FOOD PHARMACY AT OHSU KNIGHT CARDIOVASCULAR INSTITUTE: THE IMPACT OF A PILOT FRUIT AND VEGETABLE PROVISION PROGRAM ON CARDIOVASCULAR HEALTH - A SAMPLE POPULATION ANALYSIS

By

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II. ABSTRACT

This thesis presents the findings of a subpopulation analysis of The Food Pharmacy Study at OHSU KCVI, a randomized controlled trial aiming to assess the role a fruit and vegetable provision program may play in reducing cardiovascular disease risk in an at-risk patient population. This thesis' primary outcomes included sustained dietary changes, as measured by the Healthy Eating Index (HEI) Score, and perceived changes to dietary intake and meal preparation habits. It was hypothesized that HEI-scores, as well as perceived intake and use, would increase over time in the intervention group. Participants were recruited from the patient population of the Center for Preventive Cardiology. These Participants (n=9) were randomized via block randomization into two groups: intervention or control. All participants received a 60-minute nutrition counseling session with a registered dietitian (RD) focusing on dietary habits for heart health. Intervention participants were also provided funding for a 3-month weekly fruit and vegetable delivery service.

Quantitative data collected at baseline include participants' anthropometric measurements, blood pressure, plasma lipid panel, plasma blood glucose, and HbA1c levels. Derived quantitative data collected at baseline included Body Mass Indices (BMI) and HEI-scores. Qualitative data collected at baseline included survey responses from the Diet History Questionnaire (DHQ) and the Hunger Vital Sign Food Insecurity Screener. Three-month follow up data collection included HEI-scores, survey responses from the DHQ and the same food security screener, and a survey collecting subjective perceptions of behavior change. The latter survey was only administered to the intervention group.

Sample size was not large enough for adequate power for a statistical analysis, so qualitative data analysis was conducted via visual inspection only. Baseline and follow up characteristics were non-normally distributed and reported in quintiles. Medians of baseline characteristics did not differ substantially between groups, except food insecurity prevalence,

which was higher in the intervention group than the control group. Food insecurity prevalence decreased in the intervention group over time but increased in the control group. While the majority of intervention participants did report perceived increased intake of fruits and vegetables, HEI scores did not increase in the intervention group over time as hypothesized. Limitations of this research include small sample size, non-representative study population characteristics, insufficient power for statistical analysis, lack of quantitative follow up data, and differences in baseline food insecurity prevalence. These findings are not generalizable to the American adult population or those at increased risk for cardiovascular disease. These findings serve as a starting point for additional research to ascertain the role fruit and vegetable prescription programs may play in reducing the risk of cardiovascular disease.

III. INTRODUCTION

A. Significance of Fruit and Vegetable Intake in Cardiovascular Health

Adequate fruit and vegetable intake, as defined by the Dietary Guidelines for Americans, decreases the risk for chronic disease.[1-3] Cardiovascular disease is the leading cause of death for both men and women in the United States.[4] Prevention of cardiovascular disease and promotion of cardiovascular health can be effectively achieved by following a diet similar to the DASH dietary pattern, which includes: fat-free or low-fat dairy products, fish, poultry, beans, nuts, and vegetable oils, limiting foods that are high in saturated fat, limiting sugar-sweetened beverages and sweets, and eating vegetables, fruits, and whole grains.[5,6] However, less than 14.5% and 11% of Oregonians and 12% and 9% of United States residents meet the dietary recommendations for fruit and vegetable intake, respectively.[7]

Six in ten adults living in the United States have a chronic disease, and four in ten adults have two or more chronic diseases, while most United States residents do not meet recommended fruit and vegetable intake levels.[4] Interventions currently in effect to address the disparity between recommended intake and actual intake of fruits and vegetables, namely, nutrition education, can have significant impact on an individual level, but are not as impactful on a community level.[8] An effective community-based intervention strategy is essential for encouraging increased fruit and vegetable intake to decrease chronic disease prevalence. Food pharmacy programs represent a new and innovative program design to decrease the rate of chronic disease by increasing access to fruits and vegetables. Generally, food pharmacies are programs based out of a hospital or outpatient clinic which provide food to patients meeting certain criteria identified by the hospital or clinic. Many of these programs often base their eligibility criteria on an individual's socioeconomic status to target those in whom cost is a barrier to consuming fresh produce. However, the majority of U.S. adults in the highest income

bracket still do not meet the dietary recommendations for fruits and vegetables, with just 11% in compliance.[7]

In order to test whether providing Food Pharmacy Programs benefits a broader population, we proposed the current study that will assess the impact increased access to fruits and vegetables through a food delivery service can have on risk factors for chronic disease. If a decrease in these risk factors is found, programs like these may become more prominent in preventive care to aid in decreasing the American population's risk for developing chronic diseases like cardiovascular disease.

B. Study Objective

Research is lacking as to what impact, if any, these food pharmacy programs have on participant's diet and risk for chronic disease development. The goal of this project is to assess the impact increased access to fruits and vegetables, by way of a food pharmacy program, can have on diet and risk factors for developing cardiovascular disease, regardless of socioeconomic status.

C. Study Aims and Hypotheses

The overall hypothesis of this study is that increased access to fruits and vegetables will improve cardiovascular health markers. The specific aims of this project are:

i. Specific Aim 1: To determine the effect of increased access to fruits and vegetables on sustained dietary changes, as measured by the Healthy Eating Index (HEI).
   a. Hypothesis: Receipt of fruits and vegetables will lead to lasting improvements in healthy eating index scores.

ii. Specific Aim 2: To determine the effect increased access to fruits and vegetables has on perceived changes in dietary intake and cooking habits

a. Hypothesis: Receipt of fruits and vegetables will lead to perceived increases in intake and positive changes in cooking and/or meal preparation habits

IV. BACKGROUND

A. The Cardiovascular System and Its Role in Overall Health

The cardiovascular system is essential for the maintenance of homeostasis throughout the body, circulating oxygen, proteins, glucose, fatty acids, hormones, water, vitamins, minerals, and other molecules, while simultaneously removing waste products, to optimally support life.[9] All other systems, organs, and tissues of the body are dependent on the cardiovascular system. It is because of this dependency that impaired cardiovascular health carries such importance in the body's overall functionality. For example, the chronic diseases diabetes, chronic obstructive pulmonary disease (COPD), obesity, and chronic kidney disease arise from different organ systems and are all recognized comorbidities of cardiovascular impairment.[10] Impaired cardiovascular health is associated with greater risk for all-cause mortality in adults aged 65 years or older.[11-13] And, impaired cardiovascular health affects individual's ability to perform activities of daily living, significantly reducing independence of adults aged 65 years or older with cardiovascular disease (CVD) compared to those without CVD.[14,15] Complications of CVD including heart failure, myocardial infarction or heart attack, cerebrovascular accident or stroke, aneurysm, peripheral artery disease, and sudden cardiac arrest often lead to increased number of hospitalizations, polypharmacy, increased dependence, decreased quality of life, and increased morbidity and mortality.[11-16] Therefore, cardiovascular health is necessary to maintain not only quantity of life, but also quality of life.

B. Cardiovascular Disease

Cardiovascular disease is an umbrella term which refers to diseases that affect either the heart or its vasculature, such as atherosclerosis, coronary heart disease, heart failure, stroke,

cardiac hypertrophy, peripheral artery disease, and congenital heart defects.[17,18] While the pathophysiology is unique for each of these diseases, several of them share common causative pathways, such as hypertension and dyslipidemia, which predispose individuals for developing these chronic diseases later in life.[17] Hypertension is the presence of persistently elevated arterial blood pressure above either 130 mmHg systolic blood pressure, 80 mmHg diastolic blood pressure, or both.[9] This increased pressure on the arterial walls causes damage to the vessel walls and pathological changes in the heart.[9,17] Its pathophysiology is complex, as blood pressure regulation involves renal, neurohormonal, metabolic, and vascular factors.[17] However, the development of primary hypertension is attributed to an interaction of dietary and genetic factors.[9,17]

Like hypertension, hyperlipidemia (defined as elevated low-density lipoprotein (LDL) cholesterol levels, total cholesterol, lipoprotein(a) levels, or triglyceride levels above the 90th percentile, or high-density lipoprotein (HDL) cholesterol levels below the 10th percentile of the general population[19]) increases risk of cardiovascular events in large prospective cohort studies,[5,20,21] and is influenced by both environmental (dietary and lifestyle factors) and genetic factors.[19] It is for this reason that initial recommendations in the management of both primary hypertension and hyperlipidemia typically include dietary and lifestyle interventions. Examples include the DASH diet, dietary sodium restriction, reduced dietary intake of saturated fats and *trans* fats, consuming a diet emphasizing fruits, vegetables, and whole grains, weight reduction, moderate exercise, alcohol restriction, and tobacco smoking cessation.[6,17,18,22]

Additional risk factors for coronary artery disease and increased mortality include atherosclerosis, diabetes mellitus, smoking, family history, along with C-reactive protein, homocysteine, high fibrinogen, lipoprotein (a), and lipoprotein-associated phospholipase A2 (Lp-PLA2).[17,19] Briefly, atherosclerosis is the process by which the arterial wall becomes infiltrated by LDL, VLDL remnants, and chylomicron remnants, where these particles are retained,

oxidized, and taken up by macrophages, smooth muscle cells are mobilized and proliferate, and extracellular lipids accumulate within the arterial wall.[17,23] The interior of the plaque will begin to necrotize, and a fibrous cap will be formed to prevent exposure of the luminal surface to the plaque's necrotic core.[17,23] Over time, the plaque lesions will cause the arterial lumen to narrow, thus decreasing blood flow and increasing arterial pressure. In the case of plaque rupture, acute myocardial infarction and stroke can result.[17,23]

C. Prevention of Cardiovascular Disease

Risk factors for cardiovascular disease may be generally separated into two categories: fixed and modifiable. Elevated lipoprotein (a), African American, Native American, Native Hawaiian, Mexican-American, or Asian-American ethnicity, increased age, especially over age 65, male sex, and familial history of cardiovascular disease, heart attack, or stroke are genetically controlled and unmodifiable risk factors for cardiovascular disease.[18,24] Health-related conditions such as obesity, diabetes, hyperlipidemia, hypertension, and metabolic syndrome are chronic diseases or conditions, for which behavior changes and medical treatments promoting optimal management of these conditions can be modified. Other modifiable risk factors for cardiovascular disease development include tobacco use, being overweight, low fruit and vegetable intake, sedentary lifestyle, increased alcohol intake, and elevated stress levels.[17,18]

