

**Effects of Exercise on Health Outcomes and
Cardiovascular Disease Risk in Cancer
Survivors**

Kellie Louise Toohey

Student ID: u110234

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Dedication

This thesis is dedicated to Dragons Abreast - pioneers in improving the lives of those diagnosed with cancer through exercise, challenging medical thinking.

CERTIFICATE OF AUTHORSHIP OF THESIS

Except where clearly acknowledged in footnotes, quotations and the bibliography, I certify that I am the sole author of the thesis submitted today entitled - **Effects of Exercise on Health Outcomes and Cardiovascular Disease Risk in Cancer Survivors**

I certify that to the best of my knowledge the thesis contains no material previously published or written by another person except where due reference is made in the text of the thesis.

The material in the thesis has not been the basis of an award of any other degree or diploma except where due reference is made in the text of the thesis.

The thesis complies with University requirements for a thesis as set out in *Higher Degree by Research Examination Policy, Schedule Two (S2)*. Refer to <http://www.canberra.edu.au/research/hdr-policy-and-procedures>



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Signature of Candidate



.....

Signature of the chair of the supervisory panel

Date: 14th August, 2018

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Publications

The work in this thesis has been presented at scientific meetings and/or published in peer reviewed journals as listed below:

International Journals

- Toohey, K., Pumpa, K., McKune, A., Cooke, J., DuBose, K. D., Yip, D., Craft, P., Semple, S. (2018). Does low volume high-intensity interval training elicit superior benefits to continuous low to moderate-intensity training in cancer survivors? *World Journal of Clinical Oncology*, 9(1), 1.
- Toohey, K., Pumpa, K., McKune, A., Cooke, J., & Semple, S. (2018). High-intensity exercise interventions in cancer survivors: a systematic review exploring the impact on health outcomes. *Journal of Cancer Research and Clinical Oncology*, 144(1), 1-12.
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- Toohey, K., Pumpa, K., McKune, A., Cooke, J., Welvaert, M., Northey, J., & Semple, S. (2018). Autonomic Nervous System and Immune Function in Breast Cancer Survivors: An Exploration of the Impact of Exercise Intensity. *European Journal of Cancer Care*. Submitted.

- Toohey, K., Semple, S., Pumpa, K., Cooke, J., Arnold, L., Craft, P., & Yip, D. (2015). High-intensity interval training versus continuous moderate intensity training: Effects on health outcomes and cardiometabolic disease risk factors in cancer survivors: A pilot study. *Journal of Science & Medicine in sport*, 19, e94-e94.
- Toohey, K., Pumpa, K., Cooke, J., & Semple, S (2015). Effects of high vs. moderate intensity exercise on functional fitness and quality of life in cancer survivors: a pilot study. *Journal of medicine & science in sports and exercise*, 47(5S):464

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- Toohey, K., Semple, S., Pumpa, K., Cooke, J., Arnold, L., Craft, P., & Yip, D. (2015). High-intensity interval training versus continuous moderate intensity training: Effects on health outcomes and cardiometabolic disease risk factors in cancer survivors: A pilot study. *Heart Foundation, Cardiovascular Research Symposium*. May 5th 2017, Canberra, Australia. Oral Presentation.
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- Toohey, K., Pumpa, K., Cooke, J., & Semple, S. Effects of moderate vs. high intensity exercise on functional fitness & quality of life in cancer survivors. *12th Behavioural Research in Cancer Control Conference “Bridging the Gap”*, 12th May -15th May 2015, Sydney, Australia. Oral presentation.
- Toohey, K., Pumpa, K., Cooke, J., & Semple, S. Effects of high vs. moderate intensity exercise on functional fitness and quality of life in cancer survivors: a pilot study. *62nd Annual Meeting & 6th World Congress on Exercise is Medicine®*, May 26th -May 30th 2015, San Diego, United States of America. Poster presentation.
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Coursework Component of Doctorate

- Graduate Certificate of Research Methods and Design (see appendix 4)

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Abstract

Many cancer survivors are inactive, putting them at risk of developing additional diseases such as cardiovascular disease (CVD). Even though general physical activity guidelines exist, cancer survivors commonly do not meet them and engage in too much sedentary behaviour. The optimal level of physical activity and/or exercise for reducing CVD risk in cancer survivors remains unclear. High-intensity interval training (HIIT) is being used by some individuals (including those with a chronic condition such as Diabetes and CVD) as a method of achieving additional physiological benefits compared to traditional exercise modes. It remains unclear if HIIT is effective, achievable or safe for cancer survivors and if the same benefits would be seen. The studies combined in this thesis aimed to investigate the efficacy of HIIT within cancer survivors for reducing risk factors for CVD.

High-intensity exercise interventions elicited significant improvements ($p < 0.05$) in VO_2 max, strength, body mass, body fat and hip and waist circumference compared with CMIT and/or control groups. The studies reviewed showed low risk in participating in supervised high-intensity exercise interventions. A self-reported questionnaire was used to determine the changes in physical activity (PA) patterns and body weight (BW) throughout the first 12 months after a cancer diagnosis. In the 12 months post-diagnosis, cancer survivors increased their sleep time and reduced their levels of both vigorous and light PA, this may or may not be related to the increases in BW, which was observed for 60% of the participants. These negative changes in PA puts this population at risk of additional diseases such as CVD.

Cancer survivors (16) within 24 months post diagnosis, were randomly assigned into the LVHIIT or CLMIT group for 36 sessions (12 weeks) of supervised exercise.

