DIETARY RISK FACTORS FOR BONE LOSS AMONG MEN UNDERGOING ANDROGEN DEPRIVATION THERAPY FOR THE TREATMENT OF PROSTATE CANCER

by

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ABSTRACT

Androgen deprivation therapy (ADT) is the preferred mode of treatment for patients with recurrence of prostate cancer (PC) following definitive treatment and locally advanced disease. With more men commencing ADT earlier in the treatment trajectory and for longer duration, the side effects of ADT are becoming more prevalent and of greater concern to clinicians. ADT can have serious adverse effects on bone mineral density (BMD) and metabolism, leading to the development of osteopenia or osteoporosis.

This study was a cross-sectional investigation of dietary risk factors for bone loss, particularly calcium and vitamin D intakes, among men undergoing ADT for the treatment of non-metastatic PC (n = 12), hormone-naïve men with PC (n = 21) and healthy controls (n = 20). Outcome measures were dietary intake of calcium and vitamin D assessed by diet history questionnaire, as well as vitamin D status as assessed by serum 25-hydroxyvitamin D and parathyroid hormone levels. There were no between-group differences in calcium or vitamin D intake from food, supplements or both. When compared with the current Adequate Intake and treatment-specific guidelines, the majority of men did not meet current recommendations. Adherence to current dietary guidelines for the prevention of osteoporosis among men undergoing ADT was poor, with 91.7% falling short of the recommended 1500 mg of calcium per day, and no men meeting the treatment-specific recommendation of 20 mcg of daily vitamin D. In addition to inadequate calcium and vitamin D intakes, several additional dietary risk factors present among study participants further increase risk of bone loss and osteoporosis in this group of men. Vitamin D status was also not different among groups; however, serum values quantitated by the assays were well outside expected values, and it was concluded that the assays were likely not valid.

The results of this study demonstrate the need for provision of nutrition information to these men at time of therapy commencement and on an ongoing basis throughout treatment, as a means of preventing or reducing the negative effects of ADT on nutritional status and quality of life.
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"Let food be thy medicine and medicine be thy food." – Hippocrates
CHAPTER 1: INTRODUCTION

Prostate cancer (PC) is the most common solid malignancy diagnosed in Canadian men, where one in seven men will develop the disease in their lifetime. An estimated 25,500 men will be diagnosed with PC in Canada in 2009, causing 4,400 deaths; the second leading cause of cancer-related mortality (1). Increasing use of the prostate specific antigen (PSA) blood test in diagnosis and management of PC over the last several decades has led to improved detection of biochemical recurrence, a rising PSA without evidence of local progression or metastases (2). Despite advances in treatment selection and techniques, up to 35% of patients treated with surgery or radiation will have detectable PSA levels within a decade (2-4).

Androgen deprivation therapy (ADT) is the preferred mode of treatment for patients with locally advanced disease and biochemical recurrence (5,6). Preliminary evidence suggests that immediate versus delayed induction of ADT increases survival time (6). With more men commencing ADT earlier in the treatment trajectory and for longer duration (5-7), the common side effects of ADT are becoming more prevalent and of greater concern to clinicians (5,7-9). ADT can have serious adverse effects, such as hot flashes (10), weight gain, increased fat mass, decreased lean body mass (11,12) and osteoporosis (6,8,9,12), and may significantly impact quality of life (5,13). Historically, osteoporosis is seen as a disease affecting primarily postmenopausal women, yet other secondary causes of osteoporosis, such as induced hypogonadism in men undergoing ADT, have been garnering more attention (5). The baseline characteristics of this group and the routine early use of ADT increase their risk of bone loss and skeletal-related events (5,8). The importance of recognizing and preventing these adverse effects of treatment through risk identification and appropriate prevention intervention programs cannot be ignored.
CHAPTER 2: LITERATURE REVIEW

2.1. Overview

Current literature discussing the effect of hypogonadism on bone metabolism and health is dominated by research studies of postmenopausal women. While some attention to the effects of aging on bone health in men is now occurring, a paucity of literature exists on the effects of hypogonadism in men, particularly as a result of androgen deprivation therapy (ADT) for the treatment of prostate cancer (PC). The growing use of ADT among men with PC, and the substantial toxicity associated with its use, warrant closer inspection. Although ADT is known to produce side effects ranging from erectile dysfunction to hyperlipidemia, the effects of ADT on bone health are significant and pose a considerable threat to quality-of-life.

Risk factors for bone loss and osteoporosis are well documented, yet modifiable risk factors such as dietary intake, body weight, and physical activity, as well as their respective effects on bone mineral density (BMD) and fracture rate, have been inconsistently investigated in studies of men with PC. As a result, the prevalence of such risk factors is unknown, and identification of men on ADT at high-risk for osteoporosis and fracture as a means of targeting preventive strategies has not been conducted. In fact, despite recommendations related to the diagnosis and treatment of bone loss as a result of ADT, the use of risk assessment and prevention strategies in clinical practice is sporadic at best.

Although an association between vitamin D status and PC incidence has recently emerged in the literature, reports of serum 25-hydroxyvitamin D (25OHD) levels and the factors contributing to vitamin D status in men on ADT are scant. The relationship between vitamin D status and BMD, risk of osteoporosis and fracture incidence in this population is poorly understood, and represents an important new avenue for research.
The literature that underlies the above summary, and additional background information essential to its understanding, are presented in the following review. The first section describes current practices regarding ADT for the treatment of PC, as well as the significant risk of toxicity with such treatment. This is followed by discussions of bone loss in men, the factors which contribute to bone loss and the prevalence of bone loss in both the general and prostate cancer populations. The current state of knowledge regarding vitamin D is summarized, with emphasis on optimal intake, prevalence of insufficiency in the target populations and associations between vitamin D and bone health. Finally, the relationship between vitamin D and prostate cancer, including the impact of ADT on vitamin D status, is discussed.

2.2. Androgen Deprivation Therapy

The use of ADT as a treatment for PC was discovered in the early 1940s, when Charles Huggins found that diethylstilbestrol (DES) as a castrating agent in men with metastatic PC gave a complete blockade of testosterone production and favourably affected prostate cancer markers (14). Although Huggins’ work was recognized by a Nobel Prize in science in 1966, the administering of high-dose DES in men with PC has serious adverse effects, such as thromboembolism and cardiovascular events, which preclude its use in current practice.

Modern-day ADT encompasses two different modalities: surgical castration and medical or chemical castration. Surgical castration, or orchiectomy, involves the removal of the testes and results in immediate, irreversible and complete (95%) blockade of testosterone production (15). While orchiectomy is still currently used, its irreversible nature and the potential dangers of surgery have led to predominant use of medical castration in urologic practice. The most prevalent modalities of medical castration are leutinizing hormone-releasing hormone (LHRH)
agonists and gonadotropin-releasing hormone (GnRH) antagonists, available as either monthly or 3-month injections. Both modalities block the production of testosterone by interfering with the hypothalamus-pituitary axis of testosterone production (15). LHRH agonists and GnRH antagonists provide a reversible reduction in testosterone that is similar to the complete blockade induced by estrogen therapy (15), causing PSA levels to fall quickly.

The continuous use of ADT in men with PC was once the mainstay of recurrence treatment, demonstrating a primary response rate of 80–90% in the majority of men (6,16). While this initial response may last for many years, ADT is not considered to be curative as the progression of disease to a hormone-refractory or hormone-independent state is inevitable, where PC no longer responds to testosterone deprivation (16). As a result, the intermittent delivery of ADT in men with PC has been investigated as a promising mode of treatment. Intermittent ADT is generally given as a nine-month treatment course of ADT followed by a nine-month recovery period, or re-treatment at the first sign of PSA increase (6,15,16). While still in its investigative stages, it is hoped that intermittent ADT will prolong time to androgen independence and ameliorate the short- and long-term side effects of continuous treatment (6,16). Currently, intermittent ADT is the preferred mode of treatment for men with biochemical recurrence at the Vancouver Prostate Centre.

2.2.1. Toxicity of androgen deprivation therapy

ADT induces hypogonadism in men with PC, defined as a free serum testosterone level of less than 10 nmol/L (16). Hypogonadism induced by ADT is associated with substantial toxicity. Loss of libido, erectile dysfunction, vasomotor flushes and fatigue are the most commonly reported side effects in men (13,17,18). In addition to quality of life-related side
effects, ADT is also associated with significant physical morbidity, such as changes in body composition and lipid profiles, anemia, and bone loss (5,10-12).

After 48 weeks of ADT therapy, an increase in body mass index (BMI; kg/m²) of 2.4% and increases in total cholesterol and serum triglycerides of 9% and 26.5%, respectively, have been reported (11). The loss of lean body mass and subsequent development of sarcopenia provide further evidence of negative body composition changes induced by secondary hypogonadism (11,12,15). As many as 90% of men will have a 10% reduction in hemoglobin levels, and 13% may experience declines of 25% or more. The experience of anemia in men on ADT is thought to be due to the lack of testosterone and dehydrotestosterone stimulation of red blood cell precursors and a reduction in erythropoietin production (10,19).

The risk of bone loss in men undergoing ADT is not, however, associated directly with a lack of testosterone, but instead to the resulting loss of circulating estradiol due to the reduced aromatization of testosterone to estrogen (20-22). Testosterone was initially believed to be the dominant bone metabolism-regulating hormone in men, whereas estrogen was considered the dominant regulator in women. A paradigm shift was prompted by the case report of a 28-year old man presenting with osteopenia and altered bone metabolism. Although testosterone levels were normal, the man was found to have nonfunctional estrogen receptors; estrogen is now recognized as the dominant regulating hormone in both men and women (22). Several studies have been conducted in men to clarify the relationship between testosterone, estrogen and bone metabolism. Rate of bone loss and BMD in men were found to be significantly associated with circulating estrogen, with no correlation to available testosterone (20,21,23,24).
2.3. Bone Loss in Men

Osteoporosis is defined as “a skeletal disease characterized by low bone mass and micro-
architectural deterioration of bone tissue with a resulting increase in fragility and risk of
fracture” (25), accounting for an estimated $1.9 billion in treatment costs in Canada each year
(26). Historically, osteoporosis is seen as a disease affecting primarily postmenopausal women.
The Canadian Multicentre Osteoporosis Study (CaMos) (27) estimated the prevalence of low
BMD in a random sample of 10 061 men and women, assessing BMD of the lumbar spine and
femoral neck by dual-energy x-ray absorptiometry (DEXA). The combined prevalence of
osteoporosis in women age 50 years and older was estimated to be 15.8%: 12.1% and 7.9% at
the lumbar spine and femoral neck, respectively (27). Although combined prevalence of
osteoporosis was lower in men (6.6% of men 50 years of age and older) (28), the importance of
recognizing the morbidity and mortality related to osteoporosis and fragility fracture in men is
growing.

The World Health Organization (29) definition of diagnosable osteoporosis is based
upon a comparison of BMD with the mean BMD of healthy, young adults of the same gender
and ethnicity. Osteoporosis is diagnosed based upon a person’s T-score, the number of standard
deviations (SD) above or below the normal reference BMD (25). A normal BMD is considered
to be between + 2.5 and −1 SD. Osteopenia, an earlier and less severe form of bone loss, is
associated with a BMD between −1 and −2.5 SD from normal. Osteoporosis is diagnosed at a
BMD of less than or equal to 2.5 SD below the young adult mean BMD.

While these diagnostic criteria are well established in the female population, there is
currently no consensus regarding the definition of osteoporosis in men. These generated T
scores are based upon the mean BMD of healthy women, and may underestimate the true
prevalence of low BMD in men (27,30,31). The CaMos data (27) demonstrated this disparity. When the peak bone mass (PBM) of women was used as a reference for men, the prevalence of osteopenia in men 50 years of age and older was an estimated 26.7%. When the PBM of men (as was determined in the study) was used as a reference, however, the prevalence of osteopenia rose to 39.1% (27).

2.3.1. Prevalence of osteopenia and osteoporosis in men

Based on CaMos data (27), among Canadian men 50 years of age and older the estimated prevalence of osteoporosis is 6.6%: 2.9% at the lumbar spine; 4.8% at the femoral neck. The combined prevalence of osteoporosis in Canadian women, based on CaMos data, is nearly triple that of men (27). The prevalence of low BMD and significant bone loss is lower in men than women for several reasons. Men have a greater accumulation of bone mass and, therefore, a greater bone size than women, which is primarily due to the influence of testosterone on body size (25,30). There is absence of midlife hypogonadism in healthy men, in comparison to female menopause. As a result, men do not experience the menopausal reduction in circulating estrogen that has deleterious effects on bone health. Men do experience a natural decline in circulating estrogen due to declining testicular function, however, which accounts for the slower rate of bone loss in men with age (22,23,32,33).

Bone Mineral Density in Hormone-Naïve Men with Prostate Cancer. Despite eugonadal status, the baseline characteristics of men with PC prior to or without ADT suggest a significant risk of low bone mineral density exists in hormone-naïve men (12,34-39). In a study of hormone-naïve men with PC, Smith et al. (35) investigated BMD using both DEXA and quantitative computed tomography (QCT). Fourteen of 41 (34%) men in the study met WHO
criteria for low BMD: 5% had osteoporosis, and 29% had osteopenia at the lumbar spine (posterior-anterior or lateral) and/or total hip as measured by DEXA. The results of QCT measurement of trabecular lumbar spine BMD suggested that even higher proportions had low BMD (35). With QCT, the number of osteopenic men rose to 31% and those with diagnosable osteoporosis reached 63%; nearly 95% of men had T-scores of less than −1 (35). Similarly, Conde et al. (34) found a prevalence of low BMD in hormone-naïve men with PC to be 73.5%: 55.9% were osteopenic, 17.6% had osteoporosis. And in a final study, five of eight (63%) hormone-naïve men with PC fulfilled diagnostic criteria for low BMD (36).

The high prevalence of low BMD among eugonadal men with PC is significant, yet a lack of age-matched healthy controls does not allow for a comparison to the general population. The data from CaMos (27) does demonstrate far lower estimates of low BMD at the lumbar spine in healthy men 50 years of age and older (2.9%) in comparison to estimates of 17.6% (34) and 5% (35) in men with PC. The average age of diagnosis of men with PC is 65 years of age (3), and this could contribute to the higher prevalence in men with PC as compared to the general population of men aged 50 and above. Conde et al. (34) found a significant association between age and BMD of the lumbar spine (r = -0.37; P < 0.05); however, Smith et al. (35) did not detect a significant correlation between age and BMD at the total hip (r = -0.20; P > 0.05), posterior-anterior lumbar spine (r = -0.002; P > 0.05) or lateral lumbar spine (r = -0.37; P > 0.05).

Several other factors have been suggested to explain the apparently higher prevalence of low bone mass in men with PC. Poor nutrition as a contributor to low BMD has been supported by the low calcium intakes of men with PC; vitamin D intake has been estimated at 4.8 ± 5.57 mcg (34). While both Smith et al. (35) and Conde et al. (34) found mean calcium intakes to be
low (877 ± 333 mg per day and 651.3 ± 625.5, respectively), Conde et al. (34) did not find a
significant association between BMD and calcium intake; Smith et al. (35) did not report on this
relationship. The relationship between PSA and BMD has also been postulated to contribute to
the prevalence of low BMD among men with PC. Conde et al. (34) found PSA levels to
correlate negatively with BMD at the lumbar spine, femoral neck, hip and trochanter; all sites
reached significance. The mechanism for such an explanation warrants further investigation.

Despite the high prevalence of low BMD among men with PC as suggested by several
studies, small sample size renders many of these studies underpowered for detection, as is
evident by the absence of sample size justification. A lack of healthy controls in most studies,
wide variations in outcome measures and differences in statistical analysis suggest a need for
larger prospective studies including controls, which examine a multitude of factors known to
influence BMD in men.

Impact of ADT on Bone Mineral Density. Several studies examining the effect of ADT
on BMD (36,40-47) have estimated a decrease of 2 to 10% within the first year of ADT.
Compared with eugonadal men with PC, men undergoing ADT have BMD that is 6.5 – 17.3%
lower (48). In a cross-sectional study of 23 men on ADT for six months or longer, Preston et al.
(41) compared BMD at the distal forearm, lumbar spine, femoral neck, total hip and trochanter
with BMD of an age-matched control group of eugonadal men. The control group consisted of
men with normal PSA levels: men with benign prostatic hyperplasia (BPH); men with erectile
dysfunction (ED); and men with PC who had undergone definitive treatment. Significantly
lower BMD was seen in men on ADT at all sites except lumbar spine (41). In men undergoing
ADT for more than one year (n = 24), Wei et al. (36) found a significant decrease in BMD in
comparison to eugonadal men with PC (n = 8), where 88% of men treated with ADT fulfilled
diagnostic criteria for osteopenia or osteoporosis.

Few studies investigating BMD of men on ADT have been prospective in nature. Daniell et al. (43) followed 32 men with PC starting at commencement of ADT at 6 month intervals; included also were 16 men currently on ADT who had been treated for 3 to 8 years. Results showed a 1.4 to 2.6% loss of bone mass with each year of ADT treatment. In comparison to 12 healthy controls, age-corrected femoral neck BMD was significantly greater in controls than men on ADT. Kiratli et al. (44) measured hip and lumbar spine BMD of 36 men at various points in ADT trajectory (range: time of ADT initiation to year 10). A significant association between duration of ADT and decreasing BMD in men with PC was found, with the most dramatic decline in BMD at the hip (44).

In addition to reported declines in BMD, duration of ADT is also significantly associated with increases in bone resorption markers (42,45,47). Pyridinoline (PYD), deoxypyridinoline (DPD) and crosslinked N-terminal collagen-related telopeptides (NTx) have been shown to significantly increase in men undergoing ADT, with a rise in levels seen as early as 6 months after commencement of therapy and continuing to rise two years into treatment (42,45).

The prevalence of low BMD and bone loss among men treated with ADT for PC has been documented in the aforementioned cross-sectional and short-term prospective studies (36,40-47). While the relationship between BMD and several medical chart-available clinical variables, such as age, PSA level and BMI has been investigated, a paucity of literature on additional variables known to influence BMD in men exists. Biochemical indices not regularly ordered as part of urologic practice, such as serum 25OHD and parathyroid hormone (PTH) are rarely assessed (41,42,47), and if assessed are not included in analysis beyond simple description at baseline. Modifiable risk factors of low BMD and bone loss, such as dietary
intake and/or physical activity have all but been ignored save for a few studies (34,35,41,43) and are, similarly, not included in analysis. The importance of such factors and their potential for the identification of men with low BMD, development of risk modification counseling and prevention/reduction of bone loss in this population demonstrates a tremendous need for additional research.

2.3.2. Osteoporotic fracture

The most common osteoporotic fracture sites are the hip, spine and wrist (26). In 1993, 25,000 hip fractures occurred in Canada, 70% of which were osteoporosis-related (26). Hip fracture in men is associated with 32–50% mortality within one-year of fracture occurrence (30,49), as men have a greater probability of undertreatment for hip fracture in comparison to women (49).

Low BMD, bone loss and subsequent development of osteoporosis are considerable risks associated with long-term ADT, and can lead to an increased incidence of fracture (7,40,46,50-53). Fracture risk may be as high as 35% for men surviving five years or more after commencement of ADT, with men undergoing ADT at a five-fold higher risk of sustaining a fracture in comparison to hormone-naïve men with PC (51). Increasing duration of ADT has been shown to be the most significant predictor of future fracture risk (46,53). Increasing age and lower BMI are also associated with an increased risk of fracture in men on ADT (7,46,50,53).

In a population-based retrospective study, Dickman et al. (52) found an increased risk of hip fracture as early as 6 months into ADT, and this increased risk persisted for a minimum of 15 years after cessation of therapy. A recent retrospective analysis comparing fracture incidence
in 288 men on ADT with hormone-naïve men with PC was conducted. Lopez et al. (54) found a significantly higher incidence of fracture among men on ADT, and in a multivariate analysis, ADT was the only factor significantly associated with fracture risk. Similarly, current data from more than 50,000 men from the Surveillance, Epidemiology and End Results (SEER) program study (7) compared fracture risk in men on ADT and men with PC not on ADT. Shahinian et al. (7) found that men on ADT were at a higher risk of fracture after only one year of treatment, and this risk continued to increase with duration of ADT.

Although the actual incidence of ADT-induced clinical fracture is small (7,40,52,54), the risk is four- to five-fold higher for hypogonadal men in comparison to eugonadal men with PC (40,46). The true incidence of fracture may be significantly underestimated due to presence of subclinical fractures and undertreatment of fracture in men (5). A need exists for healthy, age-matched controls in these studies to compare incidence of fracture among men on ADT with eugonadal men with PC and men in the general population. Due to the retrospective nature of fracture incidence studies, fracture risk association with modifiable risk factors, such as physical activity and dietary intake in this population remain largely unknown. The potential prevention of fractures through risk modification, and the effectiveness of such modifications, are important areas for future research.

2.3.3. Diagnosis and treatment

In men with PC undergoing ADT, the majority of bone loss investigations have involved the use of medications in the treatment of diagnosed osteoporosis (10); to the present day, no studies have focused exclusively on the role of adequate nutrition for the prevention of bone loss in this population. The efficacy of bisphosphonate therapy in the management of established
osteoporosis in men is well established and has shown improvements in BMD with concurrent use of calcium and vitamin D supplements. The use of bisphosphonate therapy for the treatment of secondary osteoporosis induced by ADT is considered investigative (55). The efficacy of such treatments has been investigated in several studies (5,37,55-57).

Bisphosphonates have a strong affinity for calcium and directly inhibit the resorption of bone by osteoclasts (55). Alendronate is an orally taken bisphosphonate and in clinical investigation, treatment increases BMD among men on ADT; however, the gastrointestinal (GI) side effect profile includes GI pain, esophagitis and ulcer (10,55). When taken with LHRH agonist, intravenous (IV) administered pamidronate results in maintenance of BMD, without significant loss or gain (5). The most studied bisphosphonate is zoledronate, or zoledronic acid, which has 850 times the potency of pamidronate and is also delivered via IV (10). Among men with hormone-refractory and metastatic disease, zoledronic acid reduced skeletal-related events (SREs) (10) and prevented BMD loss in men on LHRH agonist. Side effects of both pamidronate and zoledronic acid include flu-like symptoms, injection-site reactions and occasional renal toxicity (55).

Current preventive recommendations for men on ADT include: lifestyle practice modification, including smoking cessation and moderate alcohol use; regular physical activity, particularly weight-bearing exercise; and adequate nutrition, with recommendations of 1200 – 1500 mg of calcium per day and 10 – 20 mcg of vitamin D per day (5,9,58-60). Although these recommendations are prudent and supported by research conducted among the general population, it should be noted that their efficacy has not been assessed in men with PC.

Despite significant interest in treatment of osteoporosis in men on ADT, actual physician practices with respect to prevention may not reflect current recommendations. Tanvetyanon et
(28) carried out a retrospective medical record review of 184 men on ADT for greater than one year (mean duration 32 months). Osteoporosis interventions were considered to be: (1) use of DEXA scan; (2) calcium and/or vitamin D supplement recommendation; and (3) bisphosphonate use. Only 15% of patients received one or more interventions for the prevention of osteoporosis. Calcium and vitamin D supplements and DEXA were recorded for 8.7% of participants, whereas oral bisphosphonate therapy was only prescribed in 4.9% of men. Surprisingly, cancer-related specialists, such as oncologists and urologists, were the least likely to suggest preventive measures in comparison to family and other physicians (28). In spite of a high prevalence of concurrent risk factors of osteoporosis (such as age, family history, BMI, etc.), in multiple regression analysis including risk factors and disease characteristics, only bone metastases significantly predicted use of physician-prescribed preventive strategies (28).

2.4. Risk Factors for Bone Loss and Osteoporosis

2.4.1. Non-modifiable risk factors

The clinical practice guidelines for diagnosis and management of osteoporosis in Canada (25) identify four key risk factors for fracture due to osteoporosis: increasing age, low BMD, family history of osteoporosis and previous fragility fracture. A man’s ethnicity has also been shown to influence risk of osteoporosis (32).

Age. The age-related reduction in number of the testosterone-producing Leydig cells, and subsequent reduction in circulating testosterone available for conversion to estradiol, is postulated to account for declines in bone mass experienced by men (61). Bone loss in men is estimated to begin at age 40 years, with a rate of 0.4 to 1.3% of BMD lost per year (19,27,32).

Bone Mineral Density. Low BMD has been shown to be the most important predictor of
osteoporotic fracture in men and women alike (29,32). For each standard deviation below a baseline level, whether it be peak bone mass for an individual or based on a comparison with a reference population, the risk of fracture approximately doubles (25).

**Family History.** The role of genetics in modulating bone metabolism cannot be understated; an estimated 50 – 80% of peak BMD has been shown to be due to genetic factors (25). Determining family history of osteoporosis and fracture currently involves the assessment of female first- and second-degree relative incidence. The increasing recognition and diagnosis of osteoporosis in men demonstrates a need for inclusion of male relatives’ history in risk assessment as well (25).

**Previous Fracture.** Sustaining a prior fragility fracture increases risk of second fracture in both men and women (25). Patients with vertebral or hip fracture have an increased risk of a second fracture at the same site: vertebral fracture carries a four-fold increased risk and risk of second hip fracture is 2.2 times higher than those not sustaining a fracture (25).

**Ethnicity.** Being of Caucasian or Asian ethnicity is associated with an increased risk of BMD loss (59). Those of African descent have approximately 10% higher peak bone mass in comparison with Caucasian men of a similar age, and men of Asian ethnicity have lower BMD in comparison to both groups. Despite this ethnic difference in peak bone mass, when BMI and body size are controlled for these differences are reduced. It has been suggested that intra-ethnicity differences in BMD are far greater than inter-ethnicity differences when age and body size are controlled for (32,59).
2.4.2. Lifestyle risk factors

In addition to non-modifiable risk factors, modifiable risk factors play an important role in mediating osteoporosis risk in men: BMI; physical activity level, particularly weight-bearing exercise; alcohol and tobacco use; calcium intake; and vitamin D status also contribute to osteoporosis risk (9,25,29,32,58).

**Body Mass Index.** A higher BMI is positively associated with BMD, while having a lower BMI is associated with lower BMD in men (10,11,32,34,62-64). In a recent meta-analysis of international studies, the age-adjusted risk for any type of fracture (vertebral, osteoporotic or hip) increased significantly with lower BMI (62). When compared with a BMI of 25, a BMI of 20 was associated with a nearly two-fold increase in risk for hip fracture; having a BMI of 30, however, was associated with a 17% reduction in hip fracture risk in comparison to a BMI of 25. While the increased risk of fracture with lower BMI was found to be independent of age and gender, BMD was an important determinant of BMI-modulated risk (62).

**Physical Activity.** Participating in regular physical exercise, particularly weight-baring, is positively associated with BMD in men, and may decrease the risk of falls that lead to fracture (65,66). In comparison to sedentary men, physical activity is associated with higher BMD, and greater muscle strength, coordination and balance (32,65,66).

**Alcohol and Tobacco Use.** In comparison with self-reported nonsmokers (those having never smoked), current and former smokers show decreased BMD, particularly at the distal radius and trochanter (25,30,32,63). Studies have shown a strong correlation between lower BMD and increasing duration of smoking. In a recent meta-analysis (67), a history of smoking was associated with a significantly increased risk of fracture compared with individuals with no smoking history; current smokers had a higher risk of fracture than former smokers did.
Compared with female smokers, risk ratios were significantly higher for male smokers for all types of fractures and osteoporotic fractures; no gender difference in hip fracture risk was seen (67).

While moderate alcohol is protective of BMD, excessive alcohol intakes (greater than two units per day), and prior or present alcoholism are independent risk factors for osteoporosis in men (10,30,63,68). In an analysis of three prospective cohorts investigating alcohol intake and fracture risk, Kanis et al. (68) found that alcohol intake of greater than 2 units per day was significantly associated with any fracture, osteoporotic fracture and hip fracture. Poor nutritional status due to active alcoholism, such as insufficient protein, calcium and vitamin D intakes, as well as potentially impaired liver function for hydroxylation to 25OHD, are thought to be responsible for this increased risk (69).

2.4.3. Calcium intake

Adequate calcium intake is necessary in achieving optimal peak bone mass, maintaining calcium homeostasis and minimizing bone loss. Calcium deficiency increases osteoclast activity and bone resorption, and accelerates BMD loss in the elderly (29,61).

The Dietary Reference Intakes (DRI) recommendation for calcium is in the form of an Adequate Intake (AI) (70). Men aged 50 years and older are advised to consume 1200 mg of calcium per day. The British Columbia Nutrition Survey (71) found the calcium intake of men aged 51 years and older to be well below the Adequate Intake (AI) of 1200 mg per day, with only 20% of men meeting the AI with food and supplements. The mean calcium intake from both food and supplements among these men was just 915 milligram per day (71).

Although some evidence supports an association between excessive calcium intakes
(greater than 2000 mg per day) and risk of prostate cancer, particularly advanced and metastatic
disease (72), study findings are not consistent. Despite this inconsistency, the PC population
may be predisposed to inadequate calcium intakes based on concern and confusion regarding
calcium-mediated risk of disease progression and spread. In a cross-sectional study, Smith et al.
(35) found the mean calcium intake among hormone-naïve men with PC to be just 877 mg per
day, where 88% of men had intakes below 1000 mg and 59% had intakes of less than 800 mg
per day.

There is growing clarity with respect to the dose of calcium required to reduce bone loss
and prevent fracture in older adults. In a seminal study, Dawson-Hughes et al. (73)
demonstrated significant increases in BMD and decreased fracture risk with daily
supplementation of 500 mg of calcium (with total calcium intake of approximately 1200 mg per
day) and 700 IU of vitamin D among men and women 65 years of age and older in a three-year
prospective, double-blind, randomized placebo-controlled trial. Similarly, a meta-analysis by
Tang et al. (74), which included all the randomized trials in which calcium, or calcium in
combination with vitamin D, was used to prevent fracture and osteoporotic bone loss, found
significantly reduced fracture rates (12%) at all bone sites and reduced hip and spine bone loss
with calcium and vitamin D supplementation. The treatment effect, however, was strongest for
calcium supplementation at or above 1200 mg per day with at least 800 IU vitamin D daily.
2.4.4. Vitamin D intake

The maintenance of calcium homeostasis is essential for normal functioning of the nervous system, as well as for bone growth and maintenance (70,75). Vitamin D is the chief regulator of calcium levels and maintains serum calcium through action on bone, intestinal and renal systems (75,76). When serum calcium decreases, the parathyroid glands secrete parathyroid hormone (PTH); this elevation in PTH in response to dropping serum calcium stimulates stepwise activation of vitamin D and its action on the: (1) increased intestinal absorption of calcium; (2) increased reabsorption of calcium in the kidneys; and (3) mobilization of calcium from bone via the action of osteoclast resorption (77).

In addition to low calcium intakes, research findings indicate a significant prevalence of low vitamin D intakes in the U.S. and Canada (78). Vitamin D occurs naturally in very few foods, most of which are not readily consumed in the Canadian diet such as beef liver and cod liver oil (77,78). In Canada, all fluid milk (excluding butter milk) is fortified with vitamin D, as are most margarines and soy beverages. The amount obtained through food intake, however, is not the principal source of vitamin D, as the majority is contributed by endogenous synthesis in the skin (76,79,80).

The first population-based recommendation for vitamin D was set at 10 micrograms (mcg) (400 IU), based upon the observation that one teaspoon of cod liver oil per day could prevent rickets in children; one teaspoon of cod liver oil contains the equivalent of 10 mcg of vitamin D (81). The current age-related Adequate Intakes (AI) were set at a level sufficient to maintain circulating 25-hydroxyvitamin D, the major form of vitamin D in the blood, at or above 27.5 nmol/L in the absence of sunlight for most age groups (70). The recommendation is
set as an AI because scientific evidence was not adequate to establish a Recommended Daily Allowance (RDA).

Vitamin D intakes of men in Canada from the Canadian Community Health Survey, cycle 2.2 (82) showed mean intake of vitamin D from food alone among men 51 – 70 years and 71 years and older to be 7.1 mcg and 6.3 mcg per day, respectively. British Columbia men specifically had intakes of 10.3 mcg among men 51 – 70 years and 6.8 mcg among the oldest group of men. When compared with age-specific AIs of 10 mcg per day and 15 mcg per day for men 51 – 70 years of age and 71 years and older, respectively, many men fell short of recommendations. Of those age 51 – 70 years in the nationwide sample, 20.4% of men met or exceeded the AI, while only 3.8% of men aged 71 years and older consumed 15 mcg or more of vitamin D from food. The CCHS investigated vitamin D supplement use as well, but results have not yet been released. The vitamin D intake of 34 hormone-naïve men with PC was determined by Conde et al. (34) using a food frequency questionnaire (FFQ); the mean intake of vitamin D was a mere 4.8 ± 5.7 mcg, but no information was given as to whether supplements were considered in the intake assessment.

The BC Nutrition Survey (71), however, does provide information on vitamin D-containing supplement use among British Columbian men as of 1999, when the survey was conducted. From 24-hour recall data, 17% of men aged 51-70 years and 35% of those aged 71 years and above used a vitamin D-containing supplement (median supplement dose of 10 mcg) (71). Age was a significant predictor of vitamin D supplement use, where men aged 71 years and older were more likely to use a vitamin D supplement than all other age groups of men. Although dietary vitamin D intake data was not determined, this supplement use data provides a useful indicator of vitamin D intake among older men, as food sources of vitamin D are limited.
The significant proportion of older men in British Columbia not consuming a supplement are unlikely to meet vitamin D recommendations from food alone, thereby placing themselves at high risk for vitamin D insufficiency.

Vitamin D deficiency is an established risk factor for osteoporosis, falls and fractures. The impact of vitamin D supplementation, alone or with calcium, on BMD, bone loss and fracture risk has been investigated in several studies (17,24,26,64,73,83-88,88-90,90-92), yet the associations have been most consistent when risk of fall is considered due to the proposed synergistic contribution of vitamin D supplementation to muscle strength, balance and coordination.

A meta-analysis (17) of vitamin D supplementation interventions in the elderly (mean age 60 years) found that supplemental vitamin D reduced risk of first fall by 22% in women; results were not significant in men, possibly due to lower numbers of male participants. In combination with calcium supplements (800 – 1200 mg per day), vitamin D supplements (20 mcg per day in 4 of 5 trials included in analysis) were significantly associated with reduced risk of falls.

Trivedi et al. (90) found that supplementation with 2500 mcg of vitamin D alone every four months (approximately 20 mcg per day) significantly reduced risk of fracture. In this randomized, double-blind controlled trial of men and women living in the community, after five years of supplementation, the vitamin D group had a 22% reduced risk of fracture, and a 33% reduced risk of osteoporotic fracture (90). An intention-to-treat analysis of the crude number of falls among 122 elderly women randomized to 20 mcg vitamin D and 1200 mg calcium per day, or 1200 mg calcium per day alone for eight weeks, showed a 49% reduction in risk of falling in the vitamin D supplemented group (88).
2.5. Assessment of Vitamin D Status

Cutaneous synthesis of vitamin D involves the conversion of 7-dehydrocholesterol in the skin to previtamin D₃ upon exposure to UVB radiation (wavelength 290 to 315 nm), which causes photolysis and cleavage of the steroid B-ring structure. Subsequent thermal conversion of previtamin D₃ yields the prohormone vitamin D₃ (cholecalciferol) (76). At this point, vitamin D₃ enters the circulation, either directly from capillary drainage of the skin if synthesized endogenously or via chylomicrons in the lymphatic system if obtained from the diet. Once in the circulation, vitamin D₃ is transported in the plasma in an associated complex with vitamin D-binding protein (VDBP) (75).

