Depressive Symptomatology Following Interdisciplinary Palliative Rehabilitation: Mechanisms of Change and Longitudinal Course

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Preface

This thesis is manuscript-based, containing a general introduction, three studies, and a general discussion/conclusion. The main collaborators throughout have been myself, Dr. Sophie Lebel, Ph.D. C. Psych, and Dr. Martin Chasen, MBChB, FCP(SA), MPhil(PallMed). In all three studies, I was responsible for conceptualizing and refining the research ideas, background literature searches, the ethics application to the University of Ottawa, data management (screening, cleaning), data analysis, data interpretation, manuscript preparation, and dissemination of findings at academic meetings. With the exception of few sections in Study 1, which are indicated in the manuscript, , I wrote these manuscripts.

Dr. Sophie Lebel, my research supervisor, contributed to all of my abovementioned activities as a knowledgeable and supportive supervisor. We met for weekly supervisions throughout the progress of this research. She guided and contributed to the research design, analysis, interpretation, preparation and editing of manuscripts, and dissemination of findings.

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Other authors of these articles include Dr. Neil MacDonald, CM, MD, FRCPC. Dr. MacDonald contributed to the conceptualization and refinement of research ideas, literature searches, instrument selection, selection of statistical tests and analysis, drafting and editing of the first manuscript, as well as being a supportive mentor. He contributed to writing the discussion section of the first manuscript, providing his expertise on interventions for systemic inflammation (page 69 last paragraph). Dr. José Pereira, MBChB, DA, CCFP, MSc(MEd) helped create Figure 1 in the first article (page 80) and both he

and Debbie Gravelle, RN BScN MHS, were involved in the conceptualization and refinement of research ideas and in editing the first manuscript.

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This research was approved by the local research ethics boards: The Bruyère Continuing Care Research Ethics Board (Protocol# M16-09-055), the Ottawa Health Science Network Research Ethics Board (Protocol# 2011898-01H), and the University of Ottawa Office of Research Ethics and Integrity (File# H05-15-02).

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Two of the three studies have been published in peer-reviewed journals. The pilot study entitled "An interprofessional palliative care oncology rehabilitation program: effects on function and predictors of program completion" was published in *Current Oncology* in December 2013. The theoretical article entitled "An interdisciplinary palliative rehabilitation intervention bolstering general self-efficacy to attenuate symptoms of depression in patients living with advanced cancer" was published in *Supportive Care in Cancer* in May of 2015. These have been reproduced with permission from the copyright holders. The third article entitled "The longitudinal course of depression symptomatology following a palliative rehabilitation program" has been submitted to *Psycho-Oncology*.

Only in the twisted world of cancer is ‘chronic’ disease a good thing
-Patient with metastatic lymphoma, female, age 55

General Abstract

Patients with advanced cancer (PWAC) are living months-years longer. With advances in oncological care, their illness can be considered chronic rather than terminal. This population of survivors emerged within the last two decades and their needs are not well understood nor are appropriate resources available. A particular concern is depression. Both clinical and subclinical depressive symptomatology can impede functioning and quality of life (QOL). Using secondary clinical data from a palliative rehabilitation program (PRP), the thesis objectives were to a) examine pre-post changes in functioning and QOL, b) examine the mechanisms of change in depressive symptomatology, and c) examine the longitudinal course of depressive symptomatology.

Study 1 examined pre-post changes in QOL and functioning. Outcomes from 67 PRP patients were analyzed using paired t-tests. Results revealed ameliorations in the majority of domains (e.g. physical functioning, malnutrition) including self-reported "depression." These results counter the existing literature that has shown that these typically stay stable until one month before death, when they drastically worsen. This begins to support that rehabilitation may be beneficial for PWAC.

Study 2 focused on the finding that depression scores decreased. Changes in systemic inflammation, exercise, and general self-efficacy (GSE) from 80 PRP patients were examined as predictors of change in depressive symptomatology using a hierarchical linear regression. The model accounted for 15% of change in depression symptomatology, and GSE was the only significant predictor. This suggests that a GSE theoretical framework may be helpful in reducing depressive symptomatology in interdisciplinary palliative rehabilitation.

Study 3 focused on longitudinal depressive symptomatology. Three-month follow-up data from 80 patients were analyzed using a repeated measures ANOVA for continuous data and a Cochrane's Q analysis for grouped data. Results revealed that patients maintained reduced scores

at follow-up. This counters the existing literature, in which longitudinal maintenance is poor following exercise-based interventions. Therefore, PRP may offer something beyond what other published interventions have previously. These finding will be discussed in the context of other existing literatures and the implications will be discussed.

General Introduction

The definition of *cancer survivor* has evolved alongside the evolution of cancer care. Prior to the 1960s, a survivor was a person who had lost a loved one to cancer reflecting that the patient him/herself was not expected to survive (Institute of Medicine [IOM] & National Research Council of the National Academies [NRC], 2006). In more recent decades, with increasing length of survival, it has been used in varied contexts. A survivor may describe a person who has lived for five years or more after diagnosis or treatment (Ganz, 2011; IOM & NRC, 2006), anybody who has completed treatment regardless of time elapsed (Ganz, 2011; Howell et al., 2012; IOM & NRC, 2006), or anyone who has been diagnosed regardless of time elapsed (Ganz, 2011; IOM & NRC, 2006). Definitions may also include the loved ones of patients, indicating that they also lived through the cancer experience (Ganz, 2011; National Cancer Institute [NCI], 2015; IOM & NRC, 2006). Within the last 10-15 years, advances in oncological care have allowed for the growth of a new population of survivors: Post-treatment patients living with advanced cancer (Chasen & Dippenaar, 2008).

"Advanced cancer" most commonly indicates that the tumour has spread beyond its original site, either to adjacent organs or to distant sites through the circulatory system. This is known as metastasizing and new tumours are called metastases. Advanced cancer, often denoted as stage III or IV, is more severe than earlier stage (a.k.a. localized) cancer, denoted as stage I or II. This staging system is generally accepted for treatment planning, estimating prognosis, and for communication amongst professionals although some cancer sites may have unique staging systems, such as cancers of the breast, kidney, or prostate (IOM & NRC, 2006). Advanced cancer may require more aggressive treatments and patients often present with a decreased ability to perform normal daily activities, such as meeting their own needs, satisfying roles, maintaining health (Cheville, 2001; Gerber, 2001; IOM & NRC, 2006; Victoria Hospice, 2001).

Post-treatment patients living with advanced cancer are among those who have experienced increased life expectancy due to advances in oncology screening and treatments. Some patients may gain months of life and others may gain years, qualifying them as chronically ill rather than terminally. For example, people living with advanced pancreatic cancer can now live a median of 11.1 months with newer cancer treatments as compared to 6.8 months with previous treatments (Conroy et al., 2011); 23% of patients with metastatic prostate cancer can live for over five years following diagnosis and 7% can survive for over ten years (Tangen et al., 2003).

Extended survival is a positive development in cancer care but the experience of living with advanced cancer is not exclusively so. The cancer experience takes a toll on health, functioning, sense of security, and wellbeing and the effects can continue to surface for months or years following treatment completion (Bruera & Yennurajalingam, 2012; Eades, Chasen, & Bhargava, 2009). There are social, psychological, financial, physical, personal, familial, and community issues that ensue. Given the novelty of this population, services to meet their unique needs are still sparse and they are not well represented in the literature (Haylock, 2010).

The Needs of the Patient with Advanced Cancer

After completing cancer treatment, it is crucial for patients at any phase of illness to have a coordinated plan of action to encourage healthy lifestyle changes, manage the sequelae of having gone through treatment, and to optimize quality of life (QOL)[1] and functioning (IOM & NRC, 2006). Ganz (2011) has described the needs of survivorship care as "The three P's": Palliation of symptoms,

[1] Quality of life is not universally defined. A recent theoretical review by Theofilou (2013) summarized quality of life as a multidisciplinary concept that incorporates both objective and subjective ratings of a person's functioning in domains such as physical, mental, and social. Additionally, it can include living arrangements, income, or other considerations. Health-related QOL may also incorporate perceptions of health status, treatment outcomes, fitness, life satisfaction, and wellbeing.

prevention of late-effects or of new cancers, and promotion of ongoing wellness. While this model can apply to survivors living with advanced cancer, it does not quite address their more complex needs, as discussed in this section, below). Similarly, the end-of-life model for patients with terminal illness focuses on comfort care and is also less than optimal for patients living with advanced cancer, who are able to function at a higher level than those who are at end-of-life. Therefore, the needs of this population fall somewhere between these two models of care (Park & Rosenstein, 2014). The difficulties of living with advanced cancer can include ongoing symptom burden, medical management or maintenance of disease status, emotional distress, strain on one's social network, stigma, threats to ongoing functioning (including cognitive functioning), and diminished QOL.

Following primary acute treatment, patients with advanced disease have been found to be polysymptomatic, with a median of 11 symptoms (ranging from 6 to 14). Symptoms may be physical, psychosocial, or spiritual and may result from advanced disease, its more complex treatment, or both (Esper, 2010; Mayer, 2010; Park & Rosenstein, 2014). In addition to this, patients may continue to receive treatments to manage further disease progression, which may become increasingly complex over time. This can itself induce cumulative side-effects which may further exacerbate symptoms and require additional therapies (Haylock, 2010; Mayer, 2010).

The most common emotional concerns reported by patients with advanced cancer include fear, confusion, depression, anger, and isolation (Park & Rosenstein, 2014). Cheville (2001) and Gerber (2001) found that patients with advanced cancer were especially distressed about becoming progressively more debilitated and becoming dependent on others. This is problematic because fears of burdening others in combination with painful or fear-inducing experiences, such as cancer, have been found to predict suicide or requests for euthanasia (Cheville, 2001; McPherson, Wilson, & Murray, 2007; Van Orden et al., 2010). Similarly, Rodin et al. (2009) found that physical and

psychological distress can be risk factors for depression, hopelessness, and desire for hastened death in patients with advanced cancer.

Having good social support can be helpful in emotional coping. However, for this population, it has been found that they may lack outlets to process their emotional concerns about death because their social supports find it distressing (Marcusen, 2010). Feeling isolated has also been found to be prevalent. They have reported feeling ostracized because they were considered to be "losing the battle" and represented "lack of hope," (Mayer, 2010, pp. 196) while disease-free survivors are the acceptable public face (Park & Rosenstein, 2014).

Among their reported unmet needs, receiving quality and detailed information (regarding cancer, treatment, prognosis, and coping with symptoms and side-effects) was the highest reported need (Hannon et al., 2013; Mayer, 2010). Having information can reduce distress, inform decision-making, and improve satisfaction, outcomes, and hope, although appropriate informational resources for this population are still sparse. As well, their need for information may be complicated by declines in physical and cognitive functioning: it may affect their abilities to obtain information and may negatively affect their perception of the information's quality (Marcusen, 2010).

Patients and their loved ones may feel exhausted and depleted from the high demands throughout chronic metastatic disease (Haylock, 2010; Mayer, 2010). Therefore, following their acute cancer treatment, it is imperative that patients living with advanced cancer have opportunities to bolster their informational needs, seek sources of social support, manage their side-effects and symptoms, as well as improve their functioning and QOL. Two models of care that can help achieve these goals are palliative care and cancer rehabilitation.

In the following sections, I will describe the palliative care and rehabilitation models and their histories within oncology. I will describe how the Palliative Rehabilitation Program (PRP) combined these models of care to offer a program to potentially improve functioning and QOL for

patients with advanced heterogeneous cancers. I will then discuss the salience of depressive disorders within this population and the mechanisms through which the program attempts to attenuate depressive symptomatology. Finally, I will introduce the three studies of this thesis.

Palliative Care

Palliative care was derived from the Latin verb *palliare* (meaning *to cloak*). It is today a subspecialty of medicine that strives to alleviate suffering and promote life through interdisciplinary non-curative care (MacDonald, 2009). Prior to the 1900s, cancer care was focused on symptom control while either recovery or death ran its course. This focus diminished when the potential to cure emerged in the early 20th century. For the next half-century, efforts shifted accordingly (Saunders, 2004) and those for whom "nothing more [could] be done" (Mount, 1980, p. 472) were neglected, often sent home to die without any help through the process (Clark, 2007). In the mid-20th century, a subset of clinicians began to take notice of this neglected population and their subsequent clinical and empirical efforts planted the seeds for modern palliative care (Clark, 2007; Fallon & Smyth, 2008; Saunders, 2000; Seymour, Clark, & Winslow, 2005; Shuster & Higginson, 2009).

Modern day palliative care is credited to Dame Cecily Saunders, trained nurse, medical social worker, and physician, who founded St Christopher's Hospice in London in 1967. The clinical and empirical work initiated by Saunders and her colleagues revolutionized care for dying patients with cancer. St Christopher's became an institution of integrated interdisciplinary care, research, and education. Their aim was to allow patients to live out their days more calmly, without pain or distress, and their work improved the patient experience drastically.

Their interdisciplinary approach remains a template for end-of-life care, worldwide. Saunders is credited for the notion of "total pain." This theory views pain as the product of physical, psychological, social, and emotional causes and is influenced by a person's past and present

experiences. Not coincidentally, St Christopher's developed an interdisciplinary model of care that valued each discipline equally and encouraged collaboration (Clark, 2007; Fallon & Smyth, 2008; James & Field, 1992; Saunders, 2000; Seymour et al., 2005).

Today, palliative care can help patients and loved ones find hope, attain realistic goals, and maintain their dignity (Shuster & Higginson, 2009). It is defined by the Canadian Hospice Palliative Care Association as:

> [...] treating existing issues for persons with life-threatening illness, at risk of developing it, or their loved ones and/or caregivers, preventing the development of new issues, and promoting the opportunity for those involved to create meaning, growth, and self-actualization through the experience. (Canadian Hospice and Palliative Care Association [CHPCA], 2013)

The model developed at St Christopher's is retrospectively considered the first wave (Cellarius & Upshur 2014) of palliative care. At that time, palliative care was subsequent to, and distinct from, active treatment. Accordingly, St Christopher's was not part of the cure-focused medical system but was rather supported by charities.

The second wave of palliative care arose in approximately the mid-1990s, when palliative care began to integrate with other services (Cellarius & Upshur 2014; Clark, 2007; Mount, 1980). Leading up to this, the St Christopher's model had grown internationally through correspondence, collaboration, and training. Fortuitously, American President Richard Nixon's "War on Cancer" in 1971 helped to incite new ideas, provoking support for end-of-life care and attracting a fresh influx of palliative care practitioners (Clark, 2007). The expertise of palliative care, such as symptom control, began to be more integrated in acute care throughout the 1970s (Clark, 2007; Fallon & Smyth, 2008). In the 1980s, an international network of palliative care professionals formed, allowing for support and collaboration, sharing of information, and awareness; a palliative care

medical association and scientific journal were established; and a World Health Organization (WHO) initiative to bring together medical professionals from palliative care, oncology, and pain specialties helped establish increased mutuality of curative and palliative treatment (Clark, 2007; N. MacDonald, personal communication, July 8, 2014).

The shift into the second wave of palliative care was reflected in 2002, when the WHO updated their 1989 definition of palliative care to the following:

> Palliative care is an approach that improves the QOL of patients and their families facing the problems associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual. (World Health Organization [WHO], 2013)

Its new definition clearly reflected the shift, moving away from distinct, post-treatment care for incurable disease. What remained constant since 1967 though, was its interdisciplinary approach, holistic scope, and focus on the ease of suffering for patient and loved ones.

Palliative care in Canada.

Many Canadian innovations have affected the global landscape of palliative care. There are multiple palliative care services available across the country and there is awareness of the need and benefits on the part of health care providers, government, and community (Carstairs, 2010; Wentlandt et al., 2014). Within Canada, the first two palliative care clinics opened within weeks of each other in 1974. They were located in the St. Boniface General Hospital in Winnipeg, spearheaded by Dr. David Skelton, and the Royal Victoria Hospital in Montreal, spearheaded by Dr. Balfour Mount (CHPCA, 2014; MacDonald, 2009). Both St. Boniface and the Royal Victoria were academic institutions, which was internationally unique and was influential in the growth of palliative care in Canada.

Mount was a urological oncologist and, like his palliative care predecessors at St Christopher's, recognized the acute focus on cure in oncology to the detriment of other important aspects of care (MacDonald, 2009). He became interested in the inclusion of "personhood" (Mount, 1980, p. 471) within medical care. He studied the experience of end-of-life, the needs of dying patients, and took sabbaticals to study with Saunders (Saunders, 2004). His endeavours included examining spiritual and existential issues, incorporating a humanizing approach, and including a strong contingency of volunteers in his interdisciplinary team. He was also the person who coined the name "Palliative Care." Due to early academic influences such as these, Canada has been ahead of other nations in its developments of palliative care (MacDonald, 2009; Mount, 1980; Saunders, 2004).

Other major Canadian influences have come out of Edmonton and Winnipeg. In the 1990s, Edmonton brought together professionals from acute care, primary care, long-term care, and home care, to establish comprehensive and coordinated provision of palliative care for Edmonton and surrounding regions. Programming included levels of care based on patient need: interdisciplinary hospice palliative care units for patients with terminal illness; tertiary palliative care units for patients with higher symptom control or psychosocial needs; and consultation services, such as a 24-hour on-call physician service for home care. Edmonton was also heavily involved in standardizing assessment for the assurance of standards, common practice, and eased communication amongst care providers and settings (Fainsinger, Brenneis, & Fassbender, 2007; Neil MacDonald, 2009). In Winnipeg, psychiatrist Dr. Harvey Chochinov and his colleagues have been influential in addressing psychosocial issues. Since the early 1990s, their work has illuminated issues of mental health in the terminally ill, including research on the prevalence, assessment, and intervention of depression and/or suicidal ideation (e.g. Chochinov, Tataryn, Clinch, & Dudgeon, 1999; Chochinov, Wilson, Enns, & Lander, 1994; Chochinov, Wilson, Enns, & Lander, 1998; Wilson,

Lander, & Chochinov, 2009). More recent endeavours include maintaining dignity in patients who are dying (e.g. Chochinov et al., 2013) and Canadian Virtual Hospice, a web-based resource of reliable palliative care information for patients, families, health care providers, and researchers (Canadian Virtual Hospice, 2014).

Canadian palliative care is currently transitioning into its third wave, in which it is integrating with active treatment early in the disease trajectory (Carstairs, 2010). Accordingly, the Canadian government has recommended integrating palliative care services into the greater health care system rather than reserving it for those who can no longer benefit from active treatment. Palliative care has been shown to improve symptoms, motor and cognitive functioning, as well as overall QOL (Bruera & Yennurajalingam, 2012; Cole, Scialla, & Bednarz, 2000; Cramp & Byron-Daniel, 2008; Oldervoll et al., 2006), even more so with earlier integration (Temel et al., 2010; Zimmerman et al., 2014). Research is even starting to show a survival benefit (Bruera & Yennurajalingam, 2012).

Palliative care has now spread to more than half of the world's countries, yet despite being a leader in palliative care, Canadian palliative health care can still progress. Canada is accused of being a death-denying culture (Carstairs, 2010; Williams et al., 2010), its implementation of palliative care is inconsistent, largely inpatient-based (Hannon et al., 2015), scarce outside of concentrated urban areas (Carstairs, 2010; Williams et al., 2010), and referral patterns do not yet reflect the third wave (Wentlandt et al., 2014). Although we are doing well on a global level, we are still moving forward.

Cancer Rehabilitation

Rehabilitation is defined by the World Health Organization as "... a process aimed at enabling [people with disabilities] to reach and maintain their optimal physical, sensory, intellectual, psychological and social functional levels. Rehabilitation provides disabled people with the tools

they need to attain independence and self-determination"(WHO, 2014). They define disability as "an umbrella term for impairments, activity limitations and participation restrictions. Functional limitations occur as a result of the interactions between an individual (with a health condition) and that individual's contextual factors (environmental and personal)" (WHO, 2001, p. 17). Palliative care, which aims to provide comfort and ameliorate QOL, may seem incongruent with rehabilitation, which aims to attain optimal functioning and independence. However, the two fields share commonalities and together may be a valuable combination for patients living with advanced cancer (Gagnon, Murphy, Eades, Lemoignan, Jelowicki, Carney, Amdouni, Dibble, et al., 2013; Oldervoll et al., 2006).

Palliative care and rehabilitation interventions combine commonalities of the seemingly disparate paradigms. Both rehabilitation and palliative care focus on improving functioning and QOL, rather than cure. They both have an interprofessional, biopsychosocial approach. Neither treats just the physical, but both also consider the patient, family, and environment. Each has a tradition of interdisciplinary collaboration, and accordingly, they have each emphasized the importance of providing psychosocial care (Bickenbach, Chatterji, Badley, & Ustun, 1999; Cheville, 2001; Delbruck, 2007; Downie, 1978; Kim, Fall, & Wang, 2005).

The history and theory of cancer rehabilitation.

Until the mid-1960s, rehabilitation was largely overlooked for patients with any stage of cancer or prognosis (Bickenbach et al., 1999; Dietz, 1981; Herbert, 1980). Retrospectively, this was attributed to the acute medical needs of the patient that overshadowed their potential for rehabilitation and to an omnipresent sense of hopelessness, including on the part of the physician (Dietz, 1969). Efforts were focused on discharge planning rather than independence or comfort (Dietz, 1981). Dr. J. Herbert Dietz was a pioneer in cancer rehabilitation. He first published on the

potential for rehabilitation of patients with cancer in 1969, describing a multidisciplinary approach for patients with various cancers (Dietz, 1969).

Dietz's article (1969) outlined several guidelines for providing rehabilitation for other patients with various prognoses, tumour sites, disabilities, or needs. His cancer rehabilitation model incorporated triage and multidisciplinary rehabilitation care based on four categories of need: *Preventive*- improving functioning prior to the effects of the illness or treatment*; Restorative*- aiming to restore pre-morbid functioning for patients whose disability can be controlled, avoided, or eliminated; *Supportive*- for patients who continue to live with active disease, for the purpose of attenuating disability, emotional stress, discomfort; and *Palliative*- reducing complications such as symptom burden for patients whose disease is unremitting and improve self-sufficiency.

In this article and in his subsequent work (Dietz, 1969, 1981), Dietz advocated for rehabilitation to attain the patient's best possible levels of physical, social, emotional, and vocational functioning, from diagnosis through palliation. Like Saunders, he envisioned working in coordinated teams with open communication and regular meetings. His model of basic care included physical therapy, occupational therapy, training in activities of daily living (ADLs), education, vocational services, psychosocial services, and the application of mechanical devices such as prosthetics (Dietz, 1981). He considered palliation and improvements in functioning as overall goals for all patients. He and Dr. Howard Rusk spearheaded the first program dedicated to cancer rehabilitation. This was a joint project between New York's Memorial Hospital and the Institute of Rehabilitation Medicine (Kevorkian, 2009).

Rusk was a pioneer in cancer rehabilitation and was one of the few to publish on the topic prior to 1960 (Kevorkian, 2009). In the mid-1960s, he was a member of American President Lyndon Johnson's subcommittee for the *Heart, Cancer, and Stroke Act,* which lead to the development of programs for diagnosis, treatment, and rehabilitation of patients with these conditions.

Subsequently, rehabilitation programs for the purpose of clinical care, research, and professional training began being established in medical schools and teaching hospitals (Kevorkian, 2009).

Further developments in the field of cancer rehabilitation continued through the 1970s. With the *National Cancer Act* of 1971, new cancer centers, training programs, cancer control programs, research contracts, and collaborations amongst agencies began to appear (Committee on Labor and Public Welfare, 1971). Funds were allocated for research in topics such as hospice care, pain management, and psychosocial interventions, although efforts shifted towards cure (Kevorkian, 2009). In 1972, the U.S. National Cancer Institute funded the National Cancer Rehabilitation Planning Conference, which identified four goals in cancer rehabilitation: 1) optimize physical function, 2) provide psychosocial support, 3) provide vocational counseling, and 4) enhance social function.

