Disclosure of Genetic Information for
Personalized Nutrition and Change in Dietary Intake

by

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for the degree of Doctor of Philosophy
Department of Nutritional Sciences
University of Toronto

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Abstract

**Background:** Personal genetic information has become increasingly accessible as a result of consumer genetic tests. Proponents claim that the information may motivate positive behavioural changes aimed at chronic disease prevention, however, the effects of disclosing genetic information on dietary behaviour have not been well explored.

**Objectives:** To determine the effects of DNA-based dietary advice on intakes of caffeine, vitamin C, added sugar and sodium, as well as to explore individual perceptions of genetic testing and personalized nutrition.

**Methods:** A randomized trial was conducted with men and women aged 20-35 years (n=138). Subjects in the intervention group (I) were given DNA-based dietary advice and those in the control group (C) were given general dietary recommendations. Food frequency questionnaires were collected at baseline, 3- and 12-months and general linear models were used to compare changes in intake between groups. A survey was completed at baseline, the intervention point,
and 3- and 12-months to assess perceptions between groups. The chi-square test and Wilcoxon signed-rank test were used to compare responses.

**Results:** Subjects in the intervention group were more likely to agree that the advice would be useful when considering diet (88% [I] vs. 72% [C]; p=0.02). A significant reduction in sodium intake was observed at 12-months among subjects who received DNA-based advice when compared to the control group (mean ± SE: -287.3 ± 114.1 mg/day [I] vs. 129.8 ± 118.2 mg/day [C]; p=0.008). Compared to baseline, subjects rated higher agreement with the statement “I am interested in the relationship between diet and genetics” at 3-months (mean change ± SD: 0.28 ± 0.99, p=0.0002) and 12-months (0.20 ± 1.04, p=0.02). The majority of subjects indicated that a university research lab (47%) or healthcare professional (41%) were the best sources for obtaining accurate personal genetic information, while direct-to-consumer genetic testing company received the fewest selections (12%). Most subjects (56%) considered registered dietitians to be the best source of personalized nutrition.

**Conclusions:** These findings demonstrate that DNA-based dietary advice is more effective than general dietary recommendations at motivating individuals to adopt dietary changes for certain nutrients, and therefore, may be more useful for chronic disease prevention.
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<thead>
<tr>
<th>Abbreviation</th>
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<tbody>
<tr>
<td>ACE</td>
<td>Angiotensin-converting enzyme</td>
</tr>
<tr>
<td>AD</td>
<td>Alzheimer’s disease</td>
</tr>
<tr>
<td>AI</td>
<td>Adequate intake</td>
</tr>
<tr>
<td>ANCOVA</td>
<td>Analysis of covariance</td>
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<tr>
<td>APOB</td>
<td>Apolipoprotein B</td>
</tr>
<tr>
<td>APOE</td>
<td>Apolipoprotein E</td>
</tr>
<tr>
<td>BMI</td>
<td>Body mass index</td>
</tr>
<tr>
<td>CCHS</td>
<td>Canadian Community Health Survey</td>
</tr>
<tr>
<td>CYP1A2</td>
<td>Cytochrome P450 1A2</td>
</tr>
<tr>
<td>DRI</td>
<td>Dietary Reference Intakes</td>
</tr>
<tr>
<td>DTC</td>
<td>Direct-to-consumer</td>
</tr>
<tr>
<td>EAR</td>
<td>Estimated Average Requirement</td>
</tr>
<tr>
<td>FBG</td>
<td>Fasting blood glucose</td>
</tr>
<tr>
<td>FDA</td>
<td>Food and Drug Administration</td>
</tr>
<tr>
<td>FFQ</td>
<td>Food frequency questionnaire</td>
</tr>
<tr>
<td>FH</td>
<td>Familial hypercholesterolemia</td>
</tr>
<tr>
<td>FTO</td>
<td>Fat mass and obesity associated</td>
</tr>
<tr>
<td>GMC</td>
<td>Glutathione S-transferase Mu 1</td>
</tr>
<tr>
<td>GSTT1</td>
<td>Glutathione S-transferase Theta 1</td>
</tr>
<tr>
<td>GWAS</td>
<td>Genome-wide association study</td>
</tr>
<tr>
<td>HOMA-IR</td>
<td>Homeostasis model assessment of insulin resistance</td>
</tr>
<tr>
<td>HOMA-B</td>
<td>Homeostasis model assessment of beta-cell dysfunction</td>
</tr>
<tr>
<td>IOM</td>
<td>Institute of Medicine</td>
</tr>
<tr>
<td>LDL</td>
<td>Low density lipoprotein cholesterol</td>
</tr>
<tr>
<td>LDLR</td>
<td>Low density lipoprotein receptor</td>
</tr>
<tr>
<td>MI</td>
<td>Myocardial infarction</td>
</tr>
<tr>
<td>NCD</td>
<td>Noncommunicable diseases</td>
</tr>
<tr>
<td>NOD2</td>
<td>Nucleotide-binding oligomerization domain-containing protein 2</td>
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</tbody>
</table>
PAPM - Precaution Adoption Process Model
PGT - Personal genome testing
RDA - Recommended Dietary Allowance
RD - Registered Dietitian
RFLP - Restriction fragment length polymorphism
RNI - Recommended Nutrient Intakes
RT-PCR - Real-time polymerase chain reaction
SBP - Systolic blood pressure
SIDE - Software for intake distribution estimation
SNP - Single nucleotide polymorphism
TAS1R2 - Taste receptor type 1 member 2
TC - Total cholesterol
TG - Triglycerides
TNH - Toronto Nutrigenomics and Health Study
UL - Tolerable upper intake level
USDA - United States Department of Agriculture
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Chapter 1

Introduction
1.1 Introduction

Recent advances in genomics technologies have made the acquisition of personalized genetic information easily obtainable. Consumer genetic tests claim to provide consumers with information about their genetic ancestry, ability to metabolize nutrients and drugs, and risk for developing diseases (Janssens and van Duijn, 2010). One class of genetic tests offer personalized dietary advice based on one’s DNA to improve health (Sterling, 2008). These tests are commercially available through the internet and are largely unregulated, though significant measures are being taken to regulate this emerging market in certain jurisdictions (McGuire et al., 2010). In some cases the tests are sold direct-to-consumer (DTC), without involvement of healthcare professionals. DTC genetic testing for disease susceptibility remains controversial, with opponents arguing that the tests possess limited value due to their questionable clinical validity and utility (Burke, 2009; Caulfield, 2010; Eng and Sharp, 2010). Critics note that predicted risks will continue to change as new genetic variants are discovered, and thus any risk estimates for disease based on currently known common variants are premature (Janssens et al., 2011; Mihaescu et al., 2009). Moreover, the corresponding advice with test results is not genuinely personalized since the lifestyle recommendations are generally the same, regardless of genotype.

Despite these criticisms, proponents of DTC genetic tests argue that there is public interest in genomics and that individuals should have access to their own genetic information (Bloss et al., 2011a; Caulfield, 2010). In addition, some propose that direct access to genetic information may motivate consumers to adopt lifestyle behavioural changes aimed at reducing risk of disease development (Bloss et al., 2011b; McBride et al., 2010). Therefore, a potential outcome of these genetic tests is a decrease in the prevalence of chronic diseases, such as type 2
diabetes and cardiovascular disease, due to an increase in preventative strategies through lifestyle modification. However, much debate exists about the influence of genetic information on an individual’s behaviour, and little is known about the influence on dietary behaviour in particular.
Chapter 2

Background and Literature Review
2.1 Modifiable Lifestyle Factors and Chronic Disease

Chronic diseases such as cardiovascular diseases and diabetes are becoming increasingly prevalent around the world. In a 2011 World Health Organization (WHO) report on noncommunicable diseases (NCD) in 193 countries, cardiovascular diseases and diabetes accounted for 51% of deaths globally from NCD (WHO, 2011). In Canada, cardiovascular diseases and diabetes were responsible for 36% of total deaths, regardless of age (WHO, 2011), and 58% of annual healthcare spending (equivalent to $68 billion per year) was directed to chronic diseases in 2010 (Public Health Agency of Canada, 2011). Beyond these direct healthcare costs, productivity and indirect income losses attributable to chronic diseases were estimated at $122 billion (Public Health Agency of Canada, 2011). Productivity losses are expected to rise, since the onset of chronic diseases is increasingly occurring at younger ages (Yates et al., 2012). This is due, in part, to the rising rates of obesity in North America. A recent analysis in Canada reported that adult obesity rates have tripled (from 6.1% to 18.5%) between 1985 and 2011 (Twells et al., 2014).

The WHO has identified three lifestyle factors as the most common modifiable risk factors for chronic diseases: an unhealthy diet, physical inactivity and tobacco use (Strong et al., 2006). Non-modifiable risk factors include age and genetics (WHO, 2005). These three lifestyle factors, along with age and genetics, influence intermediate risk factors of chronic disease, which include hypertension, dysglycemia, dyslipidemia, and overweight or obesity (WHO, 2005). As a result, modifying an individual’s or population’s health behaviours related to diet, physical activity and tobacco use can have a significant impact on chronic disease rates globally (Willett et al., 2006). While all three lifestyle factors are implicated in chronic disease development, the individual relative importance of each may depend on whether the goal is to achieve improved
health at an individual or population level. Indeed, in 1985 the epidemiologist Geoffrey Rose noted that individual and population approaches to health are fundamentally different, since they target different factors that influence health (Rose, 1985). While the “high-risk” individual approach identifies “causes of cases” of an outcome, the population approach identifies “causes of incidence” (Rose, 1985). Rose proposed that a population approach to health intervention could prevent more cases of a disease than an approach that targets high-risk individuals, although he acknowledged that the two are generally not in competition (Rose, 1985).

In this view, several population-based strategies have been or are being developed to target diet, physical activity and tobacco use to reduce the prevalence of chronic diseases. One of the most effective strategies to date is government taxation on tobacco products (Chaloupka et al., 2011). Tobacco taxes have reduced overall tobacco use (Becker et al., 1994; Franz, 2008; Siahpush et al., 2009; Townsend et al., 1994), smoking initiation rates among youth (Cawley et al., 2004; Lewit et al., 1981) and the total number of cigarettes consumed by persistent users (Jimenez-Martin et al., 1998). The success of this initiative has led some to propose taxing unhealthy food products as a way to target overweight and obesity in the population (Pomeranz, 2014). However, those opposed to that proposal point out that tobacco taxes were only one contributor to a decrease in smoking rates, and factors such as indoor smoking bans (Zablocki et al., 2014) and marketing limits (Pierce, 2007) also played an important role. Menu labeling, where nutrient values for calories, fat and/or sodium are clearly displayed on restaurant menus, is another population-based strategy that aims to influence consumer food choices (Wootan, 2007). While menu labeling has been shown to impact consumer behaviour (Gittelsohn et al., 2013), its effectiveness is partly mediated by the availability of healthier options that restaurants provide. To target physical activity, the Canadian government implemented the Children’s Fitness Tax
Credit in 2007, however, the effectiveness of this initiative has not been evaluated and some argue that its impact will be small, since in most cases ≤15% of the total claim is returned the year after it was made (von Tigerstrom et al., 2011). Moreover, no adult equivalent of this tax credit currently exists. Another population target for physical activity that is gaining more attention is the built environment (Trowbridge and Schmid, 2013). Factors such as land use patterns, transportation systems and design features of living places have been shown to affect the physical activity levels of residents (Frank and Engelke, 2011). An example of this relationship is neighbourhood walkability, which was recently shown to be associated with obesity and type 2 diabetes (Booth et al., 2013; Glazier et al., 2014).

Evidently, a number of population-based strategies to target physical activity and diet have been or are being developed. While some of these strategies may be effective, their overall impact on chronic disease rates remains to be determined. Moreover, although Rose argued for a population-based approach to health intervention to be the priority, more recent work raises important counter points. Since the time of Rose’s 1985 publication, there have been improvements in the accuracy with which high-risk individuals can be identified and, therefore, this could potentially lessen the need for population-based strategies (Manuel et al., 2006). In addition, population-based strategies could inadvertently increase social inequalities in health, if the population intervention disproportionately benefited those who were at lower risk to begin with (Frohlich and Potvin, 2008). One proposed approach to mediate a choice between an intervention at either an individual or population level is to focus on vulnerable groups, which are subgroups of the population made vulnerable (i.e. at “higher risk of risks”) to a health outcome because of social characteristics such as income and education (Frohlich and Potvin, 2008). However, the genomic era has provided an opportunity to characterize risk and identify
vulnerable groups based on genetic variation (Burton et al., 2012). Stratifying a population by genetic risk and determining the most appropriate intervention for the different levels of risk may be more effective and less costly than applying a single intervention to an entire population. In particular, nutrigenomics, the study of the relationship between genes and diet, provides a unique opportunity to tailor dietary recommendations to an individual’s genotype and this level of personalization may motivate positive dietary behaviour changes to a greater extent than general dietary recommendations.

2.2 Theories of Health Behaviour Change

Health promoters and healthcare practitioners often target lifestyle as a first line of defense against chronic disease. However, making changes to health behaviours is challenging and promoting dietary change, in particular, can be difficult (Ogden et al., 2007). This is especially evident in weight loss initiatives where, even if initial weight loss is successful, individuals tend to regain much of what was lost within 5 years (Anderson et al., 2001; Barte et al., 2010). The process of behaviour change is complex, with a number of different variables influencing how an individual will respond to a health intervention. Several models and theories of health behaviour change have been developed to assist in understanding the factors that influence health behaviour so that more effective interventions can be designed. Although the present thesis research does not apply a theory of health behaviour change, it is important to acknowledge the utility of these theories and propose their application in future research. Indeed, certain health interventions that apply theories of behaviour change have been shown to be more effective than those that lack a theoretical basis (Webb et al., 2010). Overall, theories of health behaviour can be divided into
three categories of social cognition models: models of individual health behaviour, interpersonal health behaviour and community/group models, however, individual models are the most applicable to research assessing the behavioural impact of genetic testing.

Models of individual health behaviour seek to identify characteristics of individuals and factors that influence individual perceptions that play a role in how a person behaves (Rimer, 2008). These include the consideration of constructs such as one’s values, expectancy beliefs, motivation and intentions (Champion and Skinner, 2008; Montano and Kasprzyk, 2008). Variables such as age, sex, education, socioeconomic status, social norms and cultural beliefs may modify individuals’ perceptions of health risks and associated health behaviours (Champion and Skinner, 2008; Montano and Kasprzyk, 2008). Examples of individual models of health behaviour include the Health Belief Model (Champion and Skinner, 2008) and the Theory of Planned Behaviour (Montano and Kasprzyk, 2008). Stage models are models of individual health behaviour that place less emphasis on the cognitive variables that influence behaviour and more emphasis on a person’s readiness to make behavioural changes (Prochaska et al., 2008). Readiness can be categorized into various stages of change that possess unique constructs and processes that influence one’s behaviour (Prochaska et al., 2008). As a result, tailoring an intervention to an individual’s stage of change may be more effective than applying one uniform intervention. Examples of stage models include the Transtheoretical Model (Prochaska et al., 2008) and the Precaution Adoption Process Model (Weinstein et al., 2008).

The most appropriate behaviour change framework to consider when designing a health intervention will depend on the questions the intervention seeks to answer as well as what constructs of behaviour change will be assessed. There is currently no evidence that suggests one particular theory related to individual health behaviour is superior to another (Brewer and Rimer,
2008). While theories of health behaviour change have been useful for understanding variables that influence human health behaviour and designing more effective interventions, some common limitations apply to all of the current models. First, no current framework accounts for how emotional factors such as fear or mood influence constructs associated with behaviour (Brewer and Rimer, 2008). Second, some argue that these models only assess behavioural intention, which is not considered to be a strong predictor of actual behaviour (Lerman et al., 2002; Persky et al., 2007). Lastly, all current frameworks assume that individuals behave in a rational way and, thus, behaviour change is presented in a manner where inputs produce predictable change in outputs in a linear fashion (Resnicow and Page, 2008). Emerging evidence suggests that the process of behaviour change may be better described by a quantum model informed by chaos theory and complex adaptive systems (Resnicow and Vaughan, 2006; Resnicow and Page, 2008). This type of model does not assume rationality in human action and proposes that behaviour change is the result of non-linear interactions between multiple components and resembles a “chaotic process that is sensitive to initial conditions, highly variable and difficult to predict” (Resnicow and Page, 2008). However, linear and quantum models of health behaviour need not be mutually exclusive. A continuum of behaviour change has been proposed such that linear and quantum frameworks can be applied in the most appropriate ways based on the goal of the research question (Resnicow and Page, 2008).

2.3 Disclosure of Genetic Information and Health Behaviour

2.3.1 Genetic Testing

Genetic testing and personal genomics raise new questions in the field of health behaviour change. As little as 10 years ago, access to genetic testing was predominantly restricted to
clinical settings and utilized under select conditions, such as to determine carrier status for inherited genetic disorders or for prenatal screening. The rise of the consumer genetic testing industry since 2007 has rapidly changed access to genomic technologies. Individuals can now purchase genetic tests over the Internet for relatively low costs that claim to provide personalized information on disease susceptibility and nutrient and drug response. Some of these tests are available directly to consumer (DTC), without need for healthcare professional involvement, while others require that a physician order the test. The DTC genetic testing industry has been heavily scrutinized (Lancet Oncology, 2014). In fact, in late 2013 the Food and Drug Administration (FDA) in the United States sent a warning letter to one of the largest DTC genetic testing companies, 23andMe, ordering them to halt the sale and marketing of their health-related genetic test (Food and Drug Administration, 2013). The federal body pointed out that the company had not provided any evidence of the clinical validity or utility of their genetic test and stated concerns that the information could cause harm to consumers. This event has implications for the entire DTC genetic testing industry and has been received with mixed response. Some believe the FDA was warranted in their action (Annas and Elias, 2014) while others feel the approach was overly cautious without sufficient reasoning (Green and Farahany, 2014). Indeed, a recent study reported benefits of direct access to \textit{BRCA} genetic test information (Francke et al., 2013). Women who discovered they were carriers of the \textit{BRCA} mutation from a DTC genetic test sought out medical advice and some chose to undergo risk-reducing procedures after confirming the DTC test result. Moreover, men who discovered they were carriers understood that their result had relevance for their female relatives and shared this information with their family members. This led to medical screening of these participants’ female relatives and additional \textit{BRCA} carriers were identified. Direct access to \textit{BRCA} mutation testing did not result in
emotional distress or inappropriate actions among either carriers or non-carriers of the mutation (Francke et al., 2013), although it is important to consider that DTC genetic test consumers may not be representative of the general population.

While the future of DTC genetic testing remains unclear, a recent trend in the industry has been for companies that began with a DTC marketing model to shift to offering their services through physicians (Allison, 2012). While in some cases this shift occurred because certain states prohibited DTC genetic testing, more broadly it is due to the fact that the DTC method attracted a select group of individuals and there was a great deal of competition between companies to possess market share (Allison, 2012). Essentially, the change has been an attempt to attract a new customer base by offering tests through physicians (Allison, 2012). With or without healthcare professional involvement, the impact of disclosing health-related personal genomic information on health behaviours is of great interest to researchers and health promoters (McBride et al., 2010) and in order to properly regulate the consumer genetic testing industry, an understanding of the public’s perceptions of and demands for this technology, in addition to evidence on how individuals respond to disclosure of health-related genetic information, is needed.

2.3.2 Public Knowledge and Attitudes

For appropriate recommendations and regulations regarding consumer personal genetic tests to be made, public knowledge and opinions of these technologies must be well understood. Surveys of the general public demonstrate substantial public interest in personal genomics. In the UK, 4,050 adult volunteers were surveyed on their interest in Internet-based personal genome testing (PGT) (Cherkas et al., 2010). While only 13% of respondents were aware of PGT, after reading a
summary about PGT half of the participants were interested in taking a test if it was free (Cherkas et al., 2010). Nearly all the respondents who would take a test reported that they would do so to encourage them to adopt a healthier lifestyle if found to be at high genetic risk of a disease (Cherkas et al., 2010). An Internet-based survey of almost 1,500 randomly sampled Americans reported that 88% would be willing to pay for a genetic test that provided disease susceptibility information (Neumann et al., 2010). In line with these findings, a Canadian survey reported that 51% of nearly 1,200 respondents would pay for genetic testing that provides information on serious diseases (Ries et al., 2010). The interest in genomics in Canada is further illustrated by the recent launch of the Canadian Personal Genome Project and the large number of volunteers (~350) who offered to participate within a number of days of the project’s announcement (Abraham, 2012). Reasons for seeking out genetic testing have been reported and include curiosity, identity-seeking, disease-risk testing that complements health care and searching for a better lifestyle (Su, 2013).

Two studies have assessed public interest in nutrigenomics testing in particular (Morin, 2009; Stewart-Knox et al., 2009). In a sample of European consumers (n=5,967), 66% reported they would be willing to undergo nutrigenomics testing and 27% would follow a personalized diet (Stewart-Knox et al., 2009). Of note, individuals who were aware that they had health problems associated with the metabolic syndrome were more favourable toward nutrigenomic intervention (Stewart-Knox et al., 2009). In addition, focus groups were conducted in Canadian cities in 2007 to examine Canadian consumers’ and health care professionals’ (HCPs) knowledge of and attitudes toward nutritional genomics (Morin, 2009). Most consumers were unfamiliar with the term “nutrigenomics” and did not relate the term “personalized nutrition” to an individual’s genetic profile (Morin, 2009). Roughly half of HCPs were aware of the term
“nutrigenomics”, and a few related “personalized nutrition” to an individual’s genetic profile (Morin, 2009). After the moderator offered an explanation of nutrigenomics, consumers were optimistic that a tailored diet could help reduce the risk of disease, while HCPs expressed more skepticism (Morin, 2009). All participants were shown a mock website selling nutrigenomics test kits and health questionnaires, ranging from $275 to $2400. Some consumers held a favourable view of such companies, though there was general discomfort with purchasing a test online (Morin, 2009). A preference for in-person testing at a clinic, in the presence of a HCP, was evident (Morin, 2009). Both consumers and HCPs agreed that more public education about nutrigenomics is necessary and that regulatory oversight should ensure consumer protection (Morin, 2009).

Results from studies assessing public perceptions of genetic testing demonstrate a great deal of interest in personal genetic testing for health-related purposes, but behavioural effects of the technology must also be elucidated. Indeed, a number of studies have begun to explore the behavioural effects of genetic information in analogue settings, clinical settings, and from DTC genetic tests.

2.3.3 Response to Analogue Studies
Analogue studies, sometimes referred to as vignette studies, involve researchers presenting hypothetical scenarios to study participants and assessing participant reactions to and perceptions of the scenarios (Persky et al., 2007). These studies possess a number of advantages including cost-effective and efficient production of study materials, ability to administer materials with little special preparation and ability to present scenarios in a standardized way (Persky et al.,
To test responses to disclosure of health-related genetic information, analogue studies generally request that participants imagine they undergo genetic testing for assessment of risk of a particular health outcome. To date, nine analogue studies examining responses to hypothetical genetic information scenarios have been published (Conradt et al., 2009; Frosch et al., 2005; Hicken and Tucker, 2002; Meisel et al., 2012; Rief et al., 2007; Sanderson and Michie, 2007; Sanderson et al., 2010; Wright et al., 2006; Wright et al., 2008). Hicken et al. (2002) assessed self-reported intentions to engage in behavioural strategies that were recommended to reduce the risk of developing a fictitious genetically determined disorder. Participants were randomized to one of three groups: positive genetic test result, negative test result, or positive family history with no genetic test. Participants were not informed that the disorder was fictitious until the completion of the study, and those randomized to a genetic test group were required to provide a saliva sample and were told the sample would be analyzed for assessment of genetic risk. The authors reported that the positive test result group and the positive family history group expressed greater intent to follow the recommended behavioural strategies (reducing dietary fat and increasing soy intake) than the negative test result group, but there was no difference in intent between the positive test result group and the family history group, indicating that genetic risk information did not provide stronger behavioural motivation than family history (Hicken and Tucker, 2002).

Five analogue studies examined participant responses to genetic testing for weight gain/obesity (Conradt et al., 2009; Frosch et al., 2005; Meisel et al., 2012; Rief et al., 2007; Sanderson et al., 2010). Frosch et al. (2005) conducted a 2x2 factorial design randomized trial that assessed behavioural intentions and perceived behavioural control to eat a healthy diet after subjects were provided with either genetic risk (increased vs. average) or hormone risk
(increased vs. average) information for obesity. Subjects who received information indicating increased obesity risk expressed greater intentions to eat a healthy diet, whether the information was genetic or hormone. Those who received information indicating greater genetic risk expressed a lower sense of behavioural control than those who received information indicating average genetic risk (Frosch et al., 2005).

Sanderson et al. (2010) compared perceived risk of obesity and intention to eat healthily among participants who were randomized to receive a genetic test result for obesity that indicated high eating-based risk or high metabolism-based risk, an enzyme test result indicating high eating-based risk or high metabolism-based risk, or no risk information but standard advice to eat a healthy diet. Those who received high risk information from either a genetic or enzyme test reported greater perceived risk of obesity and a greater intent to eat healthily compared to the no risk information group, although perceived risk was higher among the genetic information group compared to the enzyme information group (Sanderson et al., 2010).