Dietary and physical activity behavior modifications have a wide area of effect on targeted modifiable risk factors for cardiovascular disease. Small dietary behavior changes can reduce cardiovascular disease risk by improving the management of multiple high-CVD risk conditions. For example, increased fiber intake from fruits, vegetables, whole grains, nuts, and legumes have been shown to decrease cholesterol synthesis, increase gastrointestinal cholesterol excretion, decrease risk of insulin resistance by reducing the rate of glucose absorption and pancreatic insulin release, and decrease circulating LDL-c concentrations.[25] Fiber also

contributes to increased sensation of fullness in the stomach and delays gastric emptying, which has been associated with decreased caloric intake and weight loss.[25] Likewise, increased intensity and frequency of physical activity has been associated with weight loss, elevated HDL, and improved insulin sensitivity.[26-28] Diet and physical activity interventions are often not sufficient for complete prevention of cardiovascular disease in those with multiple risk factors but are an important and effective part of cardiovascular disease prevention.[17,19,22]

Perhaps the most critical part of preventive care is the detection of disease risk. In the case of cardiovascular disease specifically, individuals should be screened first for genetic and medical history risk factors and should be made aware if they are at higher risk of developing cardiovascular disease. Communication around modifiable risk factors, like diet and physical activity, and counseling on safe, appropriate interventions to reduce individual risk could lead to improved quantity of life, quality of life, and decreased medical expenses for both patient and healthcare system.[14,29]

D. Nutrition and Cardiovascular Health

Cardiovascular disease (CVD) is one of several chronic diseases influenced by diet quality.[2,3] In particular, poor cardiovascular outcomes are associated with diets which are high in saturated and *trans* fats, sodium, and energy, and low in fruits, vegetables, whole grains, and unsaturated fatty acids.[6,18] Food groups that have been identified as protective against risk for developing cardiovascular disease or cardiovascular mortality include fruits and vegetables, whole grains, seafood, and plant proteins like nuts and legumes.[6,18] However, the presence of these food groups in the diet alone does not meaningfully decrease CVD risk. Rather, it is dietary patterns that include frequent consumption of each of these food groups and reduced consumption of other nutrients, like sodium and *trans*-fat, that contribute to overall decreased risk of CVD. Model dietary patterns associated with decreased CVD risk include the Mediterranean diet, the Dietary Approaches to Stop Hypertension (DASH) diet, and other

variations of the DASH diet, such as the OmniHeart diet.[30] Additionally, a dietary pattern modeled after the Dietary Guidelines for Americans is also associated with decreased CVD risk.[1,30] Compliance with these dietary patterns can be quantified through their respective indices, such as the Healthy Eating Index (HEI-2010), Adjusted HEI (AHEI-2010), Adjusted Mediterranean Diet (aMED), and the DASH index.[30] Though the specific dietary components assessed differ among the various indices, high compliance with any of the aforementioned dietary patterns is associated with a 12-28% reduced risk for all-cause mortality, CVD mortality, and cancer mortality in both men and women.[30] Dietary components which remain constant in all of these model dietary patterns are increased intake of whole grains, plant-based proteins, fruits, and vegetables.[30]

Fruit and vegetable intake has been specifically analyzed for association with CVD risk by several studies. For example, Hung et al, in a prospective cohort study, found that over a 14-year period, higher fruit and vegetable intake (>8 servings per day) was significantly, inversely associated with relative risk for CVD.[3] Notably, the observed protective effect of higher fruit and vegetable intake was even stronger in individuals who were current smokers or did not take vitamin supplements.[3] Stewart et al. reported similar findings in a global study assessing the association between Mediterranean Diet Scores and occurrence of major adverse cardiovascular events (MACE).[31] In this study, a higher Mediterranean Diet Score was associated with a lower risk of a MACE, which remained significant across all geographic regions and countries included.[31] Mortality attributable to inadequate fruit and vegetable intake worldwide was estimated to be 2.6 million in 2000.[32] And, since increased fruit and vegetable consumption is associated with decreased CVD risk, it is not surprising that increased fruit and vegetable intake is also associated with medical cost savings. Daviglus et al report consuming >42 cups of fruits and vegetables every 28 days for 1 year would be associated with $1,568 savings per patient in the United States.[29] In other words, average fruit and vegetable intake of

approximately 1.5 cups of fruits and vegetables per day is projected to yield $1,568 cost savings per patient for CVD-related care. Despite the role fruits and vegetables play in preventing CVD, chronic disease, and reducing mortality risk, 88% and 91% of Americans, respectively, do not consume them in the recommended amounts.[1,3] Patients receiving CVD-related care persist in dietary patterns that contain subpar fruit and vegetable intake levels as well.[33] Kral et al led a prospective cohort study, during which they followed 689 patients with symptomatic heart disease and conducted one multiple pass 24-hour dietary recall to assess the participant's dietary quality one year after initial diagnosis of coronary heart disease (CHD).[33] The results of this study show that only 12.4% of subjects met or exceeded the recommended daily vegetable intake (>/= 5/day per AHEI-2010), and 7.8% met or exceeded the recommended daily fruit intake (>/= 4/day per AHEI-2010).[33]

E. Interventions to Increase Fruit and Vegetable Intake

The high prevalence of inadequate fruit and vegetable intake relates to multiple factors known to influence diet behavior. These factors include perceived health competence (a patient's belief in his or her ability to achieve health-related goals), price of fruits and vegetables, the food environment, socioeconomic status, health status, nutritional knowledge, grocery shopping skill level, meal preparation skill level, and food accessibility.[34-37] In a study analyzing the association between perceived health competence and diet behavior in over 2000 CVD inpatients at the Vanderbilt University Hospital, Bachmann et al found that perceived health competence exhibited a non-linear association with health behavior, including dietary quality, as measured by the Health Behavior Index.[34] Perceived health competence was also found to be positively, linearly associated with health-related quality of life, as measured by the Global Health Scale.[34] These results indicate that adults with CVD who have higher perceived health competence tend to also have higher health-related quality of life and more favorable health behaviors, including dietary behaviors.[34] The price of fruits and vegetables and

socioeconomic status can also significantly affect dietary behaviors and decisions. In multiple studies that either financially incentivized or reduced the cost of fruits and vegetables, intake of fruits and vegetables significantly increased.[33,35,38-41] Furthermore, Buyuktuncer et al report that participants in a fruit and vegetable prescription program identified one of the primary barriers to fruit and vegetable consumption as “the price of fruit and vegetables” and “the money available to spend on food”.[38]

Likewise, skill in the areas of food procurement and preparation also contribute to an individual’s ability to consume adequate fruits and vegetables. Especially when considering the guidelines for consuming a variety of fruits and vegetables, individuals must have the ability to prepare diverse options available in both delicious and healthy ways.[1,38] Basic nutritional knowledge may also influence the food purchase decisions made in the grocery store and guide meal preparation methods.[38] Lack thereof may partially contribute to a diet low in fruits and vegetables. Lastly, the home food environment, which is the summation of food accessibility, socioeconomic status, health status, and skill level in grocery shopping and meal preparation, significantly contributes to dietary intake.[33,39-44] In a randomized control trial studying the effects of a coupon program incentivizing healthy food purchases on fruit and vegetable intake and the household food environment, Kral et al found that obesogenic household food availability scores significantly improved over the 3 month intervention from baseline.[33] Coupled with the improved household availability scores was a significant increase in daily vegetable intake from baseline.[33] All of the aforementioned factors are interrelated, and thus form a complex interaction that influences an individual’s likelihood to consume adequate fruits and vegetables.

Presently, when the proportion of nutrients obtained away from the home continues to increase, the role of the external food environment on dietary intake must also be addressed. High-fat foods, sweet and savory snacks, and sugar-sweetened beverages are, on average, more easily accessible than fruits and vegetables.[42-44] One of the fastest growing means for

consuming meals away from the home is the restaurant industry. The convenience and ease of access to restaurants compared to preparing a meal in the home have contributed to the rise in restaurants' popularity over the past two decades.[36] In response to this trend, there have been several proposed policies and interventions to address inadequate fruit and vegetable intake at restaurants themselves, including policies surrounding increased fruit and vegetable availability and access, reduced prices and coupons for fruits and vegetables, catering policies, point-of-purchase information, and promotion and communication regarding the benefits of fruit and vegetable consumption.[36]

Alterations to the presentation of food have also been studied as an effective intervention to increase fruit and vegetable intake. Kongsbak et al studied the effect of food order in a buffet would have on fruit, vegetable, and total energy intake.[45] Both the control and intervention arms featured the same foods on a buffet table, but in a different order and with different presentation. In the control buffet, a mixed fruit and vegetable salad was placed at the end of the buffet table, and in the intervention, the components of the salad were separated into individual bowls and placed at the front of the buffet table. The changes made to the intervention buffet resulted in significantly higher amounts of self-served fruits and vegetables, and total energy was significantly lower than the control group.[45] This research highlights the strong influence convenience and ease of access have on dietary choices.[45]

Not only are people's choices influenced by access, time, and finances, but by perceived convenience as well. For example, SNAP participants in certain states are eligible for Double Up Food Bucks (DUFB) program, which doubles SNAP participants' buying power at farmers markets through fruit and vegetable vouchers.[46] However, in a study conducted by Cohen et al involving 127 adult SNAP participants, only 18% were aware of and had participated in the Double Up Food Bucks program, despite 56% reporting shopping at a farmer's market within the last year.[39] Through a brief intervention involving baseline verbal explanation and print

materials of the Double Up Food Bucks program, 69% of study participants reported participation in the Double Up Food Bucks program within the next 5 months of follow-up.[39] Therefore, not only must avenues for fruit and vegetable procurement be available, but they must be well advertised and understood for these avenues to be perceived as a convenient option.

This trend is further highlighted by survey responses from participants in the SNAP Healthy Incentives Pilot (HIP) program.[41] The HIP program incentivized fruit and vegetable purchases by providing $0.33 for every one dollar spent on eligible fruit and vegetable purchases at participating retailers, up to a monthly limit based on household size.[41] While this program did result in a significant ¼ cup equivalent increase in fruit and vegetable intake among HIP participants compared to non-participants, this positive impact may have been stunted due to limited understanding and use of the program.[41] For example, 38% of a subset of HIP participants reported that it was “hard or somewhat hard” to understand how HIP worked 4-6 months after the program’s initial launch date, and 25% of a subset of HIP participants 9-11 months after the program’s launch date reported the same difficulty.[41] Limited understanding of HIP was associated with lower spending on total fruits and vegetables using EBT benefits.[41] Efforts made in program design must be matched in marketing to improve participant understanding and utilization.