The first article to address the needs of patients with cancer was written by Lehman et al. (1978). He conducted a needs assessment of this population and his findings revealed that they struggled with ADLs, ambulation, psychological distress, and pain. By the 1980s, rehabilitation programs for patients with cancer were becoming more prevalent. They were commonly hospital-based, multidisciplinary, and integrated with rehabilitation or cancer care (Harvey, Jellinek, & Habeck, 1982). However, their growth was still limited by preconceptions of the progressive and terminal nature of the disease (Cheville, 2005), reluctance based on a lack of evidence for effectiveness, or physiatrists feeling unprepared for cancer referrals (Harvey et al., 1982). These among other potential reasons (e.g. preference of physiatrists to treat outpatients) may have contributed to the lost momentum after the first two decades (DeLisa, 2001; Harvey et al., 1982). The increase in publications on cancer rehabilitation in the last decade suggests a revival, perhaps due to ongoing growth in cancer survivorship (Fialka-Moser, Crevenna, Korpan, & Quittan, 2003; IOM & NRC, 2006). Concurrently, there is a revival in the literature in advocacy for palliative

rehabilitation (e.g. Cheville, 2001; Cheville, Khema, & O'Mahony, 2007; Marciniak, Sliwa, Spill, Heinemann, & Semik, 1996; Okamura, 2011), for the adminstration of palliative care earlier in the cancer trajectory, even as early as diagnosis (e.g. Temel et al., 2010), and the empirical examinations of such programs (Salakari, Surakka, Nurminen, & Pylkkänen, 2015). Yet, little clinical data exists on the combination of these approaches, which could potentially be beneficial clinical programming for this novel population of patients living with advanced cancer. In an attempt to combine these domains, the Palliative Rehabilitation Program (formerly the Cancer Nutrition Program) was designed.

The Palliative Rehabilitation Program

The PRP is a unique program designed specifically for the palliative rehabilitation needs of patients living with advanced cancer. In accordance with the World Health Organization's definition of Palliative Care and with Dietz' (1969) aforementioned goals of cancer palliative rehabilitation, this team aims to empower individuals who are experiencing loss of function, fatigue, malnutrition, psychological distress, or other symptoms as a result of cancer or its treatment (WHO, 2013). The PRP aims to help patients with advanced cancer improve QOL by improving general health through exercise, good nutrition, individualized psychosocial care, and management of medical complications. It incorporates the expertise of six clinicians (oncologist, nurse, physiotherapist, occupational therapist, dietician, and social worker) to thoroughly assess and deliver integrated intervention care plans to keep people as active as possible in their daily lives for as long as possible.

The composition of the PRP had two major influences in its design. First, was Dietz' aforementioned model described in his early writings on cancer rehabilitation: that it is best offered in a multidisciplinary team format with a physician at the head (e.g. oncologist, surgeon, physiatrist) and as a base, physical therapy, occupational therapy, education, vocational services, psychosocial

services, and the application of mechanical devices such as prosthetics (Dietz, 1981). The second influence on the PRP team was the composition of its predecessor, the McGill Cancer Nutrition-Rehabilitation (CNR) Program in Montreal, Canada.

The CNR was developed by Dr. Neil MacDonald, a medical oncologist and palliative care physician. He recognized that cancer rehabilitation focused largely on physiatry, to the detriment of nutritional and symptom control interventions. He proposed that a multidisciplinary approach, including pain and symptom management, nutritional counseling, and physical rehabilitation, alongside medical treatment of the tumour, could help reverse slow declines in patient functioning. This could potentially counter the limitation of usual care in which these interventions were offered: when patient functioning had already deteriorated to the point that it would be difficult to respond (MacDonald, 2002).

MacDonald's rationale included evidence from the research literature demonstrating that the physical effects of cancer and its treatment could debilitate a patient in a number of domains (MacDonald, 2002). For example, physical sequelae impact symptom burden and survival time, leading to disability and hospitalization, thereby reducing mobility and independence in self-care. In addition to the physical consequences of advancing cancer (weight loss, fatigue, constipation, chronic nausea), patients experience psychosocial consequences, such as loss of independence, increased requests for euthanasia, increased anxiety and depression, and strains in relationships with family, friends, health care providers (Bruera & Yennurajalingam, 2012; Cheville, 2001; Eades, Chasen, & Bhargava, 2009; Gerber, 2001; Haylock, 2010; IOM & NRC, 2006). The CNR's interventions aimed to counter these effects by encouraging the maintenance of weight, prevention of muscle loss, maintenance or increase in strength and mobility while patients underwent cancer treatment. It was hypothesized that patients would experience reduced fatigue, increased independence, maintained or increased feelings of utility and dignity, independence in ADLs, eased

depression, maintained or increased social capacities, and improved overall QOL (MacDonald, 2002). This program was originally running at the Jewish General Hospital in Montreal, QC.

In 2006, the CNR program opened in Montreal's Royal Victoria Hospital under the medical direction of Dr. Martin Chasen, a medical oncologist and palliative care physician. The CNR significantly evolved at this second location. The team grew to incorporate two clinical oncologists, a psychologist, clinical nurse specialist, triage nurse, physiotherapist, dietician, occupational therapist, social worker, nurse researcher, research physician, data manager, and clinic coordinator. The team decided to focus their interventions on survivors of cancer who had functional decline, fatigue, malnutrition, psychological distress, and other symptoms of cancer. Patients were offered individual treatments from team members as part of an integrated interdisciplinary care plan and both patients and their loved ones were offered psycho-educational group sessions. The CNR also began publishing from their program of research, supporting the benefit of this interdisciplinary approach on improvement of symptoms and QOL (e.g. Chasen & Bhargava, 2012; Eades et al., 2009) as well as descriptions on the needs of patients and the role of team members (e.g. Gagnon, Murphy, Eades, Lemoignan, Jelowicki, Carney, Amdouni, Di Dio, et al., 2013; Lemoignan, Chasen, & Bhargava, 2010). For an exhaustive list of CNR/PRP publications, see Appendix. These integrated clinical and empirical traditions continued when Chasen expanded the CNR to Ottawa, ON, in 2010, under the name *The Palliative Rehabilitation Program*.

Palliative rehabilitation cannot offer a cure from advanced cancer, but it can help patients to regain function, ease oncoming suffering, and attenuate further deconditioning (Chasen & Dippenaar, 2008; Cheville, 2001; Santiago-Palma & Payne, 2001). The CNR and the PRP have been timely programs for the delivery of service for this emerging population. As recently as 2012, Howell et al. (2012) conducted a systematic review of the structure of services offered to survivors at all stages of cancer. They found that follow-up care through oncologist and cancer center are not

sustainable for the ongoing care of patients who have completed their cancer treatments, especially for patients who require more complex care (i.e. patients living with advanced cancer). They also noted that behaviour change is crucial alongside ongoing oncological care and not sufficiently achieved through patient education, interdisciplinary programs are important but not yet tested, and literature is needed regarding how to implement models of care that are effective at stimulating patient action. Goals such as addressing difficulties with behaviour change, helping patients process and/or manage distress related to cancer, or grieving losses while they rehabilitate are examples of how a psychosocial oncologist may contribute to a patient's interdisciplinary care.

Psychosocial Oncology

From their respective beginnings, palliative care and cancer rehabilitation have both identified psychosocial oncology as an important component of their models. According to the Canadian Association of Psychosocial Oncology (CAPO), psychosocial oncology is:

> […] a specialty in cancer care concerned with understanding and treating the social, psychological, emotional, spiritual, quality-of-life and functional aspects of cancer, from prevention through bereavement. It is a whole-person approach to cancer care that addresses a range of very human needs that can improve QOL for people affected by cancer. (Canadian Association of Psychosocial Oncology [CAPO], 2015)

In addition, it is said to be concerned with 1) the psychological reactions of patients, families, and staff across disease stages, and 2) the psychological, social, and behavioural factors that cause or affect cancer and survival (Holland, 2002). The field of psychosocial oncology (sometimes called "psycho-oncology") was first recognized in 1975, not too long after the birth of modern palliative care and cancer rehabilitation. According to Holland, this was made possible by the reduction of the societal stigma of having cancer, sequelae of the development of curative treatments, celebrity disclosures of their own cancers, and the increase in the rights of the medically ill. Since that time, it

has been recognized that issues with mental health are amongst the most common and troublesome difficulties for patients with advanced disease (Shuster & Higginson, 2009; Standing Senate Committee on Social Affairs, 2000).

In modern day psychosocial oncology, Canada is spearheading international change in cancer care (e.g. Andersen et al., 2014; Coleman, Hession, & Connolly, 2011). Through research and advocacy by Canadian psychosocial oncologists, the Canadian government officially recognized "distress," a psychological symptom, as the sixth vital sign in cancer care (Bultz et al., 2011; Thomas & Bultz, 2008). Distress is "a multi-factorial unpleasant emotional experience which extends along a continuum, ranging from common normal feelings of vulnerability, sadness, and fear to problems that can become disabling, such as depression, anxiety, panic, social isolation, and existential and spiritual crisis" (Holland, Anderson, & Breitbart, 2007). Some distress is a normal part of having cancer but it becomes clinically significant when a person struggles with his/her general functioning, their ability to adhere to treatment, or their progression through cancer care. There are a multitude of factors that might affect distress, such as disease site or stage, personality characteristics, social support, or other factors (Levenson, 2006).

From a clinical perspective, patient distress may manifest as anxious or depressive symptoms. Patient distress may reach the threshold of a clinical disorder, such as major depressive disorder or panic disorder, or patients may experience intrusive symptoms that fall below the clinical threshold, yet their symptoms still interfere with their functioning (Li, Boquiren, Lo, & Rodin, 2011). It has been found that anxiety and depression tend to peak at different points in the cancer trajectory. Anxiety is more frequently elevated at the time of diagnosis or recurrence, times of more immediate and unavoidable threat. In contrast, depressive symptoms slowly increase over time and peak later in the trajectory, as patients have more time to reflect on the losses from the cancer, realize that it may be permanent, or have difficulty finding meaning in the threats to their identity

and wellbeing (Li et al., 2011). Therefore, depressive symptoms are a salient concern for post-treatment patients living with advanced cancer.

Depressive Disorders and Screening of Depressive Symptomatology

Depressive disorders have been found to be the most common mental health concern in patients with advanced cancer (Massie, Lloyd-Williams, Irving, & Miller, 2011). Depressive disorders are often underdiagnosed and often untreated in patients with advanced cancer (Wilson et al., 2009) and other physical illness (Gill, Klinkman, & Chen, 2010). Reasons for these oversights in the care for patients with advanced cancer likely include the misconception that depression is a normal reaction to living with advanced cancer. Another reason may be the discomfort of discussing emotions by either the patient or the health care professional (DiMatteo & Haskard-Zolnierek, 2011; Massie et al., 2011; Passik & Lowery, 2011; Wilson et al., 2009).

Depression is different than sadness. Depressive disorders are clusters of symptoms (e.g. depressed mood, lack of motivation or pleasure, fatigue, changes in sleep, changes in appetite, psychomotor agitation or retardation, difficulty concentrating, difficulties with self-esteem or guilt, suicidal ideation) that significantly interfere in a person's functioning (American Psychiatric Association [APA], 2013). At least five symptoms must be present for a minimum of two weeks for a diagnosis of Major Depressive Disorder. In the literature on depression and advanced cancer, there is also a focus on subthreshold cases of depression, i.e. cases that do not meet criteria for a Major Depressive Disorder but that do impede patient functioning. These include minor depression (2-4 symptoms), dysthymia (persistent depression with less than five symptoms for two years or more), or adjustment disorder (in response to a stressor or life event that is more pronounced than is considered normal) (Li, Fitzgerald, & Rodin, 2012; A. J. Mitchell et al., 2011; Rodin, 2013). Any of these conditions are different than sadness, which is an emotion that may be a symptom of

depression and/or may be a normal reaction during the cancer experience. Sadness itself does not impede normal functioning to the extent or duration of a depressive disorder.

Clinical and subclinical levels of depressive symptomatology have all been found to negatively affect QOL and functioning in patients with physical illness and in those without comorbid physical illness (e.g. da Silva Lima & de Almeida Fleck, 2007; Lyness et al., 2007; Meeks, Vahia, Lavretsky, Kulkarni, & Jeste, 2011; Santangelo et al., 2014). Reviews and meta-analysis have found rates of mood disorders to range from 5.1% to 30.1%, with a pooled prevalence of 16.5% for palliative care in- and outpatients. Minor depression has been found to be approximately 9.6% and is considered the most problematic because medications are ineffective for minor depressions and other resources are not available at this time. Prevalence rates have not been found to vary based on age, sex, or in/outpatient setting (Currier & Nemeroff, 2014; Mitchell et al., 2011; Rodin, 2013).

Depression, whether clinical or subclinical, is an important topic for ongoing research and programming in this population. A person with a depressive disorder may experience extreme difficulty adhering to medical treatments, engaging with others (including health care professionals), engaging in ADLs (Fann et al., 2008), and it can exacerbate other symptom burden (Delgado-Guay, Parsons, Li, Palmer, & Bruera, 2009). Depression is a predictor of mortality in patients with cancer, regardless of whether the physical illness or the depression was diagnosed first. This remains true when medical variables, such as disease stage, are controlled (Lloyd-Williams, Shiels, Taylor, & Dennis, 2009; Pinquart & Duberstein, 2010; Satin, Linden, & Phillips, 2010; Spiegel & Giese-Davis, 2003). Untreated depressive disorders also exacerbate health care overuse (Meeks et al., 2011), exarbate physical dysfunction making patients more dependent on others, which has been linked to desire for hastened death (Wilson et al, 2007) and even cause tumour progression (see section “Systemic Inflammation” below). Therefore, helping patients

overcome depressive symptomatology has the potential to make a meaningful difference in QOL, functioning, and even survival.

In the screening of depressive symptomatology, the Hospital Anxiety and Depression scale (HADS; Zigmond & Snaith, 1983) is a commonly used self-report in research involving patients with cancer. It was designed for use with medical populations of patients, including cancer. During its development, there was an emphasis on evaluating psychological symptoms of depression (e.g. lack of interest, motivation, sad mood) and a lack of emphasis on the physical symptoms (e.g. change in appetite, fatigue, sleep disturbances). This is because many of the physical symptoms of depression overlap with symptoms of physical illness, which may contribute to increased false-positives in screening (Levenson, 2006; Luckett et al., 2010).

Measuring depression.

The HADS has been well-validated for patients with heterogeneous cancers. It has been found to perform well when compared to other self-report measures of depression in patients with physical illness, mental illness, in primary care, and physically healthy adults (Bjelland, Dahl, Haug, & Neckelmann, 2002) and specifically for screening for major depressive disorder in outpatients with cancer (Walker et al., 2007). Of reviewed self-report measures of depression, it has received the most psychometric support and gives the richest data for the number of questions (Bjelland et al., 2002; Luckett et al., 2010; Mitchell, Meader, & Symonds, 2010; Vodermaier & Millman, 2011). It has also been found to be acceptable for patients who are ill or weak (Johnston, Pollard, & Hennessey, 2000).

A consideration when using the HADS is that it is not an appropriate tool for diagnosis or case-finding. The HADS is considered a screening measure that is best to rule-out patients who are not exhibiting depressive symptomatology from further assessment or as an indication of symptom severity (Lowe et al., 2004; Luckett et al., 2010; Mitchell et al., 2012; Mitchell et al., 2010). In their

meta-analysis, Mitchell et al. (2012) found that in samples of palliative patients or those with advanced cancer, the HADS had a sensitivity of 69.9% and a specificity of 74.6%. For the purpose of diagnosis, the gold standard measure is the clinical interview based on criteria of the psychiatric diagnostic manual (APA, 2013) or a combination or self-report measures and clinical interview (Meyer et al., 2001).

Although the HADS is not meant to be used as a diagnostic measure of depression, the original authors proposed that it can be used to categorize symptom severity into categories such as minimal symptomatology versus possible or probably depression (Zigmond & Snaith, 1983, p. 365). Past studies have used varying cut-off scores to qualify what defines a case (Walker et al., 2007). For patients with heterogeneous cancers, Bjelland (2002) and Mitchell (2010) reported that qualifying a score of 0-7 as minimal depressive symptomatology and a score of 8 or above as possible or probable depressive symptomatology is optimal to balance between sensitivity and specificity. As well, a change in score of 1.5 units is considered the clinically important difference, indicating a shift in clinical severity (Yost, Eton, Garcia, & Cella, 2011).

Targeting Depressive Symptomatology in the PRP

There are several interventions within the PRP that have been supported elsewhere as beneficial in reducing depressive symptomatology. These include reducing systemic inflammation, increasing physical activity, and improving sense of general self-efficacy. Each of these will be examined next, including a rationale for including them and a review of the literature linking them to attenuation of depressive symptomatology.

Systemic inflammation.

Systemic inflammation is a sign of immune activity in response to injury or infection. When the body detects an injury or pathogen, its normal state of physiological homeostasis is disrupted to create a more defensive environment, called the *acute phase response.* The acute phase response

includes a number of systemic and metabolic changes, such as changes in the synthesis of endocrine hormones, blood cells, glucose, lipids, changes to the ion charge of the blood, and most relevant to the current research: the production of inflammation. The acute phase reaction is meant to contain and/or destroy pathogens, remove or repair damaged tissue, repair organs, and return the body back to homeostasis (Black, Kushner, & Samols, 2004; Du Clos & Mold, 2004; Kushner, 1982, 1993). C-reactive protein (CRP) is one of two major acute phase proteins that increase substantially during the acute phase response. Produced in the liver in response to pro-inflammatory cytokines, specifically interlukin-6, it is sparse during homeostasis but it can increase from several 100s – 1000s% depending on the severity of bodily threat (Allin & Nordestgaard, 2011; Black et al., 2004; Du Clos & Mold, 2004; Irwin & Miller, 2007; Kushner, 1982, 1993; Lopresti, Maker, Hood, & Drummond, 2014). It is involved early in the immune process of clearing pathogens and decreases rapidly in the blood post-infection or injury, making it a particularly useful clinical measure (Black et al., 2004). It is commonly used in clinical settings due to its sensitivity and can be used for monitoring infections, post-operative complications, treatment efficacy, or disease progression.

In addition to infection or injury, acute elevations of CRP may occur from sleep deprivation (Meier-Ewert et al., 2004), psychosocial stressors (Steptoe, Hamer, & Chida, 2007), hormonal therapies (e.g. oral contraceptives; Le-Ha et al., 2014; hormone-replacement therapy; Ridker, Hennekens, Rifai, Buring, & Manson, 1999), smoking (Le-Ha et al., 2014), or heavy alcohol use, although moderate alcohol consumption showed more of a decrease in CRP level than either abstinence or heavy use (Albert, Glynn, & Ridker, 2003; Imhof et al., 2001).

Chronic inflammation.

A chronic inflammatory state (CIS) may ensue when there is persistently elevated inflammation in the body, which may be due to pro- and anti-inflammatory agents having become

dysregulated (Allin & Nordestgaard, 2011; Currier & Nemeroff, 2014; Hänsel, Hong, Cámara, & von Känel, 2010). This can be due to malignant tumours, which produce inflammation that elicit an anti-inflammatory response from the immune system. Other factors include genetics, aging, chronic illness, medical treatments, chronic psychosocial stressors, ethnicity, diet, and obesity (Black et al., 2004; Currier & Nemeroff, 2014; Frank & Caceres, 2015; Henderson et al., 2015; Hänsel et al., 2010; Irwin & Miller, 2007; Kiecolt-Glaser & Glaser, 2002; Raison et al., 2013).

Malignant tumours perpetuate inflammation because they are resilient to the immune response. Tumours are composed of local immune cells, connective tissues, and neo-vascular endothelial cells, making them similar enough to the local healthy tissue that they are not cleared from the system, meanwhile still propagating more inflammation. Mediators of the immune system also propagate tumour growth by altering DNA, and promoting angiogenesis and metastasis. Given the influence of tumours in CIS, CRP is highly associated with increased morbidity and mortality in patients with cancer and has been suggested as a better prognostic measure of survival than tumour stage (Allin & Nordestgaard, 2011; Balkwill & Mantovani, 2001; Deans & Wigmore, 2005; Hefler et al., 2008; MacDonald, 2007; Mahmoud & Rivera, 2002; Trinchieri, 2012). In addition to propagating cancer, CIS has been well-supported in the literature as a factor in acute health problems, such as delayed wound healing (Kiecolt-Glaser & Glaser, 2002), and in risk of long-term morbidity, such as cardiovascular disease, rheumatoid arthritis, inflammatory bowel disease, frailty, non-inflammatory medical conditions, and genetic polymorphisms (Black et al., 2004; Currier & Nemeroff, 2014; Frank & Caceres, 2015; Henderson et al., 2015; Noto et al., 2014; Raison et al., 2013).

Measuring CRP.

In clinical practice, blood serum CRP is the prototypical biological measure used to assess systemic inflammation (Deans & Wigmore, 2005; Mahmoud & Rivera, 2002). Research is currently examining

the use of salivary CRP as a less intrusive and cost-effective option; validation for clinical use is ongoing (Christodoulides et al., 2014; Pfaffe, Cooper-White, Beyerlein, Kostner, & Punyadeera, 2011). A serum CRP level of <10 µg/mL is usually considered within the normal range. Even if CRP levels remain below 10 µg/mL though, chronic elevations of 3 µg/mL or more are associated with increased risk for inflammation-related conditions such as cardiovascular disease, metabolic syndrome, and colon cancer.

Targeting CRP.

An optimal intervention for targeting CRP has not yet been identified. Therefore, the PRP combines several therapies that have been shown to affect CRP directly and indirectly. Directly, the PRP intervention components targets CRP biologically through medication, exercise, and nutrition. The PRP also targets inflammation indirectly, through interventions geared to reduce symptom burden, ameliorate psychosocial health, and reduce stressors, which may affect the patient's ability to function and to follow care recommendations. As a hypothesized example, a patient who is depressed may lack the motivation to follow dietary recommendations; a patient who learns strategies for energy management may experience less fatigue, be better equipped to undertake ADLs, may experience a subjective improvement in independence, and feel less overall stress as a result (Chasen & Dippenaar, 2008; Lemoignan et al., 2010; MacDonald, 2007; Townsend, Accurso-Massana, Lechman, Duder, & Chasen, 2010).

CRP and mental health.

Elevated CRP has long been recognized in patients with physical illness such as cancer but it has more recently also been recognized as a factor of mental health. For example, elevated CRP in pregnant women increases the risk of their kids developing schizophrenia later in life (Canetta et al., 2014), elevated CRP predisposes survivors of trauma to the development of PTSD (Eraly et al.,

2014), it is associated with mania symptoms in patients with bipolar disorder (e.g. Dickerson, Stallings, Origoni, Boronow, & Yolken, 2007), and is strongly associated with depression.

CRP and depression.

Robust evidence exists for the association between depression and inflammation yet how CRP and depression affect each other is still largely unknown (Noto et al., 2014; Raison et al., 2013). People with depression have ongoing low-grade inflammation (Noto et al., 2014) but inflammation is neither necessary nor sufficient to yield depression. Some authors have found elevated CRP to be predictive of future depressive episodes, even for patients with no history of depression (e.g. Currier & Nemeroff, 2014; Gimeno et al., 2009; Irwin & Miller, 2007; Noto et al., 2014; Raison et al., 2013) and others have found that depression predicts elevated CRP and not vice versa (Copeland, Shanahan, Worthman, Angold, & Costello, 2012; Chocano-Bedoya et al., 2014). Differences in findings may be due to confounding variables that complicate this relationship, such as obesity, poverty, diet, or disrupted sleep (Raison et al., 2013) or participants may differ in inflammatory profiles that make some more susceptible to depression than others (Raison et al., 2013; Rosenblat, Cha, Mansur, & McIntyre, 2014). Causation, correlation, coincidence, or other confounding/mediating/moderating variables are not yet well understood in this depression-CRP relationship (Noto et al., 2014). However, given the findings of an association between depression and inflammation, authors have started to propose that targeting inflammation may be an effective treatment for depression (Currier & Nemeroff, 2014; Irwin & Miller, 2007; Köhler et al., 2014; Udina et al., 2014). Although findings have been mixed, the most pronounced effects of CRP management on depression have been found for patients with a) higher levels of CRP and b) depressions that have been resistant to more traditional anti-depressants. This suggests that there is a subgroup of patients with treatment-resistant depression who may benefit from inflammation-lowering interventions (Raison et al., 2013).

