A prospective analysis of the functional impact of patients in an interdisciplinary cancer rehabilitation program in a tertiary care hospital setting

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ABSTRACT

A prospective analysis of the functional impact of patients in an interdisciplinary cancer rehabilitation program in a tertiary care hospital setting

Irina Uscatescu

Introduction: The number of cancer survivors is increasing and the need for multidisciplinary cancer rehabilitation centers is on the rise. The Cancer Rehabilitation and Cachexia Clinic at the McGill University Health Centre, aims to provide personalized, multidisciplinary care by introducing the concept of three patient streams based on symptom progression: restorative, supportive and cachexia. Patients at this clinic are seen by five cancer care specialists whose goal is to improve quality of life while restoring or maintaining their functional abilities. The present study evaluated the functional outcomes of the patients who participated in the multidisciplinary cancer rehabilitation clinic in 2014.

Objectives: To evaluate the functional improvement in the hand grip strength, six minute walk test, sit to stand test and the single leg stand test, of patients who took part in the interdisciplinary cancer rehabilitation clinic.

Methods: 115 patients with cancer were referred to the Cancer Rehabilitation and Cachexia Clinic from January to December 2014. Physical functional was assessed at baseline visits, follow-up visits and at the end evaluation, by performing the had-grip strength test, 6 minute walk-test, sit-to-stand test, and single leg stand test. The data was analysed for each dependent variable to determine if any baseline differences existed among the three program streams (restorative stream, supportive stream, cachexia stream) and to measure if the patients improved their functional status pre-post rehabilitation after completing the respective assigned streams.

Results: There were 48 patients assigned in the cachexia stream, 28 patients in the restorative and 39 in the supportive stream. The most predominant type of cancer was lung cancer. At baseline, the cachexia stream had significantly lower weight, BMI and higher WBC compared to the restorative stream. At baseline, patients in the supportive stream had a significant higher percentile HGS when compared to the cachexia stream ($p<0.05$). Although not statistically significant, all three streams slightly improved their hand-grip strength while being part of the program.

Conclusion: Overall function of the groups did not show improvement based upon the 6MWT and HGS. However, the supportive stream did show improvement in their percentile HGS. Thus, the interdisciplinary rehabilitation services demonstrated only mild improvements in the supportive but no measureable differences in the restorative or cachexic patient groups.

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Contents

LIST OF FIGURES, TABLE AND ILLUSTRATIONS

Figures

Tables

ABBREVIATIONS

6 MWT	6 Minute Walk Test
a-PG-SGA	Abridged Patient-Generated Subjective Global Assessment
CRCC	Cancer Rehabilitation and Cachexia Clinic
DT	Distress Thermometer
ESAS	Edmonton Symptom Assessment System
FSI	Fatigue Symptom Inventory
HGS	Handgrip Strength
LSLS	Left single leg stand
MD	Medical Doctor
MGH	Montreal General Hospital
MNUPAL	McGill Nutrition and Performance Laboratory
MOCA	Montreal Cognitive Assessment
Modified CHAMPS	Community Healthy Activity Program Model for Seniors
MUHC	McGill University Health Centre
NUR	Nurse
NUT	Nutritionist
OT	Occupational Therapist
PT	Physical Therapist
RSLS	Right single leg stand
SLS	Single leg stand
STS	Sit to stand

1. INTRODUCTION

Cancer constitutes an enormous burden on society in both more and less economically developed countries alike. The occurrence of cancer is increasing because of the growth and aging of the population, as well as an increasing prevalence of established risk factors such as smoking, overweight, physical inactivity, and changing reproductive patterns associated with urbanization and economic development (Torre et al., 2015). The number of cancer cases is expected to increase to 24 million by 2035. Based on the 2012 worldwide GLOBOCAN estimates, there were about 14.1 million new cancer cases, 8.2 million cancer deaths and 32.6 million people living with cancer (within 5 years of diagnosis).

In Canada, throughout the 29-year period from 1986 to 2015, the number of cancer cases rose steadily (figure 1) and it is estimated that by 2031 the number of new cancer cases and deaths will increase by 60%, attaining 280,000 cases and 107,000 deaths (Canadian Cancer Society, *Canadian Cancer Statistics*).

Figure 1. New cases and age-standardized incidence rates (ASIR) for all cancers, Canada, 1986–2015

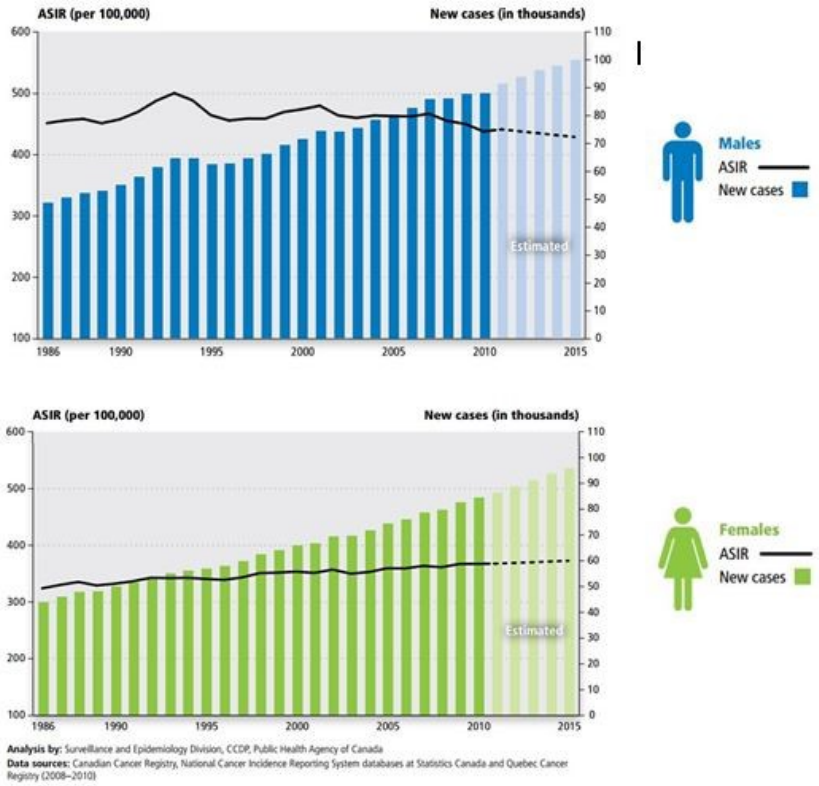
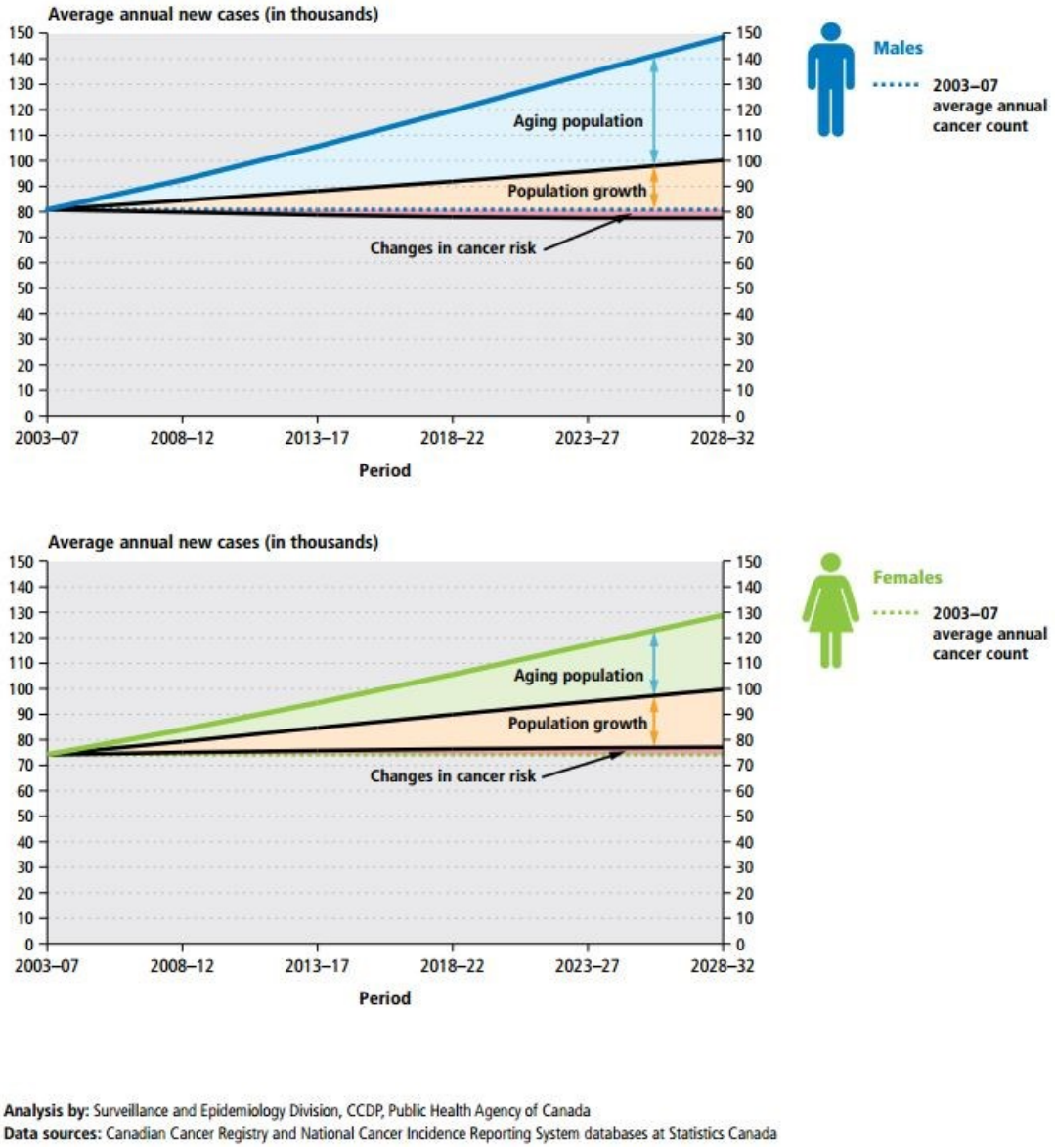


Figure 2 below illustrates that the projected rise in the number of all new cancer cases in both males and females will primarily be due to the aging of the Canadian population and, to a lesser extent, from an increase in population size (Canadian Cancer Society, *Canadian Cancer Statistics,* 2015 annual publication). Overall, cancer is the leading cause of mortality in Canada, responsible for 30% of all deaths, ahead of cardiovascular disease (Statistics Canada: *Leading cause of death*, 2014).

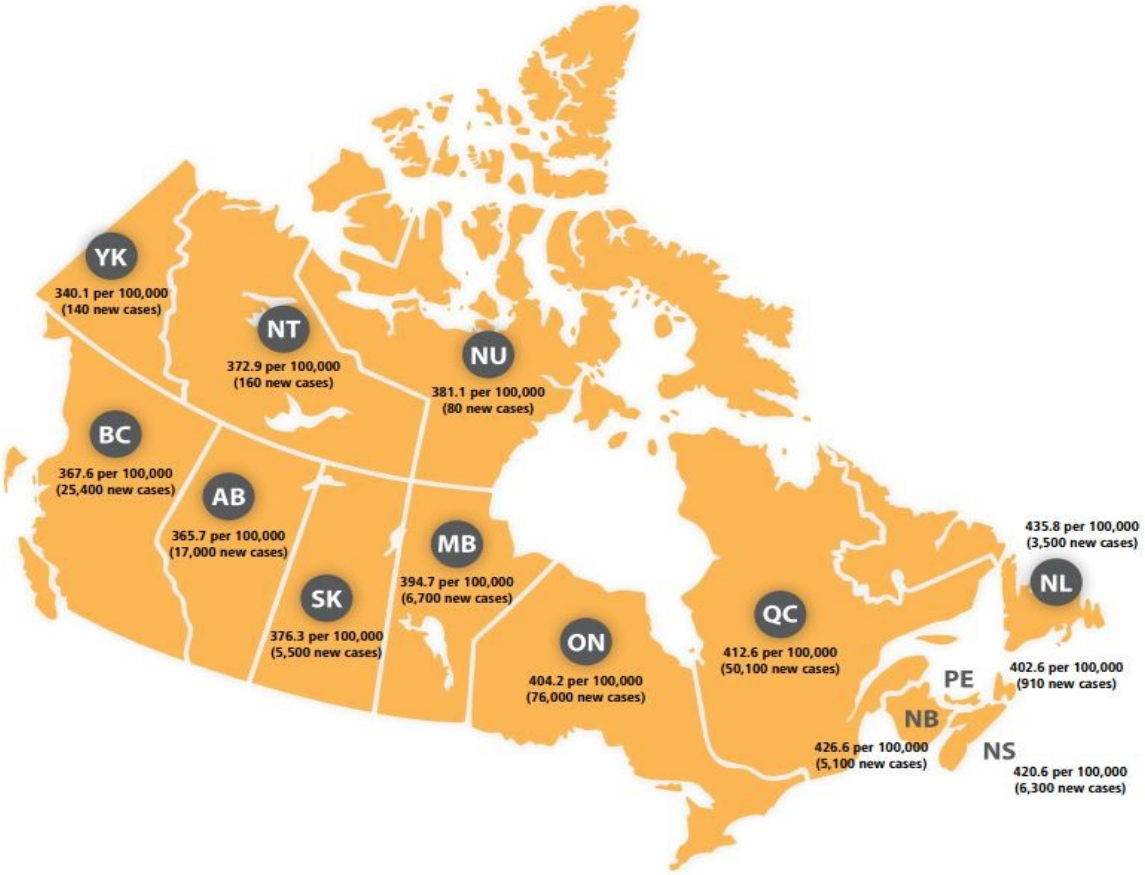
Figure 2. Trends in average annual new cases for all cancers and ages, attributed to changes in cancer risk, population growth, and aging population, Canada, 2003–2032



Analysis by: Surveillance and Epidemiology Division, CCDP, Public Health Agency of Canada
Data sources: Canadian Cancer Registry and National Cancer Incidence Reporting System databases at Statistics Canada

Figure 3 below shows new cancer cases and their distribution throughout Canada in 2015. Twenty-four percent (23.9%) of cancer diagnoses in males were prostate cancer, 13.9% were colorectal cancer and 13.5% were lung cancer. In females, breast cancer accounted for 25.9% of new cases, lung cancer for 13.5% and colorectal cancer for 11.5%. Furthermore, about 840,000 Canadians diagnosed with cancer in the previous 10 years are alive today (Canadian Cancer Society, *Canadian Cancer Statistics,* 2015 annual publication).

Figure 3. Geographic distribution of estimated new cancer cases and age-standardized incidence rates (ASIR) by province and territory, both sexes, Canada, 21015



In Quebec, the number of new cancer cases continues to increase steadily with population growth and ageing. For 2015, around 50,100 new cancer cases were predicted in Quebec along with 20,200 cancer related deaths. Around 190,000 people in Quebec diagnosed with cancer in the previous 10 years are still alive today (Canadian Cancer Society, *Canadian Cancer Statistics,* 2015 annual publication).

Cancer survival

According to the Canadian Cancer Society, the ongoing rise in the annual number of new cancer diagnoses (due to a growing and aging population), combined with an improving survival rate for most types of cancer, means that a substantial number of people are living with and beyond their cancer diagnosis. The number of newly diagnosed cancer cases in Canada is increasing, but survival rates are also increasing. These improved survival rates account for the growing number of Canadian cancer survivors (Canadian Cancer Society, Canadian Cancer Statistics, 2015 annual publication).

Based on 2006–2008 survival estimates, 63% of Canadians diagnosed with cancer are expected to survive for 5 years or more after a cancer diagnosis. Survival rates vary from low to high depending on the type of cancer. For example, based on 2006–2008 estimates (Canadian Cancer Society, cancer statistics at a glance):

- The 5-year relative survival rate for lung cancer is low (17%).
- The 5-year relative survival rate for colorectal cancer is average (64%).
- The 5-year relative survival rate is high for prostate cancer (96%) and breast cancer (88%).

Between 1992–1994 and 2006–2008, survival rates increased from 56% to 63% for all cancers combined (Canadian Cancer Society, cancer statistics at a glance). This prevalent population of people with cancer and cancer survivors is likely to have unique healthcare needs during the course of their cancer journey. Patients now have to cope longer with symptoms of cancer and the long-term consequences of cancer treatment (Canadian Cancer Society, Canadian Cancer Statistics, 2015 annual publication). As a consequence of this trend, there is a growing demand to address the increasing needs of the cancer patients and survivors. To address the complex situations that accompany long-term cancer care, chronic management teams, made up of supportive health care professionals and palliative care specialists, will be charged to provide personalized clinical services and programs. These teams will have to address many clinical, nutritional and functional challenges in this patient population.

Cancer rehabilitation

Cancer rehabilitation is a relatively new form of rehabilitation medicine focusing on restoring and maintaining the highest possible level of function, independence, and quality of life of patients at all stages of their cancer diagnosis. This includes those undergoing potentially curative therapy and those receiving palliative care, as well as cancer survivors (Stubblefield et

al., 2011; Stubblefield et al., 2013 a,b; Chasen et al., 2008). Furthermore, cancer rehabilitation assists the cancer patient to obtain maximal physical, social, psychological, and vocational functioning within the limits created by the disease and its resulting treatment. Rehabilitation specialists have proposed several general principles regarding rehabilitation interventions for patients with cancer. Rehabilitation requires an interdisciplinary team approach because of the variety of potential problems patients may face during the course of the illness. The availability of professionals from major disciplines is essential to offering comprehensive care. The patient's needs determine the team members involved.

Rehabilitation services include, but are not limited to (American College of Surgeons: Cancer program standards: ensuring patient-centered care, 2016 Edition):

- Lymphedema program
- Pain management
- Physical impairments and disabilities
- Lifestyle and weight management programs
- Physical and exercise therapy
- Reflexology and massage therapy
- Occupational therapy

Specialized cancer rehabilitation often involves a team of different healthcare professionals composed of (Canadian Cancer Society):

- Occupational therapist
- Ostomy therapist
- Physiotherapist
- Recreational therapist
- Rehabilitation nurse
- Social worker or psychologist
- Speech-language pathologist
- Spiritual care worker
- Vocational rehabilitation counsellor

These professionals have the capacity to provide their own expertise in designing and implementing multidisciplinary approaches and interventions in an individualized and personal manner.

The National's Cancer Institute definition on cancer survivors states that an individual is considered a cancer survivor from the time of diagnosis, through the balance of his or her life. Family members, friends, and caregivers are also impacted, and thus are included in the definition. Upon discharge from oncology, cancer survivors need follow up care (Nissen MJ et al., 2007). After their treatment is completed, these patients need assistance on nutritional, physical and psychosocial aspects. Family physicians are expected to provide continuity of care however; they are often unaware of the specific issues and needs of these cancer patients (Nissen MJ et al., 2007). The Montreal's Cancer Rehabilitation and Cachexia Clinic (CRCC), at the McGill University Health Centre (MUHC) is a unique model in that it contributes with five disciplines to the assessment and treatment of a cancer patients and cancer survivors. The five specialists work together to improve more than one patient outcome.

The focus of this research project was on the Montreal's CRCC at the McGill Nutrition and Performance Laboratory (MNUPAL). The purpose of this project was to evaluate if the cancer patients who took part of the CRCC clinic during 2014 improved their functional performance as evidenced by significant increases in hand grip strength, six minute walk test, sit to stand test and single leg stand test.

2. LITERATURE REVIEW

2.1 International Cancer Programs

MD Anderson Cancer Center (Texas, USA)

The University of Texas MD Anderson Cancer Center in Houston, Texas, is a comprehensive center with an acute inpatient rehabilitation unit dedicated to cancer patients (Shin et al., 2011). Patients with multiple impairments, significant functional deficit, and multiple medical co-morbidities who are receiving treatments can highly benefit from acute inpatient cancer rehabilitation composed of a comprehensive interdisciplinary team. The interdisciplinary team includes a doctor, nurse practitioner, physical therapist, occupational therapist, speech therapist, rehabilitation nursing specialist, nutritionist, pharmacist, case manager and a chaplain, working together to achieve the goal of safe patient discharge.

Shin et al., (2011) retrospectively reviewed the medical records of 1098 patients, between September 2008 and August 2009. 427 patients were admitted to the inpatient rehabilitation unit. The conclusion of the study was that after an average stay of 11 days, 324 of the 427 patients seen at the MD Anderson Cancer Center were successfully discharged. Furthermore, 72 patients went back to intensive care, 15 patients were sent to a nursing facility, 9 were discharged to palliative care and 5 were discharged to a long-term intensive care facility (Shin et al., 2011).

