A PHASE III STUDY OF THE IMPACT OF A PHYSICAL ACTIVITY PROGRAM ON DISEASE-FREE SURVIVAL IN PATIENTS WITH HIGH RISK STAGE II OR STAGE III COLON CANCER: A RANDOMIZED CONTROLLED TRIAL (CHALLENGE)

CCTG Protocol Number: CO.21

NCT number: NCT00819208

Document date: June 24, 2020

PROTOCOL AMENDMENT #5: 2020-JUN-24
CCTG TRIAL: CO.21

INITIAL VERSION: 2008-NOV-21
AMENDMENT #1: 2009-DEC-04
AMENDMENT #2: 2010-SEP-17
ADMINISTRATIVE UPDATE #1: 2011-NOV-07
AMENDMENT #3: 2013-MAR-07
AMENDMENT #4: 2014-MAR-04

CANADIAN CANCER TRIALS GROUP (CCTG)

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I have read the protocol and agree that it contains all necessary details for carrying out the study as described. I will conduct this protocol as outlined therein, and according to Good Clinical Practice and any applicable local regulations. I will make a reasonable effort to complete the study within the time designated. I confirm that I and study personnel participating under my supervision have adequate resource to fulfill their responsibilities as outlined in this protocol. I will maintain documentation of any investigator responsibilities assigned to participating study personnel.

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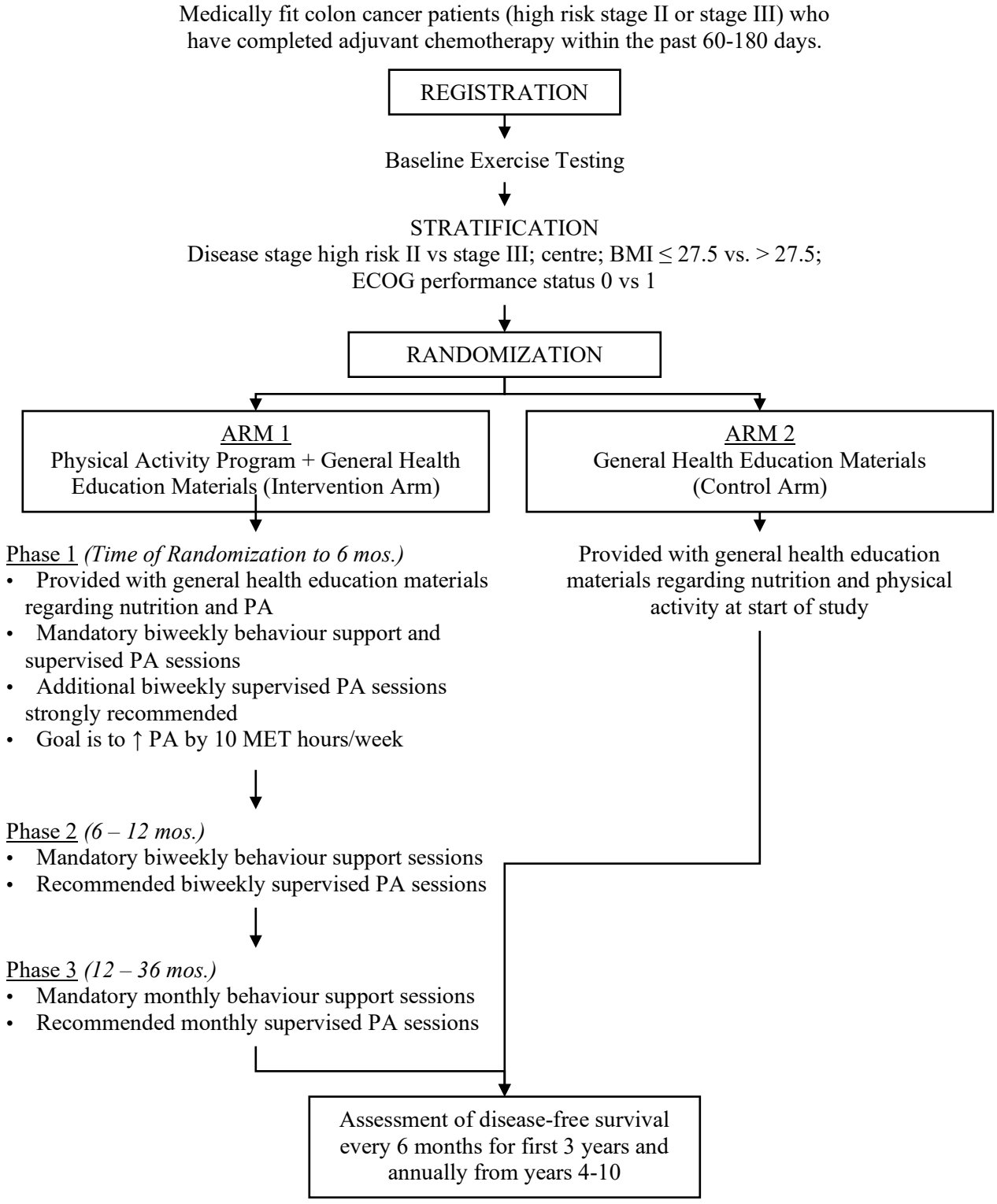
EXECUTIVE SUMMARY

The Colon Health And Life Long Exercise ChaNGE (CHALLENGE) trial is based on compelling evidence from: (a) observational studies showing that physical activity (PA) is strongly and inversely associated with colon cancer incidence, recurrence, and disease-specific and overall survival, (b) intervention studies showing that PA interventions cause changes in biologic mechanisms thought to play a role in colon cancer initiation and promotion, and (c) behavior change studies showing that it is possible to achieve a substantial increase in PA that can be maintained over an extended period of time. The general objective of this study is to determine whether a structured physical activity program plus provision of standard written material improves outcomes in comparison with provision of standard written material in patients who have completed adjuvant chemotherapy given after surgical resection of high-risk stage II or stage III colon cancer.

TREATMENT SCHEMA



Population
Medically fit patients who have completed surgical resection of high risk stage II/stage III colon cancer and have completed adjuvant chemotherapy within the past 60-180 days.

Stratification
- Disease stage (high risk II vs III)
- Centre
- BMI ($\leq$ 27.5 vs > 27.5)
- ECOG performance status(0 vs 1)

Endpoints
Primary:
- Disease-free survival

Secondary:
- Overall survival
- Patient Reported Outcomes including quality of life (using SF-36, FACIT-F, PSQI, HADS)*
- Objective markers of physical fitness (BMI, hip and waist circumference, cardiovascular fitness, physical function)
- Physical activity behaviour (TPAQ)*
- Safety profile
- Correlative biological markers including:
  - Biochemical and molecular markers associated with insulin-related growth factor
  - Cytokines associated with the mechanisms of fatigue
- Economic evaluations including:
  - Cost-effective analysis
  - Cost utility analysis
- Predictors of physical activity adherence (using Social Cognitive Determinants of Exercise)
- Specimen banking

Sample Size
Planned sample size is 962 patients.

* see glossary in Appendix I for listings of acronyms

1.0 OBJECTIVES

1.1 Primary Objective

To compare the disease-free survival (DFS) of medically fit patients who have completed surgical resection and adjuvant chemotherapy for high-risk stage II or stage III colon cancer and are allocated to participate in a structured physical activity (PA) program plus receive general health education materials OR to receive general health education materials only. Disease-free survival is measured from the time of randomization until local disease recurrence, distant disease recurrence, a new primary colon cancer malignancy, other second primary tumours or death from any cause.

1.2 Secondary Objectives

- To compare the two intervention arms with respect to:
  - Overall survival (OS)
  - Patient Reported Outcomes including QOL using the SF-36, FACIT-F, PSQI and HADS
  - Objective markers of physical fitness using BMI, hip and waist circumference, submaximal exercise testing, and the Seniors' Fitness Test
  - Physical activity behaviour using the Total Physical Activity Questionnaire Recreational Activity Module (TPAQ)
  - Safety profile as assessed by NCI Common Toxicity Criteria for Adverse Events, Version 3.0
  - Serum levels of insulin, IGF-1, IGF-2, IGFBP3
  - Cytokine levels of IL-1β, IL-6, IL-2, IL-4, IL-8, IL-10, IL-12, TNF-α, IFN-γ, and GM-CSF and C-reactive protein
  - Economic evaluations including cost-effective and cost-utility analyses
  - Predictors of physical activity adherence using the Social-Cognitive Determinants of Exercise Measure

- To evaluate in all randomized patients the potential prognostic associations of the following variables:
  - Serum levels of insulin, IGF-1, IGF-2, IGFBP3 and blood glucose, and cytokine levels of IL-1β, IL-6, IL-2, IL-4, IL-8, IL-10, IL-12, TNF-α, IFN-γ, and GM-CSF and C-reactive protein with DFS, OS, level of physical activity and level of fatigue
  - Age, gender, country, incremental increase in physical activity and change in cardiovascular fitness with DFS, OS, level of fatigue and QOL.

- To establish a comprehensive specimen bank linked to a clinical database for the further study of molecular markers of colon cancer.

2.0 BACKGROUND INFORMATION AND RATIONALE

2.1 Colorectal Cancer

There are an estimated 20 000 new cases of colo-rectal cancer (CRC) diagnosed annually, making this the third most common cancer diagnosed in Canadian men and women and the second leading cause of cancer-related death *[CCS/NCIC 2008]*. Prognosis and therapy are largely based on stage of disease. Stage I disease includes tumours confined to the submucosa and is treated with surgery alone (5-year survival > 90%). Tumours that have invaded the bowel muscularis but not spread to regional lymph nodes are stage II and have a 5-year survival of 60-85%. Based on clinical and pathological risk factors, selected stage II patients may require adjuvant chemotherapy after surgery. Patients in whom the disease has spread to regional lymph nodes are classified as stage III and have a 5 year survival 25-65%: these patients commonly receive a course of adjuvant therapy. Disease that is metastatic to distant organs is stage IV and often treated with palliative chemotherapy (median survival 16-20 months).

As will be discussed in Section 2.2, physical activity is strongly associated with reduced risk of colon cancer but not rectal cancer. For this reason only patients with colon cancer are considered eligible for this study. In addition to stage III patients, the study will also include patients with high risk stage II disease as they are felt to be at moderate risk of disease relapse and often receive adjuvant chemotherapy.

2.2 Physical Activity and Colon Cancer Risk and Disease Outcomes

Data from numerous studies as well as a recent meta-analysis *[Samad 2005]* have provided evidence that physical activity is associated with a lower risk of primary colon cancer. Of 63 studies identified, there have been 29 prospective cohort and 34 case-control studies. A statistically significant risk reduction in colon cancer risk among those who were most physically active as compared to those least active was observed in 49 (78%) of these studies. In these 49 studies, 36 studies examined whether cancer risk decreased with increasing physical activity and in 33 such an association was observed. The magnitude of the risk reduction, among the studies that found a risk decrease, was 35% in the prospective cohort studies and 40% in the case-control studies. The level of risk reduction has been classified as “convincing” *[WCRF/AICR 2007; Friedenreich 2002]*.

Although primary and secondary prevention are two distinct issues, many of the proposed mechanisms by which physical activity may reduce the incidence of primary colon cancer may also apply to recurrence. Such mechanisms include the reduction of insulin growth factor (IGF), prostaglandin E2, and gut transit time.

Recent research has evaluated whether an association exists between PA and colon cancer prognosis and recurrence. Haydon et al. *[Haydon 2006]* conducted a prospective observational study as part of the Melbourne Collaborative Cohort Study. In a sub-study, 526 participants were asked, a median of 5.3 years prior to a colorectal cancer diagnosis, how many times per week they had engaged in vigorous and moderate exercise during the previous six months. Participants were followed for a median of 5.5 years after their diagnosis. Participants that engaged in at least one vigorous or moderate exercise session per week were considered "exercisers" whereas all others were considered "non-exercisers". Analyses adjusted for known prognostic factors, including body mass index (BMI), showed that exercisers had a borderline significantly lower risk for overall mortality (0.77; 95% CI=0.58 to 1.03) and colorectal cancer-specific mortality (0.73; 95% CI=0.54 to 1.00). The unadjusted overall 5-year survival was 71% for exercisers and 57% for non-exercisers. Subgroup analyses indicated that the association of exercise with colorectal cancer-specific mortality was largely restricted to stage II/III cancers (0.49; 95% CI=0.30 to 0.79) and to cancers of the right colon (0.50; 95% CI=0.27 to 0.90) compared to the left colon (0.82; 95% CI=0.46 to 1.44) or rectum (1.00; 95% CI=0.59 to 1.69).

Meyerhardt et al. *[Meyerhart 2006b]* conducted a prospective observational study of 832 patients with stage III colon cancer enrolled in a randomized adjuvant chemotherapy trial and followed for a median of 3.8 years from trial entry. Physical activity was self-reported approximately six months after completing chemotherapy and predefined PA categories were calculated as metabolic equivalent task (MET) hours/week of < 3 (referent), 3 to 8.9, 9 to 17.9, 18 to 26.9, and 27+. Analyses adjusted for known prognostic factors, including BMI, indicated a significant negative linear association between the amount of PA and disease-free survival (p=.01), recurrence-free survival (p=.03), and overall mortality (p=.01). Specifically, compared with patients that exercised < 18 MET hours/week, patients that exercised $\geq$ 18 MET hours/week had a hazard ratio of 0.57 (95% CI=0.39 to 0.85) for disease-free survival. The 3-year DFS was 75.1% for patients who engaged in < 18 MET hours/week and 84.5% for patients who engaged in $\geq$ 18 MET hours/week. To better characterize the amount of PA necessary for benefit, a smoothing spline of log hazard versus the log of the total MET score was generated—a method independent of predetermined MET hours/week categorizations. The spline suggested that the protective benefit of PA may occur at less than 9 MET hours/week and that at a threshold of 27 MET hours/week, additional PA was not associated with further improvements. Although none of the tests for interactions were statistically significant, the association between PA and DFS appeared to be slightly stronger for women and for patients with a BMI > 25.

In a second article Meyerhardt et al. *[Meyerhart 2006a]* reported a prospective observational study of 573 women from the Nurses' Health Study who were diagnosed with stage I to III colorectal cancer. Leisure-time physical activity was self-reported prior to diagnosis (median six months) and one to four years post-diagnosis (median 22 months) and predefined PA categories were calculated as MET hours/week < 3 (referent), 3 to 8.9, 9 to 17.9, and 18+. Analyses adjusted for known prognostic factors, including BMI, showed a significant negative linear association between the amount of PA post-diagnosis and the risk of both colorectal cancer-specific mortality (p=.008) and overall mortality (p=.003). Specifically, compared with women exercising < 3 MET hours/week, the risk of colorectal cancer-specific mortality was 0.92 (95% CI=0.50 to 1.69) for 3-8.9 METs, 0.57 (95% CI=0.27 to 1.20) for 9 to 17.9 METs, and 0.39 (95% CI=0.18 to 0.82) for 18+ METs. The risk of overall mortality was 0.77 (95% CI=0.48 to 1.23) for 3-8.9 METs, 0.50 (95% CI=0.28 to 0.90) for 9 to 17.9 METs, and 0.43 (95% CI=0.25 to 0.74) for 18+ METs. Although none of the tests for interactions were statistically significant, the association between PA and colorectal-cancer specific mortality appeared to be slightly stronger for patients with a BMI > 25, over age 65, rectal cancer, and diagnosed after 1995.

In the same study, Meyerhardt et al. *[Meyerhart 2006a]* also examined the change in PA from pre-diagnosis to post-diagnosis. Compared with women who did not change their PA, women who increased their PA at least one category from pre-diagnosis had an adjusted risk of 0.48 (95% CI=0.24 to 0.97) for colorectal cancer-specific mortality and an adjusted risk of 0.51 (95% CI=0.30 to 0.85) for overall mortality. Women who decreased their PA had a non-significant increase in risk of 1.32 (95% CI=0.74 to 2.34) for colorectal cancer-specific mortality and 1.23 (95% CI=0.79 to 1.91) for overall mortality. These data were further divided into women who were performing < vs ≥ 9 MET hours/week of PA pre-diagnosis (approximately equivalent to the current public health guidelines of 150 minutes of moderate intensity exercise or 60 minutes of vigorous intensity exercise/week). Women performing < 9 MET hours/week pre-diagnosis who increased their PA by at least one category post-diagnosis (from < 3 to 3-8.9 or from 3-8.9 to 9+) had a reduced risk of colorectal cancer-specific mortality of 0.26 (95% CI=0.10 to 0.66) and overall mortality of 0.36 (95% CI=0.19 to 0.67) compared to women who did not increase their PA. Women that were performing ≥ 9 MET hours/week pre-diagnosis had a similar lower risk of colorectal cancer specific mortality and overall mortality regardless of whether they maintained or further increased their PA post-diagnosis. These data suggest that there was no additional benefit to increasing PA post-diagnosis in women that were already doing at least 9 MET hours/week before diagnosis.

While the existing literature suggests a strong association between physical activity and colon cancer, the data for rectal cancer are less convincing. This is true in the primary prevention literature and the observational studies by Meyerhardt and Haydon described above. Because of the uncertainty regarding the association in rectal cancer we have chosen to include only patients with colon cancer so as not to dilute the treatment effect.

In summary the existing literature demonstrates that higher levels of post-diagnosis exercise are associated with a reduced risk of colon cancer recurrence. Furthermore, it appears that individuals who were relatively inactive at baseline can modify their recurrence risk by increasing their level of physical activity after diagnosis. Despite the highly suggestive observational data, a randomized control trial (RCT) is needed to unequivocally establish and better define this relationship.

Randomized controlled trials (RCTs) have been launched to examine the effects of physical activity on diabetes endpoints and heart disease endpoints but no studies are currently examining cancer disease recurrence endpoints. Thus we are testing the hypothesis that a meaningful and achievable increase in PA after adjuvant therapy for high risk stage II or III colon cancer will improve disease-free survival.

2.3 Biological Plausibility of Physical Activity and Colon Cancer Disease Outcomes

Several biological mechanisms have been hypothesized to explain the association between physical activity and colon cancer. Possible mechanisms are hyperinsulinemia, obesity, decreased gut transit time, change in prostaglandin ratio, lowered bile acid secretion and altered gut flora. Furthermore physical activity may affect cancer risk indirectly through other correlated or confounding factors like diet, smoking, alcohol consumption and lifestyle habits.

Body mass index is a known prognostic factor for colon cancer progression and relapse *[McTiernan 2007]* and will therefore be used as a stratification factor in this study. In this study, participants will be stratified based on a BMI of less than or equal to 27.5 or greater than 27.5 as this is roughly an equal separation as found in Courneya et al., *[Courneya 2003a]*, who evaluated the effect of exercise on QOL for participants who had recently resected colon cancer and were undergoing adjuvant chemotherapy. The mean BMI for participants in the exercise group was 27.4 and 27.8 in the control group.

2.4 Prevalence of Physical Activity in Colon Cancer Survivors

There are data demonstrating that colon cancer survivors experience significant declines in PA during adjuvant therapy that do not return to baseline even years after treatment *[Courneya 1997]*. Moreover, colon cancer survivors report among the lowest PA participation rates of any cancer survivor group in Canada although they are not significantly different from the general population matched for age, sex, income, and ethnicity *[Courneya 2008]*. These data suggest that there is significant room for improvement in the PA behavior of colon cancer survivors.

2.5 Physical Activity Behavior Change in Colon Cancer Patients

Long term PA adherence can be achieved. During the last decade, several large and well-designed randomized trials have demonstrated that PA can be increased substantially and maintained for at least one year or longer. The APPEAL trial *[McTiernan 2006]* demonstrated that previously sedentary men and women aged 45-75 years with colon polyps were able to increase PA to over 300 minutes per week for a one year period. The PATH trial *[Irwin 2003]* demonstrated that previously sedentary and overweight women aged 50-75 years were able to increase PA to over 175 minutes per week for a one year period. The DREW trial *[Church 2007]* demonstrated that previously sedentary, overweight or obese women aged 45-75 years were able to increase PA to over 190 minutes per week for a one year period. Finally, the ALPHA trial demonstrated that previously sedentary overweight women aged 50 to 75 years were able to increase their PA by over 20 MET hours/week (unpublished data).

2.6 Choice of Physical Activity Intervention

Based on the Meyerhardt data *[Meyerhardt 2006a; 2006b]* and current pubic health recommendations for the general population *[US Department of Health and Human Services 2008; Haskell 2007]* as well as cancer survivors *[Doyle 2006]*, in this study we will aim to increase physical activity by at least 10 MET hours/week. We will focus on recreational PA for several reasons. First, previous observational studies have shown that the amount of recreational PA is associated with colorectal and other cancer outcomes *[Meyerhardt 2006a; Holmes 2005]*. Second, behavior change interventions focus on changing recreational PA defined as recreation-time PA for which the person has a choice. Third, public health recommendations advise performing approximately 10 MET hours/week of recreational PA beyond activities of daily living *[US Department of Health and Human Services 2008; Health Canada 1998]*. Fourth, activities of daily living, including household, are not reliably measured using self-report. This study will capture all activity to document changes in other types of PA over the course of the study and will encourage enhancement of activities associated with daily living, but these will not be counted towards the target increase of 10 MET hours/week goal.

Our baseline assessment of PA will take place in the post-adjuvant therapy time period, rather than the pre-diagnosis period for several reasons. First, the majority of physical activity trials reported previously captured pre-diagnosis PA prospectively. As a result, they were not subject to the biases (for example recall bias) that would be present if this was captured retrospectively on this trial. For this trial, patients would be required to recall PA levels from pre-diagnosis PA levels after an intervening time period required for surgical resection, up to six months of chemotherapy and up to six months post-chemotherapy. As well, many patients may have been diagnosed after an extended period of experiencing multiple symptoms including anemia that potentially would have decreased PA prior to diagnosis. Finally an accurate measurement of patients' current PA is required in order to design a safe and effective physical activity program that can gradually increase their recreational PA by 10 MET hours/week. In an attempt to overcome these biases this trial will use post-chemotherapy PA as the baseline level. Patients will not be permitted to be registered to the trial for a minimum of two months and a maximum of six months after completing chemotherapy. It is anticipated that patients will have resumed their "normal" physical activity level by this time. Although it will not be used to determine eligibility, pre-diagnosis physical activity participation will also be captured for this study using the Leisure Time Exercise Questionnaire (LTEQ) in order to describe the study population.

Patients will be excluded from this trial who are currently meeting the public health guidelines, which advise approximately > 10 MET hours/week of recreational activity *[Health Canada 1998]*. Given that we will exclude these patients, the remaining patients who are assessed to be sedentary in their recreation time will be asked to increase their activity to at least 10 MET hours/week and those who are almost meeting current public health guidelines will be asked to increase their physical activity from 9 to at least 19 MET hours/week. This amount of PA is consistent with Health Canada, the US Department of Health and Human Services, and the American Cancer Society's recommendations that otherwise healthy cancer survivors should aim to obtain 150-300 minutes/week of moderate PA (at least brisk walking) or 75-150 minutes/week of vigorous PA (at least jogging) on at least 3 separate days per week (i.e. 10 to 20 MET hours/week) *[US Department of Health and Human Services 2008;Doyle 2006; Health Canada 1998]* in addition to usual daily-living activities.

In order to achieve this goal, patients in the intervention arm will receive an intensive behavioural support program based on the Theory of Planned Behaviour (TPB) *[Azjen 1991]* and modeled after the successful behaviour support program in the Diabetes Prevention Program *[Knowler 2002]* and the Look AHEAD trial in diabetics *[The Look AHEAD Research Group, 2007]*. The TPB proposes that intention (motivation) to perform a behaviour (e.g. physical activity), can be predicted from attitudes toward the behaviour, subjective norms, and perceived behavioural control *[Azjen 1991]*. It incorporates social learning theory, which proposes that human behaviour is acquired and maintained through the use of behavioural, cognitive and environmental systems and therefore is amenable to change through influence over motivation *[Bandura 1977]*. This willingness to change can also be modified by successful experiences, observation of other's achievements, by persuasion from credible sources, and with inferences drawn from a person's physiological state *[Froelicher 2000]*. The behaviour support program will be provided by Physical Activity Consultants and will occur in conjunction with supervised physical activity sessions.

Patients in both arms will be provided with general health education materials including nutritional and physical activity information. Patients in the control group will continue with routine follow-up as per local centre practice including regular physician visits, imaging, bloodwork, and colonoscopy.

2.7 Choice of Primary Endpoint

Recent evidence suggests that 3-year DFS is highly correlated with overall survival in patients with resected colon cancer *[Sargent 2005]*. Based on this analysis, most adjuvant trials in CRC are now designed with 3-year DFS as the primary end-point. Furthermore, this end-point has been deemed suitable for registration trials by the Food and Drug Administration. We define DFS as the time from randomization to the first event of either recurrent disease (local or distant), new primary or death from any cause. This includes development of second colon primary tumours and all other second primary tumours *[Punt 2007]*.

2.8 Correlative Studies

2.8.1 *Insulin-like Growth Factors and Colorectal Cancer*

Accumulating observational and experimental evidence has found an association between insulin resistance and colorectal neoplasia *[Gunter 2006]*. Insulin-like growth factor 1 (IGF-1) signaling stimulates proliferation and prolongs survival of cells propagated in tissue culture *[Pollak 2004]*. Colon cancer tissue has both insulin and IGF-1 receptors and elevated levels of these molecules may have mitogenic properties *[Samad 2005]*. Recent population studies have corroborated these laboratory findings, showing an association between plasma IGF-1 and IGF-binding protein (IGFBP) levels with risk of CRC. The syndrome of insulin resistance, characterized by increased insulin levels and obesity is also associated with increased risk of CRC and may involve similar mechanisms *[Pollak 2004]*. Although several biological mechanisms have been proposed to explain the association between physical activity and CRC, hyperinsulinaemia and elevated levels of IGF-1 have received the most attention *[Samad 2005]*. A cohort study of early-stage colorectal cancer patients has reported that the beneficial association of physical activity with colorectal cancer mortality may occur through interactions with IFGBP-3 *[Haydon 2006]*. Furthermore, there are data suggesting that IGF levels are correlated with quality of life in patients with advanced colorectal cancer *[Meyerhardt 2005]*. For this reason we will investigate the role of insulin and IGF-1 levels in serum as biomarkers. Our hypothesis is that elevated IGF-1 will have prognostic and predictive properties.

2.8.2 *Cytokines in Cancer and Relationship to Survival and Fatigue*

There is increasing clinical and experimental evidence that cytokines, and their role in the inflammatory response, can lead to cancer development *[Tann 2007; deVisser 2006; Dagleish 2002; O'Byrne 2001]*, that elevated plasma concentrations of cytokines are predictive for recurrence and survival in a variety of cancers *[Tann 2007; deVisser 2006; Galon 2006; Andrews 2002; Dalgleish 2002; O'Byrne 2001]*, and are likely aetiological factors in the development of cancer associated fatigue *[Meyers 2005; Pusztai 2004; Mantovani 2002;Vener 2000]*. There are no published longitudinal studies of cytokine levels following longer treatment of patients with solid tumours. In ongoing studies, Vardy et al. *[Vardy 2007]* have found elevated cytokine levels in breast and CRC survivors compared with healthy volunteers, and a trend for higher serum cytokine levels to be associated with cognitive impairment and sustained fatigue.

Evidence has emerged that contracting skeletal muscles secrete IGF-1 and -2, IGF binding proteins, as well as a number of cytokines, including IL-6,-2,-4,-8,-15,TNFα, IFNγ and myostatin *[Pedersen, 2007b; Pedersen 2001]*. Cytokines produced by muscle have been termed 'myokines' *[Pedersen, 2001]*. Skeletal muscle-derived IL-6 is thought to be an "exercise factor," mediating metabolic and physiologic responses in other organs *[Pedersen 2007b]*, including whole body glucose homeostasis, glycogen storage and lipid oxidation *[Pedersen 2005]*. The levels of IL-6 released from skeletal muscle into the circulation, are dependent on the duration, mode and intensity of the exercise *[Pedersen 2007b]*. Although IL-6 is generally regarded as a pro-inflammatory cytokine it also has anti-inflammatory properties and suppresses TNFα production *[Pedersen 2007b; Pedersen, 2007a]*. It is thought this may protect against TNF-induced insulin resistance *[Pedersen 2007b; Pedersen 2005]*. Dekker et al have demonstrated decreased fasting IL-6 levels in previously sedentary patients after a 12-week intervention without change in body weight *[Dekker 2007]*. In summary, it appears that PA stimulates the production and release of cytokines but longer term has an anti-inflammatory response, which then influences metabolism and modifies the production of cytokines in tissues and organs. We hypothesize that those patients who have higher PA levels will have lower levels of proinflammatory cytokines, decreased fatigue and improved DFS. Cytokines we will be measuring are IL-1β, IL-6, IL-2, IL-4, IL-8, IL-10, IL-12, TNF-α, IFN-γ, and GM-CSF and C-reactive protein.

2.9 Supportive Care Outcomes of Physical Activity in Colon Cancer Patients

A burgeoning literature has examined the effects of PA on supportive care outcomes in cancer survivors including physical fitness, physical functioning, fatigue, quality of life, and others. Supportive care benefits from PA become critical in assessing the societal value of the intervention if the intervention shows no significant impact on disease-related outcomes. Previous systematic reviews *[Luctkar-Flue 2007; Monninkhof 2007; Jones 2006; Hewitt 2005; Knols 2005; Courneya 2003]*; and a meta-analysis *[Schmitz 2005]* have concluded that PA interventions during and soon after adjuvant cancer therapies often result in meaningful and reliable improvements in several important supportive care outcomes. These benefits include observed changes in physiologic measures, objective performance indicators, self-reported functioning and symptoms, psychological well-being, and overall QOL. Reviews further suggest that cancer patients may benefit from PA both during and after treatment, although benefits appear stronger in the post-adjuvant setting *[Knols 2005; Courneya 2003b]*.

Despite the mounting evidence of diverse improvements in supportive care outcomes, reviews have also concluded that the specific beneficial effects of PA may vary with stage of disease, the nature of the medical treatment, patient lifestyle, and other moderating factors. Moreover, some authors have suggested that future RCTs should use larger samples with appropriate comparison groups (to control for an attention-placebo effect), should pay greater attention to issues of motivation and adherence of patients' participating in PA programs, and should examine mechanisms for changes in QOL.

Few studies in the PA literature have focused on colon cancer survivors *[Knols 2005]*, and only one small RCT focused on colorectal cancer patients is reported *[Courneya 2003b]*. Therefore, in this study, supportive care outcomes will focus on patient reported outcomes such as QOL, fatigue, anxiety and depression, sleep, and additional measures. Each of these will be discussed briefly.

2.9.1 *Quality of Life (QOL)*

Quality of Life is relevant to cancer patients as it measures, from the patient perspective, the symptom-related and functional benefits from the PA intervention that can not be ascertained from data regarding toxicity or adverse events *[Paul 1991]*. Systematic overviews have extensively described the potential impact of PA on QOL, both in the setting of interventions during treatment and interventions initiated after treatment *[Knols 2005; Courneya 2003b]*. While the majority of studies have been done in the breast cancer setting, others studies have suggested that the benefits of PA on QOL are seen in other cancer settings *[Knols 2005; Courneya 2003b]*, and in older cancer patients *[Luctkar-Flue 2007]*.

We hypothesize that a program designed to increase PA will result in improved QOL scores in comparison to the control arm. The null hypothesis is that average change scores (tested by repeated measures statistics), and, that the proportion of patients reporting improved QOL scores (minimal clinical important difference), are not different between arms *[Osoba 2005]*.

In this study, QOL will be measured by all centres (Australia and Canada). Two measures of overall QOL will be used, one generic and one cancer-specific: the SF-36 and the FACT-F (also known as the FACIT-F). The SF-36 is a widely used and well validated measure *[Wyrwich 1999]*. It contains eight subscales or domains, which are summarized into two global scores: the physical and mental component summary (PCS and MCS) scores. The results of the two summary scores provide a global indicator of patients' quality of life. The SF-36 is scored from 0 to 100, with a higher number representing a better or favorable quality of life. The PCS and MCS are normalized so that the mean score for a representative sample of the US population is 50, with a standard deviation (SD) of 10. The physical functioning sub-scale of the SF-36 is a commonly utilized instrument in previous studies of PA in cancer patients *[Knols 2005]* and will be the primary measure of the impact of PA on physical functioning in this study. The use of the SF-36 will, thus, allow comparison of QOL scores of patients in this study between study arms (the primary QOL hypothesis), to other comparable clinical trials, and to established population norms *[Wyrwich 1999]*. Finally, SF-36 scores will allow the estimation of clinical utilities needed for the cost-utility analyses proposed below.

In addition to the SF-36, QOL will be assessed by the Functional Assessment of Cancer Therapy - Fatigue *[Ward 1999; Yellen 1997]*. The general FACT instrument provides measures on five subscales: physical well-being; social/family well-being; emotional well-being; and functional well-being. Patients are asked to rate how they have felt over the past seven days, on a scale of 0 ('not at all') to 4 ('very much'). Individual scores are compiled according to a standardized algorithm, so that each subscale is scored and then summed to provide an overall quality of life score. Higher scores indicate better quality of life. Each subscale has a maximum score of 28, except for the emotional well-being subscale, which has a maximum score of 24. The FACT has been shown to be a valid and reliable measure, and sensitive to changes in functional status. A difference between-group scores on the FACT within the range of 5–8 points, accounting for differences across samples and settings, is defined as being clinically important *[Yost 2005]*. These data will provide a more textured, cancer-specific estimate of global QOL and functional status in several domains that will be more sensitive to change in this cancer population than will be the general SF-36 modules. The focus of the analysis of FACT and FACT-F (FACIT-F) data will be QOL scores in domains other than physical functioning. Moreover, the 13 item Fatigue Scale will provide a valid and sensitive measure of fatigue with minimal redundancy beyond the core instrument.

2.9.2 *Fatigue*

Fatigue is one of the most common and most distressing patient-reported symptoms associated with cancer and with treatment of cancer *[Luctkar-Flude 2007; Hamilton 2001]*. Previous studies have shown a significant impact of cancer chemotherapy on patient fatigue scores, although few studies have focused on patients with colorectal cancer. In a previously published controlled trial in patients with colorectal cancer (68% of whom received chemotherapy), evaluation of FACT fatigue scores revealed clinically significant prevalence of fatigue (average scores 11 [scale range 0-58, high scores better] with std. deviation of 10) *[Courneya 2003a]*. Like overall QOL, as summarized above, studies evaluating the affect of PA on fatigue have demonstrated mixed findings.

