# Physical activity levels of breast cancer patients before diagnosis compared to a reference population : a cross-sectional comparative study

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***Physical activity levels of breast cancer patients***

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**Conflict of Interest**

All authors declare that they have no conflict of interest.

**Abstract**

**PURPOSE:** We hypothesize that pre-diagnosis physical activity (PA) levels of breast cancer patients are below those of a reference population without breast cancer. Therefore, the aim of the present study was to compare pre-diagnosis PA levels (including total-, occupational-, sport- and household activity levels) of breast cancer patients with activity levels of a reference population.

**METHODS: Female p**atients with primary breast cancer (n=265) filled in the Flemish Physical Activity Computerized Questionnaire (FPACQ) the day before surgery recalling the year before diagnosis. PA levels were expressed as Metabolic Equivalent Task (MET) values. Smooth reference curves of PA levels were estimated in a representative sample of 3466 women without breast cancer with the LMS method, which allowed comparison of pre-diagnosis PA data of the breast cancer sample with this reference.

**RESULTS:** Compared to women without breast cancer, total PA levels were significantly lower in the year prior to breast cancer diagnosis over all age groups (Mean $\pm$ SD z-scores (95%CI) = -1.51 ± 1.86 (-1.74 to -1.29)). More specifically, household PA levels of breast cancer patients were significantly lower between ages 40-60, while occupational PA levels were significantly higher in this age group. No differences were found between sports PA levels.

**CONCLUSIONS:** Patients with breast cancer show significantly lower total PA levels during the year prior to surgery compared to a reference population. Especially household activity levels are lower in patients between ages 40 to 60. Given this, a return to pre-diagnosis PA levels may not be sufficient for protection from disease in the future.

**KEYWORDS:** Breast cancer, physical activity, comparative study

## Introduction

It has been proven that physical inactivity is a predictor for having breast cancer [1-3]. Moreover, physical inactivity is responsible for 10% of the breast cancer burden [4]. Indeed, it has been shown that a sufficient level of physical activity (PA) before, during and after cancer treatment is associated with a better prognosis, a lower risk of recurrence, a lower risk of mortality [3, 5, 6], fewer negative treatment-related side effects [6] and a better quality of life [6-9].

The *American College of Sports Medicine (ACSM) Roundtable Report on Physical Activity, Sedentary Behavior, and Cancer Prevention and Control* recommends that adult cancer survivors should do at least 30 minutes of moderate to vigorous aerobic PA on top of their usual activities on at least three days of the week and muscle strength training at least two days per week [3, 9]. These recommendations are in line with those for healthy adults provided by the World Health Organization (WHO), namely a miminum of 150 minutes at least moderate intensity PA and twice strength training per week [3, 9, 10]. Despite these recommendations, results form a cohort of more than 9000 cancer survivors revealed that only between 30% and 47% of them met the current guidelines for general PA, which depended on tumour site [11]. In breast cancer survivors, only 32% reported regular PA[11].

Several studies compared PA levels of breast cancer survivors with PA levels of healthy adults at different time points after cancer treatment and found lower PA levels in breast cancer survivors [6, 12, 13]. To our knowledge, no studies compared pre-diagnosis PA levels of breast cancer patients with healthy controls. One study compared PA levels in healthy volunteers to the preoperative PA levels in patients with resectable gastrointestinal cancer [7]. No differences were found in patients with early stage (potentially curable) upper gastrointestinal cancer, but PA levels of those with advanced disease were significantly lower than in healthy volunteers [7]. However, it should be noted that the control group might not have been representative for the general population as they were recruited among sports athletes.

If breast cancer patients pre-diagnosis do not meet the recommended level of PA for healthy adults set by the WHO guidelines, returning to this level may not be sufficient to protect them in the future [3]. Several studies have shown that besides general PA levels, also occupational-, sport- and household activity levels have decreased after breast cancer treatment, even up to 24 months post-surgery [5, 14-17]. Additionally, a 16% lower risk of breast cancer has been described when comparing women with a high versus low occupational PA level [3]. Given this, it may be worthwhile to differentiate between types of PA besides general PA levels. A possible limitation of these studies is that they compare PA levels after treatment with those immediately before treatment or after diagnosis, which probably should not be interpreted as a normal representative baseline for PA [2, 18].

It is currently unknown whether breast cancer patients are less physically active in the year before diagnosis compared to healthy peers. Therefore, the aim of the present study is to compare PA levels (including total-, occupational-, sport- and household activity levels) of breast cancer patients the year pre-surgery to activity levels in a large reference sample of women without breast cancer. We hypothesize that the PA level of patients before surgery is lower compared to reference values. Additionally, given that higher age and higher Body Mass Index (BMI) are both associated with physical inactivity and breast cancer risk [2, 19], PA levels are compared for different age and weight categories.

## Methods

This study had approval from the Ethical Committee from University Hospitals Leuven (ML3513).