Meisel et al. (2012) examined responses to FTO genotype information indicating higher or average risk for obesity among two separate groups: middle-aged overweight or obese adults and normal weight students (mean age of 25 years). The A allele of rs9939609 in FTO has been associated with increased body mass index and a predisposition to obesity in both children and adults in an additive manner (Frayling et al., 2007), although a recent study suggests that the effect of FTO may be mediated by a nearby gene, IRX3 (Smemo et al., 2014). Among both the student and older adult group, a higher risk result was associated with greater motivation to change diet or exercise behaviour compared to the average risk result. The student group expressed a slight increase in fatalism about weight gain in response to a high risk result, while the older adult group did not (Meisel et al., 2012).
Conradt et al. (2009) found that incorporating genetic information about obesity into a weight loss consultation led to more realistic weight loss goals and greater satisfaction with a 5% weight loss. Additionally, subjects with familial predisposition to obesity reported less self-blame about eating after receiving consultations with genetic information (Conradt et al., 2009). A study by Rief et al. (2007) also found an improvement in negative mood in obese subjects with a family history of obesity when consultations included genetic information. This is important as negative thoughts and feelings about current weight have been shown to predict future weight gain (Burk-Braxton, 1996).

The remaining three analogue studies investigated the impact of health-related genetic information on smoking cessation (Sanderson and Michie, 2007; Wright et al., 2006; Wright et al., 2008). Wright et al. (2006) assessed intention to quit smoking and intention to attend an information session about quitting after providing participants with risk of developing heart disease due to genetic susceptibility to the adverse effects of smoking. Participants were randomized to receive a positive genetic test result, negative genetic test result, or no genetic testing but standard information about the risk of heart disease among smokers. Those who received a positive genetic result expressed greater intention to quit smoking and attend an information session about quitting compared to both the negative genetic result group and the no genetic test group (Wright et al., 2006). Moreover, there was no indication that receiving a negative genetic test result reduced motivation to quit smoking when responses were compared to the no test group (Wright et al., 2006). Sanderson et al. (2007) also examined the effect of providing heart disease genetic risk information on smoking cessation. Participants were randomized to receive either a low or high risk genetic test result, or a high risk oxidative stress test result. The group that received a high risk genetic test result for heart disease expressed a
greater intention to quit smoking compared to both the high risk oxidative stress group and low risk genetic test group, and also expressed greater perceived control over an ability to quit smoking compared to the low risk genetic test group (Sanderson and Michie, 2007). Finally, Wright et al. (2008) examined the impact of genetic information on motivation to quit smoking, but with genetic information related to Crohn’s disease risk. Smokers who have a sibling with Crohn’s disease and who carry at least two out of the three mutations in NOD2 that have been shown to increase risk of Crohn’s disease (Pascoe et al., 2007) have a 35% risk of developing the disease compared with a 5% risk among smokers who do not carry a mutation (Lewis et al., 2007). Wright et al. also assessed whether the nature, magnitude or display of risk information had differential effects on perceived susceptibility to Crohn’s disease and motivation to quit smoking. Participants were randomized to one of 18 groups in a 3 (nature of information: genetic test mutation positive group, genetic test mutation negative group or family history only group) x 3 (risk magnitude: 3%, 5%, 50%) x 2 (display: grouped or dispersed icons) design (Wright et al., 2008). Perceived susceptibility to Crohn’s disease was only affected by risk magnitude in the family history group (with no difference between genetic test groups). The nature of risk information had no impact on intentions to quit smoking, while risk magnitude did (Wright et al., 2008). Those who were informed they were at 50% greater risk of the disease reported a greater intention to quit smoking compared to the 3% risk group (Wright et al., 2008).

Results from analogue studies illustrate that providing genetic risk information does have an impact on health behavioural intentions, but genetic information does not consistently produce greater effects than non-genetic forms of health information. However, analogue studies assess behavioural intention, which may not reflect actual behaviour (Lerman et al., 2002; Persky et al., 2007). Individuals may have difficulty predicting their own behaviour when scenarios are
hypothetical versus real (Vallone et al., 1990). As a result, studies that truly disclose genetic information and assess health behaviour change provide stronger evidence of the utility of genetic testing for behaviour change. Such studies have been conducted with both clinical and DTC genetic tests.

2.3.4 Response to Clinical Genetic Testing

Most clinical genetic testing research to date has evaluated the effects of genetic information related to rare genetic variants, such as those involved in hereditary breast, ovarian and colon cancers, on screening behaviours (McBride et al., 2010). Genetic feedback of carrier status and cancer risk has been associated with improved screening behaviour among those carrying an at-risk gene variant (Claes et al., 2005; Collins et al., 2005; Hadley et al., 2004; Halbert et al., 2004; Kinney et al., 2006; Watson et al., 2004). However, studies have also examined the effect of incorporating genetic testing in smoking cessation programs (Audrain et al., 1997; Hishida et al., 2010; Hollands et al., 2012; Ito et al., 2006; Lerman et al., 1997; McBride et al., 2002; Sanderson et al., 2008), weight loss and chronic disease prevention (Arkadianos et al., 2007; Cho et al., 2012; Grant et al., 2013), and behaviour changes following disclosure of genetic risk for Alzheimer’s disease (Chao et al., 2008) and familial hypercholesterolemia (Marteau et al., 2004).

Studies that have examined the utility of genetic information in smoking cessation programs have reported little effect of genetic information on sustained cessation. Lerman et al. (1997) randomized smokers to one of three groups: a standard smoking cessation consultation group (SC), SC + carbon monoxide exhaled in breath information (CO), or SC + CO + genetic susceptibility (GS) to lung cancer information. The GS group received personal genotypes for \textit{CYP2D6}, which has been associated with lung cancer risk in the past (Law et al., 1989), although
more recent GWAS examining genetic risk for lung cancer have not identified this locus (Landi et al., 2009; Timofeeva et al., 2012; Zhang et al., 2014). Immediately following the intervention, the GS group expressed greater perceived risk of lung cancer, greater perceptions of cessation benefits and greater fear arousal compared to either the SC or CO group, however, after a 2-month follow-up, there were no significant differences in cessation rates between any of the groups (Lerman et al., 1997). After a 12-month follow-up, no significant differences in cessation rates were observed between any of the groups, but the GS group was two times more likely to attempt quitting smoking compared to the SC group (Audrain et al., 1997). McBride et al. (2002) incorporated genetic susceptibility feedback to tobacco-related cancers into a smoking cessation program and compared cessation rates to a group that received a standard cessation intervention. Participants in the genetic information group were counseled on their GSTM1 genotype, since individuals with lung cancer are significantly more likely to be missing GSTM1 (Bartsch et al., 1999; McWilliams et al., 1995). However, a 2008 meta-analysis of 98 genetic association studies reported that although the null variant of GSTM1 was associated with an increased risk of lung cancer overall (OR: 1.22, 95% CI: 1.14-1.30), this increased risk was only present in East Asian individuals (OR: 1.38, 95% CI: 1.24-1.55) and was not present in Caucasians (OR: 1.04, 95% CI: 0.97-1.11) (Carlsten et al., 2008). While GWAS have not identified associations between GSTM1 and lung cancer, Rotunno et al. reported in 2012 that GSTM1 was not well tagged in a reference GWAS platform (Environment and Genetics in Lung Cancer Etiology; EAGLE study) and expressed the importance of direct genotyping to investigate GSTM1 (Rotunno et al., 2012). Nevertheless, McBride et al. (2002) found that smoking cessation was greater in the group that received genetic information in the short-term (6 months following intervention), but not at the 12-month follow-up (McBride et al., 2002). Sanderson et al. (2008) also examined the effect of
GSTMI genetic test feedback on smokers’ motivation to quit smoking. Those with the GSTMI null variant reported a greater motivation to quit smoking compared to subjects with GSTMI positive variant and also smoked fewer cigarettes at 1-week follow-up (Sanderson et al., 2008). These differences were not significant at 2-months follow-up (Sanderson et al., 2008). Ito et al. (2006) assessed the utility of genetic information in a smoking cessation program among hospital outpatients in Japan, of whom approximately 30% were cancer patients (Ito et al., 2006). Participants were randomized to an intervention group (I) that received information on the MYC1 polymorphism (rs3134613), which has been associated with greater risk of lung and esophageal cancers among smokers carrying a risk variant (Kumimoto et al., 2002; Kumimoto et al., 2001), or a control group (C) that received no information for smoking cessation or genetic information. However, more recent GWAS investigating genetic risk of lung (Landi et al., 2009; Timofeeva et al., 2012; Zhang et al., 2014) and esophageal cancer (Wu et al., 2011; Levine et al., 2013) have not identified this locus. After 9-months, cessation rates did not differ between the intervention and control group (I: 17.0%, C: 18.8%, p=0.80), however, there was a significant difference among female participants who did not have cancer (Ito et al., 2006). Among those women, a greater proportion of those in the intervention group quit smoking compared to those in the control group (I: 15.0%, C: 4.2%, p=0.02) (Ito et al., 2006). There was no significant difference among men who did not have cancer (I: 11.0%, C: 12.3%, p=0.89) (Ito et al., 2006).

Hishida et al. (2010) also examined the utility of incorporating MYC1 genotype information into a smoking cessation program among bank employees in Japan and reported no difference in smoking cessation rates between the intervention group that received genetic information and the control group that received no information after 12-months of follow-up (Hishida et al., 2010). Finally, Hollands et al. (2012) assessed the impact of incorporating genetic information for risk
of Crohn’s disease into a smoking cessation program against family history risk information. These investigators had previously conducted an analogue study to examine this effect and reported no differences between genetic information or family history information on intention to quit smoking (Wright et al., 2008). In the 2012 study, subjects in the intervention group underwent genetic testing for three mutations in \textit{NOD2} (a genetic susceptibility marker for Crohn’s disease (Lewis et al., 2007) and were given personalized risk information for Crohn’s disease based on their genetic results. After a 6-month follow-up, no differences in attempts to quit smoking or the proportion of subjects who stopped smoking for 24 hours or longer were reported between the intervention and control group (Hollands et al., 2012).

Three studies have examined the impact of incorporating genetic information into weight loss programs, either solely for weight loss (Arkadianos et al., 2007), or as part of a diabetes prevention program (Cho et al., 2012; Grant et al., 2013). A study conducted in Greece evaluated the effect of personalized diets based on genetic information on weight loss among obese individuals who had a history of weight loss failures (Arkadianos et al., 2007). Individuals who opted for a nutrigenetic screening test, manufactured by the company Sciona Ltd., were given genotype-based weight loss recommendations and were compared to individuals who did not take the genetic test, but were following a weight loss diet (Arkadianos et al., 2007). There were no significant changes in BMI between the two groups in the first 100-300 days after the intervention, however, weight loss was more likely to be maintained in the nutrigenetic tested subjects compared to the control group, when subjects were followed for more than 300 days (Arkadianos et al., 2007). Fasting blood glucose levels were also significantly improved among subjects who underwent nutrigenetic testing, but did not improve significantly among the control group (Arkadianos et al., 2007). Cho \textit{et al.} (2012) examined the effect of incorporating genetic
information for type 2 diabetes risk in a diabetes prevention program. Participants were randomized to an intervention group that received standard risk assessment (SRA: consisting of fasting blood glucose, family history and BMI) plus genetic risk information (given as number of higher risk variants out of a total of 16 SNPs), or SRA alone. Primary outcome measurements included change in insulin resistance and BMI at 3- and 12-months. Preliminary results showed no differences in weight loss between the two groups at 3-months (Cho et al., 2012), although additional results have yet to be published. Grant et al. (2013) also assessed the utility of genetic information in a 12-week diabetes prevention program among overweight adults. Participants were randomized to a genetic risk testing group (intervention) or a no testing group (control) using a 4:1 allocation ratio and only those found to be in the top and bottom quartiles of genetic risk for diabetes (using the diabetes genetic risk score based on 18 risk alleles developed in the Framingham Offspring Study (Meigs et al., 2008)) were retained in the intervention group (Grant et al., 2013). Outcome measures included self-reported motivation to make lifestyle changes, number of weekly program sessions attended over the 12-weeks and weight change from baseline at 12-weeks. Overall, all participants in the study reported greater motivation to make lifestyle changes, attended approximately half of the program sessions and lost an average of approximately 8 pounds, but there were no significant differences in these outcomes between the intervention and control group (Grant et al., 2013).

Additional studies examining genetic information and behaviour have been related to Alzheimer’s disease (AD) and familial hypercholesterolemia (FH) (Chao et al., 2008; Marteau et al., 2004). Chao et al. (2008) examined whether disclosure of APOE e4 genotype altered health behaviour among asymptomatic individuals at high risk for AD. First-degree family members and those carrying 1 or 2 copies of the APOE e4 allele are at increased risk of developing AD
(Farrer et al., 1997; Green et al., 2002). The researchers found that participants who learned they were ε4 positive were significantly more likely to report AD-specific health behaviour change 1-year after disclosure, such as changing medication or vitamin use (Chao et al., 2008). Adding a vitamin E supplement was the most common change (Chao et al., 2008). Marteau *et al.* (2004) examined whether clinical diagnosis of FH, as confirmed by a genetic mutation in the *LDLR* or *APOB* genes, affected patients’ adherence to risk-reducing behaviours. The researchers found that subjects with a mutation believed less strongly in the efficacy of diet in reducing cholesterol levels, but showed a trend in believing more strongly in the efficacy of medication (Marteau *et al.*, 2004). However, confounding may have influenced this result since individuals who possessed mutations for FH may have had more severe disease and stronger family history of early CVD and were perhaps more motivated to take medication. Moreover, baseline analyses indicated that subjects who attributed more importance to genetics than lifestyle in CVD risk reported greater adherence to their cholesterol-lowering medication (Marteau *et al.*, 2004).

Results from studies assessing the impact of clinical genetic testing on health behaviour changes have reported conflicting findings. While incorporation of genetic information appears to have little impact on smoking cessation, some effects have been reported for dietary behaviours (Arkadianos *et al.*, 2007; Chao *et al.*, 2008). Overall, few of these studies have included long-term follow-up assessments of at least 1-year and the type of genetic information that has been provided varies between studies. Therefore, it is difficult to compare studies in order to draw conclusions about the effectiveness of disclosing genetic information for behaviour change. Additional studies may clarify the effect of genetic information on behaviour.
2.3.5 Response to Direct-to-consumer Genetic Testing

To date, only one study has empirically examined the effect of genetic information obtained from a DTC genetic test on behavioural outcomes and published both short-term and long-term findings (Bloss et al., 2011c; Bloss et al., 2013). Subjects in the study (n=2,037) were recruited from health and technology companies (Microsoft, Sempra Energy, Qualcomm, SDG&E, Life Technologies, Affymetrix and The Scripps Research Institute) and purchased the Navigenics “Health Compass” DTC genetic test ($999 USD) at a reduced price. To encourage enrolment early on during participant recruitment, the price of the genetic test was lowest at the start of the study at $150 USD. The price increased over time and the highest cost of the test was $470 USD during the final months of recruitment. Participant recruitment occurred between October 2008 and September 2009. The Navigenics “Health Compass” test screened DNA for 23 different health conditions (e.g. type 2 diabetes, heart disease, obesity and certain cancers) and provided estimates of one’s risk for developing them over a lifetime (Bloss et al., 2011c). Questionnaires were used to measure subjects’ level of anxiety (Speilberger State-Trait Anxiety Inventory), dietary fat intake (Block Dietary Fat Screener) and time spent exercising (Godin Leisure-Time Exercise Questionnaire) prior to genetic testing (Bloss et al., 2011c). These questionnaires were repeated at mean follow-up points of 6- and 12- months after the test results were disclosed and scores were compared to determine if the genetic information affected any outcome variable. No changes in scores were seen at either follow-up time points and the investigators concluded that the genetic information had no effect on the behavioural outcomes of interest (Bloss et al., 2011c; Bloss et al., 2013).

Although Bloss et al. were the first to investigate the effect of DTC genetic test information on behaviour, a number of study limitations should be noted. No control group was
present, which limits the interpretation of the results. As well, the corresponding lifestyle advice that was provided to the subjects was the same regardless of genotype and was not personalized. Therefore, the subjects were not aware of what specific changes they should make based on their genotypes that would mitigate their risk for the conditions. Furthermore, the questionnaire scores indicated that, at baseline, the majority of the sample had relatively low dietary fat intakes and were meeting public health recommendations for physical activity. The effects of the information may have been different in a population that consumed a greater amount of dietary fat and exercised less at baseline.

Despite that study’s null findings, other evidence suggests that information from a DTC genetic test may result in lifestyle modification. A survey of 1,055 readers of the journal *Nature* reported that 27% of respondents who had undergone genetic testing (predominantly from a DTC genetic testing company) indicated that they changed their diet, lifestyle or medication use based on their genetic test results (Maher, 2011). However, *Nature* readers are likely not a representative sample of the general population. A separate survey conducted among 1,048 DTC genetic test users reported that 43% sought out additional information about a health condition included in their test results, and that 33% were “being more careful about their diet” and 16% had changed their use of medications or supplements (Kaufman et al., 2012). These results suggest that information obtained from a DTC genetic test does impact health behaviour, particularly dietary behaviour, in a considerable proportion of users and thus warrants further study.
2.4 Dietary Recommendations

2.4.1 Population-based Dietary Guidelines

The origin of dietary guidelines can be dated back to the work of the chemist Wilbur Olin Atwater in the late 19\textsuperscript{th} century. Atwater conducted the first calorimeter experiments that measured the energy in different foods, which led to the development of the first food composition tables and dietary standards for Americans in 1894 (Atwater, 1894). These standards were updated and developed over time into recommendations for consuming specific items from different food groups until the 1941 release of the first Recommended Dietary Allowances (RDAs) by the Food and Nutrition Board of the National Academy of Sciences (National Research Council, 1941). This five page report included intake recommendations for calories and nine nutrients (protein, calcium, iron, vitamin A, thiamin, riboflavin, niacin, ascorbic acid and vitamin D). The recommendations were based on sex, activity level and age and the report notes that they only apply to individuals in good health (National Research Council, 1941). Moreover, the authors of the report acknowledged that evidence on nutrient requirements was sparse at the time and that the values would need to be revised as more knowledge became available (National Research Council, 1941). The RDAs continued to be used until the publication of the Dietary Reference Intakes (DRIs) in 1997. Canada had developed its own set of dietary standards released by the Canadian Council of Nutrition in 1939, but adopted the US RDAs in 1942 for uniformity between the two countries (Health Canada, 2010). However, in 1945 the RDAs were shown to be inappropriate for evaluating group intakes (Wilder, 1945), so the Canadian Council of Nutrition created new Canadian standards that were used from 1948-1990 (Health Canada, 2010). These standards were named the Recommended
Nutrient Intakes (RNI) in 1983 and remained as the Canadian guidelines until the publication of the DRIs in 1997 (Health Canada, 2010).

A 1994 IOM publication called for considerations of how the RDAs should be revised, since disagreement existed between scientists on the interpretation and application of the RDAs (Food and Nutrition Board, 1994). Proponents of revising the recommendations expressed that the standards did not consider the role nutrients played in chronic disease risk (Food and Nutrition Board, 1994). The first Dietary Reference Intakes report was published in 1997 after collaboration between scientists from the IOM and Health Canada and replaced the US RDAs and Canadian RNI (Food and Nutrition Board, 1997). The DRIs report included a set of reference values (rather than a single value) to describe states of average requirements, recommended allowances and upper safe limits (Food and Nutrition Board, 1997). A complete summary report of DRIs and their application was published by the IOM in 2006 (National Research Council, 2006), with a revision to the calcium and vitamin D recommendations released in late 2010 (National Research Council, 2011).

While the DRIs are an improvement from the RDAs, the values must be periodically reviewed to consider emerging scientific evidence. In fact, the IOM and Health Canada recently accepted nominations to review the DRIs and applications were received for 16 nutrients (Health Canada, 2013). One criticism of population-based dietary recommendations is that knowledge of individuals’ genetic variation affecting nutrition requirements has not been considered in their creation (Stover, 2006). Proponents of personalized nutrition argue that dietary recommendations that are tailored to an individual’s genotype will maximize the effects of nutrition on health outcomes. In addition, individuals may be more motivated to adhere to personalized dietary recommendations based on genotype. Indeed, a number of studies investigating the relationship
between nutrition and genetics have demonstrated an ability to personalize dietary recommendations based on genetic variation.

2.4.2 Evidence for Personalized Nutrition

Several significant findings in the field of nutrigenomics have formed the basis for this thesis project. A study examining the association between *CYP1A2* genotype, coffee intake and acute nonfatal myocardial infarction (MI) found that 2 or more cups per day of coffee increased the risk of nonfatal MI only among carriers of the variant allele (“slow” caffeine metabolizers) (Cornelis et al., 2006). Among slow metabolizers, the multivariate-adjusted odds (adjusted for age, sex, area of residence, waist-hip ratio, income, physical activity, history of diabetes, history of hypertension, and intakes of alcohol, total energy, and energy-adjusted saturated fat, polyunsaturated fat, trans fat, folate and sucrose) of MI increased as coffee consumption increased. The odds ratios (ORs) and 95% confidence intervals for MI when consuming less than 1, 1, 2 to 3, and 4 or more cups of coffee per day were 1.00 (reference), 0.99 (0.69-1.44), 1.36 (1.01-1.83), and 1.64 (1.14-2.34), respectively. These effects were more pronounced among individuals younger than the median age of 59 years. The multivariate-adjusted ORs for MI among slow metabolizers under 59 years when consuming less than 1, 1, 2 to 3, or 4 or more cups of coffee per day were 1.00, 1.24 (0.71-2.18), 1.67 (1.08-2.60), and 2.33 (1.39-3.89), respectively. A different study found that risk of hypertension associated with coffee intake varies according to *CYP1A2* genotype, with carriers of the slow allele being at increased risk when consuming moderate amounts of caffeine (1-3 cups of coffee per day). The multivariate-adjusted ORs (adjusted for age, sex, baseline blood pressure and follow-up length) of hypertension among slow metabolizers was 1.00 in abstainers (reference), 1.72 (1.21-2.44) in
moderate coffee drinkers and 3.00 (1.53–5.90) in heavy drinkers (Palatini et al., 2009). Fast metabolizers were not at significantly increased risk of MI or hypertension in either study at any level of coffee consumption (Cornelis et al., 2006; Palatini et al., 2009). These results suggest that individuals carrying a slow allele should limit their consumption of caffeine, potentially to no more than 2 cups of coffee per day.

Researchers studying genetic variation in vitamin C metabolism found that individuals with null variants in the GSTM1 and GSTT1 were at increased risk of serum ascorbic acid deficiency if they did not meet the Recommended Dietary Allowance (RDA) for vitamin C (Cahill et al., 2009). The multivariate-adjusted ORs and 95% confidence intervals (adjusted for BMI, energy intake, oral contraceptive use in women, C-reactive protein, ethnicity and season) for serum ascorbic acid deficiency were 2.17 (1.10, 4.28) and 12.28 (4.26, 33.42), respectively, for subjects with the GSTT1 functional and GSTT1 null genotypes and 2.29 (0.96, 5.45) and 4.03 (2.01, 8.09), respectively, for subjects with the GSTM1 functional and GSTM1 null genotypes. Serum ascorbic acid levels were also lower in subjects with a deletion of GSTT1 or GSTM1 in a different study (Horska et al., 2011). The recommended intake for vitamin C protects against serum ascorbic acid deficiency regardless of genotype, yet these results suggest that individuals with deletion genotypes for GSTM1 and GSTT1 could benefit from being particularly mindful of meeting the daily recommendation.

An intriguing area of study which is rapidly expanding is the science of chemical senses and its relation to individual food preferences (Meiselman, 1996). There is growing evidence that genetics plays a significant role in one’s ability to detect taste and smell, in turn affecting food preferences and dietary intake (Garcia-Bailo et al., 2009; Reed and Knaapila, 2010). A study examining the role of genetics in sugar consumption found that a variation in the TAS1R2 gene
(which encodes the sweet taste receptor) affected habitual consumption of sugars in two distinct populations: (1) healthy, young adults and (2) individuals with type 2 diabetes (Eny et al., 2010). Individuals possessing a variant in the TAS1R2 gene consumed more total sugars (mean ± SEM) than those without the genetic variant (population 1: 122 ± 6 g/day vs. 103 ± 6 g/day, p = 0.01; population 2: 99 ± 6 g/day vs. 83 ± 6 g/day, p = 0.04) (Eny et al., 2010). Although the mechanism for this is unknown, it is plausible that genetic variation in TAS1R2 affects sweet taste perception and may play a role in an individual’s preference for sweet tasting foods. Knowing whether one is genetically predisposed to preferring sweet foods may impact eating behaviour.

