.00 to 9.59. The average score was 2.33 (SD = 2.94). Using the dichotomous cutoff, 68 (54.8%) patients had no fatigue (PFS score of 0.00); 17 (13.7%) of these women reported mild levels of fatigue (PFS score between 1–3), 27 patients (21.8%) reported moderate levels of fatigue (PFS score between 4-7) and 12 (9.7%) reported severe levels of fatigue (PFS score between 7–10).

A Spearman's rank-order correlation was used to explore the relationship between the total piper fatigue scale score and the daily movement pattern variables. There was a weak, positive correlation between fatigue and SED, which was statistically significant ($r_s = 0.237$, $p = 0.008$). A weak, negative correlation between fatigue and LIPA, which was also statistically significant ($r_s = -0.207$, $p = 0.021$). As well as a third statistically significant correlation that was weak and positive, found between fatigue and SED bouts ($r_s = 0.177$, $p = 0.05$).

Table 2 presents statistically significant variances between the different groups of severity of fatigue and SED ($F(3,120) = 3.753$, $p = 0.013$), LIPA ($F(3,120) = 5.139$, $p = 0.002$), and SED breaks: ($F(3,120) = 2.862$, $p = 0.040$). Further, a Bonferroni post hoc test revealed that SED was significantly higher in the Moderate fatigue group compared to the No fatigue group (58.0 ± 8.0 vs. 52.0 ± 7.6). LIPA was also significantly higher in the No fatigue group (42.0 ± 6.4 min) compared to the Moderate fatigue group (35.0 ± 7.6 min). Lastly, SED breaks was significantly higher in the Mild fatigue group (78.0 ± 12.2 min) compared to the Moderate fatigue group (69.0 ± 9.5 min). There was no statistically significant difference revealed for MVPA and SED bouts within fatigue groups.
Table 2. Mean with standard deviation (SD) for the different components of the daily movement pattern within the four fatigue groups (n=124).

<table>
<thead>
<tr>
<th></th>
<th>No Fatigue</th>
<th>Mild Fatigue</th>
<th>Moderate Fatigue</th>
<th>Severe Fatigue</th>
<th>p-value ANOVA</th>
</tr>
</thead>
<tbody>
<tr>
<td>SED (% of daily wear time)</td>
<td>52.0 (7.6)</td>
<td>52.0 (10.0)</td>
<td>58.0 (8.0)*</td>
<td>54.0 (8.0)</td>
<td>0.013</td>
</tr>
<tr>
<td>LIPA (% of daily wear time)</td>
<td>42.0 (6.4)</td>
<td>41.0 (8.4)</td>
<td>35.0 (7.6)*</td>
<td>39.0 (6.5)</td>
<td>0.002</td>
</tr>
<tr>
<td>MVPA (% of daily wear time)</td>
<td>6.8 (2.9)</td>
<td>6.7 (3.7)</td>
<td>6.9 (3.1)</td>
<td>6.8 (2.8)</td>
<td>0.999</td>
</tr>
<tr>
<td>Prolonged SED Bouts (#/day)</td>
<td>4.9 (1.9)</td>
<td>4.6 (2.0)</td>
<td>5.6 (2.0)</td>
<td>5.4 (1.5)</td>
<td>0.264</td>
</tr>
<tr>
<td>Total SED breaks (#/day)</td>
<td>75.0 (11.2)</td>
<td>78.0 (12.2)</td>
<td>69.0 (9.5)*</td>
<td>75.0 (9.8)</td>
<td>0.040</td>
</tr>
</tbody>
</table>

a Significantly different from No Fatigue group
b Significantly different from Mild Fatigue group

SED = Sedentary behavior; LIPA = Low intensity physical activity; Moderate-to-vigorous physical activity