We hypothesize that a PA program designed to increase PA will result in reduced burdens of fatigue in comparison with the control arm. The null hypothesis is that average fatigue change scores (tested by repeated measures statistics), and, that the proportion of patients reporting improved fatigue scores (minimal clinical important difference), are not different between arms *[Osoba 2005]*.

As noted above, the FACT (also called FACIT) Fatigue Scale will be used to explicitly explore patient- related fatigue. The 13 item instrument is well validated in many cancer settings; scores range from 0-52 with higher scores representing less fatigue. On this study a standard deviation of 10 is anticipated. In a study using both distribution-based and anchor-based estimates of minimal clinically important difference (MCID or change), a change score of 3 on the FACIT-F estimates the MCID.

2.9.3 *Sleep*

A patient-reported subjective assessment of sleep quality is included as a secondary endpoint for a number of reasons. First, the prevalence of sleep difficulties in cancer patients following completion of treatment is clinically relevant. Second, since the main secondary endpoint in this study is fatigue, information regarding sleep quality will be important to explicate the fatigue scores at baseline and the effect of the intervention; the measurements of fatigue and QOL will assess the extent to which fatigue causes daytime sleepiness, but they do not measure to what extent poor sleep quality might contribute to fatigue.

The Pittsburgh Sleep Quality Index (PSQI) will be used to measure sleep quality *[Buysee 1989]*. The PSQI is a reliable, validated and standardized measure of sleep quality, designed to discriminate between "good" and "poor" sleepers, and to provide an index that is easy for patients to complete and for clinical researchers to interpret. It consists of 19 self-rated questions grouped into seven component scores, each (equally weighted) on a 0-3 scale. The summed score (0-21) represents the global PSQI score (higher scores indicate poor sleep quality). In the validation study (general population), scores ranged from 0-20 with a mean of 7.4 and a SD of 5.1. The null hypothesis is that average global PSQI change scores (tested by repeated measures statistics), and, that the proportion of patients reporting improved fatigue scores, are not different between arms.

2.9.4 *Psychological Distress (Anxiety and Depression)*

Lynch and colleagues have recently reviewed the prevalence of psychological distress of colorectal cancer survivors *[Lynch 2008]*. Prevalence estimates of psychological distress range from 12% to 37%. In a large Australian prospective survey psychological distress and predictive factors for distress were assessed in 1822 colorectal cancer patients *[Lynch 2008]*. The prevalence of global psychological distress was low: 8.3% and 6.7% at 6 and 12 months post-diagnosis, respectively. However, patients with medical co-morbidities (OR=1.64) or high subjective cancer threat appraisal (OR=0.85 for low threat appraisal) had significantly higher levels of distress at 12 months post-diagnosis. Taken together, these data suggest that psychological distress may be present in many patients eligible for enrolment to this protocol. Given existing evidence of a potential beneficial impact of physical activity on psychological distress, this is an important secondary outcome in this study.

The Hospital Anxiety and Depression Scale (HADS) will be used to measure psychological distress. The HADS has shown to be reliable and valid *[Zigmord 1983]*, and has been demonstrated to be more sensitive in detecting depression in patients with colorectal cancer than the emotional functioning QL domain of the EORTC QLQ-C30. The patient requirements for completing the HADS make it feasible; the instrument consists of two subscales HADS-A (anxiety) and HADS-D (depression), each consisting of seven items scored from 0 (no problems) to 3 (maximum distress). Standard scoring algorithm results in a sum score ranging from 0 to 21 for both anxiety and depression *[Zigmord 1983]*. In a recent evaluation of HADS scores in survivors with colorectal cancer, 110 patients with no evidence of recurrent disease in follow-up reported HADS-A average score (SD) of 2.9 (3.0), HADS-D of 3.5 (3.0), and HADS-T of 6.4 (5.5). The null hypothesis is that average HADS-T change scores (tested by repeated measures statistics), and, that the proportion of patients reporting improved HADS-T scores (minimal clinical important difference), are not different between arms. A change of 0.5 standard deviation of the HADS scores will be used as a measure of clinically significant difference.

2.10 Physical Activity Behaviour and Adherence Instruments

2.10.1 *Social-Cognitive Determinants of Exercise*

Baseline social-cognitive factors will be examined using the Social-Cognitive Determinants of Exercise Measure to determine if they predict adherence to a PA program. Adherence will be defined as achieving 80% of the PA goal (equal to an increase of 8 MET hours/week from baseline). This measure will also examine how social cognitive parameters change over the course of the study.

The Social-Cognitive Determinants of Exercise Measure assesses social-cognitive factors from the theory of planned behaviour perspective by assessing standard measures of attitude, subjective norm, perceived behavioral control (PBC), and intention *[Ajzen 1991]*. This is an 8-item self-report questionnaire. Patients rate each item on a 5-point scale from 1 (not at all/none) to 5 (extremely/lots). The instrumental attitude item asks about the benefits of the exercise, affective attitude item asks about the enjoyment of the exercise, the subjective norm asks about the support they get for the exercise, the perceived behavioural control items asks about the difficulty of doing the exercise, the self-efficacy item asks about their confidence in doing the exercise, the intention item asks how motivated the patients are to do the exercise, the planning item asks how detailed a plan they have for the exercise, and the environmental item asks how many opportunities they have for exercise.

These items have been used extensively with cancer survivors and have been shown to be highly reliable and to predict exercise behaviour in cross-sectional and prospective studies *[Courneya 2008; Karvinen 2007a; Karvinen 2007b]* and to partially mediate the effects of PA behaviour change interventions in cancer survivors *[Vallance 2008; Jones 2005]*.

We hypothesize that patients with more positive attitudes, subjective norms, PBC and intentions will have higher adherence rates than those that do not. The null hypothesis in this trial is that there will be no difference.

Our second hypothesis is that patients in the intervention arm will have more positive attitudes, subjective norms, PBC and intentions over time when compared to the control arm. The null hypothesis is that there will be no difference between the two arms.

2.10.2 *Total Physical Activity Questionnaire (TPAQ)*

Our primary measure of PA adherence will be self-reported recreational PA at baseline and every six to 12 months using a slight modification of the Past Year Total Physical Activity Questionnaire *[PYTPAQ; Friedenreich 1998; Friedenreich 2006]*. The PYTPAQ has been shown to have acceptable reliability and validity for measurement of past-year physical activity that is comparable to that of similar questionnaires *[Friedenreich 2006]*.

At baseline and at all follow up assessments, the PYTPAQ will be modified to refer to the month prior to its administration. This TPAQ has an open table format, rather than specific questions, and is separated into three sections to assess occupational (including transportation to and from work), household and recreational activity during that reporting period. It includes a description of the activity type as well as the frequency (months per year, days per week), duration (hours per day) and perceived intensity of the activity. Definitions of each level of intensity (1=sedentary, 2=light, 3=moderate and 4=heavy) are provided with examples in the questionnaire. Respondents are required to report household activities that involve at least standing and all types of recreational and occupational activities. A list of possible recreational activities is also given at the end of the questionnaire as a prompt for completion of this section.

The physical activity measurements include the number of hours per week spent in each type of activity (i.e. occupational, household, recreational) and total physical activity (i.e. the sum of the three types of activity). The total hours per week spent at each activity are multiplied by the estimated metabolic cost of each activity that is assigned to that activity (the MET-value) as determined from the Compendium of Physical Activities to produce a score of MET hours/week *[Ainsworth, 2000; Ainsworth 1993]*. The results are estimates of average MET hours/week for each type of activity and then total activity (estimated as the sum of the three types of activity). The estimates are the average MET hours/week for the time period under study (i.e. the past month).

While all components of the TPAQ will be completed, the delta of 10 MET hours/week will be calculated on the patients' responses in the recreational activity section of the TPAQ only.

2.10.3 *Physical Activity Logs*

Each week, patients on the intervention arm will be asked to complete a PA log for both the supervised and unsupervised activity in which they are involved. The logs include the date of the week, type of activity, duration of PA, rating of perceived exertion and heart rate achieved. If more than one activity is done in a given day, a separate row is used to record each individual activity. One sheet per week is completed by the patient and the logs are reviewed with the Physical Activity Consultant (PAC) at each follow up session, via face-to-face meeting or telephone call. The physical activity logs will be used as a motivating intervention tool for PACs and patients and will not be captured as data.

2.11 Objective Testing

2.11.1 *Submaximal Exercise Test*

A submaximal exercise test will be used to determine eligibility. The exercise testing will be conducted by a qualified exercise specialist. The Balke treadmill protocol *[American College of Sports Medicine 2006]* will be used to estimate maximum oxygen consumption from submaximal exercise intensities. Prior to the modified Balke treadmill test, patients must register to the study and have completed their rPAR-Q and have it signed by their oncologist. Throughout the test, patients' heart rate, blood pressure and rate of perceived exertion will be monitored. After each three minutes on the treadmill, the speed and/or elevation of the treadmill will be increased. Each three minute period is referred to as a stage and patients must complete at least two stages of the test in order to be considered eligible to be randomized to CO.21. The exercise test is complete when the patient has finished the stage during which they reach 85% of their maximum heart rate.

In addition to being done prior to randomization to assess eligibility and to determine baseline fitness level, the submaximal exercise test will be repeated in all patients at 6, 12, 24 and 36 months post-randomization in order to monitor changes in cardiovascular fitness over the course of the three year intervention.

2.11.2 *Seniors Fitness Test (SFT)*

The SFT is a standardized tool for assessing the functional fitness of older adults *[Rikli 1999]*. Its purpose is to measure basic physical fitness parameters associated with functional tasks and activities that are significant in the everyday living of older adults; it is comprised of six measures, 8-Foot Up-and-Go, 30-Second Chair Stand, Arm Curl, 6-Minute Walk, Chair Sit-and-Reach, and the Back Scratch. The results of the six measures are aimed to design individualized, targeted PA programs for patients. The SFT has been validated in community-living older adults *[Rikli 1999]*, and has formed the basis of PA programs developed specifically for the frail older adult population in the home *[Wieckowski 2006]*. Patients will complete the SFT prior to randomization to obtain a baseline score and then again at 6, 12, 24 and 36 months after randomization to measure change in function over the course of the three year intervention period.

2.12 Instruments and Measures to Assess Eligibility

2.12.1 *Physical Activity Readiness Questionnaire (rPAR-Q)*

The rPAR-Q is a screening questionnaire used to determine participant readiness to participate in PA. While the instrument has been validated for people aged 15 to 69, it will be used for participants of any age who are being considered for this study. It is a seven item self-report questionnaire. Patients answer 'yes' or 'no' to each of the seven items related to possible indicators of being ready or not ready for starting regular PA. If all seven questions are answered in the negative, there is reasonable certainty that a patient may participate in the activities associated with this study. If the patient answers 'yes' to one or more questions, a physician must confirm that the patient can safely become more physically active.

The rPAR-Q will be used in this trial, in conjunction with physician judgment to determine the eligibility of potential patients to participate in this study. If the patient answers 'yes' to any of the seven items, it will be up to investigator discretion to determine their medical suitability for participation in this trial.

2.12.2 *Leisure Time Exercise Questionnaire (LTEQ)*

Prospective patients will be asked to recall their PA for a typical week in the month prior to their registration using a modified version of the Leisure Time Exercise Questionnaire *[Godin 1985]*. The LTEQ contains four questions that assess the average frequency of resistance (e.g. lifting weights), light (e.g. easy walking, bowling), moderate (e.g. fast walking, folk dancing), and vigorous (e.g. running, cross-country skiing) PA during free time in a typical week in the past month. We modified the LTEQ to include the average duration of PA. An independent evaluation of the LTEQ found its reliability and validity to compare favorably to nine other self-report measures of PA based on various criteria including test-retest scores, objective activity monitors, and fitness indices *[Jacobs 1993]*.

Total minutes of vigorous PA and moderate to vigorous PA per week will be calculated. When calculating total minutes of moderate to vigorous activity per week, vigorous minutes must be double weighted. Patients will then be categorized into meeting or not meeting current guidelines for PA (i.e. $\geq$ 75 minutes of vigorous or $\geq$ 150 minutes of moderate plus vigorous physical activity per week). Patients already meeting the public health guidelines will be excluded from the trial.

At baseline, prospective patients will also be asked to recall their PA for a typical week in the 6 months preceding their diagnosis of colon cancer using the LTEQ. This information will not be used to determine eligibility of potential patients for the study but will be used to describe baseline characteristics of patients involved in the trial.

2.13 Health Economics

Health economics is important to cancer patients, health care providers, policy makers, and society, as it evaluates the value of an intervention. Value is determined by examining the costs associated with an intervention and its management and considers the benefits (including prolongation of survival and quality of life) of the intervention and its management. Determining the economic value is of particular relevance in this study as PA programs have not traditionally been publicly funded as a health intervention. If this study shows superior health outcomes, patients themselves, cancer care providers, and privately and/or publicly funded health systems will need to consider funding this intervention.

The economic analyses will compare between the randomized groups the incremental costs associated with providing a supervised PA program to patients with colon cancer including both cost-effectiveness and cost-utility. Economic evaluations will be assessed from the Ministry of Health perspective and selective societal aspects will be measured as well.

2.13.1 *Cost Effectiveness and Cost Utility Analysis*

The health economic evaluation will be completed using existing case report forms and source documentation for each subject in Canada, and Australia. Healthcare and PA-related resource utilization related to the study intervention will be documented including PAC involvement and exercise facility and equipment use, supportive care medication, laboratory tests, imaging studies, radiotherapy, transfusions, hospitalization, and outpatient care, including physician, emergency room and home care visits will be documented. To capture the use of resources associated with PA and outpatient care, additional resource utilization case report forms will be used. Utility assessments and resource utilization will be measured at baseline and at predetermined intervals on both arms of the study. Costs will be presented in Canadian currency in 2010 dollars. Unit costs will be applied to resource utilization in order to determine the cost per resource. Unit costs will be obtained from standard sources including provincial sources, literature and others.

Effectiveness will be presented as overall survival (Life Years, LYs) and quality adjusted survival. As part of the economic evaluation patient preferences, or utilities, will be measured using the SF-6D which is derived from SF-36 scoring *[Braizer 2002]*. The SF-6D index uses a 6-domain classification of health states for the purposes of economic evaluation in order to estimate quality-adjusted life years (QALYs). This validated instrument has been used in population surveys and clinical trial settings.

The primary economic hypothesis in this trial is that the patients allocated to a structured PA program will have prolonged durations of disease control that results from resource utilization that will be considered to be of high value (i.e. cost-effective). Furthermore, we hypothesize that PA will be associated with superior patient perceptions of QOL, for which value will be derived (i.e. cost-utilities).

2.13.2 *Work Productivity and Activity Impairment Scale (WPAI)*

The WPAI was created to quantify patient-reported assessments of work absenteeism, presenteeism and impairment in performing daily activities *[Reilly Associates 2008; Reilly 1993]*. The instrument exists in a form that assesses general health (WPAI:GH) and has also been adapted to assess specific heath problems. The WPAI consists of six questions that were developed through a process of literature review, patient interviews and cognitive debriefing of subjects after both interviewer-administration and self-administration. Evaluations of its construct validity and reproducibility have been reported *[Reilly 1993]*. The questions included in the instrument deal with presence or absence from work and impairment of both work and non-work related activities. The questionnaire will be self-administered at baseline and at six month intervals for three years and then yearly for years four and five.

2.14 Outcomes and Significance

Physical activity has been associated with many health benefits. As yet there is no conclusive evidence that PA will decrease the likelihood of colon cancer recurrence. Our study has the potential to reliably answer this question, and therefore we believe it is a valuable study whether the final outcome is positive or negative. In addition, it will obtain important data about the impact of PA on patient's physical functioning, body composition, QOL, mood, cytokines and the insulin pathway, and their influence on prognosis.

One of the greatest challenges to implement PA programs has been ensuring adequate support and resources to promote compliance with PA. Cancer patients are (in general) a sedentary but motivated population. Previous work has suggested good compliance and a willingness in this sub-population to pursue lifestyle modification(s) following a diagnosis of cancer. If a large RCT was able to demonstrate a significant benefit in DFS this would not only provide impetus to patients to participate in PA and oncologists to promote PA, but could potentially lead to a change in practice and policy in which patients meet with a fitness consultant to design a personalized PA regimen upon completion of adjuvant therapy.

Furthermore, in the era of molecular targeted anti-cancer therapy, funding of new and expensive agents is becoming increasingly difficult. Should a physical activity intervention be found to have a significant clinical benefit in colon cancer this could be a very cost-effective therapy with many other (i.e. non-cancer) health benefits. Finally, the magnitude of association seen for physical activity in the observational studies compares very favourably to the benefit from the use of adjuvant chemotherapy but could involve lower toxicity and cost. Importantly, the cost-effectiveness of this physical activity intervention will be evaluated prospectively as part of this clinical trial.

3.0 TRIAL DESIGN

This is a multi-national, multi-centre, randomized phase III study comparing patients allocated to a physical activity program (designed to induce increased physical activity participation) plus general health education materials arm to patients allocated to a general health education materials only arm for patients with high risk stage II/III colon cancer.

3.1 Stratification

Patients will be stratified by:
- Disease stage (high risk II vs III)
- Centre
- BMI ($\leq$ 27.5 vs > 27.5)
- ECOG performance status(0 vs 1)

3.2 Randomization

Patients will be randomized to a planned sample size of 962 to receive one of the following treatments:
- Physical activity program plus general health education materials (intervention arm)
- General health education materials (control arm)

Arm	Intervention	Duration
1	General health education materials	Provided within 14 days of randomization by cancer centre staff
	Physical activity program	3 phases Phase 1: Intensive intervention for 6 months Phase 2: Reduced intervention for months 6-12 Phase 3: Minimal intervention for months 12-36
2	General health education materials	Provided within 14 days of randomization by cancer centre staff

3.3 Sites and Collaborations

This proposed study will be led by the Canadian Cancer Trials Group and will include collaboration with the Australian Survivorship Research Group (SuRG).

Previous colorectal cancer research collaboration has shown patient population and clinical practice to be very similar between Canada and Australia. Although it is not expected that there will be differences by country, the trial design will stratify for this variable by centre. The formal assessments and questionnaires will be identical between all sites and general health education materials provided will be country-specific and identical for all patients in a given country. In order to obtain standardization, at a national level, all PACs will undergo the same training and follow up to ensure consistency. The PA program guidelines will be the same for all participating patients.

The development and oversight of the CO.21 trial is provided by the Trial Steering Committee. The Steering Committee includes the Study Chairs, Design and Conduct Committee, Senior Investigator, Coordinators for Quality of Life, Health Economics and Correlative Sciences, the Senior Biostatistician and the Study Coordinator. Because of the complexities of delivering a lifestyle intervention as well as the uniqueness of this study, four working groups were established to provide expertise in protocol development and trial implementation in four key areas: PA, PROs, health economics and correlative sciences. Each of these working groups is chaired by a member of the Trial Steering Committee with expertise in the respective fields.

The Physical Activity Working Group (PAWG) will provide oversight to the PA and behaviour support components of this study. This working group will be led by the Study Chair and will include other individuals with expertise in implementing PA programs in similar research settings. The PAWG will play a vital role in this study including leading the development of the PA and behaviour support program as well as the study materials to be provided to patients and PACs, selection of PA-related instruments for screening and follow-up, training and monitoring of PACs and selection of appropriate centres for study participation. In order to assist with standardization of the program across centres, this working group will also monitor compliance with the PA program within each participating centre.

Because of its complexity and uniqueness, the number of centres allowed to participate on this trial will initially be limited and subsequent centre activation will occur according to a systematic process. Initially 5-9 Canadian centres that have been identified based on their commitment and available personnel, facilities and previous experience successfully implementing PA trials, will be approached to participate in the study. The PAWG and Trial Steering Committee will closely monitor study implementation at these centres to ensure standardization of intervention delivery and exercise testing and to identify and problem-solve any logistical or protocol-related issues that might arise. Once the PAWG and Trial Steering Committee are confident of the service delivery and protocol implementation the study will be expanded to other sites.

To participate in the CHALLENGE trial, all centres will be judged on a number of criteria including their enthusiasm for the study, ability to recruit patients, access to a qualified PAC, and appropriate infrastructure to support the PA. Prior to initiation of a site, a pre-study site evaluation will be completed by PAWG and/or Trial Steering Committee members to ensure the site meets all of the essential criteria for participation. Each participating centre will be evaluated after allocation of 5 patients to the intervention arm and these patients have completed six months of the structured PA program. It is expected that these patients will have achieved a mean increase in PA from baseline of $\geq$ 8 MET hours/week. Centres that do not achieve an increase in PA of $\geq$ 5 MET hours/week will receive extra assistance from the PAWG including problem solving and access to tool box resources. This assistance will be provided for the duration of the next reporting period (six months). If the centre does not meet the change of at least 5 MET hours/week compared to the control arm at the next reporting period the centre will not be allowed further recruitment.

3.4 Inclusion of Women and Minorities

There are no exclusions based on gender, race or ethnicity in this trial. Recruitment to CCTG trials for disease sites that involve both males and females has been approximately in proportion to the gender incidence. Insufficient data has been collected to test a similar relationship for racial/ethnic groups. This study, however, will be presented to patients through the major cancer-treatment institutions of the Canadian provinces and internationally, to which persons of both genders and all racial/ethnic groups have equal access. The intention, therefore, is to recruit patients from each gender and from racial/ethnic groups in close approximation to the incidence of the disease in these groups. An analysis of the intervention effect on subgroups will be made, recognizing the limited statistical power of such testing.

4.0 STUDY POPULATION

Medically fit colon cancer patients (high-risk stage II or stage III) who have received their last dose of adjuvant chemotherapy within the previous 60 – 180 days. Patients are permitted to have participated in other trials evaluating adjuvant chemotherapy providing that the tested chemotherapy meets the criteria described in 4.1.2 and 4.1.3. This group has been identified as having a high risk of disease recurrence or death, being most likely to adhere to the intervention, and for whom the intervention is safe.

Patients meeting all eligibility and ineligibility criteria listed in Sections 4.1 and 4.2 can be registered onto the CO.21 study.

Registered patients must then successfully complete a baseline exercise assessment (see Section 4.3.1 and Appendix XII). Those who satisfy the eligibility criteria related to this assessment as well as the other investigations (Section 4.3) may then be randomized.

4.1 Eligibility Criteria for Registration

There will be NO EXCEPTIONS to eligibility requirements at the time of registration. Questions about eligibility criteria should be addressed PRIOR to calling for registration.

The eligibility criteria for this study have been carefully considered. Eligibility criteria are standards used to ensure that patients who enter this study are medically appropriate candidates for the intervention. For the safety of the patients, as well as to ensure that the results of this study can be useful for making treatment decisions regarding other patients with similar diseases, it is important that no exceptions be made to these criteria for admission to the study.

Patients must fulfill all of the following criteria to be eligible for admission to the study:

4.1.1 Completely resected, histologically-documented, high-risk stage II or III adenocarcinoma of the colon.

High Risk Stage II disease must include one of the following:
- T4 lesions
- Less than 12 sampled lymph nodes
- Poorly differentiated histology

Stage III disease is defined as having at least one pathologically confirmed positive lymph node or one pathologically confirmed positive tumour deposit.

Synchronous primary colon cancer is eligible. Staging classification for the intent of this protocol will be based on the highest primary tumour.

4.1.2 Adjuvant chemotherapy treatment for colon cancer with a 5-flourouracil- based regimen received with an intent to provide a complete course of treatment. While one current standard is 24 weeks of treatment, patients who are pre-planned to receive a shorter duration of chemotherapy, including as part of a research study (for example, CRC.6) will also be permitted. The actual treatment received may be less than 24 weeks; participants must have received a minimum of one treatment cycle.

4.1.3 Chemotherapy must have been completed (i.e. last dose received) a minimum of 60 days and a maximum of 180 days prior to registration.

4.1.4 Age of at least 18 years.

4.1.5 Completion of the rParQ within 14 days of registration.

If responses to any rParQ items are 'yes', these items have been discussed with the investigator and the investigator has confirmed that the patient is suitable for administration of exercise testing and for participation in a physical activity program.

4.1.6 ECOG performance status 0 or 1. (see Appendix III)

4.1.7 Adequate hematological, renal and hepatic functions, as defined by the following required laboratory values, obtained within 49 days of registration:

Absolute granulocyte count (AGC)	$\geq$ 1.0 x 10^9/L (1,000 cells/mm^3)
Platelet count	$\geq$ 100 x10^9/L (100,000/mm^3)
Hemoglobin	$\geq$ 100 g/L
Serum creatinine	$\leq$ 1.5 x UNL
Total bilirubin*	$\leq$ 1.5 x UNL
Alkaline phosphatase	< 2.5 x UNL
ALT (SGPT)	< 2 times the upper limit of normal
Carcinoembryonic antigen (CEA)	$\leq$ 5ug/L

* Total bilirubin values of > 1.5 x ULN will NOT make a patient ineligible if the cause of the hyperbilirubinemia is believed to be Gilbert's Syndrome

When laboratory testing has been performed on multiple dates within 49 days of registration, the most recently obtained laboratory tests must be applied to this criterion. Hemoglobin values must be obtained at least 6 weeks after a previous blood transfusion or administration of an erythropoietic stimulating agent.

4.1.8 Completion of chest x-ray or CT, and CT, MRI or ultrasound of abdomen within 60 days of registration; these imaging tests must not show evidence of metastatic or locally-recurrent colon cancer.

4.1.9 Current physical activity levels that do not meet the recommended guidelines ($\geq$ 150 minutes of moderate-to-vigorous or $\geq$ 75 minutes of vigorous physical activity/week) as calculated using the moderate and vigorous components of the LTEQ for physical activity in the month prior to administration (LTEQ must be completed within 14 days of registration).

4.1.10 Completion of the LTEQ within 14 days of registration to capture pre-diagnosis physical activity participation.

4.1.11 Ability (i.e. sufficiently fluent) and willingness to effectively communicate with the Physical Activity Consultant affiliated with the originating cancer centre.

4.1.12 Ability (i.e. sufficiently fluent) and willingness to complete the patient-reported outcome questionnaires, social determinants of exercise measurement, health economics and physical activity questionnaires and logs. All forms will be provided in English and French.

4.1.13 Provision of informed consent must be obtained according to local Institutional and/or University Human Experimentation Committee requirements. It will be the responsibility of the local participating investigators to obtain the necessary local clearance, and to indicate in writing to the CCTG Study Coordinator that such clearance has been obtained, before the trial can commence in that centre. Because of differing requirements, a standard consent form for the trial will not be provided but a sample form is provided. A copy of the initial full board REB approval and approved consent form must be sent to the central office. The patient must sign the consent form prior to registration and prior to exercise testing. Please note that the consent form for this study must contain a statement which gives permission for the CCTG and monitoring agencies to review patient records (see Section 15.0 for further details).

4.1.14 Accessibility for treatment and follow-up. Patients registered on this trial must receive the intervention and be followed at the participating centre (this includes its affiliated physical activity partner). Investigators must assure themselves the patients randomized on this trial will be available for complete documentation of the treatment, adverse events, and follow-up.

4.2 Ineligibility Criteria for Registration

Patients who fulfill any of the following criteria are not eligible for admission to the study:

4.2.1 Significant co-morbid conditions precluding participation in a physical activity program as determined by the investigator.

4.2.2 Loco-regional or distant metastatic disease at the time of registration.

4.2.3 Unlikeliness to participate in a physical activity program, as assessed by the investigator.

4.2.4 History of other malignancies, except: adequately treated non-melanoma skin cancer, curatively treated in-situ cancer of the cervix, or other solid tumours, Hodgkin's lymphoma or non Hodgkin's lymphoma curatively treated with no evidence of disease for > 5 years.

4.2.5 Treatment with any medications deemed by the investigator as likely to preclude participation in a physical activity program.

4.2.6 Current treatment with additional chemotherapy or radiation.

4.2.7 Inability to complete the baseline exercise test done prior to randomization.

4.2.8 Participants who are pregnant or planning to become pregnant within the next three years.

4.2.9 Prior radiation therapy as a component of treatment for primary tumour.

4.2.10 Participants with rectal cancer as determined by the investigator.

4.3 Eligibility Criteria for Randomization

Patients must fulfill all of the following criteria within 28 days after registration and within 28 days prior to randomization to be eligible for admission to the study:

4.3.1 Complete one of the following: (a) at least 2 stages of the submaximal exercise test with an acceptable heart rate and blood pressure response as defined in Appendix XII or (b) the 6 minute walk test with an acceptable heart rate and blood pressure response.

4.3.2 Completion of anthropometric testing, Seniors' Fitness Test if possible, Patient Reported Outcomes, Social-Cognitive Determinants of Exercise, and Health Economics questionnaires.

4.3.3 Completion of the TPAQ. While the patient is required to complete the TPAQ, the MET hours/week calculated by the TPAQ will not render a patient ineligible for the study.

4.3.4 Collection of mandatory blood samples for correlative studies.*

4.3.5 Fasting glucose sample collected at time of mandatory blood sample.*

4.3.6 In accordance with CCTG policy, protocol treatment is to begin within 14 days of patient randomization.

* Mandatory blood samples for correlative studies and fasting glucose sample may be taken PRIOR to (within 14 days), or AFTER registration – timing is at the discretion of the centre however both of these samples must be taken at the SAME time and only need to be taken ONE time prior to randomization. Participant must have signed informed consent for the study prior to collection of these samples.

5.0 PRE-TREATMENT EVALUATION
(See Appendix I)

Pre-registration evaluations focus on patients' current PA involvement as well as their medical eligibility for participation in the study. Pre-randomization evaluations assess baseline fitness eligibility and collect relevant baseline information. Patients must have all pre-randomization evaluations performed and be randomized within 28 days after registration.

Patients must first register for CO.21. Once patients have registered to CO.21 they will undergo exercise testing. Only those who successfully complete the submaximal exercise test (refer to eligibility criteria 4.3.1) or the 6 minute walk test will be considered eligible for randomization , the test can be done in person, or done remotely using phone calls, videolinks, or facetime if in person testing is not possible. Once the patient has been determined to be eligible based on submaximal exercise test results, he/she should then complete the remaining requirements for randomization (refer to table 5.2) including, functional assessment, anthropometric measurements, blood collection (unless completed prior to registration at the centre's discretion), and PROs. Following completion of these investigations and provided eligibility has been verified according to eligibility criterion 4.3 patients are then randomized to one of two arms. Patients who do not successfully complete the submaximal exercise test are not eligible for randomization and should not complete the remaining investigations/PROs.

It is recommended that the submaximal exercise test be completed prior to any other post-registration/pre-randomization investigations/PROs in the event that the patient is deemed ineligible based on their performance on the submaximal exercise test. However, the order of these investigations may be modified if required logistically, providing all fitness testing and questionnaires are completed after registration and prior to randomization.

Table 5.1 Evaluations Required Prior to Registration

Investigations		Timing prior to registration
History and Physical Exam including:	• Diagnosis of high risk stage II/stage III colon cancer • Major medical problems • Concomitant medications • Prior medical and therapeutic history • Smoking history • Screening questionnaire to ensure 'medically fit' for PA (rPARQ) • Screening questionnaire re: pre-registration and pre-diagnosis PA level (LTEQ) • Blood pressure, Heart rate • Height, weight, ECOG performance status	≤ 14 days
Hematology*	• Hemoglobin**, WBC, AGC, platelet count	≤ 49 days
Biochemistry*	• Bilirubin, Alkaline phosphatase, ALT • Serum Creatinine • Carcinoembryonic Antigen (CEA)	≤ 49 days
Radiology	• Chest x-ray or CT • CT or MRI or ultrasound abdomen	≤ 60 days
Adverse Event	• Baseline adverse event evaluation (to document residual adverse event from previous therapy and baseline symptoms)***	≤ 14 days

* If multiple testing performed within 49 days prior to registration, the most recently obtained lab tests must be applied to this criterion.

** Hemoglobin values must be obtained at ≥ 6 weeks after a previous blood transfusion or administration of an erythropoietic stimulating agent

*** Adverse events will be recorded and graded according to the NCI Common Terminology Criteria for Adverse Events Version 3.0 (Appendix II)

Table 5.2 Post Registration Evaluations Required for Randomization

Investigations		Timing after registration:
Fitness Testing	• Sub-maximal exercise test or 6 minute walk test	≤ 28 days (must be successfully completed prior to other pre-randomization investigations)
	• Senior's Fitness test if possible	≤ 28 days (only after successful completion of sub-maximal exercise test) **
	• Hip circumference if possible • Waist circumference if possible	
Other Investigations	• Fasting glucose+	
	• Serum/plasma collection for correlative studies and optional banking*+	
Patient Reported Outcomes	• Fatigue (FACIT-F) • QOL/Physical Functioning (SF-36) • Depression/anxiety (HADS) • Sleep (PSQI)	
Physical Activity Behaviour/ Adherence	• Physical Activity Participation (TPAQ)	
	• Social-Cognitive Determinants of Exercise	
Health Economics	• Work Productivity and Activity Impairment Questionnaire (WPAI)	

* including serum levels of insulin, IGF-1, IGF-2, IGFBP3 and cytokine levels of IL-1β, IL-6, IL-2, IL-4, IL-8, IL-10, IL-12, TNF-α, IFN-γ, and GM-CSF and C-reactive protein

+ fasting glucose and serum/plasma collection for correlative studies must be taken at the same time but it is at the centre's discretion whether these are collected post-registration or pre-registration. If taken pre-registration, informed consent to participate in the CO.21 study must have already been obtained from the participant and samples must be collected within 14 days PRIOR to registration. If taken post-registration they must be collected prior to randomization.

** this is the recommended order but may be altered due to logistical considerations

6.0 ENTRY / REGISTRATION / RANDOMIZATION PROCEDURES

6.1 Registration and Randomization

All registrations and randomizations will be done centrally by the CCTG by means of a web-based, password-operated electronic system. Complete details regarding obtaining a password, accessing the system and carrying out randomizations will be provided at the time of study activation and will also be included in the Registration/Randomization and Data Management Guidebook, posted on the CO.21 area of the CCTG web-site. If sites experience difficulties accessing the system and/or performing registrations or randomizations the CO.21 Study Coordinator should be contacted (see last page of this protocol for contact details).

