Type 2 Diabetes and Obesity: A Biological,

Behavioral, and Environmental Context

by

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ABSTRACT

According to the Centers for Disease Control and Prevention (CDC), type 2 diabetes accounts for 90-95% of diabetes (29.1 million) cases and manifests in 15-30% of prediabetes (86 million) cases, where 9 out of 10 individuals do not know they have prediabetes. Obesity, observed in 56.9% of diabetes cases, arises from the interactions among genetic, biological, environmental, and behavioral factors that are not well understood. Assessing the strength of these links in conjunction with the identification and evaluation of intervention strategies in vulnerable populations is central to the study of chronic diseases. This research addresses three issues that loosely connect three levels of organization utilizing a combination of quantitative and qualitative methods. First, the nonlinear dynamics between insulin, glucose, and free fatty acids is studied via a hypothesis-based model and validated with bariatric surgery data, demonstrating key metabolic factors for maintaining glucose homeostasis. Second, the challenges associated with the treatment or management, and prevention of diabetes is explored in the context of an individualized-based intervention study, highlighting the importance of diet and environment. Third, the importance of tailored school lunch programs and policies is studied through contagion models developed within a social-ecological framework. The Ratatouille Effect, motivated by a pilot study among PreK-8th grade Arizona students, is studied and exposes the importance of institutionalizing practical methods that factor in the culture, norms, and values of the community. The outcomes of this research illustrate an integrative framework that bridges physiological, individual, and population level approaches to study type 2 diabetes and obesity from a holistic perspective. This work reveals the significance of utilizing quantitative and qualitative methods to better elucidate underlying causes of chronic diseases and for developing solutions that lead to sustainable healthy behaviors, and more importantly, the need for translatable multilevel methodologies for the study of the progression, treatment, and prevention of chronic diseases from a multidisciplinary perspective.

To my parents, Gregorio Murillo and Anh Kim Murillo, for their love and sacrifice that I will be eternally grateful for.

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INTRODUCTION

1.1   Prevalence of Obesity and Type 2 Diabetes in the U.S.

Obesity is a complex disease, impacting nearly 1 in 3 adults and more than one-third of children and adolescents (6-to-19-year olds) are considered to be overweight or obese according to the National Institute for Diabetes and Digestive and Kidney Diseases (NIDDK) (WIN, 2012). Despite several efforts to reduce adult and childhood obesity in the U.S., the prevalence of obesity still remains to be an issue. From 1960-1970 to 2007-2008, adult obesity has increased from 13% to 33.8% and childhood obesity has increased from 5-7% to 17% (Johnson, 2012). In 2010-2011, it was estimated that now nearly 34.9% of adults 20 years of age or over are obese (Ogden, Carroll, Kit, & Flegal, 2014). Obesity increases risk of coronary heart disease, type 2 diabetes (T2D), cancer, hypertension, stroke, dyslipidemia, liver and gallbladder disease, sleep apnea, osteoarthritis, respiratory problems, and gynecological problems (see Table 1.1) (Brewis, 2011; López-Miranda et al., 2007). Although obesity was not always considered a disease until the 20th century, many organizations now consider obesity a disease including: the American Medical Association (2013), the National Institute of Health (1998), the Social Security Administration (1999), the Centers for Medicare and Medicaid Services (2004), the Obesity Society (2008), and the American Association for Clinical Endocrinology (2012) (Eknoyan, 2006).

Nearly 90-95% of diabetes cases in the U.S. are diagnosed with T2D, where of those diagnosed, 85% were overweight or obese and 56.9% were obese (Abdullah, Peeters, De Courten, & Stoelwinder, 2010; American Diabetes Association (ADA), 2014; Centers for Disease Control and Prevention (CDC), 2013b; Zimmet, Alberti, & Shaw, 2001). The

Centers for Disease Control and Prevention (CDC) estimated 29.1 million U.S. cases of diabetes in 2012, where 27.8% were undiagnosed cases. Diabetes puts individuals at higher risk for blindness, kidney failure, high blood pressure, heart disease, stroke, amputations, dental disease, depression, and pregnancy complications; thus increasing risk of morbidity and mortality. Prediabetes, or blood glucose levels higher than normal levels, impacts 86 million of U.S. individuals, where 9 out of 10 people do not know they have prediabetes and 15-30% are at risk for developing T2D within 5 years.

Table 1.1: Complications of Obesity (Centers for Disease Control and Prevention (CDC), 2015).

Description
All-causes of death (mortality)
High blood pressure (Hypertension)
High LDL cholesterol, low HDL cholesterol, or high levels of triglycerides (Dyslipidemia)
Type 2 diabetes
Coronary heart disease
Stroke
Gallbladder disease
Osteoarthritis (a breakdown of cartilage and bone within a joint)
Sleep apnea and breathing problems
Some cancers (endometrial, breast, colon, kidney, gallbladder, and liver)
Low quality of life
Mental illness such as clinical depression, anxiety, and other mental disorders
Body pain and difficulty with physical functioning
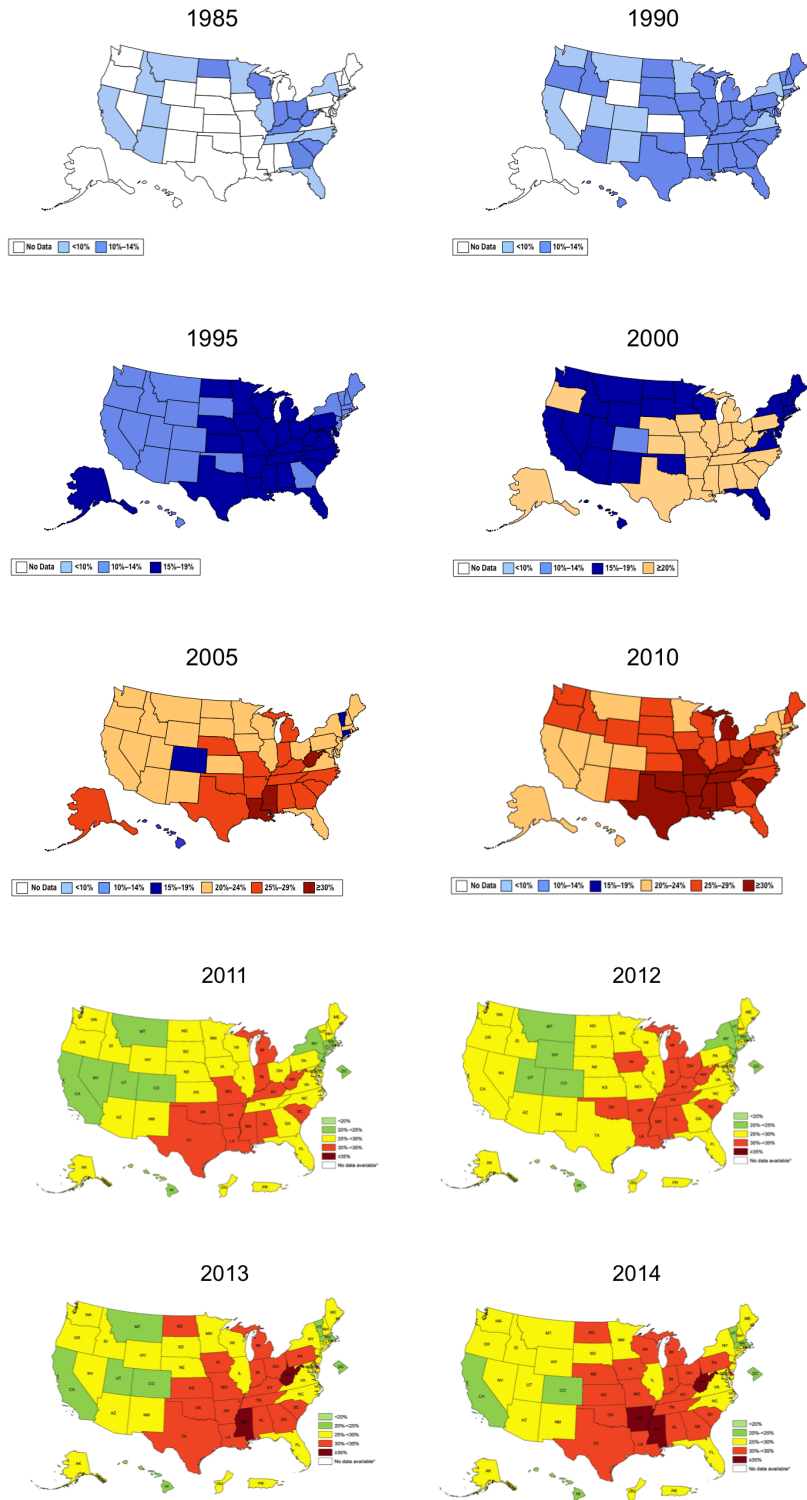
Figure 1.1: Prevalence of Obesity in the U.S. (Centers for Disease Control and Prevention (CDC), 2013a).

Racial and ethnic disparities have been observed among those impacted by diabetes and obesity. Non-hispanic black adults (37.3% men and 49.6% women) were more likely to be obese compared to both Mexican American adults (35.9% men and 45.1% women) and non-Hispanic white adults (31.9 % men and 33% women) according to the 2007-2008 National Health and Nutrition Examination Survey (NHANES), and these patterns do not differ from the 1988-1994 NHANES results (Ogden & Carroll, 2010b). Childhood and adolescent obesity has increased for all race and ethnicities. However, Mexican-American boys (26.8%) and non-Hispanic black girls (29.2%) were more likely to be obese followed by non-Hispanic black boys (19.8%) and Mexican-American girls (17.4%), and last were non-Hispanic white boys (16.7%) and non-Hispanic white girls (14.5%) (Ogden & Carroll, 2010a). Diabetes is more prevalent among American Indians and Alaska Natives (15.9%), Non-Hispanic blacks (13.2%), and Hispanics (12.8%) adults compared to Non-Hispanic whites (7.6%) and Asian Americans (9.0%). Hence, the prevalence and association between obesity and diabetes is a growing concern and needs to be addressed.
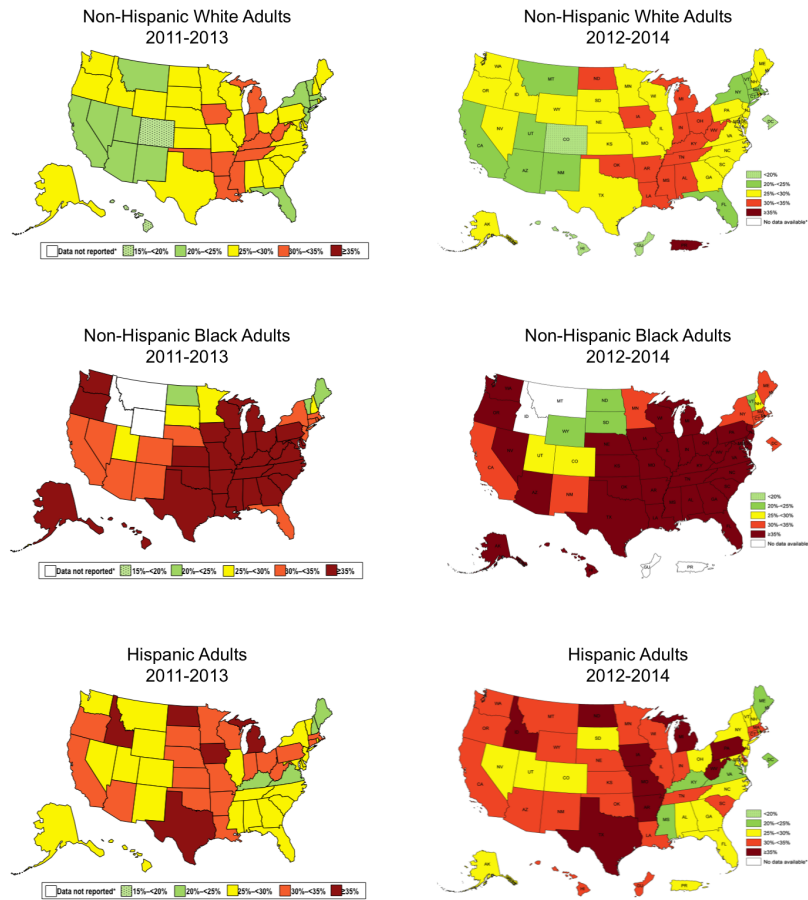
Figure 1.2: Prevalence of Obesity by Race/Ethnicity in the U.S. from (Centers for Disease Control and Prevention (CDC), 2013a).

1.2 Quantifying Body Fat

Clinical obesity refers to excessive body fat that can affect the well-being of an individual or lead to adverse health effects (Brewis, 2011). Fat is essential for life and health. Basic nutrition science reveal that dietary fat is a great source of energy, providing twice as much energy as carbohydrate or protein. In fact, lipids are a major fuel source during rest, physical activity, pregnancy, childhood, lactation, illness, and other cases when energy demand is highest (Brewis, 2011). Hence, fat storage and the process of accessing fat as a source of energy is a mechanism that is necessary for human survival and growth (Brewis, 2011). However, much research demonstrates that excessive fat can be harmful to the body and increase risk of disease and illness. A weight considered unhealthy (either underweight or overweight) is often a result of energy imbalance due to many factors underlying individuals' genetics, biology, and individual behaviors, which modify metabolism rates, energy intake, and energy expenditure.

A standard and widely used measure of total body fat is the body mass index (BMI), developed in the mid-1800s by Adolphe Quetelet, in order to have a standard measure for quantifying an individuals' weight relative to their height (Brewis, 2011). It is an easier measure to obtain, the most common way to measure body fat, and used in the medical diagnosis of negative weight gain (Brewis, 2011). Although BMI is widely and conveniently used, Brewis (2011) highlights that BMI does not distinguish between weight comprised of fat, muscle, bone, cartilage, and water weight (Romero-Corral et al., 2006) and that much variation between BMI and cutoff for disease risks vary across cultures (Brewis, 2011). and differ based on age groups (e.g., children, adolescents, elder).

Additionally, other physical measures of body fat that prior studies show are clinically relevant are central adiposity, or fat around the stomach and abdomen, such as waist circumference and waist-to-hip ratio. These measures give an approximation of subcutaneous

adipose tissue (body fat underneath the skin) and visceral adipose tissue (body fat surrounding the organs) (see Figure 1.3).
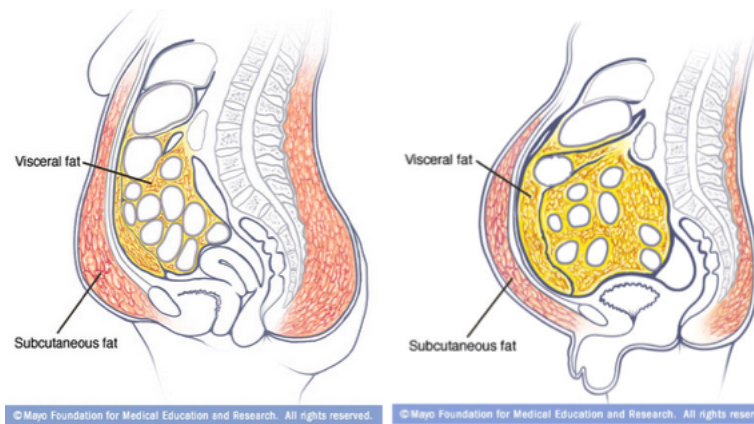
Figure 1.3: Illustration of adipose tissue in the abdominal area. Visceral adipose tissue refers to the body fat surrounding the organs and subcutaneous adipose tissue refers to the body fat underneath skin (Mayo Clinic, n.d.-a, n.d.-b).

Hence, body fat in the central area of the body is recognized as an independent risk factor for cardiovascular disease and similarly, visceral adipose tissue is acknowledged in the development of metabolic syndrome (Burks et al., 2000; S. Haffner & Taegtmeyer, 2003; Liu, Wang, Lienhard, & Keller, 1999; Numan & Russell, 1999; M. P. Reilly & Rader, 2003). Though other techniques can be used to quantify body fat (summarized in Table 1.2) these methods are not always feasible and can be costly. Other factors for diagnosing and assessing risk of metabolic-diseases include lipid biomarkers such as measures of plasma lipids such as triglycerides (TG), lipoprotein, LDL ("bad") and HDL ("good") cholesterol levels.

Table 1.2: Summary of methods used to measure body fat. Adapted from (Brewis, 2011).

Method	Description
Calipers	A measure of subcutaneous fat to estimate body fat percentage
Bioelectrical impedance analysis	A measure of the resistance of electrical flow through the body to estimate body fat where more electrical flow indicate more fat than muscle
Hydrostatic weighing	A measure of how well an individual floats after submerged in water, where more body fat leads to floating
Dual x-ray absorptiometry	Involves lab and medical scanning technique for measuring fat mass, body fat percentage, and variation in fat levels across regions of the body
MRI and CT scans	Scanning equipment to measure body fat
Other technologies (Body Volume Index, or BVI)	3D scanning to examine both volume and weight distribution, and where fat is deposited on the body

1.3 Population Heterogeneities for the Risk Assessment and Diagnosis of Metabolic-Related Diseases

Clinical studies show that insulin resistance is a major defect in people with T2D (American Diabetes Association (ADA), 1998) and a strong predictor for the development of T2D (DeFronzo, 1988; S. M. Haffner, Mykkänen, Festa, Burke, & Stern, 2000; Petersen et al., 2007). Diabetes is diagnosed when hyperglycemia, or high blood glucose levels, is observed and the likely underlying cause is insulin resistance, which refers to the inability of the body to produce enough insulin or the ineffective use of insulin. The manifestation of insulin resistance is evidenced when hyperglycemia persists in an individual. Hence, a measure of blood glucose levels to assess hyperglycemic characteristics is necessary for

diagnosing prediabetes and diabetes, though obesity remains a risk factor for both prediabetes and diabetes. Three common tests are used to diagnose prediabetes and diabetes (see Table 1.3 for a summary of clinical thresholds for the diagnosis of prediabetes and diabetes). First, A1C (also called the hemoglobin A1c, HbA1c, or glycohemoglobin test) is a blood test that captures the average percentage of blood glucose levels over the past 3 months. This test is typically used for detecting T2D and prediabetes. It does not require fasting, nor reflect daily fluctuations, and can be measured at any time of the day. Second, the fasting plasma glucose test (FPG) is used to measure blood glucose after a patient has fasted for at least 8 hours. It is typically used for detecting diabetes and prediabetes. It is the most common diagnostic test used, less expensive, more convenient, and most reliable when given in the morning. Finally, blood glucose can also be measured using the oral glucose tolerance test (OGTT) which requires a patient to fast for at least 8 hours and is given 2 hours after the patient drinks a liquid containing 7 grams of glucose dissolved in water. The OGTT is typically used for detecting diabetes, prediabetes, and gestational diabetes. It is more sensitive than the FPG and less convenient than FPG.

Prior studies demonstrated that assessing metabolic disease risk (FPG, blood pressure, HbA1C levels, LDL and HDL cholesterol levels, and TG levels) varies across many factors such as gender, ethnicity, and age (Adler-Wailes et al., 2013; Badoud, Perreault, Zulyniak, & Mutch, 2014; Golden et al., 2012; Lingvay, Szczepaniak, & Szczepaniak, 2014; Nielsen et al., 2013; Tchernof & Després, 2013). For example, gender differences have been observed in the measures of central obesity (either BMI or waist circumference) that was used to best predict insulin resistance among African Americans (A. E. Sumner, 2008; A. E. Sumner et al., 2008). These findings suggested that a good measure of central obesity was BMI within the obese range, which best predicted insulin resistance in both men and women, compared to using weight alone (A. E. Sumner, 2008; A. E. Sumner et al., 2008). Racial differences among women have been observed where a waist circumfer-

ence of 88*cm* predicts obesity in White females but overweight status in African-American women (A. E. Sumner et al., 2008). Moreover, waist circumference best predicts risk of diabetes, specifically the manifestation of insulin resistance, in African-American women is 18*cm* higher than guidelines established by the IDF ($\geq 94cm$) and 10*cm* higher than those classified by the NCEP-ATPIII ($\geq 102cm$) (A. E. Sumner, 2008; A. E. Sumner et al., 2008). Another finding indicated that African-Americans were more likely to be insulin resistant compared with Whites and Hispanics at normal TG levels (A. E. Sumner, 2009; A. E. Sumner & Cowie, 2008; A. E. Sumner et al., 2008). In addition to TG levels, insulin resistance can also be assessed by the TG:HDL ratio, where ≥ 3 indicate insulin resistance (Eckel, 1989; A. E. Sumner et al., 2008). However, the association between TG and insulin resistance was greater based on gender instead of ethnicity (A. E. Sumner et al., 2008). Moreover, these examples, demonstrate challenges in assessing risk and diagnosing disease in obese individuals when population heterogeneities are considered. Hence, more work is needed in order to fully capture and understand risk of disease and associated negative health outcomes based on physical measures of obesity and metabolic markers.

Table 1.3: Criteria for Diagnosing Prediabetes and Diabetes (Association et al., 2012).

Chacterization	HbA1C (percent)	FPG (mg/dL)	OGTT (mg/dL)
Normal	5	99 or below	139 or below
Prediabetes	5.7 to 6.4	100 to 125	140 to 199
Diabetes	6.5 or above	126 or above	200 or above

1.4   The Role of FFA on Insulin Resistance

It is widely accepted that free fatty acids (FFA), stored in adipose tissue, have a causal role in the onset of insulin resistance in skeletal muscle and liver (Bergman & Ader, 2000;

Boden & Shulman, 2002; Pankow et al., 2004). FFA mostly come from diet, in which, the energy derived from diet mostly come from macronutrients where approximately 50% from carbohydrates, 35% from fats, and 15% from proteins (Austin, Ogden, & Hill, 2011). Specifically, FFA are derived from TG and phospholipids supplied from food (see Table 1.4 for examples). FFA are either taken up to be used as a source of energy by cells (e.g., muscle cells), can be used to make lipid-containing compounds in the body, or can be stored in muscle or adipose tissue for later use (Thompson, Manore, & Vaughan, 2013). FFA are very important to the body. For example, it is a source of energy supply, it forms the myelin allowing for fast electrical communication between neurons, it provides insulation to help conserve body heat, it forms the visceral adipose tissue which protects organs, it is essential for growth and development of organs, especially the brain. FFA stored in adipose cells (i.e., adipocytes) form TG, which are made up of three FFA and one glycerol molecule. However, these adipocytes expand with increased fat storage. In consequence, stored fat, glycogen, and protein modify the chemical composition of the body, and imbalances in macronutrient consumption between dietary intake and metabolic utilization can have adverse health effects.

FFA have been identified as having a critical role in the progression of insulin resistance, that is, the inability of the body to produce enough insulin or the ineffective use of insulin. Insulin is responsible for several metabolic functions such as regulating glucose homeostasis, modifying gene expression (which regulate amino acid uptake, lipid metabolism in muscle and adipose tissue, and cell growth, development, and survival), and it also governs plasma FFA levels (Kimball, Vary, & Jefferson, 1994; Randazzo, Morey, Polishook, & Jarett, 1990; Sell, Reese, & Ossowski, 1994; Taub, Roy, Dieter, & Koontz, 1987; Yenush & White, 1997). Under normal physiological conditions, elevations in plasma glucose prompt increased insulin secretion, which in turn, stimulates glucose uptake and glycogen synthesis (Rhodes & White, 2002). Approximately 50% of insulin is removed immediately by the

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Table 1.4: Healthier and Harmful Fats (Mayo Clinic, n.d.-c).

Types of Healthier Fats	Examples
Unsaturated fats	Avocados, nuts, flaxseed, sunflower seeds, pumpkin seeds, fish, olive oil
Polyunsaturated fats *(Omega-3-Fatty Acids)*	Fish, salmon, oysters, anchovies, walnuts, kale, spinach, brussel sprouts

Types of Harmful Fats	Examples
Trans fats	Commercially-baked foods (cookies, cakes, muffins, breads), packaged snack foods (crackers, microwave popcorn, chips, candy), solid fats (stick margarine), fried foods (french fries, fried chicken), pre-mixed products (cake, milk, pancake, chocolate milk)
Saturated fats	Red meat, poultry, full-fat dairy products (Note: salmon, coconut milk and whole milk differ from pizza, french fries, and processed meat products)

liver and kidney, and the remaining insulin mediates glucose removal (insulin-dependent removal) in tissues such as muscle, adipose, and other cells. In consequence, plasma glucose returns to normal levels, then the demand for insulin is inhibited, i.e. negative feedback (see Figure 1.4 for a schematic diagram). When insulin fails to maintain glucose homeostasis over prolonged periods, the resulting outcome is hyperglycemia, implicating loss of glycemic control and in consequence, impairments in both insulin action (e.g., peripheral insulin resistance) and insulin secretion (e.g., beta-cell dysfunction) (American Diabetes Association (ADA), 1998; S. M. Haffner et al., 2000; Osei, Gaillard, & Schuster, 1997; Tripathy et al., 2000). In the long-term, persistent failure to maintain glucose homeostasis leads to beta-cell compensation, beta-cell dysfunction, and potentially beta-cell death, and possibly the manifestation of type 2 diabetes.
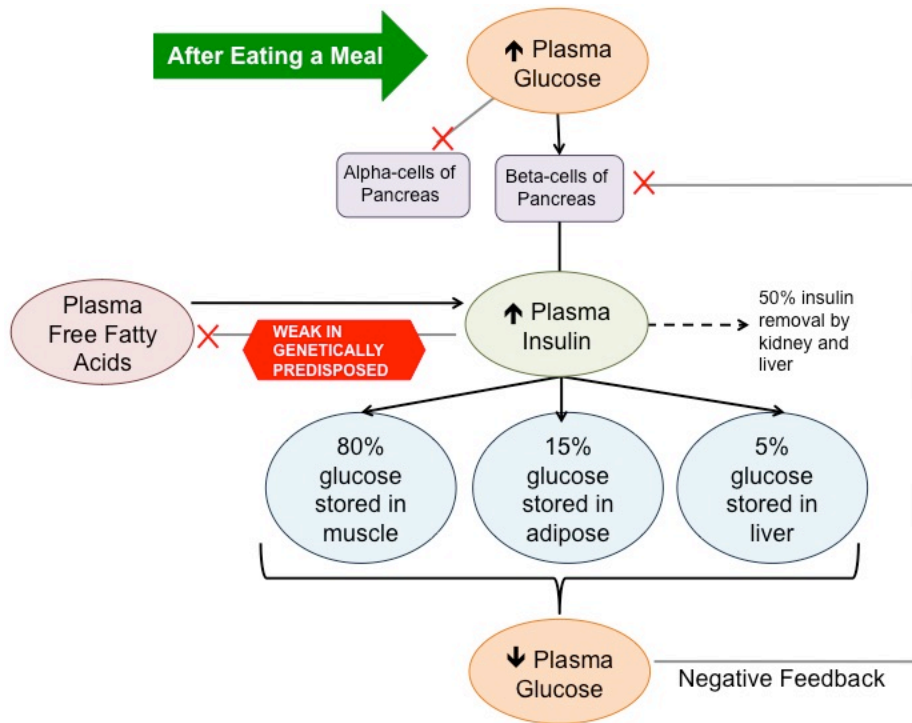
Figure 1.4: Insulin and glucose regulation after a meal. Adapted from (Texas Higher Education Coordinating Board, n.d.).

FFA is an important energy source for body tissues and is used as fuel for the liver, resting skeletal muscle, renal cortex, and myocardium (Boden & Shulman, 2002). When energy supply is low, the body adapts to provide energy and FFA often provides this additional source of energy. More specifically, demand for FFA is high during starvation, exercise, or pregnancy, and can account for more than 70% of total body energy expenditure following an overnight fast (Boden & Shulman, 2002). When demand for fuel rises, then the pancreas releases glucagon, which in turn, triggers energy supply from liver, skeletal muscle, and stimulation of adipose tissue lipolysis. FFA are released into the bloodstream mainly via lipolysis (adipose tissue-stimulated FFA production) in order to provide energy

to the body when supply is low. Hence, FFA becomes available for use while glucose is preserved for cerebral use (Boden & Shulman, 2002). However, when sufficient glucose levels are in the body, then insulin inhibits lipolysis.

Several hypotheses have been proposed to explain the role of FFA and the onset of insulin resistance (summarized in Table 1.5). In skeletal muscle, FFA may interfere with the insulin signaling transduction pathway and affect of insulin action and hinder insulin signaling. Some evidence suggests that FFA could increase glucose production in nondiabetic and diabetic individuals in liver. Prolonged circulating FFA could have direct toxic effects on beta-cells, also referred to as the "lipotoxicity" hypothesis, and thereby, impair the insulin secretary function of pancreatic beta-cells. Imbalanced regulation of FFA production via adipose tissue-stimulated lipolysis and storage of FFA in adipose tissue could create a "vicious cycle" impairing beta-cells indirectly by prompting insulin response (see Figure 1.5). Moreover, an abnormality observed in diabetic individuals is FFA enhanced basal and glucose-stimulated insulin secretion and the use of FFA as an energy source in competition with glucose (Boden & Shulman, 2002).
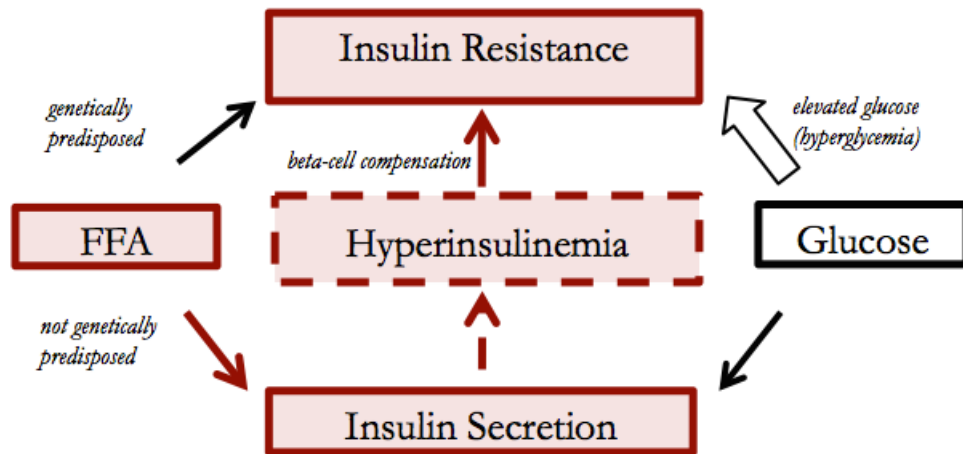
Figure 1.5: An illustration of the phenomenon that links FFA promoting insulin resistance in genetically predisposed individuals.

Table 1.5: Evidence of FFAs role in promoting the development of insulin resistance.

Organ	No.	Observation (Reference)
Skeletal Muscle	1	FFA may impair insulin signaling transduction pathway (Boden, Chen, Ruiz, White, & Rossetti, 1994) (Savage, Petersen, & Shulman, 2005; Shulman, 2000) (Wassink, Olijhoek, & Visseren, 2007)
	2	Higher FFA may interfere with the action of insulin to skeletal muscle or hinder insulin signaling (Bergman & Ader, 2000; Groop et al., 1991) (Randle, 1998)
Liver	1	High FFA levels may increase hepatic glucose production (via glycogenolysis and gluconeogenesis) in diabetes (Boden, Chen, Capulong, & Mozzoli, 2001; Wassink et al., 2007)
	2	High FFA levels may stimulate endogenous glucose production (Boden & Shulman, 2002; Wassink et al., 2007)
	3	Excessive endogenous glucose production may increase in response to a rise influx of FFA in the liver from lipolysis of visceral adipose (excessive fat surrounding internal organs) depots (Bergman & Ader, 2000; Rebrin, Steil, Getty, & Bergman, 1995)
Pancreas	1	Long-term elevated FFA levels may have toxic effects on beta-cells (e.g., "lipotoxicity hypothesis") and impair insulin secretory function (Bergman & Ader, 2000; Unger, 1995)
Adipose	1	Suppressed inhibitory effect of insulin on lipolysis increases FFA levels, creating a vicious cycle (Boden et al., 2001; Wassink et al., 2007)
	2	Increased release of FFAs from adipocytes can induce IR (Wassink et al., 2007)
	3	Imbalanced production of adipokines (e.g., adipocyte dysfunction) may promote IR (Greenberg & McDaniel, 2002; Wassink et al., 2007)

1.4.1   Bariatric Surgery as a Treatment Strategy: An Overview

Although prediabetes can be reversed by lifestyle changes including healthful eating and regular physical activity, diabetes often requires both lifestyle changes and medica-

tions to maintain glucose homeostasis. Other challenges with diabetes management include reducing the risk of alternative cardiovascular disease risk factors such as high blood pressure, high lipid levels, and eye, nerve, or kidney complications. More severe cases of type 2 diabetes require insulin delivered by injection of a pump to survive, which historically was generally given only to type 1 diabetic patients. Among diagnosed diabetes cases seeking treatment, 14% only use insulin (2.9 million adults), 56.9% use oral medication only (11.9 million adults), 14.7% use both insulin and oral medication (3.1 million adults), and 14.4% use neither insulin nor oral medication (3 million adults). An increasingly common treatment for type 2 diabetes patients who are severely obese is bariatric surgery. Some typical bariatric surgery procedures include: gastric banding (such as adjustable and nonadjustable bands), gastric bypass (such as Roux-en-Y variations or any other procedure combined with gastric bypass), gastroplasty (such as vertical banded gastriplasty), biliopancreatic diversion or duodenal switch (such as various modifications), mixed and other (biliary intestinal bypass, ileogastrostomy, jejunoileal bypass, and unspecified bariatric) (Buchwald et al., 2004).