Vitamin D₃ is not physiologically active and must be enzymatically activated by two successive hydroxylation reactions, the first of which occurs in the liver. Vitamin D₃-25-hydroxylase action in the liver produces 25OHD, the major circulating form of vitamin D₃. 25OHD is then transported to the kidney where the 1α position is hydroxylated by the mitochondrial cytochrome P450 oxidase enzyme 25OHD-1α-hydroxylase to produce the active metabolite calcitriol, 1α,25-dihydroxyvitamin D₃ (1,25(OH)₂D) (75). While the kidney is the primary site of 1,25(OH)₂D production, 1αOHase is also expressed in extra-renal tissues such as breast, intestine and prostate, allowing for local production of 1,25(OH)₂D from circulating 25OHD (75,80,93). Although 1,25(OH)₂D is the active form of vitamin D in the body, plasma levels are tightly regulated and values outside of the defined normal range (40 – 190 pmol/L) exist only with severe deficiency (75). Circulating levels of 25OHD are approximately 100 times higher, and are readily affected by external factors such as nutrition and sun exposure (75). Vitamin D deficiency is characterized by serum 25OHD of < 25 nmol/L, and vitamin D insufficiency (based upon laboratory-provided references ranges) is currently set at values...
between 25 to 50 nmol/L. Severe deficiency, as seen in frank osteomalacia, is defined as
25OHD less than 12.5 nmol/L (94).

2.5.1. Defining optimal levels of vitamin D

In the past, optimal 25OHD status was considered that of a normal reference population,
determined by measuring the circulating 25OHD in disease-free, asymptomatic men and women
(77). Due to differences in sun exposure, cutaneous synthesis capacity and other influencing
factors, the use of a sweeping reference population defined as "normal" is out-of-date.
Currently, experts agree that optimal vitamin D status and the definition of inadequacy should
be based upon functional endpoints, including serum PTH levels, calcium absorption and BMD
(77,94-96).

PTH Levels. Secondary hyperparathyroidism, increased levels of PTH caused by
chronically low serum calcium, is considered to be a biochemical hallmark of poor vitamin D
status, as a significant inverse relationship exists between circulating PTH and 25OHD (77).
The suppression of PTH levels, as a functional endpoint, is suggested to require circulating
25OHD between 40 and 80 nmol/L (96). This inverse PTH-25OHD relationship is even more
pronounced in the elderly. In a recent meta-analysis on the effect of age and immobility on PTH
response to vitamin D supplementation, Bjorkman et al. (97) found that PTH levels in the
elderly decreased less with vitamin D supplementation in comparison with younger subjects,
despite larger increases in 25OHD levels.

An inverse relationship was found between PTH and 25OHD level, where a step-like
increase in PTH was observed for 25OHD values below 40 nmol/L; suggesting a PTH
suppression level of at least 40 nmol/L for 25OHD (98). In a similar group of postmenopausal
women (mean age 63 ± 9.5 years), Jesudason et al. (83) determined the PTH suppression cutoff to occur at 25OHD of greater than 50 nmol/L; however, the most significant change in bone resorption markers occurred at 60 nmol/L. A mathematical model proposed by Vieth et al. (95) suggests that 25OHD levels of at least 80 nmol/L are required for the maximal suppression of PTH. A recent editorial by leading investigators in the field (99) suggests that optimal PTH suppression occurs at 25OHD levels of 75 to 80 nmol/L, when assay-related variability is controlled for.

**Calcium Absorption.** The use of calcium absorption as a functional endpoint has shown that as 25OHD drops below 80 nmol/L intestinal absorption of calcium is impaired in adults. In comparison to 25OHD level of 50 nmol/L, calcium absorption is 65% greater at 86.5 nmol/L (96,100). This impaired absorption results in lower serum calcium, elevated PTH and increased resorption of bone, causing loss of BMD (77).

**Bone Mineral Density.** Bischoff-Ferrari et al. (100) found a positive association between circulating levels of 25OHD of 90 – 100 nmol/L and total hip BMD based on NHANES III data; this positive association was independent of exercise. Reduced levels of circulating 25OHD are associated with increased bone turnover due to bone resorption, resulting in subsequent loss of BMD (101). Using BMD as a functional endpoint for 25OHD status, Vieth et al. (95) determined that circulating levels of 25OHD of at least 80 nmol/L were necessary to maximize BMD.
2.5.2. Risk factors for vitamin D insufficiency and deficiency

*Age.* The efficiency of subcutaneous synthesis of vitamin D declines with age due to changes in the skin and reduced amounts of vitamin D-precursors (102). The vitamin D status of the elderly may be further compromised due to reduced sun exposure and institutionalization (103) and has been demonstrated irrespective of latitude (104). Thus, serum 25OHD tends to better reflect stable lifestyle factors, including calcium and vitamin D nutrition in the elderly, as the contribution of endogenous synthesis to circulating vitamin D is reduced. Declining renal conversion of 25OHD to 1,25(OH)₂D may also account for poorer vitamin D status among the elderly (95).

*Ethnicity.* Those with dark skin, such as African descent, have a reduced capacity for endogenous synthesis of vitamin D due to greater skin pigmentation (75). Melanin, the predominant colour pigment in skin has been shown to block the UVB-induced production of vitamin D (75,102).

*Body Mass Index.* Obesity and greater total body fat has been shown to negatively impact vitamin D status (103,105,106). As vitamin D is stored in adipose tissue, it is proposed that despite a larger body pool of vitamin D, obese men and women may have slower mobilization of body stores, accounting for poorer vitamin D status (103). In a sample of 453 men and women older than 65 years of age from the Longitudinal Aging Study Amsterdam, Snijder et al. (106) measured serum 25OHD and PTH levels and determined BMI, waist circumference, waist to hip ratio, and total body fat percentage with DEXA. Higher BMI, waist circumference and skin fold sum was significantly associated with lower 25OHD and high PTH (p < 0.05) (106). Total body fat, however, showed the strongest association (p < 0.001) and
remained significant for 25OHD when PTH was controlled for. These studies demonstrate the importance of considering adiposity when measuring 25OHD.

*Disease States.* Several disease states are known to affect vitamin D status. Fat malabsorptive syndromes, inflammatory bowel diseases, chronic steatorrhea and liver disease (biliary or portal cirrhosis) negatively impact vitamin D status due to impaired intestinal absorption of dietary vitamin D. Renal impairment, parathyroid and thyroid disorders may also affect 25OHD status (75).

*Seasonality.* Seasonal variation in circulating 25OHD has been well-established in all age groups. The seasonal changes in 25OHD are associated with changes in both quality and quantity of sunlight exposure throughout the year, with lowest 25OHD found in the fall/winter months (24,103,107-109). In those living at higher latitudes, quality and quantity of UVB radiation in the winter may not be sufficient to stimulate the cutaneous synthesis of vitamin D. Webb *et al.* (109) have shown that primary residence at 53°N latitude is inadequate to generate sunlight-induced vitamin D production in the skin from October through March. In a year-long study of 188 healthy Canadian men and women, Rucker *et al.* (103) found the lowest levels of 25OHD occurring in the fall (November-December), where mean 25OHD was 52.9 nmol/L (SD, 17.2).

This seasonal inadequacy of sunlight exposure may put a significant number of Canadians at risk for vitamin D insufficiency. In a cross-sectional study of 155 institutionalized elderly subjects in Toronto, Liu *et al.* (110) found mean 25OHD to be significantly lower at the end of March (39.9 ± 19.7 nmol/L) in comparison to the zenith value in late summer (44.9 ± 16.9 nmol/L). Interestingly, the zenith value of late summer falls within the commonly used vitamin D insufficiency range (25 to 50 nmol/L). The institutionalized population in this study
further demonstrates the necessity of adequate dietary intake when sun exposure is limited, as the mean vitamin D intake based on three-day food record was a mere 4.9 ± 2.6 mcg.

*Inadequate Intake.* Estimates of optimal vitamin D status related to the functional endpoints of PTH suppression, maximal calcium absorption and maintenance of bone mass, suggest an optimal range of 75 to 80 nmol/L. To prevent vitamin D insufficiency (current definition at 50 nmol/L), an estimated intake of 15 mcg vitamin D is required in the absence of adequate endogenous synthesis, such as in the elderly or based upon season (75). To maintain an average 25OHD level of 75 nmol/L, characterized as optimal by several experts in the field (96), 20 to 25 mcg of vitamin D would be required; demonstrating the inadequacy of current vitamin D intake recommendations for many adults.

2.5.3. Prevalence of vitamin D insufficiency and deficiency

A high prevalence of vitamin D insufficiency, defined as 25OHD values of 25 to 50 nmol/L, has been reported in all age and gender groups, with particular emphasis on postmenopausal women (24,64,78,83,95,110-112). In a Swedish cross-sectional study of 104 community-dwelling elderly subjects, Melin et al. (64) found 4% of subjects to be vitamin D insufficient at a 25OHD level of < 40 nmol/L yet when 75 nmol/L was considered the cutoff for insufficiency, the prevalence of vitamin D insufficiency rose to 75%. The vitamin D status of 161 postmenopausal women referred to an osteoporosis clinic was assessed in a cross-sectional study (111). Vitamin D deficiency in this group (25OHD < 25 nmol/L) was highly prevalent, where 39.1% of women were considered deficient. In a cross-sectional study of 1741 men and women aged 19 to 47 years, Vieth *et al.* (95) found 25% of all adults not taking vitamin D supplements were vitamin D insufficient, based on 25OHD levels of < 40 nmol/L.
corrected for vitamin D intake, the prevalence of deficiency was similar for all age groups.

Recent findings from the Canadian Health Measures Survey (113) found a mean 25OHD among men and women aged 6 – 79 years of 66.9 nmol/L, with approximately 5% and 25% of the study population’s 25OHD levels as a whole falling within the accepted ranges for deficiency and insufficiency with serum levels of less than 25 nmol/L and 50 nmol/L, respectively. Specifically among older men, mean 25OHD levels were sufficient at 65.5 nmol/L and 72.4 nmol/L for men aged 51 – 70 and 71 and older, respectively. Interestingly, serum levels at each percentile tended to be higher amongst the youngest (6 – 11 years) and oldest groups (60 – 79 years) of men. These findings, while seemingly contrary to those previously reported in the literature may reflect increased supplement use with the advent of endorsement from national agencies (114).

2.6. Vitamin D and Prostate Cancer

Epidemiological data demonstrate an age, ethnic and geographic distribution pattern of prostate cancer incidence and death; this distribution pattern is proposed to be related to vitamin D status (79,80,93), though laboratory findings investigating 25OHD and PC risk have been inconsistent. Increasing age is the strongest risk factor for prostate cancer, where approximately 70% of all prostate cancers are diagnosed among men aged 65 years and older (80). This increased risk coincides with an age-related decline in endogenous vitamin D production. African American men have a nearly 60% higher age-adjusted incidence of prostate cancer in comparison to white men, and the age-adjusted mortality rate is more than twice as high in African American males (93). Impaired vitamin D synthesis due to melanin in the skin is proposed to explain this link between ethnicity and increased prostate cancer risk (79).
Prostate cancer is significantly more common at northern latitudes, such as North America and Europe, in comparison to more southern regions, like Asia and South America (79,80). In 1990, based on observations of an inverse relationship between prostate cancer mortality rates and sunlight exposure in the US, Schwartz and Hulka (115) put forth the hypothesis that vitamin D deficiency increases risk of prostate cancer.

In a nested case-control study, Ahonen et al. (116) assessed 25OHD in 149 PC patients and 596 healthy men. When 40 nmol/L was used as a cutoff point, men with 25OHD below 40 nmol/L had a 70% increased probability of PC. In men 52 years of age and younger, the increase in probability of PC diagnosis rose to 250% when 25OHD was below 40 nmol/L. Additional case-control studies have examined this proposed association between vitamin D and prostate cancer risk by measuring serum 25OHD and/or 1,25(OH)2D, yet the results have not consistently shown a significant association (93).

2.6.1. Prevalence of vitamin D deficiency among men with prostate cancer

In studies where the 25OHD status of hormone-naïve men with PC has been assessed, the prevalence of insufficiency or deficiency is rarely reported, despite the fact that mean 25OHD has been shown at approximately 40 nmol/L or below (35,41,42,47). Mittan et al. (42) assessed 25OHD as a baseline measure among 15 men with PC who had yet to start ADT. Although the mean 25OHD level of the men fell within the definition of insufficiency (40 ± 16.7 nmol/L), there was no mention of the prevalence of insufficiency. Similarly, Preston et al. (41) measured 25OHD as a baseline measure among 39 control men (BPH, ED or PC diagnosis) and found mean 25OHD to be 40.7 ± 13.5 nmol/L; again, prevalence of insufficiency was not discussed. In a study of 41 hormone-naïve men, however, Smith et al. (35) reported a mean
25OHD level of 36.7 ± 13.3 nmol/L, where seven of the 41 men (17%) were considered to be vitamin D deficient (25OHD < 25 nmol/L); however, prevalence of insufficiency at additional endpoints was not discussed.

2.6.2. Impact of ADT on vitamin D status

Several studies have investigated the effect of ADT on bone metabolism and BMD (36,37,40-44,47) yet only three studies have assessed 25OHD status among men undergoing ADT for the treatment of PC (40,41,47). To date, no studies have compared vitamin D intake and status of men with PC treated with ADT, hormone-naive men with PC and age-matched healthy controls. Preston et al. (41) assessed baseline 25OHD in 39 men with PC on ADT for longer than six months; mean 25OHD was 44 ± 16.8 nmol/L, yet prevalence of insufficiency was not indicated. Interestingly, after baseline assessment four of the participants were excluded due to ‘low’ vitamin D levels, although the cutoff for ‘low’ 25OHD was not identified. Similarly, Stoch et al. (47) assessed 25OHD in a cross-sectional study of 19 men on ADT (for longer than six months) and 41 eugonadal men with PC; BMD only was assessed in 197 healthy age-related controls. Mean 25OHD was 38.2 ± 9.7 nmol/L and 33.7 ± 11.6 nmol/L for men on ADT and eugonadal men, respectively; the difference was not statistically significant. Stoch et al. (47) did not provide an estimate of vitamin D deficiency prevalence in the population.

In a retrospective analysis of 87 Australian men with PC treated with ADT referred for evaluation of osteoporosis, Diamond et al. (40) assessed the risk factors for osteoporosis and spinal fracture. Thirty-eight (44%) men had radiographic evidence of spinal fracture. Of those with and without spinal fractures, mean 25OHD was 57.6 ± 3.3 nmol/L and 73.8 ± 3.9 nmol/L, respectively. Thirty four percent of men with spinal fractures were vitamin D deficient (< 50
nmol/L) compared with 16% deficiency prevalence among men without fracture. Longer duration of ADT was significantly associated with lower serum 25OHD, and vitamin D deficiency was significantly associated with fracture risk ($P < 0.003$). In regression analysis, only duration of ADT was a stronger predictor of fracture than 25OHD status.

These results, taken with laboratory and animal studies, suggest an estrogenic regulatory role in vitamin D metabolism, potentially optimizing concentrations of 25OHD and 1,25(OH)$_2$D. Although the precise mechanism of action has yet to be elucidated, the effect of ADT on testosterone levels, and subsequent reduction in circulating estrogen, may help to explain the negative consequences of ADT on vitamin D status in men with prostate cancer.

2.7. Summary

Based on current literature and expert opinion, a higher 25OHD than is currently noted in laboratory reference values and clinical practice may be indicative of vitamin D insufficiency. Although data are not entirely consistent, some emerging research suggests that a 25OHD level within what is currently defined as sufficient may provide inadequate protection against bone loss and potentially predispose an individual to risk of falling and increased fracture incidence. The effect of vitamin D status on fracture risk among men on ADT for the treatment of PC has been estimated in one study alone [54]. These results demonstrate the significant contribution of hypovitaminosis D to fracture risk, the primary endpoint of osteoporosis, in men on ADT. The increased risk of hip fracture in men, and subsequent morbidity and mortality due to undertreatment, further underscore the importance of assessing vitamin D status and identifying men at high-risk for fracture.

To date no studies have investigated the hypovitaminosis D prevalence of men on ADT
as a primary outcome; rather 25OHD has been included secondary to BMD in the majority of cross-sectional and longitudinal studies. As a result, the potential contribution of factors such as BMI, calcium and vitamin D intake, alcohol use and tobacco use on vitamin D status has been largely ignored. In addition, the ‘true’ prevalence of vitamin D insufficiency in men with PC on ADT compared with eugonadal men is unknown, as prevalence of men deemed insufficient/deficient is rarely reported. The inclusion of various cutoff values denoting inadequacy base on recent evidence and opinion regarding optimal vitamin D status, has not previously been conducted.

While vitamin D can be synthesized endogenously, the age-related decline in endogenous vitamin D production and impaired synthesis at northern latitudes place this group of men at increased risk for insufficient vitamin D production, further augmenting the importance of obtaining adequate dietary intakes to prevent vitamin deficiency. Current vitamin D recommendations for men undergoing ADT are placed at 20 µg vitamin D per day, yet vitamin D intake among North American men is far below recommendations.

Although the majority of research in hypovitaminosis D has been conducted in postmenopausal women, the hypogonadal state of men on ADT for the treatment of PC suggests a closer relationship of findings than between men in the general population. Recent evidence of a high prevalence of hypovitaminosis D in hormone-naïve men indicates a pre-existing impaired status due to prostate cancer, in keeping with epidemiological inverse associations between vitamin D status and prostate cancer risk. To date, no studies have compared vitamin D intake and status of men with PC treated with ADT, hormone-naïve men with PC and healthy controls.

The literature regarding the deleterious effects of ADT on bone status among men undergoing ADT focuses primarily on treatment of diagnosed osteoporosis and possible
prevention through use of bisphosphonates. There are no studies looking exclusively at the role of nutrition in the maintenance of bone mass and prevention of osteoporosis among men undergoing ADT. It is hoped that the results of the proposed study will demonstrate the need for provision of nutrition information to these men at time of therapy commencement and on an ongoing basis throughout treatment, as a means of preventing or reducing the negative effects of ADT on nutritional status and quality of life.

2.8. Statement of the Problem

Based on the present state of knowledge of this issue and identified gaps in the literature, the following hypotheses were generated:

1. The calcium and vitamin D intakes (from diet and supplements) of men undergoing androgen deprivation therapy for the treatment of non-metastatic prostate cancer will not differ from those of hormone-naïve men with prostate cancer and healthy controls, despite increased recommendations.

2. 25-hydroxyvitamin D levels (as an indicator of vitamin D status) of men undergoing androgen deprivation therapy for the treatment of non-metastatic prostate cancer will be lower than those of hormone-naïve men with prostate cancer and healthy controls.
CHAPTER 3: METHODOLOGY

3.1 Overview of Design

This is a cross-sectional descriptive study comparing the dietary intakes and vitamin D status of men undergoing ADT for the treatment of prostate cancer, hormone-naïve men with prostate cancer and healthy men without prostate cancer. Intended outcome measures were nutrient intake data (specifically calcium and vitamin D) and biochemical indices (serum testosterone, 25OHD, PTH and vitamin D binding protein (VDBP)). Anthropometric measures (height, weight, BMI) were also collected.

3.2 Setting

Men undergoing ADT for treatment of prostate cancer and hormone-naïve men with prostate cancer were recruited from the Vancouver Prostate Centre Clinic. The Vancouver Prostate Centre is a major referral centre for men with prostate cancer; about 1000 new patients are seen each year. Healthy men without prostate cancer were recruited from the Lower Mainland.

3.3 Sample Size

The original primary outcome variable for this study was vitamin D status, as represented by 25OHD level. Sample size determination was based upon a comparison of 25OHD levels in men on ADT for the treatment of PC and healthy controls without PC. Rucker et al. (103) found a nadir mean 25OHD of 52.9 ± 17.2 nmol/L among 188 Canadian men and women in a one-year study. Although no gender-specific mean was provided, this value was identified as the expected mean of healthy male controls due to similar latitude and seasonality.
effects on vitamin D status, as well as a similar mean age of study participants. The expected mean 25OHD for men on ADT with PC was based upon data provided by Stoch et al. (47). Among 19 men on ADT for six months or longer, mean 25OHD was 38.18 ± 9.68 nmol/L.

Based on these values, the effect size (d) was determined to be 1.05 (Appendix A) (117). In an unpaired t-test of a directional hypothesis, where α = 0.05, a sample size of 11.13 participants would be required in each group (n) to achieve 80% power. If a non-directional hypothesis is considered, where α = 0.05, a sample size of 14.13 would be required in each group (n) to achieve 80% power.

A secondary calculation for sample size required for an ANOVA comparing 25OHD among men undergoing ADT for the treatment of PC, hormone-naïve men with PC and healthy controls without PC yielded an effect size (f) of 0.65 (Appendix A). With an effect size of f = 0.65 and two degrees of freedom (df = 2), nine men (8.6) would be required in each of the three groups (n) to achieve power of 80%. A total sample of N = 27 would be necessary.

Although the primary objectives of this study were descriptive in nature, based on sample size calculations a total sample of 45 men (n = 15) was deemed appropriate to assess potential differences in vitamin D status (25OHD) among the three groups, with a conservative goal of 20 men per group for flexibility.

3.4. Recruitment and Participant Selection

Participants for the study were recruited from the Prostate Clinic and Lower Mainland between November 2006 and May 2007. This recruitment period was selected as 25OHD status is greatly affected by seasonal sun exposure (103), and during this time of sun inadequacy in Vancouver, a more accurate reflection of vitamin D status due to dietary intake would be
obtained. The study was approved by the University of British Columbia (Appendix B) and Vancouver Coastal Health (Appendix C) Ethics Committees. Participants were informed that they could withdraw from the study at any time and that withdrawal would not impact on their future medical care. Written, informed and voluntary consent to participate was obtained from men including consent to access medical chart information (Appendix D).

Patient charts were screened for eligibility by the writer in advance of clinic appointment. The study group included men currently undergoing treatment with ADT (Group A). Group B comprised hormone-naïve men with PC previously treated with definitive therapy (surgery or radiation) or those monitoring localized disease with active surveillance (three months or more post-diagnosis). Group C comprised healthy older men without prostate cancer. Men in this control group were recruited in two ways: 1). peer recruitment and 2). community recruitment. In an effort to maximize group homogeneity with respect to education and socioeconomic status, Group A and B participants were asked to provide the letter of invitation (Appendix E) to men within their social network who fulfilled eligibility criteria for Group C (peer recruitment). For community recruitment, a letter of invitation was posted at community centres in the surrounding area as well as circulated via email throughout Vancouver Coastal Health inviting men who met inclusion criteria and were interested in participating to contact the investigator by phone. Eligibility was based on Group C participant report and confirmed over the telephone and again at the interview.

Additional inclusion criteria for participants in Groups A and B included: biopsy-confirmed prostate cancer without evidence of bone metastases and no history of prior or present treatment with bisphosphonates. Inclusion criteria for all three groups included: ability to read and speak English; and no evidence of mental disease as identified by the attending
urologist or study investigator.

Exclusion criteria were as follows: having a pre-existing condition that may affect calcium, vitamin D or bone metabolism; prior or present renal failure; active alcoholism; liver disease; and hyperthyroidism, hyperparathyroidism or hypoparathyroidism.

3.5 Outcome Measures

3.5.1. Dietary intake

The investigator orally administered a food frequency questionnaire (FFQ) to determine each individual’s usual dietary intake by asking participants to report frequency of consumption of a list of foods over the past 12 months (Appendix G). The FFQ used in the study was the Diet History Questionnaire (DHQ) as developed by the National Institute of Health (118). This questionnaire was developed by the National Cancer Institute (NCI) and is currently in use in several epidemiological studies being conducted by the NCI. The DHQ and the DHQ nutrient database were modified for use in Canada through the collaborative efforts of The NCI Risk Factor Monitoring and Methods Branch and The Division of Population Health and Information at the Alberta Cancer Board (119). While the modifications were primarily carried out in order to develop a nutrient database that reflected Canadian nutrient fortification practices, a few questionnaire changes were also made to the DHQ (119,120).

3.5.2. Biochemical indices

Serum samples were collected on the same day as anthropometric data, personal characteristics and dietary intake information. All biochemical indices were measured in the laboratory of Dr. Emma Guns at the Vancouver Prostate Centre using standardized procedures.
Vitamin D status assessment was achieved by obtaining a serum sample from each participant and measuring 25OHD levels. 25OHD was assessed by liquid chromatography-tandem mass spectroscopy. Serum samples were diluted by a factor of 0.75 in processing. The calculated intra- and inter-assay coefficients of variation (CVs) were less than 10%, with a detection limit of 1.25 nmol/L. Normal reference range for 25OHD includes serum levels between 25 and 135 nmol/L (121).

Serum intact-parathyroid hormone (PTH) was measured with enzyme-linked immunosorbent assay kits from ALPCO Diagnostics (Windham, NH). The reference intra- and inter-assay CVs are 1.8% to 3.2% and 7% to 7.7%, respectively. The expected reference range for this assay is 0.9 – 7.16 pmol/L with a detection limit of 0.01 pmol/L. A serum level of greater than 6.4 pmol/L is considered diagnostic for hyperparathyroidism (121).

Total testosterone was measured to establish hypogonadism (< 10 nmol/L). All samples for men in Group A were collected before 11 am to account for the diurnal fluctuation of testosterone (122). Total testosterone was assessed by liquid chromatography-tandem mass spectroscopy. The serum samples were concentrated by a factor of two or four depending on volume available. The calculated intra- and inter-assay CVs were less than 5%, with a detection limit of 0.001 nmol/L. The normal laboratory reference range for testosterone includes serum levels between 10 – 30 nmol/L (121).

Vitamin D Binding Protein (VDBP) was measured with enzyme immunoassay kits from American Laboratory Products Company (Windham, NH). The reference intra- and inter-assay CVs are 3.2% to 5% and 12.7%, respectively. The expected reference range for this assay is 20 – 55 mg/dL, with a detection limit of 1.23 ng/mL.
3.6. Ancillary Information

3.6.1. Personal characteristics

Information on education level, ethnicity, tobacco use and holiday travel was obtained with the Sociodemographic Questionnaire (SDQ) found in Appendix F. Education level was divided into five strata: less than high school; high school; trade/community college certificate; undergraduate college/university; and postgraduate education. History of tobacco use was obtained from each participant, as per Daniell et al. (43) and divided into four strata: never smoked, former smoker (quit > 10 years), recent smoker (quit < 10 years) and current smoker; information on alcohol use was obtained from the DHQ (118). Due to inadequate sunlight penetration and strength for endogenous synthesis in Vancouver during the study time frame, total sunlight exposure was not determined; however, an estimation of sunlight exposure due to travel below 40 °N, as per Rucker et al. (103), was determined for each participant.

3.6.2. Clinical characteristics

Information on medical history, time since diagnosis, type (LHRH agonist/GnRH antagonist or Combined Androgen Blockade – addition of antiandrogen) and duration of hormone treatment, prior neoadjuvant hormone therapy and indication for hormone therapy was obtained from Group A and B participant charts. Pertinent medical history (exclusion criteria) was assessed for Group C participants at time of eligibility telephone call and again at time of interview.
3.6.3. Anthropometrics

Heights were measured to the nearest 0.01 centimetre at the time of interview, using a tape measure and rafter square. Measurement was taken against a wall with the participant at full inspiration, standing erect, looking straight ahead, knees straight, arms at sides and feet flat with no shoes. The rafter square was placed against the wall and lowered until it was firmly touching the crown of the participant’s head. Body weight was measured to the nearest 0.01 kilogram at time of interview in light indoor clothing and no shoes using a calibrated floor standing scale. Three measurements were taken for height and weight, with the average measurement recorded. BMI was calculated using the following formula: Weight (kg) / [Height (m)]².

3.7. Data Analyses.

With the exception of food intake and lab data, all data analyses were performed by the investigator.

3.7.1. Food intake data

The completed DHQ booklets were scanned, coded and keyed by staff at The Tomorrow Project of the Alberta Cancer Board. The DHQ forms were scanned and verified using the TELEform system and the resultant data transferred into DietCalc, which is an NCI software system modified for use with the Canadian population. The data files and transformed raw data were provided to the investigator in Excel and SPSS format. The investigator completed all subsequent analyses.
3.7.2. Statistical analysis

Statistical analyses were performed using SPSS Statistics GradPack 17.0 for Macintosh (SPSS Inc., Chicago, IL 2008). Data were entered and checked for accuracy. Any errors were corrected before statistical analyses were completed. Directional hypotheses were tested on a one-tailed basis, and general hypotheses were tested on a two-tailed basis. A 0.05 critical value of alpha was used to determine statistical significance. The following analyses were performed:

- Summary statistics for each group were calculated to obtain frequency distributions of demographic, personal and clinical characteristic variables, dietary intakes and biochemical indices.

- The analysis of variance (ANOVA) was calculated to determine differences in dietary intakes and biochemical indices between those undergoing ADT (Group A), hormone-naïve men (Group B) and control participants (Group C). Tukey’s HSD method was used post-hoc to determine the significance of pair-wise comparisons. Where data were not normally distributed, Kruskal Wallis was used.

- Chi-square and Kruskal tau tests were used to determine differences among nominal and ordinal variables.

- The independent samples t-test was done to compare the dietary intakes of men identifying as having a passive vs. active role in food preparation.

- The Pearson product-moment correlation coefficient was used to examine the relationships among the anthropometric, clinical characteristic and dietary variables. The relationship between supplemental calcium and vitamin D and dietary variables was also examined using the Pearson correlation coefficient.
3.8. Miscellaneous

Following diet information collection, participants received an information package; packages differed based on group. The Group A packages contained: the “Hormone Therapy and Bone Health” handout (Appendix H), detailing bone loss prevention strategies specific to ADT; BC Dairy Foundations Calcium Calculator© and osteoporosis prevention brochure; and a series of prostate cancer-specific nutrition handouts developed by the writer. The Group B packages contained: BC Dairy Foundations Calcium Calculator© and osteoporosis prevention brochure; and the series prostate cancer-specific nutrition handouts. The Group C packages were identical to the Group B package save for the addition of the Canadian Prostate Health Council (CPHC) brochure “Prostate Cancer Prevention.”
CHAPTER 4: RESULTS

4.1. Recruitment

Between November 2006 through May 2007, 87 men attending the Vancouver Prostate Centre clinic were deemed to meet eligibility criteria for Groups A and B and were invited to participate in the study. Of those invited, 33 men (38% of those invited to participate) consented to participation (12 men in Group A, 21 men in Group B). Among control group participants (Group C), six were recruited via peer recruitment. The community-circulated letter of invitation for additional Group C participants resulted in 45 men expressing interest in participation; of those who contacted the investigator, 14 men were deemed eligible and consented to participate. Complete anthropometric and laboratory data were obtained from 53 participants; all participants completed the questionnaires.

4.2. Participant Characteristics

Age, weight and BMI of participants are shown in Table 4.1. Average age of participants was 64.3 ± 6.0 years, with Group C significantly younger than those undergoing ADT and hormone-naïve prostate patients based on post-hoc analysis. Mean BMI did not differ by group and the majority of study participants were classified as “overweight” (n = 27) or “obese” (n = 14) based on a BMI of 25 – 29.9 and 30 or greater, respectively (data not shown).

Likewise, there were no differences in demographics or personal characteristics among the groups (Table 4.2). As a whole, participants were well-educated, Caucasian and non-smokers. The majority of men (67.9%) reported a passive role in meal preparation in their household; no information on marital status was collected. Sun exposure was classified as
"regular" or 'often’ by about one-third of participants, and 40% reported travel within the preceding three months.

Table 4.1. Age, weight and body mass index (BMI) of men with prostate cancer and healthy controls.

<table>
<thead>
<tr>
<th>Variable</th>
<th>mean ± SD</th>
<th>F</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All (N=53)</td>
<td>Group A¹ (n=12)</td>
<td>Group B² (n=21)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>64.3 ± 6.0</td>
<td>67.9 ± 6.3a</td>
<td>66.2 ± 5.1a</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>87.1 ± 13.5</td>
<td>90.1 ± 11.5</td>
<td>82.4 ± 14.8</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>27.0 ± 3.9</td>
<td>27.4 ± 2.5</td>
<td>26.0 ± 3.7</td>
</tr>
</tbody>
</table>

¹ Men with prostate cancer treated with androgen deprivation therapy
² Hormone-naïve men with prostate cancer
³ Healthy men without prostate cancer

a,b Means in the same row with different superscripts differ significantly, p < .05

Clinical characteristics and treatment history are shown in Tables 4.3 and 4.4, respectively. There were significant differences in PSA at diagnosis and most recent PSA between those undergoing ADT and hormone-naïve men with PC, with men in Group A having significantly higher PSA at both time points. Men in Group A also had more well-differentiated tumours at diagnosis, as shown by Gleason score, though no significant difference in clinical stage was seen. No clinical stage was available for one participant in Group B as the sample was obtained by transurethral prostate resection. The majority of men (81.8%) were more than one year post-diagnosis with a range of 2 – 124 months since PC diagnosis (data not shown). More men in Group B had undergone definitive, local therapy, predominantly radical prostatectomy, when compared with men in Group A.
Table 4.2. Sociodemographic and personal characteristics of men with prostate cancer and healthy controls.

<table>
<thead>
<tr>
<th></th>
<th>All (N=53)</th>
<th>Group A¹ (n=12)</th>
<th>Group B² (n=21)</th>
<th>Group C³ (n=20)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Education</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; High school</td>
<td>1 (1.9%)</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>High school</td>
<td>7 (13.2%)</td>
<td>0</td>
<td>3</td>
<td>4</td>
<td>.085</td>
</tr>
<tr>
<td>College</td>
<td>7 (13.2%)</td>
<td>0</td>
<td>2</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>University</td>
<td>27 (50.9%)</td>
<td>9</td>
<td>8</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>Graduate</td>
<td>11 (20.8%)</td>
<td>3</td>
<td>7</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Caucasian Ethnicity</td>
<td>51 (96.2%)</td>
<td>11</td>
<td>21</td>
<td>19</td>
<td>.275</td>
</tr>
<tr>
<td>Tobacco Use</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>27 (50.9%)</td>
<td>5</td>
<td>12</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>Former</td>
<td>20 (37.7%)</td>
<td>6</td>
<td>8</td>
<td>6</td>
<td>.200</td>
</tr>
<tr>
<td>Recent</td>
<td>5 (9.4%)</td>
<td>0</td>
<td>1</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Current</td>
<td>1 (1.9%)</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Food Preparation</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Self</td>
<td>13 (24.5%)</td>
<td>2</td>
<td>6</td>
<td>5</td>
<td>.704</td>
</tr>
<tr>
<td>Someone else</td>
<td>36 (67.9%)</td>
<td>10</td>
<td>13</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>Shared</td>
<td>4 (7.5%)</td>
<td>0</td>
<td>2</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Sun Exposure</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>7 (13.2%)</td>
<td>1</td>
<td>3</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Seldom</td>
<td>28 (52.8%)</td>
<td>7</td>
<td>13</td>
<td>8</td>
<td>.738</td>
</tr>
<tr>
<td>Regularly</td>
<td>11 (20.8%)</td>
<td>2</td>
<td>4</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Often</td>
<td>7 (13.2%)</td>
<td>2</td>
<td>1</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Recent Travel</td>
<td>21 (39.6%)</td>
<td>4</td>
<td>8</td>
<td>9</td>
<td>.794</td>
</tr>
</tbody>
</table>

¹. Men with prostate cancer treated with androgen deprivation therapy
². Hormone-naïve men with prostate cancer
³. Healthy men without prostate cancer

Table 4.3. Clinical characteristics of men with prostate cancer.

