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# Activity behavior and physiological profile of advanced-stage ovarian cancer survivors

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# Activity behavior and physiological profile of advanced-stage ovarian cancer survivors

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This thesis is submitted for the degree of

Master of Science (Sports Science)

By

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# ABSTRACT

**Background:** Advanced-stage ovarian cancer survivors (OCS) often experience a multitude of disease symptoms and treatment-related side-effects. Additionally, most OCS are older, have comorbidities, are overweight or obese, and report being insufficiently physically active. Ovarian cancer survivors may benefit from exercise oncology interventions to reduce symptom-burden, manage comorbidities, minimize functional decline and maximize health-related quality of life (HRQoL). However, current knowledge gaps regarding the physiological characteristics of OCS throughout the entire survivorship spectrum challenge the development of tailored exercise interventions.

**Purpose:** The overall purpose of this thesis was to provide a more comprehensive physiological and activity behavior profile of post-treatment advanced-stage OCS. Specifically, a cross-sectional research study was conducted to compare objectively measured activity behavior and physical function, body composition and musculoskeletal morphology, self-reported pelvic floor dysfunction (PFD) and HRQoL of OCS with age-matched controls. Associations between activity behavior, physiological characteristics, PFD and HRQoL for OCS were also investigated.

**Methods:** Twenty stage III-IV OCS and 20 age-matched controls underwent objective assessments of activity behavior (physical activity and sedentary time via 7-day accelerometry), physical function (400-meter walk to assess cardiorespiratory fitness, repeated chair rise to assess lower extremity function, 6-meter walking tests to assess gait speed and dynamic balance), muscle strength (1-repetition maximum chest press and single leg extension, and handgrip strength), body composition (dual-energy x-ray absorptiometry) and musculoskeletal morphology (peripheral quantitative computed tomography), and completed questionnaires assessing HRQoL (SF-36) and PFD (Australian Pelvic Floor Questionnaire).

**Results:** Compared to controls, OCS spent more time/day in prolonged sedentary bouts (i.e., uninterrupted sedentary bouts of ≥30 min; $p = 0.039$), had lower cardiorespiratory fitness ($p =$

0.041) and upper body strength (p = 0.023), had higher areal bone mineral content (p = 0.047) and volumetric trabecular density (p = 0.048), but were not different in other measures of body composition or musculoskeletal morphology (i.e., all p-values > 0.050). Compared to controls, OCS had equivalent self-reported PFD as indicated by combined bladder, bowel and pelvic organ prolapse symptoms (p = 0.277), but worse physical HRQoL indicated by a physical composite score (p = 0.013). Only 20% (n = 4) of OCS accrued ≥150 minutes/week moderate-and-vigorous physical activity (MVPA) in ≥10 min bouts. MVPA time/day in ≥10 min bouts was positively associated with cardiorespiratory fitness (p = 0.001), lower extremity function, (p = 0.019), muscle cross-sectional area (p = 0.035), less PFD (p = 0.038) and physical HRQoL (p = 0.003). Decreased physical HRQoL was associated with less MVPA (p = 0.005), more sedentary time (p = 0.047), decreased objective physical function (p-values < 0.050) and greater PFD (p = 0.043).

**Conclusion:** Post-treatment advanced-stage OCS spent more time in prolonged sedentary bouts, had lower cardiorespiratory fitness, upper body strength and physical HRQoL compared to age-matched controls. The decreased physical HRQoL of this sample of OCS compared to controls and its associations with modifiable factors such as MVPA, sedentary time, objective physical function and PFD highlights the need for ongoing supportive care and the importance of multidisciplinary interventions, including exercise oncology interventions, beyond the completion of first-line ovarian cancer treatment.

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# LIST OF PUBLICATIONS

The following chapters have been published in, submitted to, or prepared for submission to peer-reviewed academic journals:

**Chapter 2**

**Schofield C**, Newton RU, Galvão DA, Cohen PA, Peddle-McIntyre CJ. A physiological profile of ovarian cancer survivors to inform tailored exercise interventions and the development of exercise oncology guidelines. **International Journal of Gynecological Cancer**. 2017;27:1560-1567.

**Chapter 3**

**Schofield C**, Newton RU, Galvão DA, Cohen PA, McVeigh JA, Hart NH, Mohan GR, Tan J, Salfinger SG, Straker LM, Peddle-McIntyre CJ. Activity behaviors and physiological characteristics of women with advanced-stage ovarian cancer: a comprehensive cross-sectional investigation. **International Journal of Gynecological Cancer.** Under review.

**Chapter 4**

**Schofield C**, Newton RU, Galvão DA, Cohen PA, McVeigh JA, Mohan GR, Tan J, Salfinger SG, Straker LM, Peddle-McIntyre CJ. Associations of objective activity behaviors and physiological characteristics with health-related quality of life and pelvic floor dysfunction in advanced-stage ovarian cancer survivors. Manuscript prepared for submission to **Supportive Care in Cancer**, October 2017.

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# *Chapter 1*

# INTRODUCTION

## BACKGROUND

Ovarian cancer (OC) is the seventh most common cancer in women worldwide and the most fatal gynecological cancer, with an estimated 255,660 new cases and 152,000 deaths in 2015.[1] In 2018, an estimated 1613 women in Australia will be diagnosed with OC, and 1069 women will succumb to the disease.[2] Common risk factors associated with OC are older age, family history of ovarian, breast and/or colorectal cancer, inherited mutations of BRCA1 and BRCA2 genes, use of hormone replacement therapy, endometriosis and obesity.[3, 4] Factors known to reduce the risk of developing OC include oral contraceptive use, full-term pregnancy before age 26, multiple pregnancies and gynecological surgery, i.e., hysterectomy and tubal ligation.[3, 4]

Ovarian cancers are often described as a group of heterogeneous diseases of uncertain etiology, which can make diagnosis and treatment challenging.[5-8] Unfortunately, the large majority of OC cases (between 70% and 75%) are diagnosed at an advanced stage when the tumor has already spread beyond the ovaries (stage III and IV).[9] Two of the main reasons for this are the lack of effective screening tests for OC coupled with diffuse early symptoms.[10] Early signs and symptoms of OC, most commonly abdominal and pelvic pain, bloating, difficulty eating or feeling full quickly, and urinary frequency or urgency, are often vague and similar to symptoms of other more common and often less serious health conditions.[11] The five-year survival rates for women with stage III and IV OC are 39% and 17%, respectively.[12]

Standard first-line treatment for advanced OC involves primary debulking surgery (PDS) to remove as much of the tumor as possible, followed by adjuvant carboplatin-paclitaxel combination

chemotherapy.[10] Optimal tumor debulking (i.e., removal of all visible tumor) is considered the most important factor associated with prolonged OC survival.[13, 14] Whether a tumor can be optimally debulked depends on factors such as the patient's age, co-morbidities, performance status, disease stage, disease burden and location of metastatic sites.[15] In cases where optimal debulking seems unlikely, chemotherapy administered prior to debulking surgery, or neoadjuvant chemotherapy (NACT), is an alternative treatment option increasingly being utilized worldwide.[16] Although most women respond well to first-line treatment, 70% of women with advanced-stage OC and up to 30% of those with early-stage cancers will eventually relapse and require further treatment.[17 18] Due to the burden of advanced disease and often prolonged treatment, ovarian cancer survivors (OCS) frequently experience persistent symptoms and side-effects such as fatigue, poor sleep quality, peripheral neuropathy, cognitive impairment, sexual dysfunction and psychological distress.[19-23] Many of these symptoms and side-effects have been associated with reduced quality of life.[23, 24]

Complicating the burden of advanced cancer and associated treatments, 50% of OCS are 63 years and older,[25] 75% have concurrent comorbidities[26-28] and 15-30% are obese (i.e., BMI ≥30).[26, 29-33] Furthermore, between 50% and 80% of OCS report being insufficiently physically active (i.e., engage in <150 minutes of moderate and vigorous physical activity per week).[26, 27, 29, 34] Limited research, most of which include mixed samples of gynaecological cancer survivors, suggest impaired cardiorespiratory fitness and physical function in this cancer population.[34-36] Ovarian cancer survivors may benefit from supportive care interventions to reduce symptom-burden, manage comorbidities, minimize functional decline and maximize health-related quality of life.

Considerable research has demonstrated multiple benefits of physical activity and exercise after a cancer diagnosis.[35, 37-39] Physical activity is commonly defined as "any bodily movement produced by skeletal muscles that results in energy expenditure" and includes occupational, household and sport activities, and exercise. Exercise is a subset of physical activity and refers to planned, structured and repetitive activity with the purpose to improve or maintain physical fitness and health.[40] However, the majority of this evidence, as well as current physical activity (PA) and

exercise oncology guidelines endorsed by professional organizations such as the American College of Sports Medicine and American Cancer Society, are primarily based on research over the past two decades involving breast and prostate cancer survivors.[37] Research evidence for the benefits of PA and exercise in OC is limited to small, non-randomized studies.[41-43] To inform the design of OC-specific exercise oncology interventions for both research and clinical settings, a more comprehensive activity behavior and physiological profile of OCS is needed. A challenge posed by most existing OC research is the notable lack of objectively measured data describing body composition, activity behaviors (i.e., PA and sedentary behavior) and physical function. Furthermore, information on pelvic floor dysfunction (PFD), a recognized barrier to physical activity and exercise[44, 45] and associated with reduced health-related quality of life (HRQoL) in women globally,[46, 47] is limited to studies with mixed samples of gynecological cancer survivors. [48, 49] Also, most current OC studies include heterogeneous samples of participants including women with different stages of cancer, often on different treatments and at different time points in the cancer trajectory. Particularly lacking is information regarding the post first-line treatment status of advanced OCS.

## RESEARCH SIGNIFICANCE

The need for tailored supportive care interventions such as exercise prescription to reduce the impact of OC and its treatment is often highlighted in research studies.[24, 26, 33, 41, 50-52] However, a comprehensive picture of objective activity behaviors and physical function, muscle strength, body composition, musculoskeletal morphology and pelvic floor symptoms in OCS is not available. This presents a challenge for the design of tailored exercise intervention studies and exercise oncology guidelines. Results from this study will provide a more comprehensive activity behavior and physiological profile of advanced-stage OCS to empirically inform the design and application of OC-specific exercise oncology interventions for both research and clinical practice.

# RESEARCH PURPOSE AND OVERVIEW

The purpose of this research is to provide a comprehensive activity behavior and physiological profile of post-treatment advanced-stage OCS. Chapter Two is a published narrative review of existing literature relating to the physiological characteristics of OCS in terms of treatment-related side-effects, concurrent comorbidities, body weight and composition, physical fitness and function, and self-reported physical activity behavior.[53] In Chapters Three and Four we present results of an original cross-sectional research study conducted with 20 advanced-stage OCS who had received either neoadjuvant chemotherapy treatment and interval debulking surgery, or primary debulking surgery and adjuvant chemotherapy treatment. More specifically, in Chapter Three we describe objectively measured activity behaviors (PA and sedentary behavior) and physiological characteristics (physical function, muscle strength, body composition and musculoskeletal morphology) of OCS compared to age-matched controls (Manuscript under review, International Journal of Gynecological Cancer, Manuscript No. IGC-D-17-00571). In Chapter Four we compare HRQoL and self-reported PFD of OCS with age-matched controls and examine correlations between HRQoL and PFD (Manuscript prepared for submission to Supportive Care in Cancer, October 2017). Finally, in Chapter Five we provide an overall critical discussion of major findings and conclusions of our narrative review and experimental chapters, with recommendations for future research.

# REFERENCES


1. Ferlay J, Soerjomataram I, Ervik M, et al. GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 [Internet]. Lyon, France: International Agency for Research on Cancer; 2013. Available from: http:// globocan.iarc.fr. Accessed September 20, 2016.
2. Australian Institute of Health and Welfare, Summary pages for selected cancers 2017. Australian Government Web Archive [Internet]. Webarchive.nla.gov.au. 2017. Available from:http://webarchive.nla.gov.au/gov/20170424033535/http://www.aihw.gov.au/cancer/cancer-in-australia-2017/summary-pages-for-selected-cancers/. Accessed September 12, 2017.
3. American Cancer Society. What Are the Risk Factors for Ovarian Cancer? [Internet]. Cancer.org. 2017. Available from: https://www.cancer.org/cancer/ovarian-cancer/causes-risks-prevention/risk-factors.html. Accessed September 10, 2017.
4. Cancer Australia. What are the risk factors for ovarian cancer? [Internet] Available from: https://ovarian-cancer.canceraustralia.gov.au/risk-factors. Accessed September 10, 2017.
5. Wentzensen N, Poole EM, Trabert B et al. Ovarian Cancer Risk Factors by Histologic Subtype: An Analysis From the Ovarian Cancer Cohort Consortium. J Clin Oncol. 2016;34:2888-2898.
6. Goh J, Mohan GR, Ladwa R et al. Frontline treatment of epithelial ovarian cancer. Asia Pac J Clin Oncol. 2015;11(suppl 6):1-16.
7. Prat J. Staging classification for cancer of the ovary, fallopian tube, and peritoneum. Int J Gynaecol Obstet. 2014;124:1-5.
8. Rodriguez-Freixinos V, Mackay HJ, Karakasis K et al. Current and emerging treatment options in the management of advanced ovarian cancer. Expert Opin Pharmacother. 2016.
9. Sato S, Itamochi H. Neoadjuvant chemotherapy in advanced ovarian cancer: latest results and place in therapy. Ther Adv Med Oncol. 2014;6:293-304.
10. Jessmon P, Boulanger T, Zhou W et al. Epidemiology and treatment patterns of epithelial ovarian cancer. Expert Rev Anticancer Ther. 2017;17:427-437.
11. American Cancer Society. Signs and Symptoms of Ovarian Cancer [Internet] Cancer.org. 2017. Available from: https://www.cancer.org/cancer/ovarian-cancer/detection-diagnosis-staging/signs-and-symptoms.html. Accessed September 10, 2017.

12. American Cancer Society. Survival Rates for Ovarian Cancer, by Stage [Internet] Cancer.org. 2017. Available from: https://www.cancer.org/cancer/ovarian-cancer/detection-diagnosis-staging/survival-rates.html. Accessed September 10, 2017.

13. Bristow RE, Tomacruz RS, Armstrong DK et al. Survival effect of maximal cytoreductive surgery for advanced ovarian carcinoma during the platinum era: a meta-analysis. J Clin Oncol. 2002;20:1248-1259.

14. Chi DS, Eisenhauer EL, Lang J et al. What is the optimal goal of primary cytoreductive surgery for bulky stage IIIC epithelial ovarian carcinoma (EOC)? Gynecol Oncol. 2006;103:559-564.

15. Vergote I, Tropé CG, Amant F et al. Neoadjuvant chemotherapy is the better treatment option in some patients with stage IIIc to IV ovarian cancer. J Clin Oncol. 2011;29:4076-4078.

16. Leiserowitz GS, Lin JF, Tergas AI et al. Factors Predicting Use of Neoadjuvant Chemotherapy Compared With Primary Debulking Surgery in Advanced Stage Ovarian Cancer-A National Cancer Database Study. Int J Gynecol. 2017;27:675-683.

17. Ushijima K. Treatment for recurrent ovarian cancer-at first relapse. J Oncol. 2010;2010:497429.

18. Lawrie TA, Winter-Roach BA, Heus P et al. Adjuvant (post-surgery) chemotherapy for early stage epithelial ovarian cancer. Cochrane Database Syst Rev. 2015:CD004706.

19. Hay CM, Courtney-Brooks M, Lefkowits C et al. Symptom management in women with recurrent ovarian cancer: Do patients and clinicians agree on what symptoms are most important? Gynecol Oncol. 2016;143:367-370.

20. Stavraka C, Ford A, Ghaem-Maghami S et al. A study of symptoms described by ovarian cancer survivors. Gynecol Oncol. 2012;125:59-64.

21. Hopkins TG, Stavraka C, Gabra H et al. Sexual activity and functioning in ovarian cancer survivors: an internet-based evaluation. Climacteric. 2015;18:94-98.

22. Clevenger L, Schrepf A, Degeest K et al. Sleep disturbance, distress, and quality of life in ovarian cancer patients during the first year after diagnosis. Cancer. 2013;119:3234-3241.

23. Arden-Close E, Gidron Y, Moss-Morris R. Psychological distress and its correlates in ovarian cancer: a systematic review. Psychooncology. 2008;17:1061-1072.

24. Ahmed-Lecheheb D, Joly F. Ovarian cancer survivors' quality of life: a systematic review. J Cancer Surviv. 2016;10:789-801.

25. American Cancer Society. What Are the Key Statistics About Ovarian Cancer? [Internet] Cancer.org. 2017. [Available from: https://www.cancer.org/cancer/ovarian-cancer/about/key-statistics.html. Accessed September 10, 2017.

26. Smits A, Smits E, Lopes A et al. Body mass index, physical activity and quality of life of ovarian cancer survivors: Time to get moving? Gynecol Oncol. 2015;139:148-154.

27. Stevinson C, Steed H, Faught W et al. Physical activity in ovarian cancer survivors: associations with fatigue, sleep, and psychosocial functioning. Int J Gynecol Cancer. 2009;19:73-78.

28. Wenzel LB, Donnelly JP, Fowler JM et al. Resilience, reflection, and residual stress in ovarian cancer survivorship: a gynecologic oncology group study. Psychooncology. 2002;11:142-153.

29. Beesley V, Eakin E, Janda M et al. Gynecological cancer survivors' health behaviors and their associations with quality of life. Cancer Causes Control. 2008;19:775-782.

30. Backes FJ, Nagel CI, Bussewitz E et al. The impact of body weight on ovarian cancer outcomes. Int J Gynecol Cancer. 2011;21:1601-1605.

31. Hess LM, Barakat R, Tian C et al. Weight change during chemotherapy as a potential prognostic factor for stage III epithelial ovarian carcinoma: a Gynecologic Oncology Group study. Gynecol Oncol. 2007;107:260-265.

32. Aust S, Knogler T, Pils D et al. Skeletal Muscle Depletion and Markers for Cancer Cachexia Are Strong Prognostic Factors in Epithelial Ovarian Cancer. PLoS ONE. 2015;10:e0140403.

33. Stevinson C, Faught W, Steed H et al. Associations between physical activity and quality of life in ovarian cancer survivors. Gynecol Oncol. 2007;106:244-250.

34. Nayak P, Vernon SW, Savas LS et al. Functional Impairment and Physical Activity Adherence Among Gynecologic Cancer Survivors: A Population-Based Study. Int J Gynecol Cancer. 2016;26:381-388.

35. Cesari M, Cerullo F, Zamboni V et al. Functional status and mortality in older women with gynecological cancer. J Gerontol A Biol Sci Med Sci. 2013;68:1129-1133

36. Peel AB, Barlow CE, Leonard D et al. Cardiorespiratory Fitness in Survivors of Cervical, Endometrial, and Ovarian Cancer: The Cooper Center Longitudinal Study. Gynecol Oncol. 2015;138:394-397.

37. Schmitz KH, Courneya KS, Matthews C et al. American College of Sports Medicine roundtable on exercise guidelines for cancer survivors. Med Sci Sports Exerc. 2010;42:1409-1426.

38. Brown JC, Winters-Stone K, Lee A et al. Cancer, physical activity, and exercise. Comprehensive Physiology. 2012;2:2775-2809.

39. Fong DYT, Ho JWC, Hui BPH et al. Physical activity for cancer survivors: meta-analysis of randomised controlled trials. BMJ. 2012;344:e70-e70.

40. Caspersen CJ, Powell KE, Christenson GM. Physical activity, exercise, and physical fitness: definitions and distinctions for health-related research. Public Health Rep. 1985;100:126-131.

41. Moonsammy SH, Guglietti CL, Santa Mina D et al. A pilot study of an exercise & cognitive behavioral therapy intervention for epithelial ovarian cancer patients. J Ovarian Res. 2013;6:21-21.

42. Mizrahi D, Broderick C, Friedlander M et al. An Exercise Intervention During Chemotherapy for Women With Recurrent Ovarian Cancer: A Feasibility Study. Int J Gynecol Cancer. 2015;25:985-992.

43. Hwang K-H, Cho O-H, Yoo Y-S. The Effect of Comprehensive Care Program for Ovarian Cancer Survivors. Clin Nurs Res. 2016;25:192-208.

44. Nygaard I, Girts T, Fultz NH et al. Is urinary incontinence a barrier to exercise in women? Obstet Gynecol. 2005;106:307-314.

45. Bø K. Urinary incontinence, pelvic floor dysfunction, exercise and sport. Sports Med. 2004;34:451-464.

46. Kenton K, Mueller ER. The global burden of female pelvic floor disorders. BJU Int. 2006;98 Suppl 1:1-5.

47. Lowenstein L, Pierce K, Pauls R. Urogynecology and sexual function research. How are we doing? J Sex Med. 2009;6:199-204.

48. Skjeldestad FE, Hagen B. Long-term consequences of gynecological cancer treatment on urinary incontinence: a population-based cross-sectional study. Acta Obstet Gynecol Scand. 2008;87:469-475.

49. Rutledge TL, Heckman SR, Qualls C et al. Pelvic floor disorders and sexual function in gynecologic cancer survivors: a cohort study. Am J Obstet Gynecol. 2010;203:514.e511-517.

50. Rutten IJG, van Dijk DPJ, Kruitwagen RFPM et al. Loss of skeletal muscle during neoadjuvant chemotherapy is related to decreased survival in ovarian cancer patients. J Cachexia Sarcopenia Muscle. 2016;7(4):458-466.

51. Mizrahi D, Naumann F, Broderick C et al. Quantifying physical activity and the associated barriers for women with ovarian cancer. Inter J Gynecol Cancer. 2015;25(4):577-583.

52. Donnelly CM, Blaney JM, Lowe-Strong A et al. A randomised controlled trial testing the feasibility and efficacy of a physical activity behavioural change intervention in managing fatigue with gynaecological cancer survivors. Gynecol Oncol. 2011;122(3):618-624.

53. Schofield C, Newton RU, Galvão DA et al. A Physiological Profile of Ovarian Cancer Survivors to Inform Tailored Exercise Interventions and the Development of Exercise Oncology Guidelines. Int J Gynecol Cancer. 2017;27:1560-1567.

# *Chapter 2*

## LITERATURE REVIEW

"A physiological profile of ovarian cancer survivors to inform tailored exercise interventions and the development of exercise oncology guidelines"

**Schofield C**, Newton RU, Galvão DA, Cohen PA, Peddle-McIntyre CJ. International Journal of Gynecological Cancer. 2017;27:1560-1567.

# ABSTRACT

**Objective:** Physical activity has become increasingly important in supportive cancer care. However, physical activity and exercise guidelines for ovarian cancer survivors remain generic. The aim of this narrative review is to summarize existing data regarding the physiological characteristics (treatment-related adverse effects, concurrent comorbidities, body weight and composition, physical fitness and function, and physical activity behavior) of ovarian cancer survivors to further understanding of their cancer-specific physical activity and exercise needs. We also highlight gaps in the current knowledge base.

**Methods:** We undertook a narrative review of current literature on the physiological status of ovarian cancer survivors. We defined physiological status as treatment-related adverse effects, concurrent comorbidities, body weight and composition, physical fitness and function, and physical activity behavior.

**Results:** In addition to disease- and treatment-related symptoms and adverse effects, the majority of ovarian cancer survivors have comorbidities, which may adversely affect treatment effectiveness and safety, as well as survival. Despite high overweight and obesity rates, a large percentage of women are malnourished at diagnosis, with potentially compromised muscle mass and muscle density. Low muscle density at diagnosis and loss of muscle mass during treatment may be associated with worse survival outcomes. A small number of studies have observed impaired physical function and cardiorespiratory fitness in ovarian cancer survivors. The majority of ovarian cancer survivors are insufficiently active or sedentary.

**Conclusion:** Our review suggests that ovarian cancer survivors could benefit from physical activity and exercise oncology interventions aimed at addressing detrimental changes to physiological status due to disease and treatment. However, current knowledge gaps regarding the physiological characteristics of ovarian cancer survivors throughout the entire survivorship spectrum challenges the development of tailored exercise intervention studies and exercise oncology guidelines.



**Key Words:** Ovarian cancer, Comorbidities, Body composition, Physical fitness, Physical activity

# INTRODUCTION

Ovarian cancer (OC) is the seventh most common cancer in women worldwide and the most lethal gynecological malignancy, with an estimated 255,660 new cases and 163,765 deaths in 2015.[1] Due to lack of effective screening tests and the non-specific nature of symptoms, 70-75% of women with OC receive the diagnosis at an advanced stage (stages III-IV).[2] Standard treatment for OC involves either primary surgery followed by adjuvant paclitaxel-carboplatin combination chemotherapy, or neoadjuvant chemotherapy with interval debulking surgery.[3] Although most women initially respond well to treatment, recurrence rates are high, with 70% of advanced-stage OCs and up to 30% of early-stage OCs eventually relapsing and requiring further treatment.[4, 5] The aim of treatment after recurrence is to control the disease and disease-related symptoms, limit treatment toxicities and prolong time to disease progression and death, whilst optimizing quality of life.[2] Identifying appropriate, targeted adjuvant interventions to reduce symptom-burden and minimize functional decline and disability are crucial in the ongoing care of OC survivors.

Physical activity is defined as "any bodily movement produced by skeletal muscles that results in energy expenditure." Exercise as a subset of physical activity refers to planned, structured and repetitive activity with the purpose to improve or maintain physical fitness and health.[6] Physical activity is important in the management of many chronic conditions and the prescription of exercise as "medicine" should be integral in the treatment of chronic diseases such as cancer.[7] The term "cancer survivor" is based on the National Comprehensive Cancer Network definition and refers to people living with cancer, from the time of diagnosis, through all disease stages, until death.[8] Higher physical activity levels in cancer survivors have been associated with reduced disease and treatment adverse effects, increased physical and emotional well-being,[9] as well as reduced risk of recurrence, cancer-specific and all-cause mortality in certain cancer groups.[10, 11] Since the American College of Sports Medicine published initial guidelines and recommendations for exercise oncology[12] other professional and cancer organizations (e.g. American Cancer Society, National Comprehensive Cancer Network) have endorsed the concept that cancer survivors should avoid

physical inactivity and, if possible, undertake 150 minutes of aerobic exercise a week and twice-weekly resistance exercises (REs).[13] However, most of these recommendations have been based on research over the past 2 decades involving primarily breast and prostate cancer survivors. As a result, there is a logical and clinical requirement to understand and identify gaps in knowledge, particularly for understudied cancers such as OC.[14] Research to help tailor physical activity guidelines and exercise interventions to specific cancer groups is crucial to maximize the impact of physical activity and exercise interventions in clinical and research settings and to further advance the field of exercise oncology.

The purpose of this review is to synthesize published literature on treatment-related adverse effects, concurrent comorbidities, body weight and composition, physical function and fitness, and physical activity behavior of OC survivors to provide a more complete physiological profile of this cancer group. A secondary aim is to highlight key gaps in knowledge to inform future research. Improved knowledge of the multifaceted challenges faced by OC survivors will support the development of exercise oncology recommendations specifically for OC survivors. In addition, it will provide a scientific basis for the design and application of tailored exercise interventions in both research and clinical settings (Fig 1).

## METHODS

Information for this review was obtained by searching the PubMed, Medline, CINAHL and SPORTDiscus databases for relevant articles in English published between January 1970 and December 2016 pertaining to treatment-related adverse effects, comorbid conditions, body weight, body composition, physical function and fitness, and exercise and physical activity levels in OC survivors. Search terms included “OC,” “ovarian neoplasms,” “treatment” (side-effects, symptoms), “comorbidities,” “BMI,” “body composition,” “physical fitness” (muscular strength, muscular endurance, cardiorespiratory fitness, cardiovascular fitness), “physical function” (grip strength, gait speed, walking speed, mobility, balance), and “physical activity” (physical activity behavior, habits, participation, levels, exercise). Reference lists of relevant papers were also searched. Review

articles, randomized controlled trials, cross-sectional studies and observational cohort studies published in peer-reviewed journals as full-text articles were reviewed by CS. Abstracts, case reports, editorials and study protocols were excluded.

# RESULTS

## Treatment-related Adverse Effects

The cumulative adverse effects of surgery, chemotherapy, and targeted therapy can have a debilitating impact on the lives of OC survivors, both during and following treatment.[15]

Acute adverse effects commonly reported during OC treatment include fatigue, pain, appetite loss, constipation, diarrhea, nausea, vomiting and dyspnea. Abdominal discomfort (pain, bloating, cramping and indigestion), insomnia, neuropathy, sexual dysfunction, weight gain, and weight loss are also common.[16] Women with advanced stage or recurrent OC who are treated with bevacizumab in addition to chemotherapy can experience hypertension, proteinuria, wound-healing complications, thrombotic events, and gastrointestinal perforation.[17, 18]

Chronic adverse effects continue to affect at least 20% of disease-free OC survivors regardless of stage of disease.[19-21] Fatigue is the most prevalent physical burden for women with active disease.[22] Poor sleep quality, chemotherapy-related cognitive impairment and peripheral neuropathy affect 60% to 70% of survivors of stages I to IV OC at least 1 year after diagnosis.[23-25] Gastrointestinal issues such as constipation, diarrhea, indigestion and flatulence remain burdensome in 16% to 47% of OC survivors years after treatment completion.[24, 25] The majority of survivors report no sexual activity 3 years or more after treatment completion,[26, 27] and more than 70% of women who remain sexually active experience sexual discomfort.[26] Although sexual and gastrointestinal dysfunction in this group of cancer survivors is well documented, data regarding the prevalence, severity and impact of pelvic floor dysfunction are limited. Such data are crucial for the design of OC-specific exercise interventions.

About 20% of all OC survivors will experience anxiety and depression at some point in their cancer trajectory.[28] Fear of recurrence is a major cause of psychological distress for survivors of all ages, irrespective of disease stage or treatment received.[29] Depressive symptoms are strongly correlated to physical symptoms, fatigue, poor sleep quality, physical function and quality of life.[23, 30, 31] More research is needed to determine if, and how, these physical and psychological symptoms and adverse effects change over time and whether differences are treatment related (eg, neoadjuvant vs adjuvant chemotherapy).

## Concurrent Comorbidities

Cancer survivors are more likely to have multiple chronic medical conditions than age-matched control subjects.[32] Although prevalence rates vary, hypertension, arthritis, hypercholesterolemia, thyroid disorders and musculoskeletal issues are commonly reported in OC survivors.[20-22, 24, 33-35] Approximately 75% of OC survivors self-reported 1 or more comorbidities in separate cross-sectional survey studies.[21, 34, 36] By contrast, 1 or more comorbidities were identified in only 25% of survivors when information from cancer registries was used.[37] This discordance may be due to response bias and/or ascertainment bias, which are inherent in such studies. The prevalence of comorbidities does not appear to differ significantly between survivors of early- and advanced-stage OC,[38] although obese survivors are more likely to have comorbidities.[39] Research suggests that women with comorbidities are less likely to receive standard cytoreductive surgery and/or combination chemotherapy,[40] and have poorer survival outcomes.[41] Thus, knowledge about the status and severity of concurrent comorbidities throughout the survivorship spectrum, as well as a better understanding of the impact of concurrent medications on OC treatment and treatment toxicity, is crucial, especially in light of the confirmed benefit of exercise to manage chronic conditions.[7]

## Body Weight

Obesity (as indicated by a body mass index [BMI] of ≥30 kg/m²) is associated with a higher risk of recurrence and mortality in many cancer groups.[42] Obesity rates in OC range between 15% and 30%,[36, 43-47] however, findings on the impact of obesity on OC prognosis have been inconsistent. A systematic review and meta-analysis by Bae et al[48] found no association between BMI at time of diagnosis and survival. In contrast, a recent meta-analysis, which included 12,390 OC survivors from 21 studies, concluded that obesity at or before diagnosis negatively affects survival in low-grade serous, endometrioid and high-grade serous OCs, but not in clear-cell or mucinous cancers.[49] This may reflect the heterogeneity of studies in these meta-analyses. While the impact of obesity on survival after an OC diagnosis has not been fully elucidated,[48, 50] increased BMI may adversely affect treatment effectiveness and safety. Obese women are more likely to experience suboptimal chemotherapy dosing, postsurgical complications[50] and hospital readmissions.[51] Complications that delay or disrupt adjuvant chemotherapy treatment may have a negative impact on quality of life, and potentially survival.[50] The adverse effects of obesity on treatment outcomes and possibly survival warrants further investigation. For example, studies investigating the impact of increased physical activity or participation in structured and regular exercise interventions on BMI after an OC diagnosis are needed.

While several studies have addressed the impact of obesity on OC outcomes, information about the prevalence and impact of weight loss during the disease trajectory, and underweight status (as indicated by a BMI <18.5 kg/m²) is limited. Data suggest that 40% to 60% of women with advanced-stage OC lose weight during adjuvant chemotherapy.[45, 52] However, the relationship between weight loss during treatment and changes in body composition has yet to be elucidated. In addition, how weight loss impacts treatment and whether weight loss continues after completion of treatment remains unclear. Low rates of underweight women (2%-9%) have been reported across all disease stages,[53-56] and conclusions regarding the impact of underweight status on survival are conflicting. Separate studies associate BMI of less than 18.5 kg/m² at diagnosis in all disease

stages,[55] and after treatment completion in advanced stage,[53] with increased mortality. Conversely, a recent meta-analysis found no association between underweight status and disease stage or survival, but concluded that more data are needed to confirm this finding.[56] More research is needed to delineate the impact of overweight or underweight status, as well as weight change in all disease stages throughout the survivorship spectrum.

The relationship between OC survivors' body weight and nutritional status is complex. While less than 10% of women are underweight,[56] 30% to 67% are malnourished at diagnosis, based on nutrition assessment tools such as the Patient-Generated Subjective Global Assessment and the Nutritional Risk Index.[44, 52, 57, 58] The presence of ascites and a high body fat percentage at any time point will "inflate" BMI values and mask muscle wasting, a consequence of malnourishment.[59] In addition to BMI, body composition measures can provide much needed objective data to identify OC survivors with low muscle mass and/or excess body fat in need of dietary and exercise interventions.