### Subjects

Patients with breast cancer

Between September 2006 and September 2007, 398 breast cancer patients in the Multidisciplinary Breast Center of the University Hospitals Leuven were consecutively asked to participate in a study on recovery of PA levels after breast cancer surgery [14, 15]. For the purpose of the present study, inclusion criteria were female patients with axillary lymph node dissection or sentinel node biopsy in combination with mastectomy or breast conserving surgery for primary breast cancer. Patients may have had neo-adjuvant chemotherapy. Of these eligible patients, 265 agreed to participate on the day before surgery. There were no exclusion criteria.

Reference population

PA data from 3466 women without a current or prior diagnosis of breast cancer aged above 18 years were available from a population-based sample recruited (2002-2004) for a cross-sectional study commissioned by the The Flemish Policy Research Centre Sport, Physical Activity and Health with the intention to collect reference data of physical activity and physical health in general of the Flemish population [20, 21]. This cross-sectional study was conducted by the Department of Movement Sciences of KU Leuven.

Procedure

The day before surgery, BC patients meeting the criteria were asked to participate in the study. Patients who agreed to participate, completed the Flemish Physical Activity Computerized Questionnaire (FPACQ). The FPACQ is a questionnaire recalling the physical activities over the past year. The controls also completed the FPACQ for activities over a one year recall period.

The FPACQ is a reliable and valid questionnaire[22]. Scoring and interpretation of the FPACQ was performed in line with the methods used by Scheers, et al[23]. The questionnaire gives information on different PA variables: occupational status (employed or unemployed, working hours, job intensity and transport to the job), sport activities (three most frequently performed sports, frequency and duration of each sport) and household activity level (light, moderate and vigorous). Information about transport during leisure time and sedentary activities (TV and sleep) was also collected. Total energy expenditure represents the overall weekly energy expenditure and was calculated by summing the energy expenditure of all reported activities (i.e. occupational activity, sport activities, household activities, transport and sedentary activities). The physical activity level (MET) (primary outcome) was subsequently calculated by dividing total energy expenditure by 168 (=numbers of hours per week)[23].

The primary outcome in the present study was the total PA level, which is the sum of occupational-, sport-, household activity levels, active transport in leisure time and sedentary activities. The activity levels were expressed as Metabolic Equivalent Task (MET) values, which were determined using the Ainsworth compendium of activities [24].
The MET is defined as the ratio of the work metabolic rate to a standard resting metabolic rate of 1.0 kg-1 h-1, where one MET is the resting metabolic rate during quiet sitting. The calculation of each component of the FPACQ was previously described in detail in the study of Devoogdt et al, 2010 (6). The variables retrieved for the present paper are the total PA level with three PA domains:
occupational-, sport- and household activity levels.

**Statistical analysis**

The activity levels (total, occupational, sport and household) in BC patients were compared to those in a representative sample of female controls. The PA levels of patients were converted to age adjusted z-scores, using the sample of women as a reference. Z-scores less than -1 SD and less than -2 SD (compared to the reference population) were interpreted as low and very low PA levels, respectively. Based on a standard normal distribution, the theoretically expected prevalence below these thresholds is 15.9% and 2.3% in the reference population. Mean z-scores and the prevalence below these cut-offs were calculated in three age categories (< 40, 40 – 60, > 60 years) and in the total sample. One sample t-tests were used to test for a deviation from the expected mean z-score of zero in the whole group and in the three age categories separately. The prevalence of low (-1SD) and very low PA (-2SD) in patients was compared with the expected prevalence in the reference population with a binomial test. Because the present study is a subanalysis based on the sample recruited by Devoogdt et al.[14], no a priori sample size calculation was performed. However, the sample size of the present study allowed us to detect a difference in mean z-score with the reference population of approximately 0.1 SD in the total sample, 0.2 SD when testing one third of the sample, and 0.4 SD when testing one tenth of the sample (e.g. in

subgroups). The prevalence of a low or very low PA was significantly different from the reference population when it differed more than respectively 5% and 2% in the total sample, 9% and 4% when comparing on third of the sample, and 18% and 8% when testing one tenth of the sample.

An unadjusted (t-test, $Chi^2$- test) and age adjusted (multiple linear and logistic regression) comparison of mean BMI, overweight prevalence rates and prevalence rates of employed people between the patients and controls was performed to compare the demographic characteristics. The distribution of the PA levels by age in the reference population were estimated with the LMS method [25, 26]. This semi-parametric method normalizes the distribution by using a Box-Cox power transformation to correct for skewness. The LMS method produces three smooth curves: L for the Box-Cox power to remove skewness, M for the median and S for the approximate coefficient of variation. The degree of smoothing is determined by assigning a number of equivalent degrees of freedom (edf) for each curve. Data of the PA levels of breast cancer patients were graphically presented on the reference lines, and the corresponding z-scores were used for further analysis. Additionally, the mean trend by age in patients was estimated with a generalized additive model (GAM). The degree of smoothing was determined by cross validation with the mgcv package in R version 3.5 (R Foundation for Statistical Computing, Vienna, 2018). This is visually presented for the different PA levels by a smooth line and shaded area that marks the standard error.