The following information will be required:
- trial code (CCTG CO.21)
- treatment centre and investigator
- date of REB approval for study at participating centre
- version of the informed consent that the patient signed
- patient's initials, hospital number (if permitted by the local REB) and CCTG serial number
- confirmation of the requirements listed in Section 4.0, including dates of essential questionnaires and tests and actual values
- completed eligibility checklist
- stratification parameters - disease stage (high risk stage II vs stage III), centre and ECOG performance status (0 vs 1), height and weight for central calculation of BMI ($\leq$ 27.5 or > 27.5)

Centres must register eligible patients prior to administration of fitness testing.

Randomization will be performed electronically. Randomization will be given by the CCTG website and confirmed by e-mail. This notification should then immediately forwarded by the cancer centre to their physical activity partner.

Note: The validity of results of the trial depends on the authenticity of and the follow-up of all patients entered into the trial. Under no circumstances, therefore, may an allocated patient's data be withdrawn prior to final analysis unless the patient withdraws participation from the trial and asks that their collected data be removed from all future analyses.

All eligible patients admitted to the trial will be followed by the coordinating centre. It is the responsibility of the physician in charge to satisfy him/herself that the patient is indeed eligible before requesting randomization.

All randomized patients are to be followed for 10 years post-randomization.

The follow-up requirement for ineligible patients is minimal follow-up using a Form 5M.

7.0 INTERVENTION PLAN

Although the Canadian Cancer Trials Group acts as the coordinating agency for the trial, the responsibility for treatment of patients rests with the individual investigator.

In accordance with CCTG policy, protocol treatment is to begin within 14 days of patient randomization. .

The treatment plan is summarized in the following table:

Patients will be randomized to one of the following two arms :		
Arm	Intervention	Duration
1	General health education materials	Provided within 14 days of randomization by cancer centre staff
	Physical activity program	3 phases Phase 1: Intensive intervention for 6 months Phase 2: Reduced intervention for months 6-12 Phase 3: Minimal intervention for months 12-36 (refer to section 7.1.7 for details)
2	General health education materials	Provided within 14 days of randomization by cancer centre staff

7.1 Arm 1: Physical Activity Program plus General Health Education Materials

7.1.1 *General Health Education Materials*

All patients will receive general health education materials within 14 days of randomization. They will be provided at the originating cancer centre. The standard of care for provision of education materials following cancer treatment is different between countries and is reflected here.

In Canada all patients will be provided with the most up-to-date Canada Food Guide for recommendations related to nutrition and the most up-to-date Canada's Tips To Get Active (for adults aged 18- 64) and older adults (over 65) for recommendations related to physical activity.

In Australia, patients are more routinely provided with cancer-specific education materials. In this study, all Australian patients will receive cancer-specific education materials regarding nutrition (Eat For Health) and exercise (Move Your Body) published by The Cancer Council Australia. While the materials provided in Canada and Australia will have some differences relevant to their specific countries, the nature of the material will be considered to represent standard clinical practice. Please refer to Appendix XIII for copies of these general health education materials.

These materials will be the same as those provided to patients in Arm 2. This will help to ensure that the difference between the two study arms is related to the PA program not the written education information and will also provide patients on Arm 2 with appropriate health recommendations.

7.1.2 *Physical Activity Program*

The PA program consists of two components:
- Behaviour support sessions with the Physical Activity Consultant
- Supervised physical activity sessions with the Physical Activity Consultant

Each component will be described below. These sessions may occur separately and/or in combination.

7.1.3 *Physical Activity Prescription Goal*

The goal of the PA program is to increase recreational PA from baseline (calculated using the TPAQ Recreational module prior to randomization documenting weekly average PA for the month prior to its completion) by at least 10 MET hours/week to a maximum of 27 MET hours/week.

The decision to encourage patients to increase PA by more than 10 MET hours/week will depend on how well they have adapted to the initial goal of a 10 MET hours/week increase at the end of six months. The absolute goal of 20 MET hours/week is equivalent to about 5 hours (e.g. 5 days x 60 minutes/day) of moderate intensity PA/week such as brisk walking (4 METs) or 2 hours (3 days x 40 minutes/day) of vigorous intensity PA/week such as jogging (10 METs). Perhaps a minority of patients will be able and willing to achieve the goal of up to a 20 MET hours/week increase. No patients will be encouraged to increase their PA beyond 27 MET hours/week which is equivalent to about an hour a day of brisk walking for 7 days or an hour a day of jogging for 3 days of the week. No further association with the risk of reducing colon cancer death has been shown above such levels and the risk of an adverse event increases significantly with the volume of PA. It is likely that only a few select patients will be able, willing, and interested in increasing their PA to this level.

As mentioned previously the delta of 10 MET hours/week will only include recreational activities. Occupational, household, and other activities of daily living will not be counted towards the goal (or in baseline calculation of MET hours/week) but patients will be encouraged to maintain such activities and they will report their MET hours/week in all categories at baseline and at all follow up visits (using the TPAQ Employment & Volunteer and Household & Do-It-Yourself modules).

7.1.4 *Behavior Support Program*

Achieving an increase in PA from baseline of $\geq$ 10 MET hours/week will require a significant amount of behavioural support. The intervention will comprise a 36-month individualized PA and behavioural support program with a PAC. This will include a personalized PA prescription which takes into account the baseline fitness test results, PA history, performance status and patient's personal PA preferences and any barriers to activity. Most patients are likely to choose a walking program however any PA of at least moderate intensity level is acceptable.

Initially face-to-face behaviour support sessions in combination with supervised PA sessions will be preferred but not mandatory (please refer to table in 7.1.7) and may be done remotely using phone calls, videolinks, or facetime if face-to-face is not possible. Combining supervised PA with behavioral support is an efficient approach to PA change. After month six, behavioral support sessions are still mandatory however patients will have the option of receiving them by telephone* or face-to-face. Patients that choose face-to-face sessions during this time period will also have the option of combining it with a supervised PA session. Face to face sessions may be 1:1 with the PAC or in a group format. This schedule is designed to allow flexibility. Throughout all phases of the study, PACs are able to provide additional behaviour support sessions if they determine a patient is experiencing difficulty with compliance.

* *Throughout the protocol when the term "telephone" is used for type of contact or session format, video conferencing is also permissible (for example, Skype, Face Time, etc.).*

Behaviour support sessions will include training in behavioral strategies to promote adoption and maintenance of PA. Key behavioral strategies will include highlighting key benefits of PA, strategies for making PA fun and enjoyable, overcoming barriers, securing social support from family and friends, time management, self-monitoring, goal setting, planning, stimulus control, relapse prevention and self-reinforcement. At the core of the behavioural intervention will be a PA guidebook that will contain the topics and materials for the PACs to reinforce and expand upon during the counseling sessions. The guidebook will be distributed to each PA program patient to have as ongoing resource. The guidebook is modeled after one that was originally developed for breast cancer survivors and was shown to be effective for increasing motivation, PA, and QOL in post-adjuvant breast cancer survivors *[Vallance 2008; 2007a; 2007b]*. The guidebook for colon cancer patients, "Step Up to the Challenge!" will undergo preliminary evaluation for readability, accuracy and theoretical fidelity by medical oncologists, nurses, PA specialists, and colon cancer patients prior to being included in the study.

7.1.5 *Behavioral Tool Box*

Advanced behavioral strategies are considered for patients that have significant struggles in adopting or maintaining PA despite continued support from the PAC. The tool box will focus mostly on overcoming barriers to PA, many of which will likely be related to issues of opportunity in the winter. The primary approach will be to have a facility available free of charge year round. In some circumstances (for example, if it is not possible to arrange free access to a facility or for patients living beyond a reasonable distance to access the available facility) arrangements may be made for short term membership at a club or in an exercise class, however, this would be for a limited duration and no longer than the intervention period. As with all strategies, these resources may be withdrawn if the intended effects are not realized. For those out of town or who prefer to be involved in PA at home, the tool box may include provision of home exercise videos or low cost equipment (e.g. someone who wants to perform their PA at home in the winter but has no home equipment), or loan of home exercise equipment (e.g. one at each site that can be loaned and used again). All patients will be provided with pedometers to help them to calculate their PA. Selection of a particular strategy is based on the major barrier experienced by the patient.

7.1.6 *Supervised Physical Activity Sessions*

In addition to counseling sessions focusing on behavioural support, patients will also receive supervised PA sessions. As per the schedule in 7.1.7 these sessions will be combined with behaviour support sessions where feasible as well as occurring independently. The focus of these sessions will be to teach proper PA technique and monitoring. In the first six months, there are preferred supervised PA sessions, after that time they are recommended. Supervised PA sessions may be 1:1 with the PAC or in a group format. Throughout all phases of the study, PACs are able to provide additional supervised PA sessions if they determine a patient is experiencing difficulty with compliance. The majority of PA, however, will be completed with unsupervised PA in addition to the schedule noted below in order to meet the goal of increasing their baseline recreational PA by 10 MET hours/week. To accomplish this, patients may be provided access to a fitness facility at time periods outside of their supervised PA sessions, however, behaviour support and PA supervision will not be provided by the PAC at these times.

7.1.7 *Timing and Nature of Physical Activity Program*

Timing	Phase 1 Baseline to 6 mos	Phase 2 6 -12 mos	Phase 3 12-36 mos
Behaviour Support Sessions*	• 12 preferred face-to-face sessions held biweekly	• 12 mandatory sessions held biweekly – with option to have them face-to-face or by telephone ***	• Mandatory monthly sessions with option to have them face-to-face or by telephone ***
Supervised Physical Activity Sessions*♦	• 12 preferred sessions combined with mandatory sessions above • 12 additional supervised PA sessions strongly recommended on alternate weeks	• 12 recommended sessions - can be combined with biweekly sessions above for those who chose face-to-face sessions	• Monthly sessions recommended - can be combined with monthly sessions above for those who chose face-to-face sessions
Physical Activity Goal**	• Gradually increase recreational PA by 10 MET hrs/wk over baseline (to 10-19 MET hrs/wk)	• Individualized based on phase 1 results to a maximum increase of 20 MET hrs/wk (to a total of 20-27 hrs/wk)	• Individualized based on phase 2 results to a maximum total of 27 MET hrs/wk

* PACs can provide additional behavioural support and/or supervised PA sessions in any phase if they determine patient is experiencing difficulty with compliance

♦ Patients may be provided with access to a fitness facility outside of the scheduled sessions however no behaviour support or PA supervision will be provided

** All increases in PA refer to recreational activity MET hours/week only.

*** Video conferencing is also permissible (e.g. Skype, Face Time, etc.).

Phase 1 (Baseline to 6 months)

The behavior support program will begin with 12 preferred face-to-face behaviour support sessions held biweekly for the first six months. These sessions will be combined with a preferred supervised PA session. An additional supervised PA session in alternate weeks is also strongly recommended. While mandatory sessions are to be completed biweekly it is recognized that there may be circumstances that require occasional variation in this schedule. Some flexibility is permitted however participants must complete a minimum of one mandatory Behaviour Support/Supervised PA session each month and a maximum of 4 sessions per month. This allows for some flexibility when required but ensures that regular contact is maintained between the PAC and the participant for ongoing support as this is a vital component of the intervention program.

The goal for the intervention group during phase 1 of the trial is to gradually increase their PA from baseline by 10 MET hours/week (absolute range of 10-19 MET hours). Patients will be asked to increase their PA by no more than 2 MET hours/week in a month (about 1 hour of casual walking or 30 minutes of brisk walking) to achieve the 10 MET hours/week increase over six months. The PA goal can be achieved by any type of recreational PA and any combination of a frequency of 3-7 days/week, duration of 10-60 minutes per day, and a moderate-to-vigorous intensity (4-10 METs). Occupational, household, and other activities of daily living will not be counted towards the goal but patients will be encouraged to maintain such activities. Walking is the most likely unsupervised PA but any PA is allowed. METs will need to be verified for any activity that is not standard (e.g. curling). MET hours will be calculated to one decimal place. PACs may offer additional support and/or supervised PA sessions to those patients that they determine are having difficulty with compliance.

Phase 2 (6 months to 1 year)
In months six to 12, patients will receive 12 mandatory biweekly behavioural support sessions with the option of receiving them by telephone or face-to-face. Patients that choose face-to-face will have the option of combining it with the recommended supervised PA session. Supervised PA sessions will not be provided on alternate weeks. While mandatory sessions are to be completed biweekly it is recognized that there may be circumstances that require occasional variation in this schedule. Some flexibility is permitted however participants must complete a minimum of one mandatory Behaviour Support/Supervised PA session each month and a maximum of 4 sessions per month. This allows for some flexibility when required but ensures that regular contact is maintained between the PAC and the participant for ongoing support as this is a vital component of the intervention program.

The PA goal for the intervention group during phase 2 of the trial will be individualized based on how well each patient adapted to the phase 1 goal. Patients that adapt well (i.e. were able, willing, and interested) will be offered to continue the "adoption" phase of PA towards an increase of up to 20 MET hours/week over baseline (absolute range of 20-27 MET hours). Patients that found the initial increase challenging but are still able, willing, and interested will be asked to continue to either "adopt" or "maintain" the initial PA increase of 10 MET hours/week during phase 2 (absolute range of 10-19 MET hours). Patients that adapt poorly and appear unable, unwilling, or uninterested will be offered to continue the "adoption" phase of PA but with a reduced goal of an increase of 5 MET hours/week over baseline (absolute range of 5-14 MET hours). PACs may offer additional support and/or supervised PA sessions to those patients that they determine are having difficulty with compliance.

Phase 3 (1 to 3 years)
For years two and three, patients will receive mandatory monthly behaviour support sessions with the option of receiving them by telephone or face-to-face. Patients that choose face-to-face will have the option of combining it with the recommended supervised PA session. While mandatory sessions are to be completed monthly, it is recognized that there may be circumstances that require occasional variation in this schedule. Some flexibility is permitted, however, participants must complete a maximum of 2 mandatory Behaviour Support sessions per month and there should be no more than 10 weeks between sessions. This allows for some flexibility when required but ensures that regular contact is maintained between the PAC and the participant for ongoing support as this is a vital component of the intervention program.

The PA goal for the intervention group during phase 3 of the trial will depend on how well each patient adapted to the phase 2 goal. Patients that adapt well (i.e. were able, willing, and interested) to either the $\geq$ 20 MET increase, 10 MET increase, or 5 MET increase will be offered to increase their PA during phase 3 to the next level to a maximum of 27 MET hours/week. Patients that find the phase 2 goal challenging but are still able, willing, and interested will be asked to continue to adopt or maintain that goal during phase 3. Patients that adapt poorly and appear unable, unwilling, or uninterested in achieving the phase 2 goal will be offered to revert to the next lower goal to a minimum of $\geq$ 5 MET hours/week over baseline (absolute range of 5-14 MET hours). PACs may offer additional support and/or supervised PA to those patients that they determine are having difficulty with compliance.

7.1.8 *Identification of Physical Activity Consultants (PACs)*

All PA programs will be facilitated by a qualified PAC. The success of the PA intervention will depend heavily on the knowledge, skills, and abilities of PACs. Each site will have one or more PACs trained in exercise physiology, behavior change and support, and cancer.

The PAC should be an individual who is affiliated with the cancer centre, local health care institution or affiliated university (for example, physiotherapist or occupational therapist) for a multitude of logistical reasons. These include facilitation of information exchange between central office and study staff and the PAC, training and monitoring PACs and opportunity to coordinate patient appointments with the PAC as well as follow up appointments with study staff to increase patient compliance.

A major component of the pre-study site evaluation will be the centres' capability to effectively deliver the PA program. Centres interested in participating in the CO.21 study will be required to identify a potential PAC(s). Potential PAC candidates will be evaluated by the Study Chair and/or Physical Activity Working Group to ensure that they meet the required qualifications. Ideally two PACs will be identified at each centre.

7.1.9 *Training of Physical Activity Consultants*

Ideally two (but at a minimum one) PACs from each centre will receive central training and ongoing supervision throughout the trial. To ensure standardization of intervention delivery across sites, training will include education on the study protocol, reporting of data, exercise testing, PA prescription, supervision, tracking and reporting as well as the behaviour support components of the study. Centres will not be permitted to accrue any patients until this training is completed. Training and supervision will also be provided on an ongoing basis via regular conference calls that include PAWG members and the PACs from each site.

PACs will also be provided with manuals covering topics including session by session guidelines for PA program sessions, patient handouts, calculation of MET hours, 'tool box/kit' for behavioural modification and support, study protocol details and PA logs.

If a PAC does discontinue their involvement in the study, another PAC will be trained at that centre using a train the trainer model. All trained PACs will actively participate in the program to ensure consistency of intervention delivery as well as to ensure all PACs are current with ongoing developments in the study.

7.1.10 *Monitoring Physical Activity Consultants*

All centres will use the standardized materials and all PACs will be trained by PAWG members and monitored to ensure that they deliver the intervention as designed and perform exercise testing consistently. Once a site has demonstrated it can deliver the program, then oversight by the PAWG will be reduced. These procedures will help ensure standardization of the intervention across centres. In addition, to assist with minimizing differences that may arise from different PACs, randomization will be stratified by centre and session by session guidelines have been developed for PACs to follow to facilitate consistency of the intervention. Standardized forms have also been developed to ensure that the information (including the fitness test results or reasons for non-completion and components of the PA program) that is being transferred from PACs to the cancer centres is consistent across sites.

The Trial Steering Committee recognizes and accepts that this high level of monitoring and prescription of the PA program may reduce the generalizability of the results however adherence to the program is essential to achieve the required improvements in PA and to determine the effectiveness of the intervention.

7.1.11 *Patient Monitoring and Compliance*

Study patients in the PA program arm will be in contact with their PACs as per the schedule described above. For each reporting period, the results of patients' fitness testing and a summary of key components of their PA program will be submitted to the originating cancer centre in a standardized form. This will include the number of behaviour support sessions completed (noted as in-person or telephone) and reasons for non-completion, the number of supervised PA sessions attended and the reason for non-attendance, and the number of additional sessions with the PAC and the reason for the contact. Throughout all phases of the study, PACs are able to provide additional supervised PA and/or behaviour support sessions if they determine a patient is experiencing difficulty with compliance. PACs will be provided with a list of serious events that should be immediately reported by the PAC to the patient's originating cancer centre if they occur.

PACs are responsible for monitoring adverse events related to the PA program and fitness testing. PACs will solicit information about adverse events during all contacts with participants and modify the PA program or Fitness Testing appropriately. Adverse events should not be reported by the PAC to the cancer clinic as participants will be able to self-report these events at their regularly scheduled follow up visits as required. However, PACs will be provided with a list of serious events that, if they occur while the PAC is present or if the PAC becomes aware of the event, should be immediately reported by the PAC to the Investigator at the patient's originating cancer centre. It will then be the responsibility of the Investigator to determine if the event is a "reportable serious adverse event" that is subject to expedited reporting to CCTG.

Patients in this arm of the study will be required to keep a PA log book (Appendix X) with instructions to complete the log book on a weekly basis to record all PA during the previous week. Information recorded will include the type of PA performed and whether it was supervised or unsupervised, frequency, intensity (based on RPE), and duration (in minutes). The PAC will use the data recorded in the patients' PA logs to calculate the patients' average recreational MET hours/week to monitor compliance and determine patients' progress towards or success in meeting the target of increasing 10 MET hours/week. The consultant will address poor compliance with the patient during the scheduled follow-up sessions described above. Physical activity consultants will continue to work with patients until that goal of increasing PA by a minimum of 10 MET hours/week is achieved.

Physical activity logs are used for motivational and monitoring purposes but are not considered an endpoint measure of adherence.

Study patients will also be seen by study investigators as per the follow-up schedule found in table 8.1 where they will be monitored to ensure they are medically able to continue to participate in the PA program. Medical oncologists should support and encourage PA for all patients when they are seen for their follow up visits every six months. Study patients will be able to report adverse events at this time.

7.1.12 *Duration of Intervention*

The PA program will continue for 36 months or until the patient is permanently unable or unwilling to continue with the PA program (refer to section 11.1). Patients who have developed a recurrence or new primary malignancy will discontinue with the PA program.

Stopping and re-starting the PA program, while not ideal, is permissible. Patients who stop and restart their PA program for a variety of reasons (for example, injury, vacation, work responsibilities, too much time commitment) will still be considered to be 'on' protocol treatment during these absences. This information will be captured through the report of attendance/non-attendance submitted by the PAC and also at the regularly scheduled follow-up appointments.

7.2 Arm 2: General Health Education Materials Arm

7.2.1 *General Health Education Materials*

All patients within each country will receive identical general health education materials regarding nutrition and PA. The materials will be provided by the originating cancer centre within 14 days of randomization. Arm 2 patients will receive material that is identical to that provided to patients in the intervention arm (Arm 1), as indicated in section 7.1.1.

7.2.2 *Patient Monitoring and Compliance*

Patients in Arm 2 will not be asked to complete PA logs because of concerns of increasing contamination. PACs are responsible for monitoring adverse events related to the fitness testing. PACs will solicit information about adverse events during all contacts with participants and modify the Fitness Testing appropriately. Adverse events should not be reported by the PAC to the cancer clinic as participants will be able to self-report these events at their regularly scheduled follow up visits as required. However, PACs will be provided with a list of serious events that, if they occur while the PAC is present or if the PAC becomes aware of the event, should be immediately reported by the PAC to the Investigator at the patient's originating cancer centre. It will then be the responsibility of the Investigator to determine if the event is a "reportable serious adverse event" that is subject to expedited reporting to CCTG. Patients will be monitored by study investigators at follow up appointments as per schedule in Appendix II.

7.2.3 *Duration of Therapy*

Patients will only be provided with general health education materials within 14 days of randomization. Otherwise patients in Arm 2 will only participate in follow up appointments and investigations/ fitness testing.

7.3 Concomitant Therapy

7.3.1 *Not permitted*

Anti-cancer therapy including chemotherapy agents, biological agents or targeted agents.

Any medications deemed by the investigator as likely to preclude participation in a structured PA program.

8.0 EVALUATION DURING AND AFTER PROTOCOL TREATMENT

All patients entered on study must be evaluated according to the schedule outlined in Appendix II with documentation submitted according to the schedule in Appendix IV.

8.1 Evaluation During and After Protocol Treatment

Evaluations will be performed at different intervals throughout the study. If a delay occurs in the schedule of a patient's PA program, other assessments, including assessment by the investigator and PRO questionnaires, will not be delayed, but should continue at the time indicated from randomization.

Investigations		During Treatment (36 months from randomization for both arms and prior to recurrence/new malignancy)	After Treatment (4 and 5 years post randomization and prior to recurrence/new malignancy)	After Treatment (6 years to 10 years post randomization and prior to recurrence/new malignancy)
History and Physical Exam including:	• Overall survival • Clinical evidence of disease	Every 6 months	Every 12 months	Every 12 months
	• Weight • Concomitant medications • Smoking history	Every 6 months	Every 12 months	NA
Biochemistry	• Carcinoembryonic Antigen (CEA)	Every 6 months	Every 12 months	NA
Radiology	• Chest CT or x-ray • CT, MRI or U/S abdomen	Every 12 months	NA	NA
	• Colonoscopy	Once between 30 – 48 months post-randomization		NA
	• Other[+]	As clinically indicated to document recurrence or new primary malignancy		
Fitness Testing	• Submaximal exercise test • Senior's Fitness Test • Hip and waist circumference	6, 12, 24, and 36 months post randomization	NA	NA
Other Investigations	• Serum/plasma collection for correlative studies and optional banking *	Every 12 months	NA	NA
	• Fasting glucose*	Every 12 months	NA	NA
Adverse Events	• Adverse events will be recorded and graded using NCI Common Terminology Criteria for Adverse Events Version 3.0 (CTCAE) (Appendix VI).	Every 6 months	Every 12 months	NA
Patient Reported Outcomes	• Fatigue (FACIT-F) • QOL/Physical Functioning (SF-36) • Depression/Anxiety (HADS) • Sleep Quality (PSQI)	Every 6 months	Every 12 months	NA
Physical Activity Behaviour/ Adherence	• Physical activity participation (TPAQ)	Every 6 months	Every 12 months	NA
	• Social-Cognitive Determinants of Exercise	Every 6 months	NA	NA
Health Economics	• Resource Utilization Assessment • WPAI • 30-Day Resource Use Diary**	Every 6 months	Every 12 months	NA

* Blood samples collected for correlative studies and for fasting glucose should be taken at the same time
** Including first month of intervention period

8.2 Evaluations Following Local or Distant Recurrence or New Primary Malignancy

Investigations		Timing	
		From randomization to 5 years	6-10 years from randomization
History and Physical Exam	• Overall survival	q6 monthly from randomization to 36 months and then annually until 5 years	Annually
	• Weight • Smoking history • Non-protocol anti-cancer therapy	q6 monthly from randomization to 36 months and then annually until 5 years	NA
Patient Reported Outcomes	• SF-36		
Health economics	• Resource Utilization Assessment • WPAI • 30-Day Resource Use Diary		

9.0 CRITERIA FOR MEASUREMENT OF STUDY ENDPOINTS

As disease-free survival is the primary endpoint in this study, it is vital that it be adequately and precisely documented.

9.1 Definition

9.1.1 *Disease Free Survival:* Disease free survival is defined as the time from randomization to the first event that is either recurrent (local or distant) colon cancer, a new primary colon cancer, a second primary malignancy or death from any cause.

9.1.2 *Overall Survival*: Overall survival is defined as the time from randomization to death from any cause.

9.1.3 *Evaluable for Toxicity*: Adverse events and other symptoms will be graded according to the National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events, Version 3.0 (see Appendix VI).

9.1.4 *Evaluable for Patient Reported Outcomes Assessment (Including the TPAQ)*: All patients who have completed the baseline PRO questionnaire and at least one other questionnaire for each of the PROs are evaluable for patient reported outcomes.

9.1.5 *Evaluable for Social Cognitive Determinants of Exercise:* All patients who have completed the baseline questionnaire for the social cognitive determinants of exercise are evaluable for adherence outcomes.

9.2 Evidence of Disease Recurrence

Local Disease Recurrence:

Suspicious:	Suspicious imaging requiring further confirmation.
Definite:	Confirmation by cytology or histology OR Definitive imaging documenting local recurrence

Elevated CEA only or physical examination only are not sufficient as evidence of suspicious or definite local disease recurrence.

Distant Disease Recurrence:
Evidence of colon cancer at sites remote from the colon.

Suspicious:	Suspicious imaging requiring further confirmation.
Definite:	Confirmation by cytology or histology OR Definitive imaging documenting distant recurrence

New Primary Malignancy:
Evidence of new primary malignancy at any site.

Suspicious:	Suspicious imaging.
Definite:	Confirmation by cytology or histology at any site.

Imaging **cannot** be used as definite evidence for confirmation of a new primary malignancy.

9.3 Dating of First Recurrence or New Primary Malignancy

The diagnosis of recurrent disease or a new primary malignancy by radiographs or scans should be dated from the date of the first suspicious record, even when the specific imaging abnormality requires subsequent confirmation by biopsy (required for confirmation of new primary malignancy) or is otherwise determined in retrospect (e.g. bone metastases that will never be biopsied but are definitively confirmed with subsequent imaging procedures).

Initial dates of first recurrence or new primary malignancy should be made as they occur by those who are responsible for the care of the patient. Dates that are based on suspicion alone will be reviewed by the CCTG coordinating office in order to establish accuracy through subsequent clinical course.

9.4 Management Following Recurrence or New Primary Malignancy

Upon evidence of disease recurrence or a new primary malignancy, patient management (including systemic therapy, surgery, radiotherapy and any lifestyle interventions) is at the discretion of the treating physician/investigator. Patients on the intervention arm who have experienced a recurrence or a new primary malignancy will discontinue the PA program.

10.0 SERIOUS ADVERSE EVENT REPORTING

This protocol does not contain investigational agent(s), and adverse events occurring as a result of this PA program intervention should be reported to CCTG in the manner described below. In addition, your local Research Ethics Board (REB) should be notified.

Adverse events (AE) will use the descriptions and grading scales found in the revised NCI Common Terminology Criteria for Adverse Events (CTCAE). This study will utilize the CTCAE Version 3.0 for adverse event reporting. All appropriate treatment areas should have access to a copy of the CTCAE Version 3.0.

All serious adverse events (SAE) defined as per ICH guidelines (see below) and other adverse events must be recorded on case report forms. In addition, all "reportable" serious adverse events are subject to expedited reporting using the CCTG SAE form. The term 'reportable SAE' is used in the definitions which follow to describe those SAEs which are subject to expedited reporting to CCTG.

10.1 Definition of a Reportable Serious Adverse Event

- All serious adverse events which are unexpected and related to protocol treatment must be reported in an expedited manner (see Section 10.2 for reporting instructions).
- Unexpected adverse events are those which are not consistent in either nature or severity with information contained in the informed consent.
- Adverse events considered related to protocol treatment are those for which a relationship to the PA program and/or fitness testing cannot reasonably be ruled out.
- A serious adverse event (SAE) is any adverse event that at any dose:
  - results in death
  - is life-threatening
  - requires inpatient hospitalization or prolongation of existing hospitalization (excluding hospital admissions for transfusional support, scheduled elective surgery and admissions for palliative or terminal care)
  - results in persistent or significant disability or incapacity
  - is a congenital anomaly/birth defect

Medical and scientific judgement should be exercised in deciding whether expedited reporting is appropriate in other situations such as important medical events that may not be immediately life-threatening or result in death or hospitalization but may jeopardize the patient or may require intervention to prevent one of the events listed above.

10.2 Serious Adverse Event Reporting Instructions

All reportable serious adverse events must be reported as follows

Within 24 hours:	FAX preliminary Serious Adverse Event Report to: Dr. Chris O'Callaghan or Patti O'Brien Canadian Cancer Trials Group Fax: 613-533-2941
Within 10 days:	Mail CCTG CO.21 Serious Adverse Event Report (signed by the investigator and updated as much as possible)

10.3 Reporting Serious Adverse Events to Local Research Ethics Boards

CCTG will notify all Investigators of all serious adverse events from this trial that are both unexpected and related (i.e. possibly, probably, or definitely) to the PA program intervention or fitness testing as reported to CCTG. Investigators must notify their Research Ethics Boards (REBs) and file the report in their study files. The date of REB Submission for SAEs will need to be entered into the CCTG trial CO.21 web based safety monitoring utility and documentation of REB submission must be retained in the study binder on site.

For this purpose, the REB submission template letter provided by CCTG should be used. Please note:

- this letter must be either printed on institutional letterhead or contain the centre identification/ REB name;
- the date of REB submission must be provided;
- this form must be signed by one of the approved participants (according to the participants list) for this trial.

The submission of these events to your ethics board should be done as soon as possible. It is expected that these will be submitted for review within 30 days of the date of the letter to Investigator.

11.0 PROTOCOL TREATMENT DISCONTINUATION AND THERAPY AFTER STOPPING

11.1 Criteria for Discontinuing Protocol Treatment

Patients may stop protocol treatment in the following instances:

- Intercurrent illness that is determined by the investigator to preclude participation in a PA program;
- Unacceptable toxicity which renders patient unable to participate in PA program;
- Disease recurrence or a new primary malignancy as defined in Section 9.0;
- Request of the patient for any reason;
- Physician discretion;
- Completion of therapy as outlined in Section 7.0.

11.2 Therapy After Protocol Treatment is Stopped

There are no additional interventions defined after patients complete or discontinue protocol therapy.

11.3 Follow-up Off Protocol Treatment

Refer to section 8.1 and Appendix II for details of follow up and required investigations.

Efforts should be made to maintain the investigations schedule (including fitness testing unless determined by investigator to be medically contraindicated) and continue follow-up, even if patients discontinue protocol treatment prematurely and/or no longer attend the participating institution.

However, if a patient has had a documented recurrence or a new primary malignancy they will be followed as per section 8.2.

12.0 CENTRAL REVIEW PROCEDURES AND TISSUE COLLECTION

12.1 Central Radiology Review

There will be no central radiology review for this study.

12.2 Central Pathology Review

There will be no central pathology review for this study.

12.3 Serum and Plasma Collection

The collection of serum and plasma is an important and mandatory part of this trial. Failure to submit any serum and plasma samples as described in Table 5.2 will render the patient ineligible for randomization.

One sample of serum and two samples of plasma will be collected. The collected serum and plasma will be used for three purposes: (1) to assess serum levels of insulin, insulin-like growth factor-1 (IGF-1), IGF-2, IGF binding protein 3 (IGFBP3) and to evaluate their association with DFS,OS, level of PA and fatigue; (2) to assess cytokine levels IL-1β, IL-6, IL-2, IL-4, IL-8, IL-10, IL-12, TNF-α, IFN-γ, and GM-CSF and C-reactive protein and to evaluate their association with DFS, OS, level of PA and fatigue; (3) for specimen banking. The assessment of insulin and related markers and cytokine levels are mandatory analyses in this trial, but serum and plasma banking is optional. Serum and plasma will be carefully banked as part of the CCTG Tissue/Tumour/Data Bank at Queen's University in Kingston, Ontario.

At the time of providing informed consent patients will be made aware that samples are being banked for eventual analysis; permission for this will be requested in the consent form.

Instructions for the collection, handling, processing and shipping of all blood specimens can be found in the CO.21 Correlative Studies Manual.

Banking:
For patients who consent to serum and plasma banking, any residual serum and/or plasma remaining after the completion of testing for insulin, IGF-1, IGF-2, IGFBP3 and cytokine levels will be banked at the CCTG Tissue/Tumour/Data Bank.

The serum and/or plasma that will be banked by the CCTG will be used by researchers in the future to better understand the nature of cancer and how patients respond to treatment. Samples will be used for research purposes only and will not be sold. A scientific review process of any proposals to use serum and/or plasma will take place and any proposals approved will have undergone ethics approval. Patients will not be identified by name. The only identification of samples will be by a patient study number assigned at the time of randomization to the trial, patient initials and the tumour bank code. Material issued to researchers will be anonymized and only identified by a coded number.

Testing for hereditary genetic defects predisposing to malignant disease will not be carried out without the expressed consent of the patient.