There is growing evidence that depression can directly stimulate the production of proinflammatory cytokines that influence a spectrum of health conditions, including cancer. Depression can attenuate the immune response, thereby prolonging time to heal from infection or wounds. Depression may also fuel sustained proinflammatory response, thereby bolstering risk for ongoing depression, feeding CIS, and increasing risk of physical illness (Kiecolt-Glaser & Glaser, 2002). Gross et al. (2010) reported that having a history of depression increases one's risk of developing cancer (hazard ratio=1.9; 95% CI 1.2-3.0), a finding that is especially pronounced for breast cancer (hazard ratio: 4.4; 95% CI 1.08-17.6). In patients with pancreatic, esophageal, and breast cancer, those with a comorbid major depression were found to have higher IL-6 (a precursor to CRP) than non-depressed patients with cancer or healthy controls (Musselman et al., 2014). In sum, the relationships are not yet well understood but evidence suggesting that there is relationship is mounting. A theoretical discussion of the mutuality between inflammation, illness, cancer, and depression is beyond the scope of this thesis. For further information, see Currier and Nemeroff (2014), Dantzer et al. (2008), Irwin and Miller (2007), and Rosenblat et al. (2014).

Exercise.

Exercise is one of the most commonly studied areas in cancer rehabilitation (Silver & Gilchrist, 2011). Several meta-analyses have found that physical activity has small to medium effects on psychological outcomes, including depression (e.g. Fong et al., 2012; Velthuis, Agasi-Idenburg, Aufdemkampe, & Wittink, 2010). Amount of exercise has been found to be positively correlated with amount of depressive symptom relief (Brown et al., 2012). However, it is important to remember two things when interpreting this: There may be a floor-effect: patients with less depressive symptomatology are limited in how much relief they can experience from their symptomatology because it is already low (Craft, VanIterson, Helenowski, Rademaker, & Courneya, 2011), and exercise may help decrease depressive symptomatology but decreased symptomatology

also promotes one's ability to exercise more (i.e. correlation not causation). Amounts of exercise that have been found to be useful vary from 90 minutes of aerobic exercise three times per week (Courneya et al., 2014) to 3 hours throughout the week (Brown et al., 2012). It has been found to be more effective for patients earlier in the cancer trajectory (Brown et al., 2012; Mishra et al., 2012) and when it is structured according to a patient's ability (Bridle, Spanjers, Patel, Atherton, & Lamb, 2012).

However, there exist shortcomings in the literature of exercise interventions for treating depression comorbid with cancer. Research on exercise interventions tends to focus on practical outcomes, such as fatigue, QOL, or symptom relief, and when depression is included, it is often a secondary outcome (Mead et al, 2009). Perhaps related to this, the literature that exists has not targeted high levels of depression (e.g. Craft, 2011) and there are only a few longitudinal follow-up on depression as an outcome, post-intervention, for patients with cancer (e.g. Mutrie et al., 2012). Additionally, target populations are often those with non-metastatic disease (Craft et al., 2011). What has been examined regarding exercise interventions for depression supports that post-intervention maintenance may be poor (Krogh, Nordentoft, Sterne, & Lawlor, 2011; Mead et al., 2009; Mishra et al., 2012; Rimer et al., 2012). In sum, there is sparse follow-up data on depression as an outcome of exercise interventions, and like other literatures, this is especially so for patients living with advanced cancer.

There also exists little examination of the mechanisms that affects change in depression. This precludes conclusions about the anti-depressant effects of exercise. For example, do exercise interventions ease symptoms of depression biologically: e.g. exercise can change the functioning of serotonin receptors (Dey, 1994); socially: interventions involve personal coaches or group participation, which increase social integration (Musick & Wilson, 2003); or psychologically: e.g. exercise regimens permit patients to feel capable of accomplishing their goals (Salmon, 2001)?

Perhaps exercise itself is not what influences depression but rather the adjacent skills developed, such as self-efficacy, when successfully implementing a new regimen. By understanding mechanisms of change, small effect sizes may possibly be bolstered.

Self-efficacy: a theoretical mechanism of change.

General self-efficacy is a person's sense that he/she can influence events or quality of functioning, in general. It comes from Bandura's Social Cognitive Theory and it is a stable character trait (Bandura, 1977; Luszczynska, Scholz, & Schwarzer, 2005). *Domain specific self-efficacy* is different than GSE: it is a person's perception that he/she can handle a specific situation (e.g. changing a flat tire). It has been found to be more strongly associated with motivation, affect, and behaviour than are objective measures of ability. It has been supported as a universal psychological construct, i.e. its associations with other psychological constructs, such as personality and self-regulation, have been found to be common in countries that are disparate in their economic development, religious affiliations, social situations, and political situations (Luszczynska, Gutiérrez-Dona, & Schwarzer, 2005; Luszczynska, Scholz, et al., 2005; Scholz, Gutiérrez-Dona, Shonali, & Schwarzer, 2002). GSE is recommended for situations in which there are a number of competing stressors or demands, such as when living with advanced cancer and coping with the related sequelae of the disease and its treatment (Bandura, 1977; Luszczynska, Gutiérrez-Dona, et al., 2005). It has been shown to affect heart rate, serum catecholamine levels, perception of pain, psychosocial adjustment, and post-coronary recovery. It can be used to predict engagement in health behaviours such as increased exercise or flossing (Bandura, 1998; Mausbach et al., 2011).

Many studies have supported that GSE is significantly related to the quality of functioning in diverse domains of health (Bandura, 2002, p. 271). Luszczynska, Gutiérrez-Dona, and Schwarzer (2005) found positive correlations between GSE and amount of positive health behaviours in patients with cardiovascular disease. Corless et al. (2012) found that higher GSE enhanced

engagement with health care providers for patient with HIV and was associated with less reported symptom burden. Hampton (2000) found that patients in China who had spinal cord injuries had better QOL when they had higher GSE. Importantly for the present research, GSE has been negatively correlated with anxiety and depression in patients with or without a variety of chronic illnesses, including cancer (e.g. Lewin, Jöbges, & Werheid, 2013; Luszczynska, Scholz, et al., 2005; Mystakidou et al., 2013; Penninx et al., 1998).

Higher perceived GSE has been found to co-occur with less depressive symptomatology in patients with cancer (Luszczynska, Scholz, et al., 2005; Penninx et al., 1998; Ralf Schwarzer, Boehmer, Luszczynska, Mohamed, & Knoll, 2005), advanced stage renal disease (Devins et al., 1982), cardiovascular disease (Luszczynska, Scholz, et al., 2005; Penninx et al., 1998), gastrointestinal disease (Luszczynska, Scholz, et al., 2005), elderly patients with chronic hearing impairment (Kramer, Kapteyn, Kuik, & Deeg, 2002), diabetes mellitus, lung disease, and arthritis (Penninx et al., 1998). In a study examining post-stroke patients, GSE was found to be the strongest predictor of depression when compared to other psychological predictors (Lewin et al., 2013). Finally, a meta-analysis of psychological interventions found that those that employed social cognitive theory (especially the ingredients of bolstering GSE, described later in this section) were more effective on improving QOL (depression included) than interventions that were not based in social cognitive theory (Graves, 2003).

In the general psychology literature, GSE has been postulated to affect depression in a number of ways (Bandura, 2009). For example, low GSE may increase a person's experience of failures, thereby increasing their sense of hopelessness; it may increase a person's sense of difficulty in engaging in social relationships, thereby limited their social support which is known to buffer the effects of chronic stress; it may perpetuate unhelpful patterns of thinking (e.g. rumination); or it may reduce the situations or environments that a person chooses to pursue,

thereby limiting a person's pleasurable experiences and opportunities to feel that they have mastered their endeavors. People with low GSE may have a weaker commitment to their goals, give up more easily due to lack of faith in their skills, or avoid challenges altogether. Specifically in the health psychology literature, GSE has been found to affect depression by moderating perceived stressors (Kreitler, Peleg, & Ehrenfeld, 2007; Luszczynska, Scholz, et al., 2005; Ralf Schwarzer et al., 2005). More specifically, GSE affects how one perceives or copes with stressors, thereby affecting one's experience of depressive symptomatology (e.g. sad mood, disturbed sleep, self-esteem or confidence).

According to Bandura (1977, 2009), there are four ways to enhance one's GSE: Mastery experience, vicarious learning, interpretation of physical and emotional states, and verbal persuasion. Mastery experience refers to working towards one's goals in a gradual fashion with interim successes along the way. Exposure and desensitization through practice lead to experiences of success in the pursuit of goals. This is the most potent factor in building GSE. Vicarious learning refers to observing others successfully pursuing their goals. Symbolic models, such as characters in stories, may also suffice. Improving emotional and physical states refers to minimizing barriers, such as improving physical functioning or helping patients understand their emotions as informative rather than aversive. Finally, the fourth factor is verbal persuasion, which includes receiving encouragement from supportive others.

The PRP works within a theoretical framework consistent with promoting GSE[1]. For example, mastery experience: Patients receive treatment plans from PRP that are appropriate for the patient's level of functioning. They are guided through their programs systematically, with increasing intensity as appropriate. Vicarious learning: Patients have their physiotherapy sessions in

[1] Although not originally included in the CNR/PRP program, the construct of GSE was added in 2007 based on recommended improvements from a third-party program evaluation.

groups. Patients who are close to graduation work in the company of those who are just beginning. This provides neophytes an opportunity to observe others who have progressed or achieved their goals. Improving emotional and physical states: The individualized programs received by each patient have been designed to help them tackle their barriers, such as pain or discouragement, while improving their abilities, such as building strength, flexibility, and social support. Verbal persuasion: The team maintains a positive and supportive environment, in which patients are encouraged to practice their treatment plans and try new things in the company of clinicians who provide positive feedback, helping them recognize their progress and success.

The Current Research

The current research sought to examine the progression of depressive symptomatology changes throughout the program, which factors in the program framework may have been influential in changes in depressive symptomatology pre-post, and whether or not changes are maintained following program completion. As has begun to be demonstrated, depression is a condition that can have many disparate predisposing, precipitating, perpetuating, or protective influences. There are also a number of ways in which an intervention can attempt to affect depressive symptomatology.

The current thesis includes three quasi-experimental studies using secondary data of clinical measures collected through the PRP. Participants were patients with heterogeneous diagnoses of advanced cancer. They had been admitted to the program and had provided informed consent for their clinical data to be used in future studies. To be admitted, patients were considered medically stable with a Palliative Performance score of 50% or better (Victoria Hospice Society, 2001). This rating indicates that they were out of bed for at least half of the day and their life expectancy was estimated to be ≥ 6 months. They had to be motivated to participate in the program. Symptoms such as pain, anxiety, depression, nausea, weight loss, fatigue, or weakness from the disease or its

treatment were present and were interfering with functioning in everyday life. Patients were considered ineligible if they had severe cognitive impairment that would interfere with participation or if they did not meet the defined criteria. Some patients with early stage disease were admitted into the program when it was first established because there was room and they were thought to be able to benefit. These patients were not included in the current analyses. All patients signed an informed consent to participate. Approval was obtained from the three Institutional Research Ethics Board of all affiliated investigators: The Bruyère Continuing Care Research Ethics Board (Protocol# M16-09-055), the Ottawa Health Science Network Research Ethics Board (Protocol# 2011898-01H), and the University of Ottawa Office of Research Ethics and Integrity (File# H05-15-02).

Study 1- An interprofessional palliative care oncology rehabilitation program: Effects on function and predictors of program completion.

The first study conducted was a pilot study. It was an exploratory study that had the primary objective of examining the changes in physical, nutritional, social, and psychological functioning pre-post PRP in patients with advanced cancer post-cancer treatment. It was hypothesized that patients who had completed the PRP would have improved in these various domains of functioning. The results of this study were meant to help inform the PRP of preliminary outcomes of the intervention and also provided a basis for future research with this program. This manuscript was published in *Current Oncology* (Chasen, Feldstain, Gravelle, MacDonald, & Pereira, 2013).

Study 2- An interdisciplinary palliative rehabilitation intervention bolstering self-efficacy to attenuate symptoms of depression in patients living with advanced cancer.

Among other results, the pilot study suggested that patients undergoing the PRP were experiencing attenuation in their symptoms of depression. Given the aforementioned relevance of depression in this population, this theoretical study examined the mechanisms of change within the

PRP that may have affected depressive symptomatology. CRP, exercise, and GSE were selected as predictors because of their prevalence in the literature for treating depression. As well, given the interdisciplinary nature of the PRP intervention, it was thought to be an interesting mix of interdisciplinary predictor variables that are not often considered in conjunction in their respective literatures. Understanding the individual effects of these factors can be helpful in the design of future interventions, providing insight into which factors may best bolster improvements in depressive symptomatology. This manuscript was published in *Supportive Care in Cancer* (Feldstain, Lebel, Chasen, 2015).

Study 3- The longitudinal course of depressive symptomatology for patients with advanced cancer following a palliative rehabilitation program.

The third study was a longitudinal examination of depressive symptomatology three months following program completion. This was novel because there is little literature on the long-term maintenance of attenuated depressive symptomatology for patients with advanced cancer, post interdisciplinary exercise-based intervention. Additionally, what does exist on this topic does not speak favourably for the maintenance of reduced depressive symptomatology. It was hypothesized that post-PRP, patients may show more promise for maintenance of reductions in depressive symptomatology than the existing literature because a) the PRP is interdisciplinary and may therefore affect a wider range of factors that can affect depressive symptomatology, b) the unifying theoretical framework of GSE has shown promise in helping patients improve their health behaviours (Graves, 2003) and may therefore be beneficial in helping patients maintain the adaptive behaviours learnt at the PRP, thereby potentially helping them maintain reduced depressive symptomatology. This manuscript describes a preliminary 3-month longitudinal follow-up of depressive symptomatology for PRP-patients. It has been submitted to *Psycho-Oncology.*

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An interprofessional palliative care oncology rehabilitation program: Effects on function and predictors of program completion[1]

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Abstract

Purpose: After treatment, patients with active cancer face a considerable burden from the effects of both the disease and its treatment. The Palliative Rehabilitation Program is designed to ameliorate disease effects and to improve the patient's functioning. The present study evaluated predictors of program completion and changes in functioning, symptoms, and wellbeing after the program.

Methods: The program received referrals for 173 patients who had finished cancer therapy. Of those 173 patients, 116 with advanced cancer were eligible and enrolled in the 8-week interprofessional palliative rehabilitation program; 67 completed it. Measures of physical, nutritional, social, and psychological functioning were evaluated at entry to the program and at completion.

Results: Participants experienced significant improvements in physical performance ($p <$ 0.000), nutrition ($p = 0.001$), symptom severity ($p = 0.005$ to 0.001), symptom interference with functioning ($p =0.003$ to 0.001), fatigue ($p = 0.001$), and physical endurance, mobility, and balance or function ($p = 0.001$ to <0.001). Reasons that participants did not complete the program were disease progression, geographic inaccessibility, being too well (program not challenging enough), dying, and personal or unknown reasons. A normal level of C-reactive protein (<10 mg/L, $p = 0.029$) was a predictor of program completion.

Conclusions: Patients living with advanced cancers who underwent an interprofessional palliative rehabilitation program experienced significant improvement in their functioning across several domains. Program completion may be predicted by a normal level of C-reactive protein.

Keywords: Cancer, interprofessional, palliative care, rehabilitation

Many patients who have undergone cancer treatment can be limited in their activities of daily life by the symptoms caused by their disease or its treatment (Chasen & Dippenaar, 2008; Kjaer et al., 2010). Cancer rehabilitation is a process that assists the individual's physical, social, psychological, and vocational functioning within their limits (Chasen & Dippenaar, 2008; Spence, Heesch, & Brown, 2010). Post-treatment rehabilitation has been shown to improve physical symptoms such as fatigue and physical endurance (Chasen & Bhargava, 2012); nutritional symptoms such as poor appetite, unintentional weight loss, and nutritional deterioration (Isenring, Bauer, & Capra, 2007; Isenring, Capra, & Bauer, 2004); psychological symptoms such as anxiety, depression, and nervousness (Chasen & Bhargava, 2012; León-Pizarro et al., 2007); and overall quality of life (Spence et al., 2010). Qualitatively, patients who had attended a cancer rehabilitation program stated that rehabilitation was an important stepping stone and that physical and psychosocial care had been an important combination in their recovery (Korstjens, Mesters, van der Peet, Gijsen, & van den Borne, 2006). However, the above-mentioned benefits vary by disease stage (Knols, Aaronson, Uebelhart, Fransen, & Aufdemkampe, 2005) and research in patients with incurable advanced disease ("palliative care" patients) is sparse (Okamura, 2011).

Our team and others have shown evidence of benefit for treatment of symptoms by disease site, such as gastrointestinal or head-and-neck (Chasen & Bhargava, 2009, 2012; Eades et al., 2013; Isenring et al., 2004), colorectal (Bartlett, Sloots, Nowak, & Ho, 2011), prostate (Thorsen, Courneya, Stevinson, & Fosså, 2008), breast (McNeely et al., 2006; Segal et al., 2001), and central nervous system sites (Kirshblum, O'Dell, Ho, & Barr, 2001). There is also evidence for the successful treatment of symptoms by various professional disciplines, including occupational therapy (Lemoignan, Chasen, & Bhargava, 2010), physical therapy (Conn, Hafdahl, Porock, McDaniel, & Nielsen, 2006), nursing (Eades, Chasen, & Bhargava, 2009), social work (Townsend, Accurso-

Massana, Lechman, Duder, & Chasen, 2010), and dietetics (Lundholm, Daneryd, Bosaeus, Körner, & Lindholm, 2004). However, a combined interprofessional approach remains rare.

Compared with standard oncology care alone, early palliative care (as early as diagnosis) is associated with improved mood and quality of life, fewer aggressive oncology treatments at end of life, and extended survival in patients with non-small-cell lung cancer (Temel et al., 2010). The Ottawa Palliative Rehabilitation Program (PRP) at Élisabeth Bruyère Hospital in Ottawa, Canada, is a unique interprofessional program of palliative oncology rehabilitation. In accordance with the World Health Organization's definition of palliative care (World Health Organization [WHO], 2013), the goal of the PRP team is to empower individuals who are experiencing loss of function, fatigue, malnutrition, psychological distress, or other symptoms as a result of cancer or its treatment. The program is designed to help patients with life-limiting disease, even though the disease is incurable, and to improve their quality of life by enhancing their overall health condition through exercise, good nutrition, individualized psychosocial care, and management of their medical complications. It aims to keep people as active as possible in daily life for as long as possible. The clinical expertise of the six team members are combined to target each patient's specific problems by meticulously assessing individual needs so as to properly diagnose and treat their symptom burden (Chasen & Bhargava, 2009, 2012; Chasen & Dippenaar, 2008; Eades et al., 2013; Lemoignan et al., 2010; Townsend et al., 2010).

The present exploratory study had the primary objective of estimating the effect of the PRP on the physical, nutritional, social, and psychological functioning of patients with advanced cancer who have already completed cancer treatment. The hypothesis was that patients who complete the PRP will improve in the various domains of functioning. The secondary objective was to determine medical factors associated with program completion. The hypothesis was that completing the PRP

can be predicted by baseline medical variables: pulse, white blood (WBC) cell count, C-reactive protein (CRP), and Eastern Cooperative Oncology Group (ECOG) performance status (PS).

Method

Participants

Patient referrals were received from health care professionals in the Ottawa Region. Eligible patients were 18 years of age or older, with geographic accessibility, advanced disease, and an ECOG PS of 3 or better or a Palliative Performance Scale of more than 50%. Enrolled patients had already completed cancer treatment.

Patients had to be medically stable and motivated to participate in the nutritional and physical program. Symptoms such as pain, anxiety, depression, nausea, weight loss, fatigue, or weakness from the disease or its treatment had to be present and interfering with functioning in everyday life. Patients were considered ineligible if they had severe cognitive impairment that would interfere with participation or did not meet the defined criteria. Some exceptions were made for patients with localized disease who were allowed into the program. The latter patients were not included in the analysis. All patients signed an informed consent to participate. The study was approved by the local research ethics board.

Procedure

Patients underwent a 3-hour initial assessment; they met with each member of the team (physiotherapist, occupational therapist, social worker, dietician, nurse, physician) individually for 30 minutes. Each clinician obtained baseline measures using self-report questionnaires (which the patient had received in the mail before the visit) and their own clinical measurements.

After the initial assessments, the team met to discuss whether patients were eligible and could benefit from the program. If so, the team jointly formulated a tailor-made care plan for each patient. Plans included medical and nursing assessments, physical exercise, and occupational,

dietary, and psychosocial interventions. Patients accepted into the 8-week program attended group exercise sessions at a gymnasium in the hospital twice per week. The gym sessions each accommodated 4–5 patients, supervised by the physiotherapist. Before each gym session, patients were seen by other team members as required, according to need, or as requested by the patient. At the end of the PRP, final assessments identical to the initial assessments were conducted by each team member. Patients were then discharged back to the referring or family physician and were connected to appropriate community resources. A discharge summary with recommendations for follow-up was provided to the referring physician and to the family physician.

Measures

Several outcome measures were used, including 8 self-report questionnaires and several standardized clinical assessments performed by team members. The outcome measures were completed at the beginning of the PRP (baseline) and again at completion of the 8-week program (end).

Self-report questionnaires

The Edmonton Symptom Assessment System (ESAS) assesses the severity of 9 common symptoms experienced by cancer patients in palliative care. A higher score indicates worse severity of a given symptom (Chang, Hwang, & Feuerman, 2000). Initially, patients in the PRP completed the ESAS only at the beginning and at the end of the 8-week program, but later they completed it at each visit. Because weekly completion did not apply to the full cohort of patients in the study, only the baseline and end ESAS scores were analyzed.

The MD Anderson Symptom Index assesses interference in patient functioning in 6 domains: general activity, mood, work (including housework), relations with others, walking, and enjoyment of life. Higher sores indicate more interference (Cleeland et al., 2000).

The Patient-Generated Subjective Global Assessment is a nutrition assessment tool, validated for clinical and research use with cancer patients. Higher scores indicate higher nutritional risk (Leuenberger, Kurmann, & Stanga, 2010; Ottery, 1996).

The Multidimensional Fatigue Inventory assesses five domains of fatigue: general, physical, mental, decreased motivation, and decreased activity (Smets, Garssen, Bonke, & De Haes, 1995). Higher scores indicate greater fatigue.

Physiotherapy measures

The physiotherapy assessments of the patients included the Berg Balance Scale (Steffen, Hacker, & Mollinger, 2002), the Functional Reach Test for balance and function (Simmonds, 2002), the Timed Up and Go for mobility (Podsiadlo & Richardson, 1991), a grip test for muscle strength (Norman et al., 2010), and the Six Minute Walk Test for endurance (Simmonds, 2002; Steffen et al., 2002).

Nurse and physician

Patients underwent a full clinical examination, and their ECOG PS, an objective measure of functional ability (0 = no functional limitations; 4 = confined to bed (Oken et al., 1982)) was recorded.

Laboratory tests

Blood tests were performed as part of usual clinical care and included full blood count, electrolytes, C-reactive protein (CRP), serum albumin, thyroid stimulating hormone, glucose, lactate dehydrogenase.

