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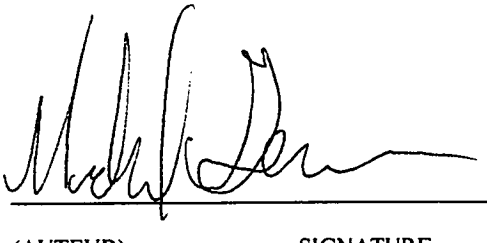

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Dietary Risk Factors for Testicular Cancer

By

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ABSTRACT

Although testicular cancer is a relatively rare cancer in Canada, accounting for only 1.1% of all malignant neoplasms in males, it is the most common cancer among men 20 to 45. Understanding of the causes of testicular cancer risk in general, and the association with diet in particular, remains limited. Data from the National Enhanced Cancer Surveillance System were used to explore the relationship of diet and testicular cancer risk. There were 601 cases of testicular cancer and 744 controls available for study. We systematically examined 17 food groups, 15 nutrients, and 7 individual foods based on data collected through a 69-item food-frequency questionnaire. Our results suggest that higher dairy product intake, specifically cheese, is associated with a higher risk of testicular cancer in Canadian males. Risk differences were observed between histological subtypes of testicular cancer. This thesis provides a basis for future studies designed to address testicular cancer etiology.

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To all my friends who still think Epidemiology is about skin...

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To the Ecclesiax community, I can't wait to see where we end up.

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This project uses data collected through the National Enhanced Cancer Surveillance System, a collaboration of the Surveillance and Risk Assessment Division, Centre for Chronic Disease Prevention and Control, Population and Public Health Branch, Health Canada and the Canadian Cancer Registries Epidemiology Research Group

"Indeed, one of the ultimate advantages of an education is simply coming to the end of it" – BF Skinner

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LIST OF ACRONYMS

MDT - Maldescendent Testicles
NECSS - National Enhanced Cancer Surveillance System
IARC - International Agency for Research on Cancer
CIS - Carcinoma in situ
DES - Diethylstilbestrol
OR - Odds Ratio
CI - Confidence Interval
BMI - Body Mass Index
SIR - Standardized Incidence Ratio
RR - Relative Risk
SES - Socio-economic status
O/E - Observed/Expected
NRC - National Research Council
Hz - Hertz
EMF - Electromagnetic Field
FFQ - Food Frequency Questionnaire
DHQ - Dietary Habits Questionnaire
PYS - Pack years
CNF - Canadian Nutrient File

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1. Introduction

1.1. Trends in Testicular Cancer Incidence

Testicular cancer accounts for 1.1% of all malignant neoplasms in Canadian males[1]. The incidence rate of testicular cancer has been increasing since the middle of the 20th century in many western countries, including Canada[1], the United States[2], the Nordic Countries[3], and Britain[4]. The trend has been especially rapid in eastern European countries such as Slovenia[5]. Countries with a sufficiently long period of cancer registration, such as Denmark, document this trend back to the first half of the 20th century[3]. In Canada a 50% increase in the incidence of testicular cancer has been observed over the last 25 years[1]. It is important to note that while this disease is an important cause of morbidity in young males, testicular cancer is one of the most curable of all solid neoplasms[6]. The five year survival rate has increased during the last 30 years from 63% to over 90%[7]. The present case fatality rate is 10-15 percent, and even in metastatic cases, cure rates are as high as 80 percent[5].

There are several risk factors for testicular cancer that are well established within the literature. These include: cryptochidism or maldescendent testicles (MDT)[8-23], carcinoma *in situ*[24;25], exposure to estrogen *in utero*[9;22;26], and the late onset of puberty (a protective effect)[11;14;20;27-29].

1.2. Nutritional Epidemiology

The field of nutritional epidemiology arises from an interest in the concept that aspects of diet may influence the occurrence of human disease[30]. Nutrition has been linked to

disease and health since ancient times when insightful observations were passed down over centuries by word of mouth[31]. Hippocrates in the fourth century BC observed a relation between health and food. He suggested that if one does not comprehend their link, we cannot understand the diseases which befall man[31]. In 1753, Lind observed the effect of diet on disease; specifically, he noted that administering lemons and oranges eliminated the effects of scurvy[32]. Contemporary nutritional epidemiology focuses primarily on the major diseases of Western Civilization, particularly heart disease and cancer[30].

In a comprehensive review of avoidable causes of cancer mortality, Doll and Peto[33], suggested that dietary factors may account for approximately 35% of cancer deaths, similar to the impact of smoking. The uncertainty associated with this estimate was high, ranging from 10% to 70%[34]. Recently, Willett summarized the major dietary risk factors linked to cancer [34]. These factors included: obesity and adult weight gain, inadequate fruit and vegetable consumption, red meat, and alcohol consumption.

1.3. Diet and Testicular Cancer Risk

The number of studies examining diet and testicular cancer risk is limited; however, their findings have suggested several dietary risk factors for testicular cancer. To date, in the peer reviewed literature, there have been three ecological studies[35-37], three case-control studies[29;38;39] and one twin study[40] examining diet and testicular cancer risk. Unfortunately, the case-control studies have been based on small sample sizes, and the study with the largest sample size does not discuss how the dietary information was gathered[29]. In addition, one study looked at fruit and vegetable consumption as a

confounder of the relationship between physical activity and testicular cancer[41]. This limited understanding the association between diet and testicular cancer risk is a shortcoming in the literature. This thesis will address the role of diet in testicular cancer etiology, through the largest case-control analysis of diet and testicular cancer conducted to date.

1.4. Research Objectives

The purpose of this thesis is to explore the relationship between testicular cancer and diet. As this relationship has yet to be extensively investigated within the cancer literature, exploration of the data for possible significant risk relationships will be important in order to direct further studies in this area. The dataset to be used is based on the National Enhanced Cancer Surveillance System. The specific research objectives are:

1.4.1. Primary Objectives

1) To explore the relationship of different food groups and nutrients to testicular cancer risk
2) To determine if there is an increased risk of testicular cancer associated with fat, meat, iron and dairy product intake
3) To examine the effect of fruits, vegetables, dietary fiber and calcium in testicular cancer

1.4.2. Secondary Objectives

1) To examine the differences in dietary risk factors in the two subtypes of testicular cancer: seminomas and non-seminomas

1.5. Outline of Thesis

This thesis consists of eight chapters beginning with an introduction and a comprehensive review of the literature surrounding testicular cancer risk. The third chapter deals with the methodology of the data set used for analysis, the National Enhanced Cancer Surveillance System. Chapter four details the methodology used to created the food groups and convert the FFQ into nutrients. In addition, chapter four reports on the methodology of analysis for both the food group and nutrient analyses. The results of the analyses are reported in three chapters: chapter five in regard to the total sample, and chapters six and seven for seminomas and non-seminomas, respectively. The final chapter provides a discussion of these results and a brief conclusion.

2. Literature Review

2.1. The biology and clinical features of Testicular Cancer

Ninety-five percent of all tumors of the testis are germ cell neoplasms, with the remaining five percent consisting of non-germinal neoplasms[42]. The International Agency for Research on Cancer (IARC) recognizes four specific types of germ cell tumours: seminomas, embryonal carcinomas, malignant teratomas and choriocarcinomas[43]. However, these can be combined into two histologies: seminomas and non-seminomas. Approximately 50% of all germ cell tumours are seminomas and 50% non-seminomas[44]. While there are several subtypes of testicular tumors, a more detailed histology is of little relevance in predicting clinical outcome or in studies of etiology[5]. As well, a large majority of the literature that stratifies analyses by histological subtype does so by seminomas and non-seminomas.

There are two theories on the histogenesis of testicular tumors. The dual origin theory hypothesizes a separate origin for seminomas and non-seminomas [45]. The holistic or single germ cell origin theory, which is favored, suggests that a single cell takes the form of CIS. These CIS cells have stem cell properties, and can give rise to both seminomas and non-seminomas[24]. Historically, seminomas have been viewed as an intermediate stage during the transformation of CIS into non-seminomas. However, it is now well accepted that seminomas are not intermediate to non-seminomas[24]. It would seem that co-factors are required to stimulate these stem cells to develop into the different types of testicular tumours. One co-factor appears to be young age. This factor is observed in that the earlier the transition from CIS into invasive cancer, the higher the probability of

developing non-seminomatous elements, with the reciprocal true as and older age of transition leads to seminomas[24].

Testicular cancer does not have any early symptoms. Cases usually present with non-specific complaints, such as a heavy feeling in the testicle[45]. Early detection can be accomplished by monthly self-examination, which requires a manual examination of the testicles for lumps or other abnormalities. While ultrasound scans can assist the diagnosis, confirmation requires a biopsy and pathologic examination of tissue[5]. At diagnosis, seminomas are more often localized and less often metastatic than non-seminomas[46].

Treatment of testicular cancer involves surgery, usually an orchiectomy, but sometimes includes a retroperitoneal lymph node dissection, depending on the stage of the cancer. Following surgery the patient usually undergoes radiation and/or chemotherapy. If the cancer is metastatic, surgery is sometimes delayed until after chemotherapy or radiation[45].

Advances in treatment have led to an increase in the five-year survival for testicular cancer during the last 30 years from 63% to over 90%[7]. As a result, current research on treatment focuses on how to individualize therapy for specific patients so that survival is not compromised while morbidity is minimized and quality of life maintained[7].

The age distribution of testicular cancer is very distinct. The major peak of incidence occurs between the ages of 25-35 in Canada[1]. A second, much smaller, peak occurs after

80 years of age[1;2;47]. This age distribution is very different than that observed for most other cancers, which normally peak much later in life. Thus, it is important to ensure that the age distribution of cases and controls are similar or that age is controlled for in statistical analyses.

2.1.1. Animal Models for Testicular Cancer

There has been a long-standing controversy about whether mice with testicular tumors are valid models of human testicular cancer[48]. Adult testicular tumors arise from CIS, consist of seminomas and non-seminomas and have consistent chromosomal abnormalities, whereas mouse tumors do not show these traits[48]. It has yet to be determined whether the same genes and molecular level pathways are involved in the development of testicular tumours in mice as in humans. This has been shown for other cancers (e.g. colon cancer[48-50]). Until this is established in mice, the generalizability of animal research will unclear.

2.2. Trends in Testicular Cancer Incidence

Testicular cancer is a rare cancer, with an age-adjusted incidence of 4.2/100,000 in 1993. Despite this low overall incidence, it is the most common cancer in young and middle-aged men[1]. In Canada, over the last 25 years a 50% increase in the incidence of testicular cancer has been observed[1]. In Ontario, over the last 30 years, the incidence has increased about 60% overall, representing an increase of 2% per annum[51]. Countries with a sufficiently long period of cancer registration, such as Denmark, can trace this trend back to the first half of the 20th century[3]. Despite the increase in testicular cancer in many western countries, the age-adjusted incidence of testicular cancer is low in all populations of the world. The lowest rates have been observed in Asian populations, African

Americans, and black populations in general[42]. The incidence rate in Denmark is in the order of 8 per 100,000, while in Japan and China and in African Americans, the incidence rate is on the order of 1 per 100,000[42].

There are several factors associated with the observed trends in testicular cancer incidence. A Canadian study by Liu *et al.*[1] found that birth cohort is a more important determinant of testicular cancer incidence than time period. Further evidence for the importance of a birth cohort effect in testicular cancer incidence is a finding from Norway. Males that were born during the Nazi Occupation (1940-1944) had a decreased risk of testicular cancer when compared to those born in the five year time periods before or after this period (1935-39 and 1945-1949)[47]. A similar trend was also found in a study of Danish data from the same time period[46]. The Nazi occupation of Norway caused many lifestyle changes, including decreased use of polluting vehicles, an increase in physical activity, and an increase in the consumption of vegetables and dietary fiber [47]. These observations suggest that exposure to environmental risk factors, including diet and environmental pollution, may be important in the development of testicular cancer.

2.3. Congenital Risk Factors

The major known risk factor for testicular cancer is cryptochidism (maldescendent testicle(s) MDT)[8-23]. "The truly cryptochid testis is the testis that lies above the external inguinal ring either within the inguinal canal or within the abdomen, and is non-palpable in the unanesthestized patient"[52]. The abnormality can be unilateral or bilateral. The association between MDT and testicular cancer was suggested as early as the beginning of the 19th century[18]. The risk for testicular cancer associated with MDT is in the order a

two to four-fold increase, with a population attributable risk of 10%[8;53]. However, some studies have found a relative risk associated with MDT in the order of 5 to 10[10;17;19;20]. There seem to be two possible links between MDT and testicular cancer. The first is that they are associated through shared risk factors, such as *in utero* exposure to estrogens. The second is that MDT may be part of a causal chain that can lead to testicular cancer. One hypothesis would be that the elevated temperature the cryptochid testes is subjected to while residing in the body cavity causes mutations that lead to malignancy or promote cellular growth. The explanation for the relationship between MDT and testicular cancer remains unclear[10].

Orchidopexy, the surgical procedure used to correct MDT, has been suggested to decrease the risk of testicular cancer associated with MDT, depending on the age of correction[10 5;14]. The optimum age at which the MDT should be corrected to maximize the protective effect on testicular cancer risk is unclear; it may be before 10 years[12;14] or even as early as 2 years of age[10]. Despite the unclear role of orchidopexy in attenuating the risk of testicular cancer in males with MDT, it is important for assisting in the early detection of testicular cancer[54], in that the testes after orchidopexy both reside in the scrotum and are accessible for palpation.

A hydrocele is a collection of watery fluid around the testicle, a common problem in newborn males that normally goes away within the first year of life[55]. One study[21] found that the presence of a hydrocele was associated with an increased risk of testicular cancer (OR=6.64; CI 1.94-22.7). However, a more recent study found no increase in risk (RR = 2.4; 95% CI = 0.6-9.0)[56].

2.4. Carcinoma *in situ*

Carcinoma *in situ* (CIS) of the testis is a distinct histological pattern preceding the development of seminomatous and non-seminomatous germ cell tumours of the testis[57]. Fifty percent of patients diagnosed with CIS of the testis develop invasive testicular cancer within five years post-diagnosis[18]. It is thought that all patients who harbour CIS cells at puberty will eventually develop testicular cancer[24]. The association between CIS and testicular cancer was first described in 1972[25]. It is now generally agreed that nearly all testicular cancer is preceded by the presence of CIS cells, with the exception of two rare tumour types: infantile germ-cell tumours, and spermatocytic seminoma, the latter which occurs in relatively older men[24]. This suggests two important methods of preventing testicular cancer: limiting the factors that cause CIS, and/or preventing the progression of the CIS to invasive cancer. The identification of individuals with CIS would be beneficial in that early detection is the key for successful treatment of testicular cancer; thus, CIS positive individuals could be more closely monitored. The type of testicular cancer (seminoma vs. non-seminoma) is also hypothesized to be linked to CIS. There is a higher probability of developing non-seminomatous elements if the transition from CIS to invasive cancer occurs at a young age[24]. The opposite is true for seminomas. At present, a surgical testicular biopsy is the most common method of diagnosing testicular CIS. Because of the invasive nature of this test, it is not useful as a screening tool for the general population[24]. There are several new non-invasive techniques, including scrotal ultrasonography (looking at the testicle for irregular echo patterns), and the analysis of semen for CIS cells [24]. Due to the difficulty in diagnosing CIS in apparently health men, it is not possible to obtain a valid estimate of the prevalence of CIS in the general population at this time.

2.5. Maternal Risk Factors

There are several maternal factors that have been associated with testicular cancer. These usually involve *in utero* exposures and surrogates. Exposures examined include ones that the mother has control over (e.g. maternal smoking), and those which are beyond her control (e.g. exposure of the fetus to endogenous estrogens).

Characteristics of the newborn can sometimes act as surrogates for the maternal *in utero* environment and associated exposures. Birth length was measured in two studies and found to be a non-significant risk factor for testicular cancer[58;59]. A twin study examining testicular cancer risk factors found no difference in the length of the case twin as compared to the healthy co-twin[40]. Five studies have examined the effect of birth weight and testicular cancer. Three found no association (OR = 1.1; CI 0.7-1.7)[9] (OR = 1.25 CI 0.7-2.5)[60] (OR =1.18; CI 0.42-3.33)[58]; two found an increased risk with low-birth weight children (<2,499g) (OR=2.6; CI 1.1-5.9)[59] (OR=3.2; $p<0.05$)[26]. Thus, no clear conclusion can be reached about the effect of birth weight on testicular cancer risk.

There is conflicting evidence on whether maternal age is a risk factor for testicular cancer. Some studies have found that older maternal age increased risk (OR=2.5; CI 1.0-6.0)[60] (OR=1.89; CI 1.14-3.20)[58] (OR=2.0; CI 1.2-3.6 seminomas only)[59], but other studies found no association (OR = 0.9; CI 0.6-1.3)[9] (OR = 1.91; $p>0.05$)[61]. The three studies finding increased risk with increasing maternal age were all case-control studies with large sample sizes[58-60]. The studies observing no association were also case-control in design, with one having a large sample size[9], and the other used a small sample of

mortality data[61]. The effect of maternal age on testicular cancer risk remains unclear. It is important to note that the impact of maternal age on testicular cancer risk in male offspring may only be present in women with no prior children[60].

A study examining maternal health characteristics found that sons of mothers with a retained placenta, at their birth, were at a significantly increased testicular cancer risk (OR=3.3; CI 1.5-7.0)[60]. As well, the presence of Rh-antibodies has been associated with an increased incidence of testicular cancer (OR=11.7; CI 2.8-48.7)[60].

The association between fetal presentation and testicular cancer risk has only been studied once[59]. They found that breech births protected against testicular cancer (OR=0.1; CI 0.0-0.6) when compared to normal presentation at birth. Conversely, the use of vacuum methods or forceps for fetal extraction, commonly used during breech, has been associated with testicular cancer risk (OR=1.6; CI 1.0-2.6)[60].

An excess of an endogenous hormone, likely estrogen, causes nausea during pregnancy[22]. Nausea in pregnancy has been associated with an increased risk of testicular cancer (OR=4.2; $p<0.05$)[26]. However, three studies examining nausea in pregnancy found no excess risk[20;22;62] and one study found a slight protective effect (OR=0.6; CI 0.5-1.0)[59]. All of the studies have small sample sizes or are subject to serious bias. Most studies examining nausea in pregnancy use self-reported questionnaires, which are subject to potential recall bias or other exposure measurement errors. Thus, no definitive conclusions can be drawn about the association of nausea in pregnancy and testicular cancer.

Several studies have indicated that children of mothers with high parity have a decreased risk of testicular cancer when compared to children of nulliparous mothers (p for trend = 0.03)[60] (nulliparous vs. multiparous OR= 1.78; CI 1.00-3.21)[58] (p for trend = 0.03)[63] (p for trend = 0.02)[64]. However, not all studies have demonstrated a protective effect for children of multiparous mothers[11;59]. It has been previously suggested that maternal endogenous estrogen levels are higher in first pregnancies when compared to subsequent ones. Since elevated levels of estrogens in utero have been found to increase risk of testicular cancer (see section 2.7), it would be expected that first-born sons would be at increased risk as a result of their increased exposure to *in utero* estrogens.

Several twin studies have looked at the effect of endogenous hormones and subsequent testicular cancer risk[65-67]. It is thought that dizygotic twin pregnancies have higher maternal hormones levels than monozygotic pregnancies[68;69]. Two studies found that dizygotic twins were at an increased risk of testicular cancer (OR=1.5; CI 1.1-2.2)[65] (O/E ratio = 2.3; CI = 1.1-4.2)[67]. This finding fits the hypothesis that higher levels of maternal estrogens elevate the risk of testicular cancer. The other twin study which looked at maternal hormones in cancer did not consider zygoticity, but examined birth order and same/opposite sex twin pairs[66]. Prenatal estrogen levels may be higher in males with a female co-twin as compared to males with a male co-twin[66]. However, the finding of increased testicular cancer in male/female twins was restricted to when the male twin was born after his female twin (OR=2.50; CI 1.11-6.15).

It has been suggested that diethylstilbestrol (DES) use during pregnancy may lead to an increased risk of testicular cancer in male offspring. DES was prescribed to about 4 million pregnant women, world-wide, from the late 1940s to the early 1970s to prevent abortions and pregnancy complications[70]. Subsequently, DES has been banned as a result of a high incidence of clear-cell adenocarcinoma of the vagina in pubertal girls exposed to DES *in utero*[71]. Currently there is insufficient evidence to support an increased risk of testicular cancer in men exposed to DES *in utero*[53;70;72]. This may be a result of small sample size and study design flaws rather than a true lack of association[53;70]. A recent study performed in the U.S.[73] suggested a possible increased risk (RR = 3.05; CI 0.65, 22.0). Unfortunately, the study was only able to obtain 7 cases in the DES-exposed group and 2 in the non-exposed group, preventing definitive conclusions.

Several studies have found an increased risk of testicular cancer associated with hormone use during pregnancy (OR=4.9; CI 1.7-13.9)[9] (RR=8.0 $p<0.05$)[26] (RR=5.00 $p=0.11$)[22]. The hormones studied have been varied and, in most studies, were not specified in detail. The observed ORs are all in excess of 4.5, and only one was non-significant[22], which seemed to be more a result of a small sample size rather than lack of an actual effect. A study by Weir *et al.*[9] found that the relationship remained significant even when stratifying by histological subtype: seminomas (OR=5.5; CI 1.4-21.8) and non-seminomas (OR=4.1; CI 1.2-14.4). One study[20] found no increased risk of testicular cancer with exogenous hormone use during pregnancy (OR = 0.5 CI 0.2-1.0).

Although smoking is a major cause of morbidity and mortality in Canada, there is some evidence that maternal smoking might be associated with a decrease risk of testicular

cancer. A study performed in Canada[9], found that sons of mothers who smoked more than 12 cigarettes per day during pregnancy had a lower risk of developing testicular cancer (OR=0.6; CI 0.4-0.9). Brown[74] found that maternal smoking had no effect on testicular cancer risk. A protective finding, while not intuitive, could possibly be due to the anti-estrogenic effect of cigarette smoking[75]. However, without a clear dose-response relationship, interpretation of these results remains difficult[9].

Consumption of alcohol during pregnancy has been assessed by one study[9]. The investigators found no significant effect of maternal drinking patterns on the risk of testicular cancer in male offspring (OR = 0.8 CI 0.5, 1.3).

Few studies have examined the effect of maternal occupation on testicular cancer risk. It is plausible that the occupation of the mother might affect germ cells or the fetus if she were working while pregnant (e.g. exposures to pesticides, fertilizers and other chemicals). To date, no studies have found a statistically significant association between testicular cancer and maternal occupation[76;77].

2.6. Personal Risk Factors

2.6.1. Personal Characteristics

Several studies have examined male infertility as a risk factor for testicular cancer[29;78-80]. In general, infertility is the failure to conceive after one year of regular unprotected intercourse with the same partner[81]. While infertility conveys a complete failure to conceive, "subfertility" seems to be a more contemporary way of classifying couples

unable to conceive, leaving the possibility of conception open. Of the four studies examining subfertility as a risk factor, the two most recent are the best designed. The first of these two studies is a case-control study[79] while the other is a cohort study[78]. Subfertility was associated with an increased risk of almost two-fold in both the case-control study (OR=1.98; CI 1.43-2.75)[79] and the cohort study (OR = 1.6; CI 1.3-1.9)[78]. The two older studies have also found an increase in risk (OR=10.0; CI 2.3-∞)[80] (OR=1.76; CI 1.08-2.86)[29]. Several measures were used to define the cohort of men with abnormal semen characteristics (subfertile): low sperm concentration, low sperm motility, and many abnormal sperm[78]. In the cohort study, it was been observed that the subfertility measures have an additive effect: one measure conferred a relative risk of 1.9 while having all three measures gave a relative risk of 9.3[78]. It is evident that subfertility is an important risk factor for testicular cancer. Whether this is through sharing common etiological factors or as part of the causal chain leading to testicular cancer is currently unclear.

The association between testicular cancer and male reproductive health is strengthened by the several investigations suggesting that male reproductive health has been declining since World War II[70]. During the same time period, the incidence of testicular cancer has increased dramatically. A meta-analysis of 61 studies has suggested a substantial decrease in sperm count and semen volume from 1938 to 1990[82]. There are several plausible hypotheses to explain this decline, including environmental chemicals disrupting endocrine function[83], *in utero* exposure to DES[70], and personal factors such as changing diet and an increase in sedentary lifestyles[84]. Change in dietary intake could be associated with increasing prosperity[85].

Males with an initial malignant testicular neoplasm have a greatly increased risk of a second tumor in the contralateral testicle[86]. Two studies have shown that having testicular cancer gives an increased risk for a contralateral tumour (RR=24.8; CI 19-38)[87] (RR=27.5; CI 14-49)[88].

Polythelia (supernumerary nipples) has been reported as a risk factor for testicular cancer[89]. Goedert *et al.* performed a case control study, which compared cases with two control groups. Using medical student controls, the relative risk was estimated to be 4.5 (CI 1.6-12.4). When using a large existing control group from the National Health and Nutrition Examination Survey (NHANES), the investigators obtained a relative risk of 31.8 (CI 13.9-72.6)[89]. The second control group was not interviewed for the study but rather relied on responses collected several years earlier.

In the late 1980s several studies were performed examining the temporality of testicular cancer, particularly month of birth[90-93]. Two of the four studies found significant results: an increasing testicular cancer risk on a four-month cycle in one study ($p<0.001$)[93], and a two-month cycle in the other ($p = 0.000$)[90]. One study found a slight indication of an annual cycle peaking in August[92]. It is currently unclear if month of birth is associated with an increase in risk for testicular cancer. There is no *a priori* reason to expect risk to vary by month of birth.

Testicular cancer incidence varies with race. Blacks and other non-white races have extremely low rates of testicular cancer in comparison with white populations[94]. The difference is so pronounced that most etiologic studies exclude non-white populations.

In the early 1970's, it was hypothesized that there might be a relationship between androgens level and testicular cancer risk, because the peak for testicular cancer incidence occurs during the time of highest androgen levels[95]. Specific androgen levels are difficult to measure in a population study; as such, surrogates are usually used. One surrogate of androgen level is male baldness since a high androgen level leads to baldness at an early age. A study by Petridou *et al.*[62] used the Norwood Hamilton scale of baldness to assess the level of baldness of subjects at the time of interview in a case control study. They found that an increase of one point on this scale was associated with an OR of 0.8 (CI 0.6-1.0 p = 0.04), supporting the hypothesis that high androgen levels may decrease testicular cancer risk.

Age at puberty is a difficult and subjective thing to measure. It appears that late age at puberty is associated with a decreased risk of testicular cancer (OR = 0.34; CI 0.18-0.66, non-seminomas only)[27] (OR=0.5; CI 0.3-0.7)[28] (OR=0.82; CI 0.58-1.14)[11] (OR=0.25; CI 0.25, 0.80)[14] (RR=0.59; CI 0.35-0.97)[29]. The reported statistics are only for studies that created a summary variable for age at puberty. Other studies have used an indicator of puberty (such as shaving, body hair, nocturnal emissions, or voice breaking) rather than defining a single age at puberty. These studies were not included in this review because of their lack of consistency in estimating age at puberty.

Studies of body mass index (BMI) and testicular cancer risk are mixed, with some finding no association (OR=0.8 CI 0.4-1.8)[96], and others reporting testicular cancer to be associated with a reduced BMI (OR=1.50; CI 1.07-2.08)[97] (OR=2.8; CI 1.2-6.4)[62]. Two studies have examined height as a risk factor for testicular cancer[29;97]. One found a statistically significant elevation in testicular cancer risk with increasing height (OR=1.60; CI 1.21-2.10)[97], while the other found an elevated, but non-significant risk (RR = 1.83; CI 0.8-4.1)[29]. Studies examining weight separately from body mass index (BMI) found no association between increased weight and testicular cancer risk[29;96].

2.6.2. Occupational exposures

Two studies have examined paternal occupation as a potential risk factor for testicular cancer. One study of paternal occupation found a significant increase in risk associated with the following occupational groups: wood processors (OR=10.46; CI 1.20-91.14), metalworkers (OR=3.28; CI 1.03-10.52), stationary engineers (OR=3.53; CI 1.05-11.87)[76]. Working in the following industries was associated with an increased risk of testicular cancer: food products (OR=2.79; CI 1.34-5.79), metal products (OR=5.77; CI 1.53-21.77), and food and beverage services (OR=4.36; CI 1.50-12.63)[76]. The other study examining paternal occupation did not find an increased risk; however, the job categories used in that study were very broad [77].

There is a sizable body of literature dealing with the relationship between occupation and testicular cancer risk. Many studies have found positive associations between occupation and testicular cancer[94;98-107]. At risk occupations include: pesticide applicators (SIR=2.37; CI 1.33-3.91)[98], plastic workers (seminoma only OR=3.7; CI 1.3-10.9)[21;99], farmers (embryonal only OR=3.1; CI 1.03-9.1)[99], metal workers (seminoma only

OR=2.05; CI 1.17-3.58)[101] (RR=2.0; CI 1.0-3.8)[102], professionals (RR=1.5; CI 1.1-2.2)[102] (seminoma only OR=2.8; CI 1.4-5.4)[103] (OR 1.13 $p<0.05$)[105] (Obs/Exp = 1.41 $p<0.01$)[94] ($p=0.02$)[107], leather workers (OR=7.2; CI 1.89-27.2)[104], work involving video display units (high exposure only OR=1.8; CI 1.1-3.2) [99], occupational use of hand-held radar (SIR = 1.3 90%; CI = 0.9-1.8)[108] (O/E 6.9 $p< 0.001$)[109], work involving asphalt (OR=3.9; CI 1.1-15)[99], electricians (RR=2.8; CI 1.2-6.4)[102] and naval automobile mechanic equivalent occupations (SIR = 3.4; CI 1.9-5.6)[106]. One study found several occupations associated with an increased risk of non-seminoma testicular cancer[100]: miners (OR=12.39; CI 2.22-69.27), food processors (OR=3.20; CI 1.39-7.35), food product manufacturing (RR=2.2; CI 1.0-4.9)[102], utilities employees (OR=3.15; CI 1.15-8.61), and other service workers (OR=1.05; CI 1.05-4.56). There is some contention around some of these associations, particularly in farmers. Numerous studies suggest that farming is not related to increased risk[110-114].

Exposures to several chemical substances have been linked to increased risk of testicular cancer. These include: fertilizers high in nitrogen (RR=1.84; CI 1.22-2.76)[115], non-specified fertilizers (OR=2.27; CI 1.3-5.0)[80], (OR=2.08; CI 1.1-5.0)[80], fumes or smoke (OR=2.83; CI 1.9-4.7)[80], pesticides (OR=2.37; CI 1.33-3.91)[98] (OR=1.7; CI 1.03-2.8)[99]. Note that these are all occupational exposures, except for the study examining fertilizers high in nitrogen, which considered exposure as a result of nutrient runoff [115]. It has also been suggested that childhood residence in an area with high-nitrate concentrations in the ground water might be associated with increased risk (OR=1.40; CI 1.09-1.81)[110].

Military service in Vietnam has been associated with an increased testicular cancer risk (OR=2.3; CI 1.0-5.5)[116]. This increase in testicular cancer risk has also been observed in dogs serving in Vietnam (OR=1.8; CI 1.2-2.7)[117]. In addition, Vietnam veterans have been found to have diminished semen quality. This decline in semen quality has been noted among soldiers with high exposures to Agent Orange[116]. However, it is unclear if exposure to Agent Orange is directly related to an increase in testicular cancer. A study of testicular cancer in current US navy personnel revealed no difference between the incidence of testicular cancer and the incidence found in the SEER dataset[106], suggesting that increased incidence may be limited to those participating in the Vietnam War.

2.6.3. Disease and Conditions

Many diseases have been examined in relation to testicular cancer. Diseases that have been studied include: mumps orchitis[5;16;21;62;79;118;119], spina bifida ($p<0.01$)[120], neonatal jaundice (OR=3.0; CI 1.4-6.6)[60], sexually transmitted diseases (OR=2.22; CI 1.46-3.39)[118], and mononucleosis (OR=0.6; CI 0.3-1.1)[20]. While mumps orchitis has been studied most frequently, the majority of the studies have failed to find a significant association[5;16;62;79;118;119]. The influence of disease on testicular cancer risk remains unclear.

Inguinal hernia has been implicated as a risk factor for testicular cancer, although the findings are mixed. Inguinal hernias are a bulge of intestine that have pushed through a weak spot in the inguinal canal, which is a triangle-shaped opening between layers of abdominal muscle near the groin[121]. Some studies have reported significant associations between testicular cancer and inguinal hernia (OR= 1.4; CI 1.0-2.1)[12] (OR=1.91; CI 1.12-

3.23)[14] (OR=2.14; CI 1.5-3.2)[80], while other studies have found no association (RR = 1.1 p>0.05)[15] (RR = 1.3; CI 0.9-1.9)[17] (OR = 1.3; CI 0.8-2.1)[20] (RR = 2.28; CI 0.85-5.59)[53]. One study[27], stratifying by seminomas and non-seminomas, found an increased risk for non-seminomas associated with inguinal hernia, but not for seminomas. The lack of histological stratification in most studies may have attenuated the potential association between of inguinal hernias and non-seminomas. It is also possible that recall bias and confusion between "hernia operations" and operations to correct MDT might have made the assessment of this risk factor difficult[122]. Hernias diagnosed before the age of 15 have been observed to increase risk for both seminomas (OR=3.12; CI 1.42-6.88) and non-seminomas (OR=2.49; CI=1.06-5.88)[27], suggesting the need for an early exposure to have an effect on the risk of testicular cancer. Another study[14] found an increased risk only in males diagnosed before the age of 15 (OR=2.64; CI 1.32-5.28).

2.6.4. Miscellaneous exposures

Over the last 15-20 years, there has been considerable interest in the possibility that 60-Hz electromagnetic fields might increase the risk of cancer. EMF exposure assessment is difficult as EMF is produced by more sources than just electric blankets[123], which as been the focus of one study[124]. This study found no increase in testicular cancer risk associated with electric blanket use[124].

Trauma to the scrotum or testicle has been associated with an elevated risk of testicular cancer (OR=1.84; CI 1.03-3.27)[118] (no analytical data)[16] (OR=2.86; CI 1.3-1.23)[80] (RR=1.9; CI 1.3-2.7)[17] (RR=2.6; CI 1.6-4.2)[119]. As well, increased risk is associated with activities that can cause persistent low level trauma, such as bicycle or motorcycle riding (OR=1.79; CI 1.1-3.1)[80]. Trauma could be hypothesized to increase mitotic activity in an

already malignant testicle[118], it may cause the victim to become aware of an already existing tumour. Furthermore, a history of testicular trauma is subject to serious recall bias.

Several studies have examined the relationship between high testicular temperatures, via occupational and non-occupational exposures may be associated with an increased risk of testicular cancer. Three occupational studies found an increased risk (excess of 26.6 degrees Celsius OR = 1.74; CI 1.2-2.6)[80] (>80 degrees F OR = 1.20; CI 0.8-1.80)[125], (OR = 1.74; CI 1.2-2.6)[80]. Non-occupational studies have examined risk associated with bathing as opposed to showering (OR = 3.11; CI 1.5-9.9)[80], and the type of underwear worn (nylon vs cotton OR = 1.81; CI 1.04-3.14)[118]. A recent large-scale case-control study in the UK found no consistent evidence of an effect of testicular temperature on cancer risk[118].

The use of exogenous hormones prior to testicular cancer diagnosis has been reported to have a protective effect (OR=0.5; CI 0.2-1.0 p=0.042)[20]. However, the specific hormone used by these men was not specified. The relationship of exogenous hormone use and testicular cancer risk has not been examined in other studies.

Studies from the late 1980s have indicated that there might be an increased risk of testicular cancer after vasectomy (SIR=4.2; CI 1.8-8.2)[126;127]. Given the wide-spread use of vasectomy around the world, the public health implications of a causal link with testicular cancer would be appreciable. As a result, a number of studies were undertaken to discover if this association could be confirmed. Two large scale studies (one cohort

study and one case-control study) have found no association between vasectomy and testicular cancer (OR = 0.9 CI 0.4-2.3)[128] (SMR = 1.0 CI 0.79-1.28)[13] (p = 0.86)[129]. A review of eight articles[130] found only one study suggesting a positive association.

2.6.5. Lifestyle

The relationship between marital status and testicular cancer risk is unclear. Studies have found both increased[131] and decreased risk[107] for single men. However, most studies have found non-significant results[22;62;107;132;133]. There is no etiological hypothesis linking testicular cancer and marital status.

The majority of the studies on the effect of socio-economic status (SES) on testicular cancer risk have used the SES indicators of social class and/or education. Testicular cancer was associated with higher social class in two studies (linear trend $p<0.05$)[105] ($\chi^2=21.72$ df=3 $p=0.0001$)[134]. Other studies have observed no such effect (OR = 1.12; CI 0.83-1.52)[11;64]. The ethnic distribution of testicular cancer (largely a white man's disease) in places such as the USA would confound the relationship between testicular cancer and SES, as the white population has higher SES and higher testicular cancer incidence. Education has also been used as a measure for SES. One study[41] controlled for education as a surrogate for SES in a multivariate regression analysis and found a positive association of testicular cancer with an increasing level of education, although the data were not presented in this paper.

The effect of physical activity on testicular cancer risk is unclear. Some studies have found that higher levels of physical activity have a protective effect (OR=0.70; CI 0.51-

0.97)[118] (p-value for trend = 0.01)[14], while others have found an adverse effect (OR=2.36; CI 1.20-4.64)[41] or no effect[135]. The studies finding the protective effect for physical activity failed to control for diet, while the study finding an adverse effect controlled for some dietary factors[41].

Smoking has not been extensively examined as a risk factor for testicular cancer. Since testicular cancer is primarily a disease of young men, it may be unlikely that the smoking duration is long enough to significantly affect the process of malignancy. However, a recent study by Srivastava and Kreiger[41] found a significant and positive association between smoking and testicular cancer risk. Unfortunately, they did not explicitly present data in support of their conclusion. Another study by Moller and Skakkebaek[11] found no increased risk (OR = 0.97 CI 0.69-1.37). Thus, the association between smoking and testicular cancer requires further study.

There have been several conflicting studies on rural and urban patterns of testicular cancer[136]. An article published in 1974 suggested a rural preponderance of testicular cancer[136]; however, more recent articles have suggested no rural/urban differences in testicular cancer[137;138]. Thus, it is unclear if having a rural dwelling adds to testicular cancer risk. If there is an increase in risk, the mechanism could be due to a variety of factors, including: genetic aggregation, lifestyle differences and exposures to pesticides.

2.7. Endogenous Estrogen Model

The exact nature of the link between estrogen exposure and testicular cancer is unclear. It has been suggested that exposure to high levels of estrogen *in utero* results in the

development of carcinoma *in situ*, which is a precursor of testicular cancer[24]. The strength of the evidence of testicular cancer risk resulting from high *in utero* exposure to estrogen is such that it suggests that estrogen may be part of the causal chain that leads from healthy testicles to a malignant tumour. The associations between estrogen exposure and testicular cancer include increased risk associated with: endogenous estrogen levels via nausea in pregnancy[26], DES exposure[70;73], and non-specified hormone use in pregnancy[9;26]. In addition to these exposures, maternal endogenous estrogen levels are higher in first pregnancies as compared to subsequent ones and several studies have found that that children of mothers with high parity have a decreased risk of testicular cancer when compared to children of nulliparous mothers[58;60;63;64]. Twin studies suggested that dizygotic twin pregnancies have higher maternal hormones than monozygotic pregnancies[65;67]. Finally, maternal smoking may be protective of testicular cancer[9], possibly be due to the anti-estrogenic effect of cigarette smoking[75]. It appears that estrogen has an important role in the etiology of testicular cancer, and warrants further study.

2.8. Genetic Factors

There is strong evidence to support genetic susceptibility to testicular cancer. There is an increased risk of testicular cancer in brothers (O/E=5.88; CI 2.2-12.8)[139] (RR=12.3; CI 3.3-31.5)[5;140;141], fathers (RR=1.96; CI 1.01-3.43)[140;141], and twin brothers (SIR=37.5; CI 12.3-115.6)[65]. These findings support the existence of a testicular cancer susceptibility gene or genes.