<table>
<thead>
<tr>
<th></th>
<th>mean ± SD</th>
<th>All (N = 33)</th>
<th>Group A¹ (n = 12)</th>
<th>Group B² (n = 21)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time since diagnosis</td>
<td>40.5 ± 35.8</td>
<td>44.9 ± 42.5</td>
<td>38.0 ± 32.3</td>
<td>.599</td>
<td></td>
</tr>
<tr>
<td>PSA³ at diagnosis</td>
<td>12.8 ± 25.6</td>
<td>22.8 ± 40.5</td>
<td>6.7 ± 4.2</td>
<td>.003*</td>
<td></td>
</tr>
<tr>
<td>Time since local therapy</td>
<td>40.3 ± 33.8</td>
<td>49.0 ± 20.3</td>
<td>36.6 ± 31.2</td>
<td>.394</td>
<td></td>
</tr>
<tr>
<td>Most recent PSA</td>
<td>1.5 ± 3.7</td>
<td>2.7 ± 5.2</td>
<td>0.8 ± 2.3</td>
<td>.006*</td>
<td></td>
</tr>
</tbody>
</table>

¹. Men with prostate cancer treated with androgen deprivation therapy
². Hormone-naïve men with prostate cancer
³. Prostate specific antigen
* significant at p < .05
† Group B n = 20
‡ Group A n = 8, Group B n = 19.
Table 4.4. Gleason score, clinical stage and treatment history of men with prostate cancer.

<table>
<thead>
<tr>
<th>Variable</th>
<th>All (N = 33)</th>
<th>Group A (n = 12)</th>
<th>Group B (n = 21)</th>
<th>P, (Χ²)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gleason score</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 7</td>
<td>16 (48.5)</td>
<td>2</td>
<td>14</td>
<td>.04*</td>
</tr>
<tr>
<td>7</td>
<td>15 (45.5)</td>
<td>9</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>&gt; 7</td>
<td>2 (6.0)</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td><strong>Clinical stage</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T1c</td>
<td>17 (53.1)</td>
<td>5</td>
<td>12</td>
<td>.177</td>
</tr>
<tr>
<td>T2a</td>
<td>7 (21.9)</td>
<td>2</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>T2b</td>
<td>4 (12.5)</td>
<td>1</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>T3</td>
<td>4 (12.5)</td>
<td>4</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td><strong>Treatment History</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None / active surveillance</td>
<td>6 (18.2)</td>
<td>4</td>
<td>2</td>
<td>.017*</td>
</tr>
<tr>
<td>Radical prostatectomy (RP)</td>
<td>24 (72.7)</td>
<td>5</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>Radiation therapy (RT)</td>
<td>2 (6.1)</td>
<td>2</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>RP ± salvage RT</td>
<td>1 (3.0)</td>
<td>1</td>
<td>-</td>
<td></td>
</tr>
</tbody>
</table>

1. Men with prostate cancer treated with androgen deprivation therapy
2. Hormone-naive men with prostate cancer
* significant at p < .05
† A higher Gleason score indicates a more well-differentiated, aggressive tumour
‡ Clinical stage based on pathology at biopsy. A T1c prostate tumour is found in the prostate only, cannot be felt during a digital rectal exam and is not visible by imaging, a T2A prostate tumour can be palpated on exam and is present in half or less than half of one lobe, a T2b tumour can be palpated on exam but is present in more than half of one lobe (but not both), and a T3 tumour has spread through the prostatic capsule; group B n = 20.

Nearly half of men in Group A had undergone neoadjuvant androgen deprivation, with four men undergoing ADT exclusively with no other local therapy history at time of data collection (Table 4.5). ADT was a post-local therapy treatment in 66.4% of those in Group A due to recurrence or locally advanced disease. The average duration of ADT was 24.3 ± 30.2 months (range 3 – 88 months). The majority of men in Group A were on an LHRH agonist with continuous therapy; for those men on intermittent ADT, the number of three-month cycles received ranged from 2 – 6 (data not shown).
Table 4.5. Type, delivery method, indication for use and duration of androgen deprivation therapy (ADT) of men undergoing ADT.

<table>
<thead>
<tr>
<th>(n = 12)</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neoadjuvant androgen deprivation therapy</td>
<td>5 (41.7)</td>
</tr>
<tr>
<td>Luteinizing hormone releasing hormone agonist</td>
<td>11 (91.7)</td>
</tr>
<tr>
<td>Continuous androgen blockage</td>
<td>3 (25.0)</td>
</tr>
<tr>
<td>Delivery</td>
<td></td>
</tr>
<tr>
<td>Continuous</td>
<td>8 (66.7)</td>
</tr>
<tr>
<td>Intermittent</td>
<td>4 (33.3)</td>
</tr>
<tr>
<td>Indication for ADT</td>
<td></td>
</tr>
<tr>
<td>Conservative management</td>
<td>1 (8.3)</td>
</tr>
<tr>
<td>Recurrence</td>
<td>6 (50.0)</td>
</tr>
<tr>
<td>Locally advanced disease</td>
<td>2 (16.4)</td>
</tr>
<tr>
<td>NADT</td>
<td>3 (25.0)</td>
</tr>
<tr>
<td>Mean duration of ADT (months)</td>
<td>24.33 (SD = 30.2)</td>
</tr>
</tbody>
</table>

4.3. Calcium and Vitamin D Intakes

4.3.1. Dietary and supplemental intakes

There were no significant differences among the groups with respect to calcium or vitamin D intake, from food sources, supplements or total intake (Table 4.6). When compared with the current Adequate Intake (AI) and treatment-specific guidelines, the majority of men did not meet current recommendations (Tables 4.7 and 4.8). For instance, 71.7% of men did not meet the calcium AI of 1200 mg per day and 91.7% of men on ADT did not meet the recommended 1500 mg per day. Most men did not meet vitamin D recommendations with 57.8% of men aged 51 – 70 years and 100% of men 71 years and older falling short of the age-specific AIs of 10 mcg and 15 mcg per day, respectively. Mean intake of men undergoing ADT was only half the treatment-specific recommendation of 20 mcg/d, and none had an intake that met the recommendation.
Table 4.6. Calcium and vitamin D intake of men with prostate cancer and healthy controls.

<table>
<thead>
<tr>
<th>Variable</th>
<th>mean ± SD</th>
<th></th>
<th></th>
<th></th>
<th>F</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All (N=53)</td>
<td>Group A¹ (n=12)</td>
<td>Group B² (n=21)</td>
<td>Group C³ (n=20)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total calcium intake (mg)</td>
<td>1117.9 ± 449.8</td>
<td>1000.4 ± 305.1</td>
<td>1226.7 ± 578.8</td>
<td>1074.2 ± 351.3</td>
<td>1.124</td>
<td>.333</td>
</tr>
<tr>
<td>Dietary calcium (mg)</td>
<td>1022.6 ± 386.2</td>
<td>876.0 ± 302.6</td>
<td>1086.3 ± 442.3</td>
<td>1043.9 ± 361.7</td>
<td>1.189</td>
<td>.313</td>
</tr>
<tr>
<td>Supplemental calcium (mg)</td>
<td>95.3 ± 207.8</td>
<td>124.4 ± 186.4</td>
<td>140.5 ± 284.4</td>
<td>30.4 ± 75.3</td>
<td>1.629</td>
<td>.206</td>
</tr>
<tr>
<td>Total vitamin D intake (mcg)</td>
<td>9.7 ± 6.2</td>
<td>10.2 ± 6.8</td>
<td>9.7 ± 5.9</td>
<td>9.5 ± 6.3</td>
<td>0.045</td>
<td>.956</td>
</tr>
<tr>
<td>Dietary vitamin D (mcg)</td>
<td>5.5 ± 2.4</td>
<td>4.6 ± 2.0</td>
<td>6.0 ± 2.4</td>
<td>5.6 ± 2.6</td>
<td>1.248</td>
<td>.296</td>
</tr>
<tr>
<td>Supplemental vitamin D (mcg)</td>
<td>4.2 ± 5.0</td>
<td>5.5 ± 5.5</td>
<td>3.8 ± 4.4</td>
<td>3.9 ± 5.5</td>
<td>0.542</td>
<td>.585</td>
</tr>
</tbody>
</table>

¹ Men with prostate cancer treated with androgen deprivation therapy
² Hormone-naïve men with prostate cancer
³ Healthy men without prostate cancer
Table 4.7. Calcium intakes from food sources and supplements of men with prostate cancer and healthy controls (expressed in mg/d).

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>mean ± SD</th>
<th>Percentiles†</th>
<th>AI‡</th>
<th>% &lt; AI</th>
<th>UL††</th>
<th>% &gt; UL</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>25th</td>
<td>50th</td>
<td>75th</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group A¹</td>
<td>12</td>
<td>1000.4 ± 305.1</td>
<td>706.8</td>
<td>999.0</td>
<td>1162.6</td>
<td>1500</td>
<td>91.7</td>
</tr>
<tr>
<td>Group B²</td>
<td>21</td>
<td>1226.7 ± 578.8</td>
<td>749.2</td>
<td>1100.0</td>
<td>1694.5</td>
<td>1200</td>
<td>57.1</td>
</tr>
<tr>
<td>Group C³</td>
<td>20</td>
<td>1074.2 ± 351.3</td>
<td>847.9</td>
<td>1042.4</td>
<td>1158.7</td>
<td>1200</td>
<td>90.0</td>
</tr>
</tbody>
</table>

¹ Men with prostate cancer treated with androgen deprivation therapy (ADT)
² Hormone-naïve men with prostate cancer
³ Healthy men without prostate cancer
† Tukey’s Hinges
‡ Adequate Intake, including AI for calcium as well as treatment-specific recommendation for men on ADT
†† Tolerable Upper Intake Level.
Table 4.8. Vitamin D intakes from food sources and supplements of men with prostate cancer and healthy controls and age (expressed in mcg/d).

<table>
<thead>
<tr>
<th>Age</th>
<th>n</th>
<th>mean ± SD</th>
<th>Percentiles†</th>
<th>AI‡</th>
<th>% &lt; AI</th>
<th>UL††</th>
<th>% &gt; UL</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>25th</td>
<td>50th</td>
<td>75th</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group A ¹</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>51 - 70</td>
<td>8</td>
<td>11.9 ± 7.3</td>
<td>3.9</td>
<td>14.1</td>
<td>18.2</td>
<td>20</td>
<td>100</td>
</tr>
<tr>
<td>71+</td>
<td>4</td>
<td>6.7 ± 4.6</td>
<td>3.4</td>
<td>5.2</td>
<td>10.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group B ²</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>51 - 70</td>
<td>17</td>
<td>11.1 ± 5.8</td>
<td>6.0</td>
<td>9.5</td>
<td>16.3</td>
<td>10</td>
<td>52.9</td>
</tr>
<tr>
<td>71+</td>
<td>4</td>
<td>4.0 ± 1.8</td>
<td>2.5</td>
<td>4.1</td>
<td>5.5</td>
<td>15</td>
<td>100</td>
</tr>
<tr>
<td>Group C ³</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>51 - 70</td>
<td>20</td>
<td>9.5 ± 6.3</td>
<td>5.3</td>
<td>8.0</td>
<td>12.1</td>
<td>10</td>
<td>65</td>
</tr>
<tr>
<td>71+</td>
<td>0</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>15</td>
<td>-</td>
</tr>
</tbody>
</table>

¹ Men with prostate cancer treated with androgen deprivation therapy (ADT)
² Hormone-naïve men with prostate cancer
³ Healthy men without prostate cancer
† Tukey’s Hinges
‡ Adequate Intake, including age-specific AI for vitamin D as well as treatment-specific recommendation for men on ADT
†† Tolerable Upper Intake Level
4.3.2. Calcium and vitamin D supplement use

There were no significant differences among the three groups when comparing use of calcium- and vitamin D-containing multivitamin-mineral (MVM) supplements or individual calcium or vitamin D supplement preparations (Table 4.9). The majority of men did not take a MVM, and among those who reported taking a MVM over the past 12 months, only half took one daily. Fewer than 30% of participants reported use of calcium and vitamin D supplements. Interestingly, of the 15 men reporting individual vitamin D supplement use, the majority (n = 11) did not take a concurrent MVM, while four men reported individual vitamin D supplement use and also taking a MVM (data not shown). Differences in MVM, calcium and vitamin D supplement use based on age group were also investigated (data not shown), however no significant differences emerged.
Table 4.9: Multivitamin-mineral (MVM), calcium and vitamin D supplement use of men with prostate cancer and healthy controls.

<table>
<thead>
<tr>
<th></th>
<th>n (%)</th>
<th>All (N=53)</th>
<th>Group A¹ (n=12)</th>
<th>Group B² (n=21)</th>
<th>Group C³ (n=20)</th>
<th>p †</th>
</tr>
</thead>
<tbody>
<tr>
<td>MVM use within last 12 months</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>30 (56.6)</td>
<td>6</td>
<td>12</td>
<td>12</td>
<td>.880</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>23 (43.4)</td>
<td>6</td>
<td>9</td>
<td>8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Daily MVM use by MVM users</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>11 (47.8)</td>
<td>2</td>
<td>5</td>
<td>4</td>
<td>.703</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>12 (52.2)</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Calcium supplement use</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>40 (75.5)</td>
<td>8</td>
<td>15</td>
<td>17</td>
<td>.431</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>13 (24.5)</td>
<td>4</td>
<td>6</td>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Frequency of calcium use by calcium users</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 3 days per week</td>
<td>3 (23.1)</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>.540</td>
<td></td>
</tr>
<tr>
<td>&gt; 3 days per week</td>
<td>10 (76.9)</td>
<td>2</td>
<td>5</td>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vitamin D supplement use</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>38 (71.7)</td>
<td>8</td>
<td>13</td>
<td>17</td>
<td>.194</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>15 (28.3)</td>
<td>4</td>
<td>8</td>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Frequency of vitamin D use by vitamin D users</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 3 days per week</td>
<td>4 (26.7)</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>.622</td>
<td></td>
</tr>
<tr>
<td>&gt; 3 days per week</td>
<td>11 (73.3)</td>
<td>4</td>
<td>6</td>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vitamin D supplement dose</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 10 mcg</td>
<td>4 (28.6)</td>
<td>0</td>
<td>4</td>
<td>1</td>
<td>.339</td>
<td></td>
</tr>
<tr>
<td>&gt; 10 mcg</td>
<td>10 (71.4)</td>
<td>4</td>
<td>4</td>
<td>2</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1. Men with prostate cancer treated with androgen deprivation therapy
2. Hormone-naïve men with prostate cancer
3. Healthy men without prostate cancer
† Based on Kruskal tau

4.4. Other Dietary Outcomes

4.4.1. Macronutrients

There were no significant differences in macronutrient intake (Table 4.10) or fatty acid intake (Table 4.11) among the three groups. Breakdown of macronutrient and alcohol contribution to total energy intake (Table 4.12) showed that Group C derived a significantly greater percentage of calories from total fat compared with Group B. When Groups A and B
were collapsed to form one PC-diagnosed group, no differences in the above were seen when compared to healthy controls (data not shown). Percentage of calories from alcohol approached, but did not reach significance. Alcohol intake varied widely among men, though abstainers (n = 5) represented a minority when compared to those drinking more than one drink (n = 34) or two drinks (n = 21) each day.

4.4.2. Micronutrients and Phytochemicals

There were few significant differences in vitamin (Table 4.13) and mineral (Table 4.14) intakes from diet and supplements among the three groups. Group A had significantly higher intakes of vitamin E when compared to the Group B and Group C. When intake was broken down into food alone vs. supplemental intake (data not shown), the significant difference was eliminated for food sources (F=2.368, p=.104), whereas the post hoc analysis showed a significantly greater intake of supplemental vitamin E (approximately 95 mg ATE) among men in Group A in comparison with those in Group B (p = .028) and Group C (p = .029). The group intakes were compared for food alone and supplements for all other micronutrients, though no other significant differences were seen (data not shown). Similarly, when Groups A and B were collapsed to form one PC-diagnosed group, no differences in the above were seen when compared to healthy controls (data not shown). There were no significant differences between the three groups with respect to phytochemical intake (Table 4.15).
Table 4.10. Macronutrient and alcohol intakes of men with prostate cancer and healthy controls.

<table>
<thead>
<tr>
<th>Variable</th>
<th>mean ± SD</th>
<th>F</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All (N=53)</td>
<td>Group A¹ (n=12)</td>
<td>Group B² (n=21)</td>
</tr>
<tr>
<td>Energy (kcal)</td>
<td>2243.5 ± 624.8</td>
<td>2022.5 ± 447.1</td>
<td>2242.0 ± 666.5</td>
</tr>
<tr>
<td>Protein (g)</td>
<td>87.4 ± 22.3</td>
<td>77.8 ± 20.1</td>
<td>86.2 ± 18.5</td>
</tr>
<tr>
<td>Total fat (g)</td>
<td>85.2 ± 30.3</td>
<td>80.5 ± 28.8</td>
<td>77.5 ± 24.8</td>
</tr>
<tr>
<td>Cholesterol (mg)</td>
<td>226.5 ± 87.3</td>
<td>225.4 ± 117.6</td>
<td>215.9 ± 78.1</td>
</tr>
<tr>
<td>Carbohydrate (g)</td>
<td>260.6 ± 80.9</td>
<td>225.0 ± 52.8</td>
<td>262.9 ± 89.1</td>
</tr>
<tr>
<td>Fibre (g)</td>
<td>27.0 ± 9.8</td>
<td>23.9 ± 8.2</td>
<td>27.1 ± 11.1</td>
</tr>
<tr>
<td>Alcohol (g)†</td>
<td>22.2 ± 28.0</td>
<td>21.5 ± 15.3</td>
<td>31.0 ± 39.1</td>
</tr>
</tbody>
</table>

¹ Men with prostate cancer treated with androgen deprivation therapy (ADT)
² Hormone-naïve men with prostate cancer
³ Healthy men without prostate cancer
† Kruskal Wallis used as alcohol intake distribution not normally distributed.
Table 4.11. Fatty acid intake of men with prostate cancer and healthy controls.

<table>
<thead>
<tr>
<th>Variable</th>
<th>All (N=53)</th>
<th>Group A (n=12)</th>
<th>Group B (n=21)</th>
<th>Group C (n=20)</th>
<th>F</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>SFA4 (g)</td>
<td>24.2 ± 8.4</td>
<td>34.3 ± 14.1</td>
<td>20.4 ± 8.9</td>
<td>18.1 ± 8.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MUFA5 (g)</td>
<td>32.8 ± 13.4</td>
<td>19.4 ± 8.5</td>
<td>17.1 ± 7.7</td>
<td>1.8 ± 6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PUFA6 (g)</td>
<td>19.4 ± 8.5</td>
<td>17.1 ± 7.7</td>
<td>16.0 ± 6.4</td>
<td>1.7 ± 6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Linoleic (g)</td>
<td>22.3 ± 7.4</td>
<td>30.8 ± 12.5</td>
<td>23.2 ± 10.7</td>
<td>20.8 ± 10.2</td>
<td>1.683</td>
<td>.196</td>
</tr>
<tr>
<td>Linolenic (g)</td>
<td>18.3 ± 6.4</td>
<td>22.2 ± 10.7</td>
<td>23.2 ± 10.7</td>
<td>20.8 ± 10.2</td>
<td>1.748</td>
<td>.185</td>
</tr>
<tr>
<td>Arachidonic (mg)</td>
<td>118.0 ± 36.8</td>
<td>108.3 ± 72.2</td>
<td>113.8 ± 56.5</td>
<td>125.5 ± 48.1</td>
<td>1.808</td>
<td>.175</td>
</tr>
<tr>
<td>EPA7 (mg)</td>
<td>83.8 ± 65.2</td>
<td>97.5 ± 106.9</td>
<td>75.7 ± 32.3</td>
<td>125.5 ± 48.1</td>
<td>1.808</td>
<td>.175</td>
</tr>
<tr>
<td>DHA8 (mg)</td>
<td>142.8 ± 95.7</td>
<td>158.3 ± 153.4</td>
<td>131.0 ± 51.5</td>
<td>146.0 ± 91.2</td>
<td>1.683</td>
<td>.196</td>
</tr>
<tr>
<td>Trans fat (g)</td>
<td>3.8 ± 1.6</td>
<td>3.1 ± 1.0</td>
<td>3.7 ± 1.56</td>
<td>4.4 ± 1.7</td>
<td>2.468</td>
<td>.095</td>
</tr>
</tbody>
</table>

1. Men with prostate cancer treated with androgen deprivation therapy (ADT)
2. Hormone-naïve men with prostate cancer
3. Healthy men without prostate cancer
4. Saturated fatty acids
5. MUFA: monounsaturated fatty acids
6. PUFA: polyunsaturated fatty acids
7. EPA: eicosapentaenoic acid
8. DHA: docosahexaenoic acid.
Table 4.12. Percentage (%) of energy derived from macronutrients and alcohol of men with prostate cancer and healthy controls.

<table>
<thead>
<tr>
<th></th>
<th>mean ± SD</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All (N=53)</td>
<td>Group A¹</td>
<td>Group B²</td>
<td>Group C³</td>
<td>F</td>
<td>p</td>
</tr>
<tr>
<td>Protein</td>
<td>15.9 ± 2.5</td>
<td>15.5 ± 3.1</td>
<td>15.9 ± 2.6</td>
<td>16.1 ± 2.2</td>
<td>.159</td>
<td>.854</td>
</tr>
<tr>
<td>Total fat</td>
<td>33.9 ± 6.3</td>
<td>35.1 ± 7.1abc</td>
<td>31.3 ± 5.9a</td>
<td>36.0 ± 5.5b</td>
<td>3.454</td>
<td>.039</td>
</tr>
<tr>
<td>SFA⁴</td>
<td>9.7 ± 2.2</td>
<td>9.8 ± 1.7</td>
<td>9.1 ± 2.4</td>
<td>10.4 ± 2.1</td>
<td>1.894</td>
<td>.161</td>
</tr>
<tr>
<td>MUFA⁵</td>
<td>13.6 ± 3.6</td>
<td>14.3 ± 4.1</td>
<td>12.4 ± 3.5</td>
<td>14.4 ± 3.1</td>
<td>2.083</td>
<td>.135</td>
</tr>
<tr>
<td>PUFA⁶</td>
<td>8.0 ± 2.1</td>
<td>8.4 ± 2.2</td>
<td>7.3 ± 1.8</td>
<td>8.6 ± 2.3</td>
<td>2.128</td>
<td>.130</td>
</tr>
<tr>
<td>Carbohydrate</td>
<td>46.9 ± 7.8</td>
<td>45.2 ± 9.1</td>
<td>47.5 ± 9.3</td>
<td>47.2 ± 5.0</td>
<td>.341</td>
<td>.713</td>
</tr>
<tr>
<td>Alcohol</td>
<td>6.4 ± 6.9</td>
<td>7.3 ± 4.8</td>
<td>8.4 ± 9.1</td>
<td>3.9 ± 4.1</td>
<td>5.636</td>
<td>.060</td>
</tr>
</tbody>
</table>

¹ Men with prostate cancer treated with androgen deprivation therapy
² Hormone-naïve men with prostate cancer
³ Healthy men without prostate cancer
⁴ Saturated fatty acids
⁵ MUFA: monounsaturated fatty acids
⁶ PUFA: polyunsaturated fatty acids

abc Means in the same row with different superscripts differ significantly, p <0.05
Table 4.13. Vitamin intake from food sources and supplements of men with prostate cancer and healthy controls.

<table>
<thead>
<tr>
<th>Variable</th>
<th>All (N=53)</th>
<th>Group A(^1) (n=12)</th>
<th>Group B(^2) (n=21)</th>
<th>Group C(^3) (n=20)</th>
<th>F</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin A (RAE)</td>
<td>1855.6 ± 784.0</td>
<td>1775.6 ± 848.5</td>
<td>1789.3 ± 814.7</td>
<td>1973.34 ± 736.9</td>
<td>0.354</td>
<td>0.704</td>
</tr>
<tr>
<td>Beta-carotene (RAE)</td>
<td>1201.4 ± 671.7</td>
<td>969.75 ± 482.4</td>
<td>1238.5 ± 849.9</td>
<td>1301.5 ± 542.1</td>
<td>0.966</td>
<td>0.387</td>
</tr>
<tr>
<td>Vitamin E (mg)</td>
<td>59.7 ± 105.8</td>
<td>131.9 ± 168.1(^a)</td>
<td>37.0 ± 66.2(^b)</td>
<td>40.3 ± 73.2(^b)</td>
<td>4.048</td>
<td>0.023</td>
</tr>
<tr>
<td>Vitamin C (mg)</td>
<td>315.0 ± 240.6</td>
<td>388.2 ± 286.9</td>
<td>330.6 ± 282.0</td>
<td>254.8 ± 140.3</td>
<td>1.237</td>
<td>0.299</td>
</tr>
<tr>
<td>Thiamin (mg)</td>
<td>3.4 ± 2.4</td>
<td>3.8 ± 2.7</td>
<td>3.2 ± 2.2</td>
<td>3.3 ± 2.6</td>
<td>0.226</td>
<td>0.799</td>
</tr>
<tr>
<td>Riboflavin (mg)</td>
<td>3.2 ± 1.7</td>
<td>3.5 ± 1.6</td>
<td>3.1 ± 1.7</td>
<td>3.1 ± 1.8</td>
<td>0.292</td>
<td>0.748</td>
</tr>
<tr>
<td>Niacin (mg)</td>
<td>35.5 ± 14.4</td>
<td>39.0 ± 15.3</td>
<td>32.9 ± 10.9</td>
<td>36.2 ± 17.2</td>
<td>0.694</td>
<td>0.504</td>
</tr>
<tr>
<td>Vitamin B(_6) (mg)</td>
<td>11.4 ± 16.0</td>
<td>15.5 ± 16.9</td>
<td>10.0 ± 17.0</td>
<td>10.5 ± 14.8</td>
<td>0.492</td>
<td>0.615</td>
</tr>
<tr>
<td>Folate (mcg)</td>
<td>570.5 ± 233.7</td>
<td>601.0 ± 210.6</td>
<td>547.0 ± 226.6</td>
<td>577.0 ± 261.8</td>
<td>0.210</td>
<td>0.812</td>
</tr>
<tr>
<td>Vitamin B(_12) (mcg)</td>
<td>7.0 ± 3.3</td>
<td>7.6 ± 3.8</td>
<td>6.4 ± 2.9</td>
<td>7.4 ± 3.4</td>
<td>0.678</td>
<td>0.512</td>
</tr>
<tr>
<td>Vitamin D (mcg)</td>
<td>9.7 ± 6.2</td>
<td>10.2 ± 6.8</td>
<td>9.7 ± 5.9</td>
<td>9.5 ± 6.3</td>
<td>0.045</td>
<td>0.956</td>
</tr>
</tbody>
</table>

\(^1\) Men with prostate cancer treated with androgen deprivation therapy (ADT)
\(^2\) Hormone-naïve men with prostate cancer
\(^3\) Healthy men without prostate cancer
\(^a,b\) Means in the same row with different superscripts differ significantly, p <0.05
Table 4.14. Mineral intake from food sources and supplements of men with prostate cancer and healthy controls.

<table>
<thead>
<tr>
<th>Variable</th>
<th>All (N=53)</th>
<th>Group A(^1) (n=12)</th>
<th>Group B(^2) (n=21)</th>
<th>Group C(^3) (n=20)</th>
<th>(F)</th>
<th>(p)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium (mg)</td>
<td>1117.9 ± 449.8</td>
<td>1000.4 ± 305.1</td>
<td>1226.7 ± 578.8</td>
<td>1074.2 ± 351.3</td>
<td>1.124</td>
<td>.333</td>
</tr>
<tr>
<td>Magnesium (mg)</td>
<td>487.0 ± 150.1</td>
<td>452.0 ± 128.3</td>
<td>490.5 ± 123.3</td>
<td>504.2 ± 187.1</td>
<td>.455</td>
<td>.637</td>
</tr>
<tr>
<td>Iron (mg)</td>
<td>22.3 ± 8.67</td>
<td>22.4 ± 8.4</td>
<td>21.6 ± 7.9</td>
<td>23.1 ± 9.9</td>
<td>.156</td>
<td>.856</td>
</tr>
<tr>
<td>Zinc (mg)</td>
<td>18.3 ± 9.2</td>
<td>19.8 ± 11.5</td>
<td>16.1 ± 10.0</td>
<td>19.9 ± 9.8</td>
<td>1.046</td>
<td>.359</td>
</tr>
<tr>
<td>Copper (mg)</td>
<td>2.6 ± 1.1</td>
<td>2.7 ± 1.2</td>
<td>2.4 ± .8</td>
<td>2.6 ± 1.2</td>
<td>.407</td>
<td>.668</td>
</tr>
<tr>
<td>Selenium (mcg)</td>
<td>122.1 ± 36.8</td>
<td>123.0 ± 45.3</td>
<td>114.8 ± 30.9</td>
<td>129.1 ± 37.4</td>
<td>.774</td>
<td>.467</td>
</tr>
<tr>
<td>Sodium (mg)  (†)</td>
<td>3262.3 ± 872.3</td>
<td>2990.7 ± 873.9</td>
<td>3220.3 ± 881.9</td>
<td>3469.1 ± 853.3</td>
<td>1.176</td>
<td>.317</td>
</tr>
<tr>
<td>Potassium (mg) (†)</td>
<td>4256.8 ± 1053.2</td>
<td>3900.7 ± 851.3</td>
<td>4457.8 ± 1062.5</td>
<td>4259.4 ± 1121.6</td>
<td>1.071</td>
<td>.350</td>
</tr>
<tr>
<td>Phosphorous (mg) (†)</td>
<td>150.2 ± 441.1</td>
<td>1348.8 ± 371.6</td>
<td>1510.7 ± 423.0</td>
<td>1659.5 ± 474.8</td>
<td>1.965</td>
<td>.151</td>
</tr>
</tbody>
</table>

\(^1\) Men with prostate cancer treated with androgen deprivation therapy (ADT)

\(^2\) Hormone-naïve men with prostate cancer

\(^3\) Healthy men without prostate cancer

\(†\) From food sources only.
### Table 4.15. Phytochemical intake of men with prostate cancer and healthy controls.

<table>
<thead>
<tr>
<th>Variable</th>
<th>mean ± SD</th>
<th>n=12</th>
<th>n=21</th>
<th>n=20</th>
<th>F</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>All (N=53)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lycopene (mg)</td>
<td>8.1 ± 5.1</td>
<td>9.1 ± 6.7</td>
<td>7.9 ± 5.3</td>
<td>7.6 ± 3.6</td>
<td>.336</td>
<td>.716</td>
</tr>
<tr>
<td>Beta-cryptoxanthin (mcg)</td>
<td>247.5 ± 111.3</td>
<td>241.2 ± 100.3</td>
<td>251.4 ± 129.2</td>
<td>247.1 ± 102.1</td>
<td>.031</td>
<td>.969</td>
</tr>
<tr>
<td>Lutein + zeaxanthin (mg)</td>
<td>3.8 ± 1.8</td>
<td>2.8 ± 1.2</td>
<td>4.1 ± 2.1</td>
<td>4.2 ± 1.5</td>
<td>2.619</td>
<td>.083</td>
</tr>
<tr>
<td>Theobromine (mg)</td>
<td>30.3 ± 26.4</td>
<td>26.7 ± 25.1</td>
<td>30.3 ± 30.0</td>
<td>32.6 ± 24.0</td>
<td>.180</td>
<td>.836</td>
</tr>
<tr>
<td>Caffeine (mg)</td>
<td>467.9 ± 378.4</td>
<td>462.4 ± 353.5</td>
<td>600.3 ± 426.9</td>
<td>332.1 ± 298.0</td>
<td>2.749</td>
<td>.074</td>
</tr>
</tbody>
</table>

1. Men with prostate cancer treated with androgen deprivation therapy (ADT)
2. Hormone-naïve men with prostate cancer
3. Healthy men without prostate cancer
4.4.3. Food Groups

There were no significant differences among the groups with respect to daily servings from each of the four food groups (Table 4.16). Within each food group, several specific categories were measured by the DHQ, such as daily servings of potato, cheese and soy products (data not shown). There were no significant group differences for any of these specific domains. In comparison to *Eating Well with Canada's Food Guide* (123), over 75% of men did not meet the recommended number of daily servings for Grain Products, Milk and Alternatives, and Meat and Alternatives. Approximately 79% of men reported consuming the recommended seven or more daily servings of Vegetables and Fruit (data not shown).

### Table 4.16: Eating Well with Canada's Food Guide daily food group servings of men with prostate cancer and healthy controls.

<table>
<thead>
<tr>
<th>Variable</th>
<th>mean ± SD</th>
<th>Group A</th>
<th>Group B</th>
<th>Group C</th>
<th>F</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All (N=53)</td>
<td>(n=12)</td>
<td>(n=21)</td>
<td>(n=20)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vegetables + Fruit</td>
<td>9.1 ± 2.78</td>
<td>8.4 ± 2.3</td>
<td>9.2 ± 3.2</td>
<td>9.5 ± 2.6</td>
<td>.611</td>
<td>.547</td>
</tr>
<tr>
<td>Grains</td>
<td>5.1 ± 2.1</td>
<td>4.4 ± 1.8</td>
<td>5.0 ± 2.4</td>
<td>5.6 ± 1.9</td>
<td>1.299</td>
<td>.282</td>
</tr>
<tr>
<td>Milk + Alternatives</td>
<td>1.7 ± 1.0</td>
<td>1.4 ± .8</td>
<td>1.6 ± 1.0</td>
<td>1.8 ± 1.0</td>
<td>.564</td>
<td>.572</td>
</tr>
<tr>
<td>Meat + Alternatives</td>
<td>2.3 ± .8</td>
<td>2.1 ± 1.0</td>
<td>2.3 ± .7</td>
<td>2.5 ± .9</td>
<td>1.123</td>
<td>.333</td>
</tr>
</tbody>
</table>

1. Men with prostate cancer treated with androgen deprivation therapy (ADT)
2. Hormone-naïve men with prostate cancer
3. Healthy men without prostate cancer

4.5. Biochemical Outcome Measures

Group A had significantly lower testosterone levels than Groups B or C, which was expected given the androgen-deprived status of men in Group A; all men in Group A were hypogonadal with serum testosterone below 10 nmol/L (Table 4.17). There were no other significant differences in biochemical indices among the groups. An independent sample t-test
showed no significant difference in 25OHD between men who had (n = 31) and had not (n = 32) traveled south in the preceding three months. Those reporting travel in the preceding three months had a mean 25OHD of 93.0 ± 29.3 nmol/L, while those who had not traveled had mean serum level of 98.6 ± 37.1 nmol/L (p = .565). Given the relationship between seasonality and vitamin D status, the effect of time of year of data collection (Fall, Winter, Spring) on 25OHD was investigated with ANOVA; no significant differences in 25OHD levels were detected among the groups (F = .379, p = .686).