## Body Composition

Low muscle mass may be associated with increased treatment toxicity and mortality in cancer survivors.[60] To date only a small number of studies have examined body composition and muscle quality in OC survivors. Low muscle mass, indicated by a skeletal muscle index below 39.0 $cm^2/m^2$, was observed in 45% of a large cohort of women with newly diagnosed advanced-stage OC.[61] The skeletal muscle index was calculated by dividing skeletal muscle area (in centimeters squared), measured preoperatively with computed tomography at the level of the third lumbar vertebra, by the height squared (in meters squared). However, current data do not confirm an association between low muscle mass at diagnosis and OC survival.[46, 59, 61] An important finding by Rutten et al.[59] is the association of skeletal muscle loss during neoadjuvant chemotherapy with decreased survival, although this finding requires further confirmation.

Recent evidence suggests that muscle density, more so than muscle mass, could be an important prognostic factor in OC. Preliminary evidence indicates a positive association between skeletal muscle attenuation (a measure of muscle density, with lower values indicating a higher muscle fat content) and survival in certain cancer groups.[62] Low skeletal muscle attenuation at diagnosis was associated with decreased overall survival in 2 separate OC studies.[46, 61] The findings of these retrospective studies require validation in future randomized controlled trials.

In addition to potential changes in muscle and fat content, OC survivors may experience alterations in bone mineral density. However, the prevalence of osteopenia and osteoporosis are seldom reported in OC studies. Although bone loss has been observed in pre- and postmenopausal OC survivors in the first year after diagnosis,[63-65] these studies included gynecological cancer survivors with only small samples of OC survivors (n = 30, 15 and 12, respectively). Given that bone-related comorbidities (eg, osteoporosis) could have a significant impact on exercise prescription, more research is needed to understand the prevalence of, and changes in, bone mineral density throughout the OC trajectory.

## Physical Fitness and Function

Physical fitness is historically defined as "the ability to carry out daily tasks with vigor and alertness, without undue fatigue." The term encompasses several measurable components, including cardiorespiratory capacity and endurance, muscular strength and endurance, body composition, and flexibility,[6] all of which potentially affect physical function in cancer survivors.[66] Information regarding OC survivors' cardiorespiratory and muscular fitness is lacking, with only a limited number of nonrandomized exercise intervention studies reporting these measures.[67, 68] Data from a small cross-sectional study suggest impaired cardiorespiratory fitness in gynecological cancer survivors many years after diagnosis, when compared with age-matched control subjects.[69] This finding is important considering the strong inverse association between cardiorespiratory fitness and cancer mortality, independent of adiposity level.[70]

Impairments in physical function predict disability, institutionalization and mortality in older people[71] and may predict mortality in cancer survivors.[72] Research regarding physical function in OC survivors is limited and mostly measures self-reported physical function with quality-of-life instruments. Only 10% of a small sample of long-term survivors of stages III to IV OC without evidence of recurrent disease reported functional limitations.[19] In contrast, impaired physical function was reported by 38% of more than 5000 gynecological cancer survivors, which included 922 OC survivors, at least one year since diagnosis. Participants were considered functionally impaired if they responded "yes" to 1 or both questions regarding limitations in activities and use of special equipment due to health problems.[73] Self-rated functional impairment in OC survivors is associated with lower physical activity levels,[36, 73] older age,[15] obesity,[36] comorbidities, fatigue,[74] peripheral neuropathy,[35] and increased psychological distress.[75] Physical function has seldom been objectively measured in OC research. One study found an association between physical function, measured objectively using the Short Physical Performance Battery and usual gait speed, and mortality in a mixed sample of older gynecological cancer survivors,[76] indicating a need for more quantitative data regarding physical function in OC survivors.

Considering evidence from other cancer groups such as breast and prostate cancer,[12] exercise interventions are likely to be an effective strategy to improve physical fitness and function in OC survivors. However, such strategies need to be tested in OC survivors in adequately powered prospective, controlled clinical trials.

## Physical Activity Participation

Ovarian cancer survivors' physical activity participation rates are low. In comparison to 27% of women and 35% of women in high-income countries, worldwide,[77] 50% to 80 % of OC survivors reported insufficient physical activity levels (ie, <150 minutes of moderate and vigorous physical activity per week) or a sedentary lifestyle (ie, no moderate and vigorous physical activity per week) after treatment completion.[34, 36, 43, 73] Research suggests that most women decrease

physical activity levels after diagnosis,[78] and many do not return to pre-diagnosis levels.[79] Interestingly, OC survivors' participation rates in RE (ie, exercise that involves performing sets of repeated movements against a resistance, such as lifting weights)[80] have not been previously reported. However, considering research in other cancer survivor populations, where participation in sufficient RE (ie, ≥ 2 sessions/wk for ≥ 30 minutes) is only 10%,[81] participation is likely to be low. Information regarding OC survivors' participation rates in RE and the feasibility of RE programs is important, especially considering the positive effects of RE on muscular strength and body composition in cancer survivors.[82]

Higher levels of physical activity after a cancer diagnosis are associated with a reduced risk of cancer-specific and all-cause mortality in breast, colorectal and prostate cancer.[10, 11] The association between physical activity after an OC diagnosis and mortality remains unclear, although prediagnostic physical activity appears to affect survival in this cancer group.[83] Ovarian cancer survivors who report being more physically active have reduced symptom burden, improved physical fitness and function, and a better quality of life.[34, 36, 67, 68, 84] However, most studies investigating physical activity in OC survivors are cross-sectional in design, which precludes inferring conclusions about causality and indicates a need for future prospective randomized controlled trials. In addition, limitations of self-reported physical activity, such as overreporting,[85] must be considered when interpreting the results of these studies. Objective assessment of physical activity should be included in future studies to provide more comprehensive, valid, and reliable data about physical activity participation and patterns of sedentary behavior.

Ovarian cancer survivors often express interest in participating in physical activity programs,[86, 87] but frequently report a combination of demographic, medical and motivational barriers to physical activity and exercise participation.[78] Demographic and medical barriers include older age, higher BMI, shorter time since diagnosis, or current disease.[88] The most commonly reported barriers to exercise are fatigue (37.8%), exercise not being part of usual routine (34.7%), and lack of self-discipline (32.6%).[78]

## SUMMARY AND AREAS FOR FUTURE RESEARCH

Women with a diagnosis of OC often experience a range of physical and psychological symptoms and adverse effects during and after cancer treatment, regardless of disease stage. In addition, about 75% of women have self-reported comorbidities,[21, 34, 36] and 15% to 30% are obese,[36, 43-47] both of which may adversely affect treatment and survival. Despite high overweight and obesity rates, a large percentage of women are malnourished at diagnosis, with potentially compromised muscle mass and muscle density. This is particularly important in OC survivors because low muscle density at diagnosis and loss of muscle mass during treatment may be associated with worse survival outcomes. A small number of studies have observed impaired physical function and cardiorespiratory fitness in OC survivors. Despite high levels of interest in physical activity programs, and some evidence for an association between physical activity and physical well-being, 50% to 80% of OC survivors are insufficiently active or sedentary because of numerous demographic, medical and behavioral barriers.[34, 36, 43, 73] Because of a current lack of scientific knowledge, physical activity and prescription of regular and structured exercise might not be optimally promoted by the OC care team.

The greatest challenge for the design and application of evidence-based exercise oncology guidelines in OC care is the heterogeneity of existing studies. To date, most studies have included women with all stages and grades of cancer, often on different treatment regimens and at different time points in the cancer trajectory. Furthermore, the majority of studies reporting on comorbidities, body weight and body composition, physical fitness and function, and physical activity habits are cross-sectional or retrospective in nature, and do not provide information on changes in physiological status of OC survivors over the course of the cancer trajectory. A further challenge is the notable lack of objectively measured data describing physical activity behavior, physical fitness and physical function.

Future research should aim to provide evidence-based objective information describing the physiological characteristics of OC survivors throughout the entire survivorship spectrum, with

careful consideration of potential differences due to disease stage, treatment regime or survivorship stage. Such information will provide a better understanding of the impact of OC and its treatment and will empirically inform the design and application of OC-specific exercise oncology guidelines, thus maximizing the potential impact of exercise medicine in both clinical and research settings.

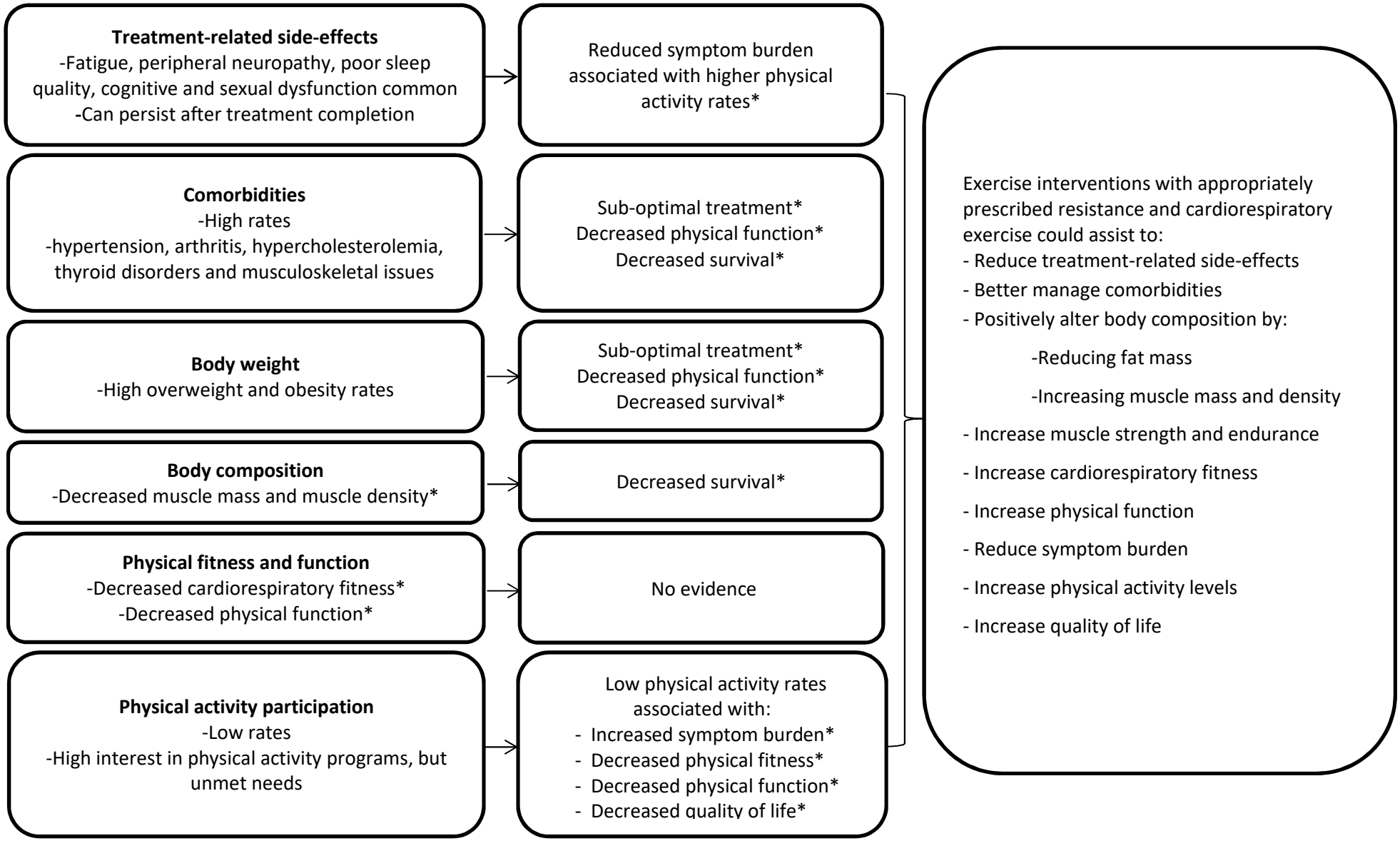


**Figure 1. Opportunities for exercise oncology interventions in OC care based on current evidence**
(* limited data) Physical activity refers to minutes of moderate and vigorous exercise/week.

# REFERENCES


1. Ferlay J, Soerjomataram I, Ervik M, et al. *GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11* [Internet]. Lyon, France: International Agency for Research on Cancer; 2013. Available from: http://globocan.iarc.fr, accessed on 20/9/2016.
2. Herzog TJ. Recurrent ovarian cancer: how important is it to treat to disease progression? Clin Cancer Res. 2004;10:7439-7449.
3. Goh J, Mohan GR, Ladwa R, et al. Frontline treatment of epithelial ovarian cancer. Asia Pac J Clin Oncol. 2015;11(suppl 6):1-16.
4. Ushijima K. Treatment for recurrent ovarian cancer-at first relapse. J Oncol. 2010;2010: 497429.
5. Lawrie TA, Winter-Roach BA, Heus P, et al. Adjuvant (post-surgery) chemotherapy for early stage epithelial ovarian cancer. Cochrane Database Syst Rev. 2015:CD004706.
6. Caspersen CJ, Powell KE, Christenson GM. Physical activity, exercise, and physical fitness: definitions and distinctions for health-related research. Public Health Rep. 1985;100:126-131.
7. Pedersen BK, Saltin B. Exercise as medicine - evidence for prescribing exercise as therapy in 26 different chronic diseases. Scand J Med Sci Sports. 2015;25:1-72.
8. Denlinger CS, Carlson RW, Are M, et al. Survivorship: introduction and definition. Clinical practice guidelines in oncology. J Natl Compr Canc Netw. 2014;12:34-45.
9. Speck RM, Courneya KS, Mâsse LC, et al. An update of controlled physical activity trials in cancer survivors: a systematic review and meta-analysis. J Cancer Surviv. 2010;4:87-100.
10. Schmid D, Leitzmann MF. Association between physical activity and mortality among breast cancer and colorectal cancer survivors: a systematic review and meta-analysis. Ann Oncol. 2014;25:1293-1311.
11. Friedenreich CM, Wang Q, Neilson HK, et al. Physical Activity and Survival After Prostate Cancer. Eur Urol. 2016;70:576-585.
12. Schmitz KH, Courneya KS, Matthews C, et al. American College of Sports Medicine roundtable on exercise guidelines for cancer survivors. Med Sci Sports Exerc. 2010;42:1409-1426.

13. Rock CL, Doyle C, Demark-Wahnefried W, et al. Nutrition and physical activity guidelines for cancer survivors. CA Cancer J Clin. 2012;62:242-274.

14. Buffart LM, Galvão DA, Brug J, et al. Evidence-based physical activity guidelines for cancer survivors: current guidelines, knowledge gaps and future research directions. Cancer Treat Rev. 2014;40:327-340.

15. Ahmed-Lecheheb D, Joly F. Ovarian cancer survivors' quality of life: a systematic review. J Cancer Surviv. 2016;10:789-801.

16. Donovan KA, Donovan HS, Cella D, et al. Recommended patient-reported core set of symptoms and quality-of-life domains to measure in ovarian cancer treatment trials. J Natl Cancer Inst. 2014;106.

17. Liang XJ, Shen J. Adverse events risk associated with angiogenesis inhibitors addition to therapy in ovarian cancer: a meta-analysis of randomized controlled trials. Eur Rev Med Pharmacol Sci. 2016;20:2701-2709.

18. Li X, Zhu S, Hong C, et al. Angiogenesis inhibitors for patients with ovarian cancer: a meta-analysis of 12 randomized controlled trials. Curr Med Res Opin. 2016;32:555-562.

19. Kornblith AB, Mirabeau-Beale K, Lee H, et al. Long-term adjustment of survivors of ovarian cancer treated for advanced-stage disease. J Psychosoc Oncol. 2010;28:451-469.

20. Matulonis UA, Kornblith A, Lee H, et al. Long-term adjustment of early-stage ovarian cancer survivors. Int J Gynecol Cancer. 2008;18:1183-1193.

21. Wenzel LB, Donnelly JP, Fowler JM, et al. Resilience, reflection, and residual stress in ovarian cancer survivorship: a gynecologic oncology group study. Psychooncology. 2002;11:142-153.

22. Hay CM, Courtney-Brooks M, Lefkowits C, et al. Symptom management in women with recurrent ovarian cancer: Do patients and clinicians agree on what symptoms are most important? Gynecol Oncol. 2016;143:367-370.

23. Clevenger L, Schrepf A, Degeest K, et al. Sleep disturbance, distress, and quality of life in ovarian cancer patients during the first year after diagnosis. Cancer. 2013;119:3234-3241.

24. Stavraka C, Ford A, Ghaem-Maghami S, et al. A study of symptoms described by ovarian cancer survivors. Gynecol Oncol. 2012;125:59-64.

25. Grover S, Hill-Kayser CE, Vachani C, et al. Patient reported late effects of gynecological cancer treatment. Gynecol Oncol. 2012;124:399-403.

26. Hopkins TG, Stavraka C, Gabra H, et al. Sexual activity and functioning in ovarian cancer survivors: an internet-based evaluation. Climacteric. 2015;18:94-98.

27. Liavaag AH, Dørum A, Bjøro T, et al. A controlled study of sexual activity and functioning in epithelial ovarian cancer survivors. A therapeutic approach. Gynecol Oncol. 2008;108:348-354.

28. Watts S, Prescott P, Mason J, et al. Depression and anxiety in ovarian cancer: a systematic review and meta-analysis of prevalence rates. BMJ Open. 2015;5:e007618.

29. Ozga M, Aghajanian C, Myers-Virtue S, et al. A systematic review of ovarian cancer and fear of recurrence. Palliat Support Care. 2015;13:1771-1780.

30. Roland KB, Rodriguez JL, Patterson JR, et al. A literature review of the social and psychological needs of ovarian cancer survivors. Psychooncology. 2013;22:2408-2418.

31. Arden-Close E, Gidron Y, Moss-Morris R. Psychological distress and its correlates in ovarian cancer: a systematic review. Psychooncology. 2008;17:1061-1072.

32. Hewitt M, Rowland JH, Yancik R. Cancer survivors in the United States: age, health, and disability. J Gerontol A Biol Sci Med Sci. 2003;58:82-91.

33. Sandadi S, Frasure HE, Broderick MJ, et al. The effect of sleep disturbance on quality of life in women with ovarian cancer. Gynecol Oncol. 2011;123:351-355.

34. Stevinson C, Steed H, Faught W, et al. Physical activity in ovarian cancer survivors: associations with fatigue, sleep, and psychosocial functioning. Int J Gynecol Cancer. 2009;19:73-78.

35. Ezendam NPM, Pijlman B, Bhugwandass C, et al. Chemotherapy-induced peripheral neuropathy and its impact on health-related quality of life among ovarian cancer survivors: results from the population-based PROFILES registry. Gynecol Oncol. 2014;135:510-517.

36. Smits A, Smits E, Lopes A, et al. Body mass index, physical activity and quality of life of ovarian cancer survivors: Time to get moving? Gynecol Oncol. 2015;139:148-154.

37. O'Malley CD, Shema SJ, Cress RD, et al. The implications of age and comorbidity on survival following epithelial ovarian cancer: summary and results from a Centers for Disease Control and Prevention study. J Womens Health. 2012;21:887-894.

38. Mirabeau-Beale KL, Kornblith AB, Penson RT, et al. Comparison of the quality of life of early and advanced stage ovarian cancer survivors. Gynecol Oncol. 2009;114:353-359.

39. Suh DH, Kim HS, Chung HH, et al. Body mass index and survival in patients with epithelial ovarian cancer. J Obstet Gynaecol Res. 2012;38:70-76

40. Jørgensen TL, Teiblum S, Paludan M, et al. Significance of age and comorbidity on treatment modality, treatment adherence, and prognosis in elderly ovarian cancer patients. Gynecol Oncol. 2012;127:367-374.

41. Jiao Y-S, Gong T-T, Wang Y-L, et al. Comorbidity and survival among women with ovarian cancer: evidence from prospective studies. Sci Rep. 2015;5:11720.

42. Ligibel JA, Alfano CM, Courneya KS, et al. American Society of Clinical Oncology position statement on obesity and cancer. J Clin Oncol. 2014;32:3568-3574.

43. Beesley V, Eakin E, Janda M, et al. Gynecological cancer survivors' health behaviors and their associations with quality of life. Cancer Causes Control. 2008;19:775-782.

44. Backes FJ, Nagel CI, Bussewitz E, et al. The impact of body weight on ovarian cancer outcomes. Int J Gynecol Cancer. 2011;21:1601-1605.

45. Hess LM, Barakat R, Tian C, et al. Weight change during chemotherapy as a potential prognostic factor for stage III epithelial ovarian carcinoma: a Gynecologic Oncology Group study. Gynecol Oncol. 2007;107:260-265.

46. Aust S, Knogler T, Pils D, et al. Skeletal Muscle Depletion and Markers for Cancer Cachexia Are Strong Prognostic Factors in Epithelial Ovarian Cancer. PLoS ONE. 2015;10:e0140403.

47. Stevinson C, Faught W, Steed H, et al. Associations between physical activity and quality of life in ovarian cancer survivors. Gynecol Oncol. 2007;106:244-250.

48. Bae HS, Kim HJ, Hong JH, et al. Obesity and epithelial ovarian cancer survival: a systematic review and meta-analysis. J Ovarian Res. 2014;7:1-8.

49. Nagle CM, Dixon SC, Jensen A, et al. Obesity and survival among women with ovarian cancer: results from the Ovarian Cancer Association Consortium. Br J Cancer. 2015;113:817-826.

50. Purcell SA, Elliott SA, Kroenke CH, et al. Impact of Body Weight and Body Composition on Ovarian Cancer Prognosis. Curr Oncol Rep. 2016;18:1-11.

51. Duska LR, Java JJ, Cohn DE, et al. Risk factors for readmission in patients with ovarian, fallopian tube, and primary peritoneal carcinoma who are receiving front-line chemotherapy on a clinical trial (GOG 218): an NRG oncology/gynecologic oncology group study (ADS-1236). Gynecol Oncol. 2015;139:221-227.

52. Yim GW, Eoh KJ, Kim SW, et al. Malnutrition Identified by the Nutritional Risk Index and Poor Prognosis in Advanced Epithelial Ovarian Carcinoma. Nutr Cancer. 2016;68:772-779.

53. Kim SI, Kim HS, Kim TH, et al. Impact of underweight after treatment on prognosis of advanced-stage ovarian cancer. J Immunol Res. 2014;2014:349546.

54. Zhou Y, Chlebowski R, Lamonte MJ, et al. Body mass index, physical activity, and mortality in women diagnosed with ovarian cancer: Results from the Women's Health Initiative. Gynecol Oncol. 2014;133:4-10.

55. Ørskov M, Iachina M, Guldberg R, et al. Predictors of mortality within 1 year after primary ovarian cancer surgery: a nationwide cohort study. BMJ Open. 2016;6:e010123.

56. Pergialiotis V, Doumouchtsis SK, Perrea D, et al. The Impact of Underweight Status on the Prognosis of Ovarian Cancer Patients: A Meta-Analysis. Nutr Cancer. 2016;68:918-925.

57. Laky B, Janda M, Bauer J, et al. Malnutrition among gynaecological cancer patients. Eur J Clin Nutr. 2007;61:642-646

58. Mardas M, Jamka M, Mdry R, et al. Dietary habits changes and quality of life in patients undergoing chemotherapy for epithelial ovarian cancer. Support Care Cancer. 2015;23:1015-1023

59. Rutten IJG, van Dijk DPJ, Kruitwagen RFPM, et al. Loss of skeletal muscle during neoadjuvant chemotherapy is related to decreased survival in ovarian cancer patients. J Cachexia Sarcopenia Muscle. 2016;7:458-466.

60. Rier HN, Jager A, Sleijfer S, et al. The Prevalence and Prognostic Value of Low Muscle Mass in Cancer Patients: A Review of the Literature. Oncologist. 2016;21:1396-1409.

61. Kumar A, Moynagh MR, Multinu F, et al. Muscle composition measured by CT scan is a measurable predictor of overall survival in advanced ovarian cancer. Gynecol Oncol. 2016;142:311-316.

62. Aubrey J, Esfandiari N, Baracos VE, et al. Measurement of skeletal muscle radiation attenuation and basis of its biological variation. Acta Physiol (Oxf). 2014;210:489-497.

63. Hui SK, Khalil A, Zhang Y, et al. Longitudinal assessment of bone loss from diagnostic computed tomography scans in gynecologic cancer patients treated with chemotherapy and radiation. Am J Obstet Gynecol. 2010;203:353e1-353e7.

64. Nishio K, Tanabe A, Maruoka R, et al. Bone mineral loss induced by anticancer treatment for gynecological malignancies in premenopausal women. Endocr Connect. 2012;2:11-17.

65. Lee SW, Yeo SG, Oh I-H, et al. Bone mineral density in women treated for various types of gynecological cancer. Asia Pac J Clin Oncol. 2016;12:e398-e404.

66. Bennett JA, Winters-Stone K, Nail L. Conceptualizing and measuring physical functioning in cancer survivorship studies. Oncol Nurs Forum. 2006;33:41-49.

67. Hwang K-H, Cho O-H, Yoo Y-S. The Effect of Comprehensive Care Program for Ovarian Cancer Survivors. Clin Nurs Res. 2016;25:192-208.

68. Mizrahi D, Broderick C, Friedlander M, et al. An Exercise Intervention During Chemotherapy for Women With Recurrent Ovarian Cancer: A Feasibility Study. Int J Gynecol Cancer. 2015;25:985-992.

69. Peel AB, Barlow CE, Leonard D, et al. Cardiorespiratory Fitness in Survivors of Cervical, Endometrial, and Ovarian Cancer: The Cooper Center Longitudinal Study. Gynecol Oncol. 2015;138:394-397.

70. Schmid D, Leitzmann MF. Cardiorespiratory fitness as predictor of cancer mortality: a systematic review and meta-analysis. Ann Oncol. 2015;26:272-278.

71. Guralnik JM, Ferrucci L, Pieper CF, et al. Lower extremity function and subsequent disability: consistency across studies, predictive models, and value of gait speed alone compared with the short physical performance battery. J Gerontol A Biol Sci Med Sci. 2000;55A:M221-M231.

72. Brown JC, Harhay MO, Harhay MN. Physical function as a prognostic biomarker among cancer survivors. Br J Cancer. 2015;112:194-198.

73. Nayak P, Vernon SW, Savas LS, et al. Functional Impairment and Physical Activity Adherence Among Gynecologic Cancer Survivors: A Population-Based Study. Int J Gynecol Cancer. 2016;26:381-388.

74. Campbell G, Hagan T, Gilbertson-White S, et al. Cancer and treatment-related symptoms are associated with mobility disability in women with ovarian cancer: A cross-sectional study. Gynecol Oncol. 2016;143:578-583.

75. Ploos van Amstel FK, van Ham MAPC, Peters EJ, et al. Self-reported distress in patients with ovarian cancer: is it related to disease status? Int J Gynecol Cancer. 2015;25:229-235.

76. Cesari M, Cerullo F, Zamboni V, et al. Functional status and mortality in older women with gynecological cancer. J Gerontol A Biol Sci Med Sci. 2013;68:1129-1133

77. World Health Organization. Physical Activity [Internet]. Geneva: World Health Organization Available from: http://www.who.int/mediacentre/factsheets/fs385/en/. Accessed on 30 March 2017.

78. Mizrahi D, Naumann F, Broderick C, et al. Quantifying physical activity and the associated barriers for women with ovarian cancer. Inter J Gynecol Cancer. 2015;25:577-583.

79. Beesley V, Price M, Butow P, et al. Physical activity in women with ovarian cancer and its association with decreased distress and improved quality of life. Psychooncology. 2011;20:1161-1169.

80. Newton RU, Galvão DA. Exercise in prevention and management of cancer. Curr Treat Options Oncol. 2008;9:135-146.

81. Forbes CC, Blanchard CM, Mummery WK, et al. Prevalence and correlates of strength exercise among breast, prostate, and colorectal cancer survivors. Oncol Nurs Forum. 2015;42:118-127.

82. Strasser B, Steindorf K, Wiskemann J, et al. Impact of resistance training in cancer survivors: a meta-analysis. Med Sci Sports Exerc. 2013;45:2080-2090.

83. Cannioto RA, LaMonte MJ, Kelemen LE, et al. Recreational physical inactivity and mortality in women with invasive epithelial ovarian cancer: evidence from the Ovarian Cancer Association Consortium. Br J Cancer. 2016;115:95-101.

84. Newton MJ, Hayes SC, Janda M, et al. Safety, feasibility and effects of an individualised walking intervention for women undergoing chemotherapy for ovarian cancer: a pilot study. BMC Cancer. 2011;11:389.

85. Sallis JF, Saelens BE. Assessment of physical activity by self-report: status, limitations, and future directions. Res Q Exerc Sport. 2000;71(suppl 2):1-14.

86. Stevinson C, Capstick V, Schepansky A, et al. Physical activity preferences of ovarian cancer survivors. Psychooncology. 2009;18:422-428.

87. Farrokhzadi L, Dhillon HM, Goumas C, et al. Physical Activity Correlates, Barriers, and Preferences for Women With Gynecological Cancer. Int J Gynecol Cancer. 2016;26:1530-1537.

88. Stevinson C, Tonkin K, Capstick V, et al. A population-based study of the determinants of physical activity in ovarian cancer survivors. J Phys Act Health. 2009;6:339-346.

# *Chapter 3*

## OBSERVATIONAL STUDY

"Activity behaviors and physiological characteristics of women with advanced-stage ovarian cancer: a comprehensive cross-sectional investigation"

**Schofield C**, Newton RU, Galvão DA, Cohen PA, McVeigh JA, Hart NH, Mohan GR, Tan J, Salfinger SG, Straker LM, Peddle-McIntyre CJ. International Journal of Gynecological Cancer. Under review.

# ABSTRACT

**Objectives:** Ovarian cancer survivors (OCS) experience many disease and treatment adverse effects. Yet, the impact of ovarian cancer and its treatment on objective activity behaviors and physiological status has not been comprehensively examined. The purpose of this study was to compare objectively measured activity behaviors and physiological characteristics of advanced-stage OCS to age-matched controls. Secondarily, OCS who underwent different treatment regimens were compared.

**Methods:** Twenty stage III-IV OCS and 20 controls completed assessments of activity behaviors (7-day accelerometry), physical function (400-meter walk as indicator of cardiorespiratory fitness, repeated chair rise, 6-meter walking tests), muscle strength (1-repetition maximum and hand grip), body composition (dual-energy x-ray absorptiometry) and musculoskeletal morphology (peripheral quantitative computed tomography).

**Results:** Compared to controls, OCS spent more time/day in prolonged sedentary bouts ($p = 0.039$), had lower cardiorespiratory fitness ($p = 0.041$) and upper body strength ($p = 0.023$), had higher areal bone mineral content ($p = 0.047$) and volumetric trabecular density ($p = 0.048$), but were not different in other measures of body composition, nor in muscle morphology (p-values $> 0.050$). Appendicular lean mass was significantly higher for women who received neoadjuvant chemotherapy compared to those who received adjuvant chemotherapy ($p = 0.045$). Only 20% ($n = 4$) of OCS accrued ≥150 minutes/week moderate-and-vigorous physical activity (MVPA) time in ≥10 min bouts. MVPA time/day in ≥10 min bouts was associated with cardiorespiratory fitness ($p = 0.001$), lower extremity function ($p = 0.019$) and muscle cross-sectional area ($p = 0.035$).

**Conclusion:** Post-treatment OCS spent more time in prolonged sedentary bouts and had lower cardiorespiratory fitness and upper body strength compared to controls. MVPA was associated with physical function and muscle cross-sectional area. Future studies should test the efficacy of exercise interventions to increase MVPA, reduce sedentary behavior, and increase cardiorespiratory fitness and muscle strength in OCS.

**Key Words:** Ovarian cancer, Sedentary behavior, Cardiorespiratory fitness, Muscle strength, Body composition

# INTRODUCTION

Ovarian cancer (OC) is the most lethal gynecological malignancy with an estimated 255,660 new cases and 163,765 deaths worldwide in 2015.[1] Most cases are diagnosed at an advanced stage.[2] Standard first-line treatment for OC involves primary debulking surgery (PDS) followed by adjuvant carboplatin-paclitaxel combination chemotherapy. Neoadjuvant chemotherapy (NACT) with interval debulking surgery is an alternative treatment for women with stage IV disease, unresectable bulky tumors and poor performance status.[3] Approximately 70% of women diagnosed with advanced OC will relapse and require additional treatment.[4]

Beyond the burden of OC, most ovarian cancer survivors (OCS) have comorbidities[5, 6] and are overweight or obese.[6-8] Between 50% and 80% report insufficient participation in physical activity (PA),[5, 6, 8, 9] with initial reports suggesting impaired physical function in this population.[9, 10] However, most studies to date have assessed PA and physiological characteristics with self-report measures in heterogeneous groups of OCS involving women with diverse stages of disease and treatment regimens across varied time-points in the disease trajectory.[11] As a result, consequences of OC and its treatment on objectively measured activity behaviors (PA and sedentary behavior [SB]), physical function, body composition, and muscle morphology (cross-sectional area [CSA] and density) remain largely undefined.

Due to a paucity of information on objectively measured activity behaviors in OC research, the relationship of objectively measured PA and sedentary behavior with physical function and body composition in this cancer population is also poorly understood. Existing research indicates a positive association between objectively measured moderate and vigorous PA (MVPA) and physical function in colon cancer survivors,[12] while objective measures of MVPA is inversely associated with waist circumference in prostate cancer survivors.[13] Objectively measured sedentary time has been inversely associated with physical function in long-term cancer survivors[14] and performance status and survival in patients with malignant pleural effusion.[15] Considering the discrepancy between self-reported and objectively measured PA and sedentary time,[16, 17]

quantification of OCS' activity behaviors and physiological characteristics, and of the association between them, is critical for development and testing of targeted interventions aimed at improving patient outcomes.

In this cross-sectional study we compared objectively measured activity behaviors and a range of objective physiological measures in a cohort of women with advanced-stage epithelial OC following first-line treatment to age-matched controls. We also examined potential differences in advanced-stage OCS treated by NACT and interval debulking surgery compared to women treated by PDS and adjuvant chemotherapy. Lastly, we explored associations of objectively measured activity behaviors with objective measures of physical function, body composition and muscle morphology in OCS.