13.0 STATISTICAL CONSIDERATIONS

13.1 Objectives and Design

The primary objective of this study is to determine, in comparison of the control arm, if participation in a PA program designed to increase recreational PA by at least 10 MET hours/week after adjuvant therapy for high risk stage II or stage III colon cancer improves DFS. Medically fit patients with resected high risk stage II or stage III colon adenocarcinoma who have received adjuvant chemotherapy will be randomized to receive a 36-month PA program plus general health education materials (Arm 1) or general health education materials only (Arm 2) in a 1:1 ratio. Patients will be stratified by centre, ECOG performance status (0 vs 1), disease stage (II vs. III), and BMI ($\leq$ 27.5 vs. > 27.5) by using the dynamic minimization method *[Tu 2003]*.

Secondary objectives of this study include a comparison of OS, PROs and health utilities, fitness and PA behavior between treatment arms, an exploration of associations between molecular markers and efficacy measures and PROs, a comparative economic evaluation, and a safety profile assessment.

13.2 Endpoints and Analysis

Disease-free survival, the primary endpoint of this study, is defined as the time from randomization to the first observation of disease recurrence or death due to any cause. Second primary colon and other primary tumours will be counted as events for the DFS. If a patient has not recurred, had a new primary malignancy or died at the time of final analysis, DFS will be censored on the date of the last disease assessment. Patients will be analyzed in the arms to which they are randomized regardless of whether they receive the assigned treatment based on the principle of intention-to-treat. The DFS of patients in both treatment groups will be described by the Kaplan-Meier method. A stratified log-rank test adjusting for the stratification factors of ECOG performance status of 0 or 1, disease stage (II vs. III) and BMI ($\leq$ 27.5 vs. > 27.5) at the time of randomization will be used as the primary method to compare the DFS between the two arms.

Secondary analyses based on stratified Cox proportional hazards model will also be performed. ECOG performance status (0 vs. 1), disease stage (II vs. III) and BMI ($\leq$ 27.5 vs. >27.5) at the time of randomization will be the stratification factors to define the stratified Cox proportional hazards model. Besides the treatment factor (PA intervention plus general health education materials vs. general health education materials only), the following factors at patient entry will be included in the stratified Cox proportional hazards model: age, gender, country. No interaction terms will be included in the model. The appropriateness of the stratified Cox proportional hazards model will be assessed using graphical methods and a test based on the Schoenfeld residuals. An exploratory Cox proportional hazards analysis seeking to identify other factors significantly related to the DFS may also be conducted. Subgroup analyses based on levels of stratification levels at baseline and other factors included in the stratified Cox model will be performed.

Overall survival is defined as the time from randomization to the time of death from any cause. Patients who are alive at the time of the final analysis or who have become lost to follow-up will be censored at their last contact date. All analyses for DFS will also be performed for OS, using similar methodology.

The BMI, waist and hip circumference and scores from submaximal exercise testing and Senior's Fitness Test are objective markers of physical fitness. Wixcon test will be used to compare the difference in these markers between two treatment arms at each assessment time point and linear mixed model for difference at all assessment time points.

All patients who have received any part of the study intervention (receipt of general health education material of provision of instruction about PA) will be included in the safety analysis. Adverse events will be graded using the NCI Common Toxicity Criteria for Adverse Events, Version 3.0 (Appendix VI). The incidence of adverse events will be summarized by type of adverse event and severity. A Fisher's exact test will be used as needed to compare the incidences of adverse events between two arms.

13.3 Patient Reported Outcomes

The patient report outcomes (PROs) will be assessed using SF-36, FACIT-F, PSQI, and HADS. For each subscale or measure, change scores from baseline and proportion of patients reporting improved scores (higher than minimal clinical important difference) at each assessment time point will be compared between two treatment groups using respectively Wilcoxon and Fisher's exact tests. Repeated measure analysis including comparison of change scores at all assessment times will also be performed using linear mixed model.

13.4 Economic Analysis

Cost Effectiveness and Cost Utility Assessment:
An exploratory cost effectiveness and utility evaluation will be performed comparing intervention, treatment and resource use related to the study intervention but not protocol driven. Data will be collected on study patients from Canada and Australia through case report forms, which capture the use of resources such as PAC intervention, medications, procedures, laboratories, imaging, and hospital stays. To capture additional resources due to the PA intervention and outpatient care, additional case report forms as well as the WPAI and 30-Day Resource Use Diary will be used. Data will be gathered and assessed using descriptive statistics. Effectiveness will be presented as survival (Life Years, LYs) and quality adjusted survival with utilities measured using the SF-6D which is derived from SF-36 scoring *[Braizer 2002]*. The incremental cost-effectiveness ratio (ICER) is the primary outcome of the economic analysis. The ICER is defined as:

$$ICER = (Cost_{\text{physical activity program}} - Cost_{\text{usual care}}) / (LY_{\text{physical activity program}} - LY_{\text{usual care}})$$

where efficacy is measured by survival in years for the analysis. Determination of incremental ratios of cost per quality adjusted survival, incorporating the SF-6D utilities data, will be considered as sensitivity analyses. Determination of incremental ratios of cost per quality adjusted survival, incorporating the SF-6D utilities data, will be considered as sensitivity analyses.

13.5 Physical Activity Behavior and Predictors of Adherence to Physical Activity

The primary measure of PA adherence will be self-reported recreational PA at baseline and every six to 12 months using a slight modification of the Past Year Total Physical Activity Questionnaire. The difference between treatment arms in the average MET hours/week for recreational activity will be compared using Wilcoxon test.

For patients randomized to Arm 1, the univariate associations between the predictors, which include those collected from Social-Cognitive Determinants of Exercise Measure, and PA (not meeting 80% of the PA guideline of increasing 10 MET hours/week from baseline vs. meeting 80% of the PA guideline) using chi-square tests for categorical variables and Wilcoxon test for continuous variables. Variables that have statistically significant or borderline univariate associations ($p < .10$) with PA behavior will be examined in a multivariate logistic regression model.

13.6 Sample Size and Duration of Study

The trial will be powered to detect a hazard ratio (HR) of 0.75 for DFS between patients randomized respectively to two treatment arms (intention-to-treat population). This hazard ratio, corresponding to 25% risk reduction, would be clinically significant and achievable based on data from previous analyses. To detect such a HR with a power of 80% and a two-tailed 0.05, we need to observe 380 events before the final analysis. The final analysis will be performed when 380 events are observed.

It is anticipated that a total of 962 patients will be randomized into this trial over three years. To project the duration of the study which will enable us to observe 380 events, we assume that the patients in the control group have a three year DFS of 75% and would not materially change their PA behaviour from baseline *[McTiernan 2006; Irwin 2003]*. It is also assumed that 10% of patients randomized to Arm 1 would not adhere with their PA programs *[McTiernan 2006; Irwin 2003]*. In this case, a hazard ratio of 0.75 between patients randomized to Arms 1 and 2 leads to a three year DFS of 81.2% for the patients adhered with their PA program (corresponding to a hazard ratio of 0.72 between Arm 1 without nonadherence and Arm 2) and also three year DFS 80.6% for the patients randomized to Arms 2 and 1. With these assumptions, it is calculated that, to observe 380 events from 962 patients randomized, 4.6 years of additional follow-up after last patient is randomized would be required, which leads to a total duration of study at around 7.6 years. The increase of nonadherence rate from 10% to 20% has minimal impact to the duration of the study, which only prolongs the duration of the study for around 1 month because of the assumption that same hazard ratio is to be detected between patients randomized to two treatment groups, but only a larger difference between two treatment arms without any cross over (HR=0.69) can be detected in this case.

13.7 Safety Monitoring

Adverse events will be monitored on an ongoing basis by the CCTG central office and their frequencies reported annually at investigators' meetings.

13.8 Interim Analysis

We are planning four interim analyses: one for feasibility, one for futility and the last two will assess efficacy. All interim data will be reviewed by the independent data safety and monitoring committee (DSMC).

The conduct of the study is dependent on patient willingness to participate in the study and compliance with the assigned intervention strategy as well as the centre’s ability to provide the recommended intervention. The first analysis will look at feasibility and will be based on accrual principles. The Trial Steering Committee will identify 5-9 pilot centres with an expressed interest in the study and who have been determined to have the required infrastructure and previous successful experience with administering similar structured physical activity programs. Accrual in each pilot centre will be monitored for 12 months after centre local activation. The accrual of each centre will be reviewed using the targeted study accrual of nine patients/year in participating study centres as a benchmark. To be considered as a ‘success’ in this feasibility phase, each pilot centre should accrue a minimum of five patients with the average for all centres meeting the target accrual of nine patients/year or greater. Results of the feasibility study will be reviewed by the Trial Steering Committee.

It is expected that all pilot centres will be locally activated within six months of central activation of this study. Consideration for broader enrolment of the study will be given at six months after the last pilot centre has been locally activated and will be based on the performance of the pilot centres in trending to meet the benchmark for accrual. Other factors including issues related to trial conduct and training the trainers will also be considered before a decision is made to locally activate the trial at additional centres. Failure of a centre to locally activate this trial within six months of central activation will lead to consideration of replacing that centre.

The second analysis will focus on the feasibility for PA behavior change and will be based on the first 25% of patients (250) completing the 1 year of the intervention phase. The trial will be stopped if observed difference in the average MET hours/week between two treatment arms is less than 5. With this stopping rule and assuming that the standard deviation of MET hours/week is 20, the probability to continue the study will be higher than 88% if the true difference in the average MET hours/week between two treatment arms is 8 or higher. If the trial is stopped in this analysis, with 250 patients, we will have 80% power and at two-sided 5% level to detect a 7 point difference between two treatment arms in the change scores from baseline at 1 year in SF-36 physical functioning subscale based on assumption that the standard deviation of change score was around 20, which was observed from a previous study of breast cancer patients.

Two formal interim analyses for DFS will be performed on all randomized subjects when respectively around one third and two thirds of the required number of events for final analysis of DFS (i.e. 125 and 250 events) have been observed, which are expected to occur respectively approximately 3.3 and 5.3 years after the first patient is randomized. These analyses will be based on the stratified logrank test adjusting for ECOG performance status (0 vs. 1), disease stage (II vs. III) and BMI (≤ 27.5 vs. > 27.5) at the time of randomization and the Lan-DeMets error spending function approach *[Lan 1983]* using an O'Brien-Fleming stopping boundary to control for a two-sided alpha of 5% at the end of the study. For example, if exactly 125 and 250 DFS events were in the locked database for these two interim analyses, the nominal p-values for stopping the study would be 0.0004 and 0.0129, respectively. A futility analysis may be performed in the second formal interim analysis and a detailed plan for this futility analysis will be developed before the analysis.

Results of the interim analyses will be supplied to the DSMC who will communicate their recommendation regarding continuation of the trial to the Director of the CCTG.

13.9 Biomarker Evaluation

The following analysis will be performed to investigate the relationship between efficacy and fatigue endpoints and serum levels of insulin (IGF-1, IGF-2, IGFBP3) and cytokine levels.

For each biomarker, Cox Proportional Hazards model and linear mixed model will be used to model the relationship between respectively efficacy endpoints (DFS and OS) and fatigue endpoints (change scores from baseline) with baseline value of the biomarker. The model will also include assigned treatment, interaction between treatment and biomarker. Additional models that include other prognostic factors may be investigated.

Exploratory analyses, additional to those described in this section, such as alternative modeling approaches and analyses of other biomarkers are expected and may be performed. All analyses described in this section are based on availability of data.

14.0 PUBLICATION POLICY

14.1 Authorship of Papers, Meeting Abstracts, Etc

14.1.1 The results of this study will be published. Prior to trial activation, the chair will decide whether to publish the trial under a group title, or with naming of individual authors. If the latter approach is taken, the following rules will apply:

- The first author will generally be the chair of the study.
- A limited number of the members of the Canadian Cancer Trials Group, may be credited as authors depending upon their level of involvement in the study.
- Additional authors, up to a maximum of 25, will be those who have made the most significant contribution to the overall success of the study. This contribution will be assessed, in part but not entirely, in terms of patients enrolled and will be reviewed at the end of the trial by the study chair.
- In the event of a separate paper dealing with the quality of life outcomes, the first author will generally be the Quality of Life Coordinator on the Trial Steering Committee.
- In the event of a separate paper dealing with the health economics, the first author will be the Health Economics Coordinator on the Trial Steering Committee.
- In the event of a separate paper dealing with predictors of physical activity adherence, the first author will be the Study Chair responsible for the Physical Activity Program.
- In the event of a separate paper dealing with correlative biomarkers, the first author will be the Correlative Sciences Coordinator on the Trial Steering Committee.

14.1.2 In an appropriate footnote, or at the end of the article, the following statement will be made:

> "A study coordinated by the Canadian Cancer Trials Group. Participating investigators included: (a list of the individuals who have contributed patients and their institutions)."

14.2 Responsibility for Publication

It will be the responsibility of the study chair to write up the results of the study within a reasonable time of its completion. If after a period of six months following the analysis of study results the draft is not substantially complete, the central office reserves the right to make other arrangements to ensure timely publication.

14.3 Submission of Material for Presentation or Publication

Material may not be submitted for presentation or publication without prior review by the CCTG senior investigator, senior biostatistician, study coordinator, and approval of the study chair. Individual participating centres may not present outcome results from their own centres separately. Supporting groups and agencies will be acknowledged.

14.4 Publication of trial results must follow the authorship policy of the CCTG that is current at the time of publication.

15.0 ETHICAL, REGULATORY AND ADMINISTRATIVE ISSUES

15.1 Institution Eligibility for Participation

All member centres in good standing of the CCTG are eligible to participate in this study. Institutions which are not CCTG members can either make application for membership or submit a single study agreement document. Any centre joining the CCTG is required to sign a Participating Centre Study Agreement and have Standard Operating Procedures regarding the conduct of clinical trials.

15.2 Investigator Qualifications

For all investigators (principal investigators and co-investigators) the following documentation must be on file with the CCTG:

- A current curriculum vitae, updated and submitted within two years at the time of randomization.
- Documentation indicating completion of training in the protection of human research participants (e.g. NCI U.S. Completion Certificate).
- Completion of the required CCTG GCP training modules.

15.3 REB (Research Ethics Board) Approval for Protocols

Each participating centre will have on file with the CCTG central office, as part of its membership/ agreement documents, a description of its ethics review process and composition of its REB.

Initial Approval
Member centres wishing to participate in a trial are required to obtain full board local ethics approval of the protocol and consent form (see below) by the appropriate REB. A completed CCTG Confirmation of Initial Ethical Approval form must be submitted to document the REB was properly constituted and there were no conflicts of interest in the REB approval process.

Annual Re-Approvals
Annual re-approval must continue until CCTG informs you that they are no longer required.

Amendments/Administrative Updates
All amendments and administrative updates to the protocol must undergo review by local REBs. Amendments/administrative updates will be circulated to all participating sites in a standard format with clear instructions regarding REB review. If full board approval of an amendment is required it will be specified.

REB Refusals
If an REB refuses to approve this protocol (or an amendment/administrative update to this protocol) the CCTG must be notified immediately of the date of refusal and the reason(s) for the refusal.

15.4 Informed Consent

Informed Consent Document
The REB of an institution must approve the consent form document which will be used at that centre prior to its local activation; changes to the consent form in the course of the study will also require REB approval.

It is essential that the consent form contain a clear statement which gives permission for 1) information to be sent to and 2) source medical records to be reviewed by the CCTG and other agencies as necessary. The consent form must include all ICH-GCP consent elements. In addition, the consent form should include all elements required by CCTG policy, and centres receiving funding from NCEHR, SSHRC and/or CIHR should include elements from the Tri Council Policy Statement (TCPS).

Informed consent forms that do not contain all ICH-GCP required elements will require an amendment and will lead to the delay of local activation. A complete list of the elements required by regulations, guidelines and CCTG policy can be found by accessing the CCTG website at http://www.ctg.queensu.ca/private/ethics/consent_RE_Checklists.html.

Consent Process/Patient Eligibility
Patients who cannot give informed consent (i.e. mentally incompetent patients, or those physically incapacitated such as comatose patients) are not to be recruited into the study. Patients competent but physically unable to sign the consent form may have the document signed by their nearest relative or legal guardian. Each patient will be provided with a full explanation of the study before consent is requested.

15.5 Retention of Patient Records and Study Files

ICH Good Clinical Practice guidelines apply to CCTG studies. It is the responsibility of CCTG to inform the investigator/institution as to when trial related records no longer need to be retained. The investigator/institution should take measures to prevent accidental or premature destruction of these documents.

CCTG will notify all the trial investigators/institutions when trial related records no longer need to be retained.

15.6 Centre Performance Monitoring

This study is eligible for inclusion in the Centre Performance Index for which there are minimum standards. The requirements for submission of data are outlined in Appendix IV.

15.7 On-Site Monitoring/Auditing

In addition to the routine review of case report forms and supporting documents sent to the central office, CCTG site monitoring will be conducted at participating centres in the course of the study as part of the overall quality assurance programme. The monitors/auditors will require access to patient medical records to verify the data, as well as essential document binders, standard operating procedures (including electronic information) and ethics documentation.

The above mentioned documentation, in addition to any submitted source documents, may be accessed remotely in the event of a public health emergency either through remote access to Electronic Medical Records or through a secure file sharing portal.

15.8 Case Report Forms

This trial will use a web-based Electronic Data Capture (EDC) system for all data collection except Patient Reported Outcomes, Determinants of Exercise, Physical Activity Behaviour and Adherence and Eligibility questionnaires, Health Economics and SAE reporting. For details of accessing the EDC system and completing the on-line forms please refer to the *"Registration/Randomization and Data Management Guidebook"* posted on the CO.21 area of the CCTG web-site (www.ctg.queensu.ca).

The following ELECTRONIC CRFs will be used for this trial;

- Web Eligibility Checklist
- Initial Evaluation
- Intervention Report (up to 3 years post-randomization)
- Follow-up Report (4 and 5 years post-randomization)
- Follow-up Report (6 to 10 years post-randomization)
- Minimum Follow-up Report for Ineligibles
- Short Follow-up Report (for patients with recurrence/new primary malignancy)
- Recurrence/New Primary Malignancy Report
- Death Report

The following PAPER CRFs will be used for this trial:

- Quality of Life Questionnaire (SF-36)
- Fatigue Questionnaire (FACIT-F))
- Depression/Anxiety Questionnaire (HADS)
- Sleep Quality Questionnaire (PSQI)
- Physical Activity Questionnaire (TPAQ)
- Exercise Screening Questionnaire (LTEQ)
- Medical Screening Questionnaire (rParQ)
- Social Cognitive Determinants of Exercise Measure
- Work Productivity and Activity Impairment Questionnaire (WPAI)
- 30-Day Resource Use Diary
- Serious Adverse Event Form
- Physical Activity Consultant Report Forms

A list of all forms (electronic and paper) to be submitted, as well as expectation dates, are to be found in Appendix IV.

16.0 REFERENCES

Ainsworth BE, Haskell WL, Leon AS, Jacobs DR, Jr., Montoye HJ, Sallis JF, Paffenbarger RS, Jr. Compendium of physical activities: Classification of energy costs of human physical activities. Med Sci Sports Exerc 1993; 25:71-80.

Ainsworth BE, Haskell WL, Whitt MC, Irwin ML, Swartz AM, Strath SJ, O'Brien WL, Bassett DR, Jr., Schmitz KH, Emplaincourt PO, Jacobs DR, Jr., Leon AS. Compendium of physical activities: An update of activity codes and MET intensities. Med Sci Sports Exerc 2000; 32: S498-S504.

American College of Sports Medicine. ACSM's guidelines for exercise testing and prescription. 7th ed. Philidelphia, PA. Lippincott, Williams & Wilkens, 2006.

Andrews B, Shariat SF, Kim JH, et al. Preoperative plasma levels of interleukin-6 and its soluble receptor predict disease recurrence and survival of patients with bladder cancer. Journal of Urology 2002; 167: 1475-81.

Azjen I. The Theory of Planned Behavior. Organizational Behavior and Human Decision Processes 1991; 50: 179-211. 1991.

Bandura A. Social learning theory. Englewood Cliffs, N.J.: Prentice Hall, 1977.

Brazier J, Roberts J, Deverill M. The estimation of a preference-based measure of health from the SF-36. Journal of Health Economics 2002; 21(2):271-92.

Buysee DJ, Reynolds CF, Monk TH, Berman SR, & Kupfer DJ. The Pittsburgh Sleep Quality Index: A new instrument for psychiatric practice and research. Psychiatric Research 1989; 28(2): 193-213. (with permission from Elsevier Science).

Canadian Cancer Society/National Cancer Institute of Canada. Canadian Cancer Statistics. Toronto, Canada; 2008.

Church TS, Earnest CP, Skinner JS, & Blair SN. Effects of different doses of physical activity on cardiorespiratory fitness among sedentary, overweight or obese postmenopausal women with elevated blood pressure: A randomized controlled trial. Journal of American Medical Association 2007: 297(19): 2081-2091.

Courneya KS[a], Friedenreich CM, Quinney HA, Fields AL, Jones LW, Fairey AS. A randomized trial of exercise and quality of life in colorectal cancer survivors. European Journal of Cancer Care 2003; 12(4):347-357.

Courneya KS, Friedenreich CM, Quinney HA, Fields AL, Jones LW, Fairey AS. Predictors of adherence and contamination in a randomized trial of exercise in colorectal cancer survivors. Psycho-oncology 2004; 13(12):857-866.

Courneya KS, Friedenreich CM, Reid RD, Gelmon K, Mackey JR, Ladhar AB, Proulx C, Vallance JK, Segal RJ (in press). Predictors of follow-up exercise behaviour six months after a randomized control trial of exercise training during breast cancer chemotherapy. Breast Cancer Research and Treatment.

Courneya KS, Friedenrich CM. Relationship between exercise pattern across the cancer experience and current quality of life in colorectal cancer survivors. The Journal of Alternative and Complementary Medicine 1997: 3(3): 215-226.

Courneya KS[b]. Exercise in cancer survivors: An overview of research. [Review] [69 refs]. Medicine & Science in Sports & Exercise 2003;35(11):1846-52.

Dalgleish AG, O'byrne KJ. Chronic immune activation and inflammation in the pathogenesis of AIDS and cancer. Advances in Cancer Research 2002; 84: 231-76.

de Visser KE, Eichten A, Coussens LM. Paradoxical roles of the immune system during cancer development. Nat Rev Cancer 2006; 6(1):24-37.

Dekker MH, Lee S, Hudson R, et al. An exercise intervention without weight loss decreases circulating interleukin-6 in lean and obese men with and without type 2 diabetes mellitus. Metabolism 2007; 56: 332-8.

Doyle C, Kushi LH, Byers T, Courneya KS, Demark-Wahnefried W, Grant B et al. Nutrition and physical activity during and after cancer treatment: An American Cancer Society guide for informed choices. CA Cancer J Clin 2006; 56(6):323-353.

Drummond M, et al. Chp 7 Cost-benefit analysis. In Methods for the Economic Evaluation of Health Care Programmes, 3rd ED. Oxford University Press 2005. Olsen JA and Smith RD. Theory versus practice: A Review of Willingness to Pay in Health and Health Care. Health Econ 2001; 10:39-52.

Friedenreich CM, Courneya KS, Bryant HE. The lifetime total physical activity questionnaire: Development and reliability. Medicine & Science in Sports & Exercise 1998; 30: 266-274.

Friedenreich CM, Courneya KS, Neilson HK, Matthews CE, Willis G, Irwin M, Troiano R, Ballard-Barbash R. Reliability and validity of the Past Year Total Physical Activity Questionnaire. American Journal of Epidemiology 2006; 163: 959-970.

Friedenreich CM, Orenstein MR. Physical activity and cancer prevention: Etiologic evidence and biological mechanisms. J Nutr 2002; 132: 3456S-64S.

Froelicher ES, Christopherson DJ. Women's initiative for nonsmoking (WINS) I: Design and methods. Heart & Lung 2000; 29(6):429-437.

Galon J, Costes A, Sanchez-Cabo F, et al. Type, density, and location of immune cells within human colorectal tumours predict clinical outcome. Science 2006; 313: 1960-4.

Godin G, Shephard, RJ. A simple method to assess exercise behavior in the community. Can. J. Appl. Sport Sci 1985; 10: 141–146.

Gunter MJ, Leitzmann MF. Obesity and colorectal cancer: epidemiology, mechanisms and candidate genes. J Nutr Biochem 2006; 17(3):145-156.

Hamilton J, Butler L, Wagenaar H, Sveinson T, Ward KA, McLean Let al. The impact and management of cancer-related fatigue on patients and families. Canadian Oncology Nursing Journal 2001; 11(4):192-8.

Haskell WL, Lee I, Pate RR, et al. Physical activity and public health: Updated recommendation for adults from the American College of Sports Medicine and the American Heart Association. Med Sci Sports Exerc 2007; 39:1423-1434

Haydon AM, MacInnis RJ, English DR, Giles GG. Effect of physical activity and body size on survival after diagnosis with colorectal cancer. Gut 2006; 55(1):62-67.

Health Canada. Handbook for Canada's physical activity guide to healthy active living. Ottawa, Ontario (1998). (Contains a 2-page pullout guide.) Available at: http://www.phac-aspc.gc.ca/pau-uap/fitness/pdf/handbook_eng.pdf.

Hewitt JA, Mokbel K, van Someren KA, Jewell AP, Garrod R. Exercise for breast cancer survival: the effect on cancer risk and cancer-related fatigue (CRF). [Review] [64 refs]. International Journal of Fertility & Women's Medicine 2005;50(5:Pt 1):t-9.

Holmes MD, Chen WY, Feskanich D, Kroenke CH, Colditz GA. Physical activity and survival after breast cancer diagnosis. JAMA 2005; 293(20):2479-2486.

Irwin ML, Yutaka Y, Ulrich CM, Bowen D, Rudolph RE, Schwartz RS, Yukawa, M, Aiello E, Potter JD, McTiernan A. Effect of exercise on total and intra-abdominal body fat in postmenopausal woman: A randomized controlled trial. Journal of American Medical Association 2003; 289(3): 323 – 330.

Jacobs DR, Ainsworth BE, Hartman TJ, Leon AS. A simultaneous evaluation of 10 commonly used physical activity questionnaires. Medicine and Science in Sports and Exercise 1993; 25: 81-91.

Jones LW, Courneya KS, Fairey AS, Mackey JR. Does the theory of planned behaviour mediate the effects of an oncologist's recommendation to exercise in newly diagnosed breast cancer survivors? Results from a randomized controlled trial. Health Psychology 2005; 24, 189-197.

Jones LW, Mark-Wahnefried W. Diet, exercise, and complementary therapies after primary treatment for cancer. [Review] [78 refs]. Lancet Oncology 2006; 7(12):1017-26.

Karvinen KH, Courneya KS, Campbell KL, Pearcey RG, Dundas G, Capstick V, Tonkin KS. Exercise preferences of endometrial cancer survivors: A population-based study. Cancer Nursing 2006; 29: 259-265.

Karvinen KH[a], Courneya KS, Campbell KL, Pearcey RG, Dundas G, Capstick V, Tonkin KS. Correlates of exercise motivation and behaviour in a population-based sample of endometrial cancer survivors: An application of the theory of planned behaviour. International Journal of Behavioural Nutrition and Physical Activity 2007; 4: 21.

Karvinen KH[b], Courneya KS, Venner P, North S. Exercise programming and counseling preferences in bladder cancer survivors: A population-based study. Journal of Cancer Survivorship 2007; 1: 27-34.

Knols R, Aaronson NK, Uebelhart D, Fransen J, Aufdemkampe G. Physical exercise in cancer patients during and after medical treatment: a systematic review of randomized and controlled clinical trials. [Review] [69 refs]. Journal of Clinical Oncology 2005; 23(16):3830-42.

Knowler WC, Barrett-Connor E, Fowler SE, Hamman RF, Lachin JM, Walker EA et al. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Engl J Med 2002; 346(6):393-403.

Lan K, DeMets DL. Discrete sequential boundaries for clinical trials. Biometrika 1983; 70:659-663.

Luctkar-Flude MF, Groll DL, Tranmer JE, Woodend K. Fatigue and physical activity in older adults with cancer: A systematic review of the literature. [Review] [90 refs]. Cancer Nursing 2007; 30(5):E35-E45.

Lynch, B.M. Describing and predicting psychological distress after colorectal cancer. Cancer 2008; 112(6): 1363-1370.

Mantovani G, Maccio A, Madeddu C. et al. Quantitative evaluation of oxidative stress, chronic inflammatory indices and leptin in cancer patients : correlation with stage and performance status. International Journal of Cancer 2002; 98: 84-91.

McTiernan A, Sorensen B, Irwin ML, Morgan A, Yasui Y, Rudolph RE, Surawicz C, Lampe JW, Lampe P, Ayub K, Potter JD. Exercise Effect on weight and body fat in men and women. Obesity 2007; 15: 1496-1512.

McTiernan A, Yasui Y, Sorensen B, Irwin ML, Morgan A, Rudolph RE, Surawicz C, Lampe JW, Ayub K, Potter JD, Lampe PD. Effect of a 12-month exercise intervention on patterns of cellular proliferation in colonic crypts: A randomized controlled trial. Cancer Epidemiology Biomarkers Prevention 2006; 15(9): 1588-1597.

Meyerhardt JA[a], Giovannucci EL, Holmes MD, Chan AT, Chan JA, Colditz GA et al. Physical activity and survival after colorectal cancer diagnosis. J Clin Oncol 2006; 24(22):3527-3534.

Meyerhardt JA[b], Heseltine D, Niedzwiecki D, Hollis D, Saltz LB, Mayer RJ et al. Impact of physical activity on cancer recurrence and survival in patients with stage III colon cancer: findings from CALGB 89803. J Clin Oncol 2006; 24(22):3535-3541.

Meyerhardt JA, Sloan JA, Sargent DJ, Goldberg RM, Pollak M, Morton RF et al. Associations between plasma insulin-like growth factor proteins and C-peptide and quality of life in patients with metastatic colorectal cancer. Cancer Epidemiol Biomarkers Prev 2005; 14(6):1402-1410.

Meyers CA, Albitar M, Estey E. Cognitive impairment, fatigue, and cytokine levels in patients with acute myelogenous leukemia or myelodysplastic syndrome. Cancer 2005; 104(4):788-793.

Monninkhof EM, Elias SG, Vlems FA, van dt I, Schuit AJ, Voskuil DW, et al. Physical activity and breast cancer: A systematic review. [Review] [75 refs]. Epidemiology 2007;18(1):137-57.

O'Brien PC, Fleming TR. A multiple testing procedure for clinical trials. Biometrics 1979; 35(3):549-556.

O'Byrne KJ, Dalgleish AG. Chronic immune activation and inflammation as the cause of malignancy. Br J Cancer 2001; 85(4):473-483.

Osoba D, Bezjak A, Brundage M, Zee B, Tu D, Pater Jet al. Analysis and interpretation of health-related quality-of-life data from clinical trials: basic approach of The National Cancer Institute of Canada Clinical Trials Group. European Journal of Cancer 2005; 41(2):280-7.

Paul N, Pater J, Whitehead M, Sadura A. Methods of toxicity data collection: and evaluation of the relative effectiveness of the case resort flow sheet, the patient symptom diary, and the quality of life questionnaire. Controlled Clinical Trials 1991;12(5):648-55.

Pedersen BK, Steensberg A., Schjerling P. Muscle-derived interleukin-6: possible biological effects. Journal of Physiology 2001; 536: 329-337.

Pedersen BK[a]. IL-6 signalling in exercise and disease. Biochem Soc Trans 2007; 35: 1295-7.

Pedersen BK[b], Akerstrom TC, Nielsen AR, et al. Role of myokines in exercise and metabolism. Journal of Applied Physiology 2007; 103: 1093-8.

Pedersen BK, Febbraio M. Muscle-derived interleukin-6 – a possible link between skeletal muscle, adiopose tissue, liver and brain. Brain Behav Immun 2005; 19: 371-6

Pollak MN, Schernhammer ES, Hankinson SE. Insulin-like growth factors and neoplasia. Nat Rev Cancer 2004; 4(7):505-518.

Punt CJA, Buyse M, Kohne CH, Hohenberger P, Labianca R, Schmoll HJ, Pahlman L, Sobrero A., Douillard JY Endpoints in adjuvant treatment trials : A systematic review of the literature in colon cancer and proposed definitions for future trials. Journal of National Cancer Institute 2007; 99: 998-1003.

Pusztai L, Mendoza TR, Reuben JM, et al. Changes in plasma levels of inflammatory cytokines in response to paclitaxel chemotherapy. Cytokine 2004; 25: 94-102.

Reilly Associates, WPAI General Information (Updated March 18, 2008). http://www.reillyassociates.net/WPAI_General.html. (Accessed July 16, 2008).

Reilly MC, Zbrozek AS, Dukes EM. The validity and reproducibility of a work productivity and activity impairment instrument. Pharmacoeconomics. 1993; 4:353–365.

Rikli R, Jones J. Development and validation of a functional fitness test for community-residing older adults. Journal of Aging and Physical Activity, 1999; 129-161.

Samad AK, Taylor RS, Marshall T, Chapman MA. A meta-analysis of the association of physical activity with reduced risk of colorectal cancer. Colorectal Dis 2005; 7(3):204-213.

Sargent DJ, Wieand HS, Haller DG, Gray R, Benedetti JK, Buyse M et al. Disease-free survival versus overall survival as a primary end point for adjuvant colon cancer studies: Individual patient data from 20,898 patients on 18 randomized trials. J Clin Oncol 2005; 23(34):8664-8670.

Schmitz KH, Holtzman J, Courneya KS, Masse LC, Duval S, Kane R. Controlled physical activity trials in cancer survivors: A systematic review and meta-analysis. [Review] [64 refs]. Cancer Epidemiology, Biomarkers & Prevention 2005;14(7):1588-95.

Tan TT, Coussens LM. Humoral immunity, inflammation and cancer. Curr Opin Immunol 2007; 19(2):209-216.

The Look AHEAD Research Group. Reduction in weight and cardiovascular disease risk factors in individuals with type 2 diabetes: One-year results of the Look AHEAD trial. Diabetes Care 2007; 30(6): 1374-1383.