Table 4.17. Testosterone, parathyroid hormone (PTH), 25-hydroxyvitamin D (25OHD) and vitamin D-binding protein (VDBP) levels of men with prostate cancer and healthy controls.

<table>
<thead>
<tr>
<th>Variable</th>
<th>mean ± SD</th>
<th>Group A¹ (n=12)</th>
<th>Group B² (n=21)</th>
<th>Group C³ (n=20)</th>
<th>F (p)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum testosterone (nmol/L)</td>
<td>97.8 ± 63.2</td>
<td>6.0 ± 3.7a</td>
<td>111.0 ± 31.9b</td>
<td>139.1 ± 50.7b</td>
<td>50.200 (&lt;0.001)</td>
</tr>
<tr>
<td>PTH (pmol/L)</td>
<td>7.1 ± 2.6</td>
<td>6.8 ± 2.6</td>
<td>7.5 ± 2.8</td>
<td>6.9 ± 2.3</td>
<td>.471 (.627)</td>
</tr>
<tr>
<td>25OHD (nmol/L)</td>
<td>96.4 ± 34.0</td>
<td>115.1 ± 30.2</td>
<td>89.4 ± 34.9</td>
<td>92.5 ± 32.6</td>
<td>2.536 (.089)</td>
</tr>
<tr>
<td>VDBP (mg/dL)</td>
<td>31.3 ± 5.0</td>
<td>32.7 ± 5.9</td>
<td>30.2 ± 5.5</td>
<td>31.5 ± 3.8</td>
<td>1.015 (.370)</td>
</tr>
</tbody>
</table>

¹ Men with prostate cancer treated with androgen deprivation therapy (ADT)
² Hormone-naïve men with prostate cancer
³ Healthy men without prostate cancer

a,b Means in the same row with different superscripts differ significantly, p < .05

The normal reference range for PTH is less than 6.4 pmol/L (121); however, the group mean for this study fell outside of normal at 7.1 ± 2.6 pmol/L. In fact, based on this reference range, nearly two-thirds of study participants would be excluded from subsequent analysis on the basis of apparent hyperparathyroidism. Based on the expected reference range for the assay kit utilized, over 40% of study participants (n = 23) had serum PTH levels about the expected
upper limit of 7.2 pmol/L. Similarly, the vitamin D status of the study group as a whole compares poorly with current literature and findings, for both the general population (124-127) and among men with PC (35,41,42,128). In our sample, over half of the participants had serum 25OHD of 80 nmol/L and above.

4.6. Effect of Demographic and Personal Characteristics

4.6.1. Effect of age on intake

The effect of age was investigated by stratifying the groups into three distinct decade-spanning groups: 51 – 60 years, 61 – 70 years and 71 years and older (Table 4.18). Total vitamin D intake and dietary vitamin D intake were significantly lower in older men (71 years and older) compared with those 61 – 70 years (p = .028 and p = .04, respectively). Analysis was also carried out to elicit the effect of age on other dietary and supplement parameters (data not shown). There was a significant main effect of age on dietary intake of DHA (F = 3.436, p = .040), with those 71 years and older having lower intakes when compared with men 61 – 70 years of age. (p = .049). Effects of age on servings of fish and seafood (F = 2.919, p = .063), total selenium intake (F = 2.758, p = .073) and EPA intake (F = 3.090, p = .054) approached, but did not reach significance.

4.6.2. Effect of education on intake

Reported educational attainment was used to assess the effect of education on dietary intake; those with less than high school and high school, trade or college diplomas were collapsed into one group (“without a degree”). There were no significant differences among the groups for calcium or vitamin D intake (Table 4.19).
Although calcium and vitamin D intakes did not differ by educational attainment, several other dietary parameters did (data not shown). Men who had obtained a graduate degree derived significantly less saturated fat ($F = 6.189, p = .004$), as percentage of total energy, than those with a university degree ($p = .041$) and those without a degree ($p = .003$). Dietary cholesterol intake ($F = 4.053, p = .023$) was significantly lower for participants with a graduate degree compared with university graduates ($p = .028$) and those with less than a university degree ($p = .043$). Similar trends were seen with theobromine intake ($F = 3.864, p = .028$), meat/poultry/fish intake ($F = 3.557, p = .036$), red meat intake ($F = 3.864, p = .028$) and arachidonic acid ($F = 3.240, p = .048$), where graduate degree attainment was associated with significantly lower intakes when compared to the other two groups. Interestingly, soy product servings were considerably higher among men with a graduate degree ($F = 18.688, p < .001$).
Table 4.18. Effect of age on calcium and vitamin D intake of men with prostate cancer and healthy controls.

<table>
<thead>
<tr>
<th></th>
<th>mean ± SD</th>
<th>F</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(N = 53)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total calcium intake (mg)</td>
<td>1117.9 ± 449.8</td>
<td>.502</td>
<td>.608</td>
</tr>
<tr>
<td>Dietary calcium (mg)</td>
<td>1022.6 ± 386.2</td>
<td>.678</td>
<td>.512</td>
</tr>
<tr>
<td>Supplemental calcium (mg)</td>
<td>95.3 ± 207.8</td>
<td>1.579</td>
<td>.216</td>
</tr>
<tr>
<td>Total vitamin D intake (mcg)</td>
<td>9.7 ± 6.2</td>
<td>3.284</td>
<td>.046*</td>
</tr>
<tr>
<td>Dietary vitamin D (mcg)</td>
<td>5.5 ± 2.4</td>
<td>1.656</td>
<td>.201</td>
</tr>
<tr>
<td>Supplemental vitamin D (mcg)</td>
<td>4.2 ± 5.0</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* significant at p < .05

Table 4.19. Effect of education on calcium and vitamin D intake of men with prostate cancer and healthy controls.

<table>
<thead>
<tr>
<th></th>
<th>mean ± SD</th>
<th>F</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(N = 53)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total calcium intake (mg)</td>
<td>1117.9 ± 449.8</td>
<td>1.936</td>
<td>.155</td>
</tr>
<tr>
<td>Dietary calcium (mg)</td>
<td>1022.6 ± 386.2</td>
<td>1.165</td>
<td>.320</td>
</tr>
<tr>
<td>Supplemental calcium (mg)</td>
<td>95.3 ± 207.8</td>
<td>.942</td>
<td>.397</td>
</tr>
<tr>
<td>Total vitamin D intake (mcg)</td>
<td>9.7 ± 6.2</td>
<td>.421</td>
<td>.659</td>
</tr>
<tr>
<td>Dietary vitamin D (mcg)</td>
<td>5.5 ± 2.4</td>
<td>1.044</td>
<td>.360</td>
</tr>
<tr>
<td>Supplemental vitamin D (mcg)</td>
<td>4.2 ± 5.0</td>
<td>.290</td>
<td>.750</td>
</tr>
</tbody>
</table>
4.6.3. Effect of food preparation role on intake

Those men who reported self-preparation or a shared role in food preparation were collapsed into one group and compared with men who had a passive role in household food preparation. There was a significant difference between a passive and active role in food preparation with respect to calcium intake, with those men reporting a passive role consuming approximately 200 mg more calcium from food sources per day ($p = .035$). Correspondingly, men not involved in food preparation had higher daily intake of Milk and Alternatives ($p = .009$) and fluid milk servings ($p = .013$) (data not shown). Similar trends were also seen with zinc (total $p = .024$, food $p = .031$), vitamin E (total $p = .015$, supplements $p = .014$), vitamin C (total $p = .036$, supplements $p = .008$) and selenium (supplements $p = .044$), where men with a passive role had higher intakes (data not shown).
Table 4.20. Effect of food preparation role on calcium and vitamin D intake of men with prostate cancer and healthy controls.

<table>
<thead>
<tr>
<th></th>
<th>mean ± SD</th>
<th></th>
<th>t</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All N=53</td>
<td>Someone else n=36</td>
<td>Shared/self n=17</td>
<td></td>
</tr>
<tr>
<td>Total calcium intake (mg)</td>
<td>1117.9 ± 449.8</td>
<td>1178.1 ± 455.9</td>
<td>990.4 ± 421.5</td>
<td>-1.432</td>
</tr>
<tr>
<td>Dietary calcium (mg)</td>
<td>1022.6 ± 386.2</td>
<td>1087.3 ± 424.4</td>
<td>885.8 ± 248.1</td>
<td>-2.169</td>
</tr>
<tr>
<td>Supplementation calcium (mg)</td>
<td>95.3 ± 207.8</td>
<td>90.9 ± 172.2</td>
<td>104.6 ± 274.5</td>
<td>.223</td>
</tr>
<tr>
<td>Total vitamin D intake (mcg)</td>
<td>9.7 ± 6.2</td>
<td>10.4 ± 6.3</td>
<td>8.3 ± 5.7</td>
<td>-1.154</td>
</tr>
<tr>
<td>Dietary vitamin D (mcg)</td>
<td>5.5 ± 2.4</td>
<td>5.7 ± 2.4</td>
<td>5.2 ± 2.3</td>
<td>-.633</td>
</tr>
<tr>
<td>Supplemental vitamin D (mcg)</td>
<td>4.2 ± 5.0</td>
<td>4.7 ± 5.3</td>
<td>3.1 ± 2.4</td>
<td>-1.211</td>
</tr>
</tbody>
</table>

* significant at p < .05
4.7 Correlation Among Outcome Measures

4.7.1. Relationship between outcome dietary measures, anthropometrics and clinical characteristics

Since participants’ physical status and disease trajectory may impact on their food choices, the relationships between dietary outcome measures, anthropometrics and clinical characteristics were examined (Table 4.21). There was no significant relationship between total calcium or vitamin D intake and age, though a significant relationship between increasing age and calcium supplement intake was found. PSA at diagnosis, time since diagnosis and duration of ADT were not affected by age. Higher weight was associated with lower intakes of total vitamin D, and higher BMI was associated with not only lower dietary and vitamin D, but lower total and supplemental calcium intakes as well.

The relationship between age, anthropometrics and clinical characteristics was examined for other dietary variables as well (data not shown). Significant relationship were seen with increasing age and lower intakes of total vitamin A (r = -.328, p = .016), supplemental vitamin A (r = -.308, p = .025), total beta-carotene (r = -.301, p = .028) and supplemental beta-carotene (r = -.301, p = .025), as well as higher intakes of supplemental vitamin E (r = .272, p = .049) and vitamin C (r = .274, p = .047).

Increasing weight was significantly associated with higher percentage of energy from saturated fat intake (r = .285, p = .039) and lower percentage of energy from carbohydrate (r = -.335, p = .014), lower intake of theobromine (r = -.298, p = .030), and greater intake of cheese (r = .378, p = .005).

Significant relationships emerged between higher BMI and lower intakes of fluid milk (r = -.271, p = 049), whole grains (r = -.286, p = .038), percentage of energy derived from
carbohydrates ($r = -0.331, p = 0.015$), total thiamin ($r = -0.284, p = 0.039$), theobromine ($r = -0.372, p = 0.006$) and supplemental vitamin C ($r = -0.276, p = 0.045$). Higher BMI was also associated with higher intake of cheese ($r = 0.359, p = 0.008$).

Time since PC diagnosis was negatively associated with servings of fluid milk ($r = -0.403, p = 0.020$) though no significant relationship between other milk product servings, calcium intake from food, or total servings of Milk and Alternatives emerged. Increasing time since diagnosis was positively associated with increased intake of fish and seafood ($r = 0.481, p = 0.005$), EPA ($r = 0.501, p = 0.003$) and DHA ($r = 0.498, p = 0.003$), and supplemental selenium ($r = 0.375, p = 0.031$). Duration of ADT was associated with higher intake of saturated fat ($r = 0.591, p = 0.043$), alcohol ($r = 0.580, p = 0.048$) and supplemental selenium ($r = 0.598, p = 0.040$).

### 4.7.2. Relationship between supplement use and dietary intake

Given that participants’ dietary intakes may influence their choice to taken supplements to augment intake, the possible relationship between supplemental intakes of calcium and vitamin D and diet were examined (Table 4.22). Higher vitamin D dietary intake was significantly associated with increasing intake of vitamin D from supplemental sources. There were no other significant associations between diet and supplemental intake of calcium and vitamin D.

### 4.7.3. Relationship between biochemical indices and dietary intake

Despite the evident discrepancy between the laboratory findings of this study, current literature and established reference ranges, correlation analyses were undertaken as a further means of attempting to assess the validity of the assays. Tables 4.23 and 4.24 examine the
possible relationships between the biochemical assays themselves, as well as between the assays and outcome dietary intakes, respectively. Surprisingly, the relationship between PTH and 25OHD levels was not significant, despite the close physiologic association between the two hormones, though an inverse relationship approached, but did not reach significance. A positive relationship between VDBP and 25OHD, however, was highly significant.

Ample literature argues that a serum 25OHD level of 80 nmol/L is the “threshold” for maximal suppression of PTH. Interestingly, when 25OHD level in our study was divided into two groups — those ‘below 80 nmol/L’ and those ‘at or above 80 nmol/L’ — and PTH level compared using the independent sample t-test, a significant relationship emerged. Those with serum 25OHD above 80 nmol/L had lower PTH levels (6.6 ± 2.4 pmol/L) compared with those with lower 25OHD (8.2 ± 2.6 pmol/L); this relationship was statistically significant at p < .05 (p = .033).

Calcium intake was not related to any of the biochemical indices. Conversely, vitamin D intake was significantly associated with 25OHD level, with the most pronounced associations between serum 25OHD and total and supplement intake. Neither PTH nor VDBP were associated with the outcome dietary measures.
Table 4.21. Relationship between outcome dietary measures, anthropometrics and clinical characteristics of men with prostate cancer and healthy controls.

<table>
<thead>
<tr>
<th></th>
<th>Dietary intakes</th>
<th></th>
<th>Supplemental intakes</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Calcium</td>
<td>Vitamin D</td>
<td>Calcium</td>
<td>Vitamin D</td>
</tr>
<tr>
<td></td>
<td>r (p)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>total diet</td>
<td>supplements</td>
<td>total diet</td>
<td>supplements</td>
</tr>
<tr>
<td>Age†</td>
<td>-.003 (.984)</td>
<td>-.166 (.236)</td>
<td>.302 (.028)*</td>
<td>-.171 (.222)</td>
</tr>
<tr>
<td>Weight†</td>
<td>-.165 (.236)</td>
<td>-.073 (.605)</td>
<td>-.223 (.108)</td>
<td>-.305 (.026)*</td>
</tr>
<tr>
<td>BMI†</td>
<td>-.271 (.049)*</td>
<td>-.141 (.315)</td>
<td>-.326 (.017)*</td>
<td>-.296 (.031)*</td>
</tr>
<tr>
<td>PSA at diagnosis‡</td>
<td>-.047 (.796)</td>
<td>-.125 (.495)</td>
<td>.140 (.444)</td>
<td>-.175 (.339)</td>
</tr>
<tr>
<td>Time since diagnosis‡</td>
<td>.062 (.731)</td>
<td>-.083 (.645)</td>
<td>.260 (.144)</td>
<td>-.069 (.705)</td>
</tr>
<tr>
<td>Duration of ADT§</td>
<td>.093 (.775)</td>
<td>.002 (.994)</td>
<td>.148 (.647)</td>
<td>.004 (.991)</td>
</tr>
</tbody>
</table>

*significant at p < .05. † n = 53; ‡ n = 23; § n = 12.

Table 4.22. Relationship between supplemental calcium and vitamin D and dietary intakes of men with prostate cancer and healthy controls.

<table>
<thead>
<tr>
<th></th>
<th>Supplemental intakes</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Calcium</td>
<td>Vitamin D</td>
<td></td>
</tr>
<tr>
<td></td>
<td>r(p)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dietary calcium intake</td>
<td>.062 (.658)</td>
<td>.086 (.540)</td>
<td></td>
</tr>
<tr>
<td>Dietary vitamin D intake</td>
<td>.059 (.675)</td>
<td>.296 (.031)*</td>
<td></td>
</tr>
<tr>
<td>Daily servings of Milk and Alternatives</td>
<td>-.202 (.147)</td>
<td>-.067 (.632)</td>
<td></td>
</tr>
<tr>
<td>Daily servings of fluid milk</td>
<td>-.138 (.326)</td>
<td>-.065 (.646)</td>
<td></td>
</tr>
<tr>
<td>Daily servings of yogurt</td>
<td>.096 (.492)</td>
<td>.115 (.411)</td>
<td></td>
</tr>
<tr>
<td>Daily servings of cheese</td>
<td>-.249 (.072)</td>
<td>-.109 (.439)</td>
<td></td>
</tr>
</tbody>
</table>

*significant at p < .05
Table 4.23. Relationship between parathyroid hormone (PTH), 25-hydroxyvitamin D (25OHD) and vitamin D-binding protein (VDBP) levels of men with prostate cancer and healthy controls.

<table>
<thead>
<tr>
<th></th>
<th>Serum PTH level</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>r (p)</td>
<td>PTH</td>
<td>25OHD</td>
</tr>
<tr>
<td>PTH</td>
<td>-</td>
<td>-260 (.060)</td>
<td>-260 (.060)</td>
</tr>
<tr>
<td>25OHD</td>
<td>-260 (.060)</td>
<td>-</td>
<td>.367 (.007)*</td>
</tr>
<tr>
<td>VDBP</td>
<td>-260 (.060)</td>
<td>.367 (.007)</td>
<td>-</td>
</tr>
</tbody>
</table>

*significant at p < .05.

Table 4.24. Relationship between outcome dietary measures and parathyroid hormone (PTH), 25-hydroxyvitamin D (25OHD) and vitamin D-binding protein (VDBP) levels of men with prostate cancer and healthy controls.

<table>
<thead>
<tr>
<th></th>
<th>Dietary Intakes</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>r (p)</td>
<td>Calcium</td>
<td>Vitamin D</td>
</tr>
<tr>
<td></td>
<td></td>
<td>total</td>
<td>diet</td>
</tr>
<tr>
<td>PTH</td>
<td></td>
<td>.155 (.269)</td>
<td>.252 (.068)</td>
</tr>
<tr>
<td>25OHD</td>
<td></td>
<td>-.042 (.766)</td>
<td>-.043 (.762)</td>
</tr>
<tr>
<td>VDBP</td>
<td></td>
<td>-.198 (.155)</td>
<td>-.233 (.094)</td>
</tr>
</tbody>
</table>

*significant at p < .05; ** significant at p < .01.
CHAPTER 5: DISCUSSION

5.1. Overview

The purpose of this study was to determine the calcium and vitamin D intakes of men undergoing ADT for the treatment of non-metastatic PC, hormone-naïve men with PC and healthy controls, and to evaluate whether men are meeting age- and treatment-specific dietary intake recommendations. Outcome measures examined included anthropometrics and nutrient intake from food sources and supplements assessed by diet history questionnaire. Assessment of vitamin D status, as indicated by serum 25-hydroxyvitamin D (25OHD) and PTH, and the prevalence of vitamin D deficiency and insufficiency among the above groups was intended, but could not be accomplished because of questionable laboratory results.

Results showed that there were no significant differences in calcium and vitamin D intakes, from food sources or supplements, among the three groups and the vast majority of men were not meeting current dietary recommendations. Although not part of the original hypotheses, further analyses were done to determine whether differences in macronutrient and micronutrient intakes existed among the three groups, particularly those linked to bone health and chemoprevention of prostate cancer, as well as to examine the effect and relationships between sociodemographic variables and dietary intakes.

In this chapter, study findings are discussed in relation to reports in the literature on dietary intakes of healthy men and those diagnosed with prostate cancer with respect to not only risk of osteoporosis and fracture, but also prostate cancer and its recurrence. Study limitations, implications for dietetic practice, areas for future research and conclusions are outlined.
5.2. Calcium and Vitamin D Intake

There were no significant differences among the groups with respect to calcium or vitamin D intake, from food sources, supplements or total intake, and most men did not meet age- or treatment-specific guidelines. When considering the DRI recommendations, 71.7% of men did not meet the calcium AI of 1200 mg per day, and 57.8% of men aged 51 – 70 years and 100% of men 71 years and older fell short of the age-specific vitamin D AIs of 10 mcg and 15 mcg per day, respectively. Although of significant concern, the poor intakes of calcium and vitamin D found in our study are comparable with those of other reports in the literature, where research shows older Canadian adults are less likely to meet the increased recommendations that correspond with age (129).

When compared with intakes among older British Columbia men (71), the proportion of men failing to meet the AI for calcium was similar at 50%. However, where mean intake is considered results of our study show higher intake of calcium from food and supplements among our participants who consumed approximately 1100 mg per day, versus means of 917 mg and 915 mg per day for men 51 – 70 years and 71 years and older, respectively, in the BCNS. Interestingly, older men in our group (over 70 years of age) also appeared to consume slightly more calcium than BC men of a similar age, with a daily mean intake of about 989 mg. Caution, however, must be exercised when comparing intake results of our study with those in the older general population given that only eight men in our study were older than 70 years of age.

Findings from the Canadian Multicentre Osteoporosis Study (CaMos) study show similar calcium intakes across older age groups (130). In this large-scale, longitudinal observational study, Poliquin et al. (130) found mean daily calcium intake among men 25 years older to be 904 ± 583 mg. When results were stratified by age groups 51 – 70 and 71 and older, younger men
consumed similar levels of calcium (908 ± 581 mg) when compared with men in the oldest category (884 ± 557 mg). Although the difference between age groups reached statistical significant, a difference of 24 mg is likely of little biological significance with respect to impact on bone health. Again, these results are in keeping with those of our study where calcium intake did not change significantly with age, though a non-significant trend towards lower intakes in the oldest age group existed. Poliquin et al. (130), however, obtained dietary information from an interviewer-administered food frequency questions, much as our study did, though only “excellent” sources of calcium considered, and total calcium intake from food was likely underestimated as a result.

Total vitamin D intakes among men in our study, while low in comparison to the AI, seem to be slightly higher than those reported in other studies of men in the general population (130,131). The mean intake of vitamin D among men 51 years and older in the United States was found to be approximately 8 mcg per day when food and supplement intake was considered versus 9.7 ± 6.2 mcg per day for food and supplemental intake in our study (131). However, Poliquin et al. (130) found a significantly lower vitamin D intakes among younger Canadian men enrolled in CaMos, where men aged 51 – 70 years consumed an average of 4.8 ± 5.3 mcg, and those aged 71 years and older with 5.0 ± 5.7 mcg vitamin D per day. Again, this represents a slight difference that is of little biological or clinical significance despite being statistically otherwise. While it appears vitamin D intake among men in our study was appreciably higher than those in CaMos, caution must be used when making comparison as Poliquin et al. only considered vitamin D intake from fluid milk and supplements.

Conversely, when intake from food alone is considered, vitamin D intakes among our study group are somewhat lower than that of other men (82). Men in our study had a mean intake
of 5.5 mcg of vitamin D from food alone (mean intake was not stratified by age group), which is considerably lower than the mean intakes reported in the Canadian Community Health Survey (CCHS) of 10.3 mcg and 6.8 mcg per day among British Columbia men age 51 – 70 years and 71 years and older, respectively. Interestingly, the CCHS showed that fewer than 50% of BC men aged 51 – 70 years were able to meet the vitamin D AI with diet alone, and only 20% of men in the national sample were able to meet the AI. A small proportion (approximately 5%) of men in the oldest age group on men in BC met 15 mcg per day with food sources. Despite considering total intake from food and supplements, only approximately 40% of men 51 – 70 years in our study met the AI with dietary means and men 71 years and older continued to fall short. This finding further demonstrates the inadequate contribution of supplemental vitamin D to augment poor dietary intakes in our study population.

While men in our study had calcium intakes comparable to or slightly higher than men in the general population, calcium intake specifically among our participants with PC was higher than previously reported intakes among men with PC in the literature. Planas et al. (132) recently investigated the dietary calcium intake and bone mineral density among 372 men with prostate cancer, including those with and without concurrent treatment with ADT. Dietary daily calcium intake was found to be 639.7 mg in hormone naïve men and 651.0 mg in those undergoing ADT. When using the National Institute of Health recommendation of 1000 mg of calcium per day, Planas et al. found intakes were inadequate in 93% of men (91.5% in hormone-naïve and 93.6% in ADT group), with no significant difference between hormone-naïve and ADT groups. When comparing calcium intake among men in our study with that of Planas et al. of note is a considerable difference in dietary data collection. While our study used a validated food frequency questionnaire and included supplemental intakes, Planas et al. only collected
information on daily dairy intake, which does not account for calcium provided by other foods or by supplemental means.

The fact that calcium intakes of the men in our study were not lower than those of men in the general population suggests that publicity stemming from a correlational study showing higher risk of prostate cancer with increased dairy and calcium intake may have abated. While excess dairy has previously been associated with increased risk (72), a recent meta-analysis (133) found that high intake (greater than 2000 – 2250 mg per day) may be associated with increased risk, though the increase appears to be small. Only four participants in our study (7.5%) had calcium intakes from food and supplements over 2000 mg per day and none surpassed the UL of 2500 mg. While initial concern regarding calcium intake and PC risk has abated in the literature, it is unclear whether the findings of recent studies, indicating that moderate dairy consumption and intake at the AI level is not associated with greater chance for PC, have been adequately disseminated to men.

To our knowledge, this is the first study of its kind to assess vitamin D intakes of men undergoing ADT for the treatment of prostate cancer. While literature is abundant with respect to serum vitamin D levels, to date only one study has also reported on the vitamin D intakes of men with prostate cancer (34). Using a food frequency questionnaire, Conde et al. (34) found that the mean intake of vitamin D among hormone-naïve men was a mere 4.8 ± 5.7 mcg; however, no information was given as to whether supplements were considered in the intake assessment. By comparison, hormone-naïve men in our study consumed approximately 9.7 mcg, 6.0 ± 2.4 mcg from food alone and supplemental vitamin D intake of 3.8 ± 4.4 mcg per day. Daily vitamin D intake was similar among men undergoing ADT at 10.2 ± 6.8 mcg, with contribution of food and supplements of approximately 4.6 and 5.5 mcg, respectively. These results demonstrate that
vitamin D intakes from food among men in our study diagnosed with PC are comparable to previous reports in the PC literature, though little research has been done in this area.

Both calcium and vitamin D supplement use was somewhat similar in our study when compared to that of community-dwelling older men in British Columbia. The majority of men in our study (56.6%) did not take a multivitamin-mineral (MVM), and among those who reported taking a MVM over the past 12 months, only half took one daily. Calcium and vitamin D supplements were used by about a quarter of participants. The BC Nutrition Survey (BCNS) (134) found that vitamin D supplement use varied with age, with 35% of men 71 years and older taking a vitamin D-containing supplement (which may have included a MVM), compared with only 17% of men aged 51-70 years. Among our study participants, there was no difference in MVM, calcium or vitamin D supplement use by age. When both vitamin D contribution from MVMs and individual supplements was considered, however, the prevalence of vitamin D-containing supplement use in our study was appreciably higher, with 34 men (64%) reporting taking either an MVM or vitamin D supplement. The lack of correlation between calcium supplemental intake and diet indicates that men with poor intakes of calcium were no more likely to take supplements to augment their intake than those with higher intakes from food sources alone. Conversely, men with higher intakes of vitamin D were more likely to also take a vitamin D-containing supplement as shown by the positive correlation between vitamin D intake in the diet and supplemental intake.

In June 2007, shortly after data collection for this study was completed, the Canadian Cancer Society (CCS) set forth new recommendations pertaining to vitamin D (114). In a media release, the CCS recommended that all adults living in Canada should consider taking vitamin D supplements of 1000 IU per day during the fall and winter due to known inadequacies in
subcutaneous synthesis in Canada. The recommendations also stipulated that those at higher risk of vitamin D insufficiency based on age, ethnicity and sun exposure, should consider taking 1000 IU vitamin D per day throughout the year. Public reaction to this recommendation was strong, as became evident with stores reporting vitamin D supplements selling out immediately after the media release, and the likelihood that vitamin D supplement use has increased substantially in Canada since 2007 is high.

In a recent population-representative telephone survey of BC adults aged 50 and older (135), 60% of respondents reported use of a supplement containing vitamin D (whether individual supplement or MVM) within the last month, representing a nearly two-fold increase in supplement use from the BCNS data (134), where 36% of respondents reported vitamin D-containing supplement use in the preceding month. Among men specifically, Barr et al. (135) found that only half (51%) used a vitamin D-containing supplement. How these population-wide supplementation recommendations have impacted supplement use among men with prostate cancer is currently unknown, though it is interesting to note that when results of our study were consolidated to include MVMs as a source of vitamin D, 64% of men reported vitamin D-containing supplement use over the past year, which is slightly higher than the recent findings of Barr et al. among older men, although men in our study were highly educated, a significant factor in vitamin D supplement use (135).

5.3. Modifiable Risk Factors for Bone Loss

The characteristics of our study group place them at high risk for bone loss due to their age, Caucasian ethnicity, and in the case of Group A, hypogonadal status. In addition to inadequate calcium and vitamin D intakes, several additional risk factors present among study
participants serve to influence risk of osteoporosis; interestingly, lifestyle factors (relative weight and smoking status) among study participants provide protection, whereas several reported dietary practices may further increase risk.

The majority of study participants (77.4%) were classified as "overweight" or "obese" based on a BMI of 25 or greater. While a risk factor for many other chronic diseases, having a greater weight-to-height ratio has been shown to significantly reduce risk of osteoporosis (10,11,32,34,62,63). In fact, men categorized as "obese" (BMI 30 or greater), as 26.4% of men in our study were, confer the greatest protective benefit against hip fracture (62).

Current literature supports the lifelong avoidance of tobacco use for maintenance of bone health, but acknowledges that quitting smoking is not without reward with respect to risk of fracture (25,67). Over half of the men in our study identified as never having smoked, which provides the greatest reduction in risk; however, only six study participants were recent or current smokers. While former smokers (having quit more than 10 years prior to data collection) are at increased risk when compared with non-smokers, reduction in risk of fracture is considerable when in comparison to those actively smoking within the past five years (67).

Although these lifestyle factors of our study participants impart a reduction in risk of osteoporosis and subsequent fracture, high intake of alcohol, caffeine and sodium oppose this benefit. While a modest alcohol intake has been shown to have a positive effect on bone status, this effect peaked among men at one to two drinks per day (8 – 16 g alcohol) (136). Studies have found alcohol intake over two units (16 g) per day in men corresponds with reduced BMD (136) and increased risk of any fracture, osteoporotic fracture and hip fracture (68). The mean alcohol intake in our study was 6.4 ± 6.9 g per day, with intakes varying widely among men and between-group differences approaching significance. While mean intake was within the
protective range, 64.2% of men drank more than one drink per day (8 g alcohol) and 39.6% had intakes greater than 16 g of alcohol each day. While the DRIs do not specifically comment on acceptable alcohol intake, the PC-diagnosed groups (Groups A and B) derived 7.3 ± 4.8% and 8.4 ± 9.1% of daily total calories from alcohol, respectively, which is considerably higher than the previously recommended less than five percent from the Nutrition Recommendations for Canadians (137). Correspondingly, alcohol intake in our study was higher than among men of a similar age group (51 – 70 years) participating in the BC Nutrition Survey (71), where mean contribution of alcohol to total energy was 3.1%. While the influence of alcohol abstainers on mean intake is apparent, one possible explanation for the high alcohol intake among our older, well-educated group of men is that alcohol intake tends to increase with age and affluence (138,139).

While the negative effect of excess caffeine and sodium intakes on bone health is less well defined than other risk factors, current guidelines recommend that both be used in moderation and limited where possible (25). The intake of caffeine considered to pose a threat to bone status is in excess of 400 mg per day; a level which was surpassed by 43.4% of study participants. At this level of caffeine intake, research demonstrates an increased risk of hip fracture among both men and women. Similarly, high dietary sodium (greater than 2100 mg per day), typically due to intake of table salt and processed foods, has been linked to reduced BMD in men and women (25). Nearly all men in this study (90.6%) had intakes above this level, with 86.8% of participants' sodium intake above the UL of 2300 mg per day. While it may seem our study group had excessively high sodium intakes, they were comparable with those found among BC men aged 51 – 70 years during the BC Nutrition Survey (71).
5.4. Diet and Chemoprevention of Prostate Cancer

There were few significant differences among the groups with respect to reported macronutrient, micronutrient and phytochemical intakes. There is little literature that examines the nutrient intakes of men after prostate cancer diagnosis; instead, a plethora of epidemiological research seeking to elucidate the effect of specific nutrients on disease risk exists. Namely, the intake of fat (particularly saturated and omega-3 fatty acids), vitamin E, selenium, zinc, lycopene, soy and vegetables has been assessed in terms of the relationship between intake, whether by diet or supplement, and primary and secondary preventive strategies (140-142).

High total fat and saturated fat intakes have been implicated in increased rates of obesity, with obesity strongly linked to both prostate cancer development and biochemical recurrence after local therapy (143,144). In two recent, large scale prospective studies, no significant association was found between total or saturated fat (SFA) intakes and risk of prostate cancer (144,145). However, a recent study by Strom et al. (143) showed that likelihood of biochemical failure was greater and time to recurrence shorter among men with SFA in the highest quartile (greater than 37.2 g per day, 14.5% of total calories or more) versus lower intakes (23.4 g per day, 9.9% of total calories or more). Of special note, Strom et al. used a validated diet tool (Block FFQ), a rarity throughout the literature and significant limitation of many prospective studies; however, the FFQ elicited dietary intake in the year prior to diagnosis and no information was collected related to potential diet change after prostate cancer diagnosis or treatment.

Within our study group, percentage of energy derived from total fat, while still within the Acceptable Macronutrient Distribution Ranges (AMDR), was at the upper end of acceptable (33.9% vs. 20 – 35%); however, mean intakes of both Groups A and C fell above the AMDR for
total fat at 35.1% and 36.0%, respectively. When compared to BCNS survey results for men aged 51 – 70 years (71), mean percentage of calories from fat was slightly higher among study participants (33.9% vs. 31.8%). With respect to saturated fat intake, our group of men had intakes similar to those found in the BCNS (24.2 g vs. 24.0 g per day), and compared favourably with the results of Strom et al. in that mean intake was substantially lower than the highest risk quartile, with 9.72 ± 2.17% of total daily calories derived from saturated fat among study participants, which falls within the lower risk quartile described in the aforementioned study (143).

The association between prostate cancer risk and polyunsaturated fatty acids, particularly omega-3 fatty acids, is considerably less clear. While results of observational studies suggested that omega-3s may have a protective role in mediating risk of prostate cancer, recent prospective studies have shown little association (144-146). Concern abounds related to the positive association between prostate cancer risk and linolenic acid intake that has been shown in several case-control studies, however, two recent meta-analyses (147,148) found that, although a modest increase in risk existed when comparing highest and lowest intakes of ALA, no definitive conclusions could be drawn with respect to risk due to study heterogeneity. One of the few prospective studies to examine ALA and risk, the Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial (149) showed no link between dietary sources of ALA and risk, regardless of quartiles of intake. Among men in our study, intake of ALA was considerably lower among study participants compared with findings of the BC Nutrition Survey (71) (1.8 g vs. 2.7 g per day), and 37.7% of individual men in our study fell short of the AI of 1.6 g per day.