The role of genetic variation in salt-sensitive hypertension has also been explored (Giner et al., 2000; Poch et al., 2001). One study found that hypertensive patients with the I variant of the intronic Insertion/Deletion (I/D) ACE gene had a significantly higher increase in both mean ± SD systolic blood pressure (SBP) and diastolic blood pressure (DBP) with high salt intake compared to those without the I variant (SBP mm Hg: 9.8 ± 8.1 (I/I), 5.0 ± 7.3 (I/D), 1.2 ± 5.9 (D/D), p = 0.01; DBP mm Hg: 5.2 ± 4.2 (I/I), 2.4 ± 6.1 (I/D), -0.2 ± 4.2 (D/D), p = 0.03) (Giner et al., 2000). The prevalence of salt-sensitive hypertension, as determined by 24-hour ambulatory mean blood pressure after high salt intake, was also higher among I/I (67%) and I/D (62%) genotypes compared with the DD genotype (19%), p = 0.01. (Giner et al., 2000). The same results were observed when this sample size was increased from 50 patients to 71 patients, and additional genotypes in other genes were examined (Poch et al., 2001). The other genes included angiotensinogen (M235T), angiotensin II type 1 receptor (A1166C), 11β HSD2 (G534A), aldosterone synthase (C-344T and Intron 2 conversion), and the mineralocorticoid receptor (G3514C and A4582C). Only 11β HSD2 and ACE were significantly associated with salt-
sensitive hypertension (Poch et al., 2001). These results suggest that the $ACE$ polymorphism may serve as a potential genetic marker of salt-sensitivity. Informing individuals of their genetic susceptibility to salt-sensitive hypertension may motivate adoption of behaviours such as limiting dietary sodium intake, which will mitigate the chance of developing this condition later in life.

The evidence highlighted above forms the rationale for the proposed research project, which is to examine how general dietary recommendations compare with targeted dietary advice based on genotypes to motivate changes in dietary intake. Dietary intake will be assessed with a food frequency questionnaire, which is discussed below along with other tools for assessing intake.

### 2.5 Dietary Assessment

In order to assess relationships between diet and health, as well as the effectiveness of an intervention in promoting dietary change, assessments of individuals’ dietary intakes are commonly made in nutrition research. The three most common tools currently available for assessing dietary intake include food records, 24-hour dietary recalls and food frequency questionnaires. However, each of these instruments possesses unique strengths and limitations.

Food records require that research subjects record everything they consume over a day as the day progresses (Buzzard, 1998). If completed correctly, data from food records are considered to be highly accurate of an individual’s actual recent intake, since memory does not play a role in the quality of reporting (Buzzard, 1998). Research participants are generally asked to record foods and beverages consumed over a period of 3-7 days and include portion sizes (or weights) and methods of preparation. The records should include intake from at least one
weekend day, as dietary intake has been shown to differ between week days and weekend days (Bhargava et al., 1994). Requesting participants to record intake on non-consecutive days is an important consideration, as capturing the true variation in dietary intake may be otherwise minimized (Larkin et al., 1991). Although considered one of the best measures of actual dietary intake, a limitation of food records includes the high level of motivation subjects require to complete the records correctly, which may affect the representativeness of the study population and limit the generalizability of findings (Buzzard, 1998). The process of completing a food record may also influence the dietary intake of the subject and thus would compromise the reliability of the data (Buzzard, 1998). In addition, food records are costly as subjects are generally compensated for their completion and study staff are required to review records for completeness and enter data manually into nutrient analysis software (Buzzard, 1998).

Twenty four hour dietary recalls are commonly used in large scale studies to obtain an estimate of recent dietary intake in a more cost-effective manner than food records (Buzzard, 1998). In this method, a trained interviewer probes a subject about the foods and beverages that were consumed over the previous day (Buzzard, 1998). Although this method only provides data on one day’s intake, a second dietary recall can be conducted among a subset of the study sample to estimate the day-to-day variation in intake of the entire sample (Hoffmann et al., 2002). This method of assessment places little burden on study subjects and allows for participation from a more representative sample of the general population, since the quality of reporting does not depend on the literacy of the subject (Buzzard, 1998). However, 24-hour recalls rely on a subject’s memory to accurately recall what was consumed over the previous day and, therefore, are prone to measurement error (Buzzard, 1998).
Food frequency questionnaires (FFQ) are commonly used in epidemiological studies to assess diet-disease relationships because they provide an estimate of usual intake, rather than recent intake (Willet, 1998). FFQs generally consist of a comprehensive list of foods, frequency response options and portion size information for either all items (quantitative), some items (semi-quantitative) or no items (Willet, 1998). The questionnaires generally collect data on dietary intake over a time period of one month to one year, although some request participants to report on dietary intake from over a year ago (particularly case-control studies where cases are asked to recall dietary intake before disease onset) (Willet, 1998). While FFQs are advantageous because they measure usual intake, can be self-administered and are processed quickly, they are prone to measurement errors such as underreporting of energy (Bedard et al., 2004; Brown, 2006) and recall bias where cases inaccurately report their dietary intake from before disease onset (Prentice, 1996).

Each of the instruments that assesses self-reported dietary intake is affected by inherent susceptibilities to measurement and reporting errors and, as a result, the validity of self-reported dietary intake data has been questioned (Schoeller, 1990). Therefore, biological markers are used to obtain more objective measures of intake and also to validate self-reported data (Hunter, 1998). Examples of biomarkers of dietary intake include doubly labeled water for total energy expenditure (Schoeller et al., 1986), urinary excretion for sodium intake (Watson and Langford, 1970), urinary nitrogen for protein intake (Bingham and Cummings, 1985) and subcutaneous adipose tissue for certain dietary fatty acids (Beynen et al., 1980). However, factors that may affect the validity of biomarkers as surrogate indicators of dietary intake include study design (e.g. cross-sectional studies need to consider whether biomarkers are affected by disease state),
whether the biomarker reflects recent or long-term intake, and issues of specimen collection, handling and storage (Jenab et al., 2009).

2.6 Summary of Literature Review and Knowledge Gaps

Chronic diseases account for a striking proportion of the world’s morbidity and mortality. Diet is one of the most common modifiable lifestyle factors that influences chronic disease risk. Therefore, interventions that target diet for health behaviour change can have a significant impact on chronic disease risk of individuals and populations. Moreover, the genomics era provides novel opportunities for designing interventions that may be more effective at promoting behaviour change. Identifying vulnerable groups of the population by characterizing genetic risk of a health outcome and customizing dietary recommendations according to an individual’s genotype may result in better adherence to recommendations than providing general population-based advice. The behavioural impact of disclosing personal genomic information related to health has been assessed in a few studies and additional randomized trials have been recently completed or are currently underway (Table 2.1). However, no previous study has assessed the impact of disclosing genetic information related to nutritional advice on dietary intake behaviour in particular. Since diet is such an important modifier of chronic disease risk and recommendations are immediately actionable, this lack of research represents a significant knowledge gap. In addition, while consumer perceptions of genomic information related to disease susceptibility have been assessed, little is known about individual perceptions regarding genetic testing for personalized nutrition. Therefore, the aim of the present thesis is to determine the effect of disclosing genetic information related to personalized nutrition on dietary intake, as well as to assess individual perceptions of genetic testing for personalized nutrition.
Table 2.1 Clinical trials investigating the behavioural impact of disclosing genetic information

<table>
<thead>
<tr>
<th>ClinicalTrials.gov Identifier</th>
<th>Dates</th>
<th>Trial Name</th>
<th>Duration</th>
<th>Outcome Measures</th>
<th>Institute</th>
</tr>
</thead>
</table>
| NCT00849563                   | April 2009- June 2013          | Effect of Type 2 Diabetes Genetic Risk Information on Health Behaviors and Outcomes | 12 months | - Percentage of weight loss  
- Change in perceptions of diabetes risk change in HOMA-IR                       | Duke University and deCode Genetics                                    |
| NCT01884545                   | July 2013- January 2016       | Genetic Risk and Health Coaching for Type 2 Diabetes and Coronary Heart Disease | 12 months | - Change in diet, exercise, smoking  
- Change in FBG, SBP, BMI, LDL, TG, TC, FRS, DRS  
- Perceived self-efficacy, worry, risk                                           | Duke University                                                       |
| NCT01766271                   | October 2012-June 2013         | GENERating Behaviour Change: An Integrating Health Coaching and Genetic Risk Testing Pilot | 6 months | - Change in diet, physical activity  
- Change in FBG, SBP, BMI, WC, LDL, TG, TC                                        | Duke University                                                       |

HOMA-IR - Homeostatic model assessment of insulin resistance; FBG - Fasting blood glucose; SBP - Systolic blood pressure; BMI - Body mass index; LDL - Low density lipoprotein cholesterol; TG - Triglycerides; TC - Total cholesterol; FRS - Framingham Risk Score; DRS- Diabetes Risk Score; WC - Waist circumference
Chapter 3

Hypothesis and Objectives
3.1 Hypothesis

Targeted dietary advice based on genetic information will influence changes in dietary intake behaviour to a greater extent than general dietary recommendations.

3.2 Objectives

1. Examine the perceptions of individuals toward genetic testing and personalized nutrition.
2. Compare the short-term and long-term effects of DNA-based dietary advice with general dietary advice on dietary intakes of caffeine, vitamin C, added sugar and sodium 3-months and 12-months after providing the advice.
3. Determine individual preferences for obtaining personal genetic information and determine if perceptions toward genetic testing and personalized nutrition changed over the course of the intervention.
Chapter 4

A randomized trial of genetic information for personalized nutrition

4.1 Abstract

Personal genetic information has become increasingly accessible to the public as a result of direct-to-consumer (DTC) genetic tests; however, concerns have been raised over their value and potential risks. We compared the effects of providing genotype-based dietary advice with general recommendations on behavioral outcomes using a randomized controlled study. Participants were men and women from the Toronto Nutrigenomics and Health Study between the ages of 20–35 years old (n=149) who completed a survey to assess their awareness of DTC genetic tests and nutrigenomics, as well as potential motivations for undergoing genetic testing. Participants were then randomized into an intervention (I) or control (C) group and were given either genotype-based personalized dietary advice or general dietary advice, respectively. A second survey was administered to assess the participants’ opinions of the dietary reports they received. A greater proportion of participants in the intervention group agreed that they understood the dietary advice they were given (93% (I) vs. 78% (C); p=0.009). Participants in the intervention group were more likely to agree that the dietary recommendations they received would be useful when considering their diet (88% (I) vs. 72% (C); p=0.02) and wanted to know more about the recommendations (95% (I) vs. 76% (C); p<0.0001). Only 9% of participants in the intervention group reported feeling uncomfortable about learning their genetic information. These findings suggest that individuals find dietary recommendations based on genetics more understandable and more useful than general dietary advice. Very few feel uneasy about receiving their genetic information that relates to personalized nutrition.
4.2 Introduction

Recent advances in genomics technologies have made the acquisition of personalized genetic information easily obtainable. Direct-to-consumer (DTC) personal genetic tests claim to provide consumers with information about their genetic ancestry, ability to metabolize nutrients and drugs, and risk for developing diseases (Janssens and van Duijn, 2010). One class of genetic tests offer personalized dietary advice based on one’s DNA to improve health (Sterling, 2008). Nutrigenomics (or nutritional genomics) is the study of the relationship between genes and diet, and is used as an umbrella term for two complimentary approaches: how nutrients affect gene function and how genetic variation affects nutrient response (Cahill and El-Sohemy, 2011). The latter is sometimes referred to as nutrigenetics (El-Sohemy, 2007) and includes the study of how genetic variations affect food intake and eating behaviours (Eny and El-Sohemy, 2010; Garcia-Bailo et al., 2009). The DTC method of marketing facilitates the sales of genetic tests without involvement of a healthcare professional (Norrgard, 2008). These tests are commercially available through the internet and are largely unregulated, though significant measures are being taken to regulate this emerging market in certain jurisdictions (McGuire et al., 2010). The cost of the different types of genetic tests available can range from approximately $99 to over $2000 USD (Bloss et al., 2011a). DTC genetic testing for disease susceptibility remains controversial, with opponents arguing that the tests possess limited value due to their questionable clinical validity and utility (Burke, 2009; Caulfield, 2010; Eng and Sharp, 2010). Critics note that predicted risks will continue to change as new genetic variants are discovered, and thus any risk estimates for disease based on currently known common variants are premature (Janssens et al., 2011; Mihaescu et al., 2009). Moreover, environmental factors such as diet, smoking and
physical activity can have a far greater impact on risk, but are often not considered when providing estimates of risk. There is also concern that consumers may experience anxiety if provided with estimates of higher risk for developing certain diseases based on their genes and may seek out potentially unnecessary health interventions (McGuire and Burke, 2008). Another criticism of most DTC genetic tests is that the corresponding advice is not genuinely personalized since the lifestyle recommendations are generally the same, regardless of genotype, although evidence for such personalized recommendations is currently scarce. Despite these criticisms, proponents of DTC genetic tests argue that there is public interest in genomics and that individuals should have access to their own genetic information (Bloss et al., 2011a; Caulfield, 2010). In addition, some propose that direct access to genetic information may motivate consumers to adopt lifestyle behavioural changes aimed at reducing risk of disease development (Bloss et al., 2011b; McBride et al., 2010). Studies have reported different findings of the effects of disclosure of genetic risk information on health-related behaviours (Arkadianos et al., 2007; Chao et al., 2008; Conradt et al., 2009; Lerman et al., 1997; Marteau et al., 2004; McBride et al., 2002; Vernarelli et al., 2010) however, only one study has investigated the impact of DTC genetic testing on behaviour and reported no short-term changes in specific dietary or exercise behaviours (Bloss et al., 2011c). A limitation of that study is that the genetic risk scores that were given to the subjects were not specifically linked to a particular lifestyle behaviour and no personalized advice to reduce the risk of developing a health condition was provided. Importantly, there was no control group in the study. A recent survey of readers of the journal Nature shows that 27% of respondents who had their genomes analyzed changed their diet, lifestyle or medication based on their genetic information, suggesting that genetic information could impact behaviour (Maher, 2011).
For appropriate recommendations and regulations regarding DTC genetic tests to be made, the public’s knowledge and opinions of these technologies need to be well understood. A number of studies have surveyed awareness of and attitudes toward DTC genetic tests either among the general public or among healthcare providers (Cherkas et al., 2010; Goddard et al., 2009; Goddard et al., 2007; Gollust et al., 2012; Kolor et al., 2009; McGuire et al., 2009; Stewart-Knox et al., 2009; Taylor, 2011). These studies report low awareness of genetic tests among the general public (13-24%) (Cherkas et al., 2010; Goddard et al., 2009; Goddard et al., 2007), but higher awareness among healthcare providers (42-44%) (Goddard et al., 2007; Kolor et al., 2009). Studies have reported an interest in genetic testing among the public, with 50-66% of subjects reporting a willingness to undergo testing (Cherkas et al., 2010; McGuire et al., 2009; Stewart-Knox et al., 2009). Focus group research has also been conducted to better understand the knowledge and attitudes of consumers and healthcare professionals toward nutrigenomics (Morin, 2009; Weir et al., 2010). Most consumers in the focus groups were unfamiliar with the term nutrigenomics and did not relate the term personalized nutrition to an individual’s genetic profile, whereas about half of healthcare professionals were aware of the term nutrigenomics (Morin, 2009). After being provided with an explanation of nutrigenomics, consumers felt that a tailored diet could help reduce the risk of disease development, while healthcare professionals expressed more skepticism (Morin, 2009). While these studies provide valuable insight into the public’s perceptions of nutrigenomics and genetic testing, they have all been either observational or qualitative in design. In addition, there has been some concern that genetic information obtained from a DTC genetic test is not always understood (Leighton et al., 2011), and no studies have examined whether DTC genetic tests that provide personalized nutrition advice are
understandable. The objectives of the present study were to conduct a randomized controlled trial to assess behavioural outcomes as well as the awareness, perceptions and understanding of nutrigenomics and genetic testing.

4.3 Methods

4.3.1 Study design and participants

The present study is a double-blinded, parallel group randomized controlled trial with a 2:1 ratio of participants in the intervention vs. control group. Ethics approval was obtained from the University of Toronto Institutional Review Board and the study was registered with www.clinicaltrials.gov (NCT 01353014). Recruitment was carried out from May to August 2011. Participants provided informed consent by mail or e-mail and then completed a baseline survey designed to assess awareness and opinions of genetic testing and nutrigenomics using 4- and 5- point Likert scales. After the baseline survey was completed, participants were randomized to an intervention (I) or control (C) group using a computer software program (Random Allocation Software) that generated a random list of assignments. A 2:1 ratio of participants in the intervention group compared to the control group was applied since the intervention group consisted of those who would have either the “risk” or “non-risk” genotype for each of the four genes. Participants were informed that they would receive DNA-based dietary advice at some point during the study and those who were randomized to the control group were given the DNA-based advice after the final follow-up assessment was completed.
Participants were recruited from the Toronto Nutrigenomics and Health Study (TNH, n=1,639), which is a cross-sectional study examining the role of genetics in food intake and food selection as well as gene-diet interactions on biomarkers of chronic disease in young men and women between the ages of 20–29 years old at the time of recruitment. The TNH cohort is multi-ethnic, with participants representing three major ethnic groups: Caucasian, East Asian and South Asian (Table 4.1). Recruitment for the TNH study was carried out at the University of Toronto from 2004–2010 by posting study advertisements around the campus, posting a notification of the study on the campus e-mail website and making announcements in lectures. Participants in the TNH study completed a general health and lifestyle questionnaire, a Toronto-modified Willett FFQ and provided a blood sample from which DNA was isolated. Genotyping was performed for several single nucleotide polymorphisms (SNPs) involved in nutrient response and metabolism.

A subset of the TNH cohort (n=354) was contacted by e-mail or phone to participate in the present study (Figure 4.1). Since the recommendations in this study were based on caffeine, vitamin C, sugar and sodium, eligible participants were those who consumed at least 100 mg of caffeine per day, 10% of total energy from total sugars per day and 1500 mg of sodium per day, and did not take vitamin C containing supplements (Table 4.2). These exclusion criteria were applied in an attempt to recruit subjects who were not already strongly adhering to the dietary recommendations that would be provided in the present study. The use of more ideal, stringent cut-offs resulted in too few subjects eligible for participation in the present study (Table 4.3). Three e-mail attempts were made and, if no response was received, one phone call was made. Eligible women who were pregnant or breastfeeding at the time of recruitment were excluded from the study.
Figure 4.1. Consolidated standards of reporting trials (CONSORT) diagram and subject flow through the trial
Table 4.1. Subject characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>All Subjects (n=149)</th>
<th>Intervention (n=92)</th>
<th>Control (n=46)</th>
<th>p-value†</th>
</tr>
</thead>
<tbody>
<tr>
<td>n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years)*</td>
<td>26 ± 4</td>
<td>27 ± 3</td>
<td>26 ± 3</td>
<td>0.82</td>
</tr>
<tr>
<td>Female</td>
<td>113 (76)</td>
<td>69 (75)</td>
<td>37 (80)</td>
<td>0.48</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
<td></td>
<td>0.57</td>
</tr>
<tr>
<td>Caucasian</td>
<td>92 (62)</td>
<td>59 (64)</td>
<td>24 (52)</td>
<td></td>
</tr>
<tr>
<td>East Asian</td>
<td>31 (21)</td>
<td>19 (21)</td>
<td>12 (26)</td>
<td></td>
</tr>
<tr>
<td>South Asian</td>
<td>16 (11)</td>
<td>9 (10)</td>
<td>6 (13)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>10 (7)</td>
<td>5 (5)</td>
<td>4 (9)</td>
<td></td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td></td>
<td></td>
<td>0.43</td>
</tr>
<tr>
<td>Some college or undergraduate training</td>
<td>20 (13)</td>
<td>9 (10)</td>
<td>8 (17)</td>
<td></td>
</tr>
<tr>
<td>College or undergraduate degree</td>
<td>76 (51)</td>
<td>50 (54)</td>
<td>22 (48)</td>
<td></td>
</tr>
<tr>
<td>Graduate degree</td>
<td>53 (36)</td>
<td>33 (36)</td>
<td>16 (35)</td>
<td></td>
</tr>
</tbody>
</table>

Note: *Values shown are mean ± standard deviation.

†p-values are for comparisons between characteristics of the intervention and control group.
Table 4.2. Number of subjects excluded using actual exclusion cut-off points

<table>
<thead>
<tr>
<th>Actual criteria</th>
<th>Number of subjects excluded within each category*</th>
<th>Number of subjects remaining after each exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>No caloric data</td>
<td>7</td>
<td>1,632</td>
</tr>
<tr>
<td>Energy intake &lt;800 kcal/day</td>
<td>35</td>
<td>1,597</td>
</tr>
<tr>
<td>Energy intake &gt;4000 kcal/day and male</td>
<td>34</td>
<td>1,563</td>
</tr>
<tr>
<td>Energy intake &gt;3500 kcal/day and female</td>
<td>50</td>
<td>1,513</td>
</tr>
<tr>
<td>Caffeine &lt;100 mg/day</td>
<td>905</td>
<td>608</td>
</tr>
<tr>
<td>Total sugars &lt;10% energy/day</td>
<td>24</td>
<td>599</td>
</tr>
<tr>
<td>Sodium &lt;1,500 mg/day</td>
<td>414</td>
<td>488</td>
</tr>
<tr>
<td>Vitamin C supplement user</td>
<td>235</td>
<td>404</td>
</tr>
<tr>
<td>Not interested in follow-up studies</td>
<td>167</td>
<td>365</td>
</tr>
<tr>
<td>Incomplete genotyping data</td>
<td>95</td>
<td>354</td>
</tr>
</tbody>
</table>

*Summing the number of subjects excluded within each category does not add up to the total number of subjects excluded after applying all exclusion criteria (n=1,285).
Table 4.3. Number of subjects excluded using ideal exclusion cut-off points

<table>
<thead>
<tr>
<th>Ideal criteria</th>
<th>Number of subjects excluded within each category*</th>
<th>Number of subjects remaining after each exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>No caloric data</td>
<td>7</td>
<td>1,632</td>
</tr>
<tr>
<td>Energy intake &lt;800 kcal/day</td>
<td>35</td>
<td>1,597</td>
</tr>
<tr>
<td>Energy intake &gt;4000 kcal/day and male</td>
<td>34</td>
<td>1,563</td>
</tr>
<tr>
<td>Energy intake &gt;3500 kcal/day and female</td>
<td>50</td>
<td>1,513</td>
</tr>
<tr>
<td>Caffeine &lt;200 mg/day</td>
<td>1,257</td>
<td>256</td>
</tr>
<tr>
<td>Total sugars &lt;25% energy/day</td>
<td>911</td>
<td>105</td>
</tr>
<tr>
<td>Sodium &lt;2,300 mg/day</td>
<td>990</td>
<td>44</td>
</tr>
<tr>
<td>Vitamin C &lt;90 mg/day and male</td>
<td>160</td>
<td>44</td>
</tr>
<tr>
<td>Vitamin C &lt;75 mg/day and female</td>
<td>214</td>
<td>42</td>
</tr>
<tr>
<td>Not interested in follow-up studies</td>
<td>167</td>
<td>34</td>
</tr>
<tr>
<td>Incomplete genotyping data</td>
<td>95</td>
<td>31</td>
</tr>
</tbody>
</table>

*Summing the number of subjects excluded within each category does not add up to the total number of subjects excluded after applying all exclusion criteria (n=1,608).

4.3.2 Intervention
Participants in the intervention group (n=92) were e-mailed a personalized dietary report providing recommendations for daily intakes of caffeine, vitamin C, sugar and sodium based on genotypes for CYP1A2 (rs762551) (Cornelis et al., 2006; Palatini et al., 2009), GSTM1 and GSTT1 (null or functional) (Cahill et al., 2009; Horska et al., 2011), TAS1R2 (rs35874116) (Eny et al., 2010) and ACE (rs4343) (Poch et al., 2001), respectively. The reports were developed in collaboration with Nutrigenomix Inc. (Toronto, Canada), which is a company that is developing a nutrigenetics test kit for registered dietitians. The reports provided participants with their
genotype for each gene, an explanation of what the genotype means in terms of the dietary component and a personalized recommendation for daily intake of the dietary component (Table 4.4). Participants in the control group (n=46) received general dietary recommendations from health organizations for the same dietary components without genetic information (Table 4.4). After participants read the dietary report, a post-intervention survey was completed to assess their opinions of the advice they were given.

Table 4.4. Sample of dietary advice for caffeine

<table>
<thead>
<tr>
<th>Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Health Canada’s recommendation for caffeine is at most 300 mg/day for women of child-bearing age and at most 400 mg/day for other adults. <strong>Since you have the CC version of the CYPIA2 gene, you might benefit from limiting your caffeine intake to no more than 200 mg/day.</strong> Caffeine is found in coffee, tea, cola beverages and energy drinks. One small (8 oz) cup of coffee contains about 100 mg of caffeine, while an 8 oz cup of tea contains about 50 mg of caffeine. One can (355 ml) of cola contains about 30 mg of caffeine, while the caffeine content of energy drinks can range from 80-200 mg depending on the serving size and brand.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Health Canada’s recommendation for caffeine is at most 300 mg/day for women of child-bearing age and at most 400 mg/day for other adults. Caffeine is found in coffee, tea, cola beverages and energy drinks. One small (8 oz) cup of coffee contains about 100 mg of caffeine, while an 8 oz cup of tea contains about 50 mg of caffeine. One can (355 ml) of cola contains about 30 mg of caffeine, while the caffeine content of energy drinks can range from 80-200 mg depending on the serving size and brand.</td>
</tr>
</tbody>
</table>
4.3.3 Surveys

Surveys were created using the online survey site SurveyMonkey (www.surveymonkey.com). Questions included were based on a literature review as well as issues raised in the Harvard University Personal Genetics Education Project (Personal Genetics Education Project, 2010). The baseline survey asked how much participants heard about DTC genetic testing to assess their awareness (Table 4.5). Participants were also asked how much they knew about nutrigenomics. Survey statements such as “I would take a genetic test to learn more about myself” were used to assess participants’ motivations to undergo genetic testing (Table 4.6). The post-intervention survey consisted of statements such as “The dietary recommendations will be useful when I consider my diet” to assess the participants’ opinions of the value of the dietary recommendations (Figure 4.2).