The LVHIIT group performed 7 x 30 second intervals ($\geq 85\%$ maximal heart rate) and the CLMIT group performed continuous aerobic training for 20 minutes ($\leq 55\%$ maximal heart rate) on a stationary bike or treadmill. Significant improvements (time) were observed for 13 of the 23 dependent variables (ES 0.05-0.61, $p < 0.05$). An interaction effect was observed for six-minute walk test (18.53% [32.43-4.63] ES 0.50, $p = < 0.01$) with the LVHIIT group demonstrating greater improvements. The study that followed incorporated a larger sample size (75) of sedentary cancer survivors ($n = 75$, aged 51 ± 12 y) within 24 months of diagnosis using the same exercise protocol. Significant improvements from baseline were observed for seven of the 22 variables (ES 0.35 – 0.97, $p \leq 0.05$). There was an interaction effect ($p < 0.01$) after 12 weeks in the LVHIIT group for six-minute walk test ($p < 0.01$; $d = 0.97$; 95% CI = 0.36, 1.56; large), sit to stand test ($p < 0.01$; $d = -0.83$; 95% CI = -1.40, -0.22; large) and waist circumference reduction ($p = 0.01$; $d = -0.48$; CI = -1.10, 0.10; medium). An interaction effect ($p < 0.01$) was also observed for quality of life in both the LVHIIT ($d = 1.11$; 95% CI = 0.50, 1.72; large) and CLMIT ($d = 0.57$; 95% CI = -0.00, 1.20; moderate) compared with the control group ($d = -0.15$; 95% CI = -0.95, 0.65; trivial). Low-volume high-intensity training showed promise as an effective exercise prescription within the cancer population, showing greater improvements in cardio-respiratory fitness, lower body strength and waist circumference compared with traditional CLMIT and control groups. Both LVHIIT and CLMIT improved quality of life.

The impact of exercise intensity on autonomic nervous system (ANS) and immune function in breast cancer survivors is not known. The final intervention included 17 participants using the same protocol except for the rest between intervals which was increased to two minutes. A significant improvement ($p \leq 0.05$) in VO_{2peak} from pre to post intervention in both exercise groups were observed. Non-significant changes were observed in ANS function

and mucosal immunity in individuals with outlying baseline levels. Both HIIT and CMIT improved cardiorespiratory fitness.

CVD remains one of the highest diagnosed comorbidities in the cancer population. Cancer survivors continue to be inactive, increasing the negative impact on their health profile, increasing CVD risk factors. Traditional and generic exercise guidelines are commonly used by clinicians to assist in prescribing recommendations for increased amounts of PA in the cancer population. In this thesis the “novel” exercise modality (supervised LVHIIT) showed increased improvements in some of the health outcomes measured, when compared with traditional CMIT however CMIT still showed significant improvements, something that we were not expecting after the short amount of exercise used. In summary, LVHIIT could be considered for use as an alternative to traditional CMIT within the cancer population for improved fitness, quality of life and compliance in those who are time poor. As shown in the final study cancer survivors who had reduced measures of HPA axis and immune functions at baseline benefited most from exercise. The studies within the thesis contributed to understanding HIIT within the cancer population. HIIT could assist in the optimisation of individualised exercise prescription to reduce risk factors for CVD in cancer.

List of Abbreviations

% - percentage

6MWT – six-minute walk test

ACSM – American College of Sports Medicine

AEP – Accredited Exercise Physiologist

AHA – American Heart Association

Aix – augmentation index

ANS – autonomic nervous system

ATP/PC – adenosine triphosphate phosphocreatine

BMI – body mass index

BPM – beats per minute

BW – body weight

CDP – central diastolic pressure

CLMIT – continuous low to moderate intensity training

cm – centimetres

CMIT – continuous moderate intensity training

CON - control

CRP – c-reactive protein

CSP – central systolic pressure

CVD – cardiovascular disease

DBP – diastolic blood pressure

DXA – dual-energy x-ray absorptiometry

EORTC – European organisationa for research and treatment of cancer

FACT-G – functional assessment of cancer therapy – general

FFT – fast fourier transformation

HIIT – high intensity interval training

HPA – hypothalamic pituitary adrenal

HRV – heart rate variability

IgA – immunoglobulin A

kg – kilograms

LA – light activity

LVHIIT -low volume high intensity interval training

m – metres

m/s – metres per second

MA – moderate activity

MAP – mean arterial pressure

mg/L – milligrams per litre

mm/Hg – millimetres of mercury

mmol/L – millimolar units per litre

mU/L – milliunits per litre

OFC – oral fluid collection

PA – physical activity

PEACE – physical activity across the cancer experience

PP – pulse pressure

POC – point of care

PRISMA – preferred reporting items for systematic reviews

PWA – pulse wave analysis

PWV – pulse wave velocity

QOL – quality of life

RHR – resting heart rate

RMSSD - root mean square of successive difference

s – seconds

SA – sedentary activity

SAA – salivary alpha amylase

SAHRV – spectral analysis of heart rate variability

SBP – systolic blood pressure

s-cortisol – salivary cortisol

SNS – sympathetic nervous system

STS – sit to stand

VA – vigorous activity

VO₂ – volume of oxygen

VO₂max – volume of oxygen maximum

VO₂peak – volume of oxygen peak

WBC – white blood cells

WHO – World Health Organisation