The genetic nature of testicular germ cell tumors in adults is well described in the literature[142]. Testicular tumours have a chromosome number in the triploid range, and are characterized by specific chromosomal gains at chromosomes 7, 8, 12, 21, and X, and by specific chromosomal losses at chromosomes 11, 13, and 18[142]. As early as 1982, a non-random genetic alteration was localized to i(12p)[143]. Studies have shown that 80% of testicular tumors have one or more copies of i(12p)[144]. It would seem that isochromosome 12p is the recurrent structural chromosomal abnormality of these tumors[145]. Recently, a susceptibility gene has been localized to Xq27[146]. One study has estimated that 33.4% of all cases of testicular cancer are in individuals with the malignant genotype[141], assuming it is a recessive trait. However, the responsible genotype is not clear. There are many other potential genetic factors involved in the development or predisposition to testicular cancer[144]; however, these are beyond the scope of this review.

2.9. Food habits and nutrition

It was noted in the 1970s that people in western countries (where diets tended to be high in animal products, fat, and sugar) had high rates of colorectal, breast, prostate, endometrial, and lung cancer. In contrast, individuals in developing countries (where diets tend to be based on one or two starchy staple foods and low intakes of animal products, fat, and sugar) had low rates of these cancers[36;147]. A recent report by the National Research Council identified several potential dietary carcinogens including: fat, linoleic acid, free fatty acids, protein, calories, alcohol, calcium, selenium, iron[148]. More recently carcinogens such as nitrosamines heterocyclic amines and acrylamide[149;150] have been identified as possible dietary carcinogens. Despite the extensive research over the

last 30 years on diet and cancer, there have been few specific dietary determinants established for cancer prevention[147].

The number of studies examining diet and testicular cancer risk is limited. However, their findings have been significant, suggesting a potential dietary component to the etiology of testicular cancer. To date, in the peer reviewed literature, there have been three ecological studies[35-37], three case-control studies[29;38;39] and one twin study[40] examining diet and testicular cancer risk. In addition, one study looked at fruit and vegetable consumption as a confounder of the association between physical activity and testicular cancer risk[41]. Unfortunately, these case-control studies have not provided conclusive evidence for or against dietary risk factors for testicular cancer. Despite the inconclusive nature of these findings, a recent article states that "The timing of the testicular cancer trend is consistent with a dietary origin, and the search for candidates should extend beyond hormonal agents to include those capable of causing genetic damage"[85].

The U.S. National Research Council (NRC) has concluded that fat exhibits the most consistent cancer-enhancing effect of all dietary factors[148]. Armstrong and Doll[36] first reported an ecological association of fat and testicular cancer in 1975. Their study found that *per capita* fat intake correlated significantly with the incidence of testicular cancer in the corresponding country. A case-control study performed in Uruguay found an association between a high-fat diet and testicular cancer[151]. A third study[38], found a significant trend of increasing testicular cancer risk with increasing fat consumption (highest vs lowest quartiles). The results were suggestive of increased risk within

different histological subtypes as well: non-seminomas (OR=6.3; CI 1.9-20.5 p-trend = 0.002), seminomas (OR=1.9; CI 0.6-5.5 p-trend = 0.08), and mixed germ cell tumours (OR=4.2; CI 0.9-18.7 p-trend = 0.051)[38]. The increased risk of testicular cancer found with higher intake of dietary fat is consistent with many reports for cancers at other hormonally influenced sites such as breast, prostate, colon, and ovary[38;152-154]. This commonality may suggest that the mechanism of carcinogenesis in testicular cancer is similar to those identified for other hormonally influenced sites. Fat intake has been associated with changing hormonal levels and breast cancer risk[30]. It may then be plausible to assume that fat intake in males will impact hormonal levels and influence risk of testicular cancer.

Considerable controversy has surrounded the putative role of iron in carcinogenesis. As a result, the NRC has stated that further investigations are needed to understand this effect[148]. There have been no studies to date examining the relationship between iron intake and testicular cancer. A recent paper hypothesizes that our "western" iron replete diet might act as a promoter of testicular cancer[155].

Muir *et al.*[156] found an ecological association between dairy products and testicular cancer. Another ecological study[35] found that there was a correlation of testicular incidence with milk (r = 0.49) and cheese (r=0.58). Most recently, an ecological study revealed a strong correlation of testicular cancer incidence and cheese (r=0.80), animal fats (r=0.77) and milk (r = 0.74)[37]. Three case control studies[29;38;39] and one twin study[40] have examined milk and dairy products in relation to testicular cancer. Findings have been mixed. Two of the case-control studies found no association[29;38] while one study

found an association with milk consumption during adolescence (OR=1.23; CI 1.09-1.38)[39]. The twin study grouped dairy products into a single category, finding no difference in total consumption of dairy products between case and co-twin[40]. Two of the case-control studies examined other dairy products, such as yogurt and cheese, and found no association between testicular cancer and dairy product intake[29;39].

Egg intake has been investigated ecologically[35], in a case-control study[29] and in a twin study[40]. No significant associations have been found.

Meat consumption, particularly red meat, has been ecologically associated with an increased risk of testicular cancer (r = 0.54)[35]. Three studies found increased consumption among testicular cancer cases[38;151;157], while another found no increase in consumption[29]. A twin study found no difference in the consumption of meat between the two twins[40]. Sigurdson *et al.*[38] examined the risk by histological subtype and found that the association seemed stronger for seminomas (OR=3.6; CI 1.1-11.1 p-trend=0.03) than non-seminomas (OR = 2.3; CI 0.8-6.8 p-trend=0.06) and mixed germ cell tumours (OR = 1.8; CI 0.6-5.6 p-trend=0.23).

Higher consumption of fruits and vegetables has been associated with a reduced risk of cancer at many sites in numerous epidemiological studies[34]. Diets low in fruit and vegetable consumption have been associated with elevated risk of testicular cancer[151;157]. Two studies found no difference in consumption between cases and controls[38;39]. A twin study[40] found a borderline significant protective effect associated with the consumption of vegetables for the co-twin of a male with testicular cancer (OR = 0.3; CI 0.1-1.0).

Excessive alcohol consumption has been linked to increased cancer risk at several sites in humans[148]. While ingestion of alcohol appears to increase the risk of cancer in susceptible individuals, it does not appear to be a genotoxic carcinogen[148]. Wine consumption has been correlated with testicular cancer in an ecologic study (r=0.63)[35]. Only one non-ecological study has looked at alcohol consumption. They found no increased risk for spirit or beer consumption but an increased risk for regular wine drinkers (RR=1.71; CI 1.21-2.43)[29].

To our knowledge, only one study has examined cholesterol intake and testicular cancer[38]. The findings were significant for non-seminomas (OR=4.6; CI 1.5-13.8 p-trend=0.01), and seminomas (OR=3.1; CI 1.1-9.0 p-trend=0.02), but not for mixed germ cell tumors[38].

Intake of dietary calcium has been suggested to have a protective effect on both prostrate and colon cancers[148]. Only one study has examined the effect of dietary calcium with testicular cancer. The study found a significant trend, with higher calcium intake associated with lower testicular cancer risk (non-seminomas only, p-trend=0.05)[38]. There was no observed effect for seminoma or mixed-germ cell tumours.

One study has looked at the relationship between dietary fibre and testicular cancer[38]. They found a significantly lower risk with low dietary fibre intake for non-seminomas only (OR=4.0; CI 1.3-12.4)[38].

2.10. Summary of Risk Factors

There are several frequently cited risk factors for testicular cancer. These include: cryptochidism (MDT), exposure to estrogen *in utero* (both endogenous and exogenous exposures), high levels of androgens (protective), age (younger age as a risk factor), and the late onset of puberty (protective). The increasing incidence of testicular cancer and the increasing levels of hormones in the environment suggest a potential role of hormones in testicular cancer development. There is also a parallel between the increased incidence of testicular cancer and the decrease in male reproductive health. Risk factors requiring more research include hernia, occupational exposures, mumps orchitis, and the effect of testicular trauma on testicular cancer risk. There has not been a significant focus on dietary risk factors for testicular cancer. However, current evidence suggests that dairy products may be associated with an increase in risk. It is possible that both calcium and fat intake may increase testicular cancer risk, while fruits and vegetables may decrease risk.

2.11. Summary of dietary risk factors for testicular cancer

Table 1. Summary of dietary literature

Study (ref #) and year	Location	No. of Subjects	Type of Study	Dietary Variables	Results	Notes
Decarli *et al.* (35), 1986	Italy	20 Italian regions	Ecological	Bread Oil Pasta Fish Meat Milk Cheese Eggs Sugar Coffee Wine	r = -0.51 r = -0.08 r = -0.63 r = -0.62 r = 0.54 r = 0.49 r = 0.58 r = 0.25 r = 0.56 r = 0.47 r = 0.63	Correlation using mortality rates
Armstrong *et al.* (36), 1975	North America, Europe, Africa, Australia, Asia	23 countries	Ecological	Cereals Sugar Meat Milk Fats + oils Calories Animal Protein Total Protein Total Fat Coffee	r = -0.50 r = 0.60 r = 0.50 r = 0.57 r = 0.76 r = 0.54 r = 0.59 r = 0.34 r = 0.76 r = 0.45	Correlation using mortality rates
Ganmaa *et al.* (37), 2002	North America, South America, Europe, Africa, Australia, Asia	42 countries	Ecological	Animal fats Butter Cheese Eggs Meat Fish Milk Cereals Fruits Vegetables Vegetable oils Alcohol Coffee Tea	r = 0.77 r = 0.63 r = 0.77 r = 0.60 r = 0.69 r = 0.05 r = 0.75 r = -0.47 r = 0.33 r = 0.08 r = 0.45 r = 0.60 r = 0.61 r = 0.08	Correlation using incidence rate
Swerdlow *et al.* (29), 1989	UK	259 cases 2 control groups of 238 and 251	Case Control	Wine Butter Milk Cheese Eggs Meat	OR = 1.71 CI 1.21-2.43 Not significant (NS), data not shown (DNS) NS, DNS NS, DNS NS, DNS NS, DNS	
Davies *et al.* (39), 1996	UK	129 cases 211 cancer controls, 184 population controls	Case Control	Milk intake at 17 Cream Yoghurt Cheese Apples Oranges Vegetable salad Fruit Salad Present milk intake	OR = 1.39 CI 1.19-1.63 NS, DNS NS, DNS NS, DNS NS, DNS NS, DNS NS, DNS NS, DNS NS, DNS	
Sigurdson *et al.* (38), 1999	Texas	82 non-seminomas 46 seminomas 136 controls	Case Control	Non-seminomas (High vs. low intake) Total fat Saturated fat Meat Cholesterol Milk Calcium	 OR = 6.3 CI 1.9-20.5 OR = 5.2 CI 1.6-17.8 OR = 2.3 CI 0.8-6.8 OR = 4.6 CI 1.5-13.8 OR = 0.5 CI 0.2-1.6 OR = 0.4 CI 0.1-1.1	

				(Low vs. High Intake) Dietary fiber Fruits Vegetables Dark green vegetables Seminomas (High vs. low intake) Total fat Saturated fat Meat Cholesterol Milk Calcium (Low vs. High Intake) Dietary fiber Fruits Vegetables Dark green vegetables	 OR = 4.0 CI 1.3-12.4 OR = 1.1 CI 0.4-3.2 OR = 1.2 CI 0.4-3.4 OR = 1.5 CI 0.5-4.4 OR = 1.9 CI 0.6-5.5 OR = 2.1 CI 0.7-6.3 OR = 3.6 CI 1.1-11.1 OR = 3.1 CI 1.1-9.0 OR = 0.6 CI 0.2-1.7 OR = 0.6 CI 0.2-1.7 OR = 1.3 CI 0.5-3.8 OR = 2.3 CI 0.7-7.4 OR = 0.6 CI 0.2-1.9 OR = 1.0 CI 0.3-2.8	
De Stefani *et al.* (147), 1998	Uruguay	Not available	Case Control	Red Meat Total Fat	Significant, DNS Significant, DNS	
Gallagher *et al.* (157), 1994	Canada	Not available	Case Control	Green Vegetables	RR = 0.5 CI 0.3-0.9	
Srivastava *et al.* (41), 2000	Ontario	212 cases 251 controls	Case control	Fruits and Vegetables	NS, DNS	
Swerdlow *et al.* (40), 1999	UK	60 twin pairs	Twin	Fruit Fruit Juice Vegetables Dairy Products Eggs Red Meat	OR = 1.0 CI 0.3-3.1 OR = 1.0 CI 0.2-5.0 OR = 0.3 CI 0.1-1.0 OR = 1.1 CI 0.4-2.7 OR = 0.8 CI 0.3-2.0 OR = 0.7 CI 0.2-2.4	

Not significant (NS), data not shown (DNS)

2.12. Dietary Measurement

Diet is a particularly difficult exposure to measure, as exposure is continuous and can change on a day-to-day or seasonal basis. As a result, complex methods have been developed to minimize the biases created by the natural changes in diet[158]. The methods used have ranged from biochemical, such as blood testing and the use of radioactive water (which are performed in special laboratories), to interview-based methods (food diaries and 24-hour recalls).

Although epidemiology is equipped to study the dietary causes of disease, the complex nature of diet has provided a difficult challenge to the discipline[159]. There are several epidemiological methods used to measure diet including: direct observation, analysis of duplicate meals, dietary recalls (24 hour recalls, food-frequency questionnaires and diet histories) and food records (weighed or estimated)[160]. Many of these methods require significant resources to be implemented in a study. Thus, the simpler and less intensive methods have become the major tools in epidemiological studies. No dietary assessment method is likely to provide a precise measure the true intake for an individual[161]. Currently, the most popular way to measure diet, especially in the study of chronic diseases, is via a "food frequency" questionnaire (FFQ), which can be included as part of a large survey or administered alone.

2.12.1. Food Frequency Questionnaire

While the initial development of food frequency questionnaires (FFQ's) took place in the 1950's[30] it was not until 1961 that Heady[162] demonstrated that the frequencies with which foods were used correlated highly with the total weights of the same food consumed over

a several-day period. During the 1980s and 1990s, FFQ's were refined, with extensive modification and evaluation to the point where the results obtained from such questionnaires are considered useful and interpretable[30]. As a result, the FFQ has widespread use in many types of scientific studies. It is especially useful in the context of large self-administered surveys, such as the NECSS.

All FFQ's have the same basic design: a list of foods for each of which respondent indicates their frequency of eating and perhaps the usual serving size. The basic design of FFQs varies mainly in the way in which the serving size aspect is implemented. One approach is to provide a reference portion size and ask subjects to adjust their frequency response to reflect the frequency with which they eat the fixed portion size. Thus, if the fixed portion is "½ a cup of juice" and the subject's regular serving is 1 cup of juice, which they drink once a week, they would need to adjust their frequency response and respond that they consume the designated serving size of juice twice a week. Another approach is to ask the subject the frequency of consumption, and then ask them to define their usual portion size. Some FFQs provide respondents with sample foods to illustrate the different serving sizes, while others rely on text descriptors (e.g. 1 cup or generic terms such as 'small').

A recent large scale study[163] of three FFQ's used frequently in nutritional epidemiology (Block[164], Willett[165], Dietary History Questionnaire (DHQ)[163]) found that the DHQ used by the National Cancer Institute and the Block FFQ were better at estimating absolute intakes than was the Willett FFQ. After energy adjustment, all three are comparable for purposes of assessing diet-disease risk. Of these three instruments, the Block and the Willett questionnaires are the major FFQs in current use[163]. The difference between them

is mainly in the approach to serving size measurement. The Willett FFQ pre-specifies the serving size, while the Block FFQ allows the subject to answer "small, medium or large". In addition, there are variations between the two in length, foods inquired about, and wording of the questions.

There has been extensive validation of both the Willett[165-167] and Block[168] questionnaires. The Willett questionnaire was validated against 1 week food records[166], while the Block questionnaire was validated against 4-day food records[168]. The validation of the Willett questionnaire produced Pearson correlations ranging from r = 0.31 for pie to r= 0.92 for coffee (average r = .59)[166]. The validation of the Block questionnaire produced correlations ranging from .42 to .68 (median = .57). The use of respondent-reported portion sizes, an important feature of the Block questionnaire, produced higher correlations than use of investigator-assigned "standard" portion sizes (median r = .43 vs. .57)[168]. The validation efforts of the questionnaire authors and the widespread use of the questionnaires in other studies of diet confirm the validity of both questionnaires.

3. Methods I – National Enhanced Cancer Surveillance System

3.1. Synopsis

The National Enhanced Cancer Surveillance System (NECSS) is a collaborative effort between Health Canada and the Provincial Cancer Registries. It is an initiative under the Action Plan on Health and the Environment, Health Canada's part of the Government of Canada's Green Plan[169]. This thesis is based on the case-control portion of the NECSS. The central database of the case-control component was built by collecting detailed information from a Canada-wide sample of 20,755 patients recently diagnosed with cancer (18 sites) and 5,039 population controls[170]. In total, eight provinces participated in the NECSS initiative: Newfoundland (NFLD), Nova Scotia (NS), Prince Edward Island (PEI), Ontario, Manitoba, Saskatchewan, Alberta, and British Columbia. The surveillance system included four major components:

1. geographic surveillance of national cancer incidence distribution to identify high risk clusters and potential determinants;
2. a national environmental quality database;
3. a case-control surveillance infrastructure to collect risk factor information from a national population-based sample of newly-diagnosed cancer cases and population controls; and
4. environment hot issue management to identify and manage emerging risk through collaboration and communication between the Laboratory Centre for Disease Control and other public health officials[169].

3.2. General Design

The NECSS adopted a case-control methodology. This design was chosen to avoid a number of limitations of ecological methods and to allow for control of many risk factors that could obscure relationships between environmental factors and cancer risk[169]. For the control sample, a frequency matching methodology was used; this matching was based upon the overall distribution of cancer within Canada by province age and sex. Information was obtained through a mailed questionnaire, which, in addition to environmental exposure questions, included questions on lifestyle factors, such as smoking, drinking, diet, drinking water, occupation, and physical activity. The full questionnaire is included in appendix A.

3.3. Ascertainment of Cases

Provincial cancer registries collect cancer incidence data for the National Cancer Incidence Reporting System. For the purposes of the NECSS, this data collection was expanded to include risk factor information for cancer cases. Subjects were recruited for 18 cancer sites: prostate, breast, colon, leukemia, bladder, kidney, rectum, non-Hodgkin's lymphoma, liver, testis, pancreas, lung, brain, stomach, bone/cartilage, salivary gland, multiple myeloma, and mesothelioma[171]. The provincial registries identified the cases and then obtained physician consent to contact them. Upon physician consent, the questionnaire was mailed to the cancer cases. The questionnaires were sent to the case within one to four months of diagnosis. The time between diagnosis and the questionnaire being mailed out varied by province and cancer site. After mailing the questionnaires, non-respondents were followed up by telephone. Case recruitment began January 1, 1994 and concluded March 1997. Based on population incidence rates, 1,570

cases of testicular cancer in all age groups would have been expected to occur during the recruitment window[171].

3.4. Ascertainment of Controls

The Provincial cancer registries were also responsible for the recruitment of controls. A quota of controls was assigned to each province by age and sex groups. The quota was determined by the overall distribution of cancer in Canada by age and sex. Controls were allocated to provinces based on census populations' net cancer numbers. In order to recruit a sufficient number of controls to allow for one-to-one matching in the analysis of young cancers, especially testicular cancer, the sample was skewed and additional young controls were recruited. The actual methodology used for control recruitment varied by province. Provincial health insurance registration databases were used in British Columbia, Saskatchewan, Manitoba, Prince Edward Island and Nova Scotia. Ontario used the Ontario Ministry of Finance Property Assessment Database to identify controls. Random digit dialing was used in Alberta and Newfoundland. Controls were collected throughout the 1996 calendar year. Financial incentives to improve response rates were used in Ontario. At final count, 5,039 controls participated in the study.

3.5. Response Rate

The overall response rate for testicular cancer cases was 61%. The breakdown of the response rate for cases is shown in figure 1. The control response rate, within males, was 63.9% and is displayed in figure 2.

Figure 1: **Breakdown of outcome of case recruitment.**

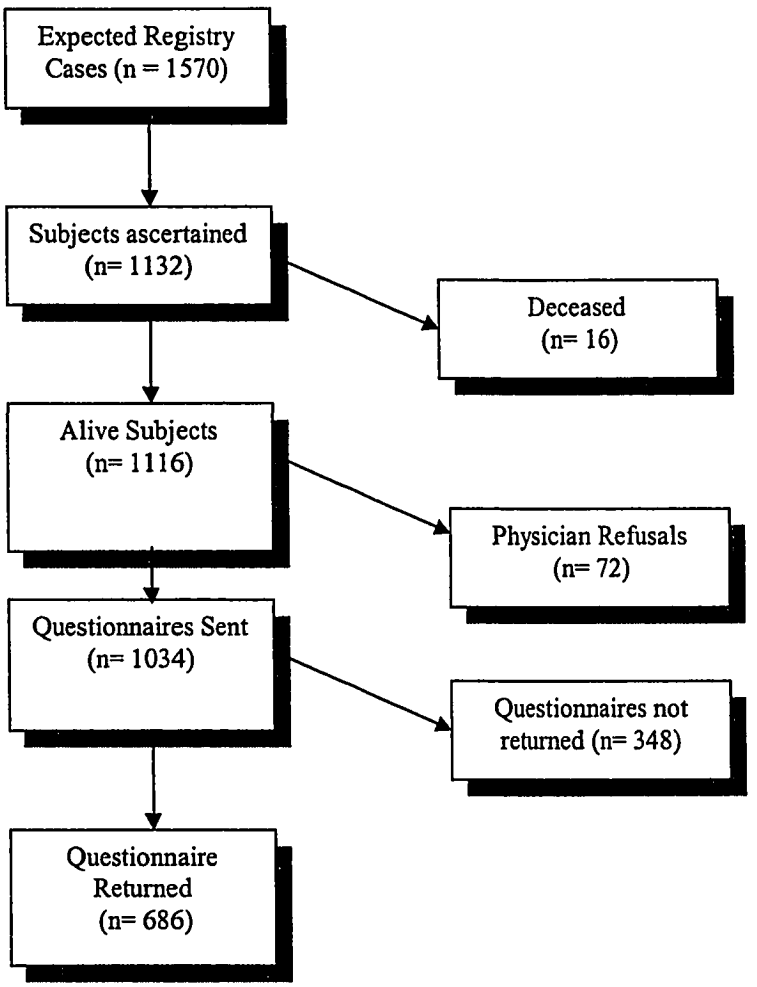
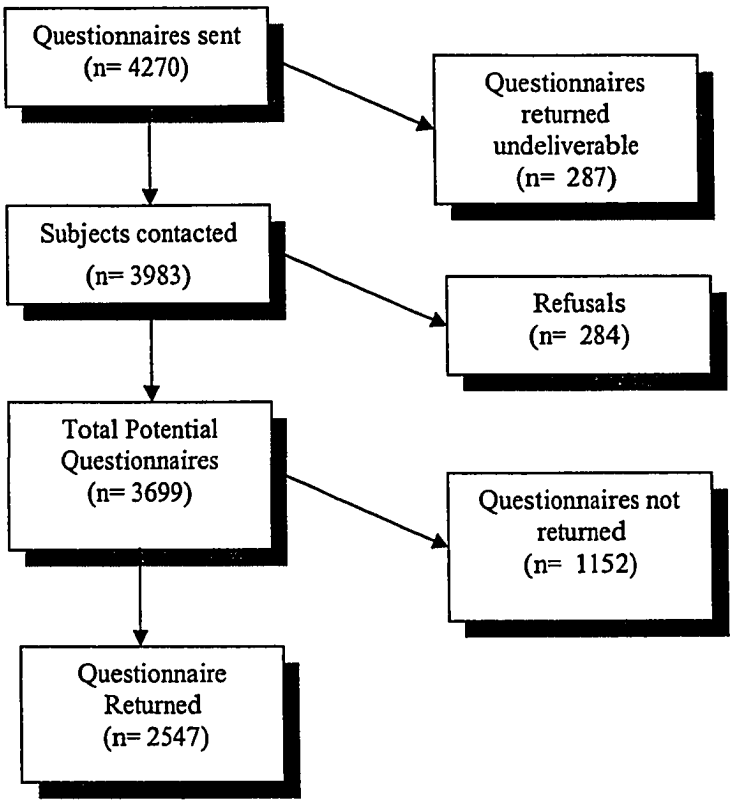


Figure 2: **Breakdown of outcome of male control recruitment.**



3.6. Survey Instrument

The NECSS collected information on occupational and residential histories, from which environmental exposures were derived. The remaining items included: general information (height, weight, and age), smoking history, diet, physical activity, socio-economic status. Females were asked additional questions regarding their reproductive history.

The diet component of the questionnaire consisted of several parts: an examination of dietary supplements (minerals and vitamins), a 69 item food frequency questionnaire (FFQ), and several additional questions regarding fat use in cooking and on foods. The only diet component used in this analysis was the FFQ. The additional dietary questions were either worded in such a way that prevented them from being quantified into daily intakes or were related to exposures at time periods inappropriate for inclusion in a study examining testicular cancer, thus neither were used in this thesis.

The food frequency questionnaire was a combination of two validated FFQ's that have been used in diet-cancer studies in the US and Canada (Ken Johnson, personal communication). These FFQ's were the reduced Block questionnaire[164] and the instrument used in the Nurses Health Study cohort[172]. Minor modifications were made to the questionnaire items to account for differences between Canadian and American diets. The FFQ is semi-quantitative in nature with a choice of frequency categories and a fixed serving size associated with each question. The FFQ asked about usual diet two years prior to the receipt of the questionnaire. The NECSS research group began with the

Willett questionnaire and used the Block questionnaire in order to guide the shortening of the questionnaire to a length deemed reasonable for the purposes of the NECSS (Ken Johnson, personal communication). The fixed serving sizes were retained from the Willett questionnaire. The revised questionnaire used in the NECSS survey has yet to be validated. However, the development of the questionnaire involved the extensive work of several experienced nutritionists in consultation with the NECSS team (Ken Johnson, personal communication). As well, the results from the dietary component of the questionnaire have been published in the peer review literature[41;173-175]. Limitations associated with the FFQ used in the NECSS are addressed in the discussion.

4. Methods II - Data Sources

This thesis is a secondary analysis of data assembled by the National Enhanced Cancer Surveillance System (NECSS). The NECSS dataset was created and is maintained by the Cancer Division of Health Canada. Once Health Canada approved the thesis, a SAS data set was provided for analysis.

The dataset contains information on incident cases of testicular cancer collected through eight Provincial cancer registries. As well, the Provincial registries collected information on controls, as described in chapter three. There were a total of 342 variables in the main data set, 686 cases of testicular cancer, and 2547 controls (all males).

4.1. Inclusion Exclusion Criteria

Subjects with the following characteristics were excluded from the study (Number of cases excluded; number of controls excluded).

- Incorrect ICD-O-Topography: cases without testicular cancer or controls with cancer (cases = 1; controls = 2)
- The subject is a proxy (cases = 2; controls = 2)
- Subject's race is black (cases = 3; controls = 20)
- Subject has a missing or invalid age (cases = 0; controls = 7)
- Subject has missing BMI (cases = 1; controls = 5)
- Subject has missing smoking status (cases = 13; controls = 15)
- Subject aged 55 or more years (cases = 43; controls = 1721)
- Subject aged less then 20 years (cases = 2; controls = 0)

- Less then 85% of the FFQ is completed (fewer than 59 of the 69 questions answered) (cases = 6; controls = 18)
- Subject had a daily energy intake of more than 5000 calories or less than 700 calories (cases = 6; controls = 8)

Black subjects were deleted because there were insufficient numbers to adjust for race in the logistic regression analyses. As well, many studies exclude black subjects from the analysis because of the extremely low incident rates among that population. All subjects aged greater than 55 years were deleted. There were only 43 cases aged greater than 55, but 1721 controls. These subjects were deleted because the large number of controls aged greater than 55 skew the dietary intake quintiles to the dietary patterns of older people, whereas for the purposes of testicular cancer research we are more interested in the risk and dietary habits of younger subjects. Finally, subjects with daily intakes of greater than 5,000 calories or less than 700 calories were deleted because of the extreme nature of their dietary responses (Bryna Shatenstein, personal communication). The subjects deleted by the energy intake criteria represented the top and bottom 1%. After applying all the inclusion/exclusion criteria, 601 cases and 744 controls were left in the final analysis data set.

4.2. Missing Values

Subjects with missing responses on their FFQ, but who had more than 85% of the questionnaire completed, were assigned "none" responses for those questions left blank under the assumption that the blanks were due to respondent fatigue with responding about foods they didn't eat.

4.3. Selection of Covariates

Age and province were included as covariates in all analyses, since the control group was selected using frequency matching on age and province. Due to the matching, it is inappropriate to compare unadjusted univariate statistic of food groups and other variables. A limited number of univariate analyses were performed in an exploratory capacity.

Smoking has been shown to cause cancer at many sites, although it is unclear if it impacts testicular cancer risk. It was decided to control for the effects of smoking in the logistic regressions. Body mass index has been shown to influence testicular cancer risk, although many conflicting results are present in the literature. Since BMI is associated with diet, we included BMI in the adjusted and energy adjusted models. Finally, there is considerable debate around the use of energy intake to adjust analysis looking at diet on a food group level. However, recent findings have deemed it important to control the food group analyses for total energy intake[163]. As a result, we present the results with and without energy adjustment.

Until recently, there has been little question about the need to control for energy intake in nutrient analyses. In a recent issue of the American Journal of Epidemiology the need for, and appropriateness of, such adjustment is discussed. One argument is that nutritional epidemiology should fundamentally be the study of dietary composition, that is, energy-adjusted intakes, in relation to disease occurrence. Absolute nutrient intakes reflect both diet composition and energy intake, making them difficult to interpret with regard to the causation or prevention of disease[176]. Conversely, nutrient requirements are

usually expressed in absolute terms rather than relative to energy intake, and thus one wants to be able to infer if the absolute level is high or low, not whether it is high or low with respect to energy intake[177]. Given these arguments we decided that it was most appropriate in the context of this study to control all nutrient analyses for total energy intake.

Three models were used for the food group analyses: model 1 (adjusted for age and province), model 2 (adjusted for age, province, BMI, and smoking), and model 3 (adjusted for age, province, BMI, smoking, and total energy intake). For the nutrient analyses only two models were required: model A (adjusted for age, province, and total energy intake), model B (adjusted for age, province, BMI, total energy intake and smoking). Please note that models 3 and B are adjusted for the same five covariates. For both the food group and the nutrient analysis model 3/model B is the primary analysis, respectively. Thus, results that reach significance in models 1, 2, or A, but not in models 3 or B, are not discussed in the text of the results section, nor commented on in the discussion.

4.3.1. Other Potential Covariates

Other potential covariates were examined for their impact on the results. These covariates were: education, income, and two measures of physical activity. All have mixed results in the literature with respect to their association with testicular cancer. Each was examined separately and the impact of the inclusion of each on the point estimates associated with the dietary variables was noted. None of these covariates materially changed the point estimates; thus, were not included in the adjusted models, and are not reported on in this thesis.

4.4. Derived Variables (BMI, smoking, age groups, province)

4.4.1. Body Mass Index (BMI)

Body mass index is used as a predictor of nutritional status among adults. It has been associated with increased risk of testicular cancer, as mentioned in chapter two. BMI is the ratio of body weight (kg) to height (m) squared. The information in the questionnaire on self-reported height and weight was used to calculate the BMI of each subject. This derived variable was present in the data set provided by Health Canada. BMI is often categorized prior to analysis. For population health purposes Health Canada recommends using four categories: 1) <20 kg/m^2; 2) 20-25 kg/m^2; 3) 25-27 kg/m^2; 4) >27 kg/m^2. For the purposes of this analysis, the upper value in the Health Canada categories was not viewed as "extreme" enough to find the possible effect of increased BMI on testicular cancer risk. As a result, a BMI variable was created that was based on quartiles of BMI in the entire sample, with the highest quartile further divided so the upper 10% of the sample could be examined separately. The resultant BMI cut points are very similar for all three analyses (Table 2).

Table 2. BMI Cutpoints for the total sample and the 2 histological subtypes

	Total	Seminomas	Non-Seminomas
1	<23.0	<23.0	<23.1
2	23.0-25.1	23.0-25.0	23.1-25.1
3	25.2-27.6	25.1-27.4	25.2-27.7
4	27.7-30.5	27.5-30.4	27.8-31.0
5	30.5+	30.4+	31.0+

4.4.2. Age

Age was derived based on the difference between date of birth and date of interview (calculations performed by Health Canada). Age was grouped into five year age groups from 20 to 54 years. The resultant groups are: 20-24, 25-29, 30-34, 35-39, 40-44, 45-49, 50-54.

4.4.3. Smoking

The questionnaire asked if the subjects had smoked more than 100 cigarettes in their lives. A positive response resulted in further questions regarding smoking length and amount. A continuous variable was then derived (by Health Canada) of pack-years of smoking for each subject. For the purposes of the present analysis the continuous smoking variable was converted into a categorical one. The cutpoints were derived from another study examining the NECSS data set and testicular cancer[41]: non-smoker, 0-5 pack years (pys), 5-12 pys, 12-24 pys, 24+ pys.

4.4.4. Province

This study included eight of the ten Canadian provinces; no information was available from New Brunswick or Quebec. The Maritime Provinces (Nova Scotia (NS), Newfoundland (NFLD) and PEI), Manitoba and Saskatchewan had small numbers of cases; thus, provinces were collapsed to create new provincial categories: PEI, NS, NFLD; Ontario; Manitoba and Saskatchewan; Alberta; and British Columbia.

4.4.5. Energy Intake

The derivation of energy intake is discussed in detail later (section 4.9). Energy intake was divided into quintiles based on all cases and controls combined using the Proc Rank procedure in SAS. The resultant quintile boundaries for the total sample, seminomas and non-seminomas are shown in Table 3.

Table 3. Energy intake quintiles for the total sample and the 2 histological subtypes

Intake Level	Total Sample kC	Seminomas kC	Non-Seminomas kC
Low Intake	700.0-1450.6	700.0-1424.7	700.0-1424.7
Low-Medium intake	1450.7-1777.7	1424.8-1759.9	1424.8-1749.4
Med Intake	1777.8-2075.7	1760.0-2062.0	1749.4-2064.2
High-Medium intake	2075.8-2553.8	2062.1-2548.3	2064.3-2548.3
High intake	>2553.9	>2548.4	>2548.4

4.5. Dietary Intake groups

Dietary intake is divided into both quartiles and quintiles in the literature; the large sample size of the NECSS allowed the division of dietary intake into quintiles. The cutpoints of each quintile were recreated for each of the 3 analyses: the total sample, the seminoma subgroup, and the non-seminoma subgroup. The quintiles were formed using the Proc Rank procedure within the SAS system. However, there were some food groups for which many people reported no intake, thus preventing the division of intake into quintiles. These situations were rare and the large majority of food groups were divided into quintiles. As well, there was one food group that required manual division into quintiles, total milk. This problem arose because of the large number of people reporting an intake of 2-3 servings of milk per day. As a result, the Proc Rank procedure automatically placed the subjects with an intake of 2-3 servings per day into the highest intake quintile. This resulted in a large number of subjects, approximately 30% being in the high intake quintile. We felt this inappropriate as these people may obscure the effect, if any associated with a high intake of milk. To correct this situation the subjects were manually placed in the medium-high intake quintile for the final analysis. The logistic regression models for milk intake were also run with the subjects in the high intake quintile, and the results were very similar for both situations.

4.6. Overview of the analysis strategy

There were two major analyses performed on the NECSS dataset, one was a food group analysis, the other a nutrient analysis. The first step of the food group analysis was to place each of the FFQ's 69 food items into the appropriate Canadian Nutrient File (CNF) food group. The allocation of these items is found in appendix B. The CNF allocation of the food items was modified in consultation with a nutritionist, as the CNF food groups

were not designed for specific use in epidemiologic studies. The consultations lead to several refinements in the contents of the food groups. The final food group allocations are shown in table 4. In addition to the food group analysis, a nutrient analysis was performed for nutrients with an *a priori* association with testicular cancer. Both the food groups and nutrients were analyzed via a logistic regression. The primary analysis used was a logistic regression model including the food group/nutrient, age group, province, BMI, smoking, and total energy intake. Individual Wald tests, tests for trend and the likelihood ratio test of heterogeneity were performed. All analyses were performed in the SAS system (version 8.2). These analyses were run on the 17 food groups, the 15 nutrients, and the 7 individual foods.

4.7. Food group analysis

4.7.1. Food group formation

The food group analysis involved examining risk associated with foods, which share nutritional properties (e.g. grouping together all dairy foods into a single exposure group). The Canadian Nutrient File (CNF) provided the initial food group classification. The 69 food items were classified into 25 groups (Appendix B). These initial groupings were then examined and discussed with a nutritional epidemiologist and a nutritionist. This lead to a number of revisions being made to the food groupings used. The major changes from the CNF allocation involved combining several of the meat food groups into one group, the division of the beverage category in alcoholic and non-alcoholic beverages, and moving "French fries" from the vegetable group to the snack food group (with potato chips). These changes were made to the initial groupings in order to group foods that had similar components potentially relating to risk together (i.e. Fat from deep

frying). As well, some groups were broad (e.g. beverages), it was decided that subgroups (alcoholic and non-alcoholic beverages) may be more applicable to risk for testicular cancer. The final food group allocations are shown in Table 4.

Table 4. The final food group composition and the associated foods from the NECSS questionnaire

No	Food Groups	Variable Names
1	DAIRY AND EGG PRODUCTS	Whole milk, 2% milk, 1% milk, skim milk, cheese, eggs, butter
2	FATS	Margarine, mayonnaise
3	MEAT	Chicken, beef as a main dish, smoked meat, liver, beef as a mixed dish, hamburger
4	SOUPS	Soups
5	LUNCHEON MEATS	Luncheon meats, sausage, bacon, hotdog
6	GRAINS	Granola, cold cereal, cooked cereal, white bread, dark bread, rice, pasta
7	FRUITS	Frozen orange juice, fresh orange juice, apples, oranges, bananas, cantaloupe, other fruit
8	VEGETABLES	Tomato juice, tomatoes, carrots, broccoli, cabbage, spinach, squash, other vegetables, potatoes, sweet potatoes
9	NUTS	Nuts
10	ALCOHOLIC BEVERAGES	Beer, wine, liquor
11	NON-ALCHOLIC BEVERAGES	Tap water, bottled water, coffee, tea, frozen juice, powdered drink, fresh juice, pop
12	FISH	Fresh fish, smoked fish
13	LEGUMES	Tofu, lentils
14	PEANUT BUTTER	Peanut butter
15	BAKED PRODUCTS	Cake, cookies, doughnut, pies
16	SWEETS	Ice cream, chocolate
17	SNACKS	Fries, chips

4.7.2. Data Analysis

The first analytical step of the food group analysis was an examination of the distribution of food group intake among cases, controls and the total sample. A brief descriptive analysis was then performed in order to obtain a general understanding of the data. These analyses are not presented, as unadjusted analyses are inappropriate for this dataset,

because the control sample was obtained by frequency matching to the case group by age and province.

Three logistic regression models were used to examine each of the 17 food groups. Model 1 examines the food group adjusting for age group (5 year categories) and province of recruitment (categorical) as covariates. Model 2 examines the food group adjusting for age group, province, BMI (categorical) and smoking (categorical) as covariates. Finally, model 3 examines the food group adjusting for age group, province, BMI, smoking and total energy intake as covariates. In model 3, total energy intake was included as a categorical variable (quintiles of intake). Model 3 provided the primary analysis for the results chapters, as well as for the discussion.

Tests for an increasing or decreasing trend of intake and risk were then performed. The trend test statistic was obtained by running the model with the food group as a continuous variable and then examining the Wald chi-square statistic for the food group. Rather than using the ordinal values of each quintile (1,2,3,4,5) to obtain the trend statistic, it was decided that the median value of each intake quintile would be used in order to account for the different intake ranges in each of the quintiles. If the resultant chi-square value was greater than or equal to 3.84, the cut point for $p = 0.05$ using a two tailed chi-square test, the trend of increasing or decreasing risk with increasing food intake was significant.