4.3.3 Statistical analysis

Statistical analyses were performed using the Statistical Analysis Software (version 9.2; SAS Institute Inc., Cary, NC). The t-test statistic was used to compare age of subjects in the intervention vs. control group. The chi square statistic was used to compare all other characteristics of subjects in the intervention vs. control group. Participants who reported “strongly agree” or “somewhat agree” to statements on the post-intervention survey were grouped (“agree”) and the chi-square test was used to compare frequency of “agree” to all other responses (“strongly disagree”, “somewhat disagree”, and “neither agree nor disagree”). Fisher’s Exact Test was used when a response category consisted of fewer than 5 counts. Significant p-values are two-sided and less than 0.05.
4.4 Results

4.4.1 Response rate and description of participants

Of the 157 participants who were sent the baseline survey, 149 participants completed the survey giving a response rate of 95% (Figure 4.1). The mean ± standard deviation age of the participants was 25 ± 4 years old and 76% were female (Table 4.1). The participants were highly educated with 87% having a university or college degree. Of the 149 participants who completed the baseline survey, 138 were randomized into an intervention or control group. The remaining 11 participants did not respond to subsequent e-mail attempts. There were no significant differences between characteristics of participants in the control or intervention group (Table 4.1).

4.4.2 Baseline survey

Approximately half of the participants (52%) reported having heard “nothing” about DTC genetic testing, while 18% reported hearing “a fair amount” or “a lot”. A smaller proportion of participants reported knowing “nothing” about nutrigenomics (30%), with just over half reporting that they knew “a little bit” about the science (52%) (Table 4.5). Interest in the relationship between diet and genetics was high, with 90% of participants reporting either “strongly agree” or “somewhat agree” to the survey statement. The majority of participants (87%) also agreed that they would benefit from learning about how their genetic make-up would affect their diet. Consistent with this, 75% of participants agreed that learning about their genetic make-up would affect what they ate. The greatest motivators participants reported for undergoing genetic testing were to learn more about themselves and to encourage themselves to adopt a healthier lifestyle (86% and 83%, respectively), while 73% of participants agreed that
they would take a genetic test to have their doctor monitor their health more closely. Only 7% of participants strongly agreed that they would be uncomfortable learning about their genetic make-up (Table 4.6).

Table 4.5. Awareness of DTC genetic tests and nutrigenomics

<table>
<thead>
<tr>
<th>Question</th>
<th>Nothing</th>
<th>A little bit</th>
<th>A fair amount</th>
<th>A lot</th>
</tr>
</thead>
<tbody>
<tr>
<td>How much have you heard about Direct-to-Consumer Personal Genetic Tests? (through media, friends, peers, etc.)</td>
<td>77 (52)</td>
<td>45 (30)</td>
<td>22 (15)</td>
<td>5 (3)</td>
</tr>
<tr>
<td>How much do you know about nutrigenomics or nutrigenetics? (the science that examines the association between genes, nutrition and health)</td>
<td>44 (30)</td>
<td>78 (52)</td>
<td>22 (15)</td>
<td>5 (3)</td>
</tr>
</tbody>
</table>
Table 4.6. Attitudes toward nutrigenomics and genetic testing

<table>
<thead>
<tr>
<th>Statement</th>
<th>Strongly Agree</th>
<th>Somewhat Agree</th>
<th>Neither Agree nor Disagree</th>
<th>Somewhat Disagree</th>
<th>Strongly Disagree</th>
</tr>
</thead>
<tbody>
<tr>
<td>I am interested in the relationship between diet and genetics.</td>
<td>68 (46)</td>
<td>65 (44)</td>
<td>5 (3)</td>
<td>8 (5)</td>
<td>3 (2)</td>
</tr>
<tr>
<td>I would benefit from learning about how my genetic make-up affects my diet.</td>
<td>99 (66)</td>
<td>32 (21)</td>
<td>10 (7)</td>
<td>4 (3)</td>
<td>4 (3)</td>
</tr>
<tr>
<td>Learning about my genetic make-up will affect what I eat.</td>
<td>25 (17)</td>
<td>86 (58)</td>
<td>29 (19)</td>
<td>7 (5)</td>
<td>2 (1)</td>
</tr>
<tr>
<td>I am uncomfortable learning about my genetic make-up.</td>
<td>11 (7)</td>
<td>11 (7)</td>
<td>13 (9)</td>
<td>22 (15)</td>
<td>92 (62)</td>
</tr>
<tr>
<td>I would take a genetic test to learn more about myself.</td>
<td>72 (48)</td>
<td>56 (38)</td>
<td>14 (10)</td>
<td>5 (3)</td>
<td>2 (1)</td>
</tr>
<tr>
<td>I would take a genetic test to encourage myself to adopt a healthier lifestyle.</td>
<td>67 (45)</td>
<td>57 (38)</td>
<td>13 (9)</td>
<td>8 (5)</td>
<td>4 (3)</td>
</tr>
<tr>
<td>I would take a genetic test to have my doctor monitor my health more closely.</td>
<td>56 (38)</td>
<td>53 (35)</td>
<td>28 (19)</td>
<td>10 (7)</td>
<td>2 (1)</td>
</tr>
</tbody>
</table>
4.4.3 Post-intervention survey

After receiving the dietary report, a greater proportion of participants in the intervention group agreed that they understood the dietary advice they received (93% (I) vs. 78% (C); p=0.009). As expected, more participants in the intervention group agreed that the recommendations they received were new to them (86% (I) vs. 28% (C); p<0.0001). Participants in the intervention group were also more likely to agree that they enjoyed learning about the recommendations (96% (I) vs. 72% (C); p<0.0001) and only 9% agreed that they felt uneasy learning about their genetics (of which only one person reported “strongly agree”). In addition, participants in the intervention group were more likely to agree that the recommendations would be useful when considering their diet (88% (I) vs. 72% (C); p=0.02) and that they would like to know more about the dietary recommendations they were given (95% (I) vs. 76% (C); p<0.0001) (Figure 4.2).
4.5 Discussion

The results of the present study demonstrate that individuals are interested in nutrigenomics and report finding dietary recommendations based on genetics more useful than general dietary recommendations. Although concern exists over the potential for genetic information to induce anxiety in some individuals, very few participants in the intervention group agreed that they felt uneasy learning about their genetic information. Rather, 96% of participants who received their genetic information agreed that they enjoyed learning about their genetic information and dietary
recommendations. This finding suggests that providing this kind of information is not likely to induce anxiety and that young adults may embrace a new era of personalized nutrition that could emerge through the advancement of personalized genomics. However, the nature of the genetic information that was provided in this study might have been perceived as less serious than genetic information related to disease risk. Although the participants in this study had an awareness of the science of nutrigenomics, only 18% reported an awareness of DTC genetic testing while 52% reported no awareness. This finding is consistent with previous surveys of the general public conducted in the UK and US (Cherkas et al., 2010; Goddard et al., 2009; Goddard et al., 2007; Kolor et al., 2009). Despite the considerable attention DTC genetic testing has received in recent years (Lynch et al., 2011), this finding suggests that media coverage of DTC genetic testing has not yet greatly impacted young adults.

Scientific literacy and communication of genetic information are important issues to consider when studying the societal impact of DTC genetic testing (McBride et al., 2010). The literacy demands and quality of informational content across DTC genetic testing websites have been shown to vary (Lachance et al., 2010) and there is concern that consumers may misinterpret or not understand DTC genetic test results (Leighton et al., 2011). In the present study, a greater proportion of participants in the intervention group agreed that they understood the dietary report they were given, suggesting that dietary recommendations based on genetics can be more understandable than general dietary recommendations. This implies that providing individuals with clear, personalized nutritional advice may result in greater understanding. An important strength of the present study is the use of a randomized controlled trial, which eliminates the possibility of confounding and allows for direct comparisons to be made between experimental groups.
In considering the results of this study, some limitations should be noted. In the present study, no in-person contact was made with study participants, potentially affecting the reliability of the results. However, DTC genetic testing can be completed without in-person contact, so the nature of this study closely mimics the nature of DTC genetic testing. Seventy-six percent of participants in this study were females and this affected our ability to report any sex-specific findings. However, excluding the males did not materially alter any of the results, suggesting that there were no major differences between men and women in this population. The age of participants in the current study was between 20-35 years old, so findings might not be representative of other age groups. In addition, the participants were highly educated and previously participated in a nutrigenomics study. This could explain the high degree of reported understanding of the gene-based dietary recommendations, although participants in the control group reported less understanding of the general dietary recommendations, yet were equally educated.

This study is the first to compare the impact of genotype-based personalized dietary advice with general dietary recommendations. Dietary recommendations based on genotype were reported to be more understandable than general dietary recommendations and were also reported to be more useful. Participants reported that they would not be uncomfortable learning about their own genetic information. Consistent with this, participants in the intervention group did not express discomfort in learning about their genetics and were more likely to report enjoyment in learning about the dietary recommendations they were given, as well as a greater desire to know more about the recommendations. Direct-to-consumer genetic tests based on personalized nutrition might, therefore, be more valuable that those based solely on disease risk predictions.
Chapter 5

Disclosure of genetic information and change in dietary intake: a randomized controlled trial

Adapted from: Nielsen DE and El-Sohemy A. (2014) Disclosure of genetic information and change in dietary intake: a randomized controlled trial. (Under review)
5.1 Abstract

Background: Proponents of consumer genetic tests claim that the information can positively impact health behaviors and aid in chronic disease prevention. However, the effects of disclosing genetic information on dietary intake behavior are not clear.

Methods: A randomized controlled trial was conducted with adults aged 20-35 years (n=138) to determine the short- and long-term effects of disclosing genetic information for personalized nutrition on caffeine, vitamin C, added sugars, and sodium intake. Food frequency questionnaires were collected at baseline, 3-months and 12-months and general linear models were used to compare changes in intake between those receiving general dietary advice and those receiving DNA-based dietary advice.

Results: Compared to the control group, no significant changes to dietary intakes of the nutrients were observed at 3-months. At 12-months, subjects in the intervention group who possessed a risk version of ACE and were advised to limit their sodium intake, significantly reduced their sodium intake (mg/day) compared to the control group (-287.3 ± 114.1 vs. 129.8 ± 118.2, p = 0.008). Those who had the non-risk version of ACE did not significantly change their sodium intake compared to the control group (12-months: -244.2 ± 150.2, p=0.11). Among those who had the risk version of ACE, 19% met the targeted recommendation of 1500 mg/day compared to 34% after 12 months (p=0.06).

Conclusions: These findings demonstrate that disclosing genetic information for personalized nutrition results in greater changes in intake for some dietary components compared to population-based dietary advice.
5.2 Introduction

Personal genetic information has become easily obtainable, in large part due to the advancement of the consumer genetic testing industry. As a result of the decreasing costs to carry out genotyping, individuals can now receive personalized feedback regarding their susceptibility to a number of different health conditions at a relatively low cost (Caulfield and McGuire, 2012). The impact that this information may have on health behaviors is of particular interest (Christensen, 2013; McBride et al., 2010), since chronic diseases such as cardiovascular disease and type 2 diabetes have become major public health concerns. There is considerable evidence that these conditions are associated with a number of modifiable health behaviors such as diet, physical activity and smoking, but lifestyle interventions aimed at achieving positive health behavior changes are often ineffective at producing the long-term changes necessary to mitigate disease risk (Desroches et al., 2011). As a result, proponents of personalized medicine claim that health recommendations tailored to an individual’s genetic profile may be more effective at producing behavior change than generic population-based recommendations. A growing body of qualitative research shows strong public interest in genomics and personalized medicine for disease prevention (Cherkas et al., 2010; Goddard et al., 2009; Kolor et al., 2012; Leighton et al., 2011; Stewart-Knox et al., 2009), but there is limited quantitative evidence to support the claim that personalized genomics can be employed as a useful prevention tool.

The study of how human genetic variations modify an individual’s response to diet on various health outcomes, often referred to as nutrigenomics is a key part of personalized medicine (Kaput, 2008) because nutrition is arguably one of the most important modifiers of chronic disease risk (Nielsen and El-Sohemy, 2012a). Genetic testing for personalized nutrition using modifier genes has the potential to be more useful than genetic testing for disease risk
using disease susceptibility genes because the advice that is given from a personalized nutrition test is more specific and actionable than advice from a disease susceptibility test. Indeed, a previous study demonstrated that individuals consider DNA-based dietary advice to be more useful and understandable than general population-based dietary recommendations, and individuals report that they would be more motivated to change their diet if provided with personalized nutrition information based on their genetics (Nielsen and El-Sohemy, 2012b). Individuals who have had their genomes analyzed report that the genetic information impacted their dietary behaviors, although the genetic information they received was not necessarily linked to any specific dietary modification (Kaufman et al., 2012; Maher, 2011). Despite this evidence, no previous study has examined the effect of disclosing personalized genetic information based on nutrigenomics testing on dietary intake behavior. In addition, previous studies investigating the impact of personal genomic information related to disease susceptibility on health behaviors have lacked long-term follow-up data. As a result, the short- and long-term effects of personal genomic information on health behavior are largely unknown. Therefore, the objective of the present study was to determine the short- and long-term effects of disclosing genetic information for personalized nutrition on dietary intake in a population of young adults using a randomized controlled trial.

5.3 Methods

5.3.1 Study design and materials

The present study was intended to mimic the nature of a direct-to-consumer genetic test and, therefore, all study materials were distributed and completed in the mail or electronically and no in-person contact was made with subjects for the present study. Ethics approval was obtained from the University of Toronto Institutional Review Board and the study is registered with
http://clinicaltrials.gov (NCT 01353014). Details on the study design have been published elsewhere (Nielsen and El-Sohemy, 2012b). Briefly, subjects (n=157) who had previously participated in a nutrigenomics research study and had provided a blood sample were invited to complete a 196-item, semi-quantitative Toronto-modified Willet food frequency questionnaire (FFQ) and were then randomized to an intervention or control group (Figure 5.1). The original Willett FFQ was modified to obtain more detailed information on caffeinated beverages and grain products to assess the glycemic index of the diet. Modifications were also made to the fruit and vegetable section of the original FFQ in order to assess particular bioactive components of certain fruits (e.g. grapefruit). The Toronto-modified Willett FFQ has been used in a number of gene-diet epidemiological studies (Fontaine-Bisson et al., 2008; Cahill et al., 2009; Eny et al., 2010; Josse et al., 2013) and has replicated gene-diet associations that have been identified using other methods of dietary assessment, such as a three day food record (Eny et al, 2010). Subjects in the present study were given information on portion sizes, which were indicated for most FFQ items, and were asked to select how frequently they consumed the items over the past month from a list of frequency responses. The FFQ was used to collect detailed information on intake of fruits and vegetables, dairy products, meats and alternatives, grain products, sweets and baked goods, processed and prepared foods, and caffeinated and non-caffeinated beverages. Nutrient analyses were carried out at the Harvard School of Public Health Channing Laboratory using the USDA National Nutrient Database for Standard Reference. Random Allocation Software was used to perform the randomization and a 2:1 ratio of subjects in the intervention group compared to the control group was applied since the intervention group consisted of those who would have either the “risk” or “non-risk” genotype for each of the four genes (Table 5.1). DNA was isolated from whole blood with the GenomicPrep Blood DNA Isolation kit (Amersham Pharmacia
Biotech Inc, Piscataway, NJ) and genotyping was completed using either real-time polymerase chain reaction on an ABI 7000 Sequence Detection System (Applied Biosystems) or a multiplex restriction fragment length polymorphism (RFLP) polymerase chain reaction method, as described previously (Cahill et al., 2009; Eny et al., 2009). Genotyping was verified by using positive control subjects in each 96-well plate as well as a second genotyping of ~5% of a random selection of samples with 100% concordance.
Figure 5.1. Consolidated standards of reporting trials (CONSORT) diagram and subject flow through the trial.
5.3.2 Dietary reports and recommendations

Subjects in the intervention group were genotyped for variants that affect caffeine metabolism (CYP1A2, rs762551) (Cornelis et al., 2006; Palatini et al., 2009), vitamin C utilization (GSTT1 and GSTM1, null or functional) (Cahill et al., 2009), sweet taste perception (TAS1R2, rs35874116) (Eny et al., 2010), and sodium-sensitivity (ACE, rs4343) (Giner et al., 2000; Poch et al., 2001) (Table 5.1). Rs4343 is in complete linkage disequilibrium with the I/D ACE variant (Glenn et al., 2009). These genes were selected as representative sample tests from consumer genetic testing companies. All subjects in the intervention group were informed of their genotypes and given a corresponding DNA-based dietary recommendation for daily intake of caffeine, vitamin C, added sugars and sodium (Nutrigenomix Inc., Toronto, Canada). Those who possessed the genotype that has been associated with increased risk of a health outcome when consuming above or below a certain daily amount were given a “targeted” dietary recommendation. For caffeine and sodium, this recommendation was more stringent than the current general recommendation for daily intake and was based on previous work that evaluated health outcomes according to genotype at different levels of intake (Cornelis et al., 2006; Palatini et al., 2009; Giner et al., 2000; Poch et al., 2001). For added sugars and vitamin C, subjects were informed to be particularly mindful of meeting the current general recommendation for daily intake, since no previous study has examined how individuals respond to consuming various levels of these nutrients according to genotype and, therefore, a different intake level could not be recommended. Subjects who possessed the genotype that has not been associated with increased risk received the current general recommendation for daily intake (Nawrot et al., 2003; Nishida et al., 2004; National Research Council, 2006). The control group was given a report of current general recommendations for the same nutrients without genetic information (Table 5.1).
Information on serving sizes and dietary sources of the dietary components were provided in the advice report. Subjects were e-mailed a monthly reminder of their dietary report and additional FFQs were collected at 3- and 12-month follow-up assessments. Subjects were given a $10 honorarium for each follow-up assessment they completed, for a total payment of $20 if they completed the full 12-month study. Dietary intakes were self-reported by participants on the FFQ with no assistance from study personnel, and the nutrient analyses were made without knowledge of study group assignment.
Table 5.1. Prevalence of risk alleles and associated risk

<table>
<thead>
<tr>
<th>Dietary Component</th>
<th>Gene</th>
<th>Risk Allele</th>
<th>Non-Risk Allele</th>
<th>Associated Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caffeine</td>
<td>CYP1A2</td>
<td>48 (52)</td>
<td>44 (48)</td>
<td>Increased risk of myocardial infarction and hypertension when consuming above 200 mg of caffeine/day</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>General recommendation: ≤ 300 mg/day for women of child-bearing age</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>≤ 400 mg/day for other adults</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Targeted Recommendation: ≤ 200 mg/day for those with risk version of CYP1A2</td>
</tr>
<tr>
<td>Vitamin C</td>
<td>GSTM1 + GSTT1</td>
<td>52 (57)</td>
<td>40 (43)</td>
<td>Increased risk of serum ascorbic acid deficiency when consuming below the RDA for vitamin C</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>General recommendation: RDA for women: ≥ 75 mg/day</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>RDA for men: ≥ 90 mg/day</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Targeted Recommendation: Same as general recommendation</td>
</tr>
<tr>
<td>Added Sugars</td>
<td>TAS1R2</td>
<td>41 (45)</td>
<td>51 (55)</td>
<td>Increased risk of over-consuming sugars</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>General recommendation: ≤ 10% energy/day</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Targeted Recommendation: Same as general recommendation</td>
</tr>
<tr>
<td>Sodium</td>
<td>ACE</td>
<td>64 (70)</td>
<td>28 (30)</td>
<td>Increased risk of sodium-sensitive hypertension when consuming above the AI for sodium</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>General recommendation: UL: ≤ 2300 mg/day</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Targeted Recommendation: AI: ≤ 1500 mg/day for those with risk version of ACE</td>
</tr>
</tbody>
</table>
5.3.3 Statistical analysis

Statistical analyses were performed using the Statistical Analysis Software (version 9.2; SAS Institute Inc., Cary, NC). The \( \alpha \) error was set at 0.05 and all reported \( p \)-values are two-sided. Subject characteristics between the intervention and control group were compared using a Chi-square test for categorical variables and a Student’s t-test for continuous variables. The distributions of nutrient intakes were examined and a log or square root transformation was applied to those that deviated from normality. In these cases, the \( p \)-values from models using transformed values are reported, but untransformed means and measures of spread are reported to facilitate interpretation. Subjects who were likely under-reporters (consuming less than 800 kcal/day) were excluded from the analyses, since dietary intake data from these individuals may not have been reliable.

Baseline mean intakes of vitamin C, sugar, sodium and caffeine were compared between ethnocultural groups using general linear models to determine if any significant dietary differences were present between groups at the start of the study. General linear models were also conducted to test for changes in dietary intakes between baseline and 3-months, and baseline and 12-months, in order to determine the effect of the dietary advice over a short- and long-term period. The Tukey-Kramer test for multiple comparisons was applied to determine whether any changes in intake of the intervention groups differed from the change in intake of the control group. The Chi-square test was used to compare the proportion of subjects meeting the recommendations for intake between baseline and the follow-up assessments. Fisher’s Exact Test was used if a proportion category consisted of fewer than 5 subjects.

Changes in dietary sources that were included in the dietary advice report were assessed
for nutrients that significantly changed between study groups at either the short-term or long-term follow-up assessment. Categorical FFQ food items were converted into continuous servings/day variables and a square root transformation was applied if a variable’s distribution deviated from normality. A general linear model with the Tukey-Kramer test for multiple comparisons was used to compare intake changes between the control and intervention groups.

5.4 Results

5.4.1 Subject characteristics

Of the 157 subjects who were randomized, 125 completed the 12-month study giving an overall retention rate of 80%. Moreover, 91% of subjects who were randomized (n=138) completed the 12-month study. The mean ± SD age of the participants was 26.5 ± 3.0 years and 78% were female. The study population was multi-ethnic with Caucasian, East Asian, and South Asian groups representing the majority of ethnic backgrounds. Over half of the population possessed at least an undergraduate degree. There were no significant differences between the characteristics of participants in the intervention group when compared to the control group (Table 5.2). However, a significant difference in baseline sodium intake (mg/day) was observed between the East Asian and Caucasian groups (mean ± SE: 1837 ± 147 vs. 2319 ± 88, p=0.03). As a result, the general linear models examining changes in dietary intakes are adjusted for ethnocultural group. At baseline, the proportion of subjects who did not meet the general recommendation for caffeine, vitamin C, added sugars and sodium were 9%, 14%, 24% and 39%, respectively. Thirty eight percent of subjects did not meet the targeted recommendation (for those with elevated risk) for caffeine intake at baseline, while 80% did not meet the targeted recommendation for sodium intake. The targeted recommendation for vitamin C and added sugars was the same as the general recommendations.
Table 5.2. Subject characteristics

<table>
<thead>
<tr>
<th></th>
<th>Intervention (n=92)</th>
<th>Control (n=46)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>n (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years)*</td>
<td>27 ± 3</td>
<td>26 ± 3</td>
<td>0.82</td>
</tr>
<tr>
<td>Female</td>
<td>69 (75)</td>
<td>37 (80)</td>
<td>0.48</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
<td>0.57</td>
</tr>
<tr>
<td>Caucasian</td>
<td>59 (64)</td>
<td>24 (52)</td>
<td></td>
</tr>
<tr>
<td>East Asian</td>
<td>19 (21)</td>
<td>12 (26)</td>
<td></td>
</tr>
<tr>
<td>South Asian</td>
<td>9 (10)</td>
<td>6 (13)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>5 (5)</td>
<td>4 (9)</td>
<td></td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td></td>
<td>0.43</td>
</tr>
<tr>
<td>Some college or</td>
<td>9 (10)</td>
<td>8 (17)</td>
<td></td>
</tr>
<tr>
<td>undergraduate training</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>College or</td>
<td>50 (54)</td>
<td>22 (48)</td>
<td></td>
</tr>
<tr>
<td>undergraduate degree</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Graduate degree</td>
<td>33 (36)</td>
<td>16 (35)</td>
<td></td>
</tr>
</tbody>
</table>

*mean ± SD

5.4.2 Changes in dietary intakes

Of the 138 subjects who were randomized, 130 were included in the 3-month follow-up analyses (n=3 lost to follow-up from baseline; n=5 under-reporters) and 123 were included in the 12-month follow-up analyses (n=10 lost to follow-up from 3-months; n=2 under-reporters). There were no differences in the baseline characteristics (e.g. age, proportion of males/females) between those who were included in the final analysis and those who were not (data not shown).
Unadjusted results are shown in Table 5.3. In the adjusted analysis, no significant changes from baseline were observed for intakes of caffeine, vitamin C, added sugars, or sodium at the 3-month follow-up among subjects in the intervention group who carried a risk version of the corresponding gene (intervention risk group) or among subjects who carried the non-risk version (intervention non-risk group) when compared to the control group. At the 12-month follow-up, subjects in the intervention group who were informed that they possessed the risk version of the *ACE* gene, and who were given the targeted advice to consume below the Adequate Intake (AI) of 1500 mg of sodium per day, significantly reduced their mean sodium intake (mg/day) from baseline when compared to the control group (mean ± SE: -287.3 ± 114.1 vs. 129.8 ± 118.2, p = 0.008), which did not receive genetic information and was given the general recommendation for sodium intake (Tolerable Upper Intake Level (UL): ≤2300 mg/day). The mean change in sodium intake among subjects who were informed that they possessed the non-risk version of the *ACE* gene, and who were advised to follow the general recommendation for sodium intake, did not differ from the change in intake of the control group at 12-months (mean ± SE: -244.2 ± 150.2 vs. 129.8 ± 118.2, p=0.11). The mean changes in intakes from baseline for caffeine, vitamin C and added sugars did not differ from the control group at the 12-month follow-up among either the intervention-risk or intervention non-risk groups (Table 5.4). Table 5.5 shows results further adjusted for energy intake, which did not materially alter the findings.