The OR for having no/mild vs. moderate/severe CRF the across tertiles of the different components of the daily movement pattern in presented in table 3. Medium and high level of SED were associated with more than four-fold higher OR of moderate/severe CRF, even after additional adjustment of confounders. With additional adjustment for MVPA, the effects of the association were even higher. Regarding LIPA, the highest tertile was associated with 70% lower OR for moderate/severe CRF in the raw analysis, and 65% lower after adjustment for confounding variables. For MVPA, the highest tertile was associated with a more than three-fold higher OR of moderate/severe CRF while adjusting for the influence confounding variables and SED. For SED bouts, the highest tertile was associated with a four-fold higher OR for moderate/severe CRF in the raw analysis, with a three-fold increase in OR after adjustment for confounding variables (borderline significant). For SED breaks, there was no significant association found between tertiles and moderate/severe CRF in neither the raw nor the adjusted analysis.
Table 3. Odds Ratio (95% CI) of having no/mild vs. moderate/severe CRF in relation to tertiles of the different components of the daily movement pattern (n=124).

<table>
<thead>
<tr>
<th></th>
<th>Raw</th>
<th>Adjusted*</th>
<th>+ MVPA or SED#</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SED (%/day)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>1.00 (ref)</td>
<td>1.00 (ref)</td>
<td>1.00 (ref)</td>
</tr>
<tr>
<td>Medium</td>
<td>3.46 (1.18-10.12)</td>
<td>3.54 (1.20-10.47)</td>
<td>6.12 (1.85-20.22)</td>
</tr>
<tr>
<td>High</td>
<td>4.70 (1.62-13.58)</td>
<td>4.59 (1.58-13.39)</td>
<td>9.52 (2.69-33.72)</td>
</tr>
<tr>
<td><strong>LIPA (%/day)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>1.00 (ref)</td>
<td>1.00 (ref)</td>
<td></td>
</tr>
<tr>
<td>Medium</td>
<td>0.52 (0.21-1.29)</td>
<td>0.67 (0.25-1.77)</td>
<td></td>
</tr>
<tr>
<td>High</td>
<td>0.29 (0.11-0.76)</td>
<td>0.35 (0.12-1.00)</td>
<td></td>
</tr>
<tr>
<td><strong>MVPA (%/day)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>1.00 (ref)</td>
<td>1.00 (ref)</td>
<td>1.00 (ref)</td>
</tr>
<tr>
<td>Medium</td>
<td>1.52 (0.59-3.86)</td>
<td>1.44 (0.52-3.96)</td>
<td>2.41 (0.79-7.29)</td>
</tr>
<tr>
<td>High</td>
<td>1.27 (0.49-3.29)</td>
<td>1.58 (0.56-4.49)</td>
<td><strong>3.76 (1.05-13.43)</strong></td>
</tr>
<tr>
<td><strong>SED Bouts (#/day)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>1.00 (ref)</td>
<td>1.00 (ref)</td>
<td></td>
</tr>
<tr>
<td>Medium</td>
<td>2.88 (0.97-8.52)</td>
<td>2.39 (0.77-7.43)</td>
<td></td>
</tr>
<tr>
<td>High</td>
<td><strong>4.21 (1.43-12.41)</strong></td>
<td>3.07 (0.99-9.51)</td>
<td></td>
</tr>
<tr>
<td><strong>SED Breaks (#/day)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>1.00 (ref)</td>
<td>1.00 (ref)</td>
<td></td>
</tr>
<tr>
<td>Medium</td>
<td>0.70 (0.28-1.8)</td>
<td>0.64 (0.23-1.79)</td>
<td></td>
</tr>
<tr>
<td>High</td>
<td>0.67 (0.23-1.92)</td>
<td>0.75 (0.25-2.32)</td>
<td></td>
</tr>
</tbody>
</table>

95% CI not including 1 are boldly marked.

*Additionally adjusted for age, body mass index, education, smoking status, comorbidities, menopause status and civil status.