The likelihood-ratio (LR) of heterogeneity of the food group OR's was also examined. This test was performed to determine if the risk associated with the food group variable intake quintiles is different across the five strata. Significance for this test was attained at

a p-value of less than 0.05. The food group analysis was run for the total sample and both of the histological subtypes, seminomas and non-seminomas. All analyses were performed in the SAS system, using Proc Logistic (Version 8.2).

4.8. Disaggregation analysis

The disaggregation analysis was undertaken in an attempt to uncover the components of the dairy product food group that were responsible for the high level of risk associated with dairy product intake. Dairy was disaggregated into milk, eggs, cheese, and butter, and then the components were individually analyzed. Milk was further disaggregated into whole, 2%, 1% and skim milk. Finally, cheese and whole milk were combined to see if the high level of fat in these two food groups combined produced even more significant results, then the results of whole milk or cheese alone. The analysis methodology used for the disaggregation analysis is the same as that used in food group analysis.

In addition to analyzing the disaggregated foods by intake quintiles, the exposure was also examined as a continuous variable. A recent paper [178] suggests that nested subsets of dietary components cannot be compared when based on quintiles or percentiles. Rather, the author suggests that subsets of dietary components, in order to compare, should be analyzed as continuous intake variables. This method has not been used extensively in the literature; it was decided that for completeness we should follow this method as well as the quintile analysis method previously described. This methodology was only applied to milk and its components (whole, 2%, 1%, and skim) and to fat (saturated, mono-unsaturated, and poly-unsaturated). For milk, the risk was calculated based on a 1

serving per day increase, and the risk associated with fat was calculated on an increase of 10 grams per day.

4.9. Nutrient analysis

4.9.1. Conversion of Foods

Prior to converting the FFQ into nutrient values, we identified micro and macronutrients of interest. The decision process to determine the nutrients to be included in the analysis involved extensive consultation with a nutritionist and a nutritional epidemiologist. From the literature, the nutrients previously examined or hypothesized to have a relationship with testicular cancer were: fat (total fat, saturated, mono-unsaturated, poly-unsaturated), protein, cholesterol, carbohydrates (total carbohydrates, dietary fibre, and total sugar), total energy, zinc, calcium, and iron. In addition to the nutrients identified from the literature, the food group analysis results were such that the nutritional consultation team suggested two additional nutrients: phosphorus and sodium.

Once the nutrients to be analyzed had been selected, each of the 69 food items was converted into 14 nutrients and energy. Prior to calculating the nutrient value of the food item, each FFQ item was linked with a known food from the 1997 CNF database[179]. This linkage was performed using the nutrient analysis program Nutriwatch[179]. Unfortunately, some of the food items were not specific to one food but were associated with 2 or more foods (e.g. a question about frozen juice that asks about both orange and grapefruit juice). Thus, to estimate nutrients, amalgams were required and used in when the food item inquired upon was associated with the more than one food. In the context of this thesis, an amalgam can be defined as a combination of foods created to obtain a nutrient

breakdown for the questions inquiring on more than one food. For example, the question on frozen orange and grapefruit juice (serving size is a 4 oz glass) required an amalgam to be created. This amalgam consisted of a combination of 2 oz of orange juice from frozen concentrate and 2 oz of grapefruit juice from frozen concentrate. The nutrients associated with this item were an average of the nutrients for all foods in the amalgam. After producing the initial amalgams, a nutritionist examined them and suggested amendments. The amalgams were then updated and approved by the nutritionist prior to use. All final amalgams defined in appendix C.

The 69 FFQ items were entered into Nutriwatch, using amalgams where necessary, and weekly nutrient intake levels for each item were generated. An example of the output from Nutriwatch is presented in appendix D. The nutrient information was then merged with the SAS datafile. The nutrient intake for each subject was obtained by multiplying the number of servings per week (indicated on the FFQ) by the nutrient value associated for each of the 69 FFQ items. This was repeated for each of the 14 nutrients and energy. This initial computation created a set of 69 values for each of the 14 nutrients and energy. The variables were then summed across the 69 FFQ items, creating 15 summary variables, one for each nutrient, containing for each subject the intake of each nutrient per week. These values were then converted to daily intakes and used as the exposure measure in the nutrient analysis.

The above methodology was used for all nutrients except for the three subtypes of fat. For each of saturated, monounsaturated, and polyunsaturated, the amount consumed for each of the 69 food items was derived by taking the total fat content of the item and

multiplying by the percentage associated with the subcategory. The percentages were included as part of the amalgam output of Nutriwatch. For example, if a serving of whole milk has 7.9 grams of fat and 62.2% of the fat is saturated, then the amount of saturated fat would be 7.9*0.622 = 4.91 grams. This value was then in turn multiplied by the weekly intake for each subject and then summed across the 69 food items to create a variable indicating weekly intake of saturated fat.

4.9.2. Data Analysis

The data analysis methodology used for the nutrient analysis was similar to the methods used for the food group analysis. The analysis performed included the examination of both the trend statistic and the likelihood ratio, along with point estimates for intake levels. The only difference in the methodology between the food group and nutrient analyses was that there are only 2 models used in the nutrient analysis. Model A examines risk associated with nutrient intake, adjusting for age group, province, and total energy intake as covariates. Model B examines risk associated with nutrient intake, adjusting for age group, province, smoking, BMI, and energy intake as covariates. The continuous disaggregation analysis used for dairy products in the food group analysis was repeated for total fat, which is a combination of saturated, mono-unsaturated and poly-unsaturated fat. As well, the descriptive statistics for each nutrient (mean, median, standard deviation and range) can be found in appendix E. Finally, it was deemed inappropriate to report on risks associated with nutrient intake without controlling that estimate for energy intake. This decision is explored in the discussion section of the thesis.

5. Results – Total Sample

5.1. Total Sample - Characteristics of Cases and Controls

5.1.1. Descriptive analysis of Covariates

The case group had a mean age of 35.2 and a median of 35.0 years. A majority of cases (57.4%) were classified as smoking at least 100 cigarettes in their lifetime. The histological breakdown of the cases was 58.7% seminomas (n=361) and 27.3% non-seminomas (n=168). The remainder of the cases (n=86, 14.0%) were classified as having "other" or missing morphological codes. The largest percentages of cases (31.4%) were recruited in Ontario, followed by British Columbia (22.4%).

The control group had a mean age of 38.8 and a median of 39.0. The largest percentage of controls (36.3%) was recruited from Ontario; the next largest province of recruitment was British Columbia (19.4%). Nearly two-thirds of the controls (61.7%) were classified as smoking at least 100 cigarettes in their lifetime. The distributions of all covariates are reported on in Table 5.

5.1.2. Analytic Analysis of Covariates

There was a small increase in risk with increasing BMI, but this did not reach statistical significance. Smoking, at any level, was not associated with an increase in testicular cancer risk. Total energy intake showed a significant linear trend of increasing testicular cancer risk with increasing energy intake ($\chi^2 = 5.7$ df =1 p= 0.02), and had an OR at high intake of 1.55. In addition, total energy intake had a significant likelihood ratio test of heterogeneity (LR χ^2=10.6 df=4 p = 0.03). The results of the analysis of the covariates are shown in Table 5.

Table 5. Multivariate analysis for the major covariates of the NECSS dataset						
Variable	Case n = 601	Control n = 744	Total n =1345	Model 1*	Model 2**	Model 3 ***
	%	%	%	Odds Ratio (95% CI)	Odds Ratio (95% CI)	Odds Ratio (95% CI)
Age Group						
20-24†	8.3	7.5	7.9	Not Applicable	Not Applicable	Not Applicable
25-29	15.5	12.5	13.8			
30-34	23.1	15.7	19.0			
35-39	24.6	17.6	20.7			
40-44	14.1	14.3	14.2			
45-49	9.7	13.7	11.9			
50-54	4.7	18.7	12.4			
Province						
Maritimes†	12.7	18.4	15.8	Not Applicable	Not Applicable	Not Applicable
Ontario	31.3	35.9	33.8			
Man & Sask	14.6	12.1	13.2			
Alberta	18.6	13.8	16.0			
BC	22.8	19.8	21.1			
Histology						
Seminoma	59.2	0.0	26.5	Not Applicable	Not Applicable	Not Applicable
Non-Seminoma	27.0	0.0	12.1			
Other	2.7	0.0	1.2			
Missing	11.2	0.0	5.0			
Not applicable	0.0	100.0	55.3			
Smoking (PY)						
0 (non-smoker) †	43.4	38.3	40.6	1.00	1.00	1.00
1-5	17.8	19.0	18.4	0.86 (0.63, 1.17)	0.86 (0.63, 1.17)	0.86 (0.63, 1.18)
5-12	17.8	18.3	18.1	0.90 (0.66, 1.24)	0.90 (0.65, 1.24)	0.89 (0.65, 1.23)
12-24	15.0	15.3	15.2	1.02 (0.72, 1.45)	1.02 (0.72, 1.45)	1.01 (0.71, 1.44)
24 +	6.0	9.1	7.7	1.11 (0.68, 1.80)	1.10 (0.67, 1.79)	1.10 (0.67, 1.80)
Trend				χ^2 = 0.0 df =1 p= 0.99	χ^2 = 0.0 df =1 p= 1.00	χ^2 = 0.0 df =1 p= 0.95
LR				χ^2=1.7 df=4 p = 0.79	χ^2=1.7 df=4 p = 0.79	χ^2=1.6 df=4 p = 0.80
BMI						
<23	24.1	24.7	24.5	1.00	1.00	1.00
23-25.2	24.5	25.5	25.1	1.02 (0.74, 1.41)	1.04 (0.75, 1.43)	1.05 (0.76, 1.44)
25.2-27.7	24.6	24.1	24.3	1.17 (0.85, 1.62)	1.19 (0.86, 1.64)	1.19 (0.86, 1.65)
27.7-30.5	16.6	15.3	15.9	1.30 (0.90, 1.87)	1.31 (0.91, 1.89)	1.34 (0.93, 1.93)
>30.5	10.2	10.4	10.3	1.31 (0.86, 2.01)	1.30 (0.85, 1.99)	1.29 (0.84, 1.99)
Trend				χ^2 = 2.9 df =1 p= 0.09	χ^2 = 3.7 df =1 p= 0.06	χ^2 = 3.5 df =1 p= 0.06
LR				χ^2=3.4 df=4 p = 0.49	χ^2=3.4 df=4 p = 0.49	χ^2=3.5 df=4 p = 0.47
Energy Intake (kC)						
700.0-1450.7†	16.8	22.6	20.0	1.00	1.00	Not Applicable
1450.7-1778.4	19.3	20.6	20.0	1.36 (0.95, 1.94)	1.37 (0.95, 1.96)	
1778.4-2081.1	21.1	19.1	20.0	1.61 (1.13, 2.30)	1.62 (1.13, 2.31)	
2081.1-2556.9	22.0	18.4	20.0	1.69 (1.18, 2.42)	1.69 (1.18, 2.42)	
2556.9+	20.8	19.4	20.0	1.53 (1.07, 2.19)	1.55 (1.08, 2.21)	
Trend				χ^2 = 5.6 df =1 p= 0.02	χ^2 = 5.7 df =1 p= 0.02	
LR				χ^2=10.5 df=4 p = 0.03	χ^2=10.6 df=4 p = 0.03	

† reference group

* includes age group and province as covariates

**includes smoking, age group, BMI, province as covariates

***includes smoking, age group, BMI, province, energy intake as covariates

5.2. Total Sample – Food group Analyses

5.2.1. Overview of Food group analyses

Three of the seventeen food groups analyzed were significantly associated with increased testicular cancer risk: dairy, luncheon meats, and baked products. The dairy food group reached peak risk in the medium-high intake quintile, rather than in the highest intake quintile as would have been expected for a monotonic dose response relationship. Baking and luncheon meats had the highest risk for subjects in the highest intake quintile as expected for a monotonic dose response relationship.

There were several foods that have been previously linked with testicular cancer that demonstrated no association in this study. Meat has been associated with an increase in cancer risk; we observed a non-significant decrease in risk at all levels, except at the highest intake quintile where the risk was 1.00. Both fruits and vegetables have been associated with a reduced risk of testicular cancer. In this study, fruits were found to have a protective effect, although non-significant. However, vegetables had a slight non-significant increase in risk associated with consumption at the highest intake level (OR = 1.18; CI 0.80, 1.74).

5.2.2. Dairy Products

Subjects with an increased consumption of dairy products over the reference group were at an elevated risk of testicular cancer. The likelihood ratio test for heterogeneity was strongly significant (χ^2=25.9 df=4 p<0.001), indicating that the ORs are different across the intake quintiles. However, there was not a significant trend in risk found with increasing consumption of dairy products (χ^2 = 2.4 df =1 p= 0.12). The risk estimates

peaked in the medium-high intake group (20.4-28.5 servings/week) with an OR of 2.56 (CI 1.73, 3.78). The risk in the highest intake quintile (28.5+ servings/week) was substantially lower (OR = 1.41; CI 0.93, 2.13). The overlap in the 95% confidence intervals for these two risks estimates shows that these estimates are not statistically different. This suggests that the apparently lower OR in the highest intake quintile is likely the result of random variation. This was confirmed by an additional logistic regression model which included a quadratic term for dairy intake; the Wald Chi-square for this term was not significant (p= 0.24).

5.2.3. Luncheon Meats

While there was not a significant risk associated with meat intake, luncheon meats were significantly associated with testicular cancer risk. The trend for test was on the borderline of significance ($\chi^2 = 3.8$ df =1 p= 0.05), suggesting that an increasing consumption of luncheon meats increases testicular cancer risk as the individual Wald tests, at the highest intake quintile, was significant and greater than one (OR = 1.49; CI 1.01, 2.19). The addition of energy intake to the models decreased the point estimates, especially in the two highest quintiles.

5.2.4. Baked Products

Baked products had a strong association with testicular cancer risk. The trend of increasing risk with increasing intake was significant ($\chi^2 = 6.2$ df =1 p= 0.01) and is the most significant trend statistic in the food group analysis. While the trend statistic did reach significance, none of the individual intake quintiles reached significance; intake of baked products at the highest level is associated with an OR of 1.47 (CI 0.99, 2.17).

Table 6. Risk of Testicular Cancer associated with Food Intake						
Variable	Case n = 601	Control n = 744	Total n= 1345	Model 1*	Model 2**	Model 3 ***
	%	%	%	Odds Ratio (95% CI)	Odds Ratio (95% CI)	Odds Ratio (95% CI)
Dairy						
Low Intake†	13.8	24.3	19.6	1.00	1.00	1.00
Low-Med Intake	19.0	21.4	20.3	1.42 (0.98, 2.04)	1.45 (1.00, 2.10)	1.39 (0.96, 2.02)
Medium Intake	21.1	19.1	20.0	1.88 (1.30, 2.70)	1.93 (1.34, 2.79)	1.79 (1.23, 2.62)
Med-High Intake	26.3	14.9	20.0	2.73 (1.89, 3.94)	2.83 (1.96, 4.10)	2.56 (1.73, 3.78)
High Intake	19.8	20.3	20.1	1.56 (1.08, 2.26)	1.58 (1.09, 2.29)	1.40 (0.93, 2.12)
Trend				χ^2= 6.6 df =1 p= 0.01	χ^2= 6.8 df =1 p= 0.01	χ^2= 2.4 df =1 p= 0.12
LR				χ^2=31.5 df=4p <0.001	χ^2=33.5 df=4 p<0.001	χ^2=25.9 df=4 p<0.001
Fats						
Low Intake†	19.0	19.9	19.5	1.00	1.00	1.00
Low-Med Intake	17.0	20.6	19.0	0.83 (0.58, 1.19)	0.84 (0.58, 1.20)	0.81 (0.56, 1.16)
Medium Intake	23.1	22.0	22.5	1.06 (0.75, 1.49)	1.06 (0.75, 1.50)	0.99 (0.69, 1.40)
Med-High Intake	20.5	19.4	19.9	1.08 (0.76, 1.55)	1.10 (0.77, 1.58)	0.98 (0.68, 1.42)
High Intake	20.5	18.2	19.2	1.30 (0.91, 1.88)	1.29 (0.89, 1.86)	1.11 (0.76, 1.64)
Trend				χ^2= 4.3 df =1 p= 0.04	χ^2= 3.8 df =1 p= 0.05	χ^2= 1.2 df =1 p= 0.28
LR				χ^2=6.1 df =4 p = 0.20	χ^2 =5.5 df =4 p = 0.24	χ^2 =2.9 df =4 p = 0.57
Meat						
Low Intake†	18.6	19.9	19.3	1.00	1.00	1.00
Low-Med Intake	19.5	22.5	21.1	0.96 (0.67, 1.36)	0.94 (0.66, 1.34)	0.86 (0.60, 1.23)
Medium Intake	20.0	20.2	20.1	1.09 (0.76, 1.55)	1.07 (0.75, 1.53)	0.94 (0.65, 1.35)
Med-High Intake	18.0	18.8	18.4	0.96 (0.67, 1.38)	0.94 (0.65, 1.35)	0.79 (0.54, 1.15)
High Intake	24.0	18.7	21.0	1.26 (0.88, 1.79)	1.23 (0.86, 1.75)	1.00 (0.67, 1.47)
Trend				χ^2= 1.8 df =1 p= 0.19	χ^2= 1.4 df =1 p= 0.23	χ^2= 0.0 df =1 p= 0.98
LR				χ^2=3.3 df =4 p = 0.51	χ^2 =3.1 df =4 p = 0.54	χ^2 =2.5 df =4 p = 0.65
Soup						
Low Intake†	12.2	12.8	12.5	1.00	1.00	1.00
Low-Med Intake	31.8	29.3	30.4	1.14 (0.78, 1.65)	1.14 (0.78, 1.66)	1.14 (0.78, 1.66)
Med-High Intake	29.3	31.9	30.7	0.96 (0.66, 1.39)	0.98 (0.67, 1.43)	0.94 (0.65, 1.38)
High Intake	26.8	26.1	26.4	1.18 (0.80, 1.73)	1.21 (0.82, 1.78)	1.12 (0.76, 1.66)
Trend				χ^2= 0.6 df =1 p= 0.44	χ^2= 0.9 df =1 p= 0.36	χ^2= 0.2 df =1 p= 0.66
LR				χ^2=2.4 df =3 p = 0.50	χ^2 =2.4 df =3 p = 0.50	χ^2 =2.1 df =3 p = 0.55
Luncheon Meats						
Low Intake†	17.1	22.7	20.2	1.00‡	1.00‡	1.00
Low-Med Intake	18.0	19.9	19.0	1.16 (0.81, 1.67)	1.15 (0.80, 1.65)	1.14 (0.79, 1.64)
Medium Intake	21.8	22.7	22.3	1.21 (0.85, 1.71)	1.19 (0.83, 1.68)	1.13 (0.79, 1.60)
Med-High Intake	19.3	17.6	18.4	1.29 (0.90, 1.85)	1.28 (0.89, 1.85)	1.15 (0.79, 1.68)
High Intake	23.8	17.1	20.1	1.68 (1.18, 2.40)	1.67 (1.16, 2.40)	1.49 (1.01, 2.19)
Trend				χ^2=8.4 df =1 p=0.004	χ^2=8.1 df=1 p= 0.004	χ^2= 3.8 df =1 p= 0.05
LR				χ^2=8.8 df =4 p = 0.07	χ^2 = 8.4 df=4 p = 0.08	χ^2 =4.5 df =4 p = 0.35
Grains						
Low Intake†	19.5	21.0	20.3	1.00	1.00	1.00
Low-Med Intake	22.3	17.9	19.9	1.36 (0.96, 1.94)	1.40 (0.98, 1.99)	1.25 (0.87, 1.81)
Medium Intake	17.3	21.4	19.6	0.94 (0.66, 1.34)	0.97 (0.68, 1.40)	0.82 (0.57, 1.20)
Med-High Intake	20.6	20.0	20.3	1.16 (0.82, 1.65)	1.19 (0.84, 1.70)	0.93 (0.64, 1.37)
High Intake	20.3	19.8	20.0	1.22 (0.86, 1.73)	1.24 (0.87, 1.76)	0.94 (0.62, 1.40)
Trend				χ^2= 0.4 df =1 p= 0.54	χ^2= 0.4 df =1 p= 0.53	χ^2= 0.7 df =1 p= 0.40
LR				χ^2=5.5 df =4 p = 0.24	χ^2 =5.5 df =4 p = 0.24	χ^2 =5.4 df =4 p = 0.25
Fruits						
Low Intake†	20.5	20.4	20.5	1.00	1.00	1.00
Low-Med Intake	19.3	19.4	19.3	0.90 (0.63, 1.28)	0.92 (0.64, 1.31)	0.90 (0.63, 1.28)
Medium Intake	19.5	20.7	20.2	0.99 (0.69, 1.41)	1.01 (0.71, 1.44)	0.96 (0.67, 1.38)
Med-High Intake	21.5	19.0	20.1	1.19 (0.84, 1.70)	1.22 (0.85, 1.74)	1.09 (0.76, 1.57)
High Intake	19.3	20.6	20.0	0.96 (0.67, 1.36)	0.97 (0.68, 1.39)	0.84 (0.58, 1.22)
Trend				χ^2= 0.1 df =1 p= 0.80	χ^2= 0.1 df =1 p= 0.01	χ^2= 0.4 df =1 p= 0.55
LR				χ^2=2.8 df =4 p = 0.66	χ^2 =2.8 df =4 p = 0.59	χ^2 =2.4 df =4 p = 0.66

Variable	Case n = 601	Control n = 744	Total n =1345	Model 1*	Model 2**	Model 3 ***
	%	%	%	Odds Ratio (95% CI)	Odds Ratio (95% CI)	Odds Ratio (95% CI)
Vegetables						
Low Intake†	19.6	19.9	19.8	1.00	1.00	1.00
Low-Med Intake	21.3	20.0	20.6	1.16 (0.82, 1.65)	1.16 (0.82, 1.65)	1.13 (0.79, 1.61)
Medium Intake	20.0	19.4	19.6	1.16 (0.81, 1.65)	1.16 (0.81, 1.66)	1.04 (0.72, 1.50)
Med-High Intake	18.8	20.6	19.8	1.12 (0.78, 1.60)	1.14 (0.79, 1.63)	0.98 (0.67, 1.43)
High Intake	20.3	20.2	20.2	1.37 (0.95, 1.96)	1.38 (0.96, 1.98)	1.18 (0.80, 1.74)
Trend				χ^2 = 2.3 df =1 p= 0.13	χ^2 = 2.5 df =1 p= 0.11	χ^2 =0.3 df =1 p= 0.56
LR				χ^2 =3.0 df =4 p = 0.56	χ^2 = 3.1 df=4 p = 0.54	χ^2 =1.5 df =4 p = 0.83
Nuts						
Low Intake†	36.8	38.8	37.9	1.00	1.00	1.00
Medium Intake	36.9	36.6	36.7	1.08 (0.83, 1.39)	1.07 (0.82, 1.38)	1.02 (0.78, 1.32)
High Intake	26.3	24.6	25.4	1.16 (0.87, 1.55)	1.17 (0.88, 1.57)	1.08 (0.81, 1.46)
Trend				χ^2 = 1.1 df =1 p= 0.30	χ^2 = 1.2 df =1 p= 0.28	χ^2 = 0.3 df =1 p= 0.61
LR				χ^2 =1.1 df =2 p = 0.58	χ^2 =1.2 df =2 p = 0.56	χ^2 =0.3 df =2 p = 0.86
Alcohol						
Low Intake†	19.6	19.4	19.5	1.00	1.00	1.00
Low-Med Intake	20.6	21.2	21.0	0.94 (0.66, 1.34)	0.96 (0.67, 1.36)	0.93 (0.65, 1.32)
Medium Intake	20.5	18.7	19.5	1.10 (0.77, 1.56)	1.11 (0.78, 1.59)	1.07 (0.74, 1.53)
Med-High Intake	21.0	19.8	20.3	1.08 (0.76, 1.53)	1.11 (0.78, 1.59)	1.05 (0.73, 1.50)
High Intake	18.3	21.0	19.8	0.98 (0.69, 1.41)	1.01 (0.70, 1.46)	0.91 (0.63, 1.33)
Trend				χ^2 = 0.0 df =1 p= 1.00	χ^2 = 0.0 df =1 p= 0.89	χ^2 = 0.2 df =1 p= 0.70
LR				χ^2 =1.0 df =4 p = 0.91	χ^2 =1.2 df =4 p = 0.89	χ^2 =1.2 df =4 p = 0.88
Non-alcoholic Beverages						
Low Intake†	19.3	20.6	20.0	1.00	1.00	1.00
Low-Med Intake	20.6	19.6	20.1	1.15 (0.81, 1.64)	1.14 (0.80, 1.63)	1.09 (0.76, 1.56)
Medium Intake	20.1	19.6	19.9	1.17 (0.82, 1.66)	1.14 (0.80, 1.62)	1.06 (0.74, 1.52)
Med-High Intake	19.6	20.4	20.1	1.11 (0.78, 1.58)	1.07 (0.74, 1.53)	0.97 (0.67, 1.40)
High Intake	20.3	19.8	20.0	1.22 (0.86, 1.74)	1.19 (0.83, 1.72)	1.04 (0.70, 1.52)
Trend				χ^2 = 0.8 df =1 p= 0.37	χ^2 = 0.5 df =1 p= 0.48	χ^2 = 0.0 df =1 p= 0.94
LR				χ^2 = 1.4 df=4 p = 0.85	χ^2 =1.1 df =4 p = 0.89	χ^2 =0.5 df =4 p = 0.97
Fish						
Low Intake†	21.1	18.6	19.7	1.00	1.00	1.00
Low-Med Intake	31.8	30.5	31.1	1.01 (0.73, 1.40)	1.02 (0.74, 1.41)	0.98 (0.71, 1.36)
Med-High Intake	27.6	28.8	28.3	0.97 (0.70, 1.35)	0.98 (0.70, 1.36)	0.92 (0.65, 1.28)
High Intake	19.5	22.2	21.0	0.95 (0.67, 1.36)	0.97 (0.68, 1.39)	0.87 (0.60, 1.25)
Trend				χ^2 = 0.1 df =1 p= 0.71	χ^2 = 0.1 df =1 p= 0.80	χ^2 = 0.7 df =1 p= 0.42
LR				χ^2 =0.2 df =3 p = 0.98	χ^2 =0.1 df =3 p = 0.99	χ^2 =0.8 df =3 p = 0.86
Legumes						
Low Intake†	52.8	49.6	51.0	1.00	1.00	1.00
Medium Intake	30.3	30.7	30.5	1.10 (0.85, 1.42)	1.10 (0.85, 1.42)	1.06 (0.82, 1.38)
High Intake	17.0	19.8	18.5	0.92 (0.68, 1.25)	0.94 (0.69, 1.29)	0.91 (0.66, 1.24)
Trend				χ^2 = 0.1 df =1 p= 0.78	χ^2 = 0.0 df =1 p= 0.88	χ^2 = 0.2 df =1 p= 0.67
LR				χ^2 =1.1 df =2 p = 0.57	χ^2 =0.9 df =2 p = 0.64	χ^2 =0.9 df =2 p = 0.64
Peanut Butter						
Low Intake†	28.0	29.6	28.9	1.00	1.00	1.00
Low-Med Intake	20.0	22.7	21.5	0.85 (0.62, 1.18)	0.85 (0.61, 1.17)	0.82 (0.59, 1.13)
Med-High Intake	17.8	18.7	18.3	0.90 (0.64, 1.26)	0.90 (0.64, 1.26)	0.86 (0.61, 1.21)
High Intake	34.3	29.0	31.4	1.18 (0.88, 1.57)	1.17 (0.88, 1.57)	1.08 (0.80, 1.46)
Trend				χ^2 = 2.9 df =1 p= 0.09	χ^2 = 2.9 df =1 p= 0.09	χ^2 = 1.3 df =1 p= 0.25
LR				χ^2 =4.8 df =3 p = 0.18	χ^2 =4.9 df =3 p = 0.18	χ^2 =3.7 df =3 p = 0.29
Baked Products						
Low Intake†	18.8	22.3	20.7	1.00	1.00	1.00
Low-Med Intake	16.3	20.2	18.4	0.91 (0.63, 1.31)	0.90 (0.63, 1.30)	0.88 (0.61, 1.27)
Medium Intake	21.6	20.6	21.0	1.11 (0.78, 1.57)	1.10 (0.78, 1.56)	1.05 (0.73, 1.49)
Med-High Intake	20.8	19.9	20.3	1.23 (0.86, 1.75)	1.24 (0.87, 1.77)	1.15 (0.80, 1.66)
High Intake	22.5	17.1	19.5	1.60 (1.12, 2.29)	1.62 (1.13, 2.32)	1.47 (0.99, 2.17)
Trend				χ^2=10.3 df=1 p=0.004	χ^2=10.7 df=1 p=0.004	χ^2 = 6.2 df =1 p= 0.01
LR				χ^2 =11.1 df=4 p =0.03	χ^2 =11.5 df=4 p= 0.02	χ^2 =7.0 df =4 p = 0.13

Variable	Case n = 601	Control n = 744	Total n =1345	Model 1*	Model 2**	Model 3 ***
	%	%	%	Odds Ratio (95% CI)	Odds Ratio (95% CI)	Odds Ratio (95% CI)
Sweets						
Low Intake†	17.6	25.5	22.0	1.00	1.00	1.00
Low-Med Intake	16.6	17.9	17.3	1.24 (0.86, 1.79)	1.25 (0.86, 1.81)	1.20 (0.83, 1.74)
Medium Intake	21.6	20.3	20.9	1.50 (1.06, 2.12)	1.49 (1.05, 2.11)	1.42 (1.00, 2.02)
Med-High Intake	26.1	20.2	22.8	1.73 (1.23, 2.43)	1.73 (1.23, 2.44)	1.59 (1.12, 2.25)
High Intake	18.0	16.1	17.0	1.50 (1.04, 2.18)	1.50 (1.03, 2.18)	1.34 (0.90, 1.98)
Trend				χ^2 = 4.4 df =1 p= 0.04	χ^2 = 4.2 df =1 p= 0.04	χ^2 = 1.7 df =1 p= 0.19
LR				χ^2=11.4 df =4 p =0.02	χ^2 =11.1 df =4 p=0.03	χ^2 =7.5 df =4 p = 0.11
Snacks						
Low Intake†	16.1	24.3	20.7	1.00	1.00	1.00
Low-Med Intake	19.0	19.5	19.3	1.37 (0.95, 1.97)	1.37 (0.95, 1.97)	1.34 (0.93, 1.94)
Medium Intake	25.3	21.4	23.1	1.62 (1.14, 2.29)	1.61 (1.14, 2.28)	1.53 (1.08, 2.18)
Med-High Intake	17.8	15.6	16.6	1.45 (0.99, 2.11)	1.42 (0.97, 2.07)	1.32 (0.90, 1.94)
High Intake	21.8	19.2	20.4	1.45 (1.01, 2.09)	1.43 (0.99, 2.06)	1.26 (0.86, 1.84)
Trend				χ^2=2.8 df =1 p= 0.09	χ^2 = 2.4 df =1 p= 0.12	χ^2 = 0.7 df =1 p= 0.42
LR				χ^2 = 8.0 df =4 p =0.09	χ^2 =7.6 df =4 p = 0.11	χ^2 = 5.9 df =4 p =0.21

† reference group

* includes age group and province as covariates

**includes smoking, age group, BMI, province as covariates

***includes smoking, age group, BMI, province, energy intake as covariates

5.3. Disaggregated Dairy Foods Analysis

The dairy food group consists of seven food items. Further analyses were conducted to determine if the risk seen with dairy intake was related to any particular component foods. The analysis proceeded by first considering large sub-groups (eg. Milk) and then specific food items (eg. 2% milk).

5.3.1. Milk

Milk is a large component of most people's dairy product consumption. Thus, the significant effect associated with dairy products could be expected to relate to milk intake (Table 7). However, we found no increasing risk associated with increasing milk intake, as the trend test was non-significant (χ^2 =1.2 df =1 p= 0.27).

Milk was further disaggregated into its components: whole milk, 2% milk, 1% milk, and skim milk. No significant results were obtained for this disaggregated analysis. However, it is important to note that the variation of intake for specific types of milk was quite limited and such that only 2% milk was divisible into more than two groups. Whole, 1% and skim were divided into low and high intake levels, while 2% milk was divided into quartiles. Because of the limited range of exposures in the categorized analyses, we also performed an analysis in which milk intake was included as a continuous variable (Table 8). This analysis did not yield any significant results.

5.3.2. Cheese

Cheese intake demonstrated the strongest association with testicular cancer risk in the disaggregated analysis. The test for a trend of increasing risk with increasing cheese intake was highly significant (χ^2=10.3 df=1 p<0.001). As well, a significant increase in

the point estimates was found at the medium intake level and above. Subjects with the two highest intake levels had very similar OR estimates (OR = 1.92; CI 1.26, 2.91) compared to (OR = 1.87; CI 1.22, 2.86). The likelihood ratio test of heterogeneity was also significant (χ^2=10.3 df=1 p<0.001). It appears that the risk associated with cheese intake was the major contributor to the increase in risk associated with dairy product intake, as opposed to milk.

5.3.3. Whole Milk and Cheese

The risk associated with the combined group of whole milk and cheese was significant, but to a lesser level than that seen in cheese. It would appear that the addition of whole milk partially attenuated the risk associated with cheese intake. However, the test for trend was significant in this food group (χ^2 =4.5 df =1 p= 0.03), and all levels of intake were significant. The highest risk estimate occurred in subjects with an intake of 3-6 servings per week (medium-high intake). The associated OR was 1.68 (CI 1.16, 2.42). The risk associated with (high) intake of >6 servings per week was 1.41 (CI 1.01, 1.98). As well, the combined variable produced a significant likelihood ratio test of heterogeneity (χ^2 =8.8 df =3 p = 0.03), indicating that the risk associated with the five intake quintiles is different.

Table 7. Risk of Testicular Cancer - Categorical Dairy Foods Disaggregation Analysis						
Variable	Case N = 601	Control n = 744	Total n =1345	Model 1*	Model 2**	Model 3 ***
	%	%	%	Odds Ratio (95% CI)	Odds Ratio (95% CI)	Odds Ratio (95% CI)
Milk						
Low Intake†	16.3	23.5	20.3	1.00	1.00	1.00
Low-Med Intake	21.1	20.4	20.7	1.40 (0.98, 2.00)	1.41 (0.99, 2.02)	1.39 (0.97, 1.99)
Medium Intake	21.5	22.5	22.0	1.23 (0.87, 1.75)	1.25 (0.88, 1.78)	1.18 (0.82, 1.68)
Med-High Intake	29.5	23.0	25.9	1.65 (1.18, 2.32)	1.68 (1.20, 2.36)	1.52 (1.08, 2.16)
High Intake	11.7	10.6	11.1	1.41 (0.92, 2.16)	1.42 (0.93, 2.17)	1.23 (0.79, 1.92)
Trend				χ^2=3.7 df=1 p= 0.06	χ^2=3.8 df=1 p= 0.05	χ^2=1.2 df=1 p= 0.27
LR				χ^2=9.1 df = 4 p = 0.06	χ^2=9.5 df= 4 p = 0.05	χ^2=6.7 df= 4 p = 0.15
Whole Milk						
Low Intake†	78.5	77.8	78.1	1.00	1.00	1.00
High Intake	21.5	22.2	21.9	0.95 (0.73, 1.25)	0.97 (0.73, 1.27)	0.93 (0.70, 1.22)
Trend				χ^2=0.1 df=1 p= 0.73	χ^2=0.1 df=1 p= 0.81	χ^2=0.3 df=1 p= 0.58
LR				χ^2 =0.1 df=1 p = 0.73	χ^2 =0.1 df=1 p = 0.81	χ^2 =0.3 df=1 p = 0.58
Two % Milk						
Low Intake†	34.9	40.3	40.3	1.00	1.00	1.00
Low-Med Intake	22.1	22.6	22.6	1.11 (0.82, 1.50)	1.10 (0.81, 1.48)	1.13 (0.84, 1.53)
Med-High Intake	25.5	21.1	21.1	1.35 (1.00, 1.81)	1.37 (1.02, 1.84)	1.34 (0.99, 1.81)
High Intake	17.5	16.0	16.0	1.18 (0.85, 1.64)	1.20 (0.86, 1.67)	1.11 (0.79, 1.56)
Trend				χ^2=1.4 df=1 p= 0.24	χ^2=1.7 df=1 p= 0.19	χ^2=0.6 df=1 p= 0.43
LR				χ^2 =4.0 df=3 p = 0.26	χ^2 =4.5 df=3 p = 0.21	χ^2 =3.4 df=3 p = 0.34
One % Milk						
Low Intake†	73.9	77.7	76.0	1.00	1.00	1.00
High Intake	26.1	22.3	24.0	1.13 (0.87, 1.47)	1.11 (0.85, 1.45)	1.09 (0.83, 1.42)
Trend				χ^2=0.8 df=1 p= 0.38	χ^2=0.6 df=1 p= 0.43	χ^2=0.4 df=1 p= 0.54
LR				χ^2 =0.8 df=1 p = 0.38	χ^2 =0.6 df=1 p = 0.43	χ^2 =0.4 df=1 p = 0.54
Skim Milk						
Low Intake†	85.2	87.9	86.7	1.00	1.00	1.00
High Intake	14.8	12.1	13.3	1.26 (0.91, 1.75)	1.26 (0.91, 1.76)	1.25 (0.90, 1.75)
Trend				χ^2=1.9 df=1 p= 0.17	χ^2=1.9 df=1 p= 0.17	χ^2=1.8 df=1 p= 0.18
LR				χ^2 =1.9 df=1 p = 0.17	χ^2 =1.9 df=1 p = 0.17	χ^2 =1.8 df=1 p = 0.18
Eggs						
Low Intake†	21.1	24.1	22.8	1.00	1.00	1.00
Low-Med Intake	22.8	24.1	23.5	1.05 (0.76, 1.46)	1.07 (0.77, 1.49)	1.06 (0.76, 1.47)
Med-High Intake	39.8	37.0	38.2	1.25 (0.93, 1.69)	1.27 (0.94, 1.71)	1.16 (0.86, 1.58)
High Intake	16.3	14.9	15.5	1.18 (0.82, 1.71)	1.20 (0.83, 1.74)	1.07 (0.73, 1.58)
Trend				χ^2=1.6 df=1 p= 0.21	χ^2=1.7 df=1 p= 0.19	χ^2=0.3 df=1 p= 0.61
LR				χ^2= 2.8 df= 3 p = 0.43	χ^2=2.8 df = 3 p = 0.42	χ^2=1.0 df = 3 p = 0.80
Butter						
Low Intake†	36.1	37.9	37.1	1.00	1.00	1.00
Low-Med Intake	13.3	12.1	12.6	1.15 (0.80, 1.65)	1.13 (0.79, 1.63)	1.13 (0.78, 1.63)
Med-High Intake	23.5	24.3	23.9	0.93 (0.69, 1.24)	0.92 (0.69, 1.24)	0.94 (0.70, 1.27)
High Intake	27.1	25.7	26.3	1.15 (0.86, 1.52)	1.15 (0.86, 1.53)	1.11 (0.83, 1.48)
Trend				χ^2=0.5 df=1 p= 0.50	χ^2=0.5 df=1 p= 0.49	χ^2=0.2 df=1 p= 0.64
LR				χ^2= 2.3 df= 3 p = 0.51	χ^2=2.3 df = 3 p = 0.51	χ^2=1.4 df = 3 p = 0.71
Cheese						
Low Intake†	12.5	20.2	16.7	1.00	1.00	1.00
Low-Med Intake	14.3	17.9	16.3	1.31 (0.88, 1.96)	1.31 (0.87, 1.96)	1.30 (0.87, 1.95)
Medium Intake	39.3	36.6	37.8	1.66 (1.18, 2.33)	1.67 (1.18, 2.35)	1.60 (1.13, 2.25)
Med-High Intake	17.5	12.2	14.6	2.04 (1.36, 3.07)	2.08 (1.38, 3.13)	1.92 (1.26, 2.91)
High Intake	16.5	13.2	14.7	2.02 (1.34, 3.04)	2.05 (1.36, 3.09)	1.87 (1.22, 2.86)
Trend				χ^2=14.8 df=1 p<0.001	χ^2=15.4 df=1 p<0.001	χ^2=10.3 df=1 p<0.001
LR				χ^2=17.5 df=4 p=0.002	χ^2=18.1 df=4 p=0.001	χ^2=12.9 df= 4 p= 0.01
Whole Milk and Cheese						
Low Intake†	21.1	30.8	26.5	1.00	1.00	1.00
Low-Med Intake	33.4	31.2	32.2	1.46 (1.08, 1.96)	1.45 (1.07, 1.95)	1.39 (1.03, 1.88)
Med-High Intake	19.0	13.7	16.1	1.80 (1.26, 2.57)	1.81 (1.26, 2.60)	1.68 (1.16, 2.42)
High Intake	26.5	24.3	25.3	1.55 (1.13, 2.12)	1.58 (1.15, 2.17)	1.41 (1.01, 1.98)
Trend				χ^2=7.9 df=1 p= 0.005	χ^2=8.7 df=1 p= 0.003	χ^2=4.5 df=1 p= 0.03
LR				χ^2=12.6 df=3 p=0.006	χ^2=13.0 df=3 p=0.004	χ^2 =8.8 df=3 p = 0.03

† reference group * includes age group and province as covariates

**includes smoking, age group, BMI, province as covariates

***includes smoking, age group, BMI, province, energy intake as covariates

Table 8. Risk of Testicular Cancer - Continuous Food Group Disaggregation Analysis*	
Food/Nutrient**	Odds Ratio (95% CI)
Total Milk	1.03 (0.95, 1.12)
Whole Milk	0.88 (0.73, 1.06)
2% Milk	0.99 (0.89, 1.10)
1% Milk	1.10 (0.95, 1.28)
Skim Milk	1.19 (0.98, 1.46)

*Model includes: food, age, province, BMI, Smoking and energy intake
** per 1 serving/week

5.4. Total Sample – Nutrient Analysis

5.4.1. Overview of the Nutrient Analysis

Few significant results were found in the nutrient analysis; only total fat, calcium, and sodium demonstrated a significant association with testicular cancer. Unfortunately, none of these results are particularly strong or compelling. The results for the nutrient analysis are shown in Table 9.