At the 12-month follow-up assessment 66% of subjects in the intervention risk group, 65% of subjects in the intervention non-risk group and 68% of subjects in the control group met the general recommendation for sodium intake of ≤2300 mg/day. In addition, 34% of subjects in the intervention risk group, 19% of subjects in the intervention non-risk group and 24% of subjects in the control group met the targeted recommendation for sodium intake of ≤1500
mg/day. These proportions were not significantly different between the control and intervention groups (data not shown). Among those in the intervention group who had the risk version of the ACE gene, 19% met the targeted recommendation of \( \leq 1500 \) mg/day at baseline compared to 34% after 12 months (\( p=0.06 \)) and 59% met the general recommendation of \( \leq 2300 \) mg/day at baseline compared to 66% after 12 months (\( p=0.41 \)). No changes were observed in food items that were included with the sodium advice between the control and intervention groups at 12-months (Table 5.6).
Table 5.3. Changes in dietary intakes after 3-months and 12-months, unadjusted results

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>3-months</th>
<th>12-months</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Mean ± SE</td>
<td>p-value‡ compared to control group</td>
</tr>
<tr>
<td><strong>Caffeine (mg/day)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intervention risk</td>
<td>45</td>
<td>174.9 ± 15.6</td>
<td>0.99</td>
</tr>
<tr>
<td>Intervention non-risk</td>
<td>43</td>
<td>195.5 ± 15.4</td>
<td>0.47</td>
</tr>
<tr>
<td>Control</td>
<td>42</td>
<td>174.9 ± 15.1</td>
<td></td>
</tr>
<tr>
<td><strong>Vitamin C (mg/day)</strong></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Intervention risk</td>
<td>49</td>
<td>189.5 ± 27.6</td>
<td>0.86</td>
</tr>
<tr>
<td>Intervention non-risk</td>
<td>39</td>
<td>226.0 ± 31.0</td>
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</tr>
<tr>
<td>Control</td>
<td>42</td>
<td>212.7 ± 29.9</td>
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</tr>
<tr>
<td><strong>Added sugars (%e/day)</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Intervention risk</td>
<td>37</td>
<td>8.1 ± 0.8</td>
<td>0.98</td>
</tr>
<tr>
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<td>51</td>
<td>7.4 ± 0.7</td>
<td>0.41</td>
</tr>
<tr>
<td>Control</td>
<td>42</td>
<td>8.8 ± 0.7</td>
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</tr>
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<td><strong>Sodium (mg/day)</strong></td>
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<td></td>
</tr>
<tr>
<td>Intervention risk</td>
<td>62</td>
<td>2212.9 ± 102.1</td>
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</tr>
<tr>
<td>Intervention non-risk</td>
<td>26</td>
<td>2358.2 ± 157.7</td>
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</tr>
<tr>
<td>Control</td>
<td>42</td>
<td>2074.8 ± 124.1</td>
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</table>

‡p-values are for log-transformed values (square root transformed for caffeine).
Table 5.4. Changes in dietary intakes after 3-months and 12-months, adjusted for ethnicity

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>3-months</th>
<th>12-months</th>
<th>p-value‡ compared to control group</th>
</tr>
</thead>
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<tr>
<td></td>
<td>n</td>
<td>Mean ± SE</td>
<td>p-value‡</td>
<td>n</td>
</tr>
<tr>
<td>Caffeine (mg/day)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intervention risk</td>
<td>45</td>
<td>182.9 ± 17.2</td>
<td>0.99</td>
<td>45</td>
</tr>
<tr>
<td>Intervention non-risk</td>
<td>43</td>
<td>195.8 ± 18.0</td>
<td>0.78</td>
<td>43</td>
</tr>
<tr>
<td>Control</td>
<td>42</td>
<td>185.6 ± 17.4</td>
<td>0.78</td>
<td>42</td>
</tr>
<tr>
<td>Caffeine (mg/day)</td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>Intervention risk</td>
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<td>204.1 ± 35.0</td>
<td>0.91</td>
<td>49</td>
</tr>
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<td>229.7 ± 35.7</td>
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<td>39</td>
</tr>
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<td>Control</td>
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<td>227.1 ± 34.6</td>
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<td>42</td>
</tr>
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<td>Vitamin C (mg/day)</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Intervention risk</td>
<td>49</td>
<td>9.4 ± 0.8</td>
<td>0.99</td>
<td>49</td>
</tr>
<tr>
<td>Intervention non-risk</td>
<td>51</td>
<td>8.3 ± 0.8</td>
<td>0.53</td>
<td>51</td>
</tr>
<tr>
<td>Control</td>
<td>42</td>
<td>9.3 ± 0.7</td>
<td>0.53</td>
<td>42</td>
</tr>
<tr>
<td>Sodium (mg/day)</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intervention risk</td>
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<td>2202.2 ± 128.5</td>
<td>0.62</td>
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</tr>
<tr>
<td>Intervention non-risk</td>
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<td>2256.7 ± 171.7</td>
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<td>26</td>
</tr>
<tr>
<td>Control</td>
<td>42</td>
<td>2082.8 ± 140.6</td>
<td>0.47</td>
<td>42</td>
</tr>
</tbody>
</table>

‡p-values are for log-transformed values (square root transformed for caffeine).
Table 5.5. Changes in dietary intakes after 3-months and 12-months, adjusted for ethnicity and energy intake

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th></th>
<th></th>
<th>3-months</th>
<th></th>
<th></th>
<th>12-months</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Mean ± SE</td>
<td>p-value&lt;sup&gt;‡&lt;/sup&gt; compared to control group</td>
<td>n</td>
<td>Mean change ± SE</td>
<td>p-value&lt;sup&gt;‡&lt;/sup&gt; compared to control group</td>
<td>n</td>
<td>Mean change ± SE</td>
<td>p-value&lt;sup&gt;‡&lt;/sup&gt; compared to control group</td>
</tr>
<tr>
<td>Caffeine (mg/day)</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Intervention risk</td>
<td>45</td>
<td>179.1 ± 16.4</td>
<td>0.89</td>
<td>45</td>
<td>-1.6 ± 14.7</td>
<td>0.94</td>
<td>41</td>
<td>-15.8 ± 18.5</td>
<td>0.87</td>
</tr>
<tr>
<td>Intervention non-risk</td>
<td>43</td>
<td>193.4 ± 17.1</td>
<td>0.90</td>
<td>43</td>
<td>-23.6 ± 15.3</td>
<td>0.44</td>
<td>41</td>
<td>4.1 ± 19.1</td>
<td>0.99</td>
</tr>
<tr>
<td>Control</td>
<td>42</td>
<td>188.2 ± 16.5</td>
<td>0.90</td>
<td>42</td>
<td>-6.4 ± 14.7</td>
<td>0.94</td>
<td>41</td>
<td>0.2 ± 17.5</td>
<td>0.94</td>
</tr>
<tr>
<td>Vitamin C (mg/day)</td>
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<td>Intervention risk</td>
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<td>0.54</td>
<td>49</td>
<td>49.0 ± 37.4</td>
<td>0.96</td>
<td>45</td>
<td>35.9 ± 43.2</td>
<td>0.73</td>
</tr>
<tr>
<td>Intervention non-risk</td>
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<td>230. ± 34.3</td>
<td>0.99</td>
<td>39</td>
<td>-6.6 ± 38.5</td>
<td>0.29</td>
<td>37</td>
<td>-61.3 ± 43.9</td>
<td>0.43</td>
</tr>
<tr>
<td>Control</td>
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<td>231.3 ± 33.1</td>
<td>0.99</td>
<td>42</td>
<td>46.0 ± 36.9</td>
<td>0.99</td>
<td>41</td>
<td>-21.6 ± 40.2</td>
<td>0.99</td>
</tr>
<tr>
<td>Added sugars (%/day)</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intervention risk</td>
<td>37</td>
<td>9.4 ± 0.8</td>
<td>0.99</td>
<td>37</td>
<td>-0.9 ± 0.9</td>
<td>0.18</td>
<td>33</td>
<td>0.4 ± 0.9</td>
<td>0.98</td>
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<tr>
<td>Intervention non-risk</td>
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<td>0.53</td>
<td>51</td>
<td>0.5 ± 0.8</td>
<td>0.99</td>
<td>49</td>
<td>-0.4 ± 0.8</td>
<td>0.85</td>
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<tr>
<td>Control</td>
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<td>0.53</td>
<td>42</td>
<td>0.6 ± 0.8</td>
<td>0.99</td>
<td>41</td>
<td>-0.4 ± 0.8</td>
<td>0.98</td>
</tr>
<tr>
<td>Sodium (mg/day)</td>
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<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Intervention risk</td>
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<td>2123.6 ± 88.3</td>
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<td>62</td>
<td>-116.4 ± 106.5</td>
<td>0.21</td>
<td>56</td>
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<tr>
<td>Intervention non-risk</td>
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<td>2242.4 ± 117.7</td>
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<td>102.2 ± 141.7</td>
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<td>-218.7 ± 141.2</td>
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</tr>
<tr>
<td>Control</td>
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<td>2129.3 ± 96.5</td>
<td>0.96</td>
<td>42</td>
<td>97.2 ± 116.1</td>
<td>0.99</td>
<td>41</td>
<td>136.5 ± 111.0</td>
<td>0.85</td>
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</table>

<sup>‡</sup>p-values are for log-transformed values (square root transformed for caffeine).
Table 5.6. Changes in sodium advice food items, adjusted for ethnicity and energy intake

<table>
<thead>
<tr>
<th>Food item (servings/day)</th>
<th>n</th>
<th>Mean ± SE</th>
<th>p-value‡ compared to control group</th>
<th>Mean change ± SE</th>
<th>p-value‡ compared to control group</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Baseline</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Canned soups</td>
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</tr>
<tr>
<td>Intervention risk</td>
<td>56</td>
<td>0.02 ± 0.01</td>
<td>0.96</td>
<td>-0.01 ± 0.01</td>
<td>0.95</td>
</tr>
<tr>
<td>Intervention non-risk</td>
<td>26</td>
<td>0.02 ± 0.01</td>
<td>0.93</td>
<td>0.00 ± 0.01</td>
<td>0.99</td>
</tr>
<tr>
<td>Control</td>
<td>41</td>
<td>0.02 ± 0.01</td>
<td>0.93</td>
<td>0.00 ± 0.01</td>
<td>0.99</td>
</tr>
<tr>
<td>Potato chips</td>
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<td></td>
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</tr>
<tr>
<td>Intervention risk</td>
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<td>0.65</td>
<td>-0.01 ± 0.03</td>
<td>0.99</td>
</tr>
<tr>
<td>Intervention non-risk</td>
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<td>0.12 ± 0.04</td>
<td>0.98</td>
<td>0.09 ± 0.04</td>
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</tr>
<tr>
<td>Control</td>
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<td>0.11 ± 0.03</td>
<td>0.98</td>
<td>-0.01 ± 0.03</td>
<td>0.99</td>
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<tr>
<td>Processed meats</td>
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</tr>
<tr>
<td>Intervention risk</td>
<td>56</td>
<td>0.46 ± 0.08</td>
<td>0.91</td>
<td>0.00 ± 0.09</td>
<td>0.84</td>
</tr>
<tr>
<td>Intervention non-risk</td>
<td>26</td>
<td>0.39 ± 0.10</td>
<td>0.96</td>
<td>0.04 ± 0.11</td>
<td>0.61</td>
</tr>
<tr>
<td>Control</td>
<td>41</td>
<td>0.42 ± 0.09</td>
<td>0.96</td>
<td>0.17 ± 0.10</td>
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</tr>
<tr>
<td>Processed cheese</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Intervention risk</td>
<td>56</td>
<td>0.60 ± 0.10</td>
<td>0.87</td>
<td>-0.13 ± 0.11</td>
<td>0.99</td>
</tr>
<tr>
<td>Intervention non-risk</td>
<td>26</td>
<td>0.70 ± 0.12</td>
<td>0.97</td>
<td>-0.19 ± 0.14</td>
<td>0.96</td>
</tr>
<tr>
<td>Control</td>
<td>41</td>
<td>0.66 ± 0.10</td>
<td>0.97</td>
<td>-0.14 ± 0.12</td>
<td></td>
</tr>
</tbody>
</table>

‡ p-values are for square root transformed values
5.5 Discussion

The present study is the first to evaluate the effect of disclosing genetic information related to personalized nutrition on dietary intake and the findings show that DNA-based dietary advice results in greater changes in self-reported intake for some dietary components compared to population-based dietary advice. Dietary modification is an important health behavior for chronic disease prevention. Changes in health behaviors have not been frequently reported in previous studies that have investigated the effect of disclosing genetic information related to disease risk (Bloss et al., 2011b; Bloss et al., 2011c; Collier, 2012; Grant et al., 2013) and a 2010 Cochrane review concluded that disclosing genetic risk information for disease has little impact on actual behavior, although it has a small effect on one’s intention to change (Marteau et al., 2010).

However, the genomic information provided in those studies was related to disease susceptibility, not personalized nutrition, and the studies lacked a long-term follow-up assessment. Moreover, participants in previous studies were not provided with personalized recommendations on what behavioural strategies should be followed to mitigate disease risk. Results from the present study provide evidence that genetic testing for personalized nutrition may be more clinically useful than testing for disease susceptibility, since a change in sodium intake was observed after 12-months among the intervention risk group. In line with this finding, a previous study comparing a personalized, gene-based weight loss diet with a traditional weight loss diet reported that subjects on the personalized diet had greater dietary adherence, longer-term maintenance of weight loss and greater improvements in fasting blood glucose levels (Arkadianos et al., 2007). In addition, a study investigating health behaviour changes after revealing genetic risk for Alzheimer’s disease reported that the addition of a vitamin E supplement was the most common change to vitamin or medication use among subjects who
were informed that they were at greater genetic risk (Chao et al., 2008).

Although changes were observed in dietary intakes of sodium among the intervention-risk group of subjects at the 12-month follow-up, no changes in intakes of caffeine, vitamin C or added sugars were observed at either follow-up assessment. This may be due to the baseline intakes of these nutrients that were already mostly in line with the recommendations that were given to the subjects who possessed a risk allele, which is a limitation of the present study. Nevertheless, variants in other genes involved in reward pathways may play a role in one’s ability to reduce consumption of some of these dietary components (Cornelis et al., 2011; Eny et al., 2009). Indeed, the National Human Genome Research Institute has recommended investigation into the potential for genomic information to improve behaviour change interventions by customizing interventions to individuals based on genetic markers of adherence (Green and Guyer, 2011; McBride et al., 2012). Despite the lack of an intervention effect on intake of these three dietary components in the present study, it is worth noting that subjects who possessed a non-risk allele for the corresponding genes did not shift to a less desirable level of intake by increasing their consumption of caffeine, sodium or added sugars, or decreasing their intake of vitamin C. Although we did not report a detrimental impact on dietary intake behaviour as a result of disclosing genetic information indicating no increased risk, proper communication of genetic test results is needed to prevent individuals from misunderstanding or misinterpreting the information and to guide them toward making appropriate lifestyle changes where necessary (Ferguson, 2012). As such, providing such information through a qualified healthcare professional might be more appropriate than providing such information direct-to-consumer. If the results of a genetic test require dietary modification then a dietitian might be best suited to guide the consumer whereas a genetic counselor would be better suited for communicating
results of tests for high penetrance genes that may require a more severe intervention, such as
*BRCA1* and breast cancer risk.

Another limitation of the present study is the use of a FFQ to assess dietary intake, which is more useful in larger, population-based studies, as it provides a measure of relative intake rather than actual intake. However, the objective of the present study was to assess change in dietary intakes, which is a relative measure of intake. In addition, the sample size was small, yet comparable to previous studies examining the impact of disclosing genetic information on particular health behaviours (Arkadianos et al., 2007; Chao et al., 2008; Grant et al., 2013), and subjects were highly educated and recruited from a previous nutrigenomics study. The reported reduction of nearly 300 mg of sodium per day in the intervention risk group was not sufficient to reduce the average sodium intake to the AI of 1500 mg/day, which was the targeted recommendation provided in the dietary report. Nevertheless, a recent Institute of Medicine report concluded that there is no benefit to sharply restricting sodium intake to the level of the AI (Institute of Medicine, 2013) and a 2010 computer-simulated model examining the effect of dietary salt reduction on future cardiovascular disease projected that a 1 g/day reduction in average population salt intake, which is equivalent to about 400 mg of sodium, would prevent up to 28,000 deaths from any cause and would be more cost-effective than using medications to manage hypertension (Bibbins-Domingo et al., 2010). Therefore, the approximate 300 mg/day reduction in sodium intake reported in the present study would be considered clinically relevant for the prevention or management of hypertension and risk of cardiovascular disease.

Strengths of the present study are the inclusion of a control group, which provided a method of comparing the utility of DNA-based dietary advice to population-based
recommendations, and the randomized design, which minimizes the potential for confounding effects. Including a 3- and 12-month follow-up assessment enabled us to examine the short- and long-term effects of the intervention. The finding that sodium intake was significantly reduced compared to the control group after 12-months among subjects in the intervention group with the risk version of the ACE gene suggests that longer-term studies are required to fully determine the impact of disclosing genetic information. Moreover, conducting the present study so that it closely resembles a consumer genetic test increases the validity of the findings to reflect the real world effects among consumer genetic test users. Early adopters of consumer genetic testing are more likely to be highly educated and Caucasian, with a substantial proportion of users between the ages of 18-49 years (Bloss et al., 2011c; Gollust et al., 2012; Kaufman et al., 2012). One study has reported a larger proportion of female consumers (Gollust et al., 2012). As a result, the subjects in the present study may be representative of the early adopters of consumer genetic testing.

The present study was the first to empirically test the effect of DNA-based personalized nutritional advice on dietary intake behaviour compared to population-based dietary advice. The findings show that DNA-based dietary advice can impact dietary intake to a greater extent than general population-based recommendations and provide supportive evidence for the clinical utility of personalized nutrition to assist in chronic disease prevention.
Chapter 6

Perceptions of genetic testing for personalized nutrition: a randomized trial of DNA-based dietary advice

6.1 Abstract

Background: Consumer genetic tests have facilitated easy access to personal genetic information related to health and nutrition, however, consumer perceptions of the nutritional information provided from these tests have not been evaluated.

Objective: To assess individual perceptions of genetic testing and personalized nutrition and to determine whether a personalized nutrition intervention modifies perceptions.

Design: A randomized controlled trial was conducted with adults aged 20-35 years (n=138). Subjects in the intervention (I) group were given a report of genotype-based dietary advice and those in the control (C) group and were given a report of general dietary advice. A survey was completed at baseline and 3- and 12-months after distributing the reports to assess perceptions of the advice between the two groups.

Results: As compared to baseline, subject responses increased significantly toward the positive end of a Likert scale at 3-months for the statements “I am interested in the relationship between diet and genetics” (mean change ± SD: 0.28 ± 0.99, p=0.0002) and “I would take a genetic test to have my healthcare professional monitor my health more closely” (mean change ± SD: 0.20 ± 1.00, p=0.02). At 12-months, subject responses for the statement “I am interested in the relationship between diet and genetics” remained significantly increased toward the positive end of the scale, as compared to baseline (mean change ± SD: 0.20 ± 1.04, p=0.02). The majority of subjects indicated that a university research lab (47%) or healthcare professional (41%) were the best sources for obtaining accurate personal genetic information, while a DTC genetic testing company received the fewest selections (12%). Most subjects (56%) considered dietitians to be
the best source of personalized nutrition followed by medical doctors (27%), naturopaths (8%) and nurses (6%).

Conclusions: These results suggest that perceptions of genetic testing and personalized nutrition changed over the course of the present intervention study. Individuals view a research lab or healthcare professional as better providers of genetic information than a DTC genetic testing company and registered dietitians are considered to be the best providers of personalized nutrition advice.
6.2 Introduction

The direct-to-consumer (DTC) genetic testing industry has provided individuals with easy access to their own personal genetic information. Many of these tests provide information on susceptibility to different diseases and some provide nutrition information (Sterling, 2008). As a result, proponents of this technology claim that the information may positively impact health behaviours such as diet, smoking and exercise in an effort to prevent the development of chronic diseases. However, controversies surrounding DTC genetic testing continue to arise, in part due to the unregulated nature of the industry. The U.S. Food and Drug Administration (FDA) recently ordered 23andMe, one of the largest DTC genetic testing companies, to stop the sales and marketing of their health-related genetic test (Coghlan, 2013), and a class action lawsuit was filed against the company shortly after claiming that the company’s advertising misled consumers (O’Connor, 2013). Concerns over the analytical validity and clinical utility of the tests, along with little information about what consumers do with the genetic test results have sparked debate on how to properly regulate this emerging technology. Government bodies around the world are working to create standards and guidelines to ensure appropriate distribution of these tests to consumers (Borry et al., 2012; Human Genetics Commission, 2010; Wagner, 2010), however, these efforts require a comprehensive understanding of the public’s perceptions of these technologies, as well as evidence of the impact of test results on consumer actions and behaviours.

Previous qualitative studies have shown substantial public interest in genetic testing and personal genomics (Cherkas et al., 2010; Goddard et al., 2009; Kolor et al., 2012), including interest in the field of nutrigenomics (Goddard et al., 2007; Ronteltap et al., 2009; Roosen et al., 2008; Stewart-Knox et al., 2009), the study of how human genetic variations modify an
individual’s response to diet on various health outcomes. The benefits of the application of nutrigenomics include the creation of gene-based dietary interventions to prevent chronic diseases, personalized dietary recommendations to optimize an individual’s dietary response and more precise public health advice for dietary intake and supplement use (Stenne et al., 2013). A European survey reported that out of 5,967 respondents, 66% were willing to undergo nutrigenomics testing and 27% would follow a personalized diet based on their test results (Stewart-Knox et al., 2009). In addition, DNA-based dietary advice was considered to be more useful and understandable than general population-based dietary recommendations in another study and individuals in that study also reported that they would be more motivated to change their diet if provided with gene-based personalized nutrition information (Nielsen and El-Sohemy, 2012b). However, individual perceptions of sources and providers of personal genetic information and personalized nutrition advice, as well as the utility of DNA-based dietary advice compared with general dietary recommendations, have not been explored. Therefore, the objective of the present study was to assess and compare perceptions of genetic testing and personalized nutrition in a population of young adults who are given DNA-based dietary advice or general dietary recommendations using a randomized controlled trial.

6.3 Methods
6.3.1 Study design and materials
Materials for the present study were distributed and completed in the mail or electronically and no in-person contact was made with subjects, since the study was intended to mimic the nature of a DTC genetic test. Ethics approval was obtained from the University of Toronto Institutional
Review Board and the study is registered with http://clinicaltrials.gov (NCT 01353014). Recruitment took place at the University of Toronto, which does not offer a dietetics program. Details on the study design have been published elsewhere (Nielsen and El-Sohemy, 2012b). Briefly, eligible subjects (n=354) who had previously participated in a nutrigenomics research study and had provided a blood sample were invited to take part in the present study. The dietary recommendations provided in this study were based on caffeine, vitamin C, sugar, and sodium, therefore, subjects were excluded if they consumed less than 100 mg of caffeine per day, less than 10% of energy from total sugars per day, less than 1,500 mg of sodium per day and if they used vitamin C-containing supplements. Women who were pregnant or breast-feeding at the time of recruitment were also excluded. A total of 157 subjects expressed interest in participating in the study and were sent a baseline survey to assess perceptions of genetic testing and personalized nutrition. Those who completed the baseline survey were randomized to an intervention or control group using Random Allocation Software (Figure 6.1). A 2:1 ratio of subjects in the intervention group compared to the control group was used to account for the proportion of subjects in the intervention group who would carry either the “risk” or “non-risk” genotype for each of the genes that were tested in the study (Table 6.1).
Figure 6.1. Consolidated standards of reporting trials (CONSORT) diagram and subject flow through the trial
6.3.2 Dietary advice reports

Subjects were given a dietary advice report that provided recommendations for daily intakes of caffeine, vitamin C, added sugars and sodium approximately one week after they completed the baseline survey. Monthly reminders of the report were e-mailed to the subjects over the course of 12-months. The report for the intervention group included the subjects’ personal genotypes for genes that affect response to each of the four dietary components and the corresponding dietary recommendation was based on the subjects’ genotype. The report for the control group provided general dietary recommendations for caffeine (Nawrot et al., 2003), vitamin C (National Research Council, 2006), added sugars (Nishida et al., 2004) and sodium (National Research Council, 2006) from recognized health institutes with no genetic information.