# SED was additionally adjusted for MVPA, and MVPA was additionally adjusted for SED.

**5. Discussion**

The purpose of this study was to examine the association between objectively-measured daily movement pattern including PA of various intensities as well SED behavior and CRF in breast cancer patients. The results showed a positive association between SED, SED bouts and MVPA with CRF. LIPA had a negative association with CRF while SED breaks had no association. These findings indicate that all aspects of the daily movement pattern should be highlighted when studying the association with CRF.
5.1 Physical activity and cancer-related fatigue

The correlation analysis showed a negative association between LIPA and CRF. No association between MVPA and CRF was found. The ANOVA and Bonferroni Post Hoc test showed that there was a statistically significant difference between the no fatigue group and the moderate fatigue group regarding LIPA. No statistically significant difference was found regarding MVPA. The binary logistic regression showed that before adjusting for confounders, the highest tertile of LIPA was associated with CRF. MVPA was found to be positively associated with CRF when adjusting for confounders and SED.

Our findings were not consistent with previous research for the relationship between MVPA and CRF that show a negative association between the two. Both subjective methods (Stagl et al., 2014) and objective methods (Phillips et. al., 2015) have found this association between MVPA and CRF. However, Timmerman et al (2015) found a moderate and positive correlation between the amount of PA done in the morning and afternoon by cancer survivors with the amount of fatigue they felt that night.

The difference in findings from previous research regarding MVPA is interesting as this study was not an intervention and the patients could perform as much or as little PA as they decided. These differences could be attributed to different cutoff points used to analyze accelerometer data as well as different scales used to measure CRF. The positive association between MVPA and CRF also could be contributed to cancer patients who engaged in MVPA prior to being diagnosed and have continued this behavior. Even though they may feel fatigued, they continue to engage in MVPA as CRF is an expected side-effect of cancer. These patients could also have been educated to understand that PA can improve CRF, motivating them to engage in MVPA without realizing that their level of CRF is higher than others doing less intense forms of PA. Future studies should continue to examine the dose-response between PA and CRF as well as cutoff points for PA intensities. Future research should also progress towards a universally accepted scale to measure CRF.
Our study was consistent with current research regarding LIPA and the positive association with CRF. A meta-analysis done by Carayol and colleagues (2013) found that LIPA consisting of between 90-120 minutes per week was found to be the most effective dose in reducing fatigue in breast cancer patients receiving adjuvant therapy. Another low-intensity (25-35% of heart rate reserve) exercise intervention found that 3 times a week for 10 weeks of doing lower-body aerobic exercise significantly decreased fatigue in cancer survivors (Burnham and Wilcox, 2002). Rogers and colleagues (2011), found in their subjective study that gardening and leisure activity was associated with less fatigue in breast cancer survivors.

5.2 Sedentary behavior and cancer-related fatigue
The correlation analysis showed a positive association between SED and CRF as well as a positive association between prolonged SED bouts and CRF. The ANOVA and Bonferroni Post Hoc test showed that there was a statistically significant difference between the no fatigue group and the moderate fatigue group regarding SED. There was also a difference between the mild fatigue group and moderate fatigue group for SED breaks. No statistically significant difference was found regarding SED bouts. The binary logistic regression showed that both the medium and high tertiles of SED were positively associated with CRF in both the raw and adjusted analyses. For the raw analysis SED bouts was positively associated with CRF. No association was found between SED breaks and CRF.

Previous research examining SED behavior and CRF has inconsistent results. Findings from a study with colorectal cancer survivors showed that greater total SED time (per 2 h/day) and prolonged SED time (per 2 h/day) were significantly associated with fatigue scores. A longer usual SED bout duration (per 15 min) was also significantly associated with fatigue scores (van Roekel et al., 2016). Hartman and colleagues (2017) also found that time spent in long SED bouts was associated with worse quality of life in 134 breast cancer survivors who also had low MVPA. In contrast, George and colleagues (2013) found no such association with CRF from self-reported SED from 710 breast cancer survivors.
5.3 Potential mechanisms that may reduce CRF through the daily movement pattern

There are several potential mechanisms that could reduce CRF when increasing PA and decreasing sedentary behavior. Engaging in PA even in healthy populations has shown to have many benefits that likely contribute to improving quality of life. Regularly engaging in PA has benefits such as improving sleep, boosting self-esteem and reducing anxiety and depression (Kirschbaum 2007). Inflammation in the body is another mechanism that could contribute to CRF, with studies showing exercise to have an anti-inflammatory effect (LaVoy et al., 2016). Inflammation is another possible mechanism from sedentary behavior that is linked to disease risk (Carter et al., 2017). The aerobic capacity of a person can decrease when a lack of movement occurs (Bower 2014). Research has shown that physiological measures such as increasing one’s aerobic capacity through increased PA could be a mechanism that decreases CRF, allowing patients to perform everyday tasks with more ease (Burnham and Wilcox, 2002).

