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Competition:

UQUAPS 2017 "Pitching Research" Competition

Submission id:	Date submitted:
UQUAPS-2017-014	**26 Aug 2017 at 15:01 AWST**

Faculty or Institute:	School:
UQ Health and Behavioural Sciences	**School of Human Movement and Nutrition Sciences**

Programme:	Load:	Level:
PhD	**Full-time**	**7-9 months**

Name:

Natalie Vear

(A) Working Title:

The effects of high-intensity exercise on endothelial and autonomic nervous system function in men with metastatic castrate-resistant prostate cancer

Word count: **1084 words**

(A) Working Title	The effects of high-intensity exercise on endothelial and autonomic nervous system function in men with metastatic castrate-resistant prostate cancer
(B) Basic Research Question	Can high-intensity aerobic and resistance exercise mitigate treatment-related endothelial and autonomic nervous system (ANS) dysfunction in men with metastatic castrate-resistant prostate cancer (MCRPC)?
(C) Key paper(s)	Gilbert, S. E., Tew, G. A., Fairhurst, C., Bourke, L., Saxton, J. M., Winter, E. M., Rosario, D. J. (2016). Effects of a lifestyle intervention on endothelial function in men on long-term androgen deprivation therapy for prostate cancer. British Journal of Cancer, 114(4), 401-408. Jones, L. W., Hornsby, W. E., Freedland, S. J., Lane, A., West, M. J., Moul, J. W., ... Eves, N. D. (2014). Effects of nonlinear aerobic training on erectile dysfunction and cardiovascular function following radical prostatectomy for clinically localized prostate cancer. European Urology, 65(5), 852-855.
(D) Motivation / Puzzle	Cancer therapies such as chemotherapy and hormone therapies extend survival, however they often result in treatment-related cardiotoxicity, subsequently increasing cardiovascular morbidity and mortality. Dysfunction to the endothelium of the arteries and the ANS has shown to precede dysfunction of the heart and thus are earlier indicators of treatment-related cardiotoxicity. Exercise has shown to be effective in improving endothelial and ANS function in other clinical populations, yet its efficacy is still not fully understood in cancer populations. If exercise is shown to reduce treatment-related toxicities, this could lead to the development of guidelines to reduce morbidity and mortality in cancer populations.
THREE	**Three** core aspects of any empirical research project i.e. the "IDioTs" guide
(E) Idea	Men with MCRPC undergo some of the most intensive and long-term cancer therapies of any cancer population and can present with significant endothelial and ANS dysfunction. Exercise, especially when performed at higher intensities, has shown to be effective in improving endothelial and ANS function in less-advanced cancer populations, yet this has not been investigated in individuals who have undergone such intensive treatment regimens as men with MCRPC. Men with MCRPC will have their endothelial and ANS function assessed before, during and after completing a structured high-intensity aerobic and resistance exercise training (HIART) intervention to identify whether this dysfunction can be reversed.
(F) Data	Qualitative analysis of the current literature - A systematic review of the literature investigating the effects of exercise interventions on cardiac, endothelial and ANS function in cancer populations was performed. This review provided an indication of the objective measures of these physiological systems employed by other researchers in the oncology field. This review also provided an indication of the design of previous exercise interventions and their potential impact on the outcome measures. Two-arm Randomised Control Trail (RCT) - Participants with MCRPC in the greater Brisbane area recruited from the larger multi-centre international RCT, named Global Action Plan 4 (GAP4), will be included. Objective assessments of endothelial and ANS function will be performed at five time points (baseline, 3, 6, 12 and 24 months) during a two-year tapered-supervision HIART intervention. Participants randomised to the control group (usual care group) will undergo the

	same assessments. A sample size calculation, based on the secondary outcome measure of flow-mediated dilation in Jones et al., 2014, determined a total of 44 participants (22 per group) is required for this study.
(G) Tools	To answer the research question, a two-armed RCT cohort design will be employed using objective assessments of endothelial and ANS function undertaken at multiple time points. The gold-standard assessment of endothelial function, flow-mediated dilation (FMD), will be measured with a Terason (GE Vingmed Ultrasound AS, Horten, Norway) system. Secondary assessments of endothelial function, including pulse wave analysis (PWA) and pulse wave velocity (PWV), will be assessed using the SphygmoCor (AtCor Medical, Sydney, Australia) system. ANS function will be assessed via heart rate variability (HRV) using electrocardiogram and analysed using a Kubios HRV (University of Eastern Finland, Finland) system. Training on the above equipment has been successfully completed, with tight test-retest reliability. Statistical analyses of raw data will be conducted on IBM SPPS Statistics for iOS. Analyses of normal distribution, within and between group differences over the five time points will be conducted using linear mixed effects models.
TWO	**Two** key questions
(H) What's New?	This will be the first exercise study to focus on men with MCRPC, a population that usually receives a variety of intense cancer treatments that can negatively affect endothelial and ANS function. A two-year exercise intervention will be employed, a duration significantly longer than any other reported intervention for these outcomes in any cancer population. A total of 44 participants will be recruited, which is the largest oncological study population to explore both endothelial and ANS function. This study will investigate the effects of high intensity exercise on endothelial and ANS function; most previous research has explored low-to-moderate intensity exercise interventions. This will also be the first study to combine high-quality measurements of these two physiological systems (endothelial and ANS).
(I) So What?	This study will help to address significant gaps within the literature, which is of paramount importance if exercise is to be promoted as an adjunct cancer treatment to mitigate treatment-related toxicities. Including an advanced cancer population, with a larger sample size over a longer exercise duration will help to identify the extent of the reversibility of these toxicities. Reporting high-quality objective measurements in both systems will provide a more extensive indication of changes in toxicity in response to exercise in this population. This study will also identify whether high-intensity exercise is an adequate 'dose' to reverse cancer-therapy toxicities and ultimately improve longevity.
ONE	**One** bottom line
(J) Contribution?	This study will determine if a HIART intervention is effective in improving endothelial and ANS function in men with MCRPC, compared to usual care.
	As the study is part of an international multi-centre RCT, collaboration with external recruiters and study co-ordinators will be required. Approval from GAP4's steering committee has been obtained to explore endothelial and ANS function. Ethics approval has been sought prior to study initiation via submission to The University of Queensland's Human Research Ethics Committee. A possible challenge for this study is slow recruitment, leading to a smaller sample size and lower power to detect significant differences between groups, as MCRPC is an advanced cancer.

(K) Other Considerations	Target journals - 'European Urology' and 'British Journal of Cancer'. "No result" risk: Low - as previous research has shown an improvement in endothelial and ANS function in smaller sample sizes of healthier cancer patients in response to exercise. "Competitor" risk: Low - this is an area which is extremely under-studied within the exercise oncology field. "Obsolesce risk": Low - the results from this study are likely to indicate that HIART could potentially improve treatment-related toxicities in men with MCRPC. This could then contribute to the development of guidelines to reduce cardiovascular morbidity and mortality in this advanced cancer population.