Z-scores of the different PA levels were compared between breast cancer patients with overweight (i.e. a BMI $\geq$ 25 kg/$m^2$ ) versus those without overweight (i.e. a BMI < 25 kg/$m^2$) with an independent t-test.

Group differences with a p-value < 0.05 were considered statistically significant. All analyses were performed with R version 3.5 (R Core Team (2019). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL https://www.R-project.org/). Descriptive analyses were performed with SPSS version 26.0 (IBM Corp. Released 2019. IBM SPSS Statistics for Macintosh, Version 26.0. Armonk, NY: IBM Corp.).

**Results**

All 265 patients with breast cancer completed the FPACQ one day before surgery. The age of the patients ranged between 21 and 90 years, with a mean (SD) of 54 (10.9) years. The age of the female controls ranged between 18 and 81 years, with a mean (SD) of 46.7 (13.9) years. The Body Mass Index (BMI) of patients ranged between 17 and 41, with a mean (SD) of 25.1 (4.4) kg/m$^2$. The BMI of controls ranged between 12.2 and 57.1 with a mean (SD) of 24.4 (4.2) kg/m$^2$ (table 1). The mean BMI and prevalence of overweight were significantly higher in patients compared to controls (respectively p = 0.02 and p = 0.01), but not when adjusted for age (p=0.92 and p=0.64). Patients were more often employed than the controls (p=0.03), also when adjusted for age (p=0.002).

*Table 1. Demographic and clinical characteristics of included female patients with breast cancer and controls. Mean (SD) and number (%) are given for continuous and categorical data, respectively.*

| | Breast cancer patients (n=265) | Controls (n=3466) |
|---|---|---|
| Age (years) | 54.5 (10.9) | 46.7 (13.9) |
| Body Mass Index (kg/m$^2$) | 25.1 (4.4) | 24.5 (4.1) |
| No overweight (< 25 kg/m$^2$) | 146 (44.9%) | 2192 (63.2%) |
| Overweight (≥ 25 kg/m$^2$) | 119 (55.1%) | 1274 (36.8%) |
| Work status | | |
| Employed | 143 (54%) | 1636 (47%) |
| Not professionally active | 42 (16%) | 996 (29%) |
| Retired | 80 (30%) | 834 (24%) |
| Tumour Stage | | |
| Tis | 7 (3%) | - |
| T1 | 123 (46%) | - |
| T2 | 105 (40%) | - |
| T3 | 18 (7%) | - |
| T4 | 12 (5%) | - |
| Lymph Node Stage | | |
| N0 | 153 (58%) | - |
| N1 | 93 (35%) | - |
| N2 | 12 (5%) | - |
| N3 | 7 (2%) | - |
| Type of Breast Surgery | | |
| Mastectomy | 119 (45%) | - |
| Breast conserving | 146 (55%) | - |
| Type of Axillary Surgery | | |

| | | |
|---|---|---|
| Axillary Dissection | 157 (59%) | - |
| Sentinel Biopsy | 108 (41%) | - |
| Radiotherapy | 229 (86%) | - |
| Chemotherapy | 136 (51%) | - |
| Neo-adjuvant chemotherapy | 14 (5%) | - |
| Hormonal therapy | 211 (80%) | - |

Table 2 shows total, household, occupational and sport physical activity levels (MET) from the female reference population. Data are presented with an interval of 20 years of age and also show the corresponding limits (± 2 SD) that include approximately 95% of the population. For household, occupational and sport PA levels, data is reported for those who reported to be physically active in household activites, employed and participating in sports activities, respectively.

*Table 2. Total, household, occupational and sport physical activity levels (MET) from the female reference population.*

| Age (years) | L | M | S | -2 SD | -1 SD | +1 SD | +2 SD |
|---|---|---|---|---|---|---|---|
| Total PA level (n=3466, 100%) | | | | | | | |
| 35 | -4.10 | 295.4 | 0.07377 | 263.2 | 277 | 322.6 | 370.5 |
| 55 | -4.10 | 288.5 | 0.06898 | 258.6 | 271.5 | 312.9 | 353.6 |
| 75 | -4.10 | 275.0 | 0.05775 | 250.2 | 261.1 | 293.7 | 321.5 |
| Household PA level (n=2684, 77%) | | | | | | | |
| 35 | 0.37 | 36.2 | 0.59420 | 7.5 | 18.5 | 61.9 | 96.8 |
| 55 | 0.37 | 45.5 | 0.54458 | 11.3 | 24.7 | 74.7 | 113.5 |
| 75 | 0.37 | 42.3 | 0.54280 | 10.5 | 23.1 | 69.3 | 105.2 |
| Occupational PA level (n=1636, 47%) | | | | | | | |
| 35 | 0.50 | 79.2 | 0.35486 | 33.0 | 53.6 | 109.9 | 145.5 |
| 55 | 0.50 | 67.3 | 0.49482 | 17.2 | 38.1 | 104.7 | 150.3 |
| Sport PA level (n=2170, 63%) | | | | | | | |
| 35 | 0.14 | 13.1 | 0.91676 | 1.6 | 4.9 | 31.1 | 66.8 |
| 55 | 0.24 | 14.7 | 0.91676 | 1.3 | 5.2 | 33.7 | 67.2 |
| 75 | 0.34 | 17.0 | 0.91676 | 1.0 | 5.7 | 37.8 | 70.9 |