5.4 Strengths and weaknesses

The sample population lives close to or in a rather large city, making it hard to generalize the findings to the entire population. Also, the participation in the study was voluntary creating the possibility of a bias.

The time of the year that the accelerometer and Piper Fatigue Scale questionnaire were taken could affect the questionnaire answers and how active the sample population were. Those that answered in late fall and winter could have much less PA and feel more fatigue because of the darkness than those who completed the questionnaire and wore the accelerometer in spring and summer.

Another limitation of the study was the cross-sectional nature of the analyses, limiting the possibility to study causality of the observed associations.
A strength of this study was using objective methods to measure PA and SED behavior. This method is less likely to encounter response and recall bias than when using a subjective method (Atkin et al., 2012).

This study contributes to previous research, emphasising the importance of staying active and reducing SED behavior during cancer treatments in order to retain a good quality of life. These findings are important as motivating a breast cancer patient to increase their LIPA and reduce their SED behavior, might be easier than motivating patients to increase MVPA.

6. Conclusion

As survivorship increases, it is important for cancer patients to continue important daily habits in order to return to normal life after treatment. Increasing low-intensity physical activity and reducing total SED time as well as SED bouts may reduce CRF in breast cancer patients.

References


Appendix 1
Literature search

**Aim:**
The aim of this study was to examine the relationship between cancer-related fatigue and daily movement patterns in breast cancer patients. My research questions are: Does physical activity have an influence on cancer-related fatigue in breast cancer patients? Does sedentary behavior have an influence on cancer-related fatigue in breast cancer patients?

**Search words used:**
Physical activity, daily movement patterns, cancer-related fatigue, breast cancer, cancer, patients, survivors, exercise, GT3X+, sedentary, sedentary patterns, sedentary behavior, accelerometer, piper fatigue scale, objectively-measured.

**Where I have searched:**
I searched using GIH’s online database as well as Pubmed.

<table>
<thead>
<tr>
<th>Database</th>
<th>Relevant Searches</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pubmed/GIH</td>
<td>-“Physical activity” AND “cancer-related fatigue” AND “breast cancer”</td>
</tr>
<tr>
<td></td>
<td>-Daily movement pattern, “cancer-related fatigue”</td>
</tr>
<tr>
<td></td>
<td>-“Physical activity” AND fatigue AND breast cancer</td>
</tr>
<tr>
<td></td>
<td>-Daily movement pattern AND breast cancer AND fatigue</td>
</tr>
<tr>
<td></td>
<td>-Sedentary AND cancer-related fatigue</td>
</tr>
<tr>
<td></td>
<td>-“Objectively-measured physical activity” AND “cancer-related fatigue”</td>
</tr>
<tr>
<td></td>
<td>-Exercise AND “cancer-related fatigue”</td>
</tr>
</tbody>
</table>
Appendix 2

Date: ______________ Qualifying Assessment ID

REVISED PIPER FATIGUE SCALE (RPFS)

Directions: Many individuals can experience a sense of unusual or excessive tiredness whenever they become ill, receive treatment, or recover from their illness/treatment. This unusual sense of tiredness is not usually relieved by either a good night’s sleep or by rest. Some call this symptom “fatigue” to distinguish it from the usual sense of tiredness.

For each of the following questions, please fill in the space provided for that response that best describes the fatigue you are experiencing now or for today. Please make every effort to answer each question to the best of your ability. If you are not experiencing fatigue now or for today, fill in the circle indicating “0” for your response. Thank you very much!