CARE Clinic, Philadelphia USA

In 2007, the Palliative Care Program at the Joan Karnell Cancer Center (JKCC) at Pennsylvania Hospital in Philadelphia developed a cancer cachexia clinic called the Cancer Appetite and Rehabilitation (CARE) Clinic, to minimize the effects of cancer cachexia and improve nutrition, function, symptom management, and quality of life (QOL) of patients with cancer. The clinic's interdisciplinary team is composed of a physician, nurse practitioner, nutritionist, physical therapist, speech and swallowing therapist, patient navigator and a program assistant. The CARE clinic is focused on patients with a high risk of cachexia but also treats patients with other types of cancer.

The interdisciplinary treatment plan includes pharmacologic and nonpharmacological approaches to symptom management, nutrition, physical therapy, and speech and swallowing therapy. The pharmacological treatment may include pro-gestational agents, glucocorticoids,

cannabinoids, antidepressants, prokinetic agents, and anabolic steroids. Nonpharmacological treatments may include exercise programs, mouth and swallowing exercises, and nutritional counseling (Adams et al., 2009; Fearon et al., 2002; Gagnon et al., 1988., MacDonald , 2007; Mattox et al., 2005; Orr et al., 2004; Osei-Hyiaman, 2007; Ottery et al., 1995; Stewart et al., 2006; Strasser et al., 2002; Tisdale , 2006; Zinna et al., 2003).

Between April 2007 and April 2009, a total of 96 patients were admitted to the CARE clinic. The CARE clinic pathway is illustrated in Appendix 1. During this pilot study, the authors looked at nutritional intake and symptom distress for the group of patients with cancer who attended the CARE Clinic at least four times (n = 11). Although not statistically significant, a tendency for improvement was observed between visit 1 and visit 4 in weight, body mass, and appetite levels (Granda-Cameron et al., 2010).

Sydney, Australia

The original Cancer Nutrition Rehabilitation Program developed by McGill University (CNRP) has been adopted by an Australian cancer center. The purpose of their study was to evaluate the outcomes of 2 months participation in the CNRP. The measures used in the CNRP included: demographics and clinical details, weight, body composition analysis, nutritional assessment (PG-SGA), laboratory parameters of inflammation (CRP, albumin), symptom assessment (ESAS), performance status (KPS), 6MWT, HGS and strength tests. Patients were eligible if they had significant anorexia/weight loss, identified by their oncologist or the Malnutrition Screening Tool. Patients who agreed to participate in the program were seen by a physician, a nutritionist and a physical therapist for a baseline assessment. Each patient was then given a nutritional intervention and exercise program to be performed either at the hospital's gym or at home, with regular monthly follow-ups for progression and re-evaluation (1, 2, 3, and 6 months). Out of the 54 patients that were recruited, 25 returned for month 2 reassessment. Among those, nutritional reassessment occurred for 22 patients whereas physical therapy reassessment was performed for 10 participants. Improvement was seen for endurance (6MWT), strength (HGS), symptoms (ESAS), and inflammatory markers (although further randomized control trials need to establish significance as only descriptive statistics were performed. Participants who remained in the program demonstrated improved nutritional and functional status, endurance, and strength, with a decrease in reported symptoms and felt better supported. Participants were significantly likely to return for re-evaluation if at baseline they were having anticancer therapy or could walk >420 m in 6 minutes.

Integrative supportive care program, Pisa, Italy

The Italian integrative supportive care program is located in an ambulatory room incorporated in an oncology unit. The team receives scheduled and unscheduled patients who are admitted to the oncology department because of complications with their treatment. During an eight month period (mid-March to October 2013) the team collected data on care provided to patients including more than 700 in person visits and more than 2,000 phone calls. Seventy three percent of patients had metastatic disease. Furthermore, 72% out of those metastatic patients were receiving active anticancer treatment. The main reason for requiring a visit were uncontrolled symptoms (54%) such as pain, fatigue, anorexia, etc. The authors concluded that 5.5% of patients, followed in the outpatient setting, were further hospitalized. Furthermore, 10% of patients needed unscheduled hospital access for supportive care mainly for disease-related symptoms and toxicities.

The management of supportive care for cancer patients inside the oncology unit could favor the accessibility of patients and help a better management of both cancer and treatment-related complications (Bandieri et al., 2012). Moreover, having an ambulatory for supportive care localized into the oncology unit might consent a more rapid admission of patients with oncological emergencies or severe toxicities that should be treated in an oncological setting (Vasile et al., 2014).

Brussels, Belgium

An outpatient rehabilitation setting in the Oncology Centre at the University Hospital Brussels in Belgium designed a pre-post evaluation on the effects of a rehabilitation program on QOL, fatigue, fear of movement, distress, anxiety, depression, and physical condition. The participants completed a questionnaire and a physical test at baseline and at the end of the 12 week program. In this study physical training was provided 3 times a week for 60 minutes, psychoeducational training was provided 8 times during the 12-week program for 90 minutes, and individual counseling was provided at the beginning of every exercise session, as well as at the end of the program. A general and significant improvement in all aspects affecting quality of life and rehabilitation was observed. Multidisciplinary rehabilitation should become part of the total care plan for patients with cancer. This program was suitable for patients who completed their cancer treatment and who experience a discrepancy between their present level of functioning and their pre-disease status (Hanssens et al., 2011)

The different worldwide (table 1) cancer programs vary greatly in size (number of patients), approach to the cancer treatment as well and the target patient population. Inpatient cancer centers are suitable for patients who are deconditioned and not for patients who are cancer free but still suffer from the long-term side effects of their chemotherapy, radiotherapy and/or surgery. Some rehabilitation programs offer pre and post assessments but do not provide any follow-ups making it more likely for the patients not to complete the program. The term “multidisciplinary team” is used in articles talking about cancer rehabilitation, often without a description of the team itself or their roles, and not necessarily in the context of an implemented program clinic but a dedicated team of cancer specialist working in a specific oncology unit.

Cancer symptoms can be managed with a multitude of different rehabilitation programs of various lengths and durations (Stubblefield et al, 2013 a,b; Chasen 2008, 2013). Studies have demonstrated that multiple consultations with the multidisciplinary team that are conducted in a single patient visit, greatly benefit cancer survivors by helping them manage symptoms like fatigue, pain, depression, nausea, weakness, etc. compared to the standard cancer care (Canestraro et al., 2013; Brar et al., 2014).

Table 1. International multidisciplinary cancer rehabilitation centers

Study ID	Program Name & Location	Population Sample	Study Design/Purpose	Results	Conclusions
USA					
Shin et al., 2011 Inpatient Cancer Rehabilitation: The experience of a National Comprehensive Cancer Center	University of Texas MD Anderson Cancer Center in Huston Texas	1098 inpatient consultations 427 admitted to the inpatient rehabilitation unit	Retrospective review of inpatient medical records of consecutive inpatients admitted to the acute inpatient cancer rehabilitation unit	1098 patients consultations, out of the 427 patients admitted, 324 were successfully discharged home	An active inpatient rehabilitation unit within a national comprehensive cancer center receives referrals from patients with a wide variety of tumor types and is able to successfully discharge home 76% of its patients.
Granda-Cameron et al., 2010 An interdisciplinary Approach to Manage Cancer Cachexia	Palliative Care Program at the Joan Karnell Cancer Center(JKCC) at Pennsylvania Hospital in Philadelphia The Cancer Appetite and Rehabilitation CARE Clinic	n = 96 total Patient with at least 4 visits n=11	Data collected to measure patient outcomes was completed at every visit included: ESAS, Karnofsky performance scale, nutrition and laboratory tests	A trend for improvement was observed between visit 1 and 4	Implementation of cancer cachexia initiative is appropriate and achievable by oncology nurses in collaboration with colleagues from nutrition and physical medicine
AUSTRALIA					
Glare et al., 2011 Establishing a cancer nutrition rehabilitation program for ambulatory patients attending an Australian cancer center.	Multidisciplinary Cancer Nutrition Rehabilitation Program (CNRP) Sydney Cancer Center Australia	41 enrolled 25 returned for week 8 assessment	Establish a multidisciplinary CNRP for the management of anorexia-cachexia syndrome (ACS) in an Australian cancer center Evaluate outcomes of 2 months participation in the CNRP Study included a nutritional intervention and an exercise program Measures were made at baseline, and on formal reviews at 1,2,3, and 6 months.	Nutritional reassessment only in 22 patients Physical reassessment only in 10 patients Improvement in: 6MWT, HGS, ESAS, inflammatory markers	Beneficial program for patients with advanced cancer & ACS
EUROPE					
Vasile et al., 2014 Dedicated supportive care team at the oncology unit: a model of simultaneous care for cancer patients	Integrative supportive care program Ambulatory room integrated into the oncology unit Pisa, Italy	700 oncology unit patients with complications from cancer treatment	Management of symptoms & toxicities suffered by cancer patients	5.5% of patients required further hospitalization Decreased cancer inpatient cost	10% patients would need unscheduled hospital visits for disease-related symptoms and toxicities An ambulatory for supportive care localized into the oncology unit might consent a more rapid admission of patients with oncological emergencies or severe toxicities that should be treated in an oncological setting.
	Outpatient rehabilitation setting in the Oncology Centre at the University Hospital Brussel Belgium	36 patients	Pre and post physical assessments and questionnaires Physical training, 3x/week for 12 weeks Psychoeducation 8 times during the 12 weeks	Sig improvements was observed in QOL, physical condition, fatigue, and depression	A general and significant improvement in all aspects affecting quality of life and rehabilitation was observed. Multidisciplinary rehabilitation should become part of the total care plan for patients with cancer

2.2 Local Cancer Programs

In Montreal, cancer rehabilitation programs are operated through either in-patient/out-patient facilities within tertiary care settings (e.g. hospital) or clinics. There are at least three of these programs currently available in the Montreal area. These include:

- The Cancer Nutrition and Rehabilitation (CNR) program
- The Peter Brojde Lung Cancer Program
- The Cancer Rehabilitation and Cachexia Clinic (CRCC)

There are “off-site” programs that are operated independently (Ville Marie Women’s Wellness Centre and Comprehensive Health Improvement Program) while others (e.g., McGill Nutrition and Performance Laboratory, Hope and Cope) are affiliated with hospital-based programs.

Each of these programs has their own personalized approach to cancer rehabilitation; however, they all rely on a multidisciplinary team of specialists (Borneman et al., 2008). Founded in April 2012 at the Jewish General Hospital, the Peter Brojde Lung Cancer Centre draws on philosophies and evidenced-based practices of western and Traditional Chinese Medicine (Grossman et al. 2012). According to their mission statement, the purpose of this program is to promote treatment efficacy, help relieve symptoms, and improve the quality of life, health and healing of patients. The program hopes to offer a holistic and personalized approach that meets the needs of patients as well as their families. According to one of the founders Dr. Jason Agulnik: "The Brojde Centre is innovative and quite unique because it was purpose-built to create an exceptional environment for merging both Western medicine with other complementary medicines".

The focus of this project was on the local cancer rehabilitation clinic (CRCC), which is part of the MUHC, and which runs its clinic at the McGill Nutrition and Performance Laboratory. The CRCC’s goal was to enhance the patient’s quality of life and help them be as self-sufficient as possible, thus keeping them out of the hospital and reducing the burden on the healthcare system. The program focused on trying to reduce the burden placed on the family and caregivers and reducing the effects of the cancer treatment as well (Gagnon et al., 2013; Glare et al., 2011).

The CRCC was the collaborative effort of different professionals working with the

patient and of an accompanying support network. The rehabilitation team provided services to patients throughout the course of illness, during all stages. Treatment plans were individualized to meet each patient's unique and specific needs. Patients at the CRCC received comprehensive symptoms assessment at their first visit followed by individualized treatment plan, from each of the five oncology specialists. The program team is composed of the following health professionals: doctor (MD), registered nurse (RN), nutritionist (NUT), physiotherapist (PT) and occupational therapist (OT). In the following paragraphs we present the role of each professional who was part of the CRCC multidisciplinary team and their individual roles in the rehabilitation program. A comprehensive listing of the assessments and evaluations performed by each professional at specific times during each visit is highlighted in Table 2.

Table 2. Role matrix by patient stream

		Restorative Rehabilitation	Supportive Rehabilitation	Cachexia
First visit (all patients)	ESAS	RN MD	RN MD	RN MD
	DT	RN MD	RN MD	RN MD
	a-PG-SGA	NUT	NUT	NUT
	6 MWT	PT	PT	
	Sit to stand	PT	PT	
	SLS	PT	PT	
	Modified CHAMPS	OT		
	Blood work	MD	MD	MD
	Vital signs			RN
	Hand grip	NUT	NUT	NUT
	Mini-Cog	MD	MD	MD
	FSI	OT	OT	OT
As needed	MOCA	OT	OT	
	Blood work	MD	MD	MD
	Pittsburgh Sleep Quality Index	RN OT	RN OT	
	Semmes Weinstein monofilament test	OT	OT	
	Trail-making	OT	OT	
	Bells-test	OT	OT	
	OT/PT referral			MD
	Referral to MNUPAL			MD
Every Visit	ESAS	RN	RN	NUT
	a-PG-SGA	NUT	NUT	NUT
	Hand grip - 1 year pilot	NUT	NUT	MD
	Blood work			MD
	Vital signs			MD
End-evaluation	ESAS	RN MD	RN MD	
	DT	RN MD	RN MD	
	a-PG-SGA	NUT	NUT	
	6 min walk	PT	PT	
	Sit to stand	PT	PT	
	SLS	PT	PT	
	Modified CHAMPS	OT	OT	
	MOCA if previously completed, for comparison	OT	OT	
	Hand grip - 1 year pilot	NUT	NUT	
	FSI if it was done during the first visit			OT
	Transition to Cancer Rehab or Day Hospital			RN

2.2.1 CRCC program team

Doctor

At the CRCC, each patient met the physician who presented the program, reviewed their medical history and interviewed them regarding their most pressing symptoms. Based on the outcome of the interview, the physician prescribed medication, made specialist referrals, or ordered for additional analysis to be performed. Laboratory test results were prescribed in order to better assess the nutritional and hormonal levels of the patients.

Nurse

For every new patient the registered nurse gathered their complete medical history which was reviewed by the interdisciplinary team at the beginning of each clinic day. A complete review of the patient's cancer history included the cancer diagnosis, previous and current cancer treatment, current medications, comorbidities and any other related symptoms. In addition to the coordination and support role of the nurse, other responsibilities included clarifying the patient's understanding of the disease and treatment, reviewing strategies for symptom management and discussing psychological distress and sexuality issues. Nurses also tried to make the patient feel more at ease by actively listening, validating feelings and normalizing the experience.

Nutritionist

The main concerns of the nutritionist were: the possible factors promoting weight loss or weight gain, oral care (e.g., mucositis), sensory changes related to nutrition (e. g., taste changes), centrally-mediated changes (e.g., dysphagia, loss of appetite), use of the dietary management of diabetes, GI tract implications (e.g., nausea and vomiting, diarrhea, and constipation), and complimentary therapy or alternative medicine (e.g., homeopathic remedies). The nutritionist assessed the weight based on the patient's usual body weight. A weight loss of more than 10% over six months or weight loss of more than 5% in one month, placed the patient at nutritional risk (Del Fabrro et al., 2011). Once the nutritional status had been assessed, the registered nutritionist strategized with the patient to meet estimated nutritional requirements. Handgrip strength (HGS) was also measured by the nutritionist during every visit. The goal of the nutritionist was to manage side effects and help malnourished patients through dietary changes, nutritional supplements, or pharmacologic agents.

Physiotherapist

The role of the physiotherapist (PT) in the CRCC was to help the patient regain their previous level of function by decreasing fatigue while building strength and endurance. The initial and end-evaluation consisted of three physical tests: six minute walk test (6MWT), single leg stand (SLS), and sit to stand (STS). The physiotherapist assessed the patient's physical activity history and their level of function. The PT provided the patient with a personalized home exercise program, taught the patient methods to manage their fatigue levels by using energy-conservation techniques and make simple life changes to increase muscle strength and tone. The patient was taught how to safely increase their activity level and their family was shown ways they could safely assist the patient with the rehabilitation program. The PT also created home strengthening programs to optimize and/or regain muscle mass and strength, cardio and balance training while addressing musculoskeletal issues, scar mobility, posture/pain-relieving positions and fall-prevention techniques.

Occupational therapist

The occupational therapist (OT) played an important role in dealing with cancer survivor's daily activities, work, leisure and social participation throughout the rehabilitation program. The OT's role was to help with the management of neuropathies, to optimize function, safety and comfort. The OT also discussed the cancer experience and helped the patient adapt to permanent life changes while actively listening and supporting them.

For this research project we focused on the physical function tests performed by the NUT and the PT. More specifically we looked at the HGS test, by cancer stream (restorative, supportive, cachexia), and compared their baseline values, as well as the improvement pre-post rehabilitation. Furthermore, for the physical function tests performed by the PT (6MWT, SLS, STS) we looked at the improvements pre-post rehabilitation by stream. The following paragraphs outline the unique concepts introduced by the CRCC (three different cancer streams).

2.2.2 The program's streams: cachexia, restorative and supportive

The CRCC team realized the need to better classify cancer patients that were recruited into the program, in order to provide a more personalized care. This is why in 2011 they moved away from a model that was treating all cancer patients in the same way to a model that had three groups of patients. The use of these three different streams allowed the team to provide a more personalized approach and set them apart from all other available cancer rehab programs. The main goal of the CRCC was to offer the best patient care possible in an efficient and personalized manner. Each patient was categorized into one of the following 3 different streams: restorative, supportive, and cachexia, based on the symptoms they display and their health status. The model of the CRCC, of grouping the cancer rehabilitation into categories followed the Dietz Classification who in 1969 introduced the concept of preventive, restorative, supportive and palliative rehabilitation, that address the scope and course of the illness (Franklin, 2007).

The patients in the restorative rehabilitation stream experienced problems secondary to cancer such as deconditioning, fatigue, weakness, nutritional and digestive problems or cognitive loss requiring an interdisciplinary approach. The goal for the restorative group was to help the patients return to their previous levels of physical, psychological, social, and vocational functioning.

The CRCC's restorative stream was designed for patients that have been off treatment for at least one month and showed no signs of active disease. For patients in this group, a fully functional recovery was expected, restorative rehabilitation envisioning a full reintegration of the patient back into society, community, school, or work (Sokolof et al., 2014).

The supportive rehabilitation stream was designed for patients in whom cancer treatments had resulted in permanent deficits (including those in whom deficits were unlikely to resolve) (Sokolof et al., 2014). The goal of supportive rehabilitation was to re-establish functional independence as much as possible (Sokolof et al., 2014). Patients in the supportive stream had an ongoing disease able to be controlled. The patient remained active and, to some degree, productive but with known residual disease and possibly slowly progressive handicap (Dietz, 1981).

At the CRCC the supportive stream was designed to help patients cope with their disabilities and to minimize debilitating changes from ongoing disease. Supportive efforts included teaching

patients how to use prosthetic devices after amputation, as well as instructing the patients on use of other devices and procedures that assist in self-management, self-care abilities, and independent functioning. Supportive efforts also included emotional support needed during the adjustment period while the patient was learning to cope with physical lifestyle changes. Furthermore, the supportive rehabilitation program was composed of patients that had a prognosis of six months or greater and displayed signs of active disease and who may or may not have undergone treatment. The patients in this group experienced similar secondary problems as the restorative group population (Sokolof et al., 2014).

Cachexia is derived from the Greek term "*kakos*" (bad) and "*hexis*" (condition). Cachexia is defined as a multifactorial syndrome characterized by progressive weight loss, frequently accompanied by anorexia, sarcopenia and chronic systemic inflammation (Tisdale, 2009).
Before death, more than 80% of patients with cancer develop cachexia. At the moment of diagnosis, about 80% of patients with upper gastrointestinal cancers and 60% of patients with lung cancer have substantial weight loss. Furthermore, patients with solid tumours (with the exception of breast cancer) have a higher frequency of cachexia. Cachexia is also more common in elderly patients and becomes more pronounced as disease progresses (Bruera, 1997).

Decrease of skeletal muscle mass is considered the most clinically relevant consequence of cachexia, irrespective of the underlying causative illness (Muscaritoli et al., 2010). Studies on sarcopenia and cachexia have shown that decreased skeletal muscle has negative clinical consequences on muscle strength, respiratory function, physical function, disability risk and QOL (Schols et al., 2005; Mantovani, 2006; Guenter et al., 1993; Morishita et al., 2012; Donohoe et al., 2011).

Factors that can influence physical function are malnutrition and/or disease-induced catabolism that are frequently accompanied by inflammation and muscle wasting. Commonly used markers of systemic inflammation available in the clinical routine are C-reactive protein (CRP) and white blood cell count (WBC). These blood markers have been proposed as indicators of abnormal metabolism or biochemistry useful aids for prognostication in patients with advanced cancer (Evans et al., 2008). High serum levels of the inflammatory marker CRP and an elevated WBC count correlate with poor prognosis and are used as a prognostic index to establish the need for nutritional/metabolic intervention.