5.4.2. Fats

Neither the trend test nor the Wald tests were significant for fat intake. However, the likelihood ratio test of heterogeneity was significant ($\chi^2 = 11.8$ df = 4 p = 0.02), indicating that the ORs are different across the intake quintiles. When fats were disaggregated into saturated, polyunsaturated and monounsaturated fat, no significant results were observed (Table 9). In the continuous disaggregation analysis (Table 10), increasing fat intake remained non-significant for all types of fat, except saturated fat (OR = 1.18; CI 1.02, 1.37).

5.4.3. Calcium

Calcium appears to be mildly associated with an increase in testicular cancer risk, although the test for trend does not reach statistical significance ($\chi^2 = 3.6$ df = 1 p = 0.06). As well, only the medium-high intake quintile has a significant point estimate (OR = 1.80; CI 1.21, 2.70). Despite the lack of significant point estimates and trend test, calcium does have a significant test of heterogeneity ($\chi^2 = 11.0$ df = 4 p = 0.03).

5.4.4. Sodium

Higher levels of sodium intake were associated with a higher risk of testicular cancer (χ^2 = 3.9 df = 1 p = 0.05). None of the individual Wald tests reach statistical significance;

however, at the highest intake quintile the associated OR is elevated (OR = 1.67; CI 0.91, 3.09).

Table 9. Risk of Testicular Cancer associated with Nutrient Intake					
Nutrient	Case n = 601	Control n = 744	Overall n = 1345	Model A*	Model B**
	%	%	%	Odds Ratio (95% CI)	Odds Ratio (95% CI)
Fat					
Low Intake†	16.6	22.7	20.0	1.00	1.00
Low-Medium Intake	21.1	19.1	20.0	1.22 (0.82, 1.82)	1.22 (0.82, 1.82)
Medium Intake	19.0	20.8	20.0	0.87 (0.55, 1.38)	0.85 (0.53, 1.35)
Medium High Intake	19.6	20.3	20.0	0.92 (0.55, 1.53)	0.90 (0.54, 1.50)
High Intake	23.6	17.1	20.0	1.70 (0.93, 3.11)	1.66 (0.91, 3.05)
Trend				$\chi^2 = 3.0$ df = 1 p = 0.08	$\chi^2 = 2.8$ df = 1 p = 0.10
LR				$\chi^2 = 11.5$ df = 4 p = 0.02	$\chi^2 = 11.8$ df = 4 p = 0.02
Saturated Fat					
Low Intake†	16.6	22.7	20.0	1.00	1.00
Low-Medium Intake	19.1	20.7	20.0	1.06 (0.73, 1.55)	1.06 (0.72, 1.55)
Medium Intake	20.1	19.9	20.0	1.10 (0.72, 1.68)	1.06 (0.69, 1.63)
Medium High Intake	22.1	18.3	20.0	1.23 (0.78, 1.95)	1.21 (0.76, 1.91)
High Intake	22.0	18.4	20.0	1.37 (0.80, 2.35)	1.34 (0.78, 2.31)
Trend				$\chi^2 = 1.5$ df = 1 p = 0.23	$\chi^2 = 1.3$ df = 1 p = 0.25
LR				$\chi^2 = 1.6$ df = 4 p = 0.82	$\chi^2 = 1.4$ df = 4 p = 0.84
Mono-Unsaturated Fat					
Low Intake†				1.00	1.00
Low-Medium Intake	18.1	21.5	20.0	0.91 (0.62, 1.33)	0.90 (0.61, 1.32)
Medium Intake	19.3	20.6	20.0	0.73 (0.47, 1.13)	0.71 (0.46, 1.10)
Medium-High Intake	19.0	20.8	20.0	0.88 (0.55, 1.41)	0.86 (0.54, 1.37)
High Intake	21.1	19.1	20.0	1.16 (0.68, 2.00)	1.12 (0.65, 1.93)
Trend	22.5	18.0	20.0	$\chi^2 = 0.8$ df = 1 p = 0.38	$\chi^2 = 0.6$ df = 1 p = 0.46
LR				$\chi^2 = 5.3$ df = 4 p = 0.26	$\chi^2 = 5.3$ df = 4 p = 0.26
Poly-Unsaturated Fat					
Low Intake†				1.00	1.00
Low-Medium Intake	17.6	21.9	20.0	0.94 (0.63, 1.40)	0.95 (0.63, 1.42)
Medium Intake	20.3	19.8	20.0	0.77 (0.49, 1.22)	0.76 (0.48, 1.21)
Medium High Intake	19.1	20.7	20.0	0.90 (0.55, 1.48)	0.90 (0.55, 1.49)
High Intake	20.5	19.6	20.0	1.20 (0.69, 2.09)	1.20 (0.68, 2.09)
Trend	22.5	18.0	20.0	$\chi^2 = 0.9$ df = 1 p = 0.35	$\chi^2 = 0.9$ df = 1 p = 0.36
LR				$\chi^2 = 4.6$ df = 4 p = 0.33	$\chi^2 = 4.7$ df = 4 p = 0.32
Protein					
Low Intake†	17.5	22.0	20.0	1.00	1.00
Low-Medium Intake	18.5	21.2	20.0	0.85 (0.56, 1.29)	0.84 (0.56, 1.28)
Medium Intake	19.6	20.3	20.0	0.84 (0.52, 1.35)	0.84 (0.52, 1.35)
Medium High Intake	21.8	18.6	20.0	1.02 (0.61, 1.71)	1.00 (0.60, 1.69)
High Intake	22.6	17.9	20.0	1.38 (0.76, 2.51)	1.35 (0.74, 2.48)
Trend				$\chi^2 = 2.3$ df = 1 p = 0.13	$\chi^2 = 2.1$ df = 1 p = 0.15
LR				$\chi^2 = 5.1$ df = 4 p =0.28	$\chi^2 = 4.8$ df = 4 p = 0.30
Carbohydrates					
Low Intake†	17.0	22.5	20.0	1.00	1.00
Low-Medium Intake	21.1	19.1	20.0	1.23 (0.80, 1.88)	1.25 (0.82, 1.91)
Medium Intake	21.0	19.2	20.0	1.04 (0.62, 1.73)	1.01 (0.60, 1.69)
Medium High Intake	20.8	19.4	20.0	0.81 (0.46, 1.45)	0.80 (0.44, 1.43)
High Intake	20.1	19.9	20.0	0.68 (0.35, 1.31)	0.67 (0.34, 1.29)
Trend				$\chi^2 = 2.4$ df = 1 p = 0.13	$\chi^2 = 2.5$ df = 1 p = 0.11
LR				$\chi^2 = 5.1$ df = 4 p = 0.28	$\chi^2 = 5.6$ df = 4 p = 0.23
Dietary Fibre					
Low Intake†	17.8	21.8	20.0	1.00	1.00
Low-Medium Intake	21.6	18.7	20.0	1.35 (0.94, 1.94)	1.38 (0.96, 2.00)
Medium Intake	19.5	20.4	20.0	1.16 (0.79, 1.71)	1.17 (0.79, 1.73)
Medium High Intake	20.8	19.4	20.0	1.23 (0.82, 1.84)	1.26 (0.84, 1.90)
High Intake	20.3	19.8	20.0	1.24 (0.80, 1.91)	1.28 (0.83, 1.99)
Trend				$\chi^2 = 0.3$ df = 1 p = 0.58	$\chi^2 = 0.5$ df = 1 p = 0.50
LR				$\chi^2 = 2.7$ df = 4 p = 0.61	$\chi^2 = 3.2$ df = 4 p = 0.52

Nutrient	Case n = 601	Control n = 744	Overall n = 1345	Model A*	Model B**
	%	%	%	Odds Ratio (95% CI)	Odds Ratio (95% CI)
Sugar					
Low Intake†	16.5	22.9	20.0	1.00	1.00
Low-Medium Intake	19.6	20.3	20.0	1.26 (0.88, 1.81)	1.27 (0.88, 1.83)
Medium Intake	21.1	19.1	20.0	1.40 (0.96, 2.05)	1.40 (0.95, 2.04)
Medium High Intake	21.0	19.2	20.0	1.24 (0.84, 1.83)	1.21 (0.81, 1.80)
High Intake	21.8	18.6	20.0	1.44 (0.94, 2.22)	1.41 (0.91, 2.17)
Trend				$\chi^2 = 1.7$ df = 1 p = 0.20	$\chi^2 = 1.3$ df = 1 p = 0.26
LR				$\chi^2 = 4.0$ df = 4 p = 0.41	$\chi^2 = 3.7$ df = 4 p = 0.45
Iron					
Low Intake†	18.1	21.5	20.0	1.00	1.00
Low-Medium Intake	19.1	20.7	20.0	0.93 (0.63, 1.38)	0.93 (0.63, 1.39)
Medium Intake	20.3	19.8	20.0	1.01 (0.64, 1.59)	1.03 (0.65, 1.62)
Medium High Intake	21.8	18.6	20.0	1.08 (0.66, 1.79)	1.10 (0.67, 1.83)
High Intake	20.6	19.5	20.0	1.02 (0.58, 1.82)	1.05 (0.58, 1.88)
Trend				$\chi^2 = 0.0$ df = 1 p = 0.85	$\chi^2 = 0.1$ df = 1 p = 0.79
LR				$\chi^2 = 0.5$ df = 4 p = 0.97	$\chi^2 = 0.6$ df = 4 p = 0.96
Calcium					
Low Intake†	15.1	23.9	20.0	1.00	1.00
Low-Medium Intake	20.8	19.4	20.0	1.56 (1.08, 2.27)	1.58 (1.09, 2.31)
Medium Intake	18.8	21.0	20.0	1.22 (0.81, 1.83)	1.25 (0.83, 1.88)
Medium High Intake	23.5	17.2	20.0	1.75 (1.17, 2.61)	1.80 (1.21, 2.70)
High Intake	21.8	18.6	20.0	1.53 (0.97, 2.40)	1.56 (0.99, 2.45)
Trend				$\chi^2 = 3.3$ df = 1 p = 0.07	$\chi^2 = 3.6$ df = 1 p = 0.06
LR				$\chi^2 = 10.4$ df = 4 p = 0.03	$\chi^2 = 11.0$ df = 4 p = 0.03
Zinc					
Low Intake†	18.1	21.5	20.0	1.00	1.00
Low-Medium Intake	19.0	20.8	20.0	0.80 (0.53, 1.21)	0.79 (0.52, 1.20)
Medium Intake	18.3	21.4	20.0	0.61 (0.37, 0.99)	0.60 (0.36, 0.98)
Medium High Intake	21.6	18.7	20.0	0.84 (0.49, 1.44)	0.83 (0.48, 1.42)
High Intake	23.0	17.6	20.0	1.14 (0.61, 2.13)	1.11 (0.59, 2.08)
Trend				$\chi^2 = 1.1$ df = 1 p = 0.30	$\chi^2 = 0.9$ df = 1 p = 0.34
LR				$\chi^2 = 9.4$ df = 4 p = 0.05	$\chi^2 = 9.4$ df = 4 p = 0.05
Phosphorous					
Low Intake†	16.8	22.6	20.0	1.00	1.00
Low-Medium Intake	18.8	21.0	20.0	1.11 (0.74, 1.67)	1.13 (0.75, 1.70)
Medium Intake	20.0	20.0	20.0	1.18 (0.76, 1.85)	1.22 (0.78, 1.91)
Medium High Intake	24.0	16.8	20.0	1.67 (1.02, 2.73)	1.72 (1.05, 2.83)
High Intake	20.5	19.6	20.0	1.19 (0.69, 2.05)	1.23 (0.71, 2.13)
Trend				$\chi^2 = 0.6$ df = 1 p = 0.44	$\chi^2 = 0.7$ df = 1 p = 0.40
LR				$\chi^2 = 6.4$ df = 4 p = 0.17	$\chi^2 = 6.7$ df = 4 p = 0.15
Sodium					
Low Intake†	18.0	21.6	20.0	1.00	1.00
Low-Medium Intake	18.0	21.6	20.0	0.90 (0.59, 1.35)	0.90 (0.59, 1.36)
Medium Intake	20.6	19.5	20.0	1.03 (0.64, 1.64)	1.03 (0.64, 1.65)
Medium High Intake	20.6	19.5	20.0	1.19 (0.71, 2.01)	1.21 (0.71, 2.04)
High Intake	22.8	17.7	20.0	1.71 (0.93, 3.15)	1.67 (0.91, 3.09)
Trend				$\chi^2 = 4.3$ df = 1 p = 0.04	$\chi^2 = 3.9$ df = 1 p = 0.05
LR				$\chi^2 = 6.0$ df = 4 p = 0.20	$\chi^2 = 5.4$ df = 4 p = 0.25
Cholesterol					
Low Intake†	18.1	21.5	20.0	1.00	1.00
Low-Medium Intake	18.5	21.2	20.0	0.96 (0.66, 1.39)	0.94 (0.64, 1.36)
Medium Intake	20.8	19.4	20.0	1.06 (0.72, 1.56)	1.06 (0.72, 1.56)
Medium High Intake	20.1	19.9	20.0	0.95 (0.63, 1.44)	0.94 (0.62, 1.42)
High Intake	22.5	18.0	20.0	1.10 (0.77, 1.88)	1.20 (0.77, 1.88)
Trend				$\chi^2 = 0.9$ df = 1 p = 0.35	$\chi^2 = 0.9$ df = 1 p = 0.35
LR				$\chi^2 = 2.1$ df = 4 p = 0.73	$\chi^2 = 2.2$ df = 4 p = 0.69

† reference group

*includes age group, province, energy intake as covariates

**includes smoking, age group, BMI, province, energy intake as covariates

Table 10. Risk of Testicular Cancer - Continuous Nutrient Disaggregation Analysis*	
Food/Nutrient**	Odds Ratio (95% CI)
Total Fat	1.06 (1.00, 1.13)
Saturated Fat	1.18 (1.02, 1.37)
Mono-Unsaturated Fat	1.09 (0.96, 1.24)
Poly-Unsaturated Fat	1.04 (0.73, 1.48)

*Model includes: food, age, province, BMI, Smoking and energy intake
** per 10 grams/week

5.5. Chapter Summary

Three of the seventeen food groups analyzed were significantly associated with increased testicular cancer risk: dairy, luncheon meats, and baked products. The dairy food group reached peak risk in the medium-high intake quintile, rather than in the highest intake quintile as would have been expected for a monotonic dose response relationship. The disaggregation of dairy products provided evidence that while milk is a large component of most people's dairy product consumption, the risk observed for milk intake was not significant. Conversely, risk associated with cheese intake was very strong, as the trend test for cheese intake was highly significant (χ^2=10.3 df=1 p<0.001). It appears that the risk associated with dairy product consumption may be more associated with the consumption of cheese rather than milk.

Baking and luncheon meats had the highest risk for subjects in the highest intake quintile as expected for a monotonic dose response relationship. As well, both baked products and luncheon meats had significant trend tests. Only two of the 14 nutrients examined reached significance, they were calcium and sodium. Of these two, only sodium had a significant trend test.

Table 11. Risk of Testicular Cancer associated with food and nutrient intake Summary table (Model 3*)

Food/Nutrient	Low Intake Odds Ratio (CI)	Low-Med Intake Odds Ratio (CI)	Medium Intake Odds Ratio (CI)	Med-High Intake Odds Ratio (CI)	High Intake Odds Ratio (CI)	P-Trend
Dairy	1.00	1.39 (0.96, 2.02)	1.79 (1.23, 2.62)	2.56 (1.73, 3.78)	1.40 (0.93, 2.12)	0.12
Luncheon Meats	1.00	1.14 (0.79, 1.64)	1.13 (0.79, 1.60)	1.15 (0.79, 1.68)	1.49 (1.01, 2.19)	0.05
Baked Products	1.00	0.88 (0.61, 1.27)	1.05 (0.73, 1.49)	1.15 (0.80, 1.66)	1.47 (0.99, 2.17)	0.01
Milk	1.00	1.39 (0.97, 1.99)	1.18 (0.82, 1.68)	1.52 (1.08, 2.16)	1.23 (0.79, 1.92)	0.27
Cheese	1.00	1.30 (0.87, 1.95)	1.60 (1.13, 2.25)	1.92 (1.26, 2.91)	1.87 (1.22, 2.86)	<0.001
Calcium	1.00	1.58 (1.09, 2.31)	1.25 (0.83, 1.88)	1.80 (1.21, 2.70)	1.56 (0.99, 2.45)	0.06
Sodium	1.00	0.90 (0.59, 1.36)	1.03 (0.64, 1.65)	1.21 (0.71, 2.04)	1.67 (0.91, 3.09)	0.05

*Model includes: food, age, province, BMI, Smoking and energy intake

6. Results II - Seminomas

6.1. Seminomas - Characteristics of Cases and Controls

6.1.1. Analysis of Covariates

The analytical results for the covariates of seminoma cases are shown in Table 12. Seminoma cases had a mean age of 37.0 years, and 41.6% of them had never smoked. The largest recruitment site for seminoma cases was in Ontario (29.4%).

There is no change in risk associated with smoking. A significant trend of increasing risk with increasing energy intake ($\chi^2 = 4.9$ df =1 p= 0.03) was observed. The peak increase in risk for total energy intake occurred in the medium-high quintile (OR = 1.65; CI 1.08, 2.52). No effect on risk was observed for BMI.

Table 12. Multivariate analysis for the major covariates of the NECSS dataset (Seminomas Only)

Variable	Case n = 356	Control n = 744	Total n= 1100	Model 1*	Model 2**	Model 3 ***
	%	%	%	Odds Ratio (95% CI)	Odds Ratio (95% CI)	Odds Ratio (95% CI)
Age Group						
20-24†	3.7	7.5	6.3	Not Applicable	Not Applicable	Not Applicable
25-29	10.7	12.5	11.9			
30-34	22.2	15.7	17.8			
35-39	27.8	17.6	20.9			
40-44	18.5	14.3	15.6			
45-49	12.4	13.7	13.3			
50-54	4.8	18.7	14.2			
LR						
Province						
Maritimes†				Not Applicable	Not Applicable	Not Applicable
Ontario	15.2	18.4	17.4			
Man & Sask	29.2	35.9	33.7			
Alberta	12.4	12.1	12.2			
BC	19.7	13.8	15.7			
LR	23.6	19.8	21.0			
Smoking (PY)						
0 (non-smoker) †	41.9	38.3	39.5	1.00	1.00	1.00
1-5	16.6	19.0	18.2	0.83 (0.57, 1.21)	0.83 (0.57, 1.20)	0.82 (0.56, 1.20)
5-12	19.1	18.3	18.6	0.93 (0.65, 1.34)	0.92 (0.64, 1.33)	0.92 (0.64, 1.32)
12-24	15.5	15.3	15.4	0.90 (0.61, 1.35)	0.89 (0.60, 1.34)	0.89 (0.59, 1.33)
24 +	7.0	9.1	8.5	1.04 (0.60, 1.80)	1.04 (0.60, 1.82)	1.03 (0.59, 1.80)
Trend				χ^2 = 0.2 df =1 p= 0.68	χ^2 = 0.2 df =1 p= 0.63	χ^2 = 0.3 df =1 p= 0.61
LR				χ^2=1.2 df=4 p = 0.88	χ^2 =1.3 df =4 p = 0.87	χ^2 =1.3 df =4 p = 0.86
BMI						
<23	25.3	24.7	24.9	1.00	1.00	1.00
23-25.2	23.3	23.3	23.3	0.94 (0.65, 1.38)	0.95 (0.65, 1.40)	0.96 (0.66, 1.41)
25.2-27.7	28.4	25.7	26.6	1.07 (0.74, 1.53)	1.07 (0.75, 1.55)	1.08 (0.75, 1.56)
27.7-30.5	14.9	14.9	14.9	1.03 (0.66, 1.58)	1.04 (0.67, 1.60)	1.05 (0.68, 1.63)
>30.5	8.2	11.4	10.4	0.81 (0.48, 1.34)	0.80 (0.48, 1.34)	0.80 (0.48, 1.33)
Trend				χ^2 = 0.1 df =1 p= 0.75	χ^2 = 0.1 df =1 p= 0.83	χ^2 = 0.0 df =1 p= 0.88
LR				χ^2=1.4 df=4 p = 0.85	χ^2 =1.5 df =4 p = 0.83	χ^2 =1.6 df =4 p = 0.81
Energy Intake (kC)						
700.0-1450.7†	16.6	21.6	20.0	1.00	1.00	Not Applicable
1450.7-1778.4	19.1	20.4	20.0	1.32 (0.86, 2.03)	1.31 (0.85, 2.02)	
1778.4-2081.1	20.8	19.6	20.0	1.50 (0.98, 2.29)	1.47 (0.96, 2.25)	
2081.1-2556.9	22.5	18.8	20.0	1.65 (1.08, 2.51)	1.66 (1.09, 2.53)	
2556.9+	21.1	19.5	20.0	1.56 (1.02, 2.37)	1.57 (1.03, 2.41)	
Trend				χ^2 = 4.5 df =1 p= 0.03	χ^2 = 4.9 df =1 p= 0.03	
LR				χ^2=6.7 df=4 p = 0.16	χ^2 =6.8 df =4 p = 0.15	

† reference group

* includes age group and province as covariates

**includes smoking, age group, BMI, province as covariates

***includes smoking, age group, BMI, province, energy intake as covariates

6.2. Seminomas - Food group analysis

6.2.1. Overview of Food group analyses

Within the seminoma histological subtype, the risk associated with food groups seems to be diminished as compared with that observed in the total sample. Only two of the food groups (dairy products and baked products) exhibited a statistically significant result, and only one (baked products) had a statistically significant trend test.

There were four food groups with notable non-significant results. Firstly, fruits have a protective effect at all quintiles other than medium-high intake. However, none of the results reached statistical significant. At high intake, the risk associated with fruit intake was almost significantly protective of testicular cancer (OR = 0.66; CI 0.42, 1.03). Risk associated with vegetable intake remained approximately at the null value at all quintiles. Meat has been associated with an increase in cancer risk; we observed a non-significant decrease in risk at all levels for the seminoma subgroup, which was similar to the result observed in the total sample analysis. Finally, luncheon meats, while significant in the total sample, were not associated with any increase in risk for the seminoma subtype (high intake; OR = 1.01; CI 0.65, 1.59). The results of the food group analysis are shown in Table 13.

6.2.2. Dairy Products

Dairy products were associated with the strongest results in the seminoma subgroup. A peak risk of OR of 2.04 (CI 1.31, 3.17) was reached in the medium intake quintile. The risk was slightly diminished risk at the medium-high intake quintile (OR = 1.93; CI 1.23, 3.03). While risk in the high intake quintile decreases substantially (OR = 1.38 CI 0.84,

2.25) as compared to the medium and medium high intake quintiles. However, the overlap in the 95% confidence intervals for these two risk estimates shows that these estimates are not statistically different. This suggests that the apparently lower OR in the highest intake quintile is likely the result of random variation. This was confirmed by an additional logistic regression model which included a quadratic term for dairy intake; the Wald Chi-square for this term was not significant (p=0.55). The test for trend was a non-significant (χ^2 =1.2 df =1 p =0.27). However, the likelihood ratio test for heterogeneity is strongly significant (χ^2=14.8 df=4 p=0.005), indicating that the ORs across the five intake strata are different.

6.2.3. Baked Products

As with the total sample, the intake of baked products had a significant test of trend (χ^2 =4.2 df =1 p =0.04) although the p-value was close to 0.05. However, none of the individual Wald tests reached statistical significance.

Table 13. Risk of Testicular Cancer associated with Food Intake (Seminomas Only)						
Variable	Case n = 354	Control n = 744	Total n= 1100	Model 1*	Model 2**	Model 3 ***
	%	%	%	Odds Ratio (95% CI)	Odds Ratio (95% CI)	Odds Ratio (95% CI)
Dairy						
Low Intake†	13.8	22.3	19.6	1.00	1.00	1.00
Low-Med Intake	17.1	21.4	20.0	1.26 (0.81, 1.98)	1.25 (0.80, 1.96)	1.22 (0.77, 1.91)
Medium Intake	24.4	18.3	20.3	2.17 (1.41, 3.34)	2.18 (1.41, 3.36)	2.04 (1.31, 3.17)
Med-High Intake	24.7	17.7	20.0	2.14 (1.39, 3.30)	2.13 (1.38, 3.29)	1.93 (1.23, 3.03)
High Intake	19.9	20.3	20.2	1.60 (1.03, 2.49)	1.58 (1.02, 2.47)	1.38 (0.84, 2.25)
Trend				χ^2=4.2 df=1 p =0.04	χ^2=4.2 df=1 p =0.04	χ^2=1.2 df=1 p =0.27
LR				χ^2=18.9 df=4 p=0.001	χ^2=18.9 df=4 p=0.001	χ^2=14.8 df=4 p=0.005
Fats						
Low Intake†	18.8	19.9	19.6	1.00	1.00	1.00
Low-Med Intake	18.8	20.6	20.0	0.92 (0.61, 1.40)	0.92 (0.60, 1.40)	0.89 (0.58, 1.37)
Medium Intake	21.1	19.6	20.1	1.10 (0.73, 1.67)	1.12 (0.74, 1.70)	1.04 (0.68, 1.60)
Med-High Intake	19.1	21.8	20.9	0.91 (0.60, 1.38)	0.91 (0.60, 1.40)	0.82 (0.53, 1.27)
High Intake	22.2	18.2	19.5	1.34 (0.88, 2.04)	1.35 (0.88, 2.07)	1.17 (0.75, 1.83)
Trend				χ^2=2.6 df=1 p =0.10	χ^2=2.6 df=1 p =0.10	χ^2=0.8 df=1 p =0.38
LR				χ^2=4.5 df = 4 p = 0.34	χ^2 = 4.7 df=4 p = 0.33	χ^2 = 3.2 df=4 p = 0.53
Meat						
Low Intake†	20.2	19.9	20.0	1.00	1.00	1.00
Low-Med Intake	17.7	19.0	18.6	0.95 (0.62, 1.45)	0.95 (0.62, 1.45)	0.87 (0.56, 1.34)
Medium Intake	21.6	21.1	21.3	1.04 (0.70, 1.57)	1.04 (0.69, 1.56)	0.92 (0.60, 1.40)
Med-High Intake	18.0	21.1	20.1	0.76 (0.50, 1.16)	0.75 (0.49, 1.15)	0.62 (0.40, 0.97)
High Intake	22.5	19.0	20.1	1.10 (0.73, 1.66)	1.12 (0.74, 1.69)	0.87 (0.55, 1.37)
Trend				χ^2=0.1 df=1 p =0.77	χ^2=0.1 df=1 p =0.73	χ^2=0.6 df=1 p =0.46
LR				χ^2= 3.6 df= 4 p= 0.46	χ^2 =3.9 df=4 p = 0.42	χ^2 =5.2 df=4 p = 0.27
Soup						
Low Intake†	13.8	12.8	13.1	1.00	1.00	1.00
Low-Med Intake	30.6	29.3	29.7	0.97 (0.63, 1.48)	0.97 (0.63, 1.49)	0.95 (0.62, 1.46)
Med-High Intake	29.8	31.9	31.2	0.86 (0.56, 1.32)	0.88 (0.57, 1.35)	0.83 (0.54, 1.28)
High Intake	25.8	26.1	26.0	0.99 (0.64, 1.54)	1.02 (0.65, 1.59)	0.93 (0.59, 1.46)
Trend				χ^2=0.0 df=1 p =0.85	χ^2=0.1 df=1 p =0.75	χ^2=0.0 df=1 p =0.88
LR				χ^2=0.9 df=3 p = 0.84	χ^2 =0.8 df=3 p = 0.84	χ^2 =1.0 df=3 p = 0.81
Luncheon Meats						
Low Intake†	18.3	18.6	18.5	1.00	1.00	1.00
Low-Med Intake	18.3	22.5	21.1	0.77 (0.50, 1.18)	0.77 (0.50, 1.18)	0.76 (0.50, 1.17)
Medium Intake	21.9	20.2	20.7	1.10 (0.72, 1.67)	1.10 (0.72, 1.67)	1.02 (0.67, 1.57)
Med-High Intake	19.1	20.4	20.0	0.86 (0.56, 1.32)	0.87 (0.57, 1.34)	0.76 (0.49, 1.19)
High Intake	22.5	18.4	19.7	1.17 (0.77, 1.79)	1.19 (0.78, 1.82)	1.01 (0.65, 1.59)
Trend				χ^2=1.4 df=1 p =0.24	χ^2=1.6 df=1 p =0.21	χ^2=0.1 df=1 p =0.75
LR				χ^2=5.5 df=4 p = 0.24	χ^2 =5.4 df=4 p = 0.25	χ^2 =4.2 df=4 p = 0.38
Grains						
Low Intake†	20.2	19.8	19.9	1.00	1.00	1.00
Low-Med Intake	20.5	19.6	19.9	1.05 (0.69, 1.58)	1.06 (0.70, 1.60)	0.93 (0.61, 1.44)
Medium Intake	17.7	21.6	20.4	0.83 (0.54, 1.26)	0.83 (0.55, 1.27)	0.70 (0.45, 1.09)
Med-High Intake	20.2	19.6	19.8	1.08 (0.72, 1.64)	1.09 (0.72, 1.66)	0.86 (0.54, 1.36)
High Intake	21.4	19.4	20.0	1.18 (0.78, 1.78)	1.19 (0.78. 1.79)	0.88 (0.55, 1.42)
Trend				χ^2=0.8 df=1 p =0.37	χ^2=0.8 df=1 p =0.36	χ^2=0.1 df=1 p =0.71
LR				χ^2=3.0 df=4 p = 0.55	χ^2 =3.0 df=4 p = 0.57	χ^2 =2.9 df=4 p = 0.57
Fruits						
Low Intake†	21.4	19.0	19.7	1.00	1.00	1.00
Low-Med Intake	19.4	20.7	20.3	0.78 (0.52, 1.18)	0.78 (0.52, 1.18)	0.75 (0.49, 1.14)
Medium Intake	18.0	20.8	19.9	0.83 (0.54, 1.26)	0.83 (0.54, 1.27)	0.78 (0.51, 1.19)
Med-High Intake	23.0	18.6	20.0	1.16 (0.77, 1.74)	1.15 (0.76, 1.73)	1.01 (0.66, 1.54)
High Intake	18.3	21.0	20.1	0.79 (0.52, 1.19)	0.79 (0.51, 1.20)	0.65 (0.42, 1.02)
Trend				χ^2=0.1 df=1 p =0.72	χ^2=0.1 df=1 p =0.74	χ^2=1.5 df=1 p =0.23
LR				χ^2=5.4 df=4 p = 0.25	χ^2 = 5.2 df=4 p = 0.26	χ^2 = 6.2 df=4 p = 0.19

Variable	Case n = 354	Control n = 744	Total n= 1100	Model 1*	Model 2**	Model 3 ***
	%	%	%	Odds Ratio (95% CI)	Odds Ratio (95% CI)	Odds Ratio (95% CI)
Vegetables						
Low Intake†	18.8	19.9	19.6	1.00	1.00	1.00
Low-Med Intake	21.9	20.0	20.6	1.19 (0.79, 1.80)	1.18 (0.78, 1.78)	1.15 (0.75, 1.74)
Medium Intake	20.8	19.4	19.8	1.15 (0.76, 1.74)	1.13 (0.74, 1.72)	1.00 (0.65, 1.54)
Med-High Intake	19.4	20.3	20.0	1.08 (0.70, 1.64)	1.07 (0.70. 1.63)	0.90 (0.58, 1.41)
High Intake	19.1	20.4	20.0	1.19 (0.78, 1.83)	1.19 (0.78, 1.83)	0.97 (0.61, 1.54)
Trend				χ^2=0.3 df=1 p=0.61	χ^2=0.3 df=1 p=0.59	χ^2=0.2 df=1 p=0.64
LR				χ^2= 1.0 df=4 p = 0.91	χ^2 = 0.9 df=4 p = 0.92	χ^2 = 1.3 df=4 p = 0.87
Nuts						
Low Intake†	36.2	38.8	38.0	1.00	1.00	1.00
Medium Intake	39.0	36.6	37.4	1.16 (0.86, 1.57)	1.16 (0.86, 1.57)	1.11 (0.82, 1.51)
High Intake	24.7	24.6	24.6	1.05 (0.75, 1.48)	1.06 (0.75, 1.49)	0.97 (0.68, 1.38)
Trend				χ^2=0.1 df=1 p=0.71	χ^2=0.2 df=1 p=0.67	χ^2=0.0 df=1 p=0.91
LR				χ^2= 1.0 df=2 p = 0.61	χ^2 = 1.0 df=2 p = 0.62	χ^2 = 0.7 df=2 p = 0.70
Alcohol						
Low Intake†	20.5	19.4	19.7	1.00	1.00	1.00
Low-Med Intake	19.1	20.2	19.8	0.92 (0.61, 1.39)	0.94 (0.62, 1.43)	0.91 (0.60, 1.39)
Medium Intake	20.8	19.8	20.1	1.06 (0.70, 1.60)	1.07 (0.70, 1.61)	1.03 (0.68, 1.56)
Med-High Intake	19.9	19.8	19.8	1.03 (0.68, 1.56)	1.04 (0.69, 1.58)	0.98 (0.64, 1.49)
High Intake	19.7	21.0	20.6	1.02 (0.68, 1.55)	1.05 (0.69, 1.60)	0.94 (0.61, 1.45)
Trend				χ^2=0.1 df=1 p=0.78	χ^2=0.1 df=1 p=0.71	χ^2=0.0 df=1 p=0.89
LR				χ^2= 0.5 df=4 p = 0.97	χ^2 = 0.4 df=4 p = 0.98	χ^2 = 0.4 df=4 p = 0.98
Non-Alcoholic Beverages						
Low Intake†	18.8	20.6	20.0	1.00	1.00	1.00
Low-Med Intake	21.4	19.6	20.2	1.13 (0.75, 1.71)	1.12 (0.74, 1.69)	1.06 (0.70, 1.62)
Medium Intake	20.2	19.8	19.9	1.06 (0.70, 1.61)	1.06 (0.69, 1.61)	0.98 (0.64, 1.49)
Med-High Intake	18.8	20.3	19.8	0.99 (0.64, 1.51)	0.98 (0.63, 1.51)	0.88 (0.57, 1.37)
High Intake	20.8	19.8	20.1	1.19 (0.78, 1.80)	1.22 (0.80, 1.88)	1.06 (0.68, 1.67)
Trend				χ^2=0.3 df=1 p=0.60	χ^2=0.4 df=1 p=0.52	χ^2=0.0 df=1 p=0.97
LR				χ^2= 1.1 df=4 p = 0.90	χ^2 = 1.4 df=4 p = 0.84	χ^2 = 1.0 df=4 p = 0.91
Fish						
Low Intake†	20.5	18.6	19.2	1.00	1.00	1.00
Low-Med Intake	33.4	30.5	31.5	0.99 (0.68, 1.44)	1.00 (0.69, 1.47)	0.97 (0.66, 1.41)
Med-High Intake	26.7	28.8	28.1	0.84 (0.57, 1.25)	0.85 (0.57, 1.26)	0.80 (0.54, 1.19)
High Intake	19.4	22.2	21.3	0.87 (0.57, 1.33)	0.88 (0.57, 1.35)	0.79 (0.51, 1.22)
Trend				χ^2=0.5 df=1 p=0.49	χ^2=0.5 df=1 p=0.50	χ^2=1.3 df=1 p=0.25
LR				χ^2 = 1.2 df=3 p = 0.75	χ^2 = 1.3 df=3 p = 0.74	χ^2 = 2.3 df=3 p = 0.52
Legumes						
Low Intake†	50.0	49.6	49.7	1.00	1.00	1.00
Medium Intake	32.3	30.7	31.2	1.19 (0.88, 1.61)	1.18 (0.87, 1.60)	1.14 (0.84, 1.55)
High Intake	17.7	19.8	19.1	1.01 (0.70, 1.45)	1.00 (0.69, 1.44)	0.96 (0.66, 1.38)
Trend				χ^2=0.1 df=1 p=0.74	χ^2=0.1 df=1 p=0.76	χ^2=0.0 df=1 p=0.97
LR				χ^2 = 1.4 df=2 p = 0.49	χ^2 = 1.3 df=2 p = 0.52	χ^2 = 1.0 df=2 p = 0.61
Peanut Butter						
Low Intake†	28.4	29.6	29.2	1.00	1.00	1.00
Low-Med Intake	22.8	22.7	22.7	1.07 (0.74, 1.55)	1.07 (0.74, 1.56)	1.04 (0.71, 1.51)
Med-High Intake	17.4	18.7	18.3	0.91 (0.61, 1.35)	0.91 (0.61, 1.35)	0.87 (0.58, 1.30)
High Intake	31.5	29.0	29.8	1.10 (0.79, 1.55)	1.11 (0.79, 1.57)	1.02 (0.72, 1.44)
Trend				χ^2=0.3 df=1 p=0.57	χ^2=0.4 df=1 p=0.54	χ^2=0.2 df=1 p=0.90
LR				χ^2 = 1.1 df=3 p = 0.78	χ^2 = 1.2 df=3 p = 0.76	χ^2 = 0.8 df=3 p = 0.84
Baked Products						
Low Intake†	20.8	22.3	21.8	1.00	1.00	1.00
Low-Med Intake	14.9	20.2	18.5	0.80 (0.52, 1.23)	0.79 (0.51, 1.22)	0.78 (0.50, 1.21)
Medium Intake	20.2	19.9	20.0	0.97 (0.65, 1.46)	0.96 (0.64, 1.44)	0.91 (0.60, 1.38)
Med-High Intake	19.7	19.8	19.7	1.08 (0.71, 1.63)	1.08 (0.71, 1.63)	1.01 (0.66, 1.54)
High Intake	24.4	17.9	20.0	1.51 (1.01. 2.25)	1.47 (1.00, 2.24)	1.34 (0.86, 2.08)
Trend				χ^2=8.0 df=1 p=0.005	χ^2=8.0 df=1 p=0.005	χ^2=4.2 df=1 p=0.04
LR				χ^2 = 9.4 df=4 p = 0.05	χ^2 = 9.5 df=4 p = 0.05	χ^2 = 5.9 df=4 p = 0.21

Variable	Case n = 354	Control n = 744	Total n= 1100	Model 1*	Model 2**	Model 3 ***
	%	%	%	Odds Ratio (95% CI)	Odds Ratio (95% CI)	Odds Ratio (95% CI)
Sweets						
Low Intake†	18.0	25.5	23.1	1.00	1.00	1.00
Low-Med Intake	18.6	17.9	18.1	1.34 (0.88, 2.05)	1.38 (0.90, 2.12)	1.35 (0.88, 2.08)
Medium Intake	21.4	20.3	20.6	1.49 (0.99, 2.25)	1.49 (0.99, 2.25)	1.46 (0.96, 2.20)
Med-High Intake	25.3	20.2	21.8	1.68 (1.13, 2.51)	1.70 (1.13, 2.54)	1.57 (1.05, 2.37)
High Intake	16.9	16.1	16.4	1.45 (0.94. 2.25)	1.47 (0.95. 2.29)	1.29 (0.81. 2.06)
Trend				χ^2=2.1 df=1 p=0.15	χ^2=2.2 df=1 p=0.14	χ^2=0.6 df=1 p=0.44
LR				χ^2 = 7.0 df=4 p = 0.14	χ^2 = 7.1 df=4 p = 0.13	χ^2 = 5.4 df=4 p = 0.25
Snacks						
Low Intake†	17.1	24.3	22.0	1.00	1.00	1.00
Low-Med Intake	22.2	19.5	20.4	1.46 (0.97, 2.22)	1.46 (0.96, 2.21)	1.43 (0.94, 2.17)
Medium Intake	25.0	21.4	22.6	1.53 (1.02, 2.29)	1.51 (1.01, 2.27)	1.42 (0.94, 2.15)
Med-High Intake	15.7	15.6	15.6	1.22 (0.78, 1.91)	1.24 (0.79, 1.95)	1.16 (0.74, 1.84)
High Intake	19.9	19.2	19.5	1.32 (0.86. 2.02)	1.33 (0.86. 2.05)	1.16 (0.74. 1.81)
Trend				χ^2=0.5 df=1 p=0.50	χ^2=0.5 df=1 p=0.47	χ^2=0.0 df=1 p=0.97
LR				χ^2 = 5.1 df=4 p = 0.28	χ^2 = 4.8 df=4 p = 0.31	χ^2 = 4.1 df=4 p = 0.39

† reference group

* includes age group and province as covariates

**includes smoking, age group, BMI, province as covariates

***includes smoking, age group, BMI, province, energy intake as covariates

6.3. Disaggregated Dairy Products analysis – Seminomas

The dairy food group consists of seven food items. Further analyses were conducted to determine if the risk seen with dairy intake was related to any particular component foods within the seminoma histological subtype. The analysis proceeded by first considering large sub-groups (eg. Milk) and then specific food items (eg. 2% milk).