Median (M), Box-Cox power to remove skewness (L) and coefficient of variation (S); SD=Standard Deviation; The distribution of the PA levels was positively skewed, which required transformation with a power < 1. The reference curve for the different PA levels were modelled as follows: 1) Total PA level: a constant Box-Cox power of -4.1, 5 edf for the median and 3 edf for the coefficient of variation; 2) Household PA level: a constant Box-Cox power of 0.4, 4 edf for the median and 5 edf for the coefficient of variation; 3) Occupational PA level: Data were square root transformed for curve fitting with a constant Box-Cox power of 0.5, and 2 edf for both the median and coefficient of variation; 4) Sport PA level: 3 edf for the skewness, 4 efd for the median line and a constant coefficient of variation. LMS coefficients and percentiles in this table are given at the precise age given in the first column.

Table 3 shows the mean ± SD z-scores for the corresponding activity components along with the prevalence of low (-1 SD) and very low (-2SD) PA levels according to the reference data. Figures 1-4 show the reference curves in the female control population for total, household, occupational and sports PA levels, respectively. The corresponding measurements in the women with breast cancer are plotted on top of these curves. Additionally, a smooth line showns the trend (± standard error) of PA level by age in the patient population.

*Table 3. Mean (SD) total, household, occupational and sports physical activity level z-scores and prevalence of low (-1 SD) and very low (-2SD) physical activity level in patients with breast cancer according to the reference data from 3466 women without breast cancer.*

| Age group (years) | n | Mean ± SD z-scores (95%CI) | Prevalence n (%) low PA (95%CI) | Prevalence n (%) very low PA (95%CI) |
|---|---|---|---|---|
| Total PA level | | | | |
| Total group | 265 | -1.51 ± 1.86 (-1.74 to -1.29)*** | 156 (58.9%) (52.7 to 64.8%)*** | 90 (33.9%) (28.3 to 40.1%)*** |
| < 40 | 14 | -1.69 ± 2.40 (-3.07 to -0.3)* | 9 (64.3%) (35.1 to 87.2%)*** | 6 (42.9%) (17.7 to 71.1%)*** |
| 40-60 | 173 | -1.15 ± 1.56 (-1.39 to -0.92)*** | 92 (53.2%) (45.5 to 60.7%)*** | 46 (26.6%) (20.3 to 33.9%)*** |
| > 60 | 78 | -2.29 ± 2.14 (-2.77 to -1.81)*** | 55 (70.5%) (59.1 to 80.3%)*** | 38 (48.7%) (37.2 to 60.3%)*** |
| Household PA level | | | | |
| Total group | 263 | -0.21 ± 0.99 (-0.33 to -0.09)*** | 60 (22.8%) (17.9 to 28.4%)** | 12 (4.6%) (2.4 to 7.8%)* |
| < 40 | 14 | -0.39 ± 1.12 (-1.04 to 0.25) | 4 (28.6%) (8.4 to 58.1%) | 0 (0 to 23.2%) |
| 40-60 | 172 | -0.18 ± 0.95 (-0.33 to -0.04)** | 37 (21.5%) (15.6 to 28.4%)* | 9 (5.2%) (2.4 to 9.7%)** |
| > 60 | 77 | -0.24 ± 1.07 (-0.48 to 0.01) | 19 (24.7%) (15.6 to 35.8%)* | 3 (3.9%) (0.8 to 11.0%) |
| Occupational PA level | | | | |
| Total group | 143 | 0.34 ± 0.94 (0.19 to 0.50)*** | 9 (6.3%) (2.9 to 11.6%)*** | 0 (0 to 2.5%) |
| < 40 | 12 | 0.60 ± 1.05 (-0.07 to 1.27) | 0 (0 to 26.5%) | 0 (0 to 26.5%) |
| 40-60 | 128 | 0.32 ± 0.94 (0.15 to 0.48)*** | 9 (7.0%) (3.3 to 12.9%)** | 0 (0 to 2.8%) |
| > 60 | 3 | 0.37 ± 1.00 (-2.12 to 2.86) | 0 (0 to 70.8%) | 0 (0 to 70.8%) |
| Sport PA level | | | | |
| Total group | 143 | 0.01 ± 0.97 (-0.15 to 0.17) | 22 (15.4%) (9.9 to 22.4%) | 3 (2.1%) (0.4 to 6.0%) |
| < 40 | 10 | -0.11 ± 0.75 (-0.64 to 0.42) | 1 (10.0%) (0.3 to 44.5%) | 0 (0 to 30.8%) |
| 40-60 | 101 | 0.01 ± 0.97 (-0.18 to 0.20) | 16 (15.8%) (9.3 to 24.4%) | 2 (2%) (0.2 to 7.0%) |
| > 60 | 32 | 0.05 ± 1.05 (-0.33 to 0.43) | 5 (15.6%) (5.3 to 32.8%) | 1 (3.1%) (0.1 to 16.2%) |

