

**PHYSICAL ACTIVITY PARTICIPATION IN OVARIAN CANCER  
SURVIVORS: PREVALENCE, DETERMINANTS AND ASSOCIATION  
WITH PATIENT REPORTED OUTCOMES**

by

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## Abstract

*Objectives:* The primary objectives were (1) to estimate the prevalence of meeting physical activity (PA) guidelines among ovarian cancer survivors in the post-treatment period and (2) to identify the determinants of meeting PA guidelines in this study population. The secondary objective was to explore the association between PA and patient reported outcomes (PROs), specifically health-related quality of life (HRQOL), anxiety and depression symptoms.

*Methods:* The Lifestyle Habits and the PRognosis of Ovarian Cancer in Quebec (HPROQ) Study is a prospective cohort study that was conducted in Montreal (2015-2018). For this thesis, a cross-sectional study was conducted on the baseline cohort. 112 ovarian cancer survivors were interviewed 6 months after treatment completion. Modified Poisson regression was used to estimate the prevalence ratio (PRs) and 95% confidence intervals (CIs) to describe the association between patient characteristics and the prevalence of meeting PA guidelines. Multivariable linear and logistic regressions were used to examine the association between meeting PA guidelines and PROs.

*Results:* 42.0% (95% CI: 32.8-51.1%) of ovarian cancer survivors met the PA guidelines of at least 150 minutes of moderate PA per week. There was no evidence of a statistically significant association between any of the potential determinants and meeting PA guidelines. Employment had the highest PR, suggesting that women who were employed had a prevalence of meeting PA guidelines that was 1.49 times greater than women who were unemployed (PR=1.49; 95% CI:0.87-2.55). There was no statistical evidence of an association between meeting PA guidelines and better HRQOL or reduced anxiety and depressive symptoms. PA was most protective for depressive symptoms, suggesting that women who met PA guidelines had odds of depressive symptoms that were 0.30 times greater than women who did not meet PA guidelines.

*Conclusions:* The prevalence of meeting PA guidelines 6 months after treatment was higher than reported in previous studies. None of the potential determinants were significantly associated with meeting PA guidelines, nor was meeting PA guidelines significantly associated with improved PROs. Due to the small sample size the study was underpowered, making it difficult to exclude chance as an explanation for some of the more suggestive associations observed in this thesis.

## **Co-Authorship**

This thesis is the work of Chloe Chow in cooperation with Dr. Anita Koushik and Dr. Harriet Richardson, as well as Dr. Anne Grundy, a Research Associate working on the Lifestyle Habits and the Prognosis of Ovarian cancer in Quebec (HPROQ) Study. The data used for this thesis was from the HPROQ Study, for which Dr. Koushik is the primary investigator. The conceptualization for this thesis was a collaborative effort between Chloe Chow, Dr. Koushik and Dr. Richardson. Chloe Chow performed the literature review, data cleaning, SAS dataset management, relevant analyses, interpretation of the results and writing of the thesis. Dr. Koushik and Dr. Richardson provided feedback and guidance, as well as editing of the thesis.

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## Table of Contents

Abstract.....	ii
Co-Authorship.....	iv
Acknowledgements.....	v
List of Tables.....	ix
List of Abbreviations.....	x
Chapter 1 Introduction.....	1
1.1 Background and Rationale.....	1
1.2 Objectives.....	3
1.3 Thesis Organization.....	3
1.4 Student Contribution.....	4
1.5 References.....	4
Chapter 2 Literature Review.....	6
2.1 Ovarian Cancer.....	6
2.1.1 Descriptive Epidemiology.....	6
2.1.2 Subtypes.....	6
2.1.3 Prevention, Prognosis and Recurrence.....	7
2.1.4 Importance of Research.....	8
2.2 Physical Activity.....	8
2.2.1 Description and Metabolic Equivalent of Tasks.....	8
2.2.2 Recommended Guidelines and Feasibility.....	9
2.2.3 Physical Activity Assessment.....	12
2.3 Physical Activity and Cancer.....	14
2.3.1 Physical Activity and Cancer Risk.....	14
2.3.2 Physical Activity and Cancer Prognosis.....	14
2.3.3 Post-Diagnosis Physical Activity and Ovarian Cancer.....	16
2.3.4 Determinants of Physical Activity Participation Among Ovarian Cancer Patients.....	18
2.4 Patient Reported Outcomes.....	20
2.4.1 Description and Assessment.....	20
2.4.2 Patient Reported Outcomes as a Prognostic Factor in Cancer.....	21
2.5 Association Between Physical Activity and Patient Reported Outcomes.....	22
2.5.1 Physical Activity and Patient Reported Outcomes in Cancer Population.....	22
2.5.2 Physical Activity and Patient Reported Outcomes in Ovarian Cancer Populations.....	23

2.5.3 Physical Activity and Patient Reported Outcomes in the General Population.....	24
2.6 Rationale.....	25
2.7 References .....	26
Chapter 3 Methods.....	32
3.1 Objectives.....	32
3.2 Study Design and Populations.....	32
3.3 Data Collection .....	33
3.3.1 Physical Activity .....	33
3.3.2 Patient Reported Outcomes.....	34
3.4 Physical Activity Assessment.....	35
3.5 Patient Reported Outcome Assessment.....	37
3.6 Covariates (patient characteristics and clinical factors) .....	37
3.7 Analysis Strategy .....	38
3.7.1 Descriptive Analysis.....	38
3.7.2 Objective 1.....	38
3.7.3 Objective 2.....	39
3.7.4 Objective 3.....	41
3.8 Power Calculation.....	42
3.9 Ethical Considerations and Data Management.....	43
3.10 References .....	44
Chapter 4 Physical Activity in Ovarian Cancer Survivors: Prevalence and Determinants of Participation	46
4.1 Abstract .....	46
4.2 Introduction .....	48
4.3 Materials and Methods.....	49
4.3.1 Study Population .....	49
4.3.2 Study Variables.....	50
4.3.3 Statistical Analysis .....	52
4.4 Results.....	53
4.5 Discussion .....	55
4.6 References .....	61
Chapter 5 Additional Analyses.....	71
5.1 Examining the Association Between Physical Activity and Patient Reported Outcomes.....	71
5.1.1 Meeting Physical Activity Guidelines and FACT-O.....	71
5.1.2 Meeting Physical Activity Guidelines and HADS .....	72

5.2 Exploratory Analysis of Lifetime and Past 10 years Physical Activity for PROVAQ Subgroup.....	73
5.3 Sensitivity Analysis.....	74
5.3.1 Logistic Regression for Determinants of Physical Activity.....	74
5.3.2 Determinants of Physical Activity with Guideline of 150 minutes including walking .....	76
5.3.3 Association Between Physical Activity (with Guideline of 150 minutes including walking) and Patient Reported Outcomes .....	78
5.4 References .....	79
Chapter 6 Discussion .....	80
6.1 Summary of Main Findings.....	80
6.2 Comparison of Study Results to Existing Literature.....	81
6.2.1 Prevalence of Physical Activity .....	81
6.2.2 Determinants of Physical Activity .....	82
6.2.3 Association between Physical Activity and Patient Reported Outcomes.....	83
6.3 Explanation of Study Results.....	84
6.3.1 Prevalence of Physical Activity .....	84
6.3.2 Determinants of Physical Activity .....	85
6.3.3 Association between Physical Activity and Patient Reported Outcomes.....	86
6.3.4 Sensitivity Analyses .....	87
6.4 Methodological Considerations .....	88
6.4.1 Strengths .....	88
6.4.2 Chance .....	90
6.4.3 Bias.....	90
6.4.4 Confounding .....	92
6.4.5 External Validity .....	93
6.5 Future Directions .....	93
6.6 Research Contributions and Overall Conclusions.....	94
6.7 References .....	95
Appendix A Ethics Clearance .....	98
Appendix B HPROQ Study Administered Questionnaire .....	100
Appendix C Specific Items Used for the Trial Outcome Index (TOI) Score .....	131
Appendix D Correlation Table for Identifying Confounders (Objective 2).....	132
Appendix E Change in Estimate Summary Tables.....	133

## List of Tables

**Table 3.1** MET energy expenditure estimates assigned to each self-reported PA category in the IPAQ based on the updated Compendium of Physical Activities

**Table 3.2** The power to detect a certain PR for a range of exposure prevalence's

**Table 3.3** The detectable mean difference with 80% power, 5% significance and 2-sided test

**Table 4.1** Descriptive characteristics of the study population

**Table 4.2** Prevalence of meeting PA guidelines

**Table 4.3** Percentage of PA participation by IPAQ domain and meeting PA guidelines

**Table 4.4** Crude and adjusted PR and 95% CI for the association between potential determinants and meeting PA guidelines

**Table 5.1** Crude and adjusted estimates with 95% CI for the relationship between meeting PA guidelines and FACT-O score which measures HRQOL

**Table 5.2** Crude and adjusted estimates with 95% CI for the relationship between meeting PA guidelines and different PROs

**Table 5.3** Past 10 years of MVPA and current MVPA participation

**Table 5.4** Lifetime MVPA and current MVPA participation

**Table 5.5** Determinants of PA using a logistic regression model in comparison to the determinants of PA using a modified Poisson model

**Table 5.6** Determinants of PA using a modified Poisson model with PA guideline defined as 150 minutes of moderate PA including walking in comparison to PA guideline not including walking

**Table 5.7** Association between PA and PROs using PA guideline of 150 minutes of MVPA, with walking included as MVPA, in comparison to results with a PA guideline of 150 minutes of MVPA without walking

## List of Abbreviations

ACSM	American College of Sports Medicine
BMI	Body mass index
CEGEP	College d'enseignement general et professionnel
CIE	Change in estimate
CI	Confidence interval
FACIT	Functional assessment of chronic illnesses therapy
FACT-O	Functional assessment of cancer therapy – ovarian cancer
HADS	Hospital anxiety and depression scale
HPROQ	Lifestyle Habits and PRognosis of Ovarian Cancer in Quebec
HRQOL	Health-related quality of life
IPAQ	International physical activity questionnaire
METs	Metabolic equivalent of tasks
MVPA	Moderate to vigorous physical activity
OC	Oral contraceptive
OR	Odds ratio
PA	Physical activity
PR	Prevalence ratio
PROs	Patient reported outcomes
PROVAQ	Prevention of OVArrian Cancer in Quebec
TOI	Trial outcome index

# Chapter 1

## Introduction

### 1.1 Background and Rationale

Ovarian cancer is the deadliest gynecological cancer in Canada and rarely diagnosed at an early stage due to an absence of early symptoms or effective secondary prevention strategies<sup>1,2</sup>. In addition to the lack of prevention strategies, symptoms related to ovarian cancer can be vague and non-specific, which often delays women to seek medical attention<sup>3</sup>. Furthermore, a high percentage of cases are classified as Type II tumours, which are highly aggressive tumours that grow rapidly<sup>4</sup>. This often results in the majority of cases being diagnosed at a later stage, leading to poor prognosis of disease.

To date, the only known factors to influence the prognosis of this disease are clinical, such as stage of diagnosis, tumour grade, histology, type of treatment, surgery and therefore, non-modifiable. With the lack of prevention strategies and the poor prognosis of ovarian cancer, emerging studies have been investigating the role that modifiable lifestyle factors may have to help improve cancer outcomes. One of the most commonly studied modifiable lifestyle factors is physical activity (PA) and among cancer populations, the recommended PA guideline is 150 minutes of moderate intensity PA, which has been deemed feasible and appropriate<sup>5,6</sup>. PA is often measured prior to diagnosis to understand its role in etiology, or during treatment to evaluate its impact on chemotherapy adherence. However, PA is rarely measured after treatment completion, and therefore its role on cancer prognosis remains unclear, especially in ovarian cancer. The ovarian cancer literature has found the prevalence of meeting PA guidelines after diagnosis to be quite low<sup>7-10</sup>. Moreover, the hardships of treatment often leave women fatigued with a loss of physical function, which make it difficult to reach these PA goals. PA measures, such as the IPAQ, collects information on duration, frequency and intensity among different PA domains,

which can help provide a better understanding of the different types of PA ovarian cancer patients prefer to engage in, as well as the contribution of these domains towards meeting PA guidelines.

Potential determinants of PA participation have not been well-established in the ovarian cancer literature, especially after diagnosis. Sociodemographic, lifestyle and clinical factors should be analyzed to determine if certain characteristics of ovarian cancer survivors are associated with being more physically active. Identifying the determinants of post-treatment PA in ovarian cancer survivors will provide crucial information when looking at survival outcomes and planning for future interventions. Other outcomes that have not been well studied after diagnosis among ovarian cancer patients are patient reported outcomes (PROs). PROs, such as health-related quality of life (HRQOL), anxiety and depression, provide insight into the patient's well-being at a critical time and have also been deemed as potential prognostic factors<sup>11,12</sup>. Moreover, increase PA has been found to be associated with better HRQOL and other PROs in breast cancer survivors<sup>13,14</sup>, which warrants the investigation in ovarian cancer, especially if an increase in PA can lead to better HRQOL after treatment completion.

Very few studies have investigated post-diagnosis and/or post-treatment PA in ovarian cancer populations, and the studies that do exist provide little information about the time period shortly after treatment. The prevalence and determinants of PA during this time remain unknown, with even less information known regarding the relationship of PA with PROs. This thesis therefore assessed PA 6 months after treatment completion for all participants in an attempt to address this gap in knowledge.

Data for this thesis came from a prospective cohort study funded through a pilot project award from the US Department of Defense Ovarian Cancer Research Program. The results from this thesis provide a baseline description of the prevalence of healthy lifestyle factors in this population. In addition, the feasibility of adopting (or maintaining) favourable lifestyle behaviours by ovarian cancer survivors will be informed by this baseline assessment. Altogether,

the results of this Pilot Award will provide support for expanding current clinical recommendations to ovarian cancer patients to incorporate the modification of lifestyle behaviours in a more holistic approach to improve prognosis.

## **1.2 Objectives**

1. To estimate the prevalence of physical activity of ovarian cancer survivors who are currently in the post-treatment period.
2. To identify determinants of post-treatment physical activity in ovarian cancer survivors.
3. To explore the association between post-treatment physical activity and patient reported outcomes (PROs) in the baseline cohort.
  - a) The association between physical activity and health-related quality of life (HRQOL).
  - b) The association between physical activity and anxiety scores from the hospital anxiety and depression scale (HADS).
  - c) The association between physical activity and depression scores from the HADS.

The hypothesis for the third objective was that women who met the PA guideline of 150 minutes of moderate activity per week will have better PROs, including higher HRQOL scores and less anxiety and fewer depression symptoms in comparison to women who did not meet PA guidelines.

## **1.3 Thesis Organization**

This thesis follows the guidelines set in place by Queen's University School of Graduate Studies and the Department of Public Health Sciences for a manuscript-based thesis. Chapter 1 provides an introduction to the topic and outlines the thesis project. Chapter 2 consists of a literature review on the background of ovarian cancer, post-treatment PA and PROs. Chapter 3

details the data source, data cleaning and the analysis techniques used to accomplish the thesis objectives. Chapter 4 is a manuscript draft that estimates the prevalence and identifies the determinants of post-treatment PA among ovarian cancer patients. Chapter 5 contains additional analyses that were conducted, investigating the association between PA and PROs. Lastly, the sixth chapter consists of a general discussion of the findings, the study validity, conclusions and important implications in the field of ovarian cancer epidemiology. References are included at the end of each chapter and extra material can be found in the appendices.

#### **1.4 Student Contribution**

To achieve the objectives above, Chloe Chow, with guidance from her supervisors and study team, was responsible for developing the research questions and objectives, critically appraising the existing literature, cleaning raw data, developing and coding definitions of all variables, conducting the statistical analyses, assessing the impact of methodological limitations on results, and writing this thesis.

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## Chapter 2

### Literature Review

#### 2.1 Ovarian Cancer

##### 2.1.1 Descriptive Epidemiology

Ovarian cancer is the deadliest gynecological cancer and the eighth most common type of cancer amongst Canadian women in 2017<sup>1</sup>. Worldwide, it was estimated that there were 239 000 new cases and 152 000 deaths due to ovarian cancer in the year 2012<sup>2</sup>. Furthermore, incidence rates are highest in more developed regions, with a rate of 9.1 per 100 000<sup>2</sup>. Mortality rates are also higher in more developed regions with 5.0 deaths per 100 000 in comparison to 3.1 deaths per 100 000 in less developed regions<sup>2</sup>.

The 5-year survival rate rapidly declines with increasing stage of cancer diagnosis (i.e. 5-year survival for stage I, 89%; stage II, 66%; stage III, 34%; and stage IV, 18%), with only 25-30% of cases diagnosed at an early stage<sup>3,4</sup>. Although the majority of women diagnosed at advanced stage will likely succumb to their disease, ovarian cancer survival can be quite variable, with 38% of women dying within the first 2 years of their diagnosis and 31% of women living 10 or more years after diagnosis<sup>5</sup>. Incidence and mortality rates increase exponentially with age, as survival is twice as high for women under the age of 65 in comparison to those who are over 65<sup>3</sup>.

##### 2.1.2 Subtypes

Traditionally, ovarian carcinomas have been suggested to originate from the ovarian surface epithelium and subtypes are classified according to the different histological types (i.e. serous, mucinous, endometrioid, and clear cell)<sup>6</sup>. However, recent studies have provided a new model for ovarian carcinogenesis, distinguishing invasive ovarian cancer into two broad categories: Type I and Type II. Type I tumours are suggested to be slow growing, appearing to be

a part of a continuum starting with benign tumours that subsequently develop towards invasive tumours<sup>6</sup>. They are often confined in the ovaries at time of diagnosis, with a stable genome and are low-grade<sup>7</sup>. On the other hand, type II tumours are suggested to be more aggressive and believed to originate from the epithelium of the fimbrial portion of fallopian tubes and/or the ovarian surface epithelium<sup>6</sup>. They grow rapidly towards the ovaries and surrounding tissues, are genetically unstable and are high-grade at, or soon after their inception<sup>7</sup>. Most screening tests can only capture Type I tumors as they are easier to detect, however, only about 25% of ovarian cancer cases are defined as Type I<sup>7</sup>.

### **2.1.3 Prevention, Prognosis and Recurrence**

The etiology of ovarian cancer remains largely unknown and proposed screening tests do not have adequate sensitivity, specificity and positive predictive values<sup>3</sup>. Consequently, ovarian cancer cannot be screened for and is rarely diagnosed at an early stage due to the absence of effective primary and secondary prevention strategies. Furthermore, symptoms related to ovarian cancer, like bloating, abdominal pain and appetite change, can be subtle and non-specific, and are often believed to be related to menopause, menstrual irregularities, aging or other non-serious conditions<sup>8</sup>. The combination of non-specific symptoms and the lack of secondary prevention strategies, often results in most patients delaying seeking medical attention until the cancer has progressed to stage III or IV, leading to poorer cancer prognosis and outcome. Thus, it is imperative to also investigate factors that may have a role in the development, prognosis and/or outcome of this disease.

Due to the small number of truly early stage cases, the rapid progression of the majority of ovarian cancer cases, and failure to identify a histological precursor, implementing primary and secondary prevention strategies for ovarian cancer has proven to be very challenging<sup>7</sup>. Moreover, cancer recurrence is quite common, with 50-75% of cases that respond to therapy

experiencing recurrence within 18 months, and once cancer is recurrent, it is rarely curable<sup>9,10</sup>. As a result, the prognosis of ovarian cancer is quite poor, which has led to emerging studies to investigate tertiary prevention strategies<sup>11,12</sup> that go beyond clinical measures, such as modifying lifestyle behaviour, to improve survival outcomes and prevent cancer recurrence.

#### **2.1.4 Importance of Research**

Many cases are diagnosed at a later stage due to the absence of appropriate screening tests and the non-specific symptoms for ovarian cancer. Late stage cancer diagnosis often results in poorer prognosis, whether it is a lower survival rate or a greater chance for cancer recurrence. In order to gain a better understanding of the prognosis of ovarian cancer, more studies should be conducted after treatment has been completed. Clinical factors that can influence cancer prognosis, such as stage of cancer, grade, surgery, etc. cannot be changed, but lifestyle factors, such as physical activity (PA), can be modified. Whether modifying lifestyle factors in ovarian cancer patients can improve cancer outcomes is still unknown, which is why it is important to investigate these factors post-diagnosis, and more specifically, post-treatment. The modifiable lifestyle factor of interest for this study is PA, as it has been well investigated in cancer, but more evidence is required for its role in ovarian cancer prognosis. Furthermore, PROs, such as HRQOL, anxiety and depression, are also important to consider as they may also have a role as a prognostic indicator and can change throughout the cancer course. It is important to research PA and PROs among ovarian cancer cases after treatment to better understand how these women are doing during this period of time and whether their disease prognosis can be improved by modifying their lifestyle behaviours.

## **2.2 Physical Activity**

### **2.2.1 Description and Metabolic Equivalent of Tasks**

In general, PA is defined as “any bodily movement produced by skeletal muscles that results in energy expenditure”<sup>13</sup>. PA is often measured by taking into account the frequency, duration and intensity of a variety of activities. Frequency and duration are often accounted for by measurements of time (i.e. hours or minutes per day; times per week), but in order to take into account exercise intensity, PA can be converted to metabolic equivalent of tasks (METs) by using guidelines provided by the Compendium of Physical Activities<sup>14</sup>. METs assess intensity by calculating the metabolic rate for different activities, with 1 MET considered a resting metabolic rate during quiet sitting<sup>15</sup>. To gain a better understanding of the different levels of PA intensities, moderate PA is equivalent to a brisk walk that noticeably accelerates the heart rate, but not to the extent of rapid breathing, whereas vigorous PA is exemplified by jogging, or activities that cause rapid breathing and a substantial increase in heart rate<sup>16</sup>. Moderate and vigorous activity can be furthered classified as expending 3-6 METs and  $\geq 6$  METs, respectively<sup>17</sup>. Hours and minutes of PA can be converted into MET-hours and MET-minutes, where 1 MET-hour or 1 MET-minute is defined as the amount of energy expended when at rest for an hour or a minute<sup>18</sup>. For example, using a moderate intensity MET estimate of 4, 150 minutes of moderate PA per week would translate to 10 MET-hours ( $2.5 \text{ hours} \times 4 \text{ METs}$ ) or 600 MET-minutes ( $150 \text{ minutes} \times 4 \text{ METs}$ ).

### **2.2.2 Recommended Guidelines and Feasibility**

For the general Canadian adult population, the recommended guidelines for PA participation is 150 minutes of MVPA per week in bouts of 10 minutes or more, in addition to muscle and bone strengthening exercises for at least 2 days per week<sup>19</sup>. In a cancer population, the same recommendation of 150 minutes per week applies, but the level of intensity of PA is not as high (i.e. moderate vs. moderate-to-vigorous). Furthermore, it is also recommended that individuals with chronic conditions, such as cancer, should be as active as their abilities and conditions allow and to avoid inactivity as much as possible<sup>20</sup>. To take into account PA intensity,

adults should aim for an energy expenditure ranging from 500-1000 MET-minutes per week based on the recommended guidelines<sup>21</sup>. PA guidelines for cancer populations ( $\geq 500$  MET-minutes per week) are on par with the PA recommendation for the general population, but on the lower end of that range, resulting in less demanding guidelines while still encouraging enough PA in order to achieve health benefits.

When assessing PA, it is important to consider different types of PA that can be included in meeting PA guidelines. Randomized controlled trials for breast cancer survivors have used aerobic and resistance training as part of the intervention regimen<sup>22</sup> and observational studies looking at ovarian cancer have focused on recreational PA<sup>23,24</sup>. However, it may be physically difficult for women who are in the post-treatment phase to reach 150 minutes of moderate-intensity recreational PA, and therefore other types of activity, such as occupational, household, yard/garden and transportation PA should also be considered<sup>14</sup>. A prospective study conducted in the Netherlands argued that measuring non-occupational PA was appropriate because during the time of recruitment, most women did not hold jobs<sup>25</sup>. Moreover, it has been suggested that women who do have physically demanding jobs, may be too tired to engage in non-occupational or domestic activity, and therefore, all forms of PA should be considered<sup>25</sup>. Men who have undergone prostate cancer treatment were most active in the domestic PA domain of the IPAQ and least active in the transport and leisure domain, implying that PA is primarily undertaken involuntarily as part of household chores, due to the side effects of treatment<sup>26</sup>. Whether domestic-related or occupation-related PA contributes more heavily to achieving a sufficient level of activity for health benefits remains unclear and needs to be further investigated.

In cancer research, the recommended PA guideline is often used as a benchmark to categorize active and non-active participants<sup>20</sup>. If PA is to be measured after diagnosis, it is important to consider the timing that ovarian cancer patients deem the most appropriate. After cancer diagnosis but during treatment may be a difficult time for women to participate in self-

directed PA, as up to 90% of women receiving chemotherapy for ovarian cancer suffer from nausea, difficulty sleeping, and pain, which has been associated with reduced physical function<sup>27</sup>. A systematic review of 56 randomized controlled trials, including a wide range of cancer patients, reported that PROs were positively impacted by PA interventions delivered post-treatment, which suggested that PA could be measured shortly after treatment completion<sup>28</sup>. However, many patients are often very fatigued and weak after treatment, resulting in 3 to 6 months post-treatment being the preferred time to engage or re-engage in PA<sup>29</sup>. Since PA participation changes over the course of cancer progression<sup>30,31</sup>, PA levels measured pre-diagnosis may not reflect post-treatment participation as research has suggested that most women decrease PA levels after diagnosis and many do not return to pre-diagnosis levels<sup>13</sup>.

Cancer populations, including ovarian cancer patients, tend to be older, which begs the question if 150 minutes of moderate PA is appropriate and feasible for an older population. A 6 month randomized controlled trial, including participants that were aged 70 and older, was used to investigate the feasibility of delivering PA counselling to elderly people<sup>32</sup>. Those who met the guidelines had a higher physical functioning and concluded that the recommendation of 150 minutes of moderate PA is still warranted for an older population, and best delivered as five, 30-minute sessions<sup>32</sup>. Another approach to encourage older individuals to participate in moderate PA is to redefine the MET values. One study that looked at the prevalence and adherence to current PA guidelines among men and women between the ages of 70 and 93, used 3 METs to define moderate PA<sup>33</sup>. An additional study used the following MET values for the different intensity levels: 5.3 for vigorous, 3 for moderate and 2.5 for walking (as opposed to 8, 4 and 3.3, respectively<sup>34</sup>). In addition, older adults are encouraged to participate in activity for bouts of at least 5-minutes, which is less than the 10-minute bouts required for the general population<sup>33</sup>. Using these modifications, the 150-minute MVPA guideline can be implemented for older individuals, as well as for those suffering from multiple chronic conditions.

There have been a number of randomized controlled trials of PA interventions for breast and colon cancer and the research community has concluded that exercise training is safe during and after cancer treatment<sup>35</sup>. The aggressive treatments and poor prognosis associated with ovarian cancer make it difficult to achieve 150 minutes of moderate intensity of PA for this population, which is reflected by the low prevalence in previous studies<sup>29,36-38</sup>. Given that PA guidelines accommodate chronic conditions, it is believed that the PA recommendations are appropriate for cancer survivors<sup>20</sup>, regardless of the poor participation rates found in the existing ovarian cancer literature. Moreover, limited research reveals that increased PA in older ovarian cancer patients is feasible and safe<sup>4</sup>. Due to the vulnerabilities of this population post-treatment, it is recommended that ovarian cancer patients should be as physically active as possible and to explicitly avoid inactivity<sup>20</sup>. Being sedentary is a risk factor for many cancers, and therefore, even small amounts of light to moderate PA could reduce the risk of cancer recurrence and all-cause mortality<sup>39</sup>.

### **2.2.3 Physical Activity Assessment**

Among the ovarian cancer literature, questionnaires are often the instrument of choice to measure PA, with some of the most common being the International Physical Activity Questionnaire (IPAQ) and the Godin-Shephard Leisure Time Exercise Questionnaire (GSLTPAQ). These questionnaires have been frequently used for cancer patient and survivor populations<sup>40</sup>. Often times, questionnaires are the most feasible method for measuring PA because they are inexpensive, convenient, and can reach a large number of participants for a study<sup>41</sup>. For the majority of PA questionnaires, the primary outcome is the amount of time spent engaging in activity, at a certain intensity (i.e. mild, moderate, vigorous), for a given week<sup>41</sup>. All items in the IPAQ and GSLTPAQ have corresponding metabolic equivalent of tasks (MET) values. From there, items from the questionnaires can be converted into METs, which permits the

comparison of PA level outcomes across different questionnaires. Both the IPAQ and GSLTPAQ have been rigorously tested for reliability by conducting test-retest studies in successive weeks, and for validity by determining the correlation between the questionnaire scores and accelerometer measures<sup>40,41</sup>. More specifically, based on a systematic review that assessed the reliability and validity of the IPAQ, the pooled spearman correlation for reliability and validity was 0.81 and 0.33, respectively<sup>41</sup>.

The accelerometer is considered one of the most accurate device-based instruments for assessing PA in an objective manner in clinical populations and can distinguish between different PA intensities<sup>40</sup>. However, accelerometers also have limitations that must be considered. First, since it primarily captures locomotor activity, it can be challenging for an accelerometer to capture bicycling, water-based activities, upper-body exercises and resistance activities such as carrying loads or stair climbing<sup>42,43</sup>, which can be included when using questionnaires. Furthermore, it was also discovered that accelerometers have difficulties accurately recording step counts and acceleration signals for the elder population as frail populations often walk more slowly and have a cautious movement pattern<sup>44</sup>. Depending on the study question and practical considerations, an accelerometer may not be able to provide important information about the context and domain in which PA has occurred<sup>45</sup>, and therefore may not provide as much descriptive information as a questionnaire. The IPAQ assesses different PA domains, such as occupational, housework, transportation, and recreational activities, which is useful for determining the source of PA for the study base. Although questionnaires are often criticized for overestimating PA participation since they are self-reported, providing all study participants with an accelerometer is often not feasible and can be very costly. Using poor quality PA measures increases the risk of misclassification and bias, but questionnaires such as the IPAQ, have demonstrated good reliability and acceptable validity<sup>14,41</sup>. To date, questionnaires are one of the

most common tools for measuring PA levels among cancer populations due to their low cost and convenience<sup>41</sup>.