Statistical Analysis

Analyses were performed using the SPSS software application (version 20: SPSS, Chicago, IL, U.S.A.). Descriptive statistics were used for patient characteristics, grouped according to whether they started and completed the program. Inferential statistics were used to assess changes from

baseline to PRP end and to examine baseline medical variables that may predict PRP completion. Pre–post changes were analyzed using paired-sample t-tests unless the distribution of the difference scores was not normal (three standard deviations or more for skewness or kurtosis), in which case a Wilcoxon signed-rank test was used. Missing values were excluded case-wise. Because of the number of pre–post tests, a p value 0.005 or less was used to determine statistical significance. The Cohen d effect size was used to assess the magnitude of the differences in pre–post measurements unless the distribution was not normal. In such cases, the formula

$$\text{effect size} = Z / \sqrt{N}$$

was used. Medical differences between groups were analyzed using a backward-selection Wald logistic regression. The variables included were CRP and WBC count measured in the blood tests, pulse as assessed by the nurse, and ECOG PS as assessed by the nurse and physician. Serum CRP was dichotomized as either normal (<10 mg/L) or elevated (≥10 mg/L) because of a positively skewed distribution and for clinical utility.

Results

Of 173 patients who underwent the initial assessment, 171 were accepted into the program (Figure 1). Of the 171 patients accepted, 55 were excluded from the analysis: 16 had localized disease, 5 patients were still in the program at the time of the analysis, and 34 patients were accepted into the program but did not start it (“non-starters”). Figure 1 shows the reasons that patients could not start the program. Of the remaining 116 patients, 67 (57.8%) completed the 8-week program, and 49 (42.2%) began the program but did not complete it. Figure 1 lists the reasons that patients did not complete the program. Table 1 presents baseline characteristics for the patients who did and did not complete the program.

In a comparison of baseline and end data (Table 2) for patients who completed the 8 weeks of the program, significant improvements (with moderate to large effect sizes) were noted across a

number of domains. Those domains included ecog ps ($p < 0.001$, $d = 0.90$), overall nutritional risk ($p = 0.001$, $d = 0.46$), severity of several symptoms [anxiety ($p = 004$, $d = 0.39$), depression ($p = 0.005$, $d = 0.37$), overall wellbeing ($p = 0.001$, $d = 0.40$), feeling tired ($p = 0.001$, $d = 0.46$)], symptom interference in several domains [mood ($p < 0.001$, $d = 0.48$), enjoyment ($p < 0.001$, $d = 0.49$), general activity ($p < 0.001$, $d = 0.47$), work ($p = 0.003$, $d = 0.38$)], fatigue [general ($p < 0.001$, $d = 0.61$), physical ($p < 0.001$, $d = 0.55$), decreased activity ($p = 0.001$, $d = 0.45$)], and physiologic functioning [Six-Minute Walk Test ($p < 0.001$, $d = 0.80$), Timed Up and Go ($p < 0.001$, $d = 0.65$), Functional Reach Test ($p = 0.001$, $d = 0.44$)].

Improvements with small effect sizes were noted in some symptoms [appetite ($p = 0.009$, $d = 0.34$), nausea ($p=0.016$, $d = 0.30$), drowsiness ($p = 0.031$, $d = 0.28$), shortness of breath ($p = 0.235$, $d = 0.15$)], symptom interference in relationships ($p = 0.090$, $d = 0.23$) and walking ($p = 0.012$, $d = 0.32$), two fatigue-related outcomes [decreased motivation ($p = 0.006$, $d = 0.35$), mental fatigue ($p = 0.272$, $d = 0.14$)], and two physiologic outcomes [Berg Balance Scale ($p = 0.008$, $d = 0.34$), grip strength ($p = 0.048$, $d = 0.27$)]. Pain did not change ($p = 1.000$, $d = 0.00$).

Patients were more likely to finish the program if their CRP level was normal than if it was elevated [Wald statistic(1) = 4.78; $p = 0.029$; relative risk: 1.52; 95% confidence interval: 0.99 to 2.34]. The ECOG PS, pulse, and WBC count were not significant predictors of program completion (Table 3). Because of missing biological data, 23 patients (8 completers, 15 non-completers) were excluded from the regression.

Discussion

Patients in our study who had advanced cancer and who completed the interprofessional PRP demonstrated a wide range of improvements. Moderate-to-large effects (defined by an effect size of 0.5 or greater) were observed in ECOG PS, endurance, mobility, general fatigue, and physical fatigue. Small-to-moderate improvements (defined by effect size between 0.2 and 0.5) were

observed in nutrition status; symptom interference in mood, enjoyment, general activity, and work; decreased activity; balance and function; and several symptoms. Some measures that did not meet statistical significance still demonstrated moderate improvement, such as severity of drowsiness and appetite symptoms; interference in relationships and walking; decreased motivation; Berg Balance Scale; and grip strength. Nonsignificant results with small effect size ($d < 0.2$) were observed for the severity of two symptoms (shortness of breath and pain) and for mental fatigue. It is important to note that patients did not experience worsening symptoms in any of the domains. Overall, our findings suggest that patients with life-limiting cancers who have undergone an interprofessional patient-centered PRP experienced improvements in many domains.

The improvements found in the current study are important because they contrast with the usual pattern seen in patients living with advanced cancer and other chronic illnesses (Lynn & Adamson, 2003). Typically, such patients have a steady burden of symptoms until the final weeks before death, at which point symptoms drastically worsen. In contrast, the results of the current research demonstrate that patients can experience many improvements. Given the contrast with the existing literature, we posit that palliative rehabilitation is a beneficial application of early palliative care. Early palliative care has been cited as a necessary next step in the advancement of care for patients living with cancer, possibly even in conjunction with active treatment (Bruera & Yennurajalingam, 2012).

In addition to direct interdisciplinary intervention, the PRP strives to foster additional sources of healing, such as social support. Social support has been found to help patients adjust to illness, to increase adherence to treatment, and to have beneficial effects on wellbeing, stress, and immunity (DiMatteo, 2004; Ell, 1984; Uchino, 2006). During the PRP, patients are encouraged to bring their caregivers to the gym sessions. The patients also bond and form friendships with their peers during the exercise sessions, and they receive support from the PRP team. All of those

contacts might improve motivation by providing friendship, solidarity, and a sense of belonging and might help patients address the initial barriers of undertaking an exercise program (for example, lacking motivation, feeling deconditioned, or having difficulty incorporating a regular exercise routine (Blaney et al., 2010)).

Normal serum CRP was found to be a significant biologic predictor of program completion. That finding was expected, because an elevated CRP alone or coupled with an elevated WBC count has been identified as an ominous indicator of shortened survival (Kasymjanova et al., 2010). In the present study, patients with normal levels of CRP were 1.52 times more likely to complete the program than were patients with elevated levels of CRP. Inflammation, as indicated by elevated CRP, promotes incapacity and suffering; compared with patients having a normal CRP, those with an elevated reading are likely to experience more rapid tumour progression (Fearon, Voss, Hustead, & Group, 2006). Although the exercise and psychosocial components of our rehabilitation program might contribute to the reduction of CRP levels (Balducci et al., 2010; Fang et al., 2010; Ford, 2002), patients with high serum CRP might find it more difficult to complete the program because they are usually more ill.

Clinically, patients reported that they were 70%–100% satisfied with the program (Savage-Larose, Gravelle, Chasen, & Bhargava, 2012). Complaints involved issues such as parking and a desire for follow-up sessions (although patients are referred to community resources for follow-up on PRP completion). Patients did not complain about the length of the 3-hour interviews or the program structure in general. [1]Given the current findings, we suggest several changes to the program, using a multipronged approach that might improve a chronic inflammatory state. Those changes might potentially increase the completion rate and perhaps generalize to functioning in

[1] Author NM wrote this paragraph from this point onwards.

overall life for the patients. From a nutrition perspective, the additional interventions could include an “anti-inflammatory diet” with increased emphasis on branched-chain amino acids (Laviano et al., 2005), vitamin D supplementation as a regular feature (Stone, Kenny, Healy, Walsh, & Lawlor, 2011), and omega-3 fatty acid supplements (Murphy, Mourtzakis, & Mazurak, 2012). From an exercise perspective, the changes would include modifications to our current balance of aerobic and resistance recommendations (Galvao & Newton, 2005; Knols et al., 2005; Spence et al., 2010). Consideration is also being given to make pharmaceutical adjustments to the program, including considering a nonsteroidal antiinflammatory drug for patients with high serum CRP otherwise judged to be at low risk for adverse reactions to such drugs. Although support in the literature for the use of nonsteroidal antiinflammatory drugs is generally positive, more research is necessary to support the efficacy of that approach (Reid, Hughes, Murray, Parsons, & Cantwell, 2012).

The major limitation of the current study is the limited availability of potential methodologic designs for this patient group. Although the results appear promising compared with those in the existing literature (Lynn & Adamson, 2003), we cannot say with certainty that our program caused the observed improvements. The next logical step would be to create control or contrast groups but some patients have only a few months to live. Withholding or replacing treatment from these patients for several months poses ethical issues. We are therefore precluded from using the usual methods to determine the unique effect of the PRP—for example, waitlist controls or randomized controlled trials. Another limitation is the lack of interim measurements. Almost 37% of the identified sample did not provide a specific reason for withdrawal. Given that the weekly ESAS data were not complete, and the ECOG PS was not assessed each week, it is difficult to draw conclusions about the experiences of the patients throughout their eight weeks. It also precludes us from contrasting the progression of symptom severity, disease status, or disease progression in patients who did and did not complete the program. Finally, patients received

individual interventions specific to their individual needs and goals—that is, the interventions were not uniform. The differences might have inflated patient improvements by focusing on areas with the worst functioning, thereby allowing for the largest possible gains to be experienced. Statistically, that approach may present a potential artifact, but clinically, it is a strength. In addition it increases external validity: individualized programs are the norm in clinical practice, and such programs are likely to be patient-centered rather than uniform.

Future research directions include examining mechanisms of change that might influence patient improvements. An analysis of that kind would be useful to better understand which elements of this complex program are the most beneficial. A pre–post examination of patient use of various health care services could also suggest whether patients are experiencing an improved level of functioning overall after having undergone such a program. The impact of the program in keeping patients functional for longer periods in the home setting warrants its continuation. Identifying the minimal program duration that can result in positive and sustained results will also be important; it is possible that benefits may be realized sooner than the full eight weeks, which would have important resource implications. Social support is another important area to examine, given its support in the current literature as an important factor in both quality of life and prognosis. Finally, longitudinal follow-up to examine if gains are maintained would better inform the evaluation of the benefits that patients are able to experience.

Conclusion

The PRP offers an interprofessional holistic approach that positions the patient at the centre of an individualized program. Each discipline offers its own expertise, but collaboration and discussion among the professionals is vital so that all the interventions complement one another. The outcomes of this program appear to be reduced symptom burden, reduced interference by symptoms in daily life, and improved nutrition, physical, and functional status and overall wellbeing.

It is expected that, through continued application of the skills acquired from the PRP, patients will demonstrate reasonable maintenance of their gains, a decreased reliance on the health care system, and fewer emergency room visits. The latter hypotheses have to be tested in future studies. By affording the opportunity for rehabilitation to palliative care patients who can manage the intensity required by such a program, “living” with cancer can be a reality for many.

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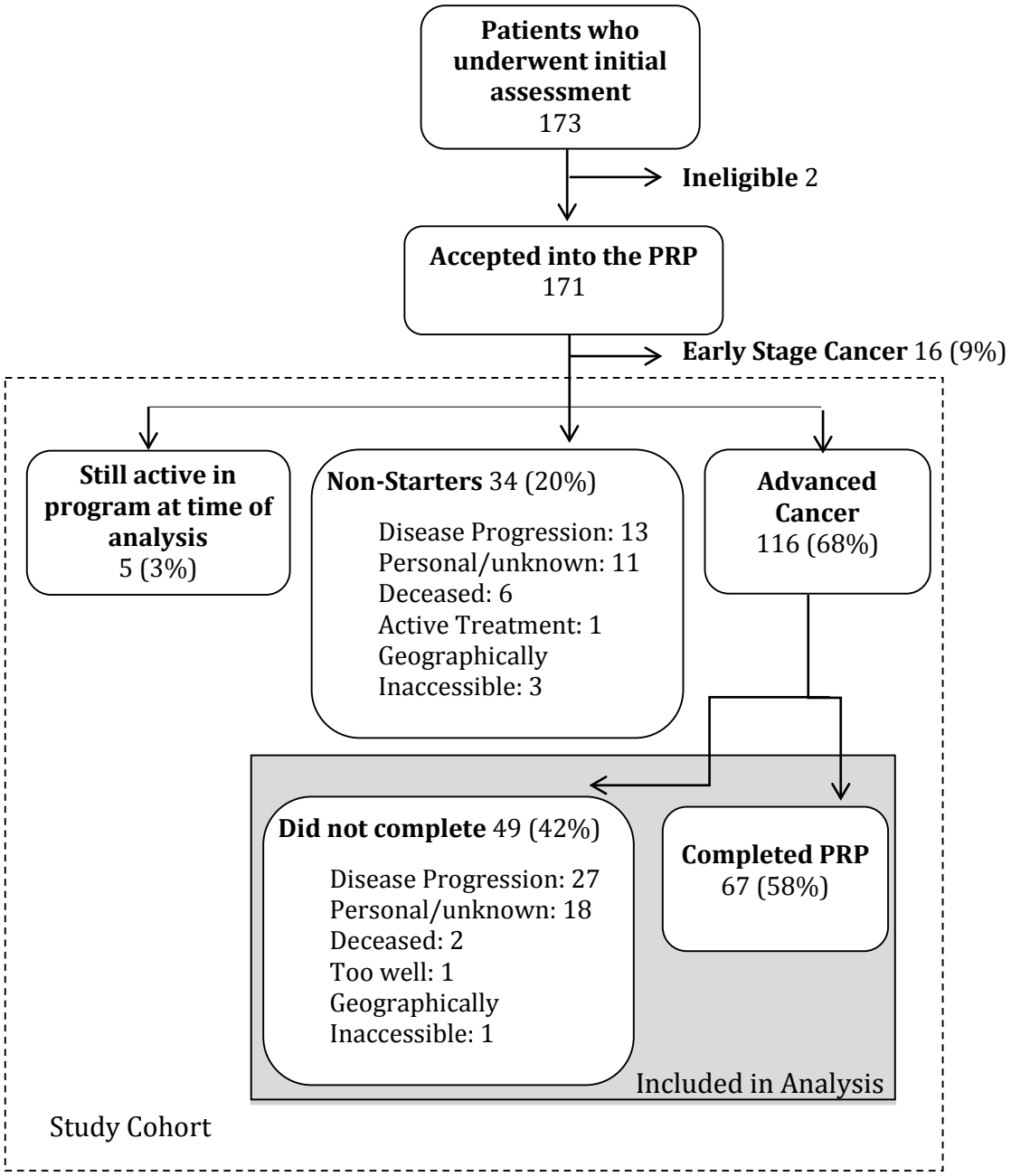

Figure 1. Flow diagram of patient recruitment.[1]

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[1]This figure was created by authors AF, MC, and JP.

Table 1

Baseline characteristics of patients who did and did not complete the Ottawa Palliative Rehabilitation Program

Characteristic	Completed program?			
	Yes		No	
	(*n*)	(%)	(*n*)	(%)
Patients (*n*)	67	57.8	49	42.2
Sex				
Men	35	52.2	27	55.1
Women	32	47.8	22	44.9
Cancer site (>30 sites)				
Head and neck	11	16.4	6	12.2
Breast	9	13.4	8	16.3
Hematologic	8	11.9	4	8.2
Lung				
Non-small-cell	7	10.4	7	14.3
Small-cell	2	3.0	3	6.1
Colorectal	5	7.5	3	6.1
Prostate	3	4.5	3	6.1
Liver bile duct	2	3.0	0	0
Esophageal	2	3.0	2	4.1
Central nervous system	2	3.0	2	4.1
Skin	2	3.0	0	0
Unknown primary	2	3.0	0	0
Urogenital	1	1.5	3	6.1
Hodgkin lymphoma	1	1.5	0	0
Other	10	14.9	8	16.4
Stage				
III	21	31.3	15	30.6
IV	46	68.7	34	69.4
ECOG performance status (PS)				
1	26	38.8	17	34.7
2	31	46.3	23	46.9
3	10	14.9	9	18.4
Mean age (years)	61.64±13.0		62.37±14.23	
Medical variables (means)				
C-Reactive protein				
Normal	3.15±2.97		3.68±3.23	
Elevated	33.46±21.64		46.94±37.84	
White blood cells	6.80±2.83		9.40±9.13	
ECOG PS score	1.76±0.70		1.84±0.72	
Pulse (bpm)	78.22±11.98		78.34±12.73	

ECOG= Eastern Cooperative Oncology Group.

Table 2

Change in functioning from baseline to end of the Ottawa Palliative Rehabilitation Program (paired t-test)

Effect size and measure	*n*	Baseline[a]	Completion[a]	*t*	*p*	*d*
Medium-to-large effect						
ECOG performance status	56	1.8±0.7	1.29±0.46	6.43	<0.001	0.90
Patient-generated SGA	60	8.15±5.29	5.98±4.14	3.49	0.001	0.46
ESAS						
Anxiety	63	3.24±2.98	2.35±2.48	3.01	0.004	0.39
Depressed	63	2.67±2.63	1.89±2.22	2.92	0.005	0.37
Wellbeing	64	4.85±2.62	3.89±2.41	3.2[b]	0.001	0.40
Tired	63	4.89±2.6	3.81±2.26	3.645	0.001	0.46
MD Anderson Symptom Index						
Mood	66	4.58±3.27	3.18±2.55	3.83	<0.001	0.48
Enjoyment	66	5.68±3.38	4.05±2.89	3.99	<0.001	0.49
General activity	66	5.5±3.12	3.89±2.7	3.8	<0.001	0.47
Work	66	5.59±3.4	4.32±3.13	3.08	0.003	0.38
Multidimensional Fatigue Inventory						
General	65	15.35±3.3	13.35±3.49	4.93	<0.001	0.61
Physical	65	15.92±3.27	14.09±3.42	4.42[b]	<0.001	0.55
Decreased activity	65	15.38±3.62	13.69±3.97	3.66	0.001	0.45
Physiologic						
Six-Minute Walk Test	60	367.38±123.24	422.68±127.6	–6.17	<0.001	0.80
Timed Up and Go	60	11.39±6.49	9.07±3.92	5.04[b]	<0.001	0.65
Functional Reach Test	61	32.69±8.03	36.01±8	–3.43	0.001	0.44
Small effect						
ESAS						
Appetite	63	4.06±3.15	3.24±2.66	2.69	0.009	0.34
Nausea	64	1.03±1.77	0.53±1.33	2.41[b]	0.016	0.30
Drowsy	63	2.71±2.61	2.02±2.17	2.21	0.031	0.28
Short of breath	63	2.3±2.76	1.92±2.48	1.2	0.235	0.15

Pain	63	3.06±2.26	3.06±2.42	0	1.000	0.00
MD Anderson Symptom Index						
Relationships	66	3.62±2.94	2.86±2.76	1.72	0.090	0.23
Walking	66	4.98±3.24	3.92±3.01	2.59	0.012	0.32
Multidimensional Fatigue Inventory						
Decreased motivation	65	12.29±4.01	10.8±3.77	2.83	0.006	0.35
Mental	65	10.92±4.04	10.29±3.79	1.11	0.272	0.14
Physiologic						
Berg Balance Scale	59	53.48±5.59	54.22±6.3	–2.64b	0.008	0.34
Grip strength	55	26.68±10.48	27.89±10.34	–1.98b	0.048	0.27

a All values, mean ± standard deviation.

b Normality not assumed. A related-samples Wilcoxon signed rank test used to test significance, and Z/√N used to calculate effect size.

Pts = patients; ECOG= Eastern Cooperative Oncology Group; SGA= Subjective Global Assessment; ESAS= Edmonton Symptom Assessment System.

Table 3

Significant medical predictors of program completion, by logistic regression

Variable	Wald statistic	*df*	*p* Value	Relative risk	95% CI	
					Lower	Upper
Significant						
C-Reactive protein	4.78	1	0.029	1.52	0.99	2.34
Nonsignificant						
ECOG performance status	0.26	1	0.614			
White blood cells	1.94	1	0.164			
Pulse	0.29	1	0.593			

CI = confidence interval; ECOG= Eastern Cooperative Oncology Group

An interdisciplinary palliative rehabilitation intervention bolstering general self-efficacy to attenuate symptoms of depression in patients living with advanced cancer[1]

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Preface to Study 2

Study 2 focuses on the finding from study 1 that self-ratings of depression were significantly attenuated. As mentioned, depression is a particular concern for patients with advanced cancer, because patients in the later stages of illness may be reflecting on their losses, learning to accept the permanence of the disease, and having difficulty finding meaning in the threat to survival. Study 2 sought to examine the mechanisms that may have influenced change in self-reported ratings of depression. Three program factors that were examined were inflammation, exercise, and general self-efficacy. Having a better understanding of how depression may have been affected can help bolster the effects of intervention.

Abstract

Purpose: Patients with advanced cancer, post-cancer treatment, are living longer than 10–20 years ago. This emerging population of survivors has unique palliative and rehabilitation needs. A particular concern is depression, which can impair functioning, quality of life, and survival. The interdisciplinary Palliative Rehabilitation Program offers holistic palliative rehabilitation for this population using a self-efficacy framework. The current study examined the unique impact of three program factors that have been shown to improve depression: inflammation, exercise, and self-efficacy. *Method:* Patients underwent a 2-month interdisciplinary intervention (up to six disciplines) and thorough pre-post assessments. Measures included serum C-reactive protein, 6-min walk test, General Self-efficacy Scale, and Hospital Anxiety and Depression Scale (depression subscale). Paired t tests analyzed pre-post changes in each variable and a hierarchical linear regression analyzed the predictors' unique contributions to changes in depression in this quasi-experimental design. *Results:* The sample included 80 patients (52.5 % females), with stages III/IV heterogeneous cancers. Results revealed that C-reactive protein (CRP) did not significantly change pre-post, from 7.39 (SD=11.99) to 9.47 mg/L (SD=16.41), $p=0.110$, exercise significantly increased, from 372.55 meters (SD=137.71) to 412.64 m (SD=144.31), $p<0.001$, self-efficacy significantly increased from 27.86 (SD=6.16) to 31.23 (SD=5.77), $p<0.001$, and depression scores significantly decreased, from 7.14 (SD=3.91) to 5.95 (SD=3.51), $p=0.002$. A hierarchical linear regression revealed that this model explained 15% of variance in changes in depression scores, $p=0.006$. Change in self-efficacy accounted for 11 % of change in depression scores ($p<0.001$). Change in CRP and exercise did not make a significant contribution. *Conclusions:* A self-efficacy framework may be a helpful ingredient in interdisciplinary intervention to decrease depressive symptomatology.

Keywords: Advanced cancer, Palliative rehabilitation, Self-efficacy, Depression, Interdisciplinary

With progress in oncological care, patients with advanced cancer may have months or years of extended life (Conroy et al., 2011; Institute of Medicine [IOM] & National Research Council of the National Academies [NRC], 2006; Tangen et al., 2003). For many, these advances may change a diagnosis of advanced cancer from terminal to chronic. However, living with chronic illness poses its own challenges, such as declines in functioning due to the disease or its treatment (Chasen & Jacobsen, 2011), and late- or long-term effects, such as depression, may continue to develop or persist (Hannon et al., 2015). Depression has been found to be the most common mental health problem in patients with advanced cancer (Massie, Lloyd-Williams, Irving, & Miller, 2011) and in palliative care (Wilson, Lander, & Chochinov, 2009). Depression increases over time following diagnosis irrespective of baseline level and tends to peak in the later or palliative stage (Mayer, Geiser, Infurna, Fiege, & Chicago, 2013; Rodin, 2013). Depression can impair a patient's functioning more than a single or multiple physical illnesses (Moussavi et al., 2007). It has been endorsed as one of the top causes of suffering in outpatients with advanced cancer (Al-Shahri, Eldali, & Al-Zahrani, 2012). This detriment in functioning is further exacerbated when depression and physical illness are comorbid. This can impair a person's ability to function and/or their quality of life (QOL). Patients with comorbid cancer and depression have been found to have shorter survival rates than patients with cancer alone, regardless of which diagnosis was received first or of potential confounding variables such as cancer stage (Hotopf, Chidgey, Addington-Hall, & Ly, 2002; Moussavi et al., 2007; Pinquart & Duberstein, 2010). Given the additional burden of depression on this population, effective clinical care is important.