1. How long have you been feeling fatigue? (Check one response only).
   1. not feeling fatigue
   2. minutes
   3. hours
   4. days
   5. weeks
   6. months
   7. other (Please describe) _____________________________________________

2. To what degree is the fatigue you are feeling now causing you distress?

   No Distress  A Great Deal

<table>
<thead>
<tr>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
</tr>
</thead>
</table>

3. To what degree is the fatigue you are feeling now interfering with your ability to complete your work or school activities?

   None  A Great Deal

33
4. To what degree is the fatigue you are feeling now interfering with your ability to socialize with your friends?

None          A Great Deal

1 2 3 4 5 6 7 8 9 10

5. To what degree is the fatigue you are feeling now interfering with your ability to engage in sexual activity?

None          A Great Deal

1 2 3 4 5 6 7 8 9 10

6. Overall, how much is the fatigue which you are now experiencing interfering with your ability to engage in the kind of activities you enjoy doing?

None          A Great Deal

1 2 3 4 5 6 7 8 9 10

7. How would you describe the degree of intensity or severity of the fatigue which you are experiencing now?

Mild          Severe

1 2 3 4 5 6 7 8 9 10

8. To what degree would you describe the fatigue which you are experiencing now as being?

Pleasant      Unpleasant

1 2 3 4 5 6 7 8 9 10

34
9. To what degree would you describe the fatigue which you are experiencing now as being?

Agreeable  
1 2 3 4 5 6 7 8 9 10

Disagreeable

10. To what degree would you describe the fatigue which you are experiencing now as being?

Protective  
1 2 3 4 5 6 7 8 9 10

Destructive

11. To what degree would you describe the fatigue which you are experiencing now as being?

Positive  
1 2 3 4 5 6 7 8 9 10

Negative

12. To what degree would you describe the fatigue which you are experiencing now as being:

Normal  
1 2 3 4 5 6 7 8 9 10

Abnormal

13. To what degree are you now feeling:

Strong  
1 2 3 4 5 6 7 8 9 10

Weak

14. To what degree are you now feeling:
### Awake vs. Sleepy

<table>
<thead>
<tr>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
</tr>
</thead>
</table>

15. To what degree are you now feeling:

- **Lively**
  | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |

- **Listless**
  | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |

16. To what degree are you now feeling:

- **Refreshed**
  | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |

- **Tired**
  | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |

17. To what degree are you now feeling:

- **Energetic**
  | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |

- **Unenergetic**
  | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |

18. To what degree are you now feeling:

- **Patient**
  | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |

- **Impatient**
  | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |

19. To what degree are you now feeling:

- **Relaxed**
  | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |

- **A Great Deal**
  | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
20. To what degree are you now feeling:

<table>
<thead>
<tr>
<th>Exhilarated</th>
<th>Depressed</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 9 8 7 6 5 4 3 2 1</td>
<td></td>
</tr>
</tbody>
</table>

21. To what degree are you now feeling:

<table>
<thead>
<tr>
<th>Able to Concentrate</th>
<th>Unable to Concentrate</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 9 8 7 6 5 4 3 2 1</td>
<td></td>
</tr>
</tbody>
</table>

22. To what degree are you now feeling:

<table>
<thead>
<tr>
<th>Able to Remember</th>
<th>Unable to Remember</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 9 8 7 6 5 4 3 2 1</td>
<td></td>
</tr>
</tbody>
</table>

23. To what degree are you now feeling:

<table>
<thead>
<tr>
<th>Able to Think Clearly</th>
<th>Unable to Think Clearly</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 9 8 7 6 5 4 3 2 1</td>
<td></td>
</tr>
</tbody>
</table>

24. Overall, what do you believe is most directly contributing to or causing your fatigue?

________________________________________________________________________

25. Overall, the best thing you have found to relieve your fatigue is:

________________________________________________________________________

26. Is there anything else you would like to add that would describe your fatigue better to us?

________________________________________________________________________

27. Are you experiencing any other symptoms right now?

________________________________________________________________________
Appendix 3

Swedish Revised Piper Fatigue Scale

Anvisningar:
Många som genomgår behandling för cancer kan oftast uppleva en ovanlig och utmattande trötthet som oftast inte lindras enbart av att sova eller vila.