## **2.3 Physical Activity and Cancer**

### **2.3.1 Physical Activity and Cancer Risk**

There has been extensive research regarding modifiable lifestyle factors, specifically the association between PA and cancers of the breast, endometrium, colon, and prostate. Studies have shown that higher levels of PA may prevent the onset of several of these cancers. A meta-analysis of 31 cohort studies that investigated the relationship of PA and breast cancer risk found that those participating in the highest level of PA had a 12% reduction for breast cancer risk in comparison to those in the lowest PA level<sup>46</sup>. This association was even greater for endometrial and colon cancer. A meta-analysis of 33 observational studies reported a 20% risk reduction for endometrial cancer,<sup>47</sup> and a meta-analysis of 52 observational studies reported a 24% risk reduction for colon cancer<sup>48</sup> among those reporting the highest levels of PA compared to the lowest. Although the magnitude of effect was not as strong in prostate cancer, a 2011 meta-analysis of 43 observational studies found that those in the high PA group had a 10% reduction in risk for prostate cancer compared to men in the low PA group<sup>49</sup>. Among highly studied cancers, an inverse relationship between PA and cancer incidence risk is well established.

### **2.3.2 Physical Activity and Cancer Prognosis**

Some studies have investigated the influence of PA post-diagnosis in relation to cancer prognosis, recurrence, survival and patient reported outcomes<sup>39,50,51</sup>, but the majority of the cancer literature has focused on lifetime or prior to diagnosis PA levels<sup>22,46-49,52,53</sup>. There is now growing evidence for a protective role of PA after diagnosis and the effect it may have on improved quality of life, cancer recurrence and survival outcomes<sup>53</sup>. Studies have shown promising findings

between post-diagnosis lifestyle factors and improved cancer outcomes in breast and colon cancers<sup>54</sup>. Results from a prospective study investigating post-diagnosis recreational PA and breast cancer mortality found that women who engaged in the greatest level of PA had a significantly lower risk of dying from breast cancer in comparison to the lowest PA level (HR, 0.44; 95% CI, 0.32 to 0.60)<sup>18</sup>. Post-diagnosis PA has also had an impact on patient reported outcomes (PROs) among several cancer populations. A randomized controlled trial of breast cancer patients receiving adjuvant chemotherapy reported that women who were in the aerobic or resistance exercise training intervention had improved PROs in comparison to women who received usual care without exercise<sup>22</sup>. Both aerobic (p=0.015) and resistance (p=0.018) training significantly improved self-esteem, and also improved HRQOL, fatigue, anxiety, and depression throughout chemotherapy treatment<sup>22</sup>. Furthermore, among stage III colon cancer patients, a prospective study found that higher post-treatment recreational PA was associated with a significant reduction in the risk of cancer recurrence (HR, 0.51; 95% CI, 0.26 to 0.97)<sup>55</sup>. The precise mechanism through which PA may influence cancer recurrence and mortality remains unknown, but suggested hypotheses include a role in adiposity, an impact on metabolic and sex hormone concentrations, altered expression of growth factors, increased immunity and decreased chronic inflammation<sup>54,56</sup>.

The literature has presented evidence that PA participation can lead to potential health benefits following a cancer diagnosis. It is estimated that 56.8-65.0% of cancer survivors are not meeting the recommended PA guidelines of 150 minutes of moderate PA per week<sup>57</sup>. The stresses of cancer, such as severity of treatment and fatigue, are common barriers to meeting PA guidelines after diagnosis, which often results in low PA prevalence. More studies conducted after diagnosis and treatment are warranted, particularly in cancers that are more commonly diagnosed at a later stage, like ovarian cancer.

### **2.3.3 Post-Diagnosis Physical Activity and Ovarian Cancer**

When considering factors that may predict disease outcome, it is important to consider different factors along the cancer trajectory that may influence prognosis. Prior to diagnosis, personal characteristics, genetic variations or environmental exposures should be considered because they may influence the type of tumour that develops; at diagnosis, factors like tumour characteristics and personal characteristics may influence access to care or effectiveness of treatments; after diagnosis, modifiable lifestyle factors, such as PA, should be explored, as they may influence disease prognosis and offer an opportunity to change the disease course<sup>58</sup>. Currently, the only factors known to influence the prognosis of ovarian cancer are clinical, such as, the stage of diagnosis, grade, histology, treatment, and surgery, and therefore non-modifiable<sup>59</sup>. There is a lack of consensus regarding the role of PA after diagnosis and health outcomes in ovarian cancer survivors. This is partially due to very few studies measuring PA during the post-diagnosis and/or post-treatment period. Furthermore, results from published studies have observed conflicting or statistically non-significant associations when examining PA and ovarian cancer outcomes<sup>60,61</sup>. This lack of consensus could also be a result of low PA participation among women suffering from ovarian cancer because of treatment and additional stresses of cancer. Ovarian cancer treatment has proven to be physically challenging for patients with the majority of the treatment population being older and undergoing a major surgical procedure, followed by significant chemotherapy. Ovarian cancer is one of the most chemotherapy-sensitive malignancies and adjuvant treatment (chemotherapy given after surgery) has a strong impact on survival<sup>4</sup>. As a result, treatment-related symptoms, such as fatigue, loss of physical functioning, and nausea, make it very difficult for women to engage in healthy lifestyle behaviours during or after adjuvant chemotherapy.

The few studies that have measured PA after diagnosis have found the prevalence of PA participation to be very low among ovarian cancer survivors. One cross-sectional study that included 359 survivors, reported that over two-thirds (68.9%) of this population were not meeting

the recommended PA guidelines and over half were completely sedentary based on self-reported questionnaires<sup>36</sup>. This study suffered from a low response of 51% and could be potentially subject to selection bias if those who chose to participate were systematically different than those who did not, which in turn would affect the internal validity of this study<sup>36</sup>. A more recent cross-sectional study (n=101) investigating the correlates, barriers and preferences of PA for gynecological cancer patients, found that 53% of their population reported sufficient PA<sup>29</sup>. However, grouping ovarian cancer with other gynecological cancers, such as cancer of the endometrium, may overestimate this prevalence estimate as women suffering from ovarian cancer are less likely to meet the PA guidelines in comparison to other gynecological cancers, which is likely a result of late stage diagnosis and poor prognosis of ovarian cancer patients<sup>29</sup>. Furthermore, this study did not strictly include women who were in the post-treatment phase, as some were in the pre-treatment or in the middle of treatment, which could influence the level of PA participation<sup>29</sup>. Another study (n=95) that included women who were undergoing treatment or were post-treatment reported low prevalence estimates with only 19% of the sample meeting PA guidelines of 150 minutes of moderate PA<sup>37</sup>. However, this study had a low response rate of 41% and the majority of the recruited participants had stage III or IV cancer, thus representing a population with more advanced stage ovarian cancer<sup>37</sup>. Abbott and colleagues explored recreational PA in African-America women, and found that only 9.1% of their study population were meeting aerobic guidelines (150 minutes of moderate recreational PA), while 49.2% were inactive at a mean time of 22.4 months since diagnosis<sup>38</sup>. Participating in sufficient levels of recreational aerobic PA may be very challenging, especially after treatment, and therefore could explain the very low prevalence. Therefore, a PA measuring tool that captures a variety of PA is warranted, as women after treatment may not be able to participate in recreational PA alone, but could potentially still participate in other forms, such as household or occupational PA.

#### **2.3.4 Determinants of Physical Activity Participation Among Ovarian Cancer Patients**

With so few studies examining PA in the post-treatment period, even fewer studies have identified potential determinants of PA participation among this population. To date, three studies have investigated potentials barriers, correlates or determinants of PA in ovarian cancer patients after diagnosis. Farrokhzadi et al. conducted a cross-sectional study that identified correlates and barriers of PA among gynecological cancer patients after diagnosis and found that certain demographic characteristics were associated with being sufficiently active<sup>29</sup>. Participants (n=101) (59% were ovarian cancer cases) reported post-diagnosis leisure-time PA using the validated self-administered Active Australia Questionnaire<sup>29</sup>. This study suggested that women who were younger (<65 vs. ≥65 years of age) (OR, 1.3; 95% CI, 0.3-5.6), who were not single (OR, 1.7; 95% CI, 0.4-8.0), and not working (includes retired and unemployed) (OR, 1.4; 95% CI, 0.4-4.5), had greater odds of meeting the PA recommendations<sup>29</sup>. However, these associations were not statistically significant. The status of a woman's cancer treatment also appeared to be important since women who had completed treatment and were disease free had significantly greater odds of being sufficiently active compared to women who were about to start treatment or were in the treatment phase (OR, 7.0; 95% CI, 1.5-33.4)<sup>29</sup>. Although this study also identified potential barriers to PA participation (fatigue, never been active, lack of time), the sample size was small, containing only 59 ovarian cancer cases with a very low response rate (24% for mail-out questionnaires)<sup>29</sup>.

Another cross-sectional study conducted by Mizrahi et al. (n=95, response=41%) focused on clinical factors, such as stage of ovarian cancer, phase of chemotherapy treatment, and months since cancer diagnosis, and reported these factors were strong correlates of participating in PA<sup>37</sup>. Post-diagnosis PA was estimated using the short form of the IPAQ, where a guideline of 150 minutes of moderate PA was used to represent adequate PA participation. Participants with stage I reported the most MVPA (average of 151 minutes per week), whereas those in stage IV reported the least (average of 47 minutes per week). In addition, only 5% of women who were undergoing

chemotherapy treatment were meeting the PA guidelines in comparison to 24% of women who were not currently undergoing chemotherapy treatment. There was a positive correlation between time since diagnosis and engaging in PA ( $\rho=0.28$ ,  $p=0.03$ ), suggesting that patients become more active over time after treatment. These initial findings provide starting points for examining the associations of sociodemographic and clinical factors with meeting PA standards. However, these studies may have been underpowered and also potentially influenced by selection bias due to their poor response<sup>29,37</sup>.

In the third study, Stevinson et al. conducted the first study that identified some determinants of PA participation in ovarian cancer survivors, but the women in this study were not at the same time point along their cancer trajectory, with some women diagnosed 20+ years ago<sup>62</sup>. Following similar trends to the two studies previously mentioned, this study observed that women who were younger, had a healthy BMI, higher education level, wealthier, were employed, had survived more than 5 years since diagnosis, had early-stage disease at diagnosis, and were currently disease free were more likely to meet PA guidelines<sup>62</sup>. Volunteer bias may be a concern for this study, as this cross-sectional study was very transparent about the focus on PA, which may have attracted more active survivors. Questionnaires were mailed out to over 1300 ovarian cancer survivors in the province of Alberta with a final sample size of 359<sup>62</sup>. Determinants of PA engagement among ovarian cancer patients during the post-treatment period has not been thoroughly investigated, with only one study exploring potential determinants and two studies identifying correlates of PA participation. Identifying the characteristics of women who participate in PA will provide crucial information when looking at survival outcomes and planning for future interventions.

Once diagnosed with ovarian cancer, women are seeking information on how lifestyle factors, such as PA, can influence their health and improve their prognosis. Preliminary research on outcomes following PA participation among ovarian cancer survivors has reported lower

levels of fatigue, better scores in quality of life, decrease peripheral neuropathy, improvement in depression and anxiety, and better sleep quality<sup>36</sup>, but the prevalence of self-directed PA is still uncertain, and varies by stage<sup>37</sup>. Reporting the prevalence of post-treatment PA, identifying the factors for increased engagement in PA, and defining reasonable levels of PA along this trajectory could provide women with new strategies for improving several health outcomes associated with ovarian cancer, including delaying recurrence and improving PROs.

## **2.4 Patient Reported Outcomes**

### **2.4.1 Description and Assessment**

Patient reported outcomes (PROs) refer to any measurement of a patient's health that come directly from the patient, usually through self-directed questionnaires or by interview<sup>63</sup>. Cancer survivors undergoing treatment often report poor psychosocial health, and therefore it is important to measure PROs after treatment<sup>64</sup>. Commonly reported PROs include psychosocial indices, including depression, anxiety, fatigue and stress, which often impact overall health-related quality of life (HRQOL)<sup>64</sup>. In addition, fear of cancer recurrence is common in ovarian cancer patients and can cause distress at various times during or after treatment, which negatively affects HRQOL<sup>10</sup>. HRQOL is a multidimensional measure that is typically comprised of an individual's physical functioning, emotional, social and psychological well-being and health perceptions<sup>65</sup>. Across studies, the Functional Assessment of Chronic Illness Therapy (FACIT) measurement system and the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC-QLQ) predominate when measuring HRQOL<sup>66</sup>. Both questionnaires include an ovarian cancer specific subscale, called the FACT-O and EORTC-QLQ-OV28, respectively. The FACT-O has demonstrated good reliability with high test-retest correlations and acceptable construct validity when compared to other HRQOL measures, such as the Functional Living Index-Cancer<sup>67</sup>. HRQOL questionnaires include different domains, such as

physical and functional well-being, which are often compared amongst different questionnaires<sup>67</sup>. Additional PROs that may be reported among cancer populations include depression and anxiety, which can be measured by the Hospital Anxiety and Depression Scale (HADS), where higher scores indicate greater psychological distress<sup>68</sup>. Scales that measure psychosocial symptoms usually have established scores that represent normal, mild, moderate, and severe symptoms, and therefore, different questionnaires can be compared by the severity level of symptoms. The HADS has been validated with the Mini-International Neuropsychiatric Interview (MINI)<sup>69</sup>, and acceptable reliability as an instrument for screening symptoms of anxiety and/or depression<sup>70</sup>.

#### **2.4.2 Patient Reported Outcomes as a Prognostic Factor in Cancer**

For some cancers, PROs and specifically HRQOL, have been deemed to have prognostic value for response to treatment and survival<sup>51,71-77</sup>. This association has been well-studied in breast cancer patients during randomized controlled trials to assess whether baseline HRQOL is associated with responding to treatment and survival<sup>72,73</sup>. The HRQOL variables that were most strongly associated with longer survival were better appetite, physical and role functioning, as well as less fatigue and pain<sup>72,73</sup>. Similar associations were observed among patients with colorectal cancer, with low role functioning scores and high fatigue scores significantly associated with lower survival<sup>71</sup>. In addition, changes in HRQOL scores from baseline to after treatment had prognostic value for advanced lung cancer patients, with a 10-point increase in pain and dysphagia associated with an increased risk of death, whereas a 10-point improvement in physical and social function was associated with a lower risk of death<sup>75</sup>. With respect to ovarian cancer, HRQOL measured during treatment has been found to be a prognostic indicator for overall survival among women receiving chemotherapy<sup>76</sup>. More specifically, the physical well-being subscale of the FACT-O seems to be the score that is the most significantly associated with overall survival in ovarian cancer patients<sup>78</sup>. In addition, one retrospective cohort study found that

a 10-point improvement in HRQOL score after the initiation of treatment was associated with a 10% decrease in risk of ovarian cancer death<sup>79</sup>. Although HRQOL has not been well-studied as a prognostic factor in ovarian cancer, there is evidence that HRQOL could affect overall survival in other cancers, which warrants more studies to explore this association in ovarian cancer. PROs have been found to be important indicators of PA interventions, and therefore future studies should continue to assess the association between PA and PROs<sup>64</sup>.

## **2.5 Association Between Physical Activity and Patient Reported Outcomes**

### **2.5.1 Physical Activity and Patient Reported Outcomes in Cancer Population**

Recently, it has been suggested that a goal of cancer research is to improve both overall survival as well as HRQOL among cancer survivors<sup>80</sup>. Psychological distress and poor HRQOL, are common amongst patients affected by cancer, especially during diagnosis and treatment<sup>68</sup>. Treatment for cancer can include a combination of modalities (surgery, chemotherapy, and radiation), which consequently take a heavy toll on the physical, functional, emotional, spiritual, and social well-being of cancer survivors<sup>52</sup>. Due to the negative side effects of cancer treatment, cancer survivors not only reported significantly lower scores of HRQOL in comparison to other non-cancer patients<sup>81</sup>, but treatment may also prevent PA participation<sup>26</sup>.

Among breast cancer patients, low HRQOL has been associated with early treatment discontinuation, cancer recurrence, and reduced overall survival<sup>81</sup>. Due to the negative consequences of having poor HRQOL among cancer populations, there is also interest in assessing whether modifiable lifestyle factors, such as PA, could be associated with improving PROs. Exercise interventions during breast cancer treatment demonstrated statistically significant beneficial effects, including improvements in fatigue, nausea, physical well-being, functional well-being, satisfaction with life and overall quality of life<sup>52,82,83</sup>. Observational studies that investigated exercise post-treatment in breast cancer survivors also found an association between

PA and improvements in satisfaction with life and overall quality of life measures<sup>52,81</sup>. Self-efficacy and health status could play a potential role in mediating the relationship between PA and quality of life among breast cancer survivors<sup>81</sup>. For ovarian cancer, recent improvements in survival have not been produced by curing the disease, but rather by the ability of chemotherapy treatment to slow the progression of disease and to extend life, which emphasizes PROs as an important outcome measure for populations with metastatic disease<sup>84,85</sup>. This also emphasizes that ovarian cancer studies should continue to examine clinical and modifiable factors that improve PROs, whether it is different kinds of treatment<sup>76</sup> or increased PA participation<sup>86</sup>.

### **2.5.2 Physical Activity and Patient Reported Outcomes in Ovarian Cancer Populations**

Studies that directly address HRQOL in ovarian cancer are sparse, with little known about the phase after treatment<sup>87</sup>, and the studies that were conducted after treatment, included women who were diagnosed years ago<sup>36,86,88-90</sup> or women at different time points on the cancer trajectory<sup>91</sup>. Both PA and HRQOL have been found to improve after treatment, with HRQOL normally decreasing after surgery and slowly improving throughout chemotherapy, and PA declining during treatment and increasing once completed<sup>31,80,92</sup>. Studies looking at the association between PA and HRQOL are more commonly conducted during chemotherapy treatment rather than after the treatment period. However, the impact of exercise on HRQOL, strength and physical functioning may be greater when initiated after treatment<sup>56</sup>. The few studies that have been conducted after treatment completion have suggested that those who are more physically active had higher HRQOL scores in comparison to those who are not as physically active. More specifically, ovarian cancer survivors' scores related to fatigue, depression, anxiety, and happiness favoured those meeting the recommend guidelines of 150 minutes of moderate intensity PA per week<sup>36</sup>. Furthermore, those who met PA guidelines or participated in more activity had higher HRQOL scores<sup>89-91</sup>. However, the majority of these studies included women

who were diagnosed years ago when examining the association of PA and HRQOL, which does not capture the participants during a vulnerable period of time. Therefore, it would be beneficial for PA data collection to occur shortly after treatment since quality of life is often compromised during treatment and has been found to be a prognostic indicator for overall survival<sup>4,76</sup>.

With cross-sectional studies, an argument could be made that the relationship between PA participation level and PROs is bidirectional, where better PROs can lead to higher PA levels instead of the other way around. Randomized controlled trials have demonstrated that women who partake in an exercise intervention, whether it be during chemotherapy<sup>31,93</sup> or after chemotherapy completion<sup>12,30,94,95</sup>, have improved HRQOL scores, mental health, physical functioning, muscular strength and fatigue. Thus, additional studies of the role for post-treatment PA in aiding PROs are needed to improve our understanding of the inter-relationships between these factors. The next steps will be to determine if PROs improve or remain compromised during post-treatment and if meeting PA guidelines could modify PROs.

### **2.5.3 Physical Activity and Patient Reported Outcomes in the General Population**

The relationship between PA level and HRQOL has also been investigated in healthy subjects. A systematic review looking at this relationship only included healthy subjects from the general adult population that were under the age of 65<sup>96</sup>. Fourteen studies were included in this review, with cross-sectional studies consistently finding that higher PA levels were associated with higher and/or better scores in various HRQOL dimensions<sup>96</sup>. Support for this association was not as strong in cohort studies and randomized controlled trials. However, another finding was that the strength of the observed effect in general populations was not as strong as in clinical populations, which suggested that the benefits of PA in healthy adults is to preserve, rather than to improve HRQOL<sup>96</sup>. These observations could also be explained by a ceiling effect, meaning that adults in the general population have a relatively high baseline HRQOL score, and therefore

it can be difficult to improve beyond baseline. Regardless, there does seem to be a consistent relationship between higher PA levels and higher HRQOL scores among healthy adults. This association has also been observed in a Canadian population. Using the 2012 Canadian Community Health Survey, individuals who were more active reported higher HRQOL scores than those who were moderately active or inactive, in both younger (age 30-59) and older (age 60+) adults<sup>97</sup>. The association between PA and HRQOL appears to be a core relationship amongst members of the general population, although it may be stronger amongst cancer populations.

## **2.6 Rationale**

The avenues for preventing ovarian cancer are limited, considering that many of the factors known to influence ovarian cancer risk, such as genetics, age of menarche and menopause are not amenable to modification. Furthermore, other factors that are linked to ovarian cancer, such as parity and OC use, are not realistic targets for cancer prevention. Primary prevention is not possible and secondary prevention is challenging to implement due to the non-specific symptoms and the rapid progression of this disease; therefore, a focus on tertiary prevention strategies is needed in order to improve the prognosis of ovarian cancer. To achieve this, modifiable lifestyle factors, such as PA, must be investigated after diagnosis. Aside from the likely benefits of PA based on evidence from other cancers, there is currently a lack of evidence concerning the potential role of lifestyle factors in influencing survival after an ovarian cancer diagnosis.

To date, only a few studies have measured PA in the post-diagnosis period, with even fewer studies specifically examining the post-treatment period when patients are in remission but not considered cancer-free. These studies have been limited by small sample sizes, low response rates, or data collection that has not occurred in a timely manner (i.e. many years after diagnosis). Estimating the prevalence of ovarian cancer survivors meeting PA guidelines will provide greater

knowledge if PA is feasible and appropriate during the post-treatment period. Exploring potential determinants of PA in this population will help to characterize barriers and facilitators of meeting PA guidelines, post-treatment. Furthermore, collecting information on PROs for this population is important, as treatment has a large impact on well-being and survival. The association between post-treatment PA and PROs is still uncertain, as existing studies have not explored this relationship shortly after treatment. Further, the prevalence and determinants of post-treatment PA among ovarian cancer patients has not been well-established. Thus, this thesis aims to address these gaps in the literature. Ovarian cancer patients have many hurdles to overcome, and a greater understanding of both the prevalence and determinants of post-treatment PA, as well as the potential association between post-treatment PA and PROs, will contribute essential knowledge to improving the prognosis of women with this disease.

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## **Chapter 3**

### **Methods**

#### **3.1 Objectives**

The primary objectives of this study were to (1) estimate the prevalence of meeting Physical Activity (PA) guidelines among ovarian cancer survivors in the post-treatment period and to (2) identify the determinants of meeting PA guidelines in this study population. The secondary objective was to explore the association between baseline PA and patient reported outcomes (PROs), specifically health-related quality of life (HRQOL), anxiety and depression symptoms in the cohort.

#### **3.2 Study Design and Populations**

The Lifestyle Habits and the Prognosis of Ovarian cancer in Quebec (HPROQ) Study is a prospective cohort study of ovarian cancer patients conducted in Montreal (2015-2018) (PI: Anita Koushik). The baseline for this study was defined as 6 months after treatment completion, which is when the first interview took place. A follow-up interview was completed 4-months after baseline, but data collection was not completed in time for inclusion in this project. Therefore, this thesis utilized a cross-sectional study design with members of the baseline cohort as participants. The study base included women diagnosed with high-grade ovarian cancer from three Montreal hospital centers (Centre hospitalier de l'Université de Montréal (CHUM), McGill University Health Centre (MUHC) and the Jewish General Hospital). The development and progression of low-grade and high-grade ovarian cancers are believed to be different<sup>1</sup>; women who have slow growing, borderline and low-grade tumors (i.e. Type I) were not eligible for this study and therefore, only women with Type II tumours, which are often aggressive and rapid-growing, were included. Furthermore, because the aim of the study was to investigate modifiable

lifestyle factors post-treatment, another inclusion criterion was that participants must have completed treatment and currently be in remission.

Recruitment for this study was based on an established recruitment infrastructure (e.g. patient identification system, access to contact information and pathology reports) that was built for a population-based case-control study investigating the etiology of ovarian cancer (PI: Anita Koushik)<sup>2</sup>. Consent was obtained from women who were recruited for the HPROQ study prior to the baseline questionnaire. Of the 162 women who were approached for this study, 25 refused, 15 were not eligible and 10 could not be reached, resulting in a total sample size of 112 with a participation of 82%.

### **3.3 Data Collection**

Data was collected using the HPROQ questionnaire and was administered to all participants. This questionnaire contained a number of questions regarding sociodemographic, menstrual and reproductive history, past contraceptive use and past hormone use. In addition, questions about the level of PA participation among different domains (transportation, occupational, housework and recreational), information on anxiety and depression symptoms, and perceived HRQOL were included. Clinical information such as stage of cancer, type of treatment and type of surgery was obtained using hospital records from the three hospital centers.

#### **3.3.1 Physical Activity**

The HPROQ study collected data on PA using the International Physical Activity Questionnaire (IPAQ). The long form of the IPAQ was administered to all participants (n=112) by telephone interview and assessed the level of PA in the past 7 days among the research participants. The IPAQ has demonstrated reliable and valid results for PA levels among different populations, including older populations, and this has been replicated in a number of countries<sup>3,4</sup>. The long form of the IPAQ assesses PA across four different domains including occupational (PA

exerted by doing paid and unpaid work outside of the home), transportation-related (travelling from place to place), housework (including housework, yard work, gardening, general maintenance and caring for family), and recreational (PA solely for recreation, sport, exercise or leisure). The IPAQ included questions about the duration (i.e. hours and minutes), frequency (i.e. how many times per week) and intensity (i.e. walking, moderate, and vigorous) of PA engaged in the 7 days prior to the interview. See Appendix B for an example of IPAQ questionnaire.

### **3.3.2 Patient Reported Outcomes**

Patient reported outcomes (PROs) were measured using two different questionnaires: the Functional Assessment of Cancer Therapy-Ovarian (FACT-O), which assessed HRQOL, and the Hospital Anxiety and Depression Scale (HADS), which provided a score for the severity of anxiety and depression symptoms (see Appendix B). The FACT-O is an ovarian cancer specific HRQOL questionnaire. The FACT-O assesses four domains of HRQOL, including physical, social/family, emotional and functional well-being, as well as an additional domain for other concerns specific to women with ovarian cancer, regarding the past 7 days<sup>5</sup>. Measures of HRQOL help capture the extent that these domains are affected by an individual's illness, health or treatment<sup>6</sup>. The FACT-O has been established to be a reliable and valid instrument to assess HRQOL among women with epithelial ovarian cancer<sup>7</sup>. The FACT-O contains 39 statements that correspond to the patient's well-being which are scored on a 0-4 Likert-type scale. With each statement, the women could respond with not at all (0), a little bit (1), somewhat (2), quite a bit (3) and very much (4)<sup>5</sup>. The other questionnaire used to evaluate PROs, the HADS, assesses depression and anxiety symptoms over the past 7 days. The HADS is a 14-item scale of which 7 items focus on anxiety symptoms and 7 items focus on depression symptoms<sup>8</sup>. Each item is rated on a Likert-type scale ranging from 0-3. The HADS has previously demonstrated good reliability and good concurrent validity among cancer patients<sup>9</sup>.

### 3.4 Physical Activity Assessment

According to the American College of Sports Medicine (ACSM), 150 minutes per week of PA at moderate intensity is the recommended guideline for cancer patients<sup>10</sup>. Ovarian cancer survivors that met this guideline were categorized as “meeting PA guidelines” and those who did not were classified as “not meeting PA guidelines”. Information collected from the IPAQ was used to estimate total PA for the past week, at a moderate intensity level or higher, for each study participant. The Compendium of Physical Activities provides metabolic equivalent of tasks (METs) conversions for each activity item on the IPAQ based on the intensity of activity<sup>11</sup> (Table 3.1). In order to take into account PA duration, frequency and intensity, MET-minutes per week were calculated as duration × frequency per week × MET intensity for each activity that was defined as moderate intensity or higher and added together to estimate total PA participation for the past week for each study participant.

The recommended PA guideline of 150 minutes of moderate PA was also converted to MET-minutes so comparisons could be made between study participant’s PA level and the recommended guideline. Moderate PA includes activities that expend between 3-6 METs<sup>3</sup>. Using a MET value of 4 to represent moderate PA, 150 minutes of moderate PA is equivalent to 600 MET-minutes (150 minutes × 4 METs = 600 MET-minutes). Therefore, once intensity was accounted for, women who participated in ≥ 600 MET-minutes of PA were considered as meeting PA guidelines and those who participated in < 600 MET-minutes of PA were considered as not meeting PA guidelines.

For this study, we chose to exclude moderate housework activities (MET value of 3) from the definition of moderate-to-vigorous physical activity (MVPA). Housework activity has been found to be weakly associated with health measures in comparison to PA in other domains<sup>12</sup>. Moreover, the amount of housework PA can often be overreported as the definition of housework

activity in the IPAQ can be interpreted as everyday activities (e.g. sweeping, general maintenance and caring for family). In addition, some studies have included walking as moderate PA<sup>13,14</sup> but other studies have not included walking in the definition of moderate PA<sup>4,15</sup>, but walking may be beneficial, especially in chronic disease populations<sup>16,17</sup>. Therefore, the prevalence of PA participation was analyzed with walking both included and not included in the definition of MVPA.