The positive effect of fish intake on CVD risk, mediated by dietary intake of docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA), is well-documented; over the
past decade, interest in these long-chain omega-3 fatty acids with respect to primary and secondary prevention of prostate cancer has grown. While there has been little consensus related to intake of DHA and EPA and mitigation of risk (146), recent findings by Chavarro et al. (150) suggest that, although fish and DHA/EPA intake were unrelated to risk of PC, eating fish more often appeared to favourably affect prostate cancer survival in those diagnosed with the disease. Mean fish intake in our study was $34.2 \pm 24.6$ g per day (range $3.3 - 150$ g per day), which corresponds to DHA and EPA intakes of $142.8 \pm 95.7$ mg and $83.8 \pm 65.2$ mg per day, respectively. Interestingly, among men diagnosed with PC in our study, increasing time since diagnosis was positively associated with increased intake of fish and seafood, DHA and EPA, suggesting that men are aware of the proposed benefits of fish with respect to prostate cancer, as well as heart disease. Men in our study had DHA and EPA intakes of approximately double that of average men in the United States (151); however, intakes fell considerably short of global recommendations, which correspond to total intake of 670 mg per day from long-chain omega-3s (based on a 2000 calorie diet); this discrepancy further highlights the need for established DRIs for both DHA and EPA (152).

Vitamin E, as a potent antioxidant, has long been touted in disease prevention, from heart disease to all realms of cancer. In 1998, the results of the Alpha Tocopherol-Beta Carotene Study found that prostate cancer risk was decreased by almost one third in a group of men who received 50 milligrams of supplemental vitamin E per day (153). While promising, this study was conducted in a group of male smokers and, as such, generalizability to the general population of men was unknown. Subsequent epidemiological research was inconclusive; indeed, several large-scale studies found no association between reduction in prostate cancer incidence and increasing dietary and supplemental intakes (140,154). The highly anticipated
SELECT (Selenium and Vitamin E Cancer Prevention Trial) study, investigating the effects of vitamin E (400 IU) and selenium (200 mcg) supplementation in 32,400 North American men, hoped to clarify these questions. While results were expected in 2012, the National Cancer Institute terminated the study early because initial results showed no benefit of supplementation with either vitamin E, selenium or both; in fact, the resultant data indicated a modest, nonsignificant increase in risk of prostate cancer with vitamin E supplementation alone (155).

While our study results showed few significant differences in vitamin and mineral intakes from diet and supplements among the three groups, Group A had significantly higher intakes of vitamin E when compared to the Group B, consuming a mean 95 mg more in supplements particularly. Upon investigation of distribution and normalcy to identify outliers, it was found that four Group A participants (25%) had supplemental vitamin E intakes above 200 mg, whereas Group B and C had only one participant per group with such supplemental intakes.

Given that Group A participants were significantly older, one might assume that this difference in vitamin E intake is merely a product of the weak relationship between age and vitamin E supplemental intakes; however, when study group was entered in bivariate analysis (data not shown), the relationship between age and intake was further attenuated. The possibility of comorbid conditions, such as cardiovascular disease (CVD) and erectile dysfunction, among the significantly-older and hypogonadal Group A participants may also have influenced this trend toward much higher supplemental vitamin E intakes, given the perceived benefits of vitamin E supplementation on libido and CVD progression and risk (156).

When one considers disease trajectory, perhaps the presence of more advanced disease, as evidenced by higher current PSA and ADT use itself, leads to increased supplement use; however, supplemental nutrient intake, as the results showed, was only higher for vitamin E. The
long-reputed connection between vitamin E and prostate cancer risk, as highlighted above, may explain this finding. Recommendations related to vitamin E supplement use and prostate cancer changed dramatically when the results of Miller et al. (157) suggested a positive association between vitamin E supplementation and all-cause mortality. Prior to this research, particularly in association with the launch of the SELECT trial, supplement dosages of 185 – 450 mg vitamin E (400 – 1000 IU) per day for primary and secondary prevention of disease were not uncommon (158). It is possible that a greater proportion of men in Group A continued to follow this outdated recommendation; however, there was no significant relationship between time since diagnosis and vitamin E supplement intake.

Much as with vitamin E, the popularity of selenium as a prostate cancer protector has waned with the release of the SELECT study results (155). Initial interest in selenium was purely coincidental; Clark et al. (159), while investigating risk of skin cancer with 200 mcg selenium supplementation, found a significant reduction in risk of prostate cancer among men receiving supplements versus placebo. Although subsequent research, from case-control, cohort and small interventional studies initially supported the protective effect of selenium, the negative SELECT study results seemed to definitely show a lack of association with reduced risk. The mean intake of selenium among men in our study was 122.1 ± 36.8 mcg per day, with no men failing to meet the EAR of 45 mcg per day. This intake is comparable to that of the average North American man (160).

Another micronutrient that has experienced a similar rise and fall in the realm of prostate cancer prevention is zinc. Initially linked to prostate health due to high concentrations of the mineral in healthy prostates, studies have failed to consistently demonstrate a link between dietary zinc, whether from food or supplements, and prostate cancer incidence. The majority of
results have been mixed with respect to zinc and risk of disease, and little to no support has been shown for the role of zinc secondary prevention of prostate cancer (161). Within the VITamins and Lifestyle (VITAL) cohort investigating dietary supplements and cancer, Gonzalez et al. (162) detected no effect of dietary zinc; long-term use of supplements appeared to decrease risk of advanced disease. Conversely, Zhang et al. (161) found long-term zinc supplementation (defined as 10 or more years) was associated with a doubling of risk in a recent case-control surveillance study of 1706 men with PC. When nutrient intakes from food sources alone are considered, 17% of our participants’ zinc intakes fell below the EAR. With the inclusion of supplemental nutrient intakes, intakes less than EAR improved somewhat but persisted for 11.3%, with one participant consuming more than the UL of 40 mg per day. Mean intake of zinc was comparable to that of BC men among men 51 – 70 years of age (71).

The intake of specific foods, particularly soy products and tomatoes, along with the phytochemicals they provide, has garnered much attention but, as with all natural food intake patterns, demonstrating consistent associations has proven difficult. Interest in soy products originated from epidemiological studies showing significantly reduced rates of prostate cancer among Japanese men; soy content of the diet was thought to be the mediating factor (163). Subsequent in vitro and in vivo studies have demonstrated the disease-reducing effect of soy on prostate cancer due to the estrogenic properties of soy isoflavones, particularly genistein and daizidein (154). Studies of diet, however, have been less conclusive and are difficult to interpret due to heterogeneity. In a recent meta-analysis investigating soy consumption and prostate cancer risk, Yan and Spitznagel (163) found soy was associated with reduction in risk of disease but results remain unclear with respect to the importance of soy food type (fermented vs. unfermented) and intake quantity. The mean soy intake among men in our study was 9.6 ± 18 g
per day (range 0 – 76.2 g); DHQ analysis did not involve quantifying isoflavone intake. It is challenging to compare intakes in our study with those shown in the literature to confer protection as some studies quantify intake, often comparing risk based on quartile of intake, while others simply report soy intake as yes or no. Sonoda et al. (164) reported soy food consumption among 140 case-control subjects and compared intake with risk of prostate cancer. When compared to the lowest quartile of intake (≤ 77 g per day), the highest quartile (≥ 187.2 g per day) had a 51% lower risk of disease development; this highest quartile intake would be equivalent to 1.2 servings of tofu daily. Given the extremely modest soy intakes among men in our study, where the upper range of intake corresponds with low intake levels in Asia, yet high intake-benefit threshold in the literature along with inconclusive isoflavone supplementation results (165), the feasibility and pragmatism of promoting increased soy and isoflavone intake at necessary levels to confer benefit among average North American men is yet to be established (166).

Although a recent review (167) failed to link vegetables and fruit as a food group to reduced risk of prostate cancer, the role of tomato intake and the antioxidant lycopene on mitigating risk continues to evolve (166). Much of the publicity surrounding lycopene stems from a Harvard study in 1995 (168), where researchers found a reduced risk of prostate cancer in men eating 10 or more servings of tomato products per week. The same study found that consuming two to four servings of tomato sauce per week was associated with reduced prostate cancer total risk and the risk of advanced disease. Men in our study consumed, on average, .77 servings of tomato per day, with a range of .7 to 1.98 daily servings. This corresponds with a mean lycopene intake 8.07 ± 5.05 mg per day (range 1.17 – 24.20 mg per day), with one participant in Group A consuming two tablespoons of tomato paste daily for lycopene content.
Intervention trials involving lycopene supplementation have generally focused on secondary prevention, particularly among those with biochemical recurrence or advanced disease, but results have been inconclusive (165). In reviews by the Food and Drug Administration (FDA), Kavanaugh et al. (169,170) found limited evidence to support a link between lycopene intake and reduced risk of prostate cancer, yet tomato consumption, especially that from cooked tomato products, showed a weak association with reduced risk.

While results are promising, conclusive findings within the literature to support dietary guidelines for the chemoprevention of prostate cancer, particularly with respect to supplementation, are currently lacking. Evidence continues to support the tenet of eating a healthy, well-balanced diet rich in vegetables, fruit, whole grains, legumes and fish for mitigation of chronic disease risk, including primary and secondary prevention of prostate cancer.

5.5. Effect of Sociodemographic Characteristics

While few differences with respect to effect of sociodemographic variables were found in this study, those that emerged relating to age, education and food preparation role will be discussed in relation to evident patterns in the literature. Age has been shown to be a strong predictor of diet quality in several studies (171-173), yet our findings relating to the effect of age were minimal and do not correspond with other studies. Age was a significant predictor of vitamin D supplement use in the BC Nutrition Survey (71), where men aged 71 years and older were more likely to use a vitamin D supplement than all other age groups of men. There was no such association in this study. When men were stratified into three age categories, no significant difference in supplemental vitamin D were found, though total vitamin D intake and dietary
vitamin D intake were significantly lower in older men (71 years and older) compared with those 61 – 70 years. Likewise, there were no significant differences on MVM or calcium and vitamin D supplement use based on age. This discrepancy may be due to the relatively small proportion (n=8, 15.1%) of “older” men (those greater than 70 years of age) in this study.

There was a significant difference in dietary intake of DHA by age group (EPA intake approached but did not reach significance), with those 71 years and older with lower intakes when compared with men 61 – 70 years of age. Correspondingly, in a study of community dwelling adults aged 65 years and older, Larrieu et al. (138) found fish intake to decrease with age; the reduced intake of protein and the Meats and Alternatives food group with age is likely a contributing factor to this trend (174).

Among our study participants, there was a significant difference in fluid milk consumption and dietary calcium intake between men who did not participate in food preparation in their household and those reporting an active role. Although data pertaining to marital status were not collected in our study, having a passive role in household food preparation is indicative of residing with at least one other person. One could, thereby, loosely interpret a passive role in food preparation as a measure of social support, as marital status often is. In a cross-sectional analysis of men enrolled in the Osteoporotic Fractures in Men (MrOS) cohort study, Shannon et al. (173) found that marital status was not an independent predictor of diet quality. Studies such as Shannon et al., looking exclusively at older men are limited in discerning differences based on marital status, as this study was with respect to food preparation role, in that the majority of older men (82.4% in Shannon et al.) are married.

Increasing education played a significant role in mediating dietary factors among our study population. The percentage of energy derived from saturated fat significantly differed
among the groups, with men who had obtained a graduate-level degree having significantly lower intake than those with a university degree and those without a degree. Similar trends were seen with dietary cholesterol, meat/poultry/fish and red meat intakes, where graduate degree attainment was associated with significantly lower intakes when compared to the other two groups. Of note, soy product servings were considerably higher among men with a graduate degree. These findings correspond with literature indicating diet quality is positively affected by educational attainment (138,171-173,175). Both Ervin (175) and Riediger and Moghadasian (171) have demonstrated that increased level of education is indicative of healthy eating, particularly in the realm of vegetable and fruit consumption, although in the present study fruit and vegetable intakes were not associated with educational attainment.

5.6. Biochemical Outcomes

While an intended primary outcome of this study, assessment of vitamin D status was complicated by assay quantification of serum levels well outside expected values. Subsequent concerns arose related to the questionable validity of serum parathyroid hormone (PTH) and 25-hydroxyvitamin D (25OHD) results in this study. The normal reference range for PTH is less than 6.4 pmol/L; however, the group mean for this study fell outside of normal at 7.11 ± 2.57 pmol/L. This is significantly higher than PTH levels documented in the literature (125,176-178). In results from the Longitudinal Aging Study Amsterdam, Kuchuk et al. (125) found mean PTH among 643 men over the age of 65 years was 3.1 pmol/L, with a minimum and maximum of 2.4 and 4.3 pmol/L, respectively. Based on the normal reference range, two-thirds of our study participants would be excluded from subsequent analysis on the basis of apparent secondary hyperparathyroidism (HPTH). The prevalence of HPTH is estimated at 1 to 4 in 1000 (179).
Incidence of secondary hyperparathyroidism is predominantly attributable to chronic renal failure (180), and the investigator carefully reviewed the medical charts of all potential participants, excluding men with documented hyperparathyroidism or kidney disease, as well as considering pertinent laboratory results for indications of the aforementioned conditions, namely previous PTH assessment or low glomerular filtration rate.

While cases of secondary hyperparathyroidism due to hypovitaminosis D in the elderly have been shown (181), corresponding vitamin D levels found in this study do not support this etiology for HPTH in our participants, given that over half of the participants had serum 25OHD of 80 nmol/L and up, and two men would be considered at risk for vitamin D intoxication with serum levels of greater than 150 nmol/L. Such levels of 25OHD have been demonstrated to lead to blunting and maximal suppression of PTH, which is clearly not the case based on our laboratory results. In a random sample of older men and women participating in the European Vertebral Osteoporosis Study (EVOS), Gomez-Alonso et al. (178) found no cases of secondary hyperparathyroidism (defined in the study as PTH greater than 6.8 pmol/L) with 25-hydroxyvitamin D levels greater than 100 nmol/L, whereas in the current study seven participants met criteria for HPTH with 25OHD levels at or above 100 nmol/L, with a total of 15 participants (28.3%) meeting criteria for HPTH with 25OHD of greater than 80 nmol/L, considered within the range for maximal PTH suppression. The investigator made every effort to control for potential confounding variables, such as seasonality, history of sun exposure and recent travel, but as shown in the results there was no significant difference in 25OHD levels based on recent travel, as well as relationship between 25OHD and date of serum collection or reported sun exposure history.
Another point of significant concern is the lack of association between PTH and 25OHD, despite intimate physiologic relationship and strong inverse relationship demonstrated throughout the literature. Given that the majority of serum 25OHD values were above the threshold thought to maximally suppress PTH (80 nmol/L), a linear relationship between 25OHD and PTH would not be expected, but rather a plateau of PTH levels above 80 nmol/L. Indeed, this “threshold effect” is supported by the finding that men in our study with serum 25OHD below 80 nmol/L did have significantly higher PTH than those with 25OHD levels above 80 nmol/L. This effect, however, does not sufficiently expound the absence of a relationship between PTH and 25OHD, as the mean PTH level of men in our study is still implausibly high, regardless of 25OHD status.

Preliminary results from the Canadian Health Measure Study (CMHS) (113) investigation of 25OHD levels in the population show a mean 25OHD among older Canadians (60 – 79 years) of 73.5 nmol/L. While the results of our study were considerably higher, they are not entirely impossible and would fall at the 90th percentile of CHMS data for older men. The type of 25OHD recovery methodology used in our study, however, was different from that utilized in the CMHS and may have contributed to the discrepancy in our results. Our study used liquid chromatography-tandem mass spectroscopy (LC/MS), whereas the CHMS was done with the DiaSorin radioimmunoassay (RIA). There is much discussion in the literature (182) as to which of several assays is superior, with some evidence suggesting better recovery and subsequent higher estimates of true 25OHD status with LC/MS (183,184). Although improved recovery could account for the higher-than-expected serum levels of 25OHD in our study, Phinney (185) from the US National Institute of Standards and Technology (NIST) recently presented about the new standard reference material NIST has developed for vitamin D.
Although NIST uses LC/MS for the assay, their "normal serum pool" (based on sera from a normal population) has a value of 65 nmol/L, approximately 30% lower than our study mean, despite the NIST population having a younger mean age than our participants.

Although our 25OHD levels compare poorly with the literature and established reference standards, it is possible that the values may have internal validity, as they were strongly associated with vitamin D intake. While it is likely that participants in our study with higher 25OHD do indeed have better vitamin D status than those with lower 25OHD, no conclusions can confidently be made with respect to the vitamin D status of men in our study group compared with either the prostate cancer or general population. Regardless of concerns regarding assay validity, most importantly, our study results do not show a difference in 25OHD among the three groups. In conjunction with the PTH results, which so poorly corresponded to established physiological patterns and research literature, it was considered probable that the assay results were flawed. As such, aside from presenting descriptive data and correlation analyses, the biochemical indices obtained were not included in additional data analysis to avoid making spurious conclusions with respect to the effects and relationships of the 25-hydroxyvitamin D, parathyroid hormone or vitamin D-binding protein results on other study outcomes.

5.7. Limitations

It is necessary to recognize the limitations of this study in interpreting findings including such issues as participants and methodology.

As a cross-sectional, descriptive study, we are limited in our ability to make causal inferences as data were collected from one time point only. However, the purpose of our research was to determine dietary calcium and vitamin D intakes of men, and the prevalence of those
failing to meet recommendations; therefore, a cross-sectional design was particularly well-suited to our goals and objectives.

The majority of men in our study sample were Caucasian and well-educated, which greatly limits the generalizability of study results to the broader group of men in the general population and those with PC in Canada. Although ethnic minorities and those with less than a university education were underrepresented in the sample, these characteristics are representative of patients currently seen at the large outpatient urology clinic where participants were recruited.

Another significant limitation of this study was sample size. As outlined in the methodology, the sample size calculation was derived from 25OHD as the primary outcome measure. The questionable validity of the 25OHD results, however, makes post-hoc assessment of statistical power challenging. While the 25OHD values obtained in this study may have some relative validity, as was examined in the discussion, and one may appropriately conclude that men treated with ADT did not have lower 25OHD than controls, no comment regarding whether statistical power was reached can be made.

With respect to dietary intake, post-hoc analysis shows that our study reached 8.9% and 4.7% power in comparing calcium and vitamin D intakes between men undergoing ADT and healthy controls, respectively. Given the small effect sizes calculated based on study results for calcium (.224) and vitamin D (.105), we would have required 314 to 1423 participants per group to reach 80% power to detect a significant difference between men in Group A and healthy controls. Statistical power reached for comparing calcium intakes between Groups A and B was slightly higher at 27.3%; however, 67 participants per group would have been necessary based on achieving 80% power.
Self-reported diet history is inherently flawed due to day-to-day fluctuations in food intake and intake-related bias, whereby participants tend to overreport socially desirable, healthy choices and underreport less desirable, unhealthy choices (186). In a recent validation study (187), the DHQ was compared with two commonly used FFQs: the 1995 NCI-Block Health Habits and History Questionnaire and the Willett (purple version) FFQ. One thousand, three hundred and one participants completed the study. Each participant first completed four reference 24-hour dietary recalls over one year, thus determining "true" nutrient intake. Participants were then randomized into one of two groups: one group completed both the DHQ and Block questionnaire; the other group completed the DHQ and Willett FFQ. Based on correlation data, the DHQ was found to be as good as or superior to these Block and Willett instruments (187). Comparable findings from our study and BCNS also lend support to the validity of the DHQ, as the BCNS utilized 24-hour recalls and a semi-quantitative FFQ to estimate nutritional intakes among a large sample of community-dwelling adults in BC.

Our study did not collect information of physical activity, an important modifiable risk factor for bone loss, which would have been a worthy inclusion given the focus on risk factors. Physical activity in men, particularly of the impact type, is associated with greater BMD, with weight-bearing exercise more efficacious than strength, endurance or non-weight-bearing activities (25). As this research was predominantly diet and nutrition-focused, however, the inclusion of a meaningful physical activity history assessment was not considered plausible within the scope and purpose of the project.

Lastly, we did not glean information regarding knowledge level of bone loss risk factors among men. It is unknown what proportion of men in Group A had been made aware of their increased risk for osteoporosis due to hypogonadal status, knew of diet and lifestyle
modifications to ameliorate risk, had been previously screened for bone loss, or had been offered prevention or treatment strategies by their physician. Based on inadequate dietary intakes of both calcium and vitamin D, without accompanying increases in calcium and vitamin D supplement use among men undergoing ADT, and the experience of the study investigator during data collection, a large proportion of men were unaware of the risk of bone loss. In a recent study from Panju et al. (188), the medical management of men undergoing ADT with respect to bone health was investigated. Researchers found that only a small proportion of men were being informed of their increased risk, lifestyle and medications were offered infrequently and physician practices regarding screening and treatment were lackluster.

5.8. Implications for Dietetic Practice

The findings of this study with respect to risk factors for bone loss and low intakes of calcium and vitamin D, in addition to reported inadequate screening and treatment practices among physicians, demonstrate the need for dietitian intervention among men about to start ADT and on an ongoing basis.

While providing patient's with education to promote greater autonomy in self-managing their risk is essential, this cannot, and will not happen without a unified and consistent approach by health care providers. As such, advocating for the inclusion of nutrition counseling recommendations into clinical practice guidelines for men undergoing ADT represents an important first step. Whether this takes the form of referral to a dietitian, provision of approved education materials or both, the incorporation of dietary education as a part of standard practice for those undergoing ADT represents an important first step in mediating risk of bone loss and optimizing quality of life.
It is unknown what access men undergoing ADT have to dietitian services or whether urologic practices commonly have a dietitian on staff. As such, identifying mechanisms for connecting patients to nutrition counseling and advice in the community is vital. A multitude of community nutrition services are available to men, such as outpatient dietitians and HealthLink BC Dietitian Services, yet awareness and use of these programs, among patients and practitioners alike, is currently lacking. Providing urologists and clinic staff with information about these services, their convenience and how to access them, whether by education sessions or simple pamphlets is crucial to ensure that men have access to timely access to reputable services.

While ideally a dietitian would be involved in formulating a nutritional care plan for men undergoing ADT, this may not be practical in all settings. Involving other health disciplines, such as nursing, in disseminating current recommendations for nutrition and physical activity is a pragmatic solution in cases where direct dietitian involvement is not feasible. For instance, men undergoing continuous ADT most often receive three-month depot injections; this time of nursing interaction could be an important teachable moment and a conduit for distributing pertinent nutrition information in this population. Dietitians must liaise with and educate nursing staff and other health disciplines involved in the care of men with prostate cancer to ensure men are made aware of risks and the importance of nutrition in this population.

While reports in the literature regarding the effect of novel, tailored interventions, such as low-fat vegan and ketogenic diets, on disease risk and trajectory are of interest and promise, mainstays of current dietetic practice, such as Eating Well with Canada’s Food Guide, remain the foundation for guiding nutrition counseling among men with prostate cancer given the current state of evidence. Although no definitive evidence exists to support any one dietary intervention
as the gold standard for the primary and secondary prevention of PC, the role of dietary interventions in promoting diet changes protective against the leading cause of death among men with PC, cardiovascular disease, seems prudent. The fact remains, nutrients implicated in PC prevention are abundant in a healthy, well-balanced diet rich in vegetables, fruit, whole grains, legumes and fish, whereas those posited to increase risk are emphasized to be eaten in moderation by the majority of dietitians. While simple and straightforward, disseminating the principles of general, healthy eating to men with and without a diagnosis of PC seems both sensible and appropriate for reduced risk of chronic disease and overall quality of life.

5.9. Directions for Further Research

Inadequate intakes of calcium and vitamin D are widely reported in the literature, yet little is known about the effect of dietary interventions tailored to men at risk for or diagnosed with osteoporosis as the majority of research is focused on post-menopausal women. Men undergoing ADT for the treatment of prostate cancer represent a niche with multiple nutrition education needs: namely reducing risk of prostate cancer progression, osteoporosis and the variety of nutrition-related health concerns associated with ADT. The development and piloting of an intervention specifically aimed at these men with prostate cancer is needed. Of interest would be the efficacy and feasibility of differing intervention styles to reduce burden on the healthcare system, such as individual versus group sessions, or face-to-face nutrition counseling in comparison with telephone intervention or print materials alone.

Bone loss is not the only nutrition-related side effect experienced by men undergoing ADT. Investigations into the effect of ADT on cardiovascular disease risk factors, such as
increased weight, serum cholesterol and triglycerides, are currently lacking but represent another important realm for possible dietitian involvement.

5.10. Conclusions

The majority of older men in this study did not meet age-specific dietary recommendations for calcium and vitamin D. Despite evidence and support indicating the importance of adequate intakes for preservation of bone mineral density among men undergoing ADT, intakes among this group were no different than hormone-naïve men with prostate cancer or healthy controls, regardless of increased recommendations. With ADT being used more frequently, there is a serious need for dietary intervention and guidance in this population of men, who may be entering ADT with compromised nutritional intakes placing them at even greater risk for bone loss.
BIBLIOGRAPHY.


APPENDICES

Appendix A – Sample Size Determination
Appendix B – University of British Columbia Ethics Approval
Appendix C – Vancouver Coastal Health Ethics Approval
Appendix D – Consent Form
Appendix E – Letter of Invitation
Appendix F – Sociodemographic Questionnaire (SDQ)
Appendix G – Diet History Questionnaire (DHQ)
Appendix H – “Hormone Therapy and Bone Health” Handout
Appendix A

Sample Size Determination
The reference values use for sample size determination were:

<table>
<thead>
<tr>
<th>Population</th>
<th>n</th>
<th>Mean 25OHD (nmol/L)</th>
<th>SD</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>A General population</td>
<td>188</td>
<td>52.9</td>
<td>17.2</td>
<td>Rucker et al. (103)</td>
</tr>
<tr>
<td>men and women</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>B Eugonadal men with PC</td>
<td>41 men</td>
<td>33.7</td>
<td>11.62</td>
<td>Stoch et al. (47)</td>
</tr>
<tr>
<td>C Men on ADT</td>
<td>19</td>
<td>38.18</td>
<td>9.68</td>
<td>Stoch et al. (47)</td>
</tr>
</tbody>
</table>

ANOVA calculation

\[ Sm = \sqrt{\frac{\sum (X_i - X_G)^2}{N}} \]

Grand mean \( X_G = 41.59 \)

\[ X_A = (41.59 - 52.9)^2 = 127.92 \]
\[ X_B = (41.59 - 33.7)^2 = 62.25 \]
\[ X_C = (41.59 - 38.18)^2 = 11.63 \]

To account for different sample sizes: \( X_i \times n \)

\[ S_p^2 = \frac{\sum SD^2 (n-1)}{n1 + n2 + n3 - 3} \]

\[ S_p^2 = 254.73 \quad \sqrt{S_p^2} = 15.96 \]

\[ f = \frac{Sm}{\sqrt{S_p^2}} = 0.65 \]

At 80% power, \( n = 8.6 \)

T-test calculation

\[ d = \frac{X_1 - X_2}{s'} \]

\[ d = \frac{52.9 - 38.18}{13.96} \]

\[ X_1 = 52.9 \]
\[ X_2 = 38.18 \]

\[ S_1^2 = (17.2)^2 = 295.84 \]
\[ S_2^2 = (9.68)^2 = 93.70 \]

\[ s' = \sqrt{\frac{S_1^2 + S_2^2}{2}} \]

\[ s' = 13.96 \]
Appendix B

University of British Columbia Ethics Approval
The University of British Columbia
Office of Research Services
Behavioural Research Ethics Board
Suite 102, 6190 Agronomy Road, Vancouver, B.C. V6T 1Z3

CERTIFICATE OF APPROVAL - MINIMAL RISK

PRINCIPAL INVESTIGATOR:

INSTITUTION / DEPARTMENT:

UBC BREC NUMBER:

INSTITUTION(S) WHERE RESEARCH WILL BE CARRIED OUT:

Other locations where the research will be conducted:

CO-INVESTIGATOR(S):

SPONSORING AGENCIES:

PROJECT TITLE:

CERTIFICATE EXPIRY DATE: October 15, 2008

DOCUMENTS INCLUDED IN THIS APPROVAL: DATED APPROVED:

The application for ethical review and the document(s) listed above have been reviewed and the procedures were found to be acceptable on ethical grounds for research involving human subjects.

Approval is issued on behalf of the Behavioural Research Ethics Board and signed electronically by one of the following:

Dr. Jim Rupart, Associate Chair
Dr. M. Judith Lynam, Chair
Dr. Laurie Ford, Associate Chair
Appendix C

Vancouver Coastal Health Ethics Approval
October 17, 2007

Dr. Joyce Davison
Urologic Sciences
Room 6175 – 2775 Laurel St.
Vancouver, B.C.
V5Z 1M9

Vancouver Coastal Health Authority Research Study # V07-0257

FINAL CERTIFICATE OF APPROVAL

TITLE: Promoting Optimum Vitamin D and Calcium Dietary Intake of Patients on Androgen Deprivation Therapy for Recurrent Prostate Cancer Following Radical Prostatectomy

Sponsor: British Columbia Foundation for Prostate Disease

This is to inform you that your project has been approved. Approval has been granted until October 15, 2008 based on the following:

1. UBC Behavioural Research Ethics Board Certificate of Approval H07-02258
2. VCHA Clinical Trials Administration Office Approval

Yours truly,

[Signature]

for:
Dr. Bernie Bressler
Vice-President Research

A joint venture in research between the Vancouver Coastal Health Authority and The University of British Columbia.
Appendix D

Consent Form
The University of British Columbia

Department of Food, Nutrition and Health
Faculty of Land and Food Systems
244 – 2205 East Mall
Vancouver, B.C., Canada V6T 1Z4

CONSENT FORM

Title of Study: Assessing Vitamin D Status of Men Undergoing Androgen Deprivation Therapy for the Treatment of Prostate Cancer

Principal Investigator:

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604-xxx-xxxx

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604-xxx-xxxx

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604-xxx-xxxx

Introduction:

You are being invited to participate in this research study because you belong to one of three groups: (1) Group A includes men with prostate cancer who are currently receiving hormone therapy; (2) Group B includes men with prostate cancer who have not received hormone therapy; or (3) Group C includes healthy men who have not been diagnosed with prostate cancer.

It is entirely up to you whether you want to take part in this study or not. The health care that you usually get will not be changed in anyway by the choice you make about taking part in this study. You can change your mind and withdraw from this study at any time.
Background:

Prostate cancer is the most commonly diagnosed cancer in men, affected one in seven men during his lifetime. Although treatments such as surgery and radiation offer a very good prognosis for the majority of men, in approximately 35% of men the prostate cancer may return. Hormone therapy (androgen deprivation) is the preferred treatment for men with recurrent prostate cancer, but may have significant side effects. One of the most serious health-related side effects of hormone therapy is bone loss, which increases a man’s risk for osteoporosis and fracture (breaking a bone).

Vitamin D plays an important role in bone health and may reduce the risk of fracture among older men and women. Despite the benefits of vitamin D on bone health, some recent evidence suggests that many men do not meet vitamin D recommendations (from food and supplements) and may have poor vitamin D status as a result. To date, no studies have compared the vitamin D intake and status of men treated with hormone therapy, those not treated and men without prostate cancer.

Purpose:

The purpose of this project will be to assess the vitamin D status of three age-matched groups: men undergoing hormone therapy for the treatment of prostate cancer; men with prostate cancer who have not received hormone therapy; and men who do not have prostate cancer.

Who can participate?

You are being asked to participate because you belong to one of three groups of men:

Group A – Men with prostate cancer who are being treated with hormone therapy (for six months of longer) with no evidence of cancer that has spread to bone and have not been prescribed bone-sparing medications.

Group B – Men with prostate cancer who have never been treated with hormone therapy, show no evidence of cancer that has spread to bone and have not been prescribed bone-sparing medications.

Group C – Healthy men who have not been diagnosed with prostate cancer.

Who should not participate?

Men who have: a pre-existing condition that may affect calcium, vitamin D or bone metabolism; prior or present kidney failure; active alcoholism; liver disease; overactive thyroid gland; over- or under-active parathyroid gland; mental illness; or are unable to read and speak English should not participate in this study.
What does the study involve?

Overview of the Study

This study is taking place at the Prostate Centre at Vancouver General Hospital and will involve the participation of 45 male volunteers assigned to one of three groups (15 men per group). The study involves a one-time blood sample for the measurement of your vitamin D status and one interview where your usual intake of specific foods will be determined.

To determine whether you meet the study criteria (Groups A and B), your medical chart will be reviewed for information on: prostate cancer diagnosis; treatment chosen; hormone therapy use and length of therapy; medical history; and prescription medications. To determine whether men in Group C are eligible, you will be asked a series of questions over the telephone.

Study Procedures

If you agree to take part in this study, the procedures you can expect will include the following:

Blood sample

You will be asked to give a blood sample at a laboratory facility of your choosing between the hours of 7:30 and 10:30 am. The blood sample should take approximately 15 minutes. This blood sample will be used to measure the amount of vitamin D (25-hydroxyvitamin D), parathyroid hormone and testosterone that is in your blood.

Interview

Once you have given a blood sample, you will be asking to complete an interview at a place most convenient for you: at your home, at the Prostate Centre clinic or at another site. The entire interview will take approximately one-and-a-half hours.

The interview will include a short questionnaire asking a few questions related to your education, ethnicity, tobacco use and holiday travel. This questionnaire will take 5 minutes to complete.

The majority of the interview will consist of a food frequency questionnaire. The food frequency questionnaire will be used to determine your usual food intake by asking you to report how often you have eaten particular foods over the past year. This food frequency questionnaire takes approximately one hour to complete. There will be time at the end of the interview for questions, should you have any.

Risk and Potential Benefits:

There are no anticipated risks or harms associated with participating in this study.

No one knows whether or not you will benefit directly from this study. There may or may not be direct benefits to you from taking part in this study. We hope that the information learned from
this study can be used in the future to benefit men with prostate cancer being treated with hormone therapy.

**Consent:**

It is entirely up to you whether you want to take part in this study or not. The health care that you usually get will not be changed in anyway by the choice you make about taking part in this study. You can change your mind and withdraw from this study at any time. By signing this consent form, you are agreeing to participate in this study and acknowledge that you have received a copy of this consent form for your own records. By signing this consent form, you do not waive any of your legal rights.

**Study Costs:**

Personal expenses may include parking costs based upon the site of interview; these costs will not be reimbursed.

You will not be paid for participating in this study. Following the interview, however, each participant will receive a package with information on: osteoporosis (bone loss) prevention; how to assess your calcium intake; and nutrition and prostate cancer.

**Confidentiality:**

Your confidentiality will be respected. All forms and responses will be kept completely confidential. All forms will be coded with a number and only the principal investigators (or their designate) will have access to the master list. Data will be kept in a locked filing cabinet and only used for the purpose of this research.

If you have any questions regarding this study or desire further information you may contact the principal investigator, Susan Barr at 604-xxx-xxxx, or Kristin Wiens at 604-xxx-xxxx.

If you have any concerns about your rights as a research subject and/or you experiences while participating in this study, you may contact the ‘Research Subject Information Line in the University of British Columbia, Office of Research Services’ at 604-822-8598.
I have read the above information and I have had a chance to ask any questions about the study and my involvement. I understand what I have to do and what will happen if I take part in this study. I freely choose to take part in this study and I have a copy of the consent form.