In a review of 134 studies (Buchwald et al., 2004), it was found that patients who underwent bariatric surgery improved diabetes-related outcomes in 76.8% of patients (n=1846) (or either resolved or improved in 85.4% of patients (n=485)). Specifically, 76.8% (70.7% to 82.9%) of patients with type 2 diabetes and impaired glucose tolerance improved, that is, they had the ability to discontinue all diabetes-related medications and maintain blood glucose levels within the normal range; and 86.0% (78.4% to 93.7%) patients either resolved or improved their condition. Nearly 99.1% (97.6% to 100%) of biliopancreatic diversion of duodenal switch patients and 96.9% (93.6% to 100%) of gastric bypass patients experiencing hyperlipidemia, hypercholesterolemia and/or hypertriglyceridemia experienced significant improvement. Hypertension resolved in 61.7% (55.6% to 67.8%) of patients or either resolved or improved in 78.5% (70.8% to 86.1%) of patients. 85.7% (79.2% to

92.2%) of patients diagnosed with obstructive sleep apnea experienced complete resolution or 83.6% (71.8% to 95.4%) experienced either resolution or improvement (Buchwald et al., 2004). Moreover, metabolic improvements include: recovery of acute insulin response, decreases of inflammatory indicators (C-reactive protein and interleukin 6), improvement in insulin sensitivity that was correlated with increases in plasma adiponectin, changes in the enteroglucagon response to glucose, a decrease in ghrelin levels, and significant improvement in beta cell function (Buchwald et al., 2004). Although bariatric surgery is shown to be successful for weight loss, life-long healthy habit changes are necessary for weight management.

1.5   Health Disparities in Arizona

The Arizona state is comprised of demographics that closely resemble that of the U.S. for age, gender, income levels, education levels, and employment status according to the U.S. Census Bureau (United States Census Bureau (USCB), 2015a; (USCB), 2015; United States Census Bureau (USCB), 2015b). However, Arizona is home to more Hispanics (29.9% in A.Z. and 16.6% in the U.S.) and more American Indian or Alaska Natives (4.0% in A.Z. and 0.7% in the U.S.), two populations who are well known to have higher risk of obesity and associated adverse health outcomes, such as diabetes mellitus (see Table 1.6). Additionally, the presence of food deserts and economical barriers puts vulnerable populations, such as the 14.3% of children (2-to-5-year olds) who live in low income households (Arizona Department of Health Services (ADHS), 2012c), at increased risk of obesity and onset of related chronic diseases. In Arizona, nearly 10.4% of children and adolescents (2-to-19-year olds) and 25.9% of adults were obese in 2009 (Arizona Department of Health Services (ADHS), 2012c) which is slightly less than the U.S. obesity prevalence of 16.9% for 2-to-19-year olds and 34.9% for adults 20 years of age or over in 2010-2011 (Ogden et al., 2014). The prevalence of overweight and obese adult residents has increased to 62%

of adults based on the 2012 Behavior Risk Factor Surveillance Survey (BRFSS) (Arizona Department of Health Services (ADHS), 2012c). Adults in households with food assistance (WIC, SNAP, and/or Free and Reduced Lunch) were more likely to be obese (37.5%) compared to those in households without food assistance (23.3%) (Arizona Department of Health Services (ADHS), 2012c). Less than 40% of the population do not consume fruits (37.6%) or vegetables (21.4%) at least once per day (Arizona Department of Health Services (ADHS), 2012a). It was found that risk of obesity was higher for those who do not consume fruits (30.3%) and vegetables (31.7%) per day compared to those who did eat fruits (24.6%) and vegetables (25.6%) at least once per day (Arizona Department of Health Services (ADHS), 2012c). Nearly half of the Arizona population report being active 53.2% (17.2% active and 36% highly active) and the remaining 46.8% were insufficiently active (18.7% insufficiently active and 28.1% inactive) in 2012 (Arizona Department of Health Services (ADHS), 2012b). It was found that obesity was less likely to occur in those who were physically active (only 22.6% who met aerobic recommendation and 20.5% who met the strength recommendation were obese) (Arizona Department of Health Services (ADHS), 2012c). Although these health disparities are reviewed here, they are not studied explicitly in this work. However, they are highlighted to show the significance of this research conducted here.

1.6 Food Deserts and Environment.

Social environments (role modeling, social and cultural norms, and interactions with family, friends, and peers), physical environments (availability and accessibility to food outlets), and economical factors (socioeconomic status, income, and cost of food) shape our eating behaviors. Food insecurity in rural communities and the study of resources in food deserts are key in addressing health disparities and developing community-based pro-

Table 1.6: Comparison of Demographics in A.Z. and the U.S. according to the 2013 estimates reported by the U.S. Census Bureau (United States Census Bureau (USCB), 2015a; (USCB), 2015; United States Census Bureau (USCB), 2015b).

Subject	Arizona Estimate (%)	United States Estimate (%)
Total Population	6,634,997	316,497,531
Age		
Under 5 years	446,556 (6.9%)	20,052,112 (6.4%)
5 − 19 years	1,360,419 (21%)	62,796,743 (20.2%)
20 − 24 years	461,534 (7.1 %)	22,099,887 (7.1 %)
25 − 44 years	827,151 (26.2 %)	40,874,162 (26.5%)
45 − 64 years	362,387 (24.4 %)	17,479,211 (26.4%)
65 years	931,722 (14.4%)	41,851,042 (13.4%)
Median Age	36.3 years (X)	37.3 years (X)
Gender		
Male	2,393,283 (49.7%)	115,463,694 (49.2%)
Female	2,465,375 (50.3%)	122,195,422 (50.8%)
Race		
White	3,716,047 (57.3%)	197,050,418 (63.3%)
Hispanic	1,935,948 (29.9%)	51,786,591 (16.6%)
American Indian or Alaska Natives	258,904 (4.0%)	2,061,752 (0.7%)
Black or African-Americans	252,752 (3.9%)	38,093,998 (12.2%)
Asian	178,627 (2.8%)	15,061,411 (4.8%)
Native Hawaiian and other Pacific Islanders	11,818 (0.2%)	488,646 (0.2%)
Other races	7,539 (0.1%)	606,356 (0.2%)
Two or more races	118,068 (1.8%)	6,387,422 (2.0%)
Education levels		
High school graduate or higher	X (85.7%)	X (86.0%)
Bachelor's degree or higher	X (26.9%)	X (28.8%)
Employment Status		
Civilian Labor Force: Employed	2,721,866 (54.0%)	141,864,697 (57.6%)
Civilian Labor Force: Unemployed	316,360 (6.3%)	15,249,189 (6.2%)
Armed Forces	18,282 (0.4%)	1,083,691 (0.4%)
Not in Labor Force	87,994,377 (35.7%)	1,983,203 (39.4%)
Households Income levels		
< 25,000	571,328 (24.1%)	27,063,516 (23.4%)
25,000 − 49,999	618,460 (26%)	27,652,909 (23.9%)
50,000 − 74,999	440,507 (18.6%)	20,744,045 (17.9%)
75,000 − 99,999	283,273 (12%)	14,107,031 (12.2%)
100,000 − 149,999	281,058 (11.9%)	14,858,239 (12.9%)
150,000 − 199,999	93,521 (3.9%)	5,651,848 (4.9%)
> 200,000	82,142 (3.5%)	5,532,628 (4.8%)
Median Income	49,774 dollars (X)	53,046 dollars (X)
Households with Supplemental Security Income	92,787 (3.9%)	5,716,592 (4.9%)
Households with Cash Public Assistance Income	60,518 (2.6%)	3,255,213 (2.8%)
Households with Food Stamp/SNAP benefits	312,330 (13.2%)	14,339,330 (12.4%)
Families Whose Income is Below Poverty Level		

grams. Food deserts are geographic areas defined as Low Income (LI) and Low Access (LA) geographic areas at 1(urban) and 10 (rural) miles away from the nearest supermarket

(see Figure 1.6). Although food deserts are not addressed in this research, the physical environment is a necessary factors to consider in the study of community-based intervention strategies.
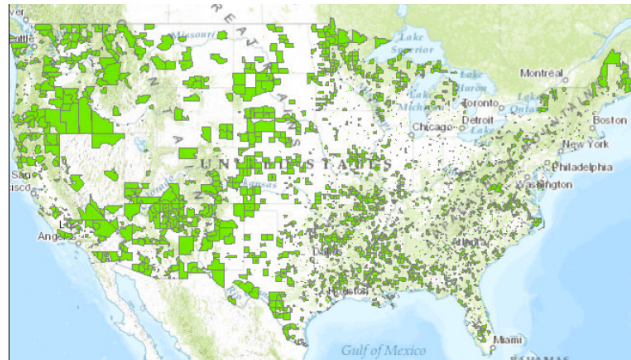
Figure 1.6: Estimated Food Deserts in the U.S. generated by the USDA Economic Research Service (United States Department of Agriculture (USDA), 2015b).

1.7 Mathematical and Statistical Methodology

Although obesity is a risk factor for chronic diseases, the etiology of obesity resulting from complex interactions between genetics, biology, behavior, and environment are not well understood. Hence, the interplay of many biological (genes and family history, metabolism, medications, health conditions, age, pregnancy), behavioral (stress, sleep, emotional, lifestyle, physical activity, diet, smoking), environmental (accessibility, availability), and other individual (culture, social influence, socioeconomic status) factors contribute to obesity; in this research we focus on a subset of these factors shown in Figure 1.7. A combination of mathematical and statistical methods are used to study the aforementioned three aims. Mathematical models are used to study the role of free fatty acids on the progression of type 2 diabetes within overweight and obese individuals at the physiological-level in aim (1). Statistical methods are used to assess the links between health characteristics, environment, and BMI at the individual-level; and to describe what an individualized-based program might look like at the community-level in aim (2). Finally, mathematical models are used to study nutrition education programs in school settings at the population-level in aim (3). Through use of both mathematical and statistical methods, we combine observational and experimental studies in addition to the study of phenomena's and mechanisms, that underly the connection between type 2 diabetes and obesity in the context of biology, behavior, and environment.

1.8 Aims of this Research

This research is structured into three parts. First, in the realm of biology, it is well-understood that FFA, released into plasma from adipose tissue, have a causal role in insulin resistance, which is a clinical marker of several metabolic-related complications, such as T2D and metabolic syndrome. The regulatory role of plasma insulin on plasma FFA levels

Physical environment: access, availability, barriers, and opportunities, e.g., home, work, neighborhoods, fast-foods

Individual factors: outcome expectations, motivation, self-efficacy

Cognition
e.g., attitudes, preferences, knowledge, values

Biological
e.g., genes, gender, age, health conditions

Lifestyle
e.g., diet, exercise, sleep, emotional eating/stress

Demographics
e.g., income, race/ethnicity, socioeconomic status (SES)

Figure 1.7: Multidisciplinary approach. Adapted from (Story et al., 2008).

is not well-understood, nor is the link between glycaemic levels and FFA in overweight and obese patients clinically well-defined. For aim (1), a delay differential equations model is proposed in order to capture the dynamics among insulin, glucose, and FFA dynamics. Key physiological parameters (insulin sensitivity, glucose effectiveness, free fatty acid clearance) are estimated to study the efficacy of insulin as a regulator of both plasma glucose and FFA levels quantitatively and qualitatively. Model validation and parameter estimation is completed using published data of patients undergoing bariatric surgery to assess when insulin effectively, or ineffectively, maintain glucose homeostasis among individuals of different glucose metabolism health statuses. In addition, the proposed model is compared with the "minimal model" to assess how well both models fit to the data. Second, an understanding of behavior-based strategies for weight management is essential for the treatment and management of diabetes in obese individuals. Previous studies show that developing healthy habits rather than focusing on weight loss alone improves cardiovascular health, that is, reversing prediabetes and improving the overall metabolic health of an individual (see Chapter 2). In aim (2), the impact of simple habit changes on weight loss and management is studied in the context of an individualized-based program pilot study implemented

at ASU. The dataset is analyzed as a cross-sectional study in order to assess the links between health factors, at the individual and environmental levels, and BMI to describe health behaviors in a college population. Additionally, this dataset is analyzed as a longitudinal study to identify what a custom-tailored intervention program might look like in a community setting and describe the healthy habits identified by the student population in building their own healthy lifestyle. Third, though many community-based programs intend to reduce the prevalence of obesity, especially, in low-income neighborhoods, long-term effects have yet to be observed. Children are an especially vulnerable population since they do not have much control over their environments and are still developing their eating behaviors. Moreover, it is suggested that eating behaviors learned early on in childhood could transition into adulthood. Food preference learning, based on classical conditioning theory, may be a possible approach for developing more effective intervention strategies (see Chapter 3). In aim (3), methods for teaching healthy eating in Arizona children are discussed emphasizing food preference learning, to instill practical methods for teaching healthier eating when economic, social, and environmental barriers are considered. Mathematical models are developed to study the dynamics of eating behaviors as a social-contagion process in school settings (see Chapter 4). Hence, this dissertation aims to assess the strength of the biological, behavioral, and environmental factors that lead to the onset of type 2 diabetes and obesity, but more broadly, chronic diseases. The outcomes of studying these distinct issues is the integrative approach and the development of frameworks that aim to bridge physiological, individual, and population level approaches to study chronic diseases from a holistic perspective. This work utilizes observational and experimental studies, as well as quantitative and qualitative methods for developing frameworks to study the progression, treatment, and prevention of chronic diseases from a multidisciplinary perspective.
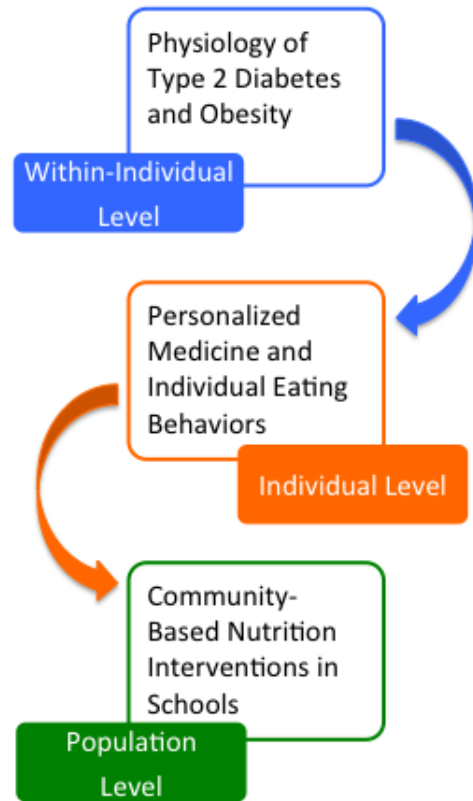
Figure 1.8: Three aims of this research.

Chapter 2

MODELING INSULIN, GLUCOSE, AND FREE FATTY ACIDS FOR AN IVGTT
PROTOCOL

2.1 Background

The intravenous glucose tolerance test (IVGTT) has been clinically considered one of the most accurate methods to determine insulin sensitivity and glucose effectiveness compared to other glucose tolerance tests (Bergman & Cobelli, 1980; Bergman, Ider, Bowden, & Cobelli, 1979; Caumo, Bergman, & Cobelli, 2000; Gresl et al., 2003; Steil, Volund, Kahn, & Bergman, 1993). In this protocol, subjects fast overnight and then are given a bolus of glucose infusion intravenously (e.g., 0.33 g/kg of body weight or 0.3 g/kg body weight of a 50% solution) which is administered into the antecubital vein in approximately 2 minutes (De Gaetano & Arino, 2000; Li, Wang, De Gaetano, Palumbo, & Panunzi, 2012). Subjects are then sampled for plasma glucose, insulin, and FFA levels over the duration of the test. The data provided through an IVGTT offer rich information and offers a more realistic picture of a subject's metabolic portrait (Li et al., 2012).

Mathematical models for an IVGTT protocol aim to capture the mechanism underlying insulin, glucose, and FFA regulation and provides a framework for quantifying two clinically relevant characteristics that cannot be measured directly: insulin sensitivity and glucose effectiveness. The dynamics studied begins with a rise in plasma glucose levels that trigger pancreatic beta-cells to produce and secrete insulin into the bloodstream. Insulin mediates glucose removal, also referred to as insulin-dependent removal, which in turn, lowers plasma glucose to normal levels and then the demand for insulin is inhibited, i.e. negative feedback. Meanwhile, FFA production is inhibited by insulin when glucose

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supply is high (see Figure 1.4). However, prior studies suggest that insulin inhibition of FFA is weak in individuals genetically predisposed to metabolic-related diseases; and FFA may enhance basal and glucose-stimulated insulin secretion among diabetic individuals (Boden & Shulman, 2002). Hence, the theoretical mechanism explored starts with the inability of insulin to regulate FFA which then leads to higher plasma FFA levels. This in turn, reduces glucose transport and leads to a "vicious cycle" promoting hyperglycemia and onset of insulin resistance in the long-term. The proposed model is built off of previous models, where a modified model is proposed to study the dynamics between insulin, glucose, and free fatty acids. This chapter is organized as follows: in Section 2.1.1 the minimal model of insulin, glucose, and FFA is described from the work by (Periwal et al., 2008), in Section 2.1.2 the explicit time delay model of insulin, glucose, and FFA incorporating the vicious cycle hypothesis with corresponding analytical results is presented, in Section 2.3 the results of the model validation and parameter estimates is shown to compare both the minimal model and explicit time delay model, and in Section 4.4 the conclusions and future work is described.

2.1.1   Minimal Model of Glucose, Insulin, and FFA

The "minimal model," developed by Bergman in 1980, was the first model to define two significant indices including the glucose effectiveness index and the insulin sensitivity index, which quantify two clinically and physiologically relevant features (Bergman & Cobelli, 1980; Bergman et al., 1979). The system of equations (2.1), define the "minimal model," where $G(t)$ represents glucose concentration (mg/dl), $I(t)$ denotes insulin concentration ($\mu U/ml$), and $X(t)$ is the remote insulin compartment accessed for insulin-dependent glucose removal ($\mu U/ml$). Parameters S_g represent glucose effectiveness, G_b bolus of glucose due to injection, p_2 insulin production, and p_3 insulin removal from the remote compartment.

$$G'(t) = S_g G_b - S_g G(t) - XG(t)$$

$$X'(t) = p_2 I(t) - p_3 X(t) \tag{2.1}$$

Insulin kinetics (e.g., first phase and second phase insulin secretion) allow us to quantify pancreatic responsiveness. Through estimation of pancreatic responsiveness, glucose disappearance, and insulin sensitivity, this model is utilized to obtain insight into an individual's glucose tolerance, or intolerance. Since then, the "minimal model" has been extended and widely used in experimental settings. The software, MINMOD, is based off of Bergman's "minimal model" and widely used among clinicians and researchers to quantify insulin sensitivity and beta-cell responsiveness for an IVGTT protocol (Boston et al., 2003).

Few mathematical models have been proposed to link insulin, glucose, and FFA (Boston & Moate, 2008; Chow et al., 2011; Periwal et al., 2008; Roy & Parker, 2006). The model presented below was developed by (Chow et al., 2011) to capture the interactions between remote insulin denoted $X(t)$, glucose denoted $G(t)$, and FFA denoted $F(t)$. Glucose enters the body intravenously and is removed by immediate use from other tissues at a constant glucose effectiveness rate S_G or through insulin-mediated removal denoted by the interaction term $S_I X G$, where S_I represents the insulin sensitivity rate. A proportion of insulin is available for use c_X, while the remainder is removed either by a natural degradation rate or by kidney and liver. The maximal lipolysis rate is given by $l_0 + l_2$. Insulin inhibition of lipolysis is denoted X_2 with the exponent A, and the clearance rate of FFA is denoted c_f. The system of equations describing these dynamics are shown below,

$$G'(t) = S_G G_b - (S_G + S_I X)G \tag{2.2}$$

$$X'(t) = c_X[I(t) - X - I_b] \tag{2.3}$$

$$F'(t) = l_0 + \frac{l_2}{1 + \left(\frac{X}{X_2}\right)^A} - c_f F, \tag{2.4}$$

where $I(t)$ represents the insulin levels in the body over time. In Bergman's model and several others, this physiological delay of insulin production and secretion into the body in response to rises in glucose levels is incorporated implicitly by the compartment-split technique in a system of ordinary differential equations (Bergman et al., 1979; Bergman & Cobelli, 1980; De Gaetano & Arino, 2000; Mukhopadhyay, De Gaetano, & Arino, 2004; Roy & Parker, 2007; Toffolo, Bergman, Finegood, Bowden, & Cobelli, 1980). The next section presents a model incorporating this time delay explicitly.

2.1.2 *Explicit Time Delay Model of Glucose, Insulin, and FFA*

A time delay for the production, secretion, and utilization of insulin in the body is key for physiologically assessing insulin sensitivity and glucose effectiveness. The "minimal model" incorporates the physiological delay implicitly by the compartment-split technique in a system of ordinary differential equations (Bergman et al., 1979; Bergman & Cobelli, 1980; De Gaetano & Arino, 2000; Mukhopadhyay et al., 2004; Roy & Parker, 2007; Toffolo et al., 1980). Alternatively, a delay can be incorporated explicitly in a system of delay differential equations in order to add a more realistic interpretation of the biological process (De Gaetano & Arino, 2000; Li et al., 2012; Smith, 2011). More recent models incorporating an explicit time delay provide more accurate quantification of insulin sensitivity and glucose effectiveness since these models are more robust (De Gaetano & Arino, 2000; Li et al., 2012). Mathematical analysis and numerical simulations (Li & Kuang, 2007; Li, Kuang, & Li, 2001; Li et al., 2012) revealed comparable results to observations in clinical

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Table 2.1: Definition of Minimal Model Parameters.

Parameter	Unit	Description
G_b	$\frac{mg}{dl}$	Basal glucose levels
I_b	$\frac{\mu U}{ml}$	Basal insulin levels
S_G	$\frac{1}{min}$	Glucose effectiveness
S_I	$\frac{ml}{\mu U \cdot min}$	Insulin sensitivity
c_X	$\frac{1}{min}$	Rate of available remote insulin
l_0	$\frac{\mu M}{min}$	Baseline nonsupressible lipolysis rate
l_2	$\frac{\mu M}{min}$	Difference between maximum and nonsuppressible lipolysis rate
X_2	$\frac{\mu U}{ml}$	Maximal inhibition rate
A	*unit less*	Hill function coefficient
c_f	$\frac{1}{min}$	Free fatty acid degradation rate

studies (Li, Kuang, & Mason, 2006; Pørksen et al., 2002; Sturis, Polonsky, Mosekilde, & Van Cauter, 1991), both in the short-term and long-term dynamics (see work by (Giang, Lenbury, De Gaetano, & Palumbo, 2008; Li & Kuang, 2007; Palumbo, Panunzi, & De Gaetano, 2007; Panunzi, Palumbo, & De Gaetano, 2007)). In (Li et al., 2012), insulin and glucose regulation for an IVGTT protocol is modeled as follows,

$$
\begin{aligned}
G'(t) &= b - aG(t)I(t) - eG(t) \\
I'(t) &= d\frac{G(t-\tau)^\gamma}{\alpha^\gamma + G(t-\tau)^\gamma} - cI(t),
\end{aligned}
$$

where γ represent the Hills function coefficient, α denote the values of half-saturation, and τ is the time delay of insulin secretion stimulated by elevated glucose level. In order to explore the theoretical hypothesis involving FFA, the model by (Li et al., 2012) is modified

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to incorporate the regulatory role of insulin on plasma FFA levels via lipolysis action and the role of FFA on plasma insulin levels via FFA-stimulated insulin secretion. Moreover, it is of clinical significance to study the dynamics of insulin, glucose, and FFA, and assess the hypothesis that higher FFA may hinder insulin signaling and reduce glucose transport, leading to onset of insulin resistance in order to elucidate the role of insulin action on lipolysis. Through model validation, parameters are estimated utilizing two datasets: the first, is an IVGTT obtained from a sample of nondiabetic and normal BMI adults, and the second, in obese adults who undergo bariatric surgery and have varying levels of glucose tolerance including, normal fasting glucose (NFG), impaired fasting glucose (IFG), or are diagnosed with T2D.

The proposed model is an extension of the insulin and glucose model studied in (Li et al., 2012) and the equation representing FFA was motivated by the work in (Chow et al., 2011). Here the interplay of glucose denoted $G(t)$, insulin denoted $I(t)$, and FFA denoted $F(t)$ is studied. Glucose enters intravenously at a constant rate b and is either immediately used from other cells at rate e or by insulin-mediated removal by the interaction term aGI, where a represents insulin sensitivity. Both glucose-stimulated and FFA-stimulated insulin production is represented by the Hill's function, that is, $d \frac{G(t-\tau)^\gamma}{\alpha^\gamma + G(t-\tau)^\gamma}$ and $p \frac{F(t)^\beta}{\sigma^\beta + F(t)^\beta}$, respectively. Here τ represents the explicit time delay for glucose-stimulated insulin production and secretion. Insulin has a natural degradation rate c and the definition of FFA dynamics is identical to the minimal model shown above. Hence, this system is governed by the following equations,

$$G'(t) = b - aG(t)I(t) - eG(t) \tag{2.5}$$

$$I'(t) = d\frac{G(t-\tau)^{\gamma}}{\alpha^{\gamma} + G(t-\tau)^{\gamma}} + p\frac{F(t)^{\beta}}{\sigma^{\beta} + F(t)^{\beta}} - cI(t) \tag{2.6}$$

$$F'(t) = g_0 + \frac{g_1}{1 + \left(\frac{I(t)}{I_2}\right)^{\kappa}} - hF(t) \tag{2.7}$$

where the parameters β and γ represent the Hills function coefficient and σ and α represent the values of half-saturation (see Table 2.2 for a description of parameters). A schematic diagram of the model is shown in Figure 2.1.
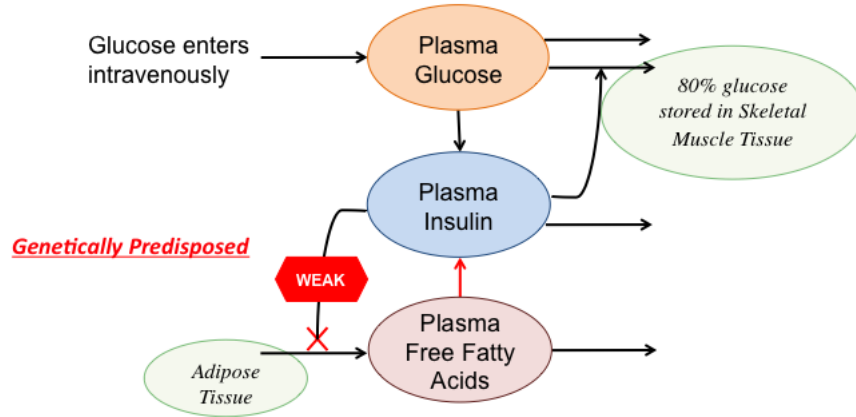
Figure 2.1: A schematic diagram of the proposed glucose, insulin and free fatty acids model.

2.2   Analysis of Solutions

The solutions must be both positive and bounded in order to ensure that the model will provide biologically relevant results. By Theorem 1, the model yields positive solutions for any positive initial conditions. In addition, by Theorem 2, the solutions are bounded for any positive initial conditions. Hence, by Theorem 1 and 2, the solutions of the proposed

Table 2.2: Definition of Explicit Time Delay Model Parameters.

Parameter	Unit	Description
a	$\frac{ml}{\mu U \cdot min}$	Insulin sensitivity
b	$\frac{mg}{dl \cdot min}$	Average rate of glucose input
c	$\frac{1}{min}$	Insulin degradation rate
d	$\frac{\mu U}{mg \cdot min}$	Max secretion rate stimulated by glucose with time delay τ
e	$\frac{1}{min}$	Glucose effectiveness rate
p	$\frac{1}{min}$	Max secretion rate stimulated by insulin
g_0	$\frac{\mu M}{min}$	Baseline nonsupressible lipolysis rate
g_1	$\frac{\mu M}{min}$	Difference between max and nonsupressible lipolysis rate
I_2	$\frac{\mu U}{ml}$	Maximal inhibition rate
h	$\frac{1}{min}$	Free fatty acid degradation rate
κ	*unit less*	Hill function coefficient
β	*unit less*	Hills function coefficient
γ	*unit less*	Hills function coefficient
α	$\frac{mg}{dl}$	half-saturation
σ	μM	half-saturation
τ	$\frac{1}{min}$	delay constant

system are biologically relevant. The proof for Theorem 1 is adapted from (Palumbo et al., 2007) and the proof of Theorem 2 is shown by differential inequalities (see Appendix A for details of these proofs).

Theorem 1. *The system of equations (2.5)-(2.7) gives positive solutions for any positive initial condition.*

Theorem 2. *The solutions for the system of equations (2.5)-(2.7) are bounded.*

Remark 1. *In conclusion of Theorems 1 and 2, the system of equations (2.5)-(2.7) permits positive bounded solutions for any positive initial conditions.*

2.2.1 Equilibria and Local Stability

The steady state is obtained by setting equations (2.5)-(2.7) equal to 0 and performing few algebraic steps (see Appendix C). Although the steady state is only attainable in an implicit form, it can be shown that the system has at least one positive steady state for a set of initial conditions. In Figure 2.2, it can be seen that $y_1(I^*)$ and $y_2(I^*)$ intersect once, and thus, there is one positive equilibrium point in the system, where

$$y_1(I^*) = d\frac{\left(\frac{b}{aI^*+e}\right)^\gamma}{\alpha^\gamma + \left(\frac{b}{aI^*+e}\right)^\gamma} + p\frac{\left(\frac{1}{h}\left(g_0 + \frac{g_1}{1+\left(\frac{I^*}{I_2}\right)^\kappa}\right)\right)^\beta}{\sigma^\beta + \left(\frac{1}{h}\left(g_0 + \frac{g_1}{1+\left(\frac{I^*}{I_2}\right)^\kappa}\right)\right)^\beta}$$

and

$$y_2(I^*) = cI^*$$

2.2.2 Local Stability

The local stability for this steady state can be found by first obtaining the characteristic equation. This is done by assuming that there exists a positive equilibrium point. To obtain the characteristic equation, let us define $A = \frac{\partial(G',I',F')}{\partial(G,I,F)}$, then,

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Plot Illustrating One Positive Equilbrium Point in the System
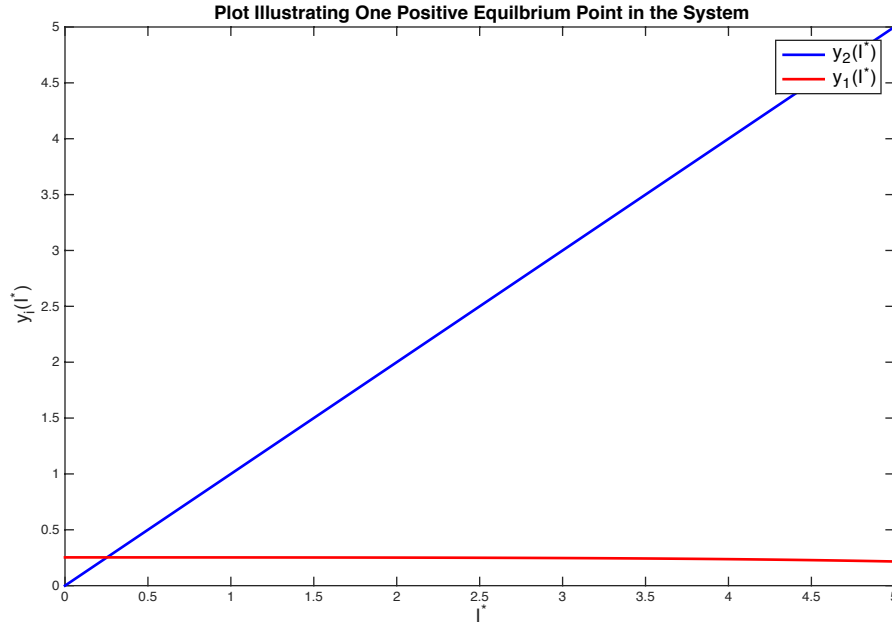
Figure 2.2: The two functions, $y_1(I^*)$ and $y_2(I^*)$, intersect at $(0.253, 0.253)$, indicating that the system has one positive equilibrium point. Parameter values are: $a = 1.060e - 7, b = 0.0005, c = 0.0355, d = 10.434, e = 0.02155, \alpha = 250.001, \gamma = 1.45483, \tau = 8.24999, g_0 = 0.3, g_1 = 40.85, I_2 = 4.1025, \kappa = 1.68, h = 0.08, \beta = 4.6, \sigma = 150$, and $p = 0.009$.

$$
A = \begin{pmatrix}
\frac{\partial G'}{\partial G} & \frac{\partial G'}{\partial I} & \frac{\partial G'}{\partial F} \\[6pt]
\frac{\partial I'}{\partial G} & \frac{\partial I'}{\partial I} & \frac{\partial F'}{\partial F} \\[6pt]
\frac{\partial F'}{\partial G} & \frac{\partial F'}{\partial I} & \frac{\partial F'}{\partial F}
\end{pmatrix}
$$

$$
= \begin{pmatrix}
-aI^* - e & -aG^* & 0 \\[10pt]
0 & -c & p\frac{\beta(F^*)^{\beta-1}\sigma^\beta}{(\sigma^\beta+(F^*)^\beta)^2} \\[10pt]
0 & \dfrac{-g_1\kappa\left(\frac{I^*}{I_2}\right)^{\kappa-1}}{I_2\left(1+\left(\frac{I^*}{I_2}\right)^\kappa\right)^2} & -h
\end{pmatrix}
$$

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and $B = \frac{\partial(G',I',F')}{\partial(G(t-\tau),I(t-\tau),F(t-\tau))}$, which yields,

$$
B = \begin{pmatrix} 0 & 0 & 0 \\ \frac{\alpha^\gamma \gamma d G(t-\tau)^{\gamma-1}}{(\alpha^\gamma + G(t-\tau)^\gamma)^2} & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix}
$$

Now defining the characteristic equation the following is obtained,

$$
H(\lambda) = \lambda I - A - B e^{-\lambda \tau}
$$

$$
= \begin{pmatrix} \lambda & 0 & 0 \\ 0 & \lambda & 0 \\ 0 & 0 & \lambda \end{pmatrix} - \begin{pmatrix} -aI^* - e & -aG^* & 0 \\ 0 & -c & p\frac{\beta(F^*)^{\beta-1}\sigma^\beta}{(\sigma^\beta+(F^*)^\beta)^2} \\ 0 & \frac{-g_1\kappa\left(\frac{I^*}{I_2}\right)^{\kappa-1}}{I_2\left(1+\left(\frac{I^*}{I_2}\right)^\kappa\right)^2} & -h \end{pmatrix} - \begin{pmatrix} 0 & 0 & 0 \\ \frac{\alpha^\gamma \gamma d G(t-\tau)^{\gamma-1}}{(\alpha^\gamma+G(t-\tau)^\gamma)^2} & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix} e^{-\lambda\tau}
$$

$$
= \begin{pmatrix} \lambda + aI^* + e & aG^* & 0 \\ -\frac{\alpha^\gamma \gamma d(G^*)^{\gamma-1}}{(\alpha^\gamma+(G^*)^\gamma)^2} e^{-\lambda\tau} & \lambda + c & -p\frac{\beta(F^*)^{\beta-1}\sigma^\beta}{(\sigma^\beta+(F^*)^\beta)^2} \\ 0 & \frac{g_1\kappa\left(\frac{I^*}{I_2}\right)^{\kappa-1}}{I_2\left(1+\left(\frac{I^*}{I_2}\right)^\kappa\right)^2} & \lambda + h \end{pmatrix}
$$

Hence, the characteristic equation is then (see Appendix D):

$$
|H(\lambda)| = \lambda^3 + \lambda^2(b_1 + b_2) + \lambda(b_1 b_2 + b_3) - \lambda b_4 e^{-\lambda\tau} + b_1 b_3 - b_4 h e^{-\lambda\tau} \quad (2.8)
$$

where

$$
b_1 = aI^* + e, \quad b_2 = c + h, \quad b_3 = ch - \hat{B}\hat{C}, \quad b_4 = aG^*\hat{A},
$$

$$\hat{A} = -\frac{\alpha^{\gamma} \gamma d (G^*)^{\gamma-1}}{(\alpha^{\gamma} + (G^*)^{\gamma})^2}, \quad \hat{B} = -p\frac{\beta (F^*)^{\beta-1} \sigma^{\beta}}{(\sigma^{\beta} + (F^*)^{\beta})^2}, \quad and \quad \hat{C} = \frac{g_1 \kappa \left(\frac{I^*}{I_2}\right)^{\kappa-1}}{I_2 \left(1 + \left(\frac{I^*}{I_2}\right)^{\kappa}\right)^2}.$$

Case with no delay. Applying Routh-Hurwitz Stability Criterion (Allen, 2007) for a cubic polynomial (see Appendix E), the equilibrium point is asymptotically stable if

$$(b_1 + b_2)(b_1 b_2 + b_3 - b_4) > b_1 b_3 - h b_4.$$

2.3   Numerical Results

Here the minimal model and the explicit time delay model are fit to two datasets in order to quantitatively estimate the physiologically relevant parameters among a metabolically heterogeneous population. Model validation and parameter estimation is completed from two published datasets that were extracted using "Plot Digitizer." The first dataset was obtained from the study (A. Sumner et al., 2004), in which, an IVGTT was performed on nineteen nondiabetic individuals (13 men and 6 women) consisting of healthy weight (N=3), overweight (N=8), and obese (N=8) individuals. The second dataset is given by (Soriguer et al., 2009), where an IVGTT was given to nondiabetic and non-obese (6 men and 6 women) individuals in the control group (N=12) and a treatment (14 men and 24 women) group (N=38) who underwent bariatric surgery consisting of 3 distinct groups who had normal fasting glucose (NFG) tolerance (N=9), impaired fasting glucose (IFG) (N=17), and T2D (N=12). A description of the data is summarized in Table 2.3 below. In both cases, the data points represents the average values over time for the samples. The

corresponding variance was not attainable from the datasets, and hence, excluded from this analysis.