**Table 3.1** MET energy expenditure estimates assigned to each self-reported PA category in the IPAQ based on the updated Compendium of Physical Activities<sup>3,11</sup>

<b>Activity Domain</b>	<b>Activity Type or Intensity</b>	<b>Self-Reported Pace</b>	<b>MET Estimate</b>	
Occupational	Vigorous		8	
	Moderate		4	
	Walking	Vigorous	5	
Transportation		Moderate	3.3	
		Slow	2.5	
	Sitting		1	
	Walking	Vigorous		5
		Moderate		3.3
		Slow		2.5
	Cycling	Vigorous		8
Moderate			6	
Slow			4	
Yard/Garden	Vigorous		5.5	
	Moderate		4	
Housework	Vigorous		3	
Recreational	Vigorous		8	
	Moderate		4	
	Walking	Vigorous		5
		Moderate		3.3
		Slow		2.5

### **3.5 Patient Reported Outcome Assessment**

Many different scores can be generated from the FACT-O questionnaire. From the 39 items on the FACT-O, subscale scores for each domain were calculated (physical, social/family, emotional and functional well-being), as well as an overall FACT-O total score, ranging from 0-152. The trial outcome index (TOI), ranging from 0-100, was also calculated which only includes the physical and functional domains, as well as additional concerns related to ovarian cancer. The TOI is often used in clinical trials because it is described to be more appropriate than the total FACT-O score as the social and emotional dimensions change quickly over time in response to health interventions<sup>18</sup>. The specific items of the FACT-O that are included in the TOI can be found in Appendix C. Higher scores generated from the FACT-O equate to better perceived HRQOL. The overall score and TOI score were used to assess HRQOL and treated as continuous variables.

The severity of anxiety and depression symptoms from the HADS is based on the score calculated for each scale. The total score for both the anxiety and depression scale ranges from 0-21. Raw scores from the HADS can be categorized and interpretation of the anxiety and depression symptom severity is as follows: normal (0-7), mild (8-10), moderate (11-14) and severe (15-21)<sup>19</sup>. With the HADS questionnaire, higher scores are associated with greater anxiety or depression symptom severity and thus, increased psychological distress. In the analyses for this thesis, the anxiety and depression scores were treated as binary variables, comparing those with normal symptoms to those that have any mild, moderate or severe symptoms of anxiety or depression.

### **3.6 Covariates (Patient Characteristics and Clinical Factors)**

Information on sociodemographic characteristics, lifestyle factors, reproductive history, and PA, was collected using the HPROQ study questionnaire. The following variables were

included in the study as covariates and categorized as follows: age (years, continuous), BMI ( $\leq 24.9$ , 25-29.9,  $\geq 30$  kg/m<sup>2</sup>), education level (high school or less, CEGEP/post-secondary), partner status (single, significant relationship), undergone a hysterectomy for cancer treatment (yes, no), past OC use (yes, no), past hormone use (yes, no), parity (nulliparous, 1, 2+), employment status (unemployed, employed on sick leave, employed), smoking duration and intensity (pack-years, continuous), self-reported ethnicity (French Canadian, Other European/Other/Mixed), menopausal status (premenopausal, postmenopausal), stage of cancer (I/II, III/IV), and type of chemotherapy (neoadjuvant, adjuvant only).

### **3.7 Analysis Strategy**

#### **3.7.1 Descriptive Analysis**

Once data collection was completed, the raw HPROQ data was cleaned before any statistical analyses were conducted. This included determining the appropriate variables among the dataset, extracting these variables to create a new dataset, converting data entries to the right unit, checking for potential outliers or improbable data points, quality checking variables between different databases, and categorizing all variables in a meaningful manner, based on prior literature or established cut-points. Descriptive statistics were used to describe baseline sociodemographic and clinical characteristics of this study population, grouped by those who met PA guidelines and those who did not. Means and standard deviations were computed for continuous variables and frequency tables were generated for categorical variables. All statistical analyses were carried out using SAS software version 9.4.

#### **3.7.2 Objective 1**

PA level was dichotomized, with a cut-off based on the 150 minutes of moderate intensity activity guideline, which is equivalent to  $\geq 600$  MET-minutes. The frequency

distribution of the number of women meeting PA guidelines was tabulated, with and without the inclusion of walking. Since the IPAQ assessed PA amongst different domains (occupational, transportation, housework, and recreational), the percentage of PA attributed to each domain was calculated by dividing the total MET-minutes in each domain by the overall total MET-minutes. This provided information on which domain or activity contributed the most to PA participation. An exploratory analysis was also conducted to analyze the association of pre-diagnosis PA and meeting PA guidelines after treatment. This was done on a subset of women (n=36) who were previously involved in the PRevention of OVArrian Cancer in Quebec (PROVAQ) study, which collected data on women's lifetime and past 10-years of PA participation. Chi-square tests were conducted to calculate PRs and to determine whether there was an association between meeting PA guidelines prior to diagnosis and currently meeting PA guidelines after cancer treatment (Chapter 5: Additional Analyses).

### **3.7.3 Objective 2**

Fourteen potential determinants of meeting PA guidelines were assessed, including sociodemographic characteristics, lifestyle factors and clinical factors. The outcome of interest for objective 2 was whether or not women met PA guidelines. Meeting PA guidelines was dichotomized into meeting and not meeting PA guidelines. Using this approach, 42% of the study population met PA guidelines. Given that the study outcome was not rare, a Modified Poisson Regression approach<sup>20</sup>, that uses a robust error variance procedure, was used to calculate the prevalence ratio (PR)<sup>21</sup> for each of the 14 determinants of interest and meeting PA guidelines. Due to the smaller sample size and the number of covariates under consideration, the log-binomial regression did not converge. In a sensitivity analysis, a logistic regression analysis was also conducted to compare the effect estimates from each of the models (Chapter 5: Additional Analyses). Each of the 14 potential determinants (patient characteristic and clinical factors) were

analyzed in separate models, to determine whether they were associated with meeting PA guidelines.

Covariates that may be confounders in the relationship between a given determinant and meeting PA guidelines were identified according to whether the covariate was associated with the determinant of interest<sup>22</sup>. In particular, spearman correlation coefficients were calculated between all covariates, and if the correlation value exceeded 0.2, then the potential confounder was included in the specific model for a given determinant (see Appendix D). This method identified potential confounders by evaluating the association between all covariates, as opposed to using statistical significance to identify confounders. There were, however, several exceptions to this approach. Variables that were believed to have an *a priori* relationship with the determinant of interest and with PA guidelines, were forced into selected models despite the absence of a correlation at the 0.2 level. Specifically, past hormone use was included in the model where BMI was the determinant of interest, and BMI was included in the past hormone use model; this was also done for education and job status.

Using the HPROQ questionnaire and medical records, models were built for the following determinants: age (years, continuous), BMI ( $\leq 24.9$ , 25-29.9,  $\geq 30$  kg/m<sup>2</sup>), education level (high school or less, CEGEP/post-secondary), partner status (single, significant relationship), hysterectomy for cancer treatment (yes, no), past OC use (yes, no) past hormone use (yes, no), parity (nulliparous, 1, 2+), employment status (unemployed, employed on sick leave, employed), smoking duration and intensity (pack-years, continuous), self-reported ethnicity (French Canadian, Other European/Other/Mixed), menopausal status (premenopausal, postmenopausal), stage of cancer (I/II, III/IV), and chemotherapy treatment (neoadjuvant, adjuvant only). Age was included in all multivariable models regardless of the correlation with the specific determinant of interest. Simple and multivariable modified Poisson regressions were used to estimate PRs and 95% confidence intervals (CIs), which represented the proportion of

those meeting PA guidelines for a specific determinant, compared to the proportion of those not meeting PA guidelines, in this study population. A sensitivity analysis was conducted, with the inclusion of “walking” in the definition of meeting MVPA guidelines, based on a minimum of 600 MET-minutes. All analyses were repeated with this revised PA outcome variable. (Chapter 5: Additional Analyses).

### **3.7.4 Objective 3**

The association between meeting PA guidelines and PROs was explored for the third objective, focusing on HRQOL, anxiety symptoms and depression symptoms. A multiple linear regression analysis was used to analyze the association between the exposure, meeting PA guidelines, and the outcome, HRQOL scores based on the FACT-O questionnaire. An analysis was conducted for the total FACT-O score (range 0-152) and the TOI score (range 0-100). Meeting PA guidelines was a binary variable, and therefore, a linear relationship between the exposure and outcome did not have to be assumed. In regard to the other assumptions of linear regression, the assumption of independence and normality were met, but homoscedasticity may have been violated. The beta parameter estimate affiliated with meeting PA guidelines represents the average difference in HRQOL score among women who met PA guidelines compared to those who did not meet PA guidelines.

Logistic regression models were built to 1) assess the relationship between meeting PA guidelines and anxiety symptoms, and 2) assess the relationship between meeting PA guidelines and depression symptoms. With the HADS questionnaire, scores ranging from 0-7 correspond to normal anxiety or depression symptoms, 8-10 for mild, 11-14 for moderate, and 15-21 severe<sup>19</sup>. Very few women presented with mild, moderate or severe depressive symptoms, and therefore the depression outcome was treated as a binary variable, with women who had symptoms of depression within the normal range versus those who had symptoms of depression that were

classified as mild, moderate or severe. To remain consistent, the anxiety outcome was also treated as a binary variable, with women who had symptoms of anxiety within the normal range versus those who had symptoms of anxiety that were classified as mild, moderate or severe. The logistic regression was the regression model of choice as the outcome was binary (normal symptoms vs. any mild/moderate/severe symptoms) and not common for the depression score (10.7%). Anxiety symptoms were more common among HPROQ participants (36.6%), but to remain consistent, logistic regression was employed to generate odds ratios (OR) and 95% (CI), representing the odds of having depression or anxiety symptoms when PA guidelines were met.

The cross-sectional analysis between PA and various PROs considered 11 covariates as potential confounders and were identified using a change in estimate (CIE) approach. Variables that were not considered as potential confounders included past behaviours, such as past OC use, past hormone use and parity, as they are not believed to have an impact on the relationship at the cross-sectional point in time. Age was forced into all models. Variables that changed the beta estimate (for FACT-O and TOI scores) or the OR estimate (for anxiety and depression scores) of meeting PA guidelines by >10%, after being removed one at a time, were included in the multivariable models. The final model contained only those variables that changed the beta estimate or OR by >10% when removed. The CIE approach is suitable for this dataset as the study sample is small with many potential covariates to consider<sup>23</sup>. A sensitivity analysis was conducted, with the inclusion of “walking” in the definition of meeting MVPA guidelines, based on a minimum of 600 MET-minutes. All analyses were repeated with the revised PA exposure variable (Chapter 5: Additional Analyses).

### **3.8 Power Calculation**

Tables 3.2 and 3.3 provide power calculations for objective 2 and 3 with an estimate of 31% of the proposed sample size (n=150) meeting PA guidelines. Table 3.2 shows that power to

detect a certain PR estimate applied to a range of exposure proportions. Table 3.3 demonstrates the mean difference that would be detectable at 80% power when looking at different PRO measurements.

**Table 3.2** The power to detect a certain PR for a range of exposure prevalence's

<b>Power to Detect</b>				
<b>Exposure Prevalence</b>	<b>PR=1.2</b>	<b>PR=1.5</b>	<b>PR=1.7</b>	<b>PR=2.0</b>
<b>10%</b>	6.75%	21.72%	36.48%	61.36%
<b>25%</b>	10.08%	35.75%	56.67%	82.27%
<b>50%</b>	11.03%	37.3%	57.31%	79.1%
<b>75%</b>	9.08%	25.35%	37.51%	54.0%

**Table 3.3** The detectable mean difference with 80% power, 5% significance and 2-sided test

	<b>Active</b>	<b>Non-Active</b>	<b>Mean Difference</b>
FACT-O	n=47	n=103	8.75
	s.d.=17.8	s.d.=17.6	
HADS (anxiety)	n=47	n=103	1.98
	s.d.=4.03	s.d.=3.99	
HADS (depression)	n=47	n=103	1.44
	s.d.=2.93	s.d.=2.89	

Table 2. Numbers used for detectable mean difference with 80% power, 5% significance and 2-sided test.

### **3.9 Ethical Considerations and Data Management**

The HPROQ study protocol was approved by the Research Ethics Committee of the Centre de recherche du Centre hospitalier de l'Université de Montreal (CRCHUM) and the three participating hospitals. Expedited ethics approval for this thesis was obtained from Queen's University Health Sciences Research Ethics Board. All data was collected from participants with informed consent. Data were stored in an anonymized form in a database on secure servers at CRCHUM. Any data analyzed by the MSc candidate was transferred via encrypted USB, on site at the CRCHUM, with personal identifiers removed to maintain participant privacy.

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## Chapter 4

# Physical Activity in Ovarian Cancer Survivors: Prevalence and Determinants of Participation

### 4.1 Abstract

*Background:* To date, there is limited knowledge on the role that physical activity (PA) may play in ovarian cancer prognosis, particularly after treatment is completed. Past studies have found that PA participation is quite low amongst ovarian cancer patients. Very few studies have investigated the prevalence of PA or what factors predict PA participation in the post-treatment period.

*Methods:* This study assessed the prevalence and determinants of post-treatment PA participation among 112 ovarian cancer survivors in a cross-sectional study. Six months after treatment completion, ovarian cancer patients were interviewed to obtain information on sociodemographic and lifestyle characteristics with PA participation collected using the International Physical Activity Questionnaire (IPAQ). Modified Poisson regression was used to estimate the prevalence ratios (PRs) and 95% confidence intervals (CI) as a measure of the association between potential determinants and the outcome of meeting PA guidelines.

*Results:* 42.0% (95% CI: 32.8-51.1%) of ovarian cancer survivors met the PA guidelines of at least 150 minutes of moderate-to-vigorous physical activity (MVPA) per week, while 37.5% (95% CI: 28.5-46.5%) of the study sample did not participate in any MVPA. Women were most active in housework-related PA, with 47.6% of all PA participation attributed to this domain. There was no evidence of a statistically significant association between any of the patient characteristics and meeting PA guidelines. Current employment had the highest PR, with the suggestion that women who were currently employed had a prevalence of meeting PA guidelines

that was 1.49 times greater than women who were unemployed (PR=1.49; 95% CI:0.87-2.55), although this could have occurred by chance given the non-significant and imprecise finding.

*Conclusion:* The prevalence of meeting PA guidelines 6 months after treatment was higher than reported in previous studies. None of the patient characteristics were significantly associated with meeting PA guidelines. Due to the small sample size, the study was underpowered, making it difficult to exclude chance as an explanation for some of the suggestive associations reported in this paper.

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## 4.2 Introduction

Ovarian cancer is the deadliest gynecological cancer in Canada and rarely diagnosed at an early stage due to the absence of effective secondary prevention strategies<sup>1,2</sup>. About 75% of invasive ovarian cancer cases are classified as Type II: tumours that grow rapidly, are highly aggressive, and high-grade at, or soon after their inception<sup>3</sup>. To date, the only factors known to influence the prognosis of ovarian cancer are clinical, such as stage of disease, surgery, chemotherapy, and thus non-modifiable by ovarian cancer patients themselves. As a result of the combined impact of the rapid progression of ovarian cancer and the high rates of cancer recurrence<sup>4,5</sup>, modifiable lifestyle factors have become a research topic of interest when investigating survivorship, as the relationship remains unclear<sup>6,7</sup>. Lifestyle factors that may influence prognosis, such as physical activity (PA), diet, and sun exposure may offer an opportunity to change the disease course<sup>8</sup>.

PA level has been established to reduce the risk of cancer of the breast, endometrium, prostate, and colon<sup>9-12</sup>. For breast and colon cancers, benefits of post-diagnosis PA, including decreased rates of mortality and recurrence, as well as improvements in patient reported outcomes (PROs), has also been established<sup>6,13-17</sup>. The precise mechanism through which PA may influence cancer recurrence and mortality has not been definitively established but ongoing research suggests reduced adiposity, changes in metabolic and sex hormones, decrease in growth factors, changes in immunological processes and decrease in chronic inflammation as possibilities<sup>6,18</sup>.

PA has been examined amongst ovarian cancer patients, however, the time frame for measurement of PA has varied across studies. For instance, some have assessed PA prior to cancer diagnosis<sup>19,20</sup>, while others have considered PA patterns over a lifetime leading to diagnosis<sup>21,22</sup>, during treatment<sup>23</sup>, amongst survivors who were diagnosed many years ago<sup>24-26</sup> or a combination of time frames along the cancer trajectory<sup>27,28</sup>. One study has shown that among women affected by ovarian cancer that PA levels do vary along the cancer trajectory, with women

decreasing their PA after diagnosis and many do not return to pre-diagnosis levels<sup>29</sup>. Only five studies have measured PA during the post-treatment period and estimates of the prevalence of PA has varied widely from 9-53% across these studies<sup>24-28</sup>. However, response rates have ranged from 41-71% in these studies<sup>24-28</sup>. PA participation was measured inconsistently, and some studies combined women at different time points along the cancer trajectory<sup>24,25,27,28</sup>, or combined different gynecological cancers<sup>27</sup> in order to increase sample size.

A recent study found that only 9% of their ovarian cancer survivors in their sample were meeting PA guidelines when only taking into account recreational PA<sup>26</sup>. However, this is a population that is often very fatigued and weak following treatment and may not be capable of participating in 150 minutes of recreational PA alone and the low prevalence rates could be a consequence of not capturing different types of PA. Moreover, there is a gap in the literature regarding determinants of PA participation for ovarian cancer patients. Three studies have looked at sociodemographic characteristics and clinical factors that are associated and correlated with being sufficiently active<sup>27,28,30</sup>. Although these studies provided some insight into the characteristics of women who are more physically active, they did not control for any potential confounders and included women prior to treatment completion.

Based on the literature to date, there are inconsistent prevalence of post-treatment PA and a gap of knowledge about post-treatment PA determinants in ovarian cancer survivors. Therefore, the aim of this study was to estimate the prevalence and to identify determinants of PA participation amongst ovarian cancer patients currently in remission, 6 months after treatment. Quantifying post-treatment PA behaviours and determinants may be useful for the development of interventions that are aimed at improving patient outcomes and improving survivorship.

## **4.3 Materials and Methods**

### **4.3.1 Study Population**

This study population consisted of 112 women from the Lifestyle Habits and the Prognosis of Ovarian Cancer in Quebec (HPROQ) Study that was conducted in Montreal, Canada (2015-2018). The cohort included women diagnosed with ovarian cancer from three participating Montreal hospital centers. Women with high-grade tumours (i.e. Type II) who had completed treatment and were currently in remission were eligible for inclusion. Out of the 162 women that were approached for this study, 10 could not be reached and 15 were not eligible. Among the eligible women contacted, 25 refused resulting in a participation of 82% (112/137). The prevalence and determinants of post-treatment PA participation among these women at baseline was assessed with a cross-sectional analysis of the baseline data, defined as 6 months after treatment was completed.

#### **4.3.2 Study Variables**

Information on sociodemographic characteristics, lifestyle factors, reproductive history, and PA, was collected in a telephone interview. Clinical data were collected through medical chart reviews. PA was assessed using the long-form of the International Physical Activity Questionnaire (IPAQ) that measured the amount of PA participation in the past 7 days. The IPAQ has shown to be both reliable and valid in assessing PA levels among general and elderly populations<sup>31,32</sup>. The IPAQ assesses PA from four different domains including occupational (PA exerted by doing paid and unpaid work outside of the home), transportation (travelling from place to place), housework (including housework, yard work, gardening, general maintenance and caring for family), and recreational (PA solely for recreation, sport, exercise or leisure). Within each domain, information on the number of hours and/or minutes of participation (duration), the number of times per week an activity was engaged in (frequency), and whether it was classified as walking, moderate or vigorous activity (intensity) was collected. This information was used to estimate total PA in the past week, at a moderate intensity level or higher (this included activities

at a moderate and/or vigorous intensity level), for each study participant. The Compendium of Physical Activities provides metabolic equivalent of tasks (MET) conversions for each activity item on the IPAQ, which is a measure of the intensity of an activity<sup>31</sup>. In order to take into account PA duration, frequency and intensity, MET-minutes per week were calculated as duration × frequency per week × MET intensity for each activity that was defined as moderate intensity or higher and added together to estimate total PA participation for the past week for each study participant.

According to the American College of Sports Medicine (ACSM), 150 minutes of PA at moderate intensity per week is the recommended guideline for cancer patients<sup>33</sup>, meaning those who met the 150 minutes per week threshold or more were classified as “meeting guidelines”, and those who do not were classified as “not meeting guidelines”. In general, moderate PA can be described as a brisk walk that noticeably accelerates the heart rate, but not to the extent of rapid breathing<sup>34</sup>. Based on the Compendium of Physical Activity, activities that expend 3-6 METs corresponds to moderate PA<sup>31,33</sup>. Since all PA participation that was collected was converted to MET-minutes, the recommended guideline of 150 minutes of at least moderate PA was also converted to MET-minutes. Using a MET value of 4 to represent moderate PA, the recommended PA guideline of 150 minutes of MVPA per week became 600 MET-minutes per week (150 minutes × 4 METs). Using the 600 MET-minute cut-off as opposed to the 150 minutes cut-off may capture exercises that were performed at a higher intensity but for a shorter amount of time. The MET conversion provides a more robust measure for categorizing the PA levels for a population that may not be as active as the general population.

For this study, we chose to exclude moderate housework activities (MET value of 3) from the definition of MVPA. Housework activity has been found to be weakly associated with health benefits, such as leanness,<sup>35</sup> and providing protection against cardiovascular disease<sup>36</sup>. Moreover, the amount of housework PA can often be overreported as the definition of housework

activity in the IPAQ can be interpreted as everyday activities (e.g. sweeping, general maintenance and caring for family).

Due to the hardships of ovarian cancer treatment (i.e. major surgery and many rounds of chemotherapy), past studies have found a low prevalence of ovarian cancer patients meeting PA guidelines after treatment. Thus, it may be important to also consider lower intensity exercises, such as walking. However, some studies have included walking in the definition of moderate PA<sup>28,37</sup>, while other studies have not included walking in the definition of moderate PA<sup>26,32</sup>. Nevertheless, walking may still contribute to overall health and be beneficial for weaker populations<sup>38,39</sup>. Therefore, in addition to determining the prevalence of MVPA participation without walking, the prevalence of PA participation with walking included in the definition of MVPA was also calculated.

#### **4.3.3 Statistical Analysis**

Baseline clinical and patient characteristics of the study population were characterized with univariate analysis. Means and standard deviations were computed for continuous variables and the frequency distribution of categorical variables were tabulated, including the number of women meeting the PA guideline to determine the prevalence of post-treatment PA. Since the IPAQ assesses PA across different domains (occupational, transportation, yard/garden, indoor housework, and recreational/leisure), the percentage of PA participation for each domain was also calculated to determine if there was a certain type of activity that contributed more towards meeting PA guidelines. Descriptive characteristics were presented for those who were categorized as meeting guidelines versus not meeting guidelines to determine if there were any baseline differences or similarities between the two groups.

A Modified Poisson regression approach<sup>40</sup> was used to model the association between each potential determinant (age, BMI, education, partner status, hysterectomy, OC use,

hysterectomy use, parity, job status, tobacco use, ethnicity, menopausal status, stage of cancer, type of chemotherapy) and the prevalence of meeting PA guidelines. A separate model was constructed for each potential determinant of PA: age (years, continuous), BMI ( $\leq 24.9$ , 25-29.9,  $\geq 30$  kg/m<sup>2</sup>), education level (high school or less, CEGEP/post-secondary), partner status (single, significant relationship), undergone a hysterectomy for cancer treatment (yes, no), past OC use (yes, no) past hormone use (yes, no), parity (nulliparous, 1, 2+), employment status (unemployed, employed on sick leave, employed), smoking duration and intensity (pack-years, continuous), self-reported ethnicity (French Canadian, Other European/Other/Mixed), menopausal status (premenopausal, postmenopausal), stage of cancer (I/II, III/IV), and chemotherapy treatment (neoadjuvant, adjuvant only). Potential confounders for each model were defined as those variables that were associated with the determinant of interest based on the Spearman correlation coefficient<sup>41</sup>. In particular, if the correlation value exceeded 0.2, then the variable was included in the model for that determinant<sup>41</sup>. This method identified potential confounders by evaluating the association between all covariates, as opposed to using statistical significance to identify confounders. Age was included in all multivariable models regardless of its correlation with the determinant. Simple and multivariable modified Poisson regression was used to estimate prevalence ratios (PRs)<sup>42</sup> and 95% confidence intervals, which represented the proportion of those meeting PA guidelines for a specific determinant, compared to the proportion of those not meeting PA guidelines, in this study population.

#### **4.4 Results**

Descriptive characteristics of the study population, categorizing women who met PA guidelines versus those that did not, are presented in Table 4.1. Those who met PA guidelines were younger, had lower BMI, a larger proportion attended post-secondary school, had a life-partner, never smoked, were French-Canadian, and have used OC in the past, compared to those

who did not meet PA guidelines. A greater proportion of women who did not meet PA guidelines were also postmenopausal.

Table 4.2 shows the prevalence of meeting PA guidelines: 42.0% (95% CI: 32.8-51.1%) of the ovarian cancer survivors were meeting the MVPA guidelines of 600 MET-minutes per week 6 months post-treatment. Conversely, 58.0% (48.8-68.8%) of the population did not meet PA guidelines, with 37.5% (28.5-46.5%) not participating in any MVPA, while 20.5% (13.1-28.0%) of these women were participating in some PA, but not meeting the recommended guidelines. With walking participation included in meeting PA guidelines, 57.1% (48.0-66.3%) of the women were meeting the guideline of 600 MET-minutes.

Table 4.3 presents the percentage of PA participation by domain. Out of all PA participation information collected, 47.6% was attributed to the housework PA domain, followed by recreational (33.6%), occupational (11.0%), and transportation (7.8%). Those who did not meet PA guidelines were most active in the housework domain, while those who did meet PA guidelines were most active in the recreational and housework domains.

Table 4.4 presents the crude and adjusted PRs (95% CI) that were calculated for the association between each potential determinant and meeting PA guidelines. None of the potential determinants under consideration were statistically significantly associated with meeting PA guidelines but many of the characteristics under consideration trended in the direction that was hypothesized. However, several of the explanatory models provide some insights on which sociodemographic, lifestyle and clinical characteristics trended towards an association with increased engagement in PA and meeting guidelines among survivors of ovarian cancer. The strongest factor associated with meeting PA guidelines was current employment status: women who were currently employed had a prevalence of meeting PA guidelines that was 1.49 times greater than women who were unemployed (PR=1.49; 95% CI:0.87-2.55). Other factors that had a suggested association with prevalence of meeting PA guidelines included single status

(PR=0.66; 95% CI: 0.38-1.18), never use of OCs in the past (PR=0.61; 95% CI: 0.30-1.23), premenopausal status (PR=1.45; 95% CI: 0.82-2.54) and non-French-Canadian ethnicity (PR=0.66; 95% CI: 0.38-1.16), although these observations could have been due to chance, given the wide and non-significant confidence intervals.

#### **4.5 Discussion**

In this population of women who had completed treatment for high-grade ovarian cancer 6 months prior, 42.0% met the PA guidelines defined as 600 MET-minutes per week and 57.1% met PA guidelines when walking was included. Among 14 potential determinants, none were found to be statistically significantly associated with meeting PA guidelines, but the magnitude of the PR estimates associated with potentially modifiable factors including current employment, partner status, past OC-users, premenopausal status and non-French-Canadian ethnicity suggested a trend towards an association with meeting PA guidelines.

The prevalence of PA participation after diagnosis among ovarian cancer patients has been measured in five past studies<sup>24-28</sup>, with the prevalence of meeting guidelines ranging from 9-53%. The study that had the highest post-diagnosis prevalence (53.0%), included other gynecological cancers, and thus the highest prevalence for only ovarian cancer patients recorded was 31.1%<sup>24</sup>. This wide prevalence range could be due to a multitude of reasons, including the inconsistent time frames that have been used to measure PA participation. Two of the past studies included women who were about to start chemotherapy treatment, during treatment and shortly after treatment<sup>27,28</sup>, which often resulted in low PA prevalence. In contrast, the three remaining studies measured PA participation amongst ovarian cancer survivors<sup>24-26</sup>, including some participants who were diagnosed with cancer years ago. Some studies have found that the most appropriate time for ovarian cancer survivors to begin or participate in PA is 3-6 months after treatment as fatigue and chemotherapy seem to be the greatest barriers for participation<sup>27,28</sup>.

Another study found that 69% of women would like to partake in PA within a year after treatment<sup>43</sup>. In our study, the time point that was chosen to measure PA (6 months after treatment) was deemed reasonable for ovarian cancer survivors. PA information was also collected consistently at the same time point for all survivors. The time point for data collection and the consistency could be reasons why the prevalence of meeting PA guidelines in this study (42.0%) was higher than what was found in past studies.

Although this study found a prevalence higher than past studies, it is slightly below what is found in the American population for women of similar age. According to Tucker et al., 46.9-59.7% of women aged 50+ were meeting the guidelines of 150 minutes of MVPA per week when taking into consideration transportation, housework and leisure activities<sup>44</sup>. A lower prevalence compared to the general healthy population is to be expected, but our study population was not too far off of the lower bound of the prevalence range for the general population for older women. Cancer recurrence is a fear that many of these women have<sup>45</sup>, which may be a motivator to modify their lifestyle during remission by participating in PA as much as possible.