Printed name of subject

Signature of subject

Witness

Signature of witness

Principal Investigator or designate

Signature of PI or designate

Date

Would you like to receive the results of this study by mail?
Yes, I would like to receive the results of this study
No, I would not like to receive the results of this study

Signature of subject

Date
Appendix E

Letter of Invitation
Vitamin D Status of Men Undergoing Androgen Deprivation Therapy for the Treatment of Prostate Cancer

We are inviting men who have been diagnosed with prostate cancer and are currently taking hormone therapy; men with prostate cancer who have not received hormone therapy; and men who do not have prostate cancer to participate in this research study.

The purpose of this study is to assess the vitamin D status of three groups: men undergoing hormone therapy for the treatment of prostate cancer; men of a similar age with prostate cancer who have not been given hormones and men of a similar age who do not have prostate cancer.

Investigator Contact: Kristin Wiens (604) xxx-xxxx

What the study involves? Approximately one to two hours of your time.

If you choose to be involved in this study, you will be asked to give a blood sample at a laboratory facility of your choosing between the hours of 7:30 and 10:30 am. The blood sample should take approximately 15 minutes.

Once you have given a blood sample, you will be asking to complete an interview with the primary investigator at your home, the Prostate Centre clinic or another place most convenient for you. The entire interview will take approximately one and a half hours. It will include a short questionnaire asking a few questions related to your education, ethnicity, tobacco use and holiday travel. This questionnaire will take 5 minutes to complete. The majority of the interview will consist of a food frequency questionnaire administered by the primary investigator. The food frequency questionnaire will be used to determine your usual dietary intake by asking you to indicate how often you have eaten particular foods over the past year. This food frequency questionnaire takes approximately one hour to complete.

All forms and responses will be kept completely confidential.

Thank you for your assistance with this very important project.
Appendix F

Sociodemographic Questionnaire (SDQ)
Sociodemographic Questionnaire

Date:_________________________ IDN:_________________________

a) 

b) 

Education: (highest level of school completed)

- 1. Less than High School Diploma
- 2. High School Diploma
- 3. Trade/Community College Certificate
- 4. University Degree
- 5. Graduate Degree (Graduate – Masters, Ph.D., M.D., etc.)

Ethnicity: To which ethnic or cultural group do you most closely identify with?

- Caucasian/white
- Black
- First Nations
- Latin American
- Arab
- Chinese
- Japanese
- Korean
- South East Asian (e.g., Vietnamese, Filipino)
- South Asian (e.g. East Indian, Pakistani…)
- Other: (please specify) ____________________________

Tobacco use: Which statement best reflects your current tobacco use?

- 1. Never smoked
- 2. Former smoker (have not smoked for 10 years or more)
- 3. Recent smoker (quit smoking less than 10 years ago)
- 4. Current smoker

Holiday travel: In the last three months, have you visited below 40°N latitude for one day or more (south of New York, NY; San Francisco, CA; Denver, CO; Beijing, China)?

- 1. No
- 2. Yes

Location(s): ____________________________________________
Appendix G

Diet History Questionnaire
[Scanned DHQ – 36 pages]
GENERAL INSTRUCTIONS:

- Answer each question as best you can. Estimate if you are not sure. A guess is better than leaving a blank.
- Use only a black ball-point pen. Do not use a pencil or felt-tip pen. Do not fold, staple, or tear the pages.
- Put an X in the box next to your answer.
- If you make any changes, cross out the incorrect answer and put an X in the box next to the correct answer. Also draw a circle around the correct answer.
- If you mark NEVER, NO, or DON'T KNOW for a question, please follow any arrows or instructions that direct you to the next question.

BEFORE TURNING THE PAGE, PLEASE COMPLETE THE FOLLOWING QUESTIONS.

Today's date:

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In what month were you born?

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Are you male or female?

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BAR CODE LABEL OR SUBJECT ID HERE
1. Over the past 12 months, how often did you drink tomato juice or vegetable juice?
   - □ NEVER (GO TO QUESTION 2)
   - □ 1 time per month or less
   - □ 2–3 times per month
   - □ 1–2 times per week
   - □ 3–4 times per week
   - □ 5–6 times per week

1a. Each time you drank tomato juice or vegetable juice, how much did you usually drink?
   - □ Less than ¾ cup (6 ounces)
   - □ ¾ to 1 cup (6 to 10 ounces)
   - □ More than 1 cup (10 ounces)

2. Over the past 12 months, how often did you drink orange juice or grapefruit juice?
   - □ NEVER (GO TO QUESTION 3)
   - □ 1 time per month or less
   - □ 2–3 times per month
   - □ 1–2 times per week
   - □ 3–4 times per week
   - □ 5–6 times per week

2a. Each time you drank orange juice or grapefruit juice, how much did you usually drink?
   - □ Less than ¾ cup (6 ounces)
   - □ ¾ to 1 cup (6 to 10 ounces)
   - □ More than 1 cup (10 ounces)

3. Over the past 12 months, how often did you drink other 100% fruit juice or 100% fruit juice mixtures (such as apple, grape, pineapple, or others)?
   - □ NEVER (GO TO QUESTION 4)
   - □ 1 time per month or less
   - □ 2–3 times per month
   - □ 1–2 times per week
   - □ 3–4 times per week
   - □ 5–6 times per week

3a. Each time you drank other fruit juice or fruit juice mixtures, how much did you usually drink?
   - □ Less than ¾ cup (6 ounces)
   - □ ¾ to 1 cup (6 to 10 ounces)
   - □ More than 1 cup (10 ounces)

4. How often did you drink other fruit drinks (such as cranberry cocktail, Hi-C, lemonade, or Kool-Aid, diet or regular)?
   - □ NEVER (GO TO QUESTION 5)
   - □ 1 time per month or less
   - □ 2–3 times per month
   - □ 1–2 times per week
   - □ 3–4 times per week
   - □ 5–6 times per week

4a. Each time you drank fruit drinks, how much did you usually drink?
   - □ Less than 1 cup (8 ounces)
   - □ 1 to 2 cups (8 to 16 ounces)
   - □ More than 2 cups (16 ounces)

4b. How often were your fruit drinks diet or sugar-free drinks?
   - □ Almost never or never
   - □ About ¼ of the time
   - □ About ½ of the time
   - □ About ¾ of the time
   - □ Almost always or always

5. How often did you drink milk as a beverage (NOT in coffee, NOT in cereal)? (Please include chocolate milk and hot chocolate.)
   - □ NEVER (GO TO QUESTION 6)
   - □ 1 time per month or less
   - □ 2–3 times per month
   - □ 1–2 times per week
   - □ 3–4 times per week
   - □ 5–6 times per week

5a. Each time you drank milk as a beverage, how much did you usually drink?
   - □ Less than 1 cup (8 ounces)
   - □ 1 to 1½ cups (8 to 12 ounces)
   - □ More than 1½ cups (12 ounces)

5b. What kind of milk did you usually drink?
   - □ Whole milk
   - □ 2% fat milk
   - □ 1% fat milk
   - □ Skim, nonfat, or ¼% fat milk
   - □ Soy milk
   - □ Rice milk
   - □ Other
This is a sample form. Do not use for scanning.

Over the **past 12 months**...

6. How often did you drink meal replacement, energy, or high-protein beverages such as Instant Breakfast, Ensure, Slimfast, Sustacal or others?
   - [ ] NEVER (GO TO QUESTION 7)
   - [ ] 1 time per month or less
   - [ ] 2–3 times per month
   - [ ] 1–2 times per week
   - [ ] 3–4 times per week
   - [ ] 5–6 times per week

6a. Each time you drank meal replacement beverages, how much did you usually drink?
   - [ ] Less than 1 cup (8 ounces)
   - [ ] 1 to 1½ cups (8 to 12 ounces)
   - [ ] More than 1½ cups (12 ounces)

7. Over the past 12 months, did you drink soft drinks, soda, or pop?
   - [ ] NO (GO TO QUESTION 8)
   - [ ] YES

7a. How often did you drink soft drinks, soda, or pop IN THE SUMMER?
   - [ ] NEVER
   - [ ] 1 time per month or less
   - [ ] 2–3 times per month
   - [ ] 1–2 times per week
   - [ ] 3–4 times per week
   - [ ] 5–6 times per week

7b. How often did you drink soft drinks, soda, or pop DURING THE REST OF THE YEAR?
   - [ ] NEVER
   - [ ] 1 time per month or less
   - [ ] 2–3 times per month
   - [ ] 1–2 times per week
   - [ ] 3–4 times per week
   - [ ] 5–6 times per week

7c. Each time you drank soft drinks, soda, or pop, how much did you usually drink?
   - [ ] Less than 12 ounces or less than 1 can or bottle
   - [ ] 12 to 16 ounces or 1 can or bottle
   - [ ] More than 16 ounces or more than 1 can or bottle

7d. How often were these soft drinks, soda, or pop diet or sugar-free?
   - [ ] Almost never or never
   - [ ] About ¼ of the time
   - [ ] About ½ of the time
   - [ ] About ¾ of the time
   - [ ] Almost always or always

7e. How often were these soft drinks, soda, or pop caffeine-free?
   - [ ] Almost never or never
   - [ ] About ¼ of the time
   - [ ] About ½ of the time
   - [ ] About ¾ of the time
   - [ ] Almost always or always

8. Over the past 12 months, did you drink beer?
   - [ ] NO (GO TO QUESTION 9)
   - [ ] YES

8a. How often did you drink beer IN THE SUMMER?
   - [ ] NEVER
   - [ ] 1 time per month or less
   - [ ] 2–3 times per month
   - [ ] 1–2 times per week
   - [ ] 3–4 times per week
   - [ ] 5–6 times per week

8b. How often did you drink beer DURING THE REST OF THE YEAR?
   - [ ] NEVER
   - [ ] 1 time per month or less
   - [ ] 2–3 times per month
   - [ ] 1–2 times per week
   - [ ] 3–4 times per week
   - [ ] 5–6 times per week

8c. Each time you drank beer, how much did you usually drink?
   - [ ] Less than a 12-ounce can or bottle
   - [ ] 1 to 3 12-ounce cans or bottles
   - [ ] More than 3 12-ounce cans or bottles

Question 8 appears in the next column

Question 9 appears on the next page
This is a sample form. Do not use for scanning.

Over the past 12 months...

9. How often did you drink wine or wine coolers?
   - NEVER (GO TO QUESTION 10)
   - 1 time per month or less
   - 2—3 times per month
   - 1—2 times per week
   - 3—4 times per week
   - 5—6 times per week

9a. Each time you drank wine or wine coolers, how much did you usually drink?
   - Less than 5 ounces or less than 1 glass
   - 5 to 12 ounces or 1 to 2 glasses
   - More than 12 ounces or more than 2 glasses

10. How often did you drink liquor or mixed drinks?
   - NEVER (GO TO QUESTION 11)
   - 1 time per month or less
   - 2—3 times per month
   - 1—2 times per week
   - 3—4 times per week
   - 5—6 times per week

10a. Each time you drank liquor or mixed drinks, how much did you usually drink?
   - Less than 1 shot of liquor
   - 1 to 3 shots of liquor
   - More than 3 shots of liquor

11. Over the past 12 months, did you eat oatmeal, grits, or other cooked cereal?
   - NO (GO TO QUESTION 12)
   - YES

11a. How often did you eat oatmeal, grits, or other cooked cereal IN THE WINTER?
   - NEVER
   - 1—6 times per winter
   - 7—11 times per winter
   - 1 time per month
   - 2—3 times per month
   - 1 time per week

11b. How often did you eat oatmeal, grits, or other cooked cereal DURING THE REST OF THE YEAR?
   - NEVER
   - 1—6 times per year
   - 7—11 times per year
   - 1 time per month
   - 2—3 times per month
   - 1 time per week

11c. Each time you ate oatmeal, grits, or other cooked cereal, how much did you usually eat?
   - Less than ¼ cup
   - ¼ to 1¼ cups
   - More than 1¼ cups

12. How often did you eat cold cereal?
   - NEVER (GO TO QUESTION 13)
   - 1—6 times per year
   - 7—11 times per year
   - 1 time per month
   - 2—3 times per month
   - 1 time per week

12a. Each time you ate cold cereal, how much did you usually eat?
   - Less than 1 cup
   - 1 to 2½ cups
   - More than 2½ cups

12b. How often was the cold cereal you ate Total, Product 19, or Right Start?
   - Almost never or never
   - About ¼ of the time
   - About ½ of the time
   - About ¾ of the time
   - Almost always or always

12c. How often was the cold cereal you ate All Bran, Fiber One, 100% Bran, or Bran Buds?
   - Almost never or never
   - About ¼ of the time
   - About ½ of the time
   - About ¾ of the time
   - Almost always or always

Question 12 appears in the next column

Question 13 appears on the next page
Over the past 12 months...

12d. How often was the cold cereal you ate some other bran or fiber cereal (such as Cheerios, Shredded Wheat, Raisin Bran, Bran Flakes, Grape-Nuts, Granola, Wheaties, or Healthy Choice)?

- Almost never or never
- About ¼ of the time
- About ½ of the time
- Almost always or always

12e. How often was the cold cereal you ate any other type of cold cereal (such as Corn Flakes, Rice Krispies, Frosted Flakes, Special K, Froot Loops, Cap'n Crunch, or others)?

- Almost never or never
- About ¼ of the time
- About ½ of the time
- Almost always or always

12f. Was milk added to your cold cereal?

- NO (GO TO QUESTION 13)
- YES

12g. What kind of milk was usually added?

- Whole milk
- 2% fat milk
- 1% fat milk
- Skim, nonfat, or ½% fat milk
- Soy milk
- Rice milk
- Other

12h. Each time milk was added to your cold cereal, how much was usually added?

- Less than ½ cup
- ½ to 1 cup
- More than 1 cup

13. How often did you eat applesauce?

- NEVER (GO TO QUESTION 14)

13a. Each time you ate applesauce, how much did you usually eat?

- Less than ½ cup
- ½ to 1 cup
- More than 1 cup

14. How often did you eat apples?

14a. Each time you ate apples, how many did you usually eat?

15. How often did you eat pears (fresh, canned, or frozen)?

15a. Each time you ate pears, how many did you usually eat?

16. How often did you eat bananas?
Over the *past 12 months*...  

16a. Each time you ate bananas, how many did you usually eat?  
- [ ] Less than 1 banana  
- [ ] 1 banana  
- [ ] More than 1 banana

17. How often did you eat dried fruit, such as prunes or raisins (not including dried apricots)?  
- [ ] NEVER (GO TO QUESTION 18)  
- [ ] 1–6 times per year  
- [ ] 7–11 times per year  
- [ ] 1 time per month  
- [ ] 2–3 times per month  
- [ ] 1 time per week  
- [ ] 2 or more times per day

17a. Each time you ate dried fruit, how much did you usually eat (not including dried apricots)?  
- [ ] Less than 2 tablespoons  
- [ ] 2 to 5 tablespoons  
- [ ] More than 5 tablespoons

18. Over the *past 12 months*, did you eat peaches, nectarines, or plums?  
- [ ] NO (GO TO QUESTION 19)  
- [ ] YES

18a. How often did you eat fresh peaches, nectarines, or plums WHEN IN SEASON?  
- [ ] NEVER  
- [ ] 1–6 times per season  
- [ ] 7–11 times per season  
- [ ] 1 time per month  
- [ ] 2–3 times per month  
- [ ] 1 time per week  
- [ ] 2 or more times per day

18b. How often did you eat peaches, nectarines, or plums (fresh, canned, or frozen) DURING THE REST OF THE YEAR?  
- [ ] NEVER  
- [ ] 1–6 times per year  
- [ ] 7–11 times per year  
- [ ] 1 time per month  
- [ ] 2–3 times per month  
- [ ] 1 time per week  
- [ ] 2 or more times per day

18c. Each time you ate peaches, nectarines, or plums, how much did you usually eat?  
- [ ] Less than 1 fruit or less than ½ cup  
- [ ] 1 to 2 fruits or ½ to ¾ cup  
- [ ] More than 2 fruits or more than ¾ cup

19. How often did you eat grapes?  
- [ ] NEVER (GO TO QUESTION 20)  
- [ ] 1–6 times per year  
- [ ] 7–11 times per year  
- [ ] 1 time per month  
- [ ] 2–3 times per month  
- [ ] 1 time per week  
- [ ] 2 or more times per day

19a. Each time you ate grapes, how much did you usually eat?  
- [ ] Less than ½ cup or less than 10 grapes  
- [ ] ½ to 1 cup or 10 to 30 grapes  
- [ ] More than 1 cup or more than 30 grapes

20. Over the *past 12 months*, did you eat cantaloupe?  
- [ ] NO (GO TO QUESTION 21)  
- [ ] YES

20a. How often did you eat fresh cantaloupe WHEN IN SEASON?  
- [ ] NEVER  
- [ ] 1–6 times per season  
- [ ] 7–11 times per season  
- [ ] 1 time per month  
- [ ] 2–3 times per month  
- [ ] 1 time per week  
- [ ] 2 or more times per day

20b. How often did you eat fresh or frozen cantaloupe DURING THE REST OF THE YEAR?  
- [ ] NEVER  
- [ ] 1–6 times per year  
- [ ] 7–11 times per year  
- [ ] 1 time per month  
- [ ] 2–3 times per month  
- [ ] 1 time per week  
- [ ] 2 or more times per day
This is a sample form. Do not use for scanning.

Over the **past 12 months**...

20c. Each time you ate cantaloupe, how much did you usually eat?

- Less than ¼ melon or less than ½ cup
- ¼ melon or ½ to 1 cup
- More than ¼ melon or more than 1 cup

21. Over the **past 12 months**, did you eat melon, other than cantaloupe (such as watermelon or honeydew)?

- NO (GO TO QUESTION 22)
- YES

21a. How often did you eat fresh melon, other than cantaloupe (such as watermelon or honeydew) **WHEN IN SEASON**?

- NEVER
- 1–6 times per season
- 7–11 times per season
- 1 time per month
- 2–3 times per month
- 1 time per week

21b. How often did you eat fresh or frozen melon, other than cantaloupe (such as watermelon or honeydew) **DURING THE REST OF THE YEAR**?

- NEVER
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per month
- 1 time per week

21c. Each time you ate melon other than cantaloupe, how much did you usually eat?

- Less than ½ cup or 1 small wedge
- ½ to 2 cups or 1 medium wedge
- More than 2 cups or 1 large wedge

22. Over the **past 12 months**, did you eat strawberries?

- NO (GO TO QUESTION 23)
- YES

22a. How often did you eat fresh strawberries **WHEN IN SEASON**?

- NEVER
- 1–6 times per season
- 7–11 times per season
- 1 time per month
- 2–3 times per month
- 1 time per week

22b. How often did you eat fresh or frozen strawberries **DURING THE REST OF THE YEAR**?

- NEVER
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per month
- 1 time per week

22c. Each time you ate strawberries, how much did you usually eat?

- Less than ¼ cup or less than 3 berries
- ¼ to ½ cup or 3 to 8 berries
- More than ½ cup or more than 8 berries

23. Over the **past 12 months**, did you eat oranges, tangerines, or tangelos?

- NO (GO TO QUESTION 24)
- YES

23a. How often did you eat fresh oranges, tangerines, or tangelos **WHEN IN SEASON**?

- NEVER
- 1–6 times per season
- 7–11 times per season
- 1 time per month
- 2–3 times per month
- 1 time per week

Question 22 appears in the next column

Question 24 appears on the next page
Over the past 12 months...

23b. How often did you eat oranges, tangerines, or tangelos (fresh or canned) DURING THE REST OF THE YEAR?

- NEVER
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per month
- 1 time per week

23c. Each time you ate oranges, tangerines, or tangelos, how many did you usually eat?

- Less than 1 fruit
- 1 fruit
- More than 1 fruit

24. Over the past 12 months, did you eat grapefruit?

- NO (GO TO QUESTION 25)
- YES

24a. How often did you eat fresh grapefruit WHEN IN SEASON?

- NEVER
- 1–6 times per season
- 7–11 times per season
- 1 time per month
- 2–3 times per month
- 1 time per week

24b. How often did you eat grapefruit (fresh or canned) DURING THE REST OF THE YEAR?

- NEVER
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per month
- 1 time per week

24c. Each time you ate grapefruit, how much did you usually eat?

- Less than ½ grapefruit
- ½ grapefruit
- More than ½ grapefruit

25. How often did you eat other kinds of fruit?

- NEVER (GO TO QUESTION 26)
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per month
- 1 time per week

25a. Each time you ate other kinds of fruit, how much did you usually eat?

- Less than ¼ cup
- ¼ to ½ cup
- More than ½ cup

26. How often did you eat COOKED greens (such as spinach, turnip, collard, mustard, chard, or kale)?

- NEVER (GO TO QUESTION 27)
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per month
- 1 time per week

26a. Each time you ate COOKED greens, how much did you usually eat?

- Less than ¼ cup
- ¼ to 1 cup
- More than 1 cup

27. How often did you eat RAW greens (such as spinach, turnip, collard, mustard, chard, or kale)? (We will ask about lettuce later.)

- NEVER (GO TO QUESTION 28)
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per month
- 1 time per week

27a. Each time you ate RAW greens, how much did you usually eat?

- Less than ¼ cup
- ¼ to 1 cup
- More than 1 cup

Question 25 appears in the next column

Question 28 appears on the next page
## Sample Form for Diet Recall

Over the past 12 months...

### 28. How often did you eat coleslaw?

- **NEVER** (GO TO QUESTION 29)
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per month
- 1 time per week

28a. Each time you ate coleslaw, how much did you usually eat?

- Less than ¼ cup
- ¼ to ½ cup
- More than ½ cup

### 29. How often did you eat sauerkraut or cabbage (other than coleslaw)?

- **NEVER** (GO TO QUESTION 30)
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per month
- 1 time per week

29a. Each time you ate sauerkraut or cabbage, how much did you usually eat?

- Less than ¼ cup
- ¼ to 1 cup
- More than 1 cup

### 30. How often did you eat carrots (fresh, canned, or frozen)?

- **NEVER** (GO TO QUESTION 31)
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per month
- 1 time per week

30a. Each time you ate carrots, how much did you usually eat?

- Less than ¼ cup or less than 2 baby carrots
- ¼ to ½ cup or 2 to 5 baby carrots
- More than ½ cup or more than 5 baby carrots

### 31. How often did you eat string beans or green beans (fresh, canned, or frozen)?

- **NEVER** (GO TO QUESTION 32)
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per month
- 1 time per week

31a. Each time you ate string beans or green beans, how much did you usually eat?

- Less than ¼ cup
- ¼ to 1 cup
- More than 1 cup

### 32. How often did you eat peas (fresh, canned, or frozen)?

- **NEVER** (GO TO QUESTION 33)
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per month
- 1 time per week

32a. Each time you ate peas, how much did you usually eat?

- Less than ¼ cup
- ¼ to ½ cup
- More than ½ cup

### 33. Over the past 12 months, did you eat corn?

- **NO** (GO TO QUESTION 34)
- **YES**

33a. How often did you eat fresh corn WHEN IN SEASON?

- **NEVER**
- 1–6 times per season
- 7–11 times per season
- 1 time per month
- 2–3 times per month
- 1 time per week

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Question 31 appears in the next column.

Question 34 appears on the next page.
Over the past 12 months...

33b. How often did you eat corn (fresh, canned, or frozen) DURING THE REST OF THE YEAR?

- NEVER
- 1—6 times per year
- 7—11 times per year
- 1 time per month
- 2—3 times per month
- 1 time per week
- 2 or more times per day

33c. Each time you ate corn, how much did you usually eat?

- Less than 1 ear or less than 1/2 cup
- 1 ear or 1/2 to 1 cup
- More than 1 ear or more than 1 cup

34. Over the past 12 months, how often did you eat broccoli (fresh or frozen)?

- NEVER (GO TO QUESTION 35)

- 1—6 times per year
- 7—11 times per year
- 1 time per month
- 2—3 times per month
- 1 time per week
- 2 or more times per day

34a. Each time you ate broccoli, how much did you usually eat?

- Less than 1/4 cup
- 1/4 to 1 cup
- More than 1 cup

35. How often did you eat cauliflower or Brussels sprouts (fresh or frozen)??

- NEVER (GO TO QUESTION 36)

- 1—6 times per year
- 7—11 times per year
- 1 time per month
- 2—3 times per month
- 1 time per week
- 2 or more times per day

35a. Each time you ate cauliflower or Brussels sprouts, how much did you usually eat?

- Less than 1/4 cup
- 1/4 to 1 cup
- More than 1/4 cup

36. How often did you eat mixed vegetables?

- NEVER (GO TO QUESTION 37)

- 1—6 times per year
- 7—11 times per year
- 1 time per month
- 2—3 times per month
- 1 time per week
- 2 or more times per day

36a. Each time you ate mixed vegetables, how much did you usually eat?

- Less than 1/2 cup
- 1/2 to 1 cup
- More than 1 cup

37. How often did you eat onions?

- NEVER (GO TO QUESTION 38)

- 1—6 times per year
- 7—11 times per year
- 1 time per month
- 2—3 times per month
- 1 time per week
- 2 or more times per day

37a. Each time you ate onions, how much did you usually eat?

- Less than 1 slice or less than 1 tablespoon
- 1 slice or 1 to 4 tablespoons
- More than 1 slice or more than 4 tablespoons

38. Now think about all the cooked vegetables you ate in the past 12 months and how they were prepared. How often were your vegetables COOKED WITH some sort of fat, including oil spray? (Please do not include potatoes.)

- NEVER (GO TO QUESTION 39)

- 1—6 times per year
- 7—11 times per year
- 1 time per month
- 2—3 times per month
- 1 time per week
- 2 or more times per day

Question 36 appears in the next column

Question 39 appears on the next page
Over the past 12 months...

38a. Which fats were usually added to your vegetables DURING COOKING? (Please do not include potatoes. Mark all that apply.)
- Margarine (including low-fat)
- Butter (including low-fat)
- Lard, fatback, or bacon fat
- Olive oil
- Canola or rapeseed oil
- Oil spray, such as Pam or others
- Other kinds of oils
- None of the above

39. Now, thinking again about all the cooked vegetables you ate in the past 12 months, how often was some sort of fat, sauce, or dressing added AFTER COOKING OR AT THE TABLE? (Please do not include potatoes.)
- NEVER (GO TO QUESTION 40)
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per month
- 1–2 times per week
- 3 or more times per week

39a. Which fats, sauces, or dressings were usually added AFTER COOKING OR AT THE TABLE? (Please do not include potatoes. Mark all that apply.)
- Margarine (including low-fat)
- Salad dressing
- Butter (including low-fat)
- Cheese sauce
- Lard, fatback, or bacon fat
- White sauce
- Other
- None of the above

39b. If margarine, butter, lard, fatback, or bacon fat was added to your cooked vegetables AFTER COOKING OR AT THE TABLE, how much did you usually add?
- Did not usually add these
- Less than 1 teaspoon
- 1 to 3 teaspoons
- More than 3 teaspoons

39c. If salad dressing, cheese sauce, or white sauce was added to your cooked vegetables AFTER COOKING OR AT THE TABLE, how much did you usually add?
- Did not usually add these
- Less than 1 tablespoon
- 1 to 3 tablespoons
- More than 3 tablespoons

40. Over the past 12 months, how often did you eat sweet peppers (green, red, or yellow)?
- NEVER (GO TO QUESTION 41)
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per month
- 1 time per week
- 2 or more times per week

40a. Each time you ate sweet peppers, how much did you usually eat?
- Less than ¼ pepper
- ¼ to ¾ pepper
- More than ¾ pepper

41. Over the past 12 months, did you eat fresh tomatoes (including those in salads)?
- NEVER (GO TO QUESTION 42)
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per month
- 1 time per week
- 2 times per day

41a. How often did you eat fresh tomatoes (including those in salads) WHEN IN SEASON?
- NEVER
- 1–6 times per season
- 7–11 times per season
- 1 time per month
- 2–3 times per month
- 1 time per week
- 2 or more times per day

41b. How often did you eat fresh tomatoes (including those in salads) DURING THE REST OF THE YEAR?
- NEVER
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per month
- 1 time per week
- 2 or more times per day

41c. Each time you ate fresh tomatoes, how much did you usually eat?
- Less than ¼ tomato
- ¼ to ¾ tomato
- More than ¾ tomato

Question 40 appears in the next column

Question 42 appears on the next page
42. How often did you eat lettuce salads (with or without other vegetables)?

☐ NEVER (GO TO QUESTION 43)
☐ 1—6 times per year ☐ 2 times per week
☐ 7—11 times per year ☐ 3—4 times per week
☐ 1 time per month ☐ 5—6 times per week
☐ 2—3 times per month ☐ 1 time per day
☐ 1 time per week ☐ 2 or more times per day

42a. Each time you ate lettuce salads, how much did you usually eat?

☐ Less than ¼ cup
☐ ¼ to 1¼ cups
☐ More than 1¼ cups

43. How often did you eat salad dressing (including low-fat) on salads?

☐ NEVER (GO TO QUESTION 44)
☐ 1—6 times per year ☐ 2 times per week
☐ 7—11 times per year ☐ 3—4 times per week
☐ 1 time per month ☐ 5—6 times per week
☐ 2—3 times per month ☐ 1 time per day
☐ 1 time per week ☐ 2 or more times per day

43a. Each time you ate salad dressing on salads, how much did you usually eat?

☐ Less than 2 tablespoons
☐ 2 to 4 tablespoons
☐ More than 4 tablespoons

44. How often did you eat sweet potatoes or yams?

☐ NEVER (GO TO QUESTION 45)
☐ 1—6 times per year ☐ 2 times per week
☐ 7—11 times per year ☐ 3—4 times per week
☐ 1 time per month ☐ 5—6 times per week
☐ 2—3 times per month ☐ 1 time per day
☐ 1 time per week ☐ 2 or more times per day

44a. Each time you ate sweet potatoes or yams, how much did you usually eat?

☐ 1 small potato or less than ¼ cup
☐ 1 medium potato or ½ to ¾ cup
☐ 1 large potato or more than ¾ cup

45. How often did you eat French fries, home fries, hash browned potatoes, or tater tots?

☐ NEVER (GO TO QUESTION 46)
☐ 1—6 times per year ☐ 2 times per week
☐ 7—11 times per year ☐ 3—4 times per week
☐ 1 time per month ☐ 5—6 times per week
☐ 2—3 times per month ☐ 1 time per day
☐ 1 time per week ☐ 2 or more times per day

45a. Each time you ate French fries, home fries, hash browned potatoes, or tater tots how much did you usually eat?

☐ Less than 10 fries or less than ¼ cup
☐ 10 to 25 fries or ¼ to 1 cup
☐ More than 25 fries or more than 1 cup

46. How often did you eat potato salad?

☐ NEVER (GO TO QUESTION 47)
☐ 1—6 times per year ☐ 2 times per week
☐ 7—11 times per year ☐ 3—4 times per week
☐ 1 time per month ☐ 5—6 times per week
☐ 2—3 times per month ☐ 1 time per day
☐ 1 time per week ☐ 2 or more times per day

46a. Each time you ate potato salad, how much did you usually eat?

☐ Less than ¼ cup
☐ ½ to 1 cup
☐ More than 1 cup

47. How often did you eat baked, boiled, or mashed potatoes?

☐ NEVER (GO TO QUESTION 48)
☐ 1—6 times per year ☐ 2 times per week
☐ 7—11 times per year ☐ 3—4 times per week
☐ 1 time per month ☐ 5—6 times per week
☐ 2—3 times per month ☐ 1 time per day
☐ 1 time per week ☐ 2 or more times per day

47a. Each time you ate baked, boiled, or mashed potatoes, how much did you usually eat?

☐ 1 small potato or less than ¼ cup
☐ 1 medium potato or ½ to 1 cup
☐ 1 large potato or more than 1 cup
Over the past 12 months...

47b. How often was sour cream (including low-fat) added to your potatoes, EITHER IN COOKING OR AT THE TABLE?

- Almost never or never (GO TO QUESTION 47d)
- About ¼ of the time
- About ½ of the time
- About ¾ of the time
- Almost always or always

47c. Each time sour cream was added to your potatoes, how much was usually added?

- Less than 1 tablespoon
- 1 to 3 tablespoons
- More than 3 tablespoons

47d. How often was margarine (including low-fat) added to your potatoes, EITHER IN COOKING OR AT THE TABLE?

- Almost never or never
- About ¼ of the time
- About ½ of the time
- About ¾ of the time
- Almost always or always

47e. How often was butter (including low-fat) added to your potatoes, EITHER IN COOKING OR AT THE TABLE?

- Almost never or never
- About ¼ of the time
- About ½ of the time
- About ¾ of the time
- Almost always or always

47f. Each time margarine or butter was added to your potatoes, how much was usually added?

- Never added
- Less than 1 teaspoon
- 1 to 3 teaspoons
- More than 3 teaspoons

47g. How often was cheese or cheese sauce added to your potatoes, EITHER IN COOKING OR AT THE TABLE?

- Almost never or never (GO TO QUESTION 48)
- About ¼ of the time
- About ½ of the time
- About ¾ of the time
- Almost always or always

47h. Each time cheese or cheese sauce was added to your potatoes, how much was usually added?

- Less than 1 tablespoon
- 1 to 3 tablespoons
- More than 3 tablespoons

48. How often did you eat salsa?

- NEVER (GO TO QUESTION 49)

48a. Each time you ate salsa, how much did you usually eat?

- Less than 1 tablespoon
- 1 to 5 tablespoons
- More than 5 tablespoons

49. How often did you eat catsup?

- NEVER (GO TO QUESTION 50)

49a. Each time you ate catsup, how much did you usually eat?

- Less than 1 teaspoon
- 1 to 6 teaspoons
- More than 6 teaspoons

50. How often did you eat stuffing, dressing, or dumplings?

- NEVER (GO TO QUESTION 51)

50a. Each time you ate stuffing, dressing, or dumplings, how much did you usually eat?

- Less than ¼ cup
- ¼ to 1 cup
- More than 1 cup
Over the past 12 months...

51. How often did you eat chili?

- NEVER (GO TO QUESTION 52)
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per month
- 1 time per week

51a. Each time you ate chili, how much did you usually eat?

- Less than ¼ cup
- ¼ to 1½ cups
- More than 1½ cups

52. How often did you eat Mexican foods (such as tacos, tostados, burritos, tamales, fajitas, enchiladas, quesadillas, and chimichangas)?

- NEVER (GO TO QUESTION 53)
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per month
- 1 time per week

52a. Each time you ate Mexican foods, how much did you usually eat?

- Less than 1 taco, burrito, etc.
- 1 to 2 tacos, burritos, etc.
- More than 2 tacos, burritos, etc.

53. How often did you eat cooked dried beans (such as baked beans, pinto, kidney, black-eyed peas, lentils, soybeans, or refried beans)? (Please don't include bean soups or chili.)

- NEVER (GO TO QUESTION 54)
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per month
- 1 time per week

53a. Each time you ate beans, how much did you usually eat?

- Less than ¼ cup
- ¼ to 1 cup
- More than 1 cup

53b. How often were the beans you ate refried beans, beans prepared with any type of fat, or with meat added?

- Almost never or never
- About ¼ of the time
- About ½ of the time
- About ¾ of the time
- Almost always or always

54. How often did you eat other kinds of vegetables?

- NEVER (GO TO QUESTION 55)
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per month
- 1 time per week

54a. Each time you ate other kinds of vegetables, how much did you usually eat?