SD=Standard Deviation; CI=Confidence Interval; *p-value<0.05; **p-value<0.01; ***p-value<0.001

***Total physical activity level***

The total PA level is slightly higher with increasing age, to a maximum at 42 years in the female reference population. Total PA level before diagnosis was significantly lower in the breast cancer population in all age groups, compared to the reference population (mean ± SD z-score (95%CI) = -1.51 ± 1.86 (-1.74 to -1.29)) (Table 2 and Figure 1). The prevalence of low and very low total PA levels in the breast cancer population ranged between 53.2% to 70.5% and 26.6% to 48.7%, respectively, depending on age groups. These prevalence rates were significantly higher than the theoretically expected prevalence rates of 15.9% and 2.3%, respectively, in the reference population. Additional analyses revealed lower z-scores for total PA level in breast cancer patients with a BMI ≥ 25 kg/m$^2$ versus those with a BMI < 25 kg/m$^2$ (-0.47; 95% CI (-0.02 to -0.92)).

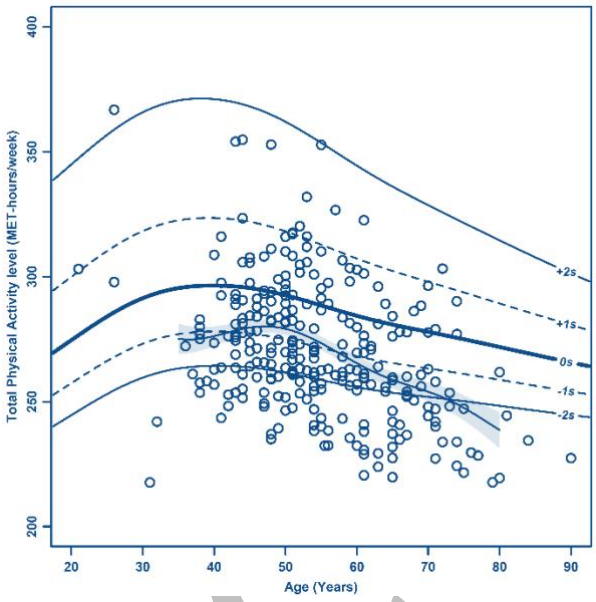


*Figure 1.* ***Total physical activity level.*** *The thick, solid curve represents the median; the dashed curves correspond to ± 1 SD and the thin, solid outer curves show the ±2 SD limits in the female reference population. Data of patients with breast cancer are plotted on top of these curves (dots). The smooth line and shaded area indicate the trend (± standard error) by age in the patient population.*

***Household physical activity level***

For household PA levels, data was limited to 2684 (77%) women from the reference sample and 263 (99%) patients with breast cancer active in household activities (Table 3 and Figure 2). Women in the reference sample without household related PA were usually below 22 years of age. In the reference sample, the highest levels of household PA were observed between the ages of 50 and 60 years. In patients with breast cancer, the level of household PA was significantly lower compared to the reference population (mean ± SD z-score (95%CI) = -0.21 ± 0.99 (-0.33 to -0.09)). In particular between 40 and 60 years of age, significantly lower levels of household PA levels were reported in the breast cancer population (mean ± SD z-score (95%CI) = -0.18 ± 0.95 (-0.33 to -0.04)). Accordingly, prevalence rates for low and very low levels of household PA were significantly higher for the total group (22.8% and 4.6%, respectively) and the age group between 40 to 60 years (21.5% and 5.2%, respectively) than expected in the reference group. Comparison of z-scores of the household PA level between breast cancer patients with and without overweight did not show any differences.

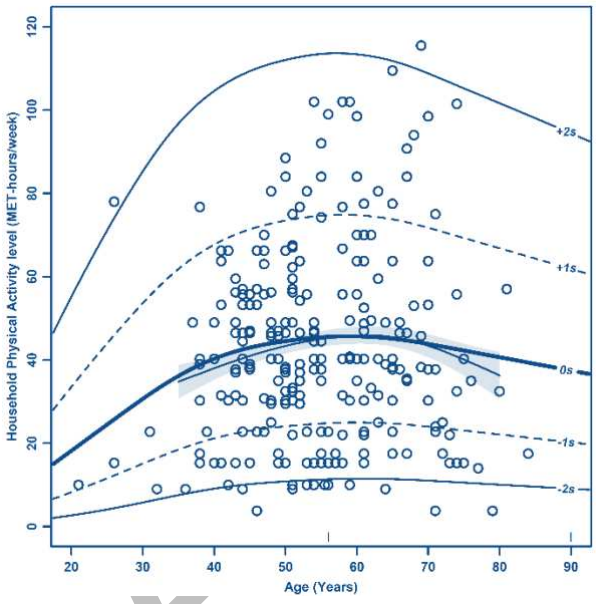


*Figure 2.* ***Household physical activity level****. The thick, solid curve represents the median; the dashed curves correspond to ± 1 SD; and the thin, solid outer curves show the ±2 SD limits in the reference population. Data of patients with breast cancer are plotted on top of these curves (dots). Zero values in patients are represented by small vertical lines at the bottom of the graph. The smooth line and shaded area indicate the trend (± standard error) by age in the patient population.*