Table 2.3: Description of IVGTT data used for model validation.

Sample Group	Age *years* [Mean ± SD]	BMI kg/m^2 [Mean ± SD]	IVGTT Duration	Reference
	36 ± 6	31.4 ± 8.3	180 minutes	(A. Sumner et al., 2004)
Control (No Surgery)	36.7 ± 1.9	23.1 ± 0.7	360 minutes	(Soriguer et al., 2009)
NFG (Pre-Surgery)	35.9 ± 3.4	48.6 ± 1.7	360 minutes	(Soriguer et al., 2009)
IFG (Pre-Surgery)	45.2 ± 2.5	58.1 ± 1.4	360 minutes	(Soriguer et al., 2009)
T2D (Pre-Surgery)	44.6 ± 2.4	53.9 ± 1.7	360 minutes	(Soriguer et al., 2009)
Control (No Surgery)	36.7 ± 1.9	23.1 ± 0.7	360 minutes	(Soriguer et al., 2009)
NFG (Post-Surgery)	35.9 ± 3.4	34.2 ± 1.4	360 minutes	(Soriguer et al., 2009)
IFG (Post-Surgery)	45.2 ± 2.5	39.6 ± 1.4	360 minutes	(Soriguer et al., 2009)
T2D (Post-Surgery)	44.6 ± 2.4	36.6 ± 1.5	360 minutes	(Soriguer et al., 2009)

2.3.1 Model Validation with Explicit Time Delay in Nondiabetic Individuals

The average glucose, insulin, and FFA data for an IVGTT protocol obtained from (A. Sumner et al., 2004) was used for validating the explicit time delay model. Qualitatively, the model captured the overall glucose, insulin, and FFA trends for an IVGTT (see Figure 2.3). Parameter estimates are shown in Table 2.4. The observed differences between the data and model might be due to the size of the sample and the variance in the sample; and hence, data of each individual test is needed in order to fully validate the model and estimate the parameters.
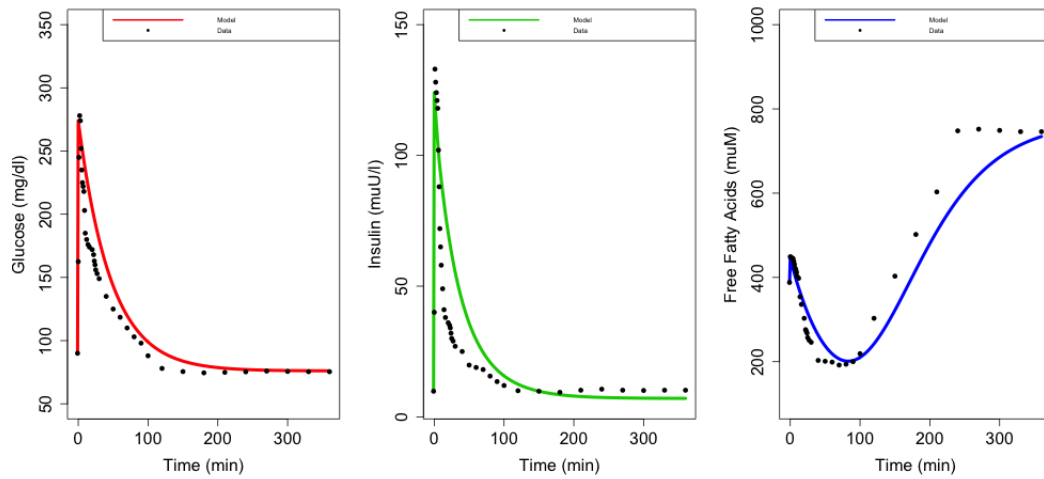
Figure 2.3: The explicit time delay model is fit to the first dataset. A detailed summary of parameter values for this fit can be found in Table 2.4.

Glucose Dynamics

Qualitatively, comparing the plasma glucose levels pre- and post-bariatric surgery, show a significant improvement, where the NFG, IFG, and T2D data nearly resembles the glucose trends of the control group. The overall glucose trends for each group pre- and post-surgery was captured by the explicit time delay model (shown in Figure 2.4). The constant rate of glucose effectiveness (e) and constant insulin sensitivity rate (a) had insignificant changes in the control group but significantly improved (e.g. increased) for the NFG, IFG, and T2D groups.
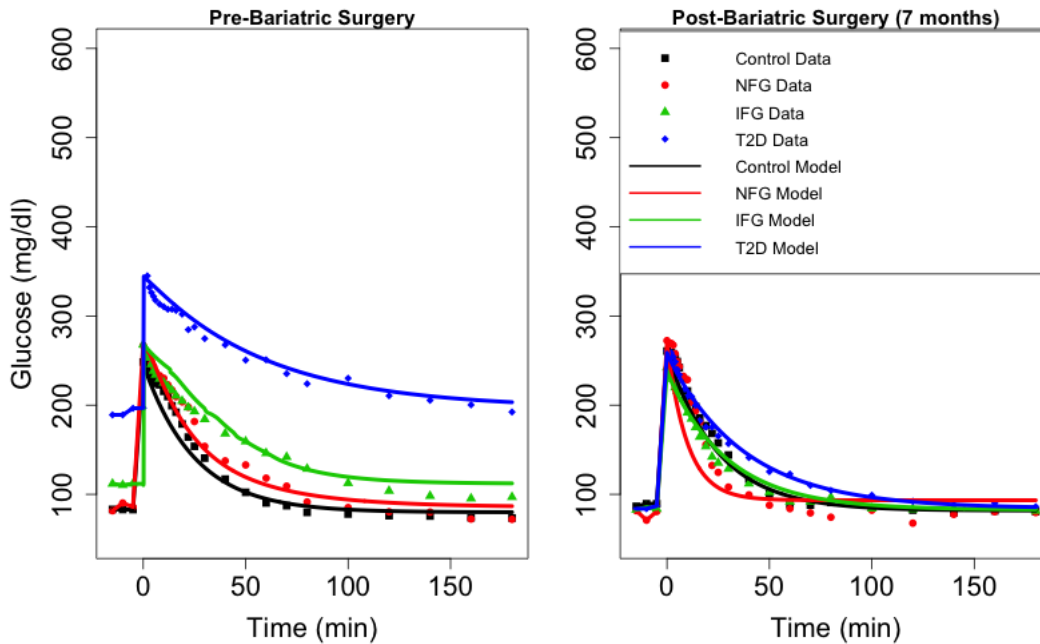
Figure 2.4: Model validation for glucose levels are shown for the explicit time delay model. A description of parameter values can be found in Tables 2.4.

Insulin Dynamics

The plasma insulin levels significantly improved comparing pre- and post-bariatric surgery results, where the NFG, IFG, and T2D data closely match the overall trends of the control group. The model fitted to the data captures the overall trends for insulin (shown in Figure 2.5). The constant insulin degradation rate (c) decreased from post- compared to pre-surgery for all groups and remained constant for the control group. The maximum secretion rate (d) decreased post-surgery for IFG and T2D but not for NFG nor control groups. The constant rate of FFA-stimulated insulin secretion (p) increased for all groups except for T2D. Finally, the time delay for insulin secretion decreased in IFG and increased in the NFG and T2D groups post-surgery.
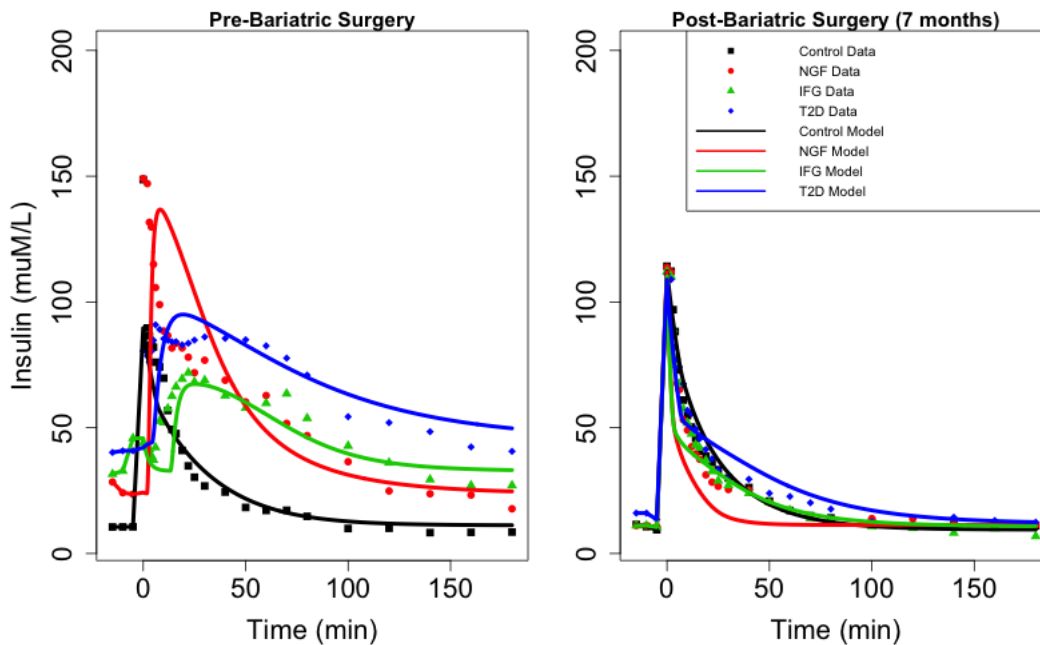
Figure 2.5: The explicit time delay model is fit to the second dataset. A description of parameter values can be found in Tables 2.4.

FFA Dynamics

The variance for plasma FFA levels significantly reduced comparing pre- and post-bariatric surgery results, where the NFG, IFG, and T2D data nearly overlap. The model results qualitatively match the overall trends, except for the NFG group (shown in Figure 2.6). The maximal lipolysis rate ($g_0 + g_1$) reduced significantly from pre- to post-surgery for the IFG and T2D groups. The insulin inhibition (I_2) rate also decreased post-surgery compared to pre-surgery in the NFG, IFG, and T2D groups, whereas no changes in FFA clearance rate (h) were observed.
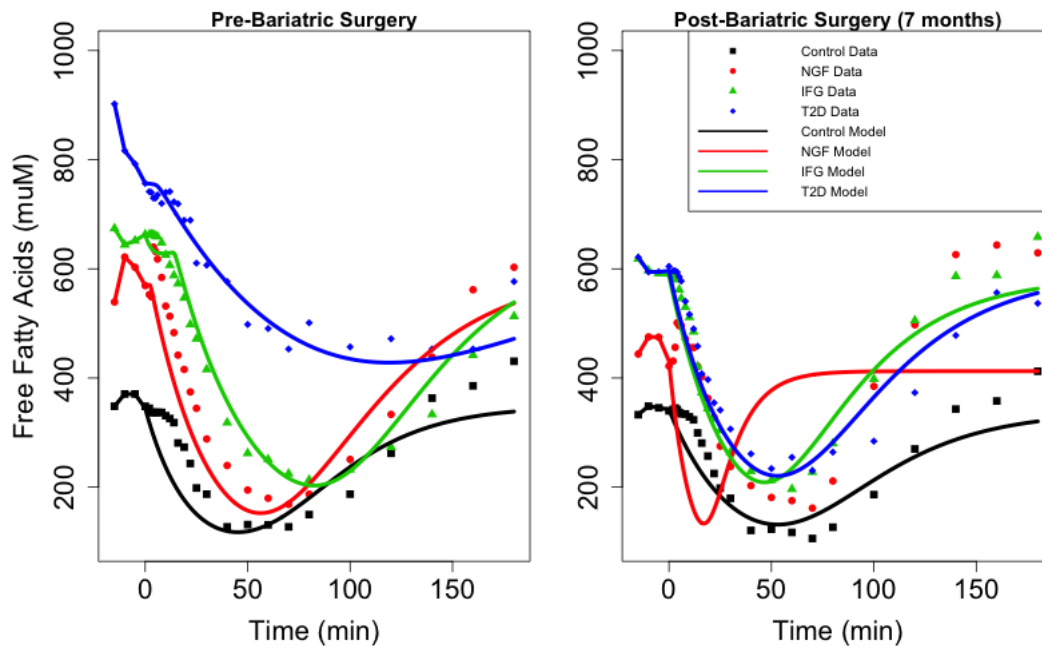
Figure 2.6: The explicit time delay model is fit to the second dataset. A description of parameter values can be found in Tables 2.4.

2.3.2 Comparison of Minimal Model with Explicit Time Delay Model

In this section, the model validation and parameter estimation for the second dataset is completed for both the minimal model and the explicit time delay model. The models fitted to plasma glucose levels is shown in Figure 2.7. Here, both models qualitatively predicted the overall trends for the control, NFG, IFG, and T2D groups. In this case, neither of the models appeared to fit better than the other. In Figure 2.8, the models are fit to plasma insulin levels. Overall, the explicit time delay model appeared to give a better fit compared to the minimal model for all groups. In particular, the steady state values produced by the minimal model estimated solutions below the actual data for the control, NFG, IFG, and T2D groups both pre- and post-surgery. In the control, NFG, and T2D groups, the minimal model falls below the actual data; and the explicit time delay model matches the data much better. For the IFG group, the explicit time delay model does much better with describing the insulin dynamics pre- and post-surgery, whereas the minimal model does not closely match the data. Qualitatively, the trends were not closely matched by the minimal model pre-surgery for the NFG, IFG, and T2D groups. In this case, the explicit time delay model approximated the overall trends more accurately then the minimal model.

Model validation for plasma FFA levels are shown in Figure 2.9. The minimal model captured the overall trends for FFA slightly better than the explicit time delay model for the NFG group, but not for the IFG or T2D group. It also appears that, qualitatively, the FFA dynamics vary more in the transient phase for the minimal model compared to the explicit time delay model. For the control group, the minimal model reached the steady states better compared to the explicit time delay model. In the NFG group, the minimal model fit the overall trends better than the explicit time delay model. However, for the IFG group, the explicit time delay model fit the data better compared to the minimal model. Similarly, in the T2D group, the explicit time delay model also fit better to the minimal model.

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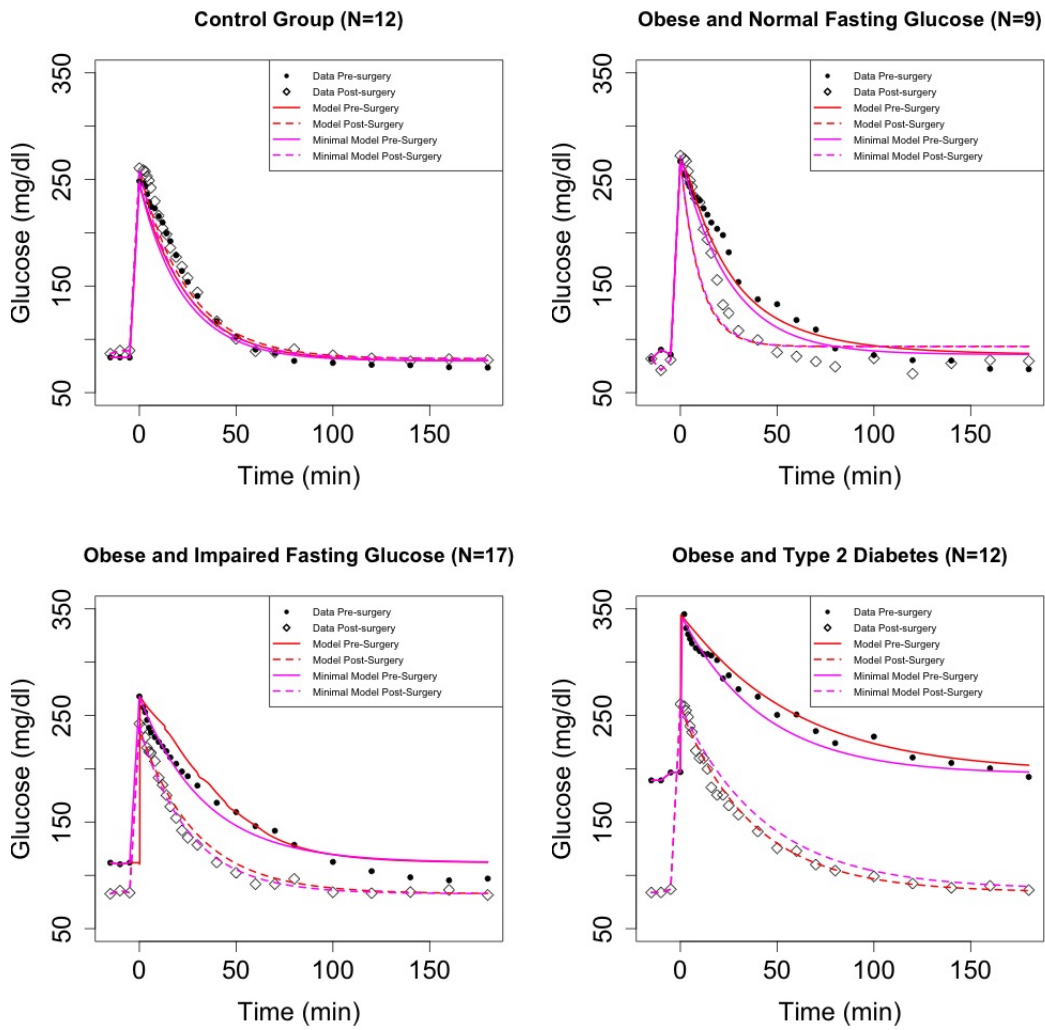
Glucose Dynamics

Figure 2.7: Both the minimal model and explicit time delay model is fit to the glucose data. A description of parameter values can be found in Tables 2.4-2.5. Here both models qualitatively predict the overall trends of glucose dynamics well.

Insulin Dynamics
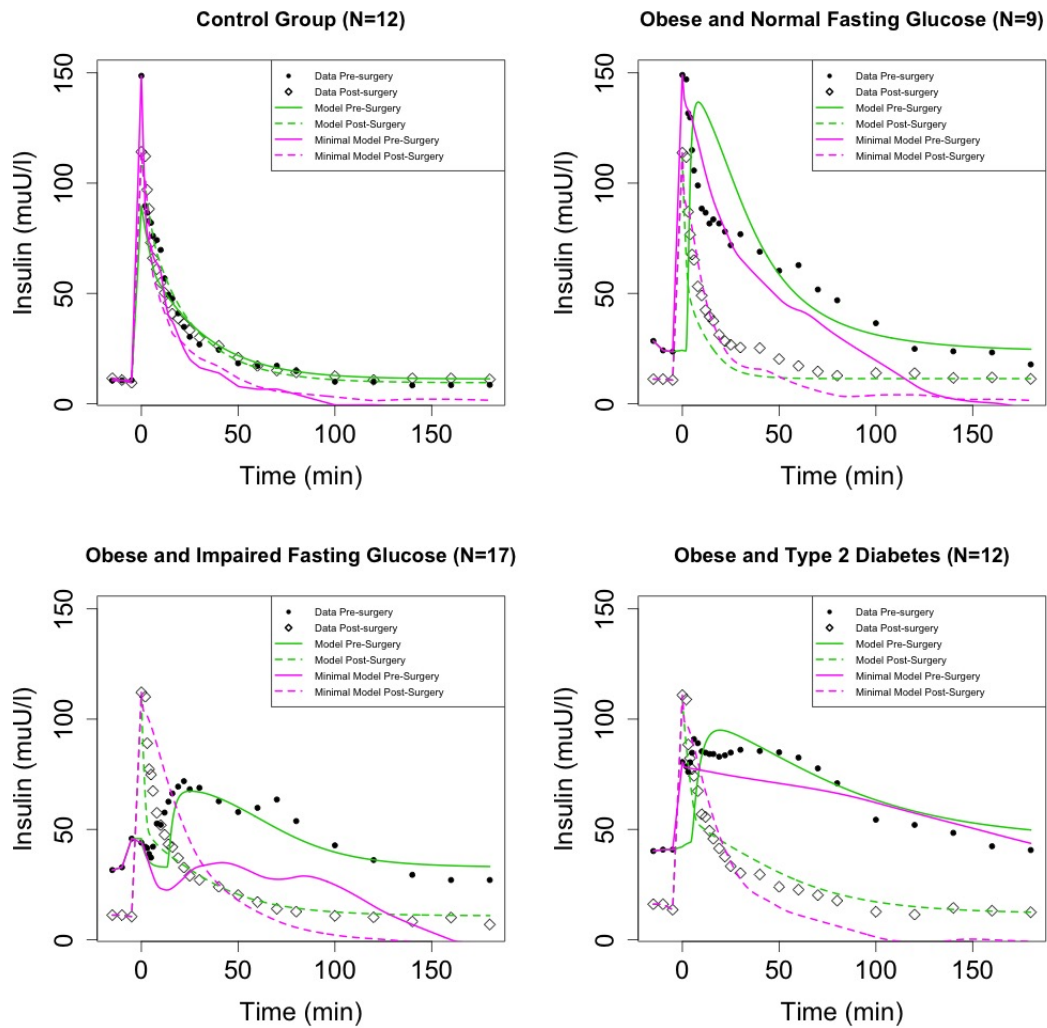
Figure 2.8: Both the minimal model and explicit time delay model is fit to the insulin data. A description of parameter values can be found in Tables 2.4-2.5. Overall, the explicit time delay model captures the qualitative trends more accurately compared to the minimal model.

FFA Dynamics
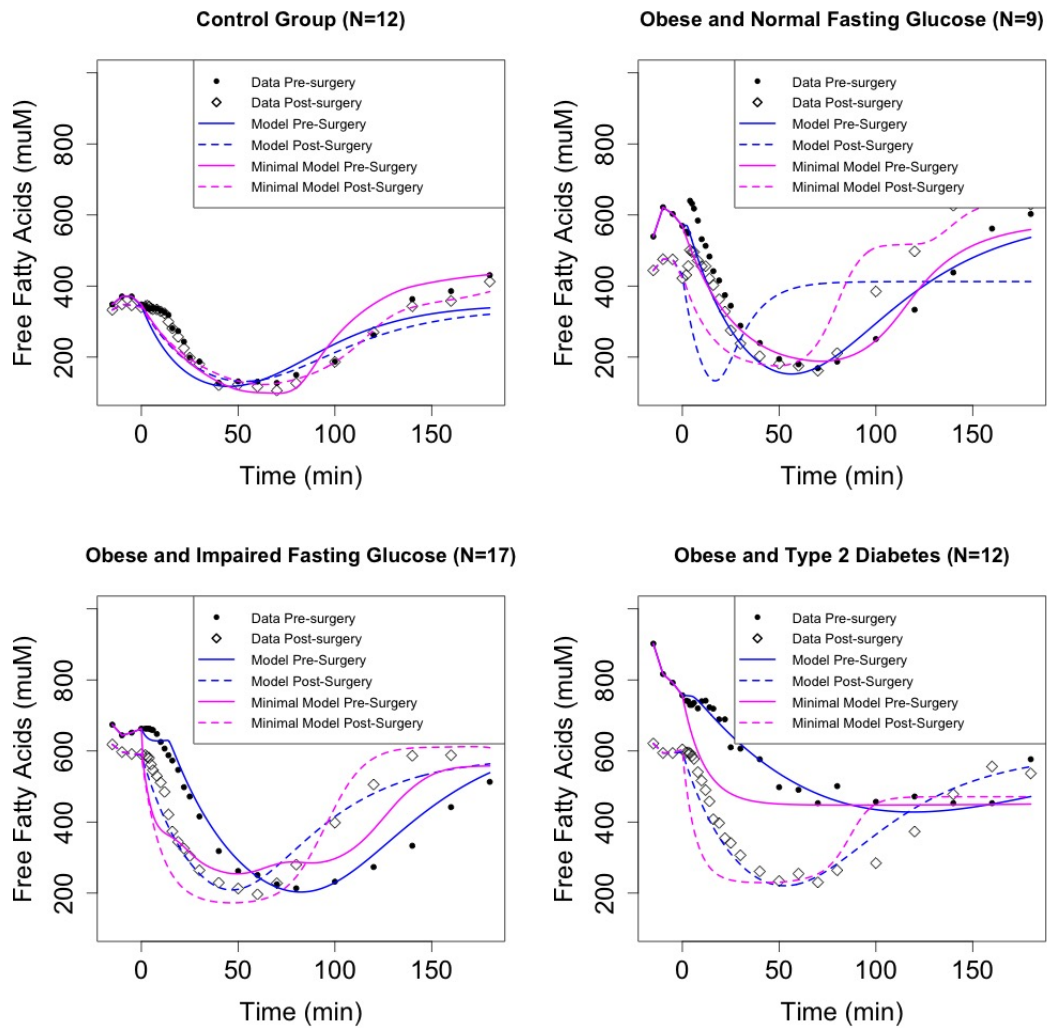
Figure 2.9: Both the minimal model and explicit time delay model is fit to the free fatty acid data. A description of parameter values can be found in Tables 2.4-2.5. The minimal model yields a better fit to the data for the control and NFG groups, whereas the explicit time delay model gave a better fit for the IFG and T2D groups.

Table 2.4: Parameter Estimates for Explicit Time Delay Model, where $*$ is from (A. Sumner et al., 2004) and $**$ is from (Soriguer et al., 2009).

Parameter	Data$*$	Control Pre	Control Post	NFG Pre	NFG Post	IFG Pre	IFG Post	T2D Pre	T2D Post
a	$1.06e-7$	$1.06e-7$	$1.06e-7$	$1.2e-4$	$1.06e-5$	$1.8e-4$	$4.06e-5$	$1.06e-5$	$4.06e-5$
b	0.0005	2.16	2.16	2.16	2.16	4.16	2.16	3.15	2.16
c	0.0355	0.072	0.072	0.8	0.3	0.4	0.3	0.25	0.12
d	10.434	10.434	10.434	12.434	12.434	20.11	12.434	25.11	12.434
e	0.02155	0.04	0.04	0.013	0.1	0.01	0.0315	0.015	0.0236
α	250	250	250	150	150	119	150	220	150
γ	1.45483	1.45	1.45	3.18	2.5	3.4	2.45	4.5	2.45
τ	8.245	8.25	8.25	3.8	4.2	15.24	4.2	6.25	8.25
g_0	0.5	2.5	1.5	0.65	0.5	1.5	0.5	1.5	0.5
g_1	40.85	30.5	18.5	28.85	38.5	30.85	19.85	26.5	18.85
I_2	4.1025	10.5	9.5	31.10	20.10	33.025	18.10	30.5	24.1025
κ	1.68	2.68	2.68	3.2	5.5	6.2	4.5	2.8	3.68
h	0.08	5.8	5.8	0.08	0.08	0.08	0.08	0.08	0.08
β	4.6	4.6	4.6	4.6	4.6	12.6	4.6	12.6	4.6
σ	150	650	650	150	150	150	150	150	150
p	0.1	0.1	0.1	0.2	0.5	0.001	0.1	1.09	0.09

2.4   Discussion

This work investigated the efficacy of insulin suppression on lipolysis and assessed the hypothesis that FFA-stimulated insulin secretion might play a vital role on the progression of insulin resistance. An explicit time delay model of delay differential equations was developed in order to describe the dynamic interplay between insulin, glucose, and FFA based on prior observations reviewed from the literature. Clinical data was obtained from the literature to validate the model and estimate parameters. The two datasets used described individuals that varied in their metabolic health, particularly, nondiabetic and nonobese to severely obese and type 2 diabetic. One of the two datasets was obtained for individuals

Table 2.5: Parameter Estimates for Minimal Model, where $*$ is from (A. Sumner et al., 2004) and $**$ is from (Soriguer et al., 2009).

Parameter	Data$*$	Data$**$							
		Control		**NFG**		**IFG**		**T2D**	
		Pre	**Post**	**Pre**	**Post**	**Pre**	**Post**	**Pre**	**Post**
S_G	NA	0.042	0.042	0.4	0.09	0.03	0.038	0.023	0.023
S_I	NA	$2.07e-5$	$2.07e-5$	$0.07e-5$	$5.07e-5$	$0.07e-5$	$5.07e-6$	$5.07e-6$	$1.07e-7$
c_X	NA	3.5	4.2	0.08	0.25	0.1	0.075	0.005	0.12
l_0	NA	0.95	2.2	5.2	10.02	20.2	16.2	40.2	34.2
l_2	NA	12.85	12.85	16.85	33.5	46.85	44.5	34.85	36.5
X_2	NA	4.25	3.25	20.25	5.2	20.25	4.2	12.25	6.2
A	NA	4.2	2.5	3.5	3.5	2.5	2.5	3.5	4.5
c_f	NA	0.0295	0.031	0.038	0.065	0.12	0.099	0.09	0.15

who underwent bariatric surgery and who significantly improved in their glucose, insulin, and FFA regulation post-surgery. Model validation was completed for the explicit time delay model and compared to the well-studied minimal model. Overall, it seems the explicit time delay model captured the overall qualitative trends well except for the NFG group. The results show that the explicit time delay model was able to better approximate the qualitative behavior compared to the minimal model. However, more work is needed in order to assess insulin suppression quantitatively. More specifically, the individual patient data is needed to more completely assess both models. Utilizing the averages eliminates the variance that needs to be quantified in each group for more realistic and accurate interpretations. The physiological parameters adjusted to fit the data matched findings from the literature on bariatric surgery, indicating that the model captures realistic phenomena. Moreover, the insulin inhibition of FFA was most significant for studying the "vicious" cycle hypothesis. The proposed model described the qualitative trends, including insulin inhibition of FFA, revealing that the proposed model might be reasonable for studying the "vicious" cycle hypothesis. Additionally, a local stability analysis was completed for the

explicit time delay model assuming a positive equilibrium point and was found if certain conditions hold. The solutions for the explicit time delay model are bounded and positive for positive initial conditions. Hence, future work would require individual patient data and possible modifications of the new model to better capture the impact of bariatric surgery on insulin regulation of glucose and FFA.