6.3.1. Milk

The findings of the disaggregated food group analysis for seminomas are presented in Table 14. Within this subgroup, total milk intake does not produce any significant result. As well, significant results do not occur when total milk intake is further disaggregated into specific types of milk (whole, 2%, 1%, and skim). The continuous disaggregated analysis (Table 14) does not produce any significant results for either total milk intake or its component subtypes.

6.3.2. Cheese

The risk associated with cheese was particularly strong in the total sample, but is moderately attenuated in the seminoma subgroup. The test for trend for cheese intake was non-significant (χ^2 =3.2 df =1 p =0.07) although the p-value did approach the nominal significance level. The point estimates of the OR's for each exposure level were all above 1.0 with a significant result for medium high intake (OR = 1.68 CI 1.03, 2.75).

Table 14. Risk of Testicular Cancer - Categorical Food Group Disaggregation Analysis (Seminomas Only)						
Variable	Case n = 356	Control n = 744	Total n =1100	Model 1*	Model 2**	Model 3 ***
	%	%	%	Odds Ratio (95% CI)	Odds Ratio (95% CI)	Odds Ratio (95% CI)
Milk						
Low Intake†	17.7	23.5	21.6	1.00	1.00	1.00
Low-Med Intake	21.1	20.4	20.6	1.37 (0.91, 2.07)	1.37 (0.90, 2.08)	1.36 (0.89, 2.06)
Medium Intake	23.6	22.5	22.8	1.33 (0.89, 1.99)	1.33 (0.89, 1.99)	1.26 (0.83, 1.89)
Med-High Intake	25.8	23.0	23.9	1.46 (0.98, 2.17)	1.46 (0.98, 2.18)	1.34 (0.89, 2.02)
High Intake	11.8	10.6	11.0	1.56 (0.95, 2.56)	1.54 (0.94, 2.54)	1.35 (0.80, 2.27)
Trend				χ^2=2.6 df=1 p=0.11	χ^2=2.5 df=1 p=0.11	χ^2=0.8 df=1 p=0.36
LR				χ^2= 4.6 df=4 p = 0.33	χ^2= 4.5 df=4 p = 0.34	χ^2= 2.7 df=4 p= 0.60
Whole Milk						
Low Intake†	77.3	77.8	77.6	1.00	1.00	1.00
High Intake	22.8	22.2	22.4	0.99 (0.72, 1.36)	0.99 (0.72, 1.37)	0.94 (0.68, 1.31)
Trend				χ^2=0.0 df=1 p=0.96	χ^2=0.0 df=1 p=0.96	χ^2=0.1 df=1 p=0.73
LR				χ^2 = 0.0 df=1 p = 0.96	χ^2 = 0.0 df=1 p = 0.96	χ^2 = 0.1 df=1 p = 0.73
Two % Milk						
Low Intake†	34.0	40.3	38.3	1.00	1.00	1.00
Low-Med Intake	22.8	22.6	22.6	1.19 (0.84, 1.70)	1.20 (0.84, 1.71)	1.24 (0.87, 1.77)
Med-High Intake	26.1	21.1	22.7	1.44 (1.02, 2.03)	1.46 (1.03, 2.06)	1.43 (1.01, 2.03)
High Intake	17.1	16.0	16.4	1.25 (0.85, 1.85)	1.26 (0.85, 1.86)	1.18 (0.79, 1.76)
Trend				χ^2=1.5 df=1 p=0.23	χ^2=1.5 df=1 p=0.23	χ^2=0.7 df=1 p=0.41
LR				χ^2 = 4.4 df=3 p = 0.22	χ^2 = 4.6 df=3 p = 0.20	χ^2 = 3.8 df=3 p = 0.29
One % Milk						
Low Intake†	76.4	77.7	77.3	1.00	1.00	1.00
High Intake	23.6	22.3	22.7	1.06 (0.77, 1.45)	1.05 (0.76, 1.44)	1.03 (0.75, 1.42)
Trend				χ^2=0.1 df=1 p=0.74	χ^2=0.1 df=1 p=0.79	χ^2=0.0 df=1 p=0.88
LR				χ^2 = 0.1 df=1 p = 0.74	χ^2 = 0.1 df=1 p = 0.79	χ^2 = 0.0 df=1 p = 0.88
Skim Milk						
Low Intake†	86.2	87.9	87.4	1.00	1.00	1.00
High Intake	13.8	12.1	12.6	1.24 (0.84, 1.83)	1.25 (0.84, 1.85)	1.23 (0.83, 1.82)
Trend				χ^2=1.2 df=1 p=0.28	χ^2=1.2 df=1 p=0.27	χ^2=1.0 df=1 p=0.31
LR				χ^2 = 1.2 df=1 p = 0.28	χ^2 = 1.2 df=1 p = 0.27	χ^2 = 1.0 df=1 p = 0.31
Eggs						
Low Intake†	22.2	24.1	23.5	1.00	1.00	1.00
Low-Med Intake	23.0	24.1	23.7	0.99 (0.67, 1.45)	1.00 (0.68, 1.47)	0.99 (0.67, 1.46)
Med-High Intake	37.1	37.0	37.0	1.05 (0.74, 1.49)	1.06 (0.74, 1.50)	0.98 (0.69, 1.41)
High Intake	17.7	14.9	15.8	1.21 (0.79, 1.84)	1.24 (0.81, 1.90)	1.10 (0.71, 1.72)
Trend				χ^2=0.9 df=1 p=0.34	χ^2=1.1 df=1 p=0.29	χ^2=0.2 df=1 p=0.69
LR				χ^2= 1.0 df=3 p = 0.79	χ^2 = 1.2 df=3 p = 0.75	χ^2 = 0.4 df=3 p = 0.95
Butter						
Low Intake†	37.4	37.9	37.7	1.00	1.00	1.00
Low-Med Intake	13.8	12.1	12.6	1.23 (0.80, 1.87)	1.22 (0.80, 1.87)	1.21 (0.79, 1.85)
Med-High Intake	22.8	24.3	23.8	0.90 (0.64, 1.27)	0.90 (0.64, 1.27)	0.93 (0.66, 1.32)
High Intake	26.1	25.7	25.8	1.06 (0.76, 1.48)	1.06 (0.75, 1.48)	1.02 (0.73, 1.44)
Trend				χ^2=0.0 df=1 p=1.00	χ^2=0.0 df=1 p=1.00	χ^2=0.0 df=1 p=0.87
LR				χ^2= 1.9 df= 3 p = 0.59	χ^2=1.9 df = 3 p = 0.60	χ^2=1.2 df = 3 p = 0.74
Cheese						
Low Intake†	13.8	20.2	18.1	1.00	1.00	1.00
Low-Med Intake	15.5	17.9	17.1	1.20 (0.75, 1.91)	1.20 (0.75, 1.91)	1.19 (0.74, 1.90)
Medium Intake	39.6	36.6	37.6	1.51 (1.02, 2.25)	1.53 (1.03, 2.28)	1.47 (0.98, 2.19)
Med-High Intake	16.0	12.2	13.5	1.79 (1.11, 2.89)	1.84 (1.14, 2.97)	1.68 (1.03, 2.75)
High Intake	15.2	13.2	13.8	1.63 (1.01, 2.63)	1.63 (1.00, 2.64)	1.43 (0.87, 2.37)
Trend				χ^2=6.0 df=1 p=0.01	χ^2=6.2 df=1 p=0.01	χ^2=3.2 df=1 p=0.07
LR				χ^2= 7.9 df=4 p = 0.10	χ^2 = 8.4 df=4 p = 0.08	χ^2 = 5.6 df=4 p = 0.23
Whole Milk and Cheese						
Low Intake†	23.6	30.8		1.00	1.00	1.00
Low-Med Intake	33.2	31.2	28.5	1.40 (1.00, 1.98)	1.36 (0.96, 1.93)	1.30 (0.92, 1.86)
Med-High Intake	17.1	13.7	31.8	1.58 (1.04, 2.40)	1.58 (1.04, 2.41)	1.47 (0.96, 2.25)
High Intake	26.1	24.3	14.8	1.47 (1.03, 2.12)	1.41 (0.98, 2.04)	1.24 (0.84, 1.83)
Trend			24.9	χ^2=3.5 df=1 p=0.06	χ^2=3.6 df=1 p=0.06	χ^2=1.3 df=1 p=0.27
LR				χ^2 = 6.6 df=3 p = 0.09	χ^2 = 5.8 df=3 p = 0.12	χ^2 = 3.6 df=3 p = 0.31

† reference group * includes age group and province as covariates

**includes smoking, age group, BMI, province as covariates

***includes smoking, age group, BMI, province, energy intake as covariates

Table 15. Risk of Testicular Cancer - Continuous Food Group Disaggregation Analysis (Seminomas Only)*	
Food/Nutrient*	Odds Ratio (95% CI)
Total Milk	1.05 (0.96, 1.15)
Whole Milk	0.93 (0.75, 1.15)
2% Milk	1.01 (0.90, 1.14)
1% Milk	1.07 (0.90, 1.28)
Skim Milk	1.23 (0.99, 1.54)

*Model includes: food, age, province, BMI, Smoking and energy intake
** per 1 serving/week

6.4. Nutrient Analysis – Seminomas

6.4.1. Overview of Nutrient Analysis

The nutrient analysis failed to produce many significant results. Both calcium and zinc obtained statistical significance in one of the tests; however, neither had a significant trend test. The results for all of the nutrients analyzed can be found in Table 16. As well, the continuous disaggregation analysis of fat did not yield any significant results, and is shown in Table 17.

6.4.2. Fats

None of the statistical tests performed on fat intake, or specific types of fat, were significant. The results for the categorical analysis of fat intake are show in Table 16, while the continuous analysis is shown in Table 17.

6.4.3. Calcium

Calcium intake is significantly associated with an increased risk of testicular cancer with the seminoma subgroup at one intake level (medium-high intake; OR = 1.67; CI 1.04, 2.67). However, the trend test was not significant ($\chi^2 = 1.1$ df = 1 p = 0.30).

6.4.4. Zinc

The likelihood ratio test for heterogeneity was significant ($\chi^2 = 10.6$ df = 4 p = 0.03) for zinc intake, suggesting that the ORs across the five intake strata are different. However, none of the individual Wald tests reached significance.

Table 16. Risk of Testicular Cancer associated with Nutrient Intake (Seminomas Only)

Nutrient	Case n = 356	Control n = 744	Total n =1100	Model A*	Model B**
	%	%	%	Odds Ratio (95% CI)	Odds Ratio (95% CI)
Fat					
Low Intake†	17.1	21.4	20.0	1.00	1.00
Low-Medium Intake	21.1	19.5	20.0	1.10 (0.69, 1.75)	1.10 (0.69, 1.75)
Medium Intake	18.5	20.7	20.0	0.78 (0.46, 1.33)	0.77 (0.45, 1.32)
Medium High Intake	19.4	20.3	20.0	0.77 (0.43, 1.38)	0.76 (0.42, 1.36)
High Intake	23.9	18.2	20.0	1.25 (0.64, 2.48)	1.24 (0.62, 2.45)
Trend				χ^2 = 0.4 df = 1 p = 0.53	χ^2 = 0.4 df = 1 p = 0.56
LR				χ^2 = 6.1 df = 4 p = 0.19	χ^2 = 6.2 df = 4 p = 0.18
Saturated Fat					
Low Intake†	16.9	21.5	20.0	1.00	1.00
Low-Medium Intake	20.2	19.9	20.0	1.15 (0.74, 1.78)	1.16 (0.75, 1.80)
Medium Intake	18.8	20.6	20.0	0.88 (0.53, 1.44)	0.88 (0.53, 1.45)
Medium High Intake	21.9	19.1	20.0	1.11 (0.66, 1.86)	1.10 (0.65, 1.85)
High Intake	22.2	19.0	20.0	1.08 (0.59, 1.99)	1.08 (0.58, 1.99)
Trend				χ^2 = 0.1 df = 1 p = 0.77	χ^2 = 0.1 df = 1 p = 0.79
LR				χ^2 = 2.0 df = 4 p = 0.74	χ^2 = 1.9 df = 4 p = 0.75
Mono-Unsaturated Fat					
Low Intake†			20.0	1.00	1.00
Low-Medium Intake	18.5	20.7	20.0	0.90 (0.57, 1.40)	0.90 (0.57, 1.41)
Medium Intake	19.7	20.2	20.0	0.66 (0.39, 1.10)	0.66 (0.39, 1.10)
Medium-High Intake	17.7	21.1	20.0	0.82 (0.48, 1.40)	0.81 (0.47, 1.39)
High Intake	21.4	19.4	20.0	0.97 (0.52, 1.80)	0.96 (0.51, 1.80)
Trend	22.8	18.7		χ^2 = 0.0 df = 1 p = 0.92	χ^2 = 0.0 df = 1 p = 0.93
LR				χ^2 = 3.7 df = 4 p = 0.44	χ^2 = 3.7 df = 4 p = 0.45
Poly-Unsaturated Fat					
Low Intake†				1.00	1.00
Low-Medium Intake	17.4	21.2	20.0	0.98 (0.62, 1.56)	0.98 (0.62, 1.56)
Medium Intake	20.2	19.9	20.0	0.83 (0.49, 1.42)	0.84 (0.49, 1.43)
Medium High Intake	19.9	20.0	20.0	0.76 (0.43, 1.35)	0.76 (0.43, 1.36)
High Intake	19.4	20.3	20.0	1.10 (0.59, 2.07)	1.11 (0.59, 2.09)
Trend	23.0	18.6	20.0	χ^2 = 0.1 df = 1 p = 0.72	χ^2 = 0.2 df = 1 p = 0.70
LR				χ^2 = 3.2 df = 4 p = 0.52	χ^2 = 3.3 df = 4 p = 0.51
Protein					
Low Intake†	18.5	20.7	20.0	1.00	1.00
Low-Medium Intake	18.5	20.7	20.0	0.76 (0.47, 1.23)	0.76 (0.47, 1.24)
Medium Intake	18.8	20.6	20.0	0.65 (0.37, 1.14)	0.65 (0.37, 1.15)
Medium High Intake	21.4	19.4	20.0	0.76 (0.41, 1.39)	0.74 (0.40, 1.38)
High Intake	22.8	18.7	20.0	0.97 (0.48, 1.98)	0.98 (0.48, 1.99)
Trend				χ^2 = 0.2 df = 1 p = 0.69	χ^2 = 0.2 df = 1 p = 0.70
LR				χ^2 = 4.0 df = 4 p =0.40	χ^2 = 4.0 df = 4 p = 0.40
Carbohydrates					
Low Intake†	18.0	21.0	20.0	1.00	1.00
Low-Medium Intake	18.8	20.6	20.0	0.90 (0.54, 1.51)	0.91 (0.54, 1.52)
Medium Intake	21.4	19.4	20.0	0.93 (0.50, 1.71)	0.91 (0.49, 1.68)
Medium High Intake	21.6	19.2	20.0	0.80 (0.40, 1.58)	0.78 (0.40, 1.56)
High Intake	20.2	19.9	20.0	0.65 (0.30, 1.40)	0.64 (0.29, 1.40)
Trend				χ^2 = 1.4 df = 1 p = 0.22	χ^2 = 1.5 df = 1 p =0.22
LR				χ^2 = 1.7 df = 4 p = 0.79	χ^2 = 1.6 df = 4 p = 0.80
Dietary Fibre					
Low Intake†	18.5	20.7	20.0	1.00	1.00
Low-Medium Intake	19.9	20.0	20.0	1.02 (0.66, 1.57)	1.03 (0.66, 1.59)
Medium Intake	18.8	20.6	20.0	0.94 (0.59, 1.49)	0.94 (0.59, 1.50)
Medium High Intake	22.5	18.8	20.0	1.19 (0.74, 1.91)	1.19 (0.74, 1.92)
High Intake	20.2	19.9	20.0	1.00 (0.61, 1.66)	1.00 (0.60, 1.68)
Trend				χ^2 = 0.0 df = 1 p = 0.84	χ^2 = 0.0 df = 1 p = 0.87
LR				χ^2 = 1.4 df = 4 p = 0.85	χ^2 = 1.4 df = 4 p = 0.85

Nutrient	Case n = 356	Control n = 744	Total n =1100	Model A*	Model B**
	%	%	%	Odds Ratio (95% CI)	Odds Ratio (95% CI)
Sugar					
Low Intake†	16.6	21.6	20.0	1.00	1.00
Low-Medium Intake	18.8	20.6	20.0	1.12 (0.73, 1.73)	1.13 (0.73, 1.75)
Medium Intake	21.9	19.1	20.0	1.34 (0.85, 2.10)	1.35 (0.85, 2.12)
Medium High Intake	21.4	19.4	20.0	1.23 (0.77, 1.97)	1.24 (0.77, 2.00)
High Intake	21.4	19.4	20.0	1.17 (0.70, 1.96)	1.19 (0.71, 1.98)
Trend				χ^2 = 0.2 df = 1 p = 0.68	χ^2 =0.2 df = 1 p = 0.66
LR				χ^2 = 1.7 df = 4 p = 0.79	χ^2 = 1.7 df = 4 p = 0.78
Iron					
Low Intake†	19.7	20.2	20.0	1.00	1.00
Low-Medium Intake	17.1	21.4	20.0	0.62 (0.38, 1.01)	0.63 (0.39, 1.03)
Medium Intake	18.3	20.8	20.0	0.63 (0.37, 1.09)	0.64 (0.37, 1.11)
Medium High Intake	24.4	17.9	20.0	0.98 (0.54, 1.77)	0.98 (0.54, 1.78)
High Intake	20.5	19.8	20.0	0.75 (0.38, 1.49)	0.75 (0.38, 1.50)
Trend				χ^2 = 0.0 df = 1 p = 0.94	χ^2 = 0.0 df = 1 p = 0.91
LR				χ^2 = 8.1 df = 4 p = 0.09	χ^2 = 7.5 df = 4 p = 0.11
Calcium					
Low Intake†	15.2	22.3	20.0	1.00	1.00
Low-Medium Intake	19.9	20.0	20.0	1.35 (0.86, 2.11)	1.36 (0.87, 2.13)
Medium Intake	19.9	20.0	20.0	1.27 (0.78, 2.05)	1.28 (0.79, 2.08)
Medium High Intake	24.7	17.7	20.0	1.68 (1.05, 2.68)	1.67 (1.04, 2.67)
High Intake	20.2	19.9	20.0	1.32 (0.78, 2.26)	1.33 (0.78, 2.28)
Trend				χ^2 = 1.1 df = 1 p = 0.29	χ^2 = 1.1 df = 1 p = 0.30
LR				χ^2 = 5.2 df = 4 p = 0.27	χ^2 = 5.0 df = 4 p = 0.29
Zinc					
Low Intake†	19.4	20.3	20.0	1.00	1.00
Low-Medium Intake	18.0	21.0	20.0	0.67 (0.41, 1.09)	0.67 (0.41, 1.10)
Medium Intake	17.1	21.4	20.0	0.49 (0.28, 0.88)	0.49 (0.27, 0.87)
Medium High Intake	21.6	19.2	20.0	0.68 (0.36, 1.27)	0.66 (0.35, 1.25)
High Intake	23.9	18.2	20.0	0.98 (0.47, 2.05)	0.98 (0.47, 2.07)
Trend				χ^2 = 0.4 df = 1 p = 0.51	χ^2 = 0.4 df = 1 p = 0.51
LR				χ^2 = 10.2 df = 4 p = 0.04	χ^2 = 10.6 df = 4 p = 0.03
Phosphorous					
Low Intake†	17.7	21.1	20.0	1.00	1.00
Low-Medium Intake	17.7	21.1	20.0	0.85 (0.53, 1.37)	0.86 (0.53, 1.39)
Medium Intake	21.6	19.2	20.0	1.09 (0.64, 1.85)	1.10 (0.65, 1.86)
Medium High Intake	23.3	18.4	20.0	1.06 (0.60, 1.90)	1.05 (0.59, 1.87)
High Intake	19.7	20.2	20.0	0.84 (0.44, 1.59)	0.83 (0.44, 1.59)
Trend				χ^2 = 0.2 df = 1 p = 0.63	χ^2 = 0.3 df = 1 p = 0.60
LR				χ^2 = 2.6 df = 4 p = 0.63	χ^2 = 2.4 df = 4 p = 0.67
Sodium					
Low Intake†	18.0	21.0	20.0	1.00	1.00
Low-Medium Intake	19.4	20.3	20.0	0.94 (0.58, 1.52)	0.94 (0.58, 1.53)
Medium Intake	20.2	19.9	20.0	0.88 (0.51, 1.54)	0.89 (0.51, 1.55)
Medium High Intake	19.9	20.0	20.0	0.86 (0.46, 1.59)	0.85 (0.46, 1.59)
High Intake	22.5	18.8	20.0	1.18 (0.58, 2.43)	1.18 (0.57, 2.44)
Trend				χ^2 = 0.4 df = 1 p = 0.53	χ^2 = 0.4 df = 1 p = 0.55
LR				χ^2 = 1.9 df = 4 p = 0.75	χ^2 = 1.9 df = 4 p = 0.76
Cholesterol					
Low Intake†	18.0	21.0	20.0	1.00	1.00
Low-Medium Intake	18.5	20.7	20.0	0.94 (0.61, 1.45)	0.94 (0.60, 1.46)
Medium Intake	21.4	19.4	20.0	1.03 (0.66, 1.61)	1.04 (0.66, 1.64)
Medium High Intake	18.0	21.0	20.0	0.76 (0.46, 1.24)	0.76 (0.46, 1.24)
High Intake	24.2	18.0	20.0	1.24 (0.74, 2.06)	1.26 (0.75, 2.11)
Trend				χ^2 = 0.8 df = 1 p = 0.37	χ^2 = 0.9 df = 1 p = 0.34
LR				χ^2 = 5.4 df = 4 p = 0.25	χ^2 = 5.8 df = 4 p = 0.21

† reference group

* includes age group, province, and energy intake as covariates

**includes smoking, age group, BMI, province, energy intake as covariates

Table 17. Risk of Testicular Cancer - Continuous Nutrient disaggregation Analysis (Seminomas Only)*	
Food/Nutrient**	Odds Ratio (95% CI)
Total Fat	1.03 (0.95, 1.10)
Saturated Fat	1.10 (0.93, 1.31)
Mono-Unsaturated Fat	1.03 (0.89, 1.19)
Poly-Unsaturated Fat	0.89 (0.59, 1.36)

*Model includes: food, age, province, BMI, Smoking and energy intake
** per 10 grams/week

6.5. Chapter Summary

The significant results from the seminoma food group and nutrient analysis are presented in table 18. Within this histological subtype, the number of significant results is less than that observed in the total sample. As well, the strength of significant for these results is diminished as compared with the total sample. Only two of the food groups (dairy products and baked products) exhibited a statistically significant result, and only baked products had a statistically significant trend test. None of the 14 nutrients examined had a significant result associated with them.

Table 18. Risk of Testicular Cancer associated with food and nutrient intake Summary table within Seminomas (Model 3*)

Food/Nutrient	Low Intake Odds Ratio (CI)	Low-Med Intake Odds Ratio (CI)	Medium Intake Odds Ratio (CI)	Med-High Intake Odds Ratio (CI)	High Intake Odds Ratio (CI)	P-Trend
Dairy	1.00	1.22 (0.77, 1.91)	2.04 (1.31, 3.17)	1.93 (1.23, 3.03)	1.38 (0.84, 2.25)	0.27
Baked Products	1.00	0.78 (0.50, 1.21)	0.91 (0.60, 1.38)	1.01 (0.66, 1.54)	1.34 (0.86, 2.08)	0.04
Cheese	1.00	1.19 (0.74, 1.90)	1.47 (0.98, 2.19)	1.68 (1.03, 2.75)	1.43 (0.87, 2.37)	0.07

*Model includes: food, age, province, BMI, Smoking and energy intake

7. Results III - Non-Seminomas

7.1. Non-Seminomas - Characteristics of Cases and Controls

7.1.1. Analysis of Covariates

The results for the analysis of covariates within the non-seminoma subtype are shown in Table 19. The non-seminoma case group had a mean age of 32.6 years and a median of 32.0 years; 41.6% of the cases were never-smokers. The case distribution among the provinces was similar to that seen in both the total sample and the seminoma subgroup, with the largest percentage of cases being recruited from Ontario (38.1%). Over one quarter (26.0%) of the non-seminoma case group had a BMI over 30.5.

There were no significant results associated with smoking level. Total energy intake showed a significant trend of increasing risk with increasing intake ($\chi^2 = 4.5$ df =1 p= 0.03) (high intake; OR = 2.04). The highest level of risk was reached at medium-high intake (OR = 2.56; CI 1.38, 4.73). The risk is lower at the high intake quintile (OR = 2.04; CI 1.09, 3.82). The overlap in the 95% confidence intervals for these two risk estimates shows that these estimates are not statistically different. This suggests that the apparently lower OR in the highest intake quintile is likely the result of random variation. A novel finding within the covariates and non-seminomas is that a significant increase in risk was found in cases above a BMI of 25.2. The highest risk was present in the highest BMI category (>31.0), as would have been expected for a monotonic dose response relationship. Subjects with BMI > 30.1 had an increase in testicular cancer risk of approximately 3.7 times the reference group (OR = 3.66; CI 1.87, 7.15). As well, there is

a highly significant trend for increasing risk with increasing BMI (χ^2 =9.9 df=1 p= 0.002) and the likelihood ratio test for heterogeneity was significant (χ^2=16.3 df=4 p=0.003).

Table 19. Multivariate analysis for the major covariates of the NECSS dataset (Non-seminomas Only)

Variable	Case n = 162	Control n = 744	Total n = 906	Model 1*	Model 2**	Model 3 ***
	%	%	%	Odds Ratio (95% CI)	Odds Ratio (95% CI)	Odds Ratio (95% CI)
Age Group						
20-24†	14.2	7.5	8.7	Not Applicable	Not Applicable	Not Applicable
25-29	23.5	12.5	14.5			
30-34	27.2	15.7	17.8			
35-39	19.8	17.6	18.0			
40-44	7.4	14.3	13.0			
45-49	4.3	13.7	12.0			
50-54	3.7	18.7	16.0			
Province						
Maritimes†	11.7	18.4	17.2	Not Applicable	Not Applicable	Not Applicable
Ontario	38.3	35.9	36.3			
Man & Sask	16.7	12.1	12.9			
Alberta	14.2	13.8	13.9			
BC	19.1	19.8	19.7			
Smoking (PY)						
0 (non-smoker) †				1.00	1.00	1.00
1-5	44.4	38.3	39.4	0.78 (0.47, 1.29)	0.82 (0.49, 1.35)	0.82 (0.49, 1.38)
5-12	17.3	19.0	18.7	0.94 (0.57, 1.57)	0.94 (0.57, 1.57)	0.92 (0.55, 1.55)
12-24	17.3	1.83	18.1	1.47 (0.85, 2.55)	1.51 (0.86, 2.64)	1.42 (0.80, 2.51)
24 +	16.1	15.3	15.5	1.52 (0.63, 3.66)	1.35 (0.55, 3.31)	1.32 (0.54, 3.25)
Trend	4.9	9.1	8.4	χ^2= 1.4 df =1 p= 0.23	χ^2= 1.5 df =1 p= 0.22	χ^2= 1.0 df =1 p= 0.31
LR				χ^2=4.6 df=4 p = 0.33	χ^2= 3.9 df=4 p = 0.42	χ^2= 3.1 df=4 p = 0.54
BMI						
<23.1	19.1	25.8	24.6	1.00	1.00	1.00
23.1-25.2	22.8	24.5	24.2	1.63 (0.94, 2.82)	1.71 (0.98, 2.96)	1.70 (0.98, 2.96)
25.2-27.8	28.4	25.3	25.8	2.08 (1.23, 3.54)	2.13 (1.25, 3.62)	2.24 (1.31, 3.85)
27.8-31.0	14.2	15.1	14.9	1.86 (1.00, 3.49)	1.88 (1.00, 3.52)	1.94 (1.03, 3.66)
>31.0	15.4	9.4	10.5	3.84 (1.99, 7.42)	3.72 (1.92, 7.22)	3.66 (1.87, 7.15)
Trend				χ^2=15.5 df=1 p<0.001	χ^2=10.3 df=1 p=0.001	χ^2=9.9 df=1 p= 0.002
LR				χ^2=17.1 df=4 p=0.001	χ^2=16.2 df=4 p=0.003	χ^2=16.3 df=4 p=0.003
Energy Intake (kC)						
700.0-1450.7†	12.4	21.6	20.0	1.00	1.00	Not Applicable
1450.7-1778.4	20.4	19.9	20.0	1.87 (1.01, 3.48)	1.88 (1.00, 3.53)	
1778.4-2081.1	19.1	20.3	20.1	1.81 (0.97, 3.39)	1.88 (1.00, 3.55)	
2081.1-2556.9	25.9	18.7	20.0	2.61 (1.42, 4.78)	2.56 (1.38, 4.73)	
2556.9+	2220	19.5	20.0	2.00 (1.09, 3.70)	2.04 (1.09, 3.82)	
Trend				χ^2= 4.5 df =1 p= 0.03	χ^2= 4.5 df =1 p= 0.03	
LR				χ^2= 9.8 df=4 p = 0.04	χ^2=9.2 df=4 p = 0.06	

† reference group

* includes age group and province as covariates

**includes smoking, age group, BMI, province as covariates

***includes smoking, age group, BMI, province, energy intake as covariates

7.2. Non-seminomas – Food group Analysis

7.2.1. Overview of the Food group Analysis

Only three food groups reached statistical significance in the non-seminoma food group analysis. These groups were dairy products, luncheon meats, and baked products. There were large effects observed for the three food groups, larger than those observed in the total or seminoma analysis. The results from all the food groups analyzed, both significant and non-significant can be found in Table 20. The sample size of the non-seminoma subgroup is smaller (n = 162) than that of the seminoma subgroup (n = 356).

The non-significant protective effects that were observed within the meat food group in both the total sample and seminomas were not seen in the non-seminoma subgroup, as the risk was non-significantly increased. Vegetable intake was not significantly related to testicular cancer risk, however the risk at the high intake level was elevated (OR = 1.61; CI 0.88, 2.95). Fruits had a non-significant increase in risk associated with them.

7.2.2. Dairy Products

The association of dairy product intake and testicular cancer risk within the non-seminoma subgroup was stronger than that seen in the total sample or the seminoma subset. The test for trend was non-significant (χ^2 =1.0 df =1 p =0.32). However, the likelihood ratio test of heterogeneity was significant (χ^2=19.0 df=4 p<0.001), indicating that the risk associated with the individual risk estimates for the intake quintiles were different. The largest risk was observed at a medium high intake (OR=3.17, 95% CI 1.65, 6.09). At the highest intake of dairy products the OR was lower at 1.36 (CI 0.67, 2.79). The overlap in the 95% confidence intervals for these two risks estimates shows

that these estimates are not statistically different. This suggests that the apparently lower OR in the highest intake quintile is likely the result of random variation. This was confirmed by an additional logistic regression model which included a quadratic term for dairy product intake; the Wald Chi-square for this term was not significant (p= 0.08).

7.2.3. Luncheon Meats

The test for trend was marginally non-significant (χ^2 =3.3 df =1 p =0.07). However, unlike seminomas, luncheon meats were significantly associated with testicular cancer risk at the highest intake level in the non-seminoma subgroup (OR = 2.11; CI 1.09, 4.08) as is expected for a monotonic dose response relationship.

7.2.4. Baked products

Consistent results were observed within the baked products food group in all three-analysis groups. The test for trend was significant within the non-seminoma subgroup (χ^2 = 6.3 df = 1 p = 0.01). As well, the risk at the highest intake level is significantly increased (OR = 2.09; CI 1.10, 3.99). These consistent results for baked products are suggestive of a real effect of baked products intake on testicular cancer risk.