A framework for post-treatment care for patients with advanced cancer is exemplified by the Palliative Rehabilitation Program (PRP). The PRP is an interdisciplinary program that was designed to meet the needs of patients living with advanced cancer (Chasen, Feldstain, Gravelle, MacDonald, & Pereira, 2013; Chasen & Dippenaar, 2008). The interdisciplinary PRP team is

composed of six clinicians (physician, nurse, physiotherapist, occupational therapist, dietician, and social worker) who offer thorough assessment and intervention to address the effects of cancer or its treatment. The goal is to help patients restore, enhance, and/or maintain their functioning and QOL. It aims to empower individuals who are experiencing loss of function, fatigue, malnutrition, psychological distress, or other symptoms. Pilot data indicated that patients with heterogeneous advanced cancer who underwent the PRP experienced improvements in a number of domains, including self-reported symptoms of depression (Chasen et al., 2013), which can be maintained 3 months following completion of the PRP (Feldstain, Lebel, & Chasen, 2014). There are a number of elements within the PRP that may contribute to improved depression scores. The current study sought to examine the contribution of three program elements: inflammation, exercise, and self-efficacy, which have previously been found to reduce depression.

Inflammation

A particular focus in PRP intervention is reducing systemic inflammation. Systemic inflammation signals immune activity, in response to injury or infection. A proxy for this is C-reactive protein (CRP), which is the prototypical biological measure used to assess systemic inflammation in clinical practice (Deans & Wigmore, 2005). CRP is an anti-inflammatory protein released by the body to counter other pro-inflammatory agents that may have been produced during the immune response. In the short term (e.g., fighting the flu, highly but acutely stressed), anti-inflammatory response is effective for regaining physical homeostasis. In the long term, e.g. when living with malignant tumors, coping with high chronic stress (Deans & Wigmore, 2005; Mahmoud & Rivera, 2002), ongoing anti-inflammatory response can itself become harmful. For patients with cancer, a chronic inflammatory state (CIS) can nourish cancer cells and perpetuate illness (MacDonald, 2011). Chronically elevated CRP in response to a CIS is highly associated with increased morbidity and mortality and is considered an indirect marker of prognosis (MacDonald,

2011; Mahmoud & Rivera, 2002). It has also been found to be a risk factor for the development of new cases of major depressive episodes and is now being considered a target for the treatment of depression especially for cases that do not respond to usual monoamine transmission anti-depressants (Miller & Raison, 2008).

An optimal intervention for targeting CRP has not yet been identified. The PRP combines several therapies that have been shown to affect CRP directly and indirectly. The PRP targets CRP directly through medication, exercise, and nutrition. Indirectly, it targets inflammation through interventions to reduce symptom burden, ameliorate psychosocial health, reduce stressors, which may affect the patient's ability to function and to follow care recommendations. For example, a patient who learns energy management strategies may experience less fatigue, be better equipped to undertake activities of daily living (ADLs), depend less on a caregiver, and feel less overall stress (Chasen & Dippenaar, 2008; MacDonald, 2007).

Exercise

All PRP patients receive group physiotherapy twice per week. Extensive reviews and meta-analyses of RCTs have been published on the effects of exercise on depression. Patients with cancer have exhibited small to moderate improvements in depression symptoms following exercise interventions (Brown et al., 2012; Mishra et al., 2012). However, depression is often a secondary outcome in interventions that target practical outcomes, such as fatigue or other symptoms (Craft, VanIterson, Helenowski, Rademaker, & Courneya, 2011; Mead et al., 2009). As well, theory on how exercise interventions affect depression is sparse in these studies (Brown et al., 2012), yet theory-driven exercise interventions have been found to be more effective than others (Brown et al., 2012). Perhaps, exercise itself is not what influences depression but rather, the adjacent skills developed, such as self-efficacy, when successfully implementing a new regimen.

Self-Efficacy: A Theoretical Mechanism of Change

Self-efficacy is a concept from social cognitive theory (SCT) that refers to one's perception that he/she can influence life events or the quality of his/her functioning. General self-efficacy (GSE) is one's subjective perception of overall ability to cope effectively with stressful or difficult situations. It is a fairly stable trait (Bandura, 1977; Luszczynska, Scholz, & Schwarzer, 2005). GSE is different than domain-specific self-efficacy, which is the perception of one's ability to cope with particular situations (e.g., changing a flat tire). GSE is recommended for measuring intentions or coping outcomes when there are a number of simultaneous activities or demands, like coping with advanced cancer, its treatments, and numerous potential side- or late-effects. GSE is related to motivation, affect, and behavior more than are objective measures of ability (Bandura, 1977; Luszczynska, Gutiérrez-Dona, & Schwarzer, 2005). In the context of health, GSE has been shown to have positive effects on objective measures of health (e.g., heart rate, serum catecholamine levels, post-coronary recovery (Bandura, 1998)), health behaviors (Bandura, 1998), functioning (Bandura, 1998), and subjective wellbeing (Bandura, O'Leary, Taylor, Gauthier, & Gossard, 1987). GSE has been negatively correlated with anxiety and depression in patients with a variety of chronic illnesses, including cancer (Kohno et al., 2010; Luszczynska, Scholz, et al., 2005).

The PRP promotes self-efficacy with the following four steps (Bandura, 1977, 1998): mastery experience, social modeling (vicarious learning), improving physical and emotional states, and verbal persuasion. Mastery experience refers to achieving small steps toward one's goal in a graded fashion; it is the most potent factor in building GSE. In the PRP, patients receive a treatment plan based on the team's assessment and the patient's individual goals/level of functioning when they are accepted into the program. The interdisciplinary treatment plans are implemented over the course of the PRP with the guidance and supervision from PRP team. Social modeling refers to viewing others in the pursuit and success toward the same goal. In the PRP, all patients enrolled in the program work in the gym together, neophytes in the company of those more advanced in their

programs, who have experienced improvements and have felt a sense of success. Improving emotional and physical states refers to removing barriers that may hinder goal achievement, such as fear, to improving their perceptions of their capabilities, such as improved mobility. In the PRP, the team works with each patient to tackle barriers, such as pain or fear, and to enhance positive factors such as improved dietary intake or social support. Finally, verbal persuasion refers to encouragement such as positive reinforcement. The PRP team provides a supportive atmosphere with plenty of positive feedback and guidance, in order to motivate patients, encourage positive changes, and help patients recognize their successes. The application of a GSE framework provides an explanation for how patients with differing presenting problems can receive reductions in depressive symptoms without standardized interventions (i.e., they receive individualized care plans commonly focusing on building self-efficacy).

While each inflammation, exercise, and GSE have been shown to help patients with symptoms of depression, they are not mutually exclusive and their unique contributions are yet unknown. The key to optimizing gains in this and other programs is to understand their independent impacts. The goal of the current study is to differentiate the predictive ability of (1) changes in CRP, (2) changes in exercise ability, and (3) changes in GSE on changes in symptoms of depression pre-post PRP. It is hypothesized that changes in CRP, exercise, and GSE will each predict a unique amount of change in depression scores from PRP beginning to completion

Methods

Participants

This was a secondary analysis of clinical data collected through the PRP. Participants were patients who completed the 8-week PRP between April 2011 and June 2014. All patients provided informed consent for their clinical measures to be used for future research; those who did not

consent were still eligible to participate in the PRP. The study was approved by the local research ethics board.

Procedure

This was a quasi-experimental design. Patients were referred by physicians in Ottawa to this 8-week outpatient interdisciplinary palliative rehabilitation. Patients received group physiotherapy twice/week and other interdisciplinary follow-ups as necessary or requested. Baseline measures were clinical assessments by each PRP team member at patient's initial clinical interview and self-report questionnaires that patients received in the mail prior to the interview. Post-PRP measures were collected at the completion interview. For more information on participants and procedure, see Chasen et al. (2013).

Measures

Patients completed the following measures before starting the PRP (T1) and upon PRP completion (T2).

Demographic information.

Demographic and medical information that may affect reported levels of depression were acquired from the patients' files and were considered as potential confounding variables. These included gender (Allin & Nordestgaard, 2011; Amyre Morris et al., 2011; Cheung, Le, Gagliese, & Zimmermann, 2011; Culleton et al., 2011; Jiménez et al., 2011; Ma et al., 2010; Zimmerman et al., 2011), age (Allin & Nordestgaard, 2011; Brant et al., 2011; Cheung et al., 2011; Dantzer, O'Connor, Freund, Johnson, & Kelley, 2008; Frank & Caceres, 2015; Jiménez et al., 2011; Kiecolt-Glaser & Glaser, 2002; Lo et al., 2010; Meeks, Vahia, Lavretsky, Kulkarni, & Jeste, 2011; Parker, Baile, de Moor, & Cohen, 2003; Rodin et al., 2009; Walsh, Donnelly, & Rybicki, 2000), marital status (Holt-Lunstad, Smith, & Layton, 2010; Mayer et al., 2013; Parker et al., 2003; Pinquart & Duberstein, 2010; Rodriguez, Mayo, & Gagnon, 2013), cancer stage (Ciaramella & Poli, 2001; Hotopf et al., 2002;

Li, Boquiren, Lo, & Rodin, 2011; Mayer et al., 2013; Rodin, 2013; Spiegel & Giese-Davis, 2003; Wilson et al., 2007), diagnosis of breast cancer versus another site (Brown et al., 2012; Mishra et al., 2012), reported smoking status (Allin & Nordestgaard, 2011; Korhonen et al., 2007; Le-Ha et al., 2014; Pasco et al., 2010) or alcohol consumption (Delgadillo, Godfrey, Gilbody, & Payne, 2013; Grant & Harford, 1995), and anti-depressant medication use.

Clinician evaluation.

Inflammation.

Inflammation was assessed by testing CRP on serum, using a serum separator tube. Samples were tested using a COBAS analyzer at the Gamma-Dynacare Medical Laboratories in Ottawa, Canada. Patients received blood requisition forms at their initial and completion interviews, and they were able to complete the blood work that day on location at the hospital.

Exercise.

The 6-min walk test (6MWT) is a common test to assess functioning in patients with cancer (Simmonds, 2002). It was originally developed to measure maximal oxygen uptake but has become a common measure of overall exercise function for patients with chronic illness. It reflects the capacity to perform day-to-day activities (Society, 2002) and it can be used to measure the impact of disease or co-morbidities on a patient's exercise capacity (Enright et al., 2003). The 6MWT was chosen as a proxy for exercise because it (a) is feasible and acceptable for this patient population and (b) reflects physical endurance, which is an objective measure of engaging in exercise behavior (Simmonds, 2002). Test-retest reliability, discriminant validity, and convergent validity have been found to be "excellent" for patients with heterogeneous cancers (Simmonds, 2002). The PRP physiotherapist completed the 6MWT at patients' initial and completion interviews.

Self-report measures.

General self-efficacy.

The General Self-efficacy Scale (GSES) is a validated self-report measure that assesses overall impression of one's ability to deal with demanding situations (Schwarzer & Jerusalem, 1995). This ten-item questionnaire requires patients to rate statements such as "I am confident that I could deal efficiently with unexpected events" and "When I am confronted with a problem, I usually find several solutions" from 1 (not at all true) to 4 (exactly true). This scale yields a single score of GSE, with higher scores indicating higher sense of GSE than lower scores.

The GSES is a reliable and valid measure of GSE (Brady, 2003). Cronbach's alpha estimates (0.88–0.91) demonstrate good internal consistency. Test-retest reliability over a period of 4 months yielded a correlation of r=0.63. Construct validity was demonstrated by a factor analysis that revealed a single factor solution that accounted for 50 % of the variance. Divergent validity was supported by the lack of association between the GSES and three measures of physical health status. The Cronbach's alpha in the current sample was 0.94 at T1 and 0.92 at T2.

Depression.

The Hospital Anxiety and Depression Scale (HADS; Zigmond & Snaith, 1983) is a 14-item self-report questionnaire that assesses symptoms of anxiety and depression. Seven of the 14 items assess symptoms of depression, such as "I still enjoy the things I used to" and "I have lost interest in my appearance." The other seven items assess anxiety, such as "I feel tense or 'wound up'." The HADS was designed for use with medical patients and has been used extensively for patients with cancer. It has been found to be the most efficient measure with the best track record for use in a population of English-speaking patients with heterogeneous cancers (Luckett et al., 2010). The HADS does not focus on the physical symptoms of depression, which may overlap with symptoms of cancer or its treatment (e.g., fatigue, weight fluctuations) but instead on psychological symptoms (e.g., sad mood, anhedonia). A systematic review of measures of emotional distress found the two HADS' subscales to be stable across samples, internally consistent, and sensitive to change for

patients with cancer (Vodermaier, Linden, & Siu, 2009). The current study will only use the depression subscale. The Cronbach's alpha of the depression subscale in the current sample was 0.79 at T1 and 0.79 at T2.

Analyses

Data were analyzed using IBM SPSS Amos. Changes in scores of depression, inflammation, exercise, and GSE were calculated using the method described by Dalecki and Willits (1991) and Gillespie and Streeter (1994). This is supported for analyzing difference scores in non-experimental analysis of change.

Using this method, T1 scores were subtracted from T2 and T1 values were also controlled within the regression. An a priori calculation of sample size using G*power (Faul, Erdfelder, Lang, & Buchner, 2007) indicated that, with all control variables previously listed included, a sample size of 78 would yield 80 % power to detect medium to large effects. The assumptions for hierarchical linear regression were met.

Multiple imputation (MI) was performed to replace missing data using NORM 2.03 (Graham, 2012; Sinharay, Stern, & Russell, 2001). Missing values were replaced for CRP (5 % at T1; 25 % at T2), 6MWT (0 % at T1;2 % at T2), GSES (0 % at T1; 2 % at T2), and HADS (2 % at T1; 10 % at T2). Age was included as an auxiliary variable in the MI due to its significant correlation with the 6MWT (T1: $r=-0.459$, $p<0.05$; T2: $r=-0.478$, $p<0.05$).

Results

Descriptive statistics were used to characterize the sample (see Table 1). The sample was composed of 80 patients who had completed the PRP: 38 males (47.5 %) and 42 females (52.5 %). The completion rate was 69 % (see Figure 1). They had been diagnosed and treated for stage 3 or 4 heterogeneous cancers prior to the PRP. The majority had ECOG performance scores (Sorensen, Klee, Palshof, & Hansen, 1993) of 2 or better (88.8 %), indicating that they were in bed less than

50% of the time. The majority of the sample reported having a partner (63.8 %), including common law or cohabitating partners. In total, 13.8 % reported being current smokers and 17.5 % reported either occasional or regular alcohol consumption. According to their PRP intake reports, 21.3 % of the sample was taking prescription anti-depressant medication. See Table 2 for a full list of reported medications[1]. A correlation analysis indicated that none of the control variables were significantly correlated with change in depression and were therefore not included in the model (Table 3). Paired sample t tests were run to determine whether the variables of interest significantly changed pre-post. It was revealed that CRP did not significantly change from a mean serum value of 7.39 mg/L at T1 (SD=11.99) to 9.47 mg/L at T2 (SD = 16.41), $t(79) = -1.62$, $p = 0.110$. Exercise significantly increased from a mean walking distance of 372.55 m at T1 (SD=137.71) to 412.64 m at T2 (SD=144.31), $t(79)=-3.91$, $p<0.001$. GSE significantly increased from a mean score of 27.86 at T1 (SD=6.16) to a mean score of 31.23 at T2 (SD=5.77), $t(79)=-5.08$, $p<0.001$.Depression scores decreased from a mean score of 7.14 at T1 (SD=3.91) to a score of 5.95 at T2 (SD=3.51), $t(79)=3.16$, $p=0.002$. A hierarchical linear regression was performed to assess the main hypothesis. Although CRP did not reveal significant pre-post change, it was maintained in the model (1) to maintain the theoretical integrity of our model and (2) to assess if the small change, albeit statistically insignificant, may still affect depression. Results revealed that the predictor variables of interest explained 15 % of variance in changes in depression scores, $F(7,72)=8.29$, $p=0.006$. When holding other predictors constant, CRP uniquely accounted for 1 % of change in depression scores: a 1 mg/L increase in CRP corresponded with a 0.03-point change in depression score, which was not significant ($p=0.304$). Exercise accounted for 3 % of the change: a 1-m increase in walking stamina

[1] Examining the effects of medications other than antidepressants was outside the scope of the current study. However, because pharmacotherapy can influence inflammation and/or depression, a table of medications is included for the interested reader.

corresponded with a 0.01 decrease in depression score, which was not significant (p=0.071). GSE accounted for 11% of the change in depression score: a 1-point increase on the GSES corresponded with a 0.23-point decrease in depression score (p<0.001; see Table 4).

Discussion

The current study examined the differential effects of three mechanisms of change that have been shown to affect symptoms of depression: inflammation, exercise, and GSE. The results revealed that, when examining their unique effects, the only factor that influenced change in depression was change in GSE.

Exercise uniquely accounted for only a small portion of change in symptoms of depression when controlling for GSE and only approached significance. This suggests that the small to moderate changes previously found in depression scores following exercise interventions may at least partially be attributable to GSE. This lends support for interventions being more effective when they are based in theory (Brown et al., 2012; although this may depend on the theory) and may help explain variations in effect sizes in the published literature. The small effect of exercise found here may also represent a well-documented publication bias: exercise studies showing an effect are more likely to be published than those that do not across a number of populations (Josefsson, Lindwall, & Archer, 2014).

GSE was the factor that accounted for most of the variance in our model although others not included herein may have also contributed. For example, the PRP offers social support in a number of ways, including peer exercise sessions, and a supportive team, and caregivers are welcomed to attend sessions with patients. The PRP also promotes behavioral activation, which is a primary component of evidence-based treatment for depression (Sturmey, 2009). Helping patients develop a schedule and providing a place to go (additionally, a place that helps them feel better), depression scores may have been affected. It may be interesting to examine these diverse

psychosocial factors in a separate model (for a brief, non-exhaustive overview of potential factors, see Figure 2) Other factors, such as encounters with clinicians (e.g. Rhondali et al., 2014) and maturation, are considerations for contrast/control groups in future research.

Mean depression scores decreased 1.2 units, which was statistically significant but was below the clinical cutoff (1.5) that indicates a change in clinically distinct group (i.e., no depression, low, moderate, severe) (Yost, Eton, Garcia, & Cella, 2011). Although patients were below the cutoff, it is worth considering that patients reported "low" symptomatology at baseline, and there may have been a floor effect. Still, this provides new information on patients with minor and subthreshold depression, which is prevalent in patients with advanced cancer and is understudied (Mead et al., 2009).

When extrapolating to clinical intervention, adopting a GSE framework across all clinicians may reduce symptoms of depression, although it is premature to conclude. Pending further empirical support, a self-efficacy framework may be considered in the future development or improvement of programming.

It may be interesting to further examine whether a self-efficacy framework affects treatment adherence, helps patients engage more fully with others in their lives, or improves their functioning and QOL in other domains. If implementing this framework, it may be helpful to provide education for clinicians on (1) the additional difficulties that patients may experience if exhibiting symptoms of depression, (2) what is GSE, and (3) how the team can promote it for patients.

Limitations and Future Directions

A limitation of this study is the lack of diagnostic assessment of clinical depression. The HADS is well validated for symptoms of depression although it does not allow for the differentiation of clinical depression from subthreshold symptomatology. Therefore, these findings cannot be generalized for treating clinical depression. Since patients may not have been clinically depressed,

there may have been a floor effect in possible symptom reduction. Contrarily, this study includes cases of subthreshold depression, which is lacking in the literature (Mead et al., 2009). Another limitation is that interventions may not have been targeted for depression unless it was specifically identified as a goal for a given patient. Patients may have also been engaging in other activities outside of the PRP, such as support groups or other mental health services. The lack of control groups is a major limitation. Since this was a secondary analysis of clinical data, control data were not collected nor was a waitlist available to measure. This is a consideration for ongoing PRP research. Meanwhile, findings cannot be attributed to the PRP intervention but rather are only correlated.

Finally, there was a larger than ideal proportion of missing data. Although MI is robust and statistically sufficient for large amounts of missing data (Dalecki & Willits, 1991; Gillespie & Streeter, 1994), one must keep these limitations in mind when interpreting results. With these limitations in mind, interesting ongoing research may include examining whether or not GSE predicts adherence to exercise program post-intervention (e.g. Loprinzi, Cardinal, Si, Bennett, & Winters-Stone, 2012) and whether GSE is a more effective framework for patients who have been diagnosed with clinical depression than for patients with minor or subthreshold depression.

Conclusion

This study found that when the unique contributions of inflammation, exercise, and GSE were considered, GSE was the only variable that accounted for a significant portion of change in depression. With the abovementioned limitations in mind, it is concluded that bolstering GSE may make more of a difference in reducing depressive symptomatology than interventions to reduce inflammation or increase exercise. Further research with more rigorous research methods is pending.

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Table 1

Baseline characteristics of patients who completed the PRP

Parameter	Completed (*N*=80)	
	N	%
Sex		
Male	38	47.5
Female	42	52.5
Cigarette use		
Non- or ex-smoker	69	86.3
Current smoker	11	13.9
Alcohol consumption		
No alcohol consumption	66	82.5
Occasional or regular consumption	14	17.5
Marital Status		
No current partner (e.g. single, widowed)	29	36.6
Current partner (e.g. spouse, common law, cohabitating)		
Cancer site		
Breast	13	16.3
Hematological	8	10
Lung		
Non-small cell	8	10
Small cell	5	6.4
Head and neck	5	6.3
Colorectal	6	7.5
Prostate	4	5
Pancreas	3	3.8
Esophageal	2	2.5
Central Nervous System	2	2.5
Urogenital	2	2.5
Rectal	2	2.5
Renal cell carcinoma	2	2.5
Gynecological	2	2.5
Other* (n=1, %=1.3)	14	17.5
Stage		
III	25	31.1
IV	55	68.8
ECOG at T1		
I	23	28.8
II	48	60
III	9	11.3
	Mean	(*SD*)
Mean age, years (*SD*)	64.04	12.50

* Cervical, Endometrial, Gastrointestinal stromal tumour, Hodgkin's Lymphoma, Leukemia, Multifocal cholangiocarcinoma, multiple primaries (Esophageal and prostate, Lymphoma and breast, Small cell lung and kidney), Neuroendocrine, Non-Hodgkin's Lymphoma, Ovarian, Sarcoma, Thymoma, Transitional cell carcinoma, Vipoma.