# METHODS

## Setting and Participants

The study was conducted at the Exercise Medicine Research Institute at Edith Cowan University and St John of God Subiaco Hospital in Perth, Western Australia. Ethical approval was granted by the Edith Cowan University (Ref. No. 12511, 23/4/2015) and St John of God Health Care Human Research Ethics Committees (Ref. No. 815, 12/6/2015). Eligibility criteria were: histologically confirmed stage III–IV epithelial OC, 3-24 months post completion of treatment, ≥18 years of age, approval from the treating oncologist or general practitioner, able to walk 400 meters, proficient in English, no existing or suspected bone metastases, no acute illness or any musculoskeletal, cardiovascular or neurological disorder that could put the participant at risk during exercise testing. The same non-cancer eligibility criteria applied for the control group. Written informed consent was obtained from all participants.

## Recruitment

Eligible patients were identified via consulting rooms of three gynecologic oncologists and were informed of the study by phone or letter. The principle investigator (CS) phoned patients to confirm interest and eligibility. Control group participants were recruited via snowball sampling, from staff at a local university and hospital, and from the wider community. A study information pack was posted to all eligible participants.

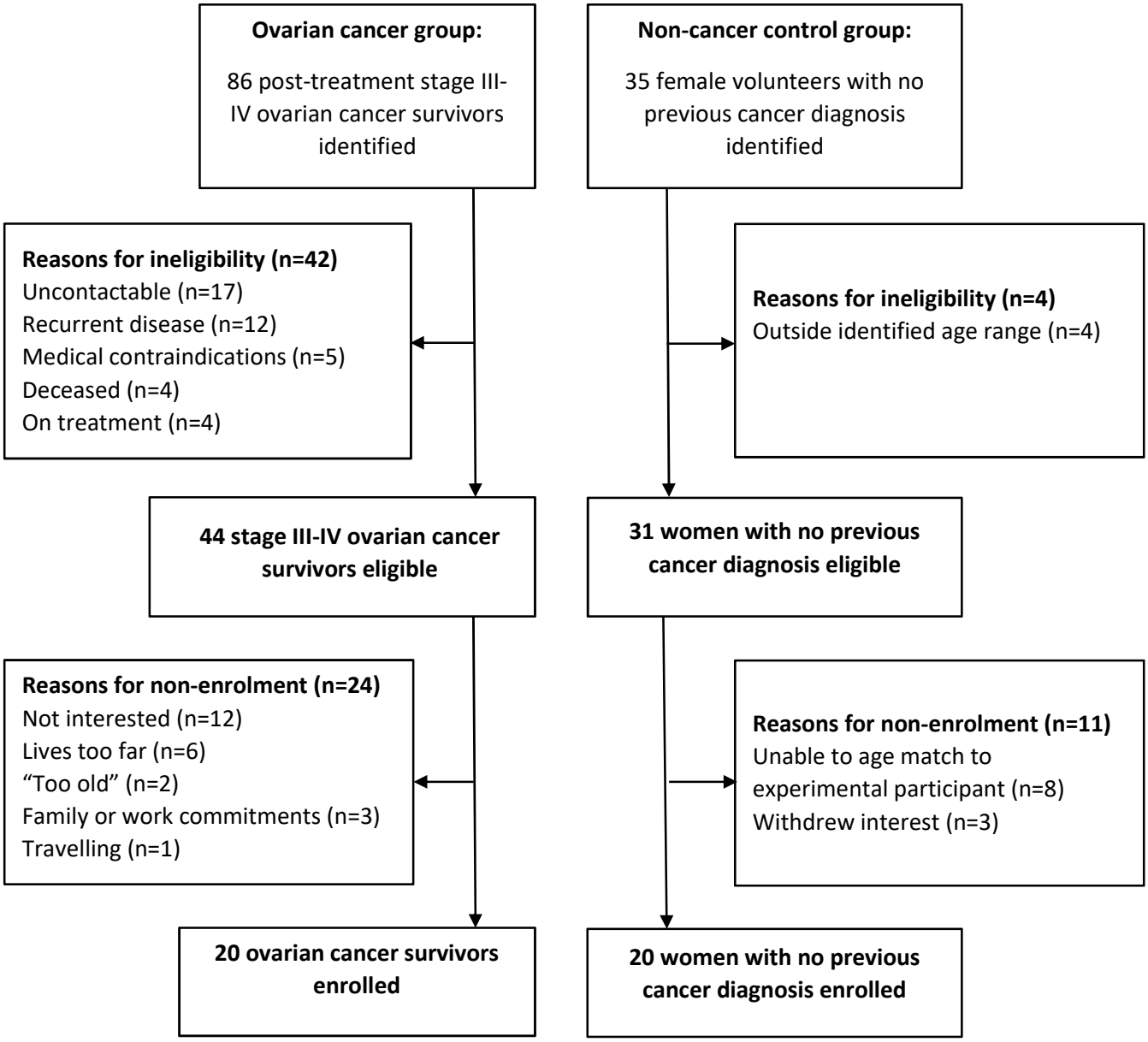


**Figure 2. Participant recruitment flowchart**

## Outcome Measures

Demographic and medical data regarding participants' age, marital status, education level, employment status and medical history were obtained by self-report questionnaire. Additional information regarding cancer diagnosis and treatment were collected from OCS. All anthropometric, body composition and objective functional data were collected at the Exercise Medicine Research Institute by one investigator (CS). Participants attended two sessions (i.e., a familiarization session followed by a testing session) no less than six, but no more than 14 days apart.

### Anthropometric Measures

Height and body weight, measured by a digital measuring-and-weighing station (Model 763, Seca, Hamburg, Germany), were used to calculate body mass index (BMI; kg/m²). Waist and hip circumference were measured at the narrowest part of the torso or between the iliac crest and 12th rib, and the maximal circumference of the hip.[18] Waist-to-hip ratio was calculated by dividing waist circumference by hip circumference.

### Physical Activity and Sedentary Behavior

Objective PA and sedentary time were measured with a hip-worn tri-axial accelerometer (ActiGraph GT3X+, ActiGraph Corp, FL, USA). Participants were asked to wear the accelerometer continuously for seven days, except when bathing/showering or participating in water-based activities. The GT3X+ was programmed to record raw data at a frequency of 30Hz, which were later reduced to vertical axis movement counts/60 s epoch

for the purpose of our analyses. Accelerometer data were downloaded with Actilife (Version 6.13.3, ActiGraph Corp, FL, USA) and processed in SAS (Version 9.3, SAS Institute Inc., NC, USA). An automated algorithm was used to identify awake wear time.[19] To render days of data collection valid, a minimum awake wear time of 600 minutes (10 hours) was required.[20] A minimum of four valid days was required for analysis. Activity counts were categorized as: sedentary (<100

counts/minute [cpm]), light intensity PA (LIPA; 100-<1952 cpm), moderate intensity PA (1952-<5275 cpm), vigorous intensity PA (≥5275 cpm), or moderate and vigorous PA (MVPA; ≥1952 cpm).[21, 22] Participants were categorized as meeting (i.e., ≥150 minutes of MVPA/week) or not meeting (i.e., <150 minutes of MVPA/week) current PA guidelines for cancer survivors.[23] Prolonged sedentary bouts were defined as uninterrupted sedentary bouts of ≥30 minutes.[15, 24]

## Physical function and muscle strength

Measures of physical function included: (1) 400-meter walk as an indicator of cardiorespiratory fitness,[25] (2) repeated chair rise to assess lower extremity function,[26] (3) 6-meter usual pace walk to assess gait speed during daily activities, (4) 6-meter fast pace walk to assess fastest self-selected gait speed and, (5) 6-meter backwards walk to assess dynamic balance.[27, 28] With the exception of the 400-meter walk test, each test was performed three times, the fastest of which was used for analysis. Measures of muscle strength included: (1) one repetition maximum (1-RM) chest press and single-leg extension to measure dynamic upper and lower body muscle strength, (2) handgrip strength test to assess isometric grip strength. Relative strength was calculated by dividing absolute strength by body weight.

## Body composition and muscle morphology

Body composition was measured by dual-energy x-ray absorptiometry (DXA, QDR-1500, Hologic Discovery A, Waltham, MA). Participants' regional and whole-body lean mass (LM), fat mass, fat percentage, areal bone mineral content (BMC), and areal bone mineral density were measured. Peripheral quantitative computed tomography (pQCT, XCT-3000, Stratec Medizintechnik, Pforzheim, Germany) scans were performed at 4%, 14%, 38% and 66% of tibial length, (medial malleolus to medial condyle), distal to proximal, to measure muscle CSA and muscle density, tibial mass, tibial CSA and tibial volumetric density across macroscopic (trabecular, cortical and total) bone material. Stress-strain index was calculated as primary marker of bone strength.[29]

### Statistical Analysis

Data were analyzed using SPSS version 23 (IBM Corp., NY, USA). Variables were assessed for normality using the Shapiro-Wilk test. Results for frequency data are presented as number/percentage, and mean/standard deviation for normally distributed data, or median/interquartile range for non-normally distributed data. Non-normally distributed data were analyzed using non-parametric tests. Differences between OCS and controls were measured using the Pearson Chi square test, Likelihood Ratio or Fisher's exact test for categorical data, and the independent t-tests or Mann-Whitney U tests for continuous variables. One-way analysis of variance (ANOVA), Kruskal-Wallis and Bonferroni post hoc tests were used to compare NACT, PDS and controls. Association between variables for OCS was determined by Pearson r or Spearman rho correlations. All tests were two-tailed, with statistical significance set at an alpha level of 0.05.

## RESULTS

### Participant Characteristics

Between July 2015 and May 2016, 20 OCS and 20 controls were recruited (Figure 1). The OCS group was on average 5.3 (range 3-18) months post cancer treatment. All women had undergone surgery, with 9 (45%) and 11 (55%) having received NACT or adjuvant chemotherapy, respectively. Demographic, health and medical characteristics of participants are presented in Table 1. Most OCS and controls were overweight or obese and reported one or more comorbidity. Compared to controls more OCS experienced shortness of breath (45% vs. 5%, $p = 0.003$) and tingling or numbness in their extremities (45% vs. 0%, $p < 0.001$), had a university degree (50% vs. 15%, $p = 0.033$) and were currently not working (20% vs. 0%, $p = 0.031$).

## Physical Activity and Sedentary Behavior

All OCS and controls provided ≥4 days of valid accelerometer data. One accelerometer worn by a control participant was faulty, resulting in lost data. There were no differences between OCS and controls for mean awake wear time (p = 0.301), or time/day spent in LIPA (p = 0.212) or MVPA (p = 0.687) (Table 2). Thirty-five percent (n = 7) of OCS vs. 53% (n = 10) of controls accrued a total MVPA time consistent with PA recommendations of ≥150 minutes/week. When considering MVPA time in ≥10-minute bouts, 20% (n = 4) of OCS vs. 10.5% (n = 2) of controls undertook ≥150 minutes/week.

Mean sedentary hours/day were similar for OCS and controls (p = 0.957). However, compared to controls, OCS spent significantly more hours/day (3.1±1.3 vs. 2.4±0.7 h, p = 0.039) and a significantly higher percentage of awake wear time/day (21.1±9.4 vs. 15.7±4.7%, p = 0.028) in prolonged sedentary bouts.

Compared to controls, there were no significant differences in average time/day spent in LIPA, MVPA or SB for NACT and PDS. However, NACT spent a significantly larger percentage of awake wear time/day in prolonged sedentary bouts compared to controls (23.8±12.1 vs. 15.7±4.7%, p = 0.032, Bonferroni p = 0.028).

## Physical function and muscle strength

The OCS group had a statistically non-significant slower median 400-meter walk time than controls [256.5 (235.0-280.2) vs. 240.4 (225.4-254.6) sec, p = 0.091; Table 3]. The exclusion of an extreme outlier (i.e., >3.0 x IQR) from the control group resulted in 400-meter walk time being significantly slower for OCS vs. controls [256.5 (235.0-280.2) vs. 239.4 (224.6-251.9) sec, p = 0.041]. Compared to controls, OCS had significantly lower absolute (21.0±6.8 vs. 26.8±9.6 kg, p = 0.044) and relative (0.29±0.09 vs. 0.38±0.13 kg/kg body weight, p = 0.023) upper body muscle strength. No significant differences were observed between groups for repeated chair rise, 6-m walk tests, handgrip strength and lower body muscle strength.

There were no significant differences between controls, NACT and PDS for functional or strength outcomes. No adverse events were reported regarding any objective measures of physical function and muscle strength.

## Body composition and muscle morphology

Fat mass, LM, muscle CSA and muscle density were not significantly different between OCS and controls (Table 4). Compared to controls, OCS had significantly higher areal BMC (2262.3±305.1 vs. 2074.9±221.4 g, p = 0.047) and volumetric trabecular density (232.5±44.4 vs. 207.2±33.1 mg/cm³, p = 0.048).

There were no significant differences between either treatment group or controls in BMI, fat mass, LM, muscle CSA or muscle density. However, compared to PDS, NACT had significantly higher appendicular LM (18.9±3.8 vs. 15.9±2.3 kg, p = 0.045, Bonferroni p = 0.047; Figure 2) and appendicular LM/height² (6.87±0.89 vs. 5.98±0.54 kg/m², p = 0.026, Bonferroni p = 0.045).

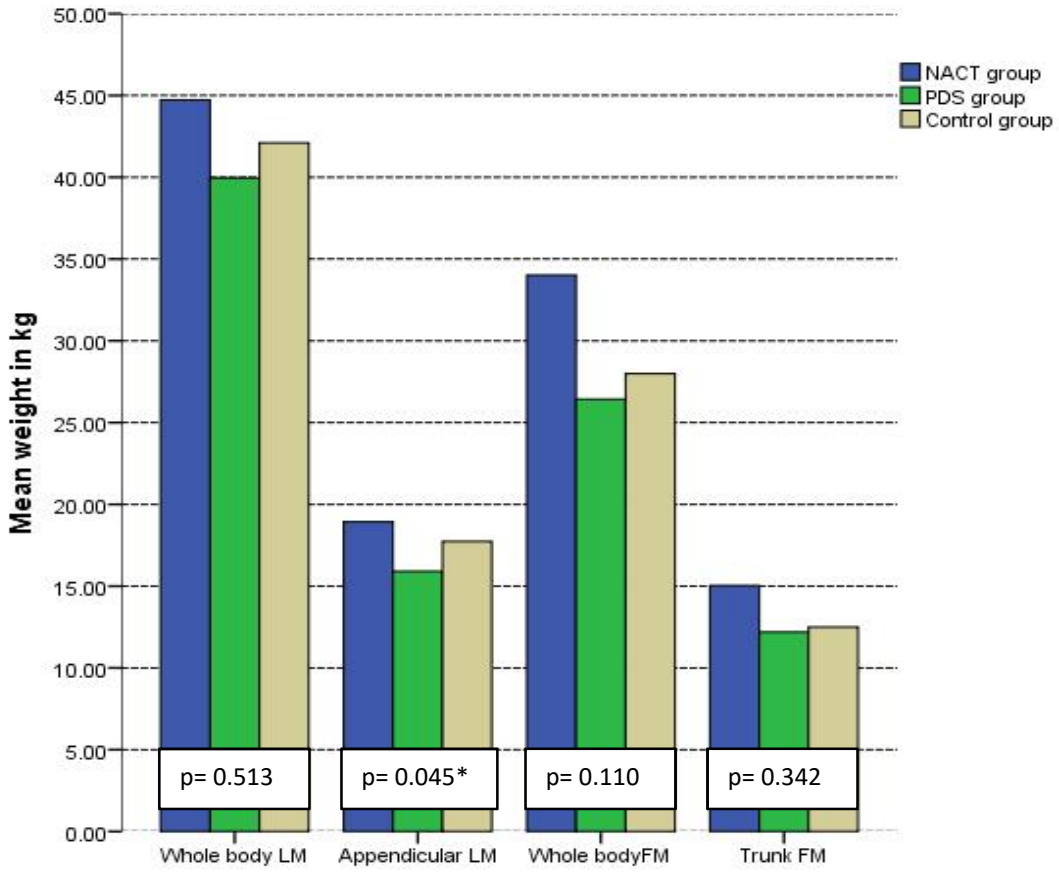


**Figure 3. Whole body and regional fat and lean mass of NACT, PDS and Control groups**
*Statistical significance (p < 0.05), CI bars = 95%

**Associations of Activity Behavior with Objective Measures of Physical Function, Body Composition and Muscle Morphology.**

Total LIPA time/day ($\rho$ = -0.481, p = 0.032), total MVPA time/day ($\rho$ = -0.737, p < 0.001) and total MVPA time/day in ≥10-minute bouts ($\rho$ = -0.702, p = 0.001) were significantly inversely correlated with 400-meter walk time. Only total MVPA time/day in ≥10-minute bouts was significantly correlated with repeated chair rise time ($\rho$ = -0.519, p = 0.019). Total MVPA time/day in ≥10 minute bouts correlated with muscle CSA ($\rho$ = 0.473, p = 0.035) and muscle density ($\rho$ = 0.438, p = 0.053). Total sedentary time/day (r = -0.713, p < 0.001), total prolonged sedentary time/day (r = -0.449, p = 0.047), and number of prolonged sedentary bouts/day (r = -0.494, p = 0.027) were significantly inversely correlated with volumetric bone mineral density. Neither PA nor sedentary time correlated with age or body composition in this sample of OCS.

# DISCUSSION

There were five main findings from our cross sectional analysis: compared to controls, OCS: (1) spent significantly more time/day in prolonged sedentary bouts; (2) had significantly lower cardiorespiratory fitness and upper body strength; (3) had significantly higher areal BMC and volumetric trabecular density; (4) had significant differences between treatment groups in appendicular LM and appendicular LM/height$^2$, but were not significantly different in BMI, LM, fat mass, and muscle morphology; and (5) for OCS, MVPA was associated with cardiorespiratory fitness, lower extremity function and muscle CSA. Our findings suggest that OCS who engage in more MVPA may experience benefits in terms of cardiorespiratory fitness, physical function and muscle morphology.

In this study, OCS did not differ significantly from controls in time spent in LIPA, MVPA and sedentary behavior. They did, however, spend significantly more time/day in prolonged sedentary bouts. This is consistent with research in breast and lung cancer survivors.[24, 30] Despite similarities in PA participation between OCS and controls, our findings confirm that most OCS are

insufficiently active, with only 20% meeting current PA guidelines for cancer survivors. In addition to low PA levels, OCS were sedentary for a large percentage of awake time (66.8±7.6%), of which 3.1 hours was spent in prolonged bouts. Higher self-reported PA in cancer survivors is associated with increased treatment tolerance, physical fitness and function, mental and physical health, and reduced risk of recurrence and cancer-specific mortality in certain cancer groups.[31] Regardless of PA, sedentary time[32] and prolonged sedentary bouts[33, 34] are associated with adverse health outcomes in adults and reduced quality of life in cancer survivors.[14, 35] Promotion of regular PA and breaking up of sedentary time in post-treatment OCS should be priorities in survivorship care.

We found that, compared to controls, OCS had significantly lower cardiorespiratory fitness and upper body strength, but were similar in other aspects of physical function. Poor cardiorespiratory fitness is associated with an increased risk of all-cause and cancer mortality.[36, 37] Impaired cardiorespiratory fitness in OCS has been observed in previous research.[38] Impaired muscle strength negatively affects functional independence and quality of life, while impaired upper body strength can have a debilitating effect on activities of daily living such as lifting, carrying, and doing housework.[39] The lack of significant differences in gait speed, balance and lower body and handgrip strength was unexpected and needs confirmation. Exercise oncology interventions to increase cardiorespiratory fitness and upper body strength in OCS are necessary and may help to increase survival[37] and preserve physical function and quality of life[39] in this population.

Our results show that OCS were comparable to controls in terms of BMI, body weight, fat and LM, and muscle morphology, but had significantly higher mean areal BMC and trabecular density. The similarities in fat mass and muscle quantity and quality, and higher BMC and trabecular density in OCS were unexpected. Many survivors in certain cancer groups experience detrimental body composition changes (i.e., increase in fat mass, loss of muscle and/or bone mass) due to the combined impact of cancer, treatment and reduced PA.[40] Furthermore, previous OC research reports low muscle mass and muscle density in 29-50% and 35% of women, respectively,

at OC diagnosis[41, 42] and bone loss in the first year after OC diagnosis.[43] Future longitudinal studies are warranted to assess body composition changes through the OC trajectory.

The differences observed between treatment groups in the current sample are notable. The NACT group, but not PDS, spent a significantly larger percentage of awake wear time in prolonged sedentary bouts compared to controls. Treatment groups did not significantly differ in terms of physical function or muscle strength, but exhibited body composition differences. Significantly higher appendicular LM in NACT did not translate into improved function or muscle strength, possibly due to their non-significantly higher fat mass (34.0±8.3 vs. 26.4±8.8 kg, $p = 0.110$). Parallels in physical function and strength might also be explained by similarities in muscle quality, confirming the previously established association between muscle quality, and physical function and muscle strength.[44, 45] It is possible that the NACT and PDS groups may have had significantly different physiological profiles pre-treatment and that our findings are due to selection bias. The observed differences between treatment groups are novel and require further investigation in large prospective studies. If confirmed, different exercise intervention strategies may be required based on treatment regimen.

Our study indicates a positive relationship between all intensities of objective PA in OCS and cardiorespiratory fitness, while MVPA in ≥10-minute bouts positively correlated with lower extremity function and muscle CSA. This finding implies that any PA is better than none, but highlights the additional advantages of higher intensity, prolonged PA bouts. The moderate correlation between MVPA and muscle morphology requires further investigation, but is notable in light of research suggesting an association between low muscle mass[46] and density[42, 47] at diagnosis and mortality in OCS. All sedentary outcome measures were negatively correlated with volumetric bone mineral density, confirming the importance of minimizing SB to maintain good bone health in OCS.

This study has important strengths and limitations that should be considered. To our knowledge, it is the first study to provide a comprehensive cross-sectional analysis of objectively

measured activity behavior, physical function and body composition in post-treatment OCS. Our sample of OCS is relatively homogenous in terms of disease and treatment stage. A further strength of the study is the inclusion of an age-matched control group. However, the small sample size limits interpretation, as the study was underpowered to detect small, but potentially meaningful differences between groups. Women with a greater interest in PA may have enrolled in the study resulting in potential selection bias. Lastly, due to the study's cross-sectional design, no inferences can be made about changes over time, or causality. Longitudinal studies are needed to objectively assess changes in OCS' activity behaviors and physiological status and to investigate the relationship between, and the impact of these changes over time. Physiological differences between NACT and PDS also require further investigation.

# CONCLUSION

In this cross-sectional study, OCS spent more time in prolonged sedentary bouts, had lower cardiorespiratory fitness and upper body strength, and higher areal BMC and volumetric trabecular density compared to age-matched controls. Women treated with NACT had higher appendicular LM compared to those treated with PDS, suggesting that different exercise intervention approaches could be required depending on treatment regimen. In OCS MVPA was associated with cardiorespiratory fitness, lower extremity function and muscle cross-sectional area, and sedentary behavior was consistently negatively correlated with bone mineral density. Collectively, our findings support the need for future studies in OCS, testing the efficacy of exercise medicine interventions to increase MVPA, reduce SB, and improve cardiorespiratory fitness and muscular strength.

**Table 1. Demographic, medical and health characteristics of Cancer and Control groups**

| | Cancer group (n = 20) | | Control group (n = 20) | | p-value |
|---|---|---|---|---|---|
| **Age** | 63.2±8.9 | | 63.0±9.1 | | 0.944 |
| **Relationship status** | **n** | **%** | **n** | **%** | 0.490 |
| Partnered | 15 | 75 | 13 | 65 | |
| Not partnered | 5 | 25 | 7 | 35 | |
| **Educational attainment** | | | | | 0.033* |
| Completed secondary school | 3 | 15 | 9 | 45 | |
| Post-secondary certificate/diploma | 7 | 35 | 8 | 40 | |
| University degree | 10 | 50 | 3 | 15 | |
| **Employment status** | | | | | 0.031* |
| Currently working | 7 | 35 | 12 | 60 | |
| Currently not working | 4 | 20 | 0 | 0 | |
| Retired | 9 | 45 | 8 | 40 | |
| **Smoking Status** | | | | | 0.055 |
| Non smoker | 13 | 65 | 9 | 45 | |
| Past smoker | 5 | 25 | 11 | 55 | |
| Current smoker | 2 | 10 | 0 | 0 | |
| **Alcohol drinks per week** | | | | | 0.791 |
| None | 8 | 40 | 7 | 35 | |
| 1-7 units | 9 | 45 | 11 | 55 | |
| ≥8 units | 3 | 15 | 2 | 10 | |
| **Body mass index** | | | | | 0.924 |
| Normal (<25.0 kg/m²) | 7 | 35 | 8 | 40 | |
| Overweight (≥25.0-29.9 kg/m²) | 7 | 35 | 7 | 35 | |
| Obese (≥30.0 kg/m²) | 6 | 30 | 5 | 25 | |
| **Number of comorbidities** | | | | | 0.426 |
| None | 5 | 25 | 4 | 20 | |
| One | 8 | 40 | 5 | 25 | |
| ≥Two | 7 | 35 | 11 | 55 | |
| **Current symptoms/side-effects** | | | | | |
| Shortness of breath | 9 | 45 | 1 | 5 | 0.003* |
| Tingling, numbness, loss of feeling§ | 9 | 45 | 0 | 0 | <0.001* |
| Swelling of feet and ankles | 8 | 40 | 6 | 30 | 0.507 |
| Pains or cramps in legs | 10 | 50 | 8 | 40 | 0.525 |
| Chest discomfort | 2 | 10 | 2 | 10 | 1.000 |

§Cancer group n = 18 due to missing data

*Statistical significance ($p < 0.05$)

**Table 2. Accelerometer-assessed sedentary time and physical activity in Cancer, Control, NACT and PDS treatment groups**

| | Cancer group (n = 20) | Control group (n = 19) | p-value T-test | NACT group (n = 9) | PDS group (n = 11) | p-value ANOVA |
|---|---|---|---|---|---|---|
| **Waking wear time, h/day** | 14.8±1.1 | 15.2±1.4 | 0.301 | 14.7±1.2 | 14.9±1.1 | 0.546 |
| **Sedentary behavior (<100 cpm)** | | | | | | |
| Total time, h/day | 9.9±1.1 | 9.9±1.1 | 0.957 | 9.7±1.4 | 10.0±0.9 | 0.864 |
| Time spent in SB (% of awake time) | 66.8±7.6 | 64.7±4.5 | 0.301 | 66.5±10.2 | 67.1±5.2 | 0.577 |
| Time in ≥30 min bouts, h/day | 3.1±1.3 | 2.4±0.7 | 0.039* | 3.5±1.7 | 2.8±1.0 | 0.052 |
| Time in ≥30 min SB bouts (% of awake time) | 21.1±9.4 | 15.7±4.7 | 0.028* | 23.8±12.1 | 18.9±6.2 | 0.032* |
| Number of ≥30 min bouts/day | 3.9±1.4 | 3.1±0.8 | 0.055 | 4.2±1.7 | 3.6±1.1 | 0.080 |
| **Light physical activity (100 to <1952 cpm)** | | | | | | |
| Total time, h/day | 4.6±1.2 | 5.0±0.8 | 0.212 | 4.6±1.5 | 4.5±0.8 | 0.455 |
| Time spent in light PA (% of awake time) | 30.6±6.6 | 32.6±4.1 | 0.278 | 31.1±9.0 | 30.2±4.2 | 0.527 |
| **Moderate physical activity (1952-<5275 cpm)** | | | | | | |
| Total time, min/day | 17.4 (34.4)† | 24.7 (22.3)† | 0.667‡ | 21.7±18.2 | 24.0±18.4 | 0.893 |
| **Vigorous physical activity (≥5275 cpm)** | | | | | | |
| Total time, min/day | 0.0 (0.1)† | 0.0 (0.0)† | 0.687‡ | 0.0(0.3)† | 0.0 (0.1)† | 0.813‡‡ |
| **MVPA** | | | | | | |
| Total time, min/day | 17.6 (34.5)† | 24.7 (26.9)† | 0.687‡ | 21.8±18.2 | 24.3±18.8 | 0.861 |
| Time in MVPA (% of awake time) | 2.6±2.0 | 2.7±1.5 | 0.776 | 2.4±2.0 | 2.7±2.1 | 0.906 |
| Consistent with ≥150 minutes/week [n (%)] | 7 (35) | 10 (52.6) | 0.267 | 3 (33.33) | 4 (36.36) | |
| Time in ≥10 min bouts, min/day | 5.2 (14.7)† | 6.1 (8.7)† | 0.835‡ | 3.1 (16.5)† | 5.6 (16.4)† | 0.791‡ |
| Consistent with ≥150 minutes/week [n (%)] | 4 (20) | 2 (10.5) | 0.661†† | 2 (22.2) | 2 (18.2) | 0.693 |
| Time in ≥10 min MVPA bouts (% of awake time) | 0.6 (1.6)† | 0.7 (0.9)† | 0.857‡ | 0.4 (1.7)† | 0.6 (1.7)† | 0.804‡ |

| | | | | | | |
|---|---|---|---|---|---|---|
| Number of ≥10 min bouts/day | 0.3 (0.6)† | 0.3 (0.4)† | 0.647‡ | 0.3 (0.8)† | 0.3 (0.7)† | 0.778‡ |

NACT = neoadjuvant chemotherapy; PDS = primary debulking surgery; cpm = counts per minute on the vertical axis of hip-worn Actigraph accelerometer; SB = sedentary bouts; PA = physical activity; MVPA = moderate-and-vigorous physical activity.

Values are presented as mean±SD unless otherwise specified

†Median (interquartile range), ‡Mann-Whitney test, ††Fisher's Exact

*Statistical significance ($p < 0.05$)

**NACT spent a significantly larger % of awake wear time/day in prolonged sedentary bouts compared to Control group (Bonferroni $p = 0.028$)

**Table 3. Physical function and muscle strength values for Cancer, Control, NACT and PDS treatment groups**

| | Cancer group (n = 20) | Control group (n = 20) | p-value T-test | NACT group (n = 9) | PDS group (n = 11) | p-value ANOVA |
|---|---|---|---|---|---|---|
| **Physical function** | | | | | | |
| 400-meter walk (s) | 256.5 (45.2)† | 240.4 (29.3)† | 0.091‡ | 256.7 (22.8)† | 244.0 (54.1)† | 0.141‡‡ |
| 400-meter walk (s)¶ | 256.5 (45.2)† | 239.4 (27.4)† | 0.041‡* | 256.7 (22.8)† | 244.0 (54.1)† | 0.072 |
| Repeated chair rise (s) | 12.0 (2.8)† | 11.0 (4.0)† | 0.242‡ | 11.8 (4.0)† | 12.1 (3.0)† | 0.418‡‡ |
| Repeated chair rise (s)¶¶ | 11.8 (2.2)† | 11.0 (4.0)† | 0.351‡ | 11.8 (4.0)† | 11.9 (2.1)† | 0.614‡‡ |
| 6-meter walk usual pace (s) | 4.2±0.5 | 4.2±0.7 | 0.817 | 4.1±0.4 | 4.2±0.6 | 0.918 |
| 6-meter walk fast pace (s) | 3.2 (0.4)† | 3.1 (0.4)† | 0.277‡ | 3.2 (0.4)† | 3.1 (0.5)† | 0.544‡‡ |
| 6-meter walk fast pace (s)¶ | 3.2 (0.4)† | 3.1 (0.3)† | 0.158‡ | 3.2 (0.4)† | 3.1 (0.5)† | 0.362 |
| 6-meter backwards walk (s) | 21.0±5.7 | 19.7±4.2 | 0.408 | 20.9±4.5 | 21.1±6.7 | 0.711 |
| **Muscle strength** | | | | | | |
| Absolute strength | | | | | | |
| Chest press 1RM (kg)§ | 21.0±6.8 | 26.8±9.6 | 0.044* | 23.3±7.4 | 18.8±5.7 | 0.070 |
| Single leg extension 1RM (kg)§§ | 24.1±9.1 | 25.2±8.4 | 0.724 | 26.9±9.4 | 21.4±8.4 | 0.384 |
| Hand grip strength, (kg)§§§ | 24.4±6.6 | 26.8±7.0 | 0.273 | 25.2±6.9 | 23.8±6.7 | 0.500 |
| Relative strength | | | | | | |
| Chest press§ | 0.29±0.09 | 0.38±0.13 | 0.023* | 0.29±0.60 | 0.29±0.12 | 0.078 |
| Single leg extension§§ | 0.33±0.10 | 0.36±0.12 | 0.342 | 0.33±0.07 | 0.32±0.13 | 0.640 |
| Hand grip strength§§§ | 0.33±0.08 | 0.38±0.09 | 0.112 | 0.31±0.05 | 0.35±0.10 | 0.156 |

NACT = neoadjuvant chemotherapy; PDS = primary debulking surgery; 1RM = one repetition maximum.