Tu D. Minimization procedure. In: Chow S-C, ed. Encyclopedia of biopharmaceutical statistics. 2nd ed., rev. New York: Marcel Dekker 2003: 614-8.

US Department of Health and Human Services physical activity guidelines for Americans. Available at www.health.gov/paguidelines .

Vallance JK [a], Courneya KS, Plotnikoff RC, Dinu I, Mackey JR. Maintenance of physical activity in breast cancer survivors after a randomized trial. Medicine & Science in Sports & Exercise 2007: 173-180.

Vallance JK, Courneya KS, Plotnikoff RC, Mackey JR.. Analyzing theoretical mechanisms of physical activity behaviour change in breast cancer survivors: Results from the activity promotion (ACTION) trial. Annals of Behavioural Medicine. 2008; 35: 150-158.

Vallance JK [b], Courneya KS, Plotnikoff RC, Yasui Y, Mackey JR. Randomized controlled trial of the effects of print materials and step pedometers on physical activity and quality of life in breast cancer survivors. J Clin Oncol 2007; 25: 2352-2359.

Vallance JKH, Courneya KS, Jones LW, Reiman T. Exercise preferences among a population-based sample of non-Hodgkin's lymphoma survivors. European Journal of Cancer Care 2006; 15, 34-43.

Vardy J, Booth C, Pond G, Galica J, Zhang J, Dhillon H, et al. Cytokine levels in patients with colorectal cancer and breast cancer and their relationship to fatigue and cognitive function. Proceedings of the American Society of Clinical Oncology Annual Meeting. Chicago, 2007.

Vener C, Guffanti A, Pomati M, et al. Soluble cytokine levels correlate with the activity and clinical stage of Hodgkin's disease at diagnosis. Leukemia and Lymphoma 2000; 37: 333-9.

Ward WL, Hahn EA, Mo F, Hernandez L, Tulsky DS, Cella D. Reliability and validity of the Functional Assessment of Cancer Therapy-Colorectal (FACT-C) quality of life instrument. Quality of Life Research 1999; 8(3):181-95.

Wieckowski J, Simmons J. Translating evidence-based physical activity interventions for frail elders. Home Health Care Service Quarterly 2006; 25: 75-94.

World Cancer Research Fund and the American Institute for Cancer research. Food, nutrition, physical activity, and the prevention of cancer: aA global perspective. American Institute for Cancer Research, 2007.

Wyrwich KW, Nienaber NA, Tierney WM, Wolinsky FD. Linking clinical relevance and statistical significance in evaluating intra-individual changes in health-related quality of life. Medical Care 1999 ;37(5):469-78.

Yellen SB, Cella DF, Webster K, Blendowski C, Kaplan E. Measuring fatigue and other anemia-related symptoms with the Functional Assessment of Cancer Therapy (FACT) measurement system. Journal of Pain & Symptom Management 1997; 13(2):63-74.

Yost KJ, Cella D, Chawla A, Holmgren E, Eton DT, Ayanian JZet al. Minimally important differences were estimated for the Functional Assessment of Cancer Therapy-Colorectal (FACT-C) instrument using a combination of distribution- and anchor-based approaches.[see comment]. Journal of Clinical Epidemiology 2005; 58(12):1241-51.

Zigmord AS, Snaith RP. the Hospital Anxiety and Depression Scale. Acta Psychatr Scand 1983; 67: 361-270.

APPENDIX I - GLOSSARY OF TERMS

AGC	Absolute granulocyte count
ALT	Alanine aminotransferase
AST	Aspartate aminotransferase
BMI	Body Mass Index
CEA	Carcinoembryonic antigen
CRC	Colorectal cancer
DFS	Disease-free survival
DSMC	Data Safety and Monitoring Committee
FACT-F	Functional Assessment of Cancer Therapy - fatigue subscale
HADS	Hospital Anxiety and Depression Scale
	HADS-A Hospital Anxiety and Depression Scale (anxiety subscale)
	HADS-D Hospital Anxiety and Depression Scale (depression subscale)
HGB	Hemoglobin
IGF	Insulin growth factor
IGFBP	Insulin growth factor binding protein

LTEQ	Leisure Time Exercise Questionnaire
LYs	Life years
MCID	Minimally clinically important difference
MET	Metabolic Equivalent Task
OS	Overall Survival
PA	Physical Activity
PAC	Physical Activity Consultant
PAWG	Physical Activity Working Group
PBC	Perceived behavioural control
PROs	Patient Reported Outcomes
PSQI	Pittsburg Sleep Quality Index
PYTPAQ	Past Year Total Physical Activity Questionnaire
QALYs	Quality Adjusted Life Years
QOL	Quality of Life
RCT	Randomized controlled trial
rPAR-Q	revised Physical Activity Readiness Questionnaire
SF-36	PCS - physical component summary
	MCS - mental component summary
SFT	Senior's Fitness Test
SuRG	Survivorship Research Group
TPAQ	Total Physical Activity Questionnaire
TPB	Theory of Planned Behaviour
UNL	Upper normal limits
WBC	White blood cells
WPI	Work Productivity and Activity Impairment Questionnaire

APPENDIX II - PATIENT EVALUATION FLOW SHEET

Required Investigations	Pre-registration	Pre-randomization	Until Recurrence/New Primary Malignancy			After Recurrence/New Primary Malignancy		
			Every 6 mths (years 1-3)	Every 12 mths (years 4-5)	Every 12 mths (6-10 years)	Every 6 mths (years 1-3)	Every 12 mths (years 4-5)	Every 12 mths (6-10 years)
History and Physical								
Blood pressure + heart rate	X							
History, physical exam, weight	X		X	X		X	X	
Height	X							
Smoking History	X		X	X		X	X	
Disease status	X		X	X	X			
Overall survival	X		X	X	X	X	X	X
ECOG performance status	X							
Exercise Screening questionnaire (LTEQ)	X							
Medical suitability for exercise questionnaire (rPAR-Q)	X							
Major Medical Problems	X							
Concomitant Medications	X		X	X				
Non-protocol anti-cancer therapy						X	X	
Hematology								
AGC + hgb + platelets + WBC	X							
Biochemistry								
LFTs (bilirubin, alkaline phos., ALT)	X							
Serum creatinine	X							
Carcinoembryonic Antigen (CEA)	X		X	X				
Radiology								
Chest x-ray or CT	X		X 12, 24 & 36 mths					
CT, MRI or U/S abdomen	X		X 12, 24 & 36 mths					
Colonoscopy			Once between 30-48 mths post-randomization					
Other			As clinically indicated to document recurrence/ new primary malignancy					
Fitness Testing								
Submaximal Exercise Test		X	X*					
Seniors' Fitness test		X	X*					
Hip and waist circumference		X	X*					
Other Investigations								
Serum and plasma collection		X+	X 12, 24 & 36 mths					
Fasting glucose		X+	X 12, 24 & 36 mths					
Adverse Events								
Adverse event assessments	X		X	X				
Patient Reported Outcomes								
FACIT-F		X	X	X				
SF-36		X	X	X		X	X	
PSQI		X	X	X				
HADS		X	X	X				
Physical Activity Behaviour/Adherence								
TPAQ		X	X	X				
Social-Cognitive Determinants of Exercise		X	X					
Health Economics								
Resource Utilization Assessment			X	X		X	X	
WPAI Questionnaire		X	X	X		X	X	
30-Day Resource Use Diary			X**	X		X	X	

* at 6, 12, 24 and 36 mths.

** including first month of intervention period

+ must be collected at the same time but may be collected within 14 days pre-registration (after informed consent obtained) or post-registration at the discretion of the centre

APPENDIX III - PERFORMANCE STATUS SCALES/SCORES

PERFORMANCE STATUS CRITERIA

Karnofsky and Lansky performance scores are intended to be multiples of 10.

ECOG (Zubrod)		Karnofsky		Lansky*	
Score	Description	Score	Description	Score	Description
0	Fully active, able to carry on all pre-disease performance without restriction.	100	Normal, no complaints, no evidence of disease.	100	Fully active, normal.
		90	Able to carry on normal activity; minor signs or symptoms of disease.	90	Minor restrictions in physically strenuous activity.
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g. light housework, office work.	80	Normal activity with effort; some signs or symptoms of disease.	80	Active, but tires more quickly.
		70	Cares for self, unable to carry on normal activity or do active work.	70	Both greater restriction of and less time spent in play activity.
2	Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours.	60	Requires occasional assistance, but is able to care for most of his/her needs.	60	Up and around, but minimal active play; keeps busy with quieter activities.
		50	Requires considerable assistance and frequent medical care.	50	Gets dressed, but lies around much of the day; no active play; able to participate in all quiet play and activities.
3	Capable of only limited selfcare; confined to bed or chair more than 50% of waking hours.	40	Disabled, requires special care and assistance.	40	Mostly in bed; participates in quiet activities.
		30	Severely disabled, hospitalization indicated. Death not imminent.	30	In bed; needs assistance even for quiet play.
4	Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair.	20	Very sick, hospitalization indicated. Death not imminent.	20	Often sleeping; play entirely limited to very passive activities.
		10	Moribund, fatal processes progressing rapidly.	10	No play; does not get out of bed.

* The conversion of the Lansky to ECOG scales is intended for NCI reporting purposes only.

APPENDIX IV - DOCUMENTATION FOR STUDY

This trial will use a web-based Electronic Data Capture (EDC) system for all data collection except Patient-Reported Outcomes, Physical Activity Behaviour and Adherence, Social Cognitive Determinants of Exercise, Health Economics and Eligibility Questionnaires and SAE reporting. For details of accessing the EDC system and completing the on-line Case Report Forms please refer to the "Registration/Randomization and Data Management Guidebook" posted on the CO.21 area of the CCTG web-site (www.ctg.queensu.ca)

The ELECTRONIC CRFs to be used in this trial are as follows:

Electronic Form	To be Completed	To be submitted electronically	Supporting Documentation Required
Eligibility Checklist/ Baseline Report	Within 2 weeks after randomization	Within 6 weeks after randomization	• Copies of signed consent form and optional blood banking consent • Relevant pathology reports • Relevant radiology reports • LTEQ (pre-registration and pre-diagnosis) • SF-36 • FACIT-F • PSQI • HADS • TPAQ • WPAI • Social-Cognitive Determinants of Exercise • PAC Testing Results form
Intervention Report	At the end of each 6 month period from randomization to 36 months	Within 6 weeks from the date patient was seen in clinic	• Chest CT or x-ray report (12, 24 and 36 months) • CT/MRI/US abdomen report (12, 24 and 36 months) • Colonoscopy report if applicable • SF-36 • FACIT-F • PSQI • HADS • TPAQ • WPAI • 30-Day Resource Use Diary • Social-Cognitive Determinants of Exercise • PAC Testing Results forms • PA Program Summary form
Follow-up Report – Year 4 and 5	Annually from 4 to 5 years post-randomization	Within 8 weeks from the date patient was seen in clinic	• Colonoscopy report if applicable • SF-36 • FACIT-F • PSQI • HADS • TPAQ • WPAI • 30-Day Resource Use Diary
Follow-up Report – Years 6-10	Annually from 6 to 10 years post-randomization	Within 8 weeks from the date patient was seen in	None required

		the clinic	

Continued on next page …

Electronic Form	To be Completed	To be submitted electronically	Supporting Documentation Required
Short Follow-up Report	*Complete ONLY for patients who have had a recurrence or new primary malignancy.* At the end of each 6 month period from randomization to 36 months and annually from 4 to 10 years	Within 8 weeks from the date patient was seen in the clinic	Until 5 years: • SF-36 • WPAI • 30-Day Resource Use Diary
Minimal Follow-up Report	*Complete ONLY for ineligible patients. Please discuss with central office staff* Annually until year 10	Within 6 weeks of contact	If available/applicable • Autopsy report • Radiology or pathology report
Death Report	When patient dies	Within 8 weeks of patient's death	Autopsy Report (if available)
Recurrence/ New Primary Malignancy Report	Upon disease recurrence or new primary malignancy	Within 8 weeks of recurrence or new primary malignancy	Relevant radiology and pathology reports

The PAPER CRFs to be used in this trial are as follows:

Paper Form	To be Completed	Due in CCTG Central Office
Serious Adverse Event Report Form*	At the time of event	To be FAXED within 24 hours of knowledge of event. Paper copy to be mailed within 10 working days.
Patient Reported Outcomes (SF-36, FACIT-F, PSQI, HADS)	See sections 5.0 and 8.0	Mail as soon as the corresponding form (WEC/Baseline Report, Intervention Report, Follow-up Report – Year 4 and 5, Short Follow-up Report) has been submitted electronically
Social-Cognitive Determinants of Exercise	See sections 5.0 and 8.0	Mail as soon as the corresponding form (WEC/Baseline Report, Intervention Report) has been submitted electronically
Total Physical Activity Questionnaire (TPAQ)	See sections 5.0 and 8.0	Mail as soon as the corresponding form (WEC/Baseline Report, Intervention Report, Follow-up Report – Year 4 and 5) has been submitted electronically
Health Economics (WPAI, 30-Day Resource Use Diary)	See sections 5.0 and 8.0	Mail as soon as the corresponding form (WEC/Baseline Report, Intervention Report, Follow-up Report – Year 4 and 5, Short Follow-up Report) has been submitted electronically
Physical Activity Consultant Forms	See sections 5.0 and 8.0	Mail as soon as the corresponding form (WEC/Baseline Report, Intervention Report) has been submitted electronically
Eligibility Questionnaires (LTEQ)	See section 5.0	Mail as soon as corresponding WEC/Baseline Report has been submitted electronically
* See Section 10.0 Serious Adverse Event Reporting for details.		

APPENDIX V - MET EQUIVALENT HOURS

Table 1. MET-Hours of Activities Surveyed	
Recreation-Time Activity	MET-Hours
Normal pace walking (2 to 2.9 mph)	3
Brisk pace walking (3 to 3.9 mph)	4
Very brisk pace walking (4_ mph)	4.5
Jogging (slower than 10 min/mile)	7
Running (faster than 10 min/mile)	12
Bicycling	7
Tennis, Squash, racquetball	7
Lap swimming	7
Calisthenics, ski or stair machine, other aerobic exercise	6
Yoga, stretching, toning, lower intensity exercise	4
Other vigorous activities (lawn mowing)	6
Abbreviations: MET – metabolic equivalent task; mph – miles per hour.	

APPENDIX VI - NCI COMMON TERMINOLOGY CRITERIA FOR ADVERSE EVENTS VERSION 3.0 (CTCAE)

This study will utilize the NCI Common Terminology Criteria for Adverse Events Version 3.0 (CTCAE) for adverse events and serious adverse event reporting. The full listing of CTCAE Version 3.0 adverse events will be used from randomization until 5 years from randomization. A copy of the CTCAE Version 3.0 can be downloaded from the CTEP home page: http://ctep.cancer.gov/reporting/ctc.html. All appropriate treatment areas should have access to a copy of the CTCAE Version 3.0.

APPENDIX VII - ELIGIBILITY QUESTIONNAIRES

(rPAR-Q, Leisure Time Exercise Questionnaires)

This study will utilize the Physical Activity Readiness Questionnaire (rPAR-Q) as a screening questionnaire to determine patients' readiness to participate in physical activity from a medical perspective. The Leisure Time Exercise Questionnaire (LTEQ) will be used to capture exercise participation prior to registration (Pre-Registration) and for the six month period preceding their diagnosis of colon cancer (Pre-Diagnosis). The Pre-Registration LTEQ will be used to determine patients' eligibility to participate in CO.21.

Please refer to Section 5.0 for schedule for completion.

The questionnaires can be downloaded at:

rPAR-Q: http://www.ctg.queensu.ca/trials/gastro-intestinal/co21/co21.html

LTEQ (Pre-Registration): http://www.ctg.queensu.ca/trials/gastro-intestinal/co21/co21.html

LTEQ (Pre-Diagnosis): http://www.ctg.queensu.ca/trials/gastro-intestinal/co21/co21.html

APPENDIX VIII - PATIENT REPORTED OUTCOMES (PROS) ASSESSMENTS

Introduction

Patient reported outcomes (such as QOL) are relevant to cancer patients as they measure, from the patient perspective, the symptom-related and functional benefits from the physical activity program intervention that can not be ascertained from data regarding toxicity or adverse events *[Paul 1991]*. The primary hypothesis related to PROs in this trial is participation in a physical activity program plus general health education materials will result in improved PROs scores in comparison to general health education materials only.

Current literature reveals interesting things; two in particular are:

- additional and useful information may be obtained from patient reported outcome measurements
- a growing consensus that the goal of medical care today for most patients is the preservation of function and well-being in everyday life.

We have reached the stage where the collection of information about psychological distress, social disruption, emotional trauma and painful side-effects is not only necessary but a routine component in many protocols.

Patient reported outcome data can be used in a variety of ways:

- to try to achieve the best possible outcome for patients
- to evaluate the extent of change in the quality of life of an individual or group across time
- to evaluate new treatments and technologies
- to try to provide the best value for health care dollars
- to compare costs and benefits of various financial and organizational aspects of health care services

In the future, approval of not only drugs but also new therapies or methods of delivery will most likely be based on a combination of quality of life, survival, response, and adverse event data.

Instructions for Administration of a Patient Reported Outcome Questionnaire. The instructions below are intended as a guide for the administration of the Patient Reported Outcome questionnaires.

1. Preamble

   Patient reported outcome data are collected for research purposes, and will usually not be used for the patient's individual medical care. The assessment is in the form of self report questionnaires. Therefore, they must be completed by the patient only, without translation, coaching or suggestions as to the "correct" answer by relatives or health care personnel.

   The usual scheduled times to obtain the questionnaires are as follows:

   - pre-randomization (baseline)
   - during treatment
   - during follow-up

   The information provided by the patient in the completed questionnaires is confidential and should not be discussed with or shown to anyone who is NOT mentioned in the consent form signed by the patient.

   If a whole questionnaire has not been completed, please document the reason(s) on the appropriate case report forms.

2. Pre-treatment Assessment

   It should be explained to the patient that the purpose of the questionnaires is to assess the impact of treatment on different areas of the patient's life, e.g. psychological distress, social disruption, side-effects, et cetera.

   The CRA should collect the questionnaires as soon as they have been completed, check to see that each question has been answered and gently remind the patient to answer any inadvertently omitted questions. If a patient states that s/he prefers not to answer some questions and gives a reason(s), the reason(s) should be noted on the questionnaire. If a specific reason is not given, this also should be noted on the questionnaire.

3. Assessments During Treatment

   The questionnaires should be given to the patient before being seen by the doctor, and prior to either a supervised physical activity session or fitness testing, as required by the schedule in the protocol. If the patient does not have a doctor visit scheduled, or if it was not possible for the patient to complete the questionnaires before being seen by the doctor, s/he should still complete the questionnaires prior to a supervised physical activity session or fitness testing.

4. Assessments During Follow-up

   The questionnaires should be given to the patient before being seen by the doctor, on follow-up visits as required by the schedule.

A patient may, on occasion, be reluctant to complete the questionnaires because they feel unwell. In that case, you may express sympathy that things are below par, but state that this is exactly the information we require if we are to understand more about how quality of life is affected.

It defeats the whole purpose of the assessment if it is delayed until the patient feels better!

5. What If . . .

   The patient should complete the questionnaires at the clinic.

   There may be circumstances when the patient does not complete the questionnaire as required in the clinic. Three situations are described below. In these cases, it is beneficial if patient reported outcome data can still be collected.

   A. The patient leaves the clinic before the questionnaires could be administered, or someone forgets to give the questionnaires to the patient.

      Contact the patient by phone informing him or her that the questionnaires were not completed. Ask the patient if s/he is willing to complete them:

      If yes, mail blank questionnaires to the patient, and make arrangements for return of the questionnaires in a timely fashion. Record the date they were mailed and the date received on the questionnaires.

If this is not feasible, then ask the patient if s/he is willing to complete questionnaires over the phone. If the patient agrees, read out the questions and range of possibilities, and record the answers. Make a note on the questionnaires that the questionnaires were completed over the phone.

If no, note the reason why the questionnaires were not completed on the appropriate case report form.

B. The patient goes on an extended vacation for several months and won't attend the clinic for regular visit(s).

Ensure that the patient has a supply of questionnaires, with instructions about when to complete them, and how to return them. If it is known beforehand, give the patient blank questionnaires at the last clinic visit; if the extended absence is not known in advance, mail the blank questionnaires to the patient. Written instructions may help ensure that the patient stays on schedule as much as possible.

C. The patient does not want to complete the questionnaires in clinic.

Should the patient not wish to answer the questionnaires in the clinic but insists on taking them home, and failing to comply with the patient's wishes is likely to result in the questionnaires not being completed at all, then the patient may take the questionnaires home with instructions that it is to be completed the same day. When the questionnaires are returned, the date on which the questionnaires were completed should be noted and a comment made on the questionnaires as to why the patient took it away from the clinic before completion.

6. Waiving the Patient Reported Outcome Component

Patient reported outcomes are mandatory components of this trial. Patient reported outcome questionnaires will be available in either English or French. Participants who are unable to complete the questionnaires in either of Canada's two official languages will not be eligible to participate in this trial. Translation of the questions is not acceptable.

7. Unwillingness to Complete Patient Reported Outcome Questionnaires

If a patient speaks and reads English or French, but does not wish to complete the questionnaires then s/he is NOT eligible and should NOT be put on study.

8. Inability to Complete Patient Reported Outcome Questionnaires (for reason other than illiteracy in English or French)

An eligible patient may be willing but physically unable to complete the questionnaires, because of blindness, paralysis, etc. If the patient is completing the PROs assessment in the clinic, the questionnaires should be read to them and the answers recorded by a health care professional (e.g. preferably the clinical research associate assigned to the trial, but another clinic nurse, a doctor or social worker who is familiar with the instructions for administering the questionnaires would be acceptable). If the patient is completing the questionnaires at home, and a telephone interview by the clinical research associate is not possible, then a spouse or friend may read the questions to the patient and record the answers. However, this method should be a last resort, and the spouse or friend should be instructed to not coach or suggest answers to the patient. Whichever method is used, it should be recorded on the questionnaires.

Patient Reported Outcomes Questionnaires

This study will utilize the SF-36, FACIT_F (FACT-F), the Pittsburgh Sleep Quality Index (PSQI) and the Hospital Anxiety and Depression Scale (HADS) as patient reported outcomes questionnaires.

Please refer to sections 5.0 and 8.0 for schedule for completion.

The questionnaires can be downloaded at:

SF-36: http://www.ctg.queensu.ca/trials/gastro-intestinal/co21/co21.html

FACIT_F (FACT-F): http://www.ctg.queensu.ca/trials/gastro-intestinal/co21/co21.html

PSQI: http://www.ctg.queensu.ca/trials/gastro-intestinal/co21/tests-questionnaires/co21-PittsburghSleepQualityIndex-PSQI-2009dec04.pdf

HADS: http://www.ctg.queensu.ca/trials/gastro-intestinal/co21/tests-questionnaires/co21-HADS-English-2009dec04.pdf

APPENDIX IX - HEALTH ECONOMICS QUESTIONNAIRES

This study will utilize the Work Productivity and Activity Impairment (WPAI) Questionnaire and the 30-Day Resource Use Diary as components of the health economics analyses.

Please refer to sections 5.0 and 8.0 for schedule for completion.

The questionnaires can be downloaded at:

WPAI: http://www.ctg.queensu.ca/trials/gastro-intestinal/co21/co21.html

30-Day Resource Use Diary: http://www.ctg.queensu.ca/trials/gastro-intestinal/co21/co21.html

APPENDIX X - PHYSICAL ACTIVITY BEHAVIOUR AND ADHERENCE QUESTIONNAIRES.

This study will utilize the Total Physical Activity Questionnaire (TPAQ), the Social Cognitive Determinants of Exercise Measure and Physical Activity Logs to monitor physical activity behaviour and adherence.

Please refer to sections 5.0 and 8.0 for schedule of completion.

The questionnaires can be downloaded at:

TPAQ: http://www.ctg.queensu.ca/trials/gastro-intestinal/co21/co21.html

Social Cognitive Determinants of Exercise Measure:
http://www.ctg.queensu.ca/trials/gastro-intestinal/co21/co21.html

Physical Activity Log: http://www.ctg.queensu.ca/trials/gastro-intestinal/co21/co21.html

APPENDIX XI - SENIORS' FITNESS TEST (SFT)

This study will use the Seniors' Fitness Test as a standardized tool for assessing the functional fitness of study participants.

Please refer to sections 5.0 and 8.0 for schedule of completion.

The test can be downloaded at:

SFT: http://www.ctg.queensu.ca/trials/gastro-intestinal/co21/co21.html

APPENDIX XII - SUB-MAXIMAL EXERCISE TESTING PROTOCOL

The sub-maximal exercise test used in this study will be a treadmill test. The purpose of the sub-maximal treadmill test is to determine whether or not the patient is physically able to exercise at moderate to vigorous intensity. The exercise testing will be conducted by the PACs affiliated with each cancer clinic. The Balke treadmill protocol will be used to estimate maximum oxygen consumption from sub-maximal exercise intensities.

Prior to the modified Balke treadmill test, the patient has had the rPAR-Q signed by the investigator – if any of the answers to the rPAR-Q are 'yes' then these items have been discussed with the investigator and the investigator has determined the patient is suitable for exercise testing and a physical activity program. This will be given to the PAC or the Clinical Research Associate will have communicated the results to the PAC. If the patient has been cleared to exercise, he/she will be asked if he/she is currently using any medications. The patient is then asked to put on a heart rate monitor. The purpose of the procedure will be explained to the patient and a resting heart rate and blood pressure will be measured.

Resting Heart Rate

Resting pulse will be taken at the beginning of the exercise test. It should be taken in a quiet area away from other activities. The patient should sit down and relax at a table and chair with both feet flat on the floor for at least five minutes before the measurement is taken. A clock or watch with a second hand is required for this procedure.

The patient should be asked to rest their arm on the table with palm turned upward. The measurement is usually taken from the radial pulse using the pads of the index and middle finger. Fingers are used to palpate until maximum pulsation is detected, pulse is counted for 15 seconds using the second hand of a watch or clock and multiplied by 4. A heart rate monitor may also be used. The heart rate is then recorded.

The resting heart rate reading should be below 99 bpm for the participant to be eligible to undertake the exercise test. Two readings should be taken if the first reading is above 99 bpm. If two readings above 99 bpm occur at the exercise test, but a lower heart rate reading was taken by the patient's physician (that has been recorded on the baseline form 1), it will supersede the readings taken at the exercise test.

Resting Blood Pressure

A conventional mercury sphygmomanometer, appropriate sized blood pressure cuff and stethoscope will be used to measure blood pressure. A clock or watch with a second hand will be required and the blood pressure measurement area should be free of excessive noise. The patient should be seated comfortably with both feet on the ground and arm resting on a table. The blood pressure reading should be below 144/94 for the participant to be eligible to undertake the exercise test. Two readings should be taken if the first reading is above 144/94. If two readings above 144/94 occur at the exercise test, but a lower blood pressure reading was taken by the patient's physician (that has been recorded on the baseline form 1), it will supersede the readings taken at the exercise test. This decision rule is to avoid exclusion of study patients on the basis of a possibly inflated blood pressure reading that is occurring because of a possible "white coat" or anxiety-driven increase in blood pressure. If the patient has underlying hypertension that had not been treated, they are ineligible for the study until their hypertension has been controlled.

Treadmill Test Procedures

The patient will then be shown how to walk on the treadmill and how to indicate to the PAC to stop the test; some time will be spent acclimatizing the subject to the treadmill.

Once the patient is ready, he/she will begin walking at 2.0 mph for three minutes with no elevation. After 3 minutes, the speed will increase to 3.0 mph, every three minutes thereafter the grade (elevation) will increase by 2.5% until the test is complete. Each three minute block is a stage of the test. The exercise test is complete when the patient has finished the stage during which he/she reached 85% of his/her maximum heart rate. Heart rate will be recorded during the last 5 seconds of each minute of the test. Blood pressure will be recorded during the last 45 seconds of each stage and rating of perceived exertion (RPE) will be recorded during the last 5 seconds of each stage. The speed may be modified to compensate for treadmills that cannot reach the required % grade for the later stages of the modified Balke protocol.

Criteria for stopping the test prematurely will include:

- Heart rate reaches:
  - 85% of maximum HR + 10 bpm or
  - 90% of maximum HR or
  - 85% of maximum HR and RPE $\geq$ 17
- For patients on beta blockers, a modified HR formula (164 – 0.7 x age) will be used to estimate their maximum heart rate. Patients on beta blockers will then have their submaximal fitness test stopped when they reach 85% of this adjusted maximum heart rate.
- Patient reaches exhaustion or volitionally reports extreme fatigue or exhaustion
- Abnormal blood pressure response to exercise:
  - An excessive rise in blood pressure as indicated by a systolic pressure ≥ 220 mmHg, and/or diastolic pressure ≥ 110 mmHg, or
  - A drop in systolic blood pressure ≥ 10 mmHg from baseline blood pressure (or failure of systolic blood pressure to increase) with increasing exercise intensity (confirm BP reading by repeating measure immediately, before stopping test).
- Chest pain
- Irregular heart rate response to exercise:
  - Failure of heart rate to increase with increasing exercise intensity, or
  - Changes to heart rhythm
- Shortness of breath, wheezing, or difficulty breathing
- Change in color (pallor) or participant disorientation
- Unusual muscle weakness, pain, or cramps
- Increasing nervous system symptoms, including ataxia (lack of coordination of muscle movements), dizziness, blurred vision, near syncope (fainting)
- Signs of poor perfusion (circulation or blood flow), including pallor (pale appearance to the skin), cyanosis (bluish discoloration), or cold and clammy skin
- Patient requests discontinuation of the test
- Opinion of tester that participant needs to stop the test for any other reason

The time on treadmill at which 85% of the maximum heart rate is reached may be recorded but is not a stopping criteria.

When the patient has reached the end of the test, he/she will actively cool down at a slower pace; after two minutes the patient will be asked to sit down and heart rate and blood pressure will be measured and recorded. The patient will remain seated for an additional three minutes; heart rate and blood pressure will be measured and recorded (five minutes post exercise). Once heart rate and blood pressure return to resting levels, the heart rate monitor will be removed and the test will be completed.

To be eligible for the CHALLENGE Trial, two stages of the test must be completed.

Equations for Predicting Maximum Oxygen Consumption

VO_2 and VO_2 max will be calculated electronically in the central database using the data provided at the end of each session using the multistage model and the ACSM metabolic equations provided for estimating maximum oxygen consumption.

A multistage model is used to predict VO_2 using the following calculations:

ACSM Calculation for predicting VO_2:

VO_2 (ml/kg/min) = 3.5 ml/kg/min + speed (m/min) x 0.1 + % grade (decimal) x speed (m/min) x 1.8

Where:

- mph = 26.8 m/min
- is the regression constant for converting m/min to ml/kg/min
- 1.8 is the regression constant for converting m/min to ml/kg/min
- % grade/100 = decimal i.e. 5%/100 = 0.05

The VO_2 will be calculated using the above equations for the last two completed stages of the test. The estimated maximum VO_2 will be calculated using the following equation

$VO_{2max} = SM2 + b (HR_{max} – HR2)$

Where:

- b is the slope b = (SM2-SM1)/(HR2-HR1)
- SM2 is the calculated VO_2 at the last stage completed
- SM1 is the calculated VO_2 at the second last stage completed
- HR2 is the heart rate at the last stage completed
- HR1 is the heart rate at the second last stage completed
- HRmax will be calculated using 220 – Age

Exercise Blood Pressure Protocol

- Any patient with high blood pressure, i.e. > 180/100 during exercise can continue if their RPE is low, i.e. < 14 and they are comfortable. Monitor blood pressure and RPE as exercise continues.
- If blood pressure is high (>180/100) and RPE is high (> 15) reduce exercise workload and monitor blood pressure for a normal response (blood pressure should decrease with a decrease in workload).
- Exercise patients with consistently high blood pressure during workout sessions should be monitored over a three-week period. If blood pressure at 60% of workload does not decrease over the three-week time frame, patient should be referred back to physician for further review.
- Any patient with an exercise blood pressure greater than 220/110 should stop exercise and see their referring physician before continuing in the CHALLENGE Trial Physical Activity Program.

APPENDIX XIII - GENERAL HEALTH EDUCATION MATERIALS

The following documents are available either from the CO.21 webpage: (http://www.ctg.queensu.ca/trials/gastro-intestinal/co21/co21.html) or from the pages towards the end of the document.

- Canada's Food Guide
- Tips to Get Active (adults and older adults versions)
- Move Your Body
- Eat for Health

APPENDIX XIV - EMERGENCY SITUATIONS AND COMPLIANCE

Management of Protocol Variances in Emergency Situations

Compliance with the trial protocol should be ensured to every extent possible, however in emergency situations, specific variances from the protocol that occur as a result of efforts to minimize or eliminate hazards and protect the safety and well-being of patients are permissible.

In these rare circumstances, minor deviations that do not impact patient safety or willingness to participate or trial integrity, which have been justified and documented in the medical record by the QI/SI will not be considered to be REB reportable deficiencies requiring action, but must be reported to CCTG (e.g. in Electronic Data Capture (EDC) or using trial specific deviation logs as directed by CCTG) within 4 weeks of the end of the Emergency Situation, unless otherwise instructed by CCTG, and to your REB at the next amendment or annual approval.

Centres should also discuss these reporting requirements with their local REB, and review the trial website for additional guidance specific to the trial.

Minor Protocol Deviations:

- Missed or delayed protocol mandated visits or investigations on treatment or in follow up.
- Changes in study drug distribution (e.g. drug distributed remotely or IV drug given at satellite site), providing permitted by local SOPs, or written procedure established and is approved by CCTG or acceptable per further instruction from CCTG. *Note there will be no exceptions for injectable/IV investigational agents as must be administered at participating site.*
- Alternative methods for safety assessments (e.g. telephone contact, virtual visit, alternative location for assessment).
- Patient care and evaluations provided by non-research staff, providing overseen by QI/SI who must make all treatment decisions and ensure that all required information and results will be reported to allow central data submission. Includes physical exam, clinical laboratory tests, research blood collections that can be shipped centrally, imaging, non-investigational drug therapy*, standard radiation therapy, surgery, and other interventions that do not require protocol-specified credentialing*.