Table 20. Risk of Testicular Cancer associated with Food Intake (Non-seminomas Only)

Variable	Case n = 162	Control n = 744	Total n = 906	Model 1*	Model 2**	Model 3 ***
	%	%	%	Odds Ratio (95% CI)	Odds Ratio (95% CI)	Odds Ratio (95% CI)
Dairy						
Low Intake†	11.7	21.9	20.1	1.00‡	1.00‡	1.00
Low-Med Intake	17.3	20.2	19.7	1.46 (0.77, 2.79)	1.59 (0.82, 3.07)	1.52 (0.78, 2.95)
Medium Intake	16.7	21.4	20.5	1.26 (0.66, 2.41)	1.40 (0.72, 2.72)	1.21 (0.61, 2.40)
Med-High Intake	35.2	16.3	19.7	3.33 (1.84, 6.03)	3.83 (2.07, 7.06)	3.17 (1.65, 6.09)
High Intake	19.1	20.3	20.1	1.51 (0.80, 2.87)	1.64 (0.85, 3.15)	1.36 (0.67, 2.79)
Trend				χ^2=3.5 df=1 p=0.06	χ^2=4.1 df=1 p=0.04	χ^2=1.0 df=1 p=0.32
LR				χ^2=23.0 df=4 p=0.001	χ^2=25.0 df=4 p<0.001	χ^2=19.0 df=4 p<0.001
Fats						
Low Intake†	21.0	19.9	20.1	1.00	1.00	1.00
Low-Med Intake	12.4	20.6	19.1	0.57 (0.31, 1.05)	0.57 (0.30, 1.07)	0.53 (0.28, 1.01)
Medium Intake	21.0	19.6	19.9	1.00 (0.58, 1.73)	0.99 (0.56, 1.73)	0.90 (0.51, 1.60)
Med-High Intake	23.5	19.2	20.0	1.16 (0.67, 2.01)	1.20 (0.69, 2.11)	0.99 (0.56, 1.60)
High Intake	22.2	20.7	21.0	1.29 (0.74, 2.24)	1.19 (0.67, 2.10)	0.96 (0.52, 1.75)
Trend				χ^2=3.4 df=1 p=0.07	χ^2=2.2 df=1 p=0.50	χ^2=0.5 df=1 p=0.50
LR				χ^2=7.6 df=4 p=0.11	χ^2=6.7 df=4 p=0.15	χ^2=4.9 df=4 p=0.29
Meat						
Low Intake†	14.2	19.9	18.9	1.00	1.00	1.00
Low-Med Intake	21.0	22.5	22.2	1.38 (0.76, 2.50)	1.24 (0.68, 2.28)	1.12 (0.60, 2.07)
Medium Intake	17.3	20.2	19.7	1.14 (0.62, 2.12)	1.07 (0.57, 2.00)	0.88 (0.46, 1.67)
Med-High Intake	19.8	18.8	19.0	1.40 (0.76, 2.55)	1.34 (0.73, 2.47)	1.12 (0.60, 2.10)
High Intake	27.8	18.7	20.3	1.80 (1.01, 3.21)	1.61 (0.89, 2.90)	1.24 (0.66, 2.33)
Trend				χ^2=3.9 df=1 p=0.05	χ^2=2.7 df=1 p=0.10	χ^2=0.6 df=1 p=0.45
LR				χ^2=4.9 df=4 p=0.30	χ^2=3.3 df=4 p=0.50	χ^2=1.6 df=4 p=0.82
Soup						
Low Intake†	11.1	12.8	12.5	1.00	1.00	1.00
Low-Med Intake	35.8	29.3	30.5	1.32 (0.72, 2.41)	1.31 (0.71, 2.42)	1.36 (0.73, 2.53)
Med-High Intake	25.3	31.9	30.7	0.83 (0.44, 1.56)	0.88 (0.46, 1.66)	0.84 (0.44, 1.61)
High Intake	27.8	26.1	26.4	1.34 (0.72, 2.51)	1.37 (0.72, 2.61)	1.26 (0.65, 2.43)
Trend				χ^2=0.7 df=1 p=0.42	χ^2=0.7 df=1 p=0.40	χ^2=0.2 df=1 p=0.68
LR				χ^2=5.2 df=3 p=0.16	χ^2=4.2 df=3 p=0.24	χ^2=4.5 df=3 p=0.21
Luncheon Meats						
Low Intake†	11.1	22.7	20.6	1.00	1.00	1.00
Low-Med Intake	19.1	19.9	19.8	1.96 (1.03, 3.73)	1.86 (0.97, 3.58)	1.88 (0.97, 3.64)
Medium Intake	16.1	18.6	18.1	1.63 (0.84, 3.19)	1.48 (0.75, 2.92)	1.34 (0.67, 2.67)
Med-High Intake	25.3	21.1	21.9	1.89 (1.02, 3.50)	1.78 (0.95, 3.34)	1.50 (0.79, 2.86)
High Intake	28.4	17.7	19.7	2.67 (1.45, 4.93)	2.53 (1.34, 4.76)	2.11 (1.09, 4.08)
Trend				χ^2=8.0 df=1 p=0.005	χ^2=6.9 df=1 p=0.01	χ^2=3.3 df=1 p=0.07
LR				χ^2=10.4 df=4 p=0.04	χ^2=9.2 df=4 p=0.06	χ^2=6.5 df=4 p=0.16
Grains						
Low Intake†	19.1	19.8	19.7	1.00	1.00	1.00
Low-Med Intake	22.2	20.2	20.5	1.10 (0.63, 1.91)	1.16 (0.66, 2.04)	0.97 (0.54, 1.74)
Medium Intake	19.1	20.0	19.9	1.02 (0.58, 1.81)	1.07 (0.60, 1.90)	0.86 (0.47, 1.57)
Med-High Intake	19.8	20.3	20.2	1.02 (0.58, 1.79)	1.06 (0.60, 1.88)	0.75 (0.41, 1.39)
High Intake	19.8	19.8	19.8	1.09 (0.62, 1.93)	1.07 (0.60, 1.91)	0.70 (0.36, 1.36)
Trend				χ^2=0.3 df=1 p=0.86	χ^2=0.0 df=1 p=0.96	χ^2=1.6 df=1 p=0.21
LR				χ^2=0.2 df=4 p=1.00	χ^2=0.3 df=4 p=0.99	χ^2=1.7 df=4 p=0.79
Fruits						
Low Intake†	19.1	20.4	20.2	1.00	1.00	1.00
Low-Med Intake	21.0	19.4	19.7	1.04 (0.59, 1.82)	1.08 (0.61, 1.92)	1.06 (0.59, 1.90)
Medium Intake	17.3	20.8	20.2	0.91 (0.51, 1.64)	1.06 (0.58, 1.94)	1.01 (0.55, 1.85)
Med-High Intake	20.4	20.0	20.1	1.19 (0.67, 2.10)	1.30 (0.73, 2.33)	1.16 (0.64, 2.10)
High Intake	22.2	19.4	19.9	1.24 (0.71, 2.18)	1.37 (0.77, 2.45)	1.14 (0.62, 2.09)
Trend				χ^2=0.9 df=1 p=0.34	χ^2=1.5 df=1 p=0.21	χ^2=0.2 df=1 p=0.63
LR				χ^2=1.5 df=4 p=0.82	χ^2=1.8 df=4 p=0.78	χ^2=0.4 df=4 p=0.98

Variable	Case n = 162	Control n = 744	Total n = 906	Model 1*	Model 2**	Model 3 ***
	%	%	%	Odds Ratio (95% CI)	Odds Ratio (95% CI)	Odds Ratio (95% CI)
Vegetables						
Low Intake†	21.6	19.8	20.1	1.00	1.00	1.00
Low-Med Intake	19.8	20.2	20.1	1.05 (0.61, 1.82)	1.07 (0.61, 1.88)	1.01 (0.57, 1.79)
Medium Intake	18.5	20.4	20.1	1.00 (0.57, 1.74)	1.04 (0.59, 1.84)	0.87 (0.49, 1.57)
Med-High Intake	16.1	20.6	19.8	1.04 (0.58, 1.87)	1.04 (0.58, 1.88)	0.85 (0.46, 1.57)
High Intake	24.1	19.1	20.0	1.84 (1.07, 3.17)	1.90 (1.09, 3.32)	1.61 (0.88, 2.95)
Trend				χ^2=4.8 df=1 p =0.03	χ^2=4.9 df=1 p =0.03	χ^2=2.0 df=1 p =0.15
LR				χ^2= 7.1 df=4 p = 0.13	χ^2 = 7.2 df=4 p = 0.13	χ^2 = 5.7 df=4 p = 0.22
Nuts						
Low Intake†	35.8	38.8	38.3	1.00	1.00	1.00
Medium Intake	34.6	36.6	36.2	0.98 (0.64, 1.49)	0.97 (0.63, 1.50)	0.89 (0.57, 1.37)
High Intake	29.6	24.6	25.5	1.45 (0.93, 2.27)	1.49 (0.94, 2.36)	1.30 (0.81, 2.09)
Trend				χ^2=2.4 df=1 p =0.13	χ^2=2.5 df=1 p =0.12	χ^2=0.9 df=1 p =0.35
LR				χ^2= 3.6 df=2 p = 0.17	χ^2 = 4.0 df=2 p = 0.14	χ^2 = 2.3 df=2 p = 0.32
Alcohol						
Low Intake†	18.5	19.4	19.2	1.00	1.00	1.00
Low-Med Intake	18.5	21.2	20.8	0.78 (0.44, 1.40)	0.78 (0.43, 1.41)	0.78 (0.43, 1.41)
Medium Intake	21.6	18.7	19.2	1.13 (0.64, 1.98)	1.07 (0.60, 1.93)	1.01 (0.56, 1.82)
Med-High Intake	24.1	19.8	20.5	1.20 (0.69, 2.08)	1.30 (0.73, 2.31)	1.18 (0.66, 2.12)
High Intake	17.3	21.0	20.3	0.94 (0.53, 1.70)	0.96 (0.52, 1.77)	0.84 (0.45, 1.57)
Trend				χ^2=0.0 df=1 p =0.85	χ^2=0.1 df=1 p =0.79	χ^2=0.1 df=1 p =0.81
LR				χ^2= 2.8 df=4 p = 0.60	χ^2 = 3.4 df=4 p = 0.50	χ^2 = 2.6 df=4 p = 0.63
Non-Alcoholic Beverages						
Low Intake†	19.1	20.3	20.1	1.00	1.00	1.00
Low-Med Intake	22.2	19.4	19.9	1.38 (0.80, 2.41)	1.35 (0.76, 2.39)	1.24 (0.70, 2.22)
Medium Intake	17.3	20.6	20.0	1.07 (0.60, 1.91)	0.98 (0.54, 1.77)	0.87 (0.47, 1.58)
Med-High Intake	21.0	20.0	20.2	1.47 (0.84, 2.58)	1.31 (0.73, 2.34)	1.13 (0.62, 2.06)
High Intake	20.4	19.8	19.9	1.39 (0.79, 2.44)	1.28 (0.70, 2.31)	1.03 (0.55, 1.94)
Trend				χ^2=1.2 df=1 p =0.27	χ^2=0.5 df=1 p =0.50	χ^2=0.0 df=1 p =0.98
LR				χ^2= 2.9 df=4 p = 0.58	χ^2 = 2.1 df=4 p = 0.72	χ^2 = 1.7 df=4 p = 0.80
Fish						
Low Intake†	21.6	18.6	19.1	1.00	1.00	1.00
Low-Med Intake	28.4	30.5	30.1	1.00 (0.60, 1.67)	0.99 (0.59, 1.68)	0.96 (0.57, 1.62)
Med-High Intake	29.6	28.8	28.9	1.14 (0.68, 1.90)	1.11 (0.66, 1.87)	1.03 (0.60, 1.74)
High Intake	20.4	22.2	21.9	1.11 (0.64, 1.94)	1.17 (0.67, 2.07)	1.01 (0.56, 1.81)
Trend				χ^2=0.2 df=1 p =0.69	χ^2=0.4 df=1 p =0.52	χ^2=0.1 df=1 p =0.92
LR				χ^2 = 0.4 df=3 p = 0.93	χ^2 = 0.5 df=3 p = 0.91	χ^2 = 0.1 df=3 p = 0.99
Legumes						
Low Intake†	59.3	49.6	51.3	1.00	1.00	1.00
Medium Intake	24.7	30.7	29.6	0.84 (0.55, 1.28)	0.86 (0.56, 1.32)	0.84 (0.54, 1.29)
High Intake	16.1	19.8	19.1	0.78 (0.47, 1.28)	0.86 (0.52, 1.43)	0.82 (0.49, 1.37)
Trend				χ^2=1.2 df=1 p =0.27	χ^2=0.5 df=1 p =0.48	χ^2=0.8 df=1 p =0.38
LR				χ^2 = 1.3 df=2 p = 0.52	χ^2 = 0.7 df=2 p = 0.72	χ^2 = 1.0 df=2 p = 0.62
Peanut Butter						
Low Intake†	25.3	29.6	28.8	1.00	1.00	1.00
Low-Med Intake	18.5	22.7	22.0	0.79 (0.46, 1.34)	0.79 (0.46, 1.36)	0.75 (0.43, 1.29)
Med-High Intake	16.7	18.7	18.3	0.93 (0.53, 1.63)	0.90 (0.51, 1.60)	0.87 (0.49, 1.55)
High Intake	39.5	29.0	30.9	1.50 (0.95, 2.37)	1.44 (0.90, 2.30)	1.30 (0.81, 2.11)
Trend				χ^2=6.2 df=1 p =0.01	χ^2=5.3 df=1 p =0.02	χ^2=3.5 df=1 p =0.06
LR				χ^2 = 7.8 df=3 p = 0.05	χ^2 = 6.6 df=3 p = 0.09	χ^2 = 5.2 df=3 p = 0.16
Baked products						
Low Intake†	14.2	22.3	20.9	1.00	1.00	1.00
Low-Med Intake	15.4	20.2	19.3	1.06 (0.56, 1.99)	1.07 (0.56, 2.05)	1.05 (0.55, 2.02)
Medium Intake	22.2	19.9	20.3	1.53 (0.85, 2.77)	1.54 (0.84, 2.82)	1.41 (0.76, 2.61)
Med-High Intake	21.0	19.6	19.9	1.60 (0.87, 2.93)	1.61 (0.87, 2.98)	1.46 (0.77, 2.76)
High Intake	27.2	18.0	19.7	2.23 (1.24, 3.99)	2.39 (1.32, 4.33)	2.09 (1.10, 3.99)
Trend				χ^2=9.3 df=1 p =0.002	χ^2=10.6 df=1 p=0.001	χ^2=6.3 df=1 p =0.01
LR				χ^2=10.2 df=4 p = 0.04	χ^2 =11.3 df=4 p =0.02	χ^2 = 6.7 df=4 p = 0.15

Variable	Case n = 162	Control n = 744	Total n = 906	Model 1*	Model 2**	Model 3 ***
	%	%	%	Odds Ratio (95% CI)	Odds Ratio (95% CI)	Odds Ratio (95% CI)
Sweets						
Low Intake†	16.7	25.5	24.0	1.00	1.00	1.00
Low-Med Intake	13.0	17.9	17.0	0.95 (0.51, 1.80)	0.90 (0.47, 1.73)	0.87 (0.45, 1.67)
Medium Intake	18.5	20.3	20.0	1.26 (0.70, 2.27)	1.18 (0.65, 2.15)	1.09 (0.59, 1.99)
Med-High Intake	30.3	20.2	22.0	1.80 (1.05, 3.10)	1.75 (1.01, 3.04)	1.57 (0.89, 2.76)
High Intake	21.6	16.1	17.1	1.66 (0.93, 2.97)	1.59 (0.88, 2.89)	1.37 (0.73, 2.57)
Trend				χ^2=5.8 df=1 p =0.02	χ^2=5.4 df=1 p =0.02	χ^2=2.8 df=1 p =0.09
LR				χ^2 = 7.8 df=4 p = 0.10	χ^2 = 7.5 df=4 p = 0.11	χ^2 = 4.8 df=4 p = 0.31
Snacks						
Low Intake†	13.0	24.3	22.3	1.00	1.00	1.00
Low-Med Intake	15.4	19.5	18.8	1.39 (0.73, 2.64)	1.38 (0.72, 2.65)	1.32 (0.68, 2.57)
Medium Intake	24.1	21.4	21.9	1.79 (0.99, 3.24)	1.79 (0.97, 3.28)	1.68 (0.91, 3.10)
Med-High Intake	19.1	15.6	16.2	1.69 (0.90, 3.16)	1.49 (0.79, 2.82)	1.32 (0.69, 2.53)
High Intake	28.4	19.2	20.9	1.89 (1.04, 3.41)	1.76 (0.96, 3.24)	1.47 (0.78, 2.76)
Trend				χ^2=3.7 df=1 p =0.05	χ^2=2.5 df=1 p =0.11	χ^2=0.8 df=1 p =0.38
LR				χ^2 = 5.4 df=4 p = 0.25	χ^2 = 4.4 df=4 p = 0.36	χ^2 = 2.8 df=4 p = 0.58

† reference group
* includes age group and province as covariates
**includes smoking, age group, BMI, province as covariates
***includes smoking, age group, BMI, province, energy intake as covariates

7.3. Non-Seminomas - Disaggregated Dairy Products Analysis

7.3.1. Milk

The results for the disaggregated food group analysis are shown in Table 21. The test of trend for milk intake was non-significant (χ^2 =1.3 df =1 p =0.26). The risk in the medium-high intake quintile is marginally significant (OR = 1.75; CI 1.00, 3.08). The likelihood ratio test produces a significant result (χ^2 = 11.4 df=4 p=0.02). The further disaggregation of milk into its components does not result in any significant findings in the categorical (Table 21) or continuous analyses (Table 22).

7.3.2. Cheese

Cheese intake is associated with a significantly increased risk of non-seminomas. The risk peaks at the medium-high intake level with an OR of 2.37 (CI 1.21, 4.67). The risk level decreases slightly at the high intake level (OR = 1.97; CI 0.95, 4.05). The overlap in the 95% confidence intervals for these two risk estimates shows that these estimates are not statistically different. This suggests that the apparently lower OR in the highest intake quintile is likely the result of random variation. This was confirmed by an additional logistic regression model which included a quadratic term for cheese intake; the Wald Chi-square for this term was not significant (p=0.18). Despite the lower risk at the high intake level, cheese intake is still associated with a significantly increasing trend of risk with increasing intake (χ^2 =5.6 df =1 p =0.02).

7.3.3. Whole Milk and Cheese

Whole milk and cheese intake was associated with an increased risk; however, it would seem that it is more a carryover from the strong effects of cheese on testicular cancer risk, rather than a combined effect of the two foods. An intake of 3-5.5 servings of whole

milk/cheese per week results in an increase of testicular cancer risk (OR = 2.03; CI 1.14, 3.64).

Table 21. Risk of Testicular Cancer - Categorical Food Group Disaggregation Analysis (Non-seminomas Only)

Variable	Case n = 162	Control n = 744	Total n =906	Model 1*	Model 2**	Model 3 ***
	%	%	%	Odds Ratio (95% CI)	Odds Ratio (95% CI)	Odds Ratio (95% CI)
Milk						
Low Intake†	16.1	23.5	22.2	1.00	1.00	1.00
Low-Med Intake	21.6	20.4	20.6	1.29 (0.73, 2.30)	1.31 (0.73, 2.36)	1.30 (0.72, 2.35)
Medium Intake	13.0	22.5	20.8	0.72 (0.38, 1.36)	0.76 (0.40, 1.45)	0.69 (0.36, 1.34)
Med-High Intake	37.7	23.0	25.6	1.96 (1.15, 3.33)	2.07 (1.20, 3.56)	1.75 (1.00, 3.08)
High Intake	11.7	10.6	10.8	1.24 (0.62, 2.48)	1.33 (0.66, 2.68)	1.09 (0.52, 2.26)
Trend				χ^2=3.2 df=1 p=0.07	χ^2=3.9 df=1 p=0.05	χ^2=1.3 df=1 p=0.26
LR				χ^2=14.5 df=4 p=0.006	χ^2=14.5 df=4 p=0.006	χ^2= 11.4 df=4 p=0.02
Whole Milk						
Low Intake†	79.6	77.8	78.2	1.00	1.00	1.00
High Intake	20.4	22.2	21.9	0.87 (0.56, 1.35)	0.91 (0.58, 1.42)	0.87 (0.55, 1.37)
Trend				χ^2=0.4 df=1 p=0.53	χ^2=0.2 df=1 p=0.70	χ^2=0.3 df=1 p=0.57
LR				χ^2 = 0.4 df=1 p = 0.53	χ^2 = 0.2 df=1 p = 0.70	χ^2 = 0.3 df=1 p = 0.57
Two % Milk						
Low Intake†	37.0	40.3	39.7	1.00	1.00	1.00
Low-Med Intake	20.4	22.6	22.2	0.85 (0.52, 1.38)	0.81 (0.47, 1.33)	0.85 (0.52, 1.40)
Med-High Intake	24.1	21.1	21.6	1.10 (0.69, 1.76)	1.18 (0.73, 1.91)	1.18 (0.73, 1.91)
High Intake	18.5	16.0	16.5	1.02 (0.61, 1.71)	1.08 (0.64, 1.82)	0.95 (0.56, 1.63)
Trend				χ^2=0.0 df=1 p=0.94	χ^2=0.2 df=1 p=0.66	χ^2=0.0 df=1 p=0.97
LR				χ^2 = 1.0 df=3 p = 0.81	χ^2 = 2.0 df=3 p = 0.58	χ^2 = 1.8 df=3 p = 0.62
One % Milk						
Low Intake†	69.8	77.7	76.3	1.00	1.00	1.00
High Intake	30.3	22.3	23.7	1.33 (0.89, 1.99)	1.37 (0.91, 2.07)	1.33 (0.88, 2.00)
Trend				χ^2=2.0 df=1 p=0.16	χ^2=1.9 df=1 p=0.16	χ^2=1.5 df=1 p=0.23
LR				χ^2 = 2.0 df=1 p = 0.16	χ^2 = 1.9 df=1 p = 0.16	χ^2 = 1.5 df=1 p = 0.23
Skim Milk						
Low Intake†	85.2	87.9	87.4	1.00	1.00	1.00
High Intake	14.8	12.1	12.6	1.23 (0.74, 2.05)	1.23 (0.73, 2.09)	1.16 (0.68, 1.98)
Trend				χ^2=0.6 df=1 p=0.43	χ^2=0.6 df=1 p=0.45	χ^2=0.3 df=1 p=0.59
LR				χ^2 = 0.6 df=1 p = 0.43	χ^2 = 0.6 df=1 p = 0.45	χ^2 = 0.3 df=1 p = 0.59
Eggs						
Low Intake†	16.7	24.1	22.7	1.00	1.00‡	1.00
Low-Med Intake	21.0	24.1	23.5	1.27 (0.72, 2.23)	1.32 (0.74, 2.35)	1.29 (0.72, 2.31)
Med-High Intake	43.8	37.0	38.2	1.79 (1.09, 2.96)	1.85 (1.11, 3.08)	1.64 (0.98, 2.77)
High Intake	18.5	14.9	15.6	1.65 (0.91, 2.98)	1.63 (0.89, 3.00)	1.40 (0.75, 2.62)
Trend				χ^2=3.8 df=1 p=0.05	χ^2=3.5 df=1 p=0.06	χ^2=1.4 df=1 p=0.24
LR				χ^2 = 6.1 df=3 p = 0.11	χ^2 = 6.3 df=3 p = 0.10	χ^2 = 3.6 df=3 p = 0.31
Butter						
Low Intake†	35.2	37.9	37.4	1.00	1.00	1.00
Low-Med Intake	10.5	12.1	11.8	0.86 (0.46, 1.59)	0.78 (0.41, 1.47)	0.79 (0.42, 1.49)
Med-High Intake	23.5	24.3	24.2	0.81 (0.51, 1.30)	0.82 (0.51, 1.32)	0.83 (0.51, 1.35)
High Intake	30.9	25.7	26.6	1.29 (0.83, 2.02)	1.34 (0.85, 2.11)	1.24 (0.78, 1.98)
Trend				χ^2=1.6 df=1 p=0.20	χ^2=2.3 df=1 p=0.13	χ^2=1.3 df=1 p=0.25
LR				χ^2= 3.9 df= 3 p = 0.28	χ^2=4.7 df = 3 p = 0.19	χ^2=3.1 df = 3 p = 0.38
Cheese						
Low Intake†	11.1	20.2	18.5	1.00	1.00	1.00
Low-Med Intake	13.6	17.9	17..1	1.39 (0.70, 2.77)	1.39 (0.69, 2.81)	1.39 (0.68, 2.81)
Medium Intake	36.4	36.6	36.5	1.66 (0.93, 2.98)	1.69 (0.93, 3.07)	1.56 (0.85, 2.86)
Med-High Intake	22.8	12.2	14.1	2.63 (1.38, 5.01)	2.69 (1.39, 5.21)	2.37 (1.21, 4.67)
High Intake	16.1	13.2	13.7	2.19 (1.11, 4.34)	2.26 (1.12, 4.54)	1.97 (0.95, 4.05)
Trend				χ^2=9.0 df=1 p=0.003	χ^2=9.0 df=1 p=0.003	χ^2=5.6 df=1 p=0.02
LR				χ^2= 10.7 df=4 p=0.03	χ^2= 10.7 df=4 p=0.03	χ^2 = 7.2 df=4 p = 0.13
Whole Milk and Cheese						
Low Intake†	17.9	30.8	28.5	1.00	1.00‡	1.00
Low-Med Intake	32.7	31.2	31.5	1.64 (0.99, 2.72)	1.60 (0.96, 2.67)	1.47 (0.87, 2.47)
Med-High Intake	23.5	13.7	15.5	2.29 (1.31, 3.99)	2.26 (1.27, 4.00)	2.03 (1.14, 3.64)
High Intake	25.9	24.3	24.6	1.67 (0.98, 2.83)	1.74 (1.01, 2.99)	1.47 (0.83, 2.60)
Trend				χ^2=4.6 df=1 p=0.03	χ^2=5.4 df=1 p=0.02	χ^2=2.7 df=1 p=0.10
LR				χ^2 = 8.7 df=3 p = 0.03	χ^2 = 8.2 df=3 p = 0.04	χ^2 = 5.8 df=3 p = 0.13

† reference group * includes age group and province as covariates

**includes smoking, age group, BMI, province as covariates

***includes smoking, age group, BMI, province, energy intake as covariates

Table 22. Risk of Testicular Cancer - Continuous Food Group Disaggregation Analysis (Non-seminomas Only)*	
Food/Nutrient**	Odds Ratio (95% CI)
Total Milk	1.02 (0.89, 1.16)
Whole Milk	0.88 (0.40, 1.49)
2% Milk	0.94 (0.80, 1.11)
1% Milk	1.21 (0.99, 1.48)
Skim Milk	1.03 (0.74, 1.42)

*Model includes: food, age, province, BMI, Smoking and energy intake
** per 1 serving/week

7.4. Non-Seminomas - Nutrient analysis

7.4.1. Overview of Nutrient Analysis

There were significant trend tests obtained for both carbohydrate and calcium intake (table 23). The disaggregated continuous fat analysis (Table 24) found that several types of fat were associated with a significantly increased risk of testicular cancer.

7.4.2. Fats

In the categorical analysis, neither total fat intake nor any of three subtypes of fat, reached statistical significance or had a significant trend test. However, the trend test for total fat intake almost reached significance ($\chi^2 = 3.3$ df = 1 p = 0.07). When fat was analyzed as a continuous variable (risk associated with a 10 gram increase in intake per week), total fat intake was significant (OR = 1.13; CI 1.03, 1.25). Furthermore, when fat is disaggregated into its three components, and analyzed continuously, saturated fat (OR = 1.35; CI 1.07, 1.71), and mono-unsaturated fat (OR = 1.24; CI 1.02, 1.51) are all associated with a statistically significant increase in risk.

7.4.3. Carbohydrates

Carbohydrate intake showed a marginally significant trend of decreasing risk with increasing intake for the non-seminoma analysis ($\chi^2 = 4.0$ df = 1 p = 0.05). This result did not occur in the total sample or seminoma analysis. As well, this was the only result of a trend of significantly decreased risk with increasing consumption in any of the analyses.

7.4.4. Calcium

Unlike carbohydrates the increase in risk associated with calcium has appeared in the other two analyses. While no individual risk estimates reached significance, a trend of

increasing risk with increasing intake of calcium was observed ($\chi^2 = 4.2$ df = 1 p = 0.04). The highest level of risk was found in the high intake quintile (OR = 1.93; CI 0.91, 4.11).

Table 23. Risk of Testicular Cancer associated with Nutrient Intake (Non-Seminomas Only)

Nutrient	Case n = 162	Control n = 744	Total n = 906	Model A*	Model B**
	%	%	%	Odds Ratio (95% CI)	Odds Ratio (95% CI)
Fat					
Low Intake†	13.6	21.4	20.0	1.00	1.00
Low-Medium Intake	20.4	19.9	20.0	1.16 (0.58, 2.32)	1.09 (0.54, 2.20)
Medium Intake	16.7	20.8	20.1	0.76 (0.35, 1.68)	0.71 (0.32, 1.58)
Medium High Intake	21.0	19.8	20.0	1.03 (0.44, 2.42)	1.01 (0.42, 2.41)
High Intake	28.4	18.2	20.0	2.20 (0.84, 5.77)	2.09 (0.79, 5.59)
Trend				$\chi^2 = 3.7$ df = 1 p = 0.05	$\chi^2 = 3.3$ df = 1 p = 0.07
LR				$\chi^2 = 8.8$ df = 4 p = 0.07	$\chi^2 = 8.5$ df = 4 p = 0.07
Saturated Fat					
Low Intake†	11.7	21.8	20.0	1.00	1.00
Low-Medium Intake	20.4	19.9	20.0	1.57 (0.81, 3.06)	1.49 (0.75, 2.94)
Medium Intake	17.9	20.6	20.1	1.18 (0.56, 2.50)	1.13 (0.53, 2.43)
Medium High Intake	22.8	19.4	20.0	1.27 (0.59, 2.75)	1.25 (0.57, 2.76)
High Intake	27.2	18.4	20.0	2.19 (0.90, 5.31)	2.18 (0.88, 5.42)
Trend				$\chi^2 = 2.6$ df = 1 p = 0.10	$\chi^2 = 2.5$ df = 1 p = 0.11
LR				$\chi^2 = 5.5$ df = 4 p = 0.24	$\chi^2 = 5.2$ df = 4 p = 0.27
Mono-Unsaturated Fat					
Low Intake†	14.8	21.1	20.0	1.00	1.00
Low-Medium Intake	19.1	20.2	20.0	1.01 (0.53, 1.95)	0.92 (0.47, 1.79)
Medium Intake	15.4	21.1	20.1	0.60 (0.29, 1.27)	0.54 (0.25, 1.16)
Medium-High Intake	22.8	19.4	20.0	0.98 (0.46, 2.13)	0.93 (0.42, 2.04)
High Intake	27.8	18.3	20.0	1.64 (0.69, 3.88)	1.45 (0.60, 3.54)
Trend				$\chi^2 = 2.6$ df = 1 p = 0.11	$\chi^2 = 2.0$ df = 1 p = 0.16
LR				$\chi^2 = 8.5$ df = 4 p = 0.08	$\chi^2 = 8.4$ df = 4 p = 0.08
Poly-Unsaturated Fat					
Low Intake†			20.0	1.00	1.00
Low-Medium Intake	16.1	20.8	20.0	0.83 (0.43, 1.59)	0.86 (0.44, 1.67)
Medium Intake	19.8	20.0	20.1	0.54 (0.26, 1.14)	0.51 (0.24, 1.09)
Medium High Intake	16.7	20.8	20.0	0.84 (0.38, 1.85)	0.86 (0.38, 1.94)
High Intake	21.6	19.6	20.0	1.20 (0.50, 2.87)	1.16 (0.47, 2.83)
Trend	25.9	18.7		$\chi^2 = 0.9$ df = 1 p = 0.34	$\chi^2 = 0.7$ df = 1 p = 0.42
LR				$\chi^2 = 6.1$ df = 4 p = 0.19	$\chi^2 = 6.6$ df = 4 p = 0.16
Protein					
Low Intake†	13.6	21.4	20.0	1.00	1.00
Low-Medium Intake	17.3	20.6	20.0	0.86 (0.42, 1.79)	0.75 (0.36, 1.58)
Medium Intake	17.9	20.6	20.1	0.87 (0.38, 1.96)	0.82 (0.36, 1.87)
Medium High Intake	24.7	19.0	20.0	1.22 (0.51, 2.92)	1.13 (0.47, 2.73)
High Intake	26.5	18.6	20.0	1.72 (0.66, 4.54)	1.61 (0.60, 4.30)
Trend				$\chi^2 = 2.8$ df = 1 p = 0.10	$\chi^2 = 2.6$ df = 1 p = 0.11
LR				$\chi^2 = 4.2$ df = 4 p =0.38	$\chi^2 = 4.6$ df = 4 p = 0.34
Carbohydrates					
Low Intake†	13.6	21.4	20.0	1.00	1.00
Low-Medium Intake	22.2	19.5	20.0	1.25 (0.61, 2.55)	1.27 (0.61, 2.63)
Medium Intake	21.6	19.8	20.1	0.97 (0.42, 2.25)	0.89 (0.37, 2.12)
Medium High Intake	22.2	19.5	20.0	0.62 (0.24, 1.60)	0.57 (0.21, 1.52)
High Intake	20.4	19.9	20.0	0.46 (0.16, 1.35)	0.42 (0.14, 1.26)
Trend				$\chi^2 = 3.5$ df = 1 p = 0.06	$\chi^2 = 4.0$ df = 1 p = 0.05
LR				$\chi^2 = 5.7$ df = 4 p = 0.23	$\chi^2 = 6.4$ df = 4 p = 0.17
Dietary Fibre					
Low Intake†	17.3	20.6	20.0	1.00	1.00
Low-Medium Intake	25.3	18.8	20.0	1.44 (0.81, 2.56)	1.50 (0.84, 2.70)
Medium Intake	17.9	20.6	20.1	0.96 (0.51, 1.82)	0.96 (0.50, 1.84)
Medium High Intake	17.3	20.6	20.0	0.81 (0.42, 1.58)	0.86 (0.44, 1.69)
High Intake	22.2	19.5	20.0	1.24 (0.62, 2.47)	1.30 (0.64, 2.63)
Trend				$\chi^2 = 0.0$ df = 1 p = 0.92	$\chi^2 = 0.1$ df = 1 p = 0.81
LR				$\chi^2 = 4.9$ df = 4 p = 0.30	$\chi^2 = 5.0$ df = 4 p = 0.29

Nutrient	Case n = 162	Control n = 744	Total n = 906	Model A*	Model B**
	%	%	%	Odds Ratio (95% CI)	Odds Ratio (95% CI)
Sugar					
Low Intake†	13.0	21.5	20.0	1.00	1.00
Low-Medium Intake	17.9	20.4	20.0	1.34 (0.71, 2.54)	1.41 (0.74, 2.70)
Medium Intake	22.2	19.6	20.1	1.58 (0.84, 2.99)	1.53 (0.80, 2.95)
Medium High Intake	22.2	19.5	20.0	1.29 (0.66, 2.51)	1.28 (0.65, 2.54)
High Intake	24.7	19.0	20.0	1.70 (0.83, 3.49)	1.58 (0.76, 3.30)
Trend				$\chi^2 = 1.3$ df = 1 p = 0.25	$\chi^2 = 0.7$ df = 1 p = 0.42
LR				$\chi^2 = 2.9$ df = 4 p = 0.58	$\chi^2 = 2.0$ df = 4 p = 0.70
Iron					
Low Intake†	16.1	20.8	20.0	1.00	1.00
Low-Medium Intake	19.1	20.2	20.0	0.97 (0.51, 1.83)	0.92 (0.48, 1.76)
Medium Intake	22.8	19.5	20.1	1.26 (0.62, 2.57)	1.22 (0.59, 2.55)
Medium High Intake	17.9	20.4	20.0	0.70 (0.31, 1.57)	0.67 (0.29, 1.54)
High Intake	24.1	19.1	20.0	1.18 (0.48, 2.94)	1.15 (0.45, 2.93)
Trend				$\chi^2 = 0.1$ df = 1 p = 0.71	$\chi^2 = 0.1$ df = 1 p = 0.78
LR				$\chi^2 = 4.8$ df = 4 p = 0.31	$\chi^2 = 4.9$ df = 4 p = 0.30
Calcium					
Low Intake†	13.0	21.5	20.0	1.00	1.00
Low-Medium Intake	18.5	20.3	20.0	1.32 (0.69, 2.51)	1.29 (0.67, 2.49)
Medium Intake	16.7	20.8	20.1	1.05 (0.52, 2.14)	1.15 (0.56, 2.37)
Medium High Intake	24.1	19.1	20.0	1.53 (0.78, 3.01)	1.78 (0.89, 3.54)
High Intake	27.8	18.3	20.0	1.84 (0.88, 3.85)	1.93 (0.91, 4.11)
Trend				$\chi^2 = 3.5$ df = 1 p = 0.06	$\chi^2 = 4.2$ df = 1 p = 0.04
LR				$\chi^2 = 4.6$ df = 4 p = 0.33	$\chi^2 = 5.1$ df = 4 p = 0.28
Zinc					
Low Intake†	13.6	21.4	20.0	1.00	1.00
Low-Medium Intake	17.3	20.6	20.0	0.93 (0.44, 1.98)	0.86 (0.40, 1.86)
Medium Intake	19.8	20.2	20.1	0.97 (0.41, 2.29)	0.96 (0.40, 2.30)
Medium High Intake	21.6	19.6	20.0	1.08 (0.43, 2.72)	1.04 (0.41, 2.65)
High Intake	27.8	18.3	20.0	2.25 (0.80, 6.28)	2.09 (0.73, 5.98)
Trend				$\chi^2 = 4.3$ df = 1 p = 0.04	$\chi^2 = 3.8$ df = 1 p = 0.05
LR				$\chi^2 = 6.5$ df = 4 p = 0.16	$\chi^2 = 5.9$ df = 4 p = 0.21
Phosphorous					
Low Intake†	16.1	20.8	20.0	1.00	1.00
Low-Medium Intake	17.9	20.4	20.0	0.75 (0.37, 1.53)	0.70 (0.34, 1.44)
Medium Intake	16.7	20.8	20.1	0.63 (0.29, 1.39)	0.67 (0.30, 1.49)
Medium High Intake	22.8	19.4	20.0	0.90 (0.39, 2.04)	0.98 (0.43, 2.27)
High Intake	26.5	18.6	20.0	1.12 (0.47, 2.67)	1.17 (0.48, 2.84)
Trend				$\chi^2 = 1.2$ df = 1 p = 0.28	$\chi^2 = 1.5$ df = 1 p = 0.22
LR				$\chi^2 = 3.9$ df = 4 p = 0.43	$\chi^2 = 4.1$ df = 4 p = 0.40
Sodium					
Low Intake†	16.7	20.7	20.0	1.00	1.00
Low-Medium Intake	13.6	21.4	20.0	0.60 (0.29, 1.26)	0.51 (0.24, 1.08)
Medium Intake	21.6	19.8	20.1	1.00 (0.46, 2.18)	0.84 (0.38, 1.89)
Medium High Intake	22.2	19.5	20.0	1.20 (0.50, 2.89)	1.01 (0.41, 2.51)
High Intake	25.9	18.7	20.0	1.77 (0.66, 4.81)	1.39 (0.50, 3.90)
Trend				$\chi^2 = 3.1$ df = 1 p = 0.08	$\chi^2 = 2.0$ df = 1 p = 0.16
LR				$\chi^2 = 6.7$ df = 4 p = 0.15	$\chi^2 = 6.8$ df = 4 p = 0.15
Cholesterol					
Low Intake†	13.0	21.5	20.0	1.00	1.00
Low-Medium Intake	19.8	20.0	20.0	1.50 (0.79, 2.84)	1.46 (0.76, 2.80)
Medium Intake	17.3	20.7	20.1	1.04 (0.53, 2.05)	1.04 (0.52, 2.06)
Medium High Intake	22.8	19.4	20.0	1.39 (0.69, 2.80)	1.44 (0.71, 2.93)
High Intake	27.2	18.4	20.0	1.76 (0.87, 3.60)	1.82 (0.88, 3.76)
Trend				$\chi^2 = 2.0$ df = 1 p = 0.16	$\chi^2 = 2.3$ df = 1 p = 0.13
LR				$\chi^2 = 4.4$ df = 4 p = 0.35	$\chi^2 = 4.6$ df = 4 p = 0.34

† reference group

*includes age group, province, and energy intake as covariates

**includes smoking, age group, BMI, province, energy intake as covariates

Table 24. Risk of Testicular Cancer - Continuous Nutrient Disaggregation Analysis (Non-seminomas Only)*	
Food/Nutrient**	Odds Ratio (95% CI)
Total Fat	1.13 (1.03, 1.25)
Saturated Fat	1.35 (1.07, 1.71)
Mono-Unsaturated Fat	1.24 (1.02, 1.51)
Poly-Unsaturated Fat	1.41 (0.82, 2.40)

*Model includes: food, age, province, BMI, Smoking and energy intake
** per 10 grams/week

7.5. Chapter Summary

The association between dietary factors and testicular cancer risk was strongest within the non-seminoma subgroup. As well, a novel finding of a strongly increased risk associated with high BMI (>31.0) was observed, as subjects of high BMI had an increase in testicular cancer risk of approximately 3.7 times the reference group. Table 25 shows a summary of the significant food group and nutrient results for the non-seminoma subgroup analysis. The non-seminoma analysis yielded the largest number of significant results, and the point estimates for each of the significant food groups within this subgroup were larger than the corresponding point estimates in either the total sample or seminoma analyses. Significant results were found for: dairy products, luncheon meats, baked products, milk, cheese, carbohydrates, calcium, and zinc. Of these, baked products, cheese, calcium, and carbohydrates had a significant trend test. Interestingly, carbohydrates had a trend of decreasing risk with increasing intake, while the other significant trends were of increasing intake leading to an increase in risk. The strongest point estimates of risk were observed in dairy products, followed closely by cheese intake. Finally, in the continuous disaggregation analysis, fat intake was associated with an increase in testicular cancer risk. This was true for total fat intake, saturated fat intake and mono-unsaturated fat intake. Poly-unsaturated fat intake had a non-significant result for the continuous disaggregated analysis.

Table 25. Risk of Testicular Cancer associated with food and nutrient intake Summary table within Non-Seminomas (Model 3)

Food/Nutrient	Low Intake Odds Ratio (CI)	Low-Med Intake Odds Ratio (CI)	Medium Intake Odds Ratio (CI)	Med-High Intake Odds Ratio (CI)	High Intake Odds Ratio (CI)	P-Trend
Dairy	1.00	1.52 (0.78, 2.95)	1.21 (0.61, 2.40)	3.17 (1.65, 6.09)	1.36 (0.67, 2.79)	0.32
Luncheon Meats	1.00	1.88 (0.97, 3.64)	1.34 (0.67, 2.67)	1.50 (0.79, 2.86)	2.11 (1.09, 4.08)	0.07
Baked Products	1.00	1.05 (0.55, 2.02)	1.41 (0.76, 2.61)	1.46 (0.77, 2.76)	2.09 (1.10, 3.99)	0.01
Milk	1.00	1.30 (0.72, 2.35)	0.69 (0.36, 1.34)	1.75 (1.00, 3.08)	1.09 (0.52, 2.26)	0.26
Cheese	1.00	1.39 (0.68, 2.81)	1.56 (0.85, 2.86)	2.37 (1.21, 4.67)	1.97 (0.95, 4.05)	0.02
Carbohydrates	1.00	1.27 (0.61, 2.63)	0.89 (0.37, 2.12)	0.57 (0.21, 1.52)	0.42 (0.14, 1.26)	0.05
Calcium	1.00	1.29 (0.67, 2.49)	1.15 (0.56, 2.37)	1.78 (0.89, 3.54)	1.93 (0.91, 4.11)	0.04
Zinc	1.00	0.86 (0.40, 1.86)	0.96 (0.40, 2.30)	1.04 (0.41, 2.65)	2.09 (0.73, 5.98)	0.05

*Model includes: food, age, province, BMI, Smoking and energy intake

8. Discussion

This thesis represents one of the largest studies ever undertaken for testicular cancer risk factors. It is our hope that the results of this investigation will inform future research directions in the attempt to understand testicular cancer etiology. Several strong and important results were found in the analyses performed. The finding relating higher dairy product intake to increased testicular cancer risk is particularly compelling. Dairy products have been associated ecologically with testicular cancer risk, but have not yet been subject to extensive analytic epidemiologic investigation. Within dairy products, cheese was a particularly significant and consistent risk factor, within the total sample and both histological subtypes. Baked products were shown to have an increasing risk associated with increasing intake in all three analyses. The association of baked products and testicular cancer risk has not yet been reported in the literature; however, the consistency of these results is strongly suggestive of a real association. The findings of this analysis should be viewed with some caution, as there are several limitations in the exposure measures, although these limitations have not prevented the results of the dietary portion of the NECSS from being reported on in the peer reviewed literature [41;173-175]. The results of this analysis should encourage other investigators to assess risk between diet and male testicular health.