Multiple policies have been modeled as effective means to increase fruit and vegetable consumption in the United States: (1) Mass media campaigns, (2) 10% fruit and vegetable price reduction, and (3) 30% fruit and vegetable price reduction.[35] A modeled one-year, mass-media campaign targeting increased intake of fruits and vegetables yielded a 7% increase in fruit and vegetable intake among the U.S. population.[35] The price reduction model illustrated significantly greater influence on fruit and vegetable intake among the U.S. population. For every 10% reduction in the prices of fruits and vegetables, average consumption increased by 14%, which

was valid up until the 50% price reduction point.[35] Fruit and Vegetable Incentive programs already in existence show similar effects on produce intake.[33,39,41] As one of the largest incentive programs launched in the United States, the HIP program described above incentivized the purchase of fruits and vegetables by providing its 7,500 participants $0.33 for every $1 spent on fruits and vegetables at participating retailers. After 1 year of this pilot program, researchers observed a 26% increase in fruit and vegetable intake of HIP participants over non-participants in a 5,000-participant subsample.[41] HIP participants also reported an 8.5% increase in expenditures on fruits and vegetables and purchasing a larger and greater variety of fruits and vegetables compared to non-HIP participants.[41] A similar, smaller study showed comparable results. In this randomized controlled trial by Kral et al, 54 participants were randomized to either an incentivized group or a non-incentivized group for 3 months.[33] Those randomized to the incentivized group qualified to receive $1 in cash for every receipt documenting purchase of a "healthy food," defined as: fruits and vegetables fresh, frozen, and canned, no calorie or low-calorie beverages, and any foods with an energy density less than 1.5 calories per gram.[33] Similar to the HIP program, incentivized participants had significantly increased vegetable purchases and intake compared to the non-incentivized group.[33] Another large U.S. fruit and vegetable incentive program is the SNAP Double Up Food Bucks (DUFB) program, which was first launched in 2009 and provides a 1:1 incentive match on any local fruit or vegetable purchase at participating farmers markets.[39] In a study by Cohen et al, SNAP participants were recruited in a waiting room of a primary care clinic and provided with verbal explanation and print materials of the DUFB program, along with an additional $10 single use fruit and vegetable voucher for use at the participant's first farmer's market visit.[39] Not only did DUFB participation increase fruit and vegetable intake during the program, but this behavior persisted beyond the program's end.[39] These results illustrate that participants who used DUFB increased their fruit and vegetable consumption by 2/3 servings per day and remained increased 5 months from baseline, 2 months longer than the DUFB season.[39]

Programs designed to increase access and reduce barriers to fruit and vegetable consumption, but do not incentivize their purchase, have also been shown to be successful at meaningfully increasing fruit and vegetable intake. For simplicity, these programs will be categorized as either Additional Access programs or Additional Benefit programs within the context of this report. Additional Access programs are those which narrow the physical or geographical gap between low-access communities, such as low-income communities or communities with large minority populations, and healthy products typically found in grocery stores.[40] Mobile produce markets targeting multiple populations, including older adults, children and adolescence, low-income communities, and minority low-income communities, have significantly increased their customers' fruit and vegetable intakes from baseline.[40] In a cross-sectional study that compared the reported intake of fruits and vegetables of four mobile produce markets' customers across the U.S., Zepeda et al found mobile produce market customers, on average, consumed 1.5 more servings of fruits and vegetables per day compared to non-mobile produce market customers.[47] In a study specifically evaluating the fruit and vegetable intake of children living in low-income neighborhoods, Gorham et al designed a mobile produce market program which included six markets, each assigned to a community organization located in a low-income census tract in Rhode Island.[48] These sites were specifically chosen to serve households more than 0.5 miles away from a grocery store or super-market. Over the 5-month intervention period, participating children's average fruit intake significantly increased from baseline by almost ¼ cup, vegetable intake increased by almost 1/3 cup, and fruit and vegetable combined increased by almost ½ cup.[48] Decreasing distance from fruit and vegetables and thereby increasing convenience to obtain fruits and vegetable significantly increased consumers' intakes. [40,47,48]

Additional Benefit programs involve the direct provision of additional fruits and vegetables at no additional cost based on income status.[40] Several initiatives are modeled in

this way, including Brighter Bites, other Farm to Family programs, and fruit and vegetable prescription programs.[49] Brighter Bites is a 16-week school-based program which distributes 50-60 servings of fruits and vegetables to families with children attending elementary schools with at least 75% of children receiving free or reduced school lunches.[49] This program included other interventions in addition to the fruit and vegetable weekly provisions, namely, the implementation of a health education curriculum known as the Coordinated Approach to Child Health (CATCH) and recipe tasting sessions featuring produce delivered in the weekly provisions.[49] Compared to children at control school sites, Brighter Bites children consumed significantly more fruits, vegetables, and fiber per day, and less added sugar per day.[49] Additionally, parents of children participating in the Brighter Bites intervention consumed significantly more fruit, vegetables, and total fruits and vegetables over time.[49] Compared to parents of children in control schools, Brighter Bites parents reported better understanding of the nutrition facts labels and increased use of the nutrition facts labels to make purchasing decisions.[49] Furthermore, the Brighter Bites intervention resulted in positive changes to family meal-time habits as well. Brighter Bites parents reported a two-fold increase in frequency of cooking from scratch and in eating dinner as a family from baseline.[49] Another, smaller fruit and vegetable provision program operating through Head Start preschools provided each participating family a bag weekly that contained 21 cup equivalents of produce during an 8 week long intervention.[50] These bags also featured recipes that met the SNAP-Ed connection recipe review criteria, ensuring that the recipes were basic and involved few ingredients.[50] Like children and parents participating in Brighter Bites, these Head Start study participants reported significant increases in combined fruit and vegetable servings, vegetable servings, and fiber intake from baseline to post-intervention follow-up.[50] Fruit and vegetable provision programs operating out of school sites have been demonstrated as effective tactics to increase the fruit and vegetable consumption of both children and their parents.[49,50]

Identifying commonly accessed sites within communities is critical for increasing the reach of an intervention. Outside of schools, clinics are another commonly used resource among communities, and have inspired the creation of programs called “food pharmacies” or “fruit and vegetable prescription (Rx) programs.” Typically, fruit and vegetable Rx programs involve the allotment of vouchers for fruits and vegetables as part of treatment for certain medical conditions, such as obesity, diabetes, or hypertension, or for identified socioeconomic conditions, such as food insecurity.[38,51] Though increasing in popularity in the U.S., limited research exists in the literature regarding the efficacy of food pharmacy programs. However, existing studies show promising results of the fruit and vegetable Rx intervention. For example, a pilot food Rx program implemented by Buyuktuncer et al in the United Kingdom resulted in participant reports of increased fruit and vegetable consumption after receiving vouchers for their purchase.[38] Another pilot fruit and vegetable program implemented by Bryce et al in the U.S. studied the effect this program would have on the HbA1c levels of patients with type 2 diabetes.[51] Study participants were allotted $10 for each visit to the farmers market (up to four times, $40 total) for the purchase of fresh fruits and vegetables from local farmers markets, which operated over a 13 week season. Although this study did not collect data on fruit and vegetable intake, the study investigators did collect data on frequency of farmers market visits.[51] Bryce et al found that 63% of participants attended a farmer’s market four times (utilizing the full stipend provided), and post-intervention HbA1c significantly decreased from baseline (9.52% to 8.83%).[51] Based on these studies, food pharmacies may be an effective strategy for targeting populations at risk for nutrition-related chronic disease.

F. The OHSU Center for Preventive Cardiology Food Pharmacy Study

Each of these aforementioned programs were successful in increasing fruit and vegetable intake in low-income, low-access, or elevated health risk-bearing individuals and families. Some also reported improved health outcomes among their study populations.

Additionally, each of these studies increased the convenience of either purchasing or consuming fruits and vegetables by increasing access or perceived access. Since convenience has been shown to weigh heavily on the consumer's dietary behaviors, and price reduction of produce has been modeled to increase fruit and vegetable intake of the entire U.S. population, regardless of socioeconomic status, a program targeting the general population and using similar intervention strategies as described above could also be effective.[35,45]

Based on the impact that increasing fruit and vegetable intake has on cardiovascular outcomes and on the findings presented in studies assessing the impact of various program designs on fruit and vegetable intake, we designed a study to assess the feasibility and efficacy of a pilot fruit and vegetable Rx program at the OHSU Knight Cardiovascular Institute's Center for Preventive Cardiology (CPC) primary clinic. The goal of this study is to assess the effect of increased convenience and access to fruits and vegetables on various health outcomes in CPC patients, including Healthy Eating Index score, fasting blood glucose, weight, waist circumference, HDL-cholesterol, LDL-cholesterol, total cholesterol, triglycerides, and blood pressure. The present analysis presents preliminary results in a small subpopulation of the larger Food Pharmacy Study at OHSU KCVI.

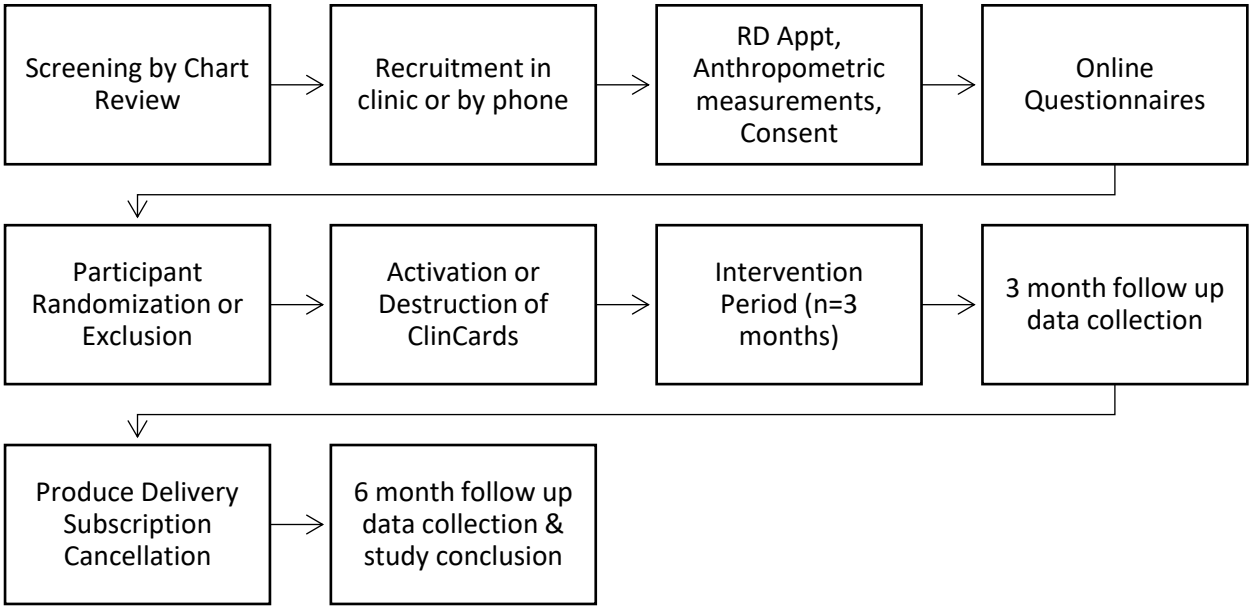
V. METHODOLOGY AND RESEARCH DESIGN

A. General Study Design

Approval for this research was obtained from the OHSU Institutional Review Board (IRB #19413). The study is an ongoing pilot and feasibility trial with a randomized controlled study design aiming to assess the impact a subscription produce delivery service has on sustained dietary changes, as measured by participants' Healthy Eating Index (HEI) scores. The target goal for the larger pilot study is 100 participants who are being recruited from the patient population of OHSU's Center for Preventive Cardiology (CPC) clinic and divided into two groups by block randomization: intervention (n=50) and control (n=50). The present thesis