At the CRCC patient in the cachexia stream were deconditioned, had a prognosis of non-curative intent and a life expectancy smaller than three months (Bruera et al., 2016). These

patients were generally patients with inoperable, incurable, metastatic cancer presenting weight loss, anorexia, sarcopenia and indicators of abnormal metabolisms (Granda-Cameron et al., 2010, Sokolof et al., 2014). All new cancer patients were being screened for the presence of nutritional problems, inflammatory markers, and related symptoms. Interventions included general symptom management, dietary counseling, nutritional supplementation, exercise prescription in accordance with the patient's physical condition (MacDonald, 2007). Furthermore, the CRCC's goals for the cachexia group included pain control and psychological support for the patient and family members.

In the following paragraphs, we describe the method used for this project, the results, the discussion and conclusion of this analysis.

3 RESEARCH QUESTIONS AND HYPOTHESES

Question 1 (Baseline)

Will we observe a statistically significant difference in the functional test outcomes (i.e., hand-grip strength, sit-to-stand, single leg stand and the 6 minute walk test) among the three streams (cachexia stream, supportive stream and restorative stream) when comparing their baseline visits?

Hypothesis 1

At baseline, patients in the restorative stream will have a significantly higher functional test results than the supportive and cachexia streams and the supportive stream will have higher results than the cachexia stream.

Question 2

Will we observe a statistically significant improvement in the functional test outcomes (i.e., hand-grip strength, sit-to-stand, single leg stand and the 6 minute walk test) of the patients after comparing the baseline visit to the final visit once their respective rehabilitation program (e.g., restorative, supportive, and cachexia) is completed?

Hypothesis 2

Patients in the restorative and supportive group will significantly improve their test results pre-post rehabilitation, while the cachectic group will not significantly improve their test results pre-post rehabilitation.

4 SIGNIFICANCE OF THE STUDY

The purpose of this prospective analysis was to measure the functional impact of patients as part of an overall assessment plan in an interdisciplinary cancer rehabilitation program situated in a tertiary care hospital setting. This study analysed the functional measurements (i.e., HGS, 6MWT, STS and SLS) of patients at baseline and during their progression through their respective rehabilitation programs (i.e., restorative, supportive, cachexia). We hope that this study will help the healthcare professionals have a deeper understanding on the cancer rehabilitation program and the impact that it has on the patient's physical function.

5 METHODS AND PROCEDURES

5.1 Study design and population

This was a prospective analysis of the functional impact in the overall assessment of patients in an interdisciplinary cancer rehabilitation program. For this study, we wanted to determine whether physical function status (HGS, 6 MWT, STS, SLS) improved amongst the restorative, supportive and cachexia streams while being part of the CRCC. Data was collected on all new patients who were enrolled in the CRCC at the MNUPAL between January and December 2014. This study was approved by the Research Ethic Board of the McGill University Health Center. Data was collected on the patient's performance during the 6MWT, HGS, STS and SLS. The study consisted of a "within program" design using an ANOVA with repeated measures (functional measure x time). The patient data was analysed for each dependent variable (6MWT, HGS, STS, SLS) to determine if any differences existed among the three program streams (e.g., restorative, supportive, and cachexia). All data was analyzed using the SAS 9.3 (Cary, NC, USA) program.

5.2 Participants' inclusion and exclusion criteria

Inclusion criteria

The following inclusion and exclusion criterion used by the team to enroll patients in the CRCC and in the different streams (restorative, supportive, cachexia) was developed over the years by the clinical team. For the purpose of this study, we will not further discuss how the three streams were developed. For this project, we used two different recruitment strategies. The inclusion criteria for the HGS test was the following: to be included in this projects, the patients had to have their initial visit in 2014 and have performed the HGS tests during their first visit. Furthermore, for the three functional tests (6 MWT, STS, SLS) performed by the PT, we have included all the patients who had seen the PT for both an initial and final assessment, in 2014. Finally, the classification into their respective streams was not done by the research team but rather by the CRCC's multidisciplinary team, who were discussing every new case at the end of the clinic day, and classified the patients in their respective streams.

Below are the inclusion and exclusion criteria that the CRCC's team used to classify patients in their respective streams. The life expectancy is the probable number of months or years remaining in the life of an individual. This is predicted by the medical team and it's affected by factors such as disease status, cancer stage, physical condition, and nutritional status of the patient.

Restorative stream:

- Age ≥ 18 years
- Histologically confirmed diagnosis of cancer.
- No clinical signs of active disease present
- At least one month off treatment

Supportive stream:

- Age ≥ 18 years
- Histologically confirmed diagnosis of advanced cancer (stage III/IV or stage II under chemo)
- Life expectancy ≥ six months
- Evidence of active disease y or may not be undergoing treatment

Cachexia stream:

- Age ≥ 18 years
- Histologically confirmed diagnosis of advanced cancer (stage III/IV)
- Inoperable and incurable metastatic cancer
- Life expectancy ≥ three months.
- Evidence of active advanced disease
- May or may not be undergoing treatment
- A score of one or two on the ECOG scale
- Pain under control

Exclusion criteria

- Impossibility for patients to fill in the questionnaires in English or French
- Life expectancy of less than three months

5.3 Data collection

The data entry for this research project was done using an iPad that ran the File Maker pro application. All the patient's information/results used for this research project was stored in a remote database. The data collected on the iPad included anthropometric measurements, hospital visits, patient functional outcomes, questionnaire results, and the patient's medical history. Data accuracy was ensured by having two members of the research team validate all data that was entered electronically. At the end of the study, the data collected was extracted from the iPad in an Excel spreadsheet for data analysis. Appendix 2 shows the different data collected and the interface of the File Maker pro application.

Baseline visit

The following paragraphs describe the functioning of the CRCC. The baseline visit was an evaluation of the patient's eligibility in the CRCC. The patients were usually referred to the program by their oncologist or any other treating professional who considers the need of cancer rehabilitation for the patient. For this research study, the NUT and PT referred all new patients who were fitting our recruitment criteria. Once referred to the program, the registered nurse called the patients to book an appointment. The nurse gathered information about the patient's symptoms and prepared a medical summary sheet for every new patient. At the beginning of the day, the nurse presented every new patient's medical history such as current illness history, past medical history, previous and current treatment, medication and any other medical problems to the interdisciplinary team.

During baseline visit, all new patients regardless of the stream in which they were assigned, had to complete four questionnaires:

- Edmonton Symptom Assessment System (ESAS)
- The Distress Screening Tool (DST)
- The abridged Patient-Generated Subjective Global Assessment (aPG-SGA)
- Fatigue Symptom Inventory (FSI)

Four physical performance tests performed by the PT and NUT:

- 6-Minute Walk Test (PT)
- Sit-to-Stand (PT)

- Single Leg Stand (PT)
- Hand Grip Strength (NUT)

The nutritionist recorded the patient's hand grip strength test results at the baseline visit and at every follow-up. At the end of the day, the professionals prepared an interdisciplinary note for every new patient. The interdisciplinary note was a resume of every professional rehabilitation plan (e.g. weight gain, muscle strengthening, symptom and pain management) for that patient.

The nutrition counselling component of the program included dietary advice tailored to patient's needs and concerns (weight loss, body weight, alterations of taste or smell, etc). The nutritional plan could range from a simple prescription of nutritional supplements (example: omega 3) or supplemental nutrition drinks (for example Ensure Plus or Boost Plus) to discussions in response to patient queries (Gagnon et al., 2013). The OT's plan in the CRCC was to provide interventions that touched on the activity domain of self-care, productivity, and leisure (Lemoignan et al., 2010). The PT's prescribed the patients a home exercise plan consisting of strength, endurance and flexibility training. The nurse was involved in the counselling, assessment and symptom care of the patient. Finally, the physician on the team was a palliative care specialist who reviewed the medical condition of the patient, conducted through symptom assessments, and provided appropriate medical interventions (Gagnon et al., 2013).

Furthermore, the team decided if the patient was accepted or not in the rehabilitation program and assigned them to their appropriate stream. According to their stream, disease and symptoms, the team decided when the next appointment should be scheduled. Each patient was scheduled for the next visit according to their needs and they did not follow the same time interval between visits.

For this project, baseline (initial assessment) demographic data was collected for 115 new patients, and baseline HGS test results was available for 86 patients. The method used to incorporate missing information was "multiple imputation". Multiple imputation is a well-established general strategy for handling missing data that makes use of available data to fill in plausible values of missing items (Belin, 2009).

In terms of the physical performance tests (6MWT, STS, SLS), out of the 115 patients seen in 2014, the PT referred 79 patients for this research project; however, only 18 patients had baseline and final assessments data, and were therefore included in this study. The remaining

61 patients who were not included in the research project did not have a final assessment with the PT.

Follow-up visit

At every follow-up visit, all patients completed 2 questionnaires (ESAS and aPG-SGA) and performed the HGS test. Patients in the restorative and supportive streams were scheduled to see all five specialists. If patients were too deconditioned or doing too well and the team considered that there was no need to see a specialist, then the patient was not scheduled to see that specific specialist. Patients in the cachexia stream were not often seen by the PT because they were too deconditioned. In some cases, patients were scheduled just for OT and PT when the focus was on physical rehabilitation only. Appendix 5 is an example of how patients were scheduled for the CRCC.

End evaluation

The last visit of the patient at the CRCC was defined as the "end evaluation visit". After this visit, patients were discharged from the program and their medical files were closed. At the end evaluation, the patient completed all four questionnaires and performed the battery of three physical tests with the PT (6 MWT, STS, SLS) and the HGS test with the NUT. The number of days between the baseline and end visit was different for all patients.

At the end of every visit, each patient's information such as completed questionnaires, a copy of the external prescription sheet and each professional's interdisciplinary note was collected and then scanned in their electronic medical record (OACIS). Furthermore, for the purpose of this research study, all demographic information, functional test scores, laboratory blood results were collected and recorded after each visit on the electronic tablet (iPad). Appendix 2 shows the iPad interface and the information that was collected.

Functional tests

Handgrip Dynamometry

The HGS dynamometer is an easy and fast tool to use in order to assess muscle strength. Although HGS reflects upper body strength, previously it has been correlated with lower body muscle strength (Lauretani et al., 2003), which is an indirect measure of whole body strength. Even though lower limbs are more important than upper limbs for gait and physical

function, handgrip strength has been well correlated with surgical outcome and with clinical improvement (Soeters et al., 2008; Cruz-Jentoft et al., 2007). Moreover, as studies have indicated, HGS has also been associated with mobility, and mortality in several clinical states (Soeters et al., 2008). Hand grip strength has been shown to predict survival and is associated with changes in body composition, nutritional status, inflammation, and functional ability in several chronic disease conditions (Kilgour et al., 2013). Peolsson et al., 2001 have studied the intra- and inter-tester reliability of the hand grip strength. The results from the reliability studies show that HGS measured with the Jamar dynamometer is a reliable method (ICC values 0.85-0.98) and is recommended for use in clinical practice (Peolsson et al., 2001, Savva et al., 2012). Research in stroke population suggests a minimal clinically important difference (MCID) of 5.0 Kg for the affected dominant hand and 6.2 Kg for the non-dominant side (Lang et al., 2008). Minimal detectable changes (MDC) values are not established for the HGS.

Functional status assessment determined by handgrip dynamometry has been recommended as a part of a complete nutrition assessment for decades (Russell, 2015). HGS measurement, a correlate of upper extremity strength, is associated with changes in functional status as well as an appropriate component of a complete nutrition assessment for cancer patients (White et al., 2012; Mendez et al., 2014; Norman et al., 2011). At the CRCC, the HGS has been used as a functional tool related to nutritional assessment (Kilgour et al., 2013). HGS was measured at every visit by the dietitian on the dominant hand using the Jamar dynamometer (Sammons Preston, Bolingbrook, IL, USA). This test was non-invasive, simple to conduct and was used to measure change in general upper body strength over time. This method has already been shown to be valid and highly reliable in measuring upper limb strength and more consistent than other tools.

The power of handgrip is the result of forceful flexion of all finger joints with the maximum voluntary force that the subject is able to exert under normal biokinetic conditions. For this test the patient was sitting in a chair with both feet planted firmly on the ground. While the dietitian was handling the upper and lower part of the device, the patient was asked to grasp the dynamometer with the dominant hand with the arm flexed at 90°. The dynamometer was set in the standard position (position number three) as recommended by the American Society of Hand Therapists and was adjusted only if the patient wasn't able to comfortably squeeze the hand dynamometer. The patient was asked to squeeze the dynamometer as hard as possible for three seconds. The dietitian informed the patient when to start and stop the performance and encouraged him/her verbally. The measurement was repeated three consecutive times with a

break of 15 seconds between each trial. The highest peak measurement of the three repetitions was recorded and used for subsequent analysis. The research team, who helped with the HGS data collection, was consistent in giving the same instructions to the patients as the dietitian. However, for the purpose of this study, the intra- and inter-tester reliability of the hand grip strength was not tested and this could affect the consistency of the data collected.

Six-minute walk test

The purpose of the 6MWT is to assess aerobic endurance. It measures the ability to perform activities of daily living such as walking, stair climbing, shopping, and sightseeing (Heyward VH, 2014). This test measures the expected performance declines across age groups and discriminates between individuals with high and low physical activity levels and functional ability. Studies have shown that the 6MWT is a valid and reliable test for healthy elderly, cardiac and pulmonary patients (Schmidt et al., 2013).

The 6 MWT is a good index of physical function and therapeutic response in patients with chronic lung disease (Holland et al., 2014; Singh et al., 2014; Enright, 2003; Swigris et al., 2010, Swigris et al., 2011). The test should be performed according to standard methods (see Appendix 3) including a practice walk to orient the patient to the procedure. During a 6MWT, healthy subjects can typically walk 400 to 700 m (Enright, 2003; Casanova et al., 2011). Studies looking at the meaningful changes in the six-minute walk distances have been conducted in several disease states. While there is some variability based on methods and study populations, the available evidence suggests that a MCID of at least 30 m has been observed (Swigris et al., 2010; Redelmeier et al., 1997; du Bois et al., 2011; Holland et al., 2009; Mathai et al., 2012; Gilbert et al., 2009; Puhan et al., 2011; Puhan et al., 2008; Wise et al., 2005)

Furthermore, in 2005, Robert A. Wise and Cynthia D. Brown in their article “Minimal Clinically Important Differences in the 6MWT” state that for COPD patients, the minimal clinical important difference (MCID) for the 6 MWT is conservatively estimated to be 54-80 meters, however, the authors concluded that for an individual patient, the 6 MWT would need to change by about 86 meters to be statistically confident that there was an improvement. Appendix 4 highlights the minimal clinically important differences (MCID) and the minimal detectable changes (MCD) across different diseased population in the 6MWT. It is worth noting that the minimum value of 54 m appears in three different research studied. Furthermore, a consensus conference by the Society of Sarcopenia, Cachexia and Wasting Disorders has concluded that sarcopenia, reduced muscle mass, with limited mobility” should be considered an important

clinical entity and that older persons should be screened for this condition. “Sarcopenia with limited mobility” is defined as a person with muscle loss whose walking speed is equal to or less than 1 m/s or who walks less than 400 m during a 6-minute walk. Minimal clinical important differences (MCID) are defined as an increase in the 6-minute walk of at least 50 meters or an increase of walking speed of at least 0.1 m/s.”

Single Leg Stand

Balance impairments are a common finding among patients experiencing disease or trauma (Springer et al., 2007). The SLS test is a simple, easy and effective method to screen for balance impairments in the older adult population (O’Loughlin, 1993; Vellas et al. 1997). Studies have shown that the ability to balance on one leg diminishes with age, therefore when timed balance tests are performed as a part of a patient's neurologic examination, the results should be interpreted in light of the patient's age (Bohannon et al., 1984). In Appendix 5 the normative data in healthy population is presented.

At the CRCC, patients were instructed to stand on one leg without support. A maximum score of 30 was recorded if the patient was able to stand on one foot for 30 seconds during one of the three trials. If not, the highest score of the 3 trials was considered the maximum score. All activities were timed with a digital stopwatch. At this point in time, there is no scientific evidence on the minimal clinical important difference (MCID) or minimal detectable changes (MCD) across any diseased population.

Sit-to-Stand Test

The Sit to Stand Test is a quick and easy to administer test of an individual’s ability to transition between sitting and standing. It measures lower body strength, functional mobility and identifies potential balance problems. It is a simple and reliable way to assess possible balance impairments or risk of falling in a geriatric population (Lewis and Shaw, 2006). For the sit-to stand test, the patient sits with arms folded across their chest and with their back against the chair. The patient is instructed to stand up and sit down 5 times as quickly as he/she can. The patient is instructed to stand fully between repetitions of the test and not to touch the back of the chair during each repetition. Timing begins at "Go" and ends when the buttocks touch the chair after the 5th repetition.

At the CRCC, the PT was using the two times sit-to-stand test rather than the standard five times sit-to-stand test. The research team has no information on how and why this test was modified from the standard test and under what circumstances. There is no scientific research on the two times sit-to-stand test. The research team was not involved in the development of the

CRCC clinic, or in the choice of the assessment tools used by each professional. For this test, (2 times sit–to-stand test) there is no scientific evidence on the minimal clinical important difference (MCID) or minimal detectable changes (MCD) across any diseased population.

The following are the instructions given by the PT to patients who took part of the CRCC in 2014. Patients were asked stand up and sit down 2 times as fast as they could in a controlled and safe manner. Each time their back had to touch the back of the chair. Starting position was with their back touching the back of the chair. If the patients felt that they needed to use their arms to do the test safely, then the use of arm was allowed. The following instructions were added to people whose judgement was questionable or who had lytic lesions or significant osteoporosis: "I don't want you falling into the chair and hurting yourself". For this test, the score was the time the patient took to do the test.

Demographics and administrative characteristics

Demographic (patient age and sex) and oncologic (cancer type, stage, type of therapy, medical history) data were collected from the computerized hospital records (OACIS). This information was collected from the patient's chart.

Blood analysis

Biological parameters considered for the purpose of this study were part of the routine blood analysis performed at the CRCC. Parameters of interest included C-reactive protein (CRP), hemoglobin (HgB), albumin (Alb), and white blood cell count (WBC). Blood samples were drawn at the MGH and analyzed onsite. WBC count laboratory results were ordered to screen for infections, since a low white blood cell count (leukopenia) leaves the cancer patient more prone to infections. CRP is a widely used systemic biomarker for diagnosing acute and chronic inflammation, promoted by the presence of a tumor (Gagnon et al., 2013). Elevated serum CRP levels predict lower survival rates in patients with cancer (Srimuninnimit et al., 2012). Alb is the most abundant protein in human blood plasma and it provides an estimation of visceral protein function and has a strong prognostic role in predicting cancer survival (Gupta and Lis, 2010). Finally, low levels of Hgb (the protein in the red blood cells that carry oxygen) have shown to negatively affect certain cancer treatment outcomes such as survival (Littlewood, 2001).

Statistical analyses

Data manipulation and handling

Data manipulation: In order to calculate changes over time, data was truncated into 2 week windows of assessment. To achieve this, the amount of days in the rehabilitation program were calculated into weeks from entry into the program (baseline), and then categorized into 2 week blocks. Week 0 to week 2 was referred to as week block 1, week 2 to week 4 was referred to as week block 2, week 4 to week 6 was referred to as week block 3 and so on. Due to a lack of participants who completed follow ups beyond 24 weeks in the program, all data beyond this point was truncated in week block 12.

Main analysis:

Baseline differences by protocol were determined by a series of general linear models (proc glm). Mixed-model approach (PROC MIXED [repeated autoregressive]) was used for the analysis of repeated measurements. Fixed effects included in the model were: sex, age, (on/off treatment, and the number of follow-ups) rehabilitation protocol (cachexia, restorative or supportive), time, and the product term of time and protocol. For the baseline analysis, the covariates used were: age, sex, on/off treatment. For the pre-post analysis, the covariates used were: age, sex, on/off treatment and number of follow-up visits. All covariates were determined at priori based on established associations with the dependent variables. Mixed models were used to examine time differences from pre-rehabilitation to post-rehabilitation in all rehabilitation protocols (cachexia, restorative and supportive), as well as a function of protocol over multiple follow up assessments (2 week blocks). All analyses were completed using SAS 9.3 (Cary, NC, USA), with significance set at $p < .05$. Occasional missing data was reflected in the degrees of freedom.

6 RESULTS

6.1 Patient demographics and clinical characteristics

A total of 115 patients (mean age 62.9 ± 13.4 y, 54% male), took part in the CRCC between January 1st 2014 and December 31st 2014. There were n=48 patients registered in the cachexia stream, n=28 in the restorative stream and n= 39 in the supportive stream. The analysis showed that there was a difference in terms of age across groups (F = 17.5; p=0.001). The post-hoc analysis showed that there was a difference between the cachexia and the restorative stream. The restorative group had an average age of 51.7 (±13.0) yrs whereas the cachexia group had an average age of 67.8 (±11.4) yrs.

In terms of sex, the analysis showed that there was a difference across groups (F = 7.52; p=0.0009). The post-hoc analysis showed that there was a significant difference between the restorative and the cachexia stream ($p<0.05$) as well as between the cachexia and the supportive stream ($p<0.05$). There were 75% males in the cachexia stream, 40% males in the restorative stream and 41% males in the supportive stream.