Chapter 3

TYPE 2 DIABETES AND WEIGHT MANAGEMENT STRATEGIES

3.1   Background and Literature Review

According to the CDC, the medical costs of those impacted by diabetes is double the
cost for those without diabetes, approximately 245 billion dollars; that is, 176 billion of
direct medical costs and 69 billion of indirect costs (disability, premature death, work ab-
sence). Specifically, type 2 diabetes can be managed by medicine-based, surgery-based,
and behavior-based strategies (or a combination of these methods). Physicians will often
recommend lifestyle changes, focusing on diet and physical activity, for patients who are
both obese and prediabetic, or diabetic, in order to encourage patients to achieve a healthier
weight level and in turn, restore glucose metabolism to a healthier state. Moreover, pre-
vious studies suggest that lifestyle changes can improve an individual's metabolic health,
including cases with no weight loss (Kelly et al., 2004; Meyer, Kundt, Lenschow, Schuff-
Werner, & Kienast, 2006; Ryder, Vega-López, Ortega, Konopken, & Shaibi, 2013; Shaibi
et al., 2012; Shaibi, Ryder, Kim, & Barraza, 2015; Watts et al., 2004; Watts, Jones, Davis,
& Green, 2005). However, there are many barriers and challenges to treatment adherence
at the economical, individual, physical environmental, and social environmental levels. For
example, studies show that college students are a particularly vulnerable population for
weight gain. For example, one study found that over 25% of the participants gained weight
in their first year of college (Wengreen & Moncur, 2009). Another study found that over-
weight and obesity was only observed in 15% of the sample during freshman year, that later
increased to 23% by the end of their senior year (Racette, Deusinger, Strube, Highstein, &
Deusinger, 2008). Hence, college adults are at higher risk for weight gain for several rea-

sons. College is a period in which students are living on their own for the first time and hence, are developing their own habits for the first time without parental supervision. A study found that weight gain during the first year of college was associated with less physical activity in college compared to high school (Wengreen & Moncur, 2009). Students who gained weight were also more likely to eat breakfast and sleep more hours compared to those who didn't gain weight (Wengreen & Moncur, 2009). Moreover, students living on campus face environmental and economical barriers, meaning they either have many or few resources for healthy living because their environmental resources are constrained. Additionally, students face challenges with what is affordable in their environment, specifically, another study showed that convenience and cost influenced perception and self-efficacy among college students, which are important factors for determining the health decisions individuals make (Deshpande, Basil, & Basil, 2009).

Intervention programs are developed using the health behavior model framework which focuses on three levels of factors including the individual, physical environment, and social environment. However, challenges still remain in assessing the overall impact of these interventions and designing targeted, or individualized-based, programs that are tailored to individuals' culture, norms, and values. Here a dataset is utilized for a qualitative analysis in order to give insight into how to create an individualized and behavior-based intervention program that is simple, feasible, and effective. Specifically, this study focuses on behavior-based strategies for weight loss or management in the context of a college setting since college students are vulnerable to weight gain, and thus have higher-risk for developing metabolic-related diseases. This statistical study is carried out in the context of a pilot study that was implemented among college students by the Conditioned Feeding Lab, Department of Psychology at Arizona State University (Fall 2014). The purpose of this research study was to develop a custom-tailored, individualized, weight intervention program that was catered to each students unhealthy habits, for example sleep, physical activity, diet,

and mindless eating. Participants in the intervention group developed three healthy habits over the 6-week period in order to focus on living a healthier lifestyle, rather than focus on caloric intake and energy expenditure. Habits varied based on the individual, for example, eating more fruits and vegetables or exercising a few times a week. Participants met weekly with lifestyle coaches in order to report progress on habit changes and for weight measures.

3.2 Description of Study and Participants

An initial screening questionnaire was used to assess eligibility and then the participants were randomly assigned to the intervention and control groups. Approximately 300 ASU students were recruited and 175 participants completed the required baseline questionnaires. Baseline questionnaires included demographic information, weight and height measures, PTC-laden strip test for taster status, Block food frequency questionnaire, sleep and eating behavior questionnaire, caffeine consumption, and neophobia was assessed (see Table 3.1). A total of 107 participants remained in the intervention study, where 54 participants were in the intervention group and 53 were in the control group. The intervention group selected three habits to change over a six week period. They attended six weekly meetings with lifestyle coaches in order to receive peer mentoring support, obtain weight measures, and track progress to lifestyle changes. The control group met with lifestyle coaches three times (every 2 weeks) for weight measures and received a nutrition booklet (see Figure 3.1).

The mean age of students was 22.66 (SD 7.3) years with a range of 17 to 55 years and mean weight was 168.8 (SD=48.2) pounds with a range of 103.2 to 405 pounds. Approximately 27.43% of the participants were male and the remaining 72.57% of the participants were female. Most students were in their freshman year (33.71%) followed by sophomore's (20.57%), junior's (18.86%), senior's (12.57%), and post baccalaureate (13.14%). Nearly 68% of students reported living off-campus. The race/ethnicity reported was mostly

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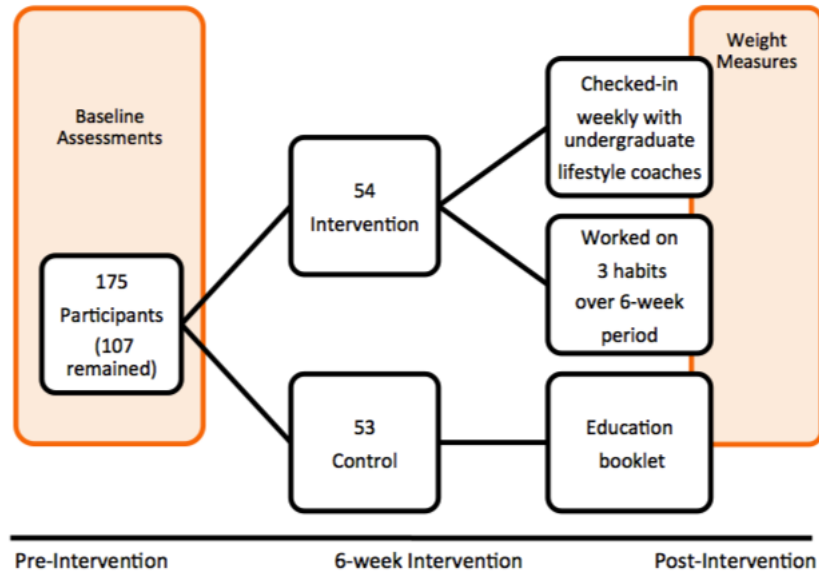
Figure 3.1: Approximately 175 participants completed baseline questionnaires and 107 participants completed the intervention study. The intervention group (N=54) worked on 3 habits over a 6-week period and the control group (N=53) received a nutrition booklet.

Caucasian (56%) followed by Hispanic (13.14%) and Asian (10.86%) participants (see Table 3.2).

Approximately 1.14% were underweight, 44% were normal weight, 28% were overweight, and 26.95% were obese. Most participants did not smoke (90.28%). Sleep health was also assessed where most participants were not at risk for sleep apnea (89.14%). However, risk for sleep insomnia was nearly identical where 40.57% were not at risk and 55.4% were at risk. Nearly 84.57% were not at risk for emotional eating but 97.71% were at risk for the inability to cope with stress (97.71%). Most participants agreed with the statement "I always eat 3 meals a day," (32.57%) which was slightly higher than those who strongly agreed (24.57%) and slightly disagreed (28.57%), and much higher than those who strongly disagreed (13.14%) (see Table 3.3).

Table 3.1: Description of the questionnaires used to assess the participants at the start of the study.

Name	Description
Demographic questionnaire	Survey of age, gender, race/ethnicity, year in school, living arrangements, smoking status, eating 3 meals a day
Block food frequency questionnaire	Survey for measuring frequency and consumption of foods and beverages (Block & Subar, 1992)
Stress and eating behavior questionnaire	Survey for measuring the likelihood of eating under stress (Ozier et al., 2007) and correlating eating habits for positive and negative emotions (Geliebter & Aversa, 2003)
Sleep behavior questionnaire	Survey to assess sleep insomnia and apnea risk, and assess quality of sleep (Bastien, Vallieres, & Morin, 2001)
Caffeine consumption	Survey to assess overall caffeine consumption
Adult neophobia scale	Survey to measure the likelihood of trying new foods (Pliner & Hobden, 1992)

Participants reported their perceived availability of fruits (Mean=2.36, SD=0.0537), vegetables (Mean=2.73, SD=0.0744), and snacks (Mean=2.47, SD=0.0562), where values between 2 to 3 indicate rarely to sometimes on an average week. Students were also assessed for neophobia, or fear of trying new things, characteristics that ranged from 5 to 38, where the higher the score indicated greater neophobia (Mean=16.48, SD=0.5785). Physical activity (minutes/day) was assessed based on self-reports to describe moderate activity (Mean=105.50, SD=11.77), vigorous activity (Mean=90.49, SD=8.24), and walking activity (Mean=192.08, SD=13.71). The average sleep time of participants was 7.29 hours/day (SD=0.08) and ranged from 4.5 to 12.85 hours/day (see Figure 3.4).

Dietary factors were assessed by completion of the Block Food Frequency Questionnaire and additional survey questions on caffeine consumption. The daily average calorie consumption was 1709.92 kcals/day (SD=55.93), where most consumption, in grams/day,

consisted of carbohydrates (M=202.23, SD=6.74) and nearly equivalent intake for both protein (Mean=67.89, SD=2.4) and fat (Mean=68.42, SD=31.53). The average daily servings of grains was highest (Mean=4.97, SD=0.19), followed by fat (Mean=2.77, SD=0.10), meat (Mean=2.39, SD=0.11), vegetables (Mean=2.25, SD=0.12), dairy (Mean=1.15, SD=0.06), and fruits (Mean=1.12, SD=0.06).

Table 3.2: Demographic characteristics of participants including gender, race/ethnicity, marital status, living arrangements, and year in college.

	All (N=175)	Intervention (N=54)	Control (N=53)
Subject	**Frequency (%)**	**Frequency (%)**	**Frequency (%)**
Gender			
Male	48/175 (27.43%)	15/54 (27.78%)	12/53 (22.64%)
Female	127/175 (72.57%)	39/54 (72.22%)	41/53 (77.36%)
Ethnicity			
African-American	5/175 (2.86 %)	1/54 (1.85 %)	2/53 (3.77%)
Asian	19/175 (10.86%)	6/54 (11.11 %)	7/53 (13.21 %)
Caucasian	98/175 (56 %)	28/54 (51.85 %)	31/53 (58.49 %)
Hispanic	23/175 (13.14 %)	11/54 (20.37 %)	5/53 (9.43 %)
Middle Eastern	2/175 (1.14 %)	0/54 (0 %)	0/53 (0%)
Mixed Race	18/175 (10.29 %)	5/54 (9.26 %)	7/53 (13.21 %)
Other	6/175 (3.43 %)	3/54 (5.56 %)	0/53 (0%)
Missing	4/175 (2.28 %)	0/54 (0%)	1/53 (1.89 %)
Marital Status			
Single	145/175 (82.86 %)	46/54 (85.19 %)	47/53 (88.68 %)
Married	20/175 (11.43 %)	6/54 (11.11 %)	3/53 (5.66 %)
Separated	0/175 (0%)	0/54 (0%)	0/53 (0 %)
Divorced	6/175 (3.43 %)	2/54 (3.7%)	2/53 (3.77 %)
Missing	4/175 (2.28 %)	0/54 (0%)	1/53 (1.89 %)
Living Arrangements			
On-campus	54/175 (30.86%)	17/54 (31.48 %)	18/53 (33.96%)
Off-campus	119/175 (68%)	37/54 (68.52 %)	34/53 (64.15 %)
Missing	2/175 (1.14%)	0/54 (0%)	1/53 (1.89 %)
Years in College			
Freshman	59/175 (33.71%)	14/54 (25.93 %)	23/53 (43.4 %)
Sophomore	36/175 (20.57%)	11/54 (20.37 %)	12/53 (22.64 %)
Junior	33/175 (18.86%)	13/54 (24.08 %)	10/53 (18.87 %)
Senior	22/175 (12.57%)	8/54 (14.81 %)	5/53 (9.43 %)
Other	23/175 (13.14%)	8/54 (14.81%)	5/53 (9.43 %)
Missing	2/175 (1.15%)	0/54 (0%)	1/53 (1.89 %)

Table 3.3: Health characteristics of participants including BMI, smoking habits, eating 3 meals a day, taster status, sleep apnea risk, sleep insomnia risk, emotional eating, and emotional stress.

Subject	All (N=175) Frequency (%)	Intervention (N=54) Frequency (%)	Control (N=53) Frequency (%)
BMI Category			
Underweight (BMI ≤ 18.5)	2/175 (1.14%)	0/54 (0%)	2/53 (3.77%)
Normal (18.5 < BMI ≤ 25)	77/175 (44 %)	25/54 (46.3 %)	24/53 (45.28 %)
Overweight (25 < BMI < 30)	49/175 (28 %)	15/54 (27.8%)	13/53 (24.53%)
Obese (BMI > 30)	47/175 (26.95 %)	14/54 (25.92 %)	14/53 (26.42 %)
Smoking Status			
(*cigarettes/day*)			
Do not smoke	158/175 (90.28%)	51/54 (94.44%)	50/53 (94.33%)
5 or less	11/175 (6.28%)	3/54 (5.55%)	2/53 (3.77%)
6-10	0/175 (0%)	0/54 (0%)	0/53 (0%)
11-15	1/175 (0.57%)	0/54 (0 %)	0/53 (0%)
16-20	3/175 (1.71%)	0/54 (0 %)	0/53 (0%)
"I always eat three meals a day"			
Strongly agree	43/175 (24.57%)	13/54 (24.07 %)	14/53 (26.41%)
Agree	57/175 (32.57%)	20/54 (37.03 %)	19/53 (35.84%)
Slightly disagree	50/175 (28.57%)	14/54 (25.92 %)	14/53 (26.41%)
Strongly disagree	23/175 (13.14%)	7/54 (12.96%)	5/53 (9.43%)
Taster status			
Nontaster	10/175 (5.71%)	1/54 (1.85%)	7/53 (13.2%)
Moderate Taster	46/175 (26.28%)	20/54 (37.03%)	14/53 (26.41%)
Taster	119/175 (68%)	33/54 (61.11%)	32/53 (60.37%)
Sleep Apnea			
Not at Risk	156/175 (89.14%)	48/54 (88.88%)	50/54 (92.59%)
At Risk	15/175 (8.57%)	4/54 (7.40%)	2/53 (3.77%)
Sleep Insomnia			
Not at Risk	71/175 (40.57%)	21/54 (38.88%)	21/53 (39.62%)
At Risk	97/175 (55.4%)	29/54 (53.7%)	31/53 (58.49%)
Emotional Eating			
Not at Risk	148/175 (84.57%)	46/54 (85.18%)	44/53 (83.01%)
At Risk	27/175 (15.42%)	8/54 (14.81%)	9/53 (16.98%)
Inability to Cope with Stress			
Not at Risk	4/175 (2.28%)	2/54 (3.70%)	1/53 (1.88%)
At Risk	171/175 (97.71%)	52/54 (96.29%)	52/53 (98.11%)

Table 3.4: A summary of perceived environmental factors (availability of fruits, availability of vegetables, availability of fruits and vegetables, availability of snacks, accessibility of fruits and vegetables), dietary behaviors, physical activity behaviors, and sleep activity.

Subject	Mean	Standard Error	Median	Range
Environmental Factors				
Average Availability of fruit	2.36	0.0537	2.33	1 - 4.73
Average Availability of vegetables	2.73	0.0744	2.7	1 - 5
Average Availability of fruit and vegetables	2.51	0.0543	2.56	1 - 4.6
Average Availability of snacks	2.47	0.0562	2.5	1 - 4.78
Individual Factor				
Neophobia	16.48	0.5785	16	5 - 38
Physical Activity Factors				
Physical activity moderate (min/day)	105.50	11.77	32.5	0 - 630
Physical activity vigorous (min/day)	90.49	8.24	60	0 - 540
Physical activity walking (min/day)	192.08	13.71	150	0 - 720
Sleep Factor				
Sleep total average ($hours/day$)	7.29	0.08	7.28	4.5-12.85
Dietary Factors				
Calories ($kcals/day$)	1709.92	55.93	1565.31	421.2 - 4000.95
Protein (gms/day)	67.89	2.4	59.34	15.83 - 184.47
Total fat (gms/day)	68.42	31.53	186.82	14.86 - 163.16
Carbohydrates (gms/day)	202.23	6.74	186.82	53.97 - 489.62
Vegetable Servings ($servings/day$)	2.25	0.12	1.87	0.04 - .37
Fruit Servings ($servings/day$)	1.12	0.06	0.923	0 - 4
Grain Servings ($servings/day$)	4.97	0.19	4.41	0.804 - 3.71
Meat Servings ($servings/day$)	2.39	0.11	2.08	0.136 - 8.73
Dairy Servings ($servings/day$)	1.15	0.06	0.975	0 - 4.46
Fat Servings ($servings/day$)	2.77	0.10	2.48	0.06 - 6.81
Caffeine morning (mg/day)	128.14	37.31	45	0 - 798
Caffeine afternoon (mg/day)	98.1	28.00	30	0 - 510.5
Caffeine evening (mg/day)	85.02	26.01	19	0 - 523
Caffeine night (mg/day)	0.24	0.24	0	0 - 6
Caffeine total (mg/day)	311.505	55.85	249	0 - 968.5

3.2.1 Description of the Control Group

The age group for the control group (N=53) ranged from 17 to 55 (Mean=21 , SD=5), where 45 were between ages 17-24, 6 between ages 25-34, and 2 between ages 35-55 (see Figure 3.2). Participants' weight ranged from 103.2 to 405 lbs (Mean=21, SD=5). Based on baseline BMI the total underweight were 2, healthy weight were 24, overweight was 13, and obese was 14 (see Figure 3.3). The distribution of race/ethnicity had larger proportions of Caucasian (31) followed by Asian (7), Hispanic (5), Mixed Race (7), Other (1), and African American (1) (see Figure 3.4). Only a small number of students were seniors (2) or were in the category "other" (5), whereas the remainder of the students were juniors (10), sophomores (12), or freshman (23) (see Figure 3.5). The majority of students were nonsmokers (50), however, some self-reported smoking 5 cigarettes/day or less (2) (see Figure 3.6). Most students agreed to the statement "I eat 3 meals a day" (19) and others strongly agreed (14), slightly disagreed (14), or strongly disagreed (5) (see Figure 3.7). The self-reported taster status can be divided into three groups. Specifically, fewer participants were considered non-taster (7) followed by moderate taster (14) and super tasters (32) (see Figure 3.8).

3.2.2 Description of the Intervention Group

The age group for the intervention group (N=53) ranged from 18 to 47 (Mean=22.67, SD=7.2), where 45 were between ages 17-24, 4 between ages 25-34, and 5 between ages 35-55 (see Figure 3.2). Measured weight ranged from 112.4 to 274 lbs (Mean=168.2, SD=56). The distribution of baseline BMI showed that none were underweight, healthy weight were 25, overweight was 15, and obese was 14 (see Figure 3.3). Most participants were Caucasian (28) followed by Hispanic (11), Asian (6), Mixed Race (5), Other (3), and African American (1) (see Figure 3.4). The year in college was distributed similarly in

the intervention group. Specifically, freshman (14), sophomore (11), junior (13), senior (8), or in "other" category (8) (see Figure 3.5). Similar to the control group, most of the students self-reported no smoking activities (51) whereas few reported smoking 5 or less cigarettes/day (3) (see Figure 3.6). Similar to the control group, most students agreed to the statement "I eat 3 meals a day" (20) and others strongly agreed (13), slightly disagreed (14), or strongly disagreed (7) (see Figure 3.7). Similar to the control group, most participants were categorized as a super taster (32), moderate taster (14), and non-taster (7) (see Figure 3.8).
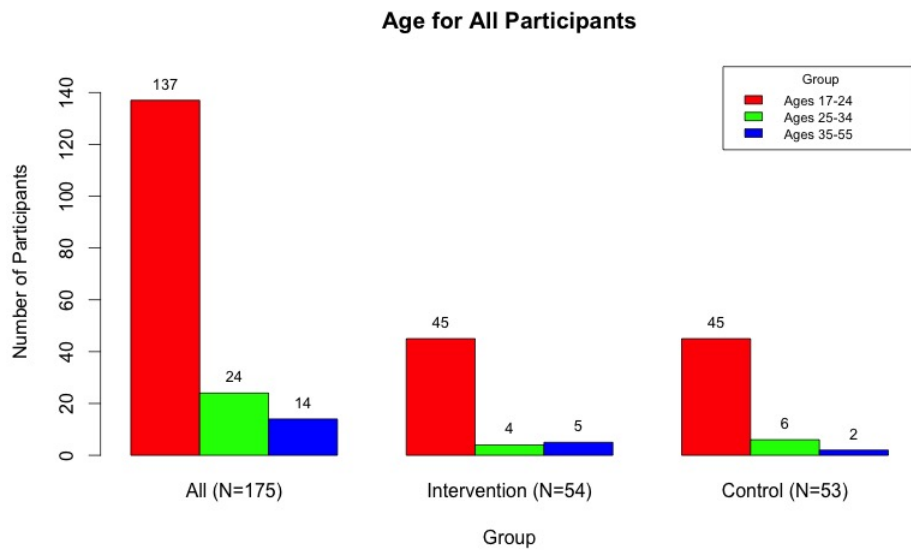
Figure 3.2: Distribution of age for all participants.
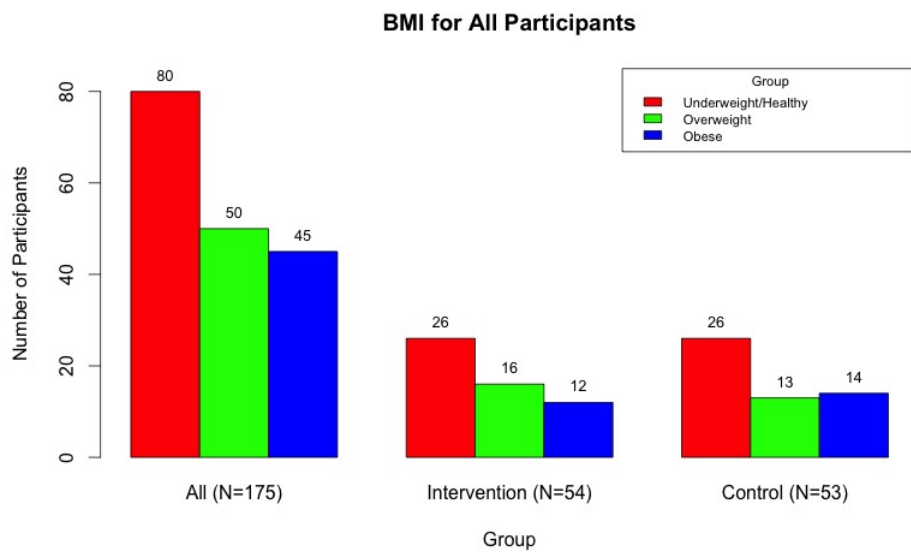
Figure 3.3: Distribution of BMI for all participants.
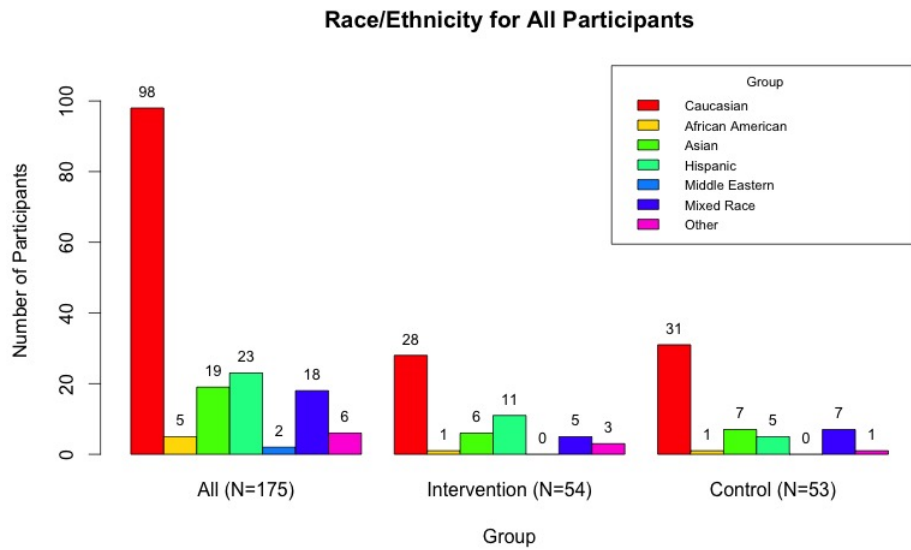
Figure 3.4: Distribution of race/ethnicity for all participants.
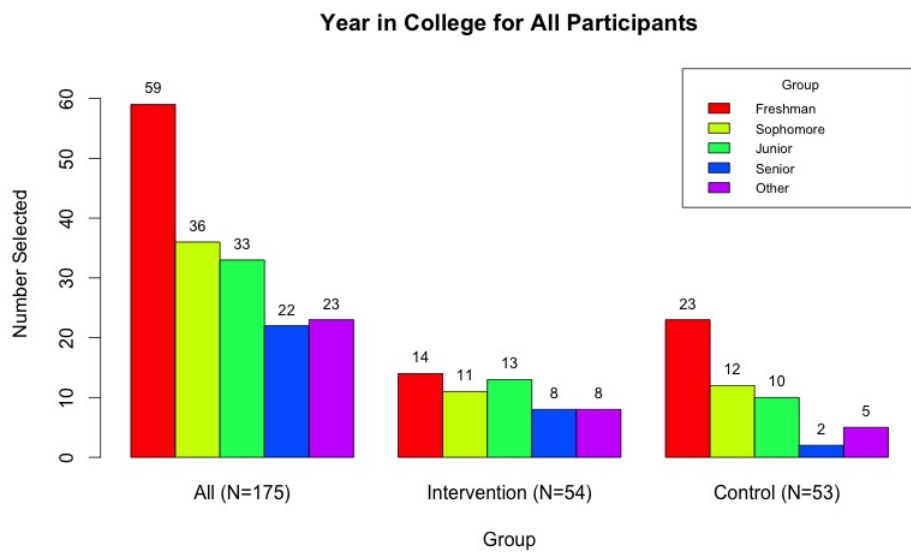
Figure 3.5: Distribution of year in college for all participants.
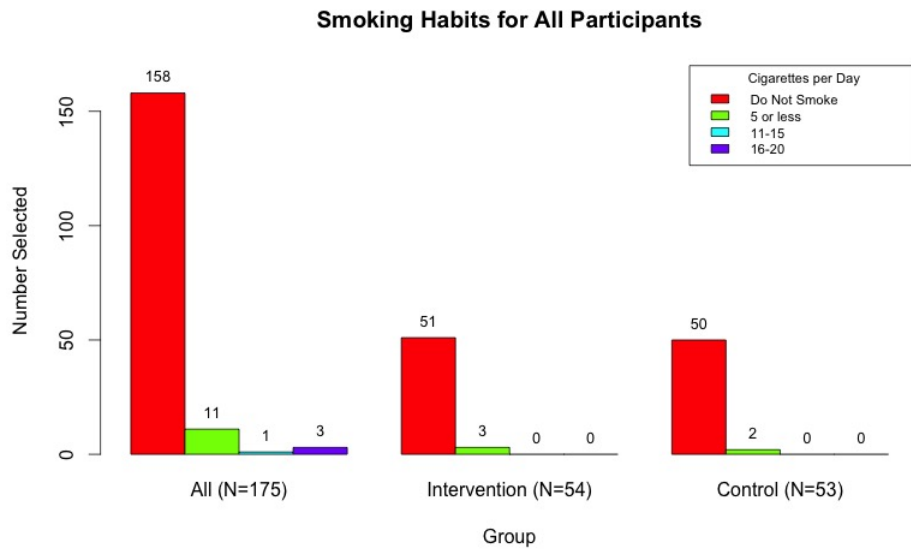
Figure 3.6: Distribution of smoking habits for all participants.
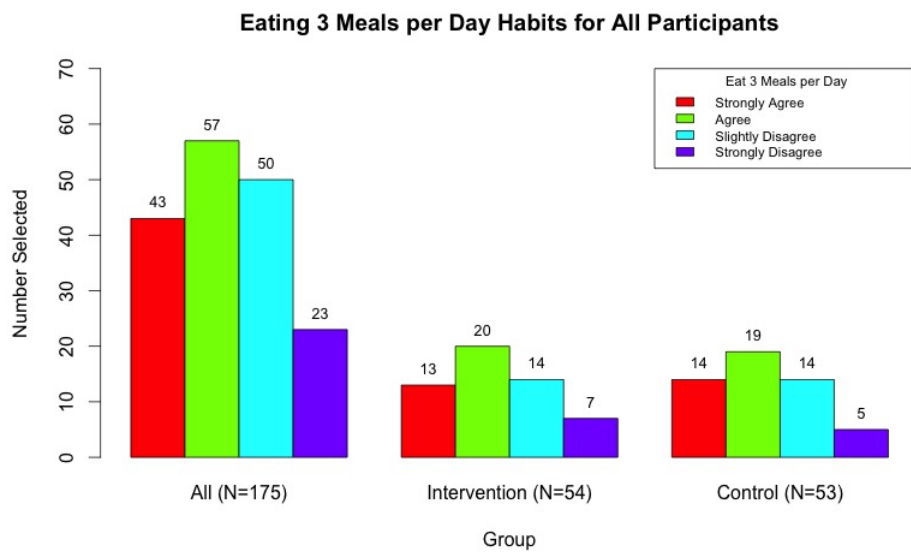
Figure 3.7: Distribution of participants' response to eating 3 meals a day for all participants.
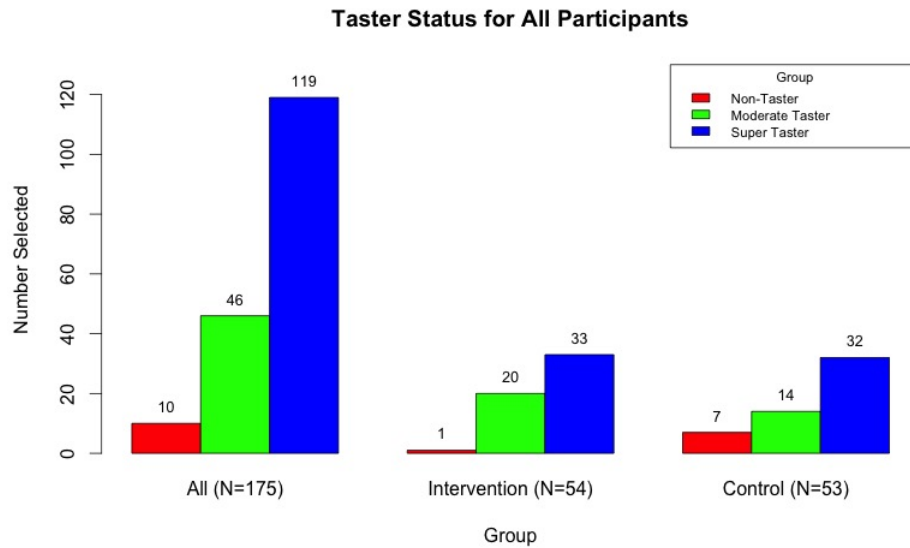
Figure 3.8: Distribution of taster status for all participants.

3.3   Statistical Methods

This section provides a broad overview of the statistical methods used for the cross-sectional and longitudinal studies.

3.3.1   One-Way Analysis of Variance (ANOVA) Fixed Effects Model

A generalizable method of the t test is called the one-way ANOVA model, which allows for the comparison of the means of an arbitrary number of groups for only one variable (Rosner, 2010). The ANOVA model assumes that:

1. Each probability distribution is normally distributed (Kutner, Nachtsheim, Neter, & Li, 2005)

2. Each probability distribution has the same variance (Kutner et al., 2005)

3. The responses for each factor level are random from the corresponding probability distributions and are independent of the responses for any other factor level (Kutner et al., 2005)

The general definition of the model is given by,

$$Y_{ij} = \mu + \alpha_i + e_{ij}, \tag{3.1}$$

where Y_{ij} represents the value of the jth observation (or person) in the ith group, μ denotes the underlying mean of all groups taken together, α_i represents the difference between the mean of the ith group and the overall mean, and e_{ij} denotes the error term capturing the random error about the mean for an individual observation for group i (Rosner, 2010).

The null hypothesis (H_0) is that the underlying mean values are equivalent across all factor levels in a group. The alternative hypothesis (H_1) states that at least one mean for one factor level is different in the group. Hence, the hypothesis to test is H_0: all $\alpha_i = 0$ vs. H_1: at least one $\alpha_i \neq 0$. This is tested using the overall F test which represents the ratio of the between group variability to the within group variability. If this ratio is large, then we reject H_0; and if it is small, then we fail to reject H_0. The significance of this F test statistic is determined by the F distribution with $k-1$ and $n-k$ df under H_0, and α level used. Thus, if $F > F_{k-1,n-k,1-\alpha}$, then reject H_0; and if $F \leq F_{k-1,n-k,1-\alpha}$, then fail to reject H_0.

3.3.2   Two-Way ANOVA

In some cases, the mean responses can be classified into groups based on two different variables. The two-way ANOVA allows for the analysis of mean effects of each variable after controlling for the effects of the other variable, where the two groups could be independent or related (or "interact") (Rosner, 2010). The following general model is defined as,

$$Y_{ijk} = \mu + \alpha_i + \beta_j + \gamma_{ij} + e_{ijk}, \tag{3.2}$$

where Y_{ijk} represents the value of the kth observation (or person) in the ith group of variable 1 and jth group of variable 2, μ denotes the underlying mean of all groups taken together, α_i represents the effect of the ith group of variable 1, β_j denotes the effect of jth group of variable 2, γ_{ij} represents the interaction effect between variables 1 and 2, and e_{ijk} denotes the error term (Rosner, 2010). Three major hypothesis tests can be investigated for the two-factor ANOVA:

1. **The presence of an effect of variable 1.** The null hypothesis (H_0) is that there are no effects of α_i after controlling for the effect of variable 2, whereas the alternative hypothesis (H_1) is that there is an effect. Hence, the hypothesis tested is H_0 : all $\alpha_i = 0$ vs. H_1 : at least one $\alpha_i \neq 0$ (Rosner, 2010).

2. **The presence of an effect of variable 2.** Similarly, to the study of the effect of variable 1, the null hypothesis (H_0) is that there are no effects of β_j after controlling for the effect of variable 1, whereas the alternative hypothesis (H_1) is that there is an effect. Hence, the hypothesis tested is H_0 : all $\beta_j = 0$ vs. H_1 : at least one $\beta_j \neq 0$ (Rosner, 2010).

3. **The presence of an interaction effect between variables 1 and 2.** Here we assess whether or not the effect of variable 1 between the levels of variable 2 differ. The null hypothesis (H_0) is that all interaction terms are equivalent, whereas the alternative hypothesis (H_1) is that at least one is not equal. Hence, the hypothesis tested is H_0 : all $\gamma_{ij} = 0$ vs. H_1 : at least one $\gamma_{ij} \neq 0$ (Rosner, 2010).