The intervention group reports were developed in collaboration with Nutrigenomix Inc., a personalized nutrition genetic testing company in Toronto, Canada. The genetic information provided included the following genes and their associated dietary response: CYP1A2 and caffeine metabolism (Cornelis et al., 2006; Palatini et al., 2009), GSTT1 and GSTM1 and vitamin C utilization (Cahill et al., 2009), TAS1R2 and sweet taste perception and ACE and sodium sensitivity (Giner et al., 2000; Poch et al., 2001) (Table 6.1). A “targeted” dietary recommendation was provided in cases where a subject carried the version of the gene that has been associated with increased risk of a health outcome when consuming above or below a certain daily amount of the corresponding dietary component. The targeted recommendation was more stringent than the current general recommendation for intake. Subjects who possessed the version of the gene that has not been associated with increased risk of a health outcome were given the current general recommendation for daily intake.
Table 6.1. Prevalence of risk alleles in intervention group and associated risk

<table>
<thead>
<tr>
<th>Gene</th>
<th>Risk Allele</th>
<th>Non-Risk Allele</th>
<th>Associated Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (%)</td>
<td>n (%)</td>
<td></td>
</tr>
<tr>
<td>CYP1A2</td>
<td>48 (52)</td>
<td>44 (48)</td>
<td>Increased risk of myocardial infarction when consuming &gt;200 mg of caffeine/day</td>
</tr>
<tr>
<td>GSTM1+</td>
<td>52 (57)</td>
<td>40 (43)</td>
<td>Increased risk of serum ascorbic acid deficiency when consuming below the RDA for vitamin C</td>
</tr>
<tr>
<td>GSTT1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TAS1R2</td>
<td>41 (45)</td>
<td>51 (55)</td>
<td>Increased risk of over-consuming sugars</td>
</tr>
<tr>
<td>ACE</td>
<td>64 (70)</td>
<td>28 (30)</td>
<td>Increased risk of sodium-sensitive hypertension when consuming above the AI for sodium</td>
</tr>
</tbody>
</table>

6.3.3 Surveys

Four surveys were collected from the intervention and control group over the course of the present study; at baseline, immediately after the advice reports were distributed, and at the 3- and 12-month follow-up assessments. The surveys were administered online and assessed subjects’ perceptions toward genetic testing and personalized nutrition. The baseline survey also collected demographic information. Specifically, items on the surveys assessed subjects’ interests in personalized nutrition, motivations for seeking out genetic testing, and perceptions of (i) sources for obtaining personal genetic information, (ii) providers of personalized nutrition advice and (iii) the utility of DNA-based dietary advice. Whether or not the information in the dietary
reports was shared with others was also assessed. The surveys consisted of five-point Likert-type scales where subjects were asked to indicate the extent to which they agreed with various statements on a scale that contained the following response options: strongly disagree, somewhat disagree, neither agree or disagree, somewhat agree and strongly agree; multiple choice questions where the subjects were instructed to select all response options that applied; and one “yes”, “no” or “no opinion” question where the subjects could only select one response. A number of items included in the surveys were adapted from questions used in a previous UK survey of public interest in personal genome testing (Cherkas et al., 2010) and four of these items that were present on the baseline survey were repeated at the follow-up points to determine if responses to these items changed after the intervention.

6.3.4 Statistical analysis

Statistical analyses were conducted using the Statistical Analysis Software version 9.2 (SAS Institute Inc., Cary, NC). Subject characteristics between the intervention and control group were compared using a chi-square test for categorical variables and a Student’s t-test for continuous variables. For the multiple choice and yes/no/no opinion questions, survey responses between the intervention and control group were compared using the chi-square test. Fisher’s exact test was used instead if a response category contained fewer than five counts. Responses of the intervention and control group were combined if significant differences were not present between the groups. To examine changes in responses to the repeated Likert-type survey items, responses were coded from 1 to 5, with 1 denoting the negative end of the scale (strongly disagree) and 5 denoting the positive end (strongly agree). Baseline responses were subtracted from follow-up responses and the non-parametric Kruskal Wallis test was used to compare
changes of mean responses between the intervention and control group. Responses were combined if a significant difference was not present between groups. The non-parametric Wilcoxon signed-rank test was used to identify significant changes in the responses between baseline and the 3- and 12-month follow-up surveys. The α error was set at 0.05 and all reported p-values are two-sided.

6.4 Results

6.4.1 Subject characteristics

Of the 157 subjects who were sent the baseline survey, 135 subjects completed the 3-month follow-up assessment and 125 completed the 12-month follow-up assessment giving an overall retention rate of 80%. There were no significant differences between the characteristics of subjects in the intervention group when compared to the control group (Table 6.2). The mean ± SD age of the subjects was 26.5 ± 3.0 years and 78% were female. The study population was multi-ethnic with Caucasian, East Asian, and South Asian groups representing the majority of ethnic backgrounds. Over half of the population possessed at least an undergraduate degree.

Some survey results from the baseline and intervention time point surveys have been published previously (Nielsen and El-Sohemy, 2012b).

Table 6.2. Subject Characteristics (See Chapter 4, Table 4.1.)
6.4.2 Opinions of sources for personal genetic information and personalized nutrition advice

On the 3-month survey, subjects were asked to indicate which source they felt would provide them with the most accurate personal genetic information. The response options were “university research lab”, “healthcare professional”, and “direct-to-consumer genetic testing company” with subjects being instructed to select all that applied. Since no significant differences were observed between the responses of the intervention group when compared to the control group (data not shown), the responses of both groups were combined. The most commonly selected response among the 135 subjects was “university research lab” (47%), followed by “healthcare professional” (41%) and “direct-to-consumer genetic testing company” (12%). Subjects were also asked to indicate which source they felt would provide them with the best personalized nutrition advice. The response options were “registered dietitian”, “medical doctor”, “registered nurse”, “naturopath”, or “other” and subjects were instructed to select all that applied. The option “other” required subjects to specify an open-ended response. Similar to the previous finding, no significant differences were observed between the responses of the intervention group when compared to the control group (data not shown), so the responses of both groups were combined. The most commonly selected response was “registered dietitian” (56%), followed by “medical doctor” (27%), “naturopath” (6%), “registered nurse” (8%), and “other” (3%). Four subjects selected “other” and the open-ended responses were either “myself” (n=3: 2 subjects from the intervention group, 1 from the control group) or “a researcher” (n=1: subject from the intervention group).
6.4.3 Changes in perceptions of personalized nutrition and genetic testing

Four statements that were included on the baseline survey to assess individual interest in personalized nutrition and motivations for seeking out genetic testing were repeated on the 3-month and 12-month survey in order to determine whether perceptions of these statements changed over the course of the study (Table 6.3). Subjects who completed the entire 12-month study were included in these analyses (n=125). No significant differences in the mean response changes were observed between the intervention and control group for any of the four statements (data not shown) and, therefore, responses of the two groups were combined. At 3-months, significant changes were observed for two statements as compared to baseline (Table 6.4). Subject responses increased significantly toward the positive end of the scale for the statements “I am interested in the relationship between diet and genetics” (mean change ± SD: 0.28 ± 0.99, p=0.0002) and “I would take a genetic test to have my healthcare professional monitor my health more closely” (mean change ± SD: 0.20 ± 1.00, p=0.02). At 12-months, subject responses for the statement “I am interested in the relationship between diet and genetics” were also significantly increased toward the positive end of the scale, as compared to baseline (mean change ± SD: 0.20 ± 1.04, p=0.02).
Table 6.3. Survey responses at baseline, 3-months and 12-months

<table>
<thead>
<tr>
<th>Survey statement</th>
<th>Strongly Disagree</th>
<th>Somewhat Disagree</th>
<th>Neither Agree nor Disagree</th>
<th>Somewhat Agree</th>
<th>Strongly Agree</th>
</tr>
</thead>
<tbody>
<tr>
<td>Numerical value</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I am interested in the relationship between diet and genetics.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>3 (2)</td>
<td>6 (5)</td>
<td>4 (3)</td>
<td>58 (46)</td>
<td>54 (43)</td>
</tr>
<tr>
<td>3-months</td>
<td>3 (2)</td>
<td>2 (2)</td>
<td>3 (2)</td>
<td>37 (30)</td>
<td>80 (64)</td>
</tr>
<tr>
<td>12-months</td>
<td>3 (2)</td>
<td>0 (0)</td>
<td>5 (4)</td>
<td>49 (39)</td>
<td>68 (54)</td>
</tr>
<tr>
<td>I would take a genetic test to learn more about myself.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>2 (2)</td>
<td>4 (3)</td>
<td>13 (10)</td>
<td>45 (36)</td>
<td>61 (49)</td>
</tr>
<tr>
<td>3-months</td>
<td>4 (3)</td>
<td>2 (2)</td>
<td>9 (7)</td>
<td>44 (35)</td>
<td>66 (53)</td>
</tr>
<tr>
<td>12-months</td>
<td>5 (4)</td>
<td>5 (4)</td>
<td>14 (11)</td>
<td>40 (32)</td>
<td>61 (49)</td>
</tr>
<tr>
<td>I would take a genetic test to encourage myself to adopt a healthier lifestyle.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>4 (3)</td>
<td>7 (6)</td>
<td>9 (7)</td>
<td>51 (41)</td>
<td>54 (43)</td>
</tr>
<tr>
<td>3-months</td>
<td>4 (3)</td>
<td>3 (2)</td>
<td>11 (9)</td>
<td>51 (41)</td>
<td>56 (45)</td>
</tr>
<tr>
<td>12-months</td>
<td>4 (3)</td>
<td>10 (8)</td>
<td>16 (13)</td>
<td>49 (39)</td>
<td>46 (37)</td>
</tr>
<tr>
<td>I would take a genetic test to have my healthcare professional monitor my health more closely.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>2 (2)</td>
<td>8 (6)</td>
<td>19 (15)</td>
<td>48 (38)</td>
<td>48 (38)</td>
</tr>
<tr>
<td>3-months</td>
<td>3 (2)</td>
<td>4 (3)</td>
<td>10 (8)</td>
<td>49 (39)</td>
<td>59 (47)</td>
</tr>
<tr>
<td>12-months</td>
<td>3 (2)</td>
<td>8 (6)</td>
<td>19 (15)</td>
<td>48 (38)</td>
<td>47 (38)</td>
</tr>
</tbody>
</table>

Percentages may not total to 100% due to rounding.
Table 6.4. Changes in perceptions of personalized nutrition and genetic testing

<table>
<thead>
<tr>
<th>Survey statement</th>
<th>Mean response ± SD</th>
<th>Mean change ± SD from baseline</th>
<th>p-value compared to baseline</th>
</tr>
</thead>
<tbody>
<tr>
<td>I am interested in the relationship between diet and genetics.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>4.23 ± 0.91</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3-months</td>
<td>4.51 ± 0.83</td>
<td>0.28 ± 0.99</td>
<td>0.0002</td>
</tr>
<tr>
<td>12-months</td>
<td>4.43 ± 0.79</td>
<td>0.20 ± 1.04</td>
<td>0.02</td>
</tr>
<tr>
<td>I would take a genetic test to have my healthcare professional monitor my health more closely.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>4.06 ± 0.97</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3-months</td>
<td>4.26 ± 0.91</td>
<td>0.20 ± 1.00</td>
<td>0.02</td>
</tr>
<tr>
<td>12-months</td>
<td>4.01 ± 1.00</td>
<td>-0.03 ± 1.08</td>
<td>0.89</td>
</tr>
<tr>
<td>I would take a genetic test to learn more about myself.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>4.27 ± 0.91</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3-months</td>
<td>4.33 ± 0.92</td>
<td>0.06 ± 0.86</td>
<td>0.32</td>
</tr>
<tr>
<td>12-months</td>
<td>4.17 ± 1.05</td>
<td>-0.10 ± 1.03</td>
<td>0.42</td>
</tr>
<tr>
<td>I would take a genetic test to encourage myself to adopt a healthier lifestyle.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>4.15 ± 1.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3-months</td>
<td>4.21 ± 0.94</td>
<td>0.06 ± 0.95</td>
<td>0.35</td>
</tr>
<tr>
<td>12-months</td>
<td>3.98 ± 1.05</td>
<td>-0.17 ± 1.05</td>
<td>0.08</td>
</tr>
</tbody>
</table>
6.4.4 Sharing of information and utility of personalized nutrition

On the 12-month survey, subjects were asked if they shared the information in the report with anyone. The available choices were “family member”, “significant other”, “friend”, “healthcare professional”, and “I did not share the information with anyone”, and subjects were instructed to select all that applied. A significantly greater proportion of subjects in the intervention group shared the information with a family member (31% (I) vs. 9% (C), p=0.005) or a friend (33% (I) vs. 7% (C), p=0.001). A significantly greater proportion of subjects in the control group selected “I did not share the information with anyone” when compared to the intervention group (10% (I) vs. 64% (C), p<0.0001). Only one subject in the study, who was in the intervention group, shared the information with a healthcare professional. At 12-months, subjects were also asked if they thought DNA-based dietary advice is more useful than general population-based dietary advice and the possible responses were “yes”, “no”, or “no opinion”. Since no significant differences were observed between the responses of the intervention group when compared to the control group (data not shown), the responses of both groups were combined. The majority of the 125 subjects (73%) selected “yes”, 14% selected “no” and 14% selected “no opinion”.

6.5 Discussion

The present study is the first randomized controlled trial to compare attitudes and perceptions of genetic testing and personalized nutrition between those who receive DNA-based dietary advice and those who receive general dietary recommendations. The findings demonstrated that certain perceptions of personalized nutrition and genetic testing changed over the course of the present study. Since proponents of consumer genetic tests claim that the test results can positively impact
health behaviour, this finding may have clinically relevant behavioural implications. Theories of health behaviour change, such as the Health Belief Model, assert that an individual’s beliefs about a health risk and the effectiveness of a particular behaviour are indicative of one’s likelihood of engaging in that behaviour (Rosenstock et al., 1988). Therefore, the reported changes in perceptions may have an influence on individual health behaviours, such as changing one’s diet or sharing genetic test results with a healthcare professional. Indeed, previous surveys of individuals who have undergone consumer genetic testing have reported that the genetic information impacted their dietary behaviours, although the information was not specifically related to dietary response (Kaufman et al., 2012; Maher, 2011). Consequently, genetic information for personalized nutrition may have an even greater impact on dietary behaviour.

A university research lab and healthcare professional were viewed more favorably than a DTC genetic testing company as providers of accurate personal genetic information, and a registered dietitian was selected as the best provider of personalized nutrition advice. The low proportion of subjects who selected DTC genetic testing company may reflect a lack of awareness of such companies, which we previously reported (Nielsen and El-Sohemy, 2012b). Nevertheless, these findings are in line with other reports of consumer preferences for healthcare professional involvement in genetic testing (Almeling and Gadarian, 2013; Morin, 2009) and highlight an important consideration. While proper communication of genetic test results is needed to prevent individuals from misinterpreting the information and to guide them toward making appropriate lifestyle changes where necessary (Ferguson, 2012), healthcare professionals in general, including dietitians, have expressed low genetic self-efficacy to be able to interpret and explain genetic test results to patients (Birmingham et al., 2013; Collins et al., 2013; Cormier et al., 2014; Weir et al., 2010). Some argue that genetic counselors should communicate genetic
test results to consumers (Harris et al., 2013), but it is important to note that genetic counselors do not possess the required training to provide dietary advice. Increasing genomics education in healthcare professional training programs is, therefore, an important priority that has been acknowledged by a number of health centers (Salari et al., 2013). In fact, a recent study demonstrated that incorporating personal genome testing in a course on personalized medicine improved both self-reported and assessed genomics knowledge among medical students who underwent testing (Salari et al., 2013). Since registered dietitians were viewed as the best providers of personalized nutrition advice in the present study, dietetics curricula may benefit from increasing education on genomics and genetic testing. Indeed, the Academy of Nutrition and Dietetics recently acknowledged that dietitians with coursework in genetics and genomics are needed to advance the field of nutrigenomics (Camp and Trujillo, 2014), while the Partnership for Dietetic Education and Practice (Canada) identified ‘genetics and nutrigenomics’ as foundational knowledge areas for dietetics students (Partnership for Dietetic Education and Practice, 2013).

Although healthcare professional involvement in personal genome testing is preferred by the general public, there is concern that use of this technology could increase the burden on healthcare systems (McBride et al., 2012). A previous study reported low levels of physician involvement and no difference in use of medical screening tests 3-months after undergoing DTC testing (Bloss et al., 2011c), but at 12-months it was reported that nearly 40% of subjects had shared their genetic test results with their healthcare professional and undergone a greater number of screening tests than those who did not share their test results (Bloss et al., 2013). However, that study did not include a control group, so the interpretation of those findings is limited. In the present study, only one subject in the intervention group shared their genetic
information with a healthcare professional, which suggests that genetic testing for personalized nutrition might not impact healthcare resources in the manner that genetic testing for disease susceptibility may. Nevertheless, subjects in the intervention group were more likely to share the information from their dietary report with a family member or friend compared with subjects in the control group, who mostly reported that they did not share their dietary information with anyone. This finding may be reflective of individuals’ interests and enthusiasm for personalized nutrition information. Indeed, the majority (73%) of subjects from both the intervention and control group in the present study indicated that DNA-based dietary advice is more useful than general recommendations. As a result, personalized dietary advice may be more effective at motivating adherence to dietary recommendations than general population-based dietary advice. Overall, the application of nutrigenomics is not considered to have substantial risk such as potentially medicalizing food, hindering individual autonomy for food choices, or obliging individuals to comply with DNA-based dietary recommendations (Hurlimann et al., 2014).

Limitations of the present study include the small sample size and selective group of subjects that may not be representative of other populations. However, previous studies that have examined individual responses following disclosure of personal genetic information have consisted of comparable sample sizes (Arkadianos et al., 2007; Chao et al., 2008; Grant et al., 2013). Moreover, while the subjects in the present study were highly educated and recruited from a previous nutrigenomics study, they are representative of the early adopters of consumer genetic testing who are more likely to be highly educated, Caucasian and between the ages of 18-49 years (Bloss et al., 2011c; Gollust et al., 2012; Kaufman et al., 2012). One previous study reported that a larger proportion of consumers were female (Gollust et al., 2012). Nevertheless,
the survey findings reported in the present study may not be generalizable to populations that are less educated, older, non-Caucasian or managing a chronic disease.

Strengths of the present study are the inclusion of a control group, which provided a method of comparing the perceptions of DNA-based dietary advice to general population-based recommendations, as well as the randomized design, which minimizes the potential for confounding effects. In addition, conducting the study in a manner that closely resembled a DTC genetic test increases the validity of the findings to reflect the perceptions among DTC genetic test users. The present study was the first to examine and compare perceptions of genetic testing and personalized nutrition among individuals who are given DNA-based advice or general dietary recommendations. The findings provide novel information on individual perceptions toward personalized nutrition and genetic testing, as well as perceptions of sources of personal genetic information, providers of personalized nutrition advice and the utility of DNA-based advice compared with general dietary recommendations.
Chapter 7

Overall Discussion
7.1 Summary

The overall aims of this thesis were to examine individual perceptions towards genetic testing for personalized nutrition and to determine whether disclosing genetic information related to dietary advice for caffeine, vitamin C, added sugars and sodium resulted in changes to dietary intakes of these nutrients.

Objective 1: Examine the perceptions of individuals toward genetic testing and personalized nutrition.

Results: At baseline, approximately half of the participants (52%) reported having heard “nothing” about DTC genetic testing, while 18% reported hearing “a fair amount” or “a lot”. A smaller proportion of participants reported knowing “nothing” about nutrigenomics (30%), with just over half reporting that they knew “a little bit” about the science (52%). Interest in the relationship between diet and genetics was high, with 90% of participants reporting either “strongly agree” or “somewhat agree” to the survey statement. The majority of participants (87%) also agreed that they would benefit from learning about how their genetic make-up would affect their diet. Consistent with this, 75% of participants agreed that learning about their genetic make-up would affect what they ate. The greatest motivators participants reported for undergoing genetic testing were to learn more about themselves and to encourage themselves to adopt a healthier lifestyle (86% and 83%, respectively), while 73% of participants agreed that they would take a genetic test to have their doctor monitor their health more closely. Only 7% of participants strongly agreed that they would be uncomfortable learning about their genetic make-up. Compared to the control group, subjects in the intervention group who received gene-based
dietary advice were more likely to agree that they understood the dietary advice they were given (93% (I) vs. 78% (C); p = 0.009), that the recommendations would be useful when considering their diet (88% (I) vs. 72% (C); p = 0.02), and wanted to know more about the recommendations (95% (I) vs. 76% (C); p<0.0001). Only 9% of subjects in the intervention group reported feeling uneasy about learning their genetic information.

**Objective 2:** Determine the effect that dietary advice based on genetic information has on dietary intake after a 3- and 12-month intervention.

**Results:** At baseline, the proportion of subjects who did not meet the general recommendation for caffeine, vitamin C, added sugars and sodium were 9%, 14%, 24% and 39%, respectively. Thirty eight percent of subjects did not meet the targeted recommendation for caffeine intake at baseline, while 80% did not meet the targeted recommendation for sodium intake. No significant changes in dietary intakes of caffeine, vitamin C, added sugars, or sodium were observed between baseline and the 3-month follow-up. At 12-months, subjects in the intervention group who possessed a risk version of the *ACE* gene, and were advised to limit their sodium intake, significantly reduced their sodium intake (mg/day) compared to the control group (mean ± SE: -287.3 ± 114.1 vs. 129.8 ± 118.2, p=0.008). Those who had the non-risk version of *ACE* did not significantly change their sodium intake compared to the control group (12-months: -244.2 ± 150.2, p=0.11). Among those with the risk version of the *ACE* gene, the proportion who met the targeted recommendation of 1500 mg/day increased from 19% at baseline to 34% after 12 months (p=0.06). No significant changes in dietary intakes of caffeine, vitamin C or added sugars were observed between baseline and the 12-month follow-up.
Objective 3: Determine individual preferences for obtaining personal genetic information and determine if perceptions toward genetic testing and personalized nutrition changed over the course of the intervention.

Results: On the 3-month survey, subjects were asked to indicate which source they felt would provide them with the most accurate personal genetic information. The most commonly selected response was “university research lab” (47%), followed by “healthcare professional” (41%) and “direct-to-consumer genetic testing company” (12%). Subjects were also asked to indicate which source they felt would provide them with the best personalized nutrition advice. The most commonly selected response was “registered dietitian” (56%), followed by “medical doctor” (27%), “naturopath” (8%), “registered nurse” (6%), and “other” (3%). On the 12-month survey, subjects were asked if they shared the information in the report with anyone. A significantly greater proportion of subjects in the intervention group shared the information with a family member (31% (I) vs. 9% (C), p=0.005) or a friend (33% (I) vs. 7% (C), p=0.001). A significantly greater proportion of subjects in the control group selected “I did not share the information with anyone” when compared to the intervention group (10% (I) vs. 64% (C), p<0.0001). Only one subject in the study, who was in the intervention group, shared the information with a healthcare professional. At 12-months, subjects were also asked if they thought DNA-based dietary advice is more useful than general population-based dietary advice. The majority of subjects (73%) selected “yes”, 14% selected “no” and 14% selected “no opinion”.

At 3-months, significant changes in survey responses were observed for two out of four repeated survey statements as compared to baseline responses among the entire sample of subjects. Subject responses increased significantly toward the positive end of a Likert-type scale for the statements “I am interested in the relationship between diet and genetics” (mean change ±
SD: 0.28 ± 0.99, p=0.0002) and “I would take a genetic test to have my healthcare professional monitor my health more closely” (mean change ± SD: 0.20 ± 1.00, p=0.02). At 12-months, subject responses for the statement “I am interested in the relationship between diet and genetics” remained significantly increased toward the positive end of the scale, as compared to baseline (mean change ± SD: 0.20 ± 1.04, p=0.02).

7.2 Other Considerations

The present thesis provides novel information on the dietary behavioural response to a personalized nutrition intervention, as well as individual perceptions toward personalized nutrition and genetic testing. However, the present project did not apply a theory of health behaviour change to its study design, so information on factors that influenced behaviour change was not obtained. One particular theoretical framework of health behaviour change that could be applied to future studies investigating the impact of genetic information on health behaviour is the Precaution Adoption Process Model (PAPM; Figure 7.1). PAPM is a stage theory that aims to explain how an individual comes to decisions to take action against a health risk and, subsequently, how (and if) the decision is translated into action (Weinstein et al., 2008).