Thirty-five of the study patients (30%) had lung cancer (including SCLC, NSCLC and mesothelioma), 22 (19%) had gastrointestinal cancers (including upper and lower GI tract) and the remaining patients had other types of cancers (see Table 3). Eighty patients (69.5%) had a history of advanced cancer stages III and IV. Out of these 80 patients, n=63 had metastases and n=17 had locally advanced cancer.

Eight of the 115 (7%) patients passed away while participating in the program, six of whom were part of the cachexia stream. Their data was included in the study analysis.

Patient demographics and clinical characteristics are described in Table 3. Patients in the supportive and cachexia stream may have been undergoing curative treatment while still being part of the program. The patients in the restorative group were cancer free and thus were not undergoing curative cancer treatment. For their treatments, patients have received either chemotherapy (n=41, 35.6%), radiotherapy (n=13, 11.3%) or both (n=42, 36.5%) cancer treatments.

In terms of body weight, at the baseline assessment, there was a difference across groups (F = 3.66; p=0.0288). However, the post-hoc analysis does not show any significant

difference between the groups. The cachexia group had an average weight of 66.3 Kg (±14.0 Kg), the supportive group had an average weight of 75.3 Kg (±21.0 Kg) and the restorative an average weight of 75.6 Kg (±18.5 Kg).

The average BMI for all patients in the cancer rehabilitation program was 25.16 Kg/m^2. The analysis showed that there was a baseline difference in BMI across groups ($F= 7.78$; $p=0.0007$). The post-hoc analysis showed that the cachexia and the restorative group were significantly different ($p<0.05$). The restorative and supportive groups had a BMI of 27.1 Kg/m^2 and 27.2 Kg/m^2 respectively, while the cachectic groups BMI was lowest with a value of 22 $Kg/m^{2.}$

Table 3. highlights the mean for all the observed laboratory characteristics at baseline (WBC, Alb, CRP and Hgb). In terms of the WBC, the analysis showed that there was a significant difference between groups, at baseline ($F = 3.84$; $p=0.0254$). The post-hoc analysis showed that there was a significant difference between the cachexia and the restorative stream ($p<0.05$). For the inflammatory marker (WBC), the cachexia group had a WBC mean value of 8.9 (±5.0 SD) whereas the restorative group has a WBC mean value of 5.9 (±1.8 SD).

In terms of number of follow–up visits with the multidisciplinary team, the analysis showed that there was a significant difference across groups ($F=2.97$; $p=0.0554$). The post-hoc analysis showed there was a difference between the restorative and the supportive stream ($p<0.05$). The patients in the cachexia group spent an average of 75 days in the program with an average of 2.5 follow-up visits. The patients in the restorative group spent an average of 97 days in the program, with an average of 3.4 follow-up visits while the patients in the supportive group spent an average of 60 days in the program with an average of 2.1 follow-up visits.

TABLE 3. Baseline demographic comparisons among the three streams

Baseline characteristics	Supportive n = 39 (mean, SD)	Restorative n = 28 (mean, SD)	Cachexia n = 48 (mean, SD)	(p, F)
Age (years)	65.1 ± 11.4	51.7 ± 13.0	67.8 ± 11.4[a]	(0.0001, 17.50)
Sex (male)	41% [c]	40%	75%[a]	(0.0009, 7.52)
Height (m)	1.66 ±0.1	1.68 ± 0.1	1.70 ± 0.1	(0.0927, 2.43)
Weight (Kg)	75.3 ± 21.0	75.6 ± 18.5	66.3 ± 14.0	(0.0288, 3.66)
Body Mass Index (Kg/m^2)	27.2 ± 7.0	27.1 ± 7.5	22.4 ± 5.2[a]	(0.0007, 7.78)
Days in the program	60.9 ± 55.5	97.8 ± 63.5	75.1 ± 69.5	(0.0688, 2.74)
Number of follow-ups in the program	2.1 ± 2.0	3.4 ± 2.0[b]	2.5 ± 2.1	(0.0554, 2.97)
Number (n) of patients by cancer type				
Breast	7	4	0	
Endocrinology	0	0	1	
Gynecology	3	3	2	
Head and Neck	0	4	2	
Hematology	2	6	1	
Liver-bile duct- Pancreas	6	0	3	
Lung	12	1	22	
Musculo-Skeletal System	1	1	1	
Neurology	0	1	1	
Skin	1	0	1	
Upper GI	1	0	7	
Lower GI	0	7	7	
Urology	5	0	2	
Baseline laboratory characteristics				
C-reactive protein (mg/L)	31.2 ± 45.2 n = 8	38.8 ± 69.1 n = 5	29.2 ± 41.7 n = 18	(0.9242, 0.08)
Hemoglobin (g/L)	112.8 ± 14.5 n = 30	111.3 ± 36.1 n = 13	114.6 ± 17.2 n = 44	(0.8574, 0.15)
Albumin (g/L)	35.9 ± 5.4 n = 30	39.3 ± 3.9 n = 10	34.8 ± 6.1 n = 36	(0.0830, 2.58)
WBC	7.0 ± 3.1 n = 30	5.9 ± 1.8 n = 13	8.9 ± 5.0[a] n = 44	(0.0254, 3.84)
Previous cancer treatment (n)				
Chemotherapy	17	11	13	
Radiotherapy	2	3	8	
Chemotherapy and radiotherapy	13	14	15	
Surgery (< 5y.)	20	21	23	
Concurrent cancer treatment (n)				
Chemotherapy	29	0	25	
Radiotherapy	1	0	1	
Chemotherapy and radiotherapy	1	0	1	
Surgery	1	0	0	

a statistical difference ($p<0.05$) between the cachexia and the restorative stream
b statistical difference ($p<0.05$) between the restorative and supportive stream
c statistical difference ($p<0.05$) between the supportive and the cachexia stream

6.2 Peak HGS and percentile HGS at baseline

The peak baseline HGS was performed by every patient at their initial visit with the NUT. The HGS percentile was then taken according to patient's age and sex using the normative data for adults in Mathiowetz et al., 1985.

The results showed that in terms of the baseline peak HGS there was a significant difference between groups at baseline (F=4.19; p=0.0186). However, the post-hoc analysis does not show any significant difference between any of the groups.

Moreover, in terms of the percentile HGS, the analysis showed that there was a significant difference between groups, at baseline (F = 5.7; p=0.0048,). The post-hoc analysis showed that there was a significant difference between the supportive and the cachexia stream ($p<0.05$). The patients in the supportive stream had the highest HGS percentile (57^{th}), while patients in the cachexia group had scores below the 50^{th} percentile. Table 4 represents the peak HGS and the percentile HGS at baseline for each stream.

Table 4. Peak HGS and HGS percentile at baseline across the three groups

	n	Peak HGS (mean, SD)	HGS percentile (mean, SD)
Restorative	20	35.6 ± 13.7	56.5 ± 22.5
Supportive	32	31.5 ± 10.3	57.2 ± 22.6[c]
Cachexia	34	31.4 ± 9.0	42.1 ± 21.3

c statistical difference ($p<0.05$) between the supportive and the cachexia stream

6.3 Pre-post analysis of the percentile HGS and peak HGS

For the peak HGS and percentile HGS, a pre-post analysis for each individual stream was performed in order to see if the patients improved their performance pre-post rehabilitation. For this analysis, the HGS measurements taken at the first visit were considered the "baseline visit" and all the HGS measurements taken at the last visit of each patient were considered the "final visit". The time in between the baseline visit and the final evaluation was different for every patient who took part in this cancer rehabilitation program. Therefore, this analysis was done to see if the patients improved while being part of the CRCC, regardless of the time spent in the program.

For the pre-post peak HGS, the analysis showed that there was an effect of protocol ($F=3.42$; $p=0.0370$) and there was also an effect of time ($F=8.64$; $p=0.0042$), however, there was no interaction effect ($F=1.58$; $p=0.2124$). Furthermore, the post-hoc analysis showed that there was no statistical difference in any of the groups (Table 5).

For the pre-post percentile HGS, the analysis shows that there was an effect of time ($F=9.94$; $p=0.0022$), however there was no effect of protocol ($p=0.1482$; $F=1.95$) and no protocol interaction ($F=1.72$; $p=0.1845$). Furthermore, the post-hoc analysis showed that there was no statistical difference in any of the groups.

Table 5. Peak HGS and percentile HGS at baseline and final evaluation regardless of the time

	Baseline (mean, SD)	Final (mean, SD)	p value
Peak hand-grip strength			
RESTORATIVE	34.5 ± 2.3	40.2 ± 2.4	0.065
SUPPORTIVE	34.4 ± 1.7	35.7 ± 1.7	0.967
CACHEXIA	30.0 ± 1.6	32.0 ± 1.6	0.811
Percentile hand-grip strength			
RESTORATIVE	49.3 ± 5.9	60.2 ± 6.0	0.083
SUPPORTIVE	53.3 ± 4.3	54.8 ± 4.3	0.997
CACHEXIA	41.1 ± 4.1	47.6 ± 4.0	0.283

6.4 Peak HGS and percentile HGS over time

A next step in our statistical analysis compared the three different streams (i.e., cachexia, restorative, supportive) amongst each other, over time. Figure 4 and Figure 5 are scatter plots of the peak HGS and percentile HGS, over time, for each cancer stream, with a line of best fit. These graphs show that all three streams increased their peak and percentile HGS, over the 12 week block interval, in a positive linear fashion. The restorative stream had the highest HGS values, followed by the supportive and then the cachexia stream. A statistical analysis was completed however due to small sample sizes, this analysis was not included.

Figure 4. Peak HGS over time across the three groups

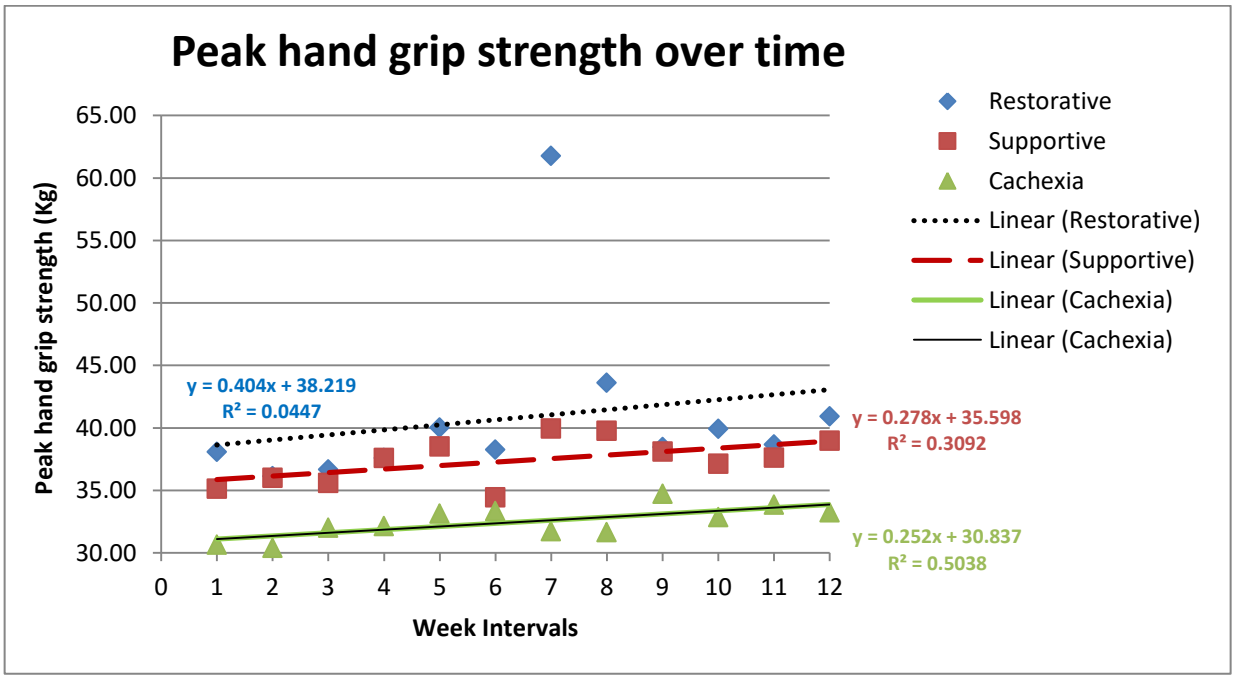
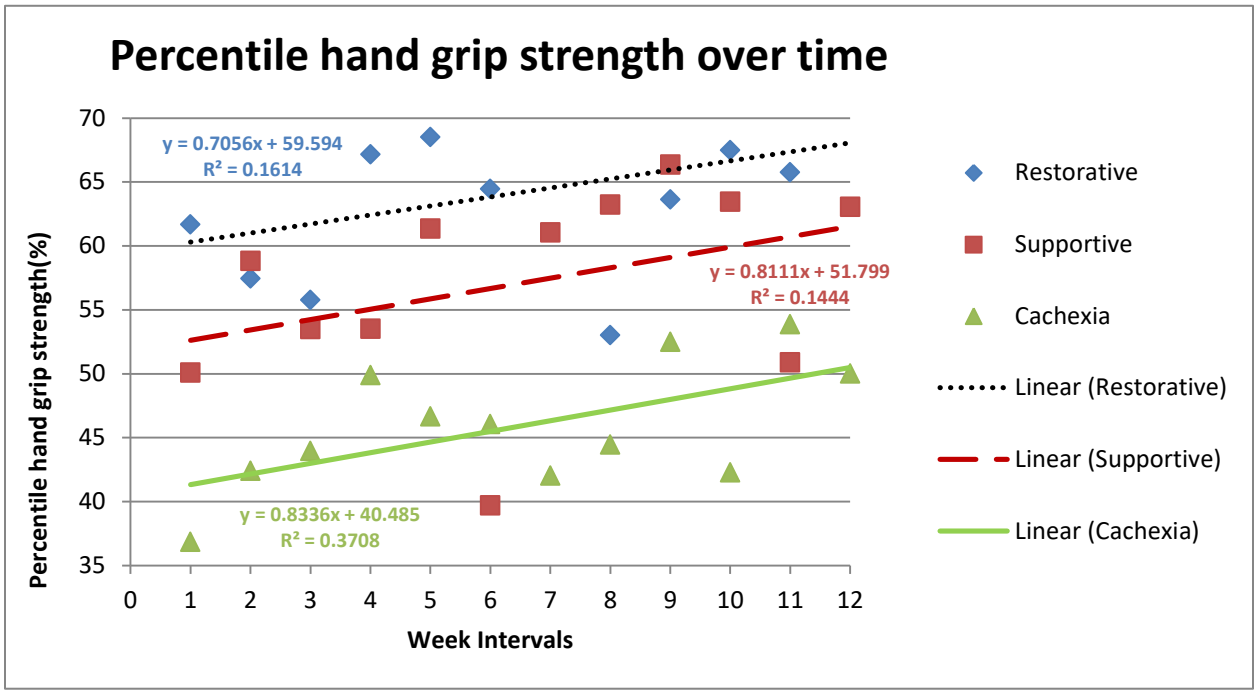


Figure 5. Percentile HGS over time across the three groups



6.5 Physiotherapy

Figure 6. Six minute walk test pre-post rehabilitation across all 3 streams

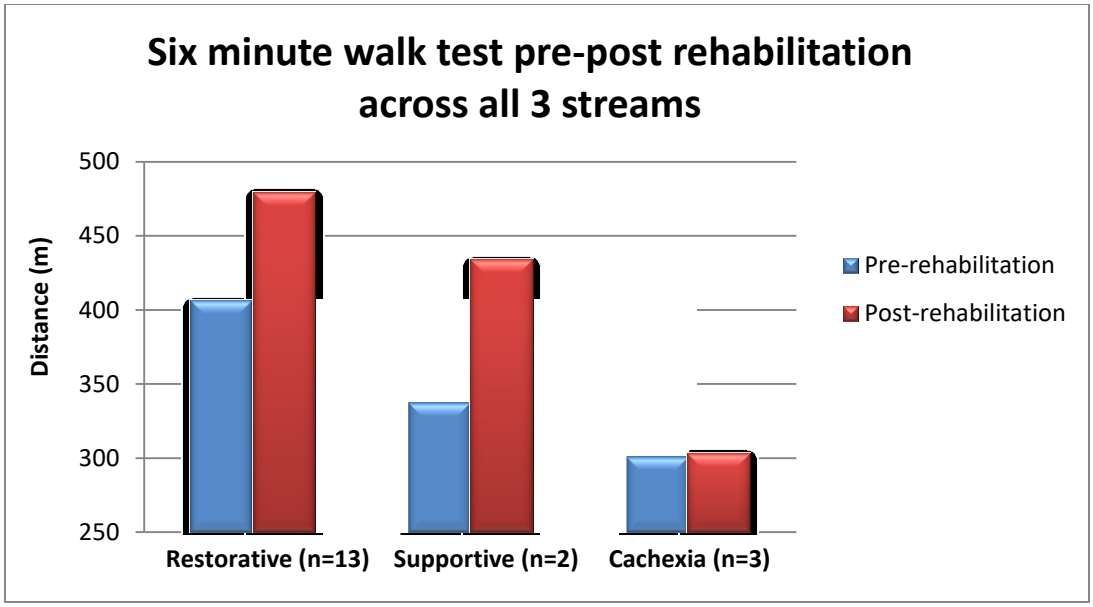


Figure 7. Left-single leg stand test pre-post rehabilitation across all three streams

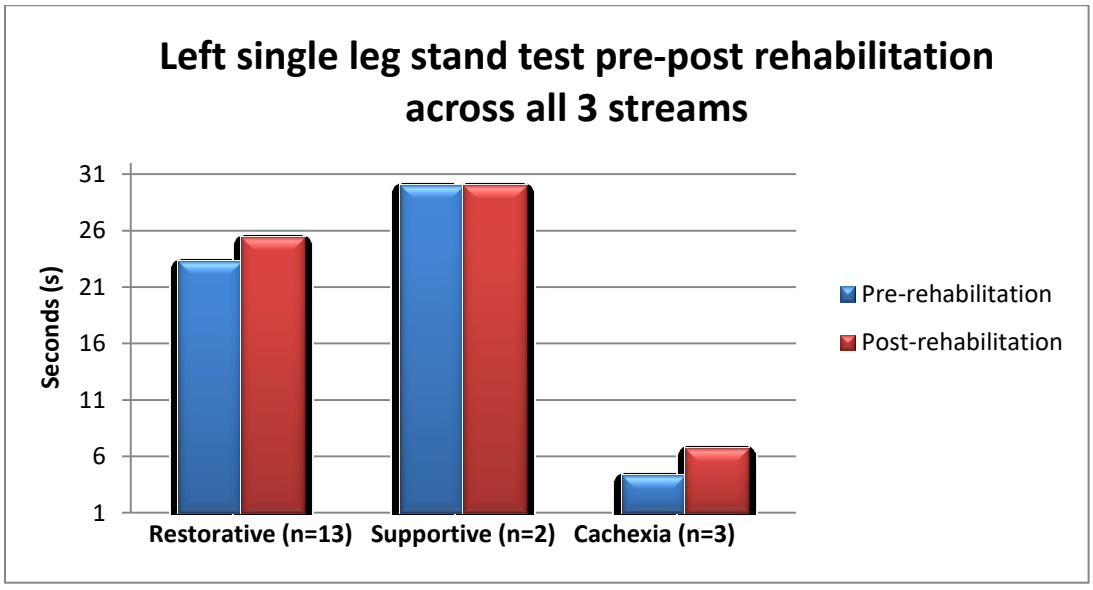


Figure 8. Right single leg stand test pre-post rehabilitation across all 3 streams