Table 2

Medications reported by patients at their baseline assessment interviews

Medication	n	%
5 alpha reductase inhibitor	1	1.3
(Dutasteride)		
ACE Sartans Direct Reninhibitor	18	22.5
(Aliskiren, Coversyl, Enalapril, Perindopril, Ramipril, Telmisartan, Trandalopril, Valsartan)		
Alphablocker	2	2.5
(Flomax, Terazosine, Tamsulosin)		
Analgesic/Narcotic	33	40.5
(Tylenol, Codeine, Fentanyl, Hydromorphone, methadone, morphine, morphine sulfate)		
Antiandrogen	2	2.5
(Bicalutamide, Casodex)		
Antiarrithmics	2	2.5
(Amiodarone, Propafenone)		
Antibiotic or antifungal medication	4	5
(antibiotics for skin, Cipro, Fluconazole, metronidazole, Sulfatrim)		
Anticoagulant	8	10
(Clopidogrel, Dalteparin, Femaram Fragmin, Rivaroxaban, Warfarin)		
Anticonvulsant	15	18.8
(Dilantin, Gabapentin, Lyrica, Pregabaline, Valproic)		
Antidepressants	17	21.3
(Amitriptyline, Bupropion, Cipralex, Citalopram, Elavil, Mirtazapine, Remeron, Trazadone)		
Anti-diabetic medications	15	18.8
(Acarbose, Gliclazide, Insulin, Insulin Lantus, Januvia, Metformin, NovoRapid, Sitagliptin)		
Antiemetics	10	12.5
(Domperidone, metoclopramide, Stemetil, metoclopramide)		
Antimuscarinics	5	6.3
(Buscopan, Butylscopolamine, Darifenacin, Tolterodine)		
Antipsychotics	5	6.3
(Phenergran, Quetiapine)		
Antiviral	1	1.3
(Acyclovir)		
Aromataseinhibitor	3	3.8
(Letrozole)		

Benzodiazepines (Alprozolan, Clonazapam, Lorazepam, Oxazepam, Temazepam)	17	21.3
Beta blockers (bisoprolol, metaprolol)	9	11.3
Bisphosphanates and other drugs for osteoporosis (Denosumab, Pamidronate, Zolendronate)	5	6.3
Bronchodilators (Atroven, Salvent, Spiriva, Symbicort, Ventolin)	10	12.5
Calcium channel blocker (Amlodipin, Nifedipine, tiazac, verapamile)	11	13.8
Chemotherapy (Capecitabine, oxaliplatin, cisplatin, Etoposide, Xeloda)	4	5
Cholesterol absorption (Ezetmibe)	2	2.5
Combined Analgesics (Percocet, Tramacet)	3	3.8
Combined corticosteroid and bronchodilator (Advair, Symbicort)	8	10
Corticosteroids (Flonase, Pulmicort)	2	2.5
Cytoprotective (Sucralfate)	2	2.5
Dimenhydrinate (Gravol)	1	1.3
Diuretics (Chlorthalidone, Furosemide, Hydrochlorthiazide, Spironolactone, Thiazide)	14	17.5
Enzymes (Creon, Intezyme forte proteolytic enzyme, pancreatic enzymes, pancrelipase)	5	6.3
Estrogen receptor antagonist (Tamoxifen)	1	1.3
Eyedrops (Dorzo-timop, Dorzolamide, Timolol, Xalatan)	4	5
Glucocorticoids (Decadron, Dexamethyazone, Prenisone)	8	10
Glycoside (Digoxin)	2	2.5
GnRH agonist (Leuprolide)	1	1.3
Histamine blockers (Hydroxyzine, Ranitidine)	10	12.5
Laxatives & other anti-diarrheals	18	22.5

(Bisakodyl, Colace, Docusate, Lactulose, Loperamide, PEG, Polyethylene glycol, Sennokot, Soflax, stool softener)		
Levothyroxine	8	10
(Eltroxin, Synthroid, Thyroxine)		
Local Hormonal treatments	2	2.5
(Biest, Estrogel, Estriol, Testosterone/progesterone cream)		
Melatonin	2	2.5
(Melatonin, Melatonin OICC)		
Methylpohenidate	1	1.3
(Methylpohenidate: Concerta)		
Monoclonal Antibodies	4	5
(Denosumab, Ipratopium bromide, Panitumumab, Trastuzuman)		
N-methyl-D-aspartate receptor blocker	1	1.3
(Meantin)		
Nonsteroidal antiinflammatory drugs	24	30
(Advil, ASA *(dose dependent)*, Celebrex)		
Ointment	3	3.8
(Androgel, Anusol, Proctosedyl)		
Proton pump inhibitors	20	25
(Esomeprazole, Omeprazole, Pantoloc, Pantoprazole, Rabeprasol, Rabeprazole)		
Sedative/hypnotic	8	10
(Zopiclone)		
Statins	22	27.5
(Atorvastatin, Crestor, Ezetrol, Lipitor, Pravastatin, Rosuvastatin, Sandostatin, Simvastatin)		
Systemic Androgen	1	1.3
(DHEA)		
Systemic Cannoboid	1	1.3
(Nabilone)		
Tyrosinekinaseinhibitor	6	7.5
(Axitinib, Erlotinib, Gleevec, Imatinib)		
Vitamins, minerals, and supplements	26	32.5
(B_{12}, Calcium, eurofer, ferrous gluconate, fish oil, folic acid, glucosamine, iron, vitamin D, K-dur, magnesium, Metamucil, multivitamin, potassium chloride, omega 3)		
No medication recorded	11	13.8

Table 3

Potential control variables and their correlations with the dependent variable

Control variable	r-value	p-value
Pearson Correlations		
Age	-0.065	0.284
Disease stage	0.067	0.277
Point Biserial Correlations		
Gender	0.141	0.105
Marital Status (no current partner versus current spouse, i.e. married, common-law, or cohabitating)	0.012	0.457
Smoking status (non- or ex-smoker versus current smoker)	0.066	0.281
Alcohol Consumption (no consumption versus occasional or regular consumption)	-0.014	0.453
Antidepressant medication	0.029	0.399
Diagnosis (breast cancer versus other)	-0.033	0.385

Table 4

Results of analysis of main hypothesis

Variables	R^2 change	p-value	Unstandardized β
Overall Model	0.153	0.006	
Change in CRP	0.01	0.304	0.027
Change in exercise	0.03	0.071	-0.006
Change in GSE	0.11	<0.001	-0.233

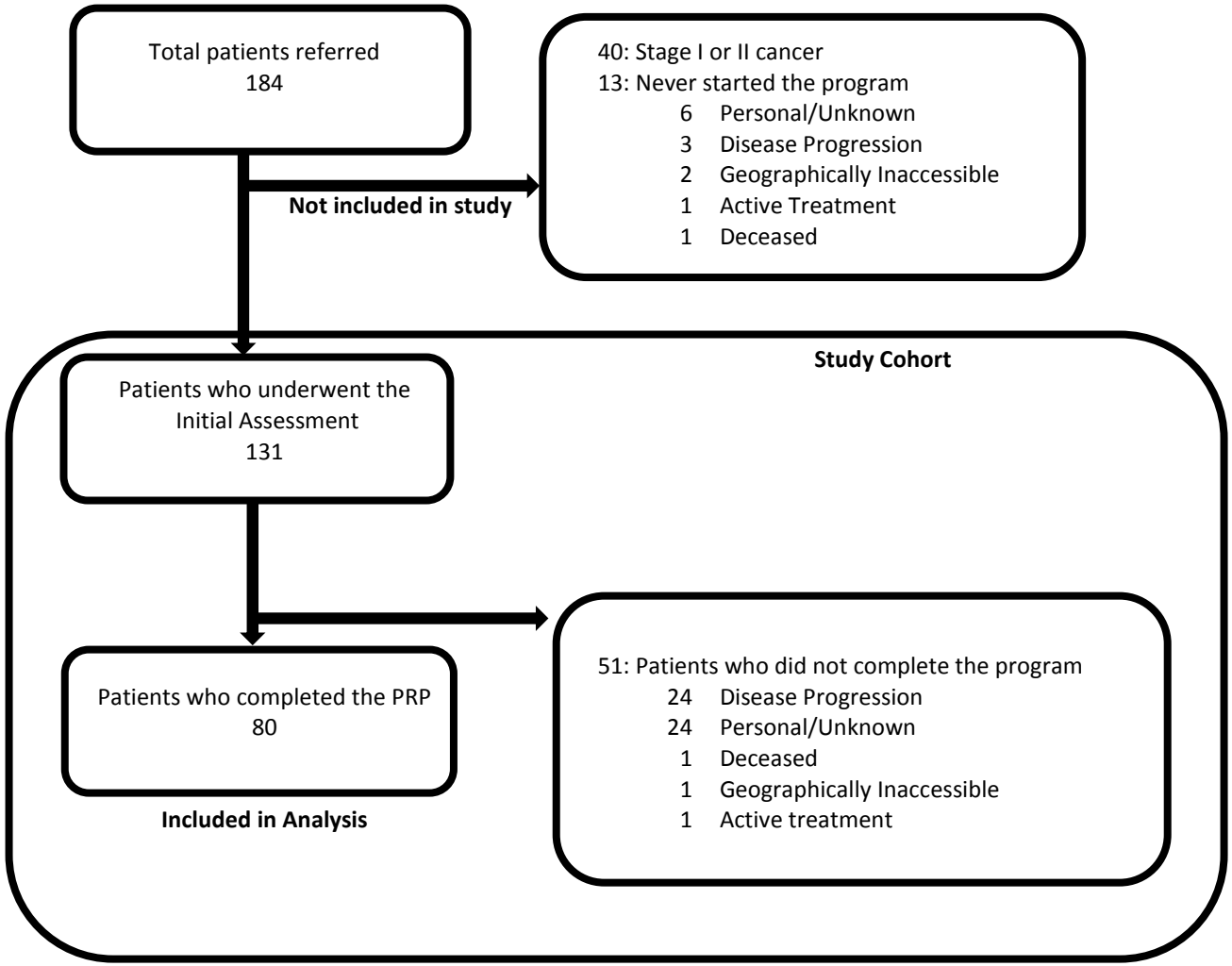

Figure 1. Flowchart of patient completion of the PRP.

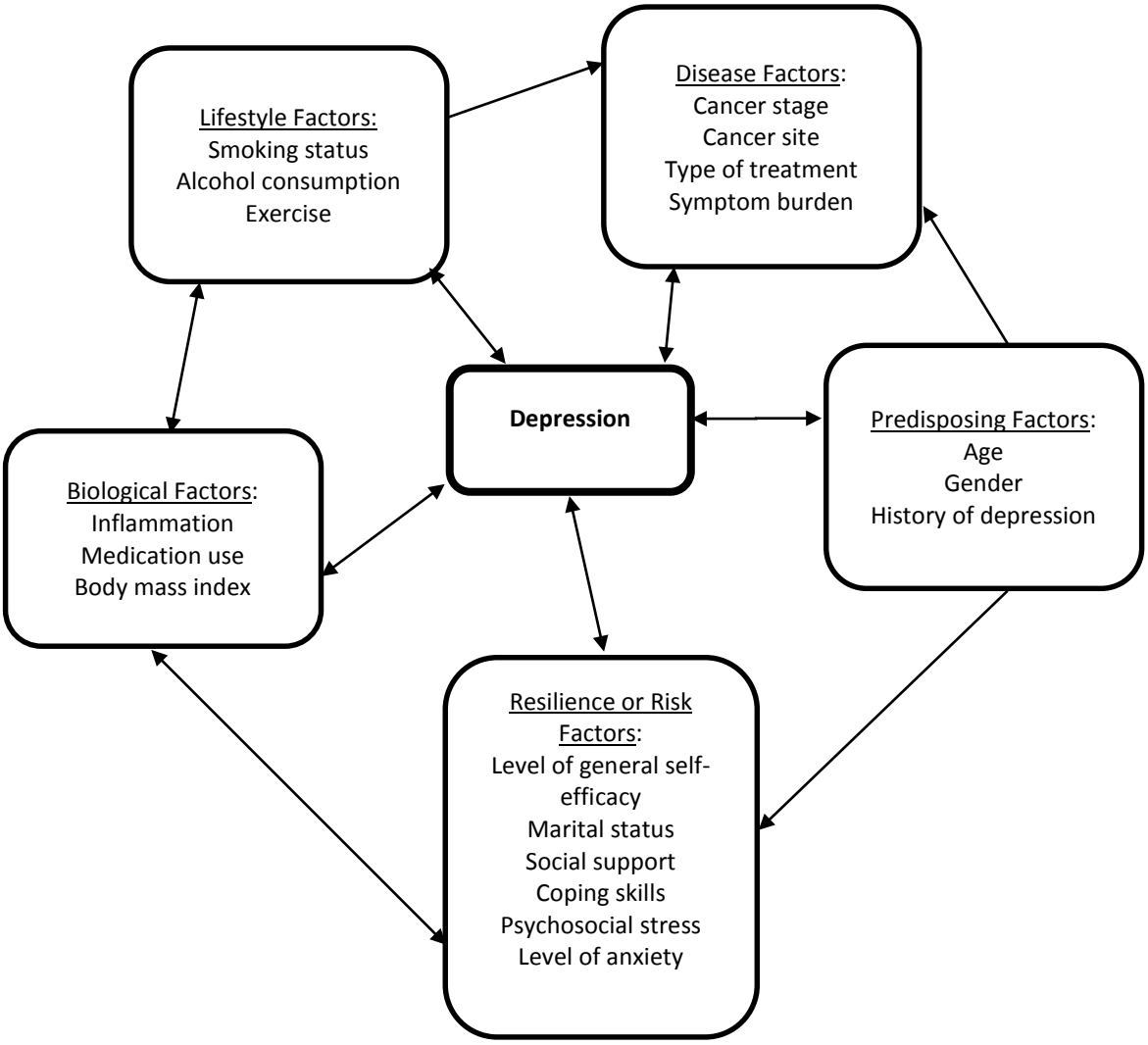

Figure 2. Brief and non-exhaustive overview of potential factors that interact with depression.

The longitudinal course of depression symptomatology following a palliative rehabilitation program

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Preface to Study 3

Studies 1 and 2 revealed that patients were reporting attenuated ratings of depressive symptomatology and that building self-efficacy may be an effective way to bolster these changes. The little literature that exists on the maintenance of reduced depressive symptomatology post-exercise intervention indicates that maintenance is poor. This study builds on the existing literature by including a multidisciplinary intervention and the unifying theory of self-efficacy. Study 3 examined the longitudinal course of the reported changes in studies 1 and 2 by examining self-reported symptomatology three months after program completion.

Abstract

Patients living with advanced cancer have an increased life expectancy due to improvements in oncological care but also suffer from ongoing long-term and late-effects. Depressive symptomatology has been found to be the most common mental health disorder in patients in this population, which can impede quality of life, functioning, and survival. The Ottawa Palliative Rehabilitation Program (PRP) is an interdisciplinary program that offers rehabilitation for this emerging population. Pilot data suggest that patients benefit in a range of domains upon completion of the PRP, including self-report ratings of feeling depressed. The current study aims to examine whether reduced ratings of depressive symptomatology can be maintained three months after PRP completion.

Methods

Participants who had previously completed the PRP (baseline measurement timepoint: T1; program completion measurement timepoint: T2) were mailed a follow-up package of questionnaires (follow-up measurement timepoint: T3) including the Hospital Anxiety and Depression Scale to complete and return by mail. Demographic and medical information were obtained from patient files. There were 44 participants with advanced stage heterogeneous cancers who participated in this quasi-experimental longitudinal study.

Results

A repeated measure ANOVA revealed a significant linear trend across the three timepoints ($p=0.007$). Statistically and clinically significant differences were revealed between T1-T2 ($p=0.042$) and T1-T3 ($p=0.007$). A Cochrane's Q analysis revealed that patients changed from cases of mild-to-severe symptomatology of depression to minimal or no symptomatology from T1-T3 ($p=0.038$).

Conclusion

Patients who undergo a palliative rehabilitation program may experience statistically and clinically significant improvements in depressive symptomatology, with improvements that can continue following program completion. Future studies using an experimental design are needed to draw firm conclusions.

Keywords: Palliative care, rehabilitation, advanced cancer, interdisciplinary intervention, depression.

Patients living with advanced cancer are among those who have experienced increased life expectancy due to improved and earlier oncological screening and treatment. Previously considered a terminal diagnosis, advanced cancer can now be considered a chronic illness as people are living with the disease for an increased number of months or years (Conroy et al., 2011; Institute of Medicine [IOM] & National Research Council of the National Academies [NRC], 2006; Tangen et al., 2003). However, living with advanced cancer has its own challenges: Post- treatment patients are polysymptomatic with a median of 11 symptoms associated with the advanced disease, its more complex treatment, ongoing and increasingly complex treatments, or any combination of these (Esper, 2010; Haylock, 2010; Mayer, 2010; Park & Rosenstein, 2014). The cancer experience takes a toll on health, functioning, sense of security, and wellbeing, and the effects can continue to surface for months or years following treatment completion (Bruera & Yennurajalingam, 2012; Eades, Chasen, & Bhargava, 2009).

Often underdiagnosed and untreated (Wilson, Lander, & Chochinov, 2009), depressive disorders have been found to be the most common mental health concern in patients with advanced cancer (Massie, Lloyd-Williams, Irving, & Miller, 2011; Rodin, 2013). Of these, subclinical disorders are the more problematic because they are not responsive to pharmacotherapy (Mitchell et al., 2011; Rodin, 2013). Pooled data reveals that 14.3% of patients across palliative settings meet criteria for major depression and 9.6% for subclinical depression, irrespective of age, sex, or in/outpatient setting (Currier & Nemeroff, 2014). Both clinical and subclinical levels of depressive symptomatology can negatively affect quality of life (QOL), functioning (Fils et al., 2010), medical compliance, engagement with others (including clinicians), and may exacerbate other symptoms, such as pain or fatigue (Delgado-Guay, Parsons, Li, Palmer, & Bruera, 2009). It is a predictor of mortality (Lloyd-Williams, Shiels, Taylor, & Dennis, 2009; Pinquart & Duberstein, 2010; Satin, Linden, & Phillips, 2010; Spiegel & Giese-Davis, 2003), health care overuse (Meeks, Vahia, Lavretsky,

Kulkarni, & Jeste, 2011), and can even perpetuate tumour progression (Currier & Nemeroff, 2014). Therefore, helping patients overcome depressive symptomatology has the potential to make a meaningful difference in QOL, functioning, and survival.

The etiology of depressive disorders is multifactorial (Li & Rodin, 2010) and may best be addressed accordingly. One such framework for care is exemplified by the Ottawa Palliative Rehabilitation Program (PRP). The PRP is an interdisciplinary program that offers rehabilitation for this population (Chasen, Feldstain, Gravelle, MacDonald, & Pereira, 2013; Chasen & Dippenaar, 2008). Their goal is to empower patients who are experiencing loss of function or QOL as a result of cancer or its treatment. It is an 8-week interdisciplinary intervention that offers thorough assessment and collaborative interdisciplinary care plans from the team's six professionals (physician, nurse, physiotherapist, occupational therapist, social worker, and dietician). The patient-centered nature of the program offers individualized interventions based on patient goals and clinical assessment, which differs by patient. Although this design lacks empirical rigour, it does offer clinical value in helping patients improve in ways that are meaningful to them. As well, the team utilizes a general self-efficacy theoretical framework to empower patients to maintain lifestyle changes and therapeutic gains. For further discussion on the theoretical framework, see Feldstain et al. (2015).

Results of a PRP pilot study of pre-post changes revealed that patient self-reports of physical function, symptom burden (including depression), symptom interference in everyday life, malnutrition, and medical ratings of performance status all improved, with no significant worsening in any dimension. This suggests that patients with advanced cancer are experiencing pre-post improvements in a range of domains (Chasen et al., 2013), which has not been found for patients with advanced disease (mostly cancer) who do not receive rehabilitation (Lynn & Adamson, 2003). This included a significant reduction of endorsing feeling "depressed" on a single screening item.

There has been little investigation into the longitudinal maintenance of improved depressive symptomatology following rehabilitation interventions, but what does exist, mostly exercise interventions, suggests that maintenance is poor (Krogh, Nordentoft, Sterne, & Lawlor, 2011; Mead et al., 2009; Mishra et al., 2012; Rimer et al., 2012). The current study will examine PRP improvements in depressive symptomatology at PRP admission, completion, and at 3-months follow-up, utilizing a validated measure rather than a single screening item. Due to the interdisciplinary, individualized, and theory-driven interdisciplinary PRP interventions that is not commonly found in the literature, it is possible that patients may report reduced and maintained depressive symptomatology, contrary to what has previously been found in the existing research. It is hypothesized that patients will a) report lower scores of depressive symptomatology at program completion than at baseline and b) report lower depressive symptomatology at 3-month follow-up than at baseline. An exploratory research question is: Do levels of self-reported depressive symptomatology change between program completion and 3-month follow-up?

Methods

Participants and Procedure

This secondary analysis of quasi-experimental data uses a subset of PRP clinical data collected during the first five years of PRP's operation. Participants were patients living with advanced cancer who had been referred to the PRP by physicians in the Ottawa region for palliative rehabilitation following completion of cancer treatment. They had also completed the eight-week PRP. Those who did not have advanced cancer or those who completed the program prior to the inclusion of the measure below were excluded from this analysis.

Referred patients who were interested in attending the PRP attended an initial assessment interview (baseline; T1) where self-report questionnaires were collected and clinical assessments were performed. The self-report questionnaires had been received in the mail one week prior to

the initial interview. Patients appropriate for the PRP received group physiotherapy twice/week for eight weeks and other interdisciplinary follow-ups as necessary or requested. At program completion (T2), patients were re-administered self-report questionnaires and clinical assessments. Three months following PRP completion, patients received the same self-report questionnaires by mail (T3), which they completed and returned by mail. Requisitions for blood work were received at all three timepoints. Only one of the administered measures will be considered herein.

Patients received a consent form alongside their T1 self-report questionnaires in the mail, informing them of the PRP's research. Patients who were interested in partaking provided informed consent for their clinical data to be used in future research; those who did not consent were still eligible to participate in the clinical program. Participants were recruited between April 2011 and June 2014. For a more complete description of the PRP procedure, structure, and team, see Chasen et al. (2013). The study received local REB approval.

Measures

Demographic information

Age, gender, marital status, ECOG performance status (Eastern Cooperative Oncology Group; Oken et al., 1982) at T1 and T2, cancer type, and stage were collected from participant files.

Self-Report Questionnaires

Symptoms of Depression. The Hospital Anxiety and Depression Scale (HADS; Zigmond & Snaith, 1983) is a fourteen item self-report questionnaire assessing symptomatology of anxiety, depression, and general distress (Mitchell, Meader, & Symonds, 2010). Seven items assess depressive symptomatology, e.g. "I still enjoy the things I used to," and "I have lost interest in my appearance." The purpose of the HADS is to focus on psychological symptomatology rather than physical, in order to reduce false positives due to the overlap of physical symptoms between depression and cancer (e.g. fatigue). It was designed for medical settings and has been validated in

patients with cancer. It has been supported as a good measure for English-speaking samples with heterogeneous cancer diagnoses (Bjelland, Dahl, Haug, & Neckelmann, 2002; Luckett et al., 2010; Mitchell et al., 2010; Vodermaier & Millman, 2011).

A concern in using the HADS is its lack of diagnostic ability, although the original authors proposed that it can still be used as an indicator of "possible" or "probable" mood disturbance (Zigmond & Snaith, 1983). Given the importance of identifying subclinical depressive symptomatology, a score of 8 or higher was used to define mild-to-severe symptoms of depression and a score of below 8 to define minimal-or-no symptoms of depression. This was recommended by Bjelland (2002) whose review found the sensitivity and specificity to both be around 0.80 and by Mitchell et al. (2010), whose meta-analysis found a sensitivity of 71.6% and a specificity of 82.6%.

Analyses

An a priori estimate of 20 participants was obtained using G*Power version 3.1 (Faul, Erdfelder, Lang, & Buchner, 2007) to yield 80% power to detect medium to large effects. Multiple imputation (MI) using NORM 2.03 (Graham, 2012) was performed to replace missing HADS data (4.55% at T1, 18.18% at T2, 4.55% at T3). This method involves using auxiliary variables that are correlated with the variables containing missing values and with missingness to improve imputations. It is recommended to include auxiliary variables from the larger dataset, even if not included in the current study (Graham, 2012; Sinharay, Stern, & Russell, 2001). Auxiliary variables included in the MI due to their correlations with the existing data were age (HADS T1: r=-0.380, p=0.016; HADS T2: r=-0.335, p=0.049) and an item from the larger study (see Chasen et al., 2013) ESAS depression (HADS T1: r=0.518, p=0.001; HADS T2: r=0.443, p=0.009). Other variables included because of their correlation with data missingness were marital status (HADS T1: r=-0.364, p=0.032) and disease stage (HADS T2: r=0.426, p=0.005).