- Less than ¼ cup
- ¼ to 1 cup
- More than 1 cup

55. How often did you eat rice or other cooked grains (such as bulgur, cracked wheat, or millet)?

- NEVER (GO TO QUESTION 56)
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per month
- 1 time per week

55a. Each time you ate rice or other cooked grains, how much did you usually eat?

- Less than ¼ cup
- ¼ to 1½ cups
- More than 1½ cups

55b. How often was butter, margarine, or oil added to your rice IN COOKING OR AT THE TABLE?

- Almost never or never
- About ¼ of the time
- About ½ of the time
- About ¾ of the time
- Almost always or always
Over the past 12 months...

56. How often did you eat pancakes, waffles, or French toast?

☐ NEVER (GO TO QUESTION 57)

☐ 1–6 times per year
☐ 7–11 times per year
☐ 1 time per month
☐ 2–3 times per month
☐ 1 time per week
☐ 2 or more times per day

56a. Each time you ate pancakes, waffles, or French toast, how much did you usually eat?

☐ Less than 1 medium piece
☐ 1 to 3 medium pieces
☐ More than 3 medium pieces

56b. How often was margarine (including low-fat) added to your pancakes, waffles, or French toast AFTER COOKING OR AT THE TABLE?

☐ Almost never or never
☐ About ¼ of the time
☐ About ½ of the time
☐ About ¾ of the time
☐ Almost always or always

56c. How often was butter (including low-fat) added to your pancakes, waffles, or French toast AFTER COOKING OR AT THE TABLE?

☐ Almost never or never
☐ About ¼ of the time
☐ About ½ of the time
☐ About ¾ of the time
☐ Almost always or always

56d. Each time margarine or butter was added to your pancakes, waffles, or French toast, how much was usually added?

☐ Never added
☐ Less than 1 teaspoon
☐ 1 to 3 teaspoons
☐ More than 3 teaspoons

56e. How often was syrup added to your pancakes, waffles, or French toast?

☐ Almost never or never (GO TO QUESTION 57)

☐ About ¼ of the time
☐ About ½ of the time
☐ About ¾ of the time
☐ Almost always or always

56f. Each time syrup was added to your pancakes, waffles, or French toast, how much was usually added?

☐ Less than 1 tablespoon
☐ 1 to 4 tablespoons
☐ More than 4 tablespoons

57. How often did you eat lasagna, stuffed shells, stuffed manicotti, ravioli, or tortellini? (Please do not include spaghetti or other pasta.)

☐ NEVER (GO TO QUESTION 58)

☐ 1–6 times per year
☐ 7–11 times per year
☐ 1 time per month
☐ 2–3 times per month
☐ 1 time per week
☐ 2 or more times per day

57a. Each time you ate lasagna, stuffed shells, stuffed manicotti, ravioli, or tortellini, how much did you usually eat?

☐ Less than 1 cup
☐ 1 to 2 cups
☐ More than 2 cups

58. How often did you eat macaroni and cheese?

☐ NEVER (GO TO QUESTION 59)

☐ 1–6 times per year
☐ 7–11 times per year
☐ 1 time per month
☐ 2–3 times per month
☐ 1 time per week
☐ 2 or more times per day

58a. Each time you ate macaroni and cheese, how much did you usually eat?

☐ Less than 1 cup
☐ 1 to 1½ cups
☐ More than 1½ cups

59. How often did you eat pasta salad or macaroni salad?

☐ NEVER (GO TO QUESTION 60)

☐ 1–6 times per year
☐ 7–11 times per year
☐ 1 time per month
☐ 2–3 times per month
☐ 1 time per week
☐ 2 or more times per day

Question 57 appears in the next column

Question 60 appears on the next page
Over the past 12 months...

59a. Each time you ate pasta salad or macaroni salad, how much did you usually eat?
- Less than ½ cup
- ½ to 1 cup
- More than 1 cup

60. Other than the pastas listed in Questions 57, 58, and 59, how often did you eat pasta, spaghetti, or other noodles?
- NEVER (GO TO QUESTION 61)
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per month
- 1 time per week
- 2 or more times per week

60a. Each time you ate pasta, spaghetti, or other noodles, how much did you usually eat?
- Less than 1 cup
- 1 to 3 cups
- More than 3 cups

60b. How often did you eat your pasta, spaghetti, or other noodles with tomato sauce or spaghetti sauce made WITH meat?
- Almost never or never
- About ¼ of the time
- About ½ of the time
- About ¾ of the time
- Almost always or always

60c. How often did you eat your pasta, spaghetti, or other noodles with tomato sauce or spaghetti sauce made WITHOUT meat?
- Almost never or never
- About ¼ of the time
- About ½ of the time
- About ¾ of the time
- Almost always or always

60d. How often did you eat your pasta, spaghetti, or other noodles with margarine, butter, oil, or cream sauce?
- Almost never or never
- About ¼ of the time
- About ½ of the time
- About ¾ of the time
- Almost always or always

61. How often did you eat bagels or English muffins?
- NEVER (GO TO INTRODUCTION TO QUESTION 62)
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per month
- 1 time per week
- 2 or more times per week

61a. Each time you ate bagels or English muffins, how many did you usually eat?
- Less than 1 bagel or English muffin
- 1 bagel or English muffin
- More than 1 bagel or English muffin

61b. How often was margarine (including low-fat) added to your bagels or English muffins?
- Almost never or never
- About ¼ of the time
- About ½ of the time
- About ¾ of the time
- Almost always or always

61c. How often was butter (including low-fat) added to your bagels or English muffins?
- Almost never or never
- About ¼ of the time
- About ½ of the time
- About ¾ of the time
- Almost always or always

61d. Each time margarine or butter was added to your bagels or English muffins, how much was usually added?
- Never added
- Less than 1 teaspoon
- 1 to 2 teaspoons
- More than 2 teaspoons

61e. How often was cream cheese (including low-fat) spread on your bagels or English muffins?
- Almost never or never (GO TO INTRODUCTION TO QUESTION 62)
- About ¼ of the time
- About ½ of the time
- About ¾ of the time
- Almost always or always
Over the past 12 months...

61f. Each time cream cheese was added to your bagels or English muffins, how much was usually added?

☐ Less than 1 tablespoon
☐ 1 to 2 tablespoons
☐ More than 2 tablespoons

The next questions ask about your intake of breads other than bagels or English muffins. First, we will ask about bread you ate as part of sandwiches only. Then we will ask about all other bread you ate.

62. How often did you eat breads or rolls AS PART OF SANDWICHES (including burger and hot dog rolls)?

☐ NEVER (GO TO QUESTION 63)

☐ 1–6 times per year ☐ 2 times per week
☐ 7–11 times per year ☐ 3–4 times per week
☐ 1 time per month ☐ 5–6 times per week
☐ 2–3 times per month ☐ 1 time per day
☐ 1 time per week ☐ 2 or more times per day

62a. Each time you ate breads or rolls AS PART OF SANDWICHES, how many did you usually eat?

☐ 1 slice or ½ roll
☐ 2 slices or 1 roll
☐ More than 2 slices or more than 1 roll

62b. How often were the breads or rolls that you used for your sandwiches white bread (including burger and hot dog rolls)?

☐ Almost never or never
☐ About ¼ of the time
☐ About ½ of the time
☐ About ¾ of the time
☐ Almost always or always

62c. How often was mayonnaise or mayonnaise-type dressing (including low-fat) added to your sandwich bread or rolls?

☐ Almost never or never (GO TO QUESTION 62e)
☐ About ¼ of the time
☐ About ½ of the time
☐ About ¾ of the time
☐ Almost always or always

62d. Each time mayonnaise or mayonnaise-type dressing was added to your sandwich breads or rolls, how much was usually added?

☐ Less than 1 teaspoon
☐ 1 to 3 teaspoons
☐ More than 3 teaspoons

62e. How often was margarine (including low-fat) added to your sandwich bread or rolls?

☐ Almost never or never
☐ About ¼ of the time
☐ About ½ of the time
☐ About ¾ of the time
☐ Almost always or always

62f. How often was butter (including low-fat) added to your sandwich bread or rolls?

☐ Never added
☐ Less than 1 teaspoon
☐ 1 to 2 teaspoons
☐ More than 2 teaspoons

62g. Each time margarine or butter was added to your sandwich breads or rolls, how much was usually added?

☐ Never added
☐ Less than 1 teaspoon
☐ 1 to 2 teaspoons
☐ More than 2 teaspoons

63. How often did you eat breads or dinner rolls, NOT AS PART OF SANDWICHES?

☐ NEVER (GO TO QUESTION 64)

☐ 1–6 times per year ☐ 2 times per week
☐ 7–11 times per year ☐ 3–4 times per week
☐ 1 time per month ☐ 5–6 times per week
☐ 2–3 times per month ☐ 1 time per day
☐ 1 time per week ☐ 2 or more times per day

63a. Each time you ate breads or dinner rolls, NOT AS PART OF SANDWICHES, how much did you usually eat?

☐ 1 slice or 1 dinner roll
☐ 2 slices or 2 dinner rolls
☐ More than 2 slices or 2 dinner rolls
Over the past 12 months...

63b. How often were the breads or rolls you ate white bread?
- [ ] Almost never or never
- [ ] About ⅓ of the time
- [ ] About ⅔ of the time
- [ ] Almost always or always

63c. How often was margarine (including low-fat) added to your breads or rolls?
- [ ] Almost never or never
- [ ] About ⅓ of the time
- [ ] About ⅔ of the time
- [ ] Almost always or always

63d. How often was butter (including low-fat) added to your breads or rolls?
- [ ] Almost never or never
- [ ] About ⅓ of the time
- [ ] About ⅔ of the time
- [ ] Almost always or always

63e. Each time margarine or butter was added to your breads or rolls, how much was usually added?
- [ ] Never added
- [ ] Less than 1 teaspoon
- [ ] 1 to 2 teaspoons
- [ ] More than 2 teaspoons

63f. How often was cream cheese (including low-fat) added to your breads or rolls?
- [ ] Almost never or never (GO TO QUESTION 64)
- [ ] About ⅓ of the time
- [ ] About ⅔ of the time
- [ ] Almost always or always

63g. Each time cream cheese was added to your breads or rolls, how much was usually added?
- [ ] Less than 1 tablespoon
- [ ] 1 to 2 tablespoons
- [ ] More than 2 tablespoons

64. How often did you eat jam, jelly, or honey on bagels, muffins, bread, rolls, or crackers?
- [ ] NEVER (GO TO QUESTION 65)
- [ ] 1–6 times per year
- [ ] 7–11 times per year
- [ ] 1 time per month
- [ ] 2–3 times per month
- [ ] 1 time per week
- [ ] 2 or more times per day

64a. Each time you ate jam, jelly, or honey, how much did you usually eat?
- [ ] Less than 1 teaspoon
- [ ] 1 to 3 teaspoons
- [ ] More than 3 teaspoons

65. How often did you eat peanut butter or other nut butter?
- [ ] NEVER (GO TO QUESTION 66)
- [ ] 1–6 times per year
- [ ] 7–11 times per year
- [ ] 1 time per month
- [ ] 2–3 times per month
- [ ] 1 time per week
- [ ] 2 or more times per day

65a. Each time you ate peanut butter or other nut butter, how much did you usually eat?
- [ ] Less than 1 tablespoon
- [ ] 1 to 2 tablespoons
- [ ] More than 2 tablespoons

66. How often did you eat roast beef or steak IN SANDWICHES?
- [ ] NEVER (GO TO QUESTION 67)
- [ ] 1–6 times per year
- [ ] 7–11 times per year
- [ ] 1 time per month
- [ ] 2–3 times per month
- [ ] 1 time per week
- [ ] 2 or more times per day

66a. Each time you ate roast beef or steak IN SANDWICHES, how much did you usually eat?
- [ ] Less than 1 slice or less than 2 ounces
- [ ] 1 to 2 slices or 2 to 4 ounces
- [ ] More than 2 slices or more than 4 ounces

Question 64 appears in the next column

Question 67 appears on the next page
Over the past 12 months...

67. How often did you eat turkey or chicken COLD CUTS (such as loaf, luncheon meat, turkey ham, turkey salami, or turkey pastrami)? (We will ask about other turkey or chicken later.)

☐ NEVER (GO TO QUESTION 68)
☐ 1–6 times per year ☐ 2 times per week
☐ 7–11 times per year ☐ 3–4 times per week
☐ 1 time per month ☐ 5–6 times per week
☐ 2–3 times per month ☐ 1 time per day
☐ 1 time per week ☐ 2 or more times per day

67a. Each time you ate turkey or chicken COLD CUTS, how much did you usually eat?

☐ Less than 1 slice
☐ 1 to 3 slices
☐ More than 3 slices

68. How often did you eat luncheon or deli-style ham? (We will ask about other ham later.)

☐ NEVER (GO TO QUESTION 68)
☐ 1–6 times per year ☐ 2 times per week
☐ 7–11 times per year ☐ 3–4 times per week
☐ 1 time per month ☐ 5–6 times per week
☐ 2–3 times per month ☐ 1 time per day
☐ 1 time per week ☐ 2 or more times per day

68a. Each time you ate luncheon or deli-style ham, how much did you usually eat?

☐ Less than 1 slice
☐ 1 to 3 slices
☐ More than 3 slices

68b. How often was the luncheon or deli-style ham you ate light, low-fat, or fat-free?

☐ Almost never or never
☐ About ¼ of the time
☐ About ½ of the time
☐ About ¾ of the time
☐ Almost always or always

69. How often did you eat other cold cuts or luncheon meats (such as bologna, salami, corned beef, pastrami, or others, including low-fat)? (Please do not include ham, turkey, or chicken cold cuts.)

☐ NEVER (GO TO QUESTION 70)
☐ 1–6 times per year ☐ 2 times per week
☐ 7–11 times per year ☐ 3–4 times per week
☐ 1 time per month ☐ 5–6 times per week
☐ 2–3 times per month ☐ 1 time per day
☐ 1 time per week ☐ 2 or more times per day

69a. Each time you ate other cold cuts or luncheon meats, how much did you usually eat?

☐ Less than 1 slice
☐ 1 to 3 slices
☐ More than 3 slices

69b. How often were the other cold cuts or luncheon meats you ate light, low-fat, or fat-free cold cuts or luncheon meats? (Please do not include ham, turkey, or chicken cold cuts.)

☐ Almost never or never
☐ About ¼ of the time
☐ About ½ of the time
☐ About ¾ of the time
☐ Almost always or always

70. How often did you eat canned tuna (including in salads, sandwiches, or casseroles)?

☐ NEVER (GO TO QUESTION 71)
☐ 1–6 times per year ☐ 2 times per week
☐ 7–11 times per year ☐ 3–4 times per week
☐ 1 time per month ☐ 5–6 times per week
☐ 2–3 times per month ☐ 1 time per day
☐ 1 time per week ☐ 2 or more times per day

70a. Each time you ate canned tuna, how much did you usually eat?

☐ Less than ¼ cup or less than 2 ounces
☐ ¼ to ½ cup or 2 to 3 ounces
☐ More than ½ cup or more than 3 ounces

70b. How often was the canned tuna you ate water-packed tuna?

☐ Almost never or never
☐ About ¼ of the time
☐ About ½ of the time
☐ About ¾ of the time
☐ Almost always or always
Over the past 12 months...

70c. How often was the canned tuna you ate prepared with mayonnaise or other dressing (including low-fat)?

☐ Almost never or never
☐ About ⅓ of the time
☐ About ⅔ of the time
☐ About ¾ of the time
☐ Almost always or always

71. How often did you eat GROUND chicken or turkey? (We will ask about other chicken and turkey later.)

☐ NEVER (GO TO QUESTION 72)

☐ 1–6 times per year
☐ 7–11 times per year
☐ 1 time per month
☐ 2–3 times per month
☐ 1 time per week

☐ 2 or more times per day

71a. Each time you ate GROUND chicken or turkey, how much did you usually eat?

☐ Less than 2 ounces or less than ⅓ cup
☐ 2 to 4 ounces or ⅓ to 1 cup
☐ More than 4 ounces or more than 1 cup

72. How often did you eat beef hamburgers or cheeseburgers?

☐ NEVER (GO TO QUESTION 73)

☐ 1–6 times per year
☐ 7–11 times per year
☐ 1 time per month
☐ 2–3 times per month
☐ 1 time per week

☐ 2 or more times per day

72a. Each time you ate beef hamburgers or cheeseburgers, how much did you usually eat?

☐ Less than 1 patty or less than 2 ounces
☐ 1 patty or 2 to 4 ounces
☐ More than 1 patty or more than 4 ounces

72b. How often were the beef hamburgers or cheeseburgers you ate made with lean ground beef?

☐ Almost never or never
☐ About ⅓ of the time
☐ About ⅔ of the time
☐ About ¾ of the time
☐ Almost always or always

73. How often did you eat ground beef in mixtures (such as meatballs, casseroles, chili, or meatloaf)?

☐ NEVER (GO TO QUESTION 74)

☐ 1–6 times per year
☐ 7–11 times per year
☐ 1 time per month
☐ 2–3 times per month
☐ 1 time per week

☐ 2 or more times per day

73a. Each time you ate ground beef in mixtures, how much did you usually eat?

☐ Less than 3 ounces or less than ⅔ cup
☐ 3 to 8 ounces or ⅔ to 1 cup
☐ More than 8 ounces or more than 1 cup

74. How often did you eat hot dogs or frankfurters? (Please do not include sausages or vegetarian hot dogs.)

☐ NEVER (GO TO QUESTION 75)

☐ 1–6 times per year
☐ 7–11 times per year
☐ 1 time per month
☐ 2–3 times per month
☐ 1 time per week

☐ 2 or more times per day

74a. Each time you ate hot dogs or frankfurters, how many did you usually eat?

☐ Less than 1 hot dog
☐ 1 to 2 hot dogs
☐ More than 2 hot dogs

74b. How often were the hot dogs or frankfurters you ate light or low-fat hot dogs?

☐ Almost never or never
☐ About ⅓ of the time
☐ About ⅔ of the time
☐ About ¾ of the time
☐ Almost always or always
This is a sample form. Do not use for scanning.

Over the past 12 months...

75. How often did you eat beef mixtures such as beef stew, beef pot pie, beef and noodles, or beef and vegetables?

☐ NEVER (GO TO QUESTION 76)

☐ 1–6 times per year  ☐ 2 times per week
☐ 7–11 times per year  ☐ 3–4 times per week
☐ 1 time per month  ☐ 5–6 times per week
☐ 2–3 times per month  ☐ 1 time per day
☐ 1 time per week  ☐ 2 or more times per day

75a. Each time you ate beef stew, beef pot pie, beef and noodles, or beef and vegetables, how much did you usually eat?

☐ Less than 1 cup
☐ 1 to 2 cups
☐ More than 2 cups

76. How often did you eat roast beef or pot roast? (Please do not include roast beef or pot roast in sandwiches.)

☐ NEVER (GO TO QUESTION 77)

☐ 1–6 times per year  ☐ 2 times per week
☐ 7–11 times per year  ☐ 3–4 times per week
☐ 1 time per month  ☐ 5–6 times per week
☐ 2–3 times per month  ☐ 1 time per day
☐ 1 time per week  ☐ 2 or more times per day

76a. Each time you ate roast beef or pot roast (including in mixtures), how much did you usually eat?

☐ Less than 2 ounces
☐ 2 to 5 ounces
☐ More than 5 ounces

77. How often did you eat steak (beef)? (Do not include steak in sandwiches)

☐ NEVER (GO TO QUESTION 78)

☐ 1–6 times per year  ☐ 2 times per week
☐ 7–11 times per year  ☐ 3–4 times per week
☐ 1 time per month  ☐ 5–6 times per week
☐ 2–3 times per month  ☐ 1 time per day
☐ 1 time per week  ☐ 2 or more times per day

77a. Each time you ate steak (beef), how much did you usually eat?

☐ Less than 3 ounces
☐ 3 to 7 ounces
☐ More than 7 ounces

77b. How often was the steak you ate lean steak?

☐ Almost never or never
☐ About 1/2 of the time
☐ About 3/4 of the time
☐ Almost always or always

78. How often did you eat pork or beef spareribs?

☐ NEVER (GO TO QUESTION 79)

☐ 1–6 times per year  ☐ 2 times per week
☐ 7–11 times per year  ☐ 3–4 times per week
☐ 1 time per month  ☐ 5–6 times per week
☐ 2–3 times per month  ☐ 1 time per day
☐ 1 time per week  ☐ 2 or more times per day

78a. Each time you ate pork or beef spareribs, how much did you usually eat?

☐ Less than 4 ribs
☐ 4 to 12 ribs
☐ More than 12 ribs

79. How often did you eat roast turkey, turkey cutlets, or turkey nuggets (including in sandwiches)?

☐ NEVER (GO TO QUESTION 80)

☐ 1–6 times per year  ☐ 2 times per week
☐ 7–11 times per year  ☐ 3–4 times per week
☐ 1 time per month  ☐ 5–6 times per week
☐ 2–3 times per month  ☐ 1 time per day
☐ 1 time per week  ☐ 2 or more times per day

79a. Each time you ate roast turkey, turkey cutlets, or turkey nuggets, how much did you usually eat? (Please note: 4 to 8 turkey nuggets = 3 ounces.)

☐ Less than 2 ounces
☐ 2 to 4 ounces
☐ More than 4 ounces

80. How often did you eat chicken as part of salads, sandwiches, casseroles, stews, or other mixtures?

☐ NEVER (GO TO QUESTION 81)

☐ 1–6 times per year  ☐ 2 times per week
☐ 7–11 times per year  ☐ 3–4 times per week
☐ 1 time per month  ☐ 5–6 times per week
☐ 2–3 times per month  ☐ 1 time per day
☐ 1 time per week  ☐ 2 or more times per day

Question 78 appears in the next column

Question 81 appears on the next page
Over the past 12 months...

80a. Each time you ate chicken as part of salads, sandwiches, casseroles, stews, or other mixtures, how much did you usually eat?
- Less than ¼ cup
- ¼ to ½ cup
- More than ½ cup

81. How often did you eat baked, broiled, roasted, stewed, or fried chicken (including nuggets)? (Please do not include chicken in mixtures.)
- NEVER (GO TO QUESTION 82)
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per month
- 1 time per week
- 2 or more times per day

81a. Each time you ate baked, broiled, roasted, stewed, or fried chicken (including nuggets), how much did you usually eat?
- Less than 2 drumsticks or wings, less than 1 breast or thigh, or less than 4 nuggets
- 2 drumsticks or wings, 1 breast or thigh, or 4 to 8 nuggets
- More than 2 drumsticks or wings, more than 1 breast or thigh, or more than 8 nuggets

81b. How often was the chicken you ate fried chicken (including nuggets)?
- Almost never or never
- About ⅓ of the time
- About ⅔ of the time
- Almost always or always

81c. How often was the chicken you ate WHITE meat?
- Almost never or never
- About ⅓ of the time
- About ⅔ of the time
- Almost always or always

81d. How often did you eat chicken WITH skin?
- Almost never or never
- About ⅓ of the time
- About ⅔ of the time
- Almost always or always

82. How often did you eat baked ham or ham steak?
- NEVER (GO TO QUESTION 83)
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per month
- 1 time per week
- 2 or more times per day

82a. Each time you ate baked ham or ham steak, how much did you usually eat?
- Less than 1 ounce
- 1 to 3 ounces
- More than 3 ounces

83. How often did you eat pork (including chops, roasts, and in mixed dishes)? (Please do not include ham, ham steak, or sausage.)
- NEVER (GO TO QUESTION 84)
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per month
- 1 time per week
- 2 or more times per day

83a. Each time you ate pork, how much did you usually eat?
- Less than 2 ounces or less than 1 chop
- 2 to 5 ounces or 1 chop
- More than 5 ounces or more than 1 chop

84. How often did you eat gravy on meat, chicken, potatoes, rice, etc.?
- NEVER (GO TO QUESTION 85)
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per month
- 1 time per week
- 2 or more times per day

84a. Each time you ate gravy on meat, chicken, potatoes, rice, etc., how much did you usually eat?
- Less than ¼ cup
- ¼ to ½ cup
- More than ½ cup
This is a sample form. Do not use for scanning.

Over the past 12 months...

85. How often did you eat liver (all kinds) or liverwurst?
   □ NEVER (GO TO QUESTION 86)
   □ 1–6 times per year □ 2 times per week
   □ 7–11 times per year □ 3–4 times per week
   □ 1 time per month □ 5–6 times per week
   □ 2–3 times per month □ 1 time per day
   □ 1 time per week □ 2 or more times per day

   85a. Each time you ate liver or liverwurst, how much did you usually eat?
   □ Less than 1 ounce
   □ 1 to 4 ounces
   □ More than 4 ounces

86. How often did you eat bacon (including low-fat)?
   □ NEVER (GO TO QUESTION 87)
   □ 1–6 times per year □ 2 times per week
   □ 7–11 times per year □ 3–4 times per week
   □ 1 time per month □ 5–6 times per week
   □ 2–3 times per month □ 1 time per day
   □ 1 time per week □ 2 or more times per day

   86a. Each time you ate bacon, how much did you usually eat?
   □ Fewer than 2 slices
   □ 2 to 3 slices
   □ More than 3 slices

   86b. How often was the bacon you ate light, low-fat, or lean bacon?
   □ Almost never or never
   □ About 1/3 of the time
   □ About 1/2 of the time
   □ About 2/3 of the time
   □ Almost always or always

87. How often did you eat sausage (including low-fat)?
   □ NEVER (GO TO QUESTION 88)
   □ 1–6 times per year □ 2 times per week
   □ 7–11 times per year □ 3–4 times per week
   □ 1 time per month □ 5–6 times per week
   □ 2–3 times per month □ 1 time per day
   □ 1 time per week □ 2 or more times per day

   87a. Each time you ate sausage, how much did you usually eat?
   □ Less than 1 patty or 2 links
   □ 1 to 3 patties or 2 to 5 links
   □ More than 3 patties or 5 links

   87b. How often was the sausage you ate light, low-fat, or lean sausage?
   □ Almost never or never
   □ About 1/3 of the time
   □ About 1/2 of the time
   □ About 2/3 of the time
   □ Almost always or always

88. How often did you eat fish sticks or fried fish (including fried seafood or shellfish)?
   □ NEVER (GO TO QUESTION 89)
   □ 1–6 times per year □ 2 times per week
   □ 7–11 times per year □ 3–4 times per week
   □ 1 time per month □ 5–6 times per week
   □ 2–3 times per month □ 1 time per day
   □ 1 time per week □ 2 or more times per day

   88a. Each time you ate fish sticks or fried fish, how much did you usually eat?
   □ Less than 2 ounces or less than 1 fillet
   □ 2 to 7 ounces or 1 fillet
   □ More than 7 ounces or more than 1 fillet

89. How often did you eat fish or seafood that was NOT FRIED (including shellfish)?
   □ NEVER (GO TO INTRODUCTION TO QUESTION 90)
   □ 1–6 times per year □ 2 times per week
   □ 7–11 times per year □ 3–4 times per week
   □ 1 time per month □ 5–6 times per week
   □ 2–3 times per month □ 1 time per day
   □ 1 time per week □ 2 or more times per day

   89a. Each time you ate fish or seafood that was NOT FRIED, how much did you usually eat?
   □ Less than 2 ounces or less than 1 fillet
   □ 2 to 5 ounces or 1 fillet
   □ More than 5 ounces or more than 1 fillet

Question 88 appears in the next column

Introduction to Question 90 appears on the next page
Over the past 12 months...

Now think about all the meat, poultry, and fish you ate in the past 12 months and how they were prepared.

90. How often was oil, butter, margarine, or other fat used to FRY, SAUTE, BASTE, OR MARINATE any meat, poultry, or fish you ate? (Please do not include deep frying.)

☐ NEVER (GO TO QUESTION 91)
☐ 1–6 times per year ☐ 2 times per week
☐ 7–11 times per year ☐ 3–4 times per week
☐ 1 time per month ☐ 5–6 times per week
☐ 2–3 times per month ☐ 1 time per day
☐ 1 time per week ☐ 2 or more times per day

90a. Which of the following fats were regularly used to prepare your meat, poultry, or fish? (Mark all that apply.)

☐ Margarine (including low-fat)
☐ Butter (including low-fat)
☐ Lard, fatback, or bacon fat
☐ Olive oil
☐ Corn oil
☐ Canola or rapeseed oil
☐ Oil spray, such as Pam or others
☐ Other kinds of oils
☐ None of the above

91. How often did you eat tofu, soy burgers, or soy meat-substitutes?

☐ NEVER (GO TO QUESTION 92)
☐ 1–6 times per year ☐ 2 times per week
☐ 7–11 times per year ☐ 3–4 times per week
☐ 1 time per month ☐ 5–6 times per week
☐ 2–3 times per month ☐ 1 time per day
☐ 1 time per week ☐ 2 or more times per day

91a. Each time you ate tofu, soy burgers, or soy meat-substitutes, how much did you usually eat?

☐ Less than 1/4 cup or less than 2 ounces
☐ 1/4 to 3/4 cup or 2 to 4 ounces
☐ More than 3/4 cup or more than 4 ounces

92. Over the past 12 months, did you eat soups?

☐ NO (GO TO QUESTION 93)
☐ YES

92a. How often did you eat soup DURING THE WINTER?

☐ NEVER
☐ 1–6 times per winter ☐ 2 times per week
☐ 7–11 times per winter ☐ 3–4 times per week
☐ 1 time per month ☐ 5–6 times per week
☐ 2–3 times per month ☐ 1 time per day
☐ 1 time per week ☐ 2 or more times per day

92b. How often did you eat soup DURING THE REST OF THE YEAR?

☐ NEVER
☐ 1–6 times per year ☐ 2 times per week
☐ 7–11 times per year ☐ 3–4 times per week
☐ 1 time per month ☐ 5–6 times per week
☐ 2–3 times per month ☐ 1 time per day
☐ 1 time per week ☐ 2 or more times per day

92c. Each time you ate soup, how much did you usually eat?

☐ Less than 1 cup
☐ 1 to 2 cups
☐ More than 2 cups

92d. How often were the soups you ate bean soups?

☐ Almost never or never
☐ About 1/4 of the time
☐ About 1/2 of the time
☐ About 3/4 of the time
☐ Almost always or always

92e. How often were the soups you ate cream soups (including chowders)?

☐ Almost never or never
☐ About 1/4 of the time
☐ About 1/2 of the time
☐ About 3/4 of the time
☐ Almost always or always
Over the past 12 months...

92f. How often were the soups you ate tomato or vegetable soups?

□ Almost never or never
□ About ¼ of the time
□ About ½ of the time
□ About ¾ of the time
□ Almost always or always

92g. How often were the soups you ate broth soups (including chicken) with or without noodles or rice?

□ Almost never or never
□ About ¼ of the time
□ About ½ of the time
□ About ¾ of the time
□ Almost always or always

93. How often did you eat pizza?

□ NEVER (GO TO QUESTION 94)

□ 1–6 times per year □ 2 times per week
□ 7–11 times per year □ 3–4 times per week
□ 1 time per month □ 5–6 times per week
□ 2–3 times per month □ 1 time per day
□ 1 time per week □ 2 or more times per day

93a. Each time you ate pizza, how much did you usually eat?

□ Less than 1 slice or less than 1 mini pizza
□ 1 to 3 slices or 1 mini pizza
□ More than 3 slices or more than 1 mini pizza

93b. How often did you eat pizza with pepperoni, sausage, or other meat?

□ Almost never or never
□ About ¼ of the time
□ About ½ of the time
□ About ¾ of the time
□ Almost always or always

94. How often did you eat crackers?

□ NEVER (GO TO QUESTION 95)

□ 1–6 times per year □ 2 times per week
□ 7–11 times per year □ 3–4 times per week
□ 1 time per month □ 5–6 times per week
□ 2–3 times per month □ 1 time per day
□ 1 time per week □ 2 or more times per day

94a. Each time you ate crackers, how many did you usually eat?

□ Fewer than 4 crackers
□ 4 to 10 crackers
□ More than 10 crackers

95. How often did you eat corn bread or corn muffins?

□ NEVER (GO TO QUESTION 96)

□ 1–6 times per year □ 2 times per week
□ 7–11 times per year □ 3–4 times per week
□ 1 time per month □ 5–6 times per week
□ 2–3 times per month □ 1 time per day
□ 1 time per week □ 2 or more times per day

95a. Each time you ate corn bread or corn muffins, how much did you usually eat?

□ Less than 1 piece or muffin
□ 1 to 2 pieces or muffins
□ More than 2 pieces or muffins

96. How often did you eat biscuits?

□ NEVER (GO TO QUESTION 97)

□ 1–6 times per year □ 2 times per week
□ 7–11 times per year □ 3–4 times per week
□ 1 time per month □ 5–6 times per week
□ 2–3 times per month □ 1 time per day
□ 1 time per week □ 2 or more times per day

96a. Each time you ate biscuits, how many did you usually eat?

□ Fewer than 1 biscuit
□ 1 to 2 biscuits
□ More than 2 biscuits

97. How often did you eat potato chips, tortilla chips, or corn chips (including low-fat, fat-free, or low-salt)?

□ NEVER (GO TO QUESTION 98)

□ 1–6 times per year □ 2 times per week
□ 7–11 times per year □ 3–4 times per week
□ 1 time per month □ 5–6 times per week
□ 2–3 times per month □ 1 time per day
□ 1 time per week □ 2 or more times per day

Question 95 appears in the next column

Question 98 appears on the next page
Over the past 12 months...

97a. Each time you ate potato chips, tortilla chips, or corn chips, how much did you usually eat?
- Fewer than 10 chips or less than 1 cup
- 10 to 25 chips or 1 to 2 cups
- More than 25 chips or more than 2 cups

97b. How often were the chips you ate WOW chips or other chips made with fat substitute (Olean or Olestra)?
- Almost never or never
- About ¼ of the time
- About ½ of the time
- About ¾ of the time
- Almost always or always

97c. How often were the chips you ate other low-fat or fat-free chips?
- Almost never or never
- About ¼ of the time
- About ½ of the time
- About ¾ of the time
- Almost always or always

98. How often did you eat popcorn (including low-fat)?
- NEVER (GO TO QUESTION 99)
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per month
- 1 time per week
- 2 or more times per day

98a. Each time you ate popcorn, how much did you usually eat?
- Less than 2 cups, popped
- 2 to 5 cups, popped
- More than 5 cups, popped

99. How often did you eat pretzels?
- NEVER (GO TO QUESTION 100)
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per month
- 1 time per week
- 2 or more times per day

99a. Each time you ate pretzels, how many did you usually eat?
- Fewer than 5 average twists
- 5 to 20 average twists
- More than 20 average twists

100. How often did you eat peanuts, walnuts, seeds, or other nuts?
- NEVER (GO TO QUESTION 101)
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per month
- 1 time per week
- 2 or more times per day

100a. Each time you ate peanuts, walnuts, seeds, or other nuts, how much did you usually eat?
- Less than ¼ cup
- ¼ to ½ cup
- More than ½ cup

101. How often did you eat energy, high-protein, or breakfast bars such as Power Bars, Balance, Cliff, or others?
- NEVER (GO TO QUESTION 102)
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per month
- 1 time per week
- 2 or more times per day

101a. Each time you ate energy, high-protein, or breakfast bars, how much did you usually eat?
- Less than 1 bar
- 1 bar
- More than 1 bar

102. How often did you eat yogurt (NOT including frozen yogurt)?
- NEVER (GO TO QUESTION 103)
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per month
- 1 time per week
- 2 or more times per day

Question 100 appears in the next column

Question 103 appears on the next page
This is a sample form. Do not use for scanning.