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3.3.3 Simple Linear Regression

Although a correlation coefficient quantifies and describes the association between two continuous variables, a simple linear regression model is a method used to assess how a single predictor (or independent) variable (X) relates to a normally distributed outcome (or dependent) variable (Y). A regression line is defined as,

$$Y = \alpha + \beta X + e, \tag{3.3}$$

where α defines the intercept, β is the slope of the line, and e denotes the error term or variance of Y among all X introduced in the model. It is assumed that e is normally distributed with mean 0 and variance σ^2 (Rosner, 2010). The method of least squares is used to estimate the regression line, in which, the least-squares line (or estimated regression line), selected is the line that minimizes the sum of squared distances of the sample points from the line given by: $S = \Sigma_{i=1}^{n} d_i^2$, for observations $i = 1, ..., n$ and sum of squared distances of the points from the line, $\Sigma_{i=1}^{n} d_i^2 = \Sigma_{i=1}^{n} (Y_i - a - bX_i)^2$, where a is the intercept and b is the slope of the line.

The null hypothesis (H_0) is that the slope is 0 and the alternative hypothesis (H_1) is that the slope is nonzero. Hence, we test $H_0 : \beta = 0$ vs. $H_1 : \beta \neq 0$ for a simple linear regression using either an F test or t test.

1. *F* **test.** A good fit of the model to the data is demonstrated when the ratio of the regression sum of squares to the residual sum of squares is large, whereas a small ratio illustrates a weak fit, following an $F_{1,n-2}$ distribution under H_0. Hence, if $F > F_{1,n-2,1-\alpha}$, then reject H_0; whereas, if $F \leq F_{1,n-2,1-\alpha}$, then fail to reject H_0. The exact p-value is given by $Pr(F_{1,n-2>F})$ (Rosner, 2010).

2. t **test.** A good fit of the model to the data is based on the estimate of the sample regression coefficient, or b, and the standard error, or $se(b)$, thus, $t = b/se(b)$ follows a t distribution with $n-2$ df. Hence, if $t > t_{n-2,1-\alpha/2}$ or $t < t_{n-2,\alpha/2} = -t_{n-2,1-\alpha/2}$, then reject H_0; whereas, if $-t_{n-2,1-\alpha/2} \le t \le t_{n-2,1-\alpha/2}$, then fail to reject H_0. The p-value is given by multiplying 2 by the area under a t_{n-2} distribution to the left of t if $t < 0$ or to the right of t if $t \ge 0$ (Rosner, 2010).

3.3.4 Multiple Regression Analysis

An extension of the simple linear regression model allows for the analysis of many independent variables, called the multiple regression analysis. For k independent variables $X_1, X_2, ..., X_k$, then a linear regression model relating to the dependent variable Y to $X_1, X_2, ..., X_k$ is given by,

$$Y = \alpha + \beta_1 X_1 + ... \beta_K X_K + e, \qquad (3.4)$$

or

$$Y = \alpha + \Sigma_{j=1}^{k} \beta_j X_j + e, \qquad (3.5)$$

where Y is an estimate of y, α is estimated by a and $\beta_1, ..., \beta_K$ is estimated by $b_1, ..., b_K$, using the method of least squares which minimizes the sum of $\left[y - \left(a + \Sigma_{j=1}^{k} b_j x_j \right) \right]^2$ (Rosner, 2010). The error term e is normally distributed with mean 0 and variance σ^2.

The null hypothesis (H_0) is that all regression coefficients are equal to zero and the alternative hypothesis (H_1) states that at least one of the regression coefficients is nonzero. Hence, the hypothesis tested is $H_0 : \beta_1 = \beta_2 = ... = \beta_k = 0$ vs. H_1 : at least one of the $\beta_j \ne 0$, applying either an F test or t test.

1. *F* **test.** The *F* test statistic is found by simplifying the ratio of the regression sum of squares to the residual sum of squares, which follows an $F_{k,n-k-1}$ distribution under H_0. Hence, if $F > F_{k,n-k-1,1-\alpha}$, then reject H_0; whereas, if $F \leq F_{k,n-k-1,1-\alpha}$, then fail to reject H_0. The exact p-value is given by the area to the right of F under an $F_{k,n-k-1}$ distribution $= Pr(F_{k,n-k-1} > F)$ (Rosner, 2010).

2. *t* **test.** A *t* test is computed by computing the ratio of the partial regression coefficient to the standard error if the partial regression coefficient,, which follows a *t* distribution with $n-k-1$ df under H_0 for a set α level. Hence, if $t < t_{n-k-1,\alpha/2}$ or $t > t_{n-k-1,1-\alpha/2}$, then reject H_0; whereas, if $-t_{n-k-1,\alpha/2} \leq t \leq t_{n-k-1,1-\alpha/2}$, then fail to reject H_0. The p-value is given by multiplying 2 by $Pr(t_{n-k-1} > t)$ if $t \geq 0$ or by $Pr(t_{n-k-1} \leq t)$ if $t < 0$ (Rosner, 2010).

3.4   Results of the Cross-Sectional Analysis Study

The aims of this cross-sectional study is to address three points. First, does the present study capture health behaviors among college students that are similar to those reported in the literature specifically for sleep health in Section 3.4.1, physical activity behavior in Section 3.4.2, and diet-related behavior in Section 3.4.3. Second, does the present study capture novel or unexpected trends related to sleep health in Section 3.4.1, physical activity behavior in Section 3.4.2, and diet-related behavior in Section 3.4.3. Third, statistical models are used to identify factors that best predict BMI in the following sample shown in Section 3.4.4 for dietary and environmental factors alone, and in Section 3.4.5 for the combination of dietary, environmental, and physical activity factors.

3.4.1   Sleep Behavior

Approximately 89.1% of the sample were not at risk for sleep apnea whereas 8.57% were at risk. The population at risk of sleep insomnia was 55.4% and not at risk was

40.57% (see Figure 3.9-3.10). The average BMI and distribution of BMI were very similar between those at risk and not at risk of sleep insomnia (see Figure 3.11). Although only 15 individuals were at risk for sleep insomnia, the BMI reported for those individuals were much higher than those not at risk (see Figure 3.12). Moreover, there does not seem to be a clear linear association between BMI and average hours of sleep per day (see Figure 3.13).
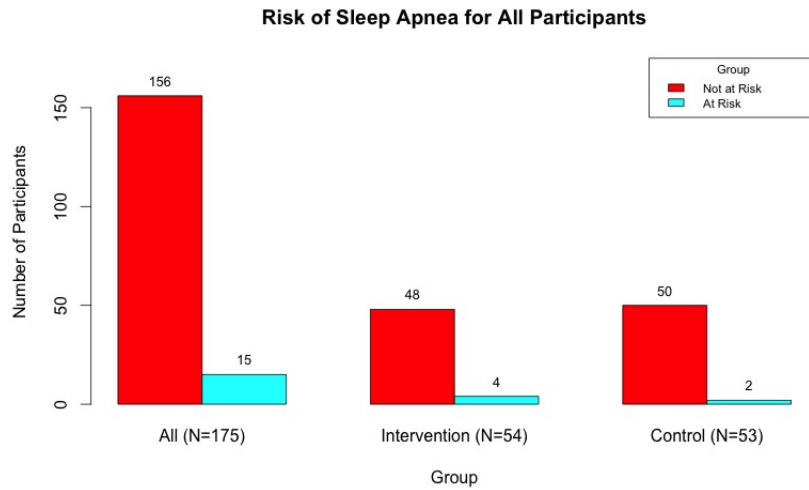
Figure 3.9: Distribution of sleep apnea for all participants.
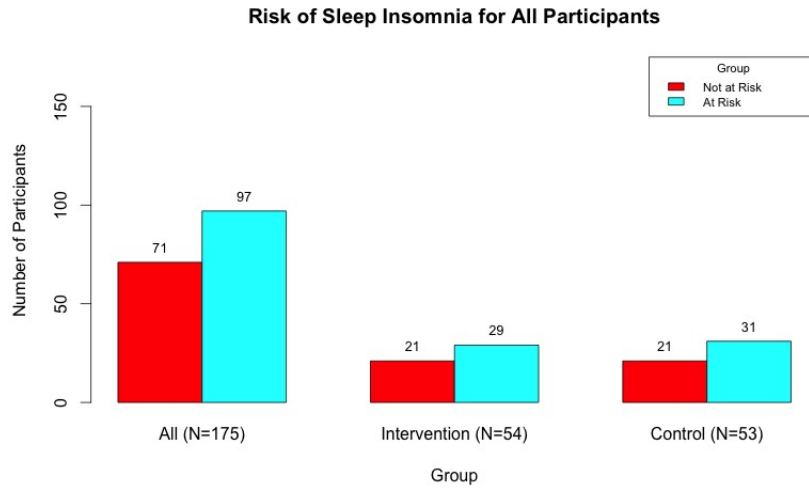
Figure 3.10: Distribution of sleep insomnia for all participants.
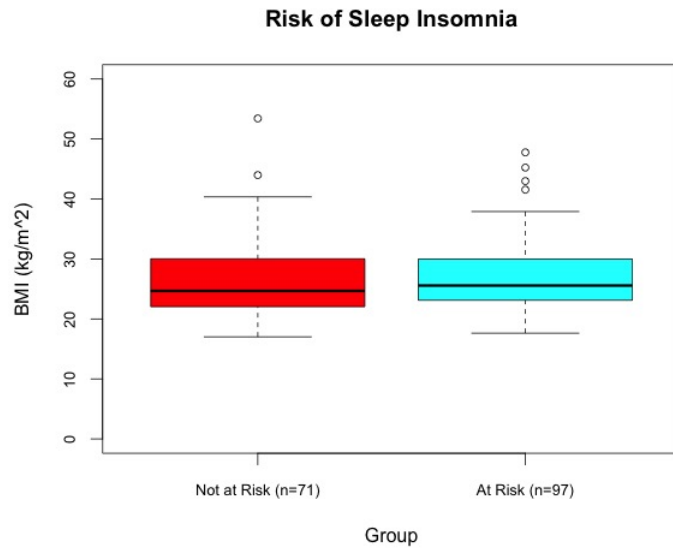
Figure 3.11: Distribution of sleep insomnia and BMI.
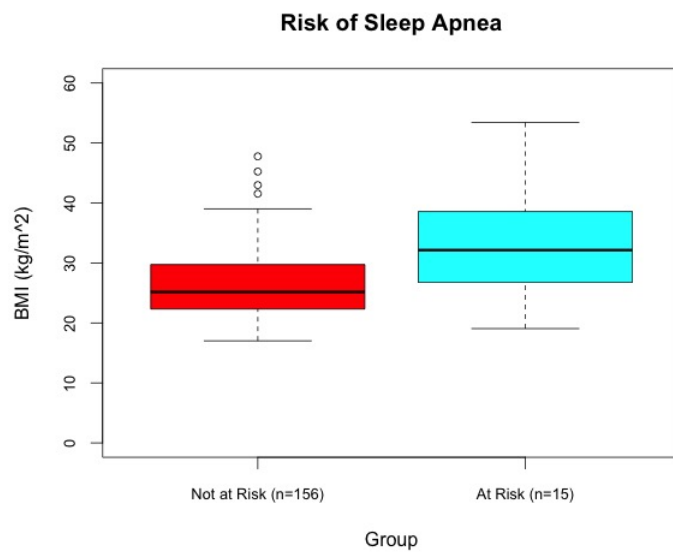
Figure 3.12: Distribution of sleep apnea and BMI.
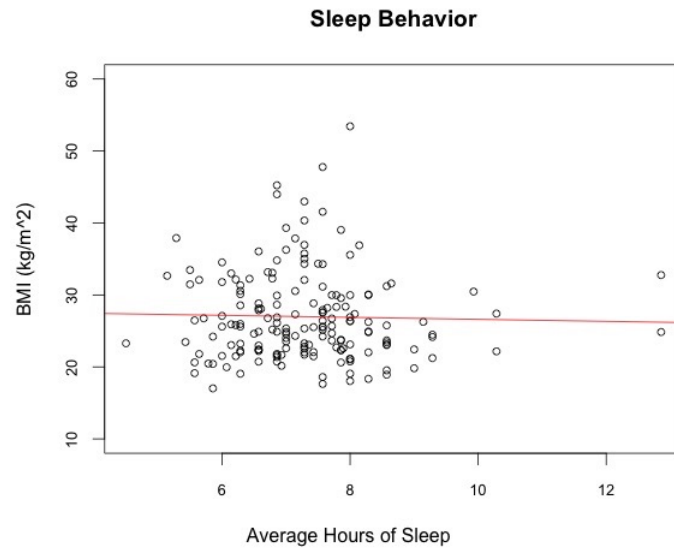
Figure 3.13: Distribution of BMI based on average hours of sleep.

Four different models were developed to assess the impact of sleep characteristics on BMI (dependent variable; continuous). These models are defined below:

- In Model 1, the independent variables included were age (continuous), gender (categorical), average hours of sleep (continuous), risk of sleep insomnia (categorical), and risk of sleep apnea (categorical).

- In Model 2, the independent variables included were age (continuous), gender (categorical), average hours of sleep (continuous), and risk of sleep apnea (categorical).

- In Model 3, the independent variables included were age (continuous), gender (categorical), average hours of sleep (continuous), and risk of sleep insomnia (categorical).

- In Model 4, the independent variables included were age (continuous), gender (categorical), risk of sleep apnea (categorical), and risk of sleep insomnia (categorical).

Table 3.5: Where *** $P < 0.001$, ** $P < 0.01$, * $P < 0.05$. The best model for predicting BMI when considering sleep factors included age, gender, and sleep apnea $AIC = 584.89$.

	Age	Gender	Average Hours Sleep	Risk of Sleep Apnea	Risk of Sleep Insomnia
Model 1	x***	x*	x	x**	x
Model 2	x***	x*	x	x**	
Model 3	x***	x*	x		x
Model 4	x***	x*		x**	x

Normal Q-Q Plot

```
Analysis of Variance Table

Response: dat$BMI
                       Df  Sum Sq Mean Sq F value    Pr(>F)
dat$AGE                 1   688.0  688.00 21.0554 8.932e-06 ***
dat$SEX                 1   149.5  149.51  4.5755  0.033940 *
dat$sleep_totalaverage  1    14.7   14.72  0.4506  0.502994
dat$InsoM_Class         1     3.5    3.45  0.1056  0.745649
dat$SleepApnea          1   345.9  345.94 10.5870  0.001388 **
Residuals             161  5260.8   32.68
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```
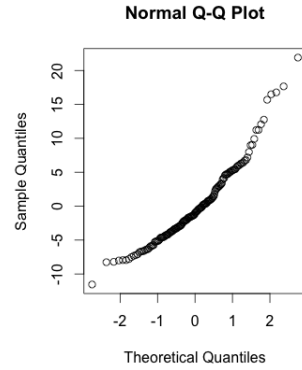
Figure 3.14: Sleep Model 1 Results.

Normal Q-Q Plot

```
Response: dat$BMI
                       Df  Sum Sq Mean Sq F value    Pr(>F)
dat$AGE                 1   708.3  708.34 21.8819 6.006e-06 ***
dat$SEX                 1   162.9  162.89  5.0319  0.026216 *
dat$sleep_totalaverage  1    13.0   12.97  0.4008  0.527550
dat$SleepApnea          1   298.5  298.54  9.2225  0.002779 **
Residuals             165  5341.2   32.37
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```
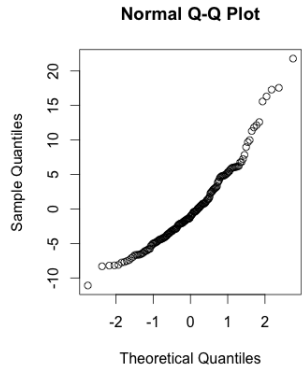
Figure 3.15: Sleep Model 2 Results.

```
Analysis of Variance Table

Response: dat$BMI
                        Df  Sum Sq Mean Sq F value    Pr(>F)
dat$AGE                   1   688.0  688.00 19.8790 1.535e-05 ***
dat$SEX                   1   149.5  149.51  4.3198   0.03925 *
dat$sleep_totalaverage   1    14.7   14.72  0.4255   0.51515
dat$InsoM_Class          1     3.5    3.45  0.0997   0.75261
Residuals              162  5606.8   34.61
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```
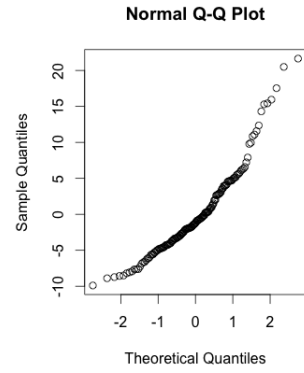
Figure 3.16: Sleep Model 3 Results.


```
Response: dat$BMI
                 Df  Sum Sq Mean Sq F value    Pr(>F)
dat$AGE           1   689.7  689.69 21.2785 7.995e-06 ***
dat$SEX           1   147.0  146.98  4.5346   0.03472 *
dat$InsoM_Class   1     4.9    4.91  0.1515   0.69764
dat$SleepApnea    1   339.3  339.32 10.4688   0.00147 **
Residuals       163  5283.2   32.41
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```
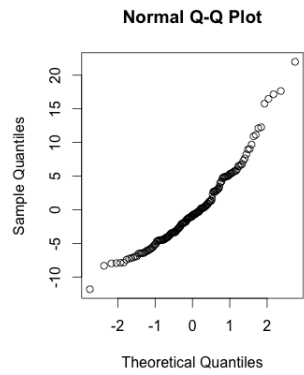
Figure 3.17: Sleep Model 4 Results.

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3.4.2 Physical Activity Behavior

The linear association between BMI and physical activity was studied. The association between BMI and walking activity was not significant (F=3.197, p-value=0.0755) (see Figure 3.18). No significant association was found between BMI and moderate activity (F=0.077, p-value=0.7816) (see Figure 3.19). Also, no significant correlation was found between BMI and vigorous activity (F=0.1541, p-value=0.6954) (see Figure 3.20). Hence, the models fit for predicting BMI when considering physical activity factors were not significant in this sample.
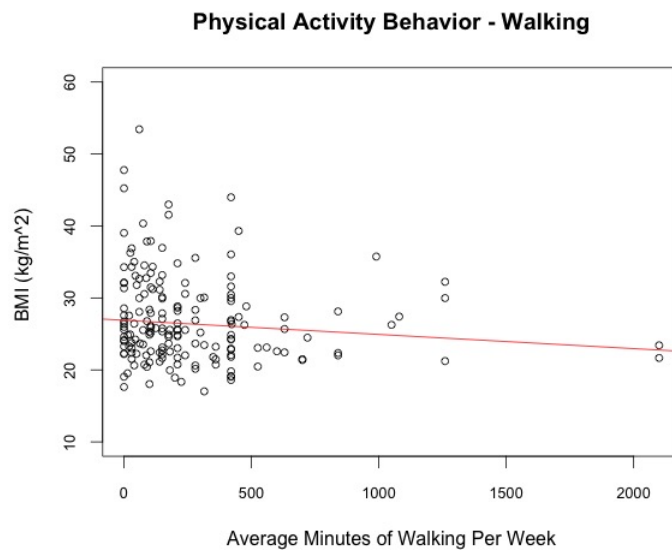
Figure 3.18: BMI and walking physical activity.
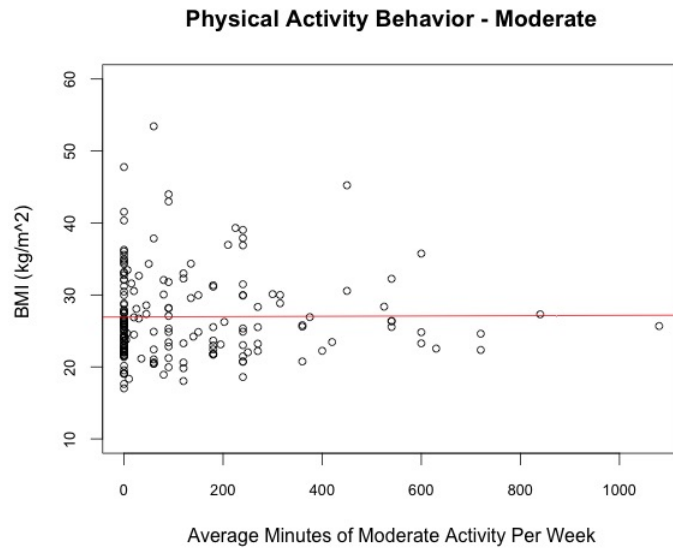
Figure 3.19: BMI and moderate physical activity.
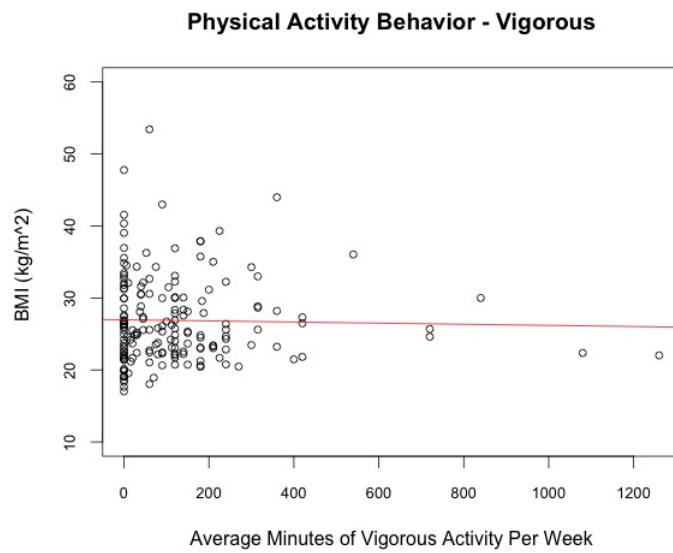
Figure 3.20: BMI and vigorous physical activity.

3.4.3 Diet Behavior

The analysis here focuses on dietary factors as the independent variables for predicting BMI. Other factors taken into account include age (continuous), gender (categorical), average daily consumption of calories (continuous), average servings of vegetables (continuous), average servings of fruits (continuous), average servings of grains (continuous), average servings of meat (continuous), average servings of fat (continuous), average servings of dairy (continuous), average macronutrient consumption of carbohydrates (continuous), average macronutrient consumption of protein (continuous), average macronutrient consumption of total fats (continuous), neophobia (continuous), and taster status (continuous). A marginally significant linear association was observed between BMI and taster status (F=3.74, p-value=0.054) (see Figure 3.21). Also, the average BMI was significantly different when taster status was divided into the three categories (non-taster, moderate taster, and super taster) (F=4.982, p-value=0.0078) (see Figure 3.22). No significant associations were observed between BMI and average daily servings of vegetables (F=0.3366, p-value=0.5626; see Figure 3.23), fruit (F=0.0225, p-value=0.8809; see Figure 3.24), grain (F=1.0134, p-value=0.3155; see Figure 3.25), fats (F=3.5687, p-value=0.0605; see Figure 3.26), and dairy (F=1.3893, p-value=0.2401; see Figure 3.27). However, a significant linear relationship was observed between BMI and daily servings of meat (F=8.66, p-value=0.0036; see Figure 3.28).
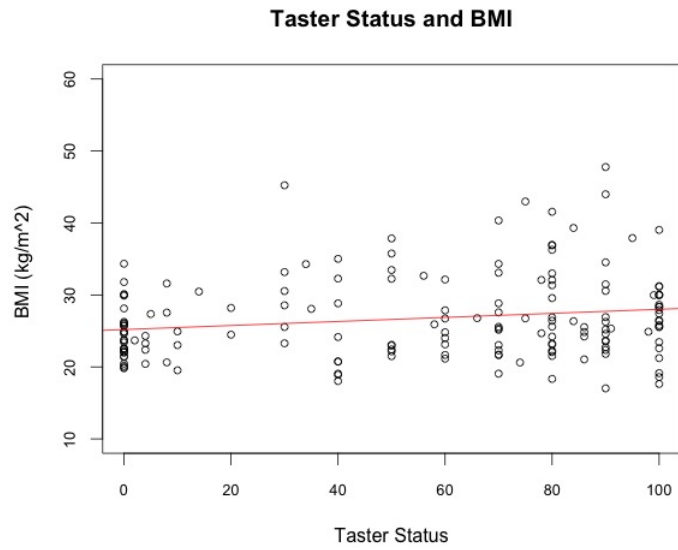
Figure 3.21: BMI and taster status as continuous variables.
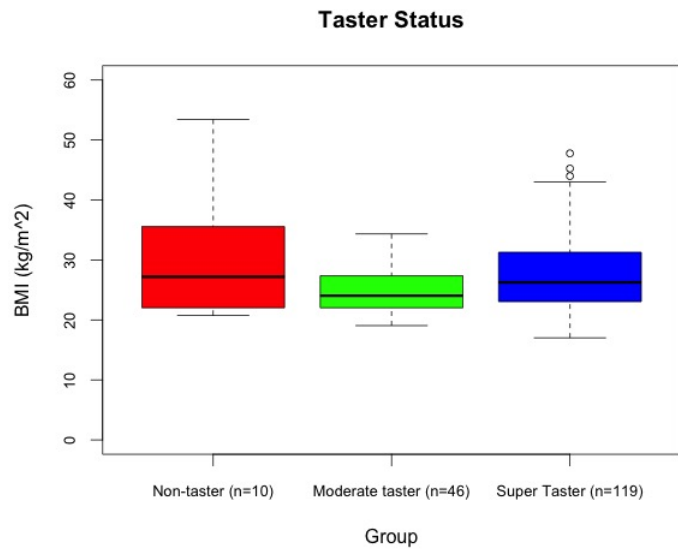
Figure 3.22: BMI as a continuous variable and taste preference as a category (non-taster, moderate taster, and super taster).

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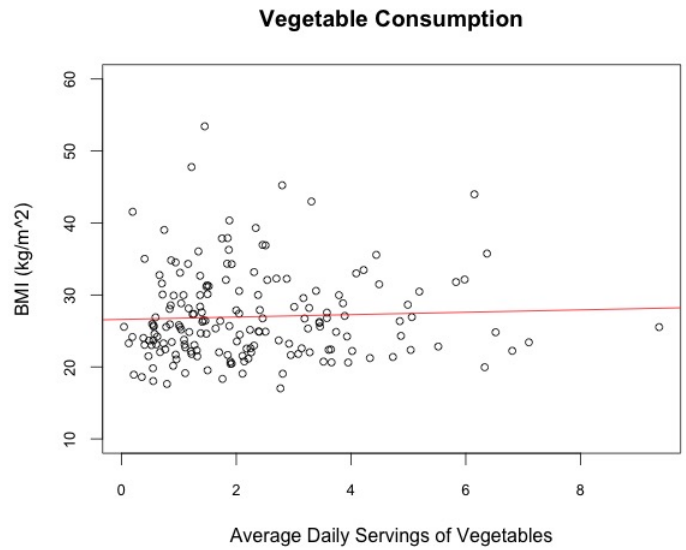
Figure 3.23: BMI and daily servings of vegetables as continuous variables.
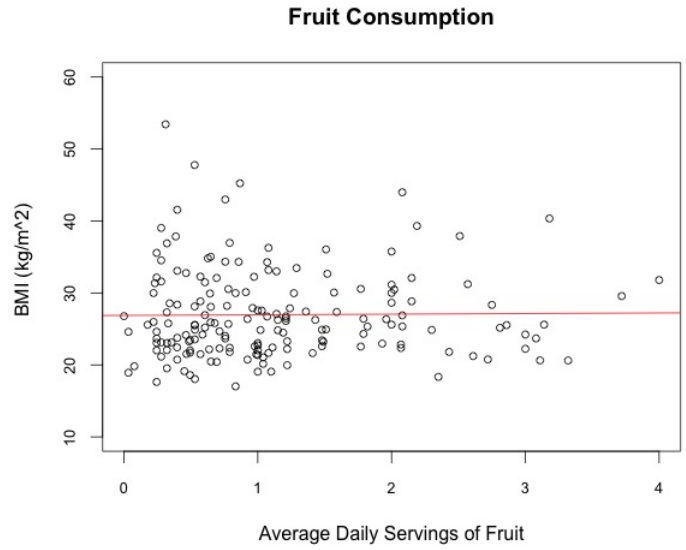
Figure 3.24: BMI and daily servings of fruit as continuous variables.
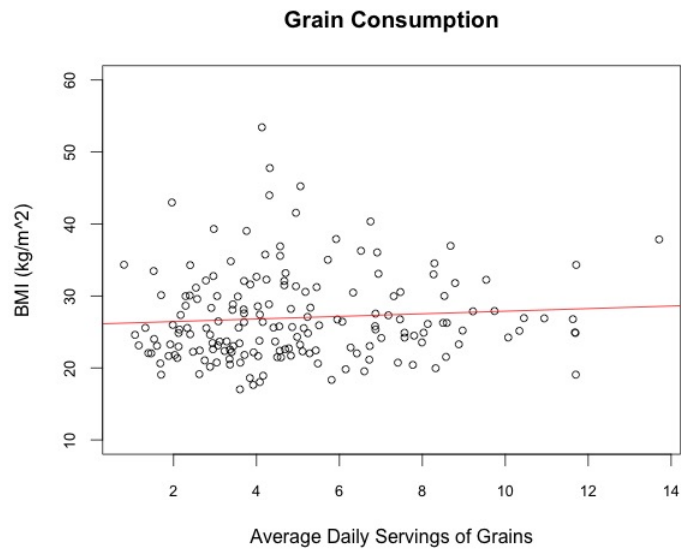
Figure 3.25: BMI and daily servings of grains as continuous variables.
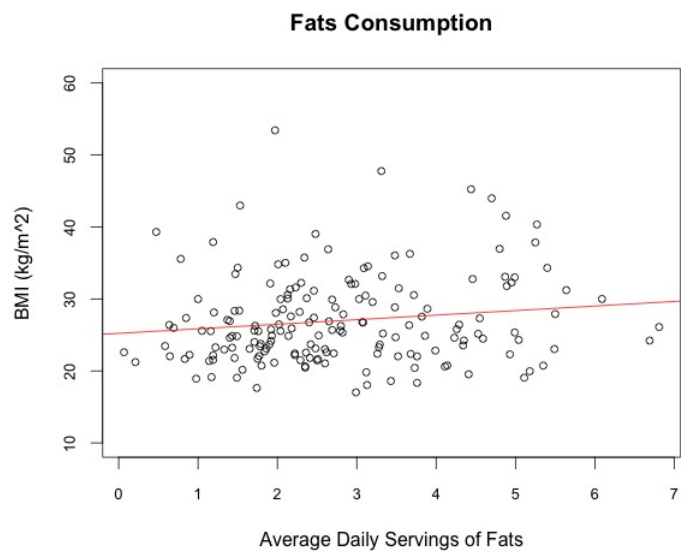
Figure 3.26: BMI and daily servings of fats as continuous variables.
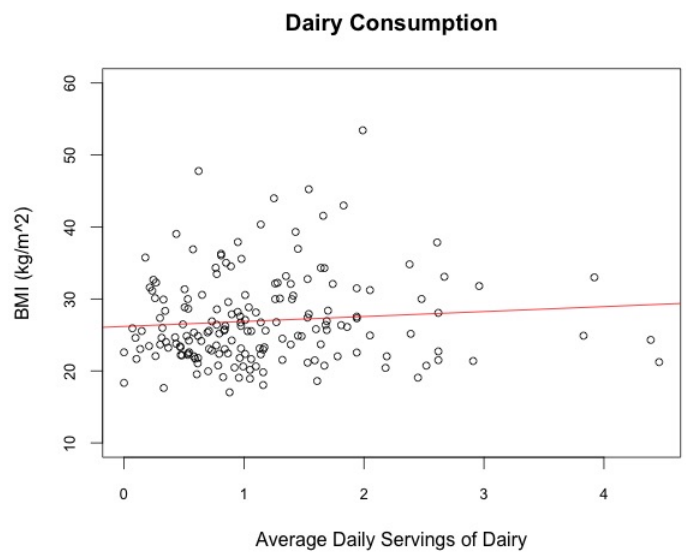
Figure 3.27: BMI and daily servings of dairy as continuous variables.
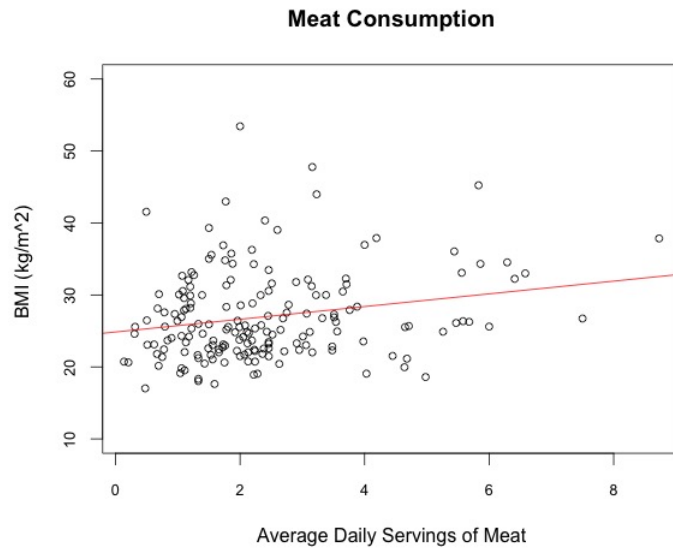
Figure 3.28: BMI and daily servings of meat as continuous variables.