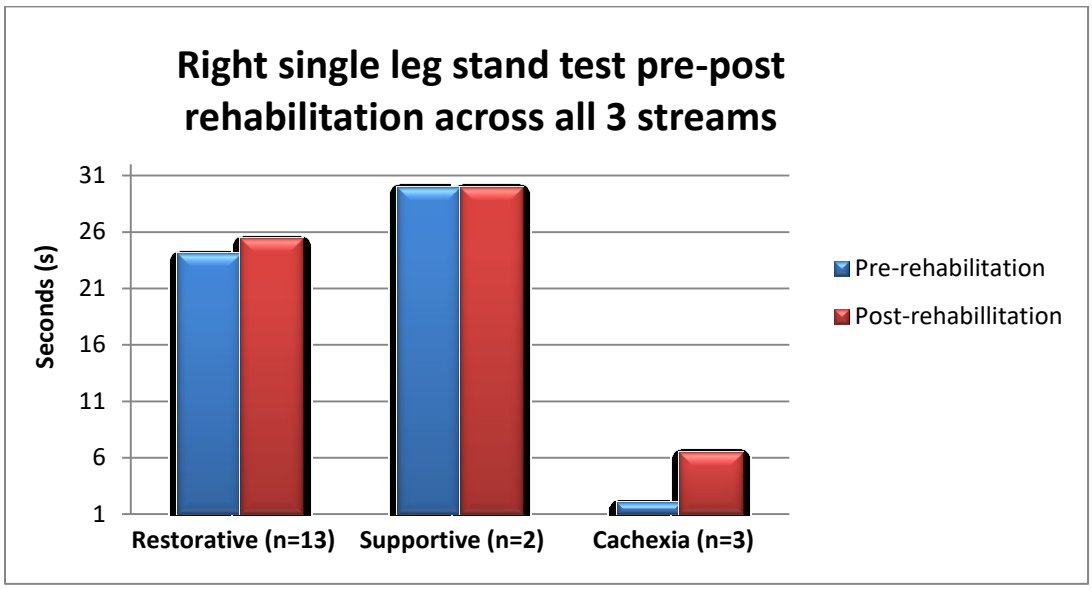
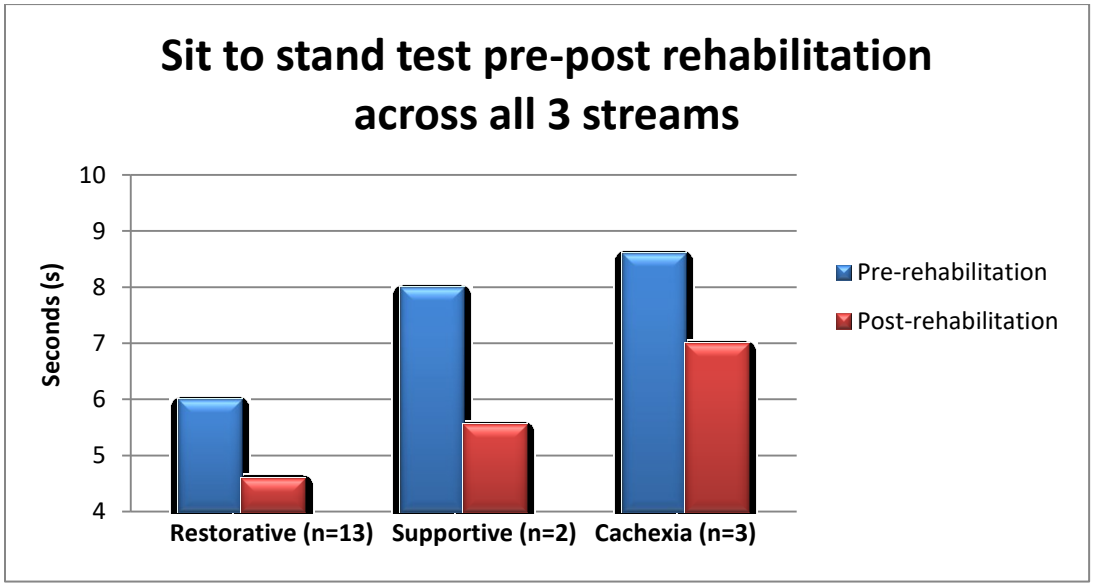


Figure 9. Sit to stand test pre-post rehabilitation in all 3 streams



The four figures above represent all the functional test results of the patients (by stream) performed by the physiotherapist during the cancer rehabilitation program in 2014. Due to the small number of patients completing the pre-post assessment with the PT, this data is purely descriptive. The patients in the restorative and supportive stream were seen by the PT however, due to the disease status of the cachectic patients, physical rehabilitation was not considered a priority for them but rather medical and nutritional interventions were prioritized.

The number of days between the initial assessment and the final assessment was different for every participant. Due to the low number of cancer patients that participated in the supportive and cachexia stream respectively, it is not possible to draw a meaningful conclusion with regards to any possible improvement (pre-post) or differences between groups.

Even if the number of subjects was small, in terms of the 6MWT, we can observe that the restorative stream was able to cover a higher distance (406.4 m, n=13) compared to the supportive (337.5 m, n=2) and to the cachexia (301.3 m, n=3). The supportive group (n=2) had a better score in the SLS test compared to the restorative (n=13) and the cachexia (n = 3).

For the restorative stream, in terms of the 6 MWT, 9 of the 13 patients had an increase in the distance walked of more than 50 meters and, as a group, the patients increased their walking distance by 73 m. Although no statistical analysis was performed, a trend for improvement is observed between pre and post rehabilitation. In terms of the SLS tests 4 out of the 13 patients had an increase in their performance, while the 9 patients kept their maximal score (30 sec). For the STS, 12 of the 13 patients had an increase in score and only one patient had a decrease in score.

The four figures above show that the cachexia group (n = 3) had the lowest results in the 6 MWT and had worse scores in the single leg stand test and sit to stand test when compared to the restorative (n=13) and the supportive (n=2). This could be explained by the fact that the patients in this group had late-stage, locally advanced inoperable and/ or incurable cancer with some having distant metastases.

7 DISCUSSION

The number of cancer survivors is increasing and as a consequence, there is a greater demand for cancer rehabilitation programs. The cancer survivors have to deal with the cancer treatment and its consequences such as physical dysfunction and decreased QOL. Physical performance assessments have the potential to contribute to a more complete understanding and therefore better management of the physical difficulties encountered by cancer patients (Simmonds, 2002). The MUHC Cancer Rehabilitation and Cachexia Clinic's mission at the MNUPAL was to improve every patient's physical performance and quality of life by offering personalized assessments and treatments by offering three different cancer rehabilitation streams (i.e., restorative, supportive, cachexia). The interdisciplinary team employed different treatment techniques but ultimately they all shared the same goal: to improve or at least maintain the patient's functional outcomes and wellbeing. The tests used (HGS, 6 MWT, SLS, STS) mimic familiar everyday tasks and could easily be incorporated into standard clinical practice.

The purpose of this study was to analyze the functional assessments (i.e., 6MWT, STS, SLS, and HGS) of the cancer patients who took part of the CRCC in 2014. First, we wanted to analyze if there were any baseline differences between the three cancer streams. Secondly, we wanted to see if the patients improved their functional assessment, pre-post rehabilitation, once they completed their respective rehabilitation program.

7.1 Hand grip strength

The HGS test is an accurate indication of upper and lower body strength. Cancer patients with higher grip strength have a higher survival rate (Kilgour et al., 2013). Research on cancer patients comparing the forearm dynamometry vs the prognostic nutritional index found that the forearm muscle dynamometry predicted the patients' mortality with a high rate of sensitivity (100%) (Kalfarentzos et al.,1989). The grip strength test is a useful, rapid, and inexpensive test to use in clinical settings. It is more accurate than the nutritional index, and can identify cancer patients at a high risk of developing major postoperative complications, and predicts the postoperative morbidity and mortality. As other sophisticated measures to assess upper body strength are not really available in clinical settings, the handgrip dynamometer is a useful clinical tool for functional and nutritional assessment as well as monitoring (Kondrup and Elia, 2011).

For our research study we compared the grip strength test results, at baseline amongst the three different streams. Our first hypothesis stated that, at baseline, patients in the restorative stream will have significantly higher functional test results than the supportive and cachexia streams and that the supportive will have better results than the cachexia stream. The results of this study show that the restorative stream had the highest peak hand grip scores, followed by the supportive and the cachexia stream. Even though at baseline, the restorative stream had the highest peak HGS, it was not statistically different than the supportive and cachexia streams ($p=0.1482$; $F=1.95$). However the supportive group had the highest percentile HGS ranking and was significantly different than the other two groups. The supportive group did not significantly improve their peak hand grip strength, pre-post rehabilitation; however, the results show a trend of improvement from week block 1 to week block 12. These findings could be explained by the fact that patients in the supportive group are not homogenous. Some patients are still on treatment while others are done with their treatment.

The restorative group was composed of patients that have been off treatment for at least one month and showed no signs of active disease and had the highest potential for improvement. This stream was intended for patients for who a full functional recovery was expected. In terms of the restorative groups, our first and second hypotheses were false. At baseline, HGS of the restorative stream was not significantly different than the other two groups and did not significantly improve pre-post rehabilitation. Although not statistically significant, the peak HGS increased from 34.5 Kg to 40.2 Kg and their percentile HGS from 49.3 to 60.2. Furthermore, for the peak HGS, the week interval 7 of the restorative group seems to have values much greater than the rest of the week intervals. The data was verified for abnormal high values but no outliers were found.

The results show that the restorative group drew the most benefits from being part of the CRCC. This study's information and design can't tell us if the restorative patients went back to full recovery as we did not have a control group, and we did not assess these patients at time of diagnosis. We cannot conclude that the physical improvements seen in this group would have been any different than not being part of the rehabilitation program. Patients in this stream could have benefited from the program but also might have improved naturally over time during the course of the rehab program. For future studies, a next step would be to randomize patients to a control group but this would present ethical problems, however, a waiting-list comparison group might be an option.

As expected, for the cachexia group, the results show that pre-post rehabilitation, there were no statistical significant changes in the peak HGS and percentile HGS over-time. However, even though the results were not clinically significant, the pre-post values for the cachexia group showed a small increase in both the percentile HGS from the 41st percentile (baseline evaluation) to the 47th percentile (final evaluation) and the peak HGS from 30 Kg (baseline) to 32 Kg (final evaluation). This group had a prognosis of non-curative intent and a life expectancy greater than three months, therefore, considering the diseased state of this cohort, maintenance of their strength over time, rather than a decrease, could be significant for this population. Therefore, although not statistically significant, a trend for improvement was observed for the cancer patients assigned to the cachexia stream.

The patients in the cachexia group had the smallest number of days spent in the program followed by the supportive group and the restorative group. This could possibly be explained, but not limited to the severity of the disease of some cachectic patients as well as issues such as getting to the MNUPAL clinic (transportation by metro or bus during the winter), multiple cancellations, or disease progression. These could result in the withdrawal of the patient from the CRCC. Referral of patients to the emergency and/or palliative care departments, or simply refusal by the patient to participate in the rehabilitation program can result in “no show visits”. If patients cancelled on multiple occasions and were not seen in many months, their files were closed with no final assessment visit. As a consequence, many patients’ data was lost.

7.2 Cachexia and Sarcopenia

For patients in the cachexia stream, disease progression and eventual cancer related death is inevitable. Many patients with advanced cancer are referred late in their disease trajectory to the CRCC, and it is likely that they are unresponsive to any interventions. It is important to note that the goal for the cachexia stream was different than the other two streams. Cachectic patients have different needs: they need to optimize nutrition and QOL. This further emphasizes the need to properly separate patients into distinct streams according to their disease progression. Our results show that patients in the cachexia group had the lowest weight, lowest BMI and highest values for the WBC. This could be explained by the fact that these patients have advanced cancer, are metastatic and some of them still undergo cancer

treatment. Advanced cancer is associated with multiple metabolic abnormalities that lead to significant body composition changes, particularly muscle loss (sarcopenia) (Baracos, 2006; Prado et al., 2011; Fearon et al., 2011). These abnormalities include the presence of catabolic host- and tumor derived factors (proinflammatory cytokines), and anorexia resulting in inadequate nutrient intake. Muscle loss may also be caused by antineoplastic therapies, as well as other common medications that these patients use. (Baracos, 2006; Prado et al., 2011). Together these factors cause an imbalance between anabolism and catabolism, which ultimately leads to skeletal muscle wasting (Baracos et al., 2005).

In the aging population, sarcopenia is defined as the degenerative loss of skeletal muscle mass (0.5–1% loss per year after the age of 50), quality, and strength associated with aging. The consequences of sarcopenia often contribute to frailty and decreased independence (Marcell, 2003). Additionally, medical journals define sarcopenia as a multifactorial disease process that may result from inadequate hormone levels or dietary protein, nutritional imbalances, lack of exercise, oxidative stress, and inflammation. All these are consequences of cancer and its treatment and characterize the cachectic patient.

Physical activity decreases with age and as a consequence, there is a down-regulation of physiological systems adapting to reduced exercise/stress levels. As cardiovascular and skeletal muscle reserve functions decrease, this contributes to an increased relative perception of effort for a similar activity as compared to when a patient was younger. If activities are perceived to be more difficult, this will increase the likelihood for avoidance of physical work. The more physical activities are avoided, the more the physical performance will decline, therefore contributing to additional physiological decrements in an individual's functional reserve capacity.

Moreover, a classification criterion for cancer cachexia was proposed by Vigano et al., 2012. It is suggested that cancer cachexia can be categorized as noncachectic, precachectic, cachectic, and in refractory cachexia. The blood biochemistry, questionnaires (ESAS and aPG-SGA), weight and activity (HGS) are tools used for this classification. The CRCC offers a model for precise diagnosing of the pathophysiology and severity of precachectic and cachectic conditions. By working closely with palliative care programs, the program may offer the best environment for a comprehensive and personalized approach to the nutritional and functional problems in advanced cancer patients (Vigano et al., 2012).

7.3 Physiotherapy

General physical exercise has been shown in many studies to have tremendous benefits in cancer survivors, including improving fatigue, QOL, mood, decreased cancer recurrence, and improved survival (Lemanne et al., 2013). 115 new patients were seen in 2014 at MNUPAL. Of those, a total of 69 were seen by the physiotherapist on their first day at the clinic (day 1). At follow-up 1, another 18 patients had "baseline" data for the PT. This inconsistency can happen by simply not having a PT on day 1 at the clinic. At follow-up 2 and follow-up 3 another 7 and 4 patients respectively had PT baseline assessments. Starting at follow-up 3, some patients had their "end-evaluation visit" while some others had their baseline visit. This inconsistency can make it difficult for the clinicians to 1) access the baseline values and 2) not doubt the true baseline of these patients. Therefore, more structured and defined appointments are needed. All baseline visits should be done on day 1 at the CRCC (or the latest at follow-up 1). After a pre-defined number of follow-ups (for example after 4 visits), all patients should have another full assessment (DXA, 6MWT, STS, SLS). This would help the team to keep track of the patient's improvement and progress.

Due to the small number of patients who have complete pre-post rehabilitation the data could not be statistically analyzed and was therefore used for purely descriptive purposes. Patients who were not eligible for the CRCC and who had only one assessment with the PT (baseline assessment) were not considered for this study. Due to the design of the clinic, the number of patients who had an initial (baseline) assessment and a final (end) evaluation was small (n = 18). The missing data for the final assessment could be due to: death, disease progression and/or hospitalization, patients drop-out without a final assessment with the PT, closure of file if patients were not seen for more than a few months, patient data may have never been uploaded on their medical chart, the team's decision that the patient would no longer benefit from PT consults. Furthermore, most of the patients in the cachexia stream were not seen by the physiotherapist due to their advanced disease status. The focus for the cachectic patients was primarily on the increase of appetite, QOL and ADLs. This could explain the small number of cachectic patients seen by the PT in 2014.

The patients in the restorative group were cancer free however they still suffered from the consequences of their treatment. Patients in this stream welcomed the idea of a cancer

rehab clinic. We did not capture the time between the completion of the oncological treatment and the beginning of the cancer rehabilitation program; however this could be interesting data to look at in future projects. We note that of the 115 new patients who started the program, complete data (initial and end physiotherapy assessment data) is available for only 13 restorative patients, two supportive patients and three cachectic patients. Therefore a comparison between groups cannot be made.

In the 13 restorative patients seen by the PT, there were slight increases in the 6 MWT, improvements in their sit to stand time, and increases in their single leg stand test time. In terms of the 6MWT, the restorative group improved their walking distance by 73 m. Studies have shown a MCID in COPD, geriatrics and stroke of more than 50 meters. The Society of Sarcopenia, Cachexia and Wasting, defines “sarcopenia with limited mobility” as a person with muscle loss whose walking speed is equal to or less than 1 m/s or who walks less than 400 m during a 6-minute walk test. Only the patients in the restorative stream had an average above 400m. The 73 m improvement in the 6 MWT, for the restorative stream, could be considered clinically significant for this population taking in consideration their age and poor functional status. However, more research studies are needed on the MCID of the cancer patients. Although not statistically significant, these positive changes in the restorative stream are encouraging. Assessment of the cachexia group by the PT could be something to be considered for the future in the CRCC.

It has been shown that cancer patients experience changes in body composition parameters such as decrease in body protein, skeletal muscle, body cell mass and fat-free mass secondary to cancer treatments (Ida et al., 2014; Tatematsu et al., 2013). Patients who are cured or have a long disease-free interval, experience long-term related sequelae that impair their functional status (Malhostras et al., 2000). The improvement in the 6MWT of the restorative group could be explained by the fact that patient in the restorative group had the highest improvement potential. Restorative patients started the CRCC program after their cancer treatment was done, therefore at a decreased functional status.

For the supportive stream, pre-post PT data was available for only two patients, and for the cachexia stream, data was available for three patients. Patients in the cachexia stream were too deconditioned, and were not usually seen by the physiotherapist, unless the team decided the PT’s intervention would be beneficial for the patients. This explains the small number of cachexia patients seen by the PT in the CRCC.

Future research projects could look at the metastatic disease of the patients, comorbidities as well as orthopedic restrictions and other limiting factors in patient's ability to perform physical rehabilitation.

7.4 Study limitations

We acknowledge that our study had several limitations. First, we did not have a control group. Without a control group, we cannot conclude that the improvements observed, would have been any different than not participating in the program. Patients were referred to the CRCC with needs already identified. It would not be appropriate to withhold services from a control population. The cancer patients who are not referred to rehabilitation and who do not have functional limitations or are very deconditioned (palliative care is needed) are significantly different from the study population and can't serve as controls (Sabers et al., 1999). However, for future studies, patients that are on the "waiting list" could be used as a control group.

This was a small non-randomized observational study in cancer patient population. This was observational data since the study was performed in a clinical setting (MNUPAL) rather than in a controlled laboratory setting. Observational studies are not reliable sources of information when looking at the safety, efficacy or effectiveness of a practice; however they can be useful to formulate hypotheses, give "real world" information about a practice and discover advantages of some therapies.

One of the most important obstacles to overcome with observational studies is the fact that the participants along with the health care provider choose the therapy the patient will follow. This means that, inevitably the patients will have different characteristics and therefore it will be almost impossible to determine if the observed effects are due to the therapy itself or just the different patient characteristics. This could over-estimated the positive results seen in the clinic. For well-designed randomized trials this is less of an issue because of the fact that patients are randomly assigned to a treatment which helps balance the effect of the patient's characteristics (Richard Nahin, retrieved from the National Center for Complementary and Integrative Health website nccih.nih.gov on April 4th 2016).

Since the referral process to the program was not based on the screening of all patients after cancer treatment, there is a risk that only patients with potential for rehabilitation were referred to the CRCC. Patients with advanced disease unlikely to respond to any form of rehabilitation might not have been referred to the CRCC and could have been referred to

palliative care. This may have overestimated the positive results of the program (Eades et al., 2011).

Another limitation of our study includes its prospective nature and incomplete data, particularly for the physiotherapy assessments. At the CRCC, patients did not have an equal number of follow-ups, and did not have an equal number of days between their physiotherapy follow-ups. The full physical assessment performed by the physiotherapist (6 MWT, SLS, STS) was performed only for the initial and end evaluation. This led to missed end-evaluations and therefore led to missing data. The missing data could over-estimate the positive results seen in the clinic. Patients with the potential for rehabilitation and interest in the rehabilitation clinic remained in the clinic, while those who were deconditioned did not return for their follow-up visits.

Patient data analysis was challenging due to the nature of the follow-up visits. This is a common challenge for studies of patients with advanced cancer and multiple follow-up visits. In general, patients who were part of the cachectic group skipped or postponed follow-ups due to various health factors. For the supportive and restorative groups, the patients seemed to adhere rigorously to the program in the beginning only to see the number of days between follow-ups grow as time progressed. After the fourth visit, the number of patients returning to the clinic decreased significantly. From the fourth to the fifth visit the number of patients reduced to half. The number of follow-ups needed and/or patients' adherence to the program is information that could be analysed in future studies.

8 CONCLUSION

Current standards of oncology care are limited in the care and needs of the growing group of cancer survivors. Multidisciplinary rehabilitation should become a part of the total care package of the patient with cancer (Hanssens et al., 2011). Few studies to date have assessed the functional benefits of interdisciplinary cancer rehabilitation, especially in advanced cancer. The interdisciplinary approach allowed multiple services to be provided with a common purpose. The CRCC team ensured that the rehabilitation program was tailored to the patient's specific needs and evolving medical status. The availability of professionals from major disciplines was essential to offering comprehensive care.

The pre-post results of the restorative stream are encouraging in that patients may benefit from an interdisciplinary rehabilitation program after completion of their oncology treatment. Even though not statistically significant, the restorative stream showed improvement pre-post rehabilitation in all physical performance tests. Furthermore, the supportive patients significantly improved their percentile hand-grip strength. Considering the disease status of the cachectic patients taking part of the CRCC, maintenance of the physical status over time, rather than a decrease in performance, could be beneficial for these patients. The results of this study are encouraging and lead to more questions and future research opportunities.

Physical assessment and rehabilitation should be considered an important and useful component in the standard care of cancer survivors. Care plans for rehabilitation must be developed to give cancer survivors the opportunity to receive help at the most beneficial time in their disease trajectory (Hanssens et al., 2011).