  **Must be approved by CCTG or acceptable per further instruction from CCTG.*
- Re-treatment following extended treatment delays if protocol specifies that excessive delays require discontinuation, providing other protocol requirements for discontinuation have not been met and either discussed with CCTG or acceptable per further instruction from CCTG.

Note:

- Applicable only to COVID-19 and other CCTG designated emergency situations.
- No waivers will be given for eligibility, including performance of protocol mandated tests/imaging.
- Deficiencies will be issued if patients are enrolled when trial is on accrual hold, for unreported Serious Adverse Events as well as changes in drug distribution/administration and/or re-treatment after extended treatment delays when not discussed and approved by CCTG or acceptable per further instruction from CCTG.
- Deviations or changes that are believed to impact patient safety, compromise the study integrity or affect willingness to participate are still considered Major Protocol Violations and must be reported to CCTG and your REB. These include more than a minimal delay in protocol therapy administration.

LIST OF CONTACTS

	Contact	Tel. #	Fax #
RANDOMIZATION AND INQUIRIES	Sara Rushton Clinical Trials Assistant CCTG Email: srushton@ctg.queensu.ca	613-533-6430	613-533-2941
STUDY SUPPLIES Forms, Protocols	Available on CCTG Website: http://www.ctg.queensu.ca under: *Clinical Trials*		
PRIMARY CONTACTS FOR GENERAL PROTOCOL-RELATED QUERIES (including eligibility questions and protocol management)	Patti O'Brien Study Coordinator CCTG Email: pobrien@ctg.queensu.ca *or* Dr. Chris O'Callaghan Senior Investigator CCTG Email: cocallaghan@ctg.queensu.ca		
STUDY CO-CHAIRS	Dr. Kerry Courneya Study Co-Chair Email: kerry.courneya@ualberta.ca *or* Dr. Christopher Booth Study Co-Chair Email: boothc@KGH.KARI.NET		
SERIOUS ADVERSE EVENT REPORTING See protocol Section 10.0 for details of reportable events.	Dr. Chris O'Callaghan Senior Investigator *or* Patti O'Brien Study Coordinator CCTG	613-533-6430	613-533-2941

LIST OF MATERIALS / QUESTIONNAIRES / TESTS

Canada's Food Guide

Tips to Get Active (Adults and Older Adults versions)

Move Your Body

Eat for Health

rPAR-Q

LTEQ (Pre-Registration)

LTEQ (Pre-Diagnosis)

SF-36

FACIT_F (FACT-F)

PSQI

HADS

WPAI

30-Day Resource Use Diary

TPAQ

Social Cognitive Determinants of Exercise Measure

Physical Activity Log

SFT

Canada's food guide

The New Food Guide

Health Canada
Office of Nutrition Policy and Promotion
2019

Health Canada Santé Canada

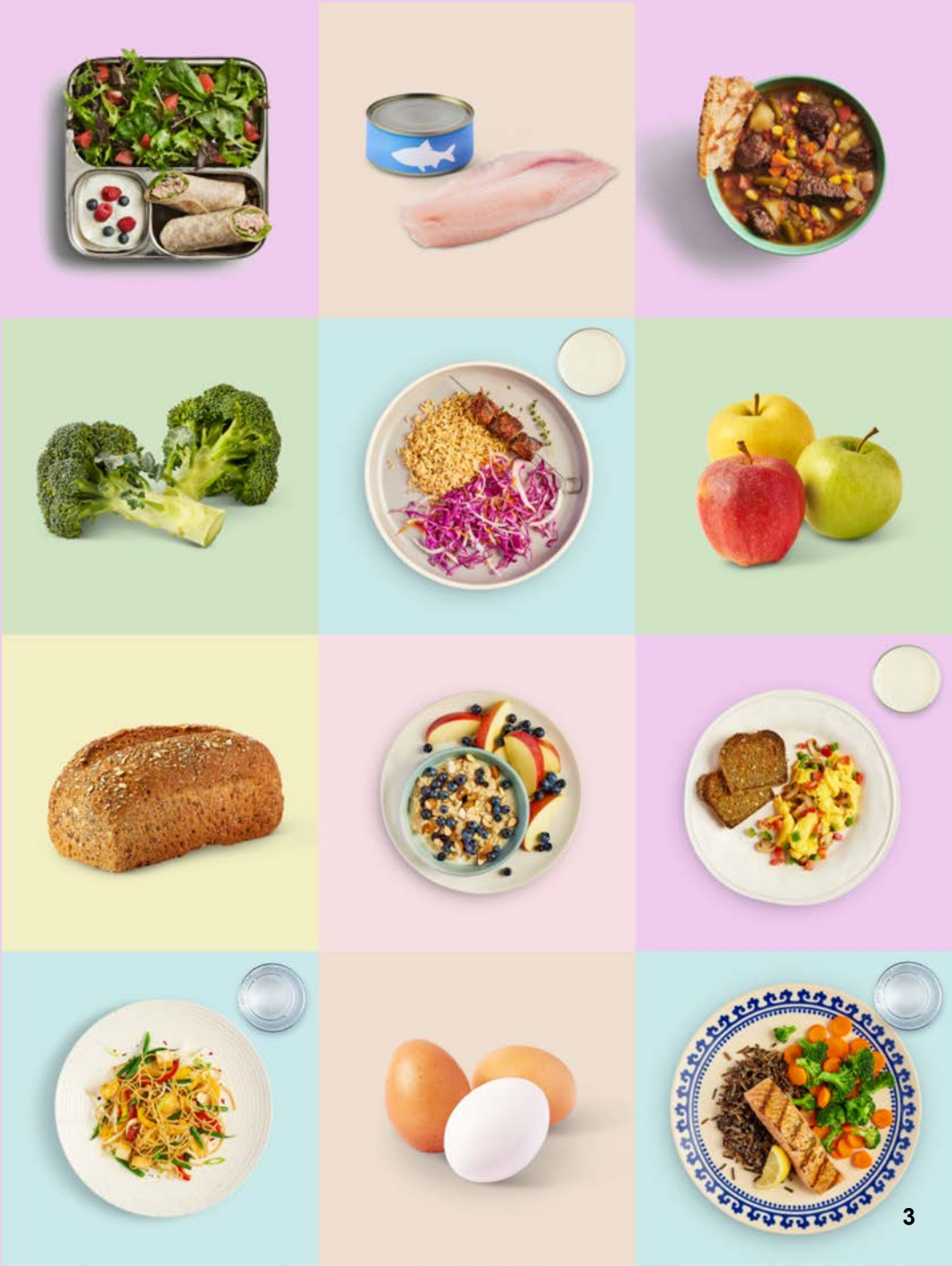
Canada

Overview

- Background
- Evidence and engagement
- What's new with Canada's Food Guide
  - For health professionals and policy makers
  - For Canadians
- Summary and next steps

Canada's food guide

Background



Why the Food Guide Matters to Canadians

Integrated widely by governments and stakeholders into nutrition policies, programs, and resources.

Taught in schools and promoted by health professionals when supporting Canadians to eat well.

Can help influence the foods served and sold in Canada's public institutions from day cares and schools, to long-term care facilities, as well as the foods Canadians choose for themselves and their families.

Why Healthy Eating Information Matters

Disease Risk

Unhealthy diet is a primary risk factor for disease burden in Canada

Complex

Nutrition information can be difficult to use and understand

Confusing

Conflicting healthy eating messages are everywhere

Credible

Canadians need credible healthy eating information

Why Revise?

To **address challenges** for users such as:

- applying recommendations in every day life, including building healthy meals and snacks
- providing the right information to the right audience

To **ensure alignment** with most current evidence on topics such as sodium, saturated fat and sugars.

Canada's food guide

Evidence and Engagement

Canada's food guide

Solid Evidence

The best available evidence was considered, including:

- only high-quality scientific reports on food and health from respected authorities including systematic reviews on over **100** food-related topics
- over **400** convincing conclusions

The *Evidence Review for Dietary Guidance 2015* and the *Food, Nutrients and Health: Interim Evidence Update 2018*, form the foundation of the new Food Guide.

Industry-commissioned reports were excluded to reduce the potential for, or the perception of, conflict of interest.

Responsible and Meaningful Engagement

Consulted extensively to ensure resources are evidence based, useful, and relevant to Canadians.

Online public consultations with Canadians and interested stakeholders helped to identify needs and expectations.

To help communicate the guidance accurately, targeted consultations were held with:

- academics
- Indigenous experts
- provincial and territorial governments
- other federal departments
- National Indigenous Organizations
- health professional regulatory bodies/organizations and health charities

Openness and Transparency

Submissions received during public consultations were summarized in *What We Heard* reports available at Canada.ca.

When Health Canada senior officials met with organizations to discuss the development of the Food Guide, details including the name of the organization and purpose of meeting, were posted on Canada.ca.

Health Canada's Office of Nutrition Policy and Promotion officials responsible for drafting the Food Guide did not meet with industry representatives to discuss the Food Guide.

Relevant and Useful

User-Centred

Public opinion research and consultations to understand how healthy eating information is used

Health Literacy

Lens applied throughout the crafting and testing of messages

Diversity

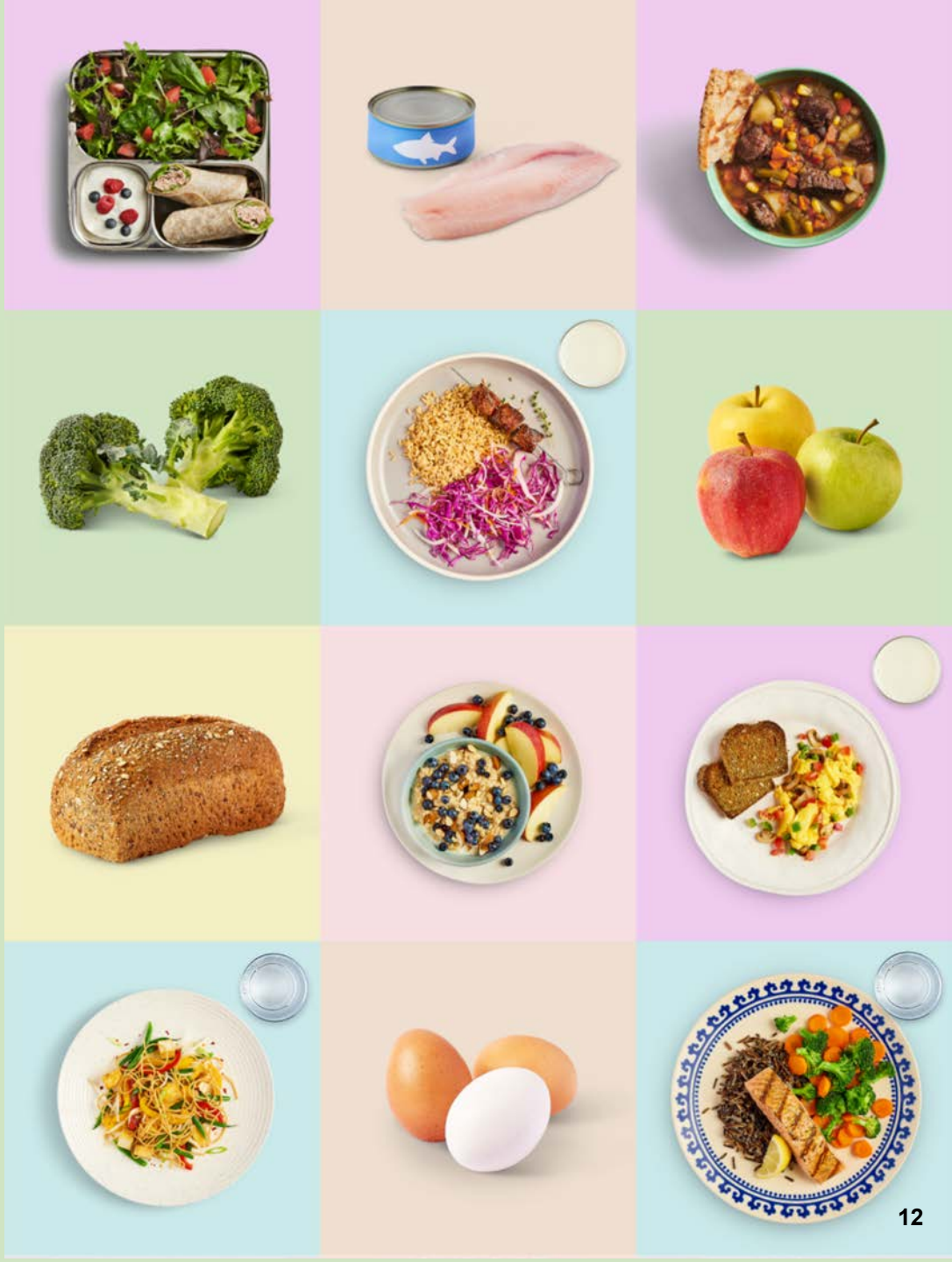
Tested with a range of ages, household incomes, locations, education levels, and cultural backgrounds

Considerations

Determinants of health, the environment, and cultural diversity, including social, cultural and historical context of Indigenous Peoples

Canada's food guide

What's New with Canada's Food Guide?



Canada’s Food Guide at a Glance

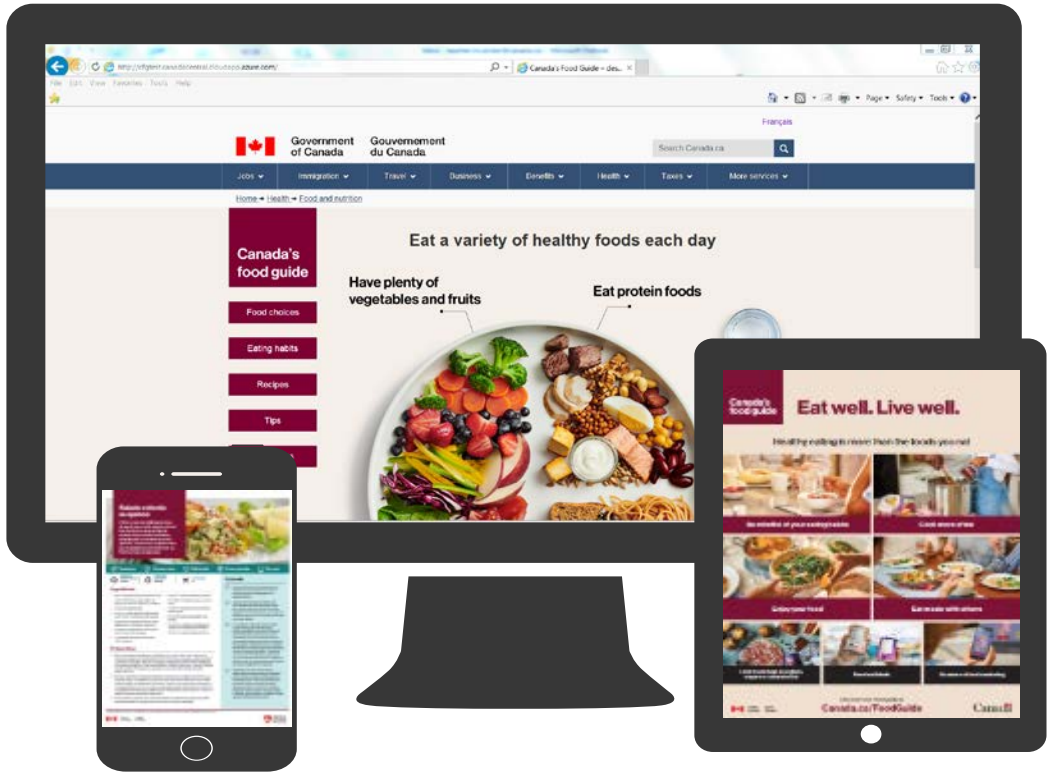
The new Food Guide is an **online suite of resources** that better meets the needs of different users including the general public, policy makers, and health professionals. Highlights include:

- Actionable advice for Canadians on healthy food choices and healthy eating habits including cooking more often and being mindful of eating habits
- Updated recommendations on saturated fat, sodium, and sugars including guidance on confectioneries and sugary drinks such as soft drinks, sweetened milk and juice
- Mobile-responsive web content to support Canadians to eat healthy whenever, and wherever they go

Canada's food guide

Online Resources
Available in English and French

- Canada's Dietary Guidelines for Health Professionals and Policy Makers
- Food Guide snapshot
- Videos, recipes and actionable advice
- Evidence including the *Evidence Review for Dietary Guidance 2015* and the *Food, Nutrients and Health: Interim Evidence Update 2018*



Canada.ca/FoodGuide

Considerations for Indigenous Peoples

As part of reconciliation, the Government of Canada acknowledges that program and policy making must support self-determination, as well as recognize the distinct nature and lived experience of First Nations, Inuit and Métis.

The integration of Indigenous considerations has been informed through engagement with Indigenous academics, health professionals and National Indigenous Organizations.

- Input to *Canada's Dietary Guidelines* addressed the social, cultural and historical factors that are determinants of healthy eating and that may influence the application of dietary guidance in Indigenous populations.

- Indigenous health professionals and health professionals with experience and expertise working with Indigenous populations provided input to inform the *Food Guide snapshot*.

Canada's food guide

Canada's Dietary Guidelines

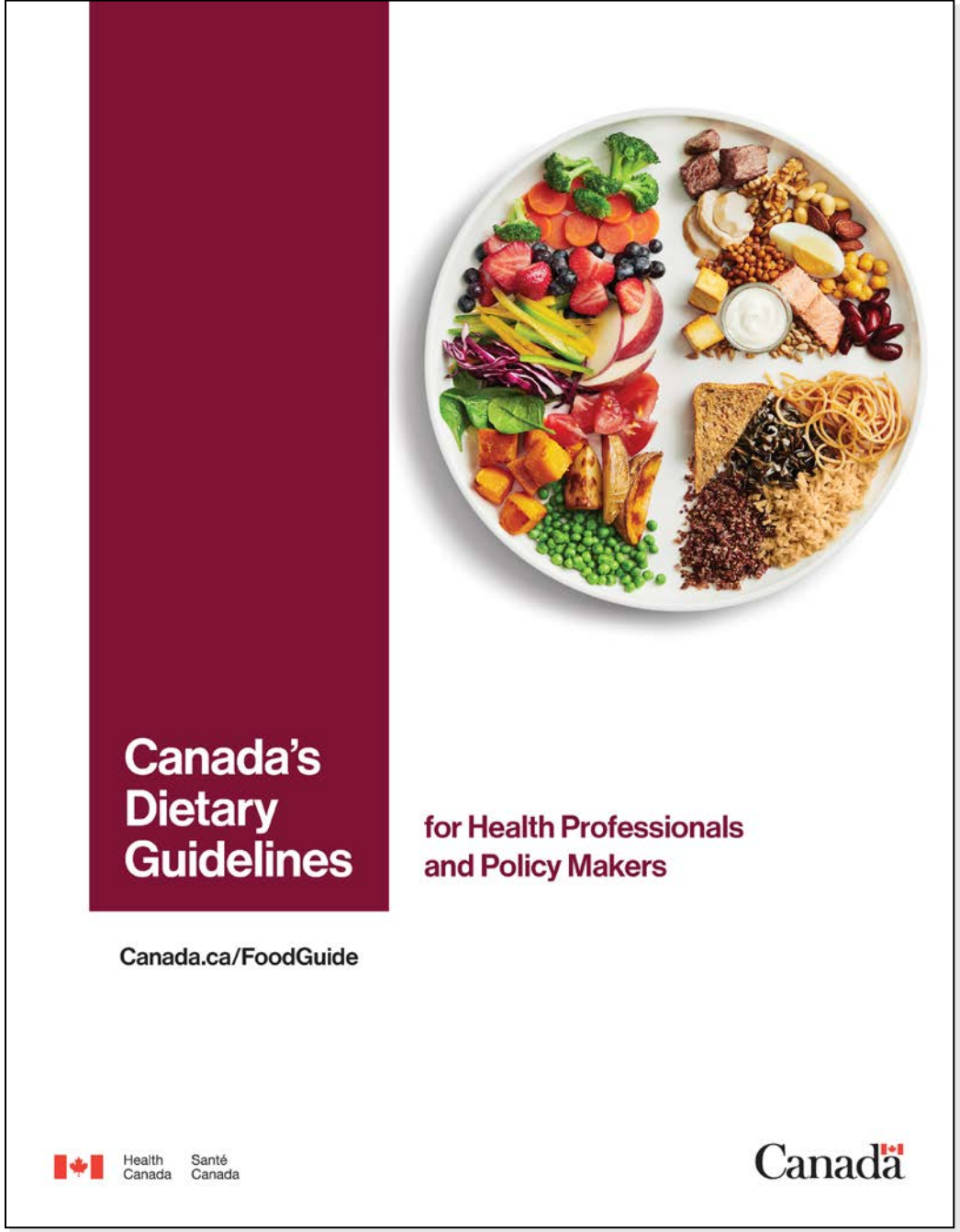
For Health Professionals and Policy Makers

For use when developing policies, programs, and educational resources.

Forms the foundation for the Food Guide resources.

Provides guidance on:

- Nutritious foods and beverages that are the foundation for healthy eating
- Foods and beverages that can have a negative impact on health when consumed on a regular basis
- Food skills as a practical way to support healthy eating
- Supportive environments for healthy eating



Canada's food guide

Guideline 1: Foundation for healthy eating

Vegetables, fruit, whole grains, and protein foods should be consumed regularly. Among protein foods, consume plant-based more often.

Why? Patterns of eating that emphasize plant-based foods typically result in higher intakes of vegetables and fruit, nuts, soy protein, and fibre; and lower intake of processed meats and foods that contain mostly saturated fat.

- ✓ Eating more vegetables and fruit is linked to a lower risk of cardiovascular disease.
- ✓ Eating more nuts or soy protein is linked to improved blood lipid levels.
- ✓ Higher fibre intake is linked to improved blood lipid levels and a lower risk of cardiovascular disease, colon cancer, and type 2 diabetes.
- ✓ Processed meat has been linked to colorectal cancer and foods that contain mostly saturated fat are linked to unfavourable blood lipid levels and a higher risk of type 2 diabetes.

Protein foods include legumes, nuts, seeds, tofu, fortified soy beverage, fish, shellfish, eggs, poultry, lean red meat including wild game, lower fat milk, lower fat yogurts, lower fat kefir, and cheeses lower in fat and sodium.

Canada's food guide

Guideline 1: Foundation for healthy eating

Foods that contain mostly unsaturated fat should replace foods that contain mostly saturated fat.

Why? Cardiovascular disease is one of the leading causes of death in Canada.

- ✓ Lowering the intake of saturated fat by replacing it with unsaturated fat decreases total and LDL-cholesterol.
- ✓ Elevated LDL-cholesterol is a well-established risk factor for cardiovascular disease.

The intention is not to reduce total fat in the diet. Rather, it is to help reduce intakes of saturated fat, while encouraging foods that contain mostly unsaturated fat.

Canada's food guide

Guideline 1: Foundation for healthy eating

Water should be the beverage of choice.

Why? Water supports health and promotes hydration without adding calories to the diet.

- ✓ Water is essential for metabolic and digestive processes.
- ✓ Adequate intake is based on the total water required to prevent the effects of dehydration.

Canada's food guide

Guideline 2: Foods and beverages that undermine healthy eating

Processed or prepared foods and beverages that contribute to excess sodium, free sugars, or saturated fat undermine healthy eating and should not be consumed regularly.

Why? Canadians are purchasing more highly processed foods.

- ✓ When consumed on a regular basis, they can contribute to excess sodium, sugars, or saturated fat. These nutrients are linked to chronic disease risk when consumed in excess.

Canada's food guide

Guideline 2: Foods and beverages that undermine healthy eating

Considerations

There are health risks associated with alcohol consumption.

Why? Alcoholic beverages can contribute a lot of calories to the diet with little to no nutritive value. They also increase the risk of developing chronic disease.

- ✓ Alcohol can be a significant source of sodium, free sugars, or saturated fat when mixed with syrups, sugary drinks, or cream-based liquors.
- ✓ Well-established health risks are associated with long-term alcohol consumption, including increased risk of many types of cancer and other serious health conditions, such as hypertension and liver disease.

Foods and beverages offered in publically funded institutions should align with Canada's Dietary Guidelines.

Why? Offering healthier options and limiting the availability of highly processed foods and beverages, such as sugary drinks and confectioneries, creates supportive environments for healthy eating.

Canada's food guide

Guideline 3: Importance of food skills

Cooking and food preparation using nutritious foods should be promoted as a practical way to support healthy eating.

Why? There has been a shift from cooking meals with basic ingredients towards use of highly processed products, which requires fewer or different skills.

- ✓ The increased use of these products has decreased the transfer of food skills to children and adolescents.
- ✓ Improving food skills by cooking and preparing food at home can contribute to improved food choices and eating behaviours among Canadians of all ages. It may also make it easier for Canadians to reduce household food waste.

Canada's food guide

Guideline 3: Importance of food skills

Food labels should be promoted as a tool to help Canadians make informed food choices.

Why? Food labels can help Canadians make informed food choices in various settings, such as grocery stores.

- ✓ Encouraging the use of food labels can be an effective strategy to promote the selection of nutritious foods and support the preparation of healthy meals and snacks.

Canada's food guide

Implementation of Dietary Guidelines

Programs and policies that align with these Guidelines provide an opportunity to create supportive environments for healthy eating.

Creating supportive environments across settings, such as schools, workplaces, recreation centres, and health care facilities, can help increase the influence of the Guidelines.

Understanding and acting on the barriers that make it challenging for Canadians to make healthy food choices are essential for the successful implementation of the Guidelines.

Food Guide Snapshot

Canada's food guide

For Canadians

At-a-glance presentation of food choices and eating habits.

An interactive, mobile-responsive online resource that is also printer-friendly.

Online entry point to Canada's healthy eating recommendations (*slides 26-28*).

Canada's food guide

Eat a Variety of Healthy Foods Each Day

Eat plenty of vegetables and fruits, whole grain foods and protein foods. Choose protein foods that come from plants more often.

- Choose foods with healthy fats instead of saturated fat.

Examples:

- Vegetables and fruit including fresh, frozen or canned options
- Whole grain foods such as whole grain pasta, brown rice and quinoa
- Protein foods such as lentils, lean meats, fish, unsweetened milk and fortified soy beverages

Canada's food guide

Eat a Variety of Healthy Foods Each Day

Make water your drink of choice.

- Replace sugary drinks with water.

Unsweetened drink options other than water can include lower fat white milk, plant-based beverages, coffee and tea

Eat a Variety of Healthy Foods Each Day

Limit highly processed foods. If you choose these foods, eat them less often and in small amounts.

- Prepare meals and snacks using ingredients that have little to no added sodium, sugars or saturated fat.

Use food labels.

Be aware that food marketing can influence your choices.

Healthy Eating is More Than the Foods You Eat

Be Mindful of Your Eating Habits. • Take time to eat. Notice when you are hungry and when you are full.	**Cook More Often.** • Involve others in planning and preparing meals.
Enjoy Your Food. • Culture and food traditions can be part of healthy eating.	**Eat Meals with Others.** • Share food traditions, across generations and cultures.

Canada's food guide

Summary and Next Steps

Canada's food guide

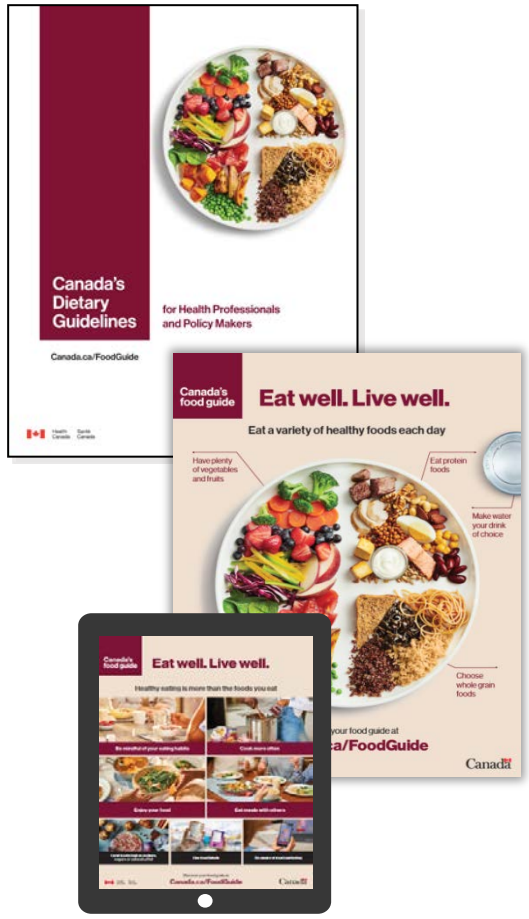
Summary

Canada's Food Guide is….

…an online **suite of resources** that better meets the needs of the general public, policy makers, and health professionals.

…based on a solid foundation of **evidence** and recommendations are aligned with many jurisdictions and trusted health authorities.

...shifting to provide more **actionable advice** for Canadians on healthy food choices and healthy eating habits.



What's Still to Come

Canada's Healthy Eating Pattern for Health Professionals and Policy Makers

- Will be released later in 2019
- For use by health professionals and policy makers
- Will build on *Canada's Dietary Guidelines* and will include a healthy eating pattern that will provide more specific guidance on amounts and types of food

Online resources

- Will be enhanced on an ongoing basis

What’s Still to Come

Considerations for Indigenous Peoples

Health Canada and Indigenous Services Canada are working with First Nations, Inuit and Métis to support the development of distinction-based healthy eating tools as part of the revision process.

Share the New Food Guide

If you wish to share messages about the Food Guide, you can access:

- Web banners and buttons
- Promotional poster
- Printer-friendly version of the Food Guide snapshot

Content can be found at Canada.ca/FoodGuide or on social media

#CanadasFoodGuide

Tips to Get Active

> Physical Activity Tips for Adults (18-64 years)

Physical activity plays an important role in your health, well-being and quality of life. Improve your health by being active as part of a healthy lifestyle.

1

Be active at least **2.5 hours a week** to achieve health benefits.

2

Focus on **moderate to vigorous aerobic activity** throughout each week, broken into sessions of 10 minutes or more.

3

Get stronger by adding activities **that target your muscles and bones** at least two days per week.

Tips to help you get active

- ☑ **Choose a variety of physical activities you enjoy.** Try different activities until you find the ones that feel right for you.
- ☑ **Get into a routine** — go to the pool, hit the gym, join a spin class or set a regular run and do some planned exercise. Make it social by getting someone to join you.
- ☑ **Limit the time you spend watching TV** or sitting in front of a computer during leisure time.
- ☑ **Move yourself** — use active transportation to get places. Whenever you can, walk, bike, or run instead of taking the car.
- ☑ **Spread your sessions of moderate to vigorous aerobic activity throughout the week.** Do at least 10 minutes of physical activity at a time.
- ☑ **Join a team** — take part in sports and recreation activities in groups. You'll make new friends and get active at the same time.

- **Set a goal**
- **Make a plan**
- **Pick a time & place**
- **Every step counts**

Public Health Agency of Canada | Agence de la santé publique du Canada

Canada

Tips to Get Active

> Physical Activity Tips for Adults (18-64 years)

Health Benefits

LIVE LONGER! LIVE HEALTHIER!

Physical activity is an important part of a healthy lifestyle. Regular physical activity can help to reduce the risk of premature death and chronic diseases such as coronary heart disease, stroke, hypertension, colon cancer, breast cancer, type-2 diabetes and osteoporosis.

EVERY STEP COUNTS!

If you're not active now, adding any amount of physical activity can bring some health benefits. Take a step in the right direction. Start now and slowly increase your physical activity to meet the recommended levels.

FEEL BETTER!

Regular physical activity can improve your overall sense of well being by improving fitness levels and self esteem, reducing the effects of stress, increasing energy and contributing to positive mental health.

What is moderate aerobic activity?

Moderate-intensity aerobic activity makes you breathe harder and your heart beat faster. You should be able to talk, but not sing.

› Examples of moderate activity include walking quickly, skating and bike riding.

What is vigorous aerobic activity?

Vigorous-intensity aerobic activity makes your heart rate increase quite a bit and you won't be able to say more than a few words without needing to catch your breath.

› Examples of vigorous activity include running, basketball, soccer and cross-country skiing.

What are strengthening activities?

Muscle-strengthening activities build up your muscles.

With bone-strengthening activities, your muscles push and pull against your bones, helping make your bones stronger.

› Examples of muscle-strengthening activities include push-ups and sit-ups, lifting weights, climbing stairs and digging in the garden.

› Examples of bone-strengthening activities include running, walking and yoga.

www.publichealth.gc.ca/paguide

Is physical activity safe for everyone?

The recommended level of physical activity applies to all adults aged 18-64 years who do not have a suspected or diagnosed medical condition. These guidelines may be appropriate if you are pregnant. Consult a health professional if you are unsure about the types and amounts of physical activity most appropriate for you.

Canadian Physical Activity Guidelines were developed by the Canadian Society for Exercise Physiology and are available at: www.csep.ca/guidelines

Cat.: HP10-16/3-2011E-PDF **ISBN:** 978-1-100-18924-6

Tips to Get Active

> Physical Activity Tips for Older Adults (65 years and older)

Physical activity plays an important role in your health, well-being and quality of life. These tips will help you improve and maintain your health by being physically active every day.

1

Take part in at least **2.5 hours of moderate- to vigorous-intensity aerobic activity each week**.

2

Spread out the activities into sessions of **10 minutes** or more.

3

It is beneficial to **add muscle and bone strengthening activities** using major muscle groups **at least twice a week**. This will help your posture and balance.

Tips to help you get active

- ☑ Find an activity you like such as swimming or cycling.
- ☑ **Minutes count** — increase your activity level 10 minutes at a time. Every little bit helps.
- ☑ **Active time can be social time** — look for group activities or classes in your community, or get your family or friends to be active with you.
- ☑ Walk wherever and whenever you can.
- ☑ Take the stairs instead of the elevator, when possible.
- ☑ Carry your groceries home.