Values are presented as mean±SD unless otherwise specified

¶Extreme outlier removed from Control group, ¶¶Extreme outlier removed from Cancer group

†Median (interquartile range), ‡Mann-Whitney test, ‡‡Kruskal-Wallis test

Relative strength was calculated by dividing absolute strength by body weight

§Cancer group n = 18, Control group n = 19, PDS group n = 9 due to inability complete upper body strength measures

§§Cancer group n = 18, Control group n = 18, PDS group n = 9 due to inability complete lower body strength measures

§§§Control group n = 19 due to inability complete hand grip strength measures

*Statistical significance ($p < 0.05$)

**Table 4. Body composition and muscle density values for Cancer, Control, NACT and PDS treatment groups**

| | Cancer group (n = 20) | Control group (n = 20) | p-value T-test | NACT group (n = 9) | PDS group (n = 11) | p-value ANOVA |
|---|---|---|---|---|---|---|
| BMI | 27.4±4.5 | 27.2±4.5 | 0.888 | 29.57±3.90 | 25.64±4.25 | 0.139 |
| Height (cm) | 163.9±7.1 | 162.9±9.4 | 0.657 | 165.3±6.5 | 162.7±7.8 | 0.630 |
| Waist to hip ratio | 0.84 (0.7)† | 0.84 (0.10)† | 0.947‡ | 0.84 (0.05)† | 0.84 (0.09)† | 0.798‡‡ |
| **DXA** | | | | | | |
| Body weight (kg) | 74.2±15.4 | 72.2±10.6 | 0.632 | 81.1±14.7 | 68.5±14.1 | 0.086 |
| Whole body fat mass (kg) | 29.8±9.2 | 28.0±7.9 | 0.500 | 34.0±8.3 | 26.4±8.8 | 0.110 |
| Trunk fat mass (kg) | 13.5±5.0 | 12.5±4.6 | 0.520 | 15.0±3.8 | 12.2±5.6 | 0.342 |
| Whole body fat percentage (%) | 39.4±5.3 | 38.1±6.6 | 0.491 | 41.6±4.7 | 37.6±5.4 | 0.264 |
| Whole body LM (kg) | 42.0 (8.5)† | 40.8 (8.0)† | 0.862‡ | 44.7±7.5 | 40.0±5.6 | 0.513‡‡ |
| Appendicular LM (kg) | 17.3±3.4 | 17.7±2.2 | 0.610 | 18.9±3.8 | 15.9±2.3 | 0.045** |
| Appendicular LM/height² (kg/m²) | 6.4±0.8 | 6.7±0.8 | 0.256 | 6.9±0.9 | 6.0±0.5 | 0.026** |
| Whole-body aBMC (g)§ | 2262.3±305.1 | 2074.9±221.4 | 0.047* | 2393.0±267.7 | 2157.7±304.6 | 0.025*** |
| Whole-body aBMD (g/cm²)§ | 1.08±0.10 | 1.05±0.08 | 0.263 | 1.11±0.10 | 1.06±0.10 | 0.257 |
| **pQCT** | | | | | | |
| Muscle area (mm²) | 5862.5±1184.4 | 6088.4±708.1 | 0.469 | 6312.1±1455.4 | 5494.6±800.0 | 0.131 |
| Muscle density (mg/cm³) | 72.4 (5.8)† | 74.2 (3.9)† | 0.221‡ | 72.8 (4.1)† | 72.0 (7.3)† | 0.423‡‡ |
| Tibial mass g/cm | 3.0±0.5 | 2.8±0.3 | 0.940 | 3.2±0.5 | 2.9±0.4 | 0.062 |
| Tibial area (mm²) | 665.0±92.5 | 632.5±64.6 | 0.205 | 675.6±103.4 | 656.4±86.7 | 0.394 |
| Tibial vBMD (mg/cm³) | 555.9±72.5 | 532.5±53.3 | 0.252 | 579.4±73.2 | 536.6±69.2 | 0.170 |
| Trabecular area (mm²) | 491.8±70.5 | 464.3±53.8 | 0.173 | 495.42=±76.0 | 488.9±69.4 | 0.390 |
| Trabecular vBMD (mg/cm³) | 232.6±44.4 | 207.3±33.2 | 0.048* | 252.9±42.7 | 216.0±40.2 | 0.015*** |
| Cortical area (mm²) | 218.6±32.7 | 212.7±23.1 | 0.514 | 228.9±33.7 | 210.1±30.8 | 0.273 |

| | | | | | | |
|---|---|---|---|---|---|---|
| Cortical vBMD (mg/cm³) | 1110.9±47.7 | 1101.4±33.6 | 0.469 | 1124.2±46.2 | 1100.0±48.3 | 0.331 |
| SSI (mm³) | 1511.7 (287.9)† | 1468.6 (244.5)† | 0.369‡ | 1654.3±332.7 | 1437.2±208.7 | 0.063 |

NACT = neoadjuvant chemotherapy, PDS = primary debulking surgery, BMI = body mass index, FM = fat mass, LM = lean mass,
aBMC = areal bone mineral content, aBMD = areal bone mineral density, vBMD = volumetric bone mineral density, SSI = stress-strain index.
Values are presented as mean±SD unless otherwise specified
†Median (interquartile range), ‡Mann-Whitney test, ‡‡Kruskal-Wallis test
§Cancer group n = 18, Control group n = 17, NACT Group n = 8, PDS Group n = 10 due to metallic surgical implants
*Statistical significance ($p < 0.05$)
**Appendicular LM (kg) and appendicular LM/height² (kg/m²) was significantly higher in NACT than PDS, Bonferroni p = 0.047 and 0.045, respectively
***BMC (g) and trabecular density (mg/cm³) was significantly higher in NACT than in Control group, Bonferroni p = 0.021 and 0.013, respectively

# REFERENCES


1. Ferlay J, Soerjomataram I, Ervik M, et al. GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 [Internet]. Lyon, France: International Agency for Research on Cancer; 2013. Available from: http://globocan.iarc.fr. Accessed September 20, 2016.
2. Herzog TJ. Recurrent ovarian cancer: how important is it to treat to disease progression? Clin Cancer Res. 2004;10:7439-7449.
3. Leiserowitz GS, Lin JF, Tergas AI, et al. Factors Predicting Use of Neoadjuvant Chemotherapy Compared With Primary Debulking Surgery in Advanced Stage Ovarian Cancer-A National Cancer Database Study. Int J Gynecol Cancer. 2017;27:675-683.
4. Ushijima K. Treatment for recurrent ovarian cancer-at first relapse. J Oncol. 2010;2010: 497429.
5. Stevinson C, Steed H, Faught W, et al. Physical activity in ovarian cancer survivors: associations with fatigue, sleep, and psychosocial functioning. Int J Gynecol Cancer. 2009;19: 73-78.
6. Smits A, Smits E, Lopes A, et al. Body mass index, physical activity and quality of life of ovarian cancer survivors: Time to get moving? Gynecol Oncol. 2015;139:148-154.
7. Stevinson C, Faught W, Steed H, et al. Associations between physical activity and quality of life in ovarian cancer survivors. Gynecol Oncol. 2007;106:244-250.
8. Beesley V, Eakin E, Janda M, et al. Gynecological cancer survivors' health behaviors and their associations with quality of life. Cancer Causes Control. 2008;19:775-782.
9. Nayak P, Vernon SW, Savas LS, et al. Functional Impairment and Physical Activity Adherence Among Gynecologic Cancer Survivors: A Population-Based Study. Int J Gynecol Cancer. 2016;26:381-388.
10. von Gruenigen VE, Huang HQ, Gil KM, et al. A comparison of quality-of-life domains and clinical factors in ovarian cancer patients: a Gynecologic Oncology Group study. J Pain Symptom Manage. 2010;39:839-846.
11. Schofield C, Newton RU, Galvão DA et al. A Physiological Profile of Ovarian Cancer Survivors to Inform Tailored Exercise Interventions and the Development of Exercise Oncology Guidelines. Int J Gynecol Cancer. 2017;27:1560-1567.

12. Vallance JK, Boyle T, Courneya KS et al. Associations of objectively assessed physical activity and sedentary time with health-related quality of life among colon cancer survivors. Cancer. 2014;120:2919-2926.

13. Lynch BM, Dunstan DW, Winkler E et al. Objectively assessed physical activity, sedentary time and waist circumference among prostate cancer survivors: findings from the National Health and Nutrition Examination Survey (2003-2006). Eur J Cancer Care. 2011;20:514-519.

14. George SM, Alfano CM, Groves J et al. Objectively measured sedentary time is related to quality of life among cancer survivors. PLoS ONE. 2014;9:e87937-e87937.

15. Jeffery E, Lee YG, McVeigh J et al. Feasibility of objectively measured physical activity and sedentary behavior in patients with malignant pleural effusion. Support Care Cancer. 2017;25:3133–3141.

16. Dyrstad SM, Hansen BH, Holme IM et al. Comparison of self-reported versus accelerometer-measured physical activity. Med Sci Sports Exerc. 2014;46:99-106.

17. Broderick JM, Hussey J, Kennedy MJ et al. Testing the 'teachable moment' premise: does physical activity increase in the early survivorship phase? Support Care Cancer: 2014;22:989-997.

18. World Health Organization. Waist Circumference and Waist–Hip Ratio: Report of a WHO Expert Consultation Geneva, 8–11 December 2008 [Internet]. Available from: http://www.who.int/nutrition/publications/obesity/WHO_report_waistcircumference_and_waisthip_ratio/en/. Accessed March 30, 2017.

19. McVeigh JA, Winkler EAH, Healy GN, et al. Validity of an automated algorithm to identify waking and in-bed wear time in hip-worn accelerometer data collected with a 24 h wear protocol in young adults. Physiol Meas. 2016;37:1636-1652.

20. Matthews CE, Hagströmer M, Pober DM, et al. Best practices for using physical activity monitors in population-based research. Med Sci Sports Exerc. 2012;44(suppl 1):68-76.

21. Freedson PS, Melanson E, Sirard J. Calibration of the Computer Science and Applications, Inc. accelerometer. Med Sci Sports Exerc. 1998;30:777-781.

22. Matthews CE, Chen KY, Freedson PS, et al. Amount of time spent in sedentary behaviors in the United States, 2003-2004. Am J Epidemiol. 2008;167:875-881.

23. Rock CL, Doyle C, Demark-Wahnefried W, et al. Nutrition and physical activity guidelines for cancer survivors. CA Cancer J Clin. 2012;62:242-274.

24. Simonsick EM, Fan E, Fleg JL. Estimating cardiorespiratory fitness in well-functioning older adults: treadmill validation of the long distance corridor walk. J Am Geriatr Soc. 2006; 54:127-132.

25. Cesari M, Kritchevsky SB, Newman AB, et al. Added value of physical performance measures in predicting adverse health-related events: results from the Health, Aging And Body Composition Study. J Am Geriatr Soc. 2009;57:251-259.

26. Peiffer JJ, Galvão DA, Gibbs Z, et al. Strength and functional characteristics of men and women 65 years and older. Rejuvenation Res. 2010;13:75-82.

27. Galvão DA, Taaffe DR. Resistance exercise dosage in older adults: single- versus multiset effects on physical performance and body composition. J Am Geriatr Soc. 2005;53:2090-2097.

28. Sheu Y, Zmuda JM, Boudreau RM, et al. Bone strength measured by peripheral quantitative computed tomography and the risk of nonvertebral fractures: the osteoporotic fractures in men (MrOS) study. J Bone Miner Res. 2011;26:63-71.

29. Shi JW, MacInnis RJ, Boyle T, et al. Physical Activity and Sedentary Behavior in Breast and Colon Cancer Survivors Relative to Adults Without Cancer. Mayo Clin Proc. 2017;92:391-398.

30. Cavalheri V, Jenkins S, Cecins N, et al. Patterns of sedentary behaviour and physical activity in people following curative intent treatment for non-small cell lung cancer. Chron Respir Dis. 2016;13:82-85.

31. Brown JC, Winters-Stone K, Lee A, et al. Cancer, physical activity, and exercise. Compr Physiol. 2012;2:2775-2809.

32. Biswas A, Oh PI, Faulkner GE et al. Sedentary time and its association with risk for disease incidence, mortality, and hospitalization in adults: a systematic review and meta-analysis. Ann Intern Med. 2015;162:123-132.

33. Dunstan DW, Thorp AA, Healy GN. Prolonged sitting: is it a distinct coronary heart disease risk factor? Curr Opin Cardiol. 2011;26:412-419.

34. Healy GN, Dunstan DW, Salmon J et al. Breaks in sedentary time: beneficial associations with metabolic risk. Diabetes Care. 2008;31:661-666.

35. van Roekel EH, Winkler EAH, Bours MJL et al. Associations of sedentary time and patterns of sedentary time accumulation with health-related quality of life in colorectal cancer survivors. Prev Med Rep. 2016;4:262-269.

36. Kodama S, Saito K, Tanaka S, et al. Cardiorespiratory fitness as a quantitative predictor of all-cause mortality and cardiovascular events in healthy men and women: a meta-analysis. JAMA. 2009;301:2024-2035.

37. Schmid D, Leitzmann MF. Cardiorespiratory fitness as predictor of cancer mortality: a systematic review and meta-analysis. Ann Oncol. 2015;26:272-278.

38. Peel AB, Barlow CE, Leonard D, et al. Cardiorespiratory Fitness in Survivors of Cervical, Endometrial, and Ovarian Cancer: The Cooper Center Longitudinal Study. Gynecol Oncol. 2015;138:394-397.

39. Warburton DE, Gledhill N, Quinney A. Musculoskeletal fitness and health. Can J Appl Physiol. 2001;26:217-237.

40. Newton RU, Galvão DA. Exercise in prevention and management of cancer. Curr Treat Options Oncol. 2008;9:135-146.

41. Rutten IJG, van Dijk DPJ, Kruitwagen RFPM, et al. Loss of skeletal muscle during neoadjuvant chemotherapy is related to decreased survival in ovarian cancer patients. J Cachexia Sarcopenia Muscle. 2016;7:458-466.

42. Aust S, Knogler T, Pils D, et al. Skeletal Muscle Depletion and Markers for Cancer Cachexia Are Strong Prognostic Factors in Epithelial Ovarian Cancer. PLoS ONE. 2015;10:e0140403.

43. Hui SK, Khalil A, Zhang Y, et al. Longitudinal assessment of bone loss from diagnostic computed tomography scans in gynecologic cancer patients treated with chemotherapy and radiation. Am J Obstet Gynecol. 2010;203:353.e1-353e7.

44. Aubrey J, Esfandiari N, Baracos VE, et al. Measurement of skeletal muscle radiation attenuation and basis of its biological variation. Acta Physiol (Oxf). 2014;210:489-497.

45. Goodpaster BH, Carlson CL, Visser M, et al. Attenuation of skeletal muscle and strength in the elderly: The Health ABC Study. J Appl Physiol (1985). 2001;90:2157-2165.

46. Bronger H, Hederich P, Hapfelmeier A, et al. Sarcopenia in Advanced Serous Ovarian Cancer. Int J Gynecol Cancer. 2017;27:223-232

47. Kumar A, Moynagh MR, Multinu F, et al. Muscle composition measured by CT scan is a measurable predictor of overall survival in advanced ovarian cancer. Gynecol Oncol. 2016;142:311-316.

# *Chapter 4*

## OBSERVATIONAL STUDY

"Associations of objective activity behaviors and physiological characteristics with health-related quality of life and pelvic floor dysfunction in advanced-stage ovarian cancer survivors"

**Schofield C,** Newton RU, Galvão DA, Cohen PA, McVeigh JA, Mohan GR, Tan J, Salfinger SG, Straker LM, Peddle-McIntyre CJ. Manuscript prepared for submission to Supportive Care in Cancer, October 2017.

# ABSTRACT

**Purpose:** Little is known about the relationship between health-related quality of life (HRQoL), pelvic floor dysfunction (PFD) and modifiable lifestyle and physiological factors for ovarian cancer survivors (OCS). This study aimed to compare post-treatment advanced-stage OCS with age-matched controls on measures of HRQoL and PFD. Associations between HRQoL, PFD, objective activity behaviors, physical function and body composition in OCS were also examined.

**Methods:** Twenty advanced-stage OCS and 20 controls completed questionnaires assessing HRQoL (SF-36) and PFD (Australian Pelvic Floor Questionnaire), and underwent objective assessments of activity behavior (7-day accelerometry), physical function (400-meter walk, repeated chair rise, 6-meter usual-pace walk, 1-repetition maximum chest press and single leg extension) and body composition (dual-energy x-ray absorptiometry).

**Results:** Compared to controls, OCS had worse physical HRQoL (-4.3 median difference, $p= 0.013$), but equivalent self-reported PFD, indicated by combined bladder, bowel and pelvic organ prolapse symptoms (0.89 mean difference, $p= 0.277$). In OCS physical HRQoL was significantly negatively associated with PFD ($r= 0.468$, $p= 0.043$). Decreased physical HRQoL and increased PFD were significantly associated with less moderate-and-vigorous physical activity in ≥ 10-minute bouts ($\rho= 0.627$, $p= 0.003$; $\rho= -0.457$, $p= 0.049$), more sedentary time ($r= -0.449$, $p= 0.047$; $r= 0.479$, $p= 0.038$) and slower 400-meter walk time ($\rho= -0.565$, $p= 0.022$; $\rho= 0.504$, $p= 0.028$).

**Conclusions:** Post-treatment advanced-stage OCS have decreased physical HRQoL, which is associated with modifiable factors such as PFD, moderate-and-vigorous physical activity, sedentary time and objective physical function. This highlights the need for ongoing supportive care and multidisciplinary interventions after first-line OC treatment.



**Key Words:** Ovarian cancer, Health-related quality of life, Pelvic floor dysfunction, Moderate-and-vigorous physical activity (MVPA), Sedentary time

# INTRODUCTION

Ovarian cancer (OC) is the seventh most common cancer among women worldwide.[1] Between 70% and 75% of OC cases are diagnosed at an advanced stage.[2] Treatment in advanced-stage OC is often palliative and aimed at controlling disease and treatment related symptoms and side-effects, whilst prolonging survival with optimal quality of life.[3] As such, health-related quality of life (HRQoL) in women with OC has received increasing attention in the last decade.[4]

Although research involving measurement of HRQoL in ovarian cancer survivors (OCS) is increasing, interpretation of results can be challenging due to heterogeneity of study design and participant groups (e.g., different disease stages and treatments). Furthermore, existing studies mostly investigate HRQoL in long-term OCS (≥ five years post-diagnosis) or in women on treatment, with little information for OCS following first-line treatment.[5] Few studies have compared HRQoL between OCS and age-matched controls drawn from the same community.[6, 7]

Health-related QoL in OCS is known to be negatively impacted by persistent treatment-related side-effects.[4] Poorer HRQoL has been linked with lifestyle factors such as obesity and insufficient self-reported physical activity (i.e., <150 minutes of moderate-and-vigorous physical activity [MVPA] per week).[8, 9] However, associations of HRQoL with body composition and objectively measured activity behaviors (i.e., physical activity [PA] and sedentary behavior [SB]) have not yet been examined. Furthermore, although most QoL instruments measure self-rated physical function, the relationship between objectively measured physical function and HRQoL in OCS has not been explored previously.

Pelvic floor dysfunction (PFD) is widely recognized as a public health issue with significant impact on HRQoL for millions of women globally.[10, 11] Although gynecological cancer treatment is often considered a risk factor for increased PFD, this association has not been firmly established.[12] Pelvic floor dysfunction is a general term that refers to clinical problems involving different organ systems in the same anatomical area. It encompasses symptoms associated with bladder, bowel and

pelvic organ prolapse (POP), and sexual dysfunction.[13] Sexual dysfunction and gastrointestinal issues such as constipation, diarrhea and indigestion after OC treatment are well documented,[14, 15] but data regarding the prevalence, severity and impact of PFD in OCS are limited.[16]

To design and implement tailored interventions aimed at improving HRQoL for OCS, it is crucial to understand the relationship between HRQoL and modifiable factors such as PFD, activity behaviors, physical function and body composition. We have previously reported that, compared to age-matched controls, OCS spent significantly more time/day in prolonged sedentary bouts of ≥30 minutes and had significantly lower cardiorespiratory fitness and upper body strength.[17] In this report we extend our previous analysis to: (1) compare HRQoL and PFD in OCS who had completed first-line treatment to age-matched controls; (2) investigate associations between HRQoL and PFD in OCS; and (3) explore associations of HRQoL and PFD with objective activity behaviors, physical function and body composition in OCS.

# METHODS

## Setting and participants

The study was conducted at the Exercise Medicine Research Institute at Edith Cowan University and St John of God Subiaco Hospital in Perth, Western Australia. The Human Research Ethics Committees of both institutions granted ethical approval (Ref. No. 12511, 23/4/2015; Ref. No. 815, 12/6/2015). Ovarian cancer survivors were eligible for participation if they had histologically confirmed stage III–IV epithelial OC, were 3-24 months post completion of first-line treatment, were ≥18 years of age, received approval from the treating oncologist or general practitioner, were able to walk 400 meters, were proficient in English, had no existing or suspected bone metastases, no acute illness or any musculoskeletal, cardiovascular or neurological disorder that could put them at risk during exercise testing. The same non-cancer eligibility criteria applied for controls. All participants provided written informed consent.

## Outcome Measures

Demographic, medical, HRQoL and pelvic floor data were obtained by self-report questionnaires. Additional information regarding cancer diagnosis and treatment were collected from OCS. All anthropometric measures (height and body weight to calculate body mass index [BMI], waist and hip circumference to calculate waist-to-hip ratio), body composition and objective functional data were collected at the Exercise Medicine Research Institute by one investigator (CS).

### Health-related Quality of Life

Health-related QoL was measured using the Medical Outcomes Study Short Form-36 (MOS SF-36) questionnaire.[18] The SF-36 is a generic instrument that comprises eight subscales measuring Physical Functioning, Role-Physical, Bodily Pain, General Health, Vitality, Social Functioning, Role-Emotional and Mental Health. Subscale scores were combined into a physical component summary score (PCS) and a mental component summary score (MCS).[19] All scores were standardized to 1998 general US population norms.[20] Higher scores reflect better HRQoL in the domain being measured.[20] The SF-36 has been established as a reliable and valid measure of QoL[21] and is often used to assess QoL of OCS.[4]

### Pelvic Floor Dysfunction

Self-reported PFD was measured with the Australian Pelvic Floor Questionnaire (APFQ).[22, 23] The APFQ has four subscales, with a range of questions each, to assess bladder, bowel and POP symptoms, and sexual function. Bladder, bowel and POP symptom scores out of 10 were calculated. We did not calculate sexual function scores due to the large percentage of women (55% of all participants) indicating sexual inactivity and thus not completing the section. Bladder, bowel and POP symptom scores out of 10 were added for a combined bladder-bowel-POP symptom score out of 30, hereafter referred to as the Pelvic Floor Score. Higher scores in all domains indicate that women are experiencing more symptoms and thus more dysfunction. The APFQ has been indicated as valid and reliable measure of all four pelvic floor domains.[22, 23]

## Physical Activity and Sedentary Behavior

Objective PA and sedentary time were measured over a seven-day period with a hip-worn tri-axial accelerometer (ActiGraph GT3X+, ActiGraph Corp, FL, USA). Data processing details have been reported previously.[17] Activity counts were categorized as: sedentary (<100 counts/minute [cpm]), light intensity PA (100-<1952 cpm), moderate intensity PA (1952-<5275 cpm), vigorous intensity PA (≥5275 cpm), or MVPA (≥1952 cpm).[24, 25] Moderate-and-vigorous PA was assessed as total MVPA time/day and MVPA time/day in strict 'bouts' of ten consecutive minutes or more with no interruption.

## Physical Function and Muscle Strength

Objective measures of physical function included: (1) 400-meter walk as an indicator of cardiorespiratory fitness,[26] (2) repeated chair rise to measure lower extremity function,[27] (3) 6-meter usual pace walk to measure gait speed during daily activities, (4) 6-meter backwards walk to measure dynamic balance.[28, 29] All tests, except for the 400-meter walk test, were performed in triplicate and the fastest of each was used for analysis. Upper and lower body muscle strength was measured with one repetition maximum (1-RM) chest press and single leg extension (dominant leg unless contraindicated), respectively. Relative strength was calculated by dividing absolute strength by body weight.

## Body Composition and Muscle Morphology

Body composition was measured by dual-energy x-ray absorptiometry (DXA, QDR-1500, Hologic Discovery A, Waltham, MA). Participants' regional and whole-body lean mass, fat mass, fat percentage, areal bone mineral content and areal bone mineral density were measured. Peripheral quantitative computed tomography (pQCT, XCT-3000, Stratec Medizintechnik, Pforzheim, Germany) scans were performed to measure muscle cross-sectional area and density, and tibial mass, cross-sectional area and volumetric density across macroscopic (trabecular, cortical and total) bone material.

### Statistical Analysis

Data were analyzed using SPSS version 23 (IBM Corp., NY, USA). The Shapiro-Wilk test was used to assess normality of variables. Results for frequency data are presented as number/percentage, and mean/standard deviation for normally distributed data, or median/interquartile range for non-normally distributed data. Non-parametric tests were used to analyze non-normally distributed data. Probability of significant differences between OCS and controls were determined using the Pearson Chi square test, Likelihood Ratio or Fisher's exact test for categorical data, and independent t-tests or Mann-Whitney U tests for continuous variables. Pearson r or Spearman rho correlations were used to determine association between variables for OCS. All tests were two-tailed, with statistical significance set at an alpha level of 0.05.

## RESULTS

Participant recruitment details and characteristics have been reported previously.[17] Briefly, 20 OCS and 20 controls were recruited between July 2015 and May 2016. Eligible OCS were recruited via the consulting rooms of three gynecologic oncologists. Controls were recruited via snowball sampling, from staff at a local university and hospital, and from the wider community. The OCS-group was on average 5.3 months (range 3-18) post cancer treatment. All OCS had undergone surgery, with 9 (45%) and 11 (55%) having received neoadjuvant or adjuvant chemotherapy, respectively. There were no differences between OCS and controls for age (63.2±8.9 vs. 63.0±9.1 years; $p = 0.944$) or BMI (27.4±4.5 vs. 27.2±4.5 kg/m²; $p = 0.888$). Most OCS and controls reported one or more comorbidities (75% vs. 80%; $p = 0.426$). More OCS than controls had obtained a university degree (50% vs. 15%; $p = 0.033$), while more controls than OCS were currently working (100% vs. 80%; $p = 0.031$).

### Health-related Quality of Life and Pelvic Floor Dysfunction

Compared to controls, OCS had significantly lower scores in three of the four physical component subscales, namely Physical Functioning ($p = 0.024$), Role Physical ($p = 0.023$) and

General Health (p = 0.021), as well as PCS (p = 0.013). No statistical differences were observed between OCS and controls for any of the mental component subscales, or MCS (Figure 4).

An extreme outlier (i.e., >3.0 x IQR) was removed from the control group for the Pelvic Floor Score. No significant differences were observed between OCS and controls for Bladder, Bowel or POP Scores, or the Pelvic Floor Score. Seventy percent (n = 14) of OCS vs. 40% (n = 8) of controls were sexually inactive (chi square = 3.636; p = 0.057) (Table 5).

## Associations between Health-related Quality of Life and Pelvic Floor Dysfunction in Ovarian Cancer Survivors

Bladder Score was significantly inversely correlated with Physical Functioning (ρ = -0.451; p = 0.046), Role Physical (r = -0.533; p = 0.016), General Health (r = -0.475; p = 0.034) and PCS (r = -0.520; p = 0.019). Bowel Score was significantly inversely correlated with Physical Functioning (ρ = -0.478; p = 0.039), Role Physical (r = -0.479; p = 0.038), General Health (r = -0.571; p = 0.011), Vitality (r = -0.554; p = 0.014), Role Emotional (ρ = -0.490; p = 0.033), Mental Health (r = -0.499; p = 0.030) and PCS (r = -0.473; p = 0.041). Pelvic Floor Score was significantly inversely correlated with Physical Functioning (ρ = -0.509; p = 0.026), Role Physical (r = -0.482; p = 0.036), General Health (r = -0.558; p = 0.013), Role Emotional (ρ = -0.509; p = 0.026) and PCS (r = -0.468; p = 0.043).

## Associations between Health-related Quality of Life and Activity Behavior, Physical Function and Body Composition in Ovarian Cancer Survivors

We have previously conducted a comprehensive cross-sectional assessment of objectively measured activity behavior and physical function, and body composition in OCS, compared to age-matched controls. Results are reported elsewhere.[17]

In this study MVPA time/day was significantly correlated with Physical Functioning (ρ = 0.532; p = 0.016), Bodily Pain (ρ = 0.521; p = 0.018), General Health (ρ = 0.511; p = 0.021), and

PCS (ρ = 0.606; p = 0.005). Moderate-and-vigorous PA time/day in ≥ 10-minute bouts was significantly correlated with Physical Functioning (ρ = 0.499; p = 0.025), Bodily Pain (ρ = 0.531; p = 0.016) and PCS (ρ = 0.627; p = 0.003). Sedentary time/day was significantly inversely correlated with Physical Functioning (ρ = -0.578; p = 0.008), Role Physical (r = -0.454; p = 0.045), General Health (r = -0.720; p = <0.001), Vitality (r = -0.656; p = 0.002), Mental Health (r = -0.636; p = 0.003) and PCS (r = -0.449; p = 0.047).

Six-meter usual walk time was significantly inversely correlated with Physical Functioning (ρ = -0.655; p = 0.002) and PCS (r = -0.588; p = 0.006). Four hundred meter walk time was significantly inversely correlated with Physical Functioning (ρ = -0.608; p = 0.004), Bodily Pain (ρ = -0.514; p = 0.020) and PCS (ρ = -0.565; p = 0.009) Relative lower body strength was significantly correlated with PCS (r = 0.537; p = 0.022).

Neither BMI nor any of the body composition components were correlated with any of the HRQoL domains.

**Associations between Pelvic Floor Dysfunction, and Activity Behavior, Physical Function and Body Composition in Ovarian Cancer Survivors**

Moderate-and-vigorous PA time/day in ≥ 10-minute bouts, but not total MVPA time/day, was significantly inversely correlated with Pelvic Floor Score (ρ = -0.457; p = 0.049). Sedentary time/day was significantly correlated with Bowel Score (r = 0.531; p = 0.019) and Pelvic Floor Score (r = 0.479; p = 0.038).

Six-meter usual walk time was significantly correlated with Bladder (r = 0.729; p = <0.001) and Pelvic Floor Scores (r = 0.514; p = 0.024). Four hundred meter walk time was significantly correlated with Bladder (ρ = 0.554; p = 0.011) and Pelvic Floor Scores (ρ = 0.504; p = 0.028). Relative upper and lower body strength were significantly inversely correlated with Bladder Score (r = -0.477; p = 0.045, r = -0.541; p = 0.020)

No significant correlations were observed between BMI or components of body composition, and PFD.

# DISCUSSION

The purpose of this cross-sectional study was to assess HRQoL and PFD in advanced-stage OCS, compared to age-matched controls. A secondary objective was to investigate associations between HRQoL, PFD, objective activity behaviors and physical function, and body composition in OCS. We found that OCS had worse physical HRQoL, but equivalent self-reported PFD compared to controls. Ovarian cancer survivors who reported more symptoms related to PFD had lower physical HRQoL. Worse physical HRQoL and greater PFD in OCS were associated with less MVPA in ≥ 10 minute bouts, more sedentary time and lower levels of objective physical function. Physical HRQoL, but not PFD, was positively associated with total MVPA time/day.

Our sample of OCS reported significantly lower physical and functional, but equivalent social, emotional and mental HRQoL compared to age-matched controls from the same community. Our findings are not consistent with a recent study which reported that stages I-IV OCS one year post-diagnosis have comparable HRQoL to the general US female population.[5] This may be due to the inclusion of women with early-stage disease who may have had better physical function[5] compared to only advanced-stage OCS in our study. We found no research that investigated HRQoL in advanced-stage OCS early after completion of first-line treatment. Studies comparing HRQoL of OCS and controls drawn from the same community have included stage I-IV OCS more than five years since diagnosis, with mixed results.[30, 31] Our findings suggest that advanced-stage OCS following first-line treatment experience physical health and functional limitations that negatively impact their daily living. Although this finding needs to be substantiated in larger studies, it highlights the need for ongoing care to address physical and functional limitations after completion of first-line OC treatment.

To our knowledge, this is the first study to examine the relationships between HRQoL, objectively measured activity behaviors and physical function, and body composition in OCS. Health-related QoL in OCS has previously been associated with symptom burden, self-reported PA and obesity.[4, 8] We found that better physical HRQoL was also associated with more MVPA, less sedentary time and better objective physical function in OCS. An association between HRQoL and MVPA, but not sedentary time, has been previously shown in colon cancer survivors.[32] Our data suggests that interventions aimed at increasing MVPA, reducing sedentary time and improving physical function could improve HRQoL for OCS.

Advanced-stage OCS in this study reported equivalent levels of PFD, as indicated by bladder, bowel and POP symptoms, but 30% higher rates of sexual inactivity, compared to controls. Research in gynecological cancer survivors indicates that rates of urinary incontinence and other pelvic floor symptoms are high even before commencement of cancer treatment; however, the prevalence of symptoms does not differ compared to non-cancer controls.[12, 33] Studies investigating PFD after completion of gynecological cancer treatment suggest that, compared to controls, gynecological cancer survivors have equivalent urinary incontinence and POP, but more fecal incontinence and sexual inactivity.[6, 7] One reason for the difference between our observation and findings in gynecological cancer survivors regarding bowel symptoms could be related to different treatment regimens. Radiation therapy is not used in first-line OC treatment, but is common in endometrial and cervical cancer treatment,[34] and is associated with detrimental radiation-induced gastrointestinal toxicities.[35] Although clearly OCS may experience severe and debilitating PFD, our data suggest that the prevalence of self-reported PFD is not different in advanced-stage OCS compared to similarly-aged women with comparable BMI in the general population.

It is notable that OCS who experienced more PFD also reported worse HRQoL, consistent with research in the general population of women.[10, 11] Existing evidence indicates that some aspects of PFD are treatable, for example, pelvic floor muscle training has been shown to be effective in treating urinary incontinence.[36] Evidence-based education and screening of OCS for

PFD at diagnosis and throughout their cancer journey is required, with appropriate referral for assessment and treatment when indicated. The level of PFD experienced by individual OCS should guide recommendations and precautions for physical activity participation, exercise testing and exercise training.

In the general female population, pelvic floor dysfunction is associated with modifiable risk factors such as low self-reported PA levels,[37] reduced physical function[38] and obesity.[39] We found that OCS with more PFD spent less time/day doing MVPA in ≥ 10-minute bouts. This is consistent with results from a recent study indicating an inverse association between MVPA in ≥ 10-minute bouts and PFD in middle-aged women from the general population.[40] These findings suggest that the prevalence of PFD may not affect participation in light, informal PA associated with daily living, but negatively affects participation in planned, purposeful and repetitive MVPA (i.e., exercise) in ≥ 10-minute bouts, which is associated with optimal health benefits.[41] In our study OCS with more PFD also accrued more sedentary time/day and had worse objective physical function. Future research is needed to determine to what extent increased PFD in OCS affects physical activity participation and sedentary behavior, and subsequently objective physical function. Best current evidence suggests that most PA does not harm the pelvic floor; however, more research is needed to fill existing knowledge gaps.[37] For OCS with multiple pelvic floor symptoms, multidisciplinary interventions aimed at treating PFD while incorporating exercise training could be beneficial. Conversely, findings from our study suggest that many OCS who have completed first-line treatment experience only a few mild pelvic floor symptoms (e.g., 58% of OCS scored ≤5/30 for combined bladder, bowel and POP symptoms). Physical activity and exercise participation for these OCS should not be restricted based on pelvic floor concerns, especially considering potential improvements in cancer survivors' HRQoL after participating in exercise programs.[42]

Notably, in this study HRQoL and PFD in OCS were not associated with BMI or components of body composition (e.g., lean mass, fat mass or fat percentage). This was a surprising finding considering that existing evidence supports associations between obesity and decreased

HRQoL in OCS[8] and between obesity and PFD in the general population.[39, 43] These findings may be due to our study being underpowered to detect such associations and require further investigation in larger prospective studies.