In addition, the different types of PA measured could influence the prevalence of PA participation. The IPAQ provided a comprehensive PA measure by including a wide range of different PA domains, such as occupational, transportation-related and housework-related, in addition to recreational PA. Very few women are capable of meeting PA guidelines when only recreational PA is taken into account, which has been shown in the study conducted by Abbott et al., where only 9.1% of the study population reached 150 minutes per week<sup>26</sup>. With an aging population that is recovering from treatment and surgery, as well as dealing with fatigue and sometimes nausea, it can be quite difficult for these women to be physically capable of participating in 150 minutes of pure recreational PA. Amongst our study population, close to half of all PA participation was from housework-related PA, which seems to follow similar trends in other cancers<sup>46</sup>. A study looking at prostate cancer patients adhering to PA guidelines found that

men were most active in the domestic domain, and least active in the transportation and recreation domain, implying PA is primarily undertaken involuntarily as household duties<sup>46</sup>. This has also been reported in the general population, where housework PA accounts for a large proportion of self-reported PA (35.6%), particularly among women and older adults<sup>35</sup>. In healthy populations, housework PA seems to be weakly associated with health benefits in comparison to leisure PA, as the energy expenditure is not as high<sup>35</sup>. Whether housework PA provides the same health benefits as recreational PA for more vulnerable populations, such as those who are older or suffering from cancer, is still unclear and will have to be investigated further.

Two previous studies did not use METs conversions for their PA measure, and therefore meeting PA guidelines was based on duration and frequency, and disregarding intensity<sup>24,27</sup>. Taking into account PA intensity, by using METs conversions for items on the IPAQ, captured participants who may have been physically active for a shorter amount of time but at a higher intensity level. In this study, vigorous PA is classified as 8 METs, while moderate PA is classified as 4 METs, and therefore, someone who participated in 75 minutes of vigorous PA in a given week, might not have been considered as meeting PA guidelines in past studies that used duration of activity to measure participation, but would have been in ours. For the general population, it is recommended that individuals participate in at least 150 minutes of moderate intensity or 75 minutes of vigorous intensity or a combination of the two that is equivalent<sup>33</sup>, and thus, not taking into account PA intensity could exclude participants that are in fact meeting guidelines.

In this study, the strength of association for 14 potential determinants and meeting PA guidelines were estimated to provide a better understanding of what characteristics of ovarian cancer patients may lead to a greater prevalence of engaging in PA after treatment. It was found that those who were younger, had a healthy BMI, had a partner, were a past OC user, were a past hormone user, currently employed, French Canadian, premenopausal, had earlier stage of cancer,

and/or received neoadjuvant chemotherapy had a greater prevalence of meeting PA guidelines, although none of the determinants were statistically significant. Only one other study has looked at potential determinants of being physically active among ovarian cancer survivors<sup>30</sup> and two studies, with sample sizes smaller than what was reported in our study (n=101; n=95) have identified correlates and barriers of being physically active<sup>27,28</sup>, but none has controlled for confounders when identifying potential determinants and/or predictors. Determinants of meeting PA guidelines were identified such as, younger age, being employed, lower BMI and earlier disease stage<sup>30</sup>; however, unlike Stevinson and colleagues, who found that higher education was associated with meeting PA guidelines, I observed a potential relationship in the opposite direction. Prior to controlling for confounders of this association, education was positively associated with meeting PA guidelines, while after controlling for age, hysterectomy, job status, smoking, menopausal status and stage of cancer, an opposite relationship was observed. Adjusting for covariates is necessary in order to have a better understanding of the determinants of meeting PA guidelines.

We did not observe statistically significant associations between the determinants assessed and meeting PA guidelines, however the magnitude of the PRs were suggestively elevated for current employment status, past OC use, premenopausal status, ethnicity and partner status. Women who were currently employed were more likely to meet PA guidelines in comparison to women who were currently unemployed. Furthermore, women who were employed but on sick leave had a similar prevalence of meeting PA guidelines as women who were unemployed. These results are to be expected as the IPAQ contains a domain to record occupational-related PA, which would only apply to women who were employed. In order for women to hold employment after cancer treatment, it would require them to be well enough to work and have a higher level of physical functioning than those who were unemployed and those who were employed but on sick leave. The level of PA participation was found to differ based on

employment status in the general female population as well, where women who were employed engaged in higher PA intensity levels, as well as spending more time participating in moderate PA compared to women who were unemployed<sup>47</sup>.

Another suggestive determinant of meeting PA guidelines was a women's history of OC use. Women who were not past OC users had a lower prevalence of meeting PA guidelines in comparison to women who had a history of OC use. The association between OC use and PA participation in older populations is not well-studied, but one study found there was a greater prevalence of OC users in more active women (moderately active, highly active and those training at a high-level) in comparison to slightly active or sedentary women<sup>48</sup>. It also may be that women who were past OC users, were more health conscience, as visits to the doctor would be required for prescription renewals, and this could also support a greater likelihood of meeting PA guidelines.

In our study, there was the suggestion that women who were single had a lower prevalence of meeting PA guidelines in comparison to women who were in a relationship or were married. Women who have a partner are believed to have greater social support, and social support can be a strong correlate for PA participation<sup>49</sup>. Among older adults, those who are married are more likely to be physically active compared to those who are single<sup>50</sup>. Furthermore, loneliness (social isolation or an absence of social support) was found to have a negative association with participation in leisure time PA, particularly in females<sup>51</sup>. Social support could be important in maintaining and/or initiating behavioural changes, such as PA participation, and therefore, social support can come from other sources, such as family members and friends<sup>51</sup>.

Certain methodological limitations should be kept in mind when assessing these results. First, the small sample size often resulted in collapsing some categories for the determinants, and therefore, some information is potentially lost due to this. Variables that may have been affected by this include: stage of cancer (stage I/II vs. stage III/IV), education ( $\leq$ high school vs. post-

secondary), ethnicity (French Canadian vs. Other/Mixed), and partner status (relationship vs. single). The relatively small sample size resulted in a lack of power to detect and label associations as statistically significant and resulted in considerable lack of precision which is seen in the width of the confidence intervals. However, the consistency of recruiting only women with Type II tumours that are 6 months post-treatment on average, could be the trade-off for having a smaller sample size. In comparison to other studies looking at ovarian cancer (sample size ranged from 95-101) or even gynecological cancers, our study size is quite reasonable.

This study exhibited many strengths that will add to the literature regarding modifiable lifestyle factors, specifically after treatment for ovarian cancer. First of all, the prevalence obtained from this study may be more accurate than past studies because of the inclusion of many different types of PA, using METs conversions for the PA measure, and measuring PA participation among all of the participants at the same time point along the cancer trajectory. This is also the first study that measured post-treatment PA without including women who were diagnosed with cancer many years ago (i.e. 10-20+ years since diagnosis), establishing a more homogenous sample of women since they were all in remission at the same time point along their cancer trajectory. When identifying potential determinants, possible confounders were controlled for, providing adjusted effect estimates that were less likely to be confounded compared to past studies. Although the study design was cross-sectional, the potential determinants that were assessed are sociodemographic, lifestyle and clinical in nature, meaning these factors do not change substantially over time (such as education or BMI) or have a specified onset (such as menopause), and reverse causality is less of a concern.

In summary, our results show that the prevalence of meeting PA guidelines after treatment is greater than what has been reported in past studies. This may, in part, be due to the consistency of our PA measurements. There is some suggestion that certain patient characteristics including current employment, past OC use, marital status (married/common-law),

premenopausal status and French-Canadian ethnicity, may be related to an increased prevalence of meeting PA guidelines. However, it is difficult to rule out chance, given the lack of statistical significance. Future research should continue to explore PA in the post-treatment phase as there is a lack of studies conducted during this period of time. Moreover, future studies that objectively measure PA may be warranted to increase the accuracy of PA participation data collection.

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**Table 4.1** Descriptive characteristics of the study population

	<b>Meeting PA Guidelines n=47 n (%)</b>	<b>Not Meeting PA Guidelines n=65 n (%)</b>	<b>p-value</b>
<b>Age (years), mean ± sd</b>	58.4 ± 8.3	61.5 ± 8.3	0.14
<b>BMI (kg/m<sup>2</sup>)</b>			
Mean ± sd	26.6 ± 5.9	27.1 ± 6.1	0.90
≤24.9 (%)	23 (48.9%)	29 (44.6%)	
25-29.9 (%)	12 (25.5%)	18 (27.7%)	
≥30 (%)	12 (25.5%)	18 (27.7%)	
<b>Education</b>			
≤High school	18 (38.3%)	27 (41.5%)	0.73
Post-secondary	29 (61.7%)	38 (58.5%)	
<b>Partner Status</b>			
Partner	37 (78.7%)	40 (61.5%)	0.05*
Single	10 (21.3%)	25 (38.5%)	
<b>Employment Status</b>			
Employed	19 (40.4%)	11 (16.9%)	0.02*
Unemployed	19 (40.4%)	41 (63.1%)	
Employed on sick leave	9 (19.2%)	13 (20.0%)	
<b>Smoking Status</b>			
Never	24 (51.1%)	27 (41.5%)	0.58
Former	20 (42.6%)	34 (52.3%)	
Current	3 (6.4%)	4 (6.2%)	
Packyears, mean ± sd	8.2 ± 20.2	9.1 ± 16.4	
<b>Ethnicity</b>			
French-Canadian	37 (78.7%)	40 (61.5%)	0.05*
Other/Mixed	10 (21.3%)	25 (38.5%)	
<b>Undergone Hysterectomy</b>			
Yes	42 (89.4%)	58 (89.2%)	0.93
No	5 (10.6%)	7 (10.8%)	
<b>Past OC use</b>			
Yes	40 (85.1%)	42 (64.6%)	0.02*
No	7 (14.9%)	23 (35.4%)	
<b>Past Hormone Use</b>			
Yes	19 (40.4%)	23 (35.4%)	0.59
No	28 (59.6%)	42 (64.6%)	
<b>Number of Pregnancies</b>			
Nulliparous	10 (21.3%)	15 (23.1%)	0.86
1	13 (27.7%)	15 (23.1%)	
≥2	24 (51.1%)	35 (53.8%)	
<b>Menopausal Status<sup>a</sup></b>			
Postmenopausal	29 (61.7%)	59 (90.8%)	0.04*
Premenopausal	18 (38.3%)	6 (9.2%)	
<b>Stage<sup>b</sup></b>			
Stage I	8 (17.0%)	13 (20.6%)	0.42
Stage II	7 (14.9%)	4 (6.4%)	
Stage III	29 (61.7%)	39 (61.9%)	
Stage IV	3 (6.4%)	7 (11.1%)	

<b>Chemotherapy</b>			
Neoadjuvant	24 (51.1%)	28 (43.1%)	0.47
Adjuvant only	23 (48.9%)	37 (56.9%)	

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<sup>a</sup> One missing information on menopausal status

<sup>b</sup> Two missing information on stage of cancer

\*statistically significant at  $\alpha=0.05$

**Table 4.2** Prevalence of meeting PA guidelines

		<b>Frequency</b>	<b>Percent (95% CI)</b>
<b>Without walking included<sup>1</sup></b>	No MVPA <sup>2</sup> <b>(not meeting guidelines)</b>	42	37.5% (28.5-46.5%)
	Between 0-600 MVPA METs <b>(not meeting guidelines)</b>	23	20.5% (13.1-28.0%)
	600 MVPA METs or more <b>(meeting guidelines)</b>	47	42.0% (32.8-51.1%)
<b>With walking included<sup>3</sup></b>	Not meeting PA guidelines (<600 METs)	48	42.9% (33.7-52.0%)
	Meeting PA guidelines (≥600 METs)	64	57.1% (48.0-66.3%)

1 Walking is not included in the definition of 150 minutes of MVPA, which is equivalent to 600 MET-minutes

2 These women did not participate in any PA at a moderate-to-vigorous intensity level (but potentially participated in lower intensity activities)

3 Walking is included in the definition of 150 minutes of MVPA

**Table 4.3** Percentage of PA participation by IPAQ domain and meeting PA guidelines

	<b>Occupational METs Percentage</b>	<b>Transportation METs Percentage</b>	<b>Housework METs Percentage</b>	<b>Recreational METs Percentage</b>	<b>Total</b>
<b>Meeting PA<sup>1</sup> Guidelines</b>	15.8%	5.2%	39.9%	39.1%	100%
<b>Not Meeting<sup>2</sup> PA Guidelines</b>	0.5%	13.6%	64.4%	21.4%	100%
<b>Overall<sup>3</sup></b>	11.0%	7.8%	47.6%	33.6%	100%

1 Percentage of PA reported that is attributed to each domain amongst women who met PA guidelines (n=47)

2 Percentage of PA reported that is attributed to each domain amongst women who did not meet PA guidelines (n=65)

3 Percentage of PA reported that is attributed to each domain amongst the study population (n=112)

**Table 4.4** Crude and adjusted PR and 95% CI for the association between potential determinants and meeting PA guidelines

Potential Determinant	n	PR <sub>crude</sub> (95% CI)	PR <sub>adjusted</sub> (95% CI)	Covariates included in multivariable model
<b>Age (for every 5 years)</b>	112	0.88 (0.75-1.04)	0.92 (0.77-1.11)	Education, hysterectomy, past hormone use, job status, ethnicity, menopausal status, stage
<b>BMI (kg/m<sup>2</sup>)</b>				
≤24.9	52	Ref.	Ref.	Age, education, past hormone use, smoking
25-29.9	30	0.90 (0.53-1.54)	0.85 (0.51-1.41)	
≥30	30	0.90 (0.53-1.54)	0.87 (0.48-1.56)	
<b>Education</b>				
≤High school	45	Ref.	Ref.	Age, BMI, job status, smoking, menopausal status, stage
Post-secondary	67	1.08 (0.69-1.70)	0.93 (0.56-1.55)	
<b>Partner Status</b>				
Relationship	77	Ref.	Ref.	Age, stage
Single	35	0.59 (0.34-1.05)	0.66 (0.38-1.18)	
<b>Undergone Hysterectomy</b>				
Yes	100	Ref.	Ref.	Age, ethnicity, chemo
No	12	0.99 (0.49-2.01)	0.99 (0.50-1.96)	
<b>Past OC Use</b>				
Yes	82	Ref.	Ref.	Age, job status, ethnicity
No	30	0.48 (0.24-0.95)	0.61 (0.30-1.23)	
<b>Past Hormone Use</b>				
No	70	Ref.	Ref.	Age, BMI, menopausal status
Yes	42	1.13 (0.73-1.75)	1.35 (0.83-2.18)	
<b>Parity (full-term births)</b>				
Nulliparous	25	Ref.	Ref.	Age, stage, chemo
1	28	1.16 (0.62-2.17)	1.09 (0.59-2.01)	
≥2	59	1.02 (0.57-1.80)	0.99 (0.55-1.78)	
<b>Job Status</b>				
Unemployed	60	Ref.	Ref.	Age, education, past OC use, menopausal status
Employed on sick leave	22	1.29 (0.69-2.41)	1.05 (0.56-1.99)	
Employed	30	2.00 (1.26-3.17)	1.49 (0.87-2.55)	
<b>Smoking (for every 18 pack-years)<sup>a</sup></b>	112	0.97 (0.72-1.31)	0.91 (0.66-1.26)	Age, BMI, education, ethnicity
<b>Ethnicity</b>				
French Canadian	77	Ref.	Ref.	Age, hysterectomy, past OC use, menopausal status
Others/Mixed	35	0.59 (0.34-1.05)	0.66 (0.38-1.16)	
<b>Menopausal Status<sup>b</sup></b>				
Postmenopausal	94	Ref.	Ref.	Age, education, past hormone use, job status
Premenopausal	17	1.69 (1.09-2.61)	1.45 (0.82-2.54)	

<b>Stage of Cancer</b> <sup>c</sup>				
Stage III/IV	78	Ref.	Ref.	Age, education, partner status, parity, chemo
Stage I/II	32	1.14 (0.73-1.80)	1.23 (0.64-2.38)	
<b>Chemo Treatment</b>				
Neoadjuvant	52	Ref.	Ref.	Age, hysterectomy, parity, stage
Adjuvant only	60	0.83 (0.54-1.28)	0.70 (0.35-1.20)	

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<sup>a</sup> Standard deviation for smoking pack-years is 18

<sup>b</sup> One missing information on menopausal status

<sup>c</sup> Two missing information on stage of cancer

## Chapter 5

### Additional Analyses

#### 5.1 Examining the Association Between Physical Activity and Patient Reported Outcomes

##### 5.1.1 Meeting Physical Activity Guidelines and FACT-O

The association between meeting physical activity (PA) guidelines and health-related quality of life (HRQOL) was examined using data collected from the Functional Assessment of Cancer Therapy-Ovarian (FACT-O) questionnaire. A trial outcome index (TOI) is a summary index of physical, functional and ovarian cancer specific outcomes. Using a multiple linear regression and the change-in-estimate (CIE) approach, the final multivariable adjusted model for the TOI score included age, partner status, job status and ethnicity. In addition to the TOI score, the total FACT-O score provides an overall, multidimensional score that includes social and emotional well-being scores in addition to the domains included in the TOI. Using the same analysis strategy with a multiple linear regression and the CIE approach, confounders identified included age, partner status, job status, ethnicity, BMI and menopausal status (see Appendix E. Table 1 and 2).

On average, those who met PA guidelines had a TOI score that was 3.21 points (-1.55, 7.96) and a total FACT-O score that was 2.17 points (-4.81, 9.15) greater than those who did not meet PA guidelines in the fully adjusted multivariable model (Table 5.1). Higher scores generated from the FACT-O equate to better perceived HRQOL. In summary, women who met PA guidelines, had a mean HRQOL score that was greater than women who did not meet PA guidelines. However, the difference in HRQOL scores was neither statistically significant nor clinically meaningful (mean difference <8 points) between those who met PA guidelines and those who did not meet PA guidelines.

**Table 5.1** Crude and adjusted estimates with 95% CI for the relationship between meeting PA guidelines and FACT-O score which measures HRQOL

FACT-O Score	Crude Estimate (95% CI)	Adjusted Estimate (95% CI)	Covariates included in the multivariable model
Trial Outcome Index Score	$\beta=3.39$ (-1.00, 7.78)	$\beta=3.21^1$ (-1.55, 7.96)	Age, partner status, job status, ethnicity
Overall HRQOL	$\beta=2.95$ (-3.68, 9.58)	$\beta=2.17^2$ (-4.81, 9.15)	Age, BMI, partner status, job status, ethnicity, menopausal status

1 Those who met PA guidelines have a TOI score that was 3.21 greater than those who did not meet PA guidelines after controlling for age, partner status, job status and ethnicity

2 Those who met PA guidelines have a total FACT-O score that was 2.17 greater than those who did not meet PA guidelines after controlling for age, partner status, job status and ethnicity

### 5.1.2 Meeting Physical Activity Guidelines and HADS

The association between meeting PA guidelines and anxiety and depression symptoms was examined by using the scores collected from the Hospital Anxiety and Depression Scale (HADS). The HADS is comprised of 7 questions that form an anxiety scale and 7 questions for a depression scale. A score of 7 or less on the respective scales corresponds to a non-case (symptoms within the normal range) while a score of 8 or greater corresponds to a diagnosis of mild (8-10), moderate (11-14) or severe symptoms (15-21)<sup>1,2</sup> of anxiety or depression, respectively. For the purpose of this analysis, non-cases (HADS anxiety/depression scores < 8) were compared to all cases with presence of anxiety (HADS anxiety  $\geq$  8) or presence of depression (HADS depression  $\geq$  8). Due to the binary nature of the outcome variables, logistic regression was employed, and the CIE approach was used to identify confounders (see Appendix E. Table 3 and 4).

Women who met PA guidelines were approximately 1.7 times (OR=1.67; 95% CI: 0.72-3.84) more likely to report symptoms of anxiety compared to women who did not meet PA guidelines, adjusted for age and ethnicity. For the depression score, women who met PA guidelines were 0.30 times (OR=0.30; 95% CI: 0.06-1.55) less likely to report depressive

symptoms compared to women who did not meet PA guidelines, adjusted for age and partner status. However, the association of meeting PA guidelines with anxiety or depression symptoms was not statistically significant, and therefore chance cannot be ruled out for the observations. Table 5.2 provides a summary of the crude and adjusted measure of effects for the association between meeting PA guidelines and outcomes from the HADS.

**Table 5.2** Crude and adjusted estimates with 95% CI for the relationship between meeting PA guidelines and different PROs

<b>HADS Outcome</b>	<b>Crude Estimate (95% CI)</b>	<b>Adjusted Estimate (95% CI)</b>	<b>Covariates included in the multivariable model</b>
Symptoms of Anxiety vs. None	OR=1.43 (0.65, 3.14)	OR=1.67 <sup>1</sup> (0.72, 3.84)	Age, ethnicity
Symptoms of Depression vs. None	OR=0.26 (0.05, 1.27)	OR=0.30 <sup>2</sup> (0.06, 1.55)	Age, partner status

1 Those who met PA guidelines have 1.67 odds of having some anxiety symptoms after adjusting for age and ethnicity

2 Those who met PA guidelines have 0.30 odds of having some depression symptoms after adjusting for age and partner status

## **5.2 Exploratory Analysis of Lifetime and Past 10 years Physical Activity for PROVAQ Subgroup**

PA participation prior to ovarian cancer diagnosis would be hypothesized to have some influence on PA participation after diagnosis. Unfortunately, information on PA prior to diagnosis was not available for all participants of the HPROQ study, but a subset of the study population was recruited from a previous study called The PRevention of OVArrian Cancer in Quebec (PROVAQ) study (PI: Anita Koushik)<sup>3</sup>. In this study, information on the past 10 years and lifetime PA participation was collected. Using this subset of participants (n=36), an exploratory analysis was conducted to determine if past PA participation had any association on PA participation after treatment. Women who met PA guidelines in the past 10 years by reaching an

average of at least 150 minutes of MVPA per week, were 1.17 (0.52, 2.64) times more likely to meet PA guidelines 6 months post-treatment compared to women who did not meet the guidelines in the past 10 years. In addition, women who had a lifetime average of at least 150 minutes of MVPA per week, were 1.60 (0.49, 5.21) times more likely to meet PA guidelines in the post-treatment period in comparison to women who did not meet these guidelines in their lifetime. Moreover, based on this subset of the study population, exactly half are meeting PA guidelines 6 months post-treatment while the other half are not (Table 5.3 and 5.4).

**Table 5.3** Past 10 years of MVPA and MVPA participation post-treatment

<b>Past 10 years of MVPA</b>	<b>MVPA Post-treatment</b>		<b>Total</b>
	<b>Meeting PA Guidelines</b>	<b>Not Meeting PA Guidelines</b>	
<b>Meeting PA Guidelines</b>	14	13	27
<b>Not Meeting PA Guidelines</b>	4	5	9
<b>Total</b>	18	18	36

**Table 5.4** Lifetime MVPA and MVPA participation post-treatment

<b>Lifetime of MVPA</b>	<b>MVPA Post-treatment</b>		<b>Total</b>
	<b>Meeting PA Guidelines</b>	<b>Not Meeting PA Guidelines</b>	
<b>Meeting PA Guidelines</b>	16	14	30
<b>Not Meeting PA Guidelines</b>	2	4	6
<b>Total</b>	18	18	36

## 5.3 Sensitivity Analysis

### 5.3.1 Logistic Regression for Determinants of Physical Activity

The choice to use a modified Poisson regression to identify potential determinants of meeting PA guidelines was due to the outcome (meeting PA guidelines) being dichotomized and considered not rare. A sensitivity analysis was conducted to determine if there were any

differences in the estimate of effects by using a logistic regression and therefore, using OR to interpret the association between potential determinants with meeting PA guidelines. In general, the odds ratios were all in the same direction as the relative risks, but the odds ratio had a larger magnitude of effect (Table 5.5).

**Table 5.5** Determinants of PA using a logistic regression model in comparison to the determinants of PA using a modified Poisson model

Potential Determinant	n	PR <sub>adjusted</sub> (95% CI) <sup>1</sup>	OR <sub>adjusted</sub> (95% CI) <sup>2</sup>	Covariates included in multivariable model
<b>Age (for every 5 years)</b>	112	0.92 (0.77-1.11)	0.85 (0.57-1.25)	Education, hysterectomy, past hormone use, job status, ethnicity, menopausal status, stage
<b>BMI (kg/m<sup>2</sup>)</b>				
≤24.9	52	Ref.	Ref.	
25-29.9	30	0.85 (0.51-1.41)	0.76 (0.29-1.99)	Age, education, past hormone use, smoking
≥30	30	0.87 (0.48-1.56)	0.79 (0.29-2.16)	
<b>Education</b>				
≤High school	45	Ref.	Ref.	
Post-secondary	67	0.93 (0.56-1.55)	0.87 (0.33-2.26)	Age, BMI, job status, smoking, menopausal status, stage
<b>Partner Status</b>				
Relationship	77	Ref.	Ref.	
Single	35	0.66 (0.38-1.18)	0.50 (0.21-1.23)	Age, stage
<b>Undergone Hysterectomy</b>				
Yes	100	Ref.	Ref.	
No	12	0.99 (0.50-1.96)	0.96 (0.25-3.62)	Age, ethnicity, chemo
<b>Past OC Use</b>				
Yes	82	Ref.	Ref.	
No	30	0.61 (0.30-1.23)	0.46 (0.16-1.32)	Age, job status, ethnicity
<b>Past Hormone Use</b>				
No	70	Ref.	Ref.	
Yes	42	1.35 (0.83-2.18)	1.75 (0.71-4.32)	Age, BMI, menopausal status
<b>Parity (full-term births)</b>				
Nulliparous	25	Ref.	Ref.	
1	28	1.09 (0.59-2.01)	1.17 (0.37-3.74)	Age, stage, chemo
≥2	59	0.99 (0.55-1.78)	0.97 (0.34-2.75)	
<b>Job Status</b>				
Unemployed	60	Ref.	Ref.	
Employed on sick leave	22	1.05 (0.56-1.99)	0.98 (0.30-3.19)	Age, education, past OC use, menopausal status
Employed	30	1.49 (0.87-2.55)	2.31 (0.83-6.40)	
<b>Smoking (for every 18</b>	112	0.91 (0.66-1.26)	0.84 (0.53-1.32)	Age, BMI, education,

pack-years) <sup>a</sup>				ethnicity
<b>Ethnicity</b>				
French Canadian	77	Ref.	Ref.	Age, hysterectomy, past OC use, menopausal status
Others/Mixed	35	0.66 (0.38-1.16)	0.46 (0.16-1.29)	
<b>Menopausal Status<sup>b</sup></b>				
Postmenopausal	94	Ref.	Ref.	Age, education, past hormone use, job status
Premenopausal	17	1.45 (0.82-2.54)	2.50 (0.64-9.80)	
<b>Stage of Cancer<sup>c</sup></b>				
Stage III/IV	78	Ref.	Ref.	Age, education, partner status, parity, chemo
Stage I/II	32	1.23 (0.64-2.38)	1.39 (0.46-4.20)	
<b>Chemo Treatment</b>				
Neoadjuvant	52	Ref.	Ref.	Age, hysterectomy, parity, stage
Adjuvant only	60	0.70 (0.35-1.20)	0.48 (0.18-1.31)	

1 The adjusted PR for each given determinant and meeting PA guidelines using a modified Poisson model (results are from Table 4.4)

2 The adjusted OR for each given determinant and meeting PA guidelines using a logistic regression model

<sup>a</sup> Standard deviation for smoking pack-years is 18

<sup>b</sup> One missing information on menopausal status

<sup>c</sup> Two missing information on stage of cancer

### 5.3.2 Determinants of Physical Activity with Guideline of 150 minutes including walking

When walking exercise is taken into consideration and is included in the definition of moderate-to-vigorous physical activity (MVPA) participation, 57.1% of the study population were meeting PA guidelines (versus 42.0% when walking is not included). Using a more liberal PA guideline definition, by including walking, the analysis for identifying potential determinants was conducted again to compare the measure of effects when more women are considered physically active. Parity became statistically significant and women who had more children were less likely to meet PA guidelines compared to women who had no children (Table 5.6). Another notable difference is that women who were employed but on sick leave were less likely to meet guidelines compared to unemployed women. With a stricter PA guideline cut-off, women who were employed but on sick leave were more likely to meet guidelines compared to unemployed women (refer to Table 4.4), although neither estimates were statistically significant. By including walking, more women who were unemployed were classified as meeting PA guidelines, and therefore, the PR for employment status and PA was attenuated.