Data were analyzed using IBM SPSS Amos. A correction for regression to the mean (RTM) was applied to decrease its threat to internal validity. RTM is a phenomenon in which early measurement tends to be further from the mean and scores center closer to the mean in subsequent measurement (Linden, 2013; Rocconi & Ethington, 2009). A correction for RTM was applied according to the method described by Rocconi and Ethington (2009) (original mean=6.80, SD=3.80; transformed mean=6.80, SD=2.29). The assumption of normality was met. The Huynh-Feldt correction was applied to correct a violation to sphericity ($p<0.001$).

Preliminary analyses were performed in order to examine pre-intervention differences between those who completed all three timepoints versus those who did not. These included chi-square analyses to examine pre-existing differences in CRP at T1, which was previously found to predict program completion (Chasen et al., 2013), gender, disease stage, and performance status; and logistic regression for pre-existing differences in age and HADS scores at T1 and T2. For the main analyses, a repeated measures ANOVA was used to assess changes in depression scores across timepoints on a continuous scale and a Cochran's Q analysis was used to examine significant differences in grouped data (little to no symptomatology: HADS<8; mild to severe symptomatology HADS≥8).

Results

There were 44 participants (46.3% of the 95 who completed the PRP) who participated in the longitudinal follow-up (45.5% male, 54.5% female). Non-completers included 13 (13.6%) who were unreachable and 38 (40%) non-responders (see Figure 1). The majority of the current sample (70.5%) had a spouse (married, common-law, cohabitating). The mean age was 64.82 (*SD*=13.03) ranging from ages 29-86. Participants had heterogeneous diagnoses of advanced cancer (see Table 1).

Preliminary analyses revealed that those who completed the longitudinal follow-up versus those who did not was not correlated with gender, age, disease stage, systemic inflammation, ECOG performance status (Sorensen, Klee, Palshof, & Hansen, 1993), or depression at T1 or at T2. When running this analysis again without "unreachable" participants, i.e. comparing those who completed only to "true" non-responders (those who presumably received the questionnaires but did not return them), age was the only significant predictor of completing T3, Wald(1)=4.046, p=0.044, β=0.036, CI=1.00-1.07. Those who were older were more likely to complete all three timepoints than those who were younger.

Descriptive statistics revealed that the mean HADS score at T1 was 6.79 (*SD*=2.29) and 47.7% of the sample scored ≥8 on the HADS; at T2, mean score was 5.23 (*SD*=3.06) and 25% scored ≥8 on the HADS; at T3, mean HADS score was 4.59 (*SD*=3.34) and 20.5% scored ≥8 on the HADS (see Figure 2). For the main analyses, the repeated measures ANOVA revealed a significant linear trend, F(1)=7.98, p=0.007 with HADS scores decreasing across timepoints. The omnibus test of within-subjects effects revealed significant differences between timepoints, F(1.56)=5.65, *p*=0.01, partial η^2=0.116. Pairwise comparisons revealed that the difference between T1-T2 was significant (mean difference=1.57, SE=0.75, p=0.042), as was the difference between T1-T3 (mean difference=2.21, SE=0.78, p=0.007). These both exceeded the clinically meaningful difference of 1.5 (Yost, Eton, Garcia, & Cella, 2011), indicating a difference large enough to impact a patient's care or wellbeing. Change between T2 and T3 was not significantly different (mean difference=0.64, SE=0.45, p=N.S.). The Cochran's Q analysis revealed that the quantity of patients who scored above or below the HADS cutoff (≥8) was significantly different across timepoints (*p*=0.026; see Table 2). Multiple comparisons using McNemar tests revealed the difference between T1 and T2 did not reach significance (p=N.S.) but the difference between T1 and T3 did reach significance (p=0.038). The

difference in number of patients who scores above or below the cutoff at T2 versus T3 was not significant (p=N.S.).

Discussion

The current study sought to examine the trajectory of depressive symptomatology for patients who underwent the PRP, during and 3-months following this interdisciplinary intervention. Results revealed that patients with advanced cancer reported significant decreased depressive symptomatology throughout the program and at longitudinal follow-up, with both post-timepoints representing significant statistical and clinical changes from baseline. These results begin to support that the PRP interventions may help patients alleviate symptoms of depression.

The current findings contrast the symptom trajectory typically found in patients with advanced disease (Lynn & Adamson, 2003). What has previously been found is that patients have a consistent symptom burden until approximately one month before death at which point symptoms worsen, including depression (Li, Fitzgerald, & Rodin, 2012; Lo et al., 2010). The statistically and clinically meaningful difference herein suggests that the PRP may have offered something beneficial for patients that, seemingly, they were able to continue applying after completing the PRP intervention itself. This is also different than what exists in the sparse literature on longitudinal maintenance of attenuated depressive symptomatology, which has not found promise for the longitudinal maintenance following exercise interventions (Krogh et al., 2011; Mead et al., 2009; Mishra et al., 2012; Rimer et al., 2012).

There are a number of elements in the PRP that may be contributing to the revealed trend. Patients may have acquired new skills that they continue to apply (e.g. techniques to reduce peripheral neuropathy, behavioural activation, dietary strategies to cope with taste changes), they may have found peers with whom they relate and continue to see, they may have experienced an overall improvement in quality of life, they may have developed an improved sense of general self-

efficacy, or it may have been a combination of these and other factors. Previous research on depression and quality of life mostly in this patient population has found social support and attenuation of physical limitations or symptoms to be the most potent factors (Goodwin et al., 2012; Lo et al., 2010; Rodin, 2013; Rodriguez, Mayo, & Gagnon, 2013).

The interdisciplinary component of the PRP may be a salient ingredient that makes a difference, above and beyond the impact of exercise. This may be because it allows patients to better target their personal triggers of depressive symptomatology. For example, one patient may feel sad, anhedonic, fatigued, and worthless due to functional declines, which can be targeted by both the physiotherapist and occupational therapist. Another patient may feel these same symptoms from being socially isolated, which can be targeted through peer-exercise, provision of survivorship resources, a supportive and encouraging team, and through empowerment by a number of individual clinical interventions, such as nursing and social work, or the team as a whole. The team would be able to approach these triggers from different perspectives, potentially better targeting the root of each patient's distress.

At each timepoint, the mean of depressive symptomatology was less than 8, indicating that there may have been a floor effect, i.e. there was a limit in how much attenuation the already low scores could exhibit. If so, results may have been more robust if the sample was exhibiting higher scores of depression at baseline. One consideration is that patients with more prominent symptomatology self-selected out of this patient population. Anhedonia is a prominent symptom of depression and the resulting inertia may have precluded patients who need such help the most from attending the PRP at all. How to reach this population of patients who are referred but disabled from comorbid depression and advanced cancer may be an interesting and important avenue for future investigation and programming. Nevertheless, a clinically meaningful difference was found. There were also a number of patients in the current sample whose scores were elevated

(47.7% scored above 8 at T1, 25% at time 2, and 20.5% at T3) and these patients seemingly experienced relief.

Limitations

There are some limitations to note: The lack of control group, the use of a self-report measure of depressive symptomatology without the gold-standard clinical interview, and considerations about the drop-outs. These data were collected for program evaluation and not for experimental purposes, therefore control data were not available. As well, the HADS is well validated in the literature for use with patients with cancer but is best used for a rule-out when considering patients for further assessment rather than as a diagnostic tool. For identifying cases of Major Depressive Disorder, a clinical assessment alongside a self-report measure is considered the gold-standard. Finally, the 3-month follow-up completion rate was 46.3% and age was found to be a significant predictor of non-response. Therefore, the findings of possible relief from depressive symptomatology may not generalize to the younger part of this cohort.

Conclusion and Future Directions

Our patients reported a reduction in depressive symptom burden that continued to decrease after the intervention completed. Depression can be a significant barrier in quality of life, one's ability to provide self-care, adhere to treatment, or engage in treatment at all (Delgado-Guay et al., 2009; Fils et al., 2010; Meeks et al., 2011). Pending further research with more rigorous methodology, an individualized interdisciplinary intervention may prove to be beneficial for post-treatment patients living with advanced cancer.

Future directions include examining motivation and care for patients who may not participate in the PRP due to symptoms of depression, such as anhedonia. Understanding which elements patients found potent and/or analyzing gain based on interventions received may speak to the development of future interdisciplinary interventions. As well, the observed effect size was

small (η^2=0.116), similar to the effects of exercise interventions alone. It may be interesting to compare the differences in outcome between this interdisciplinary intervention versus an exclusively-exercise intervention. Also of note, there is no mental health professional on the team. While patients may receive aspects of psychological intervention (e.g. behavioural activation), none of the team members specialize in treating depression. A mental health professional may be a valuable addition to such a team, affecting depressive symptomatology, and thereby other factors, such as adherence to other PRP interventions.

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Table 1.

Demographic variables as recorded at baseline (initial assessment interview), N=44.

Variable		Mean(*SD*)	Range
Age		64.89(*13.03*)	29-86
Variable		N	%
Gender	Males	20	45.5
	Females	24	54.5
Performance status at Baseline	0	12	27.3
	1	28	63.6
	2	4	9.1
Diagnosis	Hematological	7	15.9
	Multiple Primaries	5	11.4
	Breast	5	11.4
	Head and neck	5	11.4
	Lung		
	Non-small cell	5	11.4
	Small Cell	2	4.5
	Colorectal	4	9.1
	Prostate	2	4.5
	Gynecological	2	4.5
	Urogenital	2	4.5
	Neuroendocrine	1	2.3
	Sarcoma	1	2.3
	Thymoma	1	2.3
	Vipoma	1	2.3
	Gastrointestinal	1	2.3
Stage	III	20	45.5
	IV	24	54.5

Table 2.

Grouped HADS data.

	Baseline		Completion		3-month Follow-up	
	N	Mean (*SD*)	N	Mean (*SD*)	N	Mean (*SD*)
HADS < 8	23	5.05(*1.61*)	33	3.85(*2.02*)	35	3.26(*2.02*)
HADS ≥ 8	21*	8.71(*1.04*)	11	9.36(*1.50)*	9*	9.78(*2.17*)

*Significantly different, p=0.038

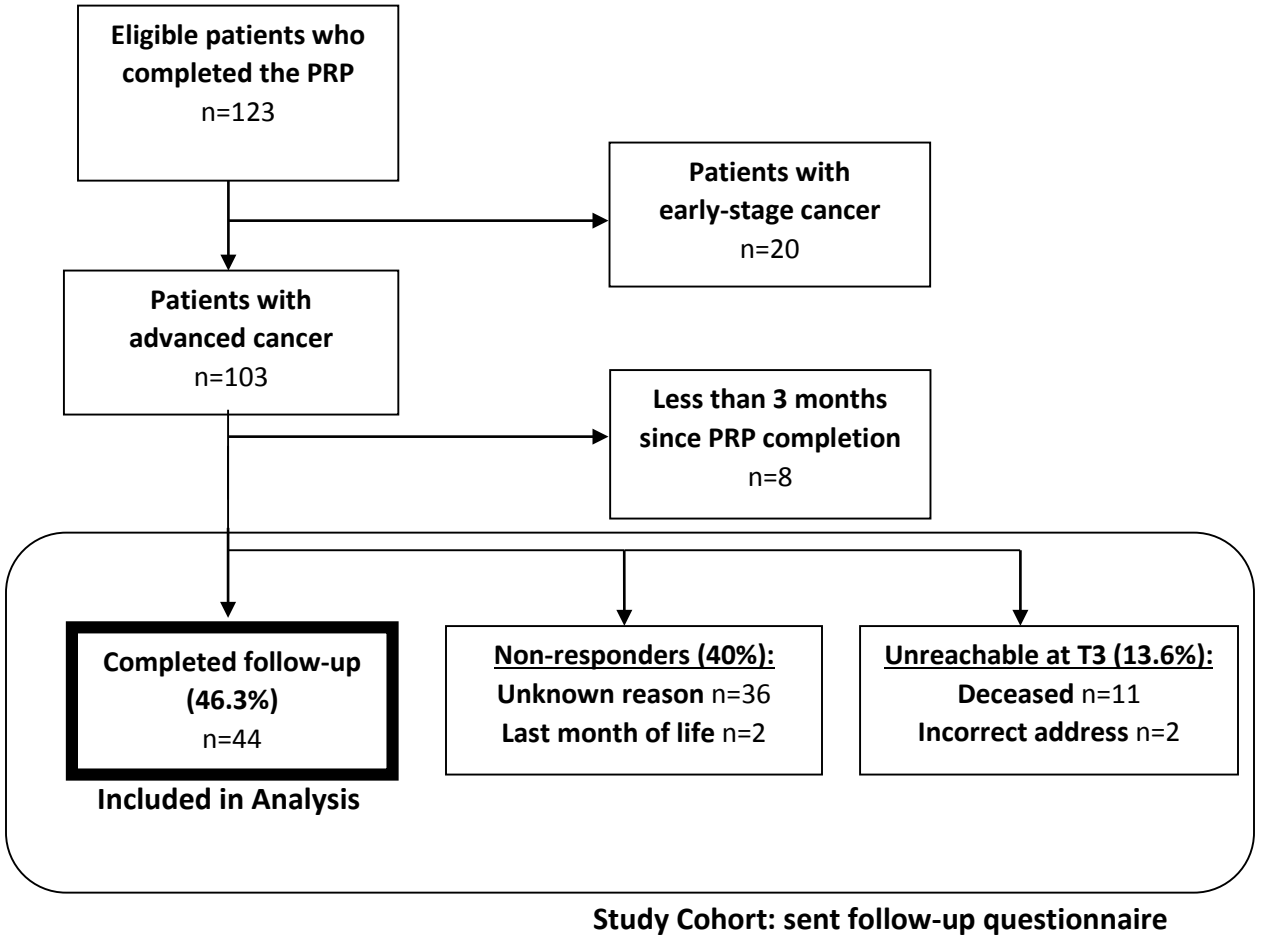

Figure 1. Flow diagram of patients through the time points.

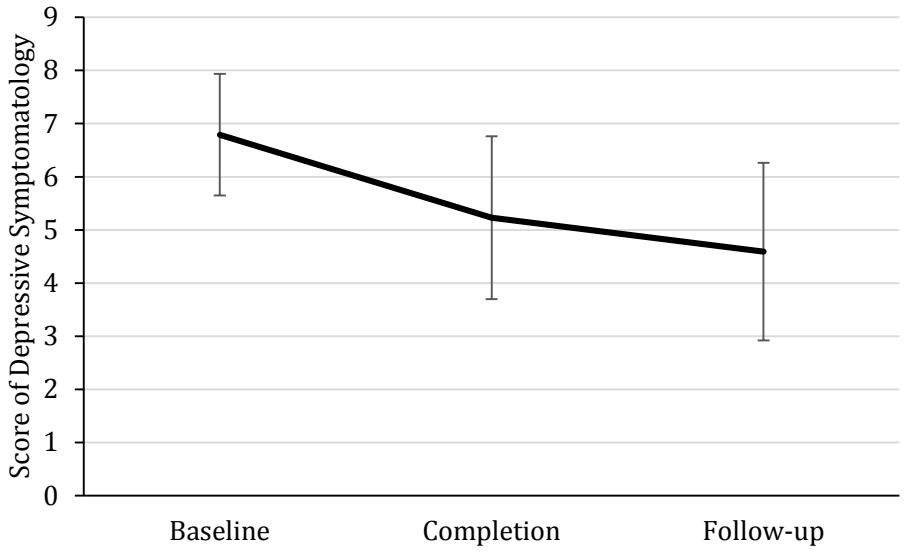

Figure 2. The linear trend of self-reported depressive symptomatology across timepoints.

General Discussion

This final discussion will present an overview of the three studies, summarize the findings and interpretations, and relate them to the existing literature. It will also provide a discussion on the limitations of this research, the clinical and empirical implications, and the recommendations for future directions.

Rationale and Overview of the Studies

Patients with advanced cancer are living months or years longer than ever before once they compete their cancer treatments. Tumours in advanced cancer have spread beyond their original location to either adjacent or distant sites. Compared to tumours that have not spread (local tumours or cancer in the "early" stages), advanced cancer requires more aggressive treatments and interferes more in patients' abilities to engage and function in their daily lives. Advanced cancer may require more aggressive treatments and patients often present with a decreased ability to perform normal daily activities, such as meeting their own needs, satisfying roles, and/or maintaining health (Cheville, 2001; Institute of Medicine [IOM]& National Research Council of the National Academies [NRC], 2006).

A particular psychological concern for patients living with advanced cancer is depression. Depression has been found to be the most prevalent mental health difficulty for this population (Massie, Lloyd-Williams, Irving, & Miller, 2011). It has also been found to peak later in the cancer trajectory, as opposed to other psychological concerns that peak earlier in the trajectory, making it a potent concern for this patient population (Li, Boquiren, Lo, & Rodin, 2011). Depression can compound the difficulties these patients face from disease and treatment, making it difficult for patients to engage in their hobbies, with others, in their daily routines, or in their medical care. It

can increase suffering and may be a predictor of mortality (Lloyd-Williams, Shiels, Taylor, & Dennis, 2009; Pinquart & Duberstein, 2010; Satin, Linden, & Phillips, 2010; Spiegel & Giese-Davis, 2003).

The Palliative Rehabilitation Program (PRP) was designed for post-treatment patients living with advanced cancer, offering interdisciplinary assessment and intervention to help patients increase functioning in a number of domains and improve quality of life (QOL). It was a unique interdisciplinary rehabilitation program that offered individually-based, interdisciplinary care plans from a collaboration of six clinicians (physician, nurse, physiotherapist, occupational therapist, dietitian, social worker) using a theoretical approach (general self-efficacy from Social Cognitive Theory; Bandura, 1997). The PRP was offering its two-month program at the Elisabeth-Bruyère hospital in Ottawa, ON from 2009 to 2015. It aimed to empower patients living with advanced cancer who were suffering from symptoms and from side- and late-effects of disease and treatment, and to improve their functioning (e.g. physical, psychological, nutritional) and QOL. The goal of this thesis is a secondary analysis of clinical outcome data that has been collected in the PRP's years of operation in order to determine if patients who underwent this program experienced improvements in their functioning and QOL, with a focus on symptoms of depression. Effectively improving depressive symptomatology can help patients engage in their lives, whether it be social engagement, medical adherence, activity participation, or in other domains. As well, being able to determine the effective mechanisms of change can help inform other existing and future programs on how to best integrate a variety of interventions, clinicians, and presenting problems to reduce depressive symptoms in people with advanced cancer. On the other hand, if depressive symptomatology is not effectively targeted, existing or future programs may benefit from this knowledge to adjust their content or theoretical framework to better intervene.

Study 1: Main Pilot Findings

The first study examined self-reported outcomes in a number of domains of functioning and QOL, including physical, psychological, nutritional, and medical. This pilot study revealed that patients reported moderate to large effects (as defined by effect size d≥ 0.5) on several measures of physical functioning/performance. Small to moderate improvements (as defined by effect size of between 0.2 and 0.5) were reported on mood and enjoyment, nutritional status, activity level, some physical function, and burden of several symptoms. Depression was in this category, with moderate and statistically significant improvement (d=0.37, t=2.92, p=0.005). However, depressive symptoms were not measured, but rather patients were asked to rate their "depression" from 0 (no depression) to 10 (worst possible depression) on a single-item screening question. Appetite, drowsiness, symptom interference in relationships and walking, motivation and some physical outcomes improved moderately (d>0.2 and d<0.5) but did not reach statistical significance. Finally, pain, grip strength, and mental fatigue did not improve (p=N.S., d<0.2). No scores worsened. It was also found that patients who had normal CRP levels, an indication of inflammation, were 1.52 times more likely to complete the program than were patients with CRP above the normal range. In sum, this pilot study suggests that patients who are well enough to complete the PRP may experience ameliorated functioning and QOL, notwithstanding the limitations discussed below.

Study 2: Main Theoretical Findings

Considering the self-reported improvements in possible depressive symptoms in the pilot study, this second study sought to examine what may influence this change. Considering the multifactorial etiology of depression (Li & Rodin, 2010) the unique influence of three different biopsychosocial clinical targets for attenuating depressive symptomatology were examined. These were changes in inflammation, exercise, and general self-efficacy (GSE). When changes in these factors were tested together as predictors of change in depressive symptomatology, our findings

suggested that the only significant predictor of change in scores was GSE. Changes in CRP and exercise were not significant predictors of change in depression, although CRP itself did not exhibit a significant change. This study suggests that perhaps GSE is responsible for at least a part of the change attributed to exercise in the literature, developing as a by-product of exercise interventions.

Study 3: Main Longitudinal Findings

Finally, study 3 examined whether reductions in depressive symptomatology could be maintained longitudinally, including a third timepoint three months after program completion. The findings supported the pilot result that self-reported scores of depressive symptomatology decreased from baseline to program completion, this time using the Hospital Anxiety and Depression Scale (Zigmond and Snaith, 1983), a validated measure for symptomatology rather than a single-item screening question. Additionally, it was found that in the 3-months following program completion, patients continued to maintain their reduced scores, which is in contrast to what exists in the literature for the longitudinal trajectory of depression scores without intervention or following exercise-based interventions (Lynn & Adamson, 2003). This suggests that there may have been elements in the PRP that were different than the programs that previous researchers examined. Suggestions of these, among others discussed below, include a) coordinated interdisciplinary care-plans that were individualized based on patient goals and clinical assessment and/or b) the theoretical framework that may bolster the likelihood that patients continue to adhere once the PRP intervention completes.

Integrating Findings with the Existing Literature

Taken together, the main findings of these three articles begin to suggest that, post-treatment, patients living with advanced cancer may experience an improved level of functioning and QOL from having undergone an individualized, theoretically-based interdisciplinary palliative

rehabilitation program. When focusing on depressive symptomatology, the most prevalent mental health concern for this population, it appears that self-reported symptomatology can be decreased throughout the course of intervention. This is fairly novel in this patient population. Previous studies have found that, without rehabilitation, improvements in functioning and QOL are not noted (Lynn and Adamson, 2003) but rather, symptom burden remains stable until one month before death. With exercise-based or interdisciplinary rehabilitation, similar findings to ours are beginning to emerge in the literature (e.g. Belchamber, Gousy, Ellis-Hill, 2013; Javier & Montagnini, 2011). What has not yet been shown, though, is the longitudinal maintenance of such intervention results. Exercise-based interventions have not found strong evidence for the longitudinal maintenance of depressive symptomatology and interdisciplinary interventions with longitudinal measurements are absent in the literature. Therefore, our longitudinal findings support that an intervention such as the PRP's may offer something unique from other programs in the literature.

The most immediate suggestion of what the PRP may offer differently than other rehabilitation interventions is their self-efficacy framework. As described in the general introduction, GSE is a fairly stable trait that refers to a person's belief that he/she can affect outcomes of difficult situations through actions and it is theorized to affect functioning through cognition, motivation, emotion, and decision-making (Bandura 1977, 1998, 2009). It has been suggested as a good target in rehabilitation programs because it is associated with active coping and emotional wellbeing (Rottman et al, 2010).

In the case of living with advanced cancer, there are a number of factors that complicate one's ability to achieve their desired outcomes. These include burden from multiple symptoms, limitations in physical functioning (e.g. due to scarring, lymphedema, or structural damage from disease or treatment), ongoing disease management (e.g. multiple medical appointments), and

stigma/shame (e.g. visible scarring, social expectation to think positive and beat cancer). The consequences of having and treating advanced disease, on its own, can pose plenty of barriers to one's perception that they can deal with stressors. Symptomatology of depression, which may include low mood, lack of interest or pleasure in activities, decreases in energy and/or self-esteem, can be a further barrier and the comorbidity of both depression and cancer may further exacerbate a person's perception of disability (Gill, Klinkman, & Chen, 2010).