- **Start slowly**
- **Listen to your body**
- **Every step counts**

Public Health Agency of Canada | Agence de la santé publique du Canada

Canada

Tips to Get Active

> Physical Activity Tips for Older Adults (65 years and older)

The Health Benefits of Being Active

- **IMPROVE YOUR BALANCE**
- **REDUCE FALLS AND INJURIES**
- **HELP YOU STAY INDEPENDENT LONGER**
- **HELP PREVENT HEART DISEASE, STROKE, OSTEOPOROSIS, TYPE 2 DIABETES, SOME CANCERS AND PREMATURE DEATH**

Aerobic activity, like **PUSHING A LAWN MOWER, TAKING A DANCE CLASS, OR BIKING TO THE STORE,** is continuous movement that makes you feel warm and breathe deeply.

Strengthening activity, like **LIFTING WEIGHTS OR YOGA,** keeps muscles and bones strong and prevents bone loss. It will also improve your balance and posture.

What is moderate aerobic activity?

Moderate-intensity aerobic activity makes you breathe harder and your heart beat faster. You should be able to talk, but not sing.

- Examples of moderate activity include walking quickly or bike riding.

What is vigorous aerobic activity?

Vigorous-intensity aerobic activity makes your heart rate increase quite a bit and you won't be able to say more than a few words without needing to catch your breath.

- Examples of vigorous activity include jogging or cross-country skiing.

What are strengthening activities?

Muscle-strengthening activities build up your muscles.

With bone-strengthening activities, your muscles push and pull against your bones. This helps make your bones stronger.

- Examples of muscle-strengthening activities include climbing stairs, digging in the garden, lifting weights, push-ups and curl-ups.
- Examples of bone-strengthening activities include yoga, walking and running.

www.publichealth.gc.ca/paguide

Every step counts!

If you're not active now, adding any amount of physical activity can bring some health benefits. Take a step in the right direction. Start now and slowly increase your physical activity to meet the recommendations.

More physical activity provides greater health benefits!

That means the more you do, the better you'll feel. Get active and see what you can accomplish! Move more!

Is physical activity safe for everyone?

The recommended level of physical activity applies to all adults aged 65 years and older who do not have a suspected or diagnosed medical condition. Consult a health professional if you are unsure about the types and amounts of physical activity most appropriate for you.

Canadian Physical Activity Guidelines were developed by the Canadian Society for Exercise Physiology and are available at: www.csep.ca/guidelines

Cat.: HP10-16/4-2011E-PDF **ISBN:** 978-1-100-18925-3

Move your body

Physical activity and cancer prevention

Physical activity and cancer prevention

We know that by being physically active every day, enjoying a healthy diet and maintaining a healthy body weight, you can lower your risk of developing cancer. We know that these factors account for at least 30 per cent of all cancers.

Physical inactivity is an important risk factor for bowel cancer and breast cancer, and possibly prostate, uterine and lung cancer. Being inactive also contributes to weight gain. Overweight and obesity also increase cancer risk.

The good news is you can lower your cancer risk by being physically active. Physical activity regulates hormones such as insulin-like growth factor and oestrogen and affects the speed that food passes through the bowel, reducing contact with any potential carcinogens.

Physical activity assists in maintaining a healthy body weight and can improve energy levels and feelings of well being.

Being more active is one of the best things you can do for yourself

For good health, put together at least 30 minutes of moderate intensity physical activity on most, preferably all days of the week. It doesn't have to be continuous, 3 x 10 minutes sessions are also good. Each activity session should last at least 10 minutes.

To reduce your cancer risk, the more physically active you are the better. As fitness improves aim for at least 60 minutes of moderate-intensity activity or 30 minutes of vigorous-intensity activity every day.

Moderate physical activity includes any activity in which you can still hold a conversation, such as brisk walking.

Vigorous physical activity includes any activity that makes you 'huff and puff', such as fast swimming, cycling, jogging etc.

Getting started

If you have not been physically active for some time, it is best to start slowly. Going too hard too early can cause pain and injury.

Tips for getting started

- Get friends to join you. They will give you company and motivation.
- Think of movement as an opportunity and plan ahead.
- Set goals and challenge yourself to build up your physical activity levels.
- If you are being active outdoors remember to be SunSmart.
- Drink water before, during and after your activity.

Tips for home

- Turn off the TV or computer and use this time to be active.
- Walk or cycle to the local shops.
- Do gardening or housework.
- Be active as a family.
- Walk your children to school.

Tips for work

- Catch public transport to work, get off a stop earlier and walk the rest of the way.
- Park your car 10-15 minutes from work, and walk the rest of the way.
- Walk with colleagues at lunchtime.
- Take the stairs, not the lift.

Being active, like healthy eating, requires some thought each day. It also needs to be kept up over a lifetime. Regular physical activity will give you extra energy and make you feel better.

Remember, if you have any concerns or questions, please contact your doctor.

Ways to reduce your cancer risk
How do you stack up?

(Tick if you need to take action)

- ☐ Quit smoking
- ☐ Be SunSmart
- ☐ Maintain a healthy body weight
- ☐ Be more physically active
- ☐ Eat a healthy, well balanced diet
- ☐ Avoid or limit alcohol intake

Where can I get reliable information?

Cancer Council Helpline 13 11 20
Information and support for you and your family for the cost of a local call anywhere in Australia.

Cancer Council Australia website
(with links to state and territory Cancer Councils)
www.cancer.org.au

Cancer Council

Eat for health

Nutrition and cancer prevention

We know that by enjoying a healthy diet, being physically active every day and maintaining a healthy body weight, you can lower your risk of developing cancer. We know that these factors account for at least 30 per cent of all cancers.

Healthy eating habits are a first step in reducing your cancer risk. Poor eating habits increase your risk of cancer at many sites in the body. Poor eating habits can also contribute to weight gain and being overweight or obese increases your risk of cancer. The good news is that a healthy diet, combined with regular physical activity and a healthy body weight can reduce cancer risk.

While there is no one food that can protect against cancer, there are steps you can take to lower your overall risk. A healthy diet may protect against cancers including cancer of the bowel, liver, oesophagus (food pipe), lung and stomach.

How much should I eat in a day?

Eat at least two serves of fruit and five serves of vegetables each day.

What is a serve?

Vegetable

½ cup cooked vegetable or cooked legumes = 1 medium potato = 1 cup salad vegetables

Fruit

1 medium piece (e.g. apple) = 2 small pieces (e.g. apricots) = 1 cup chopped or canned fruit

Tips to eat more fruit and vegetables

- Double your serving of vegetables
- Try a new fruit each week
- Use frozen vegies for convenience
- Include vegies with your lunch
- Add extra vegies to all your recipes
- Have fruit instead of sweets.

Eat for Health

- Eat a variety of raw and cooked vegetables,fruit and legumes (eg. dried beans, lentils).
- Eat plenty of cereals (including breads, rice, pasta and noodles), preferably wholegrain.
- Eat red meat no more than three to four times a week. On the other days choose fish, poultry, dried or canned beans or lentils.
- Limit processed or cured meats (eg. frankfurts, bacon and ham).
- Choose foods low in salt.
- Don't eat too much fat, especially saturated fat. Look for hidden fats (eg. snack foods, cakes and take-away foods).
- Choose low fat yoghurts, cheeses and milks.

What about taking vitamin and mineral supplements?

If you enjoy a wide variety of nutritious foods you will get the nutrients you need, reduce your cancer risk and are less likely to be overweight or obese. For most healthy people, vitamin and mineral supplements are not necessary when they eat well.

Remember, if you have any concerns or questions, please contact your doctor.

Ways to reduce your cancer risk

How do you stack up?

(Tick if you need to take action)

- ☐ Quit smoking
- ☐ Be SunSmart
- ☐ Maintain a healthy body weight
- ☐ Be more physically active
- ☐ Eat a healthy, well balanced diet
- ☐ Avoid or limit alcohol intake

Where can I get reliable information?

Cancer Council Helpline 13 11 20
Information and support for you and your family for the cost of a local call anywhere in Australia.

Cancer Council Australia website
(with links to state and territory Cancer Councils)
www.cancer.org.au

Cancer Council

This box to be completed by the clinical research associate: Pt. Serial #: _____ Pt. Initials: ____ ____ ____

Physical Activity Readiness Questionnaire - PAR-Q (revised 2002)

PAR-Q & YOU

(A Questionnaire for People Aged 15 to 69)

Regular physical activity is fun and healthy, and increasingly more people are starting to become more active every day. Being more active is very safe for most people. However, some people should check with their doctor before they start becoming much more physically active.

If you are planning to become much more physically active than you are now, start by answering the seven questions in the box below. If you are between the ages of 15 and 69, the PAR-Q will tell you if you should check with your doctor before you start. If you are over 69 years of age, and you are not used to being very active, check with your doctor.

Common sense is your best guide when you answer these questions. Please read the questions carefully and answer each one honestly: check YES or NO.

YES	NO		
☐	☐	1.	**Has your doctor ever said that you have a heart condition and that you should only do physical activity recommended by a doctor?**
☐	☐	2.	**Do you feel pain in your chest when you do physical activity?**
☐	☐	3.	**In the past month, have you had chest pain when you were not doing physical activity?**
☐	☐	4.	**Do you lose your balance because of dizziness or do you ever lose consciousness?**
☐	☐	5.	**Do you have a bone or joint problem (for example, back, knee or hip) that could be made worse by a change in your physical activity?**
☐	☐	6.	**Is your doctor currently prescribing drugs (for example, water pills) for your blood pressure or heart condition?**
☐	☐	7.	**Do you know of any other reason why you should not do physical activity?**

If you answered YES to one or more questions

Talk with your doctor by phone or in person BEFORE you start becoming much more physically active or BEFORE you have a fitness appraisal. Tell your doctor about the PAR-Q and which questions you answered YES.

- You may be able to do any activity you want — as long as you start slowly and build up gradually. Or, you may need to restrict your activities to those which are safe for you. Talk with your doctor about the kinds of activities you wish to participate in and follow his/her advice.
- Find out which community programs are safe and helpful for you.

NO to all questions

If you answered NO honestly to all PAR-Q questions, you can be reasonably sure that you can:

- start becoming much more physically active – begin slowly and build up gradually. This is the safest and easiest way to go.
- take part in a fitness appraisal – this is an excellent way to determine your basic fitness so that you can plan the best way for you to live actively. It is also highly recommended that you have your blood pressure evaluated. If your reading is over 144/94, talk with your doctor before you start becoming much more physically active.

DELAY BECOMING MUCH MORE ACTIVE:

- if you are not feeling well because of a temporary illness such as a cold or a fever – wait until you feel better; or
- if you are or may be pregnant – talk to your doctor before you start becoming more active.

PLEASE NOTE: If your health changes so that you then answer YES to any of the above questions, tell your fitness or health professional. Ask whether you should change your physical activity plan.

Informed Use of the PAR-Q: The Canadian Society for Exercise Physiology, Health Canada, and their agents assume no liability for persons who undertake physical activity, and if in doubt after completing this questionnaire, consult your doctor prior to physical activity.

NOTE: If the PAR-Q is being given to a person before he or she participates in a physical activity program or a fitness appraisal, this section may be used for legal or administrative purposes.

Please check to make sure you have answered all the questions.

Please fill in your initials to indicate that you have completed this questionnaire: _____

Today's date (Year, Month, Day): _____

Thank you.

This box to be completed by the clinical research associate: Pt. Serial #: _____ Pt. Initials: ____ ____ ____

LEISURE TIME EXERCISE QUESTIONNAIRE (LTEQ)

PRE-REGISTRATION

For this question, we would like you to recall the average amount of exercise you did **in the past 1 month.**

When answering these questions please:

- only count exercise sessions that lasted 10 minutes or longer in duration.
- only count exercise that was done during free time (i.e., not occupation or housework).
- note that the main difference between the first three categories is the intensity of the endurance (aerobic) exercise and the fourth category is for strength (resistance) exercise.
- please write the average frequency on the first line and the average duration on the second.
- if you did not do any exercise in one of the categories, please write in "0".

Considering a typical week (7 days) how many times on the average did you do the following kinds of exercise in the **past 1 month**?

	Times Per Week	Average Duration
a. VIGOROUS/STRENUOUS EXERCISE (HEART BEATS RAPIDLY, SWEATING) *(e.g. running, aerobics classes, cross country skiing, vigorous swimming, vigorous bicycling).*	_____	_____
b. MODERATE EXERCISE (NOT EXHAUSTING, LIGHT PERSPIRATION) *(e.g. fast walking, tennis, easy bicycling, easy swimming, popular and folk dancing).*	_____	_____
c. LIGHT/MILD EXERCISE (MINIMAL EFFORT, NO PERSPIRATION) *(e.g. easy walking, yoga, bowling, lawn bowling, shuffleboard).*	_____	_____
d. RESISTANCE EXERCISE *(e.g. lifting weights, push ups, sit ups therabands).*	_____	_____

Please check to make sure you have answered all the questions.

Please fill in your initials to indicate that you have completed this questionnaire: _____

Today's date (Year, Month, Day): _____

Thank you.

This box to be completed by the clinical research associate: Pt. Serial #: _____ Pt. Initials: ____ ____ ____

LEISURE TIME EXERCISE QUESTIONNAIRE (LTEQ)

PRE-DIAGNOSIS

For this question, we would like you to recall the average amount of exercise you did **in the six months BEFORE you were diagnosed with colon cancer.**

When answering these questions please:

- only count exercise sessions that lasted 10 minutes or longer in duration.
- only count exercise that was done during free time (i.e., not occupation or housework).
- note that the main difference between the first three categories is the intensity of the endurance (aerobic) exercise and the fourth category is for strength (resistance) exercise.
- please write the average frequency on the first line and the average duration on the second.
- if you did not do any exercise in one of the categories, please write in "0".

Considering a typical week (7 days) how many times on the average did you do the following kinds of exercise **in the six months BEFORE you were diagnosed with colon cancer?**

	Times Per Week	Average Duration
a. VIGOROUS/STRENUOUS EXERCISE (HEART BEATS RAPIDLY, SWEATING) *(e.g. running, aerobics classes, cross country skiing, vigorous swimming, vigorous bicycling).*	_____	_____
b. MODERATE EXERCISE (NOT EXHAUSTING, LIGHT PERSPIRATION) *(e.g. fast walking, tennis, easy bicycling, easy swimming, popular and folk dancing).*	_____	_____
c. LIGHT/MILD EXERCISE (MINIMAL EFFORT, NO PERSPIRATION) *(e.g. easy walking, yoga, bowling, lawn bowling, shuffleboard).*	_____	_____
d. RESISTANCE EXERCISE *(e.g. lifting weights, push ups, sit ups therabands).*	_____	_____

Please check to make sure you have answered all the questions.

Please fill in your initials to indicate that you have completed this questionnaire: _____

Today's date (Year, Month, Day): _____

Thank you.

This box to be completed by the clinical research associate: Pt. Serial #: _____ Pt. Initials: ____ ____ ____

The MOS 36-Item Short-Form Health Survey (SF-36)

INSTRUCTIONS: This survey asks for your views about your health. This information will help keep track of how you feel and how well you are able to do your usual activities.

Answer every question by marking the answer as indicated. If you are unsure about how to answer a question, please give the best answer you can.

1. In general, would you say your health is:

(circle one)

Excellent 1

Very good.....2

Good.....3

Fair 4

Poor 5

2. Compared to one week ago, how would you rate your health in general now?

(circle one)

Much better now than one week ago 1

Somewhat better now than one week ago.....2

About the same as one week ago 3

Somewhat worse now than one week ago 4

Much worse now than one week ago.....5

This box to be completed by the clinical research associate: Pt. Serial #: _____ Pt. Initials: ____ ____ ____

3. The following items are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much?

(circle one number on each line)

	Yes, Limited A Lot	Yes, Limited A Little	No, Not Limited At All
a. **Vigorous activities**, such as running, lifting heavy objects, participating in strenuous sports	1	2	3
b. **Moderate activities**, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf	1	2	3
c. Lifting or carrying groceries	1	2	3
d. Climbing several flights of stairs	1	2	3
e. Climbing **one** flight of stairs	1	2	3
f. Bending, kneeling, or stooping	1	2	3
g. Walking **more than a mile**	1	2	3
h. Walking **several blocks**	1	2	3
i. Walking **one block**	1	2	3
j. Bathing or dressing yourself	1	2	3

4. During the past week, have you had any of the following problems with your work or other regular daily activities as a result of your physical health?

(circle one number on each line)

	Yes	No
a. Cut down on the **amount of time** you spent on work or other activities	1	2
b. **Accomplished less** than you would like	1	2
c. Were limited in the **kind** of work or other activities	1	2
d. Had **difficulty** performing the work or other activities (for example, it took extra effort)	1	2

5. During the past week, have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)?

(circle one number on each line)

	Yes	No
a. Cut down the **amount of time** you spent on work or other activities	1	2
b. **Accomplished less** than you would like	1	2
c. Didn't do work or other activities as **carefully** as usual	1	2

6. During the past week, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbors, or groups?

(circle one)

Not at all.....1

Slightly.....2

Moderately.....3

Quite a bit.....4

Extremely.....5

7. How much bodily pain have you had during the past week?

(circle one)

None.....1

Very mild.....2

Mild.....3

Moderate.....4

Severe.....5

Very Severe 6

8. During the past week, how much did pain interfere with your normal work (including both work outside the home and housework)?

(circle one)

Not at all.....1

A little bit.....2

Moderately.....3

Quite a bit.....4

Extremely.....5

9. These questions are about how you feel and how things have been with you during the past week. For each question, please give the one answer that comes closest to the way you have been feeling. How much of the time during the past week -

(circle one number on each line)

	All of the Time	Most of the Time	A Good Bit of the Time	Some of the Time	A Little of the Time	None of the Time
a. Did you feel full of pep?	1	2	3	4	5	6
b. Have you been a very nervous person?	1	2	3	4	5	6
c. Have you felt so down in the dumps that nothing could cheer you up?	1	2	3	4	5	6
d. Have you felt calm and peaceful?	1	2	3	4	5	6
e. Did you have a lot of energy?	1	2	3	4	5	6
f. Have you felt downhearted and blue?	1	2	3	4	5	6
g. Did you feel worn out?	1	2	3	4	5	6
h. Have you been a happy person?	1	2	3	4	5	6
i. Did you feel tired?	1	2	3	4	5	6

This box to be completed by the clinical research associate: Pt. Serial #: _____ Pt. Initials: ____ ____ ____

10. During the past week, how much of the time has your physical health or emotional problems interfered with your social activities (like visiting with friends, relatives, etc.)?

(circle one)

All of the time 1

Most of the time 2

Some of the time 3

A little of the time 4

None of the time.....5

11. How TRUE or FALSE is each of the following statements for you?

(circle one number on each line)

	Definitely True	**Mostly True**	**Don't Know**	**Mostly False**	**Definitely False**
a. I seem to get sick a little easier than other people	1	2	3	4	5
b. I am as healthy as anybody I know	1	2	3	4	5
c. I expect my health to get worse	1	2	3	4	5
d. My health is excellent	1	2	3	4	5

Please check to make sure you have answered all the questions.

Please fill in your initials to indicate that you have completed this questionnaire: _____

Today's date (Year, Month, Day): _____

Thank you.

This box to be completed by the clinical research associate: Pt. Serial #: _____ Pt. Initials: ____ ____ ____

FACIT-F (Version 4)

Below is a list of statements that other people with your illness have said are important. **Please circle or mark one number per line to indicate your response as it applies to the past 7 days.**

	PHYSICAL WELL-BEING	Not at all	A little bit	Some-what	Quite a bit	Very much
GP1	I have a lack of energy	0	1	2	3	4
GP2	I have nausea	0	1	2	3	4
GP3	Because of my physical condition, I have trouble meeting the needs of my family	0	1	2	3	4
GP4	I have pain	0	1	2	3	4
GP5	I am bothered by side effects of treatment	0	1	2	3	4
GP6	I feel ill	0	1	2	3	4
GP7	I am forced to spend time in bed	0	1	2	3	4

	SOCIAL/FAMILY WELL-BEING	Not at all	A little bit	Some-what	Quite a bit	Very much
GS1	I feel close to my friends	0	1	2	3	4
GS2	I get emotional support from my family	0	1	2	3	4
GS3	I get support from my friends	0	1	2	3	4
GS4	My family has accepted my illness	0	1	2	3	4
GS5	I am satisfied with family communication about my illness	0	1	2	3	4
GS6	I feel close to my partner (or the person who is my main support)	0	1	2	3	4
Q1	*Regardless of your current level of sexual activity, please answer the following question. If you prefer not to answer it, please check this box* ☐ *and go to the next section.*					
GS7	I am satisfied with my sex life	0	1	2	3	4

Please go on to the next page

This box to be completed by the clinical research associate: Pt. Serial #: _____ Pt. Initials: ____ ____ ____

FACIT-F (Version 4)

Please circle or mark one number per line to indicate your response as it applies to the past 7 days.

	EMOTIONAL WELL-BEING	Not at all	A little bit	Some-what	Quite a bit	Very much
GE1	I feel sad	0	1	2	3	4
GE2	I am satisfied with how I am coping with my illness	0	1	2	3	4
GE3	I am losing hope in the fight against my illness	0	1	2	3	4
GE4	I feel nervous	0	1	2	3	4
GE5	I worry about dying	0	1	2	3	4
GE6	I worry that my condition will get worse	0	1	2	3	4

	FUNCTIONAL WELL-BEING	Not at all	A little bit	Some-what	Quite a bit	Very much
GF1	I am able to work (include work at home)	0	1	2	3	4
GF2	My work (include work at home) is fulfilling	0	1	2	3	4
GF3	I am able to enjoy life	0	1	2	3	4
GF4	I have accepted my illness	0	1	2	3	4
GF5	I am sleeping well	0	1	2	3	4
GF6	I am enjoying the things I usually do for fun	0	1	2	3	4
GF7	I am content with the quality of my life right now	0	1	2	3	4

Please go on to the next page

This box to be completed by the clinical research associate: Pt. Serial #: _____ Pt. Initials: ____ ____ ____

FACIT-F (Version 4)

Please circle or mark one number per line to indicate your response as it applies to the past 7 days.

	ADDITIONAL CONCERNS	Not at all	A little bit	Some-what	Quite a bit	Very much
HI7	I feel fatigued	0	1	2	3	4
HI12	I feel weak all over	0	1	2	3	4
An1	I feel listless ("washed out")	0	1	2	3	4
An2	I feel tired	0	1	2	3	4
An3	I have trouble starting things because I am tired	0	1	2	3	4
An4	I have trouble finishing things because I am tired	0	1	2	3	4
An5	I have energy	0	1	2	3	4
An7	I am able to do my usual activities	0	1	2	3	4
An8	I need to sleep during the day	0	1	2	3	4
An12	I am too tired to eat	0	1	2	3	4
An14	I need help doing my usual activities	0	1	2	3	4
An15	I am frustrated by being too tired to do the things I want to do	0	1	2	3	4
An16	I have to limit my social activity because I am tired	0	1	2	3	4

Please check to make sure you have answered all the questions.

Please fill in your initials to indicate that you have completed this questionnaire: _____

Today's date (Year, Month, Day): _____

Thank you.

This box to be completed by the clinical research associate: Pt. Serial #: _____ Pt. Initials: ____ ____ ____

Pittsburgh Sleep Quality Index (PSQI)

Instructions:
The following questions relate to your usual sleep habits during the past month only. Your answers should indicate the most accurate reply for the majority of days and nights in the past month.

Please answer all questions.

1. During the past month, when have you usually gone to bed at night?	USUAL BED TIME _____
2. During the past month, how long (in minutes) has it usually taken you to fall asleep each night?	NUMBER OF MINUTES _____
3. During the past month, when have you usually gotten up in the morning?	USUAL GETTING UP TIME _____
4. During the past month, how many hours of actual sleep did you get at night? *(This may be different than the number of hours you spend in bed.)*	HOURS OF SLEEP PER NIGHT _____

For each of the remaining questions, check the one best response. Please answer all questions.

	Not during the past month	Less than once a week	Once or twice a week	Three or more times a week
5. (a) cannot get to sleep within 30 minutes	☐	☐	☐	☐
(b) wake up in the middle of the night or early morning	☐	☐	☐	☐
(c) have to get up to use the bathroom	☐	☐	☐	☐
(d) cannot breathe comfortably	☐	☐	☐	☐
(e) cough or snore loudly	☐	☐	☐	☐
(f) feel too cold	☐	☐	☐	☐
(g) feel too hot	☐	☐	☐	☐
(h) had bad dreams	☐	☐	☐	☐
(i) have pain	☐	☐	☐	☐
(j) Other reason(s), please describe: _____				
How often in the past month have you had trouble sleeping because of this?	☐	☐	☐	☐

Please go on to the next page

This box to be completed by the clinical research associate: Pt. Serial #: _____ Pt. Initials: ____ ____ ____

6. During the past month, how would you rate your sleep quality overall?	☐ Very good ☐ Fairly good ☐ Fairly bad ☐ Very bad
7. During the past month, how often have you taken medicine (prescribed or "over the counter") to help you sleep?	☐ Not during the past month ☐ Less than once a week ☐ Once or twice a week ☐ Three or more times a week
8. During the past month, how often have you had trouble staying awake while driving, eating meals or engaging in social activity?	☐ Not during the past month ☐ Less than once a week ☐ Once or twice a week ☐ Three or more times a week
9. During the past month, how much of a problem has it been for you to keep up enough enthusiasm to get things done?	☐ No problem at all ☐ Only a very slight problem ☐ Somewhat of a problem ☐ A very big problem
10. Do you have a bed partner or roommate?	☐ No bed partner or roommate ☐ Partner/roommate in other room ☐ Partner in same room, but not same bed ☐ Partner in same bed

If you have a roommate or bed partner, ask him/her how often in the past month you have had…	Not during the past month	Less than once a week	Once or twice a week	Three or more times a week
(a) loud snoring	☐	☐	☐	☐
(b) long pauses between breaths while sleeping	☐	☐	☐	☐
(c) legs twitching or jerking while you sleep	☐	☐	☐	☐
(d) episodes of disorientation or confusion during sleep	☐	☐	☐	☐
(e) other restlessness while you sleep; please describe: _____ _____	☐	☐	☐	☐

Please check to make sure you have answered all the questions.

Please fill in your initials to indicate that you have completed this questionnaire: _____

Today's date (Year, Month, Day): _____

Thank you.

This box to be completed by the clinical research associate:

Pt. Serial #: _____ **Pt. Initials:** ____ ____ ____

Hospital Anxiety and Depression Scale (HADS)

nferNelson
understanding potential

FOLD HERE

Researchers are aware that emotions play an important part in most illnesses. This questionnaire is designed to help researchers know how you feel. Read each item below and **underline the reply** which comes closest to how you have been feeling in the past week. Ignore the numbers printed at the edge of the questionnaire.

Don't take too long over your replies, your immediate reaction to each item will probably be more accurate than a long, thought-out response.

FOLD HERE

A	D		A	D
		I feel tense and 'wound up'		
3		Most of the time		
2		A lot of the time		
1		From time to time, occasionally		
0		Not at all		
		I still enjoy the things I used to enjoy		
	0	Definitely as much		
	1	Not quite so much		
	2	Only a little		
	3	Hardly at all		
		I get a sort of frightened feeling as if something awful is about to happen		
3		Very definitely and quite badly		
2		Yes, but not too badly		
1		A little, but it doesn't worry me		
0		Not at all		
		I can laugh and see the funny side of things		
	0	As much as I always could		
	1	Not quite so much now		
	2	Definitely not so much now		
	3	Not at all		
		Worrying thoughts go through my mind		
3		A great deal of the time		
2		A lot of the time		
1		Not too often		
0		Very little		
		I feel cheerful		
	3	Never		
	2	Not often		
	1	Sometimes		
	0	Most of the time		
		I can sit at ease and feel relaxed		
0		Definitely		
1		Usually		
2		Not often		
3		Not at all		
		I feel as if I am slowed down		
		Nearly all the time		3
		Very often		2
		Sometimes		1
		Not at all		0
		I get a sort of frightened feeling like 'butterflies' in the stomach		
		Not at all	0	
		Occasionally	1	
		Quite often	2	
		Very often	3	
		I have lost interest in my appearance		
		Definitely		3
		I don't take as much care as I should		2
		I may not take quite as much care		1
		I take just as much care as ever		0
		I feel restless as if I have to be on the move		
		Very much indeed	3	
		Quite a lot	2	
		Not very much	1	
		Not at all	0	
		I look forward with enjoyment to things		
		As much as I ever did		0
		Rather less than I used to		1
		Definitely less than I used to		2
		Hardly at all		3
		I get sudden feelings of panic		
		Very often indeed	3	
		Quite often	2	
		Not very often	1	
		Not at all	0	
		I can enjoy a good book or radio or television programme		
		Often		0
		Sometimes		1
		Not often		2
		Very seldom		3

Now check that you have answered all the questions

	A	D
TOTAL		

Please fill in your initials to indicate that you have completed this questionnaire: _____

Today's date (Year, Month, Day): _____

This box to be completed by the clinical research associate: Pt. Serial #: _____ Pt. Initials: ____ ____ ____

Work Productivity and Activity Impairment (WPAI)

Specific Health Condition (Colon cancer)

The following questions ask about the effect of your health condition (i.e. recovery from prior colon cancer and its treatment) on your ability to work and perform regular daily activities. Please fill in the blanks as indicated or circle the appropriate number.

1. Are you currently employed (working for pay)? ☐ NO ☐ YES
   If NO, Check "NO" and skip to question 6

The next questions refer to the past **30 days (month)**, not including today.

2. During the past **30 days/month**, how many hours did you miss from work because of the problems associated with your colon cancer diagnosis?

   Include hours you missed on sick days, time you went in late, left early, etc because of problems associated with your health condition. Do not include time you missed to participate in this study.

   _____ Hours

3. During the past **30 days/month**, how many hours did you miss from work because of any other reason, such as vacation, holidays, time off to participate in this study?

   _____ Hours

4. During the past **30 days/month**, how many hours did you actually work?

   _____ Hours

5. During the past **30 days/month**, how much did your prior colon cancer diagnosis or treatment affect your productivity while you were working?

   Think about days you were limited in the amount or kind of work you could do, days you accomplished less than you would like, or days you could not do your work as carefully as usual because of your health condition. If your health condition affected your work only a little, choose a low number. Choose a high number if your health condition affected your work a great deal.

Colon cancer had no effect on my work	1	2	3	4	5	6	7	8	9	10	Colon cancer completely prevented me from working

CIRCLE A NUMBER

Please go on to the next page

This box to be completed by the clinical research associate: Pt. Serial #: _____ Pt. Initials: ____ ____ ____

6. During the past **30 days/month**, how much did your prior colon cancer or treatment affect your ability to do your regular daily activities, other than work at a job?
   By regular activities, we mean the usual activities you do, such as work around the house, shopping, childcare, exercising, studying, etc. Think about the times you were limited in the amount of kind of activities you do and time you accomplished less than you would like. If your health condition affected your activities only a little, choose a low number. Choose a high number if your health condition affected your activities a great deal.

Colon cancer had no effect on my daily activities	1 2 3 4 5 6 7 8 9 10	Colon cancer completely prevented me from doing my daily activities

CIRCLE A NUMBER

If you <u>ARE</u> currently employed, please answer questions #7 to 9.

If you are <u>NOT</u> currently employed answer question #9 only.

7. During the past **30 days/month**, how many hours did you miss from work because of any other health/injury concerns?

   _____ Hours

8. During the past **30 days/month**, how many hours did you miss from work because of an exercise program?

   _____ Hours

9. Were you employed within the **30 days/month** prior to your colon cancer diagnosis?

   _____ Hours

Please check to make sure you have answered all the questions.

Please fill in your initials to indicate that you have completed this questionnaire: _____

Today's date (Year, Month, Day): _____

Thank you.

NCIC CTG CO.21
30-DAY RESOURCE USE DIARY #1
ENGLISH version

Dear Sir/Madam:

As part of your participation in the NCIC CTG CO.21 Study, you have agreed to complete this diary related to the different resources used for your colon cancer care and physical activity. Each diary has a reporting period of 30 days and you will receive reminder phone calls about your diary.

THE DIARY:

- There are two diary pages to represent one day.

YOUR INSTRUCTIONS:

- There are SEVEN resource categories: doctor, wait time, facility, health professional, testing, paid services and colon cancer- (page 1) or physical activity- (page 2) related items.
- For each day during the 30 day reporting period, complete the corresponding row on the summary page. For each day, record the date and answer "Did you use any resources on this day because of your colon cancer or physical activity related issues?". If you answer "yes" to this question, complete both pages 1 and 2 of the diary for that day. If you answer "no" to that question, you do not need to complete either page 1 or 2 for that day. Repeat this process on each of the 30 days required during this reporting period.
- For each day you complete the diary, please check (✓) ALL the boxes next to the resources that were involved with your colon cancer care (page 1) or physical activity participation (page 2).
- On page 1, colon cancer-related items include purchases such as ostomy supplies, special garments, homecare equipment, and hospital/clinic parking fees because of your colon cancer.
- On page 2 , physical activity-related items include purchases such as new clothing/shoes, Physical Activity Consultant services, facility fees, home equipment, and parking fees related to physical activity participation.
- Please do **NOT** include information related to the CO.21 study (e.g. behaviour support or supervised physical activity sessions with your Physical Activity Consultant, fitness testing or any non-standard/ extra doctor visits or tests done only for the purpose of this study).

WHEN YOU ARE FINISHED:

- Please use the return envelope to mail the completed diary (including summary page) back to your clinical research associate at the cancer clinic.
- Or bring your completed diary the next time you see your clinical research associate at the cancer clinic.

Your participation in this study is greatly appreciated. Thank you.