**Table 5.6** Determinants of PA using a modified Poisson model with PA guideline defined as 150 minutes of moderate PA including walking in comparison to PA guideline not including walking

Potential Determinant	n	PR <sub>adjusted</sub> (95% CI) <sup>1</sup>	PR <sub>adjusted</sub> (95% CI) <sup>2</sup>	Covariates included in multivariable model
<b>Age (for every 5 years)</b>	112	0.92 (0.77-1.11)	0.95 (0.82-1.09)	Education, hysterectomy, past hormone use, job status, ethnicity, menopausal status, stage
<b>BMI (kg/m<sup>2</sup>)</b>				
≤24.9	52	Ref.	Ref.	Age, education, past hormone use, smoking
25-29.9	30	0.85 (0.51-1.41)	0.83 (0.57-1.22)	
≥30	30	0.87 (0.48-1.56)	0.78 (0.49-1.22)	
<b>Education</b>				
≤High school	45	Ref.	Ref.	Age, BMI, job status, smoking, menopausal status, stage
Post-secondary	67	0.93 (0.56-1.55)	1.13 (0.75-1.70)	
<b>Partner Status</b>				
Relationship	77	Ref.	Ref.	Age, stage
Single	35	0.66 (0.38-1.18)	0.79 (0.52-1.19)	
<b>Undergone Hysterectomy</b>				
Yes	100	Ref.	Ref.	Age, ethnicity, chemo
No	12	0.99 (0.50-1.96)	1.09 (0.66-1.81)	
<b>Past OC Use</b>				
Yes	82	Ref.	Ref.	Age, job status, ethnicity
No	30	0.61 (0.30-1.23)	0.66 (0.40-1.09)	
<b>Past Hormone Use</b>				
No	70	Ref.	Ref.	Age, BMI, menopausal status
Yes	42	1.35 (0.83-2.18)	1.26 (0.88-1.79)	
<b>Parity (full-term births)</b>				
Nulliparous	25	Ref.	Ref.	Age, stage, chemo
1	28	1.09 (0.59-2.01)	0.65 (0.42-1.00)	
≥2	59	0.99 (0.55-1.78)	0.66 (0.45-0.95)	
<b>Job Status</b>				
Unemployed	60	Ref.	Ref.	Age, education, past OC use, menopausal status
Employed on sick leave	22	1.05 (0.56-1.99)	0.72 (0.44-1.20)	
Employed	30	1.49 (0.87-2.55)	1.07 (0.74-1.56)	
<b>Smoking (for every 18 pack-years)<sup>a</sup></b>	112	0.91 (0.66-1.26)	1.02 (0.85-1.22)	Age, BMI, education, ethnicity
<b>Ethnicity</b>				
French Canadian	77	Ref.	Ref.	Age, hysterectomy, past OC use, menopausal status
Others/Mixed	35	0.66 (0.38-1.16)	0.84 (0.56-1.25)	
<b>Menopausal Status<sup>b</sup></b>				
Postmenopausal	94	Ref.	Ref.	Age, education, past hormone use, job status
Premenopausal	17	1.45 (0.82-2.54)	1.24 (0.78-1.97)	

<b>Stage of Cancer <sup>c</sup></b>				
Stage III/IV	78	Ref.	Ref.	Age, education, partner status, parity, chemo
Stage I/II	32	1.23 (0.64-2.38)	1.02 (0.66-1.57)	
<b>Chemo Treatment</b>				
Neoadjuvant	52	Ref.	Ref.	Age, hysterectomy, parity, stage
Adjuvant only	60	0.70 (0.35-1.20)	0.98 (0.62-1.54)	

1 The adjusted PR for each given determinant and meeting PA guidelines, with meeting PA guideline defined as participating in at least 150 minutes of MVPA (results are from Table 4.4)

2 The adjusted PR for each given determinant and meeting PA guidelines, with meeting PA guidelines defined as participating in at least 150 minutes of MVPA with walking included in the definition of MVPA

<sup>a</sup> Standard deviation for smoking pack-years is 18

<sup>b</sup> One missing information on menopausal status

<sup>c</sup> Two missing information on stage of cancer

### 5.3.3 Association Between Physical Activity (with Guideline of 150 minutes including walking) and Patient Reported Outcomes

The association between meeting PA guidelines and PROs was conducted using a more liberal PA guideline, by including walking in the definition of MVPA. We were particularly interested in whether including walking would affect anxiety and depression symptoms. The same analytic methodologies were carried out as before, by using a CIE approach to build the fully adjusted model. There were some differences in the confounders that were identified for each model (Table 5.7). The beta estimates for the TOI and FACT-O scores when comparing women who met PA guidelines to those who did not were slightly larger than what was found in the previous analysis using a stricter PA guideline definition (refer to Tables 5.1 and 5.7). Moreover, the OR for the anxiety score was attenuated when more women were considered active (OR=1.67 to 1.30), whereas the depression score had a more extreme measure of effect (OR= 0.30 to 0.13), resulting in a statistically significant difference in depression score between women who met PA guidelines and those who did not. With more women meeting PA guidelines, it did not change its association with PROs much, but did appear to have a significant impact on the depression score, with women meeting PA guidelines having a 0.13 (0.02-0.70) odds of having depression symptoms.

**Table 5.7** Association between PA and PROs using PA guideline of 150 minutes of MVPA, with walking included as MVPA, in comparison to results with a PA guideline of 150 minutes of MVPA without walking

<b>Outcome of Interest</b>	<b>Adjusted Estimate (95% CI)</b>	<b>Covariates included in the multivariable model</b>
<b>TOI Score</b>	$\beta=3.21^1$ (-1.55, 7.96)	Age, partner status, job status, ethnicity
	$\beta=3.71^3$ (-0.72, 8.14)	Age, job status, smoking, ethnicity, stage
<b>FACT-O Total Score</b>	$\beta=2.17^1$ (-4.81, 9.15)	Age, BMI, partner status, job status, ethnicity, menopausal status
	$\beta=3.39^3$ (-3.18, 9.96)	Age, job status, smoking, ethnicity, stage
<b>Anxiety Score</b>	OR=1.67 <sup>2</sup> (0.72, 3.84)	Age, ethnicity
	OR=1.30 <sup>3</sup> (0.56, 3.04)	Age, smoking, ethnicity
<b>Depression Score</b>	OR=0.30 <sup>2</sup> (0.06, 1.55)	Age, partner status
	OR=0.13 <sup>3</sup> (0.02, 0.70)	Age, education, job status, menopausal status

1 Difference in mean FACT-O scores for those who met the PA guidelines of 150 minutes of MVPA (walking not included as MVPA) and those who did not meet PA guidelines (results are from Table 5.1)

2 OR for having anxiety and depression symptoms for those who met PA guidelines of 150 minutes of MVPA (walking not included as MVPA) compared to those who did not meet PA guidelines (results are from Table 5.2)

3 Beta and OR estimates for those who met PA guidelines of 150 minutes of MVPA, with walking included in the definition of MVPA, compared to those who did not meet PA guidelines

## 5.4 References

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2. Chipperfield K, Fletcher J, Millar J, et al. Factors associated with adherence to physical activity guidelines in patients with prostate cancer. *Psychooncology.* 2013;22(11):2478-2486.
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## Chapter 6

### Discussion

#### 6.1 Summary of Main Findings

The primary objectives of this thesis were to estimate the prevalence of meeting physical activity (PA) guidelines among ovarian cancer survivors in the post-treatment period and to identify determinants of meeting PA guidelines in this study population. Additional analyses explored the association between baseline PA and patient reported outcomes (PROs), specifically health-related quality of life (HRQOL), anxiety symptoms and depression symptoms in the cohort.

Based on the recommended guidelines of 150 minutes of moderate PA per week for cancer populations, 42.0% (95% CI: 32.8-51.1%) of the study population was meeting this PA guideline (excluding walking) 6 months after treatment completion. PA participation was greatest in housework-related PA, with 47.6% of all PA participation in this study attributed to that domain. None of the potential determinants under consideration were statistically significantly associated with meeting PA guidelines but many of the characteristics under consideration trended in the direction that was hypothesized. There were some suggestive determinants that trended towards an association with meeting PA guidelines, including current employment status, history of OC use, marital status, premenopausal status and French-Canadian ethnicity. Given that this objective was aimed at generating hypotheses and the sample size was small, it is not surprising that no significant associations were reported.

This study did not provide evidence of a significant difference in PROs between women who met PA guidelines and women who did not meet PA guidelines 6 months after completing treatment. In summary, women who met PA guidelines, had a mean HRQOL score that was greater than women who did not meet PA guidelines. However, the difference in HRQOL scores

was neither statistically significant nor clinically meaningful between those who met PA guidelines and those who did not meet PA guidelines. Women who met PA guidelines were more likely to report symptoms of anxiety compared to women who did not meet PA guidelines. For the depression score, women who met PA guidelines were less likely to report depressive symptoms compared to women who did not meet PA guidelines. However, the association of meeting PA guidelines with anxiety or depression symptoms was not statistically significant, and therefore chance cannot be ruled out for the observations.

Sensitivity analyses were conducted to include walking in the definition of moderate-to-vigorous physical activity (MVPA), which resulted in classifying a greater proportion of women in this cohort as meeting the recommended PA guidelines of 150 minutes of MVPA (57.1%; 95% CI: 48.0-66.3%). The measure of effects (PRs) for many of the determinants were similar to the original analyses that did not include walking in the definition of MVPA. However, the determinant of parity became statistically significant when walking was included in the definition of MVPA. In addition, women who were employed but on sick leave were significantly less likely to meet PA guidelines as opposed to more likely when compared to women who were employed and not on sick leave. In addition, women who met PA guidelines when walking was included in the definition of MVPA were significantly less likely (OR=0.13; 95% CI: 0.02, 0.70) to have symptoms of depression.

## **6.2 Comparison of Study Results to Existing Literature**

### **6.2.1 Prevalence of Physical Activity**

The prevalence of meeting PA guidelines after diagnosis among ovarian cancer patients has been measured in five past studies, with the prevalence ranging from 9-53%<sup>1-5</sup>.

Unfortunately, these studies have measured PA participation at varying time points along the cancer trajectory (i.e. during treatment or among long-term survivors). The study with the greatest

prevalence of women meeting PA guidelines (53.0%) included other gynecological cancers, which may overestimate this prevalence if applied to ovarian cancer patients, as women suffering from ovarian cancer are less likely to meet the guidelines in comparison to other gynecological cancers<sup>2</sup>. This is often due to the poor prognosis of many women diagnosed with ovarian cancer<sup>2</sup>. On the other hand, the study with the lowest prevalence rate for meeting PA guidelines (9.1%), only considered recreational PA and therefore did not consider PA from other sources, which could partially explain the low prevalence rate<sup>5</sup>. The three remaining studies found prevalence estimates of meeting PA guidelines that were in the lower-to-middle range (19.0%, 20.8%, 31.1%)<sup>1,3,4</sup>, but included women who were still undergoing treatment and/or women who were diagnosed with ovarian cancer many years ago. In comparison to studies conducted after diagnosis among ovarian cancer populations, our findings for PA participation prevalence is higher than what has been previously reported<sup>1,3-5</sup>.

### **6.2.2 Determinants of Physical Activity**

To date, only one other study has looked at potential determinants of being physically active among ovarian cancer survivors<sup>6</sup> and two studies have identified correlates and barriers of being physically active<sup>1,2</sup>, but none of these studies controlled for confounders when identifying potential determinants and/or predictors. Determinants of meeting PA guidelines that were identified in this study, such as age, being employed, lower BMI and earlier disease stage, are consistent with the existing literature. However, unlike Stevinson and colleagues, who found that higher education was associated with meeting PA guidelines<sup>6</sup>, we found an inverse relationship. Prior to controlling for confounders of this association, education was positively associated with meeting PA guidelines, but after controlling for age, hysterectomy for cancer treatment, job status, smoking, menopausal status and stage of cancer, an inverse relationship was observed.

Adjusting for covariates is necessary in order to have a better understanding of the independent relationship between potential determinants and meeting PA guidelines.

### **6.2.3 Association between Physical Activity and Patient Reported Outcomes**

Very few observational studies have investigated the association between PA and HRQOL scores among ovarian cancer patients after diagnosis. Lowe and colleagues investigated the association between different types of PA participation and HRQOL scores among ovarian cancer survivors by categorizing PA participation into three groups: exercise and yoga, exercise only, and no exercise<sup>7</sup>. Women who participated in exercise and yoga had better HRQOL scores than women who participated in exercise alone (average difference in HRQOL score = 8.46), but exercise alone was better than no exercise at all (average difference in HRQOL score = 11.21)<sup>7</sup>. Furthermore, two studies have examined the association between meeting 150 minutes of moderate PA per week and HRQOL scores. One of those studies found that women who met PA guidelines had significantly higher global HRQOL scores compared to women who were sedentary (average difference in HRQOL score = 12.9;  $p < 0.001$ ), using the Quality of Life Questionnaire-Ovarian (QLQ-OV28) to measure HRQOL<sup>4</sup>. Similar findings were presented in a cross-sectional study that measured HRQOL using the FACT-O questionnaire, where women who participated in at least 150-minutes of PA per week had a mean FACT-O score difference of 12.5 (95% CI: 9.1-16.0) from women who did not meet guidelines<sup>3</sup>. These past studies demonstrate similar results to our study, that women who are more physically active after diagnosis tend to have better HRQOL scores; however, we were unable to provide evidence of a statistically significant difference in HRQOL between women who met PA guidelines and women who did not meet PA guidelines, nor were the observed differences as large.

The prevalence of women with symptoms of anxiety (36.6%) and depression (10.7%) in this study is similar to post-treatment prevalence rates found in a systematic review that looked at depression and anxiety in ovarian cancer patients<sup>8</sup>. The prevalence of depression symptoms tend

to decrease from pre-treatment, throughout treatment and after treatment, whereas anxiety symptoms become more prevalent across the treatment spectrum, suggesting that women may have increased fear of recurrence or cancer progression, even after treatment is completed<sup>8</sup>. At least one study has analyzed the association between meeting PA guidelines with anxiety and depression in ovarian cancer patients during the post-diagnosis period<sup>9</sup>. In this study, a significant inverse relationship between PA and psychosocial functioning was found, with women who met PA guidelines having less severe anxiety and depression symptoms in comparison to women who did not meet PA guidelines<sup>9</sup>. This thesis project observed a similar magnitude of association between increased PA and lower depression scores, but this was only statistically significant when walking was included in the definition of meeting PA guidelines based on a minimum 600 MET-minute cut-off. An opposite effect was observed in this thesis between PA and anxiety scores, such that women who met PA guidelines had increased odds of having anxiety symptoms.

## **6.3 Explanation of Study Results**

### **6.3.1 Prevalence of Physical Activity**

There could be a few reasons why the prevalence (42.0%) in this thesis was found to be higher than previous studies. First of all, the reference time for collecting PA information was consistent for all participants (6 months after treatment completion). Past studies have measured PA prevalence among patients who are undergoing chemotherapy or among long-time survivors (women diagnosed many years ago), which may bias the prevalence estimate. Those who were in the middle of treatment may have very poor physical functioning due to the hardships of chemotherapy and women who have had more time since diagnosis were more likely to participate in PA compared to women who were more recently diagnosed<sup>6</sup>. Furthermore, this study measured PA using a comprehensive questionnaire, the IPAQ, which took into account PA from different domains, such as occupational, housework and transportation, in addition to

recreational PA. This is important to consider in frailer populations, since any source of PA may have some health benefit and should be recorded. PA intensity was taken into account by converting women's PA participation into MET-minutes. This is important to note, because some previous studies did not use METs conversions, and may have missed participants that did meet guidelines by engaging in shorter bouts of PA at higher intensities<sup>2,3</sup>.

In this thesis project, women were the most active in the housework-related domain, which has also been reported in other cancer-specific studies and the general population. One study looking at prostate cancer patients adhering to PA guidelines found that men were most active in the domestic domain, and least active in the transport and recreation domain, implying PA is primarily undertaken involuntarily in the form of household duties<sup>10</sup>. Housework is often part of a daily routine and becomes a regular source of PA for many adults. This has also been reported in the general population, where housework PA accounts for a large proportion of self-reported PA (35.6%), particularly among women and older adults<sup>11</sup>. In healthy populations, housework PA seems to be weakly associated with health benefits in comparison to leisure PA, as the energy expenditure is not as high<sup>11</sup>. Whether housework PA provides the same health benefits as recreational PA for more vulnerable populations, such as those who are older or suffering from cancer, is still unclear and will have to be investigated further.

### **6.3.2 Determinants of Physical Activity**

Although the potential determinants of meeting PA guidelines analyzed in this study were not statistically significant, some of these determinants have demonstrated an association with PA in the existing literature, and were hypothesized, *a priori*, to be associated with PA in this study. Employment status and partner status were two of the determinants with the strongest suggestive association with PA participation at baseline, in this cohort of ovarian cancer survivors and there is evidence in the literature to support these observed associations. An association between

employment and higher levels of PA has been found in ovarian cancer survivors<sup>6</sup> as well as in populations of healthy women<sup>12</sup>. More specifically, one study conducted in the United States reported that women who were employed engaged in higher PA intensity levels and spent more time participating in moderate PA compared to women who were unemployed<sup>12</sup>. Women who are able to work, are more likely to have greater physical capabilities in comparison to women who are unemployed or employed but on sick leave. This relationship has been found in both the general and cancer populations. Furthermore, a cohort study identifying predictors of PA conducted in Germany observed that among older healthy adults, women who were married were more likely to be physically active compared to women who were single<sup>13</sup>. Those who have a partner or are in a significant relationship are believed to have greater social support, which can be a strong predictor for PA participation, particularly in older adults<sup>14</sup>. These studies provide support for our results that current employment and having a partner are associated with PA participation, as these sociodemographics are often indicators of good physical capabilities and greater social support.

### **6.3.3 Association between Physical Activity and Patient Reported Outcomes**

Unlike this study, past studies have found statistically significant associations among meeting PA guidelines and FACT-O scores, anxiety scores and depression scores<sup>3,4,7,9</sup>. One potential reason for this discrepancy could be that this study was underpowered, as past studies had larger sample sizes (n=209 and 359, respectively)<sup>3,4</sup>, which was achieved by including women at different time points along the cancer trajectory. Furthermore, confounders that were adjusted for in past studies included predominantly clinical factors, such as stage, cancer recurrence, and time since diagnosis, but did not control for some key sociodemographic characteristics, such as current job status and BMI. In addition, this study failed to provide evidence that women who met PA guidelines had a clinical meaningful difference in FACT-O

score compared to women who did not meet guidelines. Previous studies have found clinically meaningful differences in HRQOL scores when comparing women who are considered sufficiently active versus women who are considered insufficiently active<sup>4,7,9</sup>. A clinical meaningful difference in HRQOL is often estimated as a difference of at least 8 points or a difference of 0.5 standard deviation for the total FACT-O score<sup>15,16</sup>.

It is expected that meeting PA guidelines would result in an inverse relationship with anxiety and depression symptoms, meaning those who are more active would be less likely to have anxiety or depression symptoms. With respect to symptoms of depression, this pattern with PA was observed, but a positive relationship was observed between PA and symptoms of anxiety. While this latter observation was counter to the study hypothesis, it should be noted that these results are based on a cross-sectional analysis, and therefore the direction of the association is not known, meaning women who were more anxious may be more physically active or vice versa. At the time of data collection (6 months after treatment), women who were more anxious may have been more inclined to engage in PA to help cope with their anxiety, which could explain the positive relationship between meeting PA guidelines and anxiety symptoms. However, it is believed that as women continue to participate in PA after treatment, anxiety symptoms may decrease over time<sup>17</sup>, based on observations from longitudinal studies. Pilot studies have been conducted to assess whether exercise and walking interventions implemented during treatment could improve anxiety, depression and HRQOL<sup>18,19</sup>. These studies found no change in anxiety and depression scores<sup>18</sup> and modest changes in HRQOL<sup>19</sup> among women who participated in the intervention. Therefore, future studies should consider implementing PA interventions after treatment, once women feel more capable of participating in PA, to determine if modifying PA participation could improve PROs.

#### **6.3.4 Sensitivity Analyses**

Analyses were conducted with walking included and not included in the definition of meeting the recommended PA guideline of 150 minutes of moderate PA. In the existing literature, some studies have classified walking as moderate PA since moderate walking has a MET value of 3<sup>1,20</sup>, but other studies have not included walking<sup>5,21</sup>. Excluding walking in the definition of MVPA in this study resulted in a prevalence estimate of meeting PA guidelines among ovarian cancer survivors (42.0%) that was higher than what was reported in past studies, and therefore, future studies should consider excluding walking, as women who are in remission of ovarian cancer are capable of meeting these stricter guidelines.

By including walking in the definition of MVPA, more women who were unemployed were considered as meeting PA guidelines, and therefore, attenuating the PR for women who are employed and for women who were employed but on sick leave in comparison to women who were unemployed (refer to Table 5.6). It is hypothesized that women who were considered unemployed also included women who were retired and therefore older. Older individuals are more inclined to participate in lower intensity activities, such as walking, and by including this activity into the recommended guideline, the number of women meeting PA guidelines in the unemployed category increased. This is not for certain, as information on women's retirement status was not collected, but women who were unemployed were older on average compared to women who were employed or employed and on sick leave in this study population (results not shown). Moreover, women who are on sick leave are probably too sick to engage in a sufficient amount of PA if they are too sick to work. Including walking into MVPA participation resulted in an additional 17 women (a total of 64 out of 112 participants) as meeting PA guidelines.

## **6.4 Methodological Considerations**

### **6.4.1 Strengths**

This study exhibited several strengths that will add to the literature regarding the role of modifiable lifestyle factors in ovarian cancer survivors, specifically after treatment. First of all, an accurate prevalence of meeting PA guidelines was obtained by including many different types of PA, using METs conversion for the PA measure, and measuring PA participation among all of the participants at the same time point along the cancer trajectory. This is also the first study that measured post-treatment PA without including women who were diagnosed with cancer many years ago, establishing a homogenous sample of women, with all women in remission at the same time point along their cancer trajectory (6 months after treatment). When identifying potential determinants, possible confounders were controlled for, providing less biased measures of association compared to many of the past studies<sup>1,2,6</sup>. In addition, this study investigated several potentially important determinants of PA that have not yet been explored in the existing literature. Although the study design was cross-sectional, many of the potential determinants were not time dependent, including sociodemographic factors and clinical characteristics, in addition to some past lifestyle factors. Thus, reverse causality is less of a concern. However, one determinant that may be affected by reverse causality is current smoke status, meaning the level of PA participation could influence current smoking habits. All participants are women with ovarian cancer and currently in remission, and therefore, recall bias is not a concern when they are interviewed using the HPROQ questionnaire.

The HPROQ study from which data was used for this thesis utilized an existing recruitment infrastructure that allowed participants to be interviewed shortly after recruitment. Information regarding PA and PROs was based on activities or experience in the past 7 days, thereby decreasing the probability of recall error since participants utilized short-term recall. Since the study population was restricted to three hospitals containing specialized gynecological units, the data pertaining to tumour pathology and treatment was accurate and precise. Although a cross-sectional study design was used for the analysis of the baseline cohort, moving forward, this

study will collect follow-up data, which will provide greater insight in how PA and PROs are related to ovarian cancer outcomes over time, specifically with respect to cancer recurrence.

#### **6.4.2 Chance**

It is important to keep the limitations of this study in mind when evaluating the results of this study, such as those attributable to chance, bias, and confounding. In terms of chance, the main limitation for this study is the small sample size (n=112), which may have resulted in the analytic component to be underpowered. Results should be interpreted with caution, due to the low statistical power to detect any true effects, if they do exist. Unfortunately, literature focusing on ovarian cancer patients in the post-treatment phase is lacking, with many studies having sample sizes smaller<sup>2,19,22–25</sup> than what was reported in this study.

#### **6.4.3 Bias**

Selection bias may have occurred if participants for this study are systematically different than participants who were not recruited, based on recruitment procedures and therefore not representative of the study population<sup>26</sup> (e.g. women with ovarian cancer in the post-treatment phase from Montreal, Quebec). The study base included women who were diagnosed with ovarian cancer from three Montreal hospital centers and were recruited at the 6 months post-treatment time frame, with a participation of 82%. All patients admitted to these hospitals with ovarian cancer that met the inclusion criteria were asked to participate in this study. Selection bias, specifically volunteer bias, may have occurred if those who participated in the study were systematically more active and had better PROs (i.e. less depressed, were less anxious, and had better HRQOL) than those who did not partake in the study. As a result, volunteer bias would over-estimate the prevalence rates of these outcome measures and potentially over-estimate the measure of association between meeting PA guidelines and PRO's. However, since the data used

for this thesis came from HPROQ, a prospective cohort study and had a relatively high participation rate, selection bias will likely be less of a concern in the future cohort analyses.

The use of questionnaires for assessing PA participation could lead to non-differential misclassification since PA levels tend to be over reported when measured with a self-reported questionnaire<sup>22,27,28</sup>. Unfortunately, there is a lack of comprehensive, standardized epidemiological tools to collect data regarding the frequency, intensity and duration parameters of PA<sup>29</sup>. Nonetheless, the PA questionnaire that was used, the International Physical Activity Questionnaire (IPAQ), has shown reliability and validity and has provided a convenient method for data collection<sup>21,30,31</sup>. With non-differential misclassification of PA with respect to either the determinants of interest (exposures in objective 2) or HRQOL (outcome in objective 3), the direction of this bias can be predicted, with the measure of effect biased towards the null. In addition, PA was dichotomized (i.e. meeting 150 minute guidelines or not), which is consistent with previous studies<sup>1-5</sup>, but combining those who are somewhat active with those who are sedentary may be problematic as it prevents the ability to assess dose-response relationships and make meaningful comparisons between those who are completely sedentary versus those who participate in some PA<sup>29</sup>.

Two additional questionnaires were used for assessing PROs: the FACT-O and the Hospital Anxiety and Depression Scale (HADS). Both of these questionnaires have been evaluated for their test-retest reliability and the validity by comparing scores with other instruments<sup>32,33</sup>. These questionnaires are also based on self-report, and due to the subjective nature of self-report, there is potential for recall error, which could lead to overreporting and/or underreporting among HRQOL, anxiety and depression scores. Differential misclassification of PROs could have occurred if it was dependent on a women's PA level; if women who met PA guidelines reported more favourable PROs or women who did not meet PA guidelines reported less favourable PROs, this would result in differential misclassification and an overestimation of

the true effect. On the other hand, non-differential misclassification of PROs could have occurred if the misclassification was unrelated to women's PA level. Non-differential misclassification of PROs will most likely result in the measure of effects to be closer to the null.

It is also important to note that this thesis used a cross-sectional study design and the nature of this study design may prevent us from establishing temporality in the association between PA and PROs. Thus, it cannot be determined if meeting PA guidelines led to better PROs, or whether better PROs promoted greater PA participation.

#### **6.4.4 Confounding**

Many confounding variables were considered in the analyses. There is potential for uncontrolled confounding as there was no information on potential confounders like prior PA participation, living arrangements, alcohol consumption and social engagement. Furthermore, potential medications such as anti-anxiety or anti-depressants would be of interest when looking at the relationship between PA and PROs. Identifying confounders when assessing the determinants of PA in ovarian cancer patients has not been conducted before in the existing literature. We used a correlation coefficient of 0.2 between all potential determinants to identify confounders for each determinant of interest, which allowed for inclusive models, adjusting for any covariate that may be slightly related to the determinant. CIE approach was used for identifying confounders for the relationship between PA and PROs, which was appropriate for the study sample size and the number of covariate under consideration<sup>34</sup>. Residual confounding could be a potential for concern as it is the result of incomplete adjustment for confounders due to categories being too broad or misspecification of confounders or measurement error<sup>26</sup>. Many confounders were categorical and were collapsed into fewer categories in the interest of the small sample size and in concern for power and preserving degrees of freedom in the analysis. The variables that were collapsed into fewer categories include: education ( $\leq$ high school vs. post-

secondary), partner status (relationship vs. single), ethnicity (French Canadian vs. Other/Mixed), and stage of cancer (stage I/II vs. stage III/IV). Adjusted models often resulted in measures of effect that were attenuated, with some instances where the measure of effect increased or changed direction from the unadjusted model, however this was not common.

#### **6.4.5 External Validity**

The external validity of study results must also be evaluated which refers to the generalizability of the results<sup>26</sup>. In other words, could the results of this study be applied to populations other than the study population. If the study results are not deemed internally valid, they should not be applied to other populations. Assuming that this study is internally valid, our study population was restricted to Type II, high-grade, serous tumours, and therefore results from this study may not be applied to women diagnosed with low-grade tumours. However, about 75% of ovarian cancer cases are Type II, and therefore the prevalence of PA may be generalized to the majority of ovarian cancer patients in Quebec<sup>35</sup>. This study took place in the city of Montreal, including women over the age of 18, but included predominantly French-Canadians. Therefore, these results may be applied to other Canadian women living in a similar urban setting.

#### **6.5 Future Directions**

In total, 112 participants were included in the baseline cohort and analyzed for this thesis in a cross-sectional study. Future studies need larger sample sizes to increase the power for statistical analyses. The follow-up data for this cohort will soon be available, which will provide more insight in the relationship of modifiable lifestyle factors, such as PA, diet, and sun exposure, on ovarian cancer outcomes, specifically looking at cancer recurrence.

In the literature, exercise interventions for ovarian cancer patients do exist, but it may be beneficial to also apply these interventions during the time-frame of this study, as most studies

usually occur during chemotherapy<sup>18,19,22,23,36</sup>. While the IPAQ has proven to be a valid and reliable questionnaire to collect information on PA participation, a more objective way to measure PA may be warranted to reduce recall error and over-reporting. Objective devices that measure PA participation, such as the accelerometer, are arguably one of the best tools to measure PA in an objective manner<sup>37</sup>. However, depending on the study question and feasibility, accelerometers may not be practical and may not provide information on PA context (e.g. swimming, biking, etc.) or domain (e.g. occupational, recreational, etc.). Moreover, the IPAQ does collect information on a variety of PA domains, but it may be of interest to specifically look at exercises that could help improve psychosocial well-being such as yoga, tai chi or other mindful exercises that are appropriate for an older population. Mind-body exercises have been found to help improve mood, mental health and sleep in comparison to aerobic exercises alone<sup>38</sup>. Moreover, there is growing research that supports mind-body interventions as tools to decrease symptoms of depression, anxiety and fatigue that are commonly experienced as a result of a cancer diagnosis, treatment, and survivorship<sup>39</sup>.

Although the focus of this study was on PA as a modifiable lifestyle factor for ovarian cancer patients, it will be valuable to continue researching other modifiable lifestyle factors along with PA in determining their role in ovarian cancer prognosis. Other modifiable lifestyle factors that are not included in the HRPOQ study but could be of interest include alcohol consumption, cognitive activity (i.e. crosswords, sudoku) and social engagement.