***Occupational physical activity level***

In the reference population and breast cancer population, 1636 (47%) and 143 (54%) of women were employed, respectively (Table 1). In the reference population, the median physical activiy level related to occupation decreased linearly from 88 METs at 20 years of age to 64 METs at 60 years of age, while the variance increased linearly (Table 3 and Figure 3). In general, occupational PA levels were significantly higher in breast cancer patients during the year preceding diagnosis (mean ± SD z-score (95%CI) = (0.34 ± 0.94 (0.19 to 0.50)). When looking at the different age categories, this significant difference in occupational PA level is seen in women in the age range between 40 and 60 years in particular (mean ± SD z-score (95%CI) = 0.32 ± 0.94 (0.15 to 0.48)). This is also reflected in the significantly lower prevalence rates of low occupational PA levels in the total group of patients with breast cancer (6.3%) and age group 40 to 60 years (7.0%), compared with expected values for the reference population. Occupational PA levels did not significantly differ between breast cancer patients with and without overweight (BMI ≥ 25 kg/m$^2$).

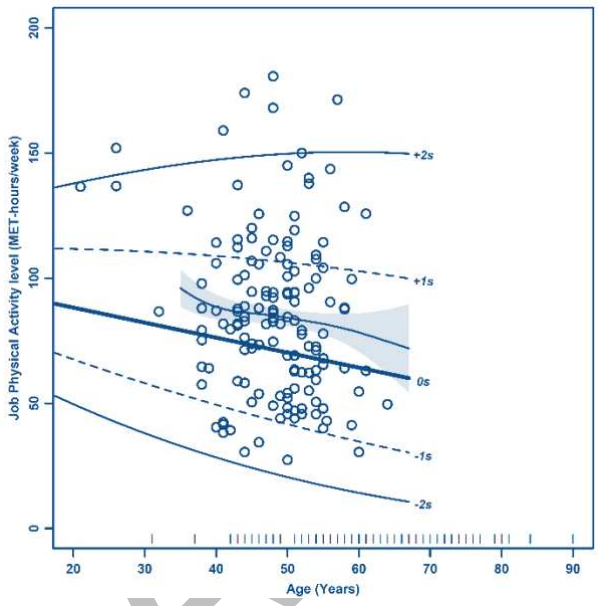


*Figure 3.* ***Occupational physical activity level****. The thick, solid curve represents the median; the dashed curves correspond to ± 1 SD; and the thin, solid outer curves represent the ±2 SD limits in the reference population. Data of patients with breast cancer are plotted on top of these curves (dots). Zero values are represented by vertical lines at the bottom of the graph. The smooth line and shaded area indicate the trend (± standard error) by age in the patient population.*

***Sports physical activity level***

In total, 2170 (63%) women in the reference population and 143 (54%) patients with breast cancer reported sports activities. No differences in sports PA level were noted between patients with breast cancer and the reference population over all age groups (Table 3 and Figure 4). Prevalence rates of decreased levels of sport PA in the breast cancer population did not significantly differ from expected rates in the reference population. No differences were found between breast cancer patients with a BMI $\geq$ 25 kg/m$^2$ versus those with a BMI < 25 kg/m$^2$.

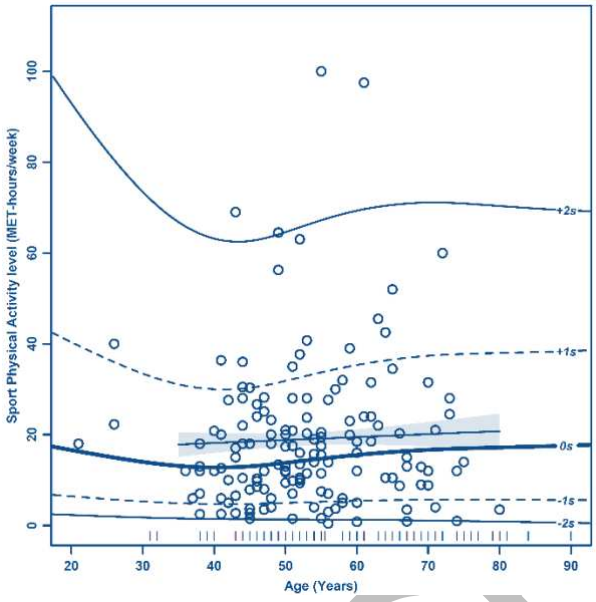


*Figure 4.* ***Sports physical activity level****. The thick, solid curve represents the median; the dashed curves correspond to ± 1 SD; and the thin, solid outer curves represent the ±2 SD limits in the reference population. Data of patients with breast cancer are plotted on top of these curves (dots). Zero values are presented with vertical lines at the bottom of the graph. The smooth line and shaded area indicate the trend (± standard error) by age in the patient population.*

## Discussion

In the present study we compared PA levels (including total-, household-, occupational- and sport-activity levels) in breast cancer patients one year before diagnosis with corresponding activity levels in women from a reference population. Our hypothesis of lower prediagnosis PA levels in women who develop breast cancer was proven for total PA, but results for the individual components are equivocal.