included a subpopulation of n = 9 participants (Intervention n = 5; Control n = 4). All participants received a blank ClinCard to be used for subscription to a produce delivery service for 12 weeks (3 months) in the event the participant was randomized to the intervention group. All participants in the study received nutrition education in clinic from the CPC's registered dietitian, Tracy Severson, as part of standard care. The present thesis included the collection of anthropometric data, a blood draw for lipid panel and fasting blood glucose concentrations, and questionnaire responses from all study participants at baseline. Original study design also indicated that these same measures be collected again at 3 months from baseline. However, due to restrictions on clinic research visits amidst the COVID19 pandemic, only questionnaire data collected at 3 months from baseline were included in the present thesis. Blood samples were collected regardless of fasting status. In the event a participant was not fasted at the time of blood draw, the participant's intake in the preceding 12 hours was recorded. Diet History Questionnaire response data was used to calculate HEI scores. See Graph 1 for flow of study design.

Graph 1. Study Design Flow



B. Study Participants, Screening, and Recruitment

Study Participants

Individuals 19 years and older who were patients of the CPC, who met the inclusion criteria, (Table 1) and did not meet any of the exclusion criteria (Table 1) were eligible for the present study. The goal study population is 100 participants. The present thesis includes a subpopulation of n = 9 participants with both baseline and 3-month follow up data. In order to enroll, participants needed to be able to stand for collection of anthropometric measurements and also needed to have internet access in order to participate in this study due to the online enrollment and account management for the produce delivery service. Ability to read English and residence in the Portland-metro area were also required for study participation, as the produce delivery service website is only available in the English language and only guarantees service for the greater Portland-metro area. Since this study aimed to assess the effect increased access to fruits and vegetables had on several health-related factors, stable prescription regimen was also required for the duration of the study. Specifically, no changes to medications for diabetes, hypertension, hypercholesterolemia, or hyperlipidemia over the 6-month study period were required in order for individuals to participate and any patients undergoing adjustments of medications for these conditions by their providers were not considered for enrollment. This was done in order to minimize confounding effects on study outcomes. For patient safety, individuals must be generally healthy and have any present medical conditions in good control to participate in this study. It is for this reason that individuals with uncontrolled hypertension, type 2 diabetes mellitus, heavy alcohol intake, triglyceride concentration greater than 500 mg/dL, or LDL-c concentration greater than 160 mg/dL were excluded. Additional exclusion criteria include females currently pregnant and those failing to provide informed consent.

Screening

Prior to recruitment, all CPC patients with either an upcoming appointment or a prior appointment with at least one CPC provider were screened for study eligibility by chart review. The most recent anthropometric data, social history, lipid lab values, and HbA1c values in CPC patient's charts were used for screening purposes. Those individuals identified as meeting study inclusion criteria and who did not meet the exclusion criteria were either contacted during their clinic appointment or by phone at the number provided within their electronic medical record for study recruitment.

Recruitment

In-person recruitment occurred either immediately preceding, during, or following an individual's encounter with their CPC provider. Recruitment over the phone involved the use of an IRB-approved script to inform patients of the study in a standardized fashion. In both recruitment methods, patients had the general study design explained to them during this initial contact. It is at this point that patients elected to state interest in participation. Patients who stated they were not interested in participating in the present study were removed from the study's screening contact list. Patients stating interest in person were consented and enrolled in the study at that time or were scheduled for a separate research appointment if the patient did not have time to undergo the consent process at that time. If the patient had not previously met with the CPC's registered dietitian, Tracy Severson, the patient scheduled an appointment at the front desk when checking out end of their current appointment. If the patient had previously met with the dietitian, this step did not occur. Patients stating interest over the phone were separately contacted by KCVI scheduling staff to schedule an appointment with the registered dietitian, Tracy Severson, for nutrition education as part of standard care and completion of the consent process.

Table 1. Inclusion and Exclusion Criteria for Study Participant Recruitment	
Inclusion Criteria	**Exclusion Criteria**
• Established patient at OHSU CPC	• Triglycerides > 500 mg/dL
• 19 years of age or older	• LDL-cholesterol > 160 mg/dL
• No changes to medication regimen required for study duration*	• Blood pressure > 140/90
• Portland-metro area resident	• HbA1c > 8.0%
• Internet access	• Healthy Eating Index (HEI) score ≥ 80
• Able to read English	• Females currently pregnant
	• Minors (≤ 18 years of age)
	• Cognitively Impaired
	• Alcohol use ≥ 3 drinks per day
	• Failure to provide informed consent
**Includes medications prescribed for management of Diabetes, Hypertension, Blood Lipid or Cholesterol disorders*	

C. Consent and Patient Confidentiality

The Consent Process

At their respective scheduled clinic appointment time, patients interested in study enrollment either met with the principal investigator, Tracy Severson, or another member of the research team, to review the study's IRB approved consent form and answer any questions patients had in regards to the present study. Risks and benefits of participation, rights of study participants, costs of participation, and confidentiality were discussed thoroughly in a private setting. Emphasis was placed on the voluntary nature of this research study, and it was made clear to interested patients that they may withdraw from the study at any time should they elect to consent. Signed consent and authorization forms were stored in a transportable file carrier locked within the principal investigator's storage locker.

Study Participant Confidentiality

Participant identifiers were removed from study data and participants were assigned a randomly generated identification number for data analysis. Study investigators were not be blinded to participant's identities for documentation purposes, but participant identifiers were not be accessible to those outside of the research team. All participant identifiers were securely

stored in one of four virtual locations: REDCap online database, OHSU Epic electronic medical record software, OHSU eCRIS, and within electronic files stored in Box, a cloud content platform protected by OHSU's firewall. Participant identifiers were also securely stored on hard copies of participant data collection documentation. These papers were stored in the same transportable file carrier and were locked within the principal investigator's storage locker when not in use. Only OHSU-approved computers with the appropriate security and encryption were used to record and store electronic data, and access to study data required an OHSU ID and password authentication.

D. Setting

Collection of baseline and follow-up anthropometric data, blood pressure, and administration of nutrition education as part of standard care took place at the OHSU CPC clinic in the OHSU Center for Health and Healing Building 1. Fasting blood draws at baseline and follow up either occurred at the OHSU CPC clinic or in the phlebotomy lab in the OHSU Center for Health and Healing Building 2. Blood samples were analyzed in the Knight Cardiovascular Institute's Lipid Core Lab in the OHSU Hatfield Research Center. Produce was delivered to participants' places of residence or address of choice, and produce was used or eaten ad libitum. Online questionnaires were completed remotely.

E. Electronic Storage of Participant Information

REDCap

All participant information was managed and stored on REDCap, a secure software created for the management of research data through OCTRI. REDCap is housed within servers located in OHSU ITG's Advanced Computing Center, protected behind the OHSU firewall and a second ACC firewall, features controlled user access, which enables primary investigators to only allow access the minimum amount of data necessary for study staff to carry out research work, and

automatic logging of all activity performed on data stored in REDCap. All web-based data transmissions are encrypted within REDCap with industry-standard SSL methods.

Epic

Recruitment of participants and study data collected as part of CPC visits was also stored and accessed within Epic, the electronic medical record system employed by OHSU. Similar to REDCap, data within Epic is protected through physical, electronic, and user access security controls. Data on study participants stored in Epic was directly entered into REDCap by study staff after cross-referencing the participant's subject ID with records in eCRIS and hard copy documentation.

Qualtrics

Data from one survey, the *Imperfect Produce Experience & Utilization Survey*, were collected and stored in Qualtrics, an online survey tool available to OHSU faculty, staff, and students. Qualtrics is approved for the collection of any kind of OHSU information, including protected health information and other confidential data, for OHSU research activity.

F. Data Collection Techniques

Anthropometric Measurements

Height was self-reported by participants and cross-checked with the recorded height in their medical chart by a medical assistant. If the participant's reported height did not match the height recorded in their medical chart, or the participant did not know their height, a medical assistant measured the participant's height in centimeters once at the baseline appointment only. The Welch-Allyn 5002 Mobile Stand-On Scale, which features an adjustable height gauge, was used for participant's height measurement. Standard protocol for height measurement in this study included shoe removal and verbal instructions for the participant to stand as straight as the

participant is able. The medical assistant recorded the height of each study participant in Epic at the time of enrollment.

Participants' weights were also measured using the Welch-Allyn 5002 Mobile Stand-On Scale at baseline and follow up appointments. A medical assistant instructed participants to remove their shoes, shed heavy outerwear, and empty their pockets prior to stepping onto the scale. A handrail is attached to the scale for additional stability if needed. The medical assistant recorded these measurements in both pounds and kilograms in Epic.

A medical assistant measured the waist circumference of each study participant at the baseline and follow up appointments using a stretch-resistant measuring tape. Each waist circumference measurement was recorded in Epic. The medical assistant was instructed to measure waist circumference using the WHO waist circumference protocol.[52] Briefly, the tape measure is wrapped around the waist, parallel to the floor, at the palpated superior posterior iliac crest. The tape is wrapped snuggly, but not in a constricting manner. The medical assistant ensures that the participant is standing upright and with feet evenly spread apart to ensure equal body weight distribution. Waist circumference was recorded in inches.