Specifically, PAPM considers an individual’s response to a new health risk, something one has recently learned about as opposed to something one has been aware of previously (Weinstein et al., 2008). Since individuals do not know what genetic variants they possess prior to undergoing genetic testing (although family history may provide an indication for disease susceptibility), PAPM can be applied to investigations of how individuals respond to genetic test results and how they come to decisions about what actions to take against new risks they may discover. Moreover, due to the concept of genetic exceptionalism, the perception that genetic information
is special, some argue that knowledge about one’s own genetic information may be a stronger motivator for change than traditional forms of health information (Green and Botkin, 2003). In the case of personalized nutrition, genetic testing reveals how an individual processes a dietary component according to one’s personal genotype and how this, in turn, modifies one’s risk of diet-related chronic diseases. According to PAPM, an individual receiving this new information would move through a series of stages and undergo a number of cognitive processes that would ultimately determine whether or not dietary modification is made. Information on how these stages and cognitive processes influence dietary behaviour may assist in developing future dietary interventions.

Figure 7.1. Precaution Adoption Process Model

Adapted from Weinstein et al., 2008
In addition, the present thesis project reported a significant reduction in sodium intake among the intervention risk group compared to the control group at 12-months (although sodium intake was decreasing among this group at 3-months). Dietary behaviour change interventions generally report success in the short-term, with long-term maintenance being difficult to achieve (Crichton et al., 2012). One potential explanation for the impact of sodium advice mainly in the long-term is the public health messaging that surrounds sodium and its association with hypertension (Papadakis et al., 2010; Petrella et al., 2005). An online search of the media archives of five leading health agencies between January 2011 and October 2012 (WHO, Centers for Disease Control and Prevention (CDC), Health Canada, Public Health Agency of Canada, and the Heart and Stroke Foundation) revealed that a greater number of media releases related to sodium were issued during and after the 3-month follow-up assessment of the present study as compared to the time that preceded the 3-month follow-up (Figure 7.2). These messages were related to either newly published research papers reporting negative health effects of consuming high amounts of sodium or to Canadian public health officials urging the federal government to make sodium reduction a national priority.
Given these observations, it is possible that public health messaging around sodium during and after the 3-month follow-up may have sensitized individuals to the DNA-based dietary advice provided in the present study. Moreover, at the 12-month follow-up the reduction in sodium intake among the intervention non-risk group compared to the control group was approaching statistical significance. This adds to the notion that media messages may have primed individuals to become more responsive to the DNA-based dietary advice, since these subjects were not advised to limit their sodium intake to the targeted recommendation. However, it is important to note that a media archive search provides an indication of message output rather than uptake. In addition, the monthly reminders that were sent over the course of the present study may have also influenced the reported long-term changes. Nevertheless, these observations suggest that knowledge of one’s genetic information related to personalized nutrition combined
with public health messaging may have the greatest impact on dietary behaviour and is a future direction that warrants exploration.

7.3 Limitations

The work performed in this thesis has some potential limitations. First, dietary intake data was assessed by self-report, which can be prone to errors such as underreporting of energy (Archer et al., 2013; Brown, 2006; Garriguet, 2008b). As a result, some of the nutrient intakes, such as for sodium or added sugars, may be underestimated. However, since the outcome measure in this project was change in dietary intake and the same FFQ was used to assess intake throughout the trial, the magnitude of change in intake should be a reliable estimate. Moreover, since the present study was a randomized trial, any measurement errors in estimating dietary intake would apply to both the intervention and control groups. As a result, the significant reduction in sodium intake reported among the intervention risk group when compared to the change in sodium intake of the control group would not be due to limitations of the dietary assessment tool used. While FFQs are often used in large, population-based epidemiological studies assessing diet-disease relationships, they have also been used in a number of intervention studies that have assessed dietary change (Bhargava and Hays, 2004; Champagne et al., 2011; Collins et al., 2011; Hebert et al., 1993; Helland-Kigen et al., 2013; Johansen et al., 2010; Kristal et al., 1994; Ochner and Lowe, 2007; Potter J.D. et al., 1990; Prosser et al., 2010; Stern et al., 1993; Wright et al., 2011). Significant changes in intakes of specific food items (Hebert et al., 1993; Helland-Kigen et al., 2013; Johansen et al., 2010), macronutrients (Bhargava and Hays, 2004; Champagne et al., 2011; Collins et al., 2011; Kristal et al., 1994; Potter J.D. et al., 1990; Stern et al., 1993) and micronutrients (Bhargava and Hays, 2004; Ochner and Lowe, 2007; Prosser et al., 2010) were
reported in each of these studies, which demonstrates the ability of FFQs to capture changes in dietary intake. However, the sensitivity of the Willett FFQ to measure within-person dietary change has not been reported.

FFQ validation studies are commonly conducted to examine how accurately the tool estimates dietary intake for certain nutrients or food items. A validation study typically involves comparing FFQ dietary intake estimates with estimates obtained from other dietary instruments such as 24-hour recalls or food records (Thompson and Byers, 1994). In the present thesis, a Toronto-modified Willett FFQ was used to assess changes in dietary intake. A comparison was made between the Toronto-modified questionnaire and a three day food record, although results have yet to be published. A subset of subjects from the TNH study (n=100) were recruited to complete a three day food record after they had completed the Toronto-modified FFQ. A minimum of 24 hours needed to pass from completing the FFQ before subjects could begin the three day food record. Nutrient intakes were assessed between the two instruments from food sources only, since data on supplement intake was not recorded in the three day food records. Pearson correlation coefficients for energy-adjusted nutrient intakes of interest to this thesis were 0.27 for sodium, 0.32 for vitamin C (food sources only), 0.57 for added sugars, and 0.84 for caffeine (unpublished results; Table 7.1). These correlation coefficients were corrected for attenuation arising from random error in within-person variability present in the data from the food records, using the method described by Rosner and Willett (Rosner and Willett, 1988).
Table 7.1. Correlation coefficients between the Toronto-modified FFQ and 3-day food records

<table>
<thead>
<tr>
<th>Nutrient</th>
<th>FFQ2 (mean ± SD)</th>
<th>3 day food record (mean ± SD)</th>
<th>Crude Pearson r</th>
<th>Deattenuated Pearson r</th>
<th>Energy-adjusted Pearson r</th>
<th>Deattenuated energy-adjusted Pearson r</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium (mg/day)</td>
<td>2050.97 ± 808.49</td>
<td>3431.41 ± 1232.87</td>
<td>0.17</td>
<td>0.20</td>
<td>0.23</td>
<td>0.27</td>
</tr>
<tr>
<td>Vitamin C (mg/day)*</td>
<td>132.67 ± 90.66</td>
<td>113.54 ± 90.65</td>
<td>0.25</td>
<td>0.28</td>
<td>0.28</td>
<td>0.32</td>
</tr>
<tr>
<td>Caffeine (mg/day)†</td>
<td>126.38 ± 102.36</td>
<td>117.19 ± 107.19</td>
<td>0.75</td>
<td>0.84</td>
<td>0.75</td>
<td>0.84</td>
</tr>
<tr>
<td>Added sugars* (% energy/day)</td>
<td>9.03 ± 4.79</td>
<td>11.44 ± 5.67</td>
<td>0.55</td>
<td>0.57</td>
<td>0.55</td>
<td>0.57</td>
</tr>
</tbody>
</table>

*Pearson correlation coefficient is for log transformed nutrient intake
†Pearson correlation coefficient is for square root transformed nutrient intake

The original Willett FFQ has also been validated in a number of other studies. Subar et al. (2001) compared results from the Willett FFQ with two other commonly used FFQs in nutritional epidemiology studies; the Block FFQ and Dietary History Questionnaire (DHQ) (Subar et al., 2001). The dietary intake estimates obtained from the FFQs were also compared with measures of dietary intake estimated from four separate 24-hour recalls that were collected over one calendar year, each administered 3 months apart (Subar et al., 2001). The nutrient intake estimates from all three FFQs were similar to one another and correlations between the FFQ estimates and 24-hour recall estimates were above r=0.40 for most nutrients after energy
adjustment (Subar et al., 2001). Therefore, Subar et al. (2001) concluded that all three FFQs yielded similar results and all are comparable for nutritional epidemiology studies (Subar et al., 2001). For the specific nutrients of interest to the present thesis, previous validation studies have demonstrated a high degree of validity between the Willett FFQ and food records for assessing caffeine ($r=0.78$ for coffee, $r=0.93$ for tea and $r=0.85$ for caffeinated soda) (Wu et al., 2005) and moderate degrees for assessing added sugars ($r=0.52-0.60$ for sucrose) and vitamin C ($r=0.53-0.73$) (Willet and Lenart, 1998). No study to date has published validation data demonstrating the original Willett FFQ’s ability to measure sodium intake against food records, but one study assessed its validity against multiple 24-hour recalls and reported correlation coefficients of $r=0.28$ and $r=0.30$ for women and men, respectively, after energy adjustment (Subar et al., 2001). For the nutrients of interest in the present study, the validity coefficients reported for the original Willett FFQ are similar to those reported above for the Toronto-modified Willett FFQ.

Moreover, FFQs are generally used to assess relative intakes by grouping individuals into quantiles of intake. The small sample size in the present study limits the ability to assess change in relative intakes, so changes in absolute intake estimates were assessed. FFQs have been documented to misclassify individual intakes (Tylavsky and Sharp, 1995), however, gross misclassification into extreme quantiles is not common (Kroke et al., 1999; Shu et al., 2004; Deschamps et al., 2007). In the present study, misclassification of dietary intake would bias the findings towards the null rather than lead to a false positive result since a randomized design was used. Nevertheless, the lower ability of the Toronto-modified Willett FFQ to estimate sodium intake is a limitation of the present thesis. While a number of studies have assessed sodium intake using FFQs (Ferreira-Sae et al., 2009; Geleijnse et al., 2007; Larsson et al., 2008; Nagata et al., 2004; Umesawa et al., 2008), objective measures of sodium intake are preferred since they
provide more accurate estimates of intake compared to self-report. Urine samples provide an objective biochemical measure of sodium intake and 24-hour urine collections, where participants collect all urine output over a period of 24-hours, is considered the gold standard because at least 90% of sodium intake is excreted in urine (Ji et al., 2012). One previous thesis project compared self-reported sodium intake from a Willett FFQ with sodium intake measured from single 24-hour urine samples and reported a correlation of r=0.66 among men (n= 127) and r=0.56 among women (n=193) (Joseph, 1994). However, that project collected only a single urine measurement. Since sodium intake varies day-to-day, multiple 24-hour urine collections are required to obtain an accurate measurement of sodium consumption. One previous study compared self-reported sodium intake from a FFQ with six 24-hour urine collections and reported a correlation of r=0.13, however, that study examined absolute rather than energy-adjusted nutrient intakes (Day et al., 2001). Moreover, 24-hour urine collections are costly, place a great amount of burden on study participants and are prone to incompleteness (Ji et al., 2012). Alternative measures, such as spot, overnight or timed urine samples, are available to assess sodium intake, but these methods are prone to measurement error since sodium levels fluctuate throughout the day (Ji et al., 2012). However, recent data from the INTERSALT study (n=5,696 men and women aged 20-59 years) provide supportive evidence for the use of spot urine samples (from either morning, afternoon or evening) in combination with equations to estimate average 24-hour urine sodium excretion among populations of healthy, Western young adults (Brown et al., 2013).

A second limitation of the present study is the selective group of subjects, who had been recruited from a previous nutrigenomics study. Subjects in the present study were young adults, mainly female and highly educated. These characteristics are representative of individuals with a
high degree of health literacy. Health literacy is defined by the WHO as “the cognitive and social skills which determine the motivation and ability of individuals to gain access to, understand and use information in ways which promote and maintain good health” (Nutbeam, 2008). Health literacy better predicts health status than variables such as age, education, income, employment and ethnicity (American Medical Association, 1999) and individuals with higher health literacy have been shown to have improved health management compared to individuals with lower health literacy in certain cases (Smith et al., 2013; Speirs et al., 2012; Taggart et al., 2012). A 2012 systematic review examined the effect of 52 different interventions aimed at increasing health literacy on changes in smoking, nutrition, alcohol consumption, physical activity, or body weight (SNAPW) (Taggart et al., 2012). Nearly all of the interventions (73%) improved health literacy and 75% improved at least one outcome measure from SNAPW (Taggart et al., 2012). Interventions that were of lower intensity (defined by the number of hours of contact with study subjects) were somewhat more effective than higher intensity interventions at improving health outcomes, and community interventions were more effective at improving nutrition and physical activity outcomes than primary care interventions (Taggart et al., 2012). Primary care interventions, however, were more effective than community interventions at supporting smoking cessation (Taggart et al., 2012). However, not all studies support a positive association between health literacy and improved health outcomes. A recent systematic review of 24 diabetes studies concluded that although higher health literacy was associated with higher diabetes knowledge, it was not associated with clinical outcomes, self-reported complications, self-efficacy or patient-provider interactions (Al Sayah et al., 2013).

Related to health literacy, nutrition literacy specifically describes “the degree to which individuals can obtain, process, and understand the basic nutrition information and services they
need to make appropriate nutrition decisions” (Carbone, 2013). This is a relatively new term and to date only one known nutrition literacy assessment exists; the 23-item Nutritional Literacy Scale designed to measure an adult’s comprehension of nutrition information (Diamond, 2007). However, this scale has only been used in one study to examine the association between nutrition literacy and health indicators (Patel et al., 2013). As a result, little insight can presently be made into the nutrition literacy of the general public.

A third limitation of the present study was the small sample size. A convenience sample of subjects who previously participated in the TNH study was selected for the research in the present thesis, since subjects’ genotypes were readily available along with dietary intake data. The number of subjects included in final analyses of the present thesis varied slightly depending on the outcome being assessed (e.g. under-reporters were excluded from dietary intake analyses, but included in survey response analyses). A limitation of a previous study examining the behavioural response to disclosure of health-related genetic information was that subjects were already meeting the corresponding lifestyle recommendations at baseline (Bloss et al., 2011b). Therefore, dietary exclusion criteria were applied to past TNH study participants prior to enrolment in order to recruit subjects who were not already adhering to the dietary recommendations that would be given in the randomized trial. The ideal dietary cut-off points would have resulted in only 31 subjects eligible to be contacted for the trial (Table 4.3). Therefore, these cut-off points were relaxed in order to increase the number of subjects who were eligible to be contacted, while still excluding participants that were likely strongly adhering to the dietary recommendations given in the trial. Although this resulted in a much larger eligible pool of subjects (n=354, Table 4.2), only about 50% of these subjects responded to invitations to participate in the present study and fewer (40%) were ultimately randomized. Re-contacting
previous study participants is a well-documented challenge in research studies and was one factor that influenced the sample size of the present study (Hunt and White, 1998). Nevertheless, the sample size of the present study is similar to previous studies that have assessed health behaviour changes following disclosure of genetic information (Arkadianos et al., 2007; Chao et al., 2008; Grant et al., 2013).

A fourth limitation of the present study was that changes in dietary intakes were assessed separately over a short and long term period. This analysis was chosen since no previous study had examined the short- and long-term effects of disclosing genetic information on health behaviours at the time the present study was designed. Since then, only one study has reported on short- and long-term outcomes, and in both cases the genetic information was not associated with changes in dietary fat intake, exercise or anxiety (Bloss et al., 2011c; Bloss et al., 2013). An alternative analysis is to use linear mixed models to assess the changes in dietary intakes over the entire 1-year duration. This approach appropriately accounts for the effect of time and correlation among measurements obtained from the same individual. As a result, linear mixed models provide greater statistical power than the ANCOVA analysis conducted in the present thesis (Sullivan, 2008).

7.3.1 Comparison of Nutrient Intake Estimates to Population Data

CCHS 2.2

The 2004 Canadian Community Health Survey, Cycle 2.2 (CCHS 2.2) collected dietary intake data from 35,107 Canadians (n=18,820 were 19 years of age or older) using 24-hour recalls. A second 24-hour recall was collected from a subset of the population in order to estimate the day-to-day variation in usual dietary intake of the population using Software for
Intake Distribution Estimation (SIDE). A comparison of the reported nutrient intakes from the present study with CCHS 2.2 data is provided below and demonstrates that the average intakes of the nutrients assessed in the present study using the Toronto-modified Willett FFQ are similar to the average intakes of the same nutrients assessed in the CCHS 2.2 using a 24-hour recall.

Caffeine

In the CCHS 2.2, coffee was the second most commonly consumed beverage following water (Garriguet, 2008a). However, this finding was largely driven by the proportion of individuals who were aged 31 years or older. Approximately 15% of women and 22% of men between the ages of 31 and 70 years consumed above the recommendation of 400 mg of caffeine per day (Garriguet, 2008a). Among younger individuals aged 19-31 years only 6.5% of women and 9% of men consumed above the recommendation (Garriguet, 2008a). Moreover, CCHS 2.2 respondents aged 19-31 years were more likely to report consuming milk than coffee on the 24-hour recall. Although population level average caffeine intakes have not been reported from the CCHS 2.2, the aforementioned results are comparable to the small proportion of subjects in the present study who consumed above 400 mg of caffeine per day at baseline and suggests that the caffeine intakes of the subjects in the present study are similar to those of the Canadian population in a similar age category.

Vitamin C

In the CCHS 2.2, nutrient intake assessments for nutrients with an EAR are made by identifying the proportion of the sample with usual intakes below (considered inadequate intake) or above (considered to meet or exceed requirements) the EAR, rather than comparing intakes to the RDA because assessments made using the RDA would overestimate the prevalence of inadequacy in a group (National Research Council, 2000). In the CCHS 2.2, 10% of females and
13% of males aged 19-30 years old had vitamin C intakes that were considered to be inadequate (below the EAR for vitamin C) (Health Canada, 2012). However, the vitamin C intake estimate from CCHS has a large coefficient of variation (16-33%) and CCHS 2.2 reports note that vitamin C intake estimates should be interpreted with caution. In the present study, only 14% of subjects consumed below the RDA for vitamin C at baseline, so even fewer would have consumed below the EAR.

**Sodium**

Median sodium intakes in the CCHS 2.2 exceeded the AI (1500 mg/day for individuals aged 9-50 years, 1300 mg/day for adults 51-70 years and 1200 mg/day for adults over 70 years (Food and Nutrition Board, 1997)) for all Canadians and also exceeded the UL (2300mg/day (Food and Nutrition Board, 1997)) for all Canadians over 19 years, with the exception of women over 70 years. Sodium intakes in the present study were also high, with 39% of subjects consuming above the UL and 80% of subjects consuming above the AI at baseline. However, the larger proportion of subjects consuming sodium levels above the UL in the CCHS 2.2 as compared to the present study indicates that sodium intakes may have been underestimated with the modified Willett FFQ, or that the sample in the present study is not representative of the broader Canadian population.

**Added Sugars**

The CCHS 2.2 dietary data provided total sugar intake as a percentage of energy per day, but did not distinguish between added and naturally occurring sugars (Langlois and Garriguet, 2011). However, the average total sugar intake of approximately 20% energy per day reported in the CCHS 2.2 (21.5% per day among respondents without diabetes) (Langlois and Garriguet, 2011) is similar to the baseline total sugar intake of 21% energy per day in the present study.
Moreover, a recent report from the Canadian Sugar Institute estimated the percentage of energy intake from added sugars per day among Canadians to be between 10-13% (Brisbois and Marsden, 2012), which is comparable to the baseline added sugars intake of 8% energy per day reported in the present study. The Canadian Sugar Institute estimate is based from the CCHS 2.2 total sugar intake data and a finding from a United States Sugars Task Force, which reported that added sugars account for roughly 50% of total sugar intake (Glinsmann et al., 1986).

7.4 Future Directions

The present thesis evaluated the effects of disclosing genetic information related to personalized nutrition in a population of healthy, university educated young adults. These results may not be generalizable to other populations, such as older individuals who may be managing risk factors for chronic disease, or individuals who possess a lower degree of health literacy. Therefore, additional studies are required to assess the effect of DNA-based dietary advice on dietary intake in populations that differ demographically from the participants of the present thesis. An assessment of health and nutrition literacy in future studies would demonstrate whether these factors are associated with the behavioural response to DNA-based dietary advice. Future studies would also benefit from collecting more objective measures of dietary intake, such as 24-hour urine collections to assess sodium intake (Ji et al., 2012). Such measures of dietary intake, as opposed to self-reported intake, would reduce the sample size required to detect an effect of the intervention (Freedman et al., 2010). In addition, assessing changes in biomarkers of health such as blood pressure, BMI, and HOMA-IR and HOMA-B, or hard outcomes (e.g. heart
attack or stroke) would demonstrate whether changes in dietary intake that follow disclosure of DNA-based dietary advice have favourable effects on clinical outcomes.

While the present study was informed by certain aspects of health behaviour change theories, such as cues to action from the Health Belief Model, a greater consideration of these theories in future studies may provide additional insight into the process of dietary behaviour change. In addition, the observation that a greater number of media messages surrounding sodium occurred predominantly after the 3-month follow-up assessment of the present project propose that an investigation into the combined impact of public health messaging and personalized nutrition should be explored. Indeed, health communication through the media is known to influence the health behaviours of individuals (Finnegan and Viswanath, 2008) and assessing how public health messages interact with personalized nutrition information to impact one’s actions may provide valuable insight on how population-based and individual-based approaches can potentially be combined.

Moreover, while this thesis sheds light on individual perceptions toward genetic testing for personalized nutrition through surveys, additional research applying qualitative research methods may provide a greater understanding of critical issues that impact the clinical application of personalized nutrition. Qualitative methods, such as focus groups and one-on-one interviews, are useful for discovering and explaining observations, and can provide answers to the “how” and “why” questions that are important to understand in order to appropriately translate research findings into clinical practice (Green and Britten, 1998; Shuval et al., 2011). Indeed, qualitative methods have been used extensively in research that examines both healthcare professional and patient attitudes, beliefs, preferences and behaviours and is therefore an important component of health services research (Mays and Pope, 1995; Pope et al., 2000;
Shuval et al., 2011). Specifically, interviews explore what research participants say about topics in great detail and are useful for uncovering themes or ideas that were not anticipated when the research was initiated (Britten, 1995). Interviews can vary in their degree of organization and fixed vs. open-ended responses (structured, semi-structured or in depth), and require a trained interviewer who is able to maintain control of the interview without influencing (or leading) the participant’s responses (Britten, 1995). Focus groups are group interviews that utilize communication between research participants to generate data (Kitzinger, 1995). They stem from a belief that group conversations assist individuals in exploring and clarifying their views on a topic (Kitzinger, 1995).

Strengths of qualitative research methods include their emphasis on “naturalism”, or understanding observations in their everyday context, as well as an ability to take an inductive approach to analysis where interpretation is derived from the data, rather than fitting data to pre-existing concepts (deductive approach) (Green and Britten, 1998; Kuper et al., 2008; Pope and Mays, 1995; Pope et al., 2000). Limitations of qualitative research are that the quality of the data can depend on the skill of the interviewer and findings from qualitative studies may not be generalizable to large populations since sample sizes are generally small (Kuper et al., 2008; Pope et al., 2000). Nevertheless, an application of qualitative methods in future studies examining the impact of DNA-based dietary advice on dietary behaviour could shed light on how participants interpret DNA-based dietary advice and what factors contribute to whether or not they decide to adhere to the advice. In addition, a qualitative component would allow for a deeper exploration of why certain types of DNA-based advice are more effective at motivating dietary change than others. For example, DNA-based advice for sodium in the present thesis appeared to be the most impactful, but it is not clear what factors contributed to this effect.
The present thesis also provided novel insight into individual preferences for obtaining personalized nutrition advice. Registered dietitians (RDs) were considered to be the best providers of personalized nutrition advice, yet RDs have expressed low levels of genomics knowledge and a lack of confidence to be able to counsel on genetic test results (Cormier et al., 2014; Rosen et al., 2006). The development of clinical practice guidelines to create a standardized approach to counselling has been proposed as one potential strategy for increasing RDs’ confidence and comfort with personalized nutrition (Cormier et al., 2014). In addition, incorporating greater genetics education in dietetics university curricula has also been proposed (Prasad et al., 2011). Indeed, the Academy of Nutrition and Dietetics recently acknowledged that dietitians with coursework in genetics and genomics are needed to advance the field of nutrigenomics (Camp and Trujillo, 2014), while the Partnership for Dietetic Education and Practice (Canada) identified ‘genetics and nutrigenomics’ as foundational knowledge areas for dietetics students (Partnership for Dietetic Education and Practice, 2013). RDs with less than five years of work experience have been reported to be the most familiar with nutrigenomics (Cormier et al., 2014), which may indicate that this group received greater exposure to the science during their educational training and could feel more comfortable with integrating personalized nutrition into clinical practice (Rosen et al., 2006). Additional studies that provide RDs with genetic tests for personalized nutrition and examine their perceptions of the testing and counselling processes with their patients would provide insight into what specific challenges may be present that would affect the clinical use of genetic tests for personalized nutrition.