**Total PA level** of breast cancer patients during the year before surgery was significantly lower compared to the reference population without breast cancer in all age groups. The literature provides strong evidence demonstrating that low levels of PA increase the risk of breast cancer up to 13% compared to high levels of PA [27, 28]. Consequently, female breast cancer patients have on average lower PA levels before surgery and a return to pre-diagnosis PA levels may not be sufficient for future protection from disease [3]. Moreover, strong evidence exists that a high level of prediagnosis PA significantly reduces breast cancer mortality as well as all-cause mortality [3]. High levels of postdiagnosis PA are also associated with a lower risk of cancer-specific mortality and all-cause mortality. These findings allow us to suggest that patients who were physically inactive before breast cancer diagnosis, should be motivated to increase their level of PA since they may benefit from a potentially protective effect of high PA levels later on [3, 9]. However, because the evidence is based on the level of physical activity before or after diagnosis, we acknowledge that further research is needed to prove changing physical activity over time is indeed related to the mentioned benefits.

Total PA level is the sum of household, occupational, sports and active transport in leisure time and sedentary activities. The strongest evidence regarding PA and the risk of developing breast cancer is available for leisure time (i.e. active recreation, exercise and sports activities) and occupational PA [3]. Protective associations were also found for household, active transport, and walking, but only in a small number of studies [3]. In the present study, significant differences with a reference population were found for household and occupational PA levels. In contrast with our hypothesis and with previous research, **occupational PA levels** were significantly higher in the breast cancer group compared to the controls. The study of Johnsson et al (23) concluded that women younger than 55 years, who were less physically active at the occupational level, had a significantly increased risk of breast cancer, but no association was found in women who were older than 55 years. Similarly, a meta-analysis by Zhou et al (24) showed that women with a history of occupational sedentary behavior had a significantly increased risk of breast cancer. A study by Moradi et al (25) also found a significant increased risk of breast cancer with decreasing level of occupational PA. All together, the report of the ACSM roundtable described a 16% lower risk of breast cancer when comparing women with a high versus low occupational PA level [3]. The unexpected higher PA levels in our study should be further explored. Possibly, the association between occupational PA and risk of breast cancer was confounded by educational level, socio-economic status and/or social support. One explanation may be that women in higher socio-economic status typically sit

more at work, but participate in higher levels of leisure time PA. Occupations with high levels of PA are often occupations associated with lower socio-economic status. Yet, in the composite measure, these are all summed into one sumscore.

To our knowledge, no study previously compared occupational activity levels in breast cancer patients with those in a reference population without breast cancer. The difference in occupational PA levels in the present study was more pronounced at ages 40 to 60 years. Interestingly, we found significantly lower levels of **household PA** levels in this same age group of breast cancer patients as well. To which extent these PA domains are interrelated should be further explored as well. At last, in the present study there was no significant difference between the patient group and reference group for **sport PA levels**. However, a recent ACSM roundtable concluded that the risk for breast cancer was up to 13% lower in high versus lower leisure time PA [3]. The relative contribution of the different PA domains to the lower general prediagnosis PA levels in breast cancer patients and the extent to which active transport in leisure time and sedentary activities also contribute to lower general PA levels has to be further explored.

In line with the differences in the mean PA levels, we also found higher **prevalence rates** of low and very low PA levels in breast cancer patients, which confirms the hypothesis that they are less physically active before diagnosis compared to a eference population. For the total PA level, more than 53% of breast cancer patients have a low PA level, which is more than three times the expected prevalence rate of 15.9%. An even higher prevalence rate (70.5%) was observed in women above 60 years of age, even though our reference curve for woman without breast cancer accounted for age differences. It has been described that PA declines dramatically across age groups between childhood and adolescence and continues to decline with age in adulthood [18]. In addition, a study of Fan et al reported that young or middle-aged persons are the least physically active age group [29]. Moreover, the risk of breast cancer increases with age as well, making middle-aged women an important target group for interventions aimed at increasing activity levels [2]. Analogous with age trends in the mean levels of household and occupational PA, prevalence rates of lower PA are also significantly higher for household activities and lower for occupational activities, particularly in the age group between 40 to 60 years.

Besides age, a higher BMI has also been associated with an increased risk of breast cancer [2]. However, in the present study, both the mean BMI and the prevalence rate of being overweight (BMI $\geq$ 25 kg/m$^2$) was similar in the breast cancer group and in the reference population (see table 1). Additionally, people with a higher BMI also tended to be less physically active. This association was confirmed in our study by a significant difference in total PA level between breast cancer patients with and without overweight, which may have increased their risk of breast cancer even more. Non-active woman with overweight may therefore be another potentially important target population for promoting PA.