Body mass index (BMI) was calculated from the directly measured height and weight from each appointment for the duration of this study as a means to assess weight status. BMI was defined as body weight in kilograms (kg) divided by height in meters (m) squared, or kg/m^2. BMI values were interpreted according to the CDC's standard interpretation, which is illustrated in Table 2.[53]

Table 2. BMI Classification	
BMI Value	**Weight Status**
<18.5	Underweight
18.5-24.9	Normal Weight
25.0 – 29.9	Overweight
30.0 – 34.9	Obese Class I
35.0 – 39.9	Obese Class II
≥ 40.0	Obese Class III

Blood Pressure

Similar to the anthropometric measurements, blood pressure was measured and recorded in Epic by a medical assistant at both the baseline and follow-up appointments. The Philips SureSign Vital Signs Monitor and blood pressure cuff was employed for collection of blood pressure values from each participant. Blood pressure measurement was obtained in the following manner: with the patient in an upright seated position with uncrossed legs firmly planted on the ground and an appropriately sized cuff wrapped around the participant's bare arm 2-3 centimeters above the elbow. Each participant was instructed to breathe normally and not to speak during the test. The blood pressure cuff was electronically inflated by the SureSigns device. Blood pressure was measured at least once at both baseline and 3-month follow up appointments. If blood pressure was over the inclusion criteria of 140/90, blood pressure was reassessed a second time. If both blood pressure measurements were above 140/90, the participant was excluded. Blood pressure was measured once at the 3-month follow up appointment.

Blood Chemistries

The OHSU Knight Cardiovascular Institute's Lipid-Atherosclerosis Lab analyzed all blood samples drawn for the purposes of the present study. Three test tubes (two 7 or 10 mL and one 2 mL) of blood were obtained from each participant for lipid panel, and plasma blood glucose

values, and all blood samples were analyzed using the Hitachi 704 Chemistry Analyzer.[54] Plasma total cholesterol concentration were directly measured in a colorimetric assay by enzymatic determination involving cholesterol esterase, oxidase, and peroxidase.[54]

Plasma triglyceride concentration was also directly measured in a colorimetric assay via enzymatic determination. Triglycerides were hydrolyzed by microbial lipase, and the remaining free glycerol was oxidized to dihydroxyacetone phosphate (DHAP) and hydroxy peroxide.[54]

Plasma High Density Lipoprotein- (HDL-) cholesterol was directly measured by quantitative determination. HDL cholesterol measurement was done through the homogenous method, which does not require additional pre-treatment or centrifugation in order to derive HDL-cholesterol concentration.[54,55]

Plasma Low Density Lipoprotein- (LDL-) cholesterol was not measured; rather, it was calculated from the measured total cholesterol, triglyceride, and HDL-cholesterol concentrations using the Friedewald equation (LDL-C = Total C – HDL-C – TG/5).[56] The Friedewald equation for deriving calculated LDL-cholesterol concentration has been shown to be highly correlated with measured LDL-cholesterol via preparative ultracentrifugation in patients with triglycerides below 400 mg/dL.[56]

Plasma blood glucose was measured via colorimetric assay using an enzymatic method involving hexokinase.

Questionnaire Responses

After consented participants' lab results were collected, individuals who were not excluded based on lab findings were emailed a secure, unique web link to both the *Diet History Questionnaire* (DHQ) and *Hunger Vital Sign Food Insecurity Screen.* The version of the *DHQ* used in this study was the *Past Month with Portion Size DHQ*. This *DHQ* version is an online food frequency questionnaire intended for use in adults 19 years of age or older consisting of

135 food and beverage line items and 26 separate questions regarding supplement use. Data from study participant's *DHQ* responses was used to calculate HEI scores. The *Hunger Vital Sign Food Insecurity Screen* is a validated 2-question survey to screen for food insecurity in individuals and families within the last 12 months.[57] The estimated time to complete both of these questionnaires was 60 minutes. Data from these questionnaires is only accessible by researchers involved in the study.

Participants were instructed to complete these questionnaires as soon as possible. These questionnaires were completed by participants away from clinic and from a computer or device of their choosing. The *DHQ* automatically generates a random participant ID code for each survey respondent. These randomly generated IDs were used in the collection of all hand-written recorded data. Questionnaires were sent to participants for completion at baseline and the 3-month follow-up period.

Healthy Eating Index Score

The Healthy Eating Index-2015 (HEI) is a tool which assesses how well an individual's diet aligns with recommendations of the *2015-2020 Dietary Guidelines for Americans*.[58] The HEI scores diets based on 13 dietary components, which reflect different food groups and key recommendations made within the *2015-2020 Dietary Guidelines for Americans*.[58] The HEI score range is from 0 to 100, with a higher score indicating increased adherence to these recommendations.[58] HEI scores were generated for each participant from their *DHQ* responses. Baseline calculated HEI score ≥ 80 resulted in exclusion of that participant from the present study. Participants excluded were notified of this and all information collected outside of their CPC appointment for the purpose of this study will be destroyed at the end of the study. Participants with an HEI score of <80 were randomized into either the intervention or control group and notified of their group assignment. Changes in HEI score over time in participants

were used to assess the impact acute receipt of fruit and vegetables had on sustained dietary changes.

Imperfect Produce Experience & Utilization Survey

The Imperfect Produce Experience & Utilization Survey was created by study staff to assess the experience and perceived behavior change reported by participants in the intervention arm of the study at the 3-month follow up appointment. Participants in the control arm of the study did not complete this survey. The first section of the survey is comprised of 20 Likert-scale questions regarding satisfaction with the produce delivery service, perceived changes in diet or cooking behavior, and how the produce was used. The latter section of the survey is comprised of 7 questions specifically regarding the participants' experiences with the service provided by the company Imperfect Produce, 5 of which offer response choices on a Likert-scale, 1 of which is dichotomous, and 1 of which is free response. These surveys were administered online over email and could be accessed through secure, unique web links. These surveys were created and administered through *Qualtrics*. Responses were manually entered into an online Excel spreadsheet housed within Box. Estimated time of completion for this survey was 5 minutes. Numerical values were assigned to the Likert scale responses for 18 of the initial 20 questions in section 1, and the sum of these values was used to calculate a composite score for each intervention participant. The composite score for this survey ranged from 0 to 90. A higher score indicates a more positive overall experience. The composite score was subdivided into the following sections to assess distinct aspects of participants' experiences during the intervention period: (1) study protocol compliance, (2) perceived convenience, (3) perceived changes in fruit and/or vegetable intake, (4) reported changes in fruit and vegetable use, and (5) degree of satisfaction with produce quality.

G. Nutrition Education

The nutrition education received by all patients interested in study participation was part of the standard care received by all patients of the Center for Preventive Cardiology (CPC). During this appointment, Tracy Severson, RD, provided individualized diet education and counseling regarding cardiovascular health for each CPC patient based on a patient's medical history, diet history, physical activity levels, supplement use, weight history, lab values, and patient's identified goals. As part of standard procedure, patients were asked to bring a 3-day food record, detailing the type and quantity of foods and liquids consumed over a 72-hour period prior to the appointment. If a food record was not available, patients were led through a 24-hour dietary recall instead, which details the type and quantity of foods and liquids a patient remembers consuming within the past 24 hours. Exact interventions and recommendations were unique for each patient. All patients received a copy of the My Heart-Healthy Plate handout (see Handout 1) and were provided information on the Heart Protection Kitchen Cooking Classes hosted by the KCVI. Patients of the CPC typically receive one 60-minute nutrition education session, though follow-up frequency is typically determined on a per patient basis. Participating patients received only one 60-minute nutrition education session for the duration of the study.

H. ClinCard

ClinCard is OHSU's approved research participant payment process supported by Greenphire.[59] The ClinCard is a secure, reloadable MasterCard debit card which is managed by research staff and is intended for use as a secure method for study participant reimbursement.[59] ClinCards, like gift cards, hold no monetary value until money is deposited into the associated account. Participants are not able to add or remove money from their ClinCard account; however, participants are able to view their current balance through any of the following options: calling the ClinCard customer service number, logging into myclincard.com, making a balance inquiry at an ATM, or asking their study investigator to

review the balance on their behalf. While certain activities incur a fee to a ClinCard user's balance, no additional fees are incurred on participants' ClinCards if they are used for their intended purpose within the present study. Additional information regarding ClinCard may be found at o2.ohsu.edu/central-financial-services/treasury/clincard.cfm.

In the present study, ClinCard was used to fund a 12-week subscription to a produce delivery service, Imperfect Produce, for participants randomized to the intervention group. Intervention participants' ClinCards each had a one-time $260 sum deposited into the respective accounts. Intervention participants were instructed to create an online account with Imperfect Produce using the ClinCard and sign up for weekly delivery of the medium mixed fruit and vegetable box, which was estimated to cost, on average, $20 per week. Participants were instructed to terminate these subscriptions at the end of the 12-week intervention period and received reminder emails and/or phone calls near the end of the intervention regarding subscription cancellation and follow-up visit scheduling.

I. Produce Delivery Service: Imperfect Produce ©

Imperfect produce is the online produce delivery service that was used in the present study. Imperfect Produce offers fully customizable grocery boxes in four sizes: small, medium, large, and extra-large. These grocery boxes are delivered to customer's residences or preferred addresses on either a weekly or biweekly basis per customer preference. Imperfect produce offers a wide variety of food items, including, but not limited to, fresh produce. Study participants were instructed to sign up for an Imperfect Produce account and select a medium, regular (conventional, rather than organic) mixed fruit and vegetable produce box to be delivered to their preferred address weekly. Additionally, participants had full control over what foods, produce or non-produce food items, were in their box each week through the Imperfect Produce web site. However, participants were instructed to only order produce through the Imperfect Produce web site, as the ClinCard accounts only hold sufficient funds for weekly,

medium, regular produce boxes for the 12-week study duration. Participants were instructed that additional funds would not be provided should their ClinCard be prematurely depleted, and that they would be instructed to terminate their subscription in that event. The Imperfect Produce Experience & Utilization Survey assessed for how frequently participants' added items to their box that were not a fruit, vegetable, or herb. Because Imperfect Produce does not deliver statewide across Oregon, study participation required that individuals reside within the company's delivery zone. This was determined by comparing individual's home zip codes, found in Epic, to delivery information found on the Imperfect Produce web site. More information on Imperfect Produce may be found at www.imperfectproduce.com.

J. Block Randomization of Study Participants

Once participating individuals had completed all baseline data collection, they were assigned to either the intervention arm or the control arm of the study via block randomization to reduce investigator bias. Participants were contacted via either telephone or email to inform them of their group assignment (intervention or control).

