The Feasibility and Efficacy of Prehabilitation for Prostate Cancer Surgery

by

William James Hilton

A Masters Thesis presented to The University of Guelph

In partial fulfillment of requirements for the degree of Master of Science in Human Health and Nutritional Sciences

Guelph, Ontario, Canada

© William James Hilton, December, 2016
ABSTRACT

THE FEASIBILITY AND EFFICACY OF PREHABILITATION FOR PROSTATE CANCER SURGERY

William James Hilton
University of Guelph, 2016

Co-Advisors:
Dr. Lawrence Spriet
Dr. Daniel Santa Mina

Physical activity and fitness are predictors of post-operative prostate cancer recovery; however the capacity to improve pre-operative fitness in this population has yet to be demonstrated in a randomized controlled trial. This study examined the feasibility and efficacy of conducting a pre-operative total-body exercise program, also known as prehabilitation, for men undergoing radical prostatectomy. Participants were prescribed home-based, moderate-intensity exercise, and/or pelvic floor muscle strengthening exercise. To estimate intervention efficacy, fitness and psychosocial outcomes were measured at baseline and ~1 week pre-operatively. From February 2014 to September 2015, 113 eligible patients were approached; 50 consented (recruitment rate = 44.2%) and were randomized to a comprehensive prehabilitation intervention or control group. Participants were mostly Caucasian and had a mean age of 61.1 years. Twelve participants withdrew pre-operatively (attrition rate = 24%). Statistically significant between-group differences were observed in body fat, waist circumference and emotional well-being in favor of the prehabilitation intervention. To our knowledge, this is the first study to assess feasibility and efficacy of a total-body exercise program in the home-based setting prior to radical prostatectomy.
Acknowledgements

To my co-advisor Dr. Daniel Santa Mina, thank you for your mentorship and guidance, and for giving me the freedom to shape my own path. Thank you for challenging me and providing me with confidence in my abilities. Your guidance has left a lasting impression on my life. To my co-advisor and committee member, Dr. Lawrence Spriet and Dr. Shabbir Alibhai, thank you for your extensive support and direction throughout my degree. Your knowledge and insight pushed me to think outside of the box and made me a better researcher. Thank you to all of the collaborators (Dr. Andrew Matthew, Dr. Francesco Carli, Dr. Hance Clarke, Dr. Paul Ritvo, Dr. John Trachtenberg, Dr. Neil Fleschner, Dr. Antonio Finelli, Dr. Michael Jewett, Dr. Robert Hamilton, Dr. Girish Kulkarni) that have helped to make this study possible. I would also like to thank Darren Au, Anika Petrella, Kristen Currie, Michael Nesbitt, Devon Woods, Blaire Jones, Judi Percell and Zahara Amaral; you have all been a pleasure to work with and have allowed for the successful completion of this study. A most gracious thank you to all my study participants, for your trust in me, your courage and willingness to help future men in your situation, and for allowing me to be a part of your journey. You have all impacted my life profoundly through the strength you have demonstrated in the face of adversity. Thank you to all my family and friends for your constant love and encouragement. Lastly, to Candace, thank you for all of your patience and support. I know at times I was not easy to deal with, and I hope you know how much it has meant to me. I appreciate everything you do.
Table of Contents

ABSTRACT .......................................................................................................................... ii

Acknowledgements .......................................................................................................... iii

Table of Contents ............................................................................................................... iv

List of Tables ....................................................................................................................... vii

List of Figures ..................................................................................................................... vii

List of Symbols, Abbreviations, or Nomenclature ............................................................... viii

CHAPTER 1: INTRODUCTION ............................................................................................. 1

1.1) Pathophysiology ........................................................................................................ 1

1.2) Treatment for Localized Prostate Cancer ................................................................. 3
   1.2.1) Side Effects of Radical Prostatectomy .............................................................. 5

1.3) Optimization of Surgical Outcomes ........................................................................... 9

1.4) Rationale for Study and Feasibility Assessment ......................................................... 15

1.5) Objectives .................................................................................................................. 16

CHAPTER 2: METHODOLOGY ............................................................................................ 18

2.1) Study Design ............................................................................................................... 18

2.2) Participants ............................................................................................................... 18

2.3) Recruitment of Participants ...................................................................................... 19

2.4) Participant Allocation to Treatment Conditions ....................................................... 21

2.5) Study Arms ............................................................................................................... 21
   2.5.1) Prehabilitation Arm .......................................................................................... 22
   2.5.2) Control Arm ...................................................................................................... 24
2.6) Outcome Measures ................................................................. 24

2.6.1) Primary Outcome Measures: Feasibility .................................. 25

2.6.2) Secondary Outcome Measures: Estimates of Intervention Efficacy .. 27

2.7) Data Management and Statistical Analysis .................................. 32

CHAPTER 3: RESULTS ........................................................................ 34

3.1) Sample Characteristics ............................................................... 34

3.2) Feasibility Assessment ............................................................... 39

3.2.2) Recruitment ................................................................. 39

3.2.3) Adherence to Group Allocation ........................................... 41

3.2.5) Adverse Events .............................................................. 42

3.3) HRQOL and Fatigue Outcomes ................................................. 44

3.4) Physical Fitness Outcomes ....................................................... 44

CHAPTER 4: DISCUSSION ................................................................. 49

4.1) Discussion of Feasibility Findings ........................................... 49

4.2) Discussion of HRQOL and Fatigue Findings .............................. 55

4.3) Discussion of Physical Fitness Findings .................................. 59

4.4) Study Limitations ............................................................... 64

4.5) Study Strengths ................................................................. 65

CHAPTER 5: CONCLUSION ................................................................. 67

References .............................................................................. i

Appendices .............................................................................. xiv

Appendix 1: REB Approval: University of Guelph .......................... xv
Appendix 2: REB Approval: University Health Network ............................................. xvi
Appendix 3: Informed Consent Form ..................................................................... xviii
Appendix 5: Email Consent Form .......................................................................... xxv
Appendix 6: Study Participant Screening Tool ...................................................... xxvi
Appendix 7: Study Recruitment Poster .................................................................. xxvii
Appendix 8: Letter of Invitation to the Study .......................................................... xxviii
Appendix 9: Web Link to Aerobic Stepping Exercise Video ................................. xxix
List of Tables

Table 1. Baseline Demographics of Study Participants
Table 2. Baseline Characteristics of Study Participants
Table 3. Baseline Demographics of Dropouts and Non-Dropouts
Table 4. Baseline Characteristics of Dropouts and Non-Dropouts
Table 5. Pre-Operative Study Length and Study Adherence
Table 6. Per Protocol Analyses of Between-Group Differences in Psychosocial Well-Being Post-Study
Table 7. Per Protocol Analyses of Within-Group Differences in Psychosocial Well-Being Post-Study
Table 8. Per Protocol Analyses of Between-Group Differences in Physical Fitness Post-Study
Table 9. Per Protocol Analyses of Within-Group Differences in Physical Fitness Post-Study

List of Figures

Figure 1. CONSORT Diagram
<table>
<thead>
<tr>
<th>Term</th>
<th>Abbreviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Activity of daily living</td>
<td>ADL</td>
</tr>
<tr>
<td>Aerobic exercise</td>
<td>AE</td>
</tr>
<tr>
<td>American College of Sports Medicine</td>
<td>ACSM</td>
</tr>
<tr>
<td>Analysis of covariance</td>
<td>ANCOVA</td>
</tr>
<tr>
<td>Androgen deprivation therapy</td>
<td>ADT</td>
</tr>
<tr>
<td>Bioelectrical impedance analysis</td>
<td>BIA</td>
</tr>
<tr>
<td>Body fat percentage</td>
<td>BF%</td>
</tr>
<tr>
<td>Body mass index</td>
<td>BMI</td>
</tr>
<tr>
<td>Consolidated standards of reporting trials</td>
<td>CONSORT</td>
</tr>
<tr>
<td>Control</td>
<td>CON</td>
</tr>
<tr>
<td>Eastern Cooperative Oncology Group</td>
<td>ECOG</td>
</tr>
<tr>
<td>Electronic patient record</td>
<td>EPR</td>
</tr>
<tr>
<td>Emotional well-being</td>
<td>EWB</td>
</tr>
<tr>
<td>Erectile dysfunction</td>
<td>ED</td>
</tr>
<tr>
<td>Food and Drug Administration</td>
<td>FDA</td>
</tr>
<tr>
<td>Functional assessment of cancer therapy-fatigue</td>
<td>FACT-F</td>
</tr>
<tr>
<td>Functional assessment of cancer therapy-prostate</td>
<td>FACT-P</td>
</tr>
<tr>
<td>Health-related quality of life</td>
<td>HRQOL</td>
</tr>
<tr>
<td>Heart rate reserve</td>
<td>HRR</td>
</tr>
<tr>
<td>High-intensity training</td>
<td>HIT</td>
</tr>
<tr>
<td>Laparoscopic radical prostatectomy</td>
<td>LRP</td>
</tr>
<tr>
<td>Term</td>
<td>Abbreviation</td>
</tr>
<tr>
<td>-------------------------------------------</td>
<td>--------------</td>
</tr>
<tr>
<td>Patient Oriented Prostate Cancer Utility Scale</td>
<td>PORPUS</td>
</tr>
<tr>
<td>Peak volume of oxygen uptake</td>
<td>VO$_2$peak</td>
</tr>
<tr>
<td>Pelvic floor muscle exercise</td>
<td>PFMX</td>
</tr>
<tr>
<td>Phosphodiesterase type 5</td>
<td>PDE5</td>
</tr>
<tr>
<td>Physical activity</td>
<td>PA</td>
</tr>
<tr>
<td>Prehabilitation</td>
<td>PREHAB</td>
</tr>
<tr>
<td>Prostate cancer</td>
<td>PCa</td>
</tr>
<tr>
<td>Prostate-specific antigen</td>
<td>PSA</td>
</tr>
<tr>
<td>Radiation therapy</td>
<td>RT</td>
</tr>
<tr>
<td>Radical prostatectomy</td>
<td>RP</td>
</tr>
<tr>
<td>Randomized controlled trial</td>
<td>RCT</td>
</tr>
<tr>
<td>Rate of perceived exertion</td>
<td>RPE</td>
</tr>
<tr>
<td>Registered Kinesiologist</td>
<td>R.Kin.</td>
</tr>
<tr>
<td>Repetitions</td>
<td>Reps</td>
</tr>
<tr>
<td>Research coordinator</td>
<td>RC</td>
</tr>
<tr>
<td>Research ethics board</td>
<td>REB</td>
</tr>
<tr>
<td>Resistance exercise</td>
<td>RE</td>
</tr>
<tr>
<td>Robot-assisted radical prostatectomy</td>
<td>RARP</td>
</tr>
<tr>
<td>Standard deviation</td>
<td>SD</td>
</tr>
<tr>
<td>Statistical Package for the Social Sciences</td>
<td>SPSS</td>
</tr>
<tr>
<td>Urinary incontinence</td>
<td>UI</td>
</tr>
<tr>
<td>Waist circumference</td>
<td>WC</td>
</tr>
<tr>
<td>World Health Organization</td>
<td>WHO</td>
</tr>
<tr>
<td>Term</td>
<td>Abbreviation</td>
</tr>
<tr>
<td>-------------------------------</td>
<td>--------------</td>
</tr>
<tr>
<td>6-minute walk test</td>
<td>6MWT</td>
</tr>
<tr>
<td>Centimeter</td>
<td>cm</td>
</tr>
<tr>
<td>Change</td>
<td>Δ</td>
</tr>
<tr>
<td>Diastolic blood pressure</td>
<td>DBP</td>
</tr>
<tr>
<td>Kilogram</td>
<td>kg</td>
</tr>
<tr>
<td>Kilogram per meter square</td>
<td>kg/m²</td>
</tr>
<tr>
<td>Meter</td>
<td>m</td>
</tr>
<tr>
<td>Milligrams per deciliter</td>
<td>mg/dL</td>
</tr>
<tr>
<td>Millimeters of mercury</td>
<td>mmHg</td>
</tr>
<tr>
<td>Systolic blood pressure</td>
<td>SBP</td>
</tr>
</tbody>
</table>
CHAPTER 1: INTRODUCTION

Prostate cancer (PCa) is the most common cancer among Canadian men with 1 in 8 developing the disease in their lifetime. Moreover, PCa is the third most common cause of cancer-related death in Canadian men with ~4,141 deaths expected yearly. In 2015, of the estimated 100,500 new cancer cases in men, ~23.9% (24,020) will be of the prostate. Throughout the early 1990’s to early 2000’s PCa incidence rates in Canada reached a peak of 27.9% of all new cancers in men. However, as a result of advancements in disease management, rates of PCa-related death have been decreasing by ~4% each year from 2001-2009. Often diagnosed in men 60-69 years of age, a majority of PCa-related deaths typically happen in men over 80 years of age. This is indicative of a slow growing disease. Worse survival in older men may be the consequence of less aggressive therapies being pursued at an older age, or age-related comorbidities compounding the negative effects of cancer, thus reducing tolerance to therapy. Nevertheless, PCa survivors are living longer and consequently greater importance has been placed upon strategies to improve or maintain health-related quality of life (HRQOL) after a diagnosis.

1.1) Pathophysiology

A healthy prostate, often compared to the size of a walnut, is typically 3-5 cm in diameter. The gland is positioned within the pelvis anterior to the rectum, with its base directly inferior to the bladder and apex in direct contact with the superior fascia of the urogenital diaphragm. A segment of the urethra (known as
The Feasibility and Efficacy of Prehabilitation for Prostate Cancer Surgery

the prostatic urethra) extending inferiorly from the bladder neck, travels through the glandular tissue and attaches superiorly to an internal sphincter and inferiorly to an external sphincter, both of which provide assistance with urinary control. A stroma of smooth musculature, fibroblasts, lymphatic vessels, and nerves surround the prostate. Growth factors essential for prostatic growth (normal or cancerous) are obtained from the stroma and the movement of glandular fluid secretions are facilitated by contractions from the smooth musculature. Ducts located within the gland are covered with secreting epithelial cells and basal cells. The secreting cells yield opaque fluid containing glycoproteins, such as prostate-specific antigen (PSA) and prostatic acid phosphatases that contribute to the composition of semen. These glycoproteins maintain the fluid consistency of sperm and support its transport through the urethra during ejaculation. The secreting epithelial cells account for the predominant cell variety of the prostate and are reliant on androgens for growth.

Evaluating PSA blood concentration is one of the least invasive strategies for detecting and monitoring abnormalities in prostatic physiology, including benign prostatic hyperplasia, prostatitis and PCa. An elevated PSA may be a reflection of some pathological process occurring within the gland, and a concentration of ≥ 4.0 ng/mL has been shown to be associated with an increased risk of PCa. In 1981, the clinical use of PSA screening was first examined and by 1994 the Food and Drug Administration (FDA) approved PSA as a PCa diagnostic marker. Yet, despite its current widespread use there has been controversy regarding the practice of measuring PSA for the early detection of
The Feasibility and Efficacy of Prehabilitation for Prostate Cancer Surgery

PCa and monitoring disease progression. Largely, the concern surrounds the risk of over-diagnosing and consequently, unnecessary or 'over-treatment' of the disease\textsuperscript{16}. Nevertheless, prior to the introduction of PSA testing and before it came into wide spread clinical use in the 1990’s men were rarely diagnosed with PCa before it had metastasized\textsuperscript{17}. Therefore, as a consequence of an increased population of men with localized disease, it is imperative that clinicians and patients address potential strategies to mitigate treatment-related sequelae, which adversely impact HRQOL.

1.2) Treatment for Localized Prostate Cancer

With the advent of PSA screening, a majority of prostatic malignancies are identified in the early stage of disease with the tumor confined within the gland. The surgical resection of the prostate and adjacent lymph nodes, referred to as radical prostatectomy (RP), is the most common and effective treatment for localized PCa with a 15 year survival rate of ~90\%\textsuperscript{18,19}. In Canada, 7,262 RP’s were performed in 2012-2013, with the most performed in Ontario (37\%; 2,742).

An RP takes 1.5-3 hours and involves resection of the prostate gland, seminal vesicles, prostatic urethra, bladder neck, and if regional metastasis is suspected, the adjacent pelvic lymph nodes\textsuperscript{20}. Throughout the procedure the surgeon is cautious to limit the extent of damage to the cavernosal nerves and blood vessels surrounding the gland, given their critical role in urinary and sexual function. After the prostate is removed, the connection between urethra and bladder neck is re-established. During the acute post-operative period (typically
The feasibility and efficacy of prehabilitation for prostate cancer surgery

10-14 days) drainage of urine is made possible through a catheter inserted into the bladder as healing proceeds\textsuperscript{20}.

The four common surgical approaches to RP include: perineal, retropubic, laparoscopic, and robot-assisted. The perineal and retropubic approaches to RP are considered ‘open’, meaning they involve a relatively large incision to create an operative field for the surgeon. The perineal approach involves an incision made between the anus and the base of the scrotum; whereas the retropubic approach involves a vertical incision between the pubic bone and the umbilicus and allows for lymph node dissection and better preservation of the cavernosal nerves near the gland. However, laparoscopic approaches to RP have grown in favour among surgeons and patients given their ‘less invasive’ nature in terms of tissue resection. Laparoscopic RP (LRP) involves five 1-1.5 cm incisions made across the abdomen to permit the insertion of a small camera and the surgical tools necessary for the procedure\textsuperscript{21}. Robot-assisted RP (RARP) follows an approach similar to the conventional open and laparoscopic procedures with the exception of employing a surgeon-operated robotic system positioned between the patient’s legs and the end of the surgical table. Precise handling of the robotic held surgical tools can mimic actual hand and wrist motion through controls manipulated by the surgeon’s index finger and thumb at the console\textsuperscript{22}. Through the aid of the robot, it is suggested that the surgeon can enhance conservation of the cavernous nerves through precise dissections and may have better assistance with suturing of the vesicourethral anastomosis (i.e. reattaching bladder neck to the urethra after prostate removal)\textsuperscript{22}. Moreover, when matched
The Feasibility and Efficacy of Prehabilitation for Prostate Cancer Surgery

against other surgical techniques some studies have shown that RARP may allow for improved convalescence of post-operative urinary incontinence\textsuperscript{23-25}. However, there is a lack of randomized controlled trials (RCT) and compelling high quality data comparing the surgical outcomes of RARP against the other RP techniques\textsuperscript{26}. Furthermore, despite the widespread use of RARP, where available, conflicting findings among current studies means that RARP cannot yet be declared as the gold standard of surgical methods for localized PCa\textsuperscript{26}.