Genom följande påståenden vill vi få en uppfattning om hur Du känt dig den senaste veckan.

Var vänlig att ringa in den siffra som bäst beskriver hur Du har det.

Det är viktigt att Du försöker svara på alla 27 frågor.

Om Du inte upplever trötthet så vänligen ringa in siffran 1 på första frågan och övergå sedan till nästa frågeformulär.

1a. Hur skulle du beskriva din trötthet?

<table>
<thead>
<tr>
<th>Ingen trötthet</th>
<th>Extremt trött</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 2 3 4 5 6 7 8 9 10</td>
<td></td>
</tr>
</tbody>
</table>

1b. Hur länge har du känt dig trött? (välj ett alternativ)

<table>
<thead>
<tr>
<th>Timmar</th>
<th>Dagar</th>
<th>Veckor</th>
<th>Månader</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Annat (beskriv) _____________________________</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

2. Hur besvärad är du av tröttheten?

<table>
<thead>
<tr>
<th>Inte alls</th>
<th>I högsta grad</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 2 3 4 5 6 7 8 9 10</td>
<td></td>
</tr>
</tbody>
</table>

3. Hur mycket störs din förmåga till daglig sysselsättning av tröttheten?

<table>
<thead>
<tr>
<th>Inte alls</th>
<th>I högsta grad</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 2 3 4 5 6 7 8 9 10</td>
<td></td>
</tr>
</tbody>
</table>

4. Hur mycket störs ditt sociala umgänge av tröttheten?

38
5. Hur mycket störs din sexuella aktivitet av tröttheten?

<table>
<thead>
<tr>
<th>Inte alls</th>
<th>I högsta grad</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 2 3 4 5 6 7 8 9 10</td>
<td></td>
</tr>
</tbody>
</table>

6. På det hela taget, hur mycket stör tröttheten dina möjligheter att delta i aktiviteter du tycker om?

<table>
<thead>
<tr>
<th>Inte alls</th>
<th>I högsta grad</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 2 3 4 5 6 7 8 9 10</td>
<td></td>
</tr>
</tbody>
</table>

7. Hur skulle du beskriva svårighetsgraden av den trötthet du känner?

<table>
<thead>
<tr>
<th>Mycket lätt</th>
<th>Mycket svår</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 2 3 4 5 6 7 8 9 10</td>
<td></td>
</tr>
</tbody>
</table>

8. I vilken utsträckning skulle du beskriva den trötthet du känner som:

<table>
<thead>
<tr>
<th>Behaglig</th>
<th>Obehaglig</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 2 3 4 5 6 7 8 9 10</td>
<td></td>
</tr>
</tbody>
</table>

9. I vilken utsträckning skulle du beskriva den trötthet du känner som:

<table>
<thead>
<tr>
<th>Hanterbar</th>
<th>Ohanterbar</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 2 3 4 5 6 7 8 9 10</td>
<td></td>
</tr>
</tbody>
</table>

10. I vilken utsträckning skulle du beskriva den trötthet du känner som:

<table>
<thead>
<tr>
<th>Uppbyggande</th>
<th>Nedbrytande</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 2 3 4 5 6 7 8 9 10</td>
<td></td>
</tr>
</tbody>
</table>

11. I vilken utsträckning skulle du beskriva den trötthet du känner som:
<table>
<thead>
<tr>
<th>Positiv</th>
<th>Negativ</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 2 3 4 5 6 7 8 9 10</td>
<td></td>
</tr>
</tbody>
</table>

12. I vilken utsträckning skulle du beskriva den trötthet du känner som:

<table>
<thead>
<tr>
<th>Vanlig</th>
<th>Ovanlig</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 2 3 4 5 6 7 8 9 10</td>
<td></td>
</tr>
</tbody>
</table>

13. I vilken utsträckning känner du dig:

<table>
<thead>
<tr>
<th>Kroppsligt stark</th>
<th>Kroppsligt svag</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 2 3 4 5 6 7 8 9 10</td>
<td></td>
</tr>
</tbody>
</table>