During this contact, participants randomized to the intervention group were directed to follow the instructions provided at the baseline RD appointment to sign up for a subscription to the produce delivery service. If participants no longer had access to their hard copy of the instructions for subscription sign-up, study staff either emailed or mailed this information to these participants per participant preference. Participants randomized to the intervention arm had $260 loaded onto the ClinCard they received at their individual baseline appointment as funding for the 12-week produce delivery subscription.

Participants randomized to the control group were instructed to destroy the blank ClinCard they received at their baseline appointment and informed that the ClinCard had no monetary value associated with it. All study participants were informed that the study

questionnaires, fasting blood draws, and anthropometric measurements were to be completed again at 3 months and 6 months from baseline.

K. Baseline Data Collection

Initial Registered Dietitian Appointment

Prior to study entrance, all interested patients who had not previously met with the CPC's dietitian were scheduled for a 60-minute appointment for nutrition education related to cardiovascular health as part of CPC standard care. At this appointment or during a separate research appointment, a medical assistant collected the following baseline measurements: weight, height, waist circumference, and blood pressure. After the appointment was complete, Tracy Severson, RD, or study staff led interested participants through the consent process. Participants who provide informed consent at this time had a blood sample drawn by a medical assistant and were provided with a blank ClinCard along with detailed, written instructions for sign up and cancellation of the produce delivery subscription. These instructions were reviewed in person with each participant to ensure complete understanding. ClinCards were provided to all study participants prior to randomization in order to prevent the intervention group from having to return to clinic to retrieve their cards. The ClinCards had no monetary value when they were provided at this baseline appointment.

Blood Draw

Lab values were measured from either a fasted or non-fasted blood sample collected at study participant's baseline appointment. If patients presented in a non-fasted state, the time of last caloric intake and contents of the last meal, snack, or calorie-containing beverage were recorded. The blood concentrations of the following indicators were assessed in the present study: triglycerides, LDL-cholesterol, HDL-cholesterol, total cholesterol, and fasting blood

glucose. All blood analysis results were recorded in REDCap and in Epic, and available for participants to review through their respective MyChart online accounts.

Questionnaires

Data from two online questionnaires completed by the study participants were also collected at baseline. The two questionnaires, the online Diet History Questionnaire (DHQ) and Hunger Vital Sign Food Insecurity Screen, were emailed to study participants after the consent process was completed and blood sample results were returned. Each questionnaire was accessible through secure web-links unique to each participant and completed away from clinic at the study participant's convenience. HEI Score was calculated based on DHQ responses.

L. Follow Up Data Collection

3 months

3 months from baseline, participants in the intervention group had received a 60-minute nutrition education appointment with the CPC's dietitian, if they had not had such an appointment previously, and 12-weeks of weekly Imperfect Produce box deliveries. Participants in the control group had only received a 60-minute nutrition education appointment with the CPC's dietitian. Intervention participants were contacted by email to notify them of the end of the subscription period and provided instructions on terminating their produce delivery subscription.

Due to restrictions placed on clinic visits related to the COVID19 pandemic, no participants included in the present thesis participated in their initially planned 3-month follow-up in-clinic appointments, and therefore they did not have blood draws or anthropometric measurements collected. All participants were informed that the same two questionnaires, the DHQ and Food Insecurity Screen, they completed at baseline would be emailed again and may be accessed through secure, unique web links within the email. Participants in the intervention group who

signed the updated consent form, dated February 11th, 2020, also completed the Imperfect Produce Experience & Utilization Survey at their 3-month follow up time point.

6 months

The present thesis only analyzed data collected at baseline and 3-month follow-up period in a smaller sub-population of the larger study's population due to program-related time restrictions. However, the study will continue through 6 months from baseline. At 6 months from baseline, all participants will be contacted via either telephone or email to inform them of the 6-month follow-up period requirements. Study researchers will inform participants that a clinic appointment scheduler will contact them to schedule an appointment for a blood draw and for measurement of their height, weight, waist circumference, and blood pressure. Results from these measurements will available to participants on OHSU MyChart. All participants will also be informed that the same questionnaires, the DHQ and the Hunger Vital Sign Food Insecurity Screen, completed at baseline and at the 3-month follow up will need to be completed one final time. Questionnaires will be emailed to participants and may be accessed through a secure, unique web link within the email. Participants will be thanked for their participation in the present research study and notified of the completion of the study once the aforementioned data is collected.

M. Data Analysis

Descriptive analyses were performed on all study variables. The distribution of each continuous variable was visually assessed through histograms overlaid with a normality curve and boxplots. Continuous, normally distributed data were summarized as means. Continuous, skewed data were summarized as medians and inter-quartile ranges. Categorical data were summarized as frequencies and percentages.

Observed differences in characteristics of the intervention and control groups were assessed via visual inspection to determine the degree to which comparable randomization was achieved between groups. Due to the small sample size and non-normal distribution, the following baseline values were reported in quintiles: HEI score, lipid panel, blood pressure, fasting blood glucose, weight, and waist circumference. Line graphs were used to visually assess differences in HEI at baseline and 3 months. Given the small sample size of this analysis, no statistical tests were used to assess the present dataset. Graphs were used to visually assess changes in outcomes between groups at baseline and 3 months and change over time from baseline to 3 months. Data collected in the Imperfect Produce Experience & Utilization Survey were visually inspected through trends in composite scores and Likert scale graphs, and qualitative analysis techniques were used to assess answers to free response questions.

Table 3. Data Analysis Summary

Specific Aim	Hypothesis	Data Analysis Method
Specific Aim 1: To determine the effect of increased access to fruits and vegetables on sustained dietary changes, as measured by the Healthy Eating Index (HEI).	**Hypothesis 1:** Receipt of fruits and vegetables will lead to lasting improvements in healthy eating index scores.	**Analysis Method 1:** The median HEI scores of each group were compared at both time points through visual inspection using tables and box plots. **Analysis Method 2:** The change in HEI over time within groups was assessed through line graphs and tables.
Specific Aim 2 (alt): To determine the effect increased access to fruits and vegetables has on perceived changes in dietary intake and cooking habits	**Hypothesis 1 (alt):** Receipt of fruits and vegetables will lead to perceived increases in intake and positive changes in cooking and/or meal preparation habits	**Analysis Method 1:** Survey questions will be categorized, and responses will be assessed through visual inspection of a diverging, stacked bar plot.

VI. RESULTS

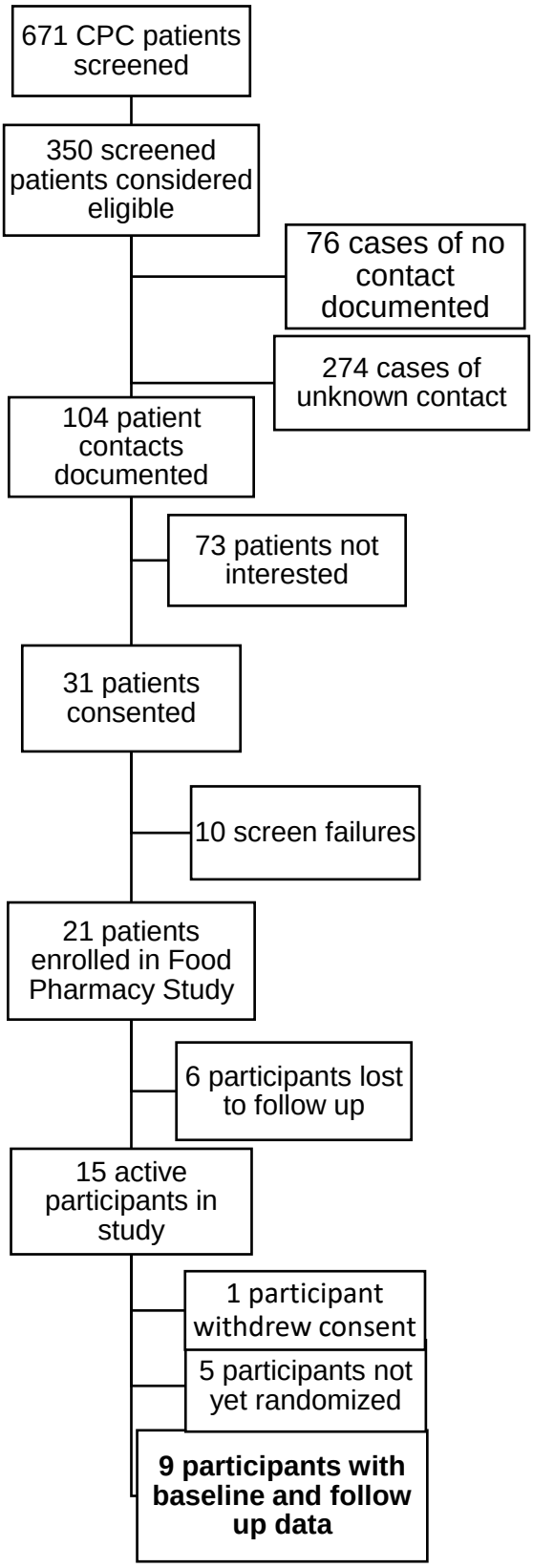
A. Population Descriptive Characteristics

A total of 671 patients at the Center for Preventive Cardiology were screened for study eligibility between September 2019 and March 2020. Approximately half of the screened patients were considered eligible for the study based on their most recent lab values and last filed vital signs (n=350). Not all of these patients were approached regarding study enrollment primarily due to lack of study personnel to reach all eligible patients and appointment cancellations. Approximately one third of the eligible patient population were approached regarding the study either in person or by phone (n=104). Of these, 31 patients approached regarding the study were consented. Of these 31, 10 participants were dropped due to screening failure: specifically, one was dropped due to LDL-cholesterol above the inclusion criterion, one due to mishandling of lab specimens, three due to HEI scores above the inclusion criterion, and the other five due to unsuccessful blood draw attempts. Of the remaining 21 study participants, at the time of this report five participants were awaiting randomization, six participants had been lost to follow up, and one participant withdrew consent after randomization. Therefore, a final population of nine participants with both baseline and follow up data are included in the present analysis. See Graph 2 for study recruitment process.

The study population (n=9) was 60% female with a mean age of 56.30 ± 11.63 years. (Table 4). The majority of the population was Non-Hispanic White and reported never smoking. No data were available in participants' medical records regarding education level. While no participants were diagnosed with diabetes, a third of participants met HbA1c criteria for pre-diabetes. The majority of participants were on stable lipid lowering medication regimens from study enrollment through follow up.