1.2.1) Side Effects of Radical Prostatectomy

While morbidity across RP approaches is relatively low\textsuperscript{27}, many PCa survivors experience ongoing adverse effects long after surgery, including: erectile dysfunction (ED), urinary incontinence (UI), fatigue and reduced physical function\textsuperscript{28,29}, that collectively contribute to diminished HRQOL. Advancements in RP operative techniques throughout the years have concentrated on lessening the risk of urological adverse effects through erectile and urinary sphincter nerve-sparing\textsuperscript{30}; however, ED and UI are still common occurrences among PCa survivors post-operatively.

With incidence of upwards to 80\%, ED is the most common negative outcome associated with RP\textsuperscript{31} and may persist long after treatment or may be a permanent consequence of surgery\textsuperscript{32,33}. Preservation of the neurovascular bundles, including the cavernous nerves, is a common indicator of post-RP success\textsuperscript{34}, as nerve-sparing has been shown to be correlated with a reduced incidence of post-operative ED\textsuperscript{35}. Moreover, the ability to achieve erections
adequate for sexual intercourse, irrespective of phosphodiesterase type 5 (PDE5) inhibitor use (e.g. Cialis® or Viagra®), is a commonly used indicator of recovered sexual function or ‘potency’\textsuperscript{35}. Several other predictors have also been demonstrated to influence sexual function up to 24 months post-RP, some of which include pre-operative sexual function and patient age\textsuperscript{36–38}. Furthermore, a variety of lifestyle considerations typically linked with comorbidities have been demonstrated to be correlated with ED\textsuperscript{39}. Litwin et al.\textsuperscript{40} observed that only 33\% of patients recouped baseline levels of erectile function at 12 months post-operatively. Moreover, incidence of ED at 12 and 24 months post-RP has shown to be significantly greater in obese patients\textsuperscript{41}; and vascular disease has exhibited some association with ED prevalence\textsuperscript{42}. Physicians most often prescribe PDE5 inhibitors and monitor recovery of sexual function as the foundation of post-RP sexual rehabilitation\textsuperscript{43}. However, post-operative sexual rehabilitation may also benefit from enhancing physical function and psychosocial well-being\textsuperscript{44}. Smith et al.\textsuperscript{45} have suggested that rehabilitation of sexual function post-RP should not only include the provision of PDE5 inhibitors, but also an evaluation of predictors for cardiovascular risk, and counsel on strategies for being more physically active.

From a urinary perspective, upwards of 40\% of patients may experience prolonged incontinence post-RP\textsuperscript{46,47}, with most men typically re-establishing partial or full continence in 12 months\textsuperscript{48}. Though a subgroup of men can suffer from UI for longer than 12 months or in some instances indefinitely, ranging from modest to severe leakage\textsuperscript{49}. The degree of symptoms can vary from post-urination dribbling, to complete incapability to resist urination\textsuperscript{48}. Post-RP UI can
The Feasibility and Efficacy of Prehabilitation for Prostate Cancer Surgery

impact clothing selection, public situations, activities of daily living (ADL), sleep quality, and self-esteem. Moreover, the effects of RP on HRQOL appear to be related to the duration and/or severity of UI symptoms. Therefore, HRQOL can be vastly diminished during times of severe UI (i.e. throughout the acute post-RP recovery period), and as continence recovers in the months following RP, HRQOL seems to improve as well. A systematic review of the RARP literature reported UI rates varying from 4-31% 12 months post-operatively. In contrast, when stratified according to problematic circumstances (i.e. body mass index \( \geq 25 \), large prostate or surgeon proficiency), UI rates were greater and varied from 4-43%. Previously examined attempts to improve post-RP UI have employed localized strategies, such as: bladder re-education, pelvic floor muscle exercise (PFMX), or biofeedback. However, a PCa management strategy should also address the global and modifiable predictors of UI (i.e. being overweight or obese; BMI \( \geq 25 \)) that can be positively influenced by healthy behaviours, such as exercise.

In addition to the urological sequelae that occur post-RP, patients also experience noticeable physical and functional limitations that endure long after localized treatment. Strassels et al. found that physical functioning 1-month post-RP was 30% below population norms and that 43% of patients were dissatisfied with their physical ability. Moreover, energy levels (vitality) and ability to work (role-physical) were 20% and 82% below population norms using the Short Form-36 HRQOL survey. At 3 months post-RP, Litwin et al. found that only 30%, 26%, and 36% of patients had returned to baseline values of physical
functioning, ability to work (role-physical), and energy (vitality), respectively; average recovery of these characteristics was 5.5 months\textsuperscript{40}. Similar reductions in physical function and ability to work (role-physical) have been observed by Ene et al.\textsuperscript{52} in RP patients 3 months post-operatively. Diminished capacity to work or perform physical duties has been shown to be a predictor of premature retirement and greater risk of death\textsuperscript{53,54}. Dahl et al.\textsuperscript{55} demonstrated poor-to-moderate levels of ability to work in 25\% of men (n = 141/563) who were working regularly up to 6 years post-RP. As the current state of PCa incidence and survival stands, a focused effort to address the functional limitations affecting RP patients post-operatively is crucial. Commencing an active lifestyle that incorporates structured exercise has not only been shown to reduce the incidence of chronic disease in the generally healthy population\textsuperscript{56}, but has also demonstrated benefits to lessening reductions in physical/functional capacity during and after cancer treatment\textsuperscript{57–60}.

In terms of treatment objectives, great importance has been placed upon extending disease-free survival. However, HRQOL throughout the post-treatment recovery period is also a significant concern for PCa survivors\textsuperscript{40}. The incidence of post-RP side effects has been shown to have a direct impact on HRQOL for 6-12 months post-operatively, or in some cases indefinitely\textsuperscript{61–64}. The definition of ‘health’ provided by the World Health Organization (WHO) is described as, “a state of complete physical, mental, and social well-being and not merely the absence of disease and infirmity”\textsuperscript{65}. In the context of the relationship between well-being, ailment, and therapeutic consequences, HRQOL is an appraisal of an
individual’s spiritual, social, mental, and physical health. In a sample of 90 RP patients, Litwin et al. showed significantly diminished HRQOL at 3 months post-operatively, as only 30-40% of the patients had recouped to pre-RP levels of HRQOL. Similarly, Strassels et al. previously reported HRQOL below population norms in n# of patients post-RP. In contrast, Ene et al. observed HRQOL recovery rates of 60% (n = 84/155) at 3 months post-RP. Individual side effects can be worsened when combined with others, which can then collectively further reduce HRQOL. For example, patients with moderate- to severe-leakage post-operatively report unsatisfactory coping levels and experience significant limitations in physical activity (PA) and ADLs. Through the evaluation of HRQOL post-RP, patients and physicians have furthered the general comprehension of disease and treatment burden; however, focus primarily on cancer and its management solely still exist. Rather, our attention must be inclusive towards improving all aspects of patient well-being, including emotional, social, psychological, and physical; areas for which exercise has been shown to be efficacious.

1.3) Optimization of Surgical Outcomes

The adverse impact on HRQOL in men with PCa begins at diagnosis with nearly 40% of men exhibiting high levels of anxiety, which continues on throughout the survivorship phases. Functional capacity and muscular strength of men with PCa are important characteristics to consider after diagnosis, as low functional ability has been shown to influence mortality risk and mobility.
issues\textsuperscript{77} in the older adults. Similarly, reduced aerobic capacity has also shown to be correlated with diminished functioning ability in cancer survivors\textsuperscript{78}. Interventions intended to enhance RP convalescence and reduce adverse effects are usually targeted at the post-operative period. Such approaches have typically focused on the urological sequelae (i.e. ED and UI) through provision of PDE5 inhibitors (e.g. Cialis ® and Viagra ®) and/or prescribing PFMX\textsuperscript{79–82}. However, research suggests that patients are usually non-compliant to post-operative interventions\textsuperscript{83}; and despite the substantial influence on HRQOL, little consideration has been given to the physical function deterioration that RP patients experience\textsuperscript{84,85}.

To overcome post-operative challenges in well-being intervening in the pre-operative period for men undergoing RP is not common, however, a growing body of literature suggests several advantages of behavioural interventions in this setting as patients carry the burden of impending cancer treatment. The often-unavoidable pre-operatively waiting period offers an opportunity to leverage potential motivation within patients to initiate in healthy behaviours, and build up physical and psychological reserves to better tolerate the effects of RP. PA is one such health behaviour that has shown great potential in relation to RP complications and better post-operative convalescence\textsuperscript{86}. In the year leading up to RP, PA levels have shown to be a predictor of HRQOL post-operatively\textsuperscript{86}. In 509 RP patients, Santa Mina et al.\textsuperscript{87} observed that men meeting the American College of Sports Medicine (ACSM) cancer-specific PA recommendations (i.e. 150 min of moderate, or 75 min of vigorous PA weekly) pre-operatively
The Feasibility and Efficacy of Prehabilitation for Prostate Cancer Surgery

experienced better HRQOL (via self-reported Patient Oriented Prostate Cancer Utility Scale (PORPUS) scores) at 6 and 26 weeks post-operatively versus those men not meeting the recommendations (meeting recommendations = 85.9; not meeting recommendations = 81.0; p < 0.001). Additionally, men meeting the recommendations pre-operatively reported less UI at 6 weeks post-RP in comparison to less active patients (meeting recommendations = 40.7%; not meeting recommendations = 59.3%; p = 0.028)\textsuperscript{87}. Wolin et al.\textsuperscript{88} has reported similarly that pre-operative PA may be an indicator of urinary recovery post-RP.

Several studies have shown the positive effects of structured exercise (i.e. resistance exercise (RE), aerobic exercise (AE) or a mixture of both) for PCa patients undergoing treatment. Galvao et al.\textsuperscript{89} demonstrated that 20 weeks of RE was efficacious in improving functional capacity, muscle endurance and balance in androgen deprived PCa patients post-treatment. Similar benefits of RE were observed by Segal et al.\textsuperscript{57} in a study of 155 PCa patients undergoing androgen deprivation therapy (ADT). Participants engaging in 12 weeks of RE demonstrated increased upper- and lower-body strength, improved HRQOL, and reduced fatigue compared to those not exercising. Segal et al.\textsuperscript{90} confirmed these findings a few years later in a comparable 24-week RE intervention in 121 PCa patients receiving radiation therapy (RT). Participants in the RE intervention arm exhibited substantial improvements in physical function, balance, HRQOL, BF\%, and energy. Windsor et al.\textsuperscript{91} demonstrated the sequelae-mitigating effects of AE in a study of 66 PCa patients receiving RT. Participants engaging in 16 weeks of AE exhibited considerably improved aerobic capacity after the intervention, this
The Feasibility and Efficacy of Prehabilitation for Prostate Cancer Surgery

was in comparison to a control arm of no exercise. Moreover, AE was beneficial in lessening treatment-related fatigue post-RT\textsuperscript{91}. AE has also shown to improve psychosocial well-being in both surgical and non-surgical PCa population, through lessening anxiety and depression, and increasing HRQOL\textsuperscript{90,91}. With respect to the specific urological side effects of RP, a possible benefit of AE on sexual function has been suggested by Belardinelli et al.\textsuperscript{92}. Authors demonstrated in chronic heart failure patients that AE stimulated improvements in peripheral artery flow–mediated dilation and VO\textsubscript{2}peak uptake, had developed in conjunction with increases in erectile function\textsuperscript{92}. These findings led authors to conclude that peripheral artery flow–mediated dilation was influential in the recovery of potency\textsuperscript{92}. Based on evidence from the literature, engaging in PA or structured exercise as an approach to dealing with the adverse effects of PCa treatment has great potential to accelerate the convalescence of physical and psychosocial well-being post-RP.

The surgical literature consistently reports that patients who are active and functioning well leading up to surgery recuperate faster, have fewer complications, and experience better recovery in comparison to patients who are less active and functioning poorly\textsuperscript{93–99}. Moreover, model surgical candidates share several characteristics, such as: few to no comorbidities, healthy body composition, and good performance status (ECOG/Karnofsky)\textsuperscript{100,101}. Accordingly, when contemplating strategies to improve patient surgical experience, one must take into consideration when the most favourable time is to commence recovery-enhancing behaviours. Apprehension for disturbing the healing process renders
The Feasibility and Efficacy of Prehabilitation for Prostate Cancer Surgery

the post-operative period as potentially undermining or aggravating to recovery. Alternatively, the pre-operative period offers great potential to take advantage of factors such as: treatment waiting times, better pre-operative physical functioning, and a ‘teachable moment’ associated with the necessity for surgery\textsuperscript{58}. Accordingly, prehabilitation is described as the process of improving physical and psychological reserves to facilitate better coping of a substantial stressor\textsuperscript{102}. In relation to the surgical experience, the objective of prehabilitation is to improve baseline reserves in preparation of functional and mental declines, and to mitigate the deterioration of post-operative HRQOL\textsuperscript{102}.

The benefits that prehabilitation offer to post-operative HRQOL have been reported throughout a variety of surgical populations, including oncology. In a systematic review of the prehabilitation literature, Moran et al.\textsuperscript{103} reported the efficacy of pre-operative interventions in patients undergoing colorectal\textsuperscript{104–106}, abdominal\textsuperscript{107–109}, upper gastrointestinal\textsuperscript{110}, hepatectomy\textsuperscript{111}, and open bariatric operations\textsuperscript{112}. In addition to the further reported benefits of prehabilitation in colorectal surgery\textsuperscript{113,114}, the literature has also shown efficacy to enhance post-operative physical and psychosocial well-being in cancer patients undergoing hysterectomy\textsuperscript{115} and lung resection\textsuperscript{116}. Studies have used a variety of conditioning approaches with patients, including: RE, AE, inspiratory muscle training, or a mixture of all. Control arms within these studies have included: no treatment, walking, low-intensity inspiratory muscle training, and/or breathing/relaxation exercises\textsuperscript{103}. Considerable enhancements to pre-operative fitness levels have been observed in these surgical patients, as assessed
through methods such as: functional exercise, cardiorespiratory, and/or inspiratory muscle strength testing\textsuperscript{103}. In a study of 38 patients to undergo colorectal cancer resection, Gillis et al.\textsuperscript{104} showed increased functional capacity via improved 6-minute walk test (6MWT) performance after \textasciitilde 24.5 days of prehabilitation. In comparison, a control group of 39 rehabilitation patients demonstrated statistically significant deterioration in post-operative functional capacity (prehabilitation = +25.2 m; rehabilitation = -16.4 m; \( p < 0.001 \)). Contrasting evidence has been reported by Carli et al.\textsuperscript{105} in 58 cancer patients also awaiting colorectal cancer resection. Despite no significant improvements to functional capacity (6MWT performance) in the intervention group (baseline = 494.1 \( \pm \) 15.5 m; pre-operatively = 502.8 \( \pm \) 15.8 m; \( p = 0.203 \)) after a pre-operative study period of \textasciitilde 40 days, participants demonstrated a statistically significant increase in VO\textsubscript{2}peak uptake (baseline = 1,395 \( \pm \) 76 mL/min; pre-operatively = 1,529 \( \pm \) 88 mL/min; \( p = 0.003 \)), as assessed via direct graded exercise testing. However, the control group of walking/breathing exercises (\( n = 54 \)) also significantly improved VO\textsubscript{2}peak uptake (baseline = 1,400 mL/min \( \pm \) 71; pre-operatively = 1,511 \( \pm \) 84 mL/min; \( p = 0.007 \)) despite no change in 6MWT performance. Authors concluded that one potential cause of this effect was an increased awareness of their low functional capacity, made evident during exercise testing, influencing motivation to improve fitness as much as possible during leading up to the operation\textsuperscript{105}. In a published re-analysis of this study's data\textsuperscript{105}, Mayo et al.\textsuperscript{113} reported that the pre-operative enhancements in functional capacity (defined as \( \pm 20 \) m increase in 6MWT distance) observed in 33% of all
The Feasibility and Efficacy of Prehabilitation for Prostate Cancer Surgery

study participants (n = 31/95), positive correlated with better self-perceived well-being (+7.8%), psychosocial well-being (+12.5%) and energy (vitality) (+14.3%). Moreover, those with greater pre-operative functional capacity exhibited a higher prevalence of recouped baseline function at ~12 weeks post-operatively compared to participants who worsened or maintained (improved = 77%; deteriorated = 32%; no change = 59%; p < 0.001). Furthermore, participants who experienced worse pre-operative function had a higher prevalence of post-operative complications and greater requirement for intensive care (control = 5/28; intervention = 1/66; p = 0.008)\(^{113}\). Lastly, the review by Moran et al.\(^{103}\) of the prehabilitation literature also reported that pre-operative interventions were beneficial in reducing the prevalence of all-cause (OR: 0.59, 95%; CI: 0.38–0.91) and pulmonary complications (OR: 0.27, 95%; CI: 0.13–0.57) post-operatively, and when compared with controls of breathing/relaxation exercises or usual care, the benefits of these interventions were most pronounced (OR: 0.35, 95%; CI: 0.17–0.71)\(^{103}\). The current body of evidence within the prehabilitation literature is of great value to PCa patients undergoing RP and investigators designing future studies; contributing to the legitimacy of prehabilitation through demonstrating that optimized pre-operative fitness may lessen post-operative complications and improve HRQOL.

1.4) Rationale for Study and Feasibility Assessment

Ultimately, it appears that the pre-operative waiting period may be an ideal time to invest in the modifiable influences that contribute to post-operative health.
The Feasibility and Efficacy of Prehabilitation for Prostate Cancer Surgery

Moreover, the literature of pre-operative interventions has demonstrated a potential role for PA and good functioning for the post-operative well-being of men undertaking RP. However, a major gap still exists in our understanding as no RCT has been conducted to establish a cause-and-effect association between pre-operative exercise and post-operative consequences in PCa patients undergoing RP. While assured of the effectiveness of RP and its widespread use in the management of localized disease, it is proposed that the mark of treatment success involve more than just cancer-free survival. Instead, it should include a thorough assessment of physical and psychosocial well-being and the rate at which patients recuperate to pre-treatments levels of HRQOL, wherein prehabilitation may play an important role.18,79

1.5) Objectives

The primary objective of this trial was to assess the feasibility of conducting an adequately powered RCT, which examined the efficacy of a comprehensive prehabilitation program (PREHAB) versus a control group (CON) of standard PFMX for men with PCa undergoing RP. The secondary objective was to assess and report estimates of efficacy on several clinically important outcomes for an RP-specific prehabilitation program including: HRQOL, fatigue, and physical fitness; these data will be used for sample size calculations in designing an adequately powered trial. We hypothesized that a comprehensive prehabilitation program comprised of total-body exercise and PFMX in the home-based setting is feasible to conduct and would produce greater pre-RP benefits.
The Feasibility and Efficacy of Prehabilitation for Prostate Cancer Surgery

to physical and psychosocial well-being compared to a control group of standard PFMX.
CHAPTER 2: METHODOLOGY

2.1) Study Design

We conducted a 2-arm, pilot RCT to examine the efficacy of a comprehensive prehabilitation program versus CON on physical and psychosocial outcomes. This study was conducted at the Princess Margaret Cancer Centre located in Toronto, Ontario. This study was granted Research Ethics Board (REB) approval by the University of Guelph (Appendix 1) and the University Health Network (Appendix 2). All participants provided written informed consent to be involved in this study (Appendix 3).

2.2) Participants

Eligible patients included men 40-80 years of age with localized PCa (stage T1c-T2c), consented for RP (any surgical method) and were proficient in English. We excluded those patients who had: i) severe coronary artery disease (Canadian Cardiovascular Society class III or greater); ii) significant congestive heart failure (New York Heart Association class III or greater); iii) uncontrolled pain; iv) neurological or musculoskeletal comorbidity inhibiting exercise; v) diagnosed psychotic, addictive, or major cognitive disorders; vi) no more than two Coronary Risk Factors as defined by the ACSM including family history of coronary disease, cigarette smoking, hypertension (i.e. SBP > 140 mmHg; DBP > 90 mmHg), known dyslipidemia, known impaired fasting glucose (i.e. > 110 mg/dL), obesity (i.e. BMI > 30 kg/m² or waist circumference (WC) > 102 cm), or physically inactive (i.e. < 150 min of moderate-intensity PA per week)\textsuperscript{117}. 
2.3) Recruitment of Participants

Eligible patients were recruited from ambulatory urology clinics at the Princess Margaret Cancer Centre by the research coordinator (RC). Attending urologists assisted in identifying eligible patients and notified the RC. The physician aided by informing the RC that the patient had completed a consent package for RP. The physician played no role in the informed consent process beyond informing the RC of eligibility and introducing the study to patients and asking if they were interested in listening to information about a research study. There was no coercion of the patient to either listen to the study description or participate in the trial. When a potential participant agreed to hear about the study, the RC provided a detailed description of the study procedures. If the patient was willing to participate, written informed consent was obtained. As part of the informed consent process, the RC discussed the voluntary nature of participation and stressed that declining to enroll would not impact the patient’s care. To protect potential study participants from feelings of coercion, the treating urologist/co-investigator was not present during the informed consent discussion. If the patient required more time to consider participation, they took home the informed consent form and contacted the RC if they wished to enroll.

Telephone and email contact information was collected to follow-up with the patients that initially expressed interest. All patients were recorded into a ‘Participant Approach List’ (Appendix 4) to record information for follow-up purposes and to describe reasons for declining participation. If the patient wished
The Feasibility and Efficacy of Prehabilitation for Prostate Cancer Surgery

to be contacted via email for follow-up purposes, they completed a ‘Communication by Email Consent Form’ (Appendix 5).

For patients that immediately expressed interest in participating, the RC completed a ‘Study Participant Screening Tool’ (Appendix 6) with them to assess their eligibility for enrollment. If eligible and agreeable, the RC obtained written consent and scheduled an initial study visit to conduct baseline testing and randomization. If ineligible, the screening measures were destroyed immediately. If the patient was not interested or refused for any other reason, reason for refusal was documented, but no recorded personal information was maintained. However, patients that refused to participate without providing a reason were informed that they did not have to give a reason as to why as per REB guidelines.

For patients that took some time to consider enrollment, they were followed-up with 7 days (± 4 days) after the initial recruitment attempt. During follow-up telephone calls the RC reviewed the study requirements and answered any additional questions. If the patient was interested, the participation screening measure was conducted over telephone conversation. If the patient was ineligible, the recruiter destroyed the screening tool. If the patient was eligible, verbal consent was obtained and they were required to bring a signed copy of the informed consent form to the initial study visit.

Patients were also recruited via study flyer/poster placed in hospital waiting areas, urology clinics, and areas of high volume for urological patients (Appendix 7). Patients responding to the study flyer were treated in the same
The Feasibility and Efficacy of Prehabilitation for Prostate Cancer Surgery

manner as those who had taken time to consider participation after meeting with the RC in clinic. In addition to these recruitment methods, the RC communicated with the treating urologists to determine whether their surgical patients may be contacted by telephone and mailed information for recruitment to the study. Agreeable to this request, their administrative assistants were communicated with for contact information (i.e. name and medical record number) of patients consented to RP. The RC screened patients for eligibility via the hospital's Electronic Patient Records (EPR) and then contacted these patients through mailing of a “Letter of Invitation to the Study” (Appendix 8) and followed up with a telephone call. No voicemail messages were left and no identifying details of the caller or calling institution were provided to anyone other than the intended patient.

2.4) Participant Allocation to Treatment Conditions

Participants were randomly allocated 1:1 to either the PREHAB or CON group prior to baseline testing. Blinded allocation of participants to their respective group was performed by via sequentially numbered opaque envelopes, which were prepared by the RC, contained group assignments and were shuffled to create a random order.

2.5) Study Arms

RP patients at the Princess Margaret Cancer Centre typically receive brief pre-operative information from a urology nurse educator regarding PFMX,
The Feasibility and Efficacy of Prehabilitation for Prostate Cancer Surgery

mobilization and general timeframes for return to normal activities following surgery. Both groups began participation in their respective study arms at the time of randomization, which was shortly after consenting to RP. The duration of the pre-operative wait-time (typically 4-8 weeks) was recorded. Both groups received a copy of a PCa-specific lifestyle support book, “Challenging Prostate Cancer: Nutrition, Exercise and You”\textsuperscript{118}, containing information on topics such as nutrition, active-living, and PFMX. Moreover, all participants were provided with parking/travel reimbursements of $20 per study visit attended.

2.5.1) Prehabilitation Arm

PREHAB participants engaged in an individualized, total-body exercise program, plus standard PFMX. The total-body exercise prescription consisted of 60 min of unsupervised exercise, performed at a moderate-intensity within the home-based setting. These sessions were completed 3-4 days per week and alternated between AE and RE. Each session was individualized based upon a baseline assessment which was conducted by a Registered Kinesiologist (R.Kin.), and included: 5 min warm-up, 25 min of AE (40-60\% of heart rate reserve (HRR))\textsuperscript{119}, 25 min of RE (five exercises targeting major muscle groups, performed at an intensity of 8-12 repetitions (reps) maximum), and a 5 min cool-down. The five RE’s were prescribed and tailored to each individual based upon their current fitness level, and included: push-ups, stability ball wall squats, seated resistance band rows, supine stability ball hamstring curls, and abdominal crunches. Progression of training intensity occurred when the participant could
complete AE with mild exertion and/or when the participant could comfortably complete 15 reps of a given RE. The program introduction included a description and demonstration of each exercise. Participants had the opportunity to try each exercise in the presence of the R.Kin., with corrective feedback and discussion around safety (i.e. posture, breathing, etc.). To facilitate exercise in the home-based setting, PREHAB participants were provided with a set of three resistance bands (i.e. light, moderate, heavy resistance), a stability ball (depending on the participant’s height; 55 or 65 cm), and a yoga mat. Participants were allowed to keep these pieces of exercise equipment at the end of the pre-operative study period. To facilitate compliance, participants were also given a heart rate monitor for AE heart rate training zone prescription (calculated by the R.Kin.). Participants were asked to return the heart rate monitor at the end of the intervention phase (i.e. ~1 week pre-operatively), with no penalty if they lost or caused damaged it.

The PFMX prescription began with instructions on how to properly contract the pelvic floor musculature, delivered by the RC trained in PFMX. The prescription included a gradual increase in reps from: 60 per day (weeks 1-2), 120 per day (weeks 3-4), to 180 per day (week 5 up to the surgical date). The total number of PFMX reps were divided equally between rhythmic (i.e. contract and relax over 1 sec) and sustained contractions (i.e. contract and hold for up to 10 sec). Participants were instructed to contract with maximal effort during all PFMX reps.
In addition to exercise equipment, the PREHAB intervention was supported with an aerobic stepping exercise video created by the co-investigating team (accessible to participants online) (Appendix 9), and a participant study manual, which described the home-based exercise program and PFMX prescription. Participant usage of the AE video was not monitored, as its purpose was to serve as an optional alternative mode of AE. The RC communicated with PREHAB participants weekly via telephone or email to ensure program compliance, support appropriate progression, and address any barriers to exercise that could have prevented ongoing participation.

2.5.2) Control Arm

The CON group received the same PFMX prescription as the PREHAB group and weekly communication from the RC regarding compliance with the PFMX prescription to provide attention-control. The CON participants were also provided with a participant study manual, which described only the PFMX prescription.

2.6) Outcome Measures

Self-reported measures and physical fitness assessments were conducted at the following time points: baseline ~4-8 weeks pre-operatively (i.e. following consenting to RP, prior to beginning group assignment), and within ~1 week pre-operatively (± 4 days). Each assessment session took place at the Princess Margaret Cancer Centre and required ~60-90 min. These assessments were
The Feasibility and Efficacy of Prehabilitation for Prostate Cancer Surgery

conducted at post-operatively at 4, 12, and 26 weeks, but are outside the scope of this thesis. Findings of the full study including both pre- and post-RP efficacy outcomes and feasibility will be reported elsewhere.

2.6.1) Primary Outcome Measures: Feasibility

Given the novelty of this type of trial, it was unclear whether there would be recruitment, adherence or attrition challenges across study arms. Accordingly, feasibility was assessed for a full-scale trial in the following ways:

2.6.1.1) Recruitment

Prior exercise trials in PCa patients on ADT and/or RT have reported recruitment rates of 14-64%, but no studies have assessed recruitment to a comprehensive home-based exercise intervention in this population pre-operatively. Thus, recruitment-success percentage and recorded reasons for non-participation were measured to better understand why men electing to undergo RP would not participate in a pre-operative exercise intervention.

2.6.1.2) Adherence to Group Allocation

Adherence to the home-based exercise program and PFMX were measured through a logbook, which was completed by the RC during the weekly communication with study participants. The RC inquired about the following information regarding AE and RE completion: number of days per week engaged in each, average duration of sessions, average rate of perceived exertion (RPE)
of sessions, types of AE performed (e.g. brisk walking, biking, etc.), average number of prescribed RE’s completed, average number of sets and reps completed, and average number of contractions achieved for PFMX. Subsequently, adherence to the PREHAB total-body exercise prescription and PFMX prescription for both groups was assessed by comparing the total training volume completed to the minimum prescribed. Full adherence to PFMX was defined as achieving the total volume (or more) of PFMX contractions, which was calculated as: total volume achieved ÷ total volume prescribed during the pre-operative study period. Full adherence to the total-body exercise program was defined as achieving the minimum of the prescribed exercise range for each training variable (i.e. duration, reps, and intensity). Completion of duration and reps were calculated as: total volume achieved ÷ total volume prescribed during the pre-operative period. Completion of exercise intensity was calculated as: average RPE achieved ÷ minimum RPE prescribed during the pre-operative period.

2.6.1.3) Study Retention

Retention was assessed through measuring attrition during the study period and at each assessment. If an enrolled participant decided to withdraw from the study, reason for dropout was documented. However, those who withdrew without providing a reason were informed that they did not have to give a reason for non-participation as per REB guidelines.
The Feasibility and Efficacy of Prehabilitation for Prostate Cancer Surgery

2.6.1.4) Adverse Events

Safety was assessed through the charting of adverse events related to the intervention, upon inquiry by the R.Kin. at the follow-up study visit (i.e. ~1 week pre-operatively). Adverse events were classified using the National Cancer Institute’s Common Terminology Criteria for Adverse Events Version 4.0^{123}.

2.6.2) Secondary Outcome Measures: Estimates of Intervention Efficacy

Participants completed self-reported psychosocial and direct physical fitness measurements at baseline (i.e. following recruitment, close to time of consenting to RP) and follow-up (i.e. ~1 week pre-operatively).

2.6.2.1) Psychosocial Measures

2.6.2.1.1) Functional Assessment of Cancer Therapy-Prostate

PCa-specific HRQOL was measured using the psychometrically validated Functional Assessment of Cancer Therapy-Prostate (FACT-P), which is a widely used 47-item scale that combines 12 items for assessing PCa-specific concerns with 35 items of the Functional Assessment of Cancer Therapy-General scale. The FACT-P has been extensively validated with high reliability and internal consistency (Cronbach’s $\alpha = 0.87 - 0.89$)\textsuperscript{124-126}.

2.6.2.1.2) Functional Assessment of Cancer Therapy-Fatigue

Cancer-specific fatigue was measured using the Functional Assessment of Cancer Therapy-Fatigue (FACT–F), which is a widely used 13-item measure.
The Feasibility and Efficacy of Prehabilitation for Prostate Cancer Surgery

with strong reliability ($r = 0.87$), excellent internal consistency (Cronbach’s $\alpha = 0.93 - 0.95$) and good validity$^{127,128}$.

2.6.2.2) Physical Fitness Measures

2.6.2.2.1) Musculoskeletal Fitness

Grip strength is an independent predictor of mortality in middle-aged and older adults; and may identify patients, including those with a high level of function, who are at risk of deteriorating health$^{129-131}$. Moreover, grip strength assessed by hand dynamometer has been used frequently as a measure of physical function in PCa patients$^{121,132}$. Participants were asked to complete two maximal effort squeezes per hand utilizing a handgrip dynamometer (Sammons Preston, model Jamar, Bolingbrook, IL, USA), while standing with elbow fully extended and arm abducted to 45 degrees$^{133}$. Grip strength was recorded to the nearest kilogram (kg), with the maximum value per hand used for outcome assessment. Grip strength measured with the Jamar dynamometer has demonstrated excellent inter-rater reliability ($r = 0.98$) and good to excellent test–retest reproducibility ($r > 0.80$)$^{134,135}$.

Musculoskeletal strength was also assessed through manual muscle testing via standardized protocols$^{117}$. A handheld digital dynamometer (Hoggan Health Industries, model Microfet2, UT, USA) was used to assess maximal upper and lower-body isometric strength associated with four different joint motions: elbow flexion, elbow extension, knee flexion, and knee extension. Resistance was applied against the dynamometer perpendicular to the limb segment tested.
The Feasibility and Efficacy of Prehabilitation for Prostate Cancer Surgery

When properly positioned, participants were instructed to gradually generate force against the dynamometer for 2 sec, and then maintain a maximal effort for another 5 sec. Upper-body isometric strength was assessed with the participant seated with elbow flexed to 90 degrees. For elbow flexion, the dynamometer was placed distal to the wrist in the participant’s palm, and they were instructed to press the device upward onto the underside of a secured table. For elbow extension, the dynamometer was placed distal to the wrist in the participant’s palm, and they were instructed to press the device downward onto the topside of a secured table. Lower-body isometric strength was tested with participant seated halfway onto a secured chair with arms, with knees bent to 90 degrees. For knee flexion, the dynamometer was placed proximal to the ankle on the posterior surface of the leg and participants were instructed to press into the device with the tester providing resistance in the opposite direction. For knee extension, the dynamometer was placed proximal to the ankle on the anterior surface of the leg and participants were instructed to press into the device with the tester providing resistance in the opposite direction. Practice of the motion for each action without any resistance was allowed prior to testing. Two trials were administered and strength was recorded to the nearest kg, with the maximum value per joint movement used for outcome assessment.

2.6.2.2.2) Aerobic Fitness

Aerobic fitness was measured using the 6-minute walk test (6MWT), which evaluates the ability of an individual to maintain a moderate level of
The Feasibility and Efficacy of Prehabilitation for Prostate Cancer Surgery

aerobic activity over a time period reflective of ADLs\textsuperscript{136}. The 6MWT is sensitive to detect changes in physical performance with strong reliability ($r = 0.73 - 0.99$) amongst a mixture of populations including chronic heart failure and apparently healthy older adults\textsuperscript{117,136-139}. The test requires the participant to walk around a 50-meter (m) linear course for 6 min. Due to a limitation in hallway length at our study site, a 30 m course was utilized. Participants were instructed to walk (not jog) as fast as possible, back and forth in a designated hallway, making sure to turn/pivot around cones placed 15 m apart. Participants were permitted to slow down or stop to rest as necessary, but resume walking as soon as they are able. If balance were an issue, the tester would walk behind and to the side of the participant to provide support as needed. At the end of the test participants cooled-down by walking at a slow pace for 1 min around the course while performing deep breathing through pursed lips. Afterwards, participants would sit down as the tester immediately recorded: heart rate, blood pressure, and RPE. The distance stopped and reason for stopping prematurely, if necessary, was noted on the data sheet. Walking distance was then recorded and calculated, with the total distance traveled recorded in meters. Motivational and time-remaining cues were standardized to the following:

1:00 – “You’re doing well. You have 5 min to go.”

2:00 – “Keep up the good work. You have 4 min to go.”

3:00 – “You’re doing well. You’re halfway done.”

4:00 – “Keep up the good work. You have 2 min left.”

5:00 – “You’re doing well. You have only 1 min to go.”
The Feasibility and Efficacy of Prehabilitation for Prostate Cancer Surgery

5:45 – "In a moment I’m going to tell you to stop. When I do, just stop right where you are and I will come to you."

2.6.2.2.3) Body Composition

Three measures of body composition were conducted: WC, BF%, and BMI. WC was measured using anthropometric tape and was performed according to protocols defined by the WHO (i.e. tape placed horizontally, midway between lowest rib cage and iliac crest)\(^{117}\). The participant was instructed to stand erect in a relaxed manner with arms hanging loosely at the sides and the measurement was taken at the end of a normal expiration to the nearest 0.5 cm. BF% was measured using bioelectrical impedance analysis (BIA) scale (Tanita Corporation, model TBF-300A, Tokyo, Japan) and performed without footwear and in light clothing (i.e. shorts or track pants and t-shirt). The BIA scale interface would prompt for the following participant information: age, gender, body type, height, and weight of clothing. A 'standard' body type and 0.45 kg for clothing weight was inputted for each test. Participants were then instructed to stand on the scale with their heels on the center of the posterior electrodes and the front part of the foot in contact with the anterior electrodes while the measurement was taken. BMI was calculated using the participant’s height (m) and weight (kg) (as indicated from the BIA scale). Total-body weight was recorded in kg to the nearest 0.1 kg.
2.7) Data Management and Statistical Analysis

All statistical analyses were done using the Statistical Package for Social Sciences (SPSS) software Version 23.0 (IBM Corporation, Armonk, NY, USA). The RC reviewed all data for completeness and accuracy. Additionally, the RC often checked data entered electronically by comparing against hard copies of the assessment documentation, and correcting to ensure completeness and accuracy. For all hypotheses testing, the alpha level was set to 0.05 to identify statistical significant differences. Participant characteristics were summarized using the appropriate parametric and non-parametric descriptive statistics (mean, standard deviation for continuous data; frequency, percentage for categorical data). The equivalence of groups at baseline in terms of demographic and clinical variables was assessed using independent samples t-tests for continuous variables and chi-square tests for categorical variables.

Reasons for exclusion, declining enrollment and withdrawing from the study were summarized using descriptive statistics (frequency, percent for categorical data). Adherence to the PREHAB and PFMX prescriptions were compared using independent samples t-tests for continuous variables (i.e. percent of training prescription achieved) and chi-square tests for categorical variables (i.e. amount of participants adhering to PREHAB and PFMX prescriptions).

Estimates of efficacy (between-group mean differences) were analyzed using an analysis of covariance (ANCOVA), controlling for the baseline value of the outcome of interest, mean days in the pre-operative study period, age and
annual income. Within-in group mean differences (between baseline and follow-up) were assessed using paired sample t-tests for continuous variables. A per-protocol analysis was conducted for this study, including only participants who completed baseline and follow-up assessments.
CHAPTER 3: RESULTS

3.1) Sample Characteristics

Baseline categorical and continuous variables for PREHAB versus CON are presented in Table 1 and 2, respectively. Study participants were mostly Caucasian (PREHAB = 18 versus CON = 19; 74%), had a mean age of 61.1 years, and pathology reports demonstrated diagnosis of PCa ranging of stage T1c-T3b. Sixty-four percent of all participants consented for robot-assisted LRP (PREHAB = 16 versus CON = 16), 32% consented for open retropubic RP (PREHAB = 8 versus CON = 8) and 4% did not go through with operation for unknown reasons (PREHAB = 1 versus CON = 1). Both study arms were similar at baseline in all categorical variables except for annual income (p = 0.004). Also, both were significantly different at baseline for the following continuous variables: FACT-P physical well-being sub-domain (PREHAB = 27.1 versus CON = 26.2; p = 0.036), FACT-P prostate-specific concerns sub-domain (PREHAB = 41.6 versus CON = 37.6; p = 0.006), and FACT-P total score (PREHAB = 135.2 versus CON = 126.2; p = 0.034). Baseline categorical and continuous variables for dropouts versus non-dropouts are presented in Table 3 and 4, respectively. Dropouts and non-dropouts did not differ, except for a statistically significant difference observed in surgical method (p = 0.033).
The Feasibility and Efficacy of Prehabilitation for Prostate Cancer Surgery

Table 1. Baseline Demographics of Study Participants

<table>
<thead>
<tr>
<th>Variable</th>
<th>PREHAB (n = 25)</th>
<th>CON (n = 25)</th>
<th>Total</th>
<th>P-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Categorical Variables</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recruitment Method</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clinic Visit</td>
<td>4 (16)</td>
<td>6 (24)</td>
<td>10 (20)</td>
<td>0.480</td>
</tr>
<tr>
<td>Contacted Patient (i.e. telephone, letter)</td>
<td>21 (84)</td>
<td>19 (76)</td>
<td>40 (60)</td>
<td></td>
</tr>
<tr>
<td>Cancer Stage (TNM Stage)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T1c</td>
<td>0 (0)</td>
<td>1 (4)</td>
<td>1 (2)</td>
<td></td>
</tr>
<tr>
<td>T2</td>
<td>3 (12)</td>
<td>3 (12)</td>
<td>6 (12)</td>
<td></td>
</tr>
<tr>
<td>T2a</td>
<td>0 (0)</td>
<td>1 (4)</td>
<td>1 (2)</td>
<td></td>
</tr>
<tr>
<td>T2c</td>
<td>6 (24)</td>
<td>9 (36)</td>
<td>15 (30)</td>
<td>0.215</td>
</tr>
<tr>
<td>T3a</td>
<td>13 (52)</td>
<td>9 (36)</td>
<td>22 (44)</td>
<td></td>
</tr>
<tr>
<td>T3b</td>
<td>3 (12)</td>
<td>0 (0)</td>
<td>3 (6)</td>
<td></td>
</tr>
<tr>
<td>Not Available</td>
<td>0 (0)</td>
<td>2 (8)</td>
<td>2 (4)</td>
<td></td>
</tr>
<tr>
<td>Gleason Score</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>1 (4)</td>
<td>0 (0)</td>
<td>1 (2)</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>3 (12)</td>
<td>0 (0)</td>
<td>3 (6)</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>20 (80)</td>
<td>23 (92)</td>
<td>43 (86)</td>
<td>0.206</td>
</tr>
<tr>
<td>8</td>
<td>0 (0)</td>
<td>1 (4)</td>
<td>1 (2)</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>1 (4)</td>
<td>0 (0)</td>
<td>1 (2)</td>
<td></td>
</tr>
<tr>
<td>Not Available</td>
<td>0 (0)</td>
<td>1 (4)</td>
<td>1 (2)</td>
<td></td>
</tr>
<tr>
<td>Surgery Type</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Open Retropubic RP</td>
<td>8 (32)</td>
<td>8 (32)</td>
<td>16 (32)</td>
<td>1.000</td>
</tr>
<tr>
<td>Robot-Assisted Laparoscopic RP</td>
<td>16 (64)</td>
<td>16 (64)</td>
<td>32 (64)</td>
<td></td>
</tr>
<tr>
<td>Not Available</td>
<td>1 (4)</td>
<td>1 (4)</td>
<td>2 (4)</td>
<td></td>
</tr>
<tr>
<td>Ancestry/Ethnicity</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White/Caucasian</td>
<td>18 (72)</td>
<td>19 (76)</td>
<td>37 (74)</td>
<td></td>
</tr>
<tr>
<td>Black/Afro-Caribbean/African</td>
<td>4 (16)</td>
<td>3 (12)</td>
<td>7 (14)</td>
<td></td>
</tr>
<tr>
<td>Latino/Hispanic</td>
<td>0 (0)</td>
<td>1 (4)</td>
<td>1 (2)</td>
<td></td>
</tr>
<tr>
<td>Arabic (e.g. Lebanon, Palestine)</td>
<td>0 (0)</td>
<td>1 (4)</td>
<td>1 (2)</td>
<td>0.654</td>
</tr>
<tr>
<td>Ashkenazi Jewish</td>
<td>1 (4)</td>
<td>0 (0)</td>
<td>1 (2)</td>
<td></td>
</tr>
<tr>
<td>East Asian (China, Korea, Japan)</td>
<td>1 (4)</td>
<td>1 (4)</td>
<td>2 (4)</td>
<td></td>
</tr>
<tr>
<td>South Asian (e.g. India, Pakistan)</td>
<td>1 (4)</td>
<td>0 (0)</td>
<td>1 (2)</td>
<td></td>
</tr>
<tr>
<td>Annual Income</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; $40,000</td>
<td>2 (8)</td>
<td>10 (40)</td>
<td>12 (24)</td>
<td>0.004*</td>
</tr>
<tr>
<td>$40,000 - $80,000</td>
<td>14 (56)</td>
<td>4 (16)</td>
<td>18 (36)</td>
<td></td>
</tr>
<tr>
<td>&gt; $80,000</td>
<td>9 (36)</td>
<td>11 (44)</td>
<td>20 (30)</td>
<td></td>
</tr>
<tr>
<td>Mental Status</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single (never married)</td>
<td>1 (4)</td>
<td>4 (16)</td>
<td>5 (10)</td>
<td></td>
</tr>
<tr>
<td>Widowed</td>
<td>1 (4)</td>
<td>1 (4)</td>
<td>2 (4)</td>
<td></td>
</tr>
<tr>
<td>Married (including common law)</td>
<td>18 (72)</td>
<td>14 (56)</td>
<td>32 (64)</td>
<td>0.661</td>
</tr>
<tr>
<td>Separated</td>
<td>1 (4)</td>
<td>1 (4)</td>
<td>2 (4)</td>
<td></td>
</tr>
<tr>
<td>Divorced</td>
<td>4 (16)</td>
<td>5 (20)</td>
<td>9 (18)</td>
<td>0.962</td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Less than High School</td>
<td>2 (8)</td>
<td>1 (4)</td>
<td>3 (6)</td>
<td></td>
</tr>
<tr>
<td>High School Graduate</td>
<td>4 (16)</td>
<td>8 (24)</td>
<td>10 (20)</td>
<td></td>
</tr>
<tr>
<td>Community College/Trade School</td>
<td>6 (24)</td>
<td>5 (20)</td>
<td>11 (22)</td>
<td></td>
</tr>
<tr>
<td>University Graduate</td>
<td>5 (20)</td>
<td>4 (16)</td>
<td>9 (18)</td>
<td></td>
</tr>
<tr>
<td>Graduate University Degree</td>
<td>7 (28)</td>
<td>8 (32)</td>
<td>15 (30)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>1 (4)</td>
<td>1 (4)</td>
<td>2 (4)</td>
<td></td>
</tr>
<tr>
<td>Work Status</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No, retired</td>
<td>10 (40)</td>
<td>7 (28)</td>
<td>17 (34)</td>
<td>0.611</td>
</tr>
<tr>
<td>No, but looking for job</td>
<td>1 (4)</td>
<td>1 (4)</td>
<td>2 (4)</td>
<td></td>
</tr>
<tr>
<td>Yes, part-time</td>
<td>5 (20)</td>
<td>5 (20)</td>
<td>10 (20)</td>
<td></td>
</tr>
<tr>
<td>Yes, full-time</td>
<td>9 (36)</td>
<td>12 (48)</td>
<td>21 (42)</td>
<td></td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>24 (96)</td>
<td>22 (88)</td>
<td>46 (92)</td>
<td>0.297</td>
</tr>
<tr>
<td>Yes</td>
<td>1 (4)</td>
<td>3 (12)</td>
<td>4 (8)</td>
<td></td>
</tr>
</tbody>
</table>

Data for categorical variables are presented as Frequency (% of the group); p-value presented for χ²; PREHAB = prehabilitation; CON = control; RP = radical prostatectomy; * statistically significant change (p ≤ 0.05).
Table 2. Baseline Characteristics of Study Participants

<table>
<thead>
<tr>
<th>Variable</th>
<th>PREHAB (n = 25)</th>
<th>CON (n = 25)</th>
<th>P-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Continuous Variables</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>61.04 (8.37)</td>
<td>61.12 (7.53)</td>
<td>0.972</td>
</tr>
<tr>
<td>FACT-P Total</td>
<td>135.15 (12.41)</td>
<td>126.16 (15.79)</td>
<td><strong>0.034</strong>*</td>
</tr>
<tr>
<td>FACT-P – PWB</td>
<td>27.14 (1.31)</td>
<td>26.21 (1.84)</td>
<td><strong>0.038</strong>*</td>
</tr>
<tr>
<td>FACT-P – SWB</td>
<td>23.28 (5.87)</td>
<td>21.54 (6.83)</td>
<td>0.349</td>
</tr>
<tr>
<td>FACT-P – EWB</td>
<td>19.24 (2.78)</td>
<td>17.96 (4.89)</td>
<td>0.275</td>
</tr>
<tr>
<td>FACT-P – FWB</td>
<td>23.88 (3.74)</td>
<td>22.89 (4.45)</td>
<td>0.412</td>
</tr>
<tr>
<td>FACT-P – PSC</td>
<td>41.60 (3.73)</td>
<td>37.56 (5.75)</td>
<td><strong>0.006</strong>*</td>
</tr>
<tr>
<td>FACT-F</td>
<td>46.91 (6.38)</td>
<td>45.88 (5.59)</td>
<td>0.553</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>79.89 (13.88)</td>
<td>79.37 (13.34)</td>
<td>0.894</td>
</tr>
<tr>
<td>Waist (cm)</td>
<td>96.96 (10.90)</td>
<td>97.74 (12.66)</td>
<td>0.817</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>25.98 (3.94)</td>
<td>26.43 (4.92)</td>
<td>0.724</td>
</tr>
<tr>
<td>Body Fat (%)</td>
<td>23.27 (5.11)</td>
<td>22.43 (7.02)</td>
<td>0.635</td>
</tr>
<tr>
<td>Grip Strength (kg)</td>
<td>74.16 (16.24)</td>
<td>72.16 (19.21)</td>
<td>0.693</td>
</tr>
<tr>
<td>Arm Strength-Elbow Flexion (kg)</td>
<td>35.23 (8.54)</td>
<td>32.19 (9.06)</td>
<td>0.228</td>
</tr>
<tr>
<td>Arm Strength-Elbow Extension (kg)</td>
<td>33.65 (6.82)</td>
<td>29.52 (8.33)</td>
<td>0.061</td>
</tr>
<tr>
<td>Leg Strength-Knee Flexion (kg)</td>
<td>37.06 (6.57)</td>
<td>36.87 (7.32)</td>
<td>0.943</td>
</tr>
<tr>
<td>Leg Strength-Knee Extension (kg)</td>
<td>41.37 (9.09)</td>
<td>44.92 (10.72)</td>
<td>0.370</td>
</tr>
<tr>
<td>6MWT Post-HR (bpm)</td>
<td>108.76 (27.18)</td>
<td>112.64 (19.35)</td>
<td>0.564</td>
</tr>
<tr>
<td>6MWT Distance (m)</td>
<td>585.08 (85.34)</td>
<td>571.72 (112.59)</td>
<td>0.638</td>
</tr>
</tbody>
</table>

Data for continuous variables are presented as Mean (SD); p-value for between-group differences using independent sample t-test; PREHAB = prehabilitation; CON = control; FACT-P = function assessment of cancer therapy-prostate; PWB = physical well-being; SWB = social well-being; EWB = emotional well-being; FWB = functional well-being; PSC = prostate cancer-specific concerns; FACT-F = functional assessment of cancer therapy-fatigue; cm = centimeters; kg = kilograms; kg/m² = kilograms per meter squared; BMI = body mass index; 6MWT = 6-minute walk test; HR = heart rate; bpm = beats per minute; m = meters; higher FACT score = better outcome; * statistically significant change (p ≤ 0.05).
## Table 3. Baseline Demographics of Dropouts and Non-Dropouts

<table>
<thead>
<tr>
<th>Variable</th>
<th>Non-Dropouts (n = 38)</th>
<th>Dropouts (n = 12)</th>
<th>Total</th>
<th>P-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Categorical Variables</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recruitment Method</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clinic Visit</td>
<td>7 (18.4)</td>
<td>3 (25)</td>
<td>10 (20)</td>
<td>0.619</td>
</tr>
<tr>
<td>Contacted Patient (i.e., telephone, letter)</td>
<td>31 (81.6)</td>
<td>9 (75)</td>
<td>50 (80)</td>
<td>0.619</td>
</tr>
<tr>
<td>Cancer Stage (TNM Stage)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T1c</td>
<td>1 (2.6)</td>
<td>0 (0)</td>
<td>1 (2)</td>
<td></td>
</tr>
<tr>
<td>T2</td>
<td>4 (10.5)</td>
<td>2 (16.7)</td>
<td>6 (12)</td>
<td></td>
</tr>
<tr>
<td>T3a</td>
<td>0 (0)</td>
<td>1 (8.3)</td>
<td>1 (2)</td>
<td>0.193</td>
</tr>
<tr>
<td>T3b</td>
<td>14 (36.8)</td>
<td>1 (8.3)</td>
<td>15 (30)</td>
<td></td>
</tr>
<tr>
<td>Not Available</td>
<td>15 (39.5)</td>
<td>7 (58.3)</td>
<td>22 (44)</td>
<td></td>
</tr>
<tr>
<td>Gleason Score</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>1 (2.6)</td>
<td>0 (0)</td>
<td>1 (2)</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>1 (2.6)</td>
<td>2 (16.7)</td>
<td>3 (6)</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>33 (86.8)</td>
<td>10 (83.3)</td>
<td>43 (86)</td>
<td>0.511</td>
</tr>
<tr>
<td>8</td>
<td>1 (2.6)</td>
<td>0 (0)</td>
<td>1 (2)</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>1 (2.6)</td>
<td>0 (0)</td>
<td>1 (2)</td>
<td></td>
</tr>
<tr>
<td>Not Available</td>
<td>1 (2.6)</td>
<td>0 (0)</td>
<td>1 (2)</td>
<td></td>
</tr>
<tr>
<td>Surgery Type</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Open Retropubic RP</td>
<td>12 (31.6)</td>
<td>4 (33.3)</td>
<td>16 (32)</td>
<td>0.033*</td>
</tr>
<tr>
<td>Robot-Assisted Laparoscopic RP</td>
<td>26 (68.4)</td>
<td>6 (50)</td>
<td>32 (64)</td>
<td></td>
</tr>
<tr>
<td>Not Available</td>
<td>0 (0)</td>
<td>2 (16.7)</td>
<td>2 (4)</td>
<td></td>
</tr>
<tr>
<td>Ancestry/Ethnicity</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White/Caucasian</td>
<td>26 (68.4)</td>
<td>11 (91.7)</td>
<td>37 (74)</td>
<td></td>
</tr>
<tr>
<td>Black/Afro-Caribbean/African</td>
<td>6 (15.8)</td>
<td>1 (8.3)</td>
<td>7 (14)</td>
<td></td>
</tr>
<tr>
<td>Latino/Hispanic</td>
<td>1 (2.6)</td>
<td>0 (0)</td>
<td>1 (2)</td>
<td>0.818</td>
</tr>
<tr>
<td>Arabic (e.g., Lebanon, Palestine)</td>
<td>1 (2.6)</td>
<td>0 (0)</td>
<td>1 (2)</td>
<td></td>
</tr>
<tr>
<td>Ashkenazi Jewish</td>
<td>1 (2.6)</td>
<td>0 (0)</td>
<td>1 (2)</td>
<td></td>
</tr>
<tr>
<td>East Asian (China, Korea, Japan)</td>
<td>2 (5.3)</td>
<td>0 (0)</td>
<td>2 (4)</td>
<td></td>
</tr>
<tr>
<td>South Asian (e.g., India, Pakistan)</td>
<td>1 (2.6)</td>
<td>0 (0)</td>
<td>1 (2)</td>
<td></td>
</tr>
<tr>
<td>Annual Income</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; $40,000</td>
<td>7 (18.4)</td>
<td>5 (41.7)</td>
<td>12 (24)</td>
<td></td>
</tr>
<tr>
<td>$40,000 - $80,000</td>
<td>14 (36.8)</td>
<td>4 (33.3)</td>
<td>18 (36)</td>
<td>0.226</td>
</tr>
<tr>
<td>&gt; $80,000</td>
<td>17 (44.7)</td>
<td>3 (25)</td>
<td>20 (40)</td>
<td></td>
</tr>
<tr>
<td>Marital Status</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single (never married)</td>
<td>2 (5.3)</td>
<td>3 (25)</td>
<td>3 (10)</td>
<td></td>
</tr>
<tr>
<td>Widowed</td>
<td>2 (5.3)</td>
<td>0 (0)</td>
<td>2 (4)</td>
<td></td>
</tr>
<tr>
<td>Married (including common law)</td>
<td>26 (68.4)</td>
<td>6 (50)</td>
<td>32 (64)</td>
<td>0.220</td>
</tr>
<tr>
<td>Separated</td>
<td>2 (5.3)</td>
<td>0 (0)</td>
<td>2 (4)</td>
<td></td>
</tr>
<tr>
<td>Divorced</td>
<td>6 (15.8)</td>
<td>3 (25)</td>
<td>9 (18)</td>
<td></td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Less than High School</td>
<td>1 (2.6)</td>
<td>2 (16.7)</td>
<td>3 (6)</td>
<td></td>
</tr>
<tr>
<td>High School Graduate</td>
<td>9 (23.7)</td>
<td>1 (8.3)</td>
<td>10 (20)</td>
<td></td>
</tr>
<tr>
<td>Community College/Trade School</td>
<td>7 (18.4)</td>
<td>4 (33.3)</td>
<td>11 (22)</td>
<td>0.245</td>
</tr>
<tr>
<td>University Graduate</td>
<td>8 (21.1)</td>
<td>1 (8.3)</td>
<td>9 (18)</td>
<td></td>
</tr>
<tr>
<td>Graduate University Degree</td>
<td>12 (31.6)</td>
<td>3 (25)</td>
<td>15 (30)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>1 (2.6)</td>
<td>1 (8.3)</td>
<td>2 (4)</td>
<td></td>
</tr>
<tr>
<td>Work Status</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No, retired</td>
<td>11 (28.9)</td>
<td>6 (50)</td>
<td>17 (34)</td>
<td></td>
</tr>
<tr>
<td>No, but looking for job</td>
<td>2 (5.3)</td>
<td>0 (0)</td>
<td>2 (4)</td>
<td></td>
</tr>
<tr>
<td>Yes, part-time</td>
<td>7 (18.4)</td>
<td>3 (25)</td>
<td>10 (20)</td>
<td>0.376</td>
</tr>
<tr>
<td>Yes, full-time</td>
<td>18 (47.4)</td>
<td>4 (33.3)</td>
<td>22 (44)</td>
<td></td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>35 (92.1)</td>
<td>11 (91.7)</td>
<td>46 (92)</td>
<td>0.961</td>
</tr>
<tr>
<td>Yes</td>
<td>3 (7.9)</td>
<td>1 (8.3)</td>
<td>4 (8)</td>
<td></td>
</tr>
</tbody>
</table>

Data for categorical variables are presented as Frequency (% of the group); p-value presented for χ²; RP = radical prostatectomy; * statistically significant change (p ≤ 0.05).
## Table 4. Baseline Characteristics of Dropouts and Non-Dropouts

<table>
<thead>
<tr>
<th>Variable</th>
<th>Non-Dropouts (n = 38)</th>
<th>Dropouts (n = 12)</th>
<th>P-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Continuous Variables</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>60.00 (7.60)</td>
<td>64.50 (8.12)</td>
<td>0.085</td>
</tr>
<tr>
<td>FACT-P Total</td>
<td>131.60 (13.96)</td>
<td>126.66 (17.67)</td>
<td>0.337</td>
</tr>
<tr>
<td>FACT-P – PWB</td>
<td>26.72 (1.54)</td>
<td>26.46 (1.63)</td>
<td>0.624</td>
</tr>
<tr>
<td>FACT-P – SWB</td>
<td>22.73 (5.73)</td>
<td>21.18 (8.46)</td>
<td>0.487</td>
</tr>
<tr>
<td>FACT-P – EWB</td>
<td>18.83 (3.79)</td>
<td>17.73 (4.86)</td>
<td>0.433</td>
</tr>
<tr>
<td>FACT-P – FWB</td>
<td>23.31 (4.09)</td>
<td>23.56 (4.37)</td>
<td>0.857</td>
</tr>
<tr>
<td>FACT-P – PSC</td>
<td>40.02 (5.61)</td>
<td>37.73 (3.44)</td>
<td>0.207</td>
</tr>
<tr>
<td>FACT-F</td>
<td>46.30 (6.29)</td>
<td>46.64 (4.82)</td>
<td>0.870</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>78.95 (12.63)</td>
<td>81.78 (16.29)</td>
<td>0.533</td>
</tr>
<tr>
<td>Waist (cm)</td>
<td>96.82 (10.33)</td>
<td>99.04 (15.69)</td>
<td>0.571</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>26.02 (3.81)</td>
<td>26.78 (6.14)</td>
<td>0.613</td>
</tr>
<tr>
<td>Body Fat (%)</td>
<td>22.79 (5.67)</td>
<td>23.09 (7.60)</td>
<td>0.887</td>
</tr>
<tr>
<td>Grip Strength (kg)</td>
<td>75.16 (17.56)</td>
<td>66.83 (17.02)</td>
<td>0.156</td>
</tr>
<tr>
<td>Arm Strength-Elbow Flexion (kg)</td>
<td>34.24 (9.02)</td>
<td>32.02 (8.41)</td>
<td>0.453</td>
</tr>
<tr>
<td>Arm Strength-Elbow Extension (kg)</td>
<td>32.78 (8.24)</td>
<td>27.80 (4.86)</td>
<td>0.054</td>
</tr>
<tr>
<td>Leg Strength-Knee Flexion (kg)</td>
<td>37.89 (6.22)</td>
<td>33.93 (8.28)</td>
<td>0.218</td>
</tr>
<tr>
<td>Leg Strength-Knee Extension (kg)</td>
<td>41.49 (9.69)</td>
<td>48.07 (9.31)</td>
<td>0.155</td>
</tr>
<tr>
<td>6MWT Post-HR (bpm)</td>
<td>109.87 (22.42)</td>
<td>113.33 (27.29)</td>
<td>0.660</td>
</tr>
<tr>
<td>6MWT Distance (m)</td>
<td>591.26 (96.18)</td>
<td>537.67 (101.24)</td>
<td>0.103</td>
</tr>
</tbody>
</table>

Data for continuous variables are presented as Mean (SD); p-value for between-group differences using independent sample t-test; FACT-P = function assessment of cancer therapy-prostate; PWB = physical well-being; SWB = social well-being; EWB = emotional well-being; FWB = functional well-being; PSC = prostate cancer-specific concerns; FACT-F = functional assessment of cancer therapy-fatigue; cm = centimeters; kg = kilograms; kg/m² = kilograms per meter squared; BMI = body mass index; 6MWT = 6-minute walk test; HR = heart rate; bpm = beats per minute; m = meters; higher FACT score = better outcome; * statistically significant change (p ≤ 0.05).
The Feasibility and Efficacy of Prehabilitation for Prostate Cancer Surgery

3.2) Feasibility Assessment

3.2.2) Recruitment

The CONSORT (Consolidated Standards of Reporting Trials) diagram is presented in Figure 1. From February 2014 to September 2015, 318 patients were screened for eligibility via EPR. Of those patients screened, 64% (n = 205/318) were excluded, and of the remaining 113 eligible patients, 56% (n = 63/113) refused to enroll. Reasons for exclusion from the study were: on active surveillance (n = 43), medical/musculoskeletal contraindication (n = 42), opted for other treatment (n = 31), could not contact (n = 23), language barrier (n = 22), on treatment (n = 12), surgery < 4 weeks (n = 12), previous cancer treatment (n = 11), non-PCa patient (n = 4), surgery at different hospital (n = 3), and enrolled in conflicting study (n = 2). Reasons for declining to enroll in the study were: lack of transportation/too far to travel (n = 25), no response to follow-up (n = 11), interested in conflicting study (n = 9), not interested/no reason (n = 9), no time (n = 8), and self-determined inability to participate (n = 1). Fifty patients were recruited out of the 113 eligible patients approached at the Princess Margaret Cancer Centre (recruitment rate = 44.2%). These men were randomly assigned 1:1 to either the PREHAB (n = 25) or CON (n = 25) study arm. The mean number of days between baseline and pre-operative follow-up for the PREHAB and CON group was 42.1 (SD = 24.8) and 45.1 (SD = 24.6), respectively (p = 0.719).
The Feasibility and Efficacy of Prehabilitation for Prostate Cancer Surgery

![ consort_diagram ]

**Figure 1. CONSORT Diagram**
3.2.3) Adherence to Group Allocation

Table 5 summarizes adherence as a percentage of participants that had achieved the minimum prescribed training for total-body exercise and/or PFMX during the pre-operative study period. With respect to PFMX, the PREHAB and CON group each demonstrated an adherence rate of 38.1% (n = 8/21) and 26.7% (n = 4/15), respectively. Moreover, when including non-adherers the PREHAB and CON group were able to achieve 75.1% (SD = 32.8) and 74.4% (SD = 43.4) of the PFMX prescription, respectively (p = 0.955). As for total-body exercise, PREHAB participants demonstrated an adherence rate of 76.2% (n = 16/21). All PREHAB participants achieved the minimum prescribed intensity/RPE (RE and AE; n = 21/21) and reps (RE; n =21/21); however, only 76.2% (n = 16/21) achieved the minimum duration of AE prescribed, which consequently reduced the overall total-body exercise adherence.

3.2.4) Study Retention

From baseline to follow-up, attrition rates were 16% (n = 4/25) and 32% (n = 8/25) for the PREHAB and CON groups, respectively. When combining dropouts in both groups, our study attrition rate was 24% (n = 12/50). This difference in attrition between groups did not reach statistical significance (p = 0.185). In the PREHAB group, reasons for dropout were: loss of interest/motivation (n = 1), self-determined inability to participate (n = 1), no time (n = 1), and lost to follow-up without explanation (n = 1) (i.e. could not be reached
The Feasibility and Efficacy of Prehabilitation for Prostate Cancer Surgery

after multiple attempts). In the CON group, the reasons for dropping out were: no time (n = 3) and lost to follow-up without explanation (n = 5).

3.2.5) Adverse Events

The comprehensive prehabilitation program was safe and there were no adverse events related to the exercise intervention. Additionally, no injuries or adverse events occurred during fitness testing at either time point (i.e. baseline and follow-up).
The Feasibility and Efficacy of Prehabilitation for Prostate Cancer Surgery

<table>
<thead>
<tr>
<th>Table 5. Pre-Operative Study Length and Study Adherence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Variables</td>
</tr>
<tr>
<td>Pre-Operative Study Length (days)¹</td>
</tr>
<tr>
<td>PFMX Adherence</td>
</tr>
<tr>
<td>Contractions²</td>
</tr>
<tr>
<td>Aerobic Training Adherence</td>
</tr>
<tr>
<td>Duration²</td>
</tr>
<tr>
<td>Intensity/RPE²</td>
</tr>
<tr>
<td>Resistance Training Adherence</td>
</tr>
<tr>
<td>Repetitions²</td>
</tr>
<tr>
<td>Intensity/RPE²</td>
</tr>
<tr>
<td>Overall Exercise Adherence²</td>
</tr>
</tbody>
</table>

¹Data for continuous variables are presented as Mean (SD); p-value for between-group differences using independent sample t-test; PREHAB = prehabilitation; CON = control. ²Data for categorical variables are presented as Frequency (% of the group); p-value presented for χ²; PFMX = pelvic floor muscle exercise; RPE = rate of perceived exertion; * statistically significant change (p ≤ 0.05).
The Feasibility and Efficacy of Prehabilitation for Prostate Cancer Surgery

3.3) HRQOL and Fatigue Outcomes

Between-group and within-group analyses for HRQOL and fatigue are presented in Table 6 and 7, respectively. There were no statistically or clinically significant differences observed to HRQOL (including sub-domains) or fatigue between groups post-study. However, PREHAB participants did demonstrate a statistically significant within-group improvement in emotion well-being (EWB) (mean within-group Δ = +0.82; p = 0.036) and a trend towards clinical and statistical significance in FACT-P total score (mean within-group Δ = +2.99; p = 0.081).

3.4) Physical Fitness Outcomes

Between-group and within-group analyses for physical fitness outcomes are presented in Table 8 and 9, respectively. A statistically significant difference in BF% was observed post-study in favour of the PREHAB group (mean between-group Δ = -1.43 %; p = 0.019). Also, a clinically (though non-statistically significant) important difference was demonstrated in favour of the PREHAB group in 6MWT distance (mean between-group Δ = +25.58 m; p = 0.344). There were no other significant differences between groups post-study. However, the PREHAB group did demonstrate statistically significant within-group differences in WC (mean within-group Δ = -1.24 cm; p < 0.001) and BF% (mean within-group Δ = -0.62 %; p = 0.003). Furthermore, throughout the duration of the pre-operative study period PREHAB participants achieved a weekly average of 236.4 min (SD = 68.6) of exercise.
The Feasibility and Efficacy of Prehabilitation for Prostate Cancer Surgery

Table 6. Per Protocol Analyses of Between-Group Differences in Psychosocial Well-Being Post-Study

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean between-group difference from baseline to pre-RP(^1)</th>
<th>F</th>
<th>P-value*</th>
<th>95% Confidence Interval for Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>FACT-P</td>
<td>0.635</td>
<td>0.036</td>
<td>0.850</td>
<td>-6.167 - 7.437</td>
</tr>
<tr>
<td>FACT-P – PWB</td>
<td>0.757</td>
<td>0.388</td>
<td>0.538</td>
<td>-1.722 - 3.237</td>
</tr>
<tr>
<td>FACT-P – SWB</td>
<td>-0.984</td>
<td>0.465</td>
<td>0.500</td>
<td>-3.926 - 1.958</td>
</tr>
<tr>
<td>FACT-P – EWB</td>
<td>0.418</td>
<td>0.109</td>
<td>0.743</td>
<td>-2.161 - 2.998</td>
</tr>
<tr>
<td>FACT-P – FWB</td>
<td>0.706</td>
<td>0.158</td>
<td>0.694</td>
<td>-2.922 - 4.335</td>
</tr>
<tr>
<td>FACT-P – PSC</td>
<td>1.109</td>
<td>0.431</td>
<td>0.516</td>
<td>-2.335 - 4.552</td>
</tr>
<tr>
<td>FACT-F</td>
<td>-1.950</td>
<td>0.797</td>
<td>0.379</td>
<td>-6.405 - 2.505</td>
</tr>
</tbody>
</table>

Per-protocol analysis; data are presented as mean between-group difference; \(^1\) = PREHAB – control; RP = radical prostatectomy; FACT-P = function assessment of cancer therapy-prostate; PWB = physical well-being; SWB = social well-being; EWB = emotional well-being; FWB = functional well-being; PSC = prostate cancer-specific concerns; FACT-F = functional assessment of cancer therapy-fatigue; F (degrees of freedom) and p-value for between-factor, 95% confidence interval (lower and upper bound), and interaction analysis are reported for ANCOVA; higher FACT score = better outcome; * statistically significant change (p ≤ 0.05).
The Feasibility and Efficacy of Prehabilitation for Prostate Cancer Surgery

Table 7. Per Protocol Analysis of Within-Group Differences in Psychosocial Well-Being Post-Study

<table>
<thead>
<tr>
<th>Variable</th>
<th>PREHAB Baseline</th>
<th>PREHAB Follow-up</th>
<th>Mean within-group difference</th>
<th>P-value*</th>
<th>CON Baseline</th>
<th>CON Follow-up</th>
<th>Mean within-group difference</th>
<th>P-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>FACT-P</td>
<td>135.66 (9.53)</td>
<td>138.65 (11.17)</td>
<td>2.99 (7.27)</td>
<td>0.081</td>
<td>126.82 (16.90)</td>
<td>127.93 (19.17)</td>
<td>1.12 (7.16)</td>
<td>0.533</td>
</tr>
<tr>
<td>FACT-P – PWB</td>
<td>27.17 (1.37)</td>
<td>26.90 (1.59)</td>
<td>-0.27 (1.32)</td>
<td>0.380</td>
<td>26.19 (1.59)</td>
<td>25.12 (3.72)</td>
<td>-1.08 (3.52)</td>
<td>0.226</td>
</tr>
<tr>
<td>FACT-P – SWB</td>
<td>23.78 (4.21)</td>
<td>24.95 (3.12)</td>
<td>1.18 (4.63)</td>
<td>0.270</td>
<td>21.49 (7.05)</td>
<td>24.40 (3.68)</td>
<td>2.91 (7.31)</td>
<td>0.121</td>
</tr>
<tr>
<td>FACT-P – EWB</td>
<td>19.13 (2.16)</td>
<td>19.95 (2.84)</td>
<td>0.82 (1.63)</td>
<td></td>
<td>18.47 (4.80)</td>
<td>18.41 (3.41)</td>
<td>-0.06 (5.19)</td>
<td>0.963</td>
</tr>
<tr>
<td>FACT-P – FWB</td>
<td>23.90 (3.23)</td>
<td>23.85 (3.82)</td>
<td>-0.05 (1.54)</td>
<td>0.886</td>
<td>22.61 (4.93)</td>
<td>21.71 (6.16)</td>
<td>-0.90 (5.68)</td>
<td>0.523</td>
</tr>
<tr>
<td>FACT-P – PSC</td>
<td>41.69 (3.72)</td>
<td>43.00 (4.03)</td>
<td>1.31 (4.13)</td>
<td>0.172</td>
<td>38.06 (6.84)</td>
<td>38.29 (8.27)</td>
<td>0.24 (3.01)</td>
<td>0.751</td>
</tr>
<tr>
<td>FACT-F</td>
<td>47.20 (6.21)</td>
<td>46.89 (7.40)</td>
<td>-0.31 (5.45)</td>
<td>0.800</td>
<td>45.24 (6.41)</td>
<td>44.21 (8.01)</td>
<td>1.03 (4.06)</td>
<td>0.312</td>
</tr>
</tbody>
</table>

Per-protocol analysis; data are presented as mean within-group difference; ¹ = follow-up – baseline; PREHAB = prehabilitation; CON = control; FACT-P = function assessment of cancer therapy-prostate; PWB = physical well-being; SWB = social well-being; EWB = emotional well-being; FWB = functional well-being; PSC = prostate cancer-specific concerns; FACT-F = functional assessment of cancer therapy-fatigue; higher FACT score = better outcome; * statistically significant change (p ≤ 0.05).
The Feasibility and Efficacy of Prehabilitation for Prostate Cancer Surgery

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean between-group difference from baseline to pre-RP</th>
<th>F</th>
<th>P-value*</th>
<th>95% Confidence Interval for Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight (kg)</td>
<td>0.299</td>
<td>0.272</td>
<td>0.606</td>
<td>-0.870, 1.469</td>
</tr>
<tr>
<td>Waist (cm)</td>
<td>-0.746</td>
<td>1.366</td>
<td>0.251</td>
<td>-2.047, 0.554</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>0.003</td>
<td>0.000</td>
<td>0.989</td>
<td>-0.519, 0.526</td>
</tr>
<tr>
<td>Body Fat (%)</td>
<td>-1.428</td>
<td>6.157</td>
<td><strong>0.019</strong>*</td>
<td>-2.599, -0.256</td>
</tr>
<tr>
<td>Grip Strength (kg)</td>
<td>-1.399</td>
<td>0.167</td>
<td>0.686</td>
<td>-8.376, 5.578</td>
</tr>
<tr>
<td>Arm Strength-Elbow Flexion (kg)</td>
<td>2.164</td>
<td>2.085</td>
<td>0.159</td>
<td>-0.889, 5.217</td>
</tr>
<tr>
<td>Arm Strength-Elbow Extension (kg)</td>
<td>0.784</td>
<td>0.274</td>
<td>0.604</td>
<td>-2.264, 3.831</td>
</tr>
<tr>
<td>Leg Strength-Knee Flexion (kg)</td>
<td>-2.877</td>
<td>0.501</td>
<td>0.491</td>
<td>-11.595, 5.840</td>
</tr>
<tr>
<td>Leg Strength-Knee Extension (kg)</td>
<td>4.260</td>
<td>1.076</td>
<td>0.317</td>
<td>-4.547, 13.067</td>
</tr>
<tr>
<td>6MWT Post-HR (bpm)</td>
<td>-7.396</td>
<td>0.913</td>
<td>0.347</td>
<td>-23.205, 8.413</td>
</tr>
<tr>
<td>6MWT Distance (m)</td>
<td>25.580</td>
<td>0.926</td>
<td>0.344</td>
<td>-28.704, 79.864</td>
</tr>
</tbody>
</table>

Per-protocol analysis; data are presented as mean between-group difference; ¹ = PREHAB – control; RP = radical prostatectomy; cm = centimeters; kg = kilograms; kg/m² = kilograms per meter squared; BMI = body mass index; 6MWT = 6-minute walk test; HR = heart rate; bpm = beats per minute; m = meters; F (degrees of freedom) and p-value for between-factor, 95% confidence interval (lower and upper bound), and interaction analysis are reported for ANCOVA; * statistically significant change (p ≤ 0.05).
The Feasibility and Efficacy of Prehabilitation for Prostate Cancer Surgery

Table 9. Per Protocol Analyses of Within-Group Differences in Physical Fitness Post-Study

<table>
<thead>
<tr>
<th>Variable</th>
<th>PREHAB Baseline</th>
<th>PREHAB Follow-up</th>
<th>Mean within-group difference</th>
<th>P-value*</th>
<th>CON Baseline</th>
<th>CON Follow-up</th>
<th>Mean within-group difference</th>
<th>P-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight (kg)</td>
<td>78.25 (11.41)</td>
<td>78.02 (11.24)</td>
<td>-0.23</td>
<td>0.324</td>
<td>79.82 (14.32)</td>
<td>79.59 (14.43)</td>
<td>-0.24</td>
<td>0.533</td>
</tr>
<tr>
<td>Waist (cm)</td>
<td>95.77 (7.79)</td>
<td>94.52 (8.10)</td>
<td>-1.24</td>
<td>&lt;0.001*</td>
<td>98.12 (12.95)</td>
<td>97.38 (13.06)</td>
<td>-0.74</td>
<td>0.111</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>25.34 (2.68)</td>
<td>25.33 (2.68)</td>
<td>-0.01</td>
<td>0.916</td>
<td>26.87 (4.82)</td>
<td>26.92 (4.92)</td>
<td>0.05</td>
<td>0.760</td>
</tr>
<tr>
<td>Body Fat (%)</td>
<td>22.67 (4.42)</td>
<td>22.04 (4.14)</td>
<td>-0.62</td>
<td>0.003*</td>
<td>22.95 (7.06)</td>
<td>23.55 (6.91)</td>
<td>0.60</td>
<td>0.166</td>
</tr>
<tr>
<td>Grip Strength (kg)</td>
<td>76.48 (16.33)</td>
<td>75.52 (13.07)</td>
<td>-0.95</td>
<td>0.634</td>
<td>73.53 (19.35)</td>
<td>75.00 (19.13)</td>
<td>1.47</td>
<td>0.385</td>
</tr>
<tr>
<td>Arm Strength-Elbow Flexion (kg)</td>
<td>35.95 (8.26)</td>
<td>36.25 (7.96)</td>
<td>0.30</td>
<td>0.753</td>
<td>32.14 (9.72)</td>
<td>32.76 (8.08)</td>
<td>0.62</td>
<td>0.546</td>
</tr>
<tr>
<td>Arm Strength-Elbow Extension (kg)</td>
<td>34.54 (6.87)</td>
<td>34.45 (6.90)</td>
<td>-0.09</td>
<td>0.910</td>
<td>30.60 (9.42)</td>
<td>31.28 (7.65)</td>
<td>0.68</td>
<td>0.521</td>
</tr>
<tr>
<td>Leg Strength-Knee Flexion (kg)</td>
<td>36.41 (6.34)</td>
<td>38.88 (7.11)</td>
<td>2.48</td>
<td>0.205</td>
<td>40.63 (5.34)</td>
<td>42.57 (5.75)</td>
<td>1.94</td>
<td>0.369</td>
</tr>
<tr>
<td>Leg Strength-Knee Extension (kg)</td>
<td>40.55 (8.91)</td>
<td>38.98 (7.66)</td>
<td>-1.57</td>
<td>0.484</td>
<td>43.23 (11.55)</td>
<td>40.06 (9.59)</td>
<td>-3.17</td>
<td>0.283</td>
</tr>
<tr>
<td>6MWT Post-HR (bpm)</td>
<td>108.67 (27.56)</td>
<td>106.00 (19.29)</td>
<td>-2.67</td>
<td>0.601</td>
<td>109.47 (12.76)</td>
<td>112.73 (20.60)</td>
<td>3.27</td>
<td>0.440</td>
</tr>
<tr>
<td>6MWT Distance (m)</td>
<td>601.05 (79.13)</td>
<td>616.52 (73.95)</td>
<td>15.48</td>
<td>0.205</td>
<td>575.47 (122.00)</td>
<td>587.07 (127.37)</td>
<td>11.60</td>
<td>0.503</td>
</tr>
</tbody>
</table>

Per-protocol analysis; data are presented as mean within-group difference; ¹ = follow-up – baseline; PREHAB = prehabilitation; CON = control; cm = centimeters; kg = kilograms; kg/m² = kilograms per meter squared; BMI = body mass index; 6MWT = 6-minute walk test; HR = heart rate; bpm = beats per minute; m = meters; * statistically significant change (p ≤ 0.05).
CHAPTER 4: DISCUSSION

4.1) Discussion of Feasibility Findings

The primary objective of this study was to assess the feasibility and safety of conducting an adequately powered, mixed-modality exercise intervention in the home-based setting for PCa patients scheduled for RP. To our knowledge no studies have assessed recruitment to a comprehensive home-based exercise intervention in the PCa population pre-operatively. Also, as it was the first pre-operative exercise intervention to be conducted at our institution's Prostate Centre, it was uncertain whether patients would be interested in participating in this type of study.

Our accrual target (n = 50) was achieved within 19 months of study initiation at a recruitment rate of 44.2%. This recruitment rate falls within the range of previously reported findings for exercise trials in men with PCa ranging from 14-64%90,91,120–122. During initial accrual, our research team observed several challenges that contributed to poor recruitment at our institution, including; i) patients consenting to RP outside of traditional clinic times (i.e. physician’s offices pre- or post-clinic), ii) high volume clinics that did not allow sufficient time for study recruiters to approach all eligible patients, and iii) competing research trials in the pre-operative PCa population. Also, due to the nature of our study design and sample population, recruiters were approaching patients at a very emotional time when many were likely overwhelmed with receiving a cancer diagnosis and/or making difficult treatment decisions. As such, our study recruiters were highly sensitive to this and avoided situations that could
The Feasibility and Efficacy of Prehabilitation for Prostate Cancer Surgery

further stress patients. To address these challenges to recruitment, ~8 months into the study, our methods were revised to include mail and telephone initiated contact with patients. Our institution’s REB and the physicians from the Division of Urology were amenable to this approach. This was facilitated through communicating with the surgeons’ administrative assistants to collect contact information of patients consented to RP. This allowed us to approach eligible patients in a less stressful environment to consider participation, and helped us to improve the rate of enrollment to the study.

In addition to these pragmatic barriers to recruitment, we observed three primary reasons for impediments to study enrollment: patients on active surveillance (n = 43/205), medical/musculoskeletal contraindications (n = 42/205) and patients opting for a different treatment (n = 31/205) (i.e. ADT, RT, focal therapy, or alternative medicine) (Figure 1). Given that our sample population was older men between 40-80 years, it is not unusual in these patients to observe some form of contraindication which may limit the ability to perform regular exercise even at a moderate-intensity, as was prescribed to our intervention group. In further relation to the barriers of our recruitment efforts, a reduction in the PCa surgical population has been evident in recent years, as demonstrated by a decline in the amount of RPs performed in Canada. In fact, between 2011-2013 a 12% decrease was observed across Canada (8,230 RPs versus 7,262 RPs), which was the greatest decline shown in the last decade. This may possibly be a consequence of a declining PCa population in Canada, as an average decrease of 3.8% in newly diagnosed cases has been observed
The Feasibility and Efficacy of Prehabilitation for Prostate Cancer Surgery

annually from 2006-2012\textsuperscript{141,142}. Moreover, the treatment trends for low-risk PCa in recent years indicate a rise in the practice of active surveillance as a management strategy for localized disease. Within Canada, active surveillance for PCa management has increased by 23.8\% (from 46.1-69.9\%) between 2010-2013\textsuperscript{143}. Similarly, this trend has been observed in other countries such as the United States, Sweden and Australia, reporting rates between 40-67\% for low-risk cases foregoing treatment and pursuing active surveillance, respectively\textsuperscript{144–147}.

Another barrier to study enrollment was lack of transportation and/or being too distant from the site (n = 25/63) (Figure 1). A recently published feasibility study of prehabilitation prior to gastrointestinal surgery for cancer also experienced a majority of eligible patients declining to participate due to travel related issues\textsuperscript{148}. Moreover, the challenge of recruiting patients to an urban-based exercise intervention due to transportation barriers (i.e. distance, expense, and time) has been previously reported in exercise literature within the cancer population\textsuperscript{60,149–152}. Our urban-based site may have been perceived as unappealing to those traveling from outside of the city due to concerns such as: parking availability, cost of gas/parking/transit, commuting time/traffic, and/or navigating through the public transit system. An attempt was made to minimize the impact of these potential burdens through the following strategies: parking/travel reimbursements ($20 per study visit), and offering to coordinate study visits with already planned hospital appointments. The second of these strategies may have been particularly important to the subsequent success of our
enrollment, as an average of participants were in their early sixties with the majority still in the work force during the study period (62%; full-time = 21/50; part-time = 10/50) (Table 1). For a phase III study, it would be ideal to expand study sites to include an urban and rural location to provide more options for eligible patients living outside of urban areas. This may potentially serve as beneficial towards improving the frequency of participant enrollment and overall study retention. However, as the primary outcome of interest in our study was feasibility, financial resources were limited for: hiring additional staff, finding another facility to conduct fitness assessments, and equipping the facility with assessment tools required; thus making a secondary rural study site as unviable.

With respect to exercise adherence, which was defined as achieving the minimum (or higher) prescribed training, the prehabilitation intervention was feasible. Over 75% of the PREHAB group adhered to the exercise prescription from baseline to pre-operative follow-up (n = 16/21) (Table 5). In comparison, previously examined home-based exercise interventions in the PCa population report moderate to high levels of adherence, ranging from 49-97%\(^{91,122,132,153–155}\). Specifically in the surgical oncology setting, prehabilitation intervention adherence rates range from 16-97%\(^{105,106,148,156}\). The level of adherence demonstrated in among the PREHAB participants may be attributed to the following factors: i) high motivation driven by a desire for optimal post-RP recovery; ii) our methods utilized to address barriers to exercising in the home-based setting (e.g. provision of exercise equipment, participant study manual, and online aerobic stepping exercise video); and iii) weekly reminders by the RC.
The Feasibility and Efficacy of Prehabilitation for Prostate Cancer Surgery

Conversely, adherence to PFMX was low overall in both study arms, as only 38.1% (n = 8/21) and 26.7% (n = 4/15) of PREHAB and CON participants fully adhered, respectively (Table 5). The difference of prescription volume achieved between groups (including non-adherers) did not reach statistical significance (PREHAB = 75.1% versus CON = 74.4%; p = 0.955). The modest adherence to PFMX was despite both groups receiving education in plain language on PFMX anatomy, function, and visualization and sensation techniques. This was reinforced with a participant study manual containing the same information for to refer back to as needed. Previous reports of adherence to PFMX interventions in the PCa surgical population range from 21-100%\textsuperscript{157,158}. Prioritizing PF MX has been shown to be facilitated by: confidence, optimism, and/or perception of anticipated training effect; all which require conscious preparation and the ability to deal with obstacles\textsuperscript{159}. Moreover, full comprehension and the mastery of the skill to achieve a sufficient PFMX contraction can support confidence and promote self-efficacy\textsuperscript{159}. During weekly RC communication, both groups had the opportunity to address concerns regarding PFMX or other areas of the study. The absence of self-perceived benefits and/or value gained by PFMX pre-operatively, when little to no issue with urinary leakage is present, may have contributed to the modest adherence in both study arms. A phase III study employing PFMX would be recommended to incorporate more sophisticated behavioural change techniques/support to facilitate better adherence and further address the concerns stated above. Still, our observed adherence to total-body exercise and PFMX should be interpreted with caution, as this information was
The Feasibility and Efficacy of Prehabilitation for Prostate Cancer Surgery

self-reported and carries the risk of a social desirability bias. To reduce the possibility of ending up with incomplete logbooks and unusable data, both groups were informed at the initial study visit that weekly contact would occur with the RC and included the monitoring of variables related to study adherence. This was a detail of the study design particularly important to emphasize, as previous studies had to limit or exclude the analysis of logbooks because of poor completion or incomplete data\textsuperscript{160,161}. The ideal design for a future phase III study would incorporate on-site training, rather than home-based exercise, to reduce the risk of a self-reporting bias and ensure training volume and intensity are actually achieved.

As for overall study withdrawals, from baseline to follow-up we observed an attrition rate of 24% (n = 12/50), which modestly exceeded our anticipated rate of 20%. This attrition rate falls within the 13-34% observed previously in PCa exercise trials\textsuperscript{57,122,132,162}. Moreover, our study also falls within varying attrition rates of 9-28% reported previously by prehabilitation interventions in the cancer population\textsuperscript{105,156,163}. Collectively, the most frequent reasons for withdrawing from the study were lost to follow-up without explanation (n = 6/12) and no time (n = 4/12). The most prevalent reason for CON dropout was lost to follow-up without explanation (n = 5/8), and all PREHAB dropouts had dissimilar reasons for withdrawing from the study such as: no time (n = 1), loss of interest/motivation (n = 1), lost to follow-up without explanation (n = 1), and self-determined inability to participate (n = 1). To address the possibility of lost contact with participants, future interventions of prehabilitation in the PCa
The Feasibility and Efficacy of Prehabilitation for Prostate Cancer Surgery

population should consider incorporating incentive strategies to better facilitate motivation to continue participation, such as partnered training with a spouse or family member\textsuperscript{164}.

Finally, the comprehensive prehabilitation program in our study was safe for participants and there were no adverse events related to the exercise intervention. Furthermore, no injuries or adverse events occurred during fitness testing at baseline or follow-up. Previously, trials of exercise in the PCa population have been safely examined with serious adverse events only described in one trial, '15 min after finishing an AE session a man with no cardiac history experienced an acute myocardial infarction resulting in hospitalization\textsuperscript{190}. Nevertheless, the observations from our study suggest the safety of pre-operative exercise for the PCa population in the home-based setting.

4.2) Discussion of HRQOL and Fatigue Findings

To our knowledge, this is the first RCT to examine the efficacy of a comprehensive home-based prehabilitation program on psychosocial well-being for men undergoing RP for PCa. There were no observed between-group differences in HRQOL or fatigue post-study (Table 6). However, the PREHAB group did demonstrate a statistically significant within-group increase in EWB (mean within-group $\Delta = +0.82; p = 0.036$) and a statistical trend toward improved overall HRQOL (mean within-group $\Delta = +2.99; p = 0.081$) (Table 7). The minimal clinically important difference for the FACT-P is 5.5 points and overall scores can
range from 0-156, with a higher score indicating better HRQOL\textsuperscript{124,126}. The high FACT-F scores demonstrated at baseline in the PREHAB group (Table 1) may have limited the opportunity for further improvement and potentially lends to the lack of change to this measure during the pre-operative period. Overall FACT-F scores can range from 0-52, with higher scores providing indication of less fatigue\textsuperscript{165}. This finding is not unexpected or unusual, as early stage PCa is typically asymptomatic at diagnosis. Therefore, this measure may not be relevant when examining the efficacy of a pre-operative exercise intervention in the PCa population; however, as physical and mental deficits are likely to occur post-RP this attribute may become more pertinent to monitor during the post-operative period. Nevertheless, our findings suggest that the comprehensive prehabilitation program of mixed-modality exercise in the home-based setting was able to positively alter EWB and overall HRQOL in PCa patients pre-RP; although, no benefits were observed to fatigue measures due the marginal concern at baseline. Similar findings have been observed previously in the cancer exercise literature. Studies report the efficacy of AE to improve psychosocial well-being in the surgical and non-surgical PCa population undergoing RT, through reducing symptoms of anxiety and depression, subsequently leading to better HRQOL\textsuperscript{90,91}. However, our findings contrast those reported in previous interventions of unsupervised and mixed-modality exercise in men with PCa undergoing ADT, as these studies observed no effect to HRQOL\textsuperscript{122,132,166}. Moreover, conflicting evidence also exists among studies of prehabilitation in the surgical population, with some reporting positive pre-operative changes to psychosocial well-being\textsuperscript{167},
The Feasibility and Efficacy of Prehabilitation for Prostate Cancer Surgery

while others suggest no effect\textsuperscript{168–170}. Further research, which examines the efficacy of pre-operative exercise in the PCa population, is required to substantiate the findings of our current study.

The negative impact to psychosocial well-being in PCa patients surfaces early on, close to diagnosis, as it has been previously shown that nearly 40% of men exhibit high levels of anxiety around this time\textsuperscript{71–75}. This undesirable effect is also common among surgical patients in general and may not only be associated with the diagnosis, but also disease management, along with the impending post-operative limitations (e.g. requirement for catheter)\textsuperscript{171}. At a time when unfavourable psychosocial detriments are likely to occur, both groups in our study demonstrated either maintenance or modest non-significant improvements to baseline HRQOL and fatigue. This preservation may be construed as an attention effect, as support above the pre-operative standard of care was provided to each study arm.

Non-intervention participants (CON) were not prohibited from engaging in PA while enrolled in the study, therefore group contamination may also explain the observed maintainence in HRQOL and fatigue in the CON arm. Though we are unable to substantiate this association as we did not foresee the need to gather data on potential contamination sources, including outside PA. Nevertheless, restricting patients from engaging in positive behaviours conducive to their health and well-being may be percieved as unethical; moreover, outside PA can be challenging to control in the research setting. All participants were well informed of the studys’ purpose and provided with clear instructions known to
The Feasibility and Efficacy of Prehabilitation for Prostate Cancer Surgery

them to follow. However, it is plausible that some had greater knowledge of exercise benefits stemming from prior experience or outside sources (e.g. family, media, etc.), and initiated or increased frequency of this behaviour. Under-reporting contamination is frequent among previous interventions of exercise in the cancer population, with rates of 15-50% being reported\textsuperscript{90,172,173}. A phase III trial would be strengthened through strict monitoring of group contamination and including an interactive control factor. Substituting the design of a non-exercising control group for low-intensity exercise, flexibility training, or breathing/meditation, may divert non-intervention participants from performing outside PA intense enough to influence physical and psychosocial outcomes. In addition to its potential use for monitoring exercise adherence, tracking daily steps or PA in general, through health-tracking applications (e.g. accelerometer, online PA diary) may be an advantageous tool for observing group contamination in exercise interventions. Furthermore, the exclusion of patients with prior exercise knowledge/experience may also reduce the risk of group contamination and better serve study outcomes, as less fit patients have previously demonstrated better adaptations to the stimulus of training\textsuperscript{113}. However, this exclusion criteria should be carefully taken into consideration as it may limit generalizability and hinder study enrollment, since these patients have the tendency to not partake in exercise interventions\textsuperscript{174}.
4.3) Discussion of Physical Fitness Findings

Participants in the PREHAB study arm demonstrated positive changes to functional capacity (i.e. 6MWT performance) and some measures of body composition (i.e. WC and BF%). However, these changes were not of statistical significance in direct comparison with the CON group, except for a difference in BF% in favor of PREHAB (mean between-group $\Delta = -1.43\%$; $p = 0.019$) (Table 8). Moreover, the PREHAB group demonstrated significant within-group changes post-study in WC (mean within-group $\Delta = -1.24\,\text{cm}$; $p < 0.001$) and BF% (mean within-group $\Delta = -0.62\,\%$; $p = 0.003$) (Table 9), indicative of improved body composition. Positive changes in body composition are of particular importance to cancer patients since earlier disease recurrence and reduced survival has been linked to adipose tissue accrual following cancer diagnosis$^{175}$. However, it is unclear whether these adaptations occurred as a direct result of the exercise intervention; it is plausible that the PREHAB group may have also been motivated to improve dietary behaviours while enrolled in the study, subsequently contributing to the positive changes demonstrated in BF% and WC. Additionally, there may have been some influence to dietary behavior from the informational booklet, ‘Challenging Prostate Cancer – Nutrition, Exercise and You’, provided to both groups at the initial study visit$^{118}$. However, we cannot verify the likelihood of this contamination since dietary behaviour was not monitored in our study. Future studies of prehabilitation in the pre-operative PCa population would be recommended to observe dietary behaviour through methods such as: a 3-day food diary or smartphone/web applications (e.g. MyFitnessPal$^\text{TM}$); and grouping
The Feasibility and Efficacy of Prehabilitation for Prostate Cancer Surgery

participants based on dietary behaviours to during analysis to evaluate the impact on body composition within an exercise intervention.

The PREHAB group also demonstrated a clinically important (although not statistically significant) between-group difference in 6MWT performance (mean between-group $\Delta = +25.58$ m; $p = 0.344$) post-study, suggestive of improved functional capacity. Previously determined in healthy elderly subjects, 20 m has been shown to represent a minimum clinically important change for the 6MWT\textsuperscript{137}. Though our limited sample size raises caution to interpretation, similar positive effects to functional capacity (i.e. sub-maximal aerobic fitness) have been reported in a recently published systematic review and meta-analysis of the PCa exercise literature\textsuperscript{176}, as well as in prehabilitation literature in the broader surgical population\textsuperscript{104,105,177,178}. Functional capacity is an important consideration after PCa diagnosis, as low functional ability has been suggested to impact mortality risk\textsuperscript{76} and mobility issues\textsuperscript{77} in the elderly. Similarly, diminished functioning ability in cancer survivors has also shown to be correlated with reduced aerobic capacity\textsuperscript{78}. However, it is worth noting that the 6MWT should not be perceived as a substitute for direct cardiorespiratory exercise testing, but rather a compliment to such testing and reflecting functional capacity\textsuperscript{179,180}. Moreover, our observed positive changes in functional capacity should be interpreted with caution, as previously, performance of the 6MWT has been shown to be influenced by a familiarization effect\textsuperscript{136,181,182}. Conversely, this test may also be less sensitive to detect changes in subjects with minimal functional limitations compared to those with more severe disability\textsuperscript{183}, therefore we may observe more significant findings
The Feasibility and Efficacy of Prehabilitation for Prostate Cancer Surgery

post-RP when physical limitations are likely to occur. This may also speak to the absence of changes to physical strength observed in our PREHAB group; therefore we may actually observe greater efficacy from the intervention in the post-operative period.

The mean duration of our PREHAB intervention (42.1 days) falls in line with recommendations published in a review of the prehabilitation literature by Carli et al.\textsuperscript{102}, which describe 4 weeks as the minimum time, required to produce sufficient benefits in a pre-operative intervention. Conversely, recent exercise literature in healthy\textsuperscript{184}, obese\textsuperscript{177}, and post-infarction heart failure populations\textsuperscript{185} indicated that 12 weeks may be the ideal intervention duration to elicit training adaptations. Moreover, previous exercise interventions of 12-18 weeks have also demonstrated the ability to enhance physical strength and aerobic fitness in the cancer survivors post-treatment\textsuperscript{186,187}. Inadequate pre-operative intervention duration may have attributed to the absence of significant physical adaptations observed in our study. However, prolonging the intervention was not possible unless patients intentionally delayed treatment. Postponing surgery for a duration sufficient enough to reach optimal physical and mental condition may benefit post-operative recovery\textsuperscript{156}; however, this may be concerning in relation to disease progression and long-term prognosis. Studies has previously shown that the modest deferrals in disease management are not correlated with worse survival in patients with lung cancer\textsuperscript{188,189}; however, this concern has not been adequately examined in other diseased populations. Therefore, acquiring REB
The Feasibility and Efficacy of Prehabilitation for Prostate Cancer Surgery

approval for a study design that incorporates delayed treatment may pose as difficult.

When examining the lack of significant physical adaptations observed in our PREHAB group, with respect to our study design, exercise intensity is an important variable to reflect upon. Despite the provision of exercise equipment and additional support (i.e. weekly calls, participant study manuals, etc.) to facilitate the intervention, the stimulus of training at a moderate-intensity may not have been sufficient to produce noticable changes over the brief pre-operative period. Moreover, the self-reported exercise intensity/RPE achieved by participants may have been overstated, and not truly reflective of the level of exertion performed. A preferable method for observing training intensity would be average exercise heart rate (via heart rate monitor) measured within exercise sessions. This would serve to reduce subjectivity, with respect to training exertion levels, and minimize the probability of a social desirability bias in future prehabilitation studies. Furthermore, interventions that incorporate resistance bands, such as ours, require familiarization and confidence to be utilized effectively; otherwise, lack of proficiency may hamper the ability to achieve the intended training intensity/stimulus. Moreover, it is also difficult to objectively monitor exercise progression when using resistance bands in comparison to systematic increases in weight possible with dumbbells or pulley machines. A 1-week on-site familiarization period, or the inclusion of in-facility booster sessions, may address the concern of equipment proficiency in future studies and ensure optimal exercise execution to best achieve the prescribed training intensity.
The Feasibility and Efficacy of Prehabilitation for Prostate Cancer Surgery

Assuming the PREHAB group actually performed the prescribed exercise intensity during the pre-operative period, given the lack of significant physiological changes observed, that may warrant the examination of high-intensity training (HIT) in future studies of a similar design. In a meta-analysis of exercise interventions in the cardiometabolic disease population, Weston et al.\textsuperscript{190} reported improvements in VO\textsubscript{2}peak uptake nearly 2-fold from HIT (19.4\% versus 10.3\%; p = ) versus continuous exercise performed at a moderate-intensity. Moreover, a growing body of literature supports the efficacy of HIT in special populations, including cancer\textsuperscript{187,191,192}. In fact, a recently published review examining training variables (i.e. frequency, intensity, time, type) used in exercise literature provides recommendations for pre-operative exercise interventions. Authors concluded that the optimal pre-operative intervention should be both effective and time-efficient. Further describing that a HIT intervention which is supervised, customized/adapted to each patient, and includes all major muscles, is efficacious for improving patient care and post-operative outcomes\textsuperscript{193}.

During the pre-operative study period, PREHAB participants achieved a weekly average of 236.4 min (SD = 68.6) of moderate-intensity exercise, which if continued regularly may offer benefits to survival and lessen disease-specific mortality\textsuperscript{68,194}. Moreover, the benefits of achieving 150 min of moderate-intensity PA were reported by Santa Mina et al.\textsuperscript{87} to improve HRQOL and UI earlier post-RP, in comparison to men not performing this volume of PA. Despite the modest pre-operative changes demonstrated in our study, our pending analysis of post-
The Feasibility and Efficacy of Prehabilitation for Prostate Cancer Surgery

RP measures (i.e. up to 6 months post-RP) may better reflect the potential utility of prehabilitation in the surgical PCa population.

4.4) Study Limitations

There are several limitations which necessitate caution when interpreting the findings of our study. The primary outcome was to evaluate feasibility for future pre-operative exercise interventions in the PCa population, and was not intended to definitively assess intervention efficacy. Our study was underpowered to conclusively demonstrate between- and within-group differences of PREHAB and CON. However, our findings still offer a meaningful preliminary investigation of a home-based and mixed-modality exercise intervention in this population. Neither study participants or assessors were unaware of group allocation. Blinding participants in exercise trials is essentially impossible. Our participants were required to follow group-specific protocols, therefore we were unable to implement blinding to intervention allocation. Moreover, blinding the principal outcome assessor (WH) was not possible, as we operated the study with limited financial reserves and staffing resources. Though, blinding should be attempted when possible to minimize the risk of assessor bias. Also, high chance of a substantial researcher's bias may be a critique of our study, as the principal outcome assessor (WH) also worked as the RC and recruiter. Given the availability of sufficient resources, future studies of this design should appoint the role of RC, outcome assesor and recruiter to separate individuals in order to minimize the risk of this potential bias.
4.5) Study Strengths

Despite the limitations of this study, there are also several strengths that deserve mention. Conducting a RCT design is one strength of our study, as it allowed for the direct comparison of the comprehensive home-based exercise intervention against a control group of standard PFMX pre-RP; something that has not been done previously in the PCa setting. Attrition and/or contamination of a non-exercising control group are concerns among exercise interventions, including ours. To maintain the CON groups’ interest during the pre-operative study period, we contacted participants on a weekly basis and provided support regarding the PFMX prescription. This communication allowed participants to address any difficulties with achieving PFMX proficiency and obstacles to study adherence. To minimize the risk of group contamination, CON participants were offered post-study exercise support (initiated after the 6 month post-operative follow-up) via our clinical program (Wellness and Exercise for Cancer Survivors) at the Princess Margaret Cancer Centre. However, this offer may not have been appealing to CON participants; as motivation to exercise resulting in group contaminating may have been greatest shortly after randomization, a time most influential to study efficacy. Nevertheless, purposefully denying a beneficial therapy (i.e. exercise) in order to demonstrate the efficacy of its modalities in others may be seen as unethical. Given the current body of literature that supports the efficacy of exercise for PCa survivors, it may have been more appropriate to address the concern of group contamination by attempting to control for the
The Feasibility and Efficacy of Prehabilitation for Prostate Cancer Surgery

volume and/or intensity of outside PA, through modalities such as: low-intensity exercise (e.g. walking, light RE), flexibility training or meditation.
CHAPTER 5: CONCLUSION

Given the rising interest and literature in this field, the effects of prehabilitation on surgical recovery is perhaps the most rapidly advancing area of exercise study. The aim of this study was to investigate the feasibility of a comprehensive home-based prehabilitation program in PCa patients scheduled for RP and examine its efficacy on physical and psychosocial well-being; to our knowledge this is the first RCT to do so in this population. We were able to demonstrate that this study design was feasible, safe, and able to elicit positive changes to HRQOL, body composition and functional capacity in favor of the PREHAB group, although no changes occurred to physical strength or fatigue. Moreover, during the pre-operative study period, PREHAB participants were able to achieve a weekly average of 236.4 min of exercise, which may provide post-operative benefits. The findings of this study build upon previous literature in surgical oncology that highlighted the benefits of pre-operative PA for post-RP convalescence. However, we cannot yet compare our prehabilitation program with others previously described in the literature, as the actual efficacy of our pre-operative exercise intervention may be demonstrated post-RP. Nevertheless, our study contributes to the overall literature of prehabilitation effects in oncology and provides a better understanding of the challenges to feasibility and pre-operative efficacy. Furthermore, these current findings not only provide beneficial insights to the field of research, but also the clinical practice setting, with respect to assisting patients and health care clinicians in further understanding the benefits and tolerability of pre-operative exercise in this specific population.
The Feasibility and Efficacy of Prehabilitation for Prostate Cancer Surgery

References


48. Powel LL. Quality of life in men with urinary incontinence after prostate


64. Smith DP, King MT, Egger S, et al. Quality of life three years after...
The Feasibility and Efficacy of Prehabilitation for Prostate Cancer Surgery

diagnosis of localised prostate cancer: population based cohort study. 


80. Molton IR, Siegel SD, Penedo FJ, et al. Promoting recovery of sexual


The Feasibility and Efficacy of Prehabilitation for Prostate Cancer Surgery


The Feasibility and Efficacy of Prehabilitation for Prostate Cancer Surgery


The Feasibility and Efficacy of Prehabilitation for Prostate Cancer Surgery

140. Canadian Institute for Health Information. The Delivery of Radical Prostatectomy to Treat Men With Prostate Cancer. 2014;(August).


169. Peddle CJ, Jones LW, Eves ND, et al. Effects of Presurgical Exercise...
The Feasibility and Efficacy of Prehabilitation for Prostate Cancer Surgery


The Feasibility and Efficacy of Prehabilitation for Prostate Cancer Surgery


Appendices

Appendix 1: REB Approval: University of Guelph
Appendix 2: REB Approval: University Health Network
Appendix 3: Informed Consent Form
Appendix 4: Participant Approach List
Appendix 5: Email Consent Form
Appendix 6: Study Participant Screening Tool
Appendix 7: Study Recruitment Poster
Appendix 8: Letter of Invitation to the Study
Appendix 9: Web Link to Aerobic Stepping Exercise Video
Appendix 1: REB Approval: University of Guelph

The members of the University of Guelph Research Ethics Board have examined the protocol which describes the participation of the human participants in the above-named research project and considers the procedures, as described by the applicant, to conform to the University’s ethical standards and the Tri-Council Policy Statement, 2nd Edition.

The REB requires that researchers:
- Adhere to the protocol as last reviewed and approved by the REB.
- Receive approval from the REB for any modifications before they can be implemented.
- Report any change in the source of funding.
- Report unexpected events or incidental findings to the REB as soon as possible with an indication of how these events affect, in the view of the Principal Investigator, the safety of the participants, and the continuation of the protocol.
- Are responsible for ascertaining and complying with all applicable legal and regulatory requirements with respect to consent and the protection of privacy of participants in the jurisdiction of the research project.

The Principal Investigator must:
- Ensure that the ethical guidelines and approvals of facilities or institutions involved in the research are obtained and filed with the REB prior to the initiation of any research protocols.
- Submit a Status Report to the REB upon completion of the project. If the research is a multi-year project, a status report must be submitted annually prior to the expiry date. Failure to submit an annual status report will lead to your study being suspended and potentially terminated.

The approval for this protocol terminates on the EXPIRY DATE, or the term of your appointment or employment at the University of Guelph whichever comes first.

Signature:  
Date: December 19, 2014

A. Papadopoulos  
Chair, Research Ethics Board-NPES
Appendix 2: REB Approval: University Health Network

Date: September 26th, 2013
To: Dr. Andrew Matthew

Re: 13-6303-CE
Prehabilitation for Prostate Cancer Surgery

ReB Review Type: Expedited
ReB Initial Approval Date: September 26th, 2013
ReB Expiry Date: September 26th, 2014

Documents Approved:
- Protocol
- Consent Form - Main
- Consent Form - Consent for E-mail Communications
- Participant Screening Tool
- Questionnaire - Prostate Outcomes Record of Psychometric and Utility Self-Report
- Questionnaire - International Index of Erectile Function (IIEF)
- Questionnaire - Pain Disability Index
- Questionnaire - Hospital Anxiety and Depression Scale
- Questionnaire - Functional Assessment of Cancer Therapy - Prostate
- Questionnaire - Demographics
- Questionnaire - Functional Assessment of Cancer Therapy - Fatigue
- Questionnaire - International Prostate Symptom Score (IPSS)
- Questionnaire - CHAMPS Activities Questionnaire for Older Adults

Documents Acknowledged:
- Data Collection Form

Version dates:
- Consent Form - Main: September 25th, 2013
- Consent Form - Consent for E-mail Communications: December 8th, 2010
- Participant Screening Tool: May 28th, 2013
- Questionnaire - Prostate Outcomes Record of Psychometric and Utility Self-Report: May 28th, 2013
- Questionnaire - International Index of Erectile Function (IIEF): May 28th, 2013
- Questionnaire - Pain Disability Index: May 28th, 2013
- Questionnaire - Hospital Anxiety and Depression Scale: May 28th, 2013
- Questionnaire - Functional Assessment of Cancer Therapy - Prostate: May 28th, 2013
- Questionnaire - Demographics: May 31st, 2013
- Questionnaire - Functional Assessment of Cancer Therapy - Fatigue: May 28th, 2013
- Questionnaire - International Prostate Symptom Score (IPSS): May 28th, 2013
- Questionnaire - CHAMPS Activities Questionnaire for Older Adults: May 28th, 2013

Received on: May 28th, 2013

The UHN Research Ethics Board operates in compliance with the Tri-Council Policy Statement: ICH Guideline for Good Clinical Practice E6(R1); Ontario Personal Health Information Protection Act (2004); Part C Division 5

Page 1 of 2

xvi
of the Food and Drug Regulations; Part 4 of the Natural Health Products Regulations and the Medical Devices Regulations of Health Canada. The approval and the views of the REB have been documented in writing.

Furthermore, members of the Research Ethics Board who are named as Investigators in research studies do not participate in discussions related to, nor vote on such studies when they are presented to the REB.

Best wishes on the successful completion of your project.

Sincerely,

Jack Holland, MD FRCPC
Co-Chair, University Health Network Research Ethics Board
Appendix 3: Informed Consent Form

Consent to Participate in a Research Study

Title: Prehabilitation for Prostate Cancer Surgery

Principal Investigators: A.G. Matthew, Ph.D. and D. Santa Mina, PhD

Co-Investigators: S.M.H. Alibhai, MD; P. Ritvo, Ph.D; L.Spriet, Ph.D; H. Clarke, MD, PhD; D. Wijeyasundera, MD, PhD; A. Finelli, MD, N. Fleshner, MD; L.E. Stefanyk, Ph.D., F. Carli, MD; J. Trachtenberg, MD

24-Hour Emergency Phone Number: t

Introduction
You are being asked to take part in a research study. Before agreeing to take part in this study, it is important that you read and understand the study procedures. The following information describes the purpose, procedures, benefits, and risks associated with this study. It also describes your right to refuse to participate or withdraw from the study at any time. In order to decide whether you want to participate in this research study, you should understand enough about its risks and benefits to be able to make an informed decision. This is known as the informed consent process. Please ask the study staff to explain any words you do not understand before signing this consent form. Make sure all your questions have been answered to your satisfaction before signing this document.

The principal investigators of this research study are Dr. Andrew Matthew and Dr. Daniel Santa Mina. The research coordinator for this study is William Hilton.

Background/Purpose
Currently, the standard of care for men with prostate cancer who choose to undergo surgery does not usually include exercise programming. However, recent studies have shown that exercise and physical fitness can help reduce some of the negative side effects related to surgery for prostate cancer. Unfortunately, little is known about the effects of an exercise program introduced prior to surgery on patients’ physical and psychological well-being. It is important to examine whether exercise introduced prior to surgery, known as prehabilitation, can benefit men with prostate cancer undergoing surgery. We are measuring the effect of a prehabilitation program (exercise program prior to surgery) for men undergoing prostate cancer surgery (radical prostatectomy) to see whether or not it can improve physical and psychological well-being after surgery. The evaluation of prehabilitation will assist in developing future programs aimed at reducing the side effects of prostate cancer treatment.

Study Design
The type of study you are asked to participate in is called a “randomized controlled trial”. This means that you will be randomly assigned to either a treatment group (prehabilitation) or a control group (standard care). Approximately 100 men with prostate cancer who are scheduled to undergo surgery (radical prostatectomy) will be asked to participate in this study, 50 of these men will be from the Princess Margaret...
The Feasibility and Efficacy of Prehabilitation for Prostate Cancer Surgery

Cancer Centre and the other 50 will be from the McGill University Health Centre.

Study Visits and Procedures
Should you decide to participate, you will be required to make 5 visits to the University Health Network (Toronto General Site). Each visit will last approximately 1 hour, except for the first visit that will be approximately 2 hours.

Screening
Prior to participating in this study, you will be asked some questions that will help us understand if you are eligible for the study. These questions will be about your health and physical fitness. Some of these questions are part of standard of care while some are being done solely for the study.

Randomization
If you agree to participate in the study, you will be randomly assigned to either the prehabilitation group or the control group. Whether you are placed in the exercise group or the control group will be decided randomly (by chance), like flipping a coin. There will be 25 men in the exercise group and 25 men in the control group.

Prehabilitation Group
If you are assigned to the prehabilitation group, you will be provided with a home-based exercise program to complete 3-4 times per week up until the date of surgery. A certified exercise specialist will individually tailor your exercise program to your physical capacity. Each exercise session will be 60 minutes long and consist of aerobic (cardiovascular) exercises and resistance training exercises that have been pre-selected by your exercise specialist. Specifically, each session will include 5 minutes of warm-up, 25 minutes of moderate intensity aerobic exercise (light step aerobics), 25 minutes of moderate intensity resistance training (using resistance bands, free weights and stability balls), and a 5 minute cool-down including some stretching. The entire exercise session is considered moderate intensity and minimal risk. You will also be asked to routinely complete exercises specifically for your pelvic floor to assist your surgical recovery. Your exercise specialist will instruct you on how to do these and will provide a specific number for you to complete on a daily basis that will likely take 5-10 minutes. To support your exercise program, you will be provided with an exercise manual (on paper or video), a set of resistance bands, a stability ball, and an exercise mat. You can keep this equipment at the end of the study. You will also be given a heart rate monitor to assist you with maintaining the appropriate cardiovascular exercise prescription. You will be asked to return the heart rate monitor at the end of the prehabilitation program; however, there will be no penalty to you should you lose or damage it. To assist you with your participation in the program, you will receive weekly telephone calls from your exercise specialist.

Control Group
If you are assigned to the control group, you will be asked to routinely complete exercises specifically for the pelvic floor to assist your surgical recovery. Your exercise specialist will instruct you on how to do these and will provide a specific number for you to complete on a daily basis that will likely take 5-10 minutes. To support your pelvic floor exercises, you will receive weekly telephone calls from your exercise specialist. These exercises are considered low intensity and minimal risk.

Study Measurements
All participants (prehabilitation and control) will be required to complete study measurements at the beginning of the trial, 1 week before surgery, and at approximately 4, 12, and 26 weeks after surgery. The study measurements are briefly described below. A certified exercise specialist will conduct all physical measurements.
The Feasibility and Efficacy of Prehabilitation for Prostate Cancer Surgery

6-Minute Walk Test
The 6-minute walk test is being conducted to test your functional cardiovascular fitness. During this test you will walk back and forth over a 15-meter path and your total distance after 6 minutes will be recorded. This is a low intensity test and requires only walking.

Physical Strength
Your physical strength will be measured through a simple test of grip strength using a small device that you will squeeze. We will also be testing your upper body strength using a small device that will require you to extend and flex your elbows against some resistance.

Body Composition
We will be measuring your height, weight, waist circumference and body fat percentage. Your body fat percentage will be measured using a device called a bioelectrical impedance analyzer (BIA) that will calculate your body fat percentage. This device requires you to stand on a scale barefoot. You will not feel anything and there are no risks related to this measurement.

Post-surgery Physical Activity Volume
While you are in the hospital following surgery, you will be provided with a small, wrist-watch device that will measure your movement. You will wear this during your hospital stay and during your time at home once you leave the hospital. You will wear this at home until you return to the hospital when you have your catheter removed. A staff member from this study will collect the device from you when you return to the hospital for this appointment. You will not feel anything and there are no risks related to this measurement.

Questionnaires
You will be asked to complete a demographics questionnaire at the beginning of the study and 4 brief questionnaires that ask about how you are currently feeling. You may choose to not answer any questions on the questionnaires that you do not feel comfortable answering.

The questionnaires included in this study are:
- Demographics Questionnaire (~5 min)
- Fatigue Questionnaire (~5 mins)
- Anxiety and Depression Questionnaire (~5 mins)
- Quality of life Questionnaire x 2 (~10 mins)
- Pain Questionnaire (~5 mins)
- Erectile Function Questionnaire (~5 mins)
- Urinary Continence Questionnaire (~5 mins)
- Physical Activity Volume Questionnaire (~10 mins)

The type of questions you will be answering in the questionnaires:
- State your marital status.
- How would you rate your fatigue?
- How often have worrying thoughts on your mind?

All information gathered during the assessments will be kept strictly confidential.

Note: If, on any questionnaire or during the fitness assessment, it is apparent that you may require additional treatment from a healthcare professional (that may or may not be a part of the study team) you will be referred to that service for appropriate consultation and treatment if necessary.

Version Date: January 29, 2014
The Feasibility and Efficacy of Prehabilitation for Prostate Cancer Surgery

Reminders
- You should not conduct heavy physical activity on the day of your assessment
- You should not drink a caffeinated beverage before your visit
- You should not smoke before your visit
- You should not eat within 2 hours of your visit
- Tell your study team about anything that worries you
- Tell your study team about any changes to your treatments or medications
- Tell your study team if you change your mind about being in the study
- Ask your study team any questions related to the study and/or exercise program

Risks and Discomforts
Before agreeing to participate in this study, you should be aware that there are some risks to the study procedures. The risks of experiencing a cardiac incident (heart attack, chest pain, etc.) involved in completing the home-based exercise sessions are very minimal (approximately 1/20000 or 0.00005%). To minimize the risk, a certified exercise specialist will create a moderate intensity exercise program based upon your exercise experience and baseline physical fitness assessment. The prescribed exercise sessions will be within the guidelines of recommended exercise duration and intensity for prostate cancer patients and has been used in previous studies.

You will also be responding to questionnaires that have been used in numerous studies. There are minimal risks associated with answering these questions. You may refuse to answer any questions that you do not feel comfortable with.

Benefits of the Research and Benefits to You
You may not receive direct medical benefit from being in this study. Information learned from this study may help men with prostate cancer undergoing surgery in the future.

Voluntary Participation
Your participation in this study is voluntary. You may decide not to be in this study, or to be in the study now and then changing your mind later. You may leave the study at any time without affecting your treatment you may be receiving, the nature of your ongoing or future relationship that you may have with the researchers or study staff, or of your relationship with the University Health Network (Princess Margaret Cancer Centre/Toronto General Hospital) or the University of Guelph-Humber. You may refuse to answer any question you do not want to answer.

We will give you new information that is learned during the study that might affect your decision to stay in the study.

Confidentiality
If you agree to join this study, the study doctor and his study team will look at your personal health information and collect only the information they need for the study. Personal health information is any information that could be used to identify you and includes your:
- name, address, date of birth
- new or existing medical records, which includes types, dates and results of medical tests or procedures.

The study doctor will keep the information that is collected for the study in a locked and secure area for 10 years. Only the study team or the people or groups listed below will be allowed to look at your records.

Version Date: January 29, 2014
Your participation in this study also may be recorded in your medical record at this hospital.

Representatives of the Research Ethics Boards from University Health Network and the University of Guelph-Humber may look at the study records and at your personal health information to check that the information collected for the study is correct and to make sure the study followed proper laws and guidelines.

All information collected during this study, including your personal health information, will be kept confidential and will not be shared with anyone outside the study unless required by law. You will not be named in any reports, publications, or presentations that may come from this study. In the event you withdraw from the study, all associated data will be immediately destroyed wherever possible.

If you decide to leave the study, the information about you that was collected before you left the study will still be used. No new information will be collected without your permission.

If prehabilitation proves to beneficial for men with prostate cancer, programming and/or resources may be developed to support standard care for radical prostatectomy. If a resource is created, all of your information will be de-identified and your personal health information will remain confidential and secure.

In Case You are Harmed in the Study (Compensation for Injury)

If you become ill or are physically injured as a result of participation in this study, medical treatment will be provided. The reasonable costs of such treatment will be covered by your health insurance for any injury or illness that is directly a result of participation in this study. In no way does signing this consent form waive your legal rights nor does it relieve the investigators, sponsors, or involved institutions from their legal and professional responsibilities. You do not give up any of your legal rights by signing this consent form.

Expenses Associated with Participating in the Study

You will not have to pay for any of the procedures or exercise programming involved in this study. At each of your 5 study visits we will be providing you with $20 for parking and travel.

Communication by E-Mail

Please note that the security of e-mail messages is not guaranteed. Messages may be forged, forwarded, kept indefinitely, or seen by others using the internet. Do not use e-mail to discuss information you think is sensitive. Do not use e-mail in an emergency since e-mail may be delayed.

Conflict of Interest

The team conducting this study comprising of the names at the beginning of this form have an interest in completing this study. Their interests should not influence your decision to participate in this study. You should not feel pressured to join this study

Questions About the Study

If you have any questions, concerns or would like to speak to the study team for any reason, please contact the research coordinator for this study, William Hilton at You may also contact the Principal Investigator, Dr. Andrew Matthew at or Dr. Daniel Santa Mina at . The 24-hour contact emergency number for this study is

If you have any questions about your rights as a research participant or have concerns about this study, call the Chair of the University Health Network Research Ethics Board (UHN REB) or the Research Ethics office number at 416-581-7849. The REB is a group of people who oversee the ethical conduct of research studies. The UHN REB is not part of the study team. Everything that you discuss will be kept confidential.
Consent
This study has been explained to me and any questions I had have been answered. I know that I may leave the study at any time. I agree to take part in this study.

Print Study Participant’s Name __________________________ Signature _______________ Date _________________
(You will be given a signed copy of this consent form)

My signature means that I have explained the study to the participant named above. I have answered all questions.

Print Name of Person Obtaining Consent __________________________ Signature _______________ Date _________________
Appendix 4: Participant Approach List

<table>
<thead>
<tr>
<th>Name</th>
<th>Phone number and/or email</th>
<th>Date of initial contact</th>
<th>Agree (A), Decline (D), Follow-up (F)</th>
<th>Notes / Reason for Refusal (Remind participants they do not have to provide a reason)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Version Date: August 27, 2013
The Feasibility and Efficacy of Prehabilitation for Prostate Cancer Surgery

Appendix 5: Email Consent Form

PATIENT CONSENT FOR E-MAIL COMMUNICATIONS

Dear Patient:

Your care provider can communicate with you or others (named below) using e-mail but you need to understand the risks of using e-mail:

- The security of e-mail messages is not guaranteed. Messages sent to, or from, your care provider may be seen by others using the Internet. E-mail is easy to forge, may be accidentally forwarded, and may exist indefinitely. For this reason, it is recommended that you do not use e-mail to discuss information you think is sensitive. If you decide to use e-mail, please tell you care provider if there are certain types of information that you do not want to discuss by e-mail.
- Do not use e-mail in an emergency because e-mail can be delayed or your care provider may not be able to read it soon enough.

Please Note:

- Your provider will talk to you about which types of conversations you are both comfortable having over e-mail (e.g. scheduling appointments). Your care provider may not feel comfortable discussing some topics by e-mail (e.g. to give test results) and will tell you if another way will be used.
- Your care provider may make decisions about your care based on information you provide in e-mail.
- If an e-mail has information that is important to your clinical care it will be copied or summarized into your medical record – much like a phone conversation.
- E-mail may be forwarded or read by other UHN staff who need the information to provide you with care. Your care provider will tell you if another person will read or reply to your e-mail on their behalf.

This consent form lets us know when we may use e-mail to communicate with you or others who are outside the hospital.

If at any time you decide that you no longer want to communicate by e-mail please tell your care provider as soon as possible. Your care provider will do the same.

By signing below, you accept the risks of using e-mail and agree to the following:

☐ Communicate with me by e-mail at ______________________________ (e-mail Address)
☐ Communicate with the person named below by e-mail (e.g. family member, friend, lawyer, etc.):
  Name: ______________________________
  Relationship: ______________________
  E-mail Address: ____________________
☐ Communicate with the following outside care providers by e-mail:

____________________________________

____________________________________

Date ________________________________

Signature of Patient/Substitute Decision Maker __________________________

Form D-2019M (12/06/2019)
Appendix 6: Study Participant Screening Tool

Patient’s initials: __________

Study Participation Screening Tool

1. What is the patient’s age: ______

2. Has the patient been diagnosed with prostate cancer? Yes / No (if yes, when ____/____ (Mon/Yr)

3. What is the stage of your prostate cancer? If so, what is it? ______

4. Has the patient received any treatments for prostate cancer?
   - Radical Prostatectomy (Surgery)
   - Radiation Therapy / Brachytherapy
   - Hormone Therapy
   - Other: _______________ (Please specify)

5. Has the patient consented for open, retropubic RP?
   - Yes (If yes, when? _______________)
   - No

6. Have you ever been diagnosed with the following (Check box [ ] if Yes):
   - Severe coronary artery disease (Canadian Cardiovascular Society class III or greater)
   - Significant congestive heart failure (New York Heart Association class III or greater)
   - Uncontrolled pain
   - Neurological or musculoskeletal co-morbidity that could inhibit exercise
   - Diagnosed psychotic, addictive, or major cognitive disorders

7. Does the patient have any of the following ACSM Coronary Risk factors (Check all that apply and measure BP/WC if uncertain)? If more than 2, the patient is ineligible.
   - Family history of coronary disease
   - Cigarette smoking
   - Hypertension (SBP > 140 mmHg; DBP > 90 mmHg)
   - Known dyslipidemia
   - Known impaired fasting, glucose (>110 mg/dL)
   - Obesity (BMI > 30 kg/m² or waist circumference > 102 cm)
   - Physically inactive (<150 min of moderate intensity physical activity per week).

Version Date: May 28, 2013
ARE YOU GOING INTO SURGERY FOR PROSTATE CANCER?

We are seeking participants for a research trial of 6 weeks of pelvic floor training or exercise with pelvic floor training on post-surgery outcomes in men with prostate cancer.

The aim of this research is to evaluate:

- Health and physical outcomes after surgery
- The effect of exercise on wellbeing and quality of life

Who are we looking for?

- Men between the ages of 40-80 years old, at least 6 weeks prior to undergoing radical prostatectomy for prostate cancer *(must not have undergone hormone and/or radiation therapy)*
- Participants must be able to travel to Toronto General Hospital (200 Elizabeth St.)

Participation Includes:

- Instructional exercise session with a certified exercise professional
- Fitness assessment performed by an exercise physiologist
- Light exercise equipment for home-based exercise
- Pre-determined reimbursement for travel and parking

If you are interested in participating in this study, please contact:

William Hilton
Email:
Appendix 8: Letter of Invitation to the Study

[ INSERT DATE ]

Dear [INSERT PATIENT’S NAME],

I hope this letter finds you well. Your physician has notified us that you might be eligible for a research study that will investigate the effects of a pre-surgery exercise program. I am following-up with you to provide additional details related to this study should you be interested in participating. Although a more detailed explanation is attached in the ‘Informed Consent Package’, a brief description of the study is provided here.

Pre-operative exercise, also known as ‘prehabilitation’ has been previously shown to improve health outcomes after surgery. Our study will investigate the role of prehabilitation in preparing men for surgery such as yours. Participants in this study will be randomly assigned to one of two groups. One group will receive a pelvic floor exercise program. The other group will receive the pelvic floor exercise program plus a total body exercise routine. The exercise routine will consist of home-based, moderate intensity aerobic and resistance training 3-4 days per week. All required exercise equipment will be provided free of charge (exercise bands, ball, and mat). Five visits to the Toronto General Hospital (across the street from the Princess Margaret Cancer Centre) are required and these visits may potentially be coordinated on days when you would normally visit to see your doctor or other healthcare professionals.

The 5 visits would occur at or close to the following times:
✓ Around the time you consent to the surgery
✓ 1 week prior to surgery
✓ 4, 12, and 26 weeks after the surgery

Participants will be reimbursed $20 for their time and travel expenses at each visit.

This program is voluntary and participants are free to leave at any time. Also, you are eligible to enroll in our ongoing exercise program (WE-Can Program) at the Princess Margaret for additional exercise support once the study is complete or if you choose not to participate. This is available to you at any time during your treatment whether you participate in this study or not.

As noted above, more details about this study are attached in the Informed Consent Document.

If you are interested in joining the study or would like more information please feel free to contact me by phone or email ( )

I look forward to hearing back from you.

Kindest Regards,

Version Date: August 11, 2014
Appendix 9: Web Link to Aerobic Stepping Exercise Video

https://www.ellicsr.ca/en/clinics_programs/we_can/exercise_fundamentals/Pages/exercise_fundamentals_aerobic.aspx