The present study had several **strengths.** First, this is the first study which uses the LMS method to estimate the distribution of PA levels by age in a female reference population. This method is widely used for the estimation of growth curves in children because it allows to summarize the median, variance and skewness in an age dependent way. The LMS method also allows for a straightforward comparison of other data (e.g. our female breast cancer population) with this population, and effectively adjusts for differences in the age distribution between the sample and the reference population. Second, this is also the first study which assesses all domains of PA (i.e. total, household, occupational and sport PA levels) before surgery in both breast cancer patients and controls.

Several limitations need to be discussed. First, a **limitation** of the study may be that people overestimate their activity levels with a self-reported PA measure. It was demonstrated by Scheers et al [23] that PA was higher and sedentary behavior lower as calculated from the FPACQ compared to a SenseWear Armband together with an electronic activity diary. This indicates that the MET values per group may be too high, however it will not affect the between group results. Second, when interpreting the results of the present study, timing of the data collection should be considered. Patients completed the self-reported PA measure - the FPACQ - one day before surgery. It has been described that after an acute illness, or in this case acute diagnosis, there is often a "sit, wait and see approach" and patients might suddenly become less physically active [30]. When hearing the cancer diagnosis, basic values, goals and one's self-image will be challenged [12]. That is why it is possible that just having had a diagnosis, even before any treatment has been given, will already result in a different PA level compared to non-diagnosed persons. This should be taken into account when interpreting these self-reported PA-levels, despite a clear instruction to recall PA one year before the diagnosis. Third, a diagnosis of a more advanced cancer may have a higher impact than a diagnosis of an early stage -possibly curable - cancer, as reported by Ferriolli et al in patients with gastrointestinal cancer [7]. In this context, the stress associated with the cancer diagnosis may also influence the responses to the questionnaire. Fourth, as discussed above, the PA levels of patients were converted to age adjusted z-scores, using the representative sample of women as a reference. However, other factors including socio-economic status, social status and education level among others, may influence PA and risk of breast cancer. These data were unfortunately not available. Also, as reported in the original manuscript patients included in the present cohort were younger and had a lower BMI as those not included[14]. Whereas this can affect the representativeness of the population, this will not have influenced the present results because we report on age and BMI controlled comparisons. Fifth, 14 (5%) breast cancer patients received neo-ajduvant chemotherapy. These patients also completed the physical activity questionnaire the day before surgery. At that time, diagnosis was made three to six months ago, followed by chemotherapy. Because this is only a small number of patients and the questionnaire questions PA levels during the past year, we do not expect this influenced the results of the present study. At last, some limitations in generalization should be mentioned. The study has been conducted in a single center in Belgium more than 10 years ago. When

looking at the trends in physical activity over time, only a very small positive evolution could be observed in The Netherlands in the period 2001-2018[31]. Data based on the National Health and Nutrition Examination Survey (NHANES) study (US) did not show any change in adherence to physical activity guidelines in the period 2007 – 2016 eather[32]. Therefore, we expect results to be reflective of the current pre-diagnosis PA levels.

For further research it would be interesting to investigate if the PA activity levels of breast cancer patients decreases from the moment of diagnosis, up to the start of the cancer treatment, although recruitment of subjects might be challenging. Additionally, it would be interesting to explore the relative contribution of different domains of PA more into detail. More specifically, the unexpected higher occupational PA level in the breast cancer population should be further explored. Further research is needed to compare the results of BC patients with controls and to look at the effect of potential confounding factors, including e.g. educational level, socio-economic status and marital status but also cancer stage.

For **clinical practice**, the results of the present study indicate that motivating female breast cancer survivors to return to their activity levels before the BC diagnosis may not be sufficient. To benefit from the protective effects of PA, moderate to high intensity activities are needed [9]. However, an important message may also be that it is certainly never too late to change lifestyle and become physically active. Second, in line with the guidelines from the ACSM roundtable from 2018, the general population should be motivated to perform aerobic activities at least three times a week for 30 minutes (at least at a moderate intensity) and do muscle strength training at least two days per week for major muscle groups, which might decrease the risk of breast cancer (and other cancers) [10].

**In conclusion**, it seems that total PA levels of female breast cancer patients are lower during the year before surgery compared to a a reference population without breast cancer, in particular household activity levels. Remarkably, occupational activity levels of breast cancer patients were higher in the year before surgery compared to female controls.

**Clinical Practice Points**

- It is currently unknown whether breast cancer patients are less physically active in the year before diagnosis compared to healthy peers.
- This study demonstrated that female patients with breast cancer show significantly lower total PA levels during the year prior to surgery compared to a female reference population without breast cancer diagnosis, especially household activity levels between ages 40 to 60 are lower.
- Returning to pre-diagnosis physical activity levels after cancer treatment may not be sufficient to protect breast cancer survivors in the future.

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