14. I vilken utsträckning känner du dig:

<table>
<thead>
<tr>
<th>Pigg</th>
<th>Sömnig</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 2 3 4 5 6 7 8 9 10</td>
<td></td>
</tr>
</tbody>
</table>

15. I vilken utsträckning känner du dig:

<table>
<thead>
<tr>
<th>Vital</th>
<th>Häglös</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 2 3 4 5 6 7 8 9 10</td>
<td></td>
</tr>
</tbody>
</table>

16. I vilken utsträckning känner du dig:

<table>
<thead>
<tr>
<th>Utvilad</th>
<th>Trött</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 2 3 4 5 6 7 8 9 10</td>
<td></td>
</tr>
</tbody>
</table>

17. I vilken utsträckning känner du dig:

<table>
<thead>
<tr>
<th>Energisk</th>
<th>Kraftlös</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 2 3 4 5 6 7 8 9 10</td>
<td></td>
</tr>
</tbody>
</table>

18. I vilken utsträckning känner du dig:

<table>
<thead>
<tr>
<th>Tålmodig</th>
<th>Otålig</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 2 3 4 5 6 7 8 9 10</td>
<td></td>
</tr>
</tbody>
</table>
19. I vilken utsträckning känner du dig:

**Avslappnad**  
1 2 3 4 5 6 7 8 9 10

**Spänd**

20. I vilken utsträckning känner du dig:

**Glad**

1 2 3 4 5 6 7 8 9 10

**Nedstämd**

21. I vilken utsträckning känner du att:

**Du kan koncentrera dig**

1 2 3 4 5 6 7 8 9 10

**Du inte kan koncentrera dig**

22. I vilken utsträckning känner du att:

**Du kan minnas**

1 2 3 4 5 6 7 8 9 10

**Du inte kan minnas**

23. I vilken utsträckning känner du att:

**Du kan tänka klart**

1 2 3 4 5 6 7 8 9 10

**Du inte kan tänka klart**

24. På det hela taget, vad tror du mest bidrar till din trötthet?

______________________________________________________________________

25. På det hela taget, hur gör du för att bäst minska din trötthet?

______________________________________________________________________

26. Är det något du vill lägga till för att ytterligare beskriva din trötthet för oss?

______________________________________________________________________

41
27. Har du just nu några andra symtom förutom trötthet? Nej Ja
Om Ja, var vänlig och beskriv
Appendix 4

**Scoring Piper Fatigue Scale (PFS) Survey Results:**

**PFS current format and scoring instructions:**

1. The PFS in its current form is composed of 22 numerically scaled, "0" to "10" items that measure four dimensions of subjective fatigue: behavioral/severity (6 items; # 2-7); affective meaning (5 items: # 8-12); sensory (5 items: # 13-17); and cognitive/mood (6 items: # 18-23). These 22 items are used to calculate the four subscale/dimensional scores and the total fatigue scores.

2. Five additional items (# 1 and # 24-27) are not used to calculate subscale or total fatigue scores but are recommended to be kept on the scale as these items furnish rich, qualitative data. Item # 1, in particular gives a categorical way in which to assess the duration of the respondent's fatigue.

3. To score the PFS, add the items contained on each specific subscale together and divide by the number of items on that subscale. This will give you a subscale score that remains on the same "0" to "10" numeric scale. Should you have missing item data, and the respondent has answered at least 75%-80% of the remaining items on that particular subscale, calculate the subscale mean score based on the number of items answered, and substitute that mean value for the missing item score (mean-item substitution).

4. Recalculate the subscale score. To calculate the total fatigue score, add the 22-item scores together and divide by 22 in order to keep the score on the same numeric "0" to "10" scale.1

**Severity Codes:**

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
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</thead>
<tbody>
<tr>
<td>0</td>
<td>NONE</td>
</tr>
<tr>
<td>1-3</td>
<td>MILD</td>
</tr>
<tr>
<td>4-6</td>
<td>MODERATE</td>
</tr>
<tr>
<td>7-10</td>
<td>SEVERE</td>
</tr>
</tbody>
</table>