## **6.6 Research Contributions and Overall Conclusions**

This study was able to make contributions to the ovarian cancer literature in terms of PA prevalence in the post-treatment period, which is novel because no other study has looked at PA exclusively in the post-treatment time frame in ovarian cancer survivors. More specifically, this study was conducted in a consistent manner, estimating an accurate prevalence of PA

participation by using a validated and comprehensive questionnaire and taking into account many aspects of PA, such as intensity and PA from different domains. Recommendations should include walking in the definition of moderate PA in future studies of ovarian cancer survivors, since the inclusion of walking increases PA participation and was associated with a significant protective effect for depression. In terms of the bigger picture, the baseline results of PA among this population will inform the future longitudinal analysis of this pilot cohort study, with the penultimate goal of describing the relationship between PA and PROs over time, and the relationship between PA and cancer recurrence and survival. Although the potential determinants under question were not statistically significant, this thesis identified suggestive associations between several patient characteristics and PA for ovarian cancer survivors 6 months after treatment and serve as hypothesis generating results for future research. Future studies should continue to focus on the post-treatment time period, because this may be the most opportune time, following the initial diagnosis and treatment, when women feel empowered to take control of their health and be motivated to make changes in their lifestyle to improve their prognosis and their quality of life.

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# Appendix A

## Ethics Clearance



### QUEEN'S UNIVERSITY HEALTH SCIENCES & AFFILIATED TEACHING HOSPITALS RESEARCH ETHICS BOARD (HSREB)

#### HSREB Initial Ethics Clearance

August 24, 2017

Ms. Chloe Chow  
Department of Public Health Sciences  
Queen's University

**ROMEO/TRAQ: #6021645**

**Department Code: EPID-589-17**

**Study Title: The Prevalence and Determinants of Post-Diagnosis Physical Activity and its Association with Patient Reported Outcomes Among Ovarian Cancer Patients**

**Co-Investigators: Dr. A. Koushik, Dr. H. Richardson**

**Review Type: Delegated**

**Date Ethics Clearance Issued: August 24, 2017**

**Ethics Clearance Expiry Date: August 24, 2018**

Dear Ms. Chow,

The Queen's University Health Sciences & Affiliated Teaching Hospitals Research Ethics Board (HSREB) has reviewed the application and granted ethics clearance for the documents listed below. Ethics clearance is granted until the expiration date noted above.

#### Documents Acknowledged:

- CORE Certificate – C. Chow
- HPROQ Study – Consent Form
- HPROQ Study Questionnaire

**Amendments:** No deviations from, or changes to the protocol should be initiated without prior written clearance of an appropriate amendment from the HSREB, except when necessary to eliminate immediate hazard(s) to study participants or when the change(s) involves only administrative or logistical aspects of the trial.

**Renewals:** Prior to the expiration of your ethics clearance you will be reminded to submit your renewal report through ROMEO. Any lapses in ethical clearance will be documented on the renewal form.

**Completion/Termination:** The HSREB must be notified of the completion or termination of this study through the completion of a renewal report in ROMEO.

**Reporting of Serious Adverse Events:** Any unexpected serious adverse event occurring locally must be reported within 2 working days or earlier if required by the study sponsor. All other serious adverse events must be reported within 15 days after becoming aware of the information.

**Reporting of Complaints:** Any complaints made by participants or persons acting on behalf of participants must be reported to the Research Ethics Board within 7 days of becoming aware of the complaint. **Note:** All documents supplied to participants must have the contact information for the Research Ethics Board.

Investigators please note that if your trial is registered by the sponsor, you must take responsibility to ensure that the registration information is accurate and complete.

Yours sincerely,



Chair, Health Sciences Research Ethics Board

*The HSREB operates in compliance with, and is constituted in accordance with, the requirements of the Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans (TCPS 2); the International Conference on Harmonisation Good Clinical Practice Consolidated Guideline (ICH GCP); Part C, Division 5 of the Food and Drug Regulations; Part 4 of the Natural Health Products Regulations; Part 3 of the Medical Devices Regulations, Canadian General Standards Board, and the provisions of the Ontario Personal Health Information Protection Act (PHIPA 2004) and its applicable regulations. The HSREB is qualified through the CTO REB Qualification Program and is registered with the U.S. Department of Health and Human Services (DHHS) Office for Human Research Protection (OHRP). Federalwide Assurance Number: FWA#:00004184, IRB#:00001173*

*HSREB members involved in the research project do not participate in the review, discussion or decision.*

**Appendix B**  
**HPROQ Study Administered Questionnaire**

**TELEPHONE SURVEY TO BE USED IN STUDY  
ENTITLED:**

**Lifestyle Habits and the Prognosis of Ovarian  
cancer in Quebec Study**

**HPROQ Study**

**OCRP Award OC140116 (PI: Dr. Anita Koushik)**

**PARTICIPANT REMINDER: Please have a paper and a pen  
handy for one section of the questionnaire.**

PARTICIPANT ID: H\_\_\_\_\_

INTERVIEWER INITIALS: \_\_\_\_\_

Today's Date:

Year	Month	Day	

Time Start:

		:		
				(24 hour clock)

**PART A: I WOULD LIKE TO START BY ASKING YOU ABOUT YOUR HEIGHT AND WEIGHT**

1. Currently, how tall are you without shoes?  
 /  or   Don't know  
ft inches cm  Prefer not to answer

2. Currently, how much do you weigh?  
 or   Don't know  
kg lbs  Prefer not to answer

3. What was your approximate weight 2 years ago?  
 or   Don't know  
kg lbs  Prefer not to answer

**PARTS B- F are for new participants only. PARTS G-P contain new information for all participants.**

**PART B: NOW I WOULD LIKE TO ASK YOU SOME QUESTIONS ABOUT YOUR BACKGROUND**

1. What is your date of birth?  Year  Month  Day

2. Which means you are how old now?  yrs old

3. Where were you born? \_\_\_\_\_  Don't know  
Country Province (if in Canada)  Prefer not to answer

4. Which ethnic categories best describes you? *(Please select all that apply)*

<input type="radio"/> French Canadian	<input type="radio"/> Black
<input type="radio"/> English, Scottish or Irish descent	<input type="radio"/> Latin American
<input type="radio"/> French	<input type="radio"/> East Indian or South Asian
<input type="radio"/> Italian	<input type="radio"/> Chinese
<input type="radio"/> Greek	<input type="radio"/> Japanese
<input type="radio"/> Portuguese	<input type="radio"/> Vietnamese
<input type="radio"/> Jewish (European descent)	<input type="radio"/> Aboriginal
<input type="radio"/> Jewish (Sephardic)	<input type="radio"/> Other (Specify) _____
<input type="radio"/> Other European (Specify) _____	<input type="radio"/> Don't know
<input type="radio"/> Maghrebian or middle-eastern	<input type="radio"/> Prefer not to answer

5. What was your religious upbringing?

<input type="radio"/> Roman Catholic	<input type="radio"/> None
<input type="radio"/> Protestant	<input type="radio"/> Don't know
<input type="radio"/> Jewish	<input type="radio"/> Prefer not to answer
<input type="radio"/> Other (specify) _____	

6. What language did you mostly speak at home while growing up?

<input type="radio"/> French	<input type="radio"/> Don't know
<input type="radio"/> English	<input type="radio"/> Prefer not to answer
<input type="radio"/> Other (specify) _____	

7. Where was your biological mother born? \_\_\_\_\_ Country \_\_\_\_\_ Province (if in Canada)  Don't know  
 Prefer not to answer
8. Where was your biological father born? \_\_\_\_\_ Country \_\_\_\_\_ Province (if in Canada)  Don't know  
 Prefer not to answer

9. Now I will ask you about your grandparents.

	Maternal Grandmother (mother's mother)	Maternal Grandfather (mother's father)	Paternal Grandmother (father's mother)	Paternal Grandfather (father's father)
In what country was he/she born?	Country	Country	Country	Country
To which ethnic or cultural group does he/she belong? Choose only one	<input type="radio"/> French Canadian <input type="radio"/> English, Scottish or Irish <input type="radio"/> French <input type="radio"/> Italian <input type="radio"/> Greek <input type="radio"/> Portuguese <input type="radio"/> Jewish (European descent) <input type="radio"/> Jewish (Sephardic) <input type="radio"/> Other European (Specify) <input type="radio"/> Maghrebian or middle-eastern <input type="radio"/> Black <input type="radio"/> Latin American <input type="radio"/> East Indian/South Asian <input type="radio"/> Chinese <input type="radio"/> Japanese <input type="radio"/> Vietnamese <input type="radio"/> Aboriginal <input type="radio"/> Other (Specify)	<input type="radio"/> French Canadian <input type="radio"/> English, Scottish or Irish <input type="radio"/> French <input type="radio"/> Italian <input type="radio"/> Greek <input type="radio"/> Portuguese <input type="radio"/> Jewish (European descent) <input type="radio"/> Jewish (Sephardic) <input type="radio"/> Other European (Specify) <input type="radio"/> Maghrebian or middle-eastern <input type="radio"/> Black <input type="radio"/> Latin American <input type="radio"/> East Indian/South Asian <input type="radio"/> Chinese <input type="radio"/> Japanese <input type="radio"/> Vietnamese <input type="radio"/> Aboriginal <input type="radio"/> Other (Specify)	<input type="radio"/> French Canadian <input type="radio"/> English, Scottish or Irish <input type="radio"/> French <input type="radio"/> Italian <input type="radio"/> Greek <input type="radio"/> Portuguese <input type="radio"/> Jewish (European descent) <input type="radio"/> Jewish (Sephardic) <input type="radio"/> Other European (Specify) <input type="radio"/> Maghrebian or middle-eastern <input type="radio"/> Black <input type="radio"/> Latin American <input type="radio"/> East Indian/South Asian <input type="radio"/> Chinese <input type="radio"/> Japanese <input type="radio"/> Vietnamese <input type="radio"/> Aboriginal <input type="radio"/> Other (Specify)	<input type="radio"/> French Canadian <input type="radio"/> English, Scottish or Irish <input type="radio"/> French <input type="radio"/> Italian <input type="radio"/> Greek <input type="radio"/> Portuguese <input type="radio"/> Jewish (European descent) <input type="radio"/> Jewish (Sephardic) <input type="radio"/> Other European (Specify) <input type="radio"/> Maghrebian or middle-eastern <input type="radio"/> Black <input type="radio"/> Latin American <input type="radio"/> East Indian/South Asian <input type="radio"/> Chinese <input type="radio"/> Japanese <input type="radio"/> Vietnamese <input type="radio"/> Aboriginal <input type="radio"/> Other (Specify)
	<input type="radio"/> Don't know <input type="radio"/> Prefer not to answer	<input type="radio"/> Don't know <input type="radio"/> Prefer not to answer	<input type="radio"/> Don't know <input type="radio"/> Prefer not to answer	<input type="radio"/> Don't know <input type="radio"/> Prefer not to answer

10. What is the highest grade you finished in school?

- No School       Prefer not to answer
- Elementary School      1   2   3   4   5   6
- High School      7   8   9   10   11   12      Equivalence Certificate
- College (CEGEP/Technical)       Pre-University program       Technology/Professional program
- University (Professional)       Bachelor's       Master's       Doctorate
- Other:

11. Have you ever been married or lived as married?

- Yes
- No
- Don't know
- Prefer not to answer

12. What is your current relationship or marital status?

- Married
- Living as married
- Significant relationship, not living together
- Widowed
- Divorced
- Separated
- Unattached/single
- Other (specify) \_\_\_\_\_
- Don't know
- Prefer not to answer

13. What was your family's financial situation when you were a child or an adolescent?

- Very difficult
- Fairly difficult
- Middle
- Fairly comfortable
- Very comfortable
- Don't know
- Prefer not to answer

14. What is the range of your family/household income now? I will read you the ranges per year.

- Less than \$10,000 per year
- \$10,000 to \$29,999 per year
- \$30,000 to \$49,999 per year
- \$50,000 to \$69,999 per year
- \$70,000 to \$89,999 per year
- \$90,000 to \$109,999 per year
- \$110,000 to \$139,999 per year
- \$140,000 or more per year
- Do not know
- Prefer not to answer

**PART C: NOW I WOULD LIKE TO ASK YOU ABOUT YOUR SUN EXPOSURE**

*Please think about the time that you spent in the sun in the last month.*

1. In the last month, have you gone on vacation to a summer climate?

- Yes
- No (Skip to Question 2)
- Don't know (Skip to Question 2)
- Prefer not to answer (Skip to Question 2)

a) How many days was this vacation? \_\_\_\_\_ days

b) While you were on this vacation, did you usually stay in the shade, keep your arms and legs covered or wear sunscreen?

- Yes, arms/legs all covered
- Yes, arms/legs partially covered
- Yes, with sunscreen
- Yes, arms/legs partially covered with sunscreen
- Stay in the shade
- No
- Don't know
- Prefer not to answer

2. In the last month, have you used a sunlamp or gone to a tanning salon or a solarium to get a suntan?

- Yes
- No (Skip to Question 3)
- Don't know (Skip to Question 3)
- Prefer not to answer (Skip to Question 3)

a) About how many sunlamp/tanning salon sessions have you had in total in the last month?  
\_\_\_\_\_ sessions

b) About how long was each sunlamp/tanning salon session? \_\_\_\_\_ minutes

3. Which color best describes the color of your eyes?
- Grey                                       Green                                       Brown  
 Blue     Blue-green                                       Hazel
4. Which color best describes your natural hair color **when you were a teenager**?
- Red     Light brown                                       Black  
 Blond or "fair"                                       Dark brown
5. What would happen to your skin if it was exposed to bright sunlight for the first time in the summer for one hour in the middle of the day without any protection?
- Get a severe sunburn with blistering                                       Go brown without any sunburn  
 Have a painful sunburn for a few days followed by peeling                                       Don't know  
 Get mildly burnt followed by some degree of tanning                                       Prefer not to answer
6. What would happen to your skin if it was repeatedly exposed to bright sunlight in the summer without any protection?
- Get very brown and deeply tanned                                       Get only freckled or no suntan at all  
 Get moderately tanned                                       Don't know  
 Get only mildly tanned due to a tendency to peel                                       Prefer not to answer
7. How would you describe the color of the skin **on the inside of your upper arm** (that is, your skin color without tanning)?
- Very fair     Light olive                                       Brown  
 Fair     Dark olive                                       Black

**PART D: MENSTRUAL HISTORY**

*The next questions relate to your menstrual cycle during periods when you were not pregnant, nursing or using birth control pills.*

1. When did you have your first menstrual period (your best guess)?

        or      
Year                      Month                      Age

- Never had periods (Skip to Question 4)  
 Don't remember  
 Prefer not to answer

2. Which category describes your menstrual status **at diagnosis**?

- Periods were still occurring (Go to A)
- Periods had stopped (Go to B)
- Don't know
- Prefer not to answer

<i>Since you were still menstruating, was it that your:</i> <b>A</b>	<i>Since you were not menstruating anymore, was it because your:</i> <b>B</b>
<input type="radio"/> Periods were still occurring naturally	<input type="radio"/> Periods had stopped naturally
<input type="radio"/> Periods were occurring on birth control or menstrual regulatory hormones	<input type="radio"/> Periods had stopped after surgical removal of your uterus
<input type="radio"/> Periods were occurring on menopausal hormones	<input type="radio"/> Periods had stopped after surgical removal of both ovaries
	<input type="radio"/> Periods had stopped after medical treatment (specify) _____
	<input type="radio"/> Pregnant or nursing

3. When did you have your last menstrual period?

        or      
 Year                      Month                      Age

- Still having periods
- Don't know
- Prefer not to answer

4. Did you ever have a tubal ligation (that is, did you ever have an operation in which your fallopian tubes were surgically tied)?

- Yes
- No (Skip to Question 6)
- Don't know (Skip to Question 6)
- Prefer not to answer (Skip to Question 6)

5. When did you have your tubal ligation?

        or         Don't know  
 Year                      Month                      Age     Prefer not to answer

6. Did you ever have a hysterectomy (that is, did you have your womb or uterus removed, causing your periods to stop)?

- Yes
- No (Skip to PART E)
- Don't know (Skip to PART E)
- Prefer not to answer (Skip to PART E)

7. When did you have your hysterectomy?

        or         Don't know  
 Year                      Month                      Age     Prefer not to answer

**PART E: NOW I WOULD LIKE TO ASK YOU SOME QUESTIONS ON YOUR CONTRACEPTIVE USE**

1. Have you ever taken birth control pills (oral contraceptives) for either birth control or any other reason?
  - Yes, currently taking
  - Yes, but not currently taking
  - No (Skip to Question 3)
  - Don't know (Skip to Question 3)
  - Prefer not to answer (Skip to Question 3)
2. For how long in total did you take birth control pills (exclude those periods when you temporarily stopped)? \_\_\_\_\_
3. Have you ever used pills other than birth control pills which contain estrogen or other female hormones, for example at menopause, after surgery, or at another time?
  - Yes, currently taking
  - Yes, but not currently taking
  - No (Skip to PART F)
  - Don't know (Skip to PART F)
  - Prefer not to answer (Skip to PART F)
4. For how long did you take estrogens or other female hormone pills, other than birth control pills (exclude those periods when you temporarily stopped)? \_\_\_\_\_

**PART F: NOW I WOULD LIKE TO ASK YOU SOME QUESTIONS ON YOUR PREGNANCY HISTORY**

1. Have you ever been pregnant?
  - Yes
  - No (Skip to Part G)
  - Don't know (Skip to Part G)
  - Prefer not to answer (Skip to Part G)

I am going to ask you for information on each pregnancy that you had in the order that they occurred, including all of your pregnancies, **even if they lasted only a few weeks and regardless of the outcome.**

	1 <sup>st</sup> Pregnancy	2 <sup>nd</sup> Pregnancy	3 <sup>rd</sup> Pregnancy
For your 1 <sup>st</sup> /2 <sup>nd</sup> /etc. pregnancy, what was the outcome?	<input type="radio"/> Single live birth <input type="radio"/> Mult. Birth, any living <input type="radio"/> Mult. Birth, none living <input type="radio"/> Stillbirth <input type="radio"/> Miscarriage <input type="radio"/> Induced abortion <input type="radio"/> Ectopic or tubal <input type="radio"/> Currently pregnant (Skip to PART G) <input type="radio"/> Other (specify) <hr/> <input type="radio"/> Don't know <input type="radio"/> Prefer not to answer	<input type="radio"/> Single live birth <input type="radio"/> Mult. Birth, any living <input type="radio"/> Mult. Birth, none living <input type="radio"/> Stillbirth <input type="radio"/> Miscarriage <input type="radio"/> Induced abortion <input type="radio"/> Ectopic or tubal <input type="radio"/> Currently pregnant (Skip to PART G) <input type="radio"/> Other (specify) <hr/> <input type="radio"/> Don't know <input type="radio"/> Prefer not to answer	<input type="radio"/> Single live birth <input type="radio"/> Mult. Birth, any living <input type="radio"/> Mult. Birth, none living <input type="radio"/> Stillbirth <input type="radio"/> Miscarriage <input type="radio"/> Induced abortion <input type="radio"/> Ectopic or tubal <input type="radio"/> Currently pregnant (Skip to PART G) <input type="radio"/> Other (specify) <hr/> <input type="radio"/> Don't know <input type="radio"/> Prefer not to answer
When did that pregnancy end?	<div style="display: flex; align-items: center; justify-content: center;"> <div style="border: 1px solid black; width: 20px; height: 20px; margin-right: 5px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px; margin-right: 5px;"></div> <div style="margin: 0 5px;">/</div> <div style="border: 1px solid black; width: 20px; height: 20px; margin-right: 5px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px; margin-right: 5px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px; margin-right: 5px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> </div> <div style="display: flex; justify-content: center; margin-top: 5px;"> <div style="margin-right: 20px;">month</div> <div>year</div> </div> <input type="radio"/> Don't know <input type="radio"/> Prefer not to answer	<div style="display: flex; align-items: center; justify-content: center;"> <div style="border: 1px solid black; width: 20px; height: 20px; margin-right: 5px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px; margin-right: 5px;"></div> <div style="margin: 0 5px;">/</div> <div style="border: 1px solid black; width: 20px; height: 20px; margin-right: 5px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px; margin-right: 5px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px; margin-right: 5px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> </div> <div style="display: flex; justify-content: center; margin-top: 5px;"> <div style="margin-right: 20px;">month</div> <div>year</div> </div> <input type="radio"/> Don't know <input type="radio"/> Prefer not to answer	<div style="display: flex; align-items: center; justify-content: center;"> <div style="border: 1px solid black; width: 20px; height: 20px; margin-right: 5px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px; margin-right: 5px;"></div> <div style="margin: 0 5px;">/</div> <div style="border: 1px solid black; width: 20px; height: 20px; margin-right: 5px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px; margin-right: 5px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> </div> <div style="display: flex; justify-content: center; margin-top: 5px;"> <div style="margin-right: 20px;">month</div> <div>year</div> </div> <input type="radio"/> Don't know <input type="radio"/> Prefer not to answer
Counting from your last menstrual period before this pregnancy, how many weeks/months did this pregnancy last?	<div style="text-align: center; margin-bottom: 5px;"> <hr style="width: 50px; margin: 0 auto;"/>           # of         </div> <input type="radio"/> Weeks <input type="radio"/> Months <input type="radio"/> Full-term <input type="radio"/> Don't know <input type="radio"/> Prefer not to answer	<div style="text-align: center; margin-bottom: 5px;"> <hr style="width: 50px; margin: 0 auto;"/>           # of         </div> <input type="radio"/> Weeks <input type="radio"/> Months <input type="radio"/> Full-term <input type="radio"/> Don't know <input type="radio"/> Prefer not to answer	<div style="text-align: center; margin-bottom: 5px;"> <hr style="width: 50px; margin: 0 auto;"/>           # of         </div> <input type="radio"/> Weeks <input type="radio"/> Months <input type="radio"/> Full-term <input type="radio"/> Don't know <input type="radio"/> Prefer not to answer
Did you breast feed this baby/any of these babies at all?	<input type="radio"/> Yes <input type="radio"/> No <input type="radio"/> Don't know <input type="radio"/> Prefer not to answer	<input type="radio"/> Yes <input type="radio"/> No <input type="radio"/> Don't know <input type="radio"/> Prefer not to answer	<input type="radio"/> Yes <input type="radio"/> No <input type="radio"/> Don't know <input type="radio"/> Prefer not to answer
How many weeks/months/years did you breast feed this/these babies?	<div style="text-align: center; margin-bottom: 5px;"> <hr style="width: 50px; margin: 0 auto;"/>           # of         </div> <input type="radio"/> Weeks <input type="radio"/> Months <input type="radio"/> Years <input type="radio"/> Don't know <input type="radio"/> Prefer not to answer	<div style="text-align: center; margin-bottom: 5px;"> <hr style="width: 50px; margin: 0 auto;"/>           # of         </div> <input type="radio"/> Weeks <input type="radio"/> Months <input type="radio"/> Years <input type="radio"/> Don't know <input type="radio"/> Prefer not to answer	<div style="text-align: center; margin-bottom: 5px;"> <hr style="width: 50px; margin: 0 auto;"/>           # of         </div> <input type="radio"/> Weeks <input type="radio"/> Months <input type="radio"/> Years <input type="radio"/> Don't know <input type="radio"/> Prefer not to answer

	4 <sup>th</sup> Pregnancy	5 <sup>th</sup> Pregnancy	6 <sup>th</sup> Pregnancy
For your 1 <sup>st</sup> /2 <sup>nd</sup> /etc. pregnancy, what was the outcome?	<input type="radio"/> Single live birth <input type="radio"/> Mult. Birth, any living <input type="radio"/> Mult. Birth, none living <input type="radio"/> Stillbirth <input type="radio"/> Miscarriage <input type="radio"/> Induced abortion <input type="radio"/> Ectopic or tubal <input type="radio"/> Currently pregnant (Skip to PART G) <input type="radio"/> Other (specify) _____ <input type="radio"/> Don't know <input type="radio"/> Prefer not to answer	<input type="radio"/> Single live birth <input type="radio"/> Mult. Birth, any living <input type="radio"/> Mult. Birth, none living <input type="radio"/> Stillbirth <input type="radio"/> Miscarriage <input type="radio"/> Induced abortion <input type="radio"/> Ectopic or tubal <input type="radio"/> Currently pregnant (Skip to PART G) <input type="radio"/> Other (specify) _____ <input type="radio"/> Don't know <input type="radio"/> Prefer not to answer	<input type="radio"/> Single live birth <input type="radio"/> Mult. Birth, any living <input type="radio"/> Mult. Birth, none living <input type="radio"/> Stillbirth <input type="radio"/> Miscarriage <input type="radio"/> Induced abortion <input type="radio"/> Ectopic or tubal <input type="radio"/> Currently pregnant (Skip to PART G) <input type="radio"/> Other (specify) _____ <input type="radio"/> Don't know <input type="radio"/> Prefer not to answer
When did that pregnancy end?	<div style="display: flex; align-items: center; justify-content: center;"> <div style="border: 1px solid black; width: 20px; height: 20px; margin-right: 5px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px; margin-right: 5px;"></div> <div style="margin: 0 5px;">/</div> <div style="border: 1px solid black; width: 20px; height: 20px; margin-right: 5px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px; margin-right: 5px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px; margin-right: 5px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> </div> <div style="display: flex; justify-content: center; margin-top: 5px;"> <div style="margin-right: 20px;">month</div> <div>year</div> </div> <input type="radio"/> Don't know <input type="radio"/> Prefer not to answer	<div style="display: flex; align-items: center; justify-content: center;"> <div style="border: 1px solid black; width: 20px; height: 20px; margin-right: 5px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px; margin-right: 5px;"></div> <div style="margin: 0 5px;">/</div> <div style="border: 1px solid black; width: 20px; height: 20px; margin-right: 5px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px; margin-right: 5px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> </div> <div style="display: flex; justify-content: center; margin-top: 5px;"> <div style="margin-right: 20px;">month</div> <div>year</div> </div> <input type="radio"/> Don't know <input type="radio"/> Prefer not to answer	<div style="display: flex; align-items: center; justify-content: center;"> <div style="border: 1px solid black; width: 20px; height: 20px; margin-right: 5px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px; margin-right: 5px;"></div> <div style="margin: 0 5px;">/</div> <div style="border: 1px solid black; width: 20px; height: 20px; margin-right: 5px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px; margin-right: 5px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> </div> <div style="display: flex; justify-content: center; margin-top: 5px;"> <div style="margin-right: 20px;">month</div> <div>year</div> </div> <input type="radio"/> Don't know <input type="radio"/> Prefer not to answer
Counting from your last menstrual period before this pregnancy, how many weeks/months did this pregnancy last?	<div style="text-align: center; margin-bottom: 5px;">_____</div> <div style="text-align: center;"># of</div> <input type="radio"/> Weeks <input type="radio"/> Months <input type="radio"/> Full-term <input type="radio"/> Don't know <input type="radio"/> Prefer not to answer	<div style="text-align: center; margin-bottom: 5px;">_____</div> <div style="text-align: center;"># of</div> <input type="radio"/> Weeks <input type="radio"/> Months <input type="radio"/> Full-term <input type="radio"/> Don't know <input type="radio"/> Prefer not to answer	<div style="text-align: center; margin-bottom: 5px;">_____</div> <div style="text-align: center;"># of</div> <input type="radio"/> Weeks <input type="radio"/> Months <input type="radio"/> Full-term <input type="radio"/> Don't know <input type="radio"/> Prefer not to answer
Did you breast feed this baby/any of these babies at all?	<input type="radio"/> Yes <input type="radio"/> No <input type="radio"/> Don't know <input type="radio"/> Prefer not to answer	<input type="radio"/> Yes <input type="radio"/> No <input type="radio"/> Don't know <input type="radio"/> Prefer not to answer	<input type="radio"/> Yes <input type="radio"/> No <input type="radio"/> Don't know <input type="radio"/> Prefer not to answer
How many weeks/months/years did you breast feed this/these babies?	<div style="text-align: center; margin-bottom: 5px;">_____</div> <div style="text-align: center;"># of</div> <input type="radio"/> Weeks <input type="radio"/> Months <input type="radio"/> Years <input type="radio"/> Don't know <input type="radio"/> Prefer not to answer	<div style="text-align: center; margin-bottom: 5px;">_____</div> <div style="text-align: center;"># of</div> <input type="radio"/> Weeks <input type="radio"/> Months <input type="radio"/> Years <input type="radio"/> Don't know <input type="radio"/> Prefer not to answer	<div style="text-align: center; margin-bottom: 5px;">_____</div> <div style="text-align: center;"># of</div> <input type="radio"/> Weeks <input type="radio"/> Months <input type="radio"/> Years <input type="radio"/> Don't know <input type="radio"/> Prefer not to answer