8.1 Future research

Future research such as monitoring the maintenance of functional gains after the program is a logical extension of this study. The CRCC's efforts are focused toward a goal of improving patients' overall quality of life despite serious disease and disability. The CRCC's rehab program goal has been to promote functional improvements in cancer patients by offering three personalized cancer rehabilitation pathways: restorative rehabilitation, supportive rehabilitation and cachexia rehabilitation. We hope that this system can be a model for other programs serving the cancer population.

9 REFERENCES

American Cancer Society. Cancer Treatment and Survivorship Facts & Figures 2014-2015.

Adams LA, Shepard N, Caruso RA, Norling MJ, Belansky H, Cunningham RS. Putting evidence into practice: evidence-based interventions to prevent and manage anorexia. Clin J Oncol Nurs. 2009 Feb;13(1):95-102. doi: 10.1188/09.CJON.95-102.

American Cancer Society; 2014. Statistics and figures taken from http://www.cancer.org/acs/groups/content/@research/documents/document/acspc-042801.pdf , in June 2016.

Bandieri E, Sichetti D, Romero M, Fanizza C, Belfiglio M, Buonaccorso L, Artioli F, Campione F, Tognoni G, Luppi M. Impact of early access to a palliative/supportive care intervention on pain management in patients with cancer. Ann Oncol. 2012 Aug;23(8):2016-20. Epub 2012 May 6.

Bohannon R, Larkin P, Cook A, Gear J, Singer J. Decrease in timed balance test scores with aging. Phys Ther 64(7):1067-70, 1984.

Borneman T, Koczywas M, Cristea M, Reckamp K, Sun V, Ferrell B. An interdisciplinary care approach for integration of palliative care in lung cancer. Clin Lung Cancer. 2008 Nov;9(6):352-60. doi: 10.3816/CLC.2008.n.051. PubMed PMID: 19073518.

Brar SS, Hong NL, Wright FC. Multidisciplinary cancer care: does it improve outcomes? J Surg Oncol. 2014 Oct;110(5):494-9. doi: 10.1002/jso.23700. Epub 2014 Jul 2.

Bruera Eduardo, Rony Dev. Palliative care: Assessment and management of anorexia and cachexia. UptoDate Apr 2016.

Bruera E. ABC of palliative care. Anorexia, cachexia, and nutrition. BMJ. 1997 Nov 8;315(7117):1219-22.

Canadian Cancer Statisctics website used in Jul 2016, https://www.cancer.ca/~/media/cancer.ca/CW/cancer%20information/cancer%20101/Canadian%20cancer%20statistics/Canadian-Cancer-Statistics-2015-EN.pdf

Canestraro A, Nakhle A, Stack M, Strong K, Wright A, Beauchamp M, Berg K, Brooks D. Oncology Rehabilitation Provision and Practice Patterns across Canada. Physiother Can. 2013 Winter;65(1):94-102. doi: 10.3138/ptc.2011-53. PubMed PMID: 24381389; PubMed Central PMCID: PMC3563384.

Casanova C, Celli BR, Barria P, et al. The 6-min walk distance in healthy subjects: reference standards from seven countries. Eur Respir J 2011; 37:150.

Chasen MR, Feldstain A, Gravelle D, Macdonald N, Pereira J. An interprofessional palliative care oncology rehabilitation program: effects on function and predictors of program completion. Curr Oncol. 2013 Dec;20(6):301-9. doi: 10.3747/co.20.1607. PubMed PMID: 24311945; PubMed Central PMCID

Chasen MR., Dippenaar A.P. Cancer nutrition and rehabilitation – its time has come! Current Oncology – Volume 15, Number 3, 2008

Cruz-Jentoft AJ, Baeyens JP, Bauer JM, Boirie Y, Cederholm T, Landi F, Martin FC, Michel JP, Rolland Y, Schneider SM, Topinková E, Vandewoude M, Zamboni M; Sarcopenia: European consensus on

definition and diagnosis: Report of the European Working Group on Sarcopenia in Older People. European Working Group on Sarcopenia in Older People. Department of Human Services. Achieving Best Practice Cancer Care: A Guide for Implementing Multidisciplinary Care. Melbourne: State Government of Victoria 2007.

Del Fabbro Egidio, M.D., David Hui, M.D., Shalini Dalal, M.D., Rony Dev, M.D., Zohra Noorhuddin, M.D., and Eduardo Bruera, M.D. Clinical Outcomes and Contributors to Weight Loss in a Cancer Cachexia Clinic. J Palliat Med. 2011 Sep; 14(9): 1004–1008.

Donohoe CL, Ryan AM, Reynolds JV. Cancer cachexia: mechanisms and clinical implications. Gastroenterol Res Pract. 2011;2011:601434. doi: 10.1155/2011/601434. Epub 2011 Jun 13.

du Bois RM, Weycker D, Albera C, et al. Six-minute-walk test in idiopathic pulmonary fibrosis: test validation and minimal clinically important difference. Am J Respir Crit Care Med 2011; 183:1231.

Enright PL. The six-minute walk test. Respir Care 2003; 48:783.

Evans WJ, Morley JE, Argilés J, Bales C, Baracos V, Guttridge D, Jatoi A, Kalantar-Zadeh K, Lochs H, Mantovani G, Marks D, Mitch WE, Muscaritoli M,Najand A, Ponikowski P, Rossi Fanelli F, Schambelan M, Schols A, Schuster M, Thomas D, Wolfe R, Anker SD. Cachexia: a new definition. Clin Nutr. 2008 Dec;27(6):793-9. doi: 10.1016/j.clnu.2008.06.013. Epub 2008 Aug 21.

Fearon K, Strasser F, Anker SD, Bosaeus I, Bruera E, Fainsinger RL, Jatoi A, Loprinzi C, MacDonald N, Mantovani G, Davis M, Muscaritoli M, Ottery F, Radbruch L, Ravasco P, Walsh D, Wilcock A, Kaasa S, Baracos VE. Definition and classification of cancer cachexia: an international consensus. Lancet Oncol. 2011 May;12(5):489-95.

Fearon KC, Moses AG. Cancer cachexia. Int J Cardiol. 2002 Sep;85(1):73-81.

Franklin Deborah Julie, MD, PhD Cancer Rehabilitation: Challenges, Approaches, and New Directions Physical Medicine and Rehabilitation. Clinics of North America Volume 18, Issue 4, November 2007, Pages 899–924

Gagnon B, Murphy J, Eades M, Lemoignan J, Jelowicki M, Carney S, Amdouni S, Di Dio P, Chasen M, Macdonald N. A prospective evaluation of an interdisciplinary nutrition-rehabilitation program for patients with advanced cancer. Curr Oncol. 2013 Dec;20(6):310-8. doi: 10.3747/co.20.1612.

Gagnon B, Bruera E. A review of the drug treatment of cachexia associated with cancer. Drugs. 1998 May;55(5):675-88.

Gilbert C, Brown MC, Cappelleri JC, et al. Estimating a minimally important difference in pulmonary arterial hypertension following treatment with sildenafil. Chest 2009; 135:137.

Glare P, Jongs W, Zafiropoulos B. Establishing a cancer nutrition rehabilitation program (CNRP) for ambulatory patients attending an Australian cancer center. Support Care Cancer. 2011 Apr;19(4):445-54. Epub 2010 Mar 5.

GLOBOCAN 2012, IARC, cancer statistics taken from the website in 2015: http://globocan.iarc.fr/Pages/fact_sheets_cancer.aspx

Granda-Cameron C, DeMille D, Lynch MP, Huntzinger C, Alcorn T, Levicoff J, Roop C, Mintzer D. An interdisciplinary approach to manage cancer cachexia. Clin J Oncol Nurs. 2010 Feb;14(1):72-80

Grossman M., Agulnik J., Batist G. The Peter Brojde Lung Cancer Centre: a model of integrative practice. Current Oncology - Volume 19, Number 3, June 2012

Guenter P, Muurahainen N, Simons G, Kosok A, Cohan GR, Rudenstein R, Turner JL. Relationships among nutritional status, disease progression, and survival in HIV infection. J Acquir Immune Defic Syndr. 1993 Oct;6(10):1130-8.

Gupta D, Lis CG. Pretreatment serum albumin as a predictor of cancer survival: a systematic review of the epidemiological literature. Nutr J. 2010 Dec 22;9:69.

Hanssens S, Luyten R, Watthy C, Fontaine C, Decoster L, Baillon C, Trullemans F, Cortoos A, De Grève J. Evaluation of a comprehensive rehabilitation program for post-treatment patients with cancer. Oncol Nurs Forum. 2011 Nov;38(6):E418-24.

Holland AE, Hill CJ, Conron M, et al. Small changes in six-minute walk distance are important in diffuse parenchymal lung disease. Respir Med 2009; 103:1430.

Holland AE, Spruit MA, Troosters T, et al. An official European Respiratory Society/American Thoracic Society technical standard: field walking tests in chronic respiratory disease. Eur Respir J 2014; 44:1428.

Ida S, Watanabe M, Karashima R, Imamura Y, Ishimoto T, Baba Y, Iwagami S, Sakamoto Y, Miyamoto Y, Yoshida N, Baba H. Changes in body composition secondary to neoadjuvant chemotherapy for advanced esophageal cancer are related to the occurrence of postoperative complications after esophagectomy. Ann Surg Oncol. 2014 Oct;21(11):3675-9. Epub 2014 May 5.

Kalfarentzos F, Spiliotis J, Velimezis G, Dougenis D, Androulakis J. Comparison of forearm muscle dynamometry with nutritional prognostic index, as a preoperative indicator in cancer patients. JPEN J Parenter Enteral Nutr. 1989 Jan-Feb;13(1):34-6. 76

Kennedy DM, Stratford PW, Wessel J, Gollish JD, Penney D. Assessing stability and change of four performance measures: a longitudinal study evaluating outcome following total hip and knee arthroplasty. BMC Musculoskelet Disord. 2005 Jan 28;6:3.

Kilgour RD, Vigano A, Trutschnigg B, Lucar E, Borod M, Morais JA. Handgrip strength predicts survival and is associated with markers of clinical and functional outcomes in advanced cancer patients. Support Care Cancer. 2013 Dec;21(12):3261-70. doi: 10.1007/s00520-013-1894-4. Epub 2013 Jul 20. PubMed PMID: 23872952.

Kondrup J, Elia M. Basic concepts in nutrition. In: Sobotka L, editor. Basics in clinical nutrition. 4th ed. Prague: Galen; 2011.p. 1-76

Lam T, Noonan VK, Eng JJ; SCIRE Research Team. A systematic review of functional ambulation outcome measures in spinal cord injury. Spinal Cord. 2008 Apr;46(4):246-54. Epub 2007 Oct 9.

Lauretani F, Russo CR, Bandinelli S, Bartali B, Cavazzini C, Di Iorio A, Corsi AM, Rantanen T, Guralnik JM, Ferrucci L. Age-associated changes in skeletal muscles and their effect on mobility: an operational diagnosis of sarcopenia. J Appl Physiol (1985). 2003 Nov;95(5):1851-60.

Lemoignan J, Chasen M, Bhargava R. A retrospective study of the role of an occupational therapist in the cancer nutrition rehabilitation program. Support Care Cancer. 2010 Dec;18(12):1589-96. Epub 2009 Dec 4.

Lewis C. and Shaw K. (2006). One-Legged (Single Limb) Stance Test. Geriatric Function, 17,10.

Littlewood TJ. The impact of hemoglobin levels on treatment outcomes in patients with cancer. Semin Oncol. 2001 Apr;28(2 Suppl 8):49-53.

MacDonald N. Cancer cachexia and targeting chronic inflammation: a unified approach to cancer treatment and palliative/supportive care. J Support Oncol. 2007 Apr;5(4):157-62; discussion 164-6, 183.

Mantovani G. Cachexia related to multiple cause. Cachexia and wasting: a modern approach, Springer (2006), pp. 161–162

Mathai SC, Puhan MA, Lam D, Wise RA. The minimal important difference in the 6-minute walk test for patients with pulmonary arterial hypertension. Am J Respir Crit Care Med 2012; 186:428.

Mattox TW. Treatment of unintentional weight loss in patients with cancer. Nutr Clin Pract. 2005 Aug;20(4):400-10.

Morishita S, Kaida K, Tanaka T, Itani Y, Ikegame K, Okada M, Ishii S, Kodama N, Ogawa H, Domen K. Prevalence of sarcopenia and relevance of body composition, physiological function, fatigue, and health-related quality of life in patients before allogeneic hematopoietic stem cell transplantation. Support Care Cancer. 2012 Dec;20(12):3161-8. Epub 2012 Apr 12.

Nissen MJ, Beran MS, Lee MW, Mehta SR, Pine DA, Swenson KK. Views of primary care providers on follow-up care of cancer patients. Fam Med. 2007 Jul-Aug;39(7):477-82.

Norman K, Stobäus N, Gonzalez MC, Schulzke JD, Pirlich M. Hand grip strength: outcome predictor and marker of nutritional status. Clin Nutr. 2011;30:135-142.

O'Loughlin J. Incidence of and risk factors for falls and injurious falls among the community-dwelling elderly. Am J Epidemiol. 137:342-354, 1993.

Orr R, Fiatarone Singh M. The anabolic androgenic steroid oxandrolone in the treatment of wasting and catabolic disorders: review of efficacy and safety. Drugs. 2004;64(7):725-50.

Osei-Hyiaman D. Endocannabinoid system in cancer cachexia. Curr Opin Clin Nutr Metab Care. 2007 Jul;10(4):443-8.

Ottery FD, Sljuka K & Hagan M (1995, January). Characterization of patients referred to nutrition clinic in a NCI-designated comprehensive cancer center: Baseline status and outcomes. Paper presented at the 19th Clinical Congress of the American Society for Parental and Enteral Nutrition in Miami, Fl.

Peolsson A, Hedlund R, Oberg B. Intra- and inter-tester reliability and reference values for hand strength. J Rehabil Med. 2001 Jan;33(1):36-41.

Perera S, Mody SH, Woodman RC, Studenski SA. Meaningful change and responsiveness in common physical performance measures in older adults. J Am Geriatr Soc. 2006 May;54(5):743-9.

Prado CM, Antoun S, Sawyer MB, Baracos VE. Two faces of drug therapy in cancer: drug-related lean tissue loss and its adverse consequences to survival and toxicity. Curr Opin Clin Nutr Metab Care. 2011 May;14(3):250-4.

Puhan MA, Chandra D, Mosenifar Z, et al. The minimal important difference of exercise tests in severe. Eur Respir J 2011; 37:784.

Puhan MA, Mador MJ, Held U, et al. Interpretation of treatment changes in 6-minute walk distance in patients with COPD. Eur Respir J 2008; 32:637.

Rasekaba T, Lee AL, Naughton MT, Williams TJ, Holland AE. The six-minute walk test: a useful metric for the cardiopulmonary patient. Intern Med J. 2009 Aug;39(8):495-501.

Redelmeier DA, Bayoumi AM, Goldstein RS, Guyatt GH. Interpreting small differences in functional status: the Six Minute Walk test in chronic lung disease patients. Am J Respir Crit Care Med 1997; 155:1278.

Ries JD, Echternach JL, Nof L, Gagnon Blodgett M. Test-retest reliability and minimal detectable change scores for the timed "up & go" test, the six-minute walk test, and gait speed in people with Alzheimer disease. Phys Ther. 2009 Jun;89(6):569-79. doi: 10.2522/ptj.20080258. Epub 2009 Apr 23.

Russell MK. Functional assessment of nutrition status. Nutr Clin Pract. 2015 Apr;30(2):211-8. doi: 10.1177/0884533615570094. Epub 2015 Feb 13.

Savva C, Karagiannis C, Rushton A. Test-retest reliability of grip strength measurement in full elbow extension to evaluate maximum grip strength. J Hand Surg Eur Vol. 2013 Feb;38(2):183-6. Epub 2012 Jun 19.

Schmidt K, Vogt L, Thiel C, Jäger E, Banzer W. Validity of the six-minute walk test in cancer patients. Int J Sports Med. 2013 Jul;34(7):631-6. doi: 10.1055/s-0032-1323746. Epub 2013 Feb 26.

Schols, R. Broekhuizen, C.A. Weling-Scheepers, E.F. Wouters. Body composition and mortality in chronic obstructive pulmonary disease. Am J Clin Nutr, 82 (2005), pp. 53–59

Shin KY, Guo Y, Konzen B, Fu J, Yadav R, Bruera E. Inpatient cancer rehabilitation: the experience of a national comprehensive cancer center. Am J Phys Med Rehabil. 2011 May;90(5 Suppl 1):S63-8.

Singh SJ, Puhan MA, Andrianopoulos V, et al. An official systematic review of the European Respiratory Society/American Thoracic Society: measurement properties of field walking tests in chronic respiratory disease. Eur Respir J 2014; 44:1447.

Soeters PB, Reijven PL, van Bokhorst-de van der Schueren MA, Schols JM, Halfens RJ, Meijers JM, van Gemert WG. A rational approach to nutritional assessment. Clin Nutr. 2008 Oct;27(5):706-16

Sokolof Jonas M, DO; Maryam Rafael Aghalar, DO; Michael D Stubblefield, MD. Physical rehabilitation for cancer survivors. Uptodate.com. This topic last updated: Jul 21, 2014.

Springer BA, Marin R, Cyhan T, Roberts H, Gill NW. Normative values for he unipedal stance test with eyes open and closed. J Geriatr Phys Ther. 2007;30(1):8-15.

Srimuninnimit V, Ariyapanya S, Nimmannit A, Wonglaksanapimon S, Akewanlop C, Soparattanapaisarn N. C-reactive protein as a monitor of chemotherapy response in advanced non-small cell lung cancer (CML study). J Med Assoc Thai. 2012 Feb;95 Suppl 2:S199-207.

Steffen T, Seney M. Test-retest reliability and minimal detectable change on balance and ambulation tests, the 36-item short-form health survey, and the unified Parkinson disease rating scale in people with parkinsonism. Phys Ther. 2008 Jun;88(6):733-46. doi: 10.2522/ptj.20070214. Epub 2008 Mar 20.

Stewart GD, Skipworth RJ, Fearon KC. Cancer cachexia and fatigue. Clin Med (Lond). 2006 Mar-Apr;6(2):140-3.

Strasser F, Bruera ED. Update on anorexia and cachexia. Hematol Oncol Clin North Am. 2002 Jun;16(3):589-617.

Stubblefield MD, Hubbard G, Cheville A, Koch U, Schmitz KH, Dalton SO. Current perspectives and emerging issues on cancer rehabilitation. Cancer. 2013a Jun 1;119 Suppl 11:2170-8. doi: 10.1002/cncr.28059. Review. PubMed PMID: 23695929.

Stubblefield MD. Cancer rehabilitation. Semin Oncol. 2011 Jun;38(3):386-93. doi: 10.1053/j.seminoncol.2011.03.008. PubMed PMID: 21600368.

Stubblefield MD. Physical Functioning and Rehabilitation for the Cancer Survivor. Semin Oncol 40:784-795; 2013b Elsevier Inc.

Swigris JJ, Olson AL, Shlobin OA, et al. Heart rate recovery after six-minute walk test predicts pulmonary hypertension in patients with idiopathic pulmonary fibrosis. Respirology 2011; 16:439.

Swigris JJ, Wamboldt FS, Behr J, et al. The 6 minute walk in idiopathic pulmonary fibrosis: longitudinal changes and minimum important difference. Thorax 2010; 65:173.

Tang A, Eng JJ, Rand D. Relationship between perceived and measured changes in walking after stroke. J Neurol Phys Ther. 2012 Sep;36(3):115-21.

Tatematsu N, Hasegawa S, Tanaka E, Sakai Y, Tsuboyama T. Impact of oesophagectomy on physical fitness and health-related quality of life in patients with oesophageal cancer. Eur J Cancer Care (Engl). 2013 May;22(3):308-13. doi: 10.1111/ecc.12030. Epub 2012 Dec 18.

Thomas R. Belin Missing Data: What a Little Can Do, and What Researchers Can Do in Response Am J Ophthalmol. Author manuscript; available in PMC 2010 Dec 1. Published in final edited form as: Am J Ophthalmol. 2009 Dec; 148(6): 820–822. doi: 10.1016/j.ajo.2009.07.027.

Tisdale M. Mechanisms of cancer cachexia. Physiol Rev 2009;89:381-410.

Tisdale MJ. Clinical anticachexia treatments. Nutr Clin Pract. 2006 Apr;21(2):168-74.

Torre LA, Bray F, Siegel RL, Ferlay J, Lortet-Tieulent J, Jemal A. Global cancer statistics, 2012. CA Cancer J Clin. 2015 Mar;65(2):87-108. Epub 2015 Feb 4.

Vasile E, Lucchesi M, Ginocchi L, Brunetti IM, Galli L, Ricci S, Falcone A, Antonuzzo A. Dedicated supportive care team at the oncology unit: a model of simultaneous care for cancer patients. Support Care Cancer. 2014 Apr;22(4):867-8. doi: 10.1007/s00520-013-2108-9. Epub 2014 Jan 5.