8.1. Covariates

Testicular cancer risk has a very distinctive age distribution. It is well established that testicular cancer occurs mainly before age forty, with incidence peaking among those aged 25-35 years [1]. The age the current sample peaked at was the latter end of that range, in the 30-34 and 35-39 year age groups. The age of the seminoma subgroup was older

than that observed for the non-seminoma subgroup. This is consistent with the understanding that seminomas develop at a later age than non-seminomas[24].

Smoking did not have a significant effect on risk; even though there were a large percentage of smokers in both the control and case groups (this was true for both seminomas and non-seminomas). The OR's associated with smoking were slightly elevated for longer durations of smoking. Smoking has not been extensively examined in the literature as a risk factor for testicular cancer[11;41], and the findings have been mixed. It is likely that smoking does not play a significant role in the etiology of this lesion. However, it is unclear why this would be. One theory is relates to the time course of exposure to tobacco-related carcinogens. Since testicular cancer occurs at a young age, before smoking becomes an established habit, the testes may not be exposed to carcinogens for a sufficiently long time to generate cancer. Alternatively, it is possible that the carcinogens in smoke do not have an impact on the testicles or do not reach testicular tissue.

The relationship between BMI and testicular cancer risk has been studied numerous times within the testicular cancer literature[62;96;97], with mixed findings. We found a non-significant but increased risk (OR = 1.29) within the total sample. A non-significant result was observed for seminomas as well. However, we found an elevated risk in the non-seminoma group. The increase in risk becomes significant at >25.2 BMI, but increases at higher BMI levels with an odds ratio of 3.42, for BMI >30.5. This finding of increased risk with increased BMI for non-seminomas is a finding that has not yet been reported on in the literature. There have been suggestions that high BMI is associated

with higher levels of estradiol and various other estrogen compounds, which have been linked testicular cancer risk. Thus, it is possible that high BMI could increase the risk of testicular cancer, either through the impact of high BMI on hormonal levels, or another unknown link.

Total energy intake was strongly associated with testicular cancer risk, such that subjects at a medium-high intake level were at a significantly increased risk over the reference group. This was observed in seminomas and non-seminomas as well as the total sample. The elevated risk associated with total energy intake has not been previously reported in the literature.

Both total energy intake and high BMI may be indicative of an energy imbalance, which has been linked to Breast, Prostate and Colon cancer[180;181]. Animal studies have observed a protective effect of energy restriction on cancer risk[182;183]. The effect of energy imbalance may be mediated by Insulin-like growth factors (IGF-I). IGF-I is a peptide growth factor produced by the liver and is responsible for regulating growth and influences body size and composition. A recent study showed a benefit of energy restriction on the cancer risk of a number of animals and further showed that this benefit was lost if IGF-I is increased to normal levels through intravenous supplementation[184]. It is currently unknown if IGF-I has a role in testicular cancer etiology, although it has been associated with CIS of the testis[185].

8.2. Dietary Analyses

8.2.1. Dairy Products

Milk and dairy products have been implicated with increasing testicular cancer risk, both in ecological[35;37;156] and case control studies[39]. One study[39] specifically designed to examine milk intake and risk of testicular cancer found a significant increase in risk associated with milk intake at 17 years of age. A major limitation of that study was the small case sample (129 cases). The study used both cancer (n = 216) and population (n = 185) controls. They did not report an increased consumption of cheese in the case group as compared to the controls, and failed to examine risk associated with cheese intake in a multivariate logistic regression model. The latest ecological study of dietary risk factors for testicular cancer, published in 2002[37], found that cheese was most strongly correlated with testicular cancer incidence, compared to all other foods.

The present study found a strongly significant association between dairy foods and testicular cancer, in each of the three analyses at medium-high intake (total sample OR = 2.56, seminomas OR = 2.01, non-seminomas OR = 3.17). The disaggregation analysis of dairy products revealed that cheese intake was responsible for much of the risk associated with dairy products. The effects of cheese intake produced significant point estimates in all three analyses, and strongly significant trend tests in the total sample and non-seminomas. The increasing trend in risk with increasing intake was not significant for seminomas (p=0.07). Within dairy products, cheese has the highest (saturated) fat level, other than butter or cream, and is made from industrial milk (no addition of vitamin D). Cheese is eaten regularly and in some quantity by substantial proportions of people

(Bryna Shatenstein, Personal Communication). Thus, risk associated with cheese intake may have an important public health implication. The individual risk estimates associated with milk intake were elevated; however, the lack of a consistent exposure-response relationship in the present study, assessed through the trend test, does not support the previously reported finding of increased risk with increased milk consumption.

With the strength of our findings, and the findings previously reported on in the literature, dairy products do seem to be a potentially important risk factor for testicular cancer, particularly cheese intake. In addition to fat, protein, and calcium, all of which may have an effect on testicular cancer risk; milk and dairy products contain considerable levels of the female sex hormones estrogens and progesterone[186]. It is reasonable to hypothesize that estrogens or progesterone in milk and dairy products could be associated with the development of testicular cancer[37]. This is also in line with the developing literature around exposure to estrogens and other hormones and testicular cancer risk. The strength of this association is further supported by the recent trend of increasing testicular cancer incidence and the excessive consumption of dairy productions in developed countries starting in the 1940s and 50s[187]. Another contributing factor to the level of estrogens in dairy products may be the increase in the treatment of cattle with hormones and antibiotics, although the impact of this on carcinogenesis is unknown. Further research is needed to understand the potential mechanisms of carcinogenesis of estrogen on the testicles, the exposure levels resulting from dairy product intake, and the dose required to cause mutagenesis within the testicles.

8.2.2. Other food groups

From an extensive review of the peer-reviewed literature, it is clear that dietary risk factors for testicular cancer have been neglected as a topic of study. In the few studies previously performed, dietary fat has been associated with increased risk of testicular cancer[36-38]. Both meat[35;38;151;157] and cholesterol[38] have also been associated with increased risk. Mixed results have been found with regard to fruits and vegetables[38-40;151;157].

Findings of significant risks associated with cholesterol or meat consumption were not duplicated in this study. Meat intake was found to be a non-significant risk factor. In this analysis luncheon meats were analyzed separately. In the total sample we found an OR of 1.49 for the high intake group. The seminoma subgroup had an increased but non-significant risk, whereas the non-seminoma subgroup had an elevated OR of 2.11 (CI 1.09, 4.08). The case-control study finding the significant increase in risk associated with meat intake[38] did not separate meats luncheon meats into a separate food group; thus it is unclear if the results of that analysis are in support of or opposed to our findings. When the mean and the luncheon meat food groups were combined, no significant results were observed. Thus, the lack of substantial evidence makes it unclear if meat intake is a risk factor for testicular cancer. The differing results found in the analysis for the luncheon meats and other meats suggest that the stratification of meats may be useful.

Mixed results have been found for fruit and vegetable consumption; however, we found a non-significant risk for both food groups. Sigurdson *et al.*[38] found that vegetables

increased risk, non-significantly, in non-seminomas and were protective in seminomas (the study did not report on overall testicular cancer risk).

A study by Srivastava *et* al.[41] has examined fruit and vegetable intake and testicular cancer; they state that the risk is decreased, but the statistics are not presented in the paper. Finally, a twin study has found a protective effect associated with consumption of vegetables that bordered on significance[40]. Thus, the role of fruits and vegetables in testicular cancer risk is unclear and warrants further study. It is also important to ensure that future research into fruit and vegetable consumption take into account pesticide use, as estrogen and endocrine modulating substances likely effect testicular cancer risk.

Consumption of baked products was associated with increased risk of testicular cancer in these analyses. It was the only food group that had a significant test for trend for each of the total sample and the two histological subtypes. It is unclear if this risk was associated with the high fat content, the milk products, sugar and eggs used in production of the foods, or the processing under high heat conditions (baking). An association between baked products and testicular cancer risk has not been reported on previously in the literature.

8.3. Nutrient Analyses

High intake of several nutrients has been associated with an increased risk of testicular cancer. These include: fat[38], iron[155], cholesterol[38], dietary fibre[38], and a protective effects has been observed for high calcium intake[38]. This study represents the first extensive examination of nutrients and testicular cancer.

Sigurdson *et al.*[38] found both an increased risk associated with total fat and saturated fat. We did not find any significant risks associated with fat intake or with its components. The role of fat in testicular cancer remains unclear and requires further research. However, the findings of dairy, cheese, luncheon meats and baked products as risk factors point to fat as being a causative agent.

Dietary calcium intake has been associated with a protective effect[38], for non-seminomas only. This study found an opposite effect, in that calcium intake was consistently associated with an increased risk of testicular cancer for both the total sample and the histological subsamples. It is unclear if this is just a spurious relationship, stemming from the high risk associated with dairy products and their high calcium content, with calcium is acting as a proxy for dairy product consumption, or if there is an actual effect resulting from higher calcium intake. The percentage of calcium from dairy products vs. other sources was 53.8% for the cases and 48.5% for the controls. The role of calcium intake in testicular cancer warrants further investigation.

Crawford[155], has hypothesized that iron replete diets will increase the risk of testicular cancer. Our study failed to find any evidence of an increase in testicular cancer risk associated with dietary iron intake.

Finally, the finding of Sigurdson[38] that cholesterol increases testicular cancer risk in both seminomas and non-seminomas was not duplicated in this study.

Several other nutrients had significant results in our analysis including phosphorus, zinc, sodium and carbohydrates. But the lack of consistent effects for these nutrients prevents conclusions regarding the risk associated with their intake. However, this is partially expected in that nutritional epidemiology does a better job describing the relation between foods and health than of assessing nutrient effects[31]. As well, none of the four nutrients for which we found significant results for have been reported on in the literature as influencing testicular cancer risk. The role of nutrient intake, for both micro and macronutrients, requires further research to clarify these findings.

8.4. Seminomas versus Non-Seminomas

As previously mentioned, it is now well accepted that seminomas are not intermediate to non-seminomas[24], and that different co-factors are required for development of either type of testicular cancer. Specifically, it appears that young age is an important cofactor in the development of a non-seminoma[24]. This is supported by the results of this thesis, as the non-seminoma sample is much younger than the seminoma group. A notable difference in the results by histological subtype is the result of BMI. BMI did not change the risk associated with seminomas. However, there was a very strong increase in risk associated with high BMI for non-seminomas. There is not a clear sense within the literature to the risk associated with BMI; this may be a result of the lack of histological stratification in these studies, where BMI, like young age, may be a cofactor in the development of non-seminomatous tumours.

The seminoma and non-seminoma analyses produced notably different results within the dietary analysis. Both seminomas and non-seminomas were associated with significant

risk increases within the dairy products group, particularly for cheese intake. It is important to note that the sample size of the case group for seminomas was 354, while only 162 cases were identified as having a non-seminomatous tumour. This difference in size leads to a lower power in the non-seminoma histological subtype. However, the risk within dairy products and its components was stronger in the non-seminoma subgroup.

Luncheon meats were associated with a non-significant increase in risk within seminomas while the same food groups produced significant results for high intake in the non-seminoma group. The nutrient analysis for seminomas yielded similar but more significant results, and there was a more pronounced protective effect of micronutrient intake on seminoma risk as compared with non-seminoma risk.

From these analyses, it would appear that diet has a stronger effect on the development of non-seminomatous tumours than for seminomatous tumours. There is only one other study that histologically stratified for tumour type and examined dietary risk factors for testicular cancer[38]. They found that the effects were larger in non-seminomas than seminomas; however, this study had a small sample size (82 non-seminomas and only 46 seminomas). Most notably, the risk associated with fat intake was markedly larger in non-seminomas (OR = 6.3; CI 1.9-20.5 for the highest intake quartile for non-seminomas, and OR = 1.9; CI 0.6-5.5 for seminomas)[38].

8.5. Analysis Issues

8.5.1. Energy Adjustment

In a recent edition of the American Journal of Epidemiology, an article examining energy adjustment in dietary analyses states that it seems to be more important to adjust for energy in situations where the FFQ used a fixed serving size, than for FFQ's with non-fixed serving sizes[163]. The NECSS FFQ used a fixed serving size. The same article proposes that energy adjustment generally appears to reduce measurement error in all FFQs[163]. But while many researchers believe that energy adjustment is essential, some are still not totally convinced[177]. Thus, for the food group analyses we include both energy adjusted and non-energy adjusted analyses. However, for the nutrient analysis we only present the energy adjusted results. The intake of most nutrients is correlated with energy intake and this correlation makes it difficult to interpret the results with regard to disease causation or prevention[188]. Energy adjustment thus allows for differentiation of the effects of total intake of the nutrient and that of diet composition[177].

8.5.2. Confounding

In this study, we identified three potential confounders of the relationship between diet and cancer (age, province, and total energy intake). In addition, we decided to control for smoking and BMI, on the basis that smoking is regularly controlled for in cancer risk analyses, and that BMI is associated with diet; however, for both BMI and smoking the risk associated with testicular cancer is unclear from the literature review. Finally, it was important to control for energy intake, as previously discussed.

There were a number of other potential variables that could have been included in the adjusted models, including income, education, and physical activity. These variables

were did not materially alter the risk estimates associated with the dietary exposures, and were thus omitted from further analyses. Some analyses of diet and testicular cancer have controlled for cryptochidism. However, we did not have this information, and cryptochidism is so rare that it is unlikely that the effect is substantial enough to appreciably alter the results of this analysis.

There were some concerns around residual confounding by age, despite the adjustment for age group. The concern stems from the fact that the age distributions between the case and control group are different. The adjustment for 5-year age group may not have been "fine" enough to prevent confounding by age. As a result, further analyses focussed on the residual effects of age. There was no change in the point estimates around the dietary exposures. Thus residual confounding was ruled out.

8.5.3. Multiple Testing

The length of the FFQ allowed for the formation of several food groups. Thus, multiple testing becomes an issue in the interpretation of the significant results, because it raises the question of what of the results came about via chance. Rothman[189] has argued that the assumption underlying the concern about multiple testing is that chance is the best first explanation for observed associations. He suggests that findings need to be examined critically and a scientific evaluation needs to be made as to their validity[188]. In addition, when a finding is unexpected, recommendations need to be withheld until the finding has been replicated in other studies. Thus, we did not adjust the p-value required for a result to be deemed significant on the basis of multiple testing.

8.5.4. Inverted U shape

In several of the food groups, especially dairy and its subcomponents, an inverted U-shape was observed for the point estimates. The peak risk in food groups with the inverted U-shape was reached at medium-high intake, rather than at the high intake level, which was expected. This could be an actual effect of the food groups, where large but not extremely large intakes of said foods are harmful, but the harm begins to decline once "high" levels are reached. However, this is not a likely explanation. More likely it is a result of random variation. As a result, we added a quadratic term to the model to examine the shape. No significant results for the quadratic term were obtained, thus we are comfortable concluding that the inverted U shape is a result of random variation rather than an actual effect.

8.5.5. Absolute vs. Relative Intake

The intake quintiles are reported as relative intake levels (low through high). This is for several reasons. The FFQ is likely systematically underestimating intake, and as such to compare the subjects' intake in this study with population based intakes would be inappropriate. As well there is a lack of a comprehensive coverage of food groups, as the questionnaire is quite short (69 items). Thus, the reported information gives intake relative to the other subjects, which will prevent the inappropriate comparison of the absolute intakes in this study with the intake of other studies.

8.6. Methodological Issues

8.6.1. NECSS issues

There are several issues surrounding the NECSS that may impact the results of this study. Firstly, the sampling of controls within each province was slightly different, as mentioned in the methods section. Although the NECSS attempted to get a population based sample

of controls, the extent for which this was successful is unclear. The different methods used to obtain the control sample in each province raises some concerns regarding it representation of the total provincial population. Secondly, the control sample was drawn to reflect the age, sex and provincial distribution of cancer in Canada. This yielded a control sample that was comparatively old for the testicular cancer case group, as most cancers occur later in life. We deleted all subjects aged greater than 55 years, which resulted in case and control groups being more similar in age. The deletion of the subjects over age 55 is appropriate in that testicular cancer primarily occurs in young men, and the inclusion of the older controls would have skewed the dietary intake quintiles to reflect the diet of subjects older than 55 years. Thus, in deleting subjects over 55 and controlling for age, we feel that the issues around the age differences are addressed, and that the results are not a surrogate of the age differences between the two groups, but an actual reflection of a pattern of risk in the NECSS dataset. Should another study be designed along the same lines as the NECSS, it would be beneficial to ensure that the control sample is drawn in the same way in each of the participating provinces.

The case ascertainment protocol was such that all incident cases of testicular cancer in the eight participating provinces were eligible for inclusion in the NECSS dataset, as all cases were identified through the cancer registry. The case recruitment resulted in a large, likely comprehensive, group representing testicular cancer cases in eight provinces.

Finally, as the NECSS was not designed to examine a specific cancer, but to look at several, there are several ways that the questionnaire might have been refined to more accurately address testicular cancer risk. It would be useful to have a series of questions

regarding other testicular cancer risk factors, including cryptochidism and carcinoma in situ diagnoses. The NECSS inquired on diet 2 years ago. It would have been beneficial for a section of the NECSS to inquire on diet during adolescence, especially dairy, as this is the time period when the testis are most susceptible to the promotion of a carcinoma in situ to a developing malignancy.

8.6.2. FFQ issues

The usefulness of FFQs in dietary assessment has been addressed earlier. However, there are some problems associated with the FFQ used in the NECSS questionnaire. Most importantly, the NECSS food frequency questionnaire is that it was not validated before use (Ken Johnson, personal communication). The source FFQs (Block and Willett) are well validated and widely used. However, combining the two FFQs does not ensure a valid resultant FFQ. As well, while American and Canadian food consumption patterns are likely similar in many respects, they are not identical. The source FFQs were altered by an experienced dietitian to account for the differences in American and Canadian diets (Ken Johnson, personal communication). It is our view that the FFQ does a good job of rank ordering both the cases and controls on exposures to foods. It is important to view the results with some caution as the FFQ is non-validated in a Canadian population. Had the NECSS undertaken a validation exercise for the FFQ, it would have been designed to ascertain the validity of the FFQ in an older population, as the majority of cancer cases and controls are significantly older than testicular cancer cases. As such, the validation may not have improved the present analysis of testicular cancer. However, without validation, it is hard to determine whether the questionnaire could accurately detect consumption of certain foods.

The portion size in the NECSS FFQ is fixed, coinciding with Willett's FFQ methodology. Unfortunately, no instructions were given to respondents that if their regular serving size were twice the fixed portion and they eat it once a week, they should respond to the frequency part as twice per week in order to portray the weekly amount of the specific food. Thus, subjects who responded to the questionnaire without making that adjustment would have systematically underestimated their intake. The extent of this effect is unknown. Finally, it is important to note that results from the FFQ portion of the NECSS have been previously published in the peer review literature[41;173-175]. Although this by no means ensures the questionnaire's validity, it does suggest its usefulness in the field of nutrition and cancer.

The NECSS FFQ's food list is short, 69 items. As a result, subjects with narrow diets completely contained within those 69 items would have their intake patterns more accurately represented, than subjects whose diets are broader based. However, it is unlikely that either the case or control group is systematically more likely to have their diets "better" represented by the food list in the NECSS FFQ.

8.6.3. Nutrient conversion

The nutrient conversion performed on the NECSS' FFQ may not be appropriate. The FFQ asks general questions about food intake. Some of these questions are not specific to one food, and may be perceived as asking about slightly different foods by different respondents. An example of this is the question that asks about fresh orange or grapefruit juice: it is unclear to which of the components the subject is responding. As a result, amalgams of foods for each question were created. Nutrient breakdowns of each of the foods comprising the amalgam were given equal weight, although some variation in

weighting is to be expected. In the case of the juice question, most subjects are likely to drink much more orange than grapefruit juice, but in the amalgam the subjects are judged to drink equal amounts. Thus, the amalgams could be improved if weights were assigned to each of the foods comprising the amalgam. For example, if Canadians drink 80% orange juice and 20% grapefruit juice, the amalgam would be more accurate if the nutrient weighted to represent the actual intake rather than the 50-50 weighing it currently has. This was not feasible in the context of this thesis.

8.7. Bias

8.7.1. Recall bias

A major limitation of nutritional epidemiology is the difficulty in validating reported exposures, particularly exposures in the distant past[188]. For hypotheses not generally recognized by the public, this source of bias may be of less importance[188]. The possible link between testicular cancer and dairy products was probably unknown to all participants.

However, it is likely that the case group were more aware of their actual diet 2 years ago, as asked for by the FFQ. Recall bias is an important consideration for all nutritional epidemiology studies of diet and disease; there is no way of measuring the extent of recall bias. Thus, the results should be interpreted and applied with caution.

8.8. Misclassification

There is a risk of misclassification of subjects into the exposure quintiles, which stems from the FFQ layout. As mentioned before, the fixed serving size may have been interpreted in several ways. This may have caused an over or underrepresentaion of

intake. As well, subjects may have been exposed to foods in a food group that were not inquired about on the FFQ. An example of this is the exposure to milk and dairy products via yogurt. Subjects who eat yogurt would have a higher actual intake of the dairy food group than was reported via the FFQ. Thus, it is important to view the findings in the light of the comprehensiveness, or lack there of, of each food group/nutrient.

Whenever dietary intake is grouped into quantiles, differential misclassification is possible to occur even if measurement error is random, and the effects of this are not known nor are they easily predictable[190]. However, it is our opinion that if the FFQ is invalid and misclassifying subjects the misclassification is likely affecting the case and control populations similarly, thus the misclassification is non-differential. Finally, as the measurement of diet was 2 years prior to receipt of the questionnaire, it is unclear if the dietary habits of the cases may have been influenced by the disease process[161].

8.9. Weight of evidence between diet and testicular cancer

In general, there are several criteria that observed associations need to meet before they can be considered "causal". These include: strength of association, consistency, specificity, temporality, and coherence. The literature surrounding testicular cancer and diet is very limited and the associations are weak. While there is a lack of knowledge of when the most important exposure period is the majority of dietary assessment measures recent diet, which may not have a direct relationship with the development of testicular cancer. The identification of specific causal agents is complicated by the fact that individual foods are made up of several chemicals and nutrients, which in addition can be

modified and new ones created in the preparation process. Finally, the extent to which a hypothesized causal association is compatible with the existing literature and knowledge is difficult in the case of testicular cancer as there is a poor understanding of the natural history of the disease.

This thesis has demonstrated a possible association between diet and testicular cancer, which needs to be evaluated in light of a number of factors both strengthening and weakening the weight of evidence for a true association. Nutritional epidemiology is fraught with evidence of weak associations [191]; however, the relative risk associated with dairy products in the present study is in the order of three and in the order of two for cheese. In addition, cheese intake demonstrates an increasing trend in risk with increasing consumption. This finding is consistent with a moderate increase in risk associated with increased intake of dairy products and cheese. A strictly monotonic exposure-response relationship was not observed. Instead of risk peaking at the highest dietary intakes, the risk for dairy products and cheese reach their highest level at medium-high intakes. The pattern observed appears to be a result of random variation, as the quadratic terms tested in the logistic regression model relating testicular cancer risk to dietary intake did not attain statistical significance. This observation does raise concerns regarding the measurement of the dietary intake. Specifically, it is possible that the FFQ leads to random non-differential misclassification of dietary intake. This type of bias leads to a conservative estimate of risk. Other factors which contribute to the variability of the observed effects include: a limited sample size, uncertainty to the optimal exposure measure (diet in early life vs. recent exposures), and a non-comprehensive coverage of foods and nutrients by the FFQ.

The effect of dairy product intake on testicular cancer risk remained consistent when adjusting for several important covariates. It is unlikely that unknown confounders of the relationship between diet and testicular cancer could explain the associations we observed, especially as the number of established risk factors for testicular cancer is limited, and none have an obvious link to dietary intake.

Measurement of the long term exposure to dietary factors is difficult; however, the FFQ is the currently the best method for measuring long term diet. The FFQ used in the NECSS dataset inquires only about the diet two years ago prior to recruitment into the study. As such it is likely that the questionnaire is measuring exposures occurring after development of partially initiated cancer cells within the testicles. This limitation is a weakness associated with the study design and time referent. The ideal situation would be to have intake measures at several points during the subjects' life, most significantly during childhood[46,47] and adolescence. This is the time at which it has been hypothesized that the changing hormonal environment associated with growth and puberty could influence the development of testicular cancer. The lack of the information to assess the temporality of the exposure is a serious limitation of this measurement method. Finally, the effect of dairy products does have some biological plausibility, especially with the emerging theories on the effect of hormones on male reproductive health, and the high levels of estrogens in dairy products.

However, our current understanding of the natural history of testicular cancer is extremely limited. In addition, the animal models that have been developed do not accurately reflect the known process of testicular cancer development. Before the link of

estrogen and testicular cancer can be confidently established, further research on the stages of testicular cancer development is required.

When the results of this thesis are viewed in the light of the strengths and limitations of the study design, the analysis methods and the exposure measurement, it would be premature to suggest causation or even a strong association between dairy products and testicular cancer. However, the results do suggest that diet may play a stronger role than previously thought in the development of testicular cancer. As such, this thesis provides a useful foundation on which to build future studies on testicular cancer etiology.

8.10. Conclusion

This study makes an important contribution to the field of risk factors for testicular cancer. As well, it adds significantly to the sparse literature on dietary risk factors for testicular cancer. The strength of these results suggest that the scientific community has incorrectly overlooked the importance of diet in testicular cancer etiology, and there must be a refocusing to address the important public health issues raised in this thesis.

The most significant results obtained are these regarding the risk associated with intake of dairy products, particularly cheese. This study has also demonstrated differences in the findings for seminomas and non-seminomas, suggesting that it is vital for studies to stratify by these histological subtypes of testicular cancer in future analyses.

It is our hope that these results will direct future research. Prospective studies looking at dairy exposure in adolescence would provide clarity on these findings. More likely, future studies will be retrospective studies similar to that of Davies[39], which inquired about dairy consumption now and during adolescence. As well, an expansion of dairy

products to other products that may have a hormonal influence or be contaminated with hormones would be useful. The high level of risk associated with cheese has only been observed in ecological studies and the current study. It is our hope that more studies will be undertaken to examine the association of cheese and testicular cancer risk.

From this thesis it is clear that despite the young age of incidence of testicular cancer, diet might play a potentially important role in the development of testicular cancer. Before recommendations to modify dietary intake can be developed, our results require confirmation and more detailed study to determine the mode of action. The cancer research community needs to be made aware of the paucity of research on diet and testicular cancer. This thesis provided a sound basis for the guidance of future studies designed to address this important public health issue.

9. References

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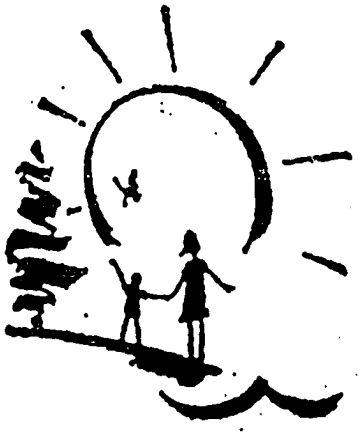
10. Appendices

10.1. Appendix A – NECSS Questionnaire

Health Canada Santé Canada



Environmental Health Survey

(Confidential when completed)

ID Number
First name/Middle name/Last name
Mailing Address: Street and Number/P.O. Box No.
Town/Province
Postal Code

This form asks a variety of questions about you and your environment, which may affect or be related to your health. The information you provide will help Canadians to understand more about preventing disease.

Please complete each question as best you can even if you are not sure of your answer.

You do not need to fill in the entire questionnaire all at once. You may wish to take a brief rest in the middle.

If you have any questions about the survey or would like help filling it out, please call

_____

at _____.

Please return this questionnaire by

Guide to filling in this Questionnaire:

Please choose answers by:
completely filling in the circle; o → ●

writing in the boxes; [ ] → [8 7]

or filling in the blank spaces provided. *April*

☐ **Si vous préférez répondre en français, veuillez cocher la case et renvoyer le questionnaire dans l'enveloppe adressée ci-jointe.**

GENERAL INFORMATION

1. Today's date *Month* _____ / *Day* [ ] / *Year* 19[ ]

2. Is anyone helping you (the person whose name appears on the front of the questionnaire) to complete this questionnaire?
   o No o Yes → o Spouse
   o Other -- Please specify: _____

3. When were you born?
   Month _____ / *Day* [ ] / *Year* 19[ ]

4. Are you
   o Female o Male

5. To which ethnic or cultural group(s) did your ancestors belong?

   Mark or specify as many as applicable.

   o French o Dutch
   o English o Jewish
   o German o Polish
   o Scottish o Black
   o Italian o Aboriginal
   o Irish o Métis
   o Ukrainian o Inuit
   o Chinese
   o Other ethnic or cultural group(s)
   -- Please specify: _____

   Examples of other ethnic or cultural groups are: Portuguese, Greek, Indian, Pakistani, Vietnamese, Japanese, Lebanese, Haitian, etc.

6. What is your marital status?
   o Single o Widowed
   o Married o Divorced/Separated
   o Common law o Other

7. What is the highest grade (or year) of high school or elementary school that you have completed?
   Grade [ ] o Never attended school

8. How many years of post-secondary school have you completed?
   [ ] years o none

[ ][ ][ ][ ][ ][ ]

9. Have you smoked at least 100 cigarettes in your entire life?
   o No → Go to 10
   o Yes
   About how old were you when you first started smoking cigarettes? [ ] years old

   About how many years in total did you smoke ? [ ] years

   Of the entire time you smoked, how many cigarettes, on the average, did you smoke per day? [ ] per day

   Do you smoke cigarettes now?

   o No → How old were you when you stopped smoking? [ ] years old

   o Yes → On the average, about how many cigarettes a day do you smoke now? [ ] per day

10. Have you ever smoked a pipe or cigars regularly?
    o No → Go to 11
    o Yes
    For how many years? [ ] years
    About how many pipes or cigars? [ ] per day or [ ] per week

11. Have you ever used chewing tobacco regularly?
    o No → Go to 12
    o Yes
    For how many years? [ ] years
    About how many plugs? [ ] per day or [ ] per week

12. How tall are you?
    [ ] feet [ ] inches or [ ] centimetres

13. How much did you weigh about 2 years ago?
    [ ] pounds or [ ] kilograms

14. What is the most you have ever weighed? (Women should not include pregnancy.)
    [ ] pounds or [ ] kilograms

RESIDENTIAL HISTORY

15. Please list each of the places in Canada you have lived for at least 1 year. Start with the most recent residence and follow back to your childhood. (If you cannot remember exact details, provide your best recollection, for example, nearest cross-street or intersection.)

	TIME PERIOD	ADDRESS			
	First Year *Last Year*	Street and Number or Lot, Concession and Township **(If you don't remember the exact address, give the nearest cross-street or intersection.)**	City, Town, or Municipality	County or District, if rural	Province
	Example: 19 8 9 to 19 9 3	*97 Greargate Rd.*	*Brandon*		*Manitoba*
	19 to 19				
	19 to 19				
	19 to 19				
	19 to 19				
	19 to 19				
5	19 to 19				
7	19 to 19				
8	19 to 19				
9	19 to 19				
10	19 to 19				
11	19 to 19				
12	19 to 19				

ADDRESS / Postal Code	Main source of **drinking water**	Primary types of home **heating** (Mark those which apply.)	Were you aware of dusts or odours from industry while living at this residence?	How many regular smokers usually lived in this home with you?
	Town/city water, Dug well, Drilled well, Bottled, Other, Don't know	Oil, Natural gas/propane, Electric, Wood, Coal, Other, Don't know	Never, At least once a month, At least once a week, At least once a day	None, 1, 2, 3 or more, Don't know
R7A 8A7	● ○ ○ ○ ○ ○	○ ○ ● ○ ○ ○ ○	○ ○ ● ○	○ ○ ○ ● ○
	○ ○ ○ ○ ○ ○	○ ○ ○ ○ ○ ○ ○	○ ○ ○ ○	○ ○ ○ ○ ○
	○ ○ ○ ○ ○ ○	○ ○ ○ ○ ○ ○ ○	○ ○ ○ ○	○ ○ ○ ○ ○
	○ ○ ○ ○ ○ ○	○ ○ ○ ○ ○ ○ ○	○ ○ ○ ○	○ ○ ○ ○ ○
	○ ○ ○ ○ ○ ○	○ ○ ○ ○ ○ ○ ○	○ ○ ○ ○	○ ○ ○ ○ ○
	○ ○ ○ ○ ○ ○	○ ○ ○ ○ ○ ○ ○	○ ○ ○ ○	○ ○ ○ ○ ○
	○ ○ ○ ○ ○ ○	○ ○ ○ ○ ○ ○ ○	○ ○ ○ ○	○ ○ ○ ○ ○
	○ ○ ○ ○ ○ ○	○ ○ ○ ○ ○ ○ ○	○ ○ ○ ○	○ ○ ○ ○ ○
	○ ○ ○ ○ ○ ○	○ ○ ○ ○ ○ ○ ○	○ ○ ○ ○	○ ○ ○ ○ ○
	○ ○ ○ ○ ○ ○	○ ○ ○ ○ ○ ○ ○	○ ○ ○ ○	○ ○ ○ ○ ○
	○ ○ ○ ○ ○ ○	○ ○ ○ ○ ○ ○ ○	○ ○ ○ ○	○ ○ ○ ○ ○
	○ ○ ○ ○ ○ ○	○ ○ ○ ○ ○ ○ ○	○ ○ ○ ○	○ ○ ○ ○ ○
	○ ○ ○ ○ ○ ○	○ ○ ○ ○ ○ ○ ○	○ ○ ○ ○	○ ○ ○ ○ ○

EMPLOYMENT HISTORY

16. Please tell us about **each job you had for at least 12 months in Canada or elsewhere.** Include seasonal work, part-time, etc., if you worked the equivalent of 12 months or more. Begin with your most recent job and continue back to your first job. Please estimate the time period if you cannot remember exact years. (Even if you have retired, we still require the information.)
If you have never been employed, check here ☐ **and continue to Question 17.**

	TIME PEROID *First Year* *Last Year*	Type of Industry, Business, or Service and Company Name	Main Job Duties
	Example: 19 8 9 to 19 9 3	*Oil industry, Bluestar Oil Company*	*Process powerhouse and sulphur plant operations.*
1	19 ☐☐ to 19 ☐☐		
2	19 ☐☐ to 19 ☐☐		
3	19 ☐☐ to 19 ☐☐		
4	19 ☐☐ to 19 ☐☐		
5	19 ☐☐ to 19 ☐☐		
6	19 ☐☐ to 19 ☐☐		
7	19 ☐☐ to 19 ☐☐		
8	19 ☐☐ to 19 ☐☐		
9	19 ☐☐ to 19 ☐☐		
10	19 ☐☐ to 19 ☐☐		

Job Location(s) *City/town and province*	Job Title	Status *Full time / Part time / Seasonal / Other*	At this workplace, were you aware of dusts or odours from industry? *Never / At least once a month / At least once a week / At least once a day*	About how many people smoked regularly in your immediate work area? *None / 1 or 2 / 3 to 5 / 6 or more / Don't know*
Rocky Mountain House, Alberta	*Gas plant operator*	● ○ ○ ○	○ ○ ○ ●	○ ○ ○ ● ○
		○ ○ ○ ○	○ ○ ○ ○	○ ○ ○ ○ ○
		○ ○ ○ ○	○ ○ ○ ○	○ ○ ○ ○ ○
		○ ○ ○ ○	○ ○ ○ ○	○ ○ ○ ○ ○
		○ ○ ○ ○	○ ○ ○ ○	○ ○ ○ ○ ○
		○ ○ ○ ○	○ ○ ○ ○	○ ○ ○ ○ ○
		○ ○ ○ ○	○ ○ ○ ○	○ ○ ○ ○ ○
		○ ○ ○ ○	○ ○ ○ ○	○ ○ ○ ○ ○
		○ ○ ○ ○	○ ○ ○ ○	○ ○ ○ ○ ○
		○ ○ ○ ○	○ ○ ○ ○	○ ○ ○ ○ ○
		○ ○ ○ ○	○ ○ ○ ○	○ ○ ○ ○ ○

17. Have you ever worked with any of the following for more than one year?

	Never	Don't know	At work	At home	How many years in total?
Asbestos	o	o	o	o	
Arsenic salts	o	o	o	o	
Chromium salts	o	o	o	o	
Cadmium salts	o	o	o	o	
Coal tar, soot, pitch, creosote, asphalt	o	o	o	o	
Mineral, cutting or lubricating oil	o	o	o	o	
Benzidine	o	o	o	o	
Benzene	o	o	o	o	
Isopropyl oil	o	o	o	o	
Dyestuffs	o	o	o	o	
Vinyl chloride	o	o	o	o	
Pesticides	o	o	o	o	
Herbicides	o	o	o	o	
Mustard gas	o	o	o	o	
Radiation sources	o	o	o	o	
Welding	o	o	o	o	
Wood dust	o	o	o	o	

You are more than halfway through the questionnaire. This is a good place to take a short break, if you wish.

DIET INFORMATION

18. During the past 20 years have you ever taken any of the following vitamin or mineral supplements?

Vitamin and Mineral type	How often?			For how many years in total?					
	No	Yes, but not regularly	Yes, fairly regularly	Less than 1 year	1 to 2 years	3 to 5 years	6 to 9 years	10 to 19 years	20 + years
Multiple vitamins	o	o	o	o	o	o	o	o	o
Vitamin A	o	o	o	o	o	o	o	o	o
Beta-carotene	o	o	o	o	o	o	o	o	o
B-complex vitamins	o	o	o	o	o	o	o	o	o
Vitamin C	o	o	o	o	o	o	o	o	o
Vitamin E	o	o	o	o	o	o	o	o	o
Calcium	o	o	o	o	o	o	o	o	o
Iron	o	o	o	o	o	o	o	o	o
Zinc	o	o	o	o	o	o	o	o	o
Selenium	o	o	o	o	o	o	o	o	o

19. This section asks about your eating habits **about two years ago.** We ask you to mark the column th best describes how often you ate or drank each of the following foods and beverages at that time.