	7 <sup>th</sup> Pregnancy	8 <sup>th</sup> Pregnancy	9 <sup>th</sup> Pregnancy
For your 1 <sup>st</sup> /2 <sup>nd</sup> /etc. pregnancy, what was the outcome?	<input type="radio"/> Single live birth <input type="radio"/> Mult. Birth, any living <input type="radio"/> Mult. Birth, none living <input type="radio"/> Stillbirth <input type="radio"/> Miscarriage <input type="radio"/> Induced abortion <input type="radio"/> Ectopic or tubal <input type="radio"/> Currently pregnant (Skip to PART G) <input type="radio"/> Other (specify) _____ <input type="radio"/> Don't know <input type="radio"/> Prefer not to answer	<input type="radio"/> Single live birth <input type="radio"/> Mult. Birth, any living <input type="radio"/> Mult. Birth, none living <input type="radio"/> Stillbirth <input type="radio"/> Miscarriage <input type="radio"/> Induced abortion <input type="radio"/> Ectopic or tubal <input type="radio"/> Currently pregnant (Skip to PART G) <input type="radio"/> Other (specify) _____ <input type="radio"/> Don't know <input type="radio"/> Prefer not to answer	<input type="radio"/> Single live birth <input type="radio"/> Mult. Birth, any living <input type="radio"/> Mult. Birth, none living <input type="radio"/> Stillbirth <input type="radio"/> Miscarriage <input type="radio"/> Induced abortion <input type="radio"/> Ectopic or tubal <input type="radio"/> Currently pregnant (Skip to PART G) <input type="radio"/> Other (specify) _____ <input type="radio"/> Don't know <input type="radio"/> Prefer not to answer
When did that pregnancy end?	<div style="display: flex; align-items: center; gap: 10px;"> <div style="border: 1px solid black; width: 20px; height: 20px; display: flex; align-items: center; justify-content: center;"> </div> <div style="border: 1px solid black; width: 20px; height: 20px; display: flex; align-items: center; justify-content: center;"> </div> <div style="font-size: 20px;">/</div> <div style="border: 1px solid black; width: 20px; height: 20px; display: flex; align-items: center; justify-content: center;"> </div> <div style="border: 1px solid black; width: 20px; height: 20px; display: flex; align-items: center; justify-content: center;"> </div> <div style="border: 1px solid black; width: 20px; height: 20px; display: flex; align-items: center; justify-content: center;"> </div> <div style="border: 1px solid black; width: 20px; height: 20px; display: flex; align-items: center; justify-content: center;"> </div> </div> <div style="display: flex; justify-content: space-around; width: 100%;"> <span>month</span> <span>year</span> </div> <input type="radio"/> Don't know <input type="radio"/> Prefer not to answer	<div style="display: flex; align-items: center; gap: 10px;"> <div style="border: 1px solid black; width: 20px; height: 20px; display: flex; align-items: center; justify-content: center;"> </div> <div style="border: 1px solid black; width: 20px; height: 20px; display: flex; align-items: center; justify-content: center;"> </div> <div style="font-size: 20px;">/</div> <div style="border: 1px solid black; width: 20px; height: 20px; display: flex; align-items: center; justify-content: center;"> </div> <div style="border: 1px solid black; width: 20px; height: 20px; display: flex; align-items: center; justify-content: center;"> </div> <div style="border: 1px solid black; width: 20px; height: 20px; display: flex; align-items: center; justify-content: center;"> </div> <div style="border: 1px solid black; width: 20px; height: 20px; display: flex; align-items: center; justify-content: center;"> </div> </div> <div style="display: flex; justify-content: space-around; width: 100%;"> <span>month</span> <span>year</span> </div> <input type="radio"/> Don't know <input type="radio"/> Prefer not to answer	<div style="display: flex; align-items: center; gap: 10px;"> <div style="border: 1px solid black; width: 20px; height: 20px; display: flex; align-items: center; justify-content: center;"> </div> <div style="border: 1px solid black; width: 20px; height: 20px; display: flex; align-items: center; justify-content: center;"> </div> <div style="font-size: 20px;">/</div> <div style="border: 1px solid black; width: 20px; height: 20px; display: flex; align-items: center; justify-content: center;"> </div> <div style="border: 1px solid black; width: 20px; height: 20px; display: flex; align-items: center; justify-content: center;"> </div> <div style="border: 1px solid black; width: 20px; height: 20px; display: flex; align-items: center; justify-content: center;"> </div> <div style="border: 1px solid black; width: 20px; height: 20px; display: flex; align-items: center; justify-content: center;"> </div> </div> <div style="display: flex; justify-content: space-around; width: 100%;"> <span>month</span> <span>year</span> </div> <input type="radio"/> Don't know <input type="radio"/> Prefer not to answer
Counting from your last menstrual period before this pregnancy, how many weeks/months did this pregnancy last?	<div style="text-align: center; margin-bottom: 5px;">_____</div> <div style="text-align: center; margin-bottom: 5px;"># of</div> <input type="radio"/> Weeks <input type="radio"/> Months <input type="radio"/> Full-term <input type="radio"/> Don't know <input type="radio"/> Prefer not to answer	<div style="text-align: center; margin-bottom: 5px;">_____</div> <div style="text-align: center; margin-bottom: 5px;"># of</div> <input type="radio"/> Weeks <input type="radio"/> Months <input type="radio"/> Full-term <input type="radio"/> Don't know <input type="radio"/> Prefer not to answer	<div style="text-align: center; margin-bottom: 5px;">_____</div> <div style="text-align: center; margin-bottom: 5px;"># of</div> <input type="radio"/> Weeks <input type="radio"/> Months <input type="radio"/> Full-term <input type="radio"/> Don't know <input type="radio"/> Prefer not to answer
Did you breast feed this baby/any of these babies at all?	<input type="radio"/> Yes <input type="radio"/> No <input type="radio"/> Don't know <input type="radio"/> Prefer not to answer	<input type="radio"/> Yes <input type="radio"/> No <input type="radio"/> Don't know <input type="radio"/> Prefer not to answer	<input type="radio"/> Yes <input type="radio"/> No <input type="radio"/> Don't know <input type="radio"/> Prefer not to answer
How many weeks/months/years did you breast feed this/these babies?	<div style="text-align: center; margin-bottom: 5px;">_____</div> <div style="text-align: center; margin-bottom: 5px;"># of</div> <input type="radio"/> Weeks <input type="radio"/> Months <input type="radio"/> Years <input type="radio"/> Don't know <input type="radio"/> Prefer not to answer	<div style="text-align: center; margin-bottom: 5px;">_____</div> <div style="text-align: center; margin-bottom: 5px;"># of</div> <input type="radio"/> Weeks <input type="radio"/> Months <input type="radio"/> Years <input type="radio"/> Don't know <input type="radio"/> Prefer not to answer	<div style="text-align: center; margin-bottom: 5px;">_____</div> <div style="text-align: center; margin-bottom: 5px;"># of</div> <input type="radio"/> Weeks <input type="radio"/> Months <input type="radio"/> Years <input type="radio"/> Don't know <input type="radio"/> Prefer not to answer

**READ:** I am going to ask you about the time you spent being physically active in the last 7 days. Please answer each question even if you do not consider yourself to be an active person. Think about the activities you do at work, as part of your house and yard work, to get from place to place, and in your spare time for recreation, exercise or sport.

**PART G: JOB-RELATED PHYSICAL ACTIVITY**

**READ:** The first questions are about your work in the past week. This includes paid jobs, farming, volunteer work, course work and any other unpaid work that you did outside your home. Do not include unpaid work you might do around your home, like housework, yard work, general maintenance, and caring for your family. I will ask you about these later.

1. Do you currently have a job or do any unpaid work outside your home? **READ ALL ANSWERS**  
[WORK; Yes=1, No=0; 8, 9]
- \_\_\_\_\_ Yes
  - \_\_\_\_\_ Yes, but I am on sick leave [Skip to PART H]
  - \_\_\_\_\_ No \_\_\_\_\_ [Skip to PART H]
  - 8. Don't Know/Not Sure [Skip to PART H]
  - 9. Refused [Skip to PART H]

**[Interviewer clarification:** This also includes credit and non-credit classes or course work. It also includes volunteer work and time spent looking for work. It does not include unpaid house or yard work, nor caring for dependents, this will be asked in a later section.

**READ:** The following questions are about all the physical activity you did as part of your paid or unpaid work. This does not include traveling to and from work.

**READ:** First, think about all the *vigorous* activities which take *hard physical effort* that you did as part of your work. Vigorous activities make you breathe much harder than normal. These may include things like heavy lifting, digging, heavy construction work, or climbing up stairs. Think about only those vigorous physical activities that you did for at least 10 minutes at a time.

2. During the **last 7 days**, on how many days did you do **vigorous** physical activities **as part of your work**? [OVDAY; Range 0-7, 8, 9]
- \_\_\_\_\_ Days per week [If respondent answers 0, skip to Question 4]
  - 8. Don't Know/Not Sure [Skip to Question 4]
  - 9. Refused [Skip to Question 4]

**[Interviewer clarification:** Think about only those physical activities that you did for at least 10 minutes at a time.]

**[Interviewer clarification:** Work includes paid and unpaid work as well as course work. Include all jobs and volunteer work.]

If this vigorous physical activity was done outdoors in the summer, for how many days was this activity done outdoors \_\_\_\_\_.

When you were doing vigorous physical activity outdoors, did you usually protect yourself from the sun (shade and/or clothes and/or sunscreen)?  Yes

No

3. How much time did you usually spend on one of those days doing **vigorous** physical activities as part of your work?

\_\_\_\_ Hours per day [OVDHRS; Range 0-16]  
\_\_\_\_ Minutes per day [OVDMIN; Range 0-960, 998, 999]  
998. Don't Know/Not Sure  
999. Refused

[Interviewer clarification: Think about only those physical activities you did for at least 10 minutes at a time.]

[Interviewer probe: An average time per day is being sought. If the respondent can't answer because the pattern of time spent varies widely from day to day, or includes time spent doing a variety of paid and unpaid work, ask: "What is the total amount of time you spent **over the last 7 days** doing vigorous physical activities as part of your work?"

\_\_\_\_ Hours per week [OVWHRS; Range 0-112]  
\_\_\_\_ Minutes per week [OVWMIN; Range 0-6720, 9998, 9999]  
9998. Don't Know/Not Sure  
9999. Refused

**READ: Now think about activities which take moderate physical effort that you did as part of your work. Moderate physical activities make you breathe somewhat harder than normal and may include activities like carrying light loads. Do not include walking. Again, think about only those moderate physical activities that you did for at least 10 minutes at a time.**

4. During the **last 7 days**, on how many days did you do **moderate** physical activities as part of your work? [OMDAY; Range 0-7, 8, 9]

\_\_\_\_ Days per week [If respondent answers 0, skip to Question 6]  
8. Don't Know/Not Sure [Skip to Question 6]  
9. Refused [Skip to Question 6]

[Interviewer clarification: Think about only those physical activities that you did for at least 10 minutes at a time.]

[Interviewer clarification: Work includes paid and unpaid work as well as course work. Include all jobs.]

If this moderate physical activity was done outdoors in the summer, for how many days was this activity done outdoors\_\_\_\_\_.

When you were doing moderate physical activity outdoors, did you usually protect yourself from the sun (shade and/or clothes and/or sunscreen)?  Yes

No

5. How much time did you usually spend on one of those days doing **moderate** physical activities as part of your work?

\_\_\_\_ Hours per day [OMDHRS; Range 0-16]  
\_\_\_\_ Minutes per day [OMDMIN; Range 0-960, 998, 999]  
998. Don't Know/Not Sure  
999. Refused

[Interviewer clarification: Think about only those physical activities you did for at least 10 minutes at a time.]

**[Interviewer probe:** An average time per day is being sought. If the respondent can't answer because the pattern of time spent varies widely from day to day, or includes time spent doing a variety of paid and unpaid work, ask: "What is the total amount of time you spent **over the last 7 days** doing moderate physical activities as part of your work?"

\_\_\_\_ Hours per week [OMWHRS; Range 0-112]  
 \_\_\_\_\_ Minutes per week [OMWMIN; Range 0-6720, 9998, 9999]  
 9998. Don't Know/Not Sure  
 9999. Refused

**READ: Now think about the time you spend walking for at least 10 minutes at a time as part of your work. Please do not count any walking you did to travel to or from work.**

6. During the **last 7 days**, on how many days did you **walk as part of your work**?

[OWDAY; Range 0-7, 8, 9]

\_\_\_\_\_ Days per week [If respondent answers 0, skip to PART H]

8. Don't Know/Not Sure [Skip to PART H]

9. Refused [Skip to PART H]

**[Interviewer clarification:** Think about only the walking that you did for at least 10 minutes at a time.]

**[Interviewer clarification:** Include all jobs.]

If you were walking outdoors in the summer, for how many days did you walk outdoors for work\_\_\_\_\_.

When you were walking outdoors for work, did you usually protect yourself from the sun (shade and/or clothes and/or sunscreen)?

<input type="checkbox"/>	Yes
<input type="checkbox"/>	No

7. How much time did you usually spend on one of those days **walking** as part of your work?

\_\_\_\_ Hours per day [OWDHRS; Range 0-16]

\_\_\_\_\_ Minutes per day [OWDMIN; Range 0-960, 998, 999]

998. Don't Know/Not Sure

999. Refused

**[Interviewer clarification:** Think about only the walking you did for at least 10 minutes at a time.]

**[Interviewer probe:** An average time per day is being sought. If the respondent can't answer because the pattern of time spent varies widely from day to day, or includes time spent doing a variety of paid and unpaid work, ask: "What is the total amount of time you spent walking **over the last 7 days** as part of your work?"

\_\_\_\_ Hours per week [OWWHRS; Range 0-112]

\_\_\_\_\_ Minutes per week [OWWMIN; Range 0-6720, 9998, 9999]

9998. Don't Know/Not Sure

9999. Refused

**PART H: TRANSPORTATION-RELATED PHYSICAL ACTIVITY**

**READ: Now, think about how you traveled from place to place, including to places like work, stores, movies and so on.**

8. During the **last 7 days**, on how many days did you **travel in a motor vehicle** like a train, bus, car or metro? [TMDAY; Range 0-7, 8, 9]

\_\_\_\_\_ Days per week [If respondent answer 0, skip to Question 10]

8. Don't Know/Not Sure [Skip to Question 10]

9. Refused [Skip to Question 10]

9. How much time did you usually spend on one of those days **traveling** in a car, bus, train or other kind of motor vehicle?

\_\_\_\_ Hours per day [TMDHRS; Range 0-16]

\_\_\_\_\_ Minutes per day [TMDMIN; Range 0-960, 998, 999]

998. Don't Know/Not Sure

999. Refused

**[Interviewer probe:** An average time per day is being sought. If the respondent can't answer because the pattern of time spent varies widely from day to day, ask: "What is the total amount of time you spent **over the last 7 days** traveling in a motor vehicle?"

\_\_\_\_ Hours per week [TMWHRS; Range 0-112]

\_\_\_\_\_ Minutes per week [TMWMIN; Range 0-6720, 9998, 9999]

9998. Don't Know/Not Sure

9999. Refused

**READ: Now think only about the bicycling you did to travel to and from work, to do errands, or to go from place to place. Only include bicycling that you did for at least 10 minutes at a time.**

10. During the **last 7 days**, on how many days did you **bicycle** to go from place to place? [TBDAY; Range 0-7, 8, 9]

\_\_\_\_\_ Days per week [If respondent answers 0, skip to Question 12]

8. Don't Know/Not Sure [Skip to Question 12]

9. Refused [Skip to Question 12]

**[Interviewer clarification:** Think only about the bicycling that you did for at least 10 minutes at a time.]

When you bicycling during the day, did you usually protect yourself from the sun (shade and/or clothes and/or sunscreen)?  Yes

No

11. How much time did you usually spend on one of those days **to bicycle** from place to place?

\_\_\_\_ Hours per day [TBDHRS; Range 0-16]

\_\_\_\_\_ Minutes per day [TBDMIN; Range 0-960, 998, 999]

998. Don't Know/Not Sure

999. Refused

**[Interviewer clarification:** Think only about the bicycling that you did for at least 10 minutes at a time.]

**[Interviewer probe:** An average time per day is being sought. If the respondent can't answer because the pattern of time spent varies widely from day to day, ask: "What is the total amount of time you spent bicycling **over the last 7 days** to travel from place to place?"

\_\_\_\_ Hours per week [TBWHRS; Range 0-112]  
\_\_\_\_ Minutes per week [TBWMIN; Range 0-6720, 9998, 9999]  
9998. Don't Know/Not Sure  
9999. Refused

**READ: Now think only about the walking you did to travel to and from work, to do errands or to go from place to place. Only include walking that you did for at least 10 minutes at a time. Do not include any recreational walking, I will ask you about that later.**

12. During the **last 7 days**, on how many days did you **walk to go from place to place**?

[TWDAY; Range 0-7, 8, 9]  
\_\_\_\_ Days per week [If respondent answers 0, skip to PART I]  
8. Don't Know/Not Sure [Skip to PART I]  
9. Refused [Skip to PART I]

**[Interviewer clarification:** Think only about the walking that you did for at least 10 minutes at a time.]

When you were walking from place to place outdoors during the daytime, did you usually protect yourself from the sun (shade and/or clothes and/or sunscreen)?  Yes

No

13. How much time did you usually spend on one of those days **walking from place to place**?

\_\_\_\_ Hours per day [TWDHRS; Range 0-16]  
\_\_\_\_ Minutes per day [TWDMIN; Range 0-960, 998, 999]  
998. Don't Know/Not Sure  
999. Refused

**[Interviewer clarification:** Think about only the walking that you did for at least 10 minutes at a time.]

**[Interviewer probe:** An average time per day is being sought. If the respondent can't answer because the pattern of time spent varies widely from day to day, ask: "What is the total amount of time you spent **over the last 7 days** walking from place to place?"

\_\_\_\_ Hours per week [TWWHRS; Range 0-112]  
\_\_\_\_ Minutes per week [TWWMIN; Range 0-6720, 9998, 9999]  
9998. Don't Know/Not Sure  
9999. Refused

### **PART I: HOUSEWORK, HOUSE MAINTENANCE AND CARING FOR FAMILY**

**READ: Now think about the physical activities you have done in the last 7 days in and around your home, like housework, gardening, yard work, general maintenance work, and caring for your family.**

**READ: First think about vigorous activities which take hard physical effort that you did in the garden or yard. Vigorous activities make you breathe much harder than normal and may include heavy lifting, chopping wood, shoveling snow, or digging. Again, think about only those vigorous physical activities that you did for at least 10 minutes at a time.**

14. During the **last 7 days**, on how many days did you do **vigorous** physical activities **in the garden or yard**? [GVDDAY; Range 0-7, 8, 9]

- \_\_\_\_\_ Days per week *[If respondent answers 0, skip to Question 16]*  
8. Don't Know/Not Sure *[Skip to Question 16]*  
9. Refused *[Skip to Question 16]*

**[Interviewer clarification:** Think about only those physical activities that you did for at least 10 minutes at a time.]

When you were doing vigorous physical activity in the garden or yard, did you usually protect yourself from the sun (shade and/or clothes and/or sunscreen)?  Yes  
 No

15. How much time did you usually spend on one of those days doing **vigorous** physical activities in the garden or yard?

- \_\_\_\_ Hours per day [GVDHRS; Range 0-16]  
\_\_\_\_ Minutes per day [GVDMIN; Range 0-960, 998, 999]  
998. Don't Know/Not Sure  
999. Refused

**[Interviewer clarification:** Think about only those physical activities that you did for at least 10 minutes at a time.]

**[Interviewer probe:** An average time per day is being sought. If the respondent can't answer because the pattern of time spent varies widely from day to day, ask: "What is the total amount of time you spent **over the last 7 days** doing vigorous physical activities in the garden or yard?"

- \_\_\_\_ Hours per week [GVWHRS; Range 0-112]  
\_\_\_\_ Minutes per week [GVWMIN; Range 0-6720, 9998, 9999]  
9998. Don't Know/Not Sure  
9999. Refused

**READ: Now think about activities which take moderate physical effort that you did in the garden or yard. Moderate physical activities make you breathe somewhat harder than normal and may include carrying light loads, sweeping, washing windows, and raking. Again, include only those moderate physical activities that you did for at least 10 minutes at a time.**

16. During the **last 7 days**, on how many days did you do **moderate** activities **in the garden or yard**? [GMDAY; Range 0-7, 8, 9]

- \_\_\_\_\_ Days per week *[If respondent answers 0, skip to Question 18]*  
8. Don't Know/Not Sure *[Skip to Question 18]*  
9. Refused *[Skip to Question 18]*

**[Interviewer clarification:** Think about only those physical activities that you did for at least 10 minutes at a time.]

When you were doing moderate physical activity in the garden or yard, did you usually protect yourself from the sun (shade and/or clothes and/or sunscreen)?  Yes  
 No

17. How much time did you usually spend on one of those days doing **moderate** physical activities in the garden or yard?

- \_\_\_ \_\_\_ Hours per day [GMDHRS; Range 0-16]  
\_\_\_ \_\_\_ \_\_\_ Minutes per day [GMDMIN; Range 0-960, 998, 999]  
998. Don't Know/Not Sure  
999. Refused

[Interviewer clarification: Think about only those physical activities that you did for at least 10 minutes at a time.]

[Interviewer probe: An average time per day is being sought. If the respondent can't answer because the pattern of time spent varies widely from day to day, ask: "What is the total amount of time you spent **over the last 7 days** doing moderate physical activities in the garden or yard?"

- \_\_\_ \_\_\_ Hours per week [GMWHRS; Range 0-112]  
\_\_\_ \_\_\_ \_\_\_ Minutes per week [GMWMIN; Range 0-6720, 9998, 9999]  
9998. Don't Know/Not Sure  
9999. Refused

**READ: Now think about activities which take at least moderate physical effort that you did inside your home. Examples include carrying light loads, washing windows, scrubbing floors, sweeping, general maintenance or other things you do when you are caring for your family. Include only those moderate physical activities that you did for at least 10 minutes at a time.**

[Interviewer clarification: Moderate activities make you breathe somewhat harder than normal.]

18. During the **last 7 days**, on how many days did you do **moderate** activities **inside your home**? [HMDAY; Range 0-7, 8, 9]

- \_\_\_ Days per week [If respondent answers 0, skip to PART J]  
8. Don't Know/Not Sure [Skip to PART J]  
9. Refused [Skip to PART J]

[Interviewer clarification: Think about only those physical activities that you did for at least 10 minutes at a time.]

[Interviewer clarification: During the last 7 days, on how many days did you do activities that take **at least moderate** effort inside your home?]

19. How much time did you usually spend on one of those days doing **moderate** physical activities inside your home?

- \_\_\_ \_\_\_ Hours per day [HMDHRS; Range 0-16]  
\_\_\_ \_\_\_ \_\_\_ Minutes per day [HMDMIN; Range 0-960, 998, 999]  
998. Don't Know/Not Sure  
999. Refused

[Interviewer clarification: Think about only those physical activities that you did for at least 10 minutes at a time.]

[Interviewer probe: An average time per day is being sought. If the respondent can't answer because the pattern of time spent varies widely from day to day, ask: "What is the total amount of time you spent **over the last 7 days** doing moderate physical activities inside your home?"

- \_\_\_ \_\_\_ Hours per week [HMWHRS; Range 0-112]  
\_\_\_ \_\_\_ \_\_\_ Minutes per week [HMWMIN; Range 0-6720, 9998, 9999]  
9998. Don't Know/Not Sure  
9999. Refused

**PART J: RECREATION, SPORT, AND LEISURE-TIME PHYSICAL ACTIVITY**

**READ: Now, think about all the physical activities that you did in the last 7 days solely for recreation, sport, exercise or leisure. Please do not include any activities you have already mentioned.**

20. Not counting any walking you have already mentioned, during the **last 7 days**, on how many days did you **walk** for at least 10 minutes at a time **in your leisure time**?

[LWDAY; Range 0-7, 8, 9]

\_\_\_\_\_ Days per week [If respondent answers 0, skip to Question 22]

8. Don't Know/Not Sure [Skip to Question 22]

9. Refused [Skip to Question 22]

**[Interviewer clarification:** Think about only the walking that you did for at least 10 minutes at a time.]

If you were walking outdoors in the summer, for how many days did you walk outdoors\_\_\_\_\_.

When you were walking outdoors, did you usually protect yourself from the sun (shade and/or clothes and/or sunscreen)?  Yes

No

21. How much time did you usually spend on one of those days **walking** in your leisure time?

\_\_\_\_\_ Hours per day [LWDHRS; Range 0-16]

\_\_\_\_\_ Minutes per day [LWDMIN; Range 0-960, 998, 999]

998. Don't Know/Not Sure

999. Refused

**[Interviewer clarification:** Think about only the walking that you did for at least 10 minutes at a time.]

**[Interviewer probe:** An average time per day is being sought. If the respondent can't answer because the pattern of time spent varies widely from day to day, ask: "What is the total amount of time you spent **over the last 7 days** walking in your leisure time?"

\_\_\_\_\_ Hours per week [LWWHRS; Range 0-112]

\_\_\_\_\_ Minutes per week [LWWMIN; Range 0-6720, 9998, 9999]

9998. Don't Know/Not Sure

9999. Refused

**READ: Now think about other physical activities you did in your leisure time for at least 10 minutes at a time.**

**READ: First, think about vigorous activities which take hard physical effort that you did in your leisure time. Examples include aerobics, running, fast bicycling, or fast swimming.**

**[Interviewer clarification:** Vigorous activities make you breathe much harder than normal.]

22. During the **last 7 days**, on how many days did you do **vigorous** physical activities **in your leisure time**? [LVDAY; Range 0-7, 8, 9]

\_\_\_\_\_ Days per week [If respondent answers 0, skip to Question 24]

8. Don't Know/Not Sure [Skip to Question 24]

9. Refused [Skip to Question 24]

**[Interviewer clarification:** Think about only those vigorous physical activities that you did for at least 10 minutes at a time.]

If vigorous physical activity was done outdoors in the summer, for how many days was this activity done outdoors\_\_\_\_\_.

When you were doing vigorous physical activity outdoors, did you usually protect yourself from the sun (shade and/or clothes and/or sunscreen)?

<input type="checkbox"/>	Yes
<input type="checkbox"/>	No

23. How much time did you usually spend on one of those days doing **vigorous** physical activities in your leisure time?

\_\_\_\_ Hours per day [LVDHRS; Range 0-16]

\_\_\_\_ Minutes per day [LVDMIN; Range 0-960, 998, 999]

998. Don't Know/Not Sure

999. Refused

**[Interviewer clarification:** Think about only those physical activities that you did for at least 10 minutes at a time.]

**[Interviewer probe:** An average time per day is being sought. If the respondent can't answer because the pattern of time spent varies widely from day to day, ask: "What is the total amount of time you spent **over the last 7 days** doing vigorous physical activities in your leisure time?"

\_\_\_\_ Hours per week [LVWHRS; Range 0-112]

\_\_\_\_ Minutes per week [LVWMIN; Range 0-6720, 9998, 9999]

9998. Don't Know/Not Sure

9999. Refused

**READ: Now think about activities which take moderate physical effort that you did in your leisure time. Examples include bicycling at a regular pace, swimming at a regular pace, and doubles tennis. Again, include only those moderate activities that you did for at least 10 minutes at a time.**

**[Interviewer clarification:** Moderate physical activities make you breathe somewhat harder than normal.]

24. During the **last 7 days**, on how many days did you do **moderate** physical activities **in your leisure time**? [LMDAY; Range 0-7, 8, 9]

\_\_\_\_ Days per week [If respondent answers 0, skip to PART K]

8. Don't Know/Not Sure [Skip to PART K]

9. Refused [Skip to PART K]

**[Interviewer clarification:** Think about only those physical activities that you did for at least 10 minutes at a time.]

If moderate physical activity was done outdoors in the summer, for how many days was this activity done outdoors\_\_\_\_\_.

When you were doing moderate physical activity outdoors, did you usually protect yourself from the sun (shade and/or clothes and/or sunscreen)?

<input type="checkbox"/>	Yes
<input type="checkbox"/>	No

25. How much time did you usually spend on one of those days doing **moderate** physical activities in your leisure time?

\_\_\_\_ Hours per day [LMDHRS; Range 0-16]  
\_\_\_\_ Minutes per day [LMDMIN; Range 0-960, 998, 999]  
998. Don't Know/Not Sure  
999. Refused

[**Interviewer clarification:** Think about only those physical activities that you did for at least 10 minutes at a time.]

[**Interviewer probe:** An average time per day is being sought. If the respondent can't answer because the pattern of time spent varies widely from day to day, ask: "What is the total amount of time you spent **over the last 7 days** doing moderate physical activities in your leisure time?"

\_\_\_\_ Hours per week [LMWHRS; Range 0-112]  
\_\_\_\_ Minutes per week [LMWMIN; Range 0-6720, 9998, 9999]  
9998. Don't Know/Not Sure  
9999. Refused

**PART K: TIME SPENT SITTING**

**READ: The last question is about the time that you spent *sitting* during the last 7 days. Include time at work, at home, while doing course work and during leisure time. This may include time spent sitting at a desk, visiting friends, reading or sitting or lying down to watch television. Do not include any time spent sitting in a motor vehicle that you have already told me about.**

26. During the **last 7 days**, how much time did you usually spend **sitting** on a **weekday**?

\_\_\_\_ Hours per day [SDHRS; Range 0-16]  
\_\_\_\_ Minutes per day [SDMIN; Range 0-960, 998, 999]  
998. Don't Know/Not Sure  
999. Refused

[**Interviewer clarification:** Include time spent lying down (awake) as well as sitting.]

[**Interviewer probe:** An average time per day is being sought. If the respondent can't answer because the pattern of time spent sitting varies widely from day to day, ask: "How much time in total did you spend sitting on **Wednesday**?"

\_\_\_\_ Hours on Wednesday [SWHRS; Range 0-16]  
\_\_\_\_ Minutes per Wednesday [SWMIN; Range 0-960, 998, 999]  
9998. Don't Know/Not Sure  
9999. Refused

If this activity was done outdoors in the summer, for how many days was this activity done outdoors\_\_\_\_\_.

When you were sitting outdoors, did you usually protect yourself from the sun (shade and/or clothes and/or sunscreen)?

<input type="checkbox"/>	Yes
<input type="checkbox"/>	No

27. During the **last 7 days**, how much time did you usually spend **sitting** on a **weekend day**?

\_\_\_\_ Hours per day [SEHRS; Range 0-16]  
\_\_\_\_ Minutes per day [SEMIN; Range 0-960, 998, 999]  
998. Don't Know/Not Sure  
999. Refused

[**Interviewer clarification:** Include time spent lying down (awake) as well as sitting.]