The average daily servings were also analyzed by BMI categories (underweight/healthy, overweight, obese). No statistical significance was found between BMI group and daily average servings of vegetables (F=0.0395, p-value=0.9612; see Figure 3.29), fruits (F=0.4515, p-value=0.6374; see Figure 3.30), grains (F=1.6899, p-value=0.1876; see Figure 3.32), dairy (F=0.7406, p-value=0.4784; see Figure 3.33), and fats (F=1.926, p-value=0.1489; see Figure 3.34). However, the average daily servings of meat was significant based on the BMI category (F=4.1039, p-value=0.018; see Figure 3.31).
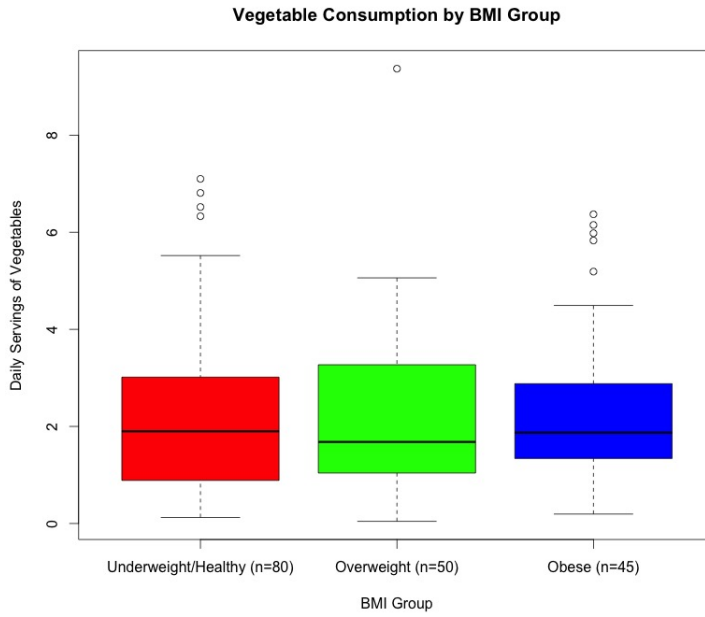
Figure 3.29: BMI group and daily servings of vegetables.
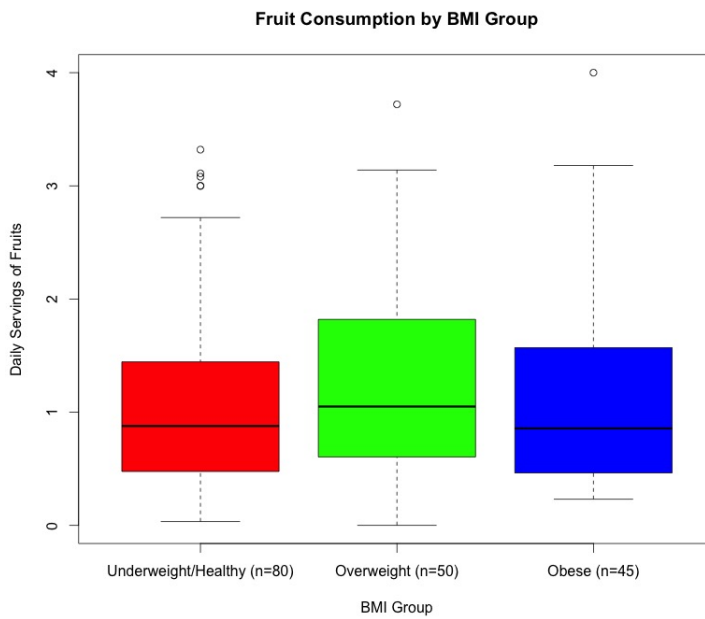
Figure 3.30: BMI group and daily servings of fruits.
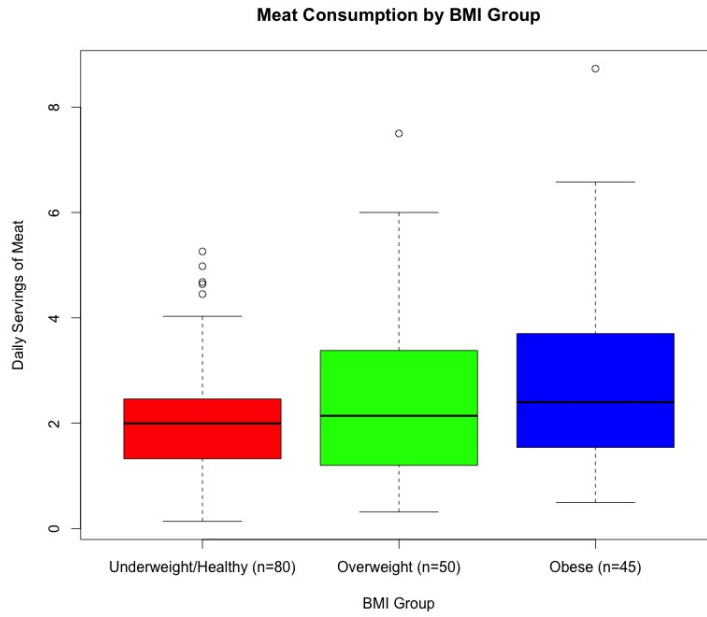
Figure 3.31: BMI group and daily servings of meats.
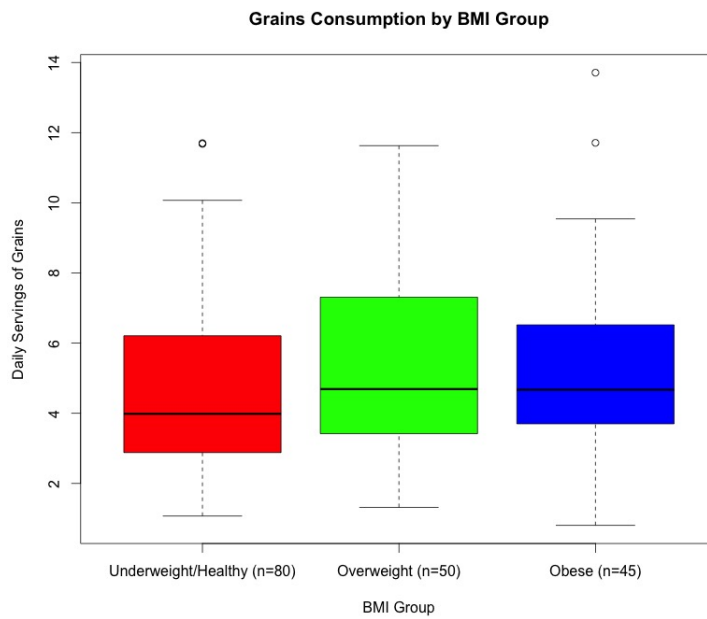
Figure 3.32: BMI group and daily servings of grains.
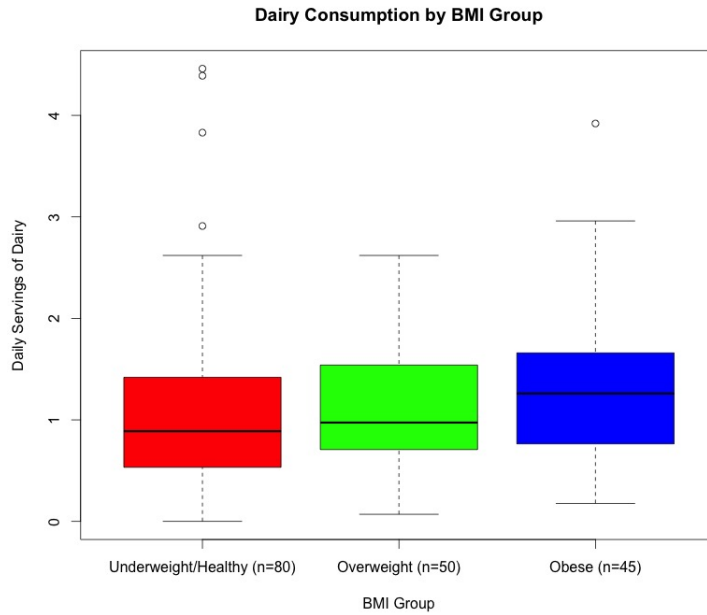
Figure 3.33: BMI group and daily servings of dairy.

The daily macronutrient consumption by BMI group was marginally significant for carbohydrates (F=3.047, P=0.05; see Figure 3.35), was significant for total fats (F=3.18, P=0.04; see Figure 3.36), and was significant for proteins (F=3.829, P=0.023; see Figure 3.37).

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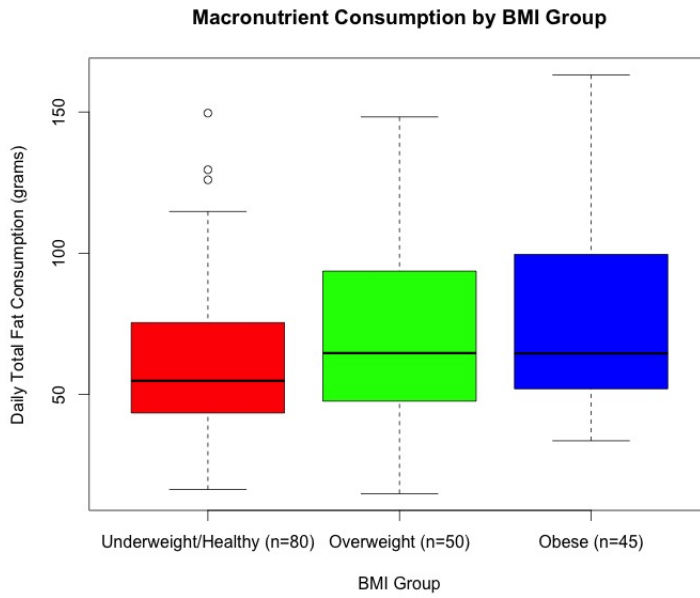
Figure 3.34: BMI group and daily servings of fats.
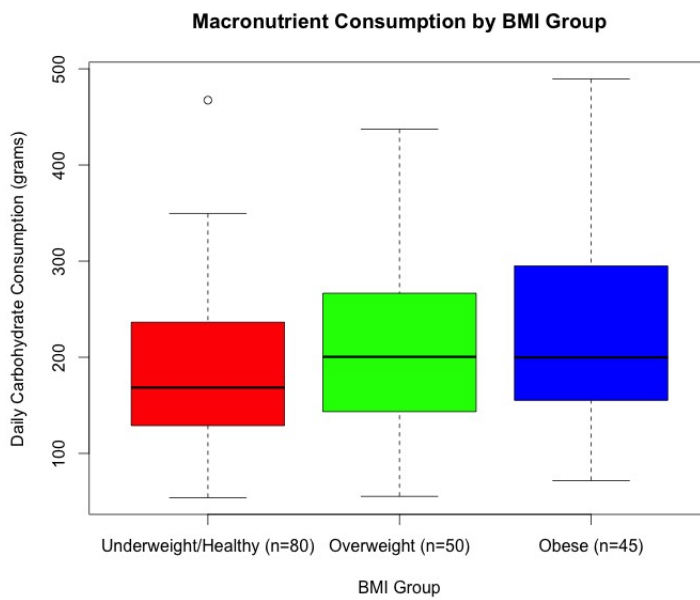
Figure 3.35: BMI group and daily consumption of carbohydrates.
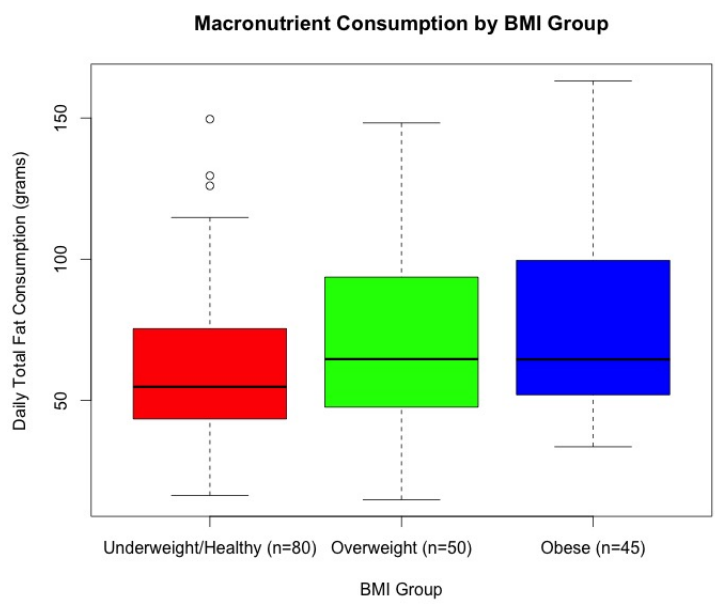
Figure 3.36: BMI group and daily consumption of total fat.
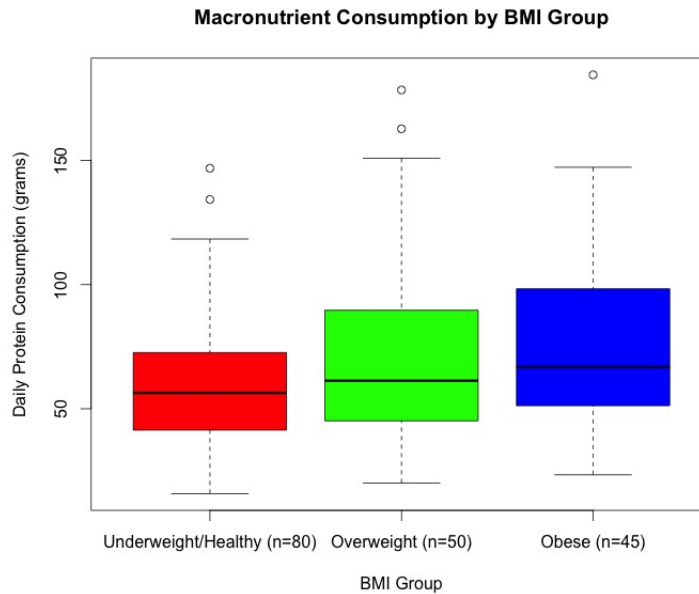
Figure 3.37: BMI group and daily consumption of protein.

This analysis consisted of 4 different models to assess the impact of diet characteristics on BMI (dependent variable; continuous).

- In Model 1, the independent variables included were age (continuous), gender (categorical), average hours of daily calories (continuous), neophobia (continuous), and taster status (continuous).

- In Model 2, the independent variables included were age (continuous), gender (categorical), average servings of vegetables (continuous), average servings of fruits (continuous), average servings of grains (continuous), average servings of meat (continuous), average servings of fat (continuous), average servings of dairy (continuous), neophobia (continuous), and taster status (continuous).

- In Model 3, the independent variables included were age (continuous), gender (categorical), average carbs (continuous), average protein (continuous), average total fats (continuous), neophobia (continuous), and taster status (continuous).

- In Model 4, the independent variables included were age (continuous), gender (categorical), average hours of daily calories (continuous), average servings of vegetables (continuous), average servings of fruits (continuous), average servings of grains (continuous), average servings of meat (continuous), average servings of fat (continuous), average servings of dairy (continuous), average carbs (continuous), average protein (continuous), average total fats (continuous), neophobia (continuous), and taster status (continuous).

```
Response: dat$BMI
                 Df Sum Sq Mean Sq F value    Pr(>F)
dat$AGE           1  588.1  588.10 20.4652 1.182e-05 ***
dat$SEX           1  129.8  129.82  4.5176   0.03509 *
dat$DT_KCAL       1  131.3  131.28  4.5684   0.03410 *
dat$Neophobia     1   19.0   19.01  0.6617   0.41718
dat$Strip2Bitter  1  146.2  146.16  5.0860   0.02548 *
Residuals       159 4569.1   28.74
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

Figure 3.38: Diet Model 1 Results.


```
Response: dat$BMI
                 Df Sum Sq Mean Sq F value    Pr(>F)
dat$AGE           1  588.1  588.10 20.7934 1.037e-05 ***
dat$SEX           1  129.8  129.82  4.5900  0.033730 *
dat$VEGSRV        1    7.0    7.02  0.2483  0.619019
dat$GRAINSRV      1   33.2   33.21  1.1740  0.280270
dat$FRUITSRV      1   46.0   45.98  1.6258  0.204207
dat$MEATSRV       1  196.2  196.21  6.9374  0.009303 **
dat$DAIRYSRV      1    0.8    0.83  0.0294  0.864033
dat$FATSRV        1   91.8   91.85  3.2475  0.073491 .
dat$Neophobia     1   21.0   21.00  0.7424  0.390221
dat$Strip2Bitter  1  113.9  113.87  4.0262  0.046550 *
Residuals       154 4355.6   28.28
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

Figure 3.39: Diet Model 2 Results.

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Table 3.6: Where *** $P < 0.001$, ** $P < 0.01$, * $P < 0.05$. The best model for predicting BMI included the following factors: age, gender, neophobia, taste preferences, kilocalories, vegetable servings, grains servings, meat servings, fat, and carbohydrate with $A1C = 554.09$.

	Age	Gender	Neophobia	Taste Pref.	Veg Srv.	Fruit Srv.	Meat Srv.	Dairy Srv.	Fat Srv.	Grain Srv.	Protein	Fat	Carb	Total Calories
Model 1	x***	x*	x	x*										x*
Model 2	x***	x*	x	x*	x	x	x**	x	x	x				
Model 3	x***	x*	x	x*							x*	x	x	
Model 4	x***	x*	x	x*	x	x	x	x	x	x	x	x	x*	x*

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```
Response: dat$BMI
                 Df Sum Sq Mean Sq F value   Pr(>F)
dat$AGE           1  588.1  588.10 20.4120 1.221e-05 ***
dat$SEX           1  129.8  129.82  4.5059  0.03535 *
dat$DT_PROT       1  140.9  140.95  4.8921  0.02842 *
dat$DT_TFAT       1   34.4   34.39  1.1935  0.27629
dat$DT_CARB       1    0.2    0.19  0.0067  0.93505
dat$Neophobia     1   19.2   19.22  0.6670  0.41533
dat$Strip2Bitter  1  147.4  147.41  5.1162  0.02508 *
Residuals       157 4523.4   28.81
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```
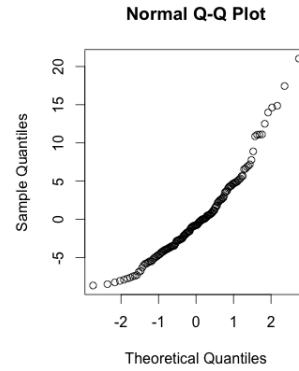

Figure 3.40: Diet Model 3 Results.

```
Response: dat$BMI
                 Df Sum Sq Mean Sq F value   Pr(>F)
dat$AGE           1  588.1  588.10 21.3741 8.129e-06 ***
dat$SEX           1  129.8  129.82  4.7182  0.03143 *
dat$DT_KCAL       1  131.3  131.28  4.7712  0.03050 *
dat$VEGSRV        1   46.5   46.49  1.6897  0.19565
dat$GRAINSRV      1   47.6   47.57  1.7288  0.19058
dat$FRUITSRV      1   40.0   39.97  1.4525  0.23003
dat$MEATSRV       1   42.8   42.78  1.5549  0.21436
dat$DAIRYSRV      1    2.6    2.55  0.0927  0.76117
dat$FATSRV        1   65.0   64.98  2.3616  0.12648
dat$WGRAINS       1    2.3    2.35  0.0853  0.77058
dat$DT_PROT       1    0.4    0.44  0.0159  0.89991
dat$DT_TFAT       1   35.6   35.61  1.2942  0.25710
dat$DT_CARB       1  184.1  184.08  6.6902  0.01065 *
dat$Neophobia     1   39.7   39.75  1.4445  0.23132
dat$Strip2Bitter  1  128.0  128.04  4.6536  0.03259 *
Residuals       149 4099.7   27.51
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```
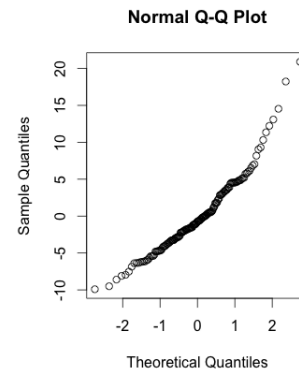

Figure 3.41: Diet Model 4 Results.

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3.4.4 Diet and Environment

This analysis consisted of 3 different models to assess the impact of diet and environmental (availability and accessibility) characteristics on BMI (dependent variable; continuous).

- In Model 1, the independent variables included were age (continuous), gender (categorical), average hours of daily calories (continuous), neophobia (continuous), taster status (continuous), availability of fruits and vegetables (continuous), and accessibility of fruits and vegetables (continuous).

- In Model 2, the independent variables included were age (continuous), gender (categorical), average servings of vegetables (continuous), average servings of fruits (continuous), average servings of grains (continuous), average servings of meat (continuous), average servings of fat (continuous), average servings of dairy (continuous), neophobia (continuous), taster status (continuous), availability of fruits and vegetables (continuous), and accessibility of fruits and vegetables (continuous).

- In Model 3, the independent variables included were age (continuous), gender (categorical), average carbs (continuous), average protein (continuous), average total fats (continuous), neophobia (continuous), taster status (continuous), availability of fruits and vegetables (continuous), and accessibility of fruits and vegetables (continuous).

```
Response: dat$BMI
                                      Df Sum Sq Mean Sq F value   Pr(>F)
dat$AGE                                1  588.1  588.10 20.6365 1.101e-05 ***
dat$SEX                                1  129.8  129.82  4.5554   0.03437 *
dat$DT_KCAL                            1  131.3  131.28  4.6066   0.03339 *
dat$Neophobia                         1   19.0   19.01  0.6672   0.41526
dat$Strip2Bitter                      1  146.2  146.16  5.1286   0.02490 *
dat$Availability_FruitandVegetable    1   89.6   89.65  3.1458   0.07806 .
dat$Accessibility_FruitandVegetable   1    5.3    5.26  0.1847   0.66794
Residuals                           157 4474.2   28.50
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

Figure 3.42: Diet and Environment Model 1 Results.


```
Response: dat$BMI
                                      Df Sum Sq Mean Sq F value   Pr(>F)
dat$AGE                                1  588.1  588.10 21.1331 8.951e-06 ***
dat$SEX                                1  129.8  129.82  4.6650  0.032351 *
dat$VEGSRV                             1    7.0    7.02  0.2523  0.616181
dat$GRAINSRV                           1   33.2   33.21  1.1932  0.276413
dat$FRUITSRV                           1   46.0   45.98  1.6523  0.200595
dat$MEATSRV                            1  196.2  196.21  7.0507  0.008768 **
dat$DAIRYSRV                           1    0.8    0.83  0.0299  0.862941
dat$FATSRV                             1   91.8   91.85  3.3005  0.071229 .
dat$Neophobia                         1   21.0   21.00  0.7546  0.386404
dat$Strip2Bitter                      1  113.9  113.87  4.0919  0.044842 *
dat$Availability_FruitandVegetable    1  125.0  124.96  4.4903  0.035714 *
dat$Accessibility_FruitandVegetable   1    0.7    0.71  0.0257  0.872964
Residuals                           152 4229.9   27.83
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

Figure 3.43: Diet and Environment Model 2 Results.

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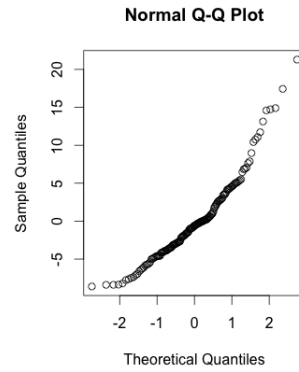
```
Response: dat$BMI
                                     Df Sum Sq Mean Sq F value     Pr(>F)
dat$AGE                               1  588.1  588.10 20.6089 1.124e-05 ***
dat$SEX                               1  129.8  129.82  4.5493   0.03451 *
dat$DT_PROT                           1  140.9  140.95  4.9393   0.02770 *
dat$DT_TFAT                           1   34.4   34.39  1.2050   0.27402
dat$DT_CARB                           1    0.2    0.19  0.0067   0.93474
dat$Neophobia                         1   19.2   19.22  0.6734   0.41311
dat$Strip2Bitter                      1  147.4  147.41  5.1655   0.02441 *
dat$Availability_FruitandVegetable    1   96.9   96.92  3.3965   0.06724 .
dat$Accessibility_FruitandVegetable   1    3.4    3.38  0.1185   0.73112
Residuals                           155 4423.1   28.54
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```
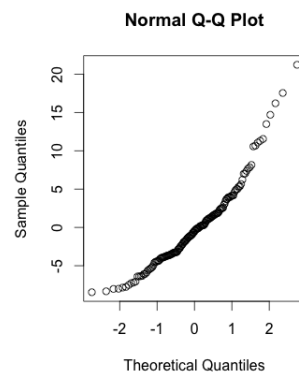

Figure 3.44: Diet and Environment Model 3 Results.
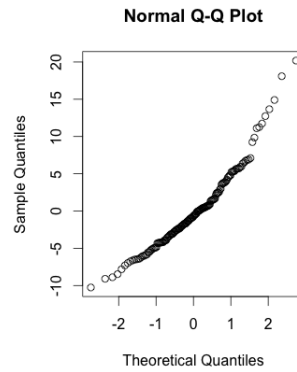
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Table 3.7: Where *** $P < 0.001$, ** $P < 0.01$, * $P < 0.05$. The best model for predicting BMI included the following factors: age, gender, neophobia, taste preferences, kilocalories, vegetable servings, meat servings, fat, carbohydrate, and availability of fruits and vegetables with $A1C = 552.12$.

	Age	Gender	Neophobia	Taste Pref.	Veg Srv.	Fruit Srv.	Meat Srv.	Dairy Srv.	Fat Srv.	Grain Srv.	Protein	Fat	Carb	Total Calories	Avail.	Access.
Model 1	x***	x*	x	x*	x	x	x**	x	x	x				x*	x	x
Model 2	x***	x*	x	x*						x					x*	x
Model 3	x***	x*	x	x*							x*	x	x		x	x

3.4.5 Diet, Environment, and Physical Activity

The analysis here consists of 3 different models to assess the impact of diet, environmental (availability and accessibility) and physical activity (moderate, vigorous, and walking) characteristics on BMI (dependent variable; continuous).

- In Model 1, the independent variables included were age (continuous), gender (categorical), average hours of daily calories (continuous), neophobia (continuous), taster status (continuous), availability of fruits and vegetables (continuous), accessibility of fruits and vegetables (continuous), average physical activity - moderate (continuous), average physical activity - vigorous (continuous), and average physical activity - walking (continuous).

- In Model 2, the independent variables included were age (continuous), gender (categorical), average servings of vegetables (continuous), average servings of fruits (continuous), average servings of grains (continuous), average servings of meat (continuous), average servings of fat (continuous), average servings of dairy (continuous), neophobia (continuous), taster status (continuous), availability of fruits and vegetables (continuous), accessibility of fruits and vegetables (continuous), average physical activity - moderate (continuous), average physical activity - vigorous (continuous), and average physical activity - walking (continuous).

- In Model 3, the independent variables included were age (continuous), gender (categorical), average carbs (continuous), average protein (continuous), average total fats (continuous), neophobia (continuous), taster status (continuous), availability of fruits and vegetables (continuous), accessibility of fruits and vegetables (continuous), average physical activity - moderate (continuous), average physical activity - vigorous (continuous), and average physical activity - walking (continuous).

Table 3.8: Where *** $P < 0.001$, ** $P < 0.01$, * $P < 0.05$, and "M" denotes "moderate physical activity," "W" denotes "walking activity", and "V" denotes "vigorous physical activity." The best model for predicting BMI included the following factors: age, gender, neophobia, taste preferences, kilocalories, vegetable servings, meat servings, fat, carbohydrate, and availability of fruits and vegetables with $A1C = 535.49$.

	Age	Gender	Neophobia	Taste Pref.	Veg Srv.	Fruit Srv.	Meat Srv.	Dairy Srv.	Fat Srv.	Grain Srv.	Prot	Fat	Carb	Total Cal	Avail.	Access.	W PA	M PA	V PA
Model 1	x***	x	x	x*										x	x	x	x	x	x
Model 2	x***	x	x	x*	x	x	x*	x	x	x					x*	x	x	x	x
Model 3	x***	x	x	x*							x	x	x		x	x	x	x	x

```
Response: dat$BMI
                                      Df Sum Sq Mean Sq F value    Pr(>F)
dat$AGE                                1  540.9  540.85 19.6645 1.753e-05 ***
dat$SEX                                1   86.2   86.21  3.1343   0.07865 .
dat$DT_KCAL                            1   97.9   97.91  3.5599   0.06109 .
dat$Neophobia                          1   10.3   10.34  0.3758   0.54076
dat$Strip2Bitter                       1  163.3  163.26  5.9358   0.01598 *
dat$Availability_FruitandVegetable     1   85.8   85.84  3.1211   0.07928 .
dat$Accessibility_FruitandVegetable    1    1.1    1.12  0.0409   0.84007
dat$physicalactivity_Moderate          1    1.4    1.39  0.0504   0.82268
dat$physicalactivity_vigorous          1    0.1    0.07  0.0027   0.95866
dat$physicalactivity_walking           1   45.7   45.67  1.6607   0.19946
Residuals                            153 4208.1   27.50
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```


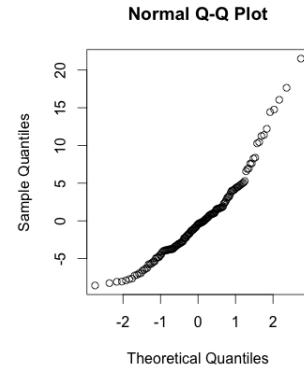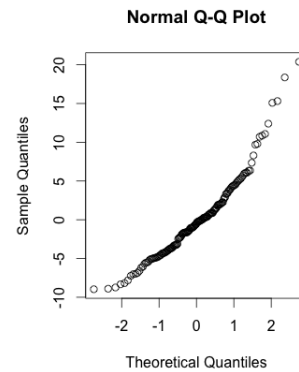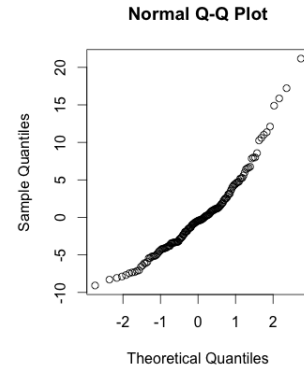Figure 3.45: Diet, Environment, and Physical Activity Model 1 Results.

```
Response: dat$BMI
                                      Df Sum Sq Mean Sq F value  Pr(>F)
dat$AGE                                1  540.9  540.85 19.7745 1.7e-05 ***
dat$SEX                                1   86.2   86.21  3.1518 0.07790 .
dat$VEGSRV                             1    8.0    7.96  0.2909 0.59046
dat$GRAINSRV                           1   36.4   36.42  1.3316 0.25037
dat$FRUITSRV                           1   49.4   49.35  1.8044 0.18124
dat$MEATSRV                            1  130.1  130.06  4.7554 0.03079 *
dat$DAIRYSRV                           1    0.6    0.58  0.0213 0.88416
dat$FATSRV                             1   65.9   65.87  2.4083 0.12283
dat$Neophobia                          1   13.2   13.20  0.4826 0.48832
dat$Strip2Bitter                       1  129.8  129.76  4.7443 0.03098 *
dat$Availability_FruitandVegetable     1  117.2  117.19  4.2848 0.04019 *
dat$Accessibility_FruitandVegetable    1    0.0    0.02  0.0006 0.98126
dat$physicalactivity_Moderate          1    0.3    0.30  0.0109 0.91702
dat$physicalactivity_vigorous          1    1.1    1.14  0.0418 0.83825
dat$physicalactivity_walking           1   13.9   13.89  0.5080 0.47715
Residuals                            148 4047.9   27.35
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```
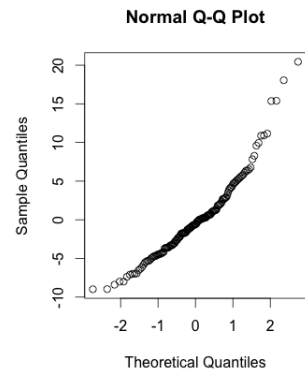

Figure 3.46: Diet, Environment, and Physical Activity Model 2 Results.