Limitations of the study include the cross-sectional study design, which does not allow inferences to be made regarding changes over time or causality. As we did not adjust data for multiple comparisons, three of our findings could be due to chance. The small sample size limits generalization of results. An objective measurement of PFD (e.g., ultrasound) and/or the inclusion of questions regarding previous treatments and known risk factors (e.g., parity and vaginal birth) for PFD would have provided a better understanding of PFD in both OCS and controls. We acknowledge the possibility of recruitment bias, as women with severe pelvic floor symptoms might not have volunteered for participation due to their perceived inability to complete functional tests. Our study provides important preliminary information about associations between HRQoL and objectively measured activity behaviors and physical function, and body composition in OCS. Furthermore, this is the first study to provide a comprehensive cross-sectional analysis of self-reported PFD and its associations with HRQoL, objectively measured activity behavior, physical function and body composition in OCS. Further strengths of our study include the relative homogeneity of our sample of OCS in terms of disease and treatment stage and the inclusion of an age-matched control group from the same community.

# CONCLUSION

In this cross-sectional study advanced-stage OCS who had completed first-line treatment had lower physical, but equivalent mental HRQoL, compared to controls. Ovarian cancer survivors who reported better physical HRQoL did more MVPA/day, spent less time/day sedentary and had better objective physical function. Pelvic floor dysfunction was not significantly different between OCS and controls. Ovarian cancer survivors with more PFD had worse physical and mental HRQoL, did less MVPA in ≥10-minute bouts, spent more time/day sedentary and had worse

objective physical function. Post-treatment advanced-stage OCS have decreased physical HRQoL, which is associated with modifiable factors such as PFD, MVPA, sedentary time and objective physical function. This highlights the need for ongoing supportive care and the importance of multidisciplinary interventions beyond the completion of first-line OC treatment.

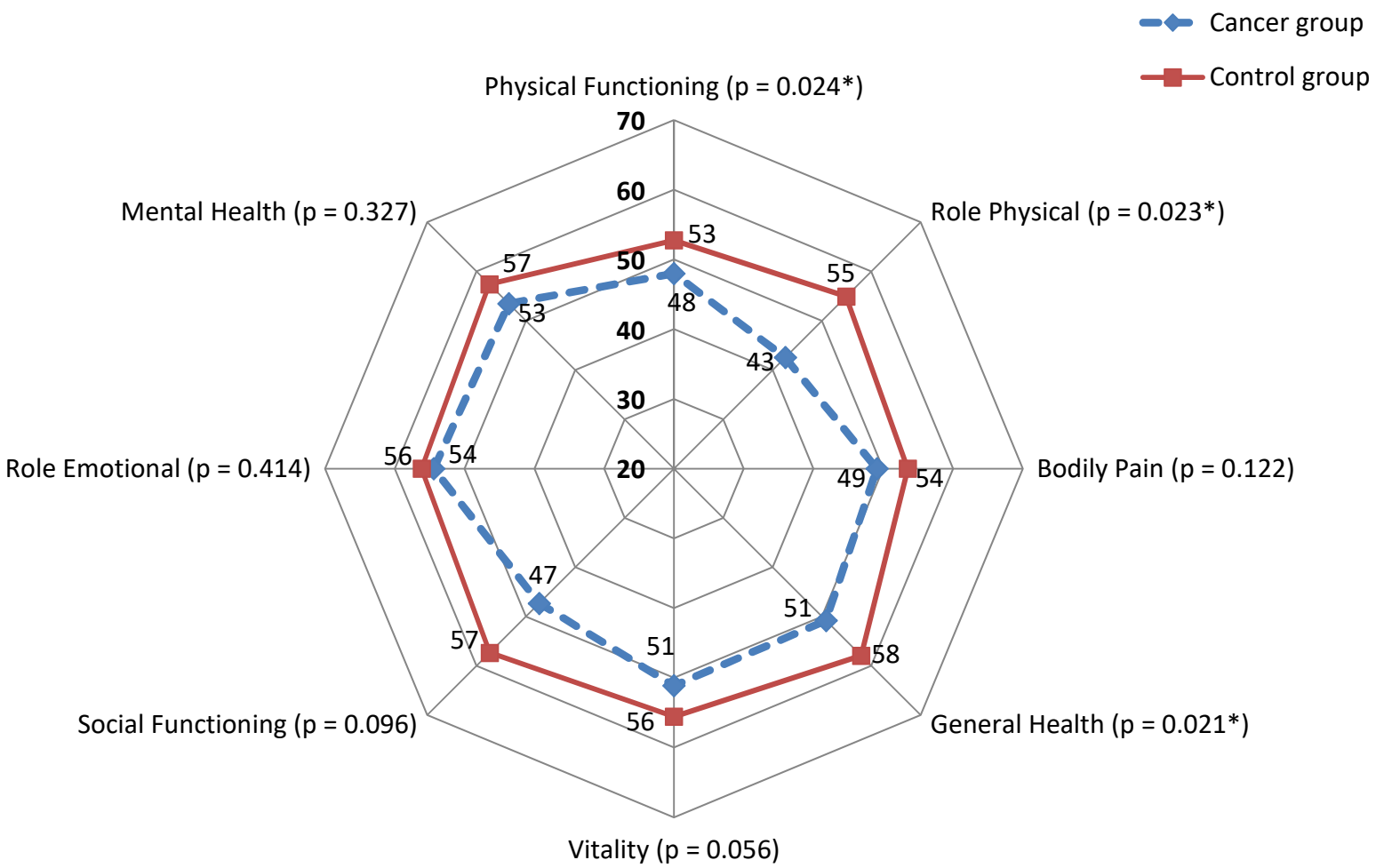


**Figure 4. Median SF-36 subscale scores for Cancer and Control groups**

*Statistical significance ($p < 0.05$)

**Table 5. Bladder, bowel and pelvic organ prolapse symptoms scores for Cancer and Control groups**

| | Cancer group | | Control group | | p-value |
|---|---|---|---|---|---|
| | (n = 20) | Median (Range) | (n = 20) | Median (Range) | T-test |
| Bladder score (/10) | 1.11 (1.89)† | 1.11 (0.00-4.00) | 1.33 (1.61)† | 1.33 (0.22-5.11) | 0.989‡ |
| Bowel score (/10)§ | 2.23±1.87 | 2.06 (0.00-6.18) | 1.97±1.38 | 2.06 (0.00-4.41) | 0.626 |
| POP score (/10)§§ | 0.00 (0.00)† | 0.00 (0.00-2.00) | 0.00 (0.00)† | 0.00 (0.00-4.67) | 0.901‡ |
| Pelvic Floor Score (/30) | 4.05 (4.85)† | 4.06 (0.00-8.71) | 3.03 (2.66)† | 3.03 (0.52-13.90) | 0.624‡ |
| Pelvic Floor Score (/30)¶ | 4.17±2.94 | 4.06 (0.00-8.71) | 3.28±1.86 | 3.03 (0.52-7.83) | 0.277 |
| Sexually active | n (%) | | n (%) | | 0.057† |
| Yes | 6 (30) | | 12 (60) | | |
| No | 14 (70) | | 8 (40) | | |

POP = Pelvic organ prolapse; Pelvic Floor Score = combined bladder, bowel and POP symptoms score for each participant

†Pearson Chi-square

Values are presented as mean±SD unless otherwise specified

†Median (interquartile range), ‡Mann-Whitney test

§Cancer group n = 19, §§Control group n = 19 due to missing data

¶Extreme outlier removed from Control group

*Statistical significance ($p < 0.05$)

# REFERENCES


1. Ferlay J, Soerjomataram I, Ervik M, et al. GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 [Internet]. Lyon, France: International Agency for Research on Cancer; 2013. Available from: http://globocan.iarc.fr. Accessed September 20, 2016.
2. Sato S, Itamochi H. Neoadjuvant chemotherapy in advanced ovarian cancer: latest results and place in therapy. Ther Adv Med Oncol. 2014;6:293-304.
3. Herzog TJ. Recurrent ovarian cancer: how important is it to treat to disease progression? Clin Cancer Res. 2004;10:7439-7449.
4. Ahmed-Lecheheb D, Joly F. Ovarian cancer survivors' quality of life: a systematic review. J Cancer Surviv. 2016;10:789-801.
5. Zhou Y, Irwin ML, Ferrucci LM et al. Health-related quality of life in ovarian cancer survivors: Results from the American Cancer Society's Study of Cancer Survivors - I. Gynecol Oncol. 2016;141:543-549.
6. Rutledge TL, Heckman SR, Qualls C et al. Pelvic floor disorders and sexual function in gynecologic cancer survivors: a cohort study. Am J Obstet Gynecol. 2010;203:514.e1-7.
7. Skjeldestad FE, Hagen B. Long-term consequences of gynecological cancer treatment on urinary incontinence: a population-based cross-sectional study. Acta Obstet Gynecol Scand. 2008;87:469-475.
8. Smits A, Smits E, Lopes A et al. Body mass index, physical activity and quality of life of ovarian cancer survivors: Time to get moving? Gynecol Oncol. 2015;139:148-154.
9. Stevinson C, Faught W, Steed H et al. Associations between physical activity and quality of life in ovarian cancer survivors. Gynecol Oncol. 2007;106:244-250.
10. Kenton K, Mueller ER. The global burden of female pelvic floor disorders. BJU Int. 2006;98(suppl 1):1-5.
11. Lowenstein L, Pierce K, Pauls R. Urogynecology and sexual function research. How are we doing? J Sex Med. 2009;6:199-204.
12. Bretschneider CE, Doll KM, Bensen JT et al. Prevalence of pelvic floor disorders in women with suspected gynecological malignancy: a survey-based study. Int Urogynecol J. 2016;27:1409-1414.

13. Davis K, Kumar D. Pelvic floor dysfunction: a conceptual framework for collaborative patient-centred care. J Adv Nurs. 2003;43:555-568.

14. Hopkins TG, Stavraka C, Gabra H et al. Sexual activity and functioning in ovarian cancer survivors: an internet-based evaluation. Climacteric. 2015;18:94-98.

15. Ferrell B, Smith S, Cullinane C et al. Symptom concerns of women with ovarian cancer. J Pain Symptom Manage. 2003;25:528-538.

16. Schofield C, Newton RU, Galvão DA et al. A Physiological Profile of Ovarian Cancer Survivors to Inform Tailored Exercise Interventions and the Development of Exercise Oncology Guidelines. Int J Gynecol Cancer. 2017;27:1560-1567.

17. Schofield C, Newton RU, Galvão DA et al. Activity behaviors and physiological characteristics of women with advanced-stage ovarian cancer: a comprehensive cross-sectional investigation. Int J Gynecol Cancer. Under review. 2017.

18. Stewart AL, Greenfield S, Hays RD et al. Functional status and well-being of patients with chronic conditions. Results from the Medical Outcomes Study. JAMA. 1989;262:907-913.

19. Lazovich D, Robien K, Cutler G et al. Quality of life in a prospective cohort of elderly women with and without cancer. Cancer. 2009;115:4283-4297.

20. Ware JE. User's Manual For The Sf-36v2 Health Survey, Second Edition,: Quality Metric Inc., Lincoln, ; 2007;81-84.

21. Schlenk EA, Erlen JA, Dunbar-Jacob J et al. Health-related quality of life in chronic disorders: a comparison across studies using the MOS SF-36. Qual Life Res. 1998;7:57-65.

22. Baessler K, O'Neill SM, Maher CF et al. Australian pelvic floor questionnaire: a validated interviewer-administered pelvic floor questionnaire for routine clinic and research. Int Urogynecol J Pelvic Floor Dysfunct. 2009;20:149-158.

23. Baessler K, O'Neill SM, Maher CF et al. A validated self-administered female pelvic floor questionnaire. International Urogynecology Journal. 2010;21:163-172.

24. Freedson PS, Melanson E, Sirard J. Calibration of the Computer Science and Applications, Inc. accelerometer. Med Sci Sports Exerc. 1998;30:777-781.

25. Matthews CE, Chen KY, Freedson PS et al. Amount of time spent in sedentary behaviors in the United States, 2003-2004. Am J Epidemiol. 2008;167:875-881.

26. Simonsick EM, Fan E, Fleg JL. Estimating cardiorespiratory fitness in well-functioning older adults: treadmill validation of the long distance corridor walk. J Am Geriatr Soc. 2006;54:127-132.

27. Cesari M, Kritchevsky SB, Newman AB et al. Added value of physical performance measures in predicting adverse health-related events: results from the Health, Aging And Body Composition Study. J Am Geriatr Soc. 2009;57:251-259.

28. Peiffer JJ, Galvão DA, Gibbs Z et al. Strength and functional characteristics of men and women 65 years and older. Rejuvenation Res. 2010;13:75-82.

29. Galvão DA, Taaffe DR. Resistance exercise dosage in older adults: single- versus multiset effects on physical performance and body composition. J Am Geriatr Soc. 2005;53:2090-2097.

30. Greimel ER, Bottomley A. Quality of life issues in gynecological cancer. Expert Rev Pharmacoecon Outcomes Res. 2001;1:93-98.

31. Liavaag AH, Dørum A, Fosså SD et al. Controlled study of fatigue, quality of life, and somatic and mental morbidity in epithelial ovarian cancer survivors: how lucky are the lucky ones? J Clin Oncol. 2007;25:2049-2056.

32. Vallance JK, Boyle T, Courneya KS et al. Associations of objectively assessed physical activity and sedentary time with health-related quality of life among colon cancer survivors. Cancer. 2014;120:2919-2926.

33. Thomas SG, Sato HRN, Glantz JC et al. Prevalence of symptomatic pelvic floor disorders among gynecologic oncology patients. Obstet Gynecol. 2013;122:976-980.

34. Pecorelli S, Angioli R, Pasinetti B et al. Systemic therapy for gynecological neoplasms: ovary, cervix and endometrium. Update Cancer Ther. 2006;1:515-538.

35. Andreyev HJN, Wotherspoon A, Denham JW et al. “Pelvic radiation disease”: New understanding and new solutions for a new disease in the era of cancer survivorship. Scand J Gastroenterol. 2011;46:389-397.

36. Dumoulin C, Hay-Smith J, Habée-Séguin GM et al. Pelvic floor muscle training versus no treatment, or inactive control treatments, for urinary incontinence in women: a short version Cochrane systematic review with meta-analysis. Neurourol Urodyn. 2015;34:300-308.

37. Nygaard IE, Shaw JM. Physical activity and the pelvic floor. Am J Obstet Gynecol. 2016;214:164-171.

38. Kafri R, Shames J, Golomb J et al. Self-report function and disability: a comparison between women with and without urgency urinary incontinence. Disabil Rehabil. 2012;34:1699-1705.

39. Pomian A, Lisik W, Kosieradzki M et al. Obesity and Pelvic Floor Disorders: A Review of the Literature. Med Sci Monit. 2016;22:1880-1886.

40. Laakkonen EK, Kulmala J, Aukee P et al. Female reproductive factors are associated with objectively measured physical activity in middle-aged women. PLoS ONE. 2017;12:e0172054.

41. Haskell WL, Lee IM, Pate RR et al. Physical activity and public health: updated recommendation for adults from the American College of Sports Medicine and the American Heart Association. Circulation. 2007;116:1081-1093.

42. Mishra SI, Scherer RW, Snyder C et al. Exercise interventions on health-related quality of life for people with cancer during active treatment. Cochrane Database Syst Rev. 2012;8:CD008465.

43. Neto IJFC, Pinto RA, Jorge JMN et al. Are Obese Patients at an Increased Risk of Pelvic Floor Dysfunction Compared to Non-obese Patients? Obes Surg. 2017;27:1822-1827.

# *Chapter 5*

# CONCLUSION

## OVERVIEW

This research aimed to provide a comprehensive profile of activity behaviors and physiological characteristics of advanced-stage OCS who have completed first-line treatment. This chapter is a summary of findings from the literature review (Chapter Two) and observational study (Chapters Three and Four), while highlighting the strengths, challenges and clinical implications of this work.

Chapter Two provides a summary of current literature relating to treatment-related side-effects, concurrent comorbidities, body weight and composition, physical fitness and function, and PA behavior of OCS. Findings from the literature review indicate that women diagnosed with OC are faced with many challenges, such as persistent disease and treatment symptoms and side-effects, concurrent comorbidities, obesity and physical inactivity. Overall, current literature is limited by a lack of objectively measured data and the heterogeneous nature of existing OC studies.

Therefore, the primary aim of the observational study was to extend current literature by assessing objectively measured activity behaviors (i.e., PA and sedentary behavior) and physical function, body composition and musculoskeletal morphology of post-treatment advanced-stage OCS compared to age-matched controls. Self-reported PFD and HRQoL of this sample of OCS were also assessed. The results were that, compared to age-matched controls, OCS spent more time in prolonged sedentary bouts, had lower cardiorespiratory fitness, upper body strength and physical HRQoL, but had equivalent self-reported PFD. Further, better physical HRQoL was associated with

more time spent doing MVPA, less time spent in sedentary behavior, better objective physical function and less PFD. These findings suggest that many of the issues associated with reduced physical HRQoL in post-treatment advanced-stage OCS are potentially modifiable with a multidisciplinary approach that includes exercise oncology interventions.

# LIMITATIONS, STRENGTHS AND IMPLICATIONS FOR PRACTICE

The study design and modest sample size limit conclusions that can be drawn from this work. Despite these limitations, the thesis provides important preliminary information about objectively measured activity behaviors and physical function, body composition, musculoskeletal morphology, self-reported PFD and HRQoL in post-treatment advanced-stage OCS. Conducting the observational study provided challenges and insights worth considering in the development of exercise intervention studies and exercise oncology guidelines.

Recruitment of participants for clinical research is known to be challenging and time-consuming. In the current study there were several factors that impacted eligibility and recruitment. A large percentage of OCS (20%) identified by clinicians as potentially eligible for the study could not be reached, despite various attempts to contact them. Another 20% had recurrent disease at the time of recruitment, or were too unwell to participate. A portion of eligible OCS (27%) declined the invitation to participate due to lack of interest. Research in cancer populations indicates that clinical trials are often considered an inconvenience to everyday life.[1] Additionally, several eligible OCS (14%) expressed interest to participate, but declined based on the fact that they lived far from the location where assessments were conducted. This is consistent with previous research reporting transportation issues and distance to trial sites as patient-related barriers to participation.[1] Similar challenges are likely to present when recruiting participants for exercise intervention studies and need to be considered when developing strategies for recruitment of OCS into exercise intervention studies.

In the observational study, no adverse events were reported as result of functional and strength testing. However, one repetition maximum (1-RM) strength testing was contra-indicated in a small percentage of OCS (10% for 1-RM chest press, 10% for with 1-RM single leg extension) with joint replacements or severe arthritis. In designing the study, a single leg extension 1-RM test was selected as a conservative measure considering the possible high prevalence of PFD after OC treatment. Based on our findings regarding the prevalence of PFD in OCS, a more functional measure of lower body strength, such as the leg press, may be considered for OCS without musculoskeletal and/or PFD contraindications. This work suggests that the majority of OCS can safely undergo functional and strength testing, but that certain tests should be modified following screening for comorbid conditions, PFD and treatment side-effects. This is likely to hold true for exercise interventions, which may require an individualized approach based on participants' treatment side-effects (e.g., peripheral neuropathy), comorbidities (e.g., arthritis, osteoporosis) and current level of physical fitness and function. As such, comprehensive screening for the prevalence and severity of persistent treatment side-effects and comorbidities, and exercise testing to determine physical fitness and function, should precede exercise interventions.

This was the first study to assess PFD in OCS. However, only self-reported PFD was assessed. Some objective measurement of PFD (e.g., ultrasound), as well as the inclusion of questions regarding previous treatments for PFD and known risk factors for PFD (e.g., parity and vaginal birth) would have provided a more complete picture of PFD for both OCS and controls. This research suggests that OCS should undergo PFD screening to identify pelvic floor symptoms that could necessitate an individualized approach to exercise testing and prescription.

# FUTURE RESEARCH

This thesis describes the activity behaviors, objective physiological characteristics, HRQoL and self-reported PFD of post-treatment advanced-stage OCS. However, possible differences that were not extensively investigated in our current study may exist based on the type of OC, treatment stage and/or treatment regime. In this research study, differences were observed regarding some activity behaviors and physiological characteristics based on type of treatment previously received. This suggests that OCS on different treatment regimens may require different exercise intervention strategies. Longitudinal studies incorporating larger sample sizes are needed to investigate potential activity behavior and physiological differences between "sub-groups" of advanced-stage OCS (e.g., women with different types of OC and on different treatment regimens). Changes in activity behavior, physiological characteristics and HRQoL of advanced-stage OCS over the entire disease spectrum also need to be investigated. Furthermore, findings of this thesis suggest that the physical HRQoL of post-treatment advanced-stage OCS are affected by potentially modifiable factors such as insufficient MVPA and reduced objective physical function. Future pilot studies and randomized controlled trials are needed to assess the feasibility and efficacy of tailored exercise interventions in advanced-stage OCS who have completed first-line treatment.

# CONCLUSION

In conclusion, this research examined activity behaviors and physiological characteristics of post-treatment advanced-stage OCS to inform the design of supportive care interventions. Overall, the findings of this research are that advanced-stage OCS who have completed first-line treatment are insufficiently physically active and have decreased physical HRQoL, which is associated with modifiable factors such as MVPA, sedentary time, objective physical function and PFD. Post-treatment OCS require ongoing multidisciplinary supportive care delivered by a team of allied health professionals that includes exercise physiologists. Future exercise intervention studies are

required to investigate the feasibility and benefits of exercise as medicine for women who have completed first-line treatment for advanced-stage OC.

## REFERENCES

1. Mills EJ, Seely D, Rachlis B et al. Barriers to participation in clinical trials of cancer: a meta-analysis and systematic review of patient-reported factors. Lancet Oncol. 2006;7:141-148.

# *Appendices*

# Appendix A – Detailed methods section

## SETTING AND PARTICIPANTS

The study was conducted at the Exercise Medicine Research Institute at Edith Cowan University and St John of God Subiaco Hospital in Perth, Western Australia. Ethical approval was granted by the Edith Cowan University (Ref. No. 12511, 23/4/2015; Appendix B) and St John of God Health Care Human Research Ethics Committees (Ref. No. 815, 12/6/2015; Appendix C). Two groups of women were recruited: (1) ovarian cancer survivors (OCS) (n = 20) and (2) similarly aged women with no previous cancer diagnosis (n = 20). We required 22 participants for each group in order to achieve 80% statistical power at an alpha level of 0.05 (two-tailed) to detect a difference in leg strength between groups. The power calculation was based on a publication in which a mean difference in leg strength (1-RM leg press) of 22.5 kg, and a pooled variance of 25.5 kg (effect size = 0.88) were reported between women with breast cancer and similarly aged women with no history of cancer.[1] Due to recruitment of OCS being slower than expected, we only managed to recruit 20 women in the allotted time frame.

Ovarian cancer survivors were eligible for participation if they had histologically confirmed stage III – IV epithelial OC and were between 3 and 24 months post cancer-related treatment (surgery and chemotherapy), were 18 years or older, able to obtain approval from their treating oncologist or general practitioner, able to walk 400 meters, able to understand and speak English, and had no existing or suspected bone metastasis, no acute illness or any musculoskeletal, cardiovascular or neurological disorder that could put them at risk during exercise testing. The same non-cancer eligibility criteria applied for the control group. Written informed consent was obtained from all participants.

## DESIGN AND RECRUITMENT

We conducted a cross-sectional study. Participants for the OC group were recruited by screening for potentially eligible participants in the rooms of three gynecological oncologists in Perth. Potentially eligible OCS were informed of the research study either via a phone call from the practice nurse or an information letter (Appendix D) and study brochure (Appendix E) sent out from the oncologists' rooms. The study coordinator (CS) then contacted potentially eligible participants by phone to determine interest and confirm eligibility.

Participants for the control group were recruited by several methods. Initially participants from the cancer group were asked if they had similarly aged female family members or friends who would be willing to participate in the study. When required, control participants were recruited from staff at the Edith Cowan University and a local cancer care center (Appendix F), and the wider community. Interested women were asked to contact the study coordinator to confirm eligibility. Women were recruited as control participants if they could be age-matched to an OC participant, i.e., if they were of similar age, or no more than two years older or younger.

A study information pack containing a cover letter (Appendix G), participant information letter (Appendix H and I), medical consent form (Appendix J and K), participant consent form (Appendix L), demographic and health history questionnaire (Appendix M) and a Day 1 letter (Appendix N) was posted to all interested and eligible participants. Follow-up telephone calls were made one week after posting the study information packs to confirm receipt, answer questions regarding the study and book assessments.

## STUDY PROCEDURES

All participants underwent two separate assessments, no less than six, but no more than 14 days apart. Assessments took 2.5-3.0 hours and 1.5-2.0 hours respectively to complete and were conducted at the Edith Cowan University Exercise Medicine Research Institute. All anthropometric,

body composition and objective functional data were collected by the study coordinator, an accredited exercise physiologist.

On commencement of the first assessment, consent forms, demographic and medical history questionnaires, and study procedures were reviewed with participants. Participants were also provided an opportunity to ask questions regarding the study. Anthropometric measures and resting heart rate and blood pressure measures were completed. In addition, each participant underwent a dual-energy X-ray absorptiometry (DXA) body composition and peripheral quantitative computed tomography (pQCT) scan, and completed a series of functional measures for familiarization purposes. At the end of the assessment, participants were provided with an ActiGraph (GT3X+) accelerometer, an instruction sheet for accelerometer use (Appendix O), an activity monitor log (Appendix P) and a second questionnaire assessing health-related quality of life (HRQoL), pelvic floor dysfunction (PFD), physical activity (PA) level and PA motivation (Appendix Q).

To minimize the learning effect, all functional tests were repeated during the second assessment. After completion of all tests on the second day, the study coordinator provided feedback and exercise advice to interested participants.

# OUTCOME MEASURES

Demographic and medical data were obtained by self-reported questionnaires and provided information regarding participants' age, marital status, educational attainment, employment status and medical history. Additional information regarding date of cancer diagnosis, date of treatment completion, cancer stage and treatment(s) received were acquired from OCS.

## Anthropometric measures

Height (m) and body weight (kg), measured by digital measuring-and-weighing station (Model 763, Seca, Hamburg, Germany), were used to calculate body mass index (BMI) in $m/kg^2$. Waist and hip circumference (cm) were measured at the narrowest part of the torso or between the

iliac crest and 12th rib, and the maximal circumference of the hip.[2] Waist-to-hip ratio was calculated by dividing waist circumference by hip circumference. For accurate set-up of the pQCT scanner, left tibial length (with one exception due to a metal implant) was measured in cm from the tibial plateau at the knee joint (proximal end) to the medial malleolus of the tibia (distal end). All measures were recorded to the nearest 0.1.

## Body composition

Whole-body DXA scans were performed using DXA (QDR-1500, Hologic Discovery A, Waltham, MA, USA) to measure participants' regional and whole-body lean and fat mass, as well as bone mineral content (g) and areal bone mineral density (g/cm²). Dual-energy X-ray absorptiometry has been established as a valid[3, 4] and reliable[5] measure of body composition and has often been used to assess body composition or components thereof in a variety of cancer populations.[6-9]

In addition to DXA scans, tibial peripheral quantitative computed tomography (pQCT) scans (pQCT, XCT-3000; Stratec Medizintechnik, Pforzheim, Germany) were conducted. In contrast to DXA, pQCT differentiates between trabecular and cortical bone and provides volumetric bone mineral density values (in mg/cm³) of bone tissue at peripheral skeletal sites, thus providing more comprehensive bone tissue information.[10] Furthermore, while DXA measures fat and muscle mass, pQCT provides information on the quality of muscle due to the ability to generate estimations of muscle density.[11] Four pQCT scan slices were measured at 4%, 14%, 38% and 66% of tibial length respectively (distal to proximal). Variables across all tibial slices were retained for analysis. Trabecular density and trabecular area were obtained from the 4% slice, cortical density and cortical area were averaged across the 14% and 38% tibial slices, muscle density and muscle area were obtained from the 66% slice, and tibial mass, total tibial area and tibial density were averaged across the 4%, 14%, and 38% tibial slices.

## Physical activity and sedentary time

Objective PA and sedentary time were measured with a hip-worn tri-axial accelerometer (ActiGraph GT3X+, ActiGraph Corp, FL, USA). Participants were asked to wear the accelerometer continuously for seven days, except when bathing/showering or participating in water-based activities. The GT3X+ was programmed to record raw data at a frequency of 30Hz, which were later reduced to vertical axis movement counts/60 s epoch for the purpose of our analyses. Accelerometer data were downloaded with Actilife (Version 6.13.3, ActiGraph Corp, FL, USA) and processed in SAS (Version 9.3, SAS Institute Inc., NC, USA). An automated algorithm was used to identify awake wear time[12] and non-wear time.[13] Non-wear time is defined as 90-minute periods of zero acceleration counts/minute [cpm], with allowance for 2-min intervals of non-zero counts for detection of accidental movement of the monitor, e.g., touching of monitor sitting on a table or nightstand).[13] To render days of data collection valid, a minimum awake wear time of 600 minutes (10 hours) was required.[14] A minimum of four valid days was required for analysis. Activity counts were categorized as: sedentary (<100 cpm), light intensity PA (LIPA; 100-<1952 cpm), moderate intensity PA (1952-<5275 cpm), vigorous intensity PA (≥5275 cpm), or moderate-to-vigorous PA (MVPA; ≥1952 cpm).[15, 16] Moderate-to-vigorous PA was assessed as total MVPA time/day and MVPA time/day in strict 'bouts' of ten consecutive minutes or more with no interruption. Participants were categorized as meeting (i.e., ≥150 minutes of MVPA/week) or not meeting (i.e., <150 minutes of MVPA/week) current PA guidelines for cancer survivors.[17] Prolonged sedentary bouts were defined as uninterrupted sedentary bouts of ≥30 minutes. Accelerometers are increasingly being used to measure time spent, and patterns of accumulation, in different intensities of physical activity and sedentary behavior.[18-20]

Self-reported physical activity was assessed by the Leisure Score Index (LSI) of the Godin Leisure Time Exercise Questionnaire (GLTEQ). The questionnaire asks participants to recall their average weekly frequency and duration of mild, moderate and strenuous activity during the past

month. The GLTEQ is considered a valid and reliable measure of self-reported physical activity[21] and is often utilized to assess physical activity behavior in gynecological cancer survivors.[22, 23]

## Objective physical function

Objective physical function was assessed through a battery of tests including: (1) a series of 6-meter walking tasks, (2) 400-meter walking test, (3) repeated chair rise, and (4) muscular strength tests. The study coordinator gave demonstrations of the 6-meter backwards walk, repeated chair rise and strength tests and allowed sufficient rest periods between different tests as well as between trials within a specific test. Participants were reminded that they could discontinue any test that caused excessive discomfort or pain.

**6-Meter walk tests** – Three separate tests were conducted: (1) a usual pace walking test to assess gait speed during daily activities, (2) a fast pace walking test to assess the fastest self-selected pace participants could safely walk at, and (3) a backwards walking test to assess dynamic balance.[23, 24] A 6-meter distance was marked with tape on the floor. Participants were instructed to start walking from the 0-meter mark when ready and to continue walking past the 6-meter mark to eliminate the effect of deceleration. For the backwards walk, participants were instructed to walk in reverse on the 6-meter line following a toe-to-heel protocol. If participants lost balance and deviated from the line, they were instructed to return to the line and continue walking. Time taken to complete each task was measured by electronic timing gates (Swift Performance Equipment, NSW, Australia) and the fastest of three trials for each 6-meter walking test was used for analysis. Both the 6-meter walk test and the 6-meter backwards walk have been reported to have good test-retest reliability.[25-27]

**400-Meter walk test** - Participants walked 400 meters by doing 10 laps of a 20-meter course, marked with cones on the floor, in a long corridor. They were instructed to start on the command “GO” after a “three-two-one” countdown, and to walk at the fastest pace they could maintain over the total distance. Time taken to complete the 400-meter walk was measured by

handheld stopwatch. The 400-meter walk test was developed as a practical alternative to maximal or submaximal treadmill testing, to measure cardiorespiratory fitness in older adults.[28] The test has been reported as a valid measure of cardiorespiratory fitness[28, 29] and mobility,[30] with excellent test-retest reliability (ICC = 0.95).[29]

**Repeated chair rise** – Participants were seated in a hard-backed chair (chair height = 46cm) with their backs against the backrest and arms folded across their chests. They were instructed to stand up to a fully upright position (knees fully extended) and to sit back down with upper backs touching the back rest, as fast as they could safely do so five times. As with the 400-meter walk test, participants were instructed to start on the command "GO" after a "three-two-one" countdown, and time taken to complete the task was measured by handheld stopwatch. The fastest of three trials was used for analysis. The repeated chair rise has been reported as a valid test for lower extremity function[31] with good test-retest reliability.[25, 32]

**Muscular strength** – One repetition maximum (1-RM) chest press and single leg extension tests were used to measure dynamic upper and lower body muscular strength respectively. In addition, isometric handgrip strength, reported to be a valid indicator of limb muscle strength,[33] was measured in all participants. All absolute strength values were divided by body weight to provide information on relative strength.

One-RM testing is considered the "gold standard" of muscular strength testing[34] and refers to the maximal weight (in kg) an individual can move once with good technique through full range of motion without compensatory movements. The 1-RM chest press was conducted on a Cybex Smith machine (Cybex International, Medway, MA, USA) and a portable flat bench. The bar was positioned at mid-sternal level and 90° elbow flexion for each participant. Lifts were only recorded as successful if executed to full elbow extension. The 1-RM single leg extension was conducted on a Cybex leg extension machine. The back rest and shin pad were adjusted after each participant was seated to ensure that the knee joint was in line with the machine pivot point and at a 90° angle, and

that the shin pad was positioned just above the ankle joint. Only movements executed to the same degree of knee extension as during the warm-up were recorded as successful. Participants received demonstrations and instructions concerning correct posture, breathing and movement execution during both the familiarization and the follow-up sessions of 1-RM testing.