**[Interviewer probe:** An average time per day is being sought. If the respondent can't answer because the pattern of time spent sitting varies widely from day to day, ask: "How much time in total did you spend sitting on **Saturday**?"

\_\_\_\_\_ Hours on Saturday [SSHRS; Range 0-16]

\_\_\_\_\_ Minutes per Saturday [SSMIN; Range 0-960, 998, 999]

9998. Don't Know/Not Sure

9999. Refused

**PART L: IN THIS NEXT SECTION, I WILL ASK A LITTLE ABOUT YOUR DIET IN THE LAST MONTH**

1. Did you eat **canned sardines** in the last month?

How often did you eat <b>canned sardines</b> ?									Each time you ate <b>canned sardines</b> at that time, how much did you usually eat?		
Never	<1 per month	1 per month	2-3 per month	1-2 per week	3-4 per week	5-6 per week	1 per day	2+ per day	< 3 small or 1½ oz	3-6 small or 1¼ to 2 ½ oz	> 6 small or 2 ½ oz
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

Don't know

Prefer not to answer

2. Did you eat **canned mackerel** in the last month?

How often did you eat <b>canned mackerel</b> ?									Each time you ate <b>canned mackerel</b> at that time, how much did you usually eat?		
Never	<1 per month	1 per month	2-3 per month	1-2 per week	3-4 per week	5-6 per week	1 per day	2+ per day	< 3 small or 1½ oz	3-6 small or 1¼ to 2 ½ oz	> 6 small or 2 ½ oz
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

Don't know

Prefer not to answer

3. Did you eat **canned salmon** in the last month?

How often did you eat <b>canned salmon</b> ?									Each time you ate <b>canned salmon</b> at that time, how much did you usually eat?		
Never	<1 per month	1 per month	2-3 per month	1-2 per week	3-4 per week	5-6 per week	1 per day	2+ per day	< ¼ cup or 2oz	¼ to ½ cup (2-3 oz)	> ½ cup (3oz)
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

Don't know

Prefer not to answer

4. Did you eat **fresh or frozen salmon** in the last month?

How often did you eat <b>fresh or frozen salmon</b> ?									Each time you ate <b>fresh or frozen salmon</b> , how much did you usually eat?		
Never	<1 per month	1 per month	2-3 per month	1-2 per week	3-4 per week	5-6 per week	1 per day	2+ per day	< ½ filet or 3 oz	½ filet or 3 to 6 oz	> ½ filet or 6 oz
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

Don't know  Prefer not to answer

5. Did you eat **smoked salmon** in the last month?

How often did you eat <b>smoked salmon</b> ?									Each time you ate <b>smoked salmon</b> at that time, how much did you usually eat?		
Never	<1 per month	1 per month	2-3 per month	1-2 per week	3-4 per week	5-6 per week	1 per day	2+ per day	<2 slices or 2 oz	2 to 3 slices or 1 to 2 oz	> 3 slices or >2 oz
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

Don't know  Prefer not to answer

6. Did you drink **Vitamin D fortified beverages, other than milk** in the last month?  
i.e. soya milk or fortified orange-juice

	How often did you drink <b>fortified beverages</b> ?									What quantity did you usually consume?		
	Never	<1 per month	1 per month	2-3 per month	1-2 per week	3-4 per week	5-6 per week	1 per day	2+ per day	< 1 cup	1 to 1½ cups	> 1½ cup
beverage	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

Don't know  Prefer not to answer

7. Did you eat **fresh or dried mushrooms** in the last month?

How often did you have <b>fresh or dried mushrooms</b> ?									Each time you ate <b>mushrooms</b> , how many did you usually eat?		
Never	<1 per month	1 per month	2-3 per month	1-2 per week	3-4 per week	5-6 per week	1 per day	2+ per day	< ½ cup	½ to 1 cup	> 1 cup
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

Don't know  Prefer not to answer

8. Did you take **cod liver oil supplements**, either in the form of a capsule or tablet in the last month?

How often did you take <b>cod liver oil supplements</b> , either in the form of a capsule or tablet?						In one day, about how much vitamin D did you take from <b>cod liver oil supplements</b> at that time?			
Never	<1 day per month	1-3 days per month	1-3 days per week	4-6 days per week	Everyday	<100 IU	100-199 IU	200-399 IU	≥ 400 IU
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

Don't know  Prefer not to answer

9. Did you consume **cod liver oil as a liquid** in the last month?

How often did you consume <b>cod liver oil as a LIQUID</b> ?									Each time you drank cod liver oil as a LIQUID at that time, how much did you usually consume?		
Never	<1 per month	1 per month	2-3 per month	1-2 per week	3-4 per week	5-6 per week	1 per day	2+ per day	< 1 tsp	1 to 2 tsp	≥2 tsp
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

Don't know

Prefer not to answer

**PART M: NOW I WILL ASK YOU ABOUT YOUR CIGARETTE SMOKING HISTORY**

1. Did you ever smoke a total of 100 cigarettes or more in your lifetime?

Yes

Don't know (Skip to Question 8)

No (Skip to Question 8)

Prefer not to answer (Skip to Question 8)

2. How old were you when you first started smoking cigarettes? \_\_\_\_\_  
Age started

Don't know

Prefer not to answer

3. At what age did you last smoke cigarettes? \_\_\_\_\_  Still smoking  
Age stopped

Don't know

Prefer not to answer

4. Have you ever stopped smoking for at least 3 months and began to smoke again, and if so, for how long in total did you stop smoking?

Never stopped smoking (Skip to 7)

Don't know

Prefer not to answer

5. When was the last time you stopped smoking before restarting?

   or           
 Year                      Month                      Age

6. And referring to this last time, when did you start smoking again?

   or           
 Year                      Month                      Age

7. During periods when you smoked, how many cigarettes did you **usually** smoke? (usually 1 package contains 25 cigarettes)

\_\_\_\_\_  
# of Cigarettes

Per day

Per week

Per month

Don't know

Prefer not to answer

8. In the last month, have any members of your household ever smoked in your presence, including caregivers?

- Yes
- No (Skip to Question 9)
- Don't know (Skip to Question 9)
- Prefer not to answer (Skip to Question 9)

On average how many cigarettes per day do you think you are exposed to from all members of your household who smoke in your presence? \_\_\_\_\_

9. Have you vaped (or smoked) an ecigarette in the last month?

- Yes
- No (Skip to PART N)
- Don't know (Skip to PART N)
- Prefer not to answer (Skip to PART N)

On average how many milliliters do you vape in a week? \_\_\_\_\_ml (average 1.5-5 ml/d; 1ml=10 cig)  
At what level of nicotine? \_\_\_\_\_mg/ml

**PART N: NOW I WILL ASK YOU ABOUT SUPPLEMENTS AND ALTERNATIVE MEDICINE**

1. Are there any complementary and alternative supplements, i.e., green tea compound or curcumin that you take more than once per week?

- Yes
- No (Skip to PART O)
- Don't know (Skip to PART O)
- Prefer not to answer (Skip to PART O)

2. Please tell me all of the supplements that you currently take more than once per week

Products	Amount	Products	Amount
Alpha lipoic acid		Glucosamine and Chondroitin	
Antioxidants		Grape seed extract	
Artemisia		Green tea (EGCC-green tea compound)	
Black cohosh		Laetrile / B17 (apricot pits)	
Calcium d-glucarate		Lycopene	
Cannabis oil		L-glutamine	
Chamomile		Melatonin	
Coenzyme Q10		Milk thistle	
Curcumin		Modified citrus pectin	
DIM indole 3 carbinol		Mushroom capsules	
Echinacea		N-acetyl-cysteine (precursor to glutathione)	
Ellagic acid		Omega 3s	
Ensure		Pomegranate	
Fish oil		Quercetin	
Flax seed oil		Resveratrol	
Garlic		Slim-Fast	
Ginger		Venus Flytrap extract	
Ginkgo Biloba		Zyflamend	
Ginseng			

**PART O: NOW I WILL ASK YOU ABOUT YOUR SLEEP PATTERNS. ALL OF THE QUESTIONS REFER TO THE PAST MONTH:**

1. What time did you usually go to bed at night? \_\_\_\_\_
2. How long (in minutes) did it usually take you to fall asleep each night? \_\_\_\_\_ mins
3. What time did you usually get up in the morning? \_\_\_\_\_
4. How many hours of actual sleep did you get at night? (this number may not be the same as the number of hours you spent in bed.) \_\_\_\_\_ hrs

**FOR THE NEXT 10 QUESTIONS PLEASE SELECT THE BEST RESPONSE FROM THE CHOICE OF 4 ANSWERS THAT I WILL READ TO YOU.**

If you would like to write them down, they are: **not during the past month, less than once a week, once or twice a week and three or more times a week.**

5. **During the past month**, how often have you had trouble sleeping because you...

	Not during the past month	Less than once a week	Once or twice a week	Three or more times a week
a. Could not get to sleep within 30 minutes?				
b. Woke up in the middle of the night or early morning?				
c. Had to get up to use the bathroom?				
d. Could not breathe comfortably				
e. Coughed or snored loudly				
f. Felt too cold				
g. Felt too hot				
h. Had bad dreams				
i. Had pain				
j. Other reason - <i>please describe</i> : _____				
How often during the past month have you had trouble sleeping because of this?				

6. **During the past month**, how would you rate your sleep quality overall?

Very good	Fairly good	Fairly bad	Very bad
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

7. **During the past month**, how often have you taken medicine to help you sleep (prescribed or over the counter)?

Not during the past month	Less than once a week	Once or twice a week	Three or more times a week
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

8. **During the past month**, how often have you had trouble staying awake while driving, eating meals, or engaging in social activity?

Not during the past month	Less than once a week	Once or twice a week	Three or more times a week
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

9. **During the past month**, how much of a problem has it been for you to keep up enough enthusiasm to get things done?

No problem at all	Only a very slight problem	Somewhat of a problem	A very big problem
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

**NOW I WILL ASK YOU ABOUT INSOMNIA IN THE PAST MONTH**

10. Please rate the **severity** of your current insomnia problems. I will read 5 different answers; please tell me which one best corresponds to your insomnia problems in the past month.

	<b>None</b>	<b>Mild</b>	<b>Moderate</b>	<b>Severe</b>	<b>Very severe</b>
a) Difficulty falling asleep	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
b) Difficulty staying asleep	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
c) Problem waking up too early	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

11. How **satisfied/dissatisfied** are you with your current sleep pattern?

Very satisfied	Satisfied	Neutral	Dissatisfied	Very dissatisfied
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

12. To what extent do you consider your sleep problem **interferes** with your daily functioning (e.g. daytime fatigue, ability to function at work/daily chores, concentration, memory, mood, etc.)?

Not at all interfering	A little interfering	Somewhat interfering	Much interfering	Very interfering
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

13. How **noticeable** to others do you think your sleeping problem is in terms of impairing the quality of your life?

Not at all noticeable	A little noticeable	Somewhat noticeable	Much noticeable	Very noticeable
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

14. How **worried / distressed** are you about your current sleep problem?

Not at all worried	A little worried	Somewhat worried	Much worried	Very worried
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

**PART P: NOW I WILL ASK YOU ABOUT HOW YOU HAVE BEEN FEELING IN THE PAST WEEK**

This section is designed to help us to know how you feel. I will read a list of statements. Please indicate the reply which comes closest to how you have been feeling **in the past week**.

Don't take too long over your replies, your immediate reaction to each item will probably be more accurate than a long, thought-out response.

HADS1	I feel tense or 'wound up'	Most of the time <input type="radio"/>	A lot of the time <input type="radio"/>	From time to time, occasionally <input type="radio"/>	Not at all <input type="radio"/>
HADS2	I still enjoy the things I used to enjoy	Definitely as much <input type="radio"/>	Not quite so much <input type="radio"/>	Only a little <input type="radio"/>	Hardly at all <input type="radio"/>
HADS3	I get a sort of frightened feeling as if something awful is about to happen	Very definitely and quite badly <input type="radio"/>	Yes, but not too badly <input type="radio"/>	A little, but it doesn't worry me <input type="radio"/>	Not at all <input type="radio"/>
HADS4	I can laugh and see the funny side of things	As much as I always could <input type="radio"/>	Not quite so much now <input type="radio"/>	Definitely not so much now <input type="radio"/>	Not at all <input type="radio"/>
HADS5	Worrying thoughts go through my mind	A great deal of the time <input type="radio"/>	A lot of the time <input type="radio"/>	Not too often <input type="radio"/>	Very little <input type="radio"/>
HADS6	I feel cheerful	Never <input type="radio"/>	Not often <input type="radio"/>	Sometimes <input type="radio"/>	Most of the time <input type="radio"/>
HADS7	I can sit at ease and feel relaxed	Definitely <input type="radio"/>	Usually <input type="radio"/>	Not often <input type="radio"/>	Not at all <input type="radio"/>
HADS8	I feel as if I am slowed down	Nearly all the time <input type="radio"/>	Very often <input type="radio"/>	Sometimes <input type="radio"/>	Not at all <input type="radio"/>
HADS9	I get a sort of frightened feeling like 'butterflies' in the stomach	Not at all <input type="radio"/>	Occasionally <input type="radio"/>	Quite often <input type="radio"/>	Very often <input type="radio"/>
HADS10	I have lost interest in my appearance	Definitely <input type="radio"/>	I don't take as much care as I should <input type="radio"/>	I may not take quite as much care <input type="radio"/>	I take just as much care as ever <input type="radio"/>
HADS11	I feel restless as if I have to be on the move	Very much indeed <input type="radio"/>	Quite a lot <input type="radio"/>	Not very much <input type="radio"/>	Not at all <input type="radio"/>
HADS12	I look forward with enjoyment to things	As much as I ever did <input type="radio"/>	Rather less than I used to <input type="radio"/>	Definitely less than I used to <input type="radio"/>	Hardly at all <input type="radio"/>
HADS13	I get sudden feelings of panic	Very often indeed <input type="radio"/>	Quite often <input type="radio"/>	Not very often <input type="radio"/>	Not at all <input type="radio"/>
HADS14	I can enjoy a good book or radio or television program	Often <input type="radio"/>	Sometimes <input type="radio"/>	Not often <input type="radio"/>	Very seldom <input type="radio"/>

1. Would you have preferred to answer the questions about how you've been feeling on your own?

- Yes  
 No  
 Don't know  
 Prefer not to answer

Now I will read a list of statements on your well-being that other people with your illness have said are important. **Please indicate your response as it applies to the past 7 days.**

If you would like to write them down, they are: **not at all, a little bit, somewhat, quite a bit and very much.**

	<b>PHYSICAL WELL-BEING</b>	<b>Not at all</b>	<b>A little bit</b>	<b>Some-what</b>	<b>Quite a bit</b>	<b>Very much</b>
GP1	I have a lack of energy .....	0	1	2	3	4
GP2	I have nausea.....	0	1	2	3	4
GP3	Because of my physical condition, I have trouble meeting the needs of my family.....	0	1	2	3	4
GP4	I have pain.....	0	1	2	3	4
GP5	I am bothered by side effects of treatment.....	0	1	2	3	4
GP6	I feel ill .....	0	1	2	3	4
GP7	I am forced to spend time in bed .....	0	1	2	3	4

	<b>SOCIAL/FAMILY WELL-BEING</b>	<b>Not at all</b>	<b>A little bit</b>	<b>Some-what</b>	<b>Quite a bit</b>	<b>Very much</b>
GS1	I feel close to my friends.....	0	1	2	3	4
GS2	I get emotional support from my family .....	0	1	2	3	4
GS3	I get support from my friends.....	0	1	2	3	4
GS4	My family has accepted my illness .....	0	1	2	3	4
GS5	I am satisfied with family communication about my illness .....	0	1	2	3	4
GS6	I feel close to my partner (or the person who is my main support) .....	0	1	2	3	4
Q1	<i>Regardless of your current level of sexual activity, please answer the following question. If you prefer not to answer it, please let me know</i> <input type="checkbox"/> Prefers not to answer					
GS7	I am satisfied with my sex life.....	0	1	2	3	4

	<b>EMOTIONAL WELL-BEING</b>	<b>Not at all</b>	<b>A little bit</b>	<b>Some-what</b>	<b>Quite a bit</b>	<b>Very much</b>
GE1	I feel sad .....	0	1	2	3	4
GE2	I am satisfied with how I am coping with my illness....	0	1	2	3	4

GE3	I am losing hope in the fight against my illness .....	0	1	2	3	4
GE4	I feel nervous .....	0	1	2	3	4
GE5	I worry about dying .....	0	1	2	3	4
GE6	I worry that my condition will get worse .....	0	1	2	3	4

	<b>FUNCTIONAL WELL-BEING</b>	<b>Not at all</b>	<b>A little bit</b>	<b>Some-what</b>	<b>Quite a bit</b>	<b>Very much</b>
GF1	I am able to work (include work at home).....	0	1	2	3	4
GF2	My work (include work at home) is fulfilling .....	0	1	2	3	4
GF3	I am able to enjoy life.....	0	1	2	3	4
GF4	I have accepted my illness .....	0	1	2	3	4
GF5	I am sleeping well .....	0	1	2	3	4
GF6	I am enjoying the things I usually do for fun .....	0	1	2	3	4
GF7	I am content with the quality of my life right now .....	0	1	2	3	4

	<b>ADDITIONAL CONCERNS</b>	<b>Not at all</b>	<b>A little bit</b>	<b>Some-what</b>	<b>Quite a bit</b>	<b>Very much</b>
O1	I have swelling in my stomach area.....	0	1	2	3	4
C2	I am losing weight.....	0	1	2	3	4
C3	I have control of my bowels .....	0	1	2	3	4
O2	I have been vomiting .....	0	1	2	3	4
B5	I am bothered by hair loss .....	0	1	2	3	4
C6	I have a good appetite .....	0	1	2	3	4
C7	I like the appearance of my body.....	0	1	2	3	4
BMT5	I am able to get around by myself .....	0	1	2	3	4
B9	I am able to feel like a woman .....	0	1	2	3	4
O3	I have cramps in my stomach area.....	0	1	2	3	4
BL4	I am interested in sex .....	0	1	2	3	4
BMT7	I have concerns about my ability to have children.....	0	1	2	3	4

	<b>FATIGUE SCALE</b>	<b>Not at all</b>	<b>A little bit</b>	<b>Some-what</b>	<b>Quite a bit</b>	<b>Very much</b>
HI7	I feel fatigued .....	0	1	2	3	4
HI12	I feel weak all over .....	0	1	2	3	4
An1	I feel listless (“washed out”).....	0	1	2	3	4
An2	I feel tired.....	0	1	2	3	4
An3	I have trouble <u>starting</u> things because I am tired .....	0	1	2	3	4
An4	I have trouble <u>finishing</u> things because I am tired .....	0	1	2	3	4
An5	I have energy.....	0	1	2	3	4
An7	I am able to do my usual activities.....	0	1	2	3	4
An8	I need to sleep during the day .....	0	1	2	3	4
An12	I am too tired to eat.....	0	1	2	3	4
An14	I need help doing my usual activities.....	0	1	2	3	4
An15	I am frustrated by being too tired to do the things I want to do .....	0	1	2	3	4
An16	I have to limit my social activity because I am tired.....	0	1	2	3	4

	<b>SECONDARY EFFECTS OF TREATMENT</b>	<b>Not at all</b>	<b>A little bit</b>	<b>Some-what</b>	<b>Quite a bit</b>	<b>Very much</b>
NTX1	I have numbness or tingling in my hands .....	0	1	2	3	4
NTX2	I have numbness or tingling in my feet.....	0	1	2	3	4
NTX3	I feel discomfort in my hands.....	0	1	2	3	4
NTX4	I feel discomfort in my feet.....	0	1	2	3	4
NTX5	I have joint pain or muscle cramps .....	0	1	2	3	4
NTX6	I have trouble hearing.....	0	1	2	3	4
NTX7	I get a ringing or buzzing in my ears.....	0	1	2	3	4
NTX8	I have trouble buttoning buttons .....	0	1	2	3	4
NTX9	I have trouble feeling the shape of small objects when they are in my hand .....	0	1	2	3	4
An6	I have trouble walking.....	0	1	2	3	4

2. Would you have preferred to answer the questions about how you've been feeling on your own?  
 Yes       No       Don't know       Prefer not to answer

3. Is there anything else that we haven't asked you that you think is important?

---

4. Do you have any feedback about this questionnaire?

---

**Thank you very much for taking the time to answer our questions.  
Your participation is greatly appreciated.**

Time Ended:   :   (24 hour clock)

## Appendix C

### Specific Items Used for the Trial Outcome Index (TOI) Score

	<b>PHYSICAL WELL-BEING</b>	<b>Not at all</b>	<b>A little bit</b>	<b>Some-what</b>	<b>Quite a bit</b>	<b>Very Much</b>
GP1	I have a lack of energy	0	1	2	3	4
GP2	I have nausea	0	1	2	3	4
GP3	Because of my physical condition, I have trouble meeting the needs of my family	0	1	2	3	4
GP4	I have pain	0	1	2	3	4
GP5	I am bothered by side effects of treatment	0	1	2	3	4
GP6	I feel ill	0	1	2	3	4
GP7	I am forced to spend time in bed	0	1	2	3	4
	<b>FUNCTIONAL WELL-BEING</b>	<b>Not at all</b>	<b>A little bit</b>	<b>Some-what</b>	<b>Quite a bit</b>	<b>Very Much</b>
GF1	I am able to work (include work at home)	0	1	2	3	4
GF2	My work (include work at home) is fulfilling	0	1	2	3	4
GF3	I am able to enjoy life	0	1	2	3	4
GF4	I have accepted my illness	0	1	2	3	4
GF5	I am sleeping well	0	1	2	3	4
GF6	I am enjoying the things I usually do for fun	0	1	2	3	4
GF7	I am content with the quality of my life right now	0	1	2	3	4
	<b>ADDITIONAL CONCERNS</b>	<b>Not at all</b>	<b>A little bit</b>	<b>Some-what</b>	<b>Quite a bit</b>	<b>Very Much</b>
O1	I have swelling in my stomach area	0	1	2	3	4
C2	I am losing weight	0	1	2	3	4
C3	I have control of my bowels	0	1	2	3	4
O4	I have been vomiting	0	1	2	3	4
B5	I am bothered by hair loss	0	1	2	3	4
C6	I have a good appetite	0	1	2	3	4
C7	I like the appearance of my body	0	1	2	3	4
BM T5	I am able to get around by myself	0	1	2	3	4
B9	I am able to feel like a woman	0	1	2	3	4
O3	I have cramps in my stomach area	0	1	2	3	4
BL4	I am interested in sex	0	1	2	3	4
BM T7	I have concerns about my ability to have children	0	1	2	3	4

## Appendix D

### Correlation Table for Identifying Confounders (Objective 2)

	Age (cont.)	BMI (normal, over, obese)	Education (<high school vs. >high)	Partner (single vs. Married)	Hyst (yes/no)	Past OC Use (yes/no)	Past Hormone Use (yes/no)	Parity (0, 1, 2+)	Job (un, sick, employed)	Smoking (packyears)	Ethnicity (French Can. vs. Other & Mixed)	Menopausal (pre/post)	Stage (I, II vs. III, IV)	Chemo (neo vs. adj)
Age (continuous)	1.00	-0.13	-0.36	0.10	-0.26	0.00	0.38	0.11	-0.44	0.06	-0.21	0.60	0.24	0.11
BMI (normal, over, obese)	-0.13	1.00	-0.20	-0.01	-0.08	-0.03	-0.18	-0.03	-0.02	0.21	-0.10	-0.01	-0.05	0.01
Education (< high school vs. >high)	-0.36	-0.20	1.00	-0.12	0.19	0.00	0.03	-0.14	0.08	-0.32	0.12	-0.25	-0.20	-0.19
Partner (single/married)	0.10	-0.01	-0.12	1.00	0.05	0.02	-0.12	-0.10	0.08	0.19	-0.04	0.18	0.20	-0.01
Hysterectomy (yes/no)	-0.26	-0.08	0.19	0.05	1.00	0.08	-0.15	-0.06	0.14	-0.06	0.24	-0.15	-0.10	-0.20
Past OC Use (yes/no)	0.00	-0.03	0.00	0.02	0.08	1.00	-0.03	0.13	0.21	0.08	-0.38	0.02	0.02	0.08
Past Hormone Use (yes/no)	0.38	-0.18	0.03	-0.12	-0.15	-0.03	1.00	-0.02	-0.11	0.00	-0.12	0.23	-0.07	-0.09
Parity (0, 1, 2+)	0.11	-0.03	-0.14	-0.10	-0.06	0.13	-0.02	1.00	-0.06	0.02	-0.10	0.07	0.20	0.21
Job Status (unemployed, sick, employed)	-0.44	-0.02	0.08	0.08	0.14	0.21	-0.11	-0.06	1.00	0.13	-0.02	-0.29	-0.08	0.00
Smoking (packyears)	0.06	0.21	-0.32	0.19	-0.06	0.08	0.00	0.02	0.13	1.00	-0.38	0.17	0.03	0.09
Ethnicity (French-Can vs. Other & Mix)	-0.21	-0.10	0.12	-0.04	0.24	-0.38	-0.12	-0.10	-0.02	-0.38	1.00	-0.15	-0.06	-0.13
Menopausal Status (pre/post)	0.60	-0.01	-0.25	0.18	-0.15	0.02	0.23	0.07	-0.29	0.17	-0.15	1.00	0.11	0.04
Stage of Cancer (I, II vs. III, IV)	0.24	-0.05	-0.20	0.20	-0.10	0.02	-0.07	0.20	-0.08	0.03	-0.06	0.11	1.00	0.54
Chemo (neo/adj)	0.11	0.01	-0.19	-0.01	-0.20	0.08	-0.09	0.21	0.00	0.09	-0.13	0.04	0.54	1.00

## Appendix E

### Change in Estimate Summary Tables

**Table 1.** Summary of CIE procedure to identify confounders for TOI score<sup>1</sup>

Step	Variable to be dropped	$\beta$ Estimate for meeting PA guidelines		% change in $\beta$ estimate <sup>2</sup>
		Variable in model	Variable removed	
1	Education	3.571	3.532	-1.1%
2	Hysterectomy	3.532	3.490	-1.2%
3	Smoking	3.490	3.547	1.6%
4	Menopause	3.547	3.703	4.4%
5	Stage	3.703	3.587	-3.1%
6	BMI	3.587	3.395	-5.4%
7	Chemotherapy	3.395	3.207 <sup>3</sup>	-5.5%

1 Starting model included age, BMI, education, partner status, hysterectomy for cancer treatment, current job status, current smoking status, ethnicity, menopausal status, stage of cancer, neoadjuvant chemotherapy

2 Refers to the comparison between the model with and without the variable

3 Additional TOI score for women who met PA guidelines in comparison to those who did not, adjusted for age, partner status, current job status and ethnicity

**Table 2.** Summary of CIE procedure to identify confounders for Total FACT-O score<sup>1</sup>

Step	Variable to be dropped	$\beta$ Estimate for meeting PA guidelines		% change in $\beta$ estimate <sup>2</sup>
		Variable in model	Variable removed	
1	Education	2.627	2.563	-2.4%
2	Hysterectomy	2.563	2.464	-3.9%
3	Smoking	2.464	2.582	4.8%
4	Stage	2.582	2.375	-8.0%
5	Chemotherapy	2.375	2.170 <sup>3</sup>	-8.6%

1 Starting model included age, BMI, education, partner status, hysterectomy for cancer treatment, current job status, current smoking status, ethnicity, menopausal status, stage of cancer, neoadjuvant chemotherapy

2 Refers to the comparison between the model with and without the variable

3 Additional total FACT-O score for women who met PA guidelines in comparison to those who did not, adjusted for age, BMI, partner status, current job status, ethnicity, menopausal status and neoadjuvant chemotherapy

**Table 3.** Summary of CIE procedure to identify confounders for anxiety score<sup>1</sup>

Step	Variable to be dropped	OR for anxiety symptoms		% change in estimate <sup>2</sup>
		Variable in model	Variable removed	
1	Education	1.966	1.967	0.1%
2	Stage	1.967	1.998	3.8%
3	Chemotherapy	1.998	1.995	-0.2%
4	Hysterectomy	1.995	2.018	1.2%
5	Smoking	2.018	1.939	-3.9%
6	Partner status	1.939	1.963	1.2%
7	BMI	1.963	1.957	-0.3%
8	Menopause	1.957	1.837	-6.5%
9	Job status	1.837	1.667 <sup>3</sup>	-9.3%

1 Starting model included age, BMI, education, partner status, hysterectomy for cancer treatment, current job status, current smoking status, ethnicity, menopausal status, stage of cancer, neoadjuvant chemotherapy

2 Refers to the comparison between the model with and without the variables

3 OR for meeting PA guidelines versus not; adjusted for age and ethnicity

**Table 4.** Summary of CIE procedure to identify confounders for depression score<sup>1</sup>

Step	Variable to be dropped	OR for depression symptoms		% change in estimate <sup>2</sup>
		Variable in model	Variable removed	
1	Stage	0.317	0.314	-0.9%
2	Job status	0.314	0.301	-4.1%
3	BMI	0.301	0.312	3.7%
4	Smoking	0.312	0.300	-3.8%
5	Education	0.300	0.300	0.0%
6	Chemotherapy	0.300	0.295	-1.7%
7	Hysterectomy	0.295	0.304	3.1%
8	Ethnicity	0.304	0.277	-8.9%
9	Menopause	0.277	0.302 <sup>3</sup>	9.0%

1 Starting model included age, BMI, education, partner status, hysterectomy for cancer treatment, current job status, current smoking status, ethnicity, menopausal status, stage of cancer, neoadjuvant chemotherapy

2 Refers to the comparison between the model with and without the variables

3 OR for meeting PA guidelines versus not; adjusted for age and partner status