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```
Response: dat$BMI
                                    Df Sum Sq Mean Sq F value    Pr(>F)
dat$AGE                              1  540.9  540.85 19.5406 1.872e-05 ***
dat$SEX                              1   86.2   86.21  3.1145   0.07962 .
dat$DT_PROT                          1   88.5   88.47  3.1963   0.07581 .
dat$DT_TFAT                          1   28.9   28.93  1.0451   0.30827
dat$DT_CARB                          1    8.9    8.87  0.3204   0.57223
dat$Neophobia                        1   11.4   11.43  0.4130   0.52140
dat$Strip2Bitter                     1  167.4  167.44  6.0494   0.01504 *
dat$Availability_FruitandVegetable   1   85.5   85.47  3.0879   0.08090 .
dat$Accessibility_FruitandVegetable  1    0.9    0.91  0.0330   0.85608
dat$physicalactivity_Moderate        1    1.1    1.05  0.0380   0.84574
dat$physicalactivity_vigorous        1    0.4    0.39  0.0141   0.90563
dat$physicalactivity_walking         1   41.3   41.30  1.4923   0.22377
Residuals                          151 4179.4   27.68
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
> qqnorm(depmodel3$res)
```
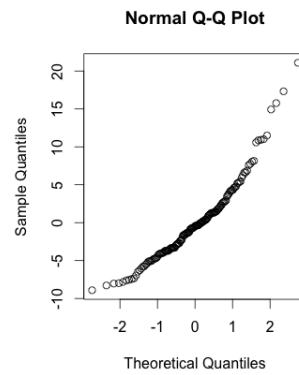

Figure 3.47: Diet, Environment ,and Physical Activity Model 3 Results.

3.5 Results of the Longitudinal Analysis Study

In this section, the data is analyzed as a longitudinal study. Participants in the intervention group selected 3 habits progressively every 2 weeks over a 6 week period. Most students selected a diet-related habit (73.58%) at the start of the study. Caffeine-related (15.09%) and exercise-related (7.54%) habits were the next most selected categories at this time. At week 2, most students added a second habit in the diet-related category (45.28%) followed by exercise-related (33.96%) and sleep-related (7.54%) categories. The third habit was chosen at week 4, where most students selected a diet-related behavior (41.50%) followed by exercise-related (18.86%) and sleep-related (13.20%) behaviors (see Table 3.9 and Figure 3.48). Furthermore, the habits are described as diet versus non-diet related categories (see Figure 3.48). No statistically significant weight loss was found between the control and intervention group over the 6-week intervention period.

Table 3.9: Choice of Habits over the Intervention Period (N=53).

	Diet (%)	Exercise (%)	Sleep (%)	Water (%)	Behavior (%)	Caffeine (%)	Total
Habit 1	39 (73.58)	4 (7.54)	1 (1.88)	0 (0)	0 (0)	8 (15.09)	52 (98.11)
Habit 2	24 (45.28)	18 (33.96)	4 (7.54)	2 (3.77)	2 (3.77)	0 (0)	50 (94.33)
Habit 3	22 (41.50)	10 (18.86)	7 (13.20)	1 (1.88)	0 (0)	5 (9.43)	45 (84.90)
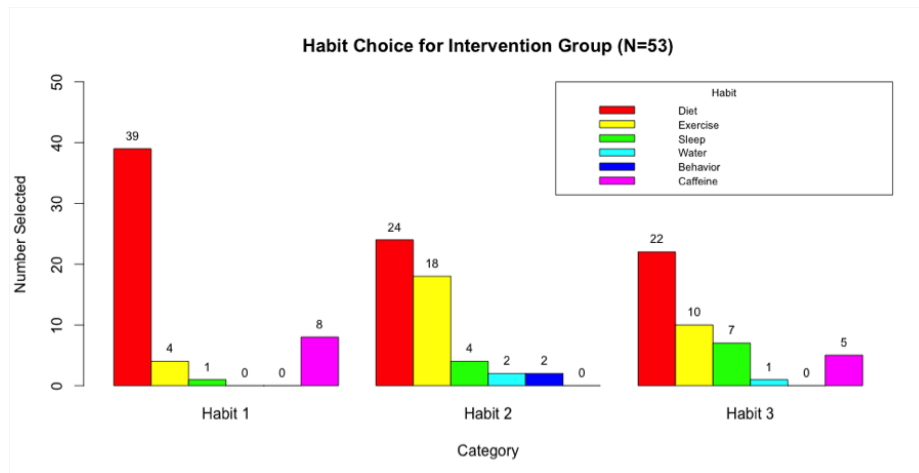
Figure 3.48: Distribution of Habits chosen by participants for all categories.
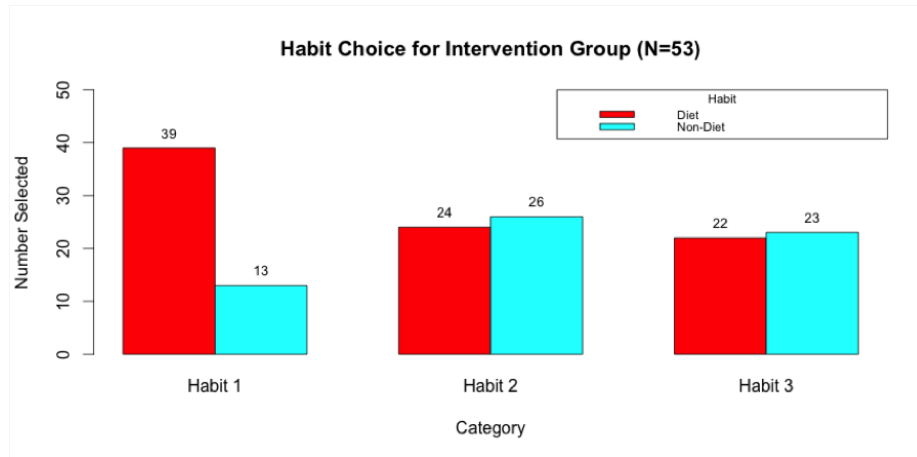
Figure 3.49: Distribution of Habits chosen by participants for diet- versus non-diet-related categories.

3.6   Conclusions

This work aimed to give insight into potential strategies for developing feasible, simple, and effective treatment and weight management programs among patients who are impacted by obesity and diabetes. This analysis utilized a dataset obtained from a pilot study that assessed the impact of an individualized-based intervention program for weight loss that focused on building healthy habits that were tailored to college students. A cross-sectional study was conducted in order to address three points: first, whether the present study captured health behaviors among college students that are similar to those reported in the literature. The factors in this intervention study that best predicted BMI agreed with prior field studies, specifically, age, gender, sleep apnea risk (Patel et al., 2008; Vorona et al., 2005; Magee, Iverson, Huang, & Caputi, 2008; Beccuti & Pannain, 2011), diet (Huang et al., 2003; Racette, Deusinger, Strube, Highstein, & Deusinger, 2005; Racette et al., 2008; Kasparek, Corwin, Valois, Sargent, & Morris, 2008), and environment (Small, Bailey-Davis, Morgan, & Maggs, 2012; Racette et al., 2008). While other studies have

shown that physical activity was a significant factor for predicting BMI, physical activity factors in this study did not seem to be statistically significant (Lowry et al., 2000; Huang et al., 2003; Racette et al., 2005, 2008; Behrens & Dinger, 2003; McArthur & Raedeke, 2009; Kasparek et al., 2008). This finding may be largely due to the self-reporting methods used since students may have overestimated or falsely reported their actual physical activity behavior; it may also be due to the small sample size of the study. The second aim of the analysis was to identify factors that could predict BMI that may not be well-studied. Taste preferences appear to be a statistically significant factor. Although many experimental studies have shown that taste preferences are important for predicting BMI, the link between taste preferences and obesity is not well-studied in intervention studies. The third aim focused on concluding which factors best predicted BMI in this study, which included: taste preferences, age, gender, risk for sleep apnea, diet, and environment. However, since this was a cross-sectional study, causal relationships could not be concluded. Moreover, the intervention did not yield statistically significant changes in weight loss for the intervention group.

Chapter 4

MODELING EATING BEHAVIORS: THE ROLE OF ENVIRONMENT AND

POSITIVE FOOD ASSOCIATION LEARNING VIA A *RATATOUILLE* EFFECT

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ABSTRACT

Eating behaviors among a large population of children are studied as a dynamic process driven by nonlinear interactions in the sociocultural school environment. The impact of food association learning on diet dynamics, inspired by a pilot study conducted among Arizona children in Pre-Kindergarten to 8th grades, is used to build simple population-level learning models. Qualitatively, mathematical studies are used to highlight the possible ramifications of instruction, learning in nutrition, and health at the community level. Model results suggest that nutrition education programs at the population-level have minimal impact on improving eating behaviors, findings that agree with prior field studies. Hence, the incorporation of food association learning may be a better strategy for creating resilient communities of healthy and non-healthy eaters. A *Ratatouille* effect can be observed when

food association learners become food preference learners, a potential sustainable behavioral change, which in turn, may impact the overall distribution of healthy eaters. In short, this work evaluates the effectiveness of population-level intervention strategies and the importance of institutionalizing nutrition programs that factor in economical, social, cultural, and environmental elements that mesh well with the norms and values in the community.

4.1 Background and Literature Review

The prevalence of childhood obesity has doubled among 2-to-5-year-olds (5-7% to 10.4%) and tripled for both 6-to-11-year-olds (6.5% to 19.6%) and 12-to-19-year-olds (5% to 18.1%) from $1971 - 1974$ to $2007 - 2008$ (Ogden & Carroll, 2010a). Childhood obesity can increase risk of cardiovascular disease (Ammerman, Lindquist, Lohr, & Hersey, 2002; Boeing et al., 2012; Ness & Powles, 1997) and cancer (Ammerman et al., 2002; Block, Patterson, & Subar, 1992; Lipkin, Reddy, Newmark, & Lamprecht, 1999), two leading causes of premature mortality and physical morbidity in adulthood (J. Reilly & Kelly, 2011). Many national efforts, such as the United States Department of Agriculture's (USDA) implementation of the "My Plate" guidelines (United States Department of Agriculture (USDA), 2015a) in schools, aim to alter the eating dynamics of young individuals (Ammerman et al., 2002). These state-mandated guidelines impact the diets of those who eat lunch (60%) and breakfast (37%) at their schools (United States Department of Agriculture Food and Nutrition Service (USDA FNS), 2014), or 99% and 78% of public schools who participate in the National School Lunch and Breakfast Programs, respectively (Fox, Hamilton, & Lin, 2004; Kaphingst & French, 2006). In short, children, in the early stages of developing their eating habits, consume most of their daily food (19 to 50% or more) in schools (Gleason, Suitor, Food, & Service, 2001; Kaphingst & French, 2006), and are members of a captive audience (10 years, 9 months, and 5 days per week) (American Diabetes Association (ADA), 1999; Pérez-Rodrigo & Aranceta, 2001). Hence, a better understanding of the overall effectiveness of these programs and the access to a captive audience is necessary for improving the overall health of children.

In this paper, we aim at shedding some light on the connections between key identified factors (Ammerman et al., 2002; Blanchette & Brug, 2005; Katz, 2009; Lytle & Achterberg, 1995) that shape eating behaviors at the population-level via contagion mathemat-

ical models, within a social-ecological framework (McLeroy, Bibeau, Steckler, & Glanz, 1988). Although schools are ideal for institutionalizing nutrition programs, a huge step in the fight against obesity-related illness, childhood obesity is still an issue and consumption of fruits and vegetables among children is low (see Figure 4.1). Using the film *Ratatouille* as a metaphor and the study by (Wadhera, Phillips, Wilkie, & Boggess, 2015), we investigate the significance of the "*Ratatouille*" effect, that is the impact of recreating 'positive' childhood eating experiences, memories, and their connection with the process of building healthy eating habits. Food preference learning has been identified as a possible influential method for developing healthier eating habits by modifying taste, the strongest predictor of children's food consumption (L. L. Birch, 1979; Domel et al., 1993; Perry et al., 2004; Story, Neumark-Sztainer, & French, 2002). Although well-studied in experimental settings, its impact is not well-understood at the population-level, and hence, we investigate this phenomenon on the diet dynamics of young individuals in this work.

4.2   Eating Behaviors in School Settings

The study of the diet dynamics of individuals at the population-level have been rarely addressed in the literature (but see (Evangelista, Ortiz, Rios-Soto, & Urdapilleta, 2004; Frerichs, Araz, & Huang, 2013; Gonzalez-Parra, Jodar, Santonja, & Villanueva, 2010; Jódar, Santonja, & González-Parra, 2008)). Building a population-level model from the knowledge that we have gathered on the daily decisions of individuals is rather challenging just as it is the construction of an epidemiological model from the study of an individuals immunological (level of the cell) response to a disease invasion. Our eating behaviors, that is, why we eat certain foods, how much to eat, when to eat, and how to eat these foods, are governed by biological, sociocultural, and psychosocial factors that are learned in a variety of settings. In this work, we assume that there are three population-level components involved on the diet-dynamics of individuals within a community. The first involves the im-

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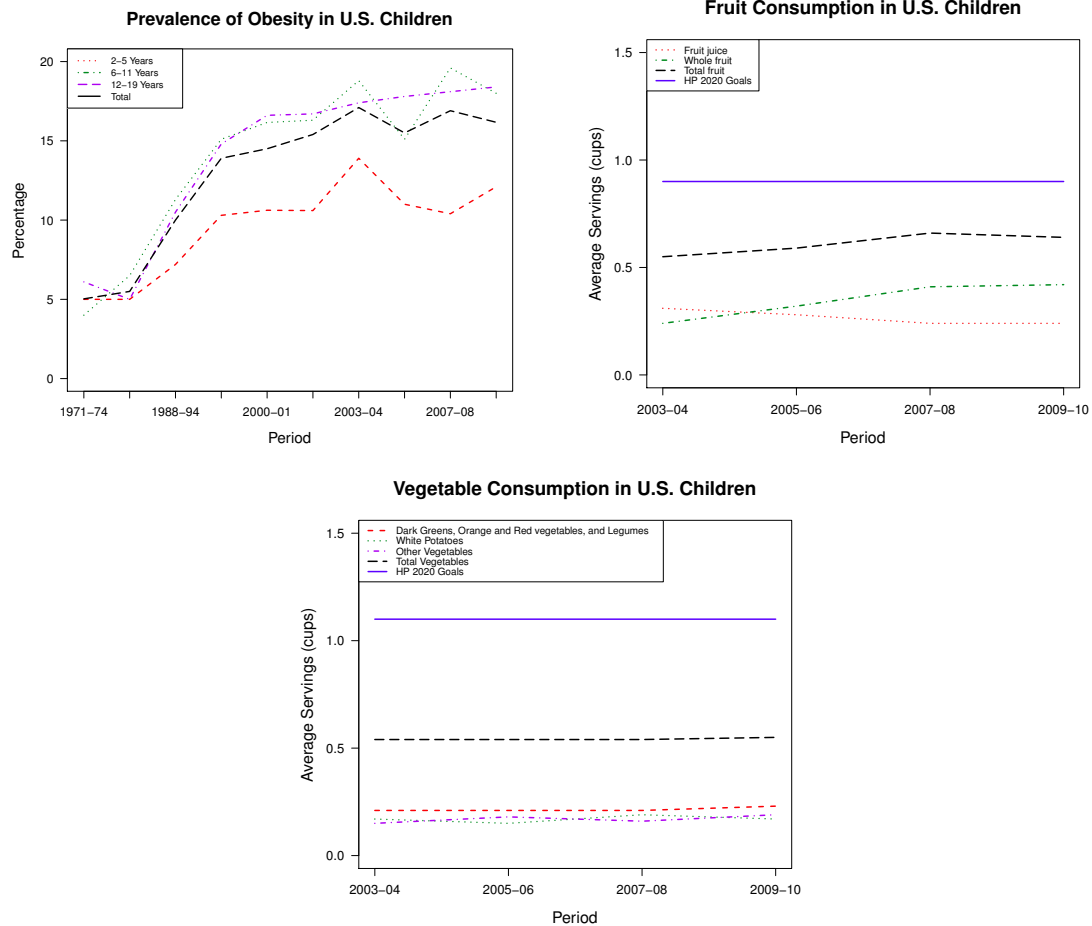
Figure 4.1: Prevalence of childhood obesity (top left). Fruit (top right) and vegetable (bottom middle) consumption in U.S. children (Centers for Disease Control and Prevention (CDC), 2014; Ogden & Carroll, 2010a).

pact of dietary programs (health awareness, communication, and skill-building) that tend to be temporary and often associated with high levels of recidivism (Cullen, Bartholomew, Parcel, & Koehly, 1998; Domel et al., 1993; Pyle et al., 2006). The second would be the social environment, here modeled simply via the day-to-day interactions among individuals with different diets. The unpalatability of healthy foods make their systematic consumption difficult, however, social and behavior-based elements have been shown effective; such as, hands-on curriculum activities (classroom lessons, taste-testing, cooking lessons), parental involvement, school gardening, peer modeling, or rewards (Ammerman et al., 2002; Birnbaum, Lytle, Story, Perry, & Murray, 2002; Lowe, Horne, Tapper, Bowdery, & Egerton, 2004; Lytle & Achterberg, 1995; Perry et al., 2004; Story et al., 2002). The third includes the physical environment, here availability and accessibility of healthier foods changes due to the nutrition programs implemented in the schools (Cullen et al., 2003; Perez-Rodrigo & Aranceta, 2003; Story et al., 2008; Van Der Horst et al., 2007). Despite our understanding of these factors, the efficacy of these interventions vary and so, more work is needed in order to fully assess their impact on the diet dynamics of young individuals.

Building 'positive' childhood memories has been identified as a possibly influential force on the long-term eating behaviors of adults based on the study in (Wadhera, Phillips, et al., 2015). Food preferences has been shown to increase with exposure, tasting (not just smelling or seeing), and a positive social experience (L. Birch, 1987; L. L. Birch, Zimmerman, & Hind, 1980). However, the unpalatability of healthier foods and the onset of neophobia, or the fear of trying something new, influences childrens food choices and can ultimately lower both dietary variety (Dovey, Staples, Gibson, & Halford, 2008; Falciglia, Couch, Gribble, Pabst, & Frank, 2000) and the consumption of fruits, vegetables, and meats (Cooke, 2007; Howard, Mallan, Byrne, Magarey, & Daniels, 2012). These issues have been addressed via exposure techniques (Wadhera, Capaldi-Phillips, & Wilkie, 2015), where familiarizing children with these foods (six to ten exposures) can improve

the liking for and intake of novel foods among preschool and school-aged children (Liem & De Graaf, 2004; Sullivan & Birch, 1990). An alternative approach for increasing liking for and consumption of vegetables is food association learning (Capaldi-Phillips & Wadhera, 2014; Fisher et al., 2012), in which, a classical conditioning paradigm is applied and considered successful when liking for a novel flavor occurs due to its pleasurable association with the calories or the liked flavor (flavor-flavor learning) it was paired repeatedly with (Capaldi, 1996). Although a few studies have shown that associative conditioning more effectively increases liking and consumption of vegetables, compared to exposure (see (Wadhera, Capaldi-Phillips, & Wilkie, 2015) for a review); its impact has been minimally studied at the population-level. In our pilot study (Wadhera, Capaldi-Phillips, & Murillo, n.d.), we studied the effect of associative conditioning among Arizona students. Among the Pre-Kindergarten to 8th grade participants, we found that our method of food association learning acted as a positive reinforcement for children who may be more likely to eat vegetables but did not improve selection or consumption for those who may be more reluctant to eat vegetables (see Figure 4.2). These results are utilized as an initial exploration of food association and food preference learning in schools.

The prevalence of childhood (10.4%) and adult (25.9%) obesity in Arizona is only slightly lower than national estimates (Arizona Department of Health Services (ADHS), 2012c; Ogden et al., 2014). Among Arizona residents, the 2012 Behavior Risk Factor Surveillance Survey (BRFSS) estimated 60% overweight or obese adults, 37.5% of obese adults living in households with food assistance (WIC, SNAP, and/or Free and Reduced Lunch), and increased adult obesity risk among non-daily consumers of fruits and vegetables (30.3% and 31.7%) compared to daily consumers (24.6% and 25.6%) (Arizona Department of Health Services (ADHS), 2012c). Although these health disparities are not studied here explicitly, the study of nutrition programs is essential for improving the overall health of Arizona residents. In U.S. children, obesity was higher among Mexican-

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American (28.8% boys and 17.4% girls) and non-Hispanic black (19.8% boys and 29.2% girls) than non-Hispanic white (16.7% boys and 14.5% girls) (Ogden & Carroll, 2010a). Arizona residents comprises demographic characteristics (age, gender, income, education, and employment status) generalizable to the nation (United States Census Bureau (USCB), 2015b). However, the presence of food deserts and the economical and environmental barriers puts vulnerable population, or 14.3% of low-income children, Hispanic (29.9% in A.Z. and 16.6% in the U.S.), and American Indian or Alaska Native (4.0% in A.Z. and 0.7% in the U.S.) (United States Census Bureau (USCB), 2015b) residents, at increased risk for insufficient consumption of essential nutrients or overconsumption of unhealthier foods high in saturated and trans fats.

Though multiple levels of detail and heterogeneity can be incorporated, such an approach could invariably lead to highly complex nonlinear models that would be difficult to analyze. In this first effort, we proceed to study the impact of the three stated factors: dietary programs, social environment, and the physical environment on the distribution of eating patterns. This effort by no means attempts to minimize or underpinned the complexities and challenges associated with understanding the forces behind the dynamics of obesity. What we are trying to do is to introduce a framework for the study of the impact of these three components on the dynamics of obesity under highly simplified conditions at the population-level. We don't expect the results of these caricature models to offer solutions. Our hope is that the population-level framework introduced, its analysis, and the interpretation of the model results would inspire others to expand and improve on this work so that a solid and tested framework would be eventually developed.

4.3   The Mathematical Modeling Framework

We develop two models to shed some light on how the interactions among individual factors, the sociocultural environment, and nutrition programs impact the dynamics of eat-
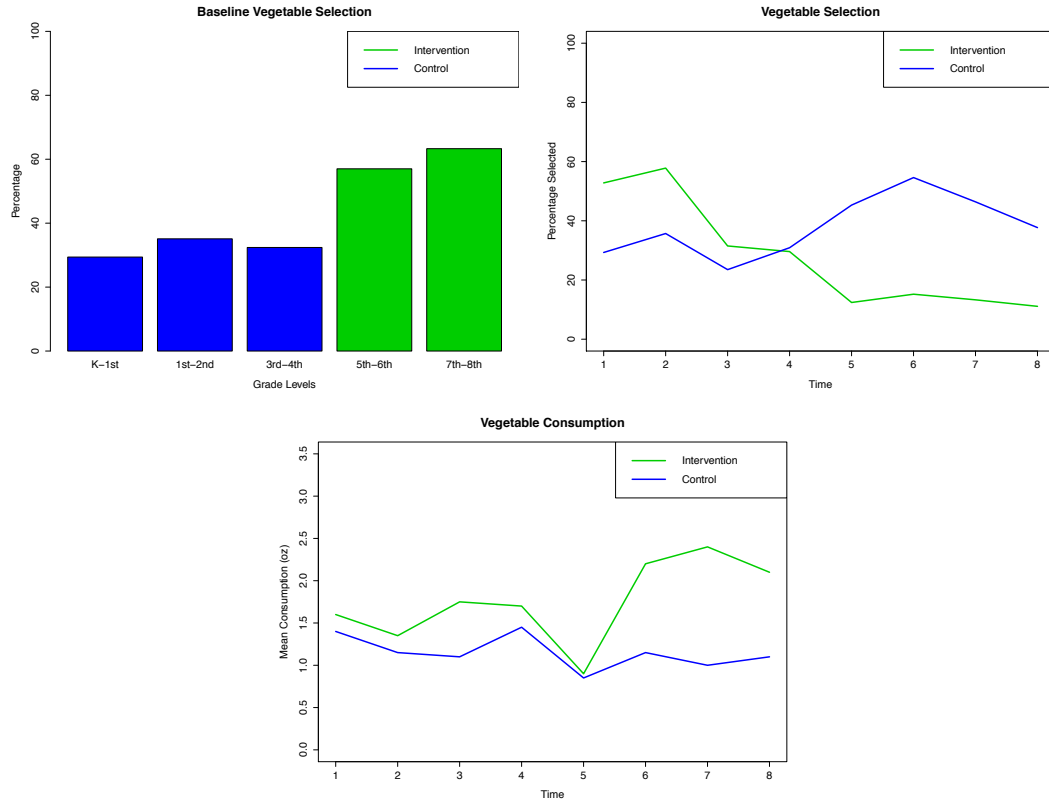
Figure 4.2: Pilot study results showing: baseline measures of participants (top left), and vegetable selection (top right) and vegetable consumption (bottom middle) where days 1 and 2 represent baseline, days 3 to 6 are the intervention period, and days 7 to 8 represent the testing period (Wadhera et al., n.d.).

ing behaviors and distribution of eaters in school settings. A typical school population can be considered to be composed of two types of students: moderately healthy individuals, denoted $M(t)$, or those who eat a 'moderate' amount of fruits, 100% fruit juice, or vegetables (FJV) (25–50% of "My Plate" guidelines) and the 'less' healthy individuals, denoted $L(t)$, or those who eat a 'low' amount of FJV (less than 25% of "My Plate" guidelines). The first model considers the simplest scenario, where school nutrition programs influence some *L*-eaters to modify their diets to become *M*-eaters but remain in the same environment. However, prior field studies suggest the impact of nutrition education is low and

hence this recovery is temporary, suggesting that *M*-eaters can break their 'good' diet, a form of recidivism. The second model, incorporates the impact of 'positive' food association learning via a *Ratatouille* effect. Both *M*- and *L*-eaters can enter a program, in which, some students learn food association techniques, denoted $A(t)$, where eventually some proportion will develop sustainable food preferences, denoted $P(t)$. In these next subsections, we describe each model, corresponding results, and the conditions under which the diet dynamics are altered.

4.3.1   Absence of Food Association, Brief Recovery, and Recidivism

The total population of students, denoted N, is made up of *M*- and *L*-eaters. The average time that a student spends in Pre-Kindergarten to 8th grades (10 years) is denoted $1/\mu$. A proportion of *L*-eaters can shift to *M*-eaters after exposure to a nutrition program, denoted ϕ, which means that *L*-eaters shift to *M*-eaters but do not change eating environments. The average time that an individual spends in the *L*-eater state before returning to the *M*-eater state is $1/\phi$. However, the diet changes are temporary due to recidivism since *M*-eaters can shift back to *L*-eaters (see Figure 4.3 for a schematic diagram and Table 4.1 for variable and parameter definitions). This system is governed by the following equations,

$$
\begin{aligned}
M' &= \Lambda - (\lambda + \mu)M + \phi L, \\
L' &= \lambda M - (\phi + \mu)L,
\end{aligned}
\tag{4.1}
$$

where $\lambda = \beta L/N$, represents the fraction of *L*-eaters in the population that interact with *M*-eaters, which in turn, lead to the conversion of *M*- into *L*-eaters at the rate β, via a social 'contagion' process. The contagion process would be considered successful as long as the interactions between *M* and *L* lead to an increase in the number of *L*'s. The number of new students entering the school per year is denoted by $\Lambda = \mu N$.
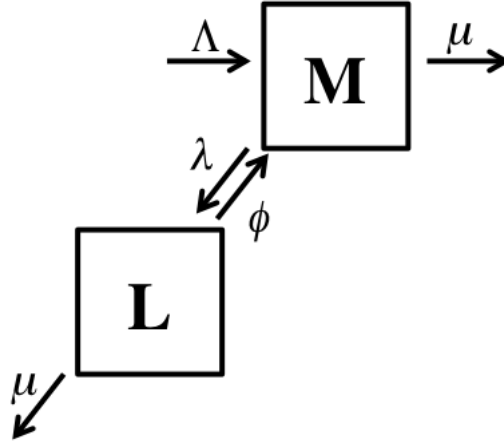
Figure 4.3: A schematic diagram of Model 1 with 'moderately' healthy eaters *M* and 'less' healthy eaters *L*.

Table 4.1: Definition of Model 1 Parameters.

Parameter	Value	Unit	Description
M/N	0.9	dimensionless	Proportion of 'moderately' healthy individuals
L/N	0.1	dimensionless	Proportion of 'less' healthy individuals
β	1.8	$\frac{1}{year}$	Peer influence rate shifting a *M*- to an *L*-eater
ϕ	varies	$\frac{1}{year}$	Exposure to nutrition programs
μ	0.10	$\frac{1}{year}$	Per-capita student entry and removal rate

The control reproduction number, $\mathscr{R}_{c,1}$, is a threshold value permitting the assessment of true success of a nutrition education program. Here, it is defined as a function of the nutrition education program rate ϕ,

$$\mathscr{R}_{c,1}(\phi) = \frac{\beta}{\mu + \phi},$$

where $1/(\mu + \phi)$ represents the total average time spent in the district as an *L*-eater before shifting to an *M*-eater following a nutrition education program. When there is no nutrition

education program, that is $\phi = 0$, then $\mathscr{R}_{c,1}(\phi)$ becomes,

$$\mathscr{R}_{c,1}(0) = \frac{\beta}{\mu},$$

that is, the threshold becomes the product of β, the effective conversion rate per L, and $1/\mu$, the average time a student remains in the education system. The above simplistic model will not be used to highlight the effectiveness or lack thereof of nutrition education on altering the prevalence of L-eaters. However, this model assumes that the educational effort (per person) modelled by ϕ remains part of the culture and it is continuously implemented. Our pilot data (Wadhera et al., n.d.) suggested that $L/N = 0.7$ (i.e., 70%), hence at equilibrium $L/N = 1 - 1/\mathscr{R}_{c,1}(0)$ and $M/N = 1/\mathscr{R}_{c,1}(0)$. With $1/\mathscr{R}_{c,1}(0) = 0.3$ and $1/\mu = 10$ years, we can estimate $\beta/\mu = 1/0.3$, or $\beta = (1/0.3) \cdot (1/10) = 1/3 \simeq 0.33$. However, this only captures observations during school lunch periods and does not consider other daily diet activities. Using slightly modified initial values, our model simulations show that increasing the nutrition programs, ϕ, will decrease the proportion of L/N eaters (see Figure 4.4). A sociocultural environment with mostly M-eaters is achieved for large values of ϕ. If $\mathscr{R}_{c,1}(\phi) > 1$, then the amount of L-eaters would increase with the proportion of non-converts decreasing. In the long-term, the model would achieve a steady state, that is, the student population will settle into a 'fixed' proportion of L-eaters (L/N) and M-eaters (M/N). If $\mathscr{R}_{c,1}(\phi) < 1$, then the population would consist of mostly M-eaters instead of L-eaters in the long-run. The system is rescaled such that $X = M/N$, $Y = L/N$, and $N/N = X + Y = 1$. There are two equilibrium points (in proportions) are: the diet-problem-free state

$$E_{0,1} = (X_{0,1}, Y_{0,1})' = (1,0)'$$

and the diet-problem-endemic state

$$E_{1,1} = (X_{1,1}, Y_{1,1})' = \left(\frac{1}{\mathscr{R}_{c,1}}, 1 - \frac{1}{\mathscr{R}_{c,1}} \right)'.$$

The prime $'$ here denotes vector transpose. We claim that $E_{1,0}$ is globally asymptotically stable *if and only if* $\mathcal{R}_{c,1} \leq 1$ while $E_{1,1}$ is globally asymptotically stable whenever it exists (i.e., *if and only if* $\mathcal{R}_{c,1} > 1$). Hence, the inequality $\mathcal{R}_{c,1} \leq 1$ is equivalent to

$$\frac{1}{\phi} \leq \frac{1/\mu}{\mathcal{R}_{c,1}(0) - 1}.$$

This means that the shorter the average time spent in the *L*-eater state is, the better chance we have to eliminate the diet problem at the population-level.
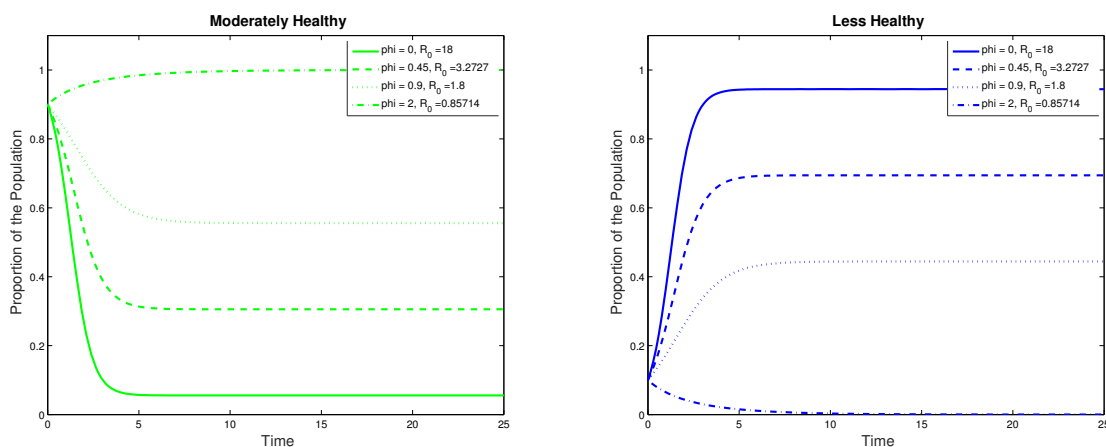
Figure 4.4: The rate of conversion from *L*- to *M*-eaters (ϕ) are varied. There is a minimal impact on the proportion of *L*-eaters compared to no education program (solid), where increasing the implementation yields mostly *M*-eaters (dashed dotted).

4.3.2 Ratatouille Effect