The 6-meter walking tasks, 400-meter walk and repeated chair rise were all conducted prior to strength testing and served as general warm-up for 1-RM tests. Participants performed two warm-up set of six and three repetitions respectively for each movement (chest press, right leg extension and left leg extension, unless contraindicated). Subsequent attempts required single movement executions at progressively heavier loads until the absolute 1-RM was determined. Rest intervals between warm-up sets and 1-RM trials were two minutes. A maximal of three to five 1-RM trials were attempted to avoid the effect of fatigue. One-RM testing, with one familiarization session 4-8 days prior, has been reported to be a safe and reliable method of maximal strength testing in older, untrained participants[34] and has been utilized to measure muscular strength in a variety of cancer populations.[35-37]

To measure handgrip strength participants were asked to stand upright whilst holding a Jamar handgrip dynamometer (Lafayette, IN, USA) in their right hand, arm slightly away from the body with approximately 20° elbow flexion, and to squeeze the dynamometer handle as forcefully as possible. After a score was recorded, the test was repeated with the left hand. Three trials were done for each hand, right and left alternatively, with a 30-second rest between each set of trials. The highest score for the right hand was used for analysis. Good inter-tester[38] and test-retest reliability[39] has been established for handgrip dynamometry and, due to ease of application, the test is often used for objective strength assessment in clinical populations, including different cancer populations.[40, 41]

### Health-related Quality of Life

Health-related quality of life was measured using the Medical Outcomes Study Short Form-36 (MOS SF-36) questionnaire.[42] The SF-36 is a generic instrument that comprises eight subscales measuring Physical Functioning, Role-Physical, Bodily Pain, General Health, Vitality, Social Functioning, Role-Emotional and Mental Health. Subscale scores were combined into a physical component summary score (PCS) and a mental component summary score (MCS).[43] All scores were standardized to 1998 general US population norms so each scale is scored to have the same average (50) and the same standard deviation (10). Higher scores reflect better HRQoL in the domain being measured.[44] The SF-36 has been established as a reliable and valid measure of quality of life[45] and is often used to assess quality of life of OCS.[46]

### Pelvic Floor Dysfunction

Self-reported PFD was measured with the Australian Pelvic Floor Questionnaire (APFQ).[47, 48] The APFQ has four subscales, with a range of questions each, to assess bladder, bowel and pelvic organ prolapse (POP) symptoms and sexual function. Bladder, bowel and POP symptom scores out of 10 were calculated. We did not calculate sexual function scores due to the large percentage of women (55% of all participants) indicating sexual inactivity and thus not completing the section. Bladder, bowel and POP symptom scores out of 10 were added for a combined bladder-bowel-POP symptom score out of 30. Higher scores in all domains indicate that women are experiencing more symptoms and thus more dysfunction. The APFQ has been indicated as valid and reliable measure of all four pelvic floor domains.[47, 48]

## STATISTICAL ANALYSIS

Data were analyzed using SPSS version 23 (IBM Corp., NY, USA). Variables were assessed for normality using the Shapiro-Wilk test. Results for frequency data are presented as number/percentage, and mean/standard deviation for normally distributed data, or

median/interquartile range for non-normally distributed data. Non-normally distributed data were analyzed using non-parametric tests. Probability of significant differences between OCS and control participants were measured using the Pearson Chi square test, Likelihood Ratio or Fisher's exact test for categorical data, and the independent t-tests or Mann-Whitney U tests for continuous variables. One-way analysis of variance (ANOVA), Kruskal-Wallis and Bonferroni post hoc tests were used to compare OCS treated with primary debulking surgery and adjuvant chemotherapy, OCS treated with neoadjuvant chemotherapy and interval debulking surgery and control participants. Association between variables for OCS was determined by Pearson r or Spearman rho correlations. All tests were two-tailed, with statistical significance set at an alpha level of 0.05.

# REFERENCES:


1. Yee J, Davis GM, Beith JM et al. Physical activity and fitness in women with metastatic breast cancer. J Cancer Surviv. 2014 Dec;8:647-656.
2. World Health Organization. Waist circumference and waist–hip ratio [Internet]. Geneva: World Health Organization, 2011. Available from: http://www.who.int/mediacentre/factsheets/fs385/en/. Accessed March 30, 2017.
3. Salamone LM, Fuerst T, Visser M et al. Measurement of fat mass using DEXA: a validation study in elderly adults. J Appl Physiol. 2000;89:345-352.
4. Visser M, Fuerst T, Lang T et al. Validity of fan-beam dual-energy X-ray absorptiometry for measuring fat-free mass and leg muscle mass. Health, Aging, and Body Composition Study--Dual-Energy X-ray Absorptiometry and Body Composition Working Group. J Appl Physiol. 1999;87:1513-1520.
5. Glickman SG, Marn CS, Supiano MA et al. Validity and reliability of dual-energy X-ray absorptiometry for the assessment of abdominal adiposity. J Appl Physiol. 2004;97:509-514.
6. Peddle-McIntyre CJ, Bell G, Fenton D et al. Feasibility and preliminary efficacy of progressive resistance exercise training in lung cancer survivors. Lung Cancer (Amsterdam, Netherlands). 2012;75:126-132.
7. Courneya KS, McKenzie DC, Mackey JR et al. Effects of exercise dose and type during breast cancer chemotherapy: multicenter randomized trial. J Natl Cancer Inst. 2013;105:1821-1832.
8. Cormie P, Newton R, Spry N et al. Safety and efficacy of resistance exercise in prostate cancer patients with bone metastases. Prostate Cancer Prostatic Dis. 2013;16:328-335.
9. Stavraka C, Maclaran K, Gabra H et al. A Study to Evaluate the Cause of Bone Demineralization in Gynecological Cancer Survivors. Oncologist. 2013;18:423-429.
10. Szabo KA, Webber CE, Gordon C et al. Reproducibility of peripheral quantitative computed tomography measurements at the radius and tibia in healthy pre- and postmenopausal women. Can Assoc Radiol J. 2011;62:183-189.
11. Sherk VD, Thiebaud RS, Chen Z et al. Associations between pQCT-based fat and muscle area and density and DXA-based total and leg soft tissue mass in healthy women and men. J Musculoskelet Neuronal Interact. 2014;14:411-417.

12. McVeigh JA, Winkler EAH, Healy GN et al. Validity of an automated algorithm to identify waking and in-bed wear time in hip-worn accelerometer data collected with a 24 h wear protocol in young adults. Physiol Meas. 2016;37:1636-1652.

13. Choi L, Liu Z, Matthews CE et al. Validation of accelerometer wear and nonwear time classification algorithm. Med Sci Sports Exerc. 2011;43:357-364.

14. Matthews CE, Hagströmer M, Pober DM et al. Best practices for using physical activity monitors in population-based research. Med Sci Sports Exerc. 2012;44(suppl 1):S68-S76.

15. Freedson PS, Melanson E, Sirard J. Calibration of the Computer Science and Applications, Inc. accelerometer. Med Sci Sports Exerc. 1998;30:777-781.

16. Matthews CE, Chen KY, Freedson PS et al. Amount of time spent in sedentary behaviors in the United States, 2003-2004. Am J Epidemiol. 2008;167:875-881.

17. Rock CL, Doyle C, Demark-Wahnefried W et al. Nutrition and physical activity guidelines for cancer survivors. CA Cancer J Clin. 2012;62:242-274.

18. Cavalheri V, Jenkins S, Cecins N et al. Patterns of sedentary behaviour and physical activity in people following curative intent treatment for non-small cell lung cancer. Chron Respir Dis. 2016;13:82-85.

19. Broderick JM, Ryan J, O'Donnell DM et al. A guide to assessing physical activity using accelerometry in cancer patients. Support Care Cancer. 2014;22:1121-1130.

20. Shi JW, MacInnis RJ, Boyle T et al. Physical Activity and Sedentary Behavior in Breast and Colon Cancer Survivors Relative to Adults Without Cancer. Mayo Clin Proc. 2017;92:391-398.

21. Shephard RJ. Godin leisure-time exercise questionnaire. / Questionnaire de Godin sur le temps de loisir passe a faire de l ' exercice physique. Med Sci Sports Exerc. 1997;29(6 Suppl.):S36-38.

22. Stevinson C, Faught W, Steed H et al. Associations between physical activity and quality of life in ovarian cancer survivors. Gynecol Oncol. 2007;106:244-250.

23. Karvinen KH, Courneya KS, Campbell KL et al. Correlates of exercise motivation and behavior in a population-based sample of endometrial cancer survivors: an application of the Theory of Planned Behavior. Int J Behav Nutr Phys Act. 2007;4:21-21.

24. Peiffer JJ, Galvão DA, Gibbs Z et al. Strength and functional characteristics of men and women 65 years and older. Rejuvenation Res. 2010;13:75-82.

25. Galvão DA, Taaffe DR. Resistance exercise dosage in older adults: single- versus multiset effects on physical performance and body composition. J Am Geriatr Soc. 2005;53:2090-2097.

26. Jette AM, Jette DU, Ng J et al. Are performance-based measures sufficiently reliable for use in multicenter trials? Musculoskeletal Impairment (MSI) Study Group. J Gerontol A Biol Sci Med Sci. 1999;54:M3-M6.

27. Tiedemann A, Sherrington C, Lord SR. Physiological and psychological predictors of walking speed in older community-dwelling people. Gerontology. 2005;51:390-395.

28. Rinne MB, Pasanen ME, Miilunpalo SI et al. Test-retest reproducibility and inter-rater reliability of a motor skill test battery for adults. Int J Sports Med. 2001;22:192-200.

29. Simonsick EM, Fan E, Fleg JL. Estimating cardiorespiratory fitness in well-functioning older adults: treadmill validation of the long distance corridor walk. J Am Geriatr Soc. 2006;54:127-132.

30. Pettee Gabriel KK, Rankin RL, Lee C et al. Test-retest reliability and validity of the 400-meter walk test in healthy, middle-aged women. J Phys Act Health. 2010;7:649-657.

31. Newman AB, Studenski SA, Harris TB et al. Association of long-distance corridor walk performance with mortality, cardiovascular disease, mobility limitation, and disability. JAMA. 2006;295:2018-2026.

32. Guralnik JM, Simonsick EM, Ferrucci L et al. A short physical performance battery assessing lower extremity function: association with self-reported disability and prediction of mortality and nursing home admission. J Gerontol. 1994;49:M85-M94.

33. Seeman TE, Charpentier PA, Berkman LF et al. Predicting changes in physical performance in a high-functioning elderly cohort: MacArthur studies of successful aging. J Gerontol. 1994;49:M97-M108.

34. Bohannon RW. Are hand-grip and knee extension strength reflective of a common construct? Percept Mot Skills. 2012;114:514-518.

35. Levinger I, Goodman C, Hare DL et al. The reliability of the 1RM strength test for untrained middle-aged individuals. J Sci Med Sport. 2009;12:310-316.

36. Peddle-McIntyre CJ, Bell G, Fenton D et al. Feasibility and preliminary efficacy of progressive resistance exercise training in lung cancer survivors. Lung Cancer. 2012;75:126-132.

37. Sellar CM, Bell GJ, Haennel RG et al. Feasibility and efficacy of a 12-week supervised exercise intervention for colorectal cancer survivors. Appl Physiol Nutr Metab. 2014;39:715-723.

38. Galvão DA, Taaffe DR, Cormie P et al. Efficacy and safety of a modular multi-modal exercise program in prostate cancer patients with bone metastases: a randomized controlled trial. BMC Cancer. 2011;11:517.

39. Mathiowetz V, Weber K, Volland G et al. Reliability and validity of grip and pinch strength evaluations. J Hand Surg. 1984;9:222-226.

40. Bohannon RW, Bubela DJ, Magasi SR et al. Relative reliability of three objective tests of limb muscle strength. Isokinet Exerc Sci. 2011;19:77-81.

41. Cesari M, Cerullo F, Zamboni V et al. Functional status and mortality in older women with gynecological cancer. J Gerontol A Biol Sci Med Sci. 2013;68:1129-1133

42. Cantarero-Villanueva I, Fernández-Lao C, Díaz-Rodríguez L et al. The Handgrip Strength Test as a Measure of Function in Breast Cancer Survivors: Relationship to Cancer-Related Symptoms and Physical and Physiologic Parameters. Am J Phys Med Rehabil. 2012;91:774-782.

43. Stewart AL, Greenfield S, Hays RD et al. Functional status and well-being of patients with chronic conditions. Results from the Medical Outcomes Study. JAMA. 1989;262:907-913.

44. Lazovich D, Robien K, Cutler G et al. Quality of life in a prospective cohort of elderly women with and without cancer. Cancer. 2009;115(S18):4283-4297.

45. Ware JE. User's Manual For The Sf-36v2 Health Survey, Second Edition,: Quality Metric Inc., Lincoln, ; 2007. p. 81 - 84.

46. Schlenk EA, Erlen JA, Dunbar-Jacob J et al. Health-related quality of life in chronic disorders: a comparison across studies using the MOS SF-36. Qual Life Res. 1998;7:57-65.

47. Ahmed-Lecheheb D, Joly F. Ovarian cancer survivors' quality of life: a systematic review. J Cancer Surviv. 2016;10:789-801.

48. Baessler K, O'Neill SM, Maher CF et al. Australian pelvic floor questionnaire: a validated interviewer-administered pelvic floor questionnaire for routine clinic and research. Int Urogynecol J Pelvic Floor Dysfunct. 2009;20:149-158.

49. Baessler K, O'Neill SM, Maher CF et al. A validated self-administered female pelvic floor questionnaire. International Urogynecology Journal. 2010;21:163-172.

# Appendix B – ECU ethical approval

AUSTRALIA ECU EDITH COWAN UNIVERSITY

JOONDALUP CAMPUS
270 Joondalup Drive, Joondalup
Western Australia 6027
☎ 134 328
www.ecu.edu.au
ABN 54 361 485 361 CRICOS IPC 00279B

28 April 2015

Mrs Christelle Schofield
9 Champaigne Drive
TAPPING WA 6065

Dear Mrs Schofield,

I am pleased to write on behalf of the Higher Degrees Committee to advise that your master's research proposal has been approved – **Physiological and disease-specific characteristics of gynaecological cancer survivors.**

I also wish to confirm that your proposal complies with the provisions contained in the University's policy for the conduct of ethical research, and your application for ethics has been approved. Your ethics approval number is **12511** and the period of approval is **23 April 2015 to 30 June 2016.**

Approval is given for your supervisory team to consist of:

| | |
|---|---|
| Principal Supervisor: | Prof Robert Newton – ECU |
| Co-Principal Supervisor: | Dr Carolyn McIntyre – ECU |
| Associate Supervisor: | Prof Daniel Galvao – ECU |

The examination requirements on completion are laid down in *Part VI of The University (Admissions, Enrolment and Academic progress) Rules for Courses Requiring the Submission of Theses* available at: http://ww.ecu.edu.au/GPPS/legal_legis/uni_rules.html

Additional information and documentation relating to the examination process can be found at the Graduate Research School website: http://research.ecu.edu.au/grs/

**Please note:** the Research Students and Scholarship Committee has resolved to restrict Master by Research (1 year) theses to a maximum of 40,000 words or a Master by Research (2 year) theses to a maximum of 60,000 words. Under special circumstances a candidate may seek approval from the Faculty Research and Higher Degrees Committee for an extension to the word length (RSSC 33/04).

I would like to take this opportunity to offer you our best wishes for your research and the development of your thesis.

Yours sincerely

Russell Tassicker
Senior Student Progress Officer
Research Assessments- SSC

| | |
|---|---|
| Principal Supervisor: | Prof Robert Newton – ECU |
| Co-Principal Supervisor: | Dr Carolyn McIntyre – ECU |
| Associate Supervisor: | Prof Daniel Galvao – ECU |
| HDR: | HES SIO |

# Appendix C – SJOG ethical approval

ST JOHN OF GOD
Subiaco Hospital

12 June 2015

Mrs Christelle Schofield
9 Champagne Drive
TAPPING WA 6065

Dear Mrs Schofield,

**Re: Physiological and disease-specific characteristics of ovarian cancer survivors** *(Our ref No: 815)*

I refer to the letter of 12 June 2015, advising of ethical approval of the above "low risk" study, as granted by the St John of God Health Care Human Research Ethics Committee.

I understand that St John of God Subiaco Hospital's involvement in this study will be restricted to the recruitment of study participants through the private consulting suites of Dr Paul Cohen, Dr Stuart Salfinger and Dr Jason Tan. There are no other resource implications for St John of God Subiaco Hospital.

Accordingly, I now confirm final approval for your study to be conducted at the St John of God Subiaco Hospital ("the participating site").

I wish you well with your research.

Yours sincerely

Dr Mark Lubliner
**Group Director Medical Services**
**St John of God Health Care**

cc. Dr Paul Cohen, Jakovich Gynae Oncology Clinical Research Fellow (via email)
cc. Adjunct Prof. Nik Zeps, Director of Research, SJG Subiaco Hospital (via email)

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# Appendix D – Letter from oncologists

Date

Dear Mrs……..

**Exercise needs in ovarian cancer survivors**

The St John of God Gynaecologic Oncology research group is collaborating with researchers at Edith Cowan University in a study which I would like to invite you to take part in. The aim of this research study is to determine what types of exercise would be most appropriate for women who have recently completed treatment for ovarian cancer.

Please find a brochure enclosed that provides further information about the research. Your participation is entirely voluntary and you are not under any obligation to be involved.

Christelle Schofield, the chief study investigator, will contact you by telephone to see if you are interested in being involved and to answer any questions that you may have.

Your participation in this would be most appreciated as it will help to improve our understanding of cancers and treatments and thus to improve care for our patients.

Yours sincerely

(Dr's Name)

# Appendix E – Study

All the research we do has to be approved by a Human Research Ethics Committee certified by the National Health & Medical Research Council. The NMHRC is responsible to the Commonwealth Minister for Health. This it to give you assurance that your health information will be used for only genuine medical research with foreseeable community benefits.

## Collaboration with other research bodies

Where appropriate your health information may be sent interstate or overseas for collaborative research purposes. This can only happen when we are sure that requisite approvals have been obtained and the necessary ethical and privacy safeguards are in place.

## Commercial gain from use of your information

The law in Australia dictates that you may not be rewarded financially for consenting for your health information to be used in research.

We are however, allowed to profit from research outcomes that are ultimately successfully commercialised. Any money we receive from commercial ventures is always put back into medical research.

## Results of Research

It is anticipated that the results of this research project will be published in medical journals or presented at scientific meetings, but you will not be identifiable in any such publication.

## If you want to change your mind

Please tell us by writing to the email address below, if you wish to withdraw your consent, which you are free to do at anytime.

If you do this, we will write back to acknowledge your wishes and to confirm the removal of your health information.

## Further information

If you require any further information concerning this project contact the principal study investigator:


Mrs Christelle Schofield, Chief Investigator

M: 0459 900 264 E: c.schofield@ecu.edu.au

Prof Robert Newton, Principle Supervisor

T: (08) 6304 3443 E: r.newton@ecu.edu.au

Dr Paul Cohen, Jakovich Gynaecological Oncology Clinical Research Fellow St John of God Subiaco Hospital

T: (08) 9468 5188 E: Paul.Cohen@sjog.org.au


Edith Cowan University
Health and Wellness Institute

vario wellness clinic

## About St John of God Health Care

St John of God Health Care is a Catholic not- for-profit healthcare provider, with hospitals, home nursing and pathology services, as well as Social Outreach services which reach out to people experiencing disadvantage to improve health and wellbeing.

We strive to serve the common good by proving holistic, ethical and person centred care and support. We aim to go beyond quality care to provide an experience for people that honours their dignity, is compassionate and affirming and leaves them with a reason to hope.


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West Perth, WA 6005

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ST JOHN OF GOD Health Care

# Physiological and disease specific characteristics of ovarian cancer survivors

Information brochure & frequently asked questions

Hospitality | Compassion | Respect | Justice | Excellence

## What is the purpose of this study?

Women with ovarian cancer often experience a significant burden of disease and treatment side-effects. Exercise has been acknowledged as a safe and effective supportive care intervention for cancer survivors. Currently it is unknown what exercise is most appropriate for addressing the disease specific and functional needs of women with ovarian cancer. The purpose of the study is to measure physical function (i.e. walking speed, balance, muscle strength), body composition (i.e. how much muscle you have, your bone mineral density), physical activity participation and pelvic floor function in ovarian cancer survivors. We plan to look at how these results relate to results of similarly aged women who have not had cancer to better understand the specific exercise needs of ovarian cancer survivors. Information obtained from this research will assist health professionals to make exercise recommendations and to design the most appropriate exercise programs for ovarian cancer survivors.

## What does this study involve?

If you agree to participate in the study, you will be asked to

1. Obtain consent from your Specialist or General Practitioner

2. Invite a female friend, colleague or relative of similar age as yourself, who has never had a diagnosis of cancer, to participate in the control group of this study. You are under no obligation to do this, but if you know someone who would be willing and interested to participate in the study, you can.

- Ask her to contact the chief investigator directly AND/ OR give her the INFORMATION LETTER TO PARTICIPANTS – CONTROL GROUP included in the package that will be posted or handed out to you

3. Complete standardised questionnaires

4. Undergo a series of assessments at the Edith Cowan University in Joondalup to measure different components of your physical fitness.

## Decision to Participate

Your decision to participate in this study is voluntary. No explanation or justification is needed if you choose not to participate. If you do decide to participate, you are free to withdraw your consent and discontinue your involvement at any time during the study. A decision not to participate will not disadvantage you or jeopardise your relationship with your care provider in any way. You will be given a copy of the Consent Form to keep for your personal record.

The Participant Information Sheet (included in the package you will receive later) will explain the study and will include details such as:

- Why this study might be suitable for you
- Possible benefits and risks of study participation
- The type, frequency and risks of any testing that you will need to have as part of this study
- What your rights and responsibilities are if you agree to participate

## Am I eligible to participate?

As an ovarian cancer survivor to participate in the study you need to

- Be 18 years or older
- Have histologically confirmed stage III – IV ovarian cancer
- Not have cancer that has spread to the bone
- Not have undergone cancer-related surgery, chemotherapy and/or radiation therapy during the last 3 months
- Not have completed your cancer-related treatment more than 6 months ago
- Not have an acute illness at the time of testing
- Not have any musculoskeletal, cardiovascular or neurological disorder that could put you at risk during exercise testing, as determined by your specialist or general practitioner

## Potential Risks

Strength and physical functional tests may result in mild discomfort and muscle soreness, or possibly muscle pulls or strains, common to any type of physical activity. Risk of falling may exist in the performance of some tasks. To minimize these risks you will be thoroughly familiarized with the physical tests through comprehensive instructions and demonstrations, and supervised at all times by the chief investigator, an accredited exercise physiologist. It is possible to experience symptoms such as abnormal blood pressure, fainting, light-headedness, nausea, and in very rare cases heart rhythm disturbances or heart attack during exercise testing. These potential risks are common to any form of physical activity. You will be asked to report any symptoms you experience during exercise testing and your safety will be of primary importance at all times. DEXA and pQCT scans are routine clinical tests, but carry a small risk to you as they involve exposure to radiation. You may experience some discomfort in answering the items in the questionnaires. Your responses will be kept strictly confidential.

## Privacy and Confidentiality

The conduct of this research involves the collection, access and/or use of your identified personal information. The information collected is confidential and will not be disclosed to third parties without your consent, except to meet government, legal or other regulatory authority requirements. A de-identified copy of this data may be used for other research purposes. However, your anonymity will be safeguarded at all times. Participants will not be referred to by name in research reports or during study discussions. If the results of the study are published in a scientific journal, as is intended, no reader will be able to identify individual patients. All records will be stored in a locked filing cabinet in a private office on the Joondalup campus of Edith Cowan University with restricted access for a minimum of five years. All computer records are restricted by password.

# Appendix F – Advertisement ECU

Edith Cowan University
Health and Wellness Institute
vario wellness clinic

**FEMALE VOLUNTEERS FOR RESEARCH STUDY RECEIVE FREE FITNESS TESTING AND EXERCISE COUNSELLING**

Ladies, would you like to volunteer to participate in the control group of a research study with gynaecological cancer survivors?

If you are eligible to participate, you will

- Undergo tests to measure your
  - **physical function** (i.e. muscle strength, walking speed, dynamic balance),
  - **body composition** (how much lean body weight and fat weight you have, what your bone density is)
  - **physical activity level**
- Receive an (optional) exercise consultation with an accredited exercise physiologist who will provide exercise advice based on your test results and answer your exercise-related questions.

*All testing will be done on the ECU Joondalup campus on days and times that suit you.*

Interested in participating?

Please contact the chief investigator to discuss your eligibility:
Mrs Christelle Schofield
Phone: 0459 900 264
E-mail: c.schofield@ecu.edu.au

# Appendix G – Cover letter

Date

Mrs……..
8 Any Street,
Suburb,
WA, 2122

Dear Mrs……..

Thank you for your interest in the research study, *Physiological and disease specific characteristics of ovarian cancer survivors*.

Please find enclosed:

1. A participant information letter outlining all aspects of the study
2. A medical doctor consent form for your GP or specialist
3. An informed consent form for you
4. A demographic and health history questionnaire
5. Details of your first appointment
6. A parking permit for the Vario Clinic/Health and Wellness Institute parking area

Please read the participant information letter carefully. If you decide to participate in the study:

1. Take the MEDICAL DOCTOR CONSENT FORM to your GP/specialist.
2. Following approval from your doctor to participate, please contact me to arrange a meeting where an orientation to the study will be provided and baseline measurements will commence.
3. Bring the medical doctor consent form, signed by your GP, with you on your first assessment appointment. Everything else you will need on the first appointment is outlined in the DAY 1 – ASSESSMENT sheet included in the package.
4. I will contact you in a few days to confirm that you have received the documents. However, if you have any questions in the meantime, please do not hesitate to contact Christelle Schofield on 0459 900 264 or via e-mail at c.schofield@ecu.edu.au.

Yours sincerely

Christelle Schofield
Accredited Exercise Physiologist
Masters Student – Edith Cowan University Health and Wellness Institute

# Appendix H – Information letter- cancer survivors


Edith Cowan University
Health and Wellness Institute
vario wellness clinic


## INFORMATION LETTER TO PARTICIPANTS – CANCER SURVIVORS

## Physiological and disease specific characteristics of ovarian cancer survivors

You are invited to participate in a research study because you have had a diagnosis of ovarian cancer. This information letter explains the purpose and nature of the study and describes what will be involved should you decide to participate. Please read the sheet carefully and do not hesitate to contact the chief investigator if anything requires further clarification or if you have additional questions or concerns. Please ensure that you do this before you sign the consent form to participate in the study.

**Contact persons**

If you have any questions about the study, you can contact:
Mrs Christelle Schofield (Chief Investigator) - 0459 900 264
Prof Robert Newton (Principle Supervisor) - 08 6304 3443

**Decision to participate**

Your decision to participate in this study is voluntary. No explanation or justification is needed if you choose not to participate. If you do decide to participate, you are free to withdraw your consent and discontinue your involvement at any time during the study. A decision not to participate will not disadvantage you or jeopardise your relationship with your care provider in any way. You will be given a copy of the Consent Form to keep for your personal record.

The Participant Information Sheet explains the study and includes details such as:

- why this study might be suitable for you
- possible benefits and risks of study participation
- the type, frequency and risks of any testing that you will need to have as part of this study
- what your rights and responsibilities are if you agree to participate

**What is the purpose of the study?**

Women with ovarian cancer often experience a significant burden of disease and treatment side-effects. Exercise has been acknowledged as a safe and effective supportive care intervention for cancer survivors. Currently it is unknown what exercise is most appropriate for addressing the disease specific and functional needs of women with ovarian cancer. The purpose of the study is to measure physical function (i.e. walking speed, balance, muscle strength), body composition (i.e.

how much muscle you have, your bone mineral density), physical activity participation and pelvic floor function in ovarian cancer survivors. We plan to look at how these results relate to results of similarly aged women who have not had cancer to better understand the specific exercise needs of ovarian cancer survivors. Information obtained from this research will assist health professionals to make exercise recommendations and to design the most appropriate exercise programs for ovarian cancer survivors.

**Am I eligible for participation?**

As an ovarian cancer survivor to participate in the study you need to

- Be 18 years or older
- Have histologically confirmed stage III – IV ovarian cancer
- Not have cancer that has spread to the bone
- Not have undergone cancer-related surgery, chemotherapy and/or radiation therapy during the last 3 months
- Not have completed your cancer-related treatment more than 24 months ago
- Not have an acute illness at the time of testing
- Not have any musculoskeletal, cardiovascular or neurological disorder that could put you at risk during exercise testing, as determined by your specialist or general practitioner

**What does participation in the study involve?**

If you agree to participate in the study, you will be asked to

- Obtain consent from your specialist or general practitioner
- Invite a female friend, colleague or relative of similar age as yourself, who has never had a diagnosis of cancer, to participate in the control group of this study. You are under no obligation to do this, but if you know someone who would be willing and interested to participate in the study, you can
  - ask her to contact the chief investigator directly AND/OR
  - give her the INFORMATION LETTER TO PARTICIPANTS – CONTROL GROUP included in your package
- Complete standardized questionnaires
- Undergo a series of assessments at the Edith Cowan University in Joondalup to measure different components of your physical fitness.

**What questionnaires do I have to complete?**

You will be asked to complete standardized questionnaires used to record demographic and health history information as well as to assess quality of life, pelvic floor function, physical activity level, physical activity motivation, and your thoughts on participating in the study. The questionnaires can be completed in the privacy of your own home and are anticipated to take you approximately half an hour.

**What do the assessments involve?**

As study participant you will undergo the following series of assessments:

- **Body Composition & Bone Mineral Density**
    - Dual Energy X-Ray Absorptiometry (DEXA) scan will be used to assess whole body composition (fat mass and lean mass) and bone mineral density of the hip and spine. These assessments involve lying still on a specially designed platform for approximately 10 minutes while a scanning arm will move above your total body and above your hip and spine (separate scans for your whole body, hip and spine). A low-dosage x-ray will pass from the scanning arm to underneath the platform.
    - Peripheral Quantitative Computed Tomography (pQCT) will be used to measure muscle density and muscle cross-sectional areas of the lower limb. The assessment involves you sitting in a chair with your leg extended and the circular scanning arm moving from your ankle to your knee.

The total radiation dose for all scans undertaken during the study is very low, only a little more than normal background radiation from an airplane flight and much less than, for example, an international flight.

- **Physical Activity Level**
  You will be asked to wear an activity monitor (triaxial accelerometer) 24 hours a day for a 7-day period in order to accurately measure your physical activity levels (i.e. how long you are active for in a day). The device is very small (4.6cm x 3.3cm x 1.5cm), lightweight (19g) and can be attached to your belt or worn around your waist using a strap.

- **Physical Function**
  A series of tests will be used to assess physical function. Before physical function tests are performed, you will receive detailed instructions regarding all tests. Where necessary, demonstrations, practice time and sufficient warm-up will be undertaken. All tests will be supervised by the chief investigator, an accredited exercise physiologist, and your safety will be observed at all times. These tests involve:

    - 6-meter walk: You will be asked to walk 6 meters at your usual pace and at a fast pace (i.e. as if you were running late for an appointment) (performed 3 times).
    - 6-meter backwards walk: As a test of balance, you will be asked to walk backwards in a toe-to-heel fashion for 6 meters (performed 3 times).
    - 400-meter corridor walk: You will be asked to walk 20 meters in a corridor, turn around and walk back to the starting position for a total of 10 times.
    - Chair rise: You will be seated in a hard-backed chair and asked to rise and sit 5 consecutive times, as fast as you can safely do so, without the use of your arms for support (performed 3 times).

- Muscle strength: You will be asked to perform an upper and lower body one repetition maximum test. During the one repetition maximum test you will be asked to lift increasingly heavy weights on a chest press and leg extension weight-training machine until you reach the most weight you can lift once using correct technique. In addition, you will be asked to perform a hand-grip strength test, which entails squeezing a hand dynamometer as hard as possible. Adequate rest will be provided in between tests to avoid fatigue.

You will be asked to do these assessments on two separate occasions as outlined below, no less than 6 but no more than 14 days apart. The purpose of the first testing session is to familiarise you with all functional assessments in order to minimise any potential learning effect. All testing will be conducted at the Edith Cowan University Health and Wellness Institute in Joondalup (see map included) and will take approximately 2-3 hours.

**OUTLINE OF TESTING SESSIONS**

| **Session 1** | **Session 2 (6-14 days after Session 1)** |
|---|---|
| The chief investigator will<br>• review consent forms, demographic and health history questionnaire and study procedures with you<br>• hand out quality of life, pelvic floor function and physical activity questionnaires<br>• provide you with an activity monitor<br>• measure your height and weight<br>• | The chief investigator will<br>• review quality of life, pelvic floor function and physical activity questionnaires with you<br>• collect the activity monitor from you<br>• provide verbal feedback and an (optional) exercise counselling to you after conducting all tests |
| You will undergo a DEXA and pQCT scan. | |
| You will undergo functional testing:<br>• 6-Meter walk test<br>  ○ Usual pace forward<br>  ○ Fast pace forward<br>  ○ Toe-to-heel backward<br>• 400-Meter walk test<br>• Chair raise<br>• Muscle strength testing<br>  ○ One repetition maximum tests<br>  ○ Grip strength test | You will undergo functional testing:<br>• 6-Meter walk test<br>  ○ Usual pace forward<br>  ○ Fast pace forward<br>  ○ Toe-to-heel backward<br>• 400-Meter walk test<br>• Chair raise<br>• Muscle strength testing<br>  ○ One repetition maximum tests<br>  ○ Grip strength |
| How long will it take?<br>• 2.5 hours for assessment<br>• 30 minutes at home to complete questionnaires | How long will it take?<br>• 2 hours for assessment<br>• 30 minutes for (optional) exercise counselling |

**What are the possible benefits of participating?**

The direct benefit for you is that all study activities, including all assessments, are provided at no cost to you. At the end of the second testing session the chief investigator will provide feedback regarding your test results. You will then be offered the choice of either:

- No exercise consultation, OR
- A brief 30-minute exercise consultation with the chief investigator immediately after the second testing session, OR
- A more comprehensive 60-minute exercise consultation with the chief investigator on another day at a time agreeable to both parties.

During the consultation of your choice the chief investigator will make exercise recommendations based on your test results and answer any exercise related questions you may have. Additionally, it is hoped that this study will contribute important new information that will be useful in the management of ovarian cancers and long-term treatment side effects.