Table 4. Population Descriptive Characteristics	
Characteristics	*Values (% or Mean ± SD)*
Female	60%
Age (Years)	56.30 ± 11.63
Non-Hispanic White	80%
Obese	30%
Never smoker	90%
Prescribed lipid lowering medication*	80%
Prescribed antihypertensive medication	50%
Diabetes Mellitus:	
Type II or Type I Diabetes Mellitus	0%
Pre-Diabetes Mellitus	30%
***Lipid lowering medication includes medications targeting triglycerides or cholesterol.**	

Graph 2. Study Recruitment



B. Baseline Characteristics

Nearly all baseline values (Table 5) were nonnormally distributed; therefore, quintiles were used to represent the data. Given the small sample size, this analysis did not include tests for statistically significant differences between groups. Visual inspection of the differences in medians between groups for each measured value shows most differences are not substantial, with the notable exceptions of triglycerides, total cholesterol, and LDL-cholesterol. Median plasma triglyceride concentration of the control group was 83 mg/dL higher than the intervention group's, and median plasma total cholesterol and LDL-cholesterol of the control group were 21 and 25 mg/dL lower than the intervention group, respectively. The large range of triglyceride concentrations can partially be explained by the variability in lipid lowering medication regimens within the study population and the variability in fasting status at time of baseline blood draw. Median BMI and waist circumference were slightly higher, while median blood pressure was lower, in the intervention group compared to the control group. Although the difference in median HEI score was not substantial, the difference between HEI score ranges of each group is illustrated in Graph 3.

Not listed in Table 5 are the responses to the Hunger Vital Sign Food Insecurity Screen. 20% of the intervention group and 100% of the control group responded "Never True" at baseline to the first part of the 2-question screener: "Within the past 12 months, we worried whether our food would run out before we got money to buy more". The remaining 80% of the intervention group responded "Sometimes True" to this question. 60% and 100% of the intervention and control groups, respectively, responded "Never True" at baseline to the second part of the screener: "Within the past 12 months, the food we bought just didn't last and we didn't have money to get more." The remaining 40% of the intervention group responded "Sometimes True" to this question. In accordance with other clinical screening

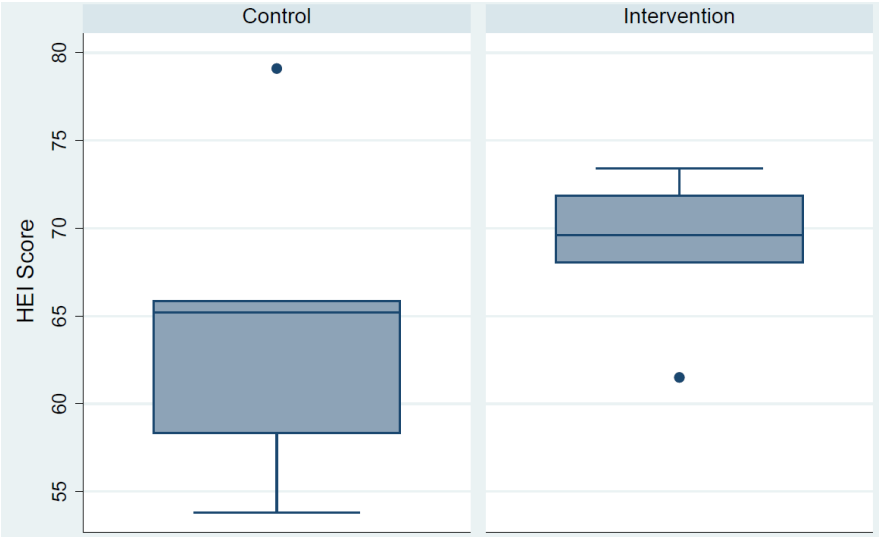
tools for food insecurity, an affirmative response to either question is interpreted as indicative of household food insecurity.[60] Therefore, at baseline, four out of five participants in the intervention group, and zero out of five participants in the control group were considered food insecure based on their responses to the Hunger Vital Sign Food Insecurity Screen.

Table 5. Baseline Values

Measured Values	***Min***	***Q1***	***Median***	***Q3***	***Max***	***Difference in Medians Between Groups***
Weight (kg)						
Intervention (n=5)	74.70	78.85	89.30	108.30	124.50	
Control (n=5)	62.10	65.95	70.90	109.20	125.00	+18.40 kg
Body Mass Index (kg/m^2)						
Intervention (n=5)	23.63	25.32	29.97	38.73	45.67	
Control (n=5)	24.47	24.75	26.01	32.81	38.45	+3.96 kg/m^2
Waist Circumference (in.)						
Intervention (n=5)	34.30	35.05	38.50	40.55	40.90	
Control (n=5)	35.00	35.20	36.20	44.30	51.60	+2.30 in.
Systolic Blood Pressure (mm Hg)						
Intervention (n=5)	96.0	108.5	128.0	133.5	139.0	
Control (n=5)	123.0	125.5	135.0	138.0	140.0	-7.0 mm Hg
Diastolic Blood Pressure (mm Hg)						
Intervention (n=5)	63.0	69.0	78.0	88.0	96.0	
Control (n=5)	69.0	70.5	87.0	88.5	89.0	-9.0 mm Hg
Triglycerides (mg/dL)						
Intervention (n=5)	76.0	89.0	243.0	253.0	262.0	
Control (n=5)	105.0	110.0	160.0	242.5	308.0	+83.0 mg/dL
Total Cholesterol (mg/dL)						
Intervention (n=5)	126.00	132.50	145.00	195.00	232.00	
Control (n=5)	157.00	160.50	166.00	198.50	222.00	-21.00 mg/dL
LDL-Cholesterol (mg/dL)						
Intervention (n=5)	56.0	57.0	60.0	109.5	140.0	
Control (n=5)	66.0	73.0	85.0	121.5	143.0	-25.0 mg/dL
HDL-Cholesterol (mg/dL)						
Intervention (n=5)	40.0	41.5	45.0	47.0	48.0	
Control (n=5)	33.0	38.0	44.0	58.5	70.0	+1.0 mg/dL
Fasting Blood Glucose (mg/dL)						

Intervention (n=5)	76.00	79.50	90.50	97.75	100.00	
Control (n=5)	80.00	80.00	88.00	99.00	100.00	+2.50 mg/dL
Healthy Eating Index Score (n)						
Intervention (n=5)	61.50	64.80	69.60	72.70	73.40	
Control (n=5)	53.80	56.05	65.20	72.50	79.10	+4.40 units

Graph 3. Baseline HEI Score Distribution



C. 3-Month Follow Up Characteristics & Change Over Time

Due to restrictions on in-person research appointments related to the COVID19 pandemic throughout the months of April and May 2020, only data that could be collected remotely were included in the 3-month follow up (Table 6). As such, neither anthropometric data nor blood parameters were collected for this sample population, leaving the Healthy Eating Index Score (HEI) and food insecurity prevalence as the post-intervention follow-up characteristics assessed in this sample population. The healthy eating index scores measured at 3-months from baseline were represented in quintiles, as they were at baseline. Visual inspection of the data indicates a 6.8-point difference in HEI scores between groups, with the control group having a higher median HEI score than the intervention group. Overall food insecurity prevalence at 3-month

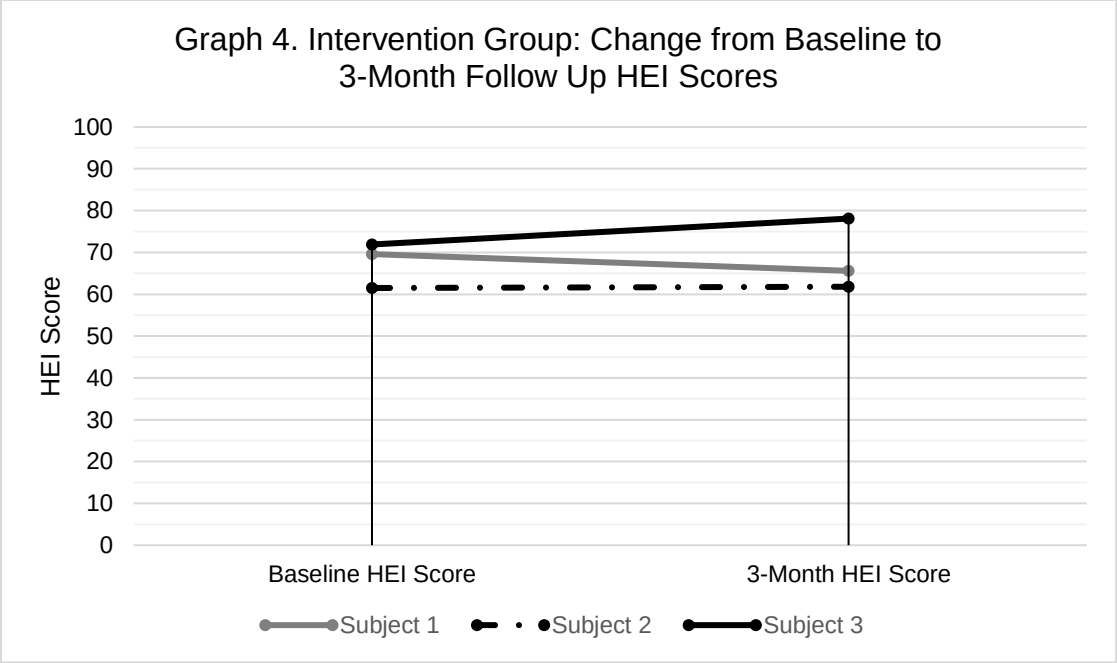
follow up was determined to be 44.44%, with a greater proportion of participants in the intervention group than the control group reporting food insecurity at 3-months from baseline.

Table 6. 3-Month Follow Up Characteristics

Measured Values	***Min***	***Q1***	***Median***	***Q3***	***Max***	***Difference in Medians between Groups***
Healthy Eating Index Score						
Intervention (n=3)	61.8	61.8	65.6	78.1	78.1	
Control (n=4)	54.8	56.7	72.4	86.8	88.2	-6.8

	Prevalence (%)
Food Insecurity	
Overall (n=9)	44.44%
Intervention (n=5)	60.00%
Control (n=4)	25.00%

Median HEI score remained relatively unchanged within the intervention group, with a four-point decrease from baseline to 3-month follow up (Table 7). However, the median HEI score of the control group increased over the 3-month period, indicating that their diets more closely aligned with the *2015-2020 Dietary Guidelines for Americans* at 3-months follow up than at baseline. Contributory factors of this discrepancy are reviewed in the discussion. Unlike the HEI score, food insecurity appears to have been impacted by the food pharmacy intervention based on visual inspection of the data. The prevalence of food insecurity in the intervention group decreased by 20% between baseline and 3-month follow up. In contrast, food insecurity prevalence of the control group, which was notably not reported by any participant in this group at baseline, was increased at 3-month follow up.