	Never or less than 1 per month	1-3 per month	1 per week	2-4 per week	5-6 per week	1 per day	2-3 per day	4-5 per day	6+ per day
BEVERAGES MADE WITH WATER									
Coffee (1 cup)	o	o	o	o	o	o	o	o	o
Tea (1 cup)	o	o	o	o	o	o	o	o	o
Orange or grapefruit juice from frozen concentrate (4 oz/115 ml glass)	o	o	o	o	o	o	o	o	o
Other juices or drinks from frozen concentrate (4 oz/115 ml glass)	o	o	o	o	o	o	o	o	o
Drinks from powdered drink crystals (4 oz/115 ml glass)	o	o	o	o	o	o	o	o	o
Tap water (8 oz/230 ml glass)	o	o	o	o	o	o	o	o	o
Bottled water (8 oz/230 ml glass)	o	o	o	o	o	o	o	o	o
OTHER BEVERAGES									
Whole milk (8 oz/230 ml glass)	o	o	o	o	o	o	o	o	o
2% milk (8 oz/230 ml glass)	o	o	o	o	o	o	o	o	o
1% milk (8 oz/230 ml glass)	o	o	o	o	o	o	o	o	o
Skim milk (8 oz/230 ml glass)	o	o	o	o	o	o	o	o	o
Orange or grapefruit juice, fresh, bottled or canned (4 oz/115 ml glass)	o	o	o	o	o	o	o	o	o
Other juices or drinks, fresh, bottled or canned (4 oz/115 ml glass)	o	o	o	o	o	o	o	o	o
Tomato or vegetable juices (4 oz/115 ml glass)	o	o	o	o	o	o	o	o	o
Soft drinks (1 glass/bottle/can)	o	o	o	o	o	o	o	o	o
Beer (1 bottle/can)	o	o	o	o	o	o	o	o	o
Wine (1 glass)	o	o	o	o	o	o	o	o	o
Liquor (1 drink or shot)	o	o	o	o	o	o	o	o	o

(continued)

9. (continued) Please mark the column that best describes how often, on average, you ate these foods **about two years ago.**

	Never or less than 1 per month	1-3 per month	1 per week	2-4 per week	5-6 per week	1 per day	2-3 per day	4-5 per day	6 + per day
FRUIT									
Apples or pears (1)	o	o	o	o	o	o	o	o	o
Oranges (1)	o	o	o	o	o	o	o	o	o
Bananas (1)	o	o	o	o	o	o	o	o	o
Cantaloupe (¼ melon)	o	o	o	o	o	o	o	o	o
Other fruit, fresh or canned (1 piece or ½ cup)	o	o	o	o	o	o	o	o	o
VEGETABLES									
Tomatoes (1 or ½ cup)	o	o	o	o	o	o	o	o	o
Carrots (1 whole or ½ cup)	o	o	o	o	o	o	o	o	o
Broccoli (½ cup)	o	o	o	o	o	o	o	o	o
Cabbage, cauliflower, brussels sprouts (½ cup)	o	o	o	o	o	o	o	o	o
Spinach or other greens (1 serving)	o	o	o	o	o	o	o	o	o
Yellow (winter) squash (½ cup)	o	o	o	o	o	o	o	o	o
Any other vegetable including green beans, corn and peas (½ cup)	o	o	o	o	o	o	o	o	o
Soups with vegetables (1 cup)	o	o	o	o	o	o	o	o	o
Potatoes: baked, boiled (1) or mashed (1 cup)	o	o	o	o	o	o	o	o	o
French fries or fried potatoes (½ cup)	o	o	o	o	o	o	o	o	o
Sweet potatoes (1 or ½ cup)	o	o	o	o	o	o	o	o	o
Tofu or soybeans (3-4 oz/115 ml)	o	o	o	o	o	o	o	o	o
Baked beans or lentils (½ cup)	o	o	o	o	o	o	o	o	o
BREADS AND CEREALS									
Bran or granola cereals, shredded wheat (1 cup)	o	o	o	o	o	o	o	o	o
Other cold cereals (1 cup)	o	o	o	o	o	o	o	o	o
Cooked cereals (1 cup)	o	o	o	o	o	o	o	o	o
White bread (1 slice) or rolls (1)	o	o	o	o	o	o	o	o	o
Dark or whole grain bread (1 slice) or rolls (1)	o	o	o	o	o	o	o	o	o
Rice (1 cup)	o	o	o	o	o	o	o	o	o
Macaroni, spaghetti or noodles (1 cup)	o	o	o	o	o	o	o	o	o

(continued)

19. (continued) Please mark the column that best describes how often, on average, you ate these foods **about two years ago.**

	Never or less than 1 per month	1-3 per month	1 per week	2-4 per week	5-6 per week	1 per day	2-3 per day	4-5 per day	6 + per day
MEAT, POULTRY, FISH, EGGS & CHEESE									
Chicken or turkey (4 oz/115 ml)	o	o	o	o	o	o	o	o	o
Beef, pork or lamb as a main dish (steak, roast, ham) (4 oz/115 ml)	o	o	o	o	o	o	o	o	o
Beef, pork or lamb as a mixed dish (stew or casserole, pasta dish) (4 oz/115 ml)	o	o	o	o	o	o	o	o	o
Hamburger (1)	o	o	o	o	o	o	o	o	o
Hot dogs (1)	o	o	o	o	o	o	o	o	o
Luncheon meats (salami, bologna) (1 piece or slice)	o	o	o	o	o	o	o	o	o
Smoked meat or corned beef (1 piece or slice)	o	o	o	o	o	o	o	o	o
Bacon (1 slice)	o	o	o	o	o	o	o	o	o
Sausage (1)	o	o	o	o	o	o	o	o	o
Liver (4 oz/115 ml)	o	o	o	o	o	o	o	o	o
Fish, fresh, frozen or canned (4 oz/115 ml)	o	o	o	o	o	o	o	o	o
Fish, smoked, salted or dried (4 oz/115 ml)	o	o	o	o	o	o	o	o	o
Eggs (1)	o	o	o	o	o	o	o	o	o
Cheese other than cottage cheese (1 slice or 1 oz)	o	o	o	o	o	o	o	o	o
SWEETS									
Cake (1 slice)	o	o	o	o	o	o	o	o	o
Cookies (1)	o	o	o	o	o	o	o	o	o
Doughnuts, pastry (1)	o	o	o	o	o	o	o	o	o
Pies (1 slice)	o	o	o	o	o	o	o	o	o
Ice cream (½ cup)	o	o	o	o	o	o	o	o	o
Chocolate (1 small bar or 1 oz)	o	o	o	o	o	o	o	o	o
MISCELLANEOUS									
Potato chips (small bag or 45g)	o	o	o	o	o	o	o	o	o
Peanut butter (1 tbsp)	o	o	o	o	o	o	o	o	o
Nuts (1 oz/30g)	o	o	o	o	o	o	o	o	o
Margarine on bread or vegetables (1 pat or tsp)	o	o	o	o	o	o	o	o	o
Butter on bread or vegetables (1 pat or tsp)	o	o	o	o	o	o	o	o	o
Mayonnaise or salad dressing on bread or in salads (1 tbsp)	o	o	o	o	o	o	o	o	o

20. About two years ago:

	Seldom or Never	Sometimes	Often or Always
How often did you **add salt** to your food?	o	o	o
How often did you **add pepper** to your food?	o	o	o
How often did you have **onions or garlic** in your food?	o	o	o
How often did you **eat the skin on chicken**?	o	o	o
How often did you **eat the fat on meat**?	o	o	o

21. What kinds of fat did you usually use in cooking about 2 years ago?
Mark only 1 or 2.

- o Block or stick margarine
- o Soft tub margarine
- o Low-calorie margarine
- o Shortening
- o Butter
- o Oil
- o Lard, baconfat, fatback
- o Non-stick spray or no fat
- o Don't know or don't cook

22. What kinds of fat did you usually put on bread, potatoes and vegetables about 2 years ago?
Mark only 1 or 2.

- o Block or stick margarine
- o Soft tub margarine
- o Low-calorie margarine
- o Butter
- o Cream cheese
- o Didn't add fat

23. Summary Questions

About 2 years ago:

	Never or less than 1 per month	Less than 1 per week	1 to 2 per week	3 to 4 per week	5 to 6 per week	1 per day	1½ per day	2 per day	3 per day	4 + per day
How often did you use **fat or oil in cooking**?	o	o	o	o	o	o	o	o	o	o
Not counting salad or potatoes, how many **servings of vegetables** did you eat?	o	o	o	o	o	o	o	o	o	o
Not counting juices, how many **servings of fruit** did you eat?	o	o	o	o	o	o	o	o	o	o
How often did you eat **fried food from a restaurant or take-out**? (for example, french fries, fried chicken, fried fish)	o	o	o	o	o	o	o	o	o	o

24. We have a few questions about your usual eating habits 20 years ago. What you have just told us about the different places you have lived and worked might help in remembering back to your eating habits at that time.

For each of the following foods and beverages, please indicate whether you usually ate or drank more or less 20 years ago than you did about 2 years ago. Please mark the appropriate column for each food or beverage.

Compared to 2 years ago, 20 years ago I used to consume:	Much less	Some-what less	About the same amount	Some-what more	Much more
Beef, pork or lamb	o	o	o	o	o
Chicken or fish	o	o	o	o	o
Milk	o	o	o	o	o
Vegetables	o	o	o	o	o
Fruit	o	o	o	o	o
Bread	o	o	o	o	o
Margarine	o	o	o	o	o
Butter	o	o	o	o	o
Fried foods	o	o	o	o	o
Sweets	o	o	o	o	o
Tea	o	o	o	o	o
Coffee	o	o	o	o	o
Soft Drinks	o	o	o	o	o
Alcohol	o	o	o	o	o

25. About how many times have you gone on a diet to lose weight during your adult life?

- o Never
- o 1 to 2 times
- o 3 to 5 times
- o 6 to 8 times
- o 9 to 11 times
- o 12 or more times

PHYSICAL ACTIVITY

26. About 2 years ago, how often did you do the following activities, on average?

	Which seasons?					How often?					Time per session			
	Never	Spring	Summer	Fall	Winter	Less than 1 per month	1-3 per month	1-2 per week	3-6 per week	Every day	Less than 15 minutes	15-30 minutes	31-60 minutes	60+ minutes
Walking for exercise	o	o	o	o	o	o	o	o	o	o	o	o	o	o
Jogging or running	o	o	o	o	o	o	o	o	o	o	o	o	o	o
Gardening or yard work	o	o	o	o	o	o	o	o	o	o	o	o	o	o
Home exercises or exercise class	o	o	o	o	o	o	o	o	o	o	o	o	o	o
Golf	o	o	o	o	o	o	o	o	o	o	o	o	o	o
Tennis or squash	o	o	o	o	o	o	o	o	o	o	o	o	o	o
Bowling or curling	o	o	o	o	o	o	o	o	o	o	o	o	o	o
Swimming or water exercises	o	o	o	o	o	o	o	o	o	o	o	o	o	o
Skiing or skating	o	o	o	o	o	o	o	o	o	o	o	o	o	o
Bicycling	o	o	o	o	o	o	o	o	o	o	o	o	o	o
Social dancing	o	o	o	o	o	o	o	o	o	o	o	o	o	o
Other strenuous exercise	o	o	o	o	o	o	o	o	o	o	o	o	o	o

OTHER GENERAL INFORMATION

27. What was the approximate total income for all household members from all sources, before income taxes, in an average year during the last 5 years?

- o less than $10,000
- o $10,000 - $19,999
- o $20,000 - $29,999
- o $30,000 - $49,999
- o $50,000 - $99,999
- o greater than $100,000
- o prefer not to answer

28. How many members are there in your household in total?

[ ] persons

WOMEN:
Please continue to the next page.

MEN:
You have now completed the questionnaire.

Please take a moment to fill in any questions you may have missed.

THANK YOU VERY MUCH
for taking the time to fill out this questionnaire. Your participation is sincerely appreciated.

Please return this completed questionnaire in the self-addressed envelope.

QUESTIONS FOR FEMALES ONLY

MENSTRUATION

29. How old were you when you had your first menstrual period?

    [ ] years old
    o Don't remember
    o Haven't menstruated → Go to 33

30. Between the ages of 10 and 30, did your menstrual periods tend to occur regularly or irregularly (menstrual cycles varied by more than 10 days in length)? Please exclude any time when you were pregnant or using birth control pills.

    o Regularly o Irregularly

31. How old were you when you had your last menstrual period?

    [ ] years old
    o Still menstruate → Go to 33

32. How did your menstrual periods stop?
    o Naturally--that is, as part of the change of life
    o As a result of a hysterectomy (removal of womb)
    o Following radiation
    o Other -- Please specify:

    _____

33. Have you had an operation to remove BOTH your ovaries?
    o No
    o Yes → At what age? If they were removed on two separate occasions, record when your second ovary was removed.
    At age [ ] years

34. Do you have mammograms (x-rays of the breast) performed on a routine basis (every two years)?
    o No
    o Yes → First mammogram at age [ ] years

PREGNANCIES

35. Have you ever been pregnant?
    o No → Go to bottom of page.
    o Yes

36. How many times have you been pregnant? Include live births, stillbirths, miscarriages, abortions and ectopic (tubal) pregnancies.
    [ ] times

37. How old were you at the end of your first pregnancy?

    [ ] years old

38. How many of your pregnancies were live births?
    [ ] live births o none

39. How old were you at the end of your first pregnancy which lasted 5 months or more?
    [ ] years old

40. For how many months in total did you breastfeed? (Add the number of months that you breastfed after each birth to give the total number of months.)
    [ ] months o never breastfed

Please take a moment to fill in any questions you may have missed.

THANK YOU VERY MUCH for taking the time to fill out this questionnaire. Your participation is sincerely appreciated.

Please return this completed questionnaire in the self-addressed envelope.

10.2. Appendix B - Initial Food group allocations

1. Frozen juice in the CNF non-specific fruit juices seem to appear in the beverage category, and thus was placed in this group
2. Fresh juice the CNF is not specific about juices, but bottled unspecified drinks are in the beverage category, thus placed in the beverage food group
3. Beef, pork or lamb as a main dish, but the CNF divides meats types down into subtypes (beef, pork...). Thus, beef, pork or lamb as a main dish were placed in beef products food group
4. Hamburger in questionnaire does not specify type, if fast food or home made, so it was assumed to be fast food and placed in fast food food group
5. Same rationale used for hamburgers was used in placing hot dogs in fast food food group
6. Smoked meat includes both smoked meat and corned beef. Corned beef was found within the beef products food group, and placed in that group.
7. Liver was assumed to be beef liver, thus placed in beef products food group
8. Smoked fish was not found in CNF, it was placed within the finfish and shellfish food group
9. Mixed beef dishes is the only mixed dish inquired about on the questionnaire, as such it was placed in beef products food group rather than the mixed dish food group.

The Canadian nutrient file food groups and the associated foods from the NECSS questionnaire		
No	Food Groups	Food Items
1	DAIRY AND EGG PRODUCTS	Whole milk, 2% milk, 1% milk, skim milk, cheese, eggs, butter
2	SPICES AND HERBS	None
3	BABYFOODS	None
4	FATS AND OILS	Margarine, Mayonnaise
5	POULTRY PRODUCTS	Chicken
6	SOUPS, SAUCES, AND GRAVIES	Soups
7	SAUSAGES AND LUNCHEON MEATS	Luncheon meats, sausage
8	BREAKFAST CEREALS	Granola, cold cereal, cooked cereal
9	FRUITS AND FRUIT JUICES	Orange juice fresh, Orange juice frozen, apples, oranges, bananas, cantaloupe, other fruit
10	PORK PRODUCTS	Bacon
11	VEGETABLES AND VEGETABLE PRODUCTS	Tomato juice, tomatoes, carrots, broccoli, cabbage, spinach, squash, other vegetables, potatoes, fries, sweet potatoes
12	NUTS AND SEEDS	Nuts
13	BEEF PRODUCTS	Beef as a main dish, smoked meat, liver, Beef as a mixed dish
14	BEVERAGES	Coffee, Tea, frozen juice, powdered drinks, tap water, bottled water, fresh juice, pop, beer, wine, liquor,
15	FINFISH AND SHELLFISH PRODUCTS	Fresh fish, smoked fish
16	LEGUMES AND LEGUME PRODUCTS	Tofu, lentils, peanut butter,
17	LAMB, VEAL, AND GAME	None
18	BAKED PRODUCTS	White bread, dark bread, cake, cookies, doughnut, pies,
19	SWEETS	Ice cream, chocolate,
20	CEREALS, GRAINS AND PASTA	Rice, pasta
21	FAST FOODS	Hamburger, hotdog,
22	MIXED DISHES	None
25	SNACKS	Chips

10.3. Appendix C - Nutrient Conversion Amalgams

Appendix C. Dietary Variable Definitions for Nutrient Conversion				
Variable Name	Serving Size In Questionnaire	Variable Description From Questionnaire	Portion Used in Nutriwatch	Decision and nutriwatch food code(s) (first number is CFC in Nutriwatch)
Whole_mi	8oz/230 ml glass	Whole Milk	230 ml	12077 - Milk, Fluid, Whole, Pasturized, Homgenized. 3.3% B.F.
two_milk	8oz/230 ml glass	2% Milk	230 ml	10079 - Milk, fluid, partly skimmed. 2% B.F.
one_milk	8oz/230 ml glass	1% Milk	230 ml	10082 - Milk. Fluid, partly skimmed 1% B.F.
skim_mil	8oz/230 ml glass	Skim Milk	230 ml	12085 - Milk, Fluid, Skim
eggs	1	Eggs	1 Large (50g)	13123 - Egg, chicken, whole, fresh or frozen. raw
cheese	1 slice/1 oz	Cheese other than Cottage cheese	1 oz/3	Amalgam of: 1) 13009 cheese cheddar 2) 10027 cheese mozzarella (48% water 25% bf) 3) 13042 cheese processed cheddar
butt_veg	1 pat or tsp	Butter on bread or vegetables	1 pat (5g)	13001 Butter, Regular
Marg_veg	1 pat or tsp	Margarine on bread or vegetables	5g/2	Amalgam of: 1) 43132 margarine, stick, unspecified veg oils 2) 43130 margarine, tub, unspecified veg oils
mayo	1 tbsp	Mayonnaise or salad dressing on bread or in salads	1 tbsp	Amalgam of: 1) 45018 - Salad dressing, commercial Mayonnaise type >35% oil 2) 45025 salad dressing, mayonnaise > 65% oil 3) 45114 salad dressing commercial, Italian (regular) 4) 45017 salad dressing, commercial, thousand island (regular) 5) 554020 salad dressing, commercial, mayonnaise, light kraft
Chicken	4 oz/ 115 ml	Chicken or Turkey	4 oz/2	Amalgam of: 1) 56060 - Chicken Broiler Breast Meat + Skin Air Chill Roasted 2) 50192 turkey all classes breast meat and skin roasted
Soups	1 cup	Soups with vegetables	1 cup	60468 - Soup, Canned, Vegetable, Vegetarian, Condensed + Water Used vegetarian version because question is in vegetable section of questionnaire and only specifies vegetables and no other soup in list was vegetable. As well used '+ water' designation under assumption that soup is prepared as per instructions on the can
Lunch_me	1 piece/slice	Luncheon Meats (salami/bologna)	1) 1x1/6 175G slice/3, 2) 29.2 g/3 3) 1X1DMx0.3 SL/3	Amalgam of: 1) 73068 - salami cooked beef 2) 76009 Salami pork cooked 3) 73008 Bologna, Beef and Pork
sausage	1	Sausage	1) 1x3DMx10 Link/2 2) 1Xlink/2	Amalgam of: 1) 70075 smoked link sausage pork and beef 2)70089 Italian Sausage Fresh pork cooked

Granola	1 cup	Bran or granola cereals, shredded wheat	1 Cup/5	Amalgam of: 1) 87001 - Cereal. RTE. All bran. Kellogg's 2) 86005 - cereal RTE bran flakes post 3) 80037 - cereal RTE granola homemade 4) 86018 Cereal RTE harvest crunch original Quaker 5) 86148 cereal RTE Shredded Wheat Spoon size post (picked because normal can't be converted into cups)
cld_cere	1 cup	Other cold cereals	1 cup/3	Amalgam of: 1) 87013 cereal RTE Cheerios General mills 2) 86020 cereal rte corn flakes Kellogg's 3) 86065 cereal rte rice krispies Kellogg's
ck_cerea	1 cup	Cooked cereals	1 cup/5	Amalgam of: 1) 86503 cereal hot cream of wheat regular ppd nabisco 2) 86523 cereal hot oats instant; regular ppd quaker 3) 86578 cereal hot oats large flake ppd quaker 4) 86541 cereal hot oats porridge ppd rogers 5) 86545 cereal, hot, red river, ppd, robin hood
Orang_fz	4 oz/115 ml glass	Orange or grapefruit juice from frozen concentrate	115 ml/2	Amalgam of: 1) 93215 orange juice frozen concentrate diluted 2) 93126 grapefruit juice frozen concentrate diluted
orang_fr	4 oz/115 ml glass	Orange or grapefuit juice, fresh, bottled or canned	115 ml/3	Amalgam of : 1) 93207 orange juice canned 2) 90124 grapefruit juice canned sweetened 3) 93123 grapefruit juice canned unsweetened
apples	1	Apples or pears	1)1x7cm fruit/2 2) 1x8.9x6.4 fruit/2	Amalgam of: 1) 93003 apples raw with skin 2) 93252 pears raw with skin
oranges	1	Oranges	1x6.7 dm fruit	93200 oranges all commercial varieties raw
bananas	1	Bananas	1x22x3.6 fruit dm	93040 bananas raw
cantalou	1/4 melon	Canaloupe	.5x.5x1.2 13 dm fruit	93181 melons cantaloupe raw

fruit	1 piece or 1/2 cup	Other fruit, fresh or canned	½ cup/16	Amalgam of: 1) 93132 grapes 2) 90070 cherry 3) 93236 peaches 4) 93266 pineapple 5) 93279 prunes 6) 93316 strawberries 7) 90021 apricots 8) 90176 mangoes 9) 93302 raspberries 10) 93050 blueberries 11) 90107 gooseberries 12) 90097 fruit salad 13) 93104 fruit salad 14) 90100 fruit salad 15) 93089 figs 16) 93087 dates
Bacon	1 slice	Bacon	1xmedium slice	103123 pork cured bacon raw
Tom_juic	4oz/115 ml glass	Tomato or vegetable juices	115 ml	Amalgam of: 1) 113540 tomato juice canned 2) 113578 vegetable juice cocktail canned
tomatoes	1 or 1/2 cup	Tomatoes	1x6.6dm tomato	113529 tomatoes red ripe raw
carrots	1 whole or 1/2 cup	Carrots	1) 1x20cmx2.5cm dm/2 2) .5xcup/2	Amalgam of: 1) 113124 carrots raw 2) 113125 carrots boiled drained
broccoli	1/2 cup	Broccoli	.5xcup/2	Amalgam of: 1) 113090 broccoli raw 2) 113091 broccoli boiled drained
cabbage	1/2 cup	Cabbage, cauliflower, brussels sprouts	.5 cup/6	Amalgam of: 1) 112109 cabbage raw 2) 112110 cabbage boiled drained 3) 113135 cauliflower raw 4) 110136 cauliflower boiled drained 5) 113098 Brussels sprouts raw 6) 113099 Brussels sprouts boiled drained
spinach	1 serving	Spinach or other greens	1/2 cup/2	Amalgam of: 1) 110457 spinach raw 2) 110458 spinach boiled drained
squash	1/2 cup	Yellow (winter) squash	.5 cup	113486 - squash winter butternut baked
other_ve	1/2 cup	Any other vegetables including green beans, corn and peas	.5 cup/7	Amalgam of: 1) 113053 beans, snap (Italian/yellow/green) boiled, drained 2) 110168 - corn sweet on or off cob boiled drained 3) 113179 corn sweet yellow frozen kernels off cob boiled drained 4) 113911 corn sweet white frozen kernels off cob boiled - salt 5) 113313 peas green frozen boiled drained 6) 113305 peas green boiled drained 7) 113308 peas green canned drained solids
potatoes	1 or 1 cup	Baked, boiled or mashed	1) 1x12x6 dm potato/3 2) 1 cup/3 3) 1 cup/3	Amalgam of: 1) 113674 potatoes baked flesh and skin 2) 113367 potatoes boiled cooked without skin flesh drained 3) 110657 potatoes mashed home-prepared + whole milk (no non-milk option, only milk or milk and butter/margarine)

fries	1/2 cup	French fries or fried potatoes	.5 cup/3	Amalgam of: 1) 113403 potatoes french-fried frozen home prepared in oven - salt 2) 110370 potatoes hashed brown home prepared 3) 113404 potatoes french-fried frozen restaurant ppd veg oil
sw_potat	1 or 1/2 cup	Sweet potatoes	.5 cup	110508 sweet potatoes baked in skin
Nuts	1 oz/ 30 g	Nuts	1 oz/3	Amalgam of: 1) 120635 nuts mixed dry roasted with peanuts salt added 2) 120637 nuts mixed oil roasted with peanuts salt added 3) 122138 nuts mixed oil roasted without peanuts salt added
Beef_mai	4 oz/ 115 ml	Beef, pork or lamb as a main dish (steak, roast, ham)	4 oz	Composite dish of: 1) 131306 beef ground medium broiled well done 2) 170225 lamb, American, ground, broiled 3) 170143 veal ground broiled 4) 100220 pork, fresh, ground, cooked
smk_meat	1 piece or slice	Smoked meat or corned beef	1 slice	133348 beef cured corned beef canned
liver	4 oz/ 115 ml	Liver	4 oz/2	Amalgam of: 1) 130326 beef liver braised 2) 130327 beef liver pan-fried
Beef_mix	4 oz/ 115 ml	Beef, pork or lamb as a mixed dish (stew or casserole, pasta dish)	4 oz/2	Composite dish of: 1) 60160 – soup, home-prepared, beef stew 2) 372 beef and vegetable stew: canned
Coffee	1 cup	Coffee	1 cup/2	Amalgam of: 1) 140209 coffee brewed 2) 140215 coffee instant regular powder + water
Tea	1 cup	Tea	1 cup/3	Amalgam of: 1) 140355 tea brewed 2) 140545 tea chamomile brewed 3) 140381 tea herb brewed
juice_fz	4 oz/115 ml	Other juices or drinks from frozen concentrate	115 ml/3	Amalgam of: 1) 90018 apple juice frozen concentrate diluted added no vitamin C 2)140406 fruit punch juice drink frozen concentrate + water 3) 93137 grape juice frozen concentrate sweetened diluted + vit c
pwd_drin	4 oz/115 ml	Drinks from powdered drink crystals	115 ml/3	Amalgam of: 1) 141408 orange flavour drink + vitamin C powder + water 2) 146266 fruit punch flavour drink powder + water 3) 146297 lemonade flavour drink powder + water
tap_wate	8 oz/ 230 ml glass	Tap water	230 ml	140429 water municipal
bot_wate	8 oz/230 ml glass	Bottled water	230 ml/2	Amalgam of: 1) 140384 water mineral bottled perrier 2) 140385 water mineral bottled poland springs

juice_fr	4 oz/ 115 ml glass	Other juices or drinks, fresh, bottled or canned	115 ml/3	Amalgam of: 1) 90016 apple juice canned or bottled without added vit c 2) 90135 grape juice canned or bottled 3) 91080 cranberry juice cocktail bottled
pop	1 glass/bottle/can	Soft drinks	355 ml/4	Amalgam of: 1) 140400 carbonated drinks pop cola coke/pepsi soda 2) 140416 carbonated drinks pop cola coke/pepsi aspartame sweetened 3)140136 carbonated drinks pop ginger ale soda 4) 140150 carbonated drinks pop orange soda
beer	1 bottle/can	Beer	341 ml bottle	141003 alcoholic beer regular (5% alcohol by volume)
wine	1 glass	Wine	4 fluid oz	140084 alcoholic wine table all (11.5% alcohol by volume)
liquor	1 drink or shot	Liquor	1 fluid oz/3	Amalgam of: 1) 140050 alcoholic rum (40% alcohol by volume) 2) 140051 alcoholic vodka (40% alcohol by volume) 3) 140037 alcoholic whisky (40% alcohol by volume)
Fresh_fi	4oz/115 ml	Fish, fresh, frozen or canned	4oz/6	Amalgam of: 1) 150186 tuna white canned in water, drained unsalted 2) 150185 tuna white canned in oil drained unsalted 3) 153182 salmon sockeye (red) canned solids + bone + liquid - salt 4)153181 salmon pink (humpback) canned solids+bone+liquid - salt 5) 150027 fish portions and sticks frozen and reheated 6) 210047 fast food fish fillet battered or breaded fried
smk_fish	4oz/115 ml	Fish, smoked, salted or dried	4oz/2	Amalgam of: 1) 150075 sablefish (black cod) smoked 2) 150131 whitefish lake mixed species smoked
Tofu	3-4 oz/115ml	Tofu or soybeans	3.5 oz/4	Amalgam of: 1) 163427 tofu, regular raw prepared with calcium sulfate 2) 163127 tofu, regular raw prepared with magnesium sulfate 3) 163429 tofu, fried (prepared with calcium sulfate) 4) 163129 tofu, fried (prepared with magnesium sulfate)
Lentils	1/2 cup	Baked beans or lentils	.5 cup/2	Amalgam of: 1) 160006 beans baked canned plain or vegetarian 2) 163070 lentils boiled

Peanut_b	1 tbsp	Peanut butter	1 tbsp/4	Amalgam of: 1) 160397 peanut butter chunk type fat and sugar added 2) 160097 peanut butter chunk type fat sugar and salt added 3) 163398 peanut butter smooth type fat and sugar added 4) 163098 peanut butter smooth type fat sugar and salt added
Wht_brea	1 slice or 1 roll	White bread or rolls	1) 1 slice/2 2) 1 roll/2	Amalgam of: 1) 183069 bread white (includes soft crumbs commercial 2) 183342 rolls dinner plain (+brown and serve) commercial
dark_bre	1 slice or roll	Dark or whole grain bread or rolls	1) 1 slice/3 2) 1 slice/3 3) 1 roll/3	Amalgam of: 1) 180035 bread mixed-grain (+ whole-grain 7-grain) 2)183075 bread whole wheat commercial 3) 180348 rolls dinner whole-wheat
cake	1 slice	Cake	1/12 of a cake/5	Amalgam of: 1) 180088 cake angelfood dry mix prepared 2) 180100 cake chocolate (devil's food fudge) dry mix prepared 3) 180451 cake pound commercial 1.2% fat 4) 180133 cake sponge commercial 5) 180138 cake white dry mix regular prepared without icing
Cookies	1	Cookies	1) 1x5.7 cm dm/5 2) 1xcookie/5 3) 1x6.7cm dm/5 4) 1xcookie/5 5) 1xcookie/5	Amalgam of: 1) 180159 cookies chocolate chip commercial 18-28% fat 2)553021 cookies chocolate sandwich oreo fat christie 3)180178 cookies oatmeal (+ or - raisins) commercial 4) 180185 cookies peanut butter commercial 5) 180204 cookies sugar commercial
Doughnut	1	Doughnuts or pastry	1) 1x10.8 cm dm/5 2-3) 1x9.5cm dm/5 4-5) 1x8.9x6.3/5	Amalgam of: 1) 180246 danish pastry fruit (apple, raisin, lemon, raspberry etc) 2) 181251 doughnuts cake-type chocolate sugared or glazed 3)180250 doughnuts cake type plain sugared or glazed 4) 180254 doughnuts yeast-leavened crème filled 5) 180256 doughnuts yeast-leavened jelly filled
Pies	1 slice	Pies	1-3) 1x1/8 23 cm dm/6 4-6) 1x1/6 20 cm dm/6	Amalgam of: 1) 180301 pie apple commercial 2 crusts 2) 181305 pie blueberry commercial 2 crusts 3) 181308 pie cherry commercial 2 crusts 4) 180320 pie lemon meringue commercial 5) 180310 pie chocolate crème commercial 6) 181326 pie pumpkin commercial

Ice_crea	1/2 cup	Ice cream	.5 cup/3	Amalgam of: 1) 190270 dessert frozen icecream chocolate 2)190271 dessert frozen ice cream strawberry 3) 190095 dessert frozen ice cream vanilla 11% bf
Chocolat	1 small bar or 1 oz	Chocolate	1) 1xbar 50g/2 2) 1x41g bar/2	Amalgam of: 1) 190120 candies bars or chips milk chocolate plain 2) 190081 candies bars sweet chocolate
Rice	1 cup	Rice	1 cup/2	Amalgam of: 1) 203037 grain rice brown long-grain cooked 2) 203445 grain rice white long-grain regular cooked
Pasta	1 cup	Macaroni, spaghetti or noodles	1 cup/3	Amalgam of: 1) 203100 pasta macaroni (elbow) cooked 2) 200121 pasta spaghetti cooked 3) 200110 pasta noodles egg cooked
Hamburge	1	Hamburger	1 burger	210107 hamburger regular single patty plain
Hotdog	1	Hot dogs	1 hotdog	210118 fastfood hotdog plain
Chips	Small bags or 45g	Potato chips	45 grams	196411 snacks potato chips plain

10.4. Appendix D – Nutriwatch Output

This day contains the following nutrients:

Protein g	0.7	1%	Tot Fat g	0.1	0%	Carbohyd g	12.4	
Calories kC	52	2%	Sugars T g	6.5	?	Choleste mg	?	
Diet Fib g	0.5	3%	Fibre In g	0.0	?	Pectin g	0.5	
Sodium mg	1	0%	Potassiu mg	198	9%	Magnesiu mg	13	
Selenium ug	?	?	Calcium mg	10	1%	Phosphor mg	18	
Iron mg	0.14	2%	Zinc mg	0.06	1%	Tot Caro RE	5	
Vit A RE	5	1%	Vit C mg	44	110%	Vit D ug	?	
Thiamin mg	0.07	7%	Riboflav mg	0.02	2%	Niacin NE	0.3	
Vit B6 mg	0.053	6%	Vit B12 ug	?	?	Panto Ac mg	0.21	
Folate ug	28.9	13%	Tryptoph g	0.001	?	Threonin g	0.005	
Isoleuci g	0.004	?	Leucine g	0.008	?	Lysine g	0.005	
Methioni g	0.002	?	Phenylal g	0.005	?	Valine g	0.007	
FA Sat T g	0.02	0%	FA Mono g	0.02	?	FA Poly g	0.03	
Vit E(Al mg	0.08	1%	Price $	?	?	Caffeine mg	?	
Alcohol g	?	?	Copper mg	0.0	2%	Manganes mg	0	

Energy Breakdown:		
Protein	6%	(recommended 15-20%)
Fat	2%	(recommended < 30%)
Carbohydrate	95%	(recommended > 50%)

Ratios - Calc/Phosph: 0.6 Sodium/Potassium: 0.0
Fat breakdown - Sat: 13.7% Monosat: 14.7% Polyunsat: 23.1% Est Trans:

10.5. Appendix E – Descriptive Statistics for Nutrient Analysis

Descriptive Statistics for Nutrient analysis – Total Analysis				
Nutrient (amount)	Mean	Median	Standard Deviation	Range
Fat (g/day)				
Case	73.9	69.0	33.2	18.0 – 254.4
Control	68.4	63.9	30.6	14.4-204.6
Saturated Fat (g/day)				
Case	25.2	22.5	12.3	5.3-88.3
Control	23.0	21.1	11.2	3.5-81.5
Mono-Unsaturated Fat (g/day)				
Case	30.4	27.8	14.7	6.8-119.5
Control	28.3	25.8	13.7	5.0-92.0
Poly-Unsaturated Fat (g/day)				
Case	11.0	10.2	4.9	1.9-38.7
Control	10.5	9.6	5.0	1.6-40.6
Protein (g/day)				
Case	75.7	71.8	28.4	20.8-244.9
Control	71.7	66.9	28.8	21.0-381.7
Carbohydrates (g/day)				
Case	270.0	253.7	103.9	71.5-747.9
Control	260.6	242.2	100.3	64.8-824.4
Dietary Fibre (g/day)				
Case	17.2	15.6	8.7	2.1-78.6
Control	17.2	15.6	9.4	2.2-90.7
Sugar (g/day)				
Case	65.4	57.1	39.0	4.7-303.3
Control	61.0	52.6	37.1	2.6-270.8
Energy (kcal/day)				
Case	2086.4	1962.6	738.0	700.2-4909.7
Control	1994.6	1888.3	709.7	706.6-4847.6
Iron (mg/day)				
Case	13.1	12.2	5.1	3.6-42.3
Control	12.6	11.8	4.9	3.3-32.3
Calcium (mg/day)				
Case	905.0	810.3	488.7	164.2-3677.0
Control	830.1	698.9	471.1	82.9-3885.0
Zinc (mg/day)				
Case	10.2	9.8	3.8	3.1-28.4
Control	9.6	9.0	3.6	3.0-33.3
Phosphorous (mg/day)				
Case	1330.9	1278.3	532.7	351.1-3914.3
Control	1259.7	1150.0	536.7	304.1-5333.5
Sodium (mg/day)				
Case	2156.0	2012.0	945.6	485.3-10394.6
Control	2019.8	1866.9	867.3	266.8-6052.1
Cholesterol (mg/day)				
Case	267.4	236.5	160.4	52.6-1631.3
Control	251.3	224.1	147.9	16.4-1140.9

Descriptive Statistics for Nutrient analysis - Seminomas				
Nutrient (amount)	Mean	Median	Standard Deviation	Range

Fat (g/day)				
Case	72.6	67.6	32.0	19.0 – 212.9
Control	68.4	63.9	30.6	14.4-204.6
Saturated Fat (g/day)				
Case	24.7	22.1	12.1	5.9-83.0
Control	23.0	21.1	11.2	3.5-81.5
Mono-Unsaturated Fat (g/day)				
Case	29.9	27.6	14.1	6.8-88.5
Control	28.3	25.8	13.7	5.0-92.0
Poly-Unsaturated Fat (g/day)				
Case	10.9	10.2	4.7	1.9-32.9
Control	10.5	9.6	5.0	1.6-40.6
Protein (g/day)				
Case	74.6	70.5	27.5	24.8-206.0
Control	71.7	66.9	28.8	21.0-381.7
Carbohydrates (g/day)				
Case	267.0	256.8	99.3	71.5-731.6
Control	260.6	242.2	100.3	64.8-824.4
Dietary Fibre (g/day)				
Case	17.2	16.2	8.5	2.1-60.1
Control	17.2	15.6	9.4	2.2-90.7
Sugar (g/day)				
Case	63.9	57.0	36.6	8.0-253.7
Control	61.0	52.6	37.1	2.6-270.8
Energy (kcal/day)				
Case	2062.1	1976.6	704.9	700.2-4786.1
Control	1994.6	1888.3	709.7	706.6-4847.6
Iron (mg/day)				
Case	12.9	12.4	4.8	3.6-33.9
Control	12.6	11.8	4.9	3.3-32.3
Calcium (mg/day)				
Case	889.0	796.9	511.0	183.7-3677.0
Control	830.1	698.9	471.1	82.9-3885.0
Zinc (mg/day)				
Case	10.1	9.6	3.8	3.9-28.4
Control	9.6	9.0	3.6	3.0-33.3
Phosphorous (mg/day)				
Case	1318.7	1264.1	546.1	485.3-10394.6
Control	1259.7	1150.0	536.7	304.1-5333.5
Sodium (mg/day)				
Case	2156.0	2012.0	945.6	485.3-10394.6
Control	2019.8	1866.9	867.3	266.8-6052.1
Cholesterol (mg/day)				
Case	266.4	233.9	169.0	61.5-1631.3
Control	251.3	224.1	147.9	16.4-1140.9

Descriptive Statistics for Nutrient analysis – Non-Seminomas				
Nutrient (amount)	Mean	Median	Standard Deviation	Range
Fat (g/day)				
Case	78.5	71.4	36.0	18.0 – 221.6
Control	68.4	63.9	30.6	14.4-204.6
Saturated Fat (g/day)				
Case	26.9	24.0	12.1	5.3-75.6
Control	23.0	21.1	11.2	3.5-81.5
Mono-Unsaturated Fat (g/day)				
Case	32.4	29.8	15.8	7.5-101.3
Control	28.3	25.8	13.7	5.0-92.0
Poly-Unsaturated Fat (g/day)				
Case	11.6	10.5	5.6	3.0-38.7
Control	10.5	9.6	5.0	1.6-40.6
Protein (g/day)				
Case	78.7	75.7	30.6	20.8-244.9
Control	71.7	66.9	28.8	21.0-381.7
Carbohydrates (g/day)				
Case	280.0	250.4	117.9	111.5-747.9
Control	260.6	242.2	100.3	64.8-824.4
Dietary Fibre (g/day)				
Case	17.6	14.7	10.1	4.7-78.6
Control	17.2	15.6	9.4	2.2-90.7
Sugar (g/day)				
Case	69.4	60.8	43.1	14.3-303.3
Control	61.0	52.6	37.1	2.6-270.8
Energy (kcal/day)				
Case	2177.0	2023.7	836.6	764.4-4909.7
Control	1994.6	1888.3	709.7	706.6-4847.6
Iron (mg/day)				
Case	13.6	12.2	5.8	4.4-42.3
Control	12.6	11.8	4.9	3.3-32.3
Calcium (mg/day)				
Case	943.7	865.4	480.0	164.2-2594.8
Control	830.1	698.9	471.1	82.9-3885.0
Zinc (mg/day)				
Case	10.6	9.9	4.1	3.1-28.1
Control	9.6	9.0	3.6	3.0-33.3
Phosphorous (mg/day)				
Case	1370.9	1310.5	551.0	351.1-3083.6
Control	1259.7	1150.0	536.7	304.1-5333.5
Sodium (mg/day)				
Case	2236.4	2077.9	951.7	746.9-5367.2
Control	2019.8	1866.9	867.3	266.8-6052.1
Cholesterol (mg/day)				
Case	281.7	256.2	152.3	52.6-955.7
Control	251.3	224.1	147.9	16.4-1140.9