**What are the possible side effects and risks?**

Prior to any testing, your specialist or GP will review your medical history and the study protocols to make sure that it is safe for you to take part in the assessments involved in the study. However, any strength and physical functional testing may result in mild discomfort and muscle soreness. There is also the possibility of muscle pulls or strains, common to any type of physical activity. Risk of falling may exist in the performance of some tasks. In order to minimize these risks you will be thoroughly familiarized with the movements involved in this investigation through comprehensive instructions and demonstrations, and supervised at all times by the chief investigator, an accredited exercise physiologist. Furthermore, during exercise testing it is possible to experience symptoms such as abnormal blood pressure, fainting, light-headedness, nausea, and in very rare cases heart rhythm disturbances or heart attack. These potential risks are common to any form of physical activity. You will be asked to report any symptoms you experience during exercise testing and your safety will be of primary importance at all times. In the event that an emergency occurs, medical assistance will be obtained according to established emergency procedures at the ECU Health and Wellness Institute.

DEXA and pQCT scans are routine clinical tests, but carry a small risk to you as they involve exposure to radiation. The level of radiation exposure is exceedingly small (10-30 microSieverts [μSv]) in comparison to the natural annual radiation dose in western communities (approximately 3000 μSv). A person would receive radiation exposure of approximately 80 μSv on an airline flight of 8 hours or 30 to 40 μSv during a typical chest x-ray.

You may experience some discomfort in answering the items in the questionnaires. Your responses will be kept strictly confidential. Some of the questions will ask about the level of distress you are experiencing. If our study identifies that you are experiencing significant distress you will be contacted and your permission will be sought to inform your GP or

cancer specialist so that referral to appropriate services can be made. In addition, if you should experience and express any distress at any stage during participation in the study, the chief investigator will offer you the opportunity to contact a support person of your choice (i.e. your husband or a friend). It is also recommended that you obtain permission from your GP to be contacted if you feel you would rather contact him/her in case you experience significant distress.

**Privacy and confidentiality**

The conduct of this research involves the collection, access and/or use of your identified personal information. The information collected is confidential and will not be disclosed to third parties without your consent, except to meet government, legal or other regulatory authority requirements. A de-identified copy of this data may be used for other research purposes. However, your anonymity will be safeguarded at all times. Participants will not be referred to by name in research reports or during study discussions. If the results of the study are published in a scientific journal, as is intended, no reader will be able to identify individual patients. All records will be stored in a locked filing cabinet in a private office on the Joondalup campus of Edith Cowan University with restricted access for a minimum of five years. All computer records are restricted by password.

**Are there any costs involved?**

If you choose to participate in the study, you will be asked to attend two testing sessions at ECU in Joondalup. Parking for visitors is available on campus at a cost of $1.50 per hour. The parking permit included in the package will allow you access to the Health and Wellness Institute's parking area close to the building where you will undergo testing (indicated on the included campus map). Please note that you still have to pay for parking and that tickets can be purchased at vending machines located in the parking area. To help cover travel and parking expenses, you will be provided with a $25.00 voucher at your second testing session.

**Will I receive any feedback?**

You will receive verbal feedback regarding your test results at the end of the second testing session. If you would like to discuss your results and ask questions about exercise, you have the choice of either a brief 30-minute exercise consultation with the chief investigator immediately after the second session or a more comprehensive 60-minute exercise consultation on another day at a time agreeable to both parties. During the consultation of your choice the chief investigator will make exercise recommendations based on your test results and answer your exercise-related questions. A summary of study results will be made available to all interested participants upon completion of the study.

**Contacting the investigators**

We are happy to answer any questions you may have at this time. If you have any queries later, please do not hesitate to contact either:


| | | |
|---|---|---|
| Mrs Christelle Schofield | Phone: 0459 900 264 | E-mail: c.schofield@ecu.edu.au |
| Prof Robert Newton | Phone: (08) 6304 3443 | E-mail: r.newton@ecu.edu.au |


**Independent Contact Person**

The ECU Human Research Ethics Committee and the Human Research Ethics Committee at St John of God Hospital, Subiaco have approved this project. If you have any concerns or complaints about the research project and wish to talk to an independent person, you may contact:


Research Ethics Officer
Edith Cowan University
270 Joondalup Drive
JOONDALUP WA 6027
Phone: (08) 6304 2170
Email: research.ethics@ecu.edu.au


-ECU Health & Wellness Institute is located in building 21 on the Joondalup Campus of Edith Cowan University.

-Please come to the Institute entrance located between building 21 and building 19 and check in with reception.

-Parking is available for ECU Health & Wellness Institute clients directly behind building 19.

-Parking charges are $1.50/hour.

-If you have any problems locating the parking area please contact Christelle on 0459 900 264.

**DIRECTIONS FROM THE FREEWAY**:

- Take the Hodges Drive exit
- Turn Right onto Hodges Drive
- Turn right onto Joondalup Drive
- Turn left onto Lakeside Drive
- Turn left onto Chancellors Pass
- Turn left at the round-a-bout
- Take the first right into the Institute Client Car Park (to your right)

# Appendix I – Information letter- control

ST JOHN OF GOD Health Care

Edith Cowan University Health and Wellness Institute

vario wellness clinic

ECU AUSTRALIA EDITH COWAN UNIVERSITY

## INFORMATION LETTER TO PARTICIPANTS – CONTROL GROUP

## Physiological and disease specific characteristics of ovarian cancer survivors

You are invited to participate in a research study because you have expressed an interest to participate in the control group of an ovarian cancer study. This information sheet explains the purpose and nature of the study and describes what will be involved should you decide to participate. Please read the sheet carefully and do not hesitate to contact the chief investigator if anything requires further clarification or if you have additional questions or concerns. Please ensure that you do this before you sign the consent form to participate in the study.

**Contact persons**

If you have any questions about the study, you can contact:
Mrs Christelle Schofield (Chief Investigator) - 0459 900 264
Prof Robert Newton (Principle Supervisor) - 08 6304 3443

**Decision to participate**

Your decision to participate in this study is voluntary. No explanation or justification is needed if you choose not to participate. If you do decide to participate, you are free to withdraw your consent and discontinue your involvement at any time during the study. A decision not to participate will not disadvantage you or jeopardise your relationship with your care provider in any way. You will be given a copy of the Consent Form to keep for your personal record.

The Participant Information Sheet explains the study and includes details such as:

- why this study might be suitable for you
- possible benefits and risks of study participation
- the type, frequency and risks of any testing that you will need to have as part of this study
- what your rights and responsibilities are if you agree to participate

**What is the purpose of the study?**

Women with ovarian cancer often experience a significant burden of disease and treatment side-effects. Exercise has been acknowledged as a safe and effective supportive care intervention for cancer survivors. Currently it is unknown what exercise is most appropriate for women with ovarian cancer to address their disease specific physical functioning needs. The purpose of the study is to measure physical function (i.e. walking speed, balance, muscle strength), body composition (i.e. how much muscle you have, your bone mineral density), physical activity participation and pelvic floor function in ovarian cancer survivors. We plan to look at how these results relate to results of similarly aged women who have not had cancer to better understand the specific exercise needs of ovarian cancer survivors. Information obtained from this research will assist health professionals to make exercise recommendations and to design the most appropriate exercise programs for ovarian cancer survivors.

**Am I eligible for participation?**

To participate in the partner/control group of the study you need to

- Be 18 years or older
- Never have had a diagnosis of cancer or history of cancer (other than non-melanoma skin cancer)
- Not have an acute illness at the time of testing
- Not have any musculoskeletal, cardiovascular or neurological disorder that could put you at risk during exercise testing, as determined by your specialist or general practitioner

**What does participation in the study involve?**

If you agree to participate in the study, you will be asked to

- Obtain consent from your specialist or general practitioner
- Complete standardized questionnaires
- Undergo a series of assessments at the Edith Cowan University in Joondalup to measure different components of your physical fitness.

**What questionnaires do I have to complete?**

You will be asked to complete standardized questionnaires used to record demographic and health history information as well as to assess quality of life, pelvic floor function, physical activity level, physical activity motivation, and your thoughts on participating in the study. The questionnaires can be completed in the privacy of your own home and are anticipated to take you approximately half an hour to complete.

**What do the assessments involve?**

As study participant you will undergo the following series of assessments:

- **Body Composition & Bone Mineral Density**

- Dual Energy X-Ray Absorptiometry (DEXA) scan will be used to assess whole body composition (fat mass and lean mass) and bone mineral density of the hip and spine. These assessments involve lying still on a specially designed platform for approximately 10 minutes while a scanning arm will move above your total body and above your hip and spine (separate scans for your whole body, hip and spine). A low-dosage x-ray will pass from the scanning arm to underneath the platform.
- Peripheral Quantitative Computed Tomography (pQCT) will be used to measure muscle density and muscle cross-sectional areas of the lower limb. The assessment involves you sitting in a chair with your leg extended and the circular scanning arm moving from your ankle to your knee.

The total radiation dose for all scans undertaken during the study is very low, only a little more than normal background radiation from an airplane flight and much less than, for example, an international flight.

- **Physical Activity Level**

  You will be asked to wear an activity monitor (triaxial accelerometer) for a 7-day period in order to accurately measure your physical activity levels (i.e. how long you are active for in a day). The device is very small (4.6cm x 3.3cm x 1.5cm), lightweight (19g) and can be attached to your belt or worn around your waist using a strap.

- **Physical Function**

  A series of tests will be used to assess physical function. Before physical function tests are performed, you will receive detailed instructions regarding all tests. Where necessary, demonstrations, practice time and sufficient warm-up will be undertaken. All tests will be supervised by the chief investigator, an accredited exercise physiologist, and your safety will be observed at all times. These tests involve:

  - 6-meter walk: You will be asked to walk 6 meters at your usual pace and at a fast pace (i.e. as if you were running late for an appointment) (performed 3 times).
  - 6-meter backwards walk: As a test of balance, you will be asked to walk backwards in a toe-to-heel fashion for 6 meters (performed 3 times).
  - 400-meter corridor walk: You will be asked to walk 20 meters in a corridor, turn around and walk back to the starting position for a total of 10 times.
  - Chair rise: You will be seated in a hard-backed chair and asked to rise and sit 5 consecutive times, as fast as you can safely do so, without the use of your arms for support (performed 3 times).
  - Muscle strength: You will be asked to perform an upper and lower body one repetition maximum test. During the one repetition maximum test you will be

asked to lift increasingly heavy weights on a chest press and leg extension weight-training machine until you reach the most weight you can lift once using correct technique. In addition, you will be asked to perform a hand-grip strength test, which entails squeezing a hand dynamometer as hard as possible. Adequate rest will be provided in between tests to avoid fatigue.

You will be asked to do these assessments twice in two testing sessions (outlined below) no less than 6 but no more than 14 days apart. The purpose of the first testing session is to familiarise you with all functional assessments in order to minimise any potential learning effect. All testing will be conducted at the Edith Cowan University Health and Wellness Institute in Joondalup (see map included) and will take approximately 2-3 hours.

**OUTLINE OF TESTING SESSIONS**

| **Session 1** | **Session 2 (6-14 days after Session 1)** |
|---|---|
| The chief investigator will<br>• review consent forms, demographic and health history questionnaire and study procedures with you<br>• hand out quality of life, pelvic floor function and physical activity questionnaires<br>• provide you with an activity monitor<br>• measure your height and weight<br>• | The chief investigator will<br>• review quality of life, pelvic floor function and physical activity questionnaires with you<br>• collect the activity monitor from you<br>• provide verbal feedback and (optional) exercise counselling to you after conducting all tests |
| You will undergo a DEXA and pQCT scan. | |
| You will undergo functional testing:<br>• 6-Meter walk test<br>o Usual pace forward<br>o Fast pace forward<br>o Toe-to-heel backward<br>• 400-Meter walk test<br>• Chair raise<br>• Muscle strength testing<br>o One repetition maximum tests<br>o Grip strength test<br>o | You will undergo functional testing:<br>• 6-Meter walk test<br>o Usual pace forward<br>o Fast pace forward<br>o Toe-to-heel backward<br>• 400-Meter walk test<br>• Chair raise<br>• Muscle strength testing<br>o One repetition maximum tests<br>o Grip strength |
| How long will it take?<br>• 2.5 hours for assessment<br>• 30 minutes at home to complete questionnaires | How long will it take?<br>• 1 hours for assessment<br>• 30 minutes for (optional) exercise counselling |

**What are the possible benefits of participating?**

The direct benefit for you is that all study activities, including all assessments, are provided at no cost to you. At the end of the second testing session the chief investigator will provide feedback regarding your test results. You will then be offered the choice of either:

- No exercise consultation, OR
- A brief 30-minute exercise consultation with the chief investigator immediately after the second testing session, OR
- A more comprehensive 60-minute exercise consultation with the chief investigator on another day at a time agreeable to both parties.

During the consultation of your choice the chief investigator will make exercise recommendations based on your test results and answer any exercise related questions you may have. Additionally, it is hoped that this study will contribute important new information that will be useful in the management of ovarian cancers and long-term treatment side effects.

**What are the possible side effects and risks?**

Prior to any testing, your GP will review your medical history and the study protocols to make sure that you are medically ready for the study procedures. However, any strength and physical functional testing may result in mild discomfort and muscle soreness. There is also the possibility of muscle pulls or strains, common to any type of physical activity. Risk of falling may exist in the performance of some tasks. In order to minimize these risks you will be thoroughly familiarized with the movements involved in this investigation through comprehensive instructions and demonstrations, and supervised at all times by the chief investigator, an accredited exercise physiologist. Furthermore, during exercise testing it is possible to experience symptoms such as abnormal blood pressure, fainting, light-headedness, nausea, and in very rare cases heart rhythm disturbances or heart attack. These potential risks are common to any form of physical activity. You will be asked to report any symptoms you experience during exercise testing and your safety will be of primary importance at all times. In the event that an emergency occurs, medical assistance will be obtained according to established emergency procedures at the ECU Health and Wellness Institute.

DEXA and pQCT scans are routine clinical tests, but carry a small risk to you as they involve exposure to radiation. The level of radiation exposure is exceedingly small (10-30 microSieverts [μSv]) in comparison to the natural annual radiation dose in western communities (approximately 3000 μSv). A person would receive radiation exposure of approximately 80 μSv on an airline flight of 8 hours or 30 to 40 μSv during a typical chest x-ray.

You may experience some discomfort in answering the items in the questionnaires. Your responses will be kept strictly confidential. Some of the questions will ask about the level of distress you are experiencing. If our study identifies that you are experiencing significant distress you will be contacted and your permission will be sought to inform your GP or

cancer specialist so that referral to appropriate services can be made. In addition, if you should experience and express any distress at any stage during participation in the study, the chief investigator will offer you the opportunity to contact a support person of your choice (i.e. your husband or a friend). It is also recommended that you obtain permission from your GP to be contacted if you feel you would rather contact him/her in case you experience significant distress.

**Privacy and confidentiality**

The conduct of this research involves the collection, access and/or use of your identified personal information. The information collected is confidential and will not be disclosed to third parties without your consent, except to meet government, legal or other regulatory authority requirements. A de-identified copy of this data may be used for other research purposes.

However, your anonymity will be safeguarded at all times. Participants will not be referred to by name in research reports or during study discussions. If the results of the study are published in a scientific journal, as is intended, no reader will be able to identify individual patients. All records will be stored in a locked filing cabinet in a private office on the Joondalup campus of Edith Cowan University with restricted access for a minimum of five years. All computer records are restricted by password.

**Are there any costs involved?**

If you choose to participate in the study, you will be asked to attend two testing sessions at ECU in Joondalup. Parking for visitors is available on campus at a cost of $1.50 per hour. The parking permit included in the package will allow you access to the Health and Wellness Institute's parking area close to the building where you will undergo testing (indicated on the included campus map). Please note that you still have to pay for parking and that tickets can be purchased at vending machines located in the parking area. To help cover travel and parking expenses, you will be provided with a $25.00 voucher at your second testing session.

**Will I receive any feedback?**

You will receive verbal feedback regarding your test results at the end of the second testing session. If you would like to discuss your results and ask questions about exercise, you have the choice of either a brief 30-minute exercise consultation with the chief investigator immediately after the second session or a more comprehensive 60-minute exercise consultation on another day at a time agreeable to both parties. During the consultation of your choice the chief investigator will make exercise recommendations based on your test results and answer your exercise-related questions. A summary of study results will be made available to all interested participants upon completion of the study.

**Contacting the investigators**

We are happy to answer any questions you may have at this time. If you have any queries later, please do not hesitate to contact either:


| | | |
|---|---|---|
| Mrs Christelle Schofield | Phone: 0459 900 264 | E-mail: c.schofield@ecu.edu.au |
| Prof Robert Newton | Phone: (08) 6304 3443 | E-mail: r.newton@ecu.edu.au |


**Independent Contact Person**

The ECU Human Research Ethics Committee and the Human Research Ethics Committee at St John of God Hospital, Subiaco have approved this project. If you have any concerns or complaints about the research project and wish to talk to an independent person, you may contact:


Research Ethics Officer
Edith Cowan University
270 Joondalup Drive
JOONDALUP WA 6027
Phone: (08) 6304 2170
Email: research.ethics@ecu.edu.au


ECU Health & Wellness Institute is located in building 21 on the Joondalup Campus of Edith Cowan University.

• Please come to the Institute entrance located between building 21 and building 19 and check in with reception.

• Parking is available for ECU Health & Wellness Institute clients directly behind building 19.

• Parking charges are $1.50 p/hour.

• If you have any problems locating the parking area please contact Christelle on 0459 900 264.

**DIRECTIONS FROM THE FREEWAY:**

• Take the Hodges Drive exit

• Turn Right onto Hodges Drive

• Turn right onto Joondalup Drive

• Turn left onto Lakeside Drive

• Turn left onto Chancellors Pass

• Turn left at the round-a-bout

• Take the first right into the Institute Client Car Park (will be to your right)

# Appendix J –Medical consent- cancer survivors

# MEDICAL DOCTOR CONSENT FORM

**Project Title: Physiological and disease specific characteristics of ovarian cancer survivors**

**Researchers:**
Mrs Christelle Scofield, Masters Student - E: c.schofield@ecu.edu.au - T: 0459 900 264
Prof Robert Newton, PhD - E: r.newton@ecu.edu.au - T: (08) 6304 5037
Dr Carolyn McIntyre, PhD - E: c.mcintyre@ecu.edu.au - T: (08) 6304 3987
Prof Daniel Galvão, PhD - E: d.galvao@ecu.edu.au - T: (08) 6304 3420

**Institute:** Edith Cowan University Health and Wellness Institute
St John of God, Subiaco

Dear Doctor,

The Edith Cowan University Health and Wellness Institute is undertaking a research study in collaboration with The St John of God Gynaecologic Oncology research group investigating the physiological and disease specific characteristics of ovarian cancer survivors. Women with ovarian cancer often experience a significant burden of disease and treatment side-effects. Exercise has been acknowledged as a safe and effective supportive care intervention for cancer survivors. Currently it is unknown what exercise is most appropriate for women with ovarian cancer to address their disease and treatment specific adverse side-effects. To better understand their exercise needs and to design appropriate exercise interventions for both research and clinical settings, we aim to identify unique physiological and disease specific characteristics of women with ovarian cancer. The purpose of this study is to determine the physiological and disease specific characteristics of ovarian cancer survivors and to explore differences in physiological characteristics between women with ovarian cancer and similarly aged women who have never been diagnosed with cancer.

Outcome measures in the study:

- Self-reported and objectively measured physical function. Objective physical function tests include:
    - muscle strength - measured by a 1-RM (repetition maximum) bench press and single leg extension test, as well as by a handgrip strength test
    - gait speed - measured by a 6-meter normal and fast pace walk
    - dynamic balance - measured by a 6-meter backwards walk
    - ability to get up from and sit back down in a chair – measured by a chair rise test

- cardiorespiratory fitness and mobility – measured by a 400-meter walk (not on a treadmill)
- Self-reported and objective (measured by an accelerometer) physical activity
- Body composition (total and trunk fat mass, lean mass, bone mineral density), muscle density and bone strength – measured by DEXA and pQCT scans respectively
- Self-reported pelvic floor function

Information obtained from this research will assist health professionals in making exercise recommendations and in designing the most appropriate exercise interventions for ovarian cancer survivors.

As ovarian cancer survivors (cancer group) will be compared to similarly aged women who have never been diagnosed with cancer (control group), two groups of 22 participants each are required for the study. Your patient has expressed interest to participate in the cancer group of the study.

Participants for the cancer group must meet all the following criteria:

- Histologically confirmed stage III – IV ovarian cancer
- No evidence or suspicion of bone metastasis
- Be 18 years or older
- Not have had cancer-related treatment during the last 3 months (e.g. surgery, chemotherapy and/or radiation therapy)
- Not have completed cancer-related treatment more than 24 months ago
- No acute illness at the time of testing or any musculoskeletal, cardiovascular or neurological disorder that could put the participant at risk of injury or illness during exercise testing

The study has been approved by the Human Research Ethics Committees at Edith Cowan University and St John of God Hospital, Subiaco and subjects will be free to withdraw from the study at any time.

**The concern of the researchers is of past and/or present medical conditions that may compromise the individual's ability to participate in the exercise testing involved with this study, as described above. For these reasons all potential participants have been asked to seek their medical doctor's approval prior to involvement in the study**.

_____ is in sufficient health to participate in this study.
Participant's Name

| _____ | _____ | _____ |
|---|---|---|
| Doctors Name (please print) | Doctors Signature | Date |

**Please complete this letter and return it, along with any relevant records via facsimile to Mrs Christelle Schofield on 08 9206 3807 at your earliest convenience, or by hand to the participant.**

If you would like to refer patients, or if you require more information, please feel free to contact me or any of my supervisors. We will be happy to provide study outcomes to you as per your request.

Yours sincerely

Christelle Schofield (AEP ESSAM)
Master of Science (Exercise Science) Student
Edith Cowan University Health and Wellness Institute

# Appendix K –Medical consent- control

# MEDICAL DOCTOR CONSENT FORM

**Project Title: Physiological and disease specific characteristics of ovarian cancer survivors**

**Researchers:**
Mrs Christelle Scofield, Masters Student - E: c.schofield@ecu.edu.au - T: 0459 900 264
Prof Robert Newton, PhD - E: r.newton@ecu.edu.au - T: (08) 6304 5037
Dr Carolyn McIntyre, PhD - E: c.mcintyre@ecu.edu.au - T: (08) 6304 3987
Prof Daniel Galvão, PhD - E: d.galvao@ecu.edu.au - T: (08) 6304 3420

**Institute:** Edith Cowan University Health and Wellness Institute
St John of God, Subiaco

Dear Doctor,

The Edith Cowan University Health and Wellness Institute is undertaking a research study in collaboration with The St John of God Gynaecologic Oncology research group investigating the physiological and disease specific characteristics of ovarian cancer survivors. Women with ovarian cancer often experience a significant burden of disease and treatment side-effects. Exercise has been acknowledged as a safe and effective supportive care intervention for cancer survivors. Currently it is unknown what exercise is most appropriate for women with ovarian cancer to address their disease and treatment specific adverse side-effects. To better understand their exercise needs and to design appropriate exercise interventions for both research and clinical settings, we aim to identify unique physiological and disease specific characteristics of women with ovarian cancer. The purpose of this study is to determine the physiological and disease specific characteristics of ovarian cancer survivors and to explore differences in physiological characteristics between women with ovarian cancer and similarly aged women who have never been diagnosed with cancer.

Outcome measures in the study:

- Self-reported and objectively measured physical function. Objective physical function tests include:
  - muscle strength - measured by a 1-RM (repetition maximum) bench press and single leg extension test, as well as by a handgrip strength test
  - gait speed - measured by a 6-meter normal and fast pace walk
  - dynamic balance - measured by a 6-meter backwards walk
  - ability to get up from and sit back down in a chair – measured by a chair rise test

- cardiorespiratory fitness and mobility – measured by a 400-meter walk (not on a treadmill)
- Self-reported and objective (measured by an accelerometer) physical activity
- Body composition (total and trunk fat mass, lean mass, bone mineral density), muscle density and bone strength – measured by DEXA and pQCT scans respectively
- Self-reported pelvic floor function

Information obtained from this research will assist health professionals in making exercise recommendations and in designing the most appropriate exercise interventions for ovarian cancer survivors.

As ovarian cancer survivors (cancer group) will be compared to similarly aged women who have never been diagnosed with cancer (control group), two groups of 22 participants each are required for the study. Your patient has expressed interest to participate in the control group of the study.

Participants for the control group must meet all the following criteria:

- Be 18 years or older
- Have never had a diagnosis of cancer or history of cancer (other than non-melanoma skin cancer)
- Must not have an acute illness at the time of testing or any musculoskeletal, cardiovascular or neurological disorder that could put the participant at risk of injury or illness during exercise testing

The study has been approved by Human Research Ethics Committees at Edith Cowan University and St John of God Hospital, Subiaco and subjects will be free to withdraw from the study at any time.

**The concern of the researchers are of past and/or present medical conditions that may compromise the individual's ability to participate in the exercise testing involved with this study, as described above. For these reasons all potential participants have been asked to seek their medical doctor's approval prior to involvement in the study**.

_____ is in sufficient health to participate in this study.
Participant's Name

_____ _____ _____
Doctors Name (please print) Doctors Signature Date

**Please complete this letter and return it, along with any relevant records via facsimile to Mrs Christelle Schofield on 08 9206 3807 at your earliest convenience, or by hand to the participant.**

If you would like to refer patients, or if you require more information, please feel free to contact me or any of my supervisors. We will be happy to provide study outcomes to you as per your request.

Yours sincerely

Christelle Schofield (AEP ESSAM)
Master of Science (Exercise Science) Student
Edith Cowan University Health and Wellness Institute

# Appendix L – Participant consent form

## PARTICIPANT CONSENT FORM

## Physiological and disease specific characteristics of ovarian cancer survivors

Participant Name: _____

- I have read and understood the information letter and this participant consent form.
- I understand that the study will be carried out as described in the information letter, a copy of which I have retained.
- I have obtained approval from my doctor to complete the activities required for participation in the study.
- The nature and possible effects of the study have been explained to me.
- Any questions that I have asked have been answered to my satisfaction.
- I understand that all research data will be treated as confidential.
- I agree to participate in this study and give my consent freely.
- I realise that my participation in this research study is voluntary and whether or not I decide to participate is solely my decision.
- I also realize that I can withdraw from the study at any time and that I do not have to give any reasons for withdrawing.
- I agree that research data gathered for the study may be published provided my name or other identifying information is not disclosed.

**Participant:**

| _____ | _____ | _____ |
|---|---|---|
| Name | Signature | Date |

**Witness:**

| _____ | _____ | _____ |
|---|---|---|
| Name | Signature | Date |

# Appendix M – demographic information and health history questionnaire

## DEMOGRAPHIC INFORMATION AND HEALTH HISTORY QUESTIONNAIRE

**ID No: _____ Initials: _____**

**Date:**

_____ _____

First Name Last Name Middle Initial

_____ _____ _____

Date of Birth Age Sex

_____

_____

Postal Address

_____ _____ _____

Home Phone Mobile Phone Email Address

_____ _____

Family Physician Name Practice or Phone Number

_____ _____ _____

Emergency Contact Name Phone Number Relationship

**1. What is your current marital status?**

| | | |
|---|---|---|
| Single | Married | Defacto |
| Separated | Divorced | Widowed |

**2. What is the highest level of education you have completed?**

| | | |
|---|---|---|
| Primary | Secondary | Trade |
| Certificate/Diploma | Bachelor degree | Higher degree |

Other

_____

**3. What is your current level of employment (please circle)?**

Retired Unemployed Casual Part-time Full time Volunteer

If employed, what is your current occupation?

_____

If employed, how many hours/days do you work in a typical week?

_____ hours/day

_____ days/week

**4. Are you or have you ever been a smoker?** Yes No

If yes:

**a.** Are you a past or current smoker?

_____

**b.** Age you started smoking:

_____

**c.** Age you quit smoking (for past smokers only):

_____

**d.** Average number of cigarettes smoked per day:

_____

**5. How many alcoholic drinks do you usually have per week?**

_____

**6. Has your weight fluctuated more than a few kilos in the last 12 months?**

Yes No

**a.** If yes, has your weight gone up or down? _____

**b.** Approximately how many kilograms? _____

7. **Do you experience shortness of breath while walking with others of your age?** Yes No

8. **Do you experience sudden tingling, numbness, or loss of feeling in arms, hands, legs, feet, or face?** Yes No

9. **Do you experience swelling of your feet and ankles?** Yes No

10. **Do you get pains or cramps in your legs?** Yes No

11. **Do you experience any discomfort in your chest?** Yes No

12. **Have you ever been told that your blood pressure was abnormal?** Yes No

    If yes, do you currently take any medication (please provide details)?

    _____

    _____

13. **Have you ever been told that your serum cholesterol or triglyceride level was high?**

    Yes No

    If yes, do you currently take any medication (please provide details)?

    _____

    _____

14. **Have you ever been told that you have cardiovascular disease?** Yes No

    If yes, please provide details of condition and how it is controlled.

    _____

    _____

15. **Have you ever been told that you have diabetes?** Yes No

    If yes, how is it controlled?

    _____

    _____

**16. Have you ever been told that you have osteoporosis?** Yes No

If yes, how is it controlled?

_____

_____

**17. Has a doctor or nurse ever told you that you had any of the following conditions?**

| | | | | | |
|---|---|---|---|---|---|
| Heart attack…….. | Yes | No | Stroke…… | Yes | No |
| Emphysema…….. | Yes | No | Chronic bronchitis……. | Yes | No |
| Arthritis…… | Yes | No | Thyroid Disease……. | Yes | No |
| Peripheral Vascular Disease | Yes | No | Angina..…….. (chest pain) | Yes | No |

If yes, please provide details

_____

_____

_____

**18. When were you diagnosed with cancer?** Month: _____ Year: _____

**19. What form of gynaecological cancer have you been diagnosed with?**

_____

**20. Have you been diagnosed with a secondary cancer?** Yes No

a. If yes, what form?

_____

b. When?

_____

**21. Which types of treatment have you undertaken? (circle all that apply)**

**Surgery** **Radiation** **Chemotherapy**

Please indicate if you have received any other the type of treatment

_____

**22. Please specify the start date, duration and other important details of each treatment**

**Surgery (if applicable)**

_____

_____

_____

_____

_____

**Chemotherapy (if applicable)**

_____

_____

_____

_____

_____

**Radiation (if applicable)**

_____

_____

_____

_____

**23. In addition to the above, do you have any other medical conditions (chronic or serious illness)?** Yes No

If yes, please provide details:

_____

_____

_____

_____

_____

**24. Please list below the prescription medications you are currently taking. Fill out every column for each medication you list.**

| Medication | Duration (in years and months) | Reason for taking (i.e. which medical condition) and other comments |
|---|---|---|
| | | |
| | | |
| | | |
| | | |
| | | |
| | | |
| | | |

**26. Have you ever had any surgery (unrelated to cancer)** Yes No

**If yes, please provide details about the type, date and reason for the surgery**

| Type of Surgery | Date of Surgery (month & year) | Reason for Surgery & details of any continuing impairments |
|---|---|---|
| | | |
| | | |
| | | |
| | | |
| | | |

# Appendix N – Day 1 letter

## DAY 1 – ASSESSMENT

### Appointment Details

**Date:** Please call Christelle Schofield on 0459 900 264 to arrange an assessment date at your convenience after you have received permission from your doctor to take part in the study.

**Venue:** Edith Cowan University, Health and Wellness Institute
Level 2, Building 21
270 Joondalup Drive
Joondalup, WA, 6027

**Parking:** Visitor Car Parking is available in Car Park 13 next to the Health and Wellness Institute at $1.50 per hour. (Enter off Lakeside Drive). Please display your purchased parking ticket as well as the parking permit included in this package on your vehicle's dashboard.

It would be advisable to remove all jewellery and wear loose, unrestrictive clothing and training shoes to both assessment sessions if possible.

Things to remember:

- Please eat your breakfast and take any medications as usual.
- Please bring
  - change for parking
  - the signed letter from your specialist/GP
  - your signed consent form
  - the completed Demographic and Health History Questionnaire
- If you use a hearing aid or glasses, please ensure you have them with you on the day.
- Wear clothing and footwear suitable for exercise.

The DAY 1 schedule will involve:

- Information about the study and time for asking questions
- Review of questionnaires (please bring your reading glasses)
- DEXA and PQCT scans of your bone density and body composition
- Tests of your physical performance

**If a problem arises on the day (for example you are running late or get lost), please contact Christelle on 0459 900 264.**

# Appendix O - Activity monitor instructions

## ACTIVITY MONITOR INSTRUCTIONS

The activity monitor measures the amount of physical activity you do in your everyday life. It is also used to measure the amount and quality of your sleep.

## 1. Please start wearing the monitor from:

_____

## 2. Please take off the monitor:

_____

**If you have any questions about the activity monitor please call the chief study investigator, Christelle Schofield, on 0459 900 264.**
If there is no answer, please leave a message. Your call will be responded to as soon as possible.

**Where do I wear the activity monitor?**

- The monitor needs to be worn at the hip area of your waist with the black button facing the top (Do not twist the button).
- The monitor can be worn either above or beneath clothing, and it is not necessary for it to make contact with the skin.
- The monitor must be held snugly against the body to work properly (i.e. must be secure and not bounce or slide when you're moving).

- **How long do I wear the activity monitor for?**
  - We ask that you wear the monitor for a period of 7 days.
  - To get the most accurate information, it is very important to wear the monitor 24 hours a day if possible.
  - This includes when you are asleep at night.
  - The monitor should be taken off to bath/shower.
  - You need to take off the activity monitor on the date and time listed above.

- **What happens if I get the activity monitor wet?**
    - It's preferable if the monitor doesn't get wet, but it is water resistant and will not be affected by getting slightly wet.
    - If you are a swimmer please take the device off before getting into the pool/ocean.
    - Note the device is water *resistant* and not water *proof*.

- **How do I return the monitor?**
    - If you complete the 7-day period before your second assessment, please bring the monitor with you when you return to the ECU Health and Wellness Institute for your second assessment.
    - If you complete the 7-day period after your second assessment you will be provided with a prepaid envelope to post the monitor back to the Institute via any red Australia Post mailbox.
    - If you choose to withdraw from the study after the first assessment and after you have received the monitor, Christelle will contact you to make arrangements for the monitor to be returned to the Institute.