A slightly modified version of Model (4.1) permits the study of food association learning with varying levels of effectiveness. Here, *M*-eaters will enter the food association learning program at the per-capita rate γ_1. After association learning, a portion p will become food preference learners (*P*-eaters) at the combined rate $p\alpha$, in which, we consider the food association learning program successful. Recidivism of *A*-eaters, where they return to old ways of eating, as *M*-eaters occurs at the rate $(1 - p)\alpha$, or as *L*-eaters after

social interactions with L-eating peers occurs at rate $r\lambda$, where $\lambda = \beta L/N$. The M-eaters who do not enter the food association program would either maintain current eating habits or by social interactions with peers, λ, they would become L-eaters. Finally, L-eaters can shift to M-eaters at rate ϕ or they join the food association program and therefore transit to A-eaters at rate γ_2 (see Table 4.2 for variable and parameter definitions and Figure 4.5 for a schematic diagram). This new model is governed by the following equations,

$$
\begin{aligned}
M' &= \Lambda - (\mu + \lambda + \gamma_1)M + \phi L + (1-p)\alpha A, \\
A' &= \gamma_1 M + \gamma_2 L - (r\lambda + \mu + \alpha)A, \\
L' &= \lambda M - (\phi + \gamma_2 + \mu)L + r\lambda A, \\
P' &= p\alpha A - \mu P,
\end{aligned}
\tag{4.2}
$$

where the total population is $N = M + L + A + P$ and student school entry rate is $\Lambda = \mu N$. Model (4.2) is rescaled in terms of sub-population proportions: $X = M/N, W = A/N, Y = L/N$, and $Z = P/N$. The diet-problem-free equilibrium is $E_{0,2} = (X_{0,2}, W_{0,2}, 0, Z_{0,2})'$, where

$$
\begin{aligned}
X_{0,2} &= \frac{\mu(\alpha + \mu)}{(\alpha + \mu)(\gamma_1 + \mu) - (1-p)\alpha\gamma_1}, \\
W_{0,2} &= \frac{\mu\gamma_1}{(\alpha + \mu)(\gamma_1 + \mu) - (1-p)\alpha\gamma_1}, \\
Z_{0,2} &= 1 - X_{0,2} - W_{0,2}.
\end{aligned}
$$

It is locally asymptotically stable *if and only if*

$$
\mathscr{R}_{c,2} = (1-q)\mathscr{R}_{c,1},
\tag{4.3}
$$

where $\mathscr{R}_{c,2}$ is the control reproduction number for the model with the *ratatouille* effect. The proportion, $q = \frac{(p\alpha + (1-r)\mu)\gamma_1}{\mu(\alpha + \mu + \gamma_1) + p\alpha\gamma_1}$, represents the reduction in the control reproduction number $\mathscr{R}_{c,1}$ due to the application of the education association program. The analysis reveals further that the rescaled model shows the existence of subcritical endemic states (backward bifurcation phenomenon) *if and only if* the following set of inequalities is held

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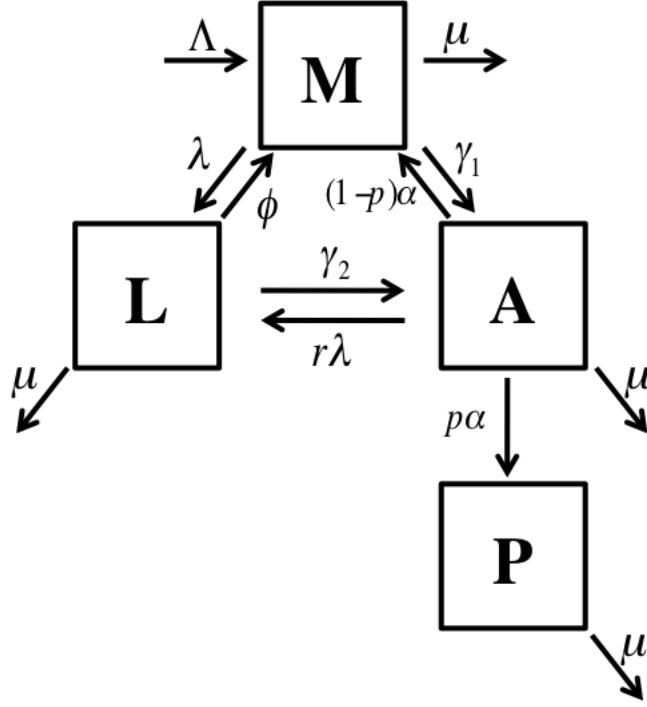
Figure 4.5: A schematic diagram of Model 2 with 'moderately' healthy eaters M, 'less' healthy eaters L, food association learners A, and food preference learners P.

$$\phi > \phi^c, \quad r_1 < r < r_2, \quad p > p^c, \tag{4.4}$$

that is, if $\frac{1}{\phi}$ is small enough, the susceptibility is within some pre-specified range, and the proportion of preference learners is high enough where

$$
\phi^c = \frac{\mu(\gamma_2 + \gamma_1 + 2\mu) + 2(\gamma_1 + \mu)\sqrt{\mu(\gamma_2 + \mu)}}{\gamma_1},
$$

$$
r_1 = \frac{\alpha + \mu}{2(\phi + \mu + \gamma_1)}\left[\frac{\gamma_2}{\gamma_1} + \frac{\phi}{\mu} - 1 - \sqrt{\left(\frac{\gamma_2}{\gamma_1} + \frac{\phi}{\mu} - 1\right)^2 - 4\left(\frac{\gamma_2 + \mu}{\gamma_1}\right)\left(1 + \frac{\gamma_1 + \phi}{\mu}\right)}\right],
$$

$$
r_2 = \frac{\alpha + \mu}{2(\phi + \mu + \gamma_1)}\left[\frac{\gamma_2}{\gamma_1} + \frac{\phi}{\mu} - 1 + \sqrt{\left(\frac{\gamma_2}{\gamma_1} + \frac{\phi}{\mu} - 1\right)^2 - 4\left(\frac{\gamma_2 + \mu}{\gamma_1}\right)\left(1 + \frac{\gamma_1 + \phi}{\mu}\right)}\right],
$$

$$
p^c = \frac{\mu\left[(r\gamma_1 + \alpha + \mu)^2 + (r-1)[r\gamma_1(\phi + \mu) - \gamma_2(\alpha + \mu)]\right]}{\alpha[r\gamma_1(\phi + \mu) - \gamma_2(\alpha + \mu)]}.
$$

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Table 4.2: Definition of Model 2 Parameters.

Parameter	Value	Unit	Description
M/N	0.4	dimensionless	Proportion of 'moderately' healthy individuals
L/N	0.1	dimensionless	Proportion of 'less' healthy individuals
A/N	0.2	dimensionless	Proportion of food association learners
P/N	0.3	dimensionless	Proportion of food preference learners
β	1.8	$\frac{1}{year}$	Peer influence rate shifting a M- to an L-eater
γ_1	0.35	$\frac{1}{year}$	Entry rate into food association program as an M-eater
γ_2	0.06	$\frac{1}{year}$	Entry rate into food association program as an L-eater
p	varies	dimensionless	Proportion of those who become "preference learners"
α	0.4	$\frac{1}{year}$	Effectiveness rate of food association learning
ϕ	0.6	$\frac{1}{year}$	Recidivism rate from a L- to an M-eater
r	0.1	dimensionless	Denotes the relative susceptibility of A-eaters with respect to M-eaters who shift to an L-eater
μ	0.10	$\frac{1}{year}$	Per-capita student entry and removal rate

Thus, if Condition (4.4) holds, then the model has two diet-problem-endemic equilibria for $\mathscr{R}_{c,2} < 1$. Figure 4.6 shows the bifurcation diagram for the ratatouille model in the plane $(\mathscr{R}_{c,2}, Y)$, where the solid curve corresponds to a diet-problem-endemic equilibrium with higher level of the endemic prevalence of L-eaters and the dotted curve corresponds to a diet-problem-endemic equilibrium with lower level of L-eaters' endemic prevalence, and both exist when $\mathscr{R}_{c,2} < 1$. Further, as $\mathscr{R}_{c,2}$ decreases, both curves approach each other until reaching the turning point (Safan, Heesterbeek, & Dietz, 2006) at which both of them coalesce. The value of the control reproduction number at this turning point is given by $\mathscr{R}_{c,2}^{\star 1}$, where

$$\mathscr{R}_{c,2}^{\star 1} = \frac{(\alpha + \mu + r\gamma_1)[\gamma_2(p\alpha + \mu) + \mu(r(\phi + \mu - \gamma_1) - (\alpha + \mu)) + 2\sqrt{D_{R_{c,2}}}]}{r(\phi + \gamma_2 + \mu)[(\alpha + \mu)(\gamma_1 + \mu) - (1 - p)\alpha\gamma_1]} \qquad (4.5)$$

and

$$D_{R_{c,2}} = r\gamma_1\gamma_2\mu^2 + \mu[p\alpha + (1-r)\mu][r\gamma_1(\phi+\mu) - \gamma_2(\alpha+\mu)].$$
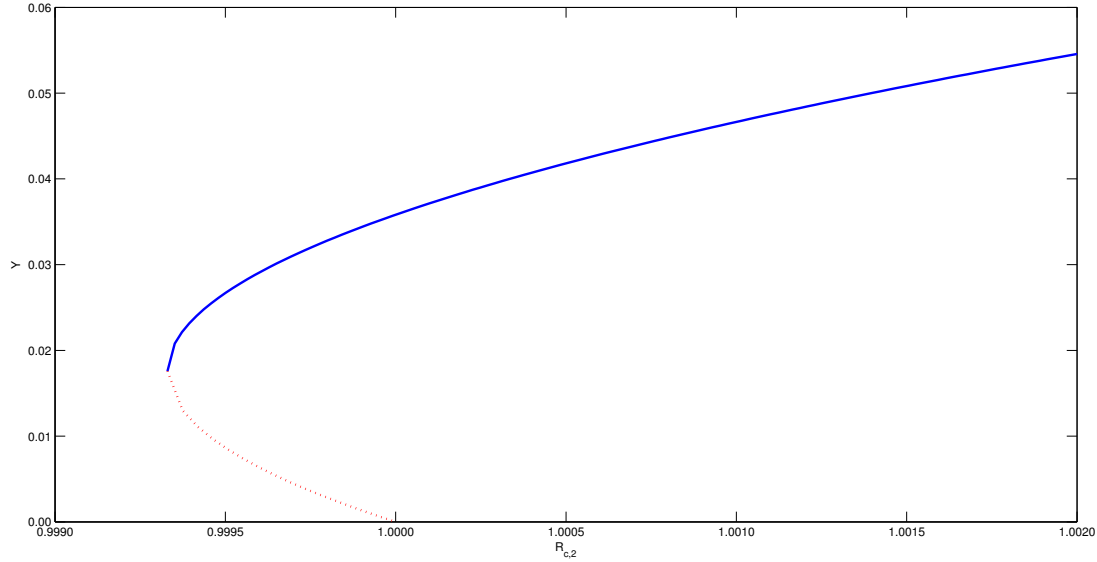
Figure 4.6: The proportion of unhealthy-eaters, or *L*-eaters, at equilibrium as a function of the control reproduction number $\mathscr{R}_{c,2}$. Simulations are done for $\mu = 0.1, \gamma_1 = 0.35, \gamma_2 = 0.06, \alpha = 0.4, \phi = 0.06, r = 0.8258$ and $p = 0.9298$.

In fact, the value $\mathscr{R}_{c,2} = \mathscr{R}_{c,2}^{\star 1}$ is, a threshold value, that determines the nonexistence and existence of diet-problem-endemic states. If at least one of the conditions (4.4) is not satisfied, then the model shows the existence of forward bifurcation (supercritical endemic state), in which, a unique diet-problem-endemic equilibrium exists and is stable for $\mathscr{R}_{c,2} > 1$, while no endemic state exists for $\mathscr{R}_{c,2} < 1$. Hence, $\mathscr{R}_{c,2} = 1$ is the threshold level that indicate the nonexistence and existence of diet-problem-endemic states. Thus, we summarize the above results as follows: the critical control reproduction number below which diet-problem-endemic equilibria do not exist is given by

$$
\mathscr{R}_{c,2}^{\star} = \begin{cases} \mathscr{R}_{c,2}^{\star 1} & \text{if the bifurcation is backward,} \\ \\ 1 & \text{if the bifurcation is forward.} \end{cases} \tag{4.6}
$$

Diet-problem containment possibility

Addressing the possibility of containing (getting rid of) the diet problem is certainly of utmost importance. Here, we discuss the existence of necessary and sufficient conditions required to eliminate the diet-endemic problem based on the implementation of a food association program with effectiveness $p \in [0, 1]$. In the literature of mathematical epidemiology, the basic reproduction number $\mathscr{R}_0$ is a key concept, the public health cornerstone used to determine the minimum effort required to eliminate an infection when the model doesn't exhibit the existence of multiple endemic equilibria. However, in the last two decades several models exhibited bistable endemic states, where backward bifurcation and hysteresis phenomena are shown to exist. In such cases, $\mathscr{R}_0 < 1$ is a necessary but not sufficient condition for eliminating the infection. For a model with backward bifurcation, it has been shown in (Safan et al., 2006) that the ratio $\mathscr{R}_0/\mathscr{R}_0^{\star}$ could be interpreted as a reproduction number and so, reducing this ratio to below one ensures an effective control of the infection. Thus, if we solve the inequality $\mathscr{R}_{c,2}/\mathscr{R}_{c,2}^{\star} < 1$ in terms of the probability p, we get

$$
p > p^{\star} = \begin{cases} p_1^{\star} & \text{if the bifurcation is backward,} \\ \\ p_2^{\star} & \text{if the bifurcation is forward} \end{cases} \tag{4.7}
$$

where

$$
\begin{aligned}
p_1^{\star} &= 1 - \frac{1}{\alpha \gamma_2^2}\left[Q_1 + \sqrt{Q_1^2 - \gamma_2^2 Q_2} \right], \\
p_2^{\star} &= 1 - \frac{1}{\alpha \gamma_1}\left[(\alpha + \mu)(\gamma_1 + \mu) - \frac{\mu \beta(\alpha + \mu + r\gamma_1)}{\phi + \mu} \right]
\end{aligned}
$$

and

$$Q_1 = \gamma_2[(\alpha+\mu)(\gamma_2+\mu)+r\mu(\phi+\gamma_1+\mu-\beta)] - 2r\mu\gamma_1(\phi+\gamma_2+\mu),$$

$$Q_2 = [(\alpha+\mu)(\gamma_2+\mu)+r\mu(\phi+\gamma_1+\mu-\beta)]^2 -$$
$$4r\mu[(\phi+\gamma_2+\mu)(\alpha+\mu)(\gamma_1+\mu)-\mu\beta(\alpha+\mu+r\gamma_1)].$$

Formula (4.7) determines the critical probability $(p^\star)$ of effectiveness of a food associa-tion program above which the diet-problem-endemic state(s) disappear. Figure 4.7 shows the critical level of the food association effectiveness $p^\star$ as a function of the contact rate β. The vertical line $\beta = \beta^-$ separates between nonexistence and existence of a back-ward bifurcation. Therefore, for $\beta \leq \beta^-$, the curve $p = p_2^\star$ separates between existence and nonexistence of diet-problem-endemic equilibria. Thus, a probability of effectiveness slightly above $p_2^\star$ ensures an effective control of the diet-endemic problem. However, if $\beta^- < \beta < \beta^+$, then backward bifurcation exists and $p = p_1^\star$ is the threshold above which diet-problem-endemic equilibria do not exist. Thus, a food association program with prob-ability of effectiveness slightly higher than $p_1^\star$ exhibits a die-out of the diet-endemic prob-lem, where

$$\beta^- = \phi+\mu-\gamma_1 - \frac{\alpha+\mu}{r} + \frac{\gamma_2}{r}\left(1+\frac{\alpha}{\mu}p^c\right),$$

$$\beta^+ = \phi+\mu-\gamma_1 - \frac{\alpha+\mu}{r}\left(1-\frac{\gamma_2}{\mu}\right) +$$
$$2\sqrt{\frac{\gamma_1\gamma_2}{r} + \frac{\alpha+(1-r)\mu}{r\mu}\left(\gamma_1(\phi+\mu)-\frac{\gamma_2(\alpha+\mu)}{r}\right)}.$$

Here, the level $\beta = \beta^+$ represents the value at which $p_1^\star$ hits the upper bound $p = 1$. Thus, for $\beta > \beta^+$, there is no feasible value of p that ensures a wash out of the diet-endemic problem and we may seek another control strategy to first reduce the contact rate β to below β^+ and then apply a food association program with high enough probability of effectiveness. This ensures an effective control of the diet-problem.
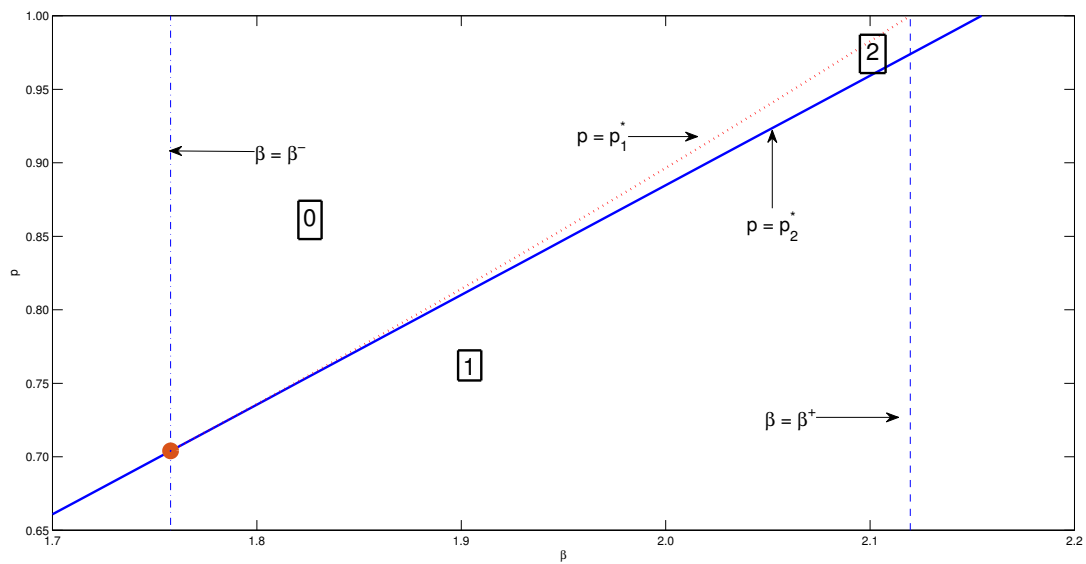
Figure 4.7: The critical probability of effectiveness $p^\star$ subdivides the (β, p) plane into regions (denoted by $0, 1$, and 2) according to the number of diet-problem-endemic equilibria.

Figure 4.8 shows a time series analysis for the model for a fixed β and four different levels of p. The proportion of L-eaters approaches zero when $p = 0.5$ and $p = 1$, while when $p = 0$ and $p = 0.25$, it approaches a constant value. This implies that if the efficacy of the program is 50% or greater, then the M- and A-eaters are reduced, while L-eaters approach zero, and P-eaters are largest, compared to a program with lower efficacy ($p < 0.5$). Hence, a food association program that leads to food preference learning can be an effective nutrition intervention strategy. However, this would require knowledge on the culture, norms, and values of the community to create and implement such a program.
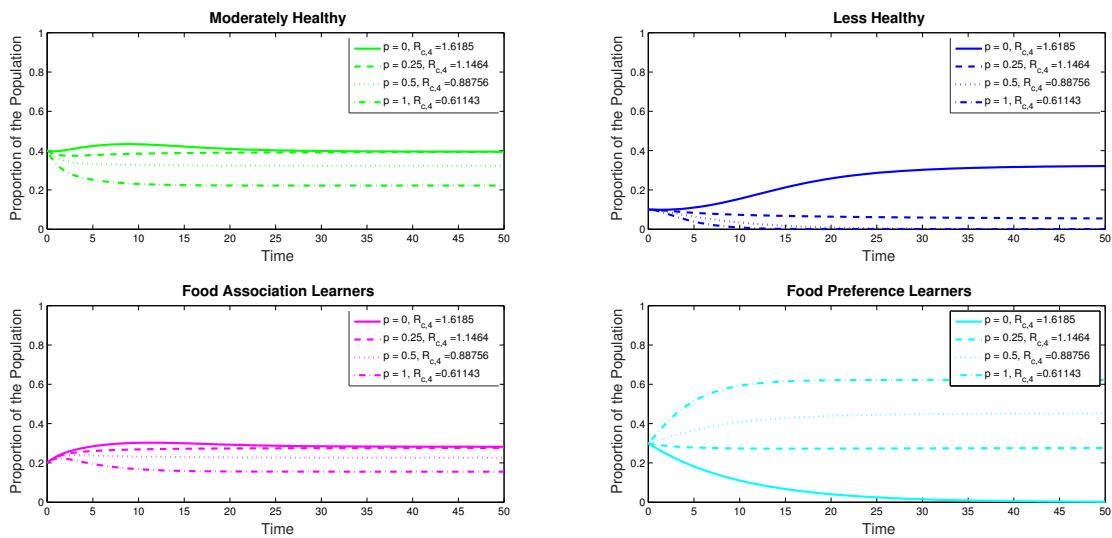
Figure 4.8: Time series analysis for the subpopulation proportions for different values of the food association efficacy probability p and the control reproduction number $\mathscr{R}_{c,2}$.

4.4 Discussion

The goals of many nutrition programs are to instill healthy and sustainable eating habits among young individuals. Since food association learning has been identified as a more effective approach, we study its potential impact at the population-level through use of mathematical models. Two models were developed in order to study eating behavior learn-

ing and the resulting diet dynamics of young individuals. The first model considered the case when there is no food association learning program and the second incorporated food association and food preference learning. Results of Model (1) indicate that some nutrition program at schools are better than none at all. If effective, or p large enough, then the food association learning program is a potential impactful strategy at reducing the proportion of L-eaters shown by the results of Model (2). These results demonstrate the importance of nutrition education curriculum, learning, and socialization in schools. However, more work is needed to understand how to create and implement an effective program so that it incorporates the culture, norms, and values of the community, supporting the conclusions of other studies (American Diabetes Association (ADA), 1999; Pérez-Rodrigo & Aranceta, 2001; Perez-Rodrigo & Aranceta, 2003; Story et al., 2008). Future work would more effectively incorporate data from the literature. The parameter values we chose (see Tables 4.1 and 4.2) were qualitatively estimated based on observations from our pilot study (Wadhera et al., n.d.) and the literature, but more work is needed to quantify these values.

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Chapter 5

EPILOGUE

The aim of this dissertation research was to address three issues related to type 2 diabetes and obesity utilizing quantitative and qualitative methods. Specifically, the progression, treatment, management, and prevention of type 2 diabetes and obesity. First, a theoretical model was developed to describe the dynamics between insulin, glucose, and free fatty acids. The explicit time delay model fitted to data and comparison with the minimal model showed that the proposed model could predict the qualitative trends of insulin, glucose, and free fatty acids relatively well. Second, statistical analyses of an individualized-based intervention program revealed that diet and environment are important factors for weight management. Third, contagion models were developed to assess the impact of food association learning on eating behaviors in school settings, where results demonstrated that this approach can be an impactful strategy. In conclusion, the value of this dissertation research is in integrating multiple disciplines and methods bridging physiological, individual, and population level approaches to address type 2 diabetes and obesity from a holistic perspective. These approaches can be extended to study chronic diseases and for the development of sustainable healthy behaviors.

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APPENDIX A

ANALYSIS OF SOLUTIONS: PROOF OF POSITIVE SOLUTIONS

Proof. Let $G(t) > 0$. The continuity of the solution of a differential equation indicate that $G(t)$ would be non-positive if there existed a $t_0 > 0$ such that $G(t_0) = 0$ and $G(t) > 0$ for any $0 \leq t < t_0$. Moreover, then $\frac{dG}{dt}|_{t=t_0} \leq 0$, which is a contradiction since,

$$\begin{aligned} \frac{dG}{dt}\Big|_{t=t_0} &= b - aG(t_0)I(t_0) - eG(t_0) \\ &= b > 0 \end{aligned} \tag{A.1}$$

This proves that, if $G(0) > 0$, then $G(t)$ will not disappear and is always positive. Similarly, we can show that if $I(0) > 0$, then $I(t)$ will also not vanish and that it is always positive. Therefore, let $I(0) > 0$ and assume that $\exists\, t_0 > 0$ such that $I(t_0) = 0$ and $I(t) > 0$ for any $0 \leq t < t_0$. Moreover, then, $\frac{dI}{dt}|_{t=t_0} \leq 0$, which is a contradiction because,

$$\frac{dI}{dt}\Big|_{t=t_0} = df_1(G(t_0)) + pf_2((F_0)) - cI(t_0) = df_1(G(t_0)) + pf_2((F_0)) > 0 \tag{A.2}$$

This proves that, if $I(0) > 0$, then $I(t)$ will not disappear and is always positive. Finally, taking a similar approach, we can show that if $F(0) > 0$, then $F(t)$ will also not vanish and that it is always positive. Therefore, let $F(0) > 0$ and assume that $\exists\, t_0 > 0$ such that $F(t_0) = 0$ and $F(t) > 0$ for any $0 \leq t < t_0$. Moreover, then, $\frac{dF}{dt}|_{t=t_0} \leq 0$, which is a contradiction because,

$$\frac{dF}{dt}\Big|_{t=t_0} = g_0 + \frac{g_1}{1 + \left(\frac{I(t_0)}{I_2}\right)^\kappa} - hF(t_0) = g_0 + \frac{g_1}{1 + \left(\frac{I(t_0)}{I_2}\right)^\kappa} > 0 \tag{A.3}$$

In conclusion, this proves that if $F(0) > 0$, then $F(t)$ will not disappear and is always positive.

$\square$

APPENDIX B

ANALYSIS OF SOLUTIONS: PROOF OF BOUNDED SOLUTIONS

Proof. It can be shown that for $G'(t) \leq b - eG$, then G is bounded by $0 \leq G \leq \frac{b}{e}$ if $G_0 < \frac{b}{e}$.

Similarly, it can be shown that $F'(t) \leq g_0 + g_1 - hF$ then F is bounded by $0 \leq F \leq \frac{g_0 + g_1}{h}$ if $F_0 \leq \frac{g_0 + g_1}{h}$.

Lastly, it can be shown that since both G and I are bounded then when $I'(t) \leq \Lambda - CI$, I is bounded by $0 \leq I \leq \frac{\Lambda}{c}$ if $I_0 < \frac{\Lambda}{c}$ where $\Lambda = d \frac{\left(\frac{b}{e} \right)^{\gamma}}{\alpha^{\gamma} + \left(\frac{b}{e} \right)^{\gamma}} + p \frac{\left(\frac{g_0 + g_1}{h} \right)^{\beta}}{\sigma^{\beta} + \left(\frac{g_0 + g_1}{h} \right)^{\beta}}$.

$\square$

APPENDIX C

ANALYSIS OF SOLUTIONS: EQUILIBRIUM POINT

The steady state is obtained by setting equations (2.5)-(2.7) equal to 0,

$$0 = b - aG^*I^* - eG^* \tag{C.1}$$

$$0 = d\frac{(G^*)^\gamma}{\alpha^\gamma + (G^*)^\gamma} + p\frac{(F^*)^\beta}{\sigma^\beta + (F^*)^\beta} - cI^* \tag{C.2}$$

$$0 = g_0 + \frac{g_1}{1 + \left(\frac{I^*}{I_2}\right)^\kappa} - hF(t) \tag{C.3}$$

Rearranging terms, we can express G^* (from equation C.1) and F^* (from equation C.3) as follows:

$$G^* = \frac{b}{aI^* + e},$$

and

$$F^* = \frac{1}{h}\left(g_0 + \frac{g_1}{1 + \left(\frac{I^*}{I_2}\right)^\kappa}\right)$$

Substituting G^* and F^* into equation (C.2), yields the equilibrium point implicitly in terms of I^*:

$$0 = d\frac{\left(\frac{b}{aI^*+e}\right)^\gamma}{\alpha^\gamma + \left(\frac{b}{aI^*+e}\right)^\gamma} + p\frac{\left(\frac{1}{h}\left(g_0 + \frac{g_1}{1+\left(\frac{I^*}{I_2}\right)^\kappa}\right)\right)^\beta}{\sigma^\beta + \left(\frac{1}{h}\left(g_0 + \frac{g_1}{1+\left(\frac{I^*}{I_2}\right)^\kappa}\right)\right)^\beta} - cI^* \tag{C.4}$$

In order to determine the number of roots in the system, we plot the two functions:

$$y_1(I^*) = d\frac{\left(\frac{b}{aI^*+e}\right)^\gamma}{\alpha^\gamma + \left(\frac{b}{aI^*+e}\right)^\gamma} + p\frac{\left(\frac{1}{h}\left(g_0 + \frac{g_1}{1+\left(\frac{I^*}{I_2}\right)^\kappa}\right)\right)^\beta}{\sigma^\beta + \left(\frac{1}{h}\left(g_0 + \frac{g_1}{1+\left(\frac{I^*}{I_2}\right)^\kappa}\right)\right)^\beta}$$

$$y_2(I^*) = cI^*$$

In Figure 2.2, we see that $y_1(I^*)$ and $y_2(I^*)$ intersect once, and thus, there is one positive equilibrium point in the system.

APPENDIX D

ANALYSIS OF SOLUTIONS: CHARACTERISTIC EQUATION

We analyze the stability here by first obtaining the characteristic equation. Let us define $A = \frac{\partial(G',I',F')}{\partial(G,I,F)}$, then,

$$A = \begin{pmatrix} \frac{\partial G'}{\partial G} & \frac{\partial G'}{\partial I} & \frac{\partial G'}{\partial F} \\ \frac{\partial I'}{\partial G} & \frac{\partial I'}{\partial I} & \frac{\partial I'}{\partial F} \\ \frac{\partial F'}{\partial G} & \frac{\partial F'}{\partial I} & \frac{\partial F'}{\partial F} \end{pmatrix}$$

$$= \begin{pmatrix} -aI^* - e & -aG^* & 0 \\ 0 & -c & p\frac{\beta(F^*)^{\beta-1}\sigma^\beta}{(\sigma^\beta+(F^*)^\beta)^2} \\ 0 & \frac{-g_1\kappa\left(\frac{I^*}{I_2}\right)^{\kappa-1}}{I_2\left(1+\left(\frac{I^*}{I_2}\right)^\kappa\right)^2} & -h \end{pmatrix}$$

and $B = \frac{\partial(G',I',F')}{\partial(G(t-\tau),I(t-\tau),F(t-\tau))}$, which yields,

$$B = \begin{pmatrix} 0 & 0 & 0 \\ \frac{\alpha^\gamma \gamma d G(t-\tau)^{\gamma-1}}{(\alpha^\gamma+G(t-\tau)^\gamma)^2} & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix}$$

Now defining the characteristic equation we obtain the following,

$$H(\lambda) = \lambda I - A - Be^{-\lambda\tau}$$

$$= \begin{pmatrix} \lambda & 0 & 0 \\ 0 & \lambda & 0 \\ 0 & 0 & \lambda \end{pmatrix} - \begin{pmatrix} -aI^* - e & -aG^* & 0 \\ 0 & -c & p\frac{\beta(F^*)^{\beta-1}\sigma^\beta}{(\sigma^\beta+(F^*)^\beta)^2} \\ 0 & \frac{-g_1\kappa\left(\frac{I^*}{I_2}\right)^{\kappa-1}}{I_2\left(1+\left(\frac{I^*}{I_2}\right)^\kappa\right)^2} & -h \end{pmatrix} - \begin{pmatrix} 0 & 0 & 0 \\ \frac{\alpha^\gamma \gamma d G(t-\tau)^{\gamma-1}}{(\alpha^\gamma+G(t-\tau)^\gamma)^2} & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix} e^{-\lambda\tau}$$

$$= \begin{pmatrix} \lambda + aI^* + e & aG^* & 0 \\ -\frac{\alpha^\gamma \gamma d (G^*)^{\gamma-1}}{(\alpha^\gamma+(G^*)^\gamma)^2}e^{-\lambda\tau} & \lambda + c & -p\frac{\beta(F^*)^{\beta-1}\sigma^\beta}{(\sigma^\beta+(F^*)^\beta)^2} \\ 0 & \frac{g_1\kappa\left(\frac{I^*}{I_2}\right)^{\kappa-1}}{I_2\left(1+\left(\frac{I^*}{I_2}\right)^\kappa\right)^2} & \lambda + h \end{pmatrix}$$

To simplify the calculation, let

$$\hat{A} = -\frac{\alpha^\gamma \gamma d (G^*)^{\gamma-1}}{(\alpha^\gamma+(G^*)^\gamma)^2}, \qquad \hat{B} = -p\frac{\beta(F^*)^{\beta-1}\sigma^\beta}{(\sigma^\beta+(F^*)^\beta)^2}, \qquad \text{and} \qquad \hat{C} = \frac{g_1\kappa\left(\frac{I^*}{I_2}\right)^{\kappa-1}}{I_2\left(1+\left(\frac{I^*}{I_2}\right)^\kappa\right)^2}.$$

Now we have:

$$|H(\lambda)| = \begin{vmatrix} \lambda + aI^* + e & aG^* & 0 \\ \hat{A}e^{-\lambda\tau} & \lambda + c & \hat{B} \\ 0 & \hat{C} & \lambda + h \end{vmatrix}$$

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Evaluating the determinant gives:

$$= (\lambda + aI^* + e) \begin{vmatrix} \lambda + c & \hat{B} \\ \hat{C} & \lambda + h \end{vmatrix} - aG^* \begin{vmatrix} \hat{A}e^{-\lambda\tau} & \hat{B} \\ 0 & \lambda + h \end{vmatrix} + 0 \begin{vmatrix} \hat{A}e^{-\lambda\tau} & \lambda + c \\ 0 & \hat{C} \end{vmatrix}$$

After few algebraic steps, we can expand the equation,

$$
\begin{aligned}
&= (\lambda + aI^* + e)\left[(\lambda + c)(\lambda + h) - \hat{B}\hat{C}\right] - aG^*\left[\hat{A}e^{-\lambda\tau}(\lambda + h) - \hat{B}\cdot 0\right] + 0 \\
&= (\lambda + aI^* + e)\left[\lambda^2 + (c+h)\lambda + ch - \hat{B}\hat{C}\right] - aG^*(\lambda + h)\hat{A}e^{-\lambda\tau}
\end{aligned}
$$

Then, we can combine like terms and simplify to obtain the following,

$$
\begin{aligned}
&= \lambda^3 + \lambda^2 aI^* + \lambda^2 e + \lambda^2(c+h) + \lambda aI^*(c+h) + \lambda e(c+h) + \lambda ch + chaI^* + che - \lambda\hat{B}\hat{C} \\
&\quad - \hat{B}\hat{C}aI^* - \hat{B}\hat{C}e - \lambda aG^*\hat{A}e^{-\lambda\tau} - aG^*h\hat{A}e^{-\lambda\tau} \\
&= \lambda^3 + \lambda^2\left[aI^* + e + c + h\right] + \lambda\left[aI^*(c+h) + e(c+h) + ch - \hat{B}\hat{C}\right] - \lambda aG^*\hat{A}e^{-\lambda\tau} \\
&\quad + chaI^* + che - \hat{B}\hat{C}aI^* - \hat{B}\hat{C}e - aG^*h\hat{A}e^{-\lambda\tau}
\end{aligned}
$$

Now, let us define $b_1 = aI^* + e$, $b_2 = c + h$, $b_3 = ch - \hat{B}\hat{C}$, $b_4 = aG^*\hat{A}$ which gives the following characteristic equation:

$$|H(\lambda)| = \lambda^3 + \lambda^2(b_1 + b_2) + \lambda(b_1b_2 + b_3) - \lambda b_4 e^{-\lambda\tau} + b_1b_3 - b_4h e^{-\lambda\tau} \quad \text{(D.1)}$$

APPENDIX E

ANALYSIS OF SOLUTIONS: LOCAL STABILITY

In order to look at the local stability of some positive equilibrium point (G^*, I^*, F^*) for our system, let us consider first the case when there is no delay and thus, assume $\tau = 0$. Evaluating equation (D.1) at $\lambda = 0$ gives,

$$|H(\lambda)| = \lambda^3 + \lambda^2(b_1 + b_2) + \lambda(b_1 b_2 + b_3 - b_4) + b_1 b_3 - h b_4 \qquad \text{(E.1)}$$

Applying Routh-Hurwitz Stability Criterion (Allen, 2007) for a cubic polynomial, that is, for the cubic polynomial:

$$a_0 s^3 + a_1 s^2 + a_2 s + a_3 = 0,$$

where all the a_i are positive. The Routh array is

$$\begin{bmatrix} s^3 & a_0 & a_2 \\ s^2 & a_1 & a_3 \\ s^1 & \frac{a_1 a_2 - a_0 a_3}{a_1} & \\ s^0 & a_3 & \end{bmatrix}$$

so the condition that all roots have negative real parts is $a_1 a_2 > a_0 a_3$. Therefore, in this case, the equilibrium point is asymptotically stable if

$$(b_1 + b_2)(b_1 b_2 + b_3 - b_4) > b_1 b_3 - h b_4.$$

APPENDIX F

PERMISSION TO INCORPORATE MANUSCRIPT IN DISSERTATION

The co-authors of the manuscript entitled, "Modeling Eating Behaviors: The Role of Environment and Positive Food Association Learning via a *Ratatouille* Effect," grant permission to the author, Anarina Murillo, to use this article in this dissertation.