Vellas BJ, Wayne S, Romero L, et al. One-leg balance is an important predictor of injurious falls in older persons. J Amer Geriatr Soc. 45:735-738, 1997

White JW, Guenter P, Jensen J, et al. Consensus statement of the Academy of Nutrition and Dietetics/American Society for Parenteral and Enteral Nutrition: characteristics recommended for

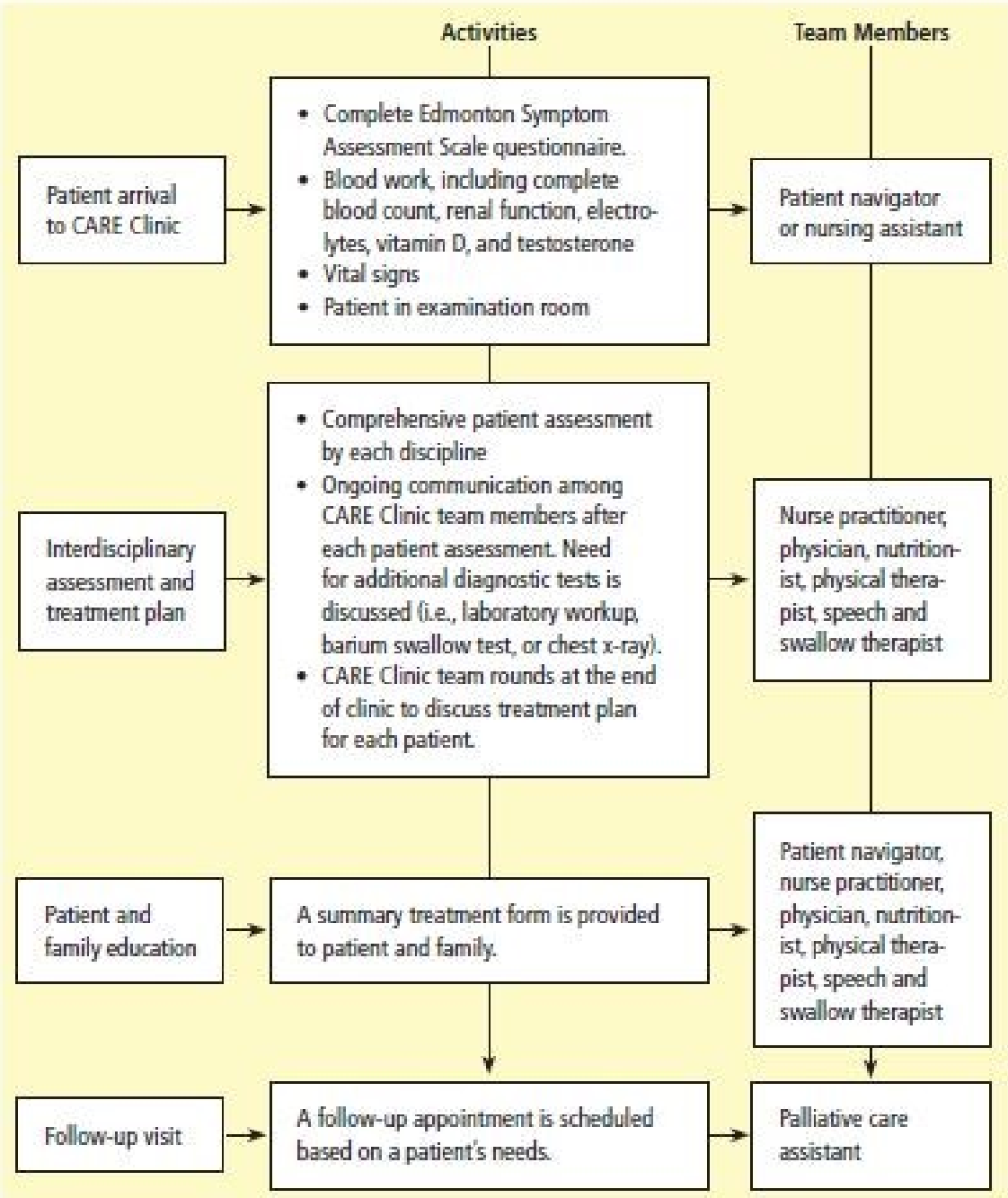
identification and documentation of adult malnutrition (undernutrition). J Acad Nutr Diet. 2012;112:730-738.

Wise RA, Brown CD. Minimal clinically important differences in the six-minute walk test and the incremental shuttle walking test. COPD 2005; 2:125.

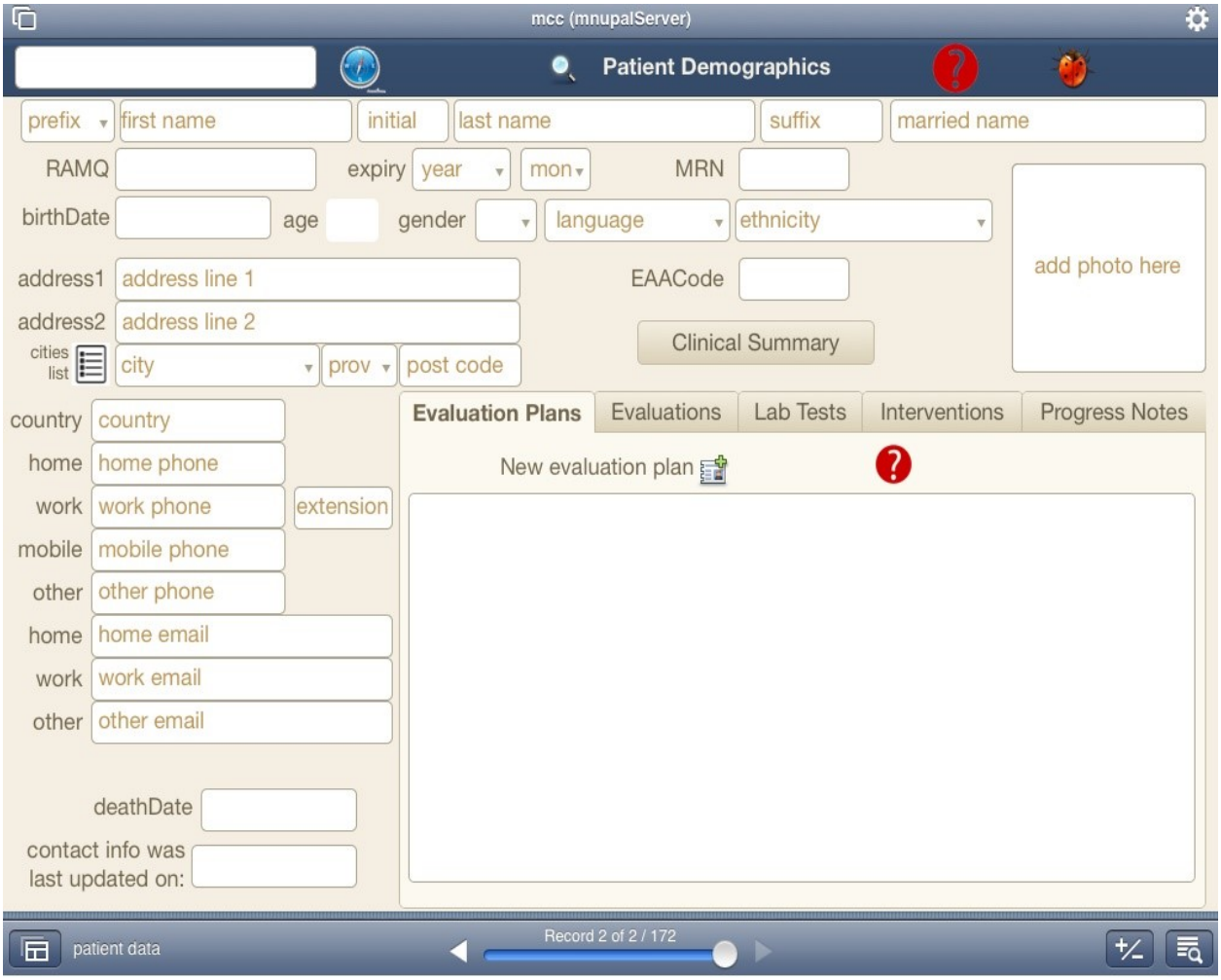
Zinna EM, Yarasheski KE. Exercise treatment to counteract protein wasting of chronic diseases. Curr Opin Clin Nutr Metab Care. 2003 Jan;6(1):87-93.