# Appendix P - Activity monitor log

## ACTIVITY MONITOR LOG

Study ID: _____

Date: ____/____/____

Please use this form to document any time that you didn't wear the monitor during the 7-day period, or any issues you had wearing the monitor.

| | DETAILS |
|---|---|
| **Day 1** | |
| **Day 2** | |
| **Day 3** | |
| **Day 4** | |
| **Day 5** | |
| **Day 6** | |
| **Day 7** | |

# Appendix Q - Questionnaires


Edith Cowan University
Health and Wellness Institute
vario wellness clinic


## QUESTIONNAIRES

Name: _____ Date: _____

- Please take your time completing these important questionnaires and answer all questions as honestly as you can. Please note that there are questions on both sides of each page in this package.

- Your responses provide extremely valuable information regarding the impact of cancer and cancer-related treatment on cancer survivors and have the potential to influence the information and services provided to all cancer survivors and specifically ovarian cancer survivors worldwide.

- We really appreciate your time and value the contribution you are making to advancing the scientific knowledge surrounding the exercise needs of ovarian cancer survivors.

- If you have any questions whatsoever don't hesitate to contact:

  Christelle Schofield
  Chief Study Investigator
  Phone: 0459 900 264
  E-mail: c.schofield@ecu.edu.au

- Please return the questionnaires to Christelle on your next testing session.

THANK YOU!

# YOUR HEALTH AND WELL-BEING

This questionnaire asks for your views about your health. This information will help keep track of how you feel and how well you are able to do your usual activities. For each of the following questions, please circle the one number that best describes your answer.

1. In general, would you say your current health is:

| Excellent | Very Good | Good | Fair | Poor |
|---|---|---|---|---|
| 1 | 2 | 3 | 4 | 5 |

2. Compared to one year ago, how would you rate your health in general now?

| Much better now than one year ago | Somewhat better now than one year ago | About the same as one year ago | Somewhat worse now than one year ago | Much worse now than one year ago |
|---|---|---|---|---|
| 1 | 2 | 3 | 4 | 5 |

3. The following questions are about activities you might do during a typical day. Does **your health now limit you** in these activities? If so, how much?

| | Yes, limited a lot | Yes, limited a little | No, not limited at all |
|---|---|---|---|
| a) **Vigorous activities**, such as running, lifting heavy objects, participating in strenuous sports. | 1 | 2 | 3 |
| b) **Moderate activities**, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf. | 1 | 2 | 3 |
| c) Lifting or carrying groceries. | 1 | 2 | 3 |
| d) Climbing **several** flights of stairs. | 1 | 2 | 3 |
| e) Climbing **one** flight of stairs. | 1 | 2 | 3 |
| f) Bending, kneeling, or stooping. | 1 | 2 | 3 |
| g) Walking **more than a mile**. | 1 | 2 | 3 |
| h) Walking **several hundred yards**. | 1 | 2 | 3 |
| i) Walking **one hundred yards**. | 1 | 2 | 3 |
| j) Bathing or dressing yourself | 1 | 2 | 3 |

4. During the **past 4 weeks**, how much of the time have you had any of the following problems with your work or other regular daily activities **as a result of your physical health**?

| | **All of the time** | **Most of the time** | **Some of the time** | **A little of the time** | **None of the time** |
|---|---|---|---|---|---|
| a) Cut down on the **amount of time** you spent on work or other activities. | **1** | **2** | **3** | **4** | **5** |
| b) **Accomplished less** than you would like. | **1** | **2** | **3** | **4** | **5** |
| c) Were limited in the **kind** of work or other activities. | **1** | **2** | **3** | **4** | **5** |
| d) Had **difficulty** performing the work or other activities (for example, it took extra effort). | **1** | **2** | **3** | **4** | **5** |

5. During the **past 4 weeks**, how much of the time have you had any of the following problems with your work or other regular daily activities **as a result of any emotional problems** (such as feeling depressed or anxious)?

| | **All of the time** | **Most of the time** | **Some of the time** | **A little of the time** | **None of the time** |
|---|---|---|---|---|---|
| a) Cut down on the **amount of time** you spent on work or other activities. | **1** | **2** | **3** | **4** | **5** |
| b) **Accomplished less** than you would like. | **1** | **2** | **3** | **4** | **5** |
| c) Did work or other activities **less carefully than usual**. | **1** | **2** | **3** | **4** | **5** |

6. During the **past 4 weeks**, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbours, or groups?

| **Not at all** | **Slightly** | **Moderately** | **Quite a bit** | **Extremely** |
|---|---|---|---|---|
| **1** | **2** | **3** | **4** | **5** |

7. How much **bodily** pain have you had during the **past 4 weeks**?

| None | Very mild | Mild | Moderate | Severe | Very severe |
|---|---|---|---|---|---|
| 1 | 2 | 3 | 4 | 5 | 6 |

8. During the **past 4 weeks**, how much did **pain** interfere with your normal work (including both work outside the home and housework)?

| Not at all | A little bit | Moderately | Quite a bit | Extremely |
|---|---|---|---|---|
| 1 | 2 | 3 | 4 | 5 |

9. These questions are about how you feel and how things have been with you **during the past 4 weeks**. For each question, please give the one answer that comes closest to the way you have been feeling. How much of the time during the **past 4 weeks**…

| | All of the time | Most of the time | Some of the time | A little of the time | None of the time |
|---|---|---|---|---|---|
| a) Did you feel full of life? | 1 | 2 | 3 | 4 | 5 |
| b) Have you been very nervous? | 1 | 2 | 3 | 4 | 5 |
| c) Have you felt so down in the dumps that nothing could cheer you up? | 1 | 2 | 3 | 4 | 5 |
| d) Have you felt calm and peaceful? | 1 | 2 | 3 | 4 | 5 |
| e) Did you have a lot of energy? | 1 | 2 | 3 | 4 | 5 |
| f) Have you felt downhearted and depressed? | 1 | 2 | 3 | 4 | 5 |
| g) Did you feel worn out? | 1 | 2 | 3 | 4 | 5 |
| h) Have you been happy? | 1 | 2 | 3 | 4 | 5 |
| i) Did you feel tired? | 1 | 2 | 3 | 4 | 5 |

10. During the **past 4 weeks**, how much of the time has your **physical health or emotional problems** interfered with your social activities (like visiting friends, relatives, etc.)?

| All of the time | Most of the time | Some of the time | A little of the time | None of the time |
|---|---|---|---|---|
| **1** | **2** | **3** | **4** | **5** |

11. How TRUE or FALSE is **each** of the following statements for you?

| | Definitely true | Mostly true | Don't know | Mostly false | Definitely false |
|---|---|---|---|---|---|
| a) I seem to get sick a little easier than other people. | **1** | **2** | **3** | **4** | **5** |
| b) I am as healthy as anybody I know. | **1** | **2** | **3** | **4** | **5** |
| c) I expect my health to get worse. | **1** | **2** | **3** | **4** | **5** |
| d) My health is excellent. | **1** | **2** | **3** | **4** | **5** |

# PHYSICAL ACTIVITY LEVEL

For this next question, we would like you to recall your average weekly exercise in the PAST MONTH.

When answering these questions please:

- Only count exercise sessions that lasted 10 minutes or longer in duration.
- Only count exercise that was done during free time (i.e., not occupation or housework).
- Note that the main difference between the three categories is the **intensity** of the exercise.

1. Considering a typical week (7 days) how many times on the average did you do the following kinds of exercise in the PAST MONTH?

| | Average Frequency | Average Duration |
|---|---|---|
| a. STRENUOUS EXERCISE<br>(HEART BEATS RAPIDLY, SWEATING)<br>(e.g. running, aerobics classes,<br>vigorous swimming, vigorous bicycling). | _____times/week | _____ minutes |
| b. MODERATE EXERCISE<br>(NOT EXHAUSTING, LIGHT PERSPIRATION)<br>(e.g. fast walking, tennis, easy bicycling,<br>easy swimming, popular and folk dancing). | _____ times/week | _____ minutes |
| c. MILD EXERCISE<br>(MINIMAL EFFORT, NO PERSPIRATION)<br>(e.g. easy walking, yoga, lawn bowling,). | _____ times/week | _____ minutes |
| d. RESISTANCE EXERCISE<br>(e.g., repetitively lifting weights using<br>your own body weight, dumbbells, weight<br>machines, or resistance bands) | _____ times/week | _____ minutes |

2. During a typical **7-Day period (a week),** in your leisure time, how often do you engage in any regular activity long enough to work up a sweat (heart beats rapidly)?

| Often | Sometimes | Never/Rarely |
|---|---|---|
| 1 | 2 | 3 |

# PELVIC FLOOR FUNCTION

**For each of the following questions, please circle the one number that best describes your answer.**

**Consider your experiences during the last month.**

## Bladder function

1. How many times do you pass urine in the day?

| Up to 7 | between 8 and 10 | between 11 and 15 | more than 15 |
|---|---|---|---|
| 0 | 1 | 2 | 3 |

2. How many times do you get up at night to pass urine?

| 0-1 | 2 | 3 | More than 3 |
|---|---|---|---|
| 0 | 1 | 2 | 3 |

3. Do you wet the bed before you wake up at night?

| never | occasionally (less than once per week) | frequently (once or more per week) | always (every night) |
|---|---|---|---|
| 0 | 1 | 2 | 3 |

4. Do you need to rush or hurry to pass urine when you get the urge?

| never | occasionally (less than once per week) | frequently (once or more per week) | daily |
|---|---|---|---|
| 0 | 1 | 2 | 3 |

5. Does urine leak when you rush or hurry to the toilet or can't you make it in time?

| never | occasionally (less than once per week) | frequently (once or more per week) | daily |
|---|---|---|---|
| 0 | 1 | 2 | 3 |

6. Do you leak urine with coughing, sneezing, laughing or exercising?

| never | occasionally (less than once per week) | frequently (once or more per week) | daily |
|---|---|---|---|
| 0 | 1 | 2 | 3 |

7. Is your urinary stream (urine flow) weak, prolonged or slow?

| never | occasionally (less than once per week) | frequently (once or more per week) | daily |
|---|---|---|---|
| 0 | 1 | 2 | 3 |

8. Do you have a feeling of incomplete bladder emptying?

| never | occasionally (less than once per week) | frequently (once or more per week) | daily |
|---|---|---|---|
| 0 | 1 | 2 | 3 |

9. Do you need to strain to empty your bladder?

| never | occasionally (less than once per week) | frequently (once or more per week) | daily |
|---|---|---|---|
| 0 | 1 | 2 | 3 |

10. Do you have to wear pads because of urinary leakage?

| never | As a precaution | When exercising /during a cold | daily |
|---|---|---|---|
| 0 | 1 | 2 | 3 |

11. Do you limit your fluid intake to decrease urinary leakage?

| never | before going out | moderately | always |
|---|---|---|---|
| 0 | 1 | 2 | 3 |

12. Do you have frequent bladder infections?

| no | 1-3 per year | 4-12 per year | more than 1 per month |
|---|---|---|---|
| 0 | 1 | 2 | 3 |

13. Do you have pain in your bladder or urethra when you empty your bladder?

| never | occasionally (less than once per week) | frequently (once or more per week) | daily |
|---|---|---|---|
| 0 | 1 | 2 | 3 |

14. Does urine leakage affect your routine activities like recreation, socialising, sleeping, shopping etc.?

| not at all | slightly | moderately | greatly |
|---|---|---|---|
| 0 | 1 | 2 | 3 |

15. How much does your bladder problem bother you?

| not at all | slightly | moderately | greatly |
|---|---|---|---|
| 0 | 1 | 2 | 3 |

## Bowel function

16. How often do you usually open your bowels?

| every other day or daily | less than every 3 days | less than once per week | more than once per day |
|---|---|---|---|
| 0 | 1 | 2 | 3 |

17. How is the consistency of your usual stool?

| soft, firm or hard (pebbles) | variable | watery |
|---|---|---|
| 0 | 1 | 2 |

18. Do you have to strain a lot to empty your bowels?

| never | occasionally (less than once per week) | frequently (once or more per week) | daily |
|---|---|---|---|
| 0 | 1 | 2 | 3 |

19. Do you use laxatives to empty your bowels?

| never | occasionally (less than once per week) | frequently (once or more per week) | daily |
|---|---|---|---|
| 0 | 1 | 2 | 3 |

20. Do you feel constipated?

| never | occasionally (less than once per week) | frequently (once or more per week) | daily |
|---|---|---|---|
| 0 | 1 | 2 | 3 |

21. When you get wind or flatus, can you control it or does wind leak?

| never | occasionally (less than once per week) | frequently (once or more per week) | daily |
|---|---|---|---|
| 0 | 1 | 2 | 3 |

22. Do you get an overwhelming sense of urgency to empty your bowels?

| never | occasionally (less than once per week) | frequently (once or more per week) | daily |
|---|---|---|---|
| 0 | 1 | 2 | 3 |

23. Do you leak watery stool when you don't mean to?

| never | occasionally (less than once per week) | frequently (once or more per week) | daily |
|---|---|---|---|
| 0 | 1 | 2 | 3 |

24. Do you leak normal stool when you don't mean to?

| never | occasionally (less than once per week) | frequently (once or more per week) | daily |
|---|---|---|---|
| 0 | 1 | 2 | 3 |

25. Do you have a feeling of incomplete bowel emptying?

| never | occasionally (less than once per week) | frequently (once or more per week) | daily |
|---|---|---|---|
| 0 | 1 | 2 | 3 |

26. Do you have to use finger pressure to help empty your bowels?

| never | occasionally (less than once per week) | frequently (once or more per week) | daily |
|---|---|---|---|
| 0 | 1 | 2 | 3 |

27. How much does your bowel problem bother you?

| not at all | slightly | moderately | greatly |
|---|---|---|---|
| 0 | 1 | 2 | 3 |

**Prolapse symptoms**

28. Do you have a sensation of tissue protrusion or a lump or bulging in your vagina?

| never | occasionally (less than once per week) | frequently (once or more per week) | daily |
|---|---|---|---|
| 0 | 1 | 2 | 3 |

29. Do you experience vaginal pressure or heaviness or a dragging sensation?

| never | occasionally (less than once per week) | frequently (once or more per week) | daily |
|---|---|---|---|
| 0 | 1 | 2 | 3 |

30. Do you have to push back your prolapse in order to void?

| never | occasionally (less than once per week) | frequently (once or more per week) | daily |
|---|---|---|---|
| 0 | 1 | 2 | 3 |

31. Do you have to push back your prolapse to empty your bowels?

| never | occasionally (less than once per week) | frequently (once or more per week) | daily |
|---|---|---|---|
| 0 | 1 | 2 | 3 |

32. How much does your prolapse bother you?

| not at all | slightly | moderately | greatly |
|---|---|---|---|
| 0 | 1 | 2 | 3 |

**Sexual function**

33. Are you sexually active? (please tick the box relevant to you)

☐ no

☐ less than once per week

☐ once or more per week

☐ daily or most days

***If you are not sexually active, please continue to answer questions 34 and 42 only***

34. If you are not sexually active, please tell us why: (please tick the box relevant to you)

☐ I do not have a partner

☐ I am not interested

☐ my partner is unable

☐ vaginal dryness

☐ too painful

☐ embarrassment due to the prolapse or incontinence

other reasons: _____

35. Do you have sufficient natural vaginal lubrication during intercourse?

| yes | no |
|---|---|
| 0 | 1 |

36. During intercourse vaginal sensation is:

| normal/pleasant | minimal | painful | none |
|---|---|---|---|
| 0 | 1 | 1 | 3 |

37. Do you feel that your vagina is too loose or lax?

| never | occasionally | frequently | always |
|---|---|---|---|
| 0 | 1 | 2 | 3 |

38. Do you feel that your vagina is too tight?

| never | occasionally | frequently | always |
|---|---|---|---|
| 0 | 1 | 2 | 3 |

39. Do you experience pain with sexual intercourse?

| never | occasionally | frequently | always |
|---|---|---|---|
| 0 | 1 | 2 | 3 |

40. Where does the pain during intercourse occur?

| Not applicable, I do not have pain | at the entrance to the vagina | deep inside, in the pelvis | both at the entrance and in the pelvis |
|---|---|---|---|
| 0 | 1 | 2 | 3 |

41. Do you leak urine during sexual intercourse?

| never | occasionally | frequently | always |
|---|---|---|---|
| 0 | 1 | 2 | 3 |

42. How much do these sexual issues bother you?

☐ not applicable, I do not have problems

| not at all | slightly | moderately | greatly |
|---|---|---|---|
| 0 | 1 | 2 | 3 |

Baessler K., O'Neill S.M., Maher C.F., Battistutta D. (2010) A validated self-administered female pelvic floor questionnaire. Int Urogynecol J 21: 163-172

# YOUR FEELING ABOUT EXERCISE

The following questions ask you to rate how you feel about **exercising on your own over the next month.** Please note that this study is **not** an exercise intervention study. However, the information you provide regarding your feelings about exercise will be extremely useful in the design and implementation of exercise intervention programs for women with ovarian cancer.

Exercise, for the purpose of the questionnaire, is defined as planned, structured and repetitive activity with the purpose to improve or maintain physical fitness and health. It excludes occupational, household and leisure activities. Ideally an exercise program should consist of:

- 2 strength or resistance training sessions/week using for instance your own body weight, weight machines, resistance bands or dumbbells.
- 150 minutes of moderate intensity aerobic-type exercise/week, for instance brisk walking, cycling, swimming or tennis.
- Stretching exercises for mobility.

Please pay careful attention to the words and descriptors at the end of each scale and circle the number that best represents how you feel. Please answer all items from (a) to (f).
**I think that doing exercise over the next month would be:**

(a)

| 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|
| Extremely Useless | Quite Useless | Slightly Useless | Neutral | Slightly Useful | Quite Useful | Extremely Useful |

(b)

| 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|
| Extremely Unenjoyable | Quite Unenjoyable | Slightly Unenjoyable | Neutral | Slightly Enjoyable | Quite Enjoyable | Extremely Enjoyable |

(c)

| 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|
| Extremely Harmful | Quite Harmful | Slightly Harmful | Neutral | Slightly Beneficial | Quite Beneficial | Extremely Beneficial |

(d)

| 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|
| Extremely Painful | Quite Painful | Slightly Painful | Neutral | Slightly Beneficial | Quite Beneficial | Extremely Beneficial |

(e)

| 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|
| Extremely Unimportant | Quite Unimportant | Slightly Unimportant | Neutral | Slightly Important | Quite Important | Extremely Important |

(f)

| 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|
| Extremely Boring | Quite Boring | Slightly Boring | Neutral | Slightly Fun | Quite Fun | Extremely Fun |

This next set of questions asks you to rate how other people in your life may feel about you doing exercise **over the next month**. Please pay careful attention to the words and descriptors at the end of each scale and circle the number that best represents how they might feel. Please answer all items from (a) to (c).

**I think that if I do exercise over the next month, most people who are important to me would be**:

(a)

| 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|
| Extremely disapproving | Quite disapproving | Slightly disapproving | Neutral | Slightly approving | Quite approving | Extremely approving |

(b)

| 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|
| Extremely discouraging | Quite discouraging | Slightly discouraging | Neutral | Slightly encouraging | Quite encouraging | Extremely encouraging |

(c)

| 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|
| Extremely unsupportive | Quite unsupportive | Slightly unsupportive | Neutral | Slightly supportive | Quite supportive | Extremely supportive |

This next question asks you to rate how active (how much exercise) you think other people in your life are likely to do **over the next month**.

**I think that over the next month, most people who are important to me will themselves be**:

(a)

| 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|
| Extremely inactive | Quite inactive | Slightly inactive | Neutral | Slightly active | Quite active | Extremely active |

This next set of questions asks you to rate how motivated you are to do exercise training **over the next month**. Pay careful attention to the words at the end of each scale and circle the number

that best represents your level of motivation.

(a) How motivated are you to do exercise **over the next month?**

| 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|
| Extremely unmotivated | Quite unmotivated | Slightly unmotivated | Neutral | Slightly motivated | Quite motivated | Extremely motivated |

(b) I strongly intend to do everything I can to do exercise **over the next month**.

| 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|
| Strongly disagree | Moderately disagree | Slightly disagree | Neutral | Slightly agree | Moderately agree | Strongly agree |

(c) How committed are you to doing exercise **over the next month?**

| 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|
| Extremely uncommitted | Quite uncommitted | Slightly uncommitted | Neutral | Slightly committed | Quite committed | Extremely committed |

These next questions ask you to rate how likely you feel it is that you will be able to do exercise **over the next month** if you were really motivated. Pay careful attention to the words at the end of each scale and circle the number that best represents how you feel.

**If you were really motivated…**

(a) How controllable would it be for you to do exercise training **over the next month**?

| 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|
| Extremely uncontrollable | Quite uncontrollable | Slightly uncontrollable | Neutral | Slightly controllable | Quite controllable | Extremely controllable |

(b) How confident would you be that you could do exercise **over the next month**?

| 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|
| Extremely unconfident | Quite unconfident | Slightly unconfident | Neutral | Slightly confident | Quite confident | Extremely confident |

(c) Do you feel that whether or not you do exercise **over the next month** would be completely up to you?

| 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|
| Strongly disagree | Moderately disagree | Slightly disagree | Neutral | Slightly agree | Moderately agree | Strongly agree |

(d) How easy or difficult would it be for you to do exercise training **over the next month?**

| 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|
| Extremely difficult | Quite difficult | Slightly difficult | Neutral | Slightly easy | Quite easy | Extremely easy |

(e) Do you feel you would have complete control over whether or not you do exercise **over the next month?**

| 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|
| Strongly disagree | Moderately disagree | Slightly disagree | Neutral | Slightly agree | Moderately agree | Strongly agree |

(f) How certain or uncertain would you be that you could do exercise **over the next month**?

| 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|
| Extremely uncertain | Quite uncertain | Slightly uncertain | Neutral | Slightly certain | Quite certain | Extremely certain |

Do you have a specific plan for where, when, and how you are going to exercise **over the next month**?

| 1 | 2 | 3 | 4 | 5 |
|---|---|---|---|---|
| Not at all | A little bit | Somewhat | Quite a bit | Very much |

# END OF QUESTIONNAIRE PACK

Thank you very much for your time and contribution to this important research!

# Appendix R – Data collection Sheet

## DATA COLLECTION SHEET

**ID No:** _____ **Initials:** _____

**Date:** _____

☐ **Familiarization**

☐ **Baseline**

**Assessor:**

1. ☐ **Informed Consent** ☐ **GP Consent** ☐ **Demographic Info & Health History**
2. **Medical History**: (conditions that may impact function/require tests to be modified)

_____

_____

_____

_____

3. **Body Composition:**

**Height**: _____cm **Weight**: _____kg BMI: _____ (kg/$m^{2)}$

4. **Circumferences**: Min of 2 trials with the 3rd trial necessary if a 2mm difference between trials

**Waist**: _____cm _____cm _____cm

**Hip**: _____cm _____cm _____cm

5. **DEXA full body scan**: remove shoes, socks, ALL metal (jewellery, underwire bra) and any prosthetics

Completed ☐

**PQCT scan:** **Tibia Length (left): _____**

Completed ☐

6. **Resting Blood Pressure & HR:** (taken after resting in a supine position for 5 minutes)**Blood**

**Pressure:** _____mmHg _____mmHg _____mmHg

**Heart Rate:** _____bpm _____bpm _____bpm

7. **6m Walk Tests:**

**Normal**: _____sec _____sec _____sec **BEST**: _____sec

**Fast**: _____sec _____sec _____sec **BEST**: _____sec

**Backwards**: _____sec _____sec _____sec **BEST**: _____sec

8. **400 meter Walk:**

**Heart rate:** Before test: _____ bpm Immediately after: _____ bpm

1 minute after: _____ bpm 2 minutes after: _____ bpm

**Warm-up Lap** ("walk from 1 marker to the other in as few strides as possible")

**Number of strides:** (for initial 20 meters) _____

**Laps:** 1 2 3 4 5 6 7 8 9 10 **400m Walk Time:** _____

9. **Repeated Chair Rise:** 2min rest between trials

Trial 1: _____sec Trial 2: _____sec Trial 3: _____sec **BEST**: _____sec

10. **Strength Testing**

a. **1 RM horizontal Chest Press:**

Bar Start: _____ Pillow Used: _____

Bench Position: _____cm Step Height: _____

Grip Distance: _____cm

**Warm-up:** 6 x 60% 1RM = _____kg (2min) 3 x 80% 1RM = _____kg (2min)

**1RM Attempts:** Trial 1: _____kg (2min) Trial 2: _____kg (2min)

Trial 3: _____kg (2min) Trial 4: _____kg (2min)

Trial 5: _____kg **Actual 1RM = _____kg**

NOTES:

_____

_____

b. **1 RM single Leg Extension:** (Alternate legs)

Back Rest: _____ Leg Rest: _____

Lifting Arm (Knees at $90^{o}$): _____

| RIGHT LEG | LEFT LEG |
|---|---|
| **Warm-up:** 6 x 60% 1RM = _____kg (2min) | **Warm-up:** 6 x 60% 1RM = _____kg (2min) |
| 3 x 80% 1RM = _____kg (2min) | 3 x 80% 1RM = _____kg (2min) |
| **1RM Attempts:** Trial 1: _____kg (2min) | **1RM Attempts:** Trial 1: _____kg (2min) |
| Trial 2: _____kg (2min) | Trial 2: _____kg (2min) |
| Trial 3: _____kg (2min) | Trial 3: _____kg (2min) |
| Trial 4: _____kg (2min) | Trial 4: _____kg (2min) |
| Trial 5: _____kg | Trial 5: _____kg |
| **Actual 1RM = _____kg** | **Actual 1RM = _____kg** |

NOTES:

_____

_____

c. **Hand Grip Dynamometer: (Alternate hands – 20-30 sec rest between trails)**

| RIGHT HAND | LEFT HAND |
|---|---|
| Trial 1: _____kg | Trial 1: _____kg |
| Trial 2: _____kg | Trial 2: _____kg |
| Trial 3: _____kg | Trial 3: _____kg |
| Mean of three : _____kg | Mean of three: _____kg |

11. **Questionnaires: (n/a for familiarization)**

Completed all questions ☐

12. **Collect/Give out:**

**Familiarization**
Give out:
- ☐ Questionnaires
- ☐ ActiGraph Monitor
- ☐ Explain ActiGraph Instructions

**Baseline**
Collect:
- ☐ ActiGraph Monitor
- ☐ Questionnaires

NOTES:

_____

_____

_____

# Appendix S – Co-author declarations

Signed declarations from all co-authors of papers to confirm that I, Christelle Schofield, contributed as significant manuscript writer and was responsible for all data acquisition, as well as the majority of data analysis and interpretation.

To whom it may concern

I, Christelle Schofield, confirm that, with reference to the papers titled:

1. "A Physiological Profile of Ovarian Cancer Survivors to Inform Tailored Exercise Interventions and the Development of Exercise Oncology Guidelines" (Schofield C, Newton RU, Galvão DA et al. Int J Gynecol Cancer. 2017; 27: 1560-1567).
2. "Activity behaviors and physiological characteristics of women with advanced-stage ovarian cancer: a comprehensive cross-sectional investigation" (Schofield C, Newton RU, Galvão DA et al. Int J Gynecol Cancer. Under review).
3. "Associations of objective activity behaviors and physiological characteristics with health-related quality of life and pelvic floor dysfunction in advanced-stage ovarian cancer survivors" (Schofield C, Newton RU, Galvão DA et al. Prepared for submission).

I contributed as significant manuscript writer and was responsible for all data acquisition, as well as the majority of data analysis and interpretation.

Signature: Schofield

I, as Co-Author, endorse that this level of contribution by the Candidate indicated above is appropriate.

**Prof Robert U. Newton, PhD**

Signature: _____ Date: 22/09/2017

Co-Director, Exercise Medicine Research Institute, Edith Cowan University, Joondalup, Australia

Associate Dean, School of Medical and Health Sciences, Edith Cowan University, Joondalup, Australia

To whom it may concern

I, Christelle Schofield, confirm that, with reference to the papers titled:

1. "A Physiological Profile of Ovarian Cancer Survivors to Inform Tailored Exercise Interventions and the Development of Exercise Oncology Guidelines" (Schofield C, Newton RU, Galvão DA et al. Int J Gynecol Cancer. 2017; 27: 1560-1567).
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I contributed as significant manuscript writer and was responsible for all data acquisition, as well as the majority of data analysis and interpretation.

Signature: Schofield

I, as Co-Author, endorse that this level of contribution by the Candidate indicated above is appropriate.

**Dr. Carolyn J. Peddle-McIntyre, PhD**

Signature: _____ Date: 21.9.2017.

Post-Doctoral Research Fellow in Exercise and Cancer, Exercise Medicine Research Institute, Edith Cowan University, Joondalup, Australia

To whom it may concern

I, Christelle Schofield, confirm that, with reference to the papers titled:

1. "A Physiological Profile of Ovarian Cancer Survivors to Inform Tailored Exercise Interventions and the Development of Exercise Oncology Guidelines" (Schofield C, Newton RU, Galvão DA et al. Int J Gynecol Cancer. 2017; 27: 1560-1567).
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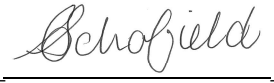
Signature: 

I, as Co-Author, endorse that this level of contribution by the Candidate indicated above is appropriate.

**Dr. Paul A. Cohen, MD**

Signature:  Date: 21.09.2017

Director Gynaecological Cancer Research Group, St John of God Hospital, Subiaco, Australia
Clinical Senior Lecturer, Department of Obstetrics and Gynaecology, School of Medicine, University of Western Australia, Australia
Adjunct Professor, Institute for Health Research, University of Notre Dame Australia, Fremantle, Australia

To whom it may concern

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1. "A Physiological Profile of Ovarian Cancer Survivors to Inform Tailored Exercise Interventions and the Development of Exercise Oncology Guidelines" (Schofield C, Newton RU, Galvão DA et al. Int J Gynecol Cancer. 2017; 27: 1560-1567).
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I contributed as significant manuscript writer and was responsible for all data acquisition, as well as the majority of data analysis and interpretation.

Signature: Schofield

I, as Co-Author, endorse that this level of contribution by the Candidate indicated above is appropriate.

**Prof Daniel A. Galvão, PhD**

Signature: _____ Date: 21/09/2017

Co-Director, Exercise Medicine Research Institute, Edith Cowan University, Joondalup, Australia

To whom it may concern

I, Christelle Schofield, confirm that, with reference to the papers titled:

1. "Activity behaviors and physiological characteristics of women with advanced-stage ovarian cancer: a comprehensive cross-sectional investigation" (Schofield C, Newton RU, Galvão DA et al. Int J Gynecol Cancer. Under review).
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I contributed as significant manuscript writer and was responsible for all data acquisition, as well as the majority of data analysis and interpretation.

Signature: Schofield

I, as Co-Author, endorse that this level of contribution by the Candidate indicated above is appropriate.

**Dr. Joanne A. McVeigh, PhD**

Signature: _____ Date: _27.09.17_____

Senior Lecturer, Faculty of Health Sciences, School of Occupational Therapy and Social Work, Curtin University, Bentley, Australia

To whom it may concern

I, Christelle Schofield, confirm that, with reference to the papers titled:

1. "Activity behaviors and physiological characteristics of women with advanced-stage ovarian cancer: a comprehensive cross-sectional investigation" (Schofield C, Newton RU, Galvão DA et al. Int J Gynecol Cancer. Under review).
2. "Associations of objective activity behaviors and physiological characteristics with health-related quality of life and pelvic floor dysfunction in advanced-stage ovarian cancer survivors" (Schofield C, Newton RU, Galvão DA et al. Prepared for submission).

I contributed as significant manuscript writer and was responsible for all data acquisition, as well as the majority of data analysis and interpretation.

Signature: Schofield

I, as Co-Author, endorse that this level of contribution by the Candidate indicated above is appropriate.

**Dr. Ganendra R. Mohan, MD**

Signature: _____ Date: 21/9/2017

Certified Gynaecologic Oncologist
Clinical Senior Lecturer, Department of Obstetrics and Gynaecology, School of Medicine, University of Western Australia, Australia
Clinical Senior Lecturer, University of Notre Dame Australia, Fremantle, Australia

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**Dr. Jason Tan, MD**

Signature:  Date: 5/9/17

Certified Gynaecologic Oncologist
Lead Clinician (Gynaecology/Gynaecological Oncology), Western Australia Cancer & Palliative Care Network, Department of Health, Government of Western Australia, Australia
Clinical Senior Lecturer, University of Notre Dame Australia, Fremantle, Australia

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Signature: Schofield

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**Dr. Stuart G. Salfinger, MD**

Signature: _____ Date: 21.9.17

Certified Gynaecologic Oncologist
Clinical Senior Lecturer, School of Women's and Infants' Health, University of Western Australia, Australia
Senior Lecturer and Clinical Mentor, University of Notre Dame Australia, Fremantle, Australia

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Signature: Schofield

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**Prof Leon M. Straker, PhD**

Signature: _____ Date: 21/9/2017

John Curtin Distinguished Professor

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1. Vallance JK, Boyle T, Courneya KS et al. Associations of objectively assessed physical activity and sedentary time with health-related quality of life among colon cancer survivors. Cancer. 2014;120(18):2919-2926.

2. Lynch BM, Dunstan DW, Winkler E et al. Objectively assessed physical activity, sedentary time and waist circumference among prostate cancer survivors: findings from the National Health and Nutrition Examination Survey (2003-2006). Eur J Cancer Care (Engl). 2011;20(4):514-519.
3. George SM, Alfano CM, Groves J et al. Objectively measured sedentary time is related to quality of life among cancer survivors. PLoS ONE. 2014;9(2):e87937-e87937.
4. Jeffery E, Lee YG, McVeigh J et al. Feasibility of objectively measured physical activity and sedentary behavior in patients with malignant pleural effusion. Supportive Care In Cancer: Official Journal Of The Multinational Association Of Supportive Care In Cancer. 2017.
5. Dyrstad SM, Hansen BH, Holme IM et al. Comparison of self-reported versus accelerometer-measured physical activity. Med Sci Sports Exerc. 2014;46(1):99-106.
6. Broderick JM, Hussey J, Kennedy MJ et al. Testing the 'teachable moment' premise: does physical activity increase in the early survivorship phase? Supportive Care In Cancer: Official Journal Of The Multinational Association Of Supportive Care In Cancer. 2014;22(4):989-997.