Over the past 12 months...

102a. Each time you ate yogurt, how much did you usually eat?
- Less than ½ cup or less than 1 container
- ½ to 1 cup or 1 container
- More than 1 cup or more than 1 container

103. How often did you eat cottage cheese (including low-fat)?
- NEVER (GO TO QUESTION 104)

103a. Each time you ate cottage cheese, how much did you usually eat?
- Less than ¼ cup
- ¼ to 1 cup
- More than 1 cup

104. How often did you eat cheese (including low-fat; including on cheeseburgers or in sandwiches or subs)?
- NEVER (GO TO QUESTION 105)

104a. Each time you ate cheese, how much did you usually eat?
- Less than ½ ounce or less than 1 slice
- ½ to 1/2 ounces or 1 slice
- More than 1/2 ounces or more than 1 slice

104b. How often was the cheese you ate light or low-fat cheese?
- Almost never or never
- About ¼ of the time
- About ½ of the time
- About ¾ of the time
- Almost always or always

105. How often did you eat frozen yogurt, sorbet, or ices (including low-fat or fat-free)?
- NEVER (GO TO QUESTION 106)

105a. Each time you ate frozen yogurt, sorbet, or ices, how much did you usually eat?
- Less than ¼ cup or less than 1 scoop
- ¼ to 1 cup or 1 to 2 scoops
- More than 1 cup or more than 2 scoops

106. How often did you eat ice cream, ice cream bars, or sherbet (including low-fat or fat-free)?
- NEVER (GO TO QUESTION 107)

106a. Each time you ate ice cream, ice cream bars, or sherbet, how much did you usually eat?
- Less than ½ cup or less than 1 scoop
- ½ to 1/2 cups or 1 to 2 scoops
- More than 1/2 cups or more than 2 scoops

106b. How often was the ice cream you ate light, low-fat, or fat-free ice cream or sherbet?
- Almost never or never
- About ¼ of the time
- About ½ of the time
- About ¾ of the time
- Almost always or always

Question 105 appears in the next column

Question 107 appears on the next page
Over the past 12 months...

107. How often did you eat cake (including low-fat or fat-free)?

- NEVER (GO TO QUESTION 108)
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per month
- 1 time per week

107a. Each time you ate cake, how much did you usually eat?

- Less than 1 medium piece
- 1 medium piece
- More than 1 medium piece

107b. How often was the cake you ate light, low-fat, or fat-free cake?

- Almost never or never
- About ½ of the time
- About 3/4 of the time
- Almost always or always

108. How often did you eat cookies or brownies (including low-fat or fat-free)?

- NEVER (GO TO QUESTION 109)
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per month
- 1 time per week

108a. Each time you ate cookies or brownies, how much did you usually eat?

- Less than 2 cookies or 1 small brownie
- 2 to 4 cookies or 1 medium brownie
- More than 4 cookies or 1 large brownie

108b. How often were the cookies or brownies you ate light, low-fat, or fat-free cookies or brownies?

- Almost never or never
- About ½ of the time
- About ¾ of the time
- Almost always or always

109. How often did you eat doughnuts, sweet rolls, Danish, or pop-tarts?

- NEVER (GO TO QUESTION 110)
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per month
- 1 time per week

110a. Each time you ate doughnuts, sweet rolls, Danish, or pop-tarts, how much did you usually eat?

- Less than 1 piece
- 1 to 2 pieces
- More than 2 pieces

110. How often did you eat sweet muffins or dessert breads (including low-fat or fat-free)?

- NEVER (GO TO QUESTION 111)
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per month
- 1 time per week

110a. Each time you ate sweet muffins or dessert breads, how much did you usually eat?

- Less than 1 medium piece
- 1 medium piece
- More than 1 medium piece

110b. How often were the sweet muffins or dessert breads you ate light, low-fat, or fat-free sweet muffins or dessert breads?

- Almost never or never
- About ½ of the time
- About ¾ of the time
- Almost always or always

111. How often did you eat fruit crisp, cobbler, or strudel?

- NEVER (GO TO QUESTION 112)
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per month
- 1 time per week
Over the past 12 months...

111a. Each time you ate fruit crisp, cobbler, or strudel, how much did you usually eat?
   - Less than \( \frac{1}{3} \) cup
   - \( \frac{1}{2} \) to 1 cup
   - More than 1 cup

112. How often did you eat pie?
   - NEVER (GO TO QUESTION 113)
   - 1–6 times per year
   - 7–11 times per year
   - 1 time per month
   - 2–3 times per month
   - 1 time per week
   - 2 or more times per day

112a. Each time you ate pie, how much did you usually eat?
   - Less than \( \frac{1}{4} \) of a pie
   - About \( \frac{1}{2} \) of a pie
   - More than \( \frac{1}{2} \) of a pie

The next four questions ask about the kinds of pie you ate. Please read all four questions before answering.

112b. How often were the pies you ate fruit pie (such as apple, blueberry, others)?
   - Almost never or never
   - About \( \frac{1}{2} \) of the time
   - About \( \frac{3}{4} \) of the time
   - Almost always or always

112c. How often were the pies you ate cream, pudding, custard, or meringue pie?
   - Almost never or never
   - About \( \frac{1}{2} \) of the time
   - About \( \frac{3}{4} \) of the time
   - Almost always or always

112d. How often were the pies you ate pumpkin or sweet potato pie?
   - Almost never or never
   - About \( \frac{1}{2} \) of the time
   - About \( \frac{3}{4} \) of the time
   - Almost always or always

112e. How often were the pies you ate pecan pie?
   - Almost never or never
   - About \( \frac{1}{4} \) of the time
   - About \( \frac{1}{2} \) of the time
   - About \( \frac{3}{4} \) of the time
   - Almost always or always

113. How often did you eat chocolate candy?
   - NEVER (GO TO QUESTION 114)
   - 1–6 times per year
   - 7–11 times per year
   - 1 time per month
   - 2–3 times per month
   - 1 time per week
   - 2 or more times per day

113a. Each time you ate chocolate candy, how much did you usually eat?
   - Less than 1 average bar or less than 1 ounce
   - 1 average bar or 1 to 2 ounces
   - More than 1 average bar or more than 2 ounces

114. How often did you eat other candy?
   - NEVER (GO TO QUESTION 115)
   - 1–6 times per year
   - 7–11 times per year
   - 1 time per month
   - 2–3 times per month
   - 1 time per week
   - 2 times per week
   - 3–4 times per week
   - 5–6 times per week
   - 1 time per day
   - 2 or more times per day

114a. Each time you ate other candy, how much did you usually eat?
   - Fewer than 2 pieces
   - 2 to 9 pieces
   - More than 9 pieces

115. How often did you eat eggs, egg whites, or egg substitutes (NOT counting eggs in baked goods and desserts)? (Please include eggs in salads, quiche, and soufflés.)
   - NEVER (GO TO QUESTION 116)
   - 1–6 times per year
   - 7–11 times per year
   - 1 time per month
   - 2–3 times per month
   - 1 time per week
   - 2 times per week
   - 3–4 times per week
   - 5–6 times per week
   - 1 time per day
   - 2 or more times per day

115a. How often did you eat eggs, egg whites, or egg substitutes (NOT counting eggs in baked goods and desserts)? (Please include eggs in salads, quiche, and soufflés.)
Over the past 12 months...

115a. Each time you ate eggs, how many did you usually eat?
- [ ] 1 egg
- [ ] 2 eggs
- [ ] 3 or more eggs

115b. How often were the eggs you ate egg substitutes?
- [ ] Almost never or never
- [ ] About ¼ of the time
- [ ] About ½ of the time
- [ ] About ¾ of the time
- [ ] Almost always or always

115c. How often were the eggs you ate egg whites only?
- [ ] Almost never or never
- [ ] About ¼ of the time
- [ ] About ½ of the time
- [ ] About ¾ of the time
- [ ] Almost always or always

115d. How often were the eggs you ate regular whole eggs?
- [ ] Almost never or never
- [ ] About ¼ of the time
- [ ] About ½ of the time
- [ ] About ¾ of the time
- [ ] Almost always or always

115e. How often were the eggs you ate cooked in oil, butter, or margarine?
- [ ] Almost never or never
- [ ] About ¼ of the time
- [ ] About ½ of the time
- [ ] About ¾ of the time
- [ ] Almost always or always

115f. How often were the eggs you ate part of egg salad?
- [ ] Almost never or never
- [ ] About ¼ of the time
- [ ] About ½ of the time
- [ ] About ¾ of the time
- [ ] Almost always or always

116. How many cups of coffee, decaffeinated or caffeinated, did you drink?
- [ ] NEVER (GO TO QUESTION 117)
  - [ ] Less than 1 cup per month
  - [ ] 1—3 cups per month
  - [ ] 1 cup per week
  - [ ] 2—4 cups per week
  - [ ] 5—6 cups per week
  - [ ] 1 cup per day
  - [ ] 2—3 cups per day
  - [ ] 4—5 cups per day
  - [ ] 6 or more cups per day

116a. How often was the coffee you drank decaffeinated?
- [ ] Almost never or never
- [ ] About ¼ of the time
- [ ] About ½ of the time
- [ ] About ¾ of the time
- [ ] Almost always or always

117. How many glasses of ICED tea, decaffeinated or caffeinated, did you drink?
- [ ] NEVER (GO TO QUESTION 118)
  - [ ] Less than 1 cup per month
  - [ ] 1—3 cups per month
  - [ ] 1 cup per week
  - [ ] 2—4 cups per week
  - [ ] 5—6 cups per week
  - [ ] 1 cup per day
  - [ ] 2—3 cups per day
  - [ ] 4—5 cups per day
  - [ ] 6 or more cups per day

117a. How often was the iced tea you drank decaffeinated or herbal tea?
- [ ] Almost never or never
- [ ] About ¼ of the time
- [ ] About ½ of the time
- [ ] About ¾ of the time
- [ ] Almost always or always

118. How many cups of HOT tea, decaffeinated or caffeinated, did you drink?
- [ ] NEVER (GO TO QUESTION 119)
  - [ ] Less than 1 cup per month
  - [ ] 1—3 cups per month
  - [ ] 1 cup per week
  - [ ] 2—4 cups per week
  - [ ] 5—6 cups per week
  - [ ] 1 cup per day
  - [ ] 2—3 cups per day
  - [ ] 4—5 cups per day
  - [ ] 6 or more cups per day

118a. How often was the hot tea you drank decaffeinated or herbal tea?
- [ ] Almost never or never
- [ ] About ¼ of the time
- [ ] About ½ of the time
- [ ] About ¾ of the time
- [ ] Almost always or always

Question 116 appears in the next column

Question 119 appears on the next page
Over the past 12 months...

119. How often did you add sugar or honey to your coffee or tea?

- NEVER (GO TO QUESTION 120)
- Less than 1 cup per month
- 1–3 cups per month
- 1 cup per week
- 2–4 cups per week

119a. Each time sugar or honey was added to your coffee or tea, how much was usually added?

- Less than 1 teaspoon
- 1 to 3 teaspoons
- More than 3 teaspoons

120. How often did you add artificial sweetener to your coffee or tea?

- NEVER (GO TO QUESTION 121)
- Less than 1 time per month
- 1–3 times per month
- 1 time per week
- 2–4 times per week

120a. What kind of artificial sweetener did you usually use?

- Equal or aspartame
- Sweet N Low or saccharin

121. How often was non-dairy creamer added to your coffee or tea?

- NEVER (GO TO QUESTION 122)
- Less than 1 time per month
- 1–3 times per month
- 1 time per week
- 2–4 times per week

121a. Each time non-dairy creamer was added to your coffee or tea, how much was usually used?

- Less than 1 teaspoon
- 1 to 3 teaspoons
- More than 3 teaspoons

121b. What kind of non-dairy creamer did you usually use?

- Regular powdered
- Low-fat or fat-free powdered
- Regular liquid
- Low-fat or fat-free liquid

122. How often was cream or half and half added to your coffee or tea?

- NEVER (GO TO QUESTION 123)
- Less than 1 time per month
- 1–3 times per month
- 1 time per week
- 2–4 times per week

122a. Each time cream or half and half was added to your coffee or tea, how much was usually added?

- Less than 1 tablespoon
- 1 to 2 tablespoons
- More than 2 tablespoons

123. How often was milk added to your coffee or tea?

- NEVER (GO TO QUESTION 124)
- Less than 1 time per month
- 1–3 times per month
- 1 time per week
- 2–4 times per week

123a. Each time milk was added to your coffee or tea, how much was usually added?

- Less than 1 tablespoon
- 1 to 3 tablespoons
- More than 3 tablespoons

123b. What kind of milk was usually added to your coffee or tea?

- Whole milk
- 2% milk
- 1% milk
- Skim, nonfat, or ½% milk
- Evaporated or condensed (canned) milk
- Soy milk
- Rice milk
- Other
Over the past 12 months...

124. How often was sugar or honey added to foods you ate? (Please do not include sugar in coffee, tea, other beverages, or baked goods.)

- NEVER (GO TO INTRODUCTION TO QUESTION 125)
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per month
- 1 time per week
- 2 times per week
- 3–4 times per week
- 5–6 times per week
- 1 time per day
- 2 or more times per day

124a. Each time sugar or honey was added to foods you ate, how much was usually added?

- Less than 1 teaspoon
- 1 to 3 teaspoons
- More than 3 teaspoons

The following questions are about the kinds of margarine, mayonnaise, sour cream, cream cheese, and salad dressing that you eat. If possible, please check the labels of these foods to help you answer.

125. Over the past 12 months, did you eat margarine?

- NO (GO TO QUESTION 126)
- YES

125a. How often was the margarine you ate regular-fat margarine (stick or tub)?

- Almost never or never
- About ¼ of the time
- About ½ of the time
- About ¾ of the time
- Almost always or always

125b. How often was the margarine you ate light or low-fat margarine (stick or tub)?

- Almost never or never
- About ¼ of the time
- About ½ of the time
- About ¾ of the time
- Almost always or always

126. Over the past 12 months, did you eat butter?

- NO (GO TO QUESTION 127)
- YES

126a. How often was the butter you ate light or low-fat butter?

- Almost never or never
- About ¼ of the time
- About ½ of the time
- About ¾ of the time
- Almost always or always

127. Over the past 12 months, did you eat mayonnaise or mayonnaise-type dressing?

- NO (GO TO QUESTION 128)
- YES

127a. How often was the mayonnaise you ate regular-fat mayonnaise?

- Almost never or never
- About ¼ of the time
- About ½ of the time
- About ¾ of the time
- Almost always or always

127b. How often was the mayonnaise you ate light or low-fat mayonnaise?

- Almost never or never
- About ¼ of the time
- About ½ of the time
- About ¾ of the time
- Almost always or always
Over the past 12 months...

127c. How often was the mayonnaise you ate fat-free mayonnaise?

☐ Almost never or never
☐ About ¼ of the time
☐ About ½ of the time
☐ About ¾ of the time
☐ Almost always or always

128. Over the past 12 months, did you eat sour cream?

☐ NO (GO TO QUESTION 129)
☐ YES

128a. How often was the sour cream you ate regular-fat sour cream?

☐ Almost never or never
☐ About ¼ of the time
☐ About ½ of the time
☐ About ¾ of the time
☐ Almost always or always

128b. How often was the sour cream you ate light, low-fat, or fat-free sour cream?

☐ Almost never or never
☐ About ¼ of the time
☐ About ½ of the time
☐ About ¾ of the time
☐ Almost always or always

129. Over the past 12 months, did you eat cream cheese?

☐ NO (GO TO QUESTION 130)
☐ YES

129a. How often was the cream cheese you ate regular-fat cream cheese?

☐ Almost never or never
☐ About ¼ of the time
☐ About ½ of the time
☐ About ¾ of the time
☐ Almost always or always

129b. How often was the cream cheese you ate light, low-fat, or fat-free cream cheese?

☐ Almost never or never
☐ About ¼ of the time
☐ About ½ of the time
☐ About ¾ of the time
☐ Almost always or always

130. Over the past 12 months, did you eat salad dressing?

☐ NO (GO TO INTRODUCTION TO QUESTION 131)
☐ YES

130a. How often was the salad dressing you ate regular-fat salad dressing (including oil and vinegar dressing)?

☐ Almost never or never
☐ About ¼ of the time
☐ About ½ of the time
☐ About ¾ of the time
☐ Almost always or always

130b. How often was the salad dressing you ate light or low-fat salad dressing?

☐ Almost never or never
☐ About ¼ of the time
☐ About ½ of the time
☐ About ¾ of the time
☐ Almost always or always

130c. How often was the salad dressing you ate fat-free salad dressing?

☐ Almost never or never
☐ About ¼ of the time
☐ About ½ of the time
☐ About ¾ of the time
☐ Almost always or always

The following two questions ask you to summarize your usual intake of vegetables and fruits. Please do not include salads, potatoes, or juices.

131. Over the past 12 months, how many servings of vegetables (not including salad or potatoes) did you eat per week or per day?

☐ Less than 1 per week
☐ 1–2 per week
☐ 3–4 per week
☐ 5–6 per week
☐ 1 per day

☐ 2 per day
☐ 3 per day
☐ 4 per day
☐ 5 or more per day
Over the past 12 months...

132. Over the past 12 months, how many servings of fruit (not including juices) did you eat per week or per day?

□ Less than 1 per week □ 2 per day
□ 1–2 per week □ 3 per day
□ 3–4 per week □ 4 per day
□ 5–6 per week □ 5 or more per day
□ 1 per day

133. Over the past month, which of the following foods did you eat AT LEAST THREE TIMES? (Mark all that apply.)

□ Avocado, guacamole □ Olives
□ Cheesecake □ Oysters
□ Chocolate, fudge, or butterscotch toppings or syrups □ Pickles or pickled vegetables or fruit
□ Chow mein noodles □ Plantains
□ Croissants □ Pork neckbones, hock, head, feet
□ Dried apricots □ Pudding or custard
□ Egg rolls □ Veal, venison, lamb
□ Granola bars □ Whipped cream, regular
□ Hot peppers □ Whipped cream, substitute
□ Jello, gelatin □ NONE
□ Milksakes or ice-cream sodas

134. For ALL of the past 12 months, have you followed any type of vegetarian diet?

□ NO (GO TO INTRODUCTION TO QUESTION 135)
□ YES

134a. Which of the following foods did you TOTALLY EXCLUDE from your diet? (Mark all that apply.)

□ Meat (beef, pork, lamb, etc.)
□ Poultry (chicken, turkey, duck)
□ Fish and seafood
□ Eggs
□ Dairy products (milk, cheese, etc.)

The next questions are about your use of fiber supplements or vitamin pills.

135. Over the past 12 months, did you take any of the following types of fiber or fiber supplements on a regular basis (more than once per week for at least 6 of the last 12 months)? (Mark all that apply.)

□ NO, didn't take any fiber supplements on a regular basis (GO TO QUESTION 136)
□ YES, psyllium products (such as Metamucil, Fiberall, Serutan, Perdiem, Correctol)
□ YES, methylcellulose/cellulose products (such as Citrucel, Unifiber)
□ YES, Fibercon
□ YES, Bran (such as wheat bran, oat bran, or bran wafers)

136. Over the past 12 months, did you take any multivitamins, such as One-a-Day-, Theragran-, or Centrum-type multivitamins (as pills, liquids, or packets)?

□ NO (GO TO INTRODUCTION TO QUESTION 138)
□ YES

137. How often did you take One-a-Day-, Theragran-, or Centrum-type multivitamins?

□ Less than 1 day per month
□ 1–3 days per month
□ 1–3 days per week
□ 4–6 days per week
□ Every day

137a. Does your multivitamin usually contain minerals (such as iron, zinc, etc.)?

□ NO
□ YES
□ Don't know

137b. For how many years have you taken multivitamins?

□ Less than 1 year
□ 1–4 years
□ 5–9 years
□ 10 or more years
Over the past 12 months...

137c. Over the past 12 months, did you take any vitamins, minerals, or other herbal supplements other than your multivitamin?

☐ NO

Thank you very much for completing this questionnaire! Because we want to be able to use all the information you have provided, we would greatly appreciate it if you would please take a moment to review each page making sure that you:

• Did not skip any pages and
• Crossed out the incorrect answer and circled the correct answer if you made any changes.

☐ YES (GO TO INTRODUCTION TO QUESTION 138)

These last questions are about the vitamins, minerals, or herbal supplements you took that are NOT part of a One-a-day-, Theragran-, or Centrum-type of multivitamin.

Please include vitamins taken as part of an antioxidant supplement.

138. How often did you take Beta-carotene (NOT as part of a multivitamin in Question 137)?

☐ NEVER (GO TO QUESTION 139)

☐ Less than 1 day per month
☐ 1–3 days per month
☐ 1–3 days per week
☐ 4–6 days per week
☐ Every day

138a. When you took Beta-carotene, about how much did you take in one day?

☐ Less than 10,000 IU
☐ 10,000–14,999 IU
☐ 15,000–19,999 IU
☐ 20,000–24,999 IU
☐ 25,000 IU or more
☐ Don’t know

138b. For how many years have you taken Beta-carotene?

☐ Less than 1 year
☐ 1–4 years
☐ 5–9 years
☐ 10 or more years

139. How often did you take Vitamin A (NOT as part of a multivitamin in Question 137)?

☐ NEVER (GO TO QUESTION 140)

☐ Less than 1 day per month
☐ 1–3 days per month
☐ 1–3 days per week
☐ 4–6 days per week
☐ Every day

139a. When you took Vitamin A, about how much did you take in one day?

☐ Less than 8,000 IU
☐ 8,000–9,999 IU
☐ 10,000–14,999 IU
☐ 15,000–24,999 IU
☐ 25,000 IU or more
☐ Don’t know

139b. For how many years have you take Vitamin A?

☐ Less than 1 year
☐ 1–4 years
☐ 5–9 years
☐ 10 or more years

140. How often did you take Vitamin C (NOT as part of a multivitamin in Question 137)?

☐ NEVER (GO TO QUESTION 141)

☐ Less than 1 day per month
☐ 1–3 days per month
☐ 1–3 days per week
☐ 4–6 days per week
☐ Every day

140a. When you took Vitamin C, about how much did you take in one day?

☐ Less than 500 mg
☐ 500–999 mg
☐ 1,000–1,499 mg
☐ 1,500–1,999 mg
☐ 2,000 mg or more
☐ Don’t know

140b. For how many years have you taken Vitamin C?

☐ Less than 1 year
☐ 1–4 years
☐ 5–9 years
☐ 10 or more years

Question 139 appears in the next column

Question 141 appears on the next page
Over the past 12 months...

141. How often did you take Vitamin E (NOT as part of a multivitamin in Question 137)?

☐ NEVER (GO TO QUESTION 142)
☐ Less than 1 day per month
☐ 1–3 days per month
☐ 1–3 days per week
☐ 4–6 days per week
☐ Every day

141a. When you took Vitamin E, about how much did you take in one day?

☐ Less than 400 IU
☐ 400–799 IU
☐ 800–999 IU
☐ 1,000 IU or more
☐ Don’t know

141b. For how many years have you taken Vitamin E?

☐ Less than 1 year
☐ 1–4 years
☐ 5–9 years
☐ 10 or more years

142. How often did you take Calcium or Calcium-containing antacids (NOT as part of a multivitamin in Question 137)?

☐ NEVER (GO TO QUESTION 143)
☐ Less than 1 day per month
☐ 1–3 days per month
☐ 1–3 days per week
☐ 4–6 days per week
☐ Every day

142a. When you took Calcium or Calcium-containing antacids, about how much elemental calcium did you take in one day? (If possible, please check the label for elemental calcium.)

☐ Less than 500 mg
☐ 500–599 mg
☐ 600–999 mg
☐ 1,000 mg or more
☐ Don’t know

142b. For how many years have you taken Calcium or Calcium-containing antacids?

☐ Less than 1 year
☐ 1–4 years
☐ 5–9 years
☐ 10 or more years

The last two questions ask you about other supplements you took more than once per week.

143. Please mark any of the following single supplements you took more than once per week (NOT as part of a multivitamin in Question 137):

☐ 8-6
☐ B-complex
☐ Brewer’s yeast
☐ Cod liver oil
☐ Coenzyme Q
☐ Fish oil
☐ (Omega-3 fatty acids)
☐ Folic acid/folate
☐ Glucosamine
☐ Hydroxytryptophan (HTP)
☐ Iron
☐ Niacin
☐ Selenium
☐ Zinc

144. Please mark any of the following herbal or botanical supplements you took more than once per week.

☐ Aloe Vera
☐ Astragalus
☐ Bilberry
☐ Cascara sagrada
☐ Cat’s claw
☐ Cayenne
☐ Cranberry
☐ Dong Kuai (Tangkwei)
☐ Echinacea
☐ Evening primrose oil
☐ Feverfew
☐ Garlic
☐ Ginger
☐ Ginko biloba
☐ Ginseng (American or Asian)
☐ Goldenseal
☐ Grapeseed extract
☐ Kava, kava
☐ Milk thistle
☐ Saw palmetto
☐ Siberian ginseng
☐ St. John’s wort
☐ Valerian
☐ Other

Thank you very much for completing this questionnaire! Because we want to be able to use all the information you have provided, we would greatly appreciate it if you would please take a moment to review each page making sure that you:

• Did not skip any pages and
• Crossed out the incorrect answer and circled the correct answer if you made any changes.
Appendix H

“Hormone Therapy and Bone Health” Handout
Hormone therapy (also called Androgen Deprivation Therapy or ADT) is the preferred therapy for patients with prostate cancer recurrence, and may also be given prior to surgical or radiation treatment.

Hormone therapy reduces testosterone (male hormone) levels in the body by preventing its production. This reduction in testosterone level is associated with the potential for side effects such as hot flashes, fatigue, weight gain and anemia (iron deficiency).

Bone loss is another serious side effect of hormone therapy. With reduced levels of testosterone, estrogen (female hormone) levels are also reduced. Bone loss may occur in men on hormone therapy because estrogen is the primary bone-protecting hormone in the body.

Within the first year of hormone therapy, men can lose up to 10% of their bone mass \(^1\), an amount greater than in postmenopausal women. Without proper preventive action, this bone loss can lead to osteoporosis. Additional risk factors for osteoporosis include: increasing age, family history and previous fragility fracture (breaking a bone).

Bone loss naturally occurs with age, and some men with prostate cancer may already have low bone density. Approximately 30% of men with prostate cancer may have medically significant bone loss or even osteoporosis prior to starting hormone therapy \(^1\). Several studies have investigated the effect of hormone therapy on bone, estimating a decrease of 2 to 10% within the first year of therapy \(^2,3\).

In men undergoing hormone therapy for more than one year, researchers found a significant decrease in bone density. Eighty-eight percent of these men showed bone loss or were diagnosed with osteoporosis \(^2\). The longer a man is on hormone therapy, the greater the potential for bone loss and development of osteoporosis.

The development of osteoporosis leads to an increased risk of fracture. The most common fracture site in men is the hip. Fracture risk may be as high as 35% for men five years or more after starting hormone therapy \(^1\). Men on hormone therapy are at a five-fold higher risk of fracture in comparison to men not on hormone therapy \(^3\).

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What can a man do to reduce his risk of bone loss? Proper nutrition and exercise is key to preventing the loss of bone. The following pages describe some important nutrients for bone health, current recommendations and how you can reduce your risk of developing osteoporosis with diet and lifestyle changes.

Calcium is essential for bone health and an adequate intake of calcium has been shown to prevent bone loss. For men on hormone therapy, the current recommendation for calcium is 1500 milligrams (mg) per day. While milk and milk products are the primary calcium contributors in our diet, other excellent calcium-rich sources include broccoli, almonds, fortified soy milk, tofu and bok choy.

<table>
<thead>
<tr>
<th>Food item</th>
<th>Serving</th>
<th>Calcium content (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Milk (skim, 1%, 2%, whole)</td>
<td>1 cup (250 ml)</td>
<td>300</td>
</tr>
<tr>
<td>Yogurt, plain</td>
<td>¾ cup (175 ml)</td>
<td>300</td>
</tr>
<tr>
<td>Hard cheese (cheddar, Swiss, gouda)</td>
<td>2 oz (55 g)</td>
<td>360 – 400</td>
</tr>
<tr>
<td>Salmon, canned with bones</td>
<td>½ can (100 g)</td>
<td>230</td>
</tr>
<tr>
<td>Almonds, dry roasted</td>
<td>½ cup (35 g)</td>
<td>80</td>
</tr>
<tr>
<td>Bok choy, cooked</td>
<td>½ cup (125 ml)</td>
<td>75</td>
</tr>
<tr>
<td>Cottage cheese, 1%</td>
<td>½ cup (125 ml)</td>
<td>70</td>
</tr>
<tr>
<td>Lentils &amp; beans (kidney, garbanzo, lima)</td>
<td>1 cup (250 ml)</td>
<td>40 – 80</td>
</tr>
<tr>
<td>Orange</td>
<td>1 medium</td>
<td>65</td>
</tr>
<tr>
<td>Bread, whole grain</td>
<td>2 slices</td>
<td>30</td>
</tr>
<tr>
<td>Broccoli, cooked</td>
<td>½ cup (125 ml)</td>
<td>30</td>
</tr>
<tr>
<td>Antacids (Tums®, Rolaids®)</td>
<td>1 tablet</td>
<td>200 – 600</td>
</tr>
</tbody>
</table>


Many men may find this increased need for calcium difficult to meet with diet alone. In fact, the average intake of calcium from food and supplements among British Columbian men aged 51 to 70 years is just 917 mg per day. If you think that your diet is not providing enough calcium, a multivitamin or calcium supplement may be a consideration. Most multivitamins provide between 125 – 225 mg of calcium, so read the label.

If your diet and a multivitamin do not provide you with enough calcium and you wish to take a supplement, there are some important points to consider. Calcium carbonate and calcium citrate are the two most common forms available in supplements. While both are absorbed equally well, calcium carbonate tends to be less expensive. Just remember that calcium carbonate must be taken with food because it requires stomach acid to be properly absorbed. Calcium citrate does not need to be taken with food. Calcium supplements are best taken in doses lower than 500 milligrams as our body can only absorb small amounts of elemental calcium at one time. To determine the appropriate calcium supplement dose for you, talk to a dietitian.

Ensure that you are not getting more than 2500 milligrams of calcium each day from food and supplements. Excess amounts of calcium can lead to high blood calcium levels, kidney stone formation and serious kidney damage.

Vitamin D is also important for bone health, as vitamin D and calcium are closely involved in the protection of bone. Adequate vitamin D levels actually increase the absorption of calcium by up to 80% \(^4\). Although vitamin D is made by our body with exposure of our skin to sunlight, at northern latitudes (like in Canada), the sunlight may not be strong enough during the late fall and winter months to make vitamin D in adequate amounts \(^6\). In addition, the efficiency of vitamin D production by the body declines with age.

Men on hormone therapy are encouraged to get **800 IU (20 micrograms) of vitamin D each day**. Vitamin D occurs naturally in very few foods, most of which are not readily consumed in the North American diet (such as beef liver and cod liver oil). In Canada, all fluid milk (excluding buttermilk) is fortified with vitamin D, as are most margarines and soy milk.

<table>
<thead>
<tr>
<th>Food item</th>
<th>Serving</th>
<th>Vitamin D content</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cod liver oil</td>
<td>1 tbsp (15 ml)</td>
<td>1280</td>
</tr>
<tr>
<td>Salmon, cooked</td>
<td>3 oz (100 g)</td>
<td>328</td>
</tr>
<tr>
<td>Mackerel, cooked</td>
<td>3 oz (100 g)</td>
<td>108</td>
</tr>
<tr>
<td><strong>Milk, fortified (skim, 1%, 2%, whole)</strong></td>
<td>1 cup (250 ml)</td>
<td>100</td>
</tr>
<tr>
<td>Soy milk, fortified</td>
<td>1 cup (250 ml)</td>
<td>100</td>
</tr>
<tr>
<td>Sardines, canned in oil</td>
<td>1 can (92 g)</td>
<td>84</td>
</tr>
<tr>
<td>Margarine, fortified</td>
<td>1 tbsp (15 ml)</td>
<td>60</td>
</tr>
<tr>
<td>Beef liver, cooked</td>
<td>3 oz (100 g)</td>
<td>28</td>
</tr>
<tr>
<td>Egg yolk</td>
<td>1 large</td>
<td>25</td>
</tr>
</tbody>
</table>


These increased recommendations may be hard to meet with diet alone. The average vitamin D intake among North American men aged 51 years and older is only 5 micrograms (mcg) per day \(^7\), half of what is considered the Adequate Intake (AI) and one-quarter of the recommendation for men on hormone therapy. For Canadian men aged 50 years and older, and those on hormone therapy, vitamin D supplements may be a consideration.

Generally, the dose in most multivitamins (400 IU) is sufficient and safe; if you are thinking about a higher dose of vitamin D, talk to your doctor or a dietitian. If you are currently taking a calcium supplement, make sure to read the label as many contain 50 – 200 IU of vitamin D as well.

If you decide to take additional vitamin D, ensure that you are not getting more than 50 micrograms (2000 IU) of vitamin D each day. Excess amounts of vitamin D can cause increased blood calcium, nausea, vomiting and confusion.

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Ensure an Adequate Intake of Protein. Ensuring that your diet contains an adequate amount of protein is important for bone health, and may reduce the risk of hip fracture. Protein comes from animal sources (like meat, fish, poultry, eggs and milk products) and non-animal sources (like beans, nuts, lentils and soy). Canada's Food Guide to Healthy Eating recommends choosing: lower fat milk products; leaner cuts of meat, poultry and fish; and non-animal sources of protein more often.

Reduce Your Intake of Caffeine. Monitoring your intake of caffeine from sources like coffee, tea, chocolate and soft drinks is important, as high caffeine intakes have negative effects on bone; four or more cups of coffee per day significantly increases your risk of hip fracture.

Limit the Amount of Salt in your Diet. High salt (sodium) intakes (greater than 2100 milligrams per day) have a negative effect on bone health. The average sodium intake of British Columbian men aged 51–70 years is 3500 milligrams per day. Compare that to our body's minimum requirement for salt, which is only 115 milligrams. You can lower your sodium intake by limiting processed foods (like crackers, canned soups and sauces, and convenience/fast foods) and reducing the amount of salt that you add at the table and during cooking. Together, processed foods and this added salt contribute approximately 90% of the sodium in our diets.

Adopt a Healthy Lifestyle. In addition to dietary changes, men on hormone therapy are encouraged to adopt a healthy lifestyle, including staying physically active and not smoking. Not only is smoking bad for your heart and general health, smokers tend to have lower bone mass and are at greater risk for bone loss.

Physical activity acts directly on bone to increase bone mass and density by stimulating the growth of new bone. Being physically active also improves muscle strength, coordination and balance, helping to reduce the potential for falls that can lead to fractures.

Participating in weight-bearing activities reduces the risk of fractures in men. Weight bearing activities include brisk walking, jogging, climbing stairs, lifting weights, hiking, doing aerobics and participating in racquet sports. Even carrying groceries and dancing are considered weight-bearing activities. Check with your doctor before starting a new exercise program.

If you are currently on hormone therapy and think that you may be at risk for bone loss, talk to your doctor about the risk factors for osteoporosis. For more information on preventing bone loss with diet, talk to a dietitian.