This box to be completed by the clinical research associate: Pt. Serial #: _____ Pt. Initials: ____ ____ ____

NCIC CTG CO.21
30-Day Resource Use Diary #1
Summary page

Day #	Date (yyyy-mmm-dd)	Did you use any resources on this day because of your colon cancer *or* physical activity related issues? (please check "yes" or "no")	
		Yes (please complete page 1 and 2 of diary for **this** day)	No (no forms to complete for **this** day)
1			
2			
3			
4			
5			
6			
7			
8			
9			
10			
11			
12			
13			
14			
15			
16			
17			
18			
19			
20			
21			
22			
23			
24			
25			
26			
27			
28			
29			
30			

Please fill in your initials to indicate that you have completed this questionnaire: _____

Today's date (Year, Month, Day): _____

Please go on to the next page

This box to be completed by the clinical research associate: Pt. Serial #: _____ Pt. Initials: ____ ____ ____

DAY 1: __ __ __ __ - __ __ __ - __ __
yyyy mmm dd

1. I saw these doctors today because of my colon cancer:
   - ☐ Oncologist
   - ☐ Cardiologist
   - ☐ Emergency room doctor
   - ☐ Family Doctor
   - ☐ Internist
   - ☐ Neurologist
   - ☐ Psychiatrist
   - ☐ Rehab Specialist
   - ☐ Surgeon
   - ☐ Other_____
   - ☐ I did not see a doctor

2. How long did you wait before being seen by the doctor(s)?
   - ☐ No wait
   - ☐ Less than 30 minutes
   - ☐ 30 minutes to 60 minutes
   - ☐ More than 60 minutes
   - ☐ I did not see a doctor

3. I visited these facilities today because of my colon cancer:
   - ☐ Family doctor's office
   - ☐ Oncology outpatient clinic/office
   - ☐ Emergency room
   - ☐ Hospital inpatient
   - ☐ ICU Inpatient
   - ☐ Nursing Home
   - ☐ Rehab Inpatient
   - ☐ Rehab Outpatient
   - ☐ Other _____
   - ☐ I did not visit a facility

4. I saw these other health professionals today because of my colon cancer:
   - ☐ Dietician
   - ☐ Nurse
   - ☐ Occupational therapist
   - ☐ Physiotherapist
   - ☐ Social worker
   - ☐ Other_____
   - ☐ I did not see a health professional

5. I got these tests done today because of my colon cancer :
   - ☐ Blood test
   - ☐ CT scan
   - ☐ MRI
   - ☐ Ultrasound
   - ☐ X-ray
   - ☐ Other _____
   - ☐ I did not get any tests done

6. I used these services because of my colon cancer :
   - ☐ Paid caretaker
   - ☐ Paid housekeeper (cook, clean)
   - ☐ Paid nurse
   - ☐ Paid professional (chiropractor)
   - ☐ Transportation (taxi, other service)
   - ☐ Other_____
   - ☐ I did not use any services

7. I paid for colon cancer-related items such as ostomy supplies, bowel incontinence liners/garments, or homecare equipment today:
   - ☐ $1 to $99
   - ☐ $100 to $499
   - ☐ $500 or more
   - ☐ I did not pay for colon cancer -related items

Please go on to the next page

This box to be completed by the clinical research associate: Pt. Serial #: _____ Pt. Initials: ____ ____ ____

DAY 1: __ __ __ __ - __ __ __ - __ __
yyyy mmm dd

1. I saw these doctors today because of physical activity-related issues:

   ☐ Oncologist
   ☐ Cardiologist
   ☐ Emergency room doctor
   ☐ Family Doctor
   ☐ Internist
   ☐ Neurologist
   ☐ Psychiatrist
   ☐ Rehab Specialist
   ☐ Surgeon
   ☐ Other _____
   ☐ I did not see a doctor

2. How long did you wait before being seen by the doctor(s)?

   ☐ No wait
   ☐ Less than 30 minutes
   ☐ 30 minutes to 60 minutes
   ☐ More than 60 minutes
   ☐ I did not see a doctor

3. I visited these facilities today because of physical activity-related issues:

   ☐ Family doctor's office
   ☐ Oncology outpatient clinic/office
   ☐ Emergency room
   ☐ Hospital inpatient
   ☐ ICU Inpatient
   ☐ Nursing Home
   ☐ Rehab Inpatient
   ☐ Rehab Outpatient
   ☐ Other _____
   ☐ I did not visit a facility

4. I saw these other health professionals today because of physical activity-related issues:

   ☐ Dietician
   ☐ Nurse
   ☐ Occupational therapist
   ☐ Physiotherapist
   ☐ Physical activity consultant
   ☐ Social worker
   ☐ Other _____
   ☐ I did not see a health professional

5. I got these tests done today because of physical activity-related issues:

   ☐ Blood test
   ☐ CT scan
   ☐ MRI
   ☐ Ultrasound
   ☐ X-ray
   ☐ Other_____
   ☐ I did not get any tests done

6. I used these services because of physical activity-related issues:

   ☐ Paid caretaker
   ☐ Paid housekeeper (cook, clean)
   ☐ Paid nurse
   ☐ Paid professional (chiropractor)
   ☐ Transportation (taxi, other service)
   ☐ Kinesiologist/Exercise physiologist/ Physical activity consultant
   ☐ I did not use any services

7. I paid for physical activity-related items such as physical activity consultant services, physical activity program/facility fees, or home exercise equipment today:

   ☐ $1 to $99
   ☐ $100 to $499
   ☐ $500 or more
   ☐ I did not pay for physical activity-related items

Please check to make sure you have answered all the questions necessary.

Please fill in your initials to indicate that you have completed this questionnaire: _____

Today's date (Year, Month, Day): _____

This box to be completed by the clinical research associate: Pt. Serial #: _____ Pt. Initials: ____ ____ ____

CO.21 Total Physical Activity Questionnaire (TPAQ)

The Total Physical Activity Questionnaire is one of the questionnaires that will describe your physical activity in the past month as you begin to participate in CHALLENGE cancer research study.

The questions are about your physical activities in the past month (i.e. four weeks), including:

- Employment & Volunteer activities
- Household & Do-it-yourself activities
- Recreation & Leisure activities

This questionnaire may take about 15-20 minutes to answer. If you are not sure of how to answer a question, please feel free to contact your cancer clinic.

Directions:

- First, record the types of activities you took part in over the past 1 month.
- Next, record how often you took part in each activity, for how long, and at what intensity level.
- The timing and intensity of your activities may have varied over the 1 month. Do your best to estimate your average or usual activity pattern.
- Do not "double-count" hours – your total activity hours should add up to no more than the hours you are awake.
- In each section, the top pages provide examples of how to fill in the charts. Read through the examples and then fill in your activities on the bottom pages.
- **If a whole page does not apply to you, please write NA in the first column. We will then know you did not miss the page.**

Please go on to the next page

This box to be completed by the clinical research associate: Pt. Serial #: _____ Pt. Initials: ____ ____ ____

Employment & Volunteer Activities

PHYSICAL INTENSITY LEVELS: *Choose the one that best describes your experience*.

1 = Activities done mainly **sitting** down

2 = Activities done mainly **standing**, that **do not increase your heart rate** & cause **no sweating**

3 = Activities that cause **your heart rate to increase slightly** & cause **some light sweating**

4 = Activities that cause **your heart rate to increase substantially** & cause **heavy sweating**

Examples:

Activity 1:

- In the past 1 month, Joe's job has been **farming**.
- His main physical activities = **drive** equipment, **walk** & **shovel.**
- He farmed **4 weeks** last month, **6** days a week, **9.5** hours a day.
- He **drives** and **walks 8.5** hours a day and rates his physical intensity level for those activities as **2**.
- He **shovels 1.0** hours a day and rates his physical intensity level for shoveling as **4**.

Activity 2:

- In the past month, Joe has also been **volunteering for a 4H Club.**
- His physical activities are **sitting** and **standing**.
- He volunteers **1** day a week, **2** hours a day.
- He rates his physical intensity level as **1** because his main activity is sitting.

	Job Title employment and volunteer work	**Main Physical Activities** List up to 3 **main** activities that you did on the job in the past month. *e.g. sit, stand, walk, carry loads*	**Weeks** per month	**Days** per week	**Hours** per day	**Physical Intensity Level 1,2,3,4** *Choose the level for you*
1	farmer	drive, walk	4	6	8.5	2
2	farmer	shovel	4	6	1.0	4
3	4H Club volunteer	sit, stand	4	1	2	1

Please go on to the next page

This box to be completed by the clinical research associate: Pt. Serial #: _____ Pt. Initials: ____ ____ ____

Your Employment & Volunteer Activities

1. Start a new line for each job that you did in the past 1 month (paid or volunteer).
2. Start a new line when the pattern changed, such as when the activities, intensity level, or the number of weeks, days or hours of the job changed.
3. Remember to deduct weeks you were on vacation.
4. If you are involved in a volunteer or work activity less than once a week, record the days and the appropriate interval in the "Days per week" column, e.g. "Bingo 1 day/month".

	Job Title employment and volunteer work	**Main Physical Activities** List up to 3 **main** activities that you did on the job in the past month. *e.g. sit, stand, walk, carry loads*	**Weeks** per month	**Days** per week	**Hours** per day	**Physical Intensity Level 1,2,3,4** *Choose the level for you*
1						
2						
3						
4						
5						
6						
7						
8						

Please go on to the next page

Walking, Biking to and from Employment & Volunteer Activities

PHYSICAL INTENSITY LEVELS: *Choose the one that best describes your experience*.

2 = Activities (walking, biking etc.) that **do not increase your heart rate** & cause **no sweating**

3 = Activities that cause **your heart rate to increase slightly** & cause **some light sweating**

4 = Activities that cause **your heart rate to increase substantially** & cause **heavy sweating**

Examples:

Activity 1:

- Sandra works part-time as a **nurse** in a community health centre near her home.
- She **walks** to and from work **3** days a week, **(15 minutes each way)**; the rest of the week she drives.
- She rates her physical intensity level for **walking** as **2**.

Activity 2:

- Sandra also **volunteers** 1 day a week at her children's school
- She **bikes** to and from the school **(30 minutes each way)**
- She rates her physical activity level for **biking** as **3**.

	Job Title employment and volunteer work from page 3	**Type of Activity** to go to and from work or volunteer activity *e.g. walk, bike, in-line skate etc.*	**Weeks** per month	**Days** per week	**Minutes** per day	**Physical Intensity Level 2,3,4** *Choose the level for you*
1	Nurse	Walk	4	3	30 min	2
2	School volunteer	Bike	4	1	60 min	3

Please go on to the next page

This box to be completed by the clinical research associate: Pt. Serial #: _____ Pt. Initials: ____ ____ ____

Your Walking, Biking to and from Employment & Volunteer Activities

1. Start a new line for each job from page 3 (paid or volunteer) that involves walking or biking to and/or from work in the past month.
2. Do not include walking that is part of your job *at* work. (Walking *at* work should be recorded on page 3.)
3. Include any other means of transportation you use for getting to work, like in-line skating etc.
4. Include the time you walk to and from the bus or your car.
5. Record your time in minutes. (This is the only section that asks for your answer in minutes – continue to enter your time in hours in the rest of the questionnaire.)
6. **OR: If this section does not apply to you, please write NA on the first line.**

	Job Title employment and volunteer work from page 3	**Type of Activity** to go to and from work or volunteer activity *e.g. walk, bike, in-line skate etc.*	**Weeks** per month	**Days** per week	**Minutes** per day	**Physical Intensity Level 2,3,4** *Choose the level for you*
1						
2						
3						
4						
5						
6						
7						
8						

Please go on to the next page

This box to be completed by the clinical research associate: Pt. Serial #: _____ Pt. Initials: ____ ____ ____

Household, Childcare & Do-It-Yourself Activities

Including:

HOUSEWORK (e.g. cook, clean, do laundry, iron, vacuum, shop for groceries)
CHILDCARE (e.g. dress, feed, play with own children)
YARD WORK (e.g. cut grass, shovel snow, wash the car, garden)
DO-IT-YOURSELF JOBS (e.g. do renovations & repairs at home or at a cabin)

For this category, DO NOT include activities that are done SEATED (e.g. sewing, paying bills)**.**

PHYSICAL INTENSITY LEVELS: *Choose the one that best describes your experience*.

2 = Activities done mainly **standing**, that **do not increase your heart rate** & cause **no sweating**
3 = Activities that cause **your heart rate to increase slightly** & cause **some light sweating**
4 = Activities that cause **your heart rate to increase substantially** & cause **heavy sweating**

Examples:

Activities 1 and 2:

- Sandra shares the **housework** (meals, dishes & laundry) and **childcare** (feeding, dressing, playing) with her family.
- She does housework **4** weeks a month, **7** days a week for an average of **2** hours a day at an intensity level of **2.**
- She cares for her children **4** weeks a month, **7** days a week for an average of **3** hours a day at an intensity level of **3**.

Activity 3:

- Sandra also shares the yard work with her husband **(gardening, cutting grass).**
- She does yard work **3** days a week, and averages about **1.5** hours a day.
- She rates her physical intensity level for **yard work** as **3**.

	Type of Activity	**Weeks** per month	**Days** per week	**Hours** per day	**Physical Intensity Level 2,3,4** *Choose the level for you*
1	meals, dishes, laundry	4	7	2	2
2	feed, dress, play with kids	4	7	3	3
3	garden, cut grass	4	3	1.5	3

Please go on to the next page

This box to be completed by the clinical research associate: Pt. Serial #: _____ Pt. Initials: ____ ____ ____

Your Household, Childcare & Do-It-Yourself Activities

1. Start a new line when the pattern changed, such as when the intensity level, or the number of months, days or hours changed in the past 1 month.
2. Report seasonal activities like gardening or snow shoveling separately from year round activities.
3. If you are being paid to provide childcare, report this activity on page 3.

	Type of Activity	**Weeks** per month	**Days** per week	**Hours** per day	**Physical Intensity Level 2,3,4** *Choose the level for you*
1					
2					
3					
4					
5					
6					
7					
8					
9					

Please go on to the next page

This box to be completed by the clinical research associate: Pt. Serial #: _____ Pt. Initials: ____ ____ ____

Recreation & Leisure Activities

For this category, DO NOT include activities that are done SEATED (e.g. playing cards, reading, etc)**.**

PHYSICAL INTENSITY LEVELS: *Choose the one that best describes your experience*.

2 = Activities done mainly **standing**, that **do not increase your heart rate** & cause **no sweating**

3 = Activities that cause **your heart rate to increase slightly** & cause **some light sweating**

4 = Activities that cause **your heart rate to increase substantially** & cause **heavy sweating**

Examples:

Activity 1:

- Greg went on a 5-day **fishing** trip this past month.
- He fished about **4** hours each day.
- For him, fishing is a level **2**.

Activity 2:

- Greg also **walks** regularly.
- He walks **4** days a week, for **30** minutes.
- For him, walking is a level **3**

Activity 3:

- Greg also **cycles** regularly.
- He cycles **4** days a month, for **3** hours.
- For him, cycling is a level **4**.

	Recreation or Leisure Activity	**Frequency** Please specify how many days: • per day • per month	**Hours** per day	**Physical Intensity Level 2,3,4** *Choose the level for you*
1	fishing	5 days per month	4	2
2	walking	4 days per week	0.5	3
3	cycling	4 days per month	3	4

Please go on to the next page

This box to be completed by the clinical research associate: Pt. Serial #: _____ Pt. Initials: ____ ____ ____

Your Recreation & Leisure Activities

1. Start a new line when the pattern changed, such as when the activity, intensity level, or the number of days or hours of your recreational activities in the past month changed.
2. Do not include walking that you did as part of your job or volunteer activities – this type of walking should be recorded on page 3.
3. See next page for examples before you start… 

	Recreation or Leisure Activity Please be specific when possible	**Frequency** Please specify how many days and whether the activity is: • per week • per month	**Hours** per day	**Physical Intensity Level 2,3,4** *Choose the level for you*
1		____ days per _____		
2				
3				
4				
5				
6				
7				
8				
9				
10				

Please check! Did you record whether your activity was weekly or monthly in the column above?

Please go on to the next page

This box to be completed by the clinical research associate: Pt. Serial #: _____ Pt. Initials: ____ ____ ____

Examples of Recreation & Leisure Activities

Aerobics
Aquacize
Archery
Backpacking
Badminton
Basketball
Bicycling
Billiards
Boating
Bowling
Boxing
Broomball
Calisthenics
Canoeing
Circuit training
Climbing (rock, wall)
Coaching
Cricket
Curling
Dancing
Darts
Deepwater running
Diving
Fishing
Football
Frisbee
Golf
Gymnastics
Handball
Hang gliding
Hiking
Hockey
Horseback riding
Horseshoe pitching
Hunting
Ice-skating
Jogging
Judo
Jujitsu
Karate
Kayaking
Lacrosse
Motor cross
Orienteering
Paddleball
Ping-pong
Racquetball
Rowing
Rugby
Running
Sailing
Scuba diving
Shuffleboard
Skateboarding
Skiing, downhill
Skiing, cross-country
Sledding
Snorkeling
Snow shoeing
Snowboarding
Soccer
Softball
Squash
Stair climber
Stationary bicycling
Stretching
Surfing
Swimming
Tai chi
Tennis
Tobogganing
Track & field
Treadmill
Volleyball
Walking
Water polo
Water volleyball
Water skiing
Weight lifting
Whitewater rafting
Wrestling
Yoga

Please check to make sure you have answered all the questions.

Please fill in your initials to indicate that you have completed this questionnaire: _____

Today's date (Year, Month, Day): _____

Thank you.

This box to be completed by the clinical research associate: Pt. Serial #: _____ Pt. Initials: ____ ____ ____

Social Cognitive Determinates of Exercise

The following questions ask you to rate how you currently feel about exercising regularly. Please pay careful attention to the words for each scale and circle the number that best represents how you currently feel.

---

1. How beneficial is it for you to exercise regularly right now?

1	2	3	4	5
not at all	slightly	moderately	quite	extremely

2. How enjoyable is it for you to exercise regularly right now?

1	2	3	4	5
not at all	slightly	moderately	quite	extremely

3. How much support do you have for exercising regularly right now?

1	2	3	4	5
none at all	a little	some	quite a bit	a lot

4. How difficult is it for you to exercise regularly right now?

1	2	3	4	5
not at all	slightly	moderately	quite	extremely

5. How confident are you that you can exercise regularly right now?

1	2	3	4	5
not at all	slightly	moderately	quite	extremely

6. How motivated are you to exercise regularly right now?

1	2	3	4	5
not at all	slightly	moderately	quite	extremely

7. How detailed of a plan do you have for exercising regularly right now?

1	2	3	4	5
none	a little	some	very	extremely

8. How many opportunities do you have for exercising regularly right now?

1	2	3	4	5
none at all	a few	some	quite a few	lots

Please check to make sure you have answered all the questions.

Please fill in your initials to indicate that you have completed this questionnaire: _____

Today's date (Year, Month, Day): _____

Thank you.

This box to be completed by the clinical research associate: Pt. Serial #: _____ Pt. Initials: ____ ____ ____

CO.21 Physical Activity Log Instructions

1. Please PRINT.

2. Use a new page each week.

3. Record your physical activity after each session (before you forget!).

4. If you do more than one type of activity in a day (for example, walking and bicycling), fill a **different row** for **each** activity.

Day: please record the day of the week for each activity. You do not need to complete a row for days you didn't exercise.

Exercise time: this is how long you spent at the activity with your heart are in the target range. It does not include warm-up or cool-down time.

Heart rate: this number is heart rate that you maintained during the aerobic exercise (not a peak heart rate that you only reached briefly).

RPE: this stands for Rate of Perceived Exertion.
This value is a number between 6 and 20.
Use the bar at the right to evaluate your RPE.

Comments: you are not required to add comments. You may wish to add comments occasionally to explain unusual activity, or to record your feelings or reasons for not completing an exercise day.

This box to be completed by the clinical research associate: Pt. Serial #: _____________ Pt. Initials: ____ ____ ____

NCIC CTG CO.21 – Week of: ____

Please start a new page each week!

Day	Activity	Exercise time	Heart rate	RPE	Comments
	☐ Walking ☐ Bicycling ☐ Other (specify below) ____________	__ __ minutes	__ __ __ beats per minute	__ __ (on a scale of 6-20)	
	☐ Walking ☐ Bicycling ☐ Other (specify below) ____________	__ __ minutes	__ __ __ beats per minute	__ __ (on a scale of 6-20)	
	☐ Walking ☐ Bicycling ☐ Other (specify below) ____________	__ __ minutes	__ __ __ beats per minute	__ __ (on a scale of 6-20)	
	☐ Walking ☐ Bicycling ☐ Other (specify below) ____________	__ __ minutes	__ __ __ beats per minute	__ __ (on a scale of 6-20)	
	☐ Walking ☐ Bicycling ☐ Other (specify below) ____________	__ __ minutes	__ __ __ beats per minute	__ __ (on a scale of 6-20)	
	☐ Walking ☐ Bicycling ☐ Other (specify below) ____________	__ __ minutes	__ __ __ beats per minute	__ __ (on a scale of 6-20)	
	☐ Walking ☐ Bicycling ☐ Other (specify below) ____________	__ __ minutes	__ __ __ beats per minute	__ __ (on a scale of 6-20)	
	☐ Walking ☐ Bicycling ☐ Other (specify below) ____________	__ __ minutes	__ __ __ beats per minute	__ __ (on a scale of 6-20)	
	☐ Walking ☐ Bicycling ☐ Other (specify below) ____________	__ __ minutes	__ __ __ beats per minute	__ __ (on a scale of 6-20)	
	☐ Walking ☐ Bicycling ☐ Other (specify below) ____________	__ __ minutes	__ __ __ beats per minute	__ __ (on a scale of 6-20)	
	☐ Walking ☐ Bicycling ☐ Other (specify below) ____________	__ __ minutes	__ __ __ beats per minute	__ __ (on a scale of 6-20)	

Please fill in your initials to indicate that you have completed this PA log: ______________

Today's date (Year, Month, Day): ________________________________

Thank you.

FUNCTIONAL FITNESS TEST FOR OLDER ADULTS

Following are specific directions for administering each of the test items. To ensure scoring accuracy and interpretation, strict adherence to all instructions is essential. Throughout all testing, participants should be instructed to *do the best they can on the tests but to never push themselves to a point of overexertion or beyond what they think is safe for them.* Prior to testing, participants must do a 5- to 10-min warm-up and general stretching routine.

Based on guidelines established by the ACSM (1995) and on input from medical consultants, these tests are safe for the majority of community-residing older adults without medical screening and pose risks similar to those in engaging in other forms of moderate physical activity. People who *should not* take the tests without physician approval are those who

- Have been advised by their doctors not to exercise because of a medical condition
- Are currently experiencing chest pain, dizziness, or have exertional angina (chest tightness, pressure, pain, heaviness) during exercise
- Have had congestive heart failure
- Have uncontrolled high blood pressure (greater than 160/100)

30-Second Chair Stand

Purpose. To assess lower body strength.

Equipment. Stopwatch, straight-back or folding chair (without arms), height approximately 17 in. For safety purposes, the chair should be placed against a wall or in some other way stabilized to prevent it from moving during the test.

Protocol. The test begins with the participant seated in the middle of the chair, back straight and feet flat on the floor. Arms are crossed at the wrists and held against the chest. On the signal "go" the participant rises to a full stand and then returns to a fully seated position. The participant is encouraged to complete as many full stands as possible within 30 s. After a demonstration by the tester, a practice trial of one to three repetitions should be done to check for proper form, followed by one 30-s test trial.

Scoring. The score is the total number of stands executed correctly within 30 s. If the participant is more than half-way up at the end of 30 s, it counts as a full stand.

Arm Curl

Purpose. To assess upper body strength.

Equipment. Wristwatch with second hand, straight-back or folding chair (without arms), hand weights (dumbbells—5 lb for women, 8 lb for men).

Protocol. The participant is seated on a chair, back straight and feet flat on the floor, with the dominant side of the body close to the side edge of the chair. The weight is held at the side in the dominant hand (handshake grip). The test begins with the arm down beside the chair, perpendicular to the floor. At the signal "go" the participant turns the palm up while curling the arm through a full range of motion and then returns to the fully extended position. At the down position the weight should have returned to the handshake grip position.

The examiner kneels (or sits in a chair) next to the participant on the dominant-arm side, placing his or her fingers on the person's mid-biceps to prevent the upper arm from moving and to ensure that a full curl is made (participant's forearm should squeeze examiner's fingers). It is important that the participant's upper arm remain stabilized (still) throughout the test.

The examiner may also need to position his or her other hand behind the participant's elbow so that the participant will know when full extension has been reached, as well as to prevent a back-swinging motion of the arm.

The participant is encouraged to execute as many curls as possible within the 30-s time limit. After a demonstration by the examiner, a practice trial of one or two repetitions should be given to check for proper form, followed by one 30-s trial.

Scoring. The score is the total number of curls made correctly within 30 s. If the arm is more than halfway up at the end of the 30 s, it counts as a curl.

6-Minute Walk

Purpose. To assess aerobic endurance.

Equipment. Stopwatch, long measuring tape, cones, popsicle sticks, chalk, masking tape (or some other type of marker). For safety purposes, chairs should be positioned at several points alongside the walkway.

Set-Up. The test involves assessing the maximum distance that can be walked in 6 min along a 50-yd course marked into 5-yd segments (see Figure A1). The inside perimeter of the measured distance should be marked with cones, and the

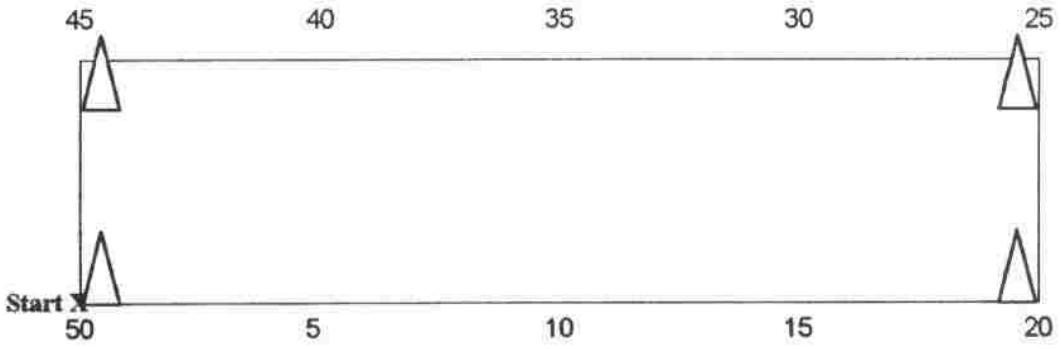


Figure A1. 50 yd measured into 5-yd segments.

5-yd segments with masking tape or chalk. The walking area, which can be indoors or outdoors, should be well lit, with a nonslippery, level surface.

Protocol. To keep track of distance walked, a popsicle stick (or similar object) can be given to the participant each time he or she rounds a cone, or a partner can mark a score card each time a lap is completed. Two or more participants should be tested at a time, with starting times staggered (10 s apart) so that participants do not walk in clusters or pairs. When testing several people at once, numbers should be placed on the participants to indicate the order of starting and stopping. On the signal "go," participants are instructed to walk as fast as possible (not run) around the course as many times as they can in 6 min. If necessary, participants may stop and rest (on provided chairs), then resume walking. The timer should move to the inside of the marked area after everyone has started. To assist with pacing, elapsed time should be called out when participants are approximately half done, when 2 min are left, and when 1 min is left. Encouragement phrases such as "you are doing well" and "keep up the good work" should be called out at approximately 30-s intervals. At the end of 6 min, participants (staggered every 10 s) are instructed to stop and move to the right, where an assistant will record their score. To assist with proper pacing and to improve scoring accuracy, a practice test should be given prior to the actual test day.

Safety. The test should be discontinued if at any time a participant shows signs of dizziness, pain, nausea, or undue fatigue. At the end of the test each participant should *slowly* walk around for about a minute to cool down.

Scoring. The score is the total number of yards walked in 6 min, to the nearest 5 yd. The test administrator or aide records the nearest 5-yd mark.

2-Minute Step-in-Place (An Alternative to the 6-Min Walk Test)

Purpose. To assess aerobic endurance.

Equipment. Stopwatch, tape measure or 30-in. piece of cord, masking tape, mechanical counter (if possible) to ensure accurate counting of steps.

Set-Up. The proper (minimum) knee-stepping height for each participant is at a level even with the midway point between the patella (middle of the knee cap) and the iliac crest (top hip bone). This point can be determined using a tape measure or by simply stretching a piece of cord from the patella to the iliac crest, then folding

it in half to determine the midway point. To monitor correct knee height when stepping, books can be stacked on an adjacent table or a ruler can be attached to a chair or wall with masking tape to mark the proper knee height.

Protocol. On the signal "go" the participant begins stepping (not running) in place, starting with the right leg, and completes as many steps as possible within the time period. Although both knees must be raised to the correct height to be counted, the tester only counts the number of times the right knee reaches it. The counter also serves as a spotter in case of loss of balance and ensures that the participant maintains proper knee height. As soon as proper knee height can no longer be maintained, the participant is asked to stop—or to stop and rest until proper form can be regained. Stepping may be resumed if the 2-min time period has not elapsed. If necessary, the participant can place one hand on the table or chair to assist in maintaining balance.

To assist with proper pacing and to improve scoring accuracy, a practice test should be given prior to the test day. On test day, the examiner should demonstrate the procedure and allow the participants to practice briefly to recheck their understanding of the protocol.

Safety. At the end of the test the participant should slowly walk around for about a minute to cool down.

Scoring. The score is the total number of times the right knee reaches the minimum height. To assist with pacing, participants should be told when 1 min has passed and when there are 30 s to go.

Chair Sit-and-Reach

Purpose. To assess lower body (primarily hamstring) flexibility.

Equipment. Straight-back or folding chair (approximately 17-in. seat height), 18-in. ruler. For safety purposes, the chair should be placed against a wall and checked to see that it remains stable (doesn't tip forward) when the participant sits on the front edge.

Protocol. Starting in a sitting position on a chair, the participant moves forward until she or he is sitting on the front edge. The crease between the top of the leg and the buttocks should be even with the edge of the chair seat. Keeping one leg bent and *foot flat on the floor,* the other leg (the preferred leg*) is extended straight in front of the hip, with heel on floor and foot flexed (at approximately 90°; see the picture).

With the extended leg as straight as possible (but not hyperextended), the participant slowly bends forward *at the hip joint* (spine should remain as straight as possible, with head in line with spine, not tucked) sliding the hands (one on top of

*The preferred leg is defined as the one that results in the better score. Obviously, it is important to work on flexibility on both sides of the body, but for the sake of time, only the "better" side has been used in developing norms.

the other with the tips of the middle fingers even) down the extended leg in an attempt to touch the toes. The reach must be held for 2 s. If the extended knee starts to bend, ask the participant to slowly sit back until the knee is straight before scoring. Participants should be reminded to exhale as they bend forward; to avoid bouncing or rapid, forceful movements; and to never stretch to the point of pain.

After a demonstration by the tester, the participant is asked to determine the preferred leg. The participant is then given two practice (stretching) trials on that leg, followed by two test trials.

Scoring. Using an 18-in. ruler, the scorer records the number of inches a person is short of reaching the toe (minus score) or reaches beyond the toe (plus score). The middle of the toe at the end of the shoe represents a zero score. Record both test scores to the nearest 1/2 in., and circle the best score. The best score is used to evaluate performance. Be sure to indicate "minus" or "plus" on the score card.

Back Scratch

Purpose. To assess upper body (shoulder) flexibility.

Equipment. 18-in. ruler (half of a yardstick).

Protocol. In a standing position, the participant places the preferred hand* behind the same-side shoulder, palm toward back and fingers extended, reaching down the middle of the back as far as possible (elbow pointed up). The participant places the other hand behind the back, palm out, reaching up as far as possible in an attempt to touch or overlap the extended middle fingers of both hands.

Without moving the participant's hands, the tester helps to see that the middle fingers of each hand are directed toward each other. The participant is not allowed to grab his or her fingers together and pull.

After a demonstration by the tester, the participant is asked to determine the preferred hand, and is then given two practice (stretching) trials, followed by two test trials.

*The preferred hand is defined as the one that results in the better score. Although it is important to work on flexibility on both sides of the body, only the "better" side has been used in developing norms.

Scoring. The distance of overlap or distance between the tips of the middle fingers is measured to the nearest 1/2 in. A minus score (–) is given to represent a distance short of touching; a plus score (+) represents the amount of an overlap. Record both test scores and circle the best one. The best score is used to evaluate performance. Be sure to indicate "minus" or "plus" on the score card.

8-Foot Up-and-Go

Purpose. To assess agility/dynamic balance.

Equipment. Stopwatch, tape measure, cone (or similar marker), straight-back or folding chair (seat height approximately 17 in.).

Set-Up. The chair should be positioned against a wall or in some other way secured so that it does not move during testing. It should also be in a clear, unobstructed area, facing a cone marker exactly 8 ft away (measured from a point on the floor even with the front edge of the chair to the back of the marker). There should be at least 4 ft of clearance beyond the cone to allow ample turning room for the participant.

Protocol. The test begins with the participant fully seated in the chair (erect posture), hands on thighs and feet flat on the floor (one foot slightly in front of the other). On the signal "go" the participant gets up from the chair (pushing off thighs or chair is allowed), walks as quickly as possible around the cone (on either side), and returns to the chair. The participant should be told that this is a timed test and that the object is to walk as quickly as possible (without running) around the cone and back to the chair. The tester should serve as a spotter, standing midway between the chair and the cone, ready to assist the participant in case of loss of balance. For reliable scoring, the tester must start the timer on "go," whether or not the participant has started to move, and stop the timer at the exact instant the participant sits in the chair.

After a demonstration, the participant walks through the test one time as a practice and then is given two test trials. Participants should be reminded that the timing does not stop until they are fully seated in the chair.

Scoring. The score is the time elapsed from the signal "go" until the participant returns to a seated position in the chair. Record both test scores to the nearest 1/10th s and circle the best score (lowest time). The best score is used to evaluate performance.

GUIDELINES FOR CONVERTING NONMETRIC MEASURES TO METRIC UNITS

Test item	U.S. measure	Metric equivalent
Chair stand	17-in. seat height	43.18-cm seat height
Arm curl	5-lb dumbbell 8-lb dumbbell	2.27-kg dumbbell 3.63-kg dumbbell
Chair sit-and-reach	17-in. seat height 18-in. ruler scores recorded to nearest 1/2 in.	43.18-cm seat height 45.72-cm ruler scores recorded to nearest cm
Back scratch	18-in. ruler scores recorded to nearest 1/2 in.	45.72-cm ruler scores recorded to nearest cm
6-min walk	50-yd course marked into 5-yd segments	45.72-m course marked into 4.57-m segments
2-min step	30-in. cord or tape measure	76.2-cm cord or tape measure
8-ft up-and-go	17-in. seat height 8-ft distance to cone 4-ft clearance past cone	43.18-cm seat height 2.44-m distance to cone 1.22-m clearance past cone