Finally, the selection process for identifying genetic variants to include in a nutrigenomics test should be considered in future studies. The present thesis examined the behavioural response to genetic information derived from candidate gene analyses, some of
which had been replicated in independent studies. However, replication of an initial finding should be a requirement for inclusion of a genetic variant in a genetic test. Methodologies, such as genome-wide association studies (GWAS), are being used and provide novel genotype-phenotype associations, including associations for caffeine and macronutrient intake (Cornelis et al., 2011; Chu et al., 2013; Tanaka et al., 2013). The validity of initial findings (either from candidate gene or genome-wide approaches) must be confirmed through replication studies, as a number of false positives have been reported (Lohmueller et al., 2003; Tabangin et al., 2009; Sionis et al., 2010). The National Cancer Institute-National Human Genome Research Institute (NCI-NHGRI) assembled a working group to propose principles for the replication of genotype-phenotype associations. Their report provided points for researchers and editors to consider when evaluating initial association findings and their replication (Chanock et al., 2007). The following criteria were suggested to establish a positive replication: the sample size of the replication should be sufficient to distinguish the proposed effect from no effect, independent data sets should be used consisting of a similar study population, the same or a very similar phenotype should be assessed, the same genetic model used in the initial study should be used in replication analyses, the effect size and statistical significance should be similar and the same SNP or a SNP in very high linkage disequilibrium should be assessed (Chanock et al., 2007). These criteria should be considered when identifying genetic variants to include in a nutrigenomics test.
7.5 Implications

The present study is the first randomized trial to evaluate the effects of disclosing genetic information related to personalized nutrition on dietary intake and also the first trial to compare perceptions of genetic testing and personalized nutrition between those who receive DNA-based dietary advice and those who receive general dietary recommendations. The findings show that DNA-based dietary advice results in greater changes in intake for some dietary components compared to population-based dietary advice. Changes in health behaviours have not been frequently reported in previous studies that have investigated the effect of disclosing genetic information related to disease risk (Bloss et al., 2011b; Bloss et al., 2011c; Collier, 2012; Grant et al., 2013) and a 2010 Cochrane review concluded that disclosing genetic risk information for disease has little impact on actual behaviour, although it has a small effect on one’s intention to change (Marteau et al., 2010). However, the genomic information provided in those studies was related to disease susceptibility, not personalized nutrition, and the studies lacked a long-term follow-up assessment. Moreover, participants in previous studies were not provided with personalized recommendations on what behavioural strategies should be followed to mitigate disease risk.

Results from the present study provide evidence that genetic testing for personalized nutrition may be more clinically useful than testing for disease susceptibility, since a change in sodium intake was observed after 12-months among the intervention risk group. Excessive sodium intake at the population level is a significant public health issue and population-wide strategies are being developed in an attempt to reduce the levels of sodium consumption. In fact, Ontario recently proposed a bill requiring menu-labeling in restaurants to include sodium content.
in addition to calories on menu items to target consumer behaviours (Ogilve, 2014). Providing personalized DNA-based dietary advice for sodium intake may be a useful strategy for reducing sodium intake among individuals who would benefit the most from sodium reduction, and could potentially enhance the impact of public health messages around sodium and cardiovascular health. In addition, the findings from the present thesis provide the first evidence of individual preferences for obtaining personal genetic information and personalized nutritional advice. A university research lab and healthcare professional were viewed more favorably than a DTC genetic testing company as providers of accurate personal genetic information, and a registered dietitian was selected as the best provider of personalized nutrition advice. Perceptions of personalized nutrition and nutrigenomics testing changed over the course of the study, which may have impacted dietary intake behaviour. Results from the present thesis demonstrate the dietary behavioural response to disclosure of genetic information for personalized nutrition and suggest that DNA-based dietary advice may be more useful than general population-based recommendations at motivating individuals to adopt favourable dietary changes.
References


Coghlan, A. 2013. 23andMe ordered to stop selling $99 genetic test. New Scientist. 18(51).


following genetic counseling and BRCA1 mutation testing in an African American kindred. *J Genet Couns.* 15:293-305.


Appendix
Sample pages from FFQ
4. (Continued) Please fill in your average total use, during the past month, of each specified food.

<table>
<thead>
<tr>
<th>Food Type</th>
<th>Frequency Options</th>
</tr>
</thead>
<tbody>
<tr>
<td>100% apple juice or cider</td>
<td>○ Never&lt;br&gt; ○ Less than once per month&lt;br&gt; ○ 1–3 glasses per month&lt;br&gt; ○ 1 glass per week&lt;br&gt; ○ 2–4 glasses per week&lt;br&gt; ○ 5–6 glasses per week&lt;br&gt; ○ 1 glass per day&lt;br&gt; ○ 2–3 glasses per day&lt;br&gt; ○ 4 or more glasses per day</td>
</tr>
<tr>
<td>Oranges, tangerines, clementines (1)</td>
<td>○ Never&lt;br&gt; ○ Less than once per month&lt;br&gt; ○ 1–3 times per month&lt;br&gt; ○ 1 glass per week&lt;br&gt; ○ 2–4 times per week&lt;br&gt; ○ 5–6 times per week&lt;br&gt; ○ 1 glass per day&lt;br&gt; ○ 2–3 times per day&lt;br&gt; ○ 4 or more glasses per day</td>
</tr>
<tr>
<td>100% orange juice (small glass)</td>
<td>○ Never&lt;br&gt; ○ Less than once per month&lt;br&gt; ○ 1–3 glasses per month&lt;br&gt; ○ 1 glass per week&lt;br&gt; ○ 2–4 glasses per week&lt;br&gt; ○ 5–6 glasses per week&lt;br&gt; ○ 1 glass per day&lt;br&gt; ○ 2–3 glasses per day&lt;br&gt; ○ 4 or more glasses per day</td>
</tr>
<tr>
<td>Grapefruit (1/2)</td>
<td>○ Never&lt;br&gt; ○ Less than once per month&lt;br&gt; ○ 1–3 times per month&lt;br&gt; ○ Once per week&lt;br&gt; ○ 2–4 times per week&lt;br&gt; ○ 5–6 times per week&lt;br&gt; ○ Once per day&lt;br&gt; ○ 2–3 times per day&lt;br&gt; ○ 4 or more times per day</td>
</tr>
<tr>
<td>100% grapefruit juice (small glass)</td>
<td>○ Never&lt;br&gt; ○ Less than once per month&lt;br&gt; ○ 1–3 glasses per month&lt;br&gt; ○ 1 glass per week&lt;br&gt; ○ 2–4 glasses per week&lt;br&gt; ○ 5–6 glasses per week&lt;br&gt; ○ 1 glass per day&lt;br&gt; ○ 2–3 glasses per day&lt;br&gt; ○ 4 or more glasses per day</td>
</tr>
<tr>
<td>Other 100% fruit juices (small glass)</td>
<td>○ Never&lt;br&gt; ○ Less than once per month&lt;br&gt; ○ 1–3 glasses per month&lt;br&gt; ○ 1 glass per week&lt;br&gt; ○ 2–4 glasses per week&lt;br&gt; ○ 5–6 glasses per week&lt;br&gt; ○ 1 glass per day&lt;br&gt; ○ 2–3 glasses per day&lt;br&gt; ○ 4 or more glasses per day</td>
</tr>
<tr>
<td>Strawberries, raspberries or blackberries, fresh or frozen (1/2 cup)</td>
<td>○ Never&lt;br&gt; ○ Less than once per month&lt;br&gt; ○ 1–3 times per month&lt;br&gt; ○ Once per week&lt;br&gt; ○ 2–4 times per week&lt;br&gt; ○ 5–6 times per week&lt;br&gt; ○ Once per day&lt;br&gt; ○ 2–3 times per day&lt;br&gt; ○ 4 or more times per day</td>
</tr>
<tr>
<td>Blueberries, fresh or frozen (1/2 cup)</td>
<td>○ Never&lt;br&gt; ○ Less than once per month&lt;br&gt; ○ 1–3 times per month&lt;br&gt; ○ Once per week&lt;br&gt; ○ 2–4 times per week&lt;br&gt; ○ 5–6 servings per week&lt;br&gt; ○ Once per day&lt;br&gt; ○ 2–3 times per day&lt;br&gt; ○ 4 or more times per day</td>
</tr>
<tr>
<td>Peaches, apricots, plums or nectarines, fresh (1)</td>
<td>○ Never&lt;br&gt; ○ Less than once per month&lt;br&gt; ○ 1–3 per month&lt;br&gt; ○ Once per week&lt;br&gt; ○ 2–4 per week&lt;br&gt; ○ 5–6 per week&lt;br&gt; ○ Once per day&lt;br&gt; ○ 2–3 per day&lt;br&gt; ○ 4 or more per day</td>
</tr>
<tr>
<td>Tropical fruit, not banana, - pineapple, kiwi, mango, papaya, guava, fresh figs, etc. (1/2 cup)</td>
<td>○ Never&lt;br&gt; ○ Less than once per month&lt;br&gt; ○ 1–3 times per month&lt;br&gt; ○ Once per week&lt;br&gt; ○ 2–4 times per week&lt;br&gt; ○ 5–6 times per week&lt;br&gt; ○ Once per day&lt;br&gt; ○ 2–3 times per day&lt;br&gt; ○ 4 or more times per day</td>
</tr>
<tr>
<td>Canned fruit, all kinds (1/2 cup)</td>
<td>○ Never&lt;br&gt; ○ Less than once per month&lt;br&gt; ○ 1–3 times per month&lt;br&gt; ○ Once per week&lt;br&gt; ○ 2–4 times per week&lt;br&gt; ○ 5–6 times per week&lt;br&gt; ○ Once per day&lt;br&gt; ○ 2–3 times per day&lt;br&gt; ○ 4 or more times per day</td>
</tr>
<tr>
<td>What type of canned fruit do you usually eat?</td>
<td>○ Don't usually eat canned fruit&lt;br&gt; ○ Canned in juice&lt;br&gt; ○ Canned in light syrup&lt;br&gt; ○ Canned in heavy syrup&lt;br&gt; ○ Canned in water&lt;br&gt; ○ Other&lt;br&gt; ○ Don't know</td>
</tr>
</tbody>
</table>
8. (Continued) Please fill in your average total use, during the past month, of each specified food.

<table>
<thead>
<tr>
<th>Tea (8 oz. cup), Not herbal, green or iced</th>
<th>Decaffeinated coffee (8 oz. cup)</th>
<th>Regular coffee with caffeine (8 oz. cup), Not latte, cappuccino, mocha, iced coffee, espresso, etc.</th>
</tr>
</thead>
<tbody>
<tr>
<td>○ Never</td>
<td>○ Never</td>
<td>○ Never</td>
</tr>
<tr>
<td>○ 1 cup per week or less</td>
<td>○ 1 cup per week or less</td>
<td>○ 1 cup per week or less</td>
</tr>
<tr>
<td>○ 2–4 cups per week</td>
<td>○ 2–4 cups per week</td>
<td>○ 2–4 cups per week</td>
</tr>
<tr>
<td>○ 5–6 cups per week</td>
<td>○ 5–6 cups per week</td>
<td>○ 5–6 cups per week</td>
</tr>
<tr>
<td>○ 1 cup per day</td>
<td>○ 1 cup per day</td>
<td>○ 1 cup per day</td>
</tr>
<tr>
<td>○ 2 cups per day</td>
<td>○ 2 cups per day</td>
<td>○ 2 cups per day</td>
</tr>
<tr>
<td>○ 3 cups per day</td>
<td>○ 3 cups per day</td>
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<tr>
<td>○ 4 cups per day</td>
<td>○ 4 cups per day</td>
<td>○ 4 cups per day</td>
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<tr>
<td>○ 5 cups per day</td>
<td>○ 5 cups per day</td>
<td>○ 5 cups per day</td>
</tr>
<tr>
<td>○ 6+ cups per day</td>
<td>○ 6+ cups per day</td>
<td>○ 6+ cups per day</td>
</tr>
</tbody>
</table>

Coffee drinks with caffeine - e.g., latte, cappuccino, mocha, iced coffee, etc. (8 oz. cup) or espresso (1 oz. cup)

○ Never
○ 1 cup per week or less
○ 2–4 cups per week
○ 5–6 cups per week
○ 1 cup per day
○ 2 cups per day
○ 3 cups per day
○ 4 cups per day
○ 5 cups per day
○ 6+ cups per day

How often are your coffees or coffee drinks purchased outside of home or work (i.e., ready-to-drink)?

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

Where do you usually purchase your ready-to-drink coffee or coffee drinks?

○ Starbucks or Second Cup
○ Timothy’s, Tim Hortons, Coffee Time, Country Style
○ Other, please specify

If you make your coffee at home or work, how is it usually prepared?

○ Paper filter drip
○ Permanent filter (plastic or metal) drip
○ Percolated
○ French press (e.g., Bodum)
○ Instant
○ Other, please specify

Are there any other caffeinated beverages not mentioned above that you usually drink at least once per week (e.g., Jolt, root beer, hot chocolate, cocoa, etc.)?

<table>
<thead>
<tr>
<th>Other caffeinated beverages</th>
<th>Usual serving size in ounces</th>
<th>Servings per week</th>
</tr>
</thead>
<tbody>
<tr>
<td>(a)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(b)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(c)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Dietary Advice Report

Control Group
Dietary Recommendations

Caffeine

Health Canada’s recommendation for caffeine is at most 300 mg/day for women of child-bearing age and at most 400 mg/day for other adults.\(^1\) Caffeine is found in coffee, tea, cola beverages and energy drinks. One small (8 oz) cup of coffee contains about 100 mg of caffeine, while an 8 oz cup of tea contains about 50 mg of caffeine. One can (355 ml) of cola contains about 30 mg of caffeine, while the caffeine content of energy drinks can range from 80 mg to 200 mg depending on the serving size and brand.

\(^1\)http://www.hc-sc.gc.ca/hl-vs/ivy-vsv/food-aliment/caffeine-eng.php

Vitamin C

The Recommended Dietary Allowance (RDA) for vitamin C is 75 mg/day for women and 90 mg/day for men. Smokers require an additional 35 mg/day.\(^2\) Oranges, strawberries, red and green peppers, broccoli and a number of fruit juices are examples of foods that are excellent sources of vitamin C. One piece of fruit (i.e. one orange) equals one serving, while ½ cup of fresh or frozen vegetables or fruit juice equals one serving.

\(^2\)http://www.hc-sc.gc.ca/fn-an/nutrition/reference/table/index-eng.php

Sugar

The World Health Organization recommends no more than 10% of daily energy consumption be from added sugars.\(^3\) This equals about 12 teaspoons (48 grams) of added sugar per day based on an average 2000-calorie diet. Added sugars are defined as sugars and syrups that are added to foods during processing or preparation and include high-fructose corn syrup, white table sugar, sucrose, honey, and maple syrup.

\(^3\)http://www.who.int/dietphysicalactivity/publications/trs916/download/en/index.html

Sodium

The Tolerable Upper Intake Level (UL) for sodium is 2300 mg/day for men and women aged 19-50.\(^4\) The UL includes intake of sodium from all sources; what is found naturally in foods, as well as sodium that is added to food during processing or preparation and salt added at the table. The UL is equivalent to 1 teaspoon (5 grams) of salt per day, from all sources. It is recommended that individuals consume below the UL for sodium. Foods that are high in sodium include canned soups, fast foods, processed meats and processed cheese.

\(^4\)http://www.hc-sc.gc.ca/fn-an/nutrition/reference/table/index-eng.php
Dietary Advice Report

Intervention Group

Non-Risk
### Personalized Dietary Advice for Daiva Nielsen

#### Report Summary

<table>
<thead>
<tr>
<th>Gene</th>
<th>Result</th>
<th>Dietary Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>CYP1A2</td>
<td>AA</td>
<td>Limit your caffeine consumption to 300 mg/day.</td>
</tr>
<tr>
<td>GSTT1 + GSTM1</td>
<td>1* + 1*</td>
<td>Meet the RDA for vitamin C, which is 75 mg/day for women and 90 mg/day for men. Smokers require an additional 35 mg/day.</td>
</tr>
<tr>
<td>TAS1R2</td>
<td>CT</td>
<td>Avoid consuming more than 10% of your total caloric intake from added sugars.</td>
</tr>
<tr>
<td>ACE</td>
<td>GG</td>
<td>Limit your sodium consumption to 2300 mg/day.</td>
</tr>
</tbody>
</table>

*Orange boxes represent genetic variants that may increase your risk of diet-related health conditions.*
Your Genetic Profile

Caffeine

The CYP1A2 gene is involved in the break down of caffeine. Individuals can break down caffeine slowly or quickly depending on the version of the CYP1A2 gene they have. Research has shown that individuals with the CA or CC version of the gene have a reduced ability to break down caffeine and may be at increased risk for caffeine-related health issues when consuming more than 200 mg/day of caffeine. Individuals with the AA version of the gene do not appear to be at increased risk of caffeine-related health issues.1

Your result for the CYP1A2 gene: AA

Vitamin C

Glutathione S-transferases (GSTM1 and GSTT1) are genes that play a role in vitamin C metabolism. A common deletion of the GSTM1 (*0) and GSTT1 (*0) genes results in a reduced ability to process vitamin C. Research has shown that individuals with the GSTM1*0 or GSTT1*0 versions of the genes may be at increased risk of vitamin C deficiency (low blood levels) if they do not meet the RDA. Individuals with a functional version of both GSTM1 (*1) and GSTT1 (*1) do not appear to be at increased risk of vitamin C deficiency.2

Your result for the GSTM1 gene: *1
Your result for the GSTT1 gene: *1

Sugar

Taste may be the most important determinant of food preferences and dietary habits. The TAS1R2 gene is responsible for sweet taste perception. Research has shown that individuals with the TT version of the TAS1R2 gene tend to consume more sugar than individuals with the CC or CT version.3

Your result for TAS1R2 gene: CT

Sodium

The angiotensin-converting enzyme (ACE) gene is known to play a role in the response of blood pressure to dietary sodium intake. Research has shown that individuals with the AA or AG version of the ACE gene may be at greater risk of experiencing increased blood pressure when higher amounts of sodium are consumed. Individuals with the GG version of the gene do not appear to be at greater risk.4

Your result for the ACE gene is: GG

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Your Personalized Dietary Report

Caffeine

Health Canada’s recommendation for caffeine is at most 300 mg/day for women of childbearing age and at most 400 mg/day for other adults. Since you have the AA version of the CYP1A2 gene, following Health Canada’s caffeine recommendation is appropriate for you. Caffeine is found in coffee, tea, cola beverages and energy drinks. One small (8 oz) cup of coffee contains about 100 mg of caffeine, while an 8 oz cup of tea contains about 50 mg of caffeine. One can (355 ml) of cola contains about 30 mg of caffeine, while the caffeine content of energy drinks can range from 80 mg to 200 mg depending on the serving size and brand.

Vitamin C

The Recommended Dietary Allowance (RDA) for vitamin C is 75 mg/day for women and 90 mg/day for men. For smokers, the requirements are 110 mg/day for women and 125 mg/day for men. Since you have the 1* + 1* versions of the GSTT1 and GSTM1 genes, ensure you meet the RDA for vitamin C. Oranges, strawberries, red and green peppers, broccoli and a number of fruit juices are examples of foods that are good sources of vitamin C. One piece of fruit (i.e. one orange) equals one serving, while ½ cup of fresh or frozen vegetables, or fruit juice, equals one serving.

Sugar

The World Health Organization recommends no more than 10% of daily energy consumption be from added sugars. This equals about 12 teaspoons (48 grams) of added sugar per day based on an average 2000-calorie diet. Since you have the CT version of the TAS1R2 gene, following the World Health Organization’s sugar recommendation is appropriate for you. Added sugars are defined as sugars and syrups that are added to foods during processing or preparation and include high-fructose corn syrup, white table sugar, sucrose, honey, and maple syrup.

Sodium

The Tolerable Upper Intake Level (UL) for sodium is 2300 mg/day and it is recommended that individuals consume below the UL for sodium. This equals about 1 teaspoon (5 grams) of salt per day, which includes sodium that is naturally found in food, as well as salt that is added to food during processing or preparation, and salt added at the table. Since you have the GG version of the ACE gene, following the recommendation to consume below the UL for sodium is appropriate for you. Foods that are high in sodium include canned soups, potato chips, processed meats and processed cheese.
Dietary Advice Report

Intervention Group

Risk
# Personalized Dietary Advice for Daiva Nielsen

## Report Summary

<table>
<thead>
<tr>
<th>Gene</th>
<th>Result</th>
<th>Dietary Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>CYP1A2</td>
<td>CA</td>
<td>Limit your caffeine consumption to 200 mg/day.</td>
</tr>
<tr>
<td>GSTT1 + GSTM1</td>
<td>1* + 0*</td>
<td>Ensure you meet the RDA for vitamin C, which is 75 mg/day for women and 90 mg/day for men. Smokers require an additional 35 mg/day.</td>
</tr>
<tr>
<td>TAS1R2</td>
<td>TT</td>
<td>Avoid consuming more than 10% of your total caloric intake from added sugars.</td>
</tr>
<tr>
<td>ACE</td>
<td>AG</td>
<td>Limit your sodium consumption to 1500 mg/day.</td>
</tr>
</tbody>
</table>

*Orange boxes represent genetic variants that may increase your risk of diet-related health conditions.
Your Genetic Profile

Caffeine

The *CYP1A2* gene is involved in the break down of caffeine. Individuals can break down caffeine slowly or quickly depending on the version of the *CYP1A2* gene they have. Research has shown that individuals with the CA or CC version of the gene have a reduced ability to break down caffeine and may be at increased risk for caffeine-related health issues when consuming more than 200 mg/day of caffeine. Individuals with the AA version of the gene do not appear to be at increased risk of caffeine-related health issues.¹


Your result for the *CYP1A2* gene: CA

Vitamin C

Glutathione S-transferases (*GSTM1* and *GSTT1*) are genes that play a role in vitamin C metabolism. A common deletion of the *GSTM1* (*0*) and *GSTT1* (*0*) genes results in a reduced ability to process vitamin C. Research has shown that individuals with the *GSTM1*/*0* or *GSTT1*/*0* versions of the genes may be at increased risk of vitamin C deficiency (low blood levels) if they do not meet the RDA. Individuals with a functional version of both *GSTM1* (*1*) and *GSTT1* (*1*) do not appear to be at increased risk of vitamin C deficiency.²


Your result for the *GSTM1* gene: *1*
Your result for the *GSTT1* gene: *0*

Sugar

Taste may be the most important determinant of food preferences and dietary habits. The *TAS1R2* gene is responsible for sweet taste perception. Research has shown that individuals with the TT version of the *TAS1R2* gene tend to consume more sugar than individuals with the CC or CT version.³


Your result for *TAS1R2* gene: TT

Sodium

The angiotensin-converting enzyme (ACE) gene is known to play a role in the response of blood pressure to dietary sodium intake. Research has shown that individuals with the AA or AG version of the ACE gene may be at greater risk of experiencing increased blood pressure when higher amounts of sodium are consumed. Individuals with the GG version of the gene do not appear to be at greater risk.⁴


Your result for the *ACE* gene is: AG
Your Personalized Dietary Report

Caffeine
Health Canada’s recommendation for caffeine is at most 300 mg/day for women of child-bearing age and at most 400 mg/day for other adults.\(^5\) Since you have the CA version of the \textit{CYP1A2} gene, you might benefit from limiting your caffeine intake to no more than 200 mg/day. Caffeine is found in coffee, tea, cola beverages and energy drinks. One small (8 oz) cup of coffee contains about 100 mg of caffeine, while an 8 oz cup of tea contains about 50 mg of caffeine. One can (355 ml) of cola contains about 30 mg of caffeine, while the caffeine content of energy drinks can range from 80 mg to 200 mg depending on the serving size and brand.
\(\text{http://www.hc-sc.gc.ca/hl-vs/iyh-vsv/food-aliment/caffeine-eng.php#he}\)

Vitamin C
The Recommended Dietary Allowance (RDA) for vitamin C is 75 mg/day for women and 90 mg/day for men. Smokers require an additional 35 mg/day.\(^6\) Since you have the 1\(^*\) + 0\(^*\) versions of the \textit{GSTT1} and \textit{GSTM1} genes, you should ensure you meet the RDA for vitamin C to reduce the risk of deficiency. Oranges, strawberries, red and green peppers, broccoli and a number of fruit juices are examples of foods that are excellent sources of vitamin C. One piece of fruit (i.e. one orange) equals one serving, while \(\frac{1}{2}\) cup of fresh or frozen vegetables, or fruit juice, equals one serving.
\(\text{http://www.hc-sc.gc.ca/hn-an/nutrition/reference/table/index-eng.php}\)

Sugar
The World Health Organization recommends no more than 10% of daily energy consumption be from added sugars.\(^7\) This equals about 12 teaspoons (48 grams) of added sugar per day based on an average 2000-calorie diet. Since you have the TT version of the \textit{TAS1R2} gene, you may have a tendency to over consume sugar and might benefit from limiting your consumption of sweetened foods and beverages with added sugars. Added sugars are defined as sugars and syrups that are added to foods during processing or preparation and include high-fructose corn syrup, white table sugar, sucrose, honey, and maple syrup.
\(\text{http://www.who.int/dietphysicalactivity/publications/trs916/download/en/index.html}\)

Sodium
The Tolerable Upper Intake Level (UL) for sodium is 2300 mg/day.\(^8\) This equals about 1 teaspoon (5 grams) of salt per day, which includes sodium that is naturally found in food as well as salt that is added to food during processing or preparation. Since you have the AG version of the \textit{ACE} gene, limiting your sodium consumption to the Adequate Intake (AI) level of 1500 mg/day should reduce the risk of increased blood pressure associated with high sodium intake. The AI is equivalent to \(\frac{3}{4}\) teaspoon (3.75 grams) of salt per day, from all sources. Foods that are high in sodium include canned soups, potato chips, processed meats and processed cheese.
\(\text{http://www.hc-sc.gc.ca/hn-an/nutrition/reference/table/index-eng.php}\)