Graph 4. Intervention Group: Change from Baseline to 3-Month Follow Up HEI Scores
HEI Score
100
90
80
70
60
50
40
30
20
10
0
Baseline HEI Score
3-Month HEI Score
Subject 1
Subject 2
Subject 3

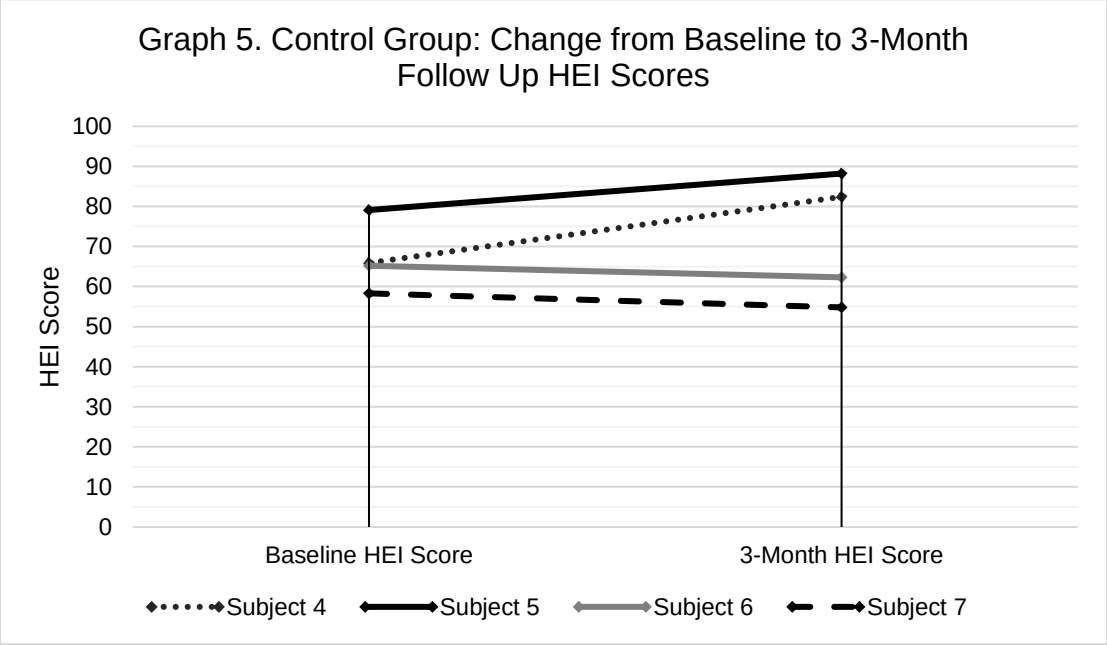

Graph 5. Control Group: Change from Baseline to 3-Month Follow Up HEI Scores
HEI Score
100
90
80
70
60
50
40
30
20
10
0
Baseline HEI Score
3-Month HEI Score
Subject 4
Subject 5
Subject 6
Subject 7

Table 7. Change Over Time in Characteristics (Baseline to 3-Month Follow Up)

Measured Values	**Baseline Median Score**	**3-Month Median Score**	***Δ in Median Score Over Time***
HEI Score			
Intervention (n=3)	69.6*	65.6	**-4.0**
Control (n=4)	65.5*	72.4	**+6.9**

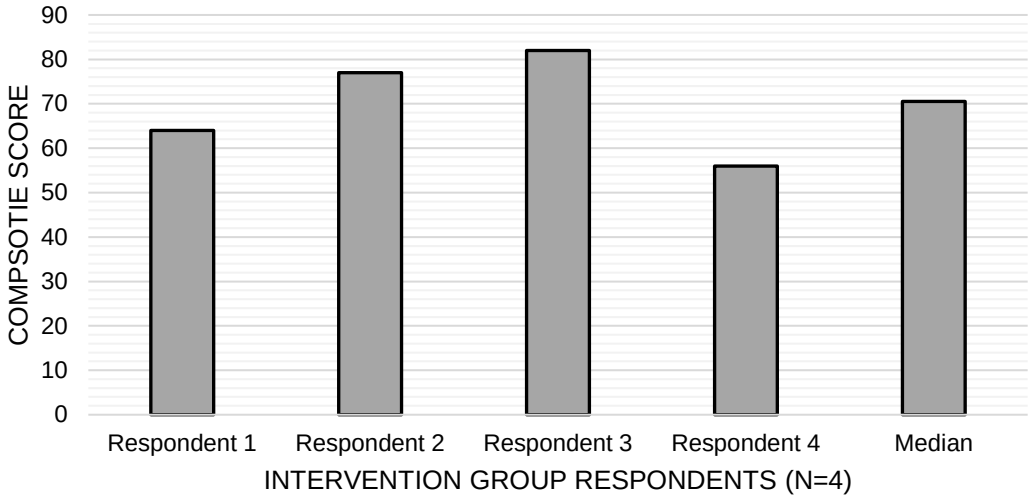
	Baseline Prevalence	**3-Month Prevalence**	***Δ in Prevalence Over Time***
Food Insecurity			
Overall (n=9)	40.00%*	44.44%	**+4.44%**
Intervention (n=5)	80.00%*	60.00%	**-20.00%**
Control (n=4)	0.00%*	25.00%	**+25.00%**

**Values derived from participants with both baseline and 3-month values*

D. Experiences of Intervention Participants with Imperfect Produce

Intervention participants within the sample population had a median composite score of 70.5 out of 90 on the Imperfect Produce Experience and Utilization Survey, indicating that participants overall reported more positive experiences and perceptions of the produce delivery service provided by Imperfect Produce. Composite scores from each survey respondent are detailed in Graph 6. A higher composite score on the Imperfect Produce Experience & Utilization Survey corresponds with greater (1) compliance with study protocol, (2) perceived convenience, (3) perceived improvement in fruit and vegetable intake, (4) perceived increase in use of fruits and vegetables, (5) satisfaction with produce quality, and (6) satisfaction with quantity of produce provided weekly.

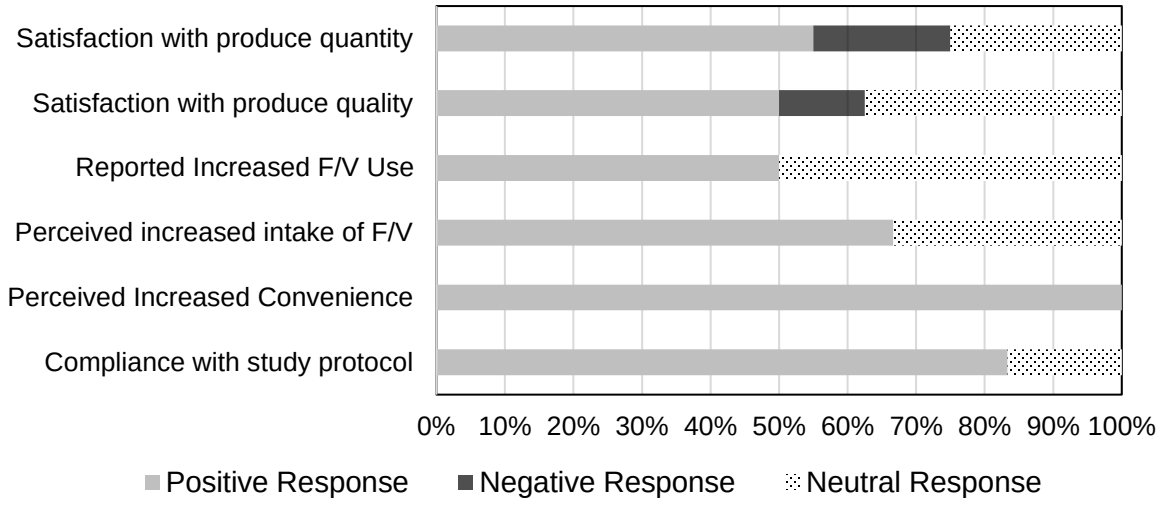
Graph 6. Imperfect Produce Experience & Utilization Survey Composite Score Distribution



Graph 7 highlights the trend in responses to the six aspects listed above, and categorizes responses as positive, negative, or neutral. Positive responses indicate a benefit or improvement was experienced by the respondent, while negative responses indicate a detriment was experienced. Responses were labeled neutral if they indicated little to no change. Fifty to seventy percent of responses were positive for the categories of produce quantity and quality, fruit and vegetable intake, and fruit and vegetable use in meals and recipes. One hundred percent of respondents reported they felt the produce delivery service was more convenient than shopping at the grocery store. Additionally, 83% of responses indicated high compliance with study protocol, indicating that the majority of participants report only ordering fruits, vegetables, or herbs to be delivered during the intervention. Two categories received negative responses: produce quantity and quality. Approximately 20% of responses indicated respondents either felt there was too much produce in their weekly delivered box, had to discard more than half of the produce received, or both. Reported satisfaction with produce quality was mixed, with 13% of responses indicating respondents did not eat the delivered produce due to poor quality, and 38% of responses indicating neutral feelings regarding the quality of the produce received. And, while the majority of responses show perceived improvements in fruit

and vegetable intake, the remaining 33% report no change in intake. Interestingly, half of respondents reported increased use of delivered produce into meals and recipes, while the other half reported no change in incorporation of fresh produce into meals and recipes. Not included in Graph 6 is sharing behavior associated with the produce boxes. All participants report that they shared the produce delivered with others in their household, which was permitted by study protocol.

Graph 7. Imperfect Produce Experience & Utilization Response Trends



Survey respondents indicated that no issues were experienced regarding delivery of the weekly produce boxes to the correct address or use of the ClinCard to fund the produce subscription. Incidence of spoiled produce found in a box at the time of delivery was low, with participants indicating this happened no more than two times over the 3-month period. However, variance in delivery date was a more prevalent issue, with one respondent indicating this happened one to two times, and another indicating this happened three to four times. Overall, respondents from the intervention group report they felt their experience with Imperfect Produce was either “good” or “great”, with only one participant rating their experience as “okay”. Echoing the universally perceived increase in convenience with the produce delivery service, one

respondent stated they “enjoyed / not having to go looking for the items [them]selves.” Multiple respondents mentioned the COVID-19 pandemic in their free responses. One respondent shared, “[The deliveries] were great, especially for the current situation.” Another stated they felt the deliveries were “more convenient than going to the store, especially during the COVID-19 pandemic.” However, when asked to compare the quality of the delivered produce to their preferred grocery store, two respondents indicated the delivered produce was of worse quality, with the other two reporting the produce being of either the same or better quality.

VII. DISCUSSION

Acknowledging the preliminary nature of our