APPENDIX 1

Cancer Appetite and Rehabilitation (CARE) Clinic Pathway



APPENDIX 2


mcc (mnupalServer)
Patient Demographics
prefix
first name
initial
last name
suffix
married name
RAMQ
expiry
year
mon
MRN
birthDate
age
gender
language
ethnicity
add photo here
address1
address line 1
EAACode
address2
address line 2
Clinical Summary
cities list
city
prov
post code
country
country
home
home phone
work
work phone
extension
mobile
mobile phone
other
other phone
home
home email
work
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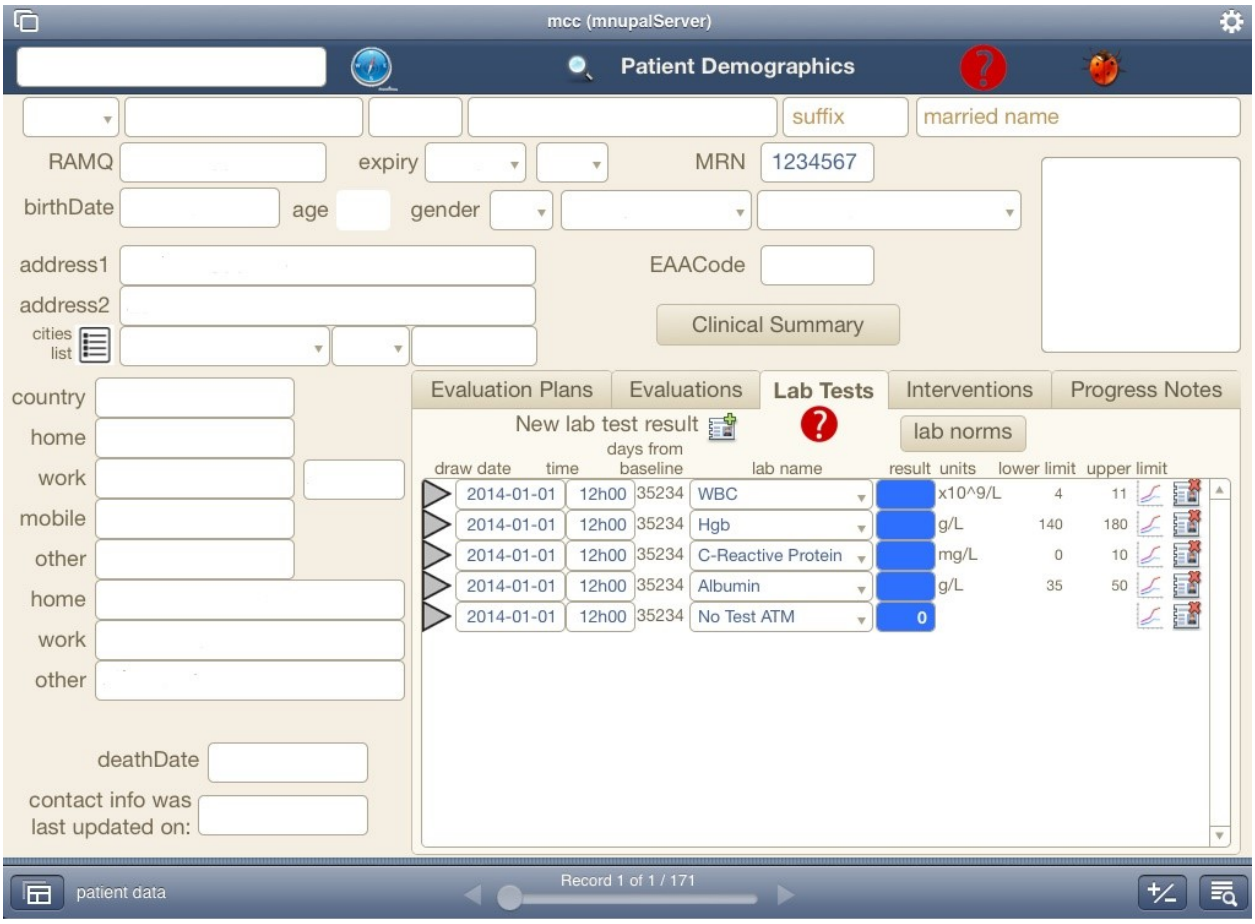
Evaluation Plans
Evaluations
Lab Tests
Interventions
Progress Notes
New evaluation plan
deathDate
contact info was last updated on:
patient data
Record 2 of 2 / 172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age
gender
address1
address2
cities list
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Clinical Summary
country
home
work
mobile
other
home
work
other
deathDate
contact info was last updated on:
Evaluation Plans
Evaluations
Lab Tests
Interventions
Progress Notes
New lab test result
lab norms
draw date
time
days from baseline
lab name
result
units
lower limit
upper limit
2014-01-01 12h00 35234 WBC x10^9/L 4 11
2014-01-01 12h00 35234 Hgb g/L 140 180
2014-01-01 12h00 35234 C-Reactive Protein mg/L 0 10
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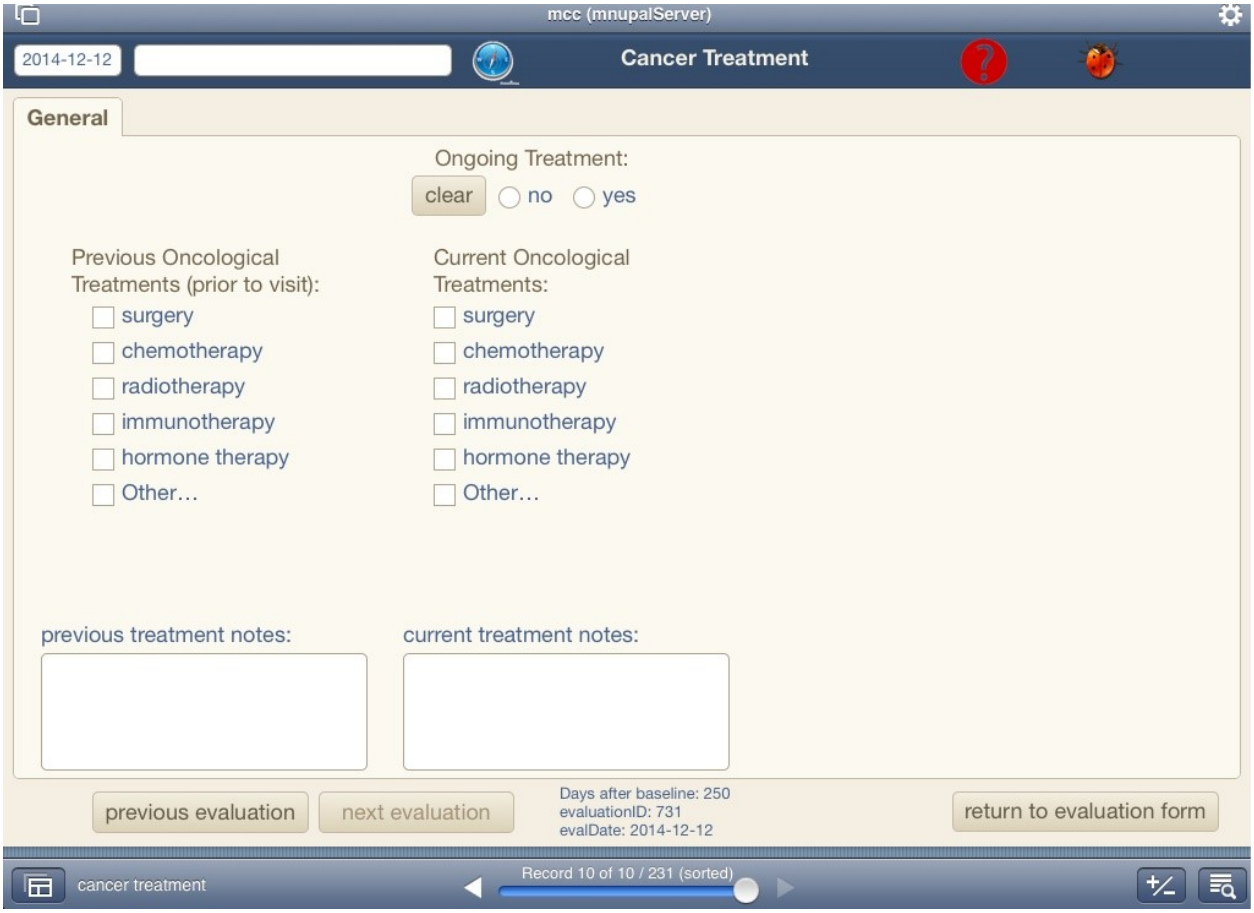
patient data
Record 1 of 1 / 171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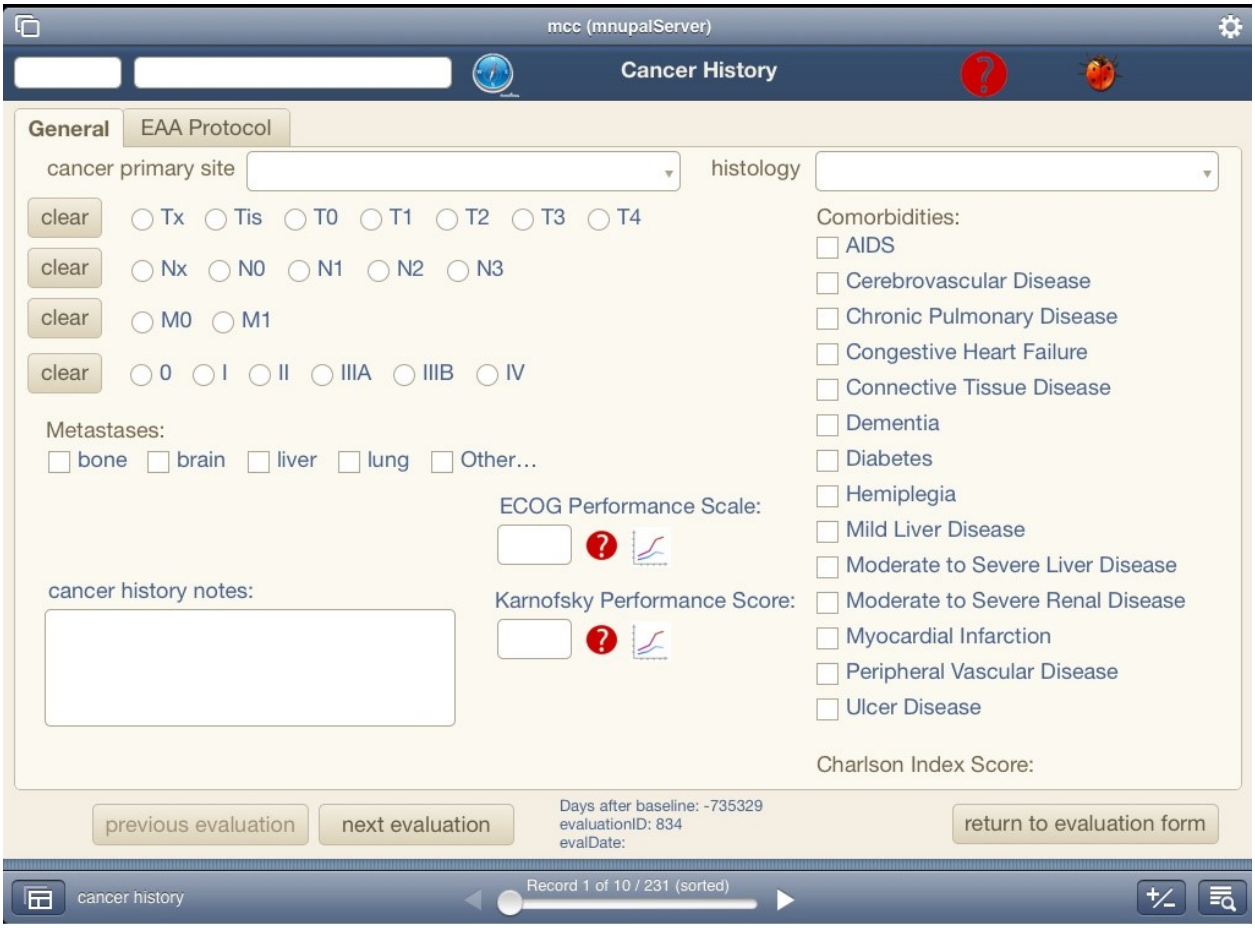
2014-12-12
Cancer Treatment
General
Ongoing Treatment:
clear
no
yes
Previous Oncological Treatments (prior to visit):
surgery
chemotherapy
radiotherapy
immunotherapy
hormone therapy
Other…
Current Oncological Treatments:
surgery
chemotherapy
radiotherapy
immunotherapy
hormone therapy
Other…
previous treatment notes:
current treatment notes:
previous evaluation
next evaluation
Days after baseline: 250
evaluationID: 731
evalDate: 2014-12-12
return to evaluation form
cancer treatment
Record 10 of 10 / 231 (sorted)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Cancer History
General
EAA Protocol
cancer primary site
histology
clear
Tx Tis T0 T1 T2 T3 T4
clear
Nx N0 N1 N2 N3
clear
M0 M1
clear
0 I II IIIA IIIB IV
Metastases:
bone brain liver lung Other…
ECOG Performance Scale:
Karnofsky Performance Score:
cancer history notes:
Comorbidities:
AIDS
Cerebrovascular Disease
Chronic Pulmonary Disease
Congestive Heart Failure
Connective Tissue Disease
Dementia
Diabetes
Hemiplegia
Mild Liver Disease
Moderate to Severe Liver Disease
Moderate to Severe Renal Disease
Myocardial Infarction
Peripheral Vascular Disease
Ulcer Disease
Charlson Index Score:
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next evaluation
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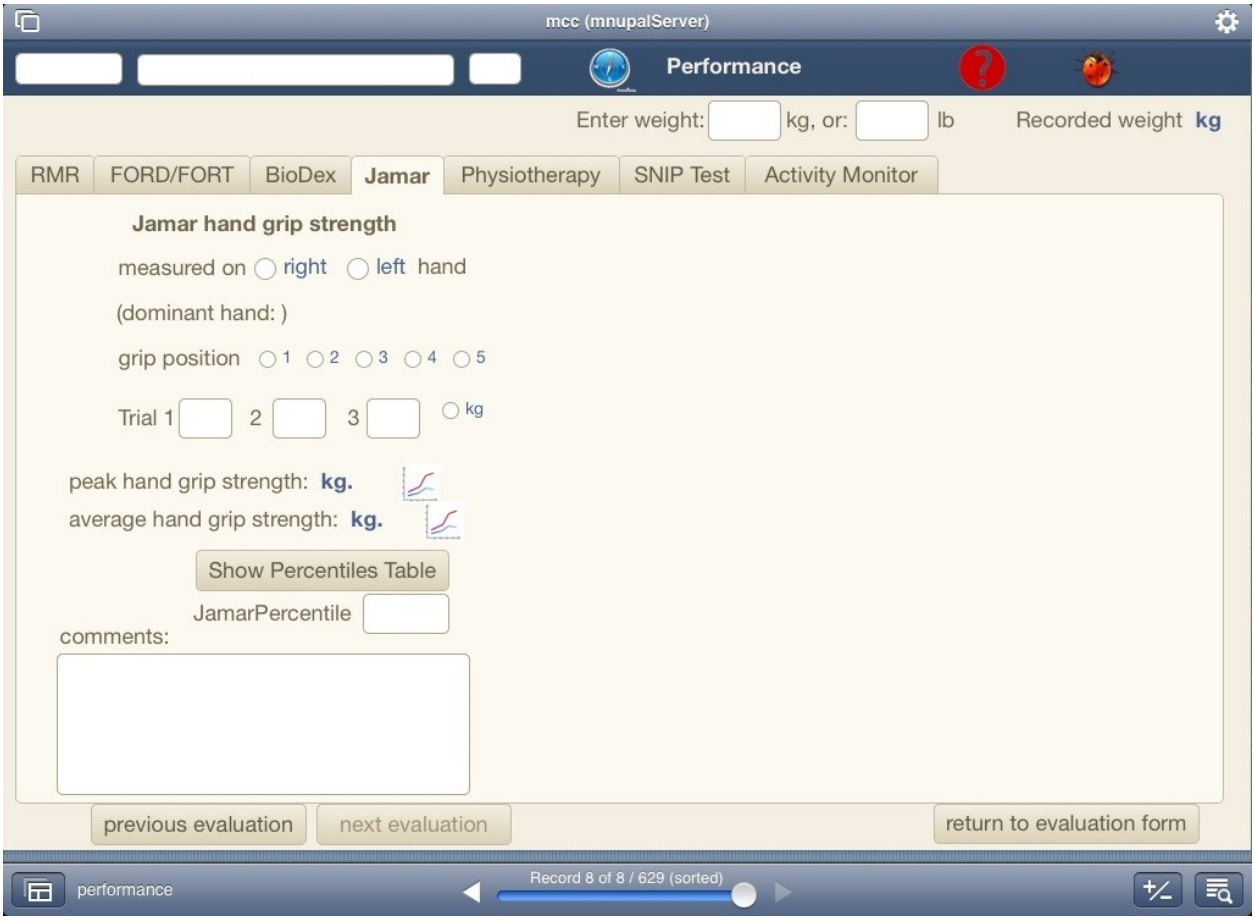
cancer history
Record 1 of 10 / 231 (sorted)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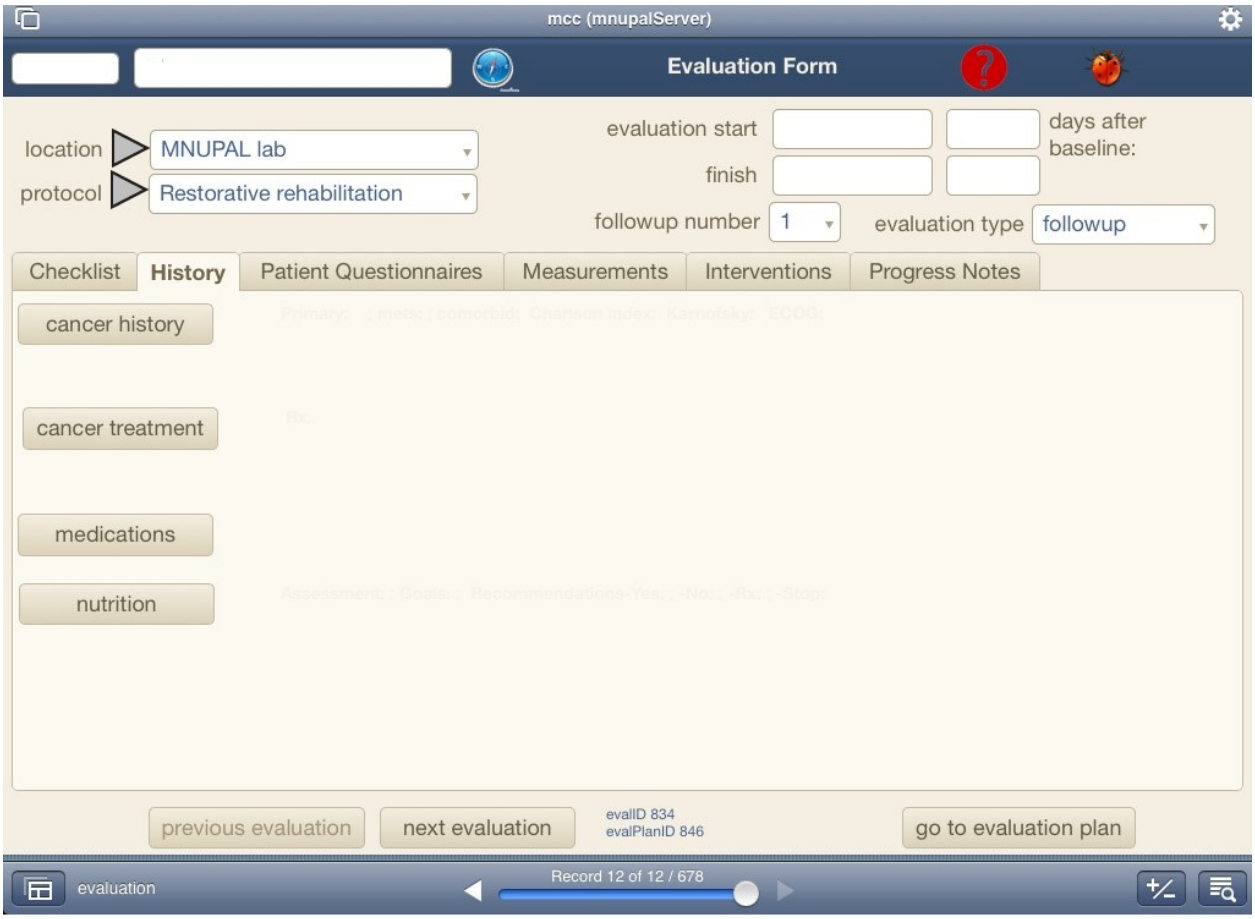
Performance
Enter weight: kg, or: lb
Recorded weight kg
RMR
FORD/FORT
BioDex
Jamar
Physiotherapy
SNIP Test
Activity Monitor
Jamar hand grip strength
measured on right left hand
(dominant hand:)
grip position 1 2 3 4 5
Trial 1 2 3 kg
peak hand grip strength: kg.
average hand grip strength: kg.
Show Percentiles Table
JamarPercentile
comments:
previous evaluation
next evaluation
return to evaluation form
performance
Record 8 of 8 / 629 (sorted)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Evaluation Form
location
MNUPAL lab
protocol
Restorative rehabilitation
evaluation start
finish
days after baseline:
followup number
1
evaluation type
followup
Checklist
History
Patient Questionnaires
Measurements
Interventions
Progress Notes
cancer history
cancer treatment
medications
nutrition
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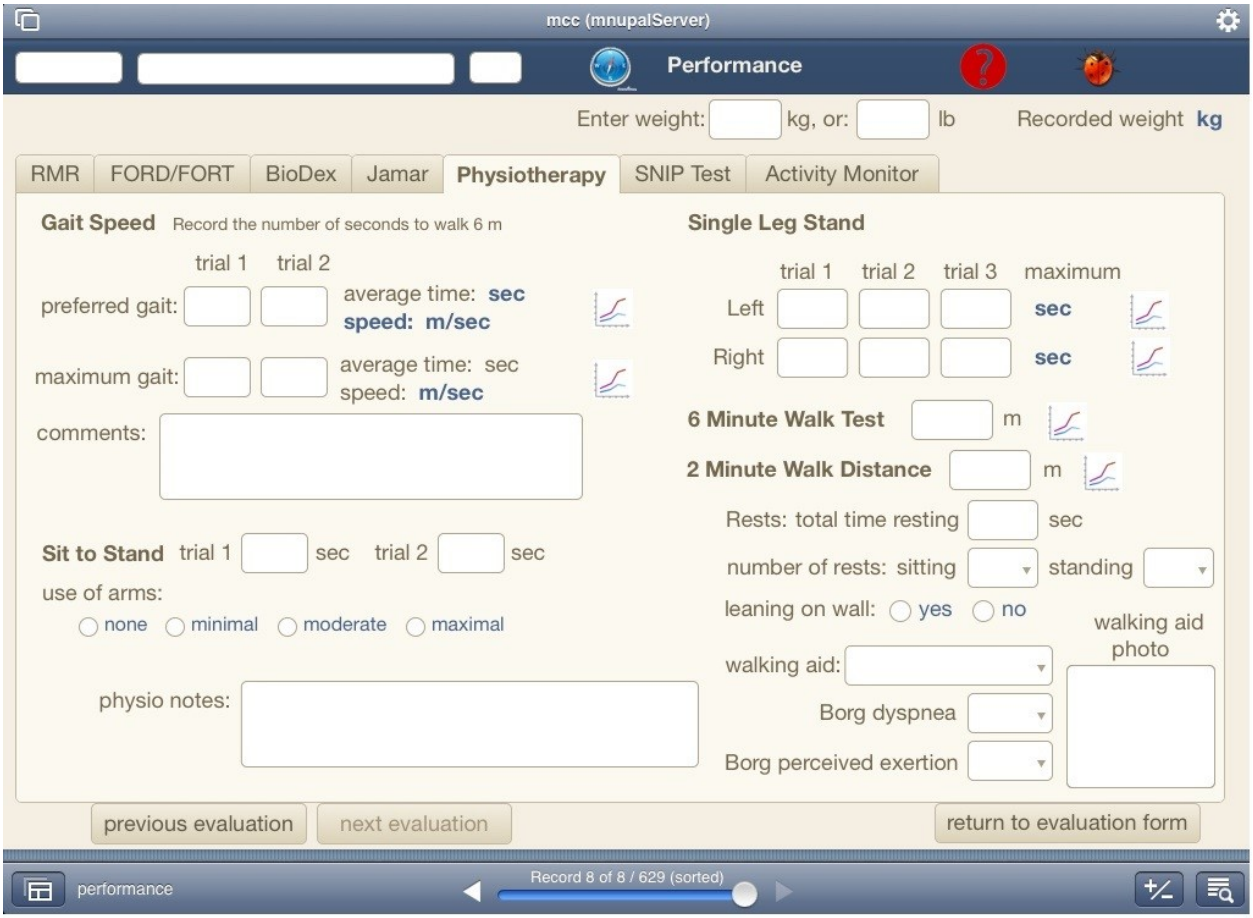
evaluation
Record 12 of 12 / 678


mcc (mnupalServer)
Performance
Enter weight: kg, or: lb
Recorded weight kg
RMR
FORD/FORT
BioDex
Jamar
Physiotherapy
SNIP Test
Activity Monitor
Gait Speed
Record the number of seconds to walk 6 m
trial 1
trial 2
preferred gait:
average time: sec
speed: m/sec
maximum gait:
average time: sec
speed: m/sec
comments:
Sit to Stand
trial 1
sec
trial 2
sec
use of arms:
none
minimal
moderate
maximal
physio notes:
Single Leg Stand
trial 1
trial 2
trial 3
maximum
Left
sec
Right
sec
6 Minute Walk Test
m
2 Minute Walk Distance
m
Rests: total time resting
sec
number of rests: sitting
standing
leaning on wall:
yes
no
walking aid:
Borg dyspnea
Borg perceived exertion
walking aid photo
previous evaluation
next evaluation
return to evaluation form
performance
Record 8 of 8 / 629 (sorted)

APPENDIX 3

SIX MINUTE WALK TEST PROTOCOL
Flat, straight corridor 30 m (100 feet) in length
Turnaround points marked with a cone
Patient should wear comfortable clothes and shoes
Patient rests in chair for at least 10 minutes prior to test (no warm-up period)
Record baseline heart rate and pulse oxygen saturation (SpO_2); monitoring pulse oxygen saturation during test is optional
If the patient is using supplemental oxygen, record the flow rate and type of device
Have patient stand and rate baseline dyspnea and overall fatigue using Borg scale
Set lap counter to zero and timer to six minutes
Instruct the patient: Remember that the object is to walk AS FAR AS POSSIBLE for 6 minutes, but don't run or jog. Pivot briskly around the cone.
At each minute mark, inform the patient of the time remaining. It is okay to say, "you are doing well" or "keep up the good work", but do not use words of encouragement to speed up.
At the end of the test, mark the spot where the patient stopped on the floor
If using a pulse oximeter, measure the pulse rate and SpO_2 and record
After the test record the Borg dyspnea and fatigue levels
Ask, "What, if anything, kept you from walking farther?"
Calculate the distance walked and record

APPENDIX 4

Minimally Clinical Important Differences (MCID) and Minimal Detectable Change (MDC) for the 6MWT

MCID					
	YEAR PUBLISHED	**TITLE OF THE ARTICLE**	**JOURNAL**	**POPULATION**	**MCID (m)**
Wise and Brown	2009	Minimal clinically important differences in the 6MWT	COPD: Journal of Chronic Obstructive Pulmonary Disease	COPD	54-80
Rasekaba et al	2009	The six-minute walk test: a useful metric for the cardiopulmonary patient	Internal Medicine Journal	COPD	54
Perera et al	2006	Meaningful change and responsiveness in common physical performance measures in older adults	Journal of the American Geriatrics Society	Geriatrics and stoke	58.21
Tang et al	2012	Relationship between perceived and measured changes in walking after stroke	J Neurol Phys Ther	Stroke	34.3
MDC					
Ries et al	2009	Test-retest reliability and minimal detectable change scores for the timed "up & go" test, the six-minute walk test, and gait speed in people with Alzheimer disease	Phys The	Alzheimer's Disease	33.47
Redelmeier et al	1997	Interpreting small differences in functional status: the six minute walk test in chronic lung disease patients.	American journal of respiratory and critical care medicine	COPD	54
Perera et al	2006	Meaningful change and responsiveness in common physical performance measures in older adults	Journal of the American Geriatrics Society	Geriatrics	58.21
Kennedy et al	2005	Assessing stability and change of four performance measures: a longitudinal study evaluating outcome following total hip and knee arthroplasty	BMC Musculoskelet Disord	Osteoarthritis	61.34
Steffen and Seney	2008	Test-retest reliability and minimal detectable change on balance and ambulation tests, the 36-item short-form health survey, and the unified Parkinson disease rating scale in people with parkinsonism	Physical Therapy	Parkinsonism	82
Lam et al	2008	A systematic review of functional ambulation outcome measures in spinal cord injury	Spinal Cord	Spinal Cord Injury	45.8
Perera et al	2006	Meaningful change and responsiveness in common physical performance measures in older adults	J Am Geriatr Soc	Stroke	20-50

APPENDIX 5

Unipedal stance test time by age group and gender for eyes open and closed

Age & Gender Groups	Eyes Open Best of 3 trials (sec) Mean (SE)	Eyes Open Mean of 3 trials (sec) Mean (SE)	Eyes Closed Best of 3 trials (sec) Mean (SE)	Eyes Closed Mean of 3 trials (sec) Mean (SE)
18-39				
Female (n = 44)	45.1 (0.1)	43.5 (3.8)	13.1 (12.3)	8.5 (9.1)
Male (n = 54)	44.4 (4.1)	43.2 (6.0)	16.9 (13.9)	10.2 (9.6)
Total (n = 98)	44.7 (3.1)	43.3 (5.1)	15.2 (13.3)	9.4 (9.4)
40-49				
Female (n = 47)	42.1 (9.5)	40.4 (10.1)	13.5 (12.4)	7.4 (6.7)
Male (n = 51)	41.6 (10.2)	40.1 (11.5)	12.0 (13.5)	7.3 (7.4)
Total (n = 98)	41.9 (9.9)	40.3 (10.8)	12.7 (12.9)	7.3 (7.0)
50-59				
Female (n = 50)	40.9 (10.0)	36.0 (12.8)	7.9 (8.0)	5.0 (5.6)
Male (n = 48)	41.5 (10.5)	38.1 (12.4)	8.6 (8.8)	4.5 (3.8)
Total (n = 98)	41.2 (10.2)	37.0 (12.6)	8.3 (8.4)	4.8 (4.8)
60-69				
Female (n = 50)	30.4 (16.4)	25.1 (16.5)	3.6 (2.3)	2.5 (1.5)
Male (n = 51)	33.8 (16.0)	28.7 (16.7)	5.1 (6.8)	3.1 (2.7)
Total (n = 101)	32.1 (16.2)	26.9 (16.6)	4.4 (5.1)	2.8 (2.2)
70-79				
Female (n = 45)	16.7 (15.0)	11.3 (11.2)	3.7 (6.2)	2.2 (2.1)
Male (n = 50)	25.9 (18.1)	18.3 (15.3)	2.6 (1.7)	1.9 (0.9)
Total (n = 95)	21.5 (17.3)	15.0 (13.9)	3.1 (4.5)	2.0 (1.6)
80-99				
Female (n = 22)	10.6 (13.2)	7.4 (10.7)	2.1 (1.1)	1.4 (0.6)
Male (n = 37)	8.7 (12.6)	5.6 (8.4)	1.8 (0.9)	1.3 (0.6)
Total (n = 59)	9.4 (12.8)	6.2 (9.3)	1.9 (1.0)	1.3 (0.6)
Total (all ages)				
Female (n=258)	33.0 (16.8)	29.2 (17.4)	7.7 (9.6)	4.7 (6.0)
Male (n = 291)	33.8 (17.1)	30.2 (17.7)	8.2 (10.8)	4.9 (6.4)
Total (n = 549)	33.4 (16.9)	29.8 (17.5)	8.0 (10.3)	4.9 (6.2)

From : Springer BA, Marin R, Cyhan T, Roberts H, Gill NW. Normative values for the unipedal stance test with eyes open and closed. J Geriatr Phys Ther. 2007;30(1):8-15.

APPENDIX 6

Example of a Cancer Rehabilitation and Cachexia Clinic schedule

Cancer Rehab Clinic/Cachexia					
Date:					
8:15 – 9:00	Meeting – case presentation (NP + FU)				
	MD	Nurse	NUT	PT	OT
9:00 – 9:30	Smith	McDonald	Brown	Miller	
9:30 – 10:00	Jones	Smith	McDonald	Brown	Miller
10:00 – 10:30	Miller	Jones	Smith	McDonald	Brown
10:30 – 11:00	Brown	Miller	Jones	Rodriguez	McDonald
11:00 – 11:30	McDonald	Brown	Miller		Rodriguez
11:30 – 12:15	Meeting Lunch				
12:15 – 13:15					

	ROOM	Patient	MGH #	
AM	1	Smith		Cachexia FU
	2	Jones		Cachexia FU
	3	Miller		Rehab end eval
	4	Brown		Rehab new patient
	5	McDonald		Rehab FU
	6	Rodriguez		FU PT and OT only

Thank you!