Given the cumulative effect of depression and cancer on a person's functioning, the GSE-framework aims to incrementally increase a person's successful experience of working towards and achieving their goals. Because PRP treatment plans are not uniform, GSE is a unifying approach taken by team members. In the theoretical study, change in GSE was entered into a regression model with change in other empirically validated targets for reducing depression: inflammation and exercise. It was found that GSE accounted for the majority of variance in change in depressive symptomology (11% of the 14%) and was the only significant predictor. These results suggest that GSE may be a useful target in attaining change in depressive symptomatology.

Examining the model more closely, it may be that GSE is the most effective target of these three predictors to affect change rather than the only one that is effective. Change in exercise stamina, used as a proxy for having engaged in exercise throughout the program, did increase although it did not predict change in depressive symptomatology in this model. Exercise has been found to have a small to moderate effect on depression (Fong et al., 2012; Velthuis, Agasi-Idenburg, Aufdemkampe, & Wittink, 2010) and there is little empirical examination as to why or how it may affect depression (Brown, 2012). The current study begins to challenge that it is exercise alone that affects depression but rather the accompanying skills that may develop when successfully implementing a new exercise regimen, such as self-efficacy. At the same time, exercise releases

endorphins and has other biological effects that, at least in the short term, can attenuate depressive symptomatology. Therefore, it may be accurate to say that exercise is more immediately helpful in reducing symptomatology while self-efficacy may be effective to elicit sustained changes.

Inflammation was the predictor that showed the least predictive ability in the model. In the literature, anti-inflammatory agents have been found to be effective in treating depression, especially cases that are non-responsive to more mainstream anti-depressant medications. This may be explained by the little change in inflammation found in Study 2: It was the only variable that did not show statistically significant change from baseline to PRP completion. Therefore, perhaps it was not a lack of predictive ability but rather a lack in successful targeting of inflammation within the intervention. As mentioned in the general introduction, optimal interventions for inflammation are not yet determined and inflammation is involved in mutually-reinforcing relationships with tumours and depression. Therefore, conclusions about GSE being the only factor to affect change in depression would be premature. A more accurate conclusion is that self-efficacy may be the most effective of the examined targets for affecting depression in the current program.

An interesting discrepancy was found in examining who is more/less likely to complete the program. In the pilot study, the logistic regression revealed that patients with abnormal CRP (≥10 mg/L; indicating more inflammation/immune activity and likely worse disease) were less likely to complete the program than those whose CRP was in the normal range (CRP<10 mg/L). Yet, at three month follow-up, neither CRP nor disease stage were found to predict completing the longitudinal timepoint. Perhaps this indicates that the patients who were the most ill discontinued before the 8-week program had elapsed. Therefore, those who were eligible for the longitudinal study were already a biased sample of patients who were less ill, negating findings of differences in disease-progression between those who did or did not complete the longitudinal follow-up.

Using these results to help with the interpretation of the longitudinal article, GSE may also help explain how patients maintained their gains at longitudinal follow-up, contrary to the poor maintenance results that other studies have found (Krogh et al., 2011; Mead et al., 2009; Mishra et al., 2012; Rimer et al., 2012). Perhaps patients may have adapted a stronger sense of GSE and carried it forward, leaving them better prepared to cope with difficulties as they arise and better able to handle threats of relapse. In accordance with this interpretation, several authors have found that higher self-efficacy has been correlated with better illness adjustment, lower distress, better emotional functioning, and less symptom interference in QOL (Beckham, Burker, Lytle, Feldman, & Costakis, 1997; Jones, Cheng, Jackman, Rodin, Walton, & Catton, 2010; Zhang, Zheng, Liu, Wu, Liu, 2015). At this point, GSE seems like a parsimonious explanation but it is too early to conclude given the quasi-experimental design. More rigorous methods will be necessary to further test this hypothesis. In the meantime, there are other empirically-based elements in the PRP that may have been effective in reducing depressive symptomatology. Following are some suggestions of other elements that may have contributed to improvements in reported depressive symptomatology. The contributions of different elements, such as these, need to be further tested to determine whether or not GSE is the potent ingredient such programming.

Social support.

Social support is defined as the perceived availability of help (Graham, Christian, & Kiecolt-Glaser, 2007) or satisfaction with help (Lutgendorf et al, 2005) when it is needed. This includes social integration, which refers to “the extent of ties to friends, family, and the community” (Kiecolt-Glaser, Gouin, & Hantsoo, 2010) or feelings of belonging within a social network (Lutgendorf et al, 2011).

Current research supports that social support status benefits psychosocial and biological functioning (Uchino, Cacioppo, & Kiecolt-Glaser, 1996). Those with existing high social support demonstrate improved morbidity and mortality (Uchino, Cacioppo, & Kiecolt-Glaser, 1996), increased adherence to medical treatments (DiMatteo, 2004), and may be a more influential indicator of health than smoking or alcohol consumption (Holt-Lunstad, Smith, & Layton, 2010). It has also been found to be the strongest predictor of QOL scores in patients with advanced cancer (Rodriguez, Mayo, Gagnon, 2013)

The PRP provides patients with many different opportunities for social support. For example, patients are encouraged to bring their caregivers to their gym sessions, they bond and form friendships with their peers during their group exercise sessions, and they receive support from the PRP team, who aim to be encouraging, helpful, and supportive. All of the above may improve QOL by increasing social integration and support by providing friendship, solidarity, and sense of belonging. Although social support has been shown to be a major contributor to patient's overall QOL (Rodriguez, Mayo, Gagnon, 2013), there have not been any studies on palliative rehabilitation interventions that weave social integration into the intervention framework. Social support may actually have been a mediator of GSE, which is one of the indirect pathways that GSE has been found to affect depression (Holahan & Holahan, 1987).

Behavioural activation.

Behavioural activation is an evidence-based intervention for depression. It involves having patients implement scheduling of their activities during a week, track their associated mood, and set small achievable goals to incrementally increase pleasant activities (Sturmey, 2009). It is often a component of a larger psychotherapeutic intervention. Through work with a number of the team's clinicians, patients may have engaged in behavioural activation.

Individualized programs.

Evidence for individualized programs is difficult to find in the existing literature, perhaps because it counters good research methodology. Considering that the RCT is considered the gold-standard of research studies and experimental control is key to assuring internal validity, it is of course necessary to properly hold as many other variables constant as possible when assessing a variable of interest. At the same time, assuring internal validity can threaten external validity, which may be the case in many published intervention-based studies. In the PRP, the patients arrive at their initial interview and are immediately recruited in the process of designing their intervention. They meet with the various team members, they are asked for their personal goals, and they begin their programs within the week. This can be a motivating factor for patients in that they are granted a portion of control of their own program. Also, interventions are clearly geared towards discussed goals, rather than overarching goals of the program or of our research. Patients can spend their time targeting what troubles them the most. Consider the difference if these patients were to meet with the team and receive uniform goals and uniform interventions: They may feel less empowered and less motivated by the program's goals than they would their own. Therefore, it may be due to this incongruence with what is well-controlled research that makes comparable literature hard to find. There is not a body of existing evidence on such individualized programs yet it may be a helpful element in such an interdisciplinary program for patients with various goals and various diseases.

Other theoretical models that may account for change in depressive symptomatology.

General self-efficacy (and more broadly, Social Cognitive Theory; Bandura 2001; 2011) are appealing for studying depression because it is a psychological variable, it can be bolstered in interventions in a fairly direct way, and can translate into improved functioning in a number of domains that may affect depression (e.g. behavioural, social). There are also other theories often

used in health psychology that are worth discussing herein because they may also provide explanatory value of changes in depression. It is important to note that they were not chosen for the current research because they are largely behavioural whereas GSE was considered more inclusive of the multidimensional nature of depression.

Theory of Planned Behavior.

This theory (Azjen, 1986) proposes that behaviours develop from intentions, which are a function of attitudes, subjective norms (e.g. family expectations), and perceived behavioural control. It may be useful to examine how the elements of this theory may influence patients' behaviour in attenuating depression, such as their abilities to attend the program, engage in the interventions, and how these contribute to their experience of reduced symptomatology.

Health Belief Model.

This model (Becker, 1974) proposes that health behaviours can be predicted by perceived susceptibility to a health threat, severity of health threat, efficacy of the behavior in protecting one from the threat, and the benefits and barriers to engaging in this behavior. Like the Health Belief Model, this theory may have been useful in gaining understanding of what may have influenced patients to complete the program or engage in other wellness-related behaviours.

Each of these two posit on how to bolster specific behaviours (e.g. program attendance) that may mediate depression. They do not necessarily predict change in depressive symptomatology directly. Accordingly, the existing literature reflects this by using these in a mediator-like capacity, i.e. the theory can be used to bolster behaviours (use of mental health services: Henshaw & Freedman-Doan, 2009; medication compliance: Cohen, Parikh, & Kennedy, 2000), which in turn mediates depression.

Theory of Activity Restriction.

This theory posits that illness and disability are stressors and they may lead to depression through a patient's restricted activity. It has been proposed as a model to predict level of depression for patients who are experiencing activity limitations (Williamson, 2000).

Theory of Illness Intrusiveness.

Not too dissimilar from the theory of activity restriction, the theory of illness intrusiveness posits that the effects of disease and/or treatment on one's ability to participate in valued activities affects their emotional and psychosocial wellbeing (Devins, 2006). These two theories are similar in that they conceptualize depression as an outcome of restricted activity. However, they lack focus on social or psychological mechanisms that may also contribute to depression as well as a mechanism that may bolster longitudinal maintenance.

Despite the difference, any of these could be measured within the PRP framework and be used to help explain changes in depression. None of these are mutually-exclusive and they may even have coincided or interacted to influence the reduction of symptomatology reported.

A clinical benefit of the GSE framework is that it has a clinical application that can be incorporated easily-enough to different interventions, and encompasses a number of the abovementioned elements in a parsimonious manner. For example, interventions implemented according to either the theory of restricted activity and of illness intrusiveness can potentially be considered within the self-efficacy framework under *Removing physical and emotional barriers*. Likewise, increasing social support can be considered as a way to bolster *verbal persuasion*. As well, given the heterogeneous cancer sites, treatment plans, individualized goals, and disparate

biopsychosocial factors in the development of depressive disorders, GSE provides a clinical approach to work within when patients' presentations are vastly different.

Limitations

It is important to note that these results are preliminary for a number of reasons. First, there are measurement concerns. A clinical interview alongside a self-report measure is considered the gold-standard in assessment for depression and, having used a self-report measure, there is some pertinent information lacking. The clinical interview allows the opportunity to further question the onset, frequency, antecedents, intensity, and duration of symptoms, whereas the self-report measure provides information only on presence and severity. Therefore, a more informed assessment or diagnosis is possible with the interview. For example, a patient who reports sadness, anhedonia, decreased appetite, increased sleep, and fatigue for most of the day, most days for the last month may meet criteria for a diagnosis of major depressive disorder. With a clinical interview, though, the clinician may be able to determine that this patient is actually experiencing a food aversion for days following each chemotherapy treatment, which drastically reduces his calorie intake, thereby reducing his energy, ability to engage with others or his hobbies, and bolstering his hypersomnia. When he takes a break from his treatment, these symptoms largely dissipate. This distinction is possible with an interview but obscured with a self-report measure. As well, the self-report measure does not provide information on subjective ratings of a symptom's interference in one's life above and beyond the interference due to the disease or treatment. Therefore, these findings cannot be generalized further than statements about reported depressive symptomatology.

Another limitation in the design, which precludes more certain conclusions, is the lack of control or contrast groups. This was an unfortunate omission that was due to this novel program

having been designed clinically (not empirically) as well as the lack of an available waitlist. Nevertheless, valuable information was gleaned from these studies that support the need for further research with more empirical rigour. Control group options for ongoing research include quasi-RCT's (such as randomization by cluster) or pragmatic designs such as cohort studies (Aoun & Kristjanson, 2005; Grande & Todd, 2000).

Patients could be referred to the PRP regardless of cancer site, which makes the program inclusive but this may also affect potential outcomes. Patients with different cancer sites may experience different limitations in various domains of functioning or QOL. For example, patients who have undergone treatment to the head or neck may experience more disfigurement and consequent shame about their appearance than might a patient who had treatment for a gynecological cancer. Contrarily, a patient with gynecological cancer may experience more concern or grief for fertility or intimacy in her relationship. Therefore, having such a wide variety of cancer sites (up to 28 sites in the theoretical study) also likely increased the variability in the etiology and perpetuating factors of depressive symptomatology. Also, with such a large number of sites, it is difficult to control for site within the analyses, which precluded our ability to examine tumour site as a predictor or control variable. Nonetheless, such heterogeneity does provide evidence for interventions that may be beneficial for patients with tumour sites that are not often studied and allows generalization to a larger population.

As previously mentioned, patients were not exhibiting severe depressive symptomatology, on average. In addition to not being able to conclude about clinical depression, it is also not possible to conclude about more severe symptomatology. Therefore, these results generalize to a population of patients who may be exhibiting some symptomatology. We do not know how patients with more severe symptomatology may respond to this sort of intervention. On one hand,

it may provide relief and on the other hand, it may not be focused enough on depression. Also, the studies within may have been subject to a floor effect: If scores were not very high to begin with, they can only decrease a small amount. Nonetheless, the advantage herein is that subclinical depression has been called more problematic for this population because medications are not effective for low levels of depression (Rodin 2013) and presumably it is harder to detect, especially without the expertise of a mental health professional.

There were a large number of withdrawals from the program (pilot study: 42%, theoretical study: 31%, longitudinal study: 47.3%). Anecdotally, the team attributed this to the nature of the population. As mentioned, they are dealing with a large burden from their illness, treatment, and ongoing medical appointments. At least two extra appointments per week may have been strenuous for them and their support networks. Looking more closely at each study, in the pilot, the cohort was among the earliest patients to undergo the program. The team was admitting people for whom the program may not have been the best fit: for example, those who were functioning too well, lived too far away. This may have impacted the drop-out rate. This was likely a factor because, as can be seen in the theoretical article, the completion rate improved as time went on, referrals increased as admission became more restricted. Finally, in the third study, the drop-out rate increased once again. This was likely due to the mail-out methodology and to the hospital portion of the program being complete. Patients may have felt less inclined to complete the questionnaires when they had already graduated from the clinical portion three months prior. Patients who were younger in age were less likely to complete the longitudinal study. Barriers to this younger part of the cohort completing the study may have included more distress than older patients, due to the demands of young families, the higher likelihood of being employed, and busier social support networks (Carlson et al, 2004; Jones et al., 2010; Mor, Allen, Siegel & Houts, 1992).

Focusing on completers was likely a source of bias. From referral onwards, there were many opportunities for patients to self-select. For example, those who were more severely depressed may never have followed through on the referral to the PRP in the first place, may not have attended their initial appointment or subsequent appointments, or may not have bothered with the follow-up questionnaires. Although I use severity of depression as an example herein, other factors may have affected completion rate, such as anxiety (e.g. social anxiety or agoraphobia).

Being a secondary analysis of the data, I did not get to choose my measures according to my preferences or my own theoretical orientation. Ideas of measures I may have liked to include would have been a measure of social support and a measure of attachment. Clinically, I am an integrative therapist, meaning that I draw from a number of evidence-based practices, but I conceptualize the difficulties my patients experience from an interpersonal lens. It would have been interesting for me to examine depression in the context of interpersonal relationships for patients who are living with advanced cancer, a disease that imposes a large burden on patients and their loved ones. Considering the social support integrated in the team, it would have been interesting to understand the level of interpersonal functioning patients were exhibiting prior to starting the program compared to when they completed it. Subsequently, I would have liked to examine how changes in these interpersonal domains affected scores of depression. In addition to these measures, I would have liked to conduct a semi-structured interview to achieve a more thorough understanding of how these elements (social support, attachment, depression) affected patients at both the beginning and end of the program. Moving forward, I would also like to integrate social support into my findings from this thesis. As mentioned, social support and GSE interact and, paradoxically, having healthy interpersonal relationships can impact a person's ability to be increasingly trusting and confident in their own abilities.

Finally, data on which professionals were accessed, the duration and quantity of sessions, and attendance data in general was not tracked in a consistent or reliable way. This raises the question of whether or not the program was actually interdisciplinary. It is possible that optional clinicians (dietician, occupational therapy, social work) were accessed by a negligible percentage of the patients herein. Although it can be estimated that this is unlikely, given that the program maintained all six clinical positions over the 5-6 years of operation, the data is not available to prove this is the case. See Table 1 for estimates of service provided by discipline as estimated by the team's clinicians, although thorough tracking would be pertinent in ongoing research.

Improvement of the current design.

Improvements in the development stage.

If redesigning this program, the Medical Research Council's recommendations for evaluating complex interventions (Medical Research Council [MRC], 2006) would be useful and arguably necessary to guide the design and inform the evaluation. According to the report, given the quantity and variability of outcomes in the program as well as the flexibility of interventions, it would be important to ask these two questions from the beginning 1) is this intervention practical? and 2) what makes this intervention effective? These can be addressed by using the existing evidence-base and choosing an appropriate theory to guide the development of the program. It would be important to plan the progression of evaluations (i.e. pilot, exploratory, and then more complete evaluation) from the beginning and implementing them progressively as the program operates and grows (MRC, 2006).

Improvements in the clinical application.

A new hypothetical design to address the current limitations can include a randomization-by-cluster design (Aoun & Kristjanson, 2005; Grande & Todd, 2000; MRC, 2006). This involves the program running in two cities: one that offers the PRP and another that does not. Upon patient referral in either city, a team member contacts each patient to discuss their involvement and arrange an initial interview. Ideally, this team member will be trained in motivational interviewing, which is a technique in which the clinician helps the patient address their reluctance to participate in the program. This may help boost motivation to attend the program for patients who may benefit the most (e.g. those with a more severe depression who may be experiencing clinically significant difficulties in engaging in their lives). Following this triage, patients who are participating receive the consent form and questionnaire package in the mail to prepare for their initial interview. On the morning of their initial interview, patients undergo a similar format (meeting with each clinician) although the team would include a mental health practitioner who is able to provide a diagnostic interview. At minimum, this would include information on depressive and anxious symptomatology. Next, patients in the city with the PRP would attend the 8-week program as above and the patients in the other city would not. An addition at the start of the intervention would include psychoeducation on GSE for patients and caregivers, in order weave the theory more fully into the program framework. After 8-weeks, patients return for their completion interview. To boost number of data at completion, phone calls can be made to those who did not attend the completion interview or who dropped out of the program. Additionally, data analysis would include using multiple imputation to estimate missing values to further improve completeness of data.

Implications and Future Directions

The current studies brought to light a number of interesting lines of research and considerations for clinical practice.

Interdisciplinary intervention.

Two Cochrane Reviews found that exercise-interventions for depression have not been found to be more effective than other evidence-based treatments, in both samples of patients with cancer and those without physical comorbidity (Mead et al 2009; Rimer et al, 2012). It would be interesting to compare uni-disciplinary interventions to interdisciplinary interventions to see if the latter builds upon the benefits of individual evidence-based therapies or if there is value added to having multiple collaborative clinicians. In addition, it would be interesting to examine individualized care-plans, as offered by the PRP, to a more structured a uniform care plan, to see whether earlier arguments about internal versus external validity are supported.

Theoretical framework.

According to the current investigation, it appears that GSE may be a possible explanation for the reduction in depressive symptomatology however, in accordance with earlier discussion, this is still a preliminary investigation. It may be interesting to compare different theories of change within a model to examine their unique contributions. With so many competing theories, the literature may benefit from an understanding of which are most potent. As well, it may be interesting to hear the clinicians' perspectives of the advantages/disadvantages of working in this framework so perhaps conducting interviews with patients and clinicians might help.

GSE has been recommended over domain-specific self-efficacy when multiple stressful demands are concurrent (Bandura, 1977; Luszczynska, Gutiérrez-Dona, & Schwarzer, 2005), which is aligned with the research questions herein. Interesting future directions can include general versus task-specific self-efficacy. For example, different tasks that are developed throughout the program (e.g. exercise or coping self-efficacy) can be compared to GSE to tease apart their unique effects on outcomes such as depression or program completion. This would be particularly meaningful

because exercise is at the foundation of the program and could speak to whether or not there is benefit to other interventions. Additionally, a path analysis may be interesting to determine if general self-efficacy affects domain specific self-efficacies or perhaps vice-versa.

Clinically, programs may consider adopting a GSE framework for any intervention in which the patient needs to gain a skill. Administrators may choose to educate their clinicians on this framework to help patients achieve their goals and increase feelings of success, motivation, coping, or others. Patients may begin to feel that they have these four steps (mastery, vicarious learning, removing barriers, and positive reinforcement) as tools to overcome ongoing hurdles and feel less burdened by their previous perceived limitations.

Severity of depressive symptomatology.

Considering the aforementioned discussion of whether or not patients with the more severe cases of depression are going to attend a hospital-based tertiary care program, their recruitment is interesting for ongoing research. To begin, it may be informative to have screening information from the referral source. This would understandably also be a measure of symptomatology rather than clinical diagnosis unless a structured clinical interview was conducted.

Clinically speaking, it may be useful to transmit distress-screening information along with referrals amongst professionals and program because it may help capture patients who are too depressed to follow-through. All oncology programs across Canada are required to implement screening programs for distress (Bultz, 2011), which could be useful for deciding who or how to triage a patient. For example, patients who score above a certain cut-off score on the depression item should perhaps be contacted by a team member who is a mental health professional. If done this way, the clinician may be able to speak to that patient's needs more directly or apply an evidence-based intervention for helping a patient work through ambiguity (e.g. motivational

interviewing). This approach may not only improve recruitment to the program but may also make a difference for a patient suffering from severe depression. It may also save some lives, because people who are depressed and those who fear burdening others while facing painful or fear-inducing events are at risk of increased suicidality or desire for hastened death (American Psychiatric Association [APA], 2013; Cheville, 2001; McPherson, Wilson, & Murray, 2007; Rodin, Lo, Mikulincer, Donner, Gagliese, & Zimmermann, 2009; van Orden, Witte, Cukrowicz, Braithwaite, Selby, & Joiner, 2010; Wilson et al., 2007).

Future avenues of research from here may include investigations of follow-through with referral based on screening scores, or qualitative interviews with all patients who are referred to understand their reasons for following-through or not. Information from these lines of research may be clinically valuable and may speak to a gap in care that exists: Those who need the services the most may be too limited in their psychological functioning to obtain them. From here, it may also be worthwhile to examine whether working within a GSE framework impacts patients with more depressive symptomatology than those with less.

Longitudinal impacts of the PRP.

The longitudinal study within this thesis begins to explore follow-up data, and there exists much more that can be analyzed in future research. At the same time, it would be interesting to hear qualitatively from patients how the PRP affected their functioning and QOL. We are currently conducting qualitative research with patients to understand their experience of social support within the program. It may be interesting to also collect open-ended subjective accounts of how the program did or did not affect them. This could be beneficial in the development of ongoing programming for this population of survivors with advanced cancer.

Conclusion

The results of these studies begin to support what may be a beneficial approach for helping patients cope with depressive symptomatology. It is a salient issue for this population. It is hoped that these studies will contribute to the budding and growing literature on palliative rehabilitation for survivors with advanced cancer and also have a beneficial impact on their care.

THE END

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Table 1.

Utilization of clinical PRP services, as estimated by team clinicians.

Clinical Discipline	Percentage of all PRP patients seen	Number of visits (range)	Duration of visits (minutes)
Physician	100%	1-3	15-45
Nurse	100%	1-3	15-45
Physiotherapist	100%	1-2/week	45
Occupational Therapist	70%	1-5*	30-45
Dietician	60-70%	1-5*	30-60
Social Worker	40%	1-8*	30-60

*In addition to booked appointments, clinician dropped-in to the PRP gym for unofficial follow-ups.

An exhaustive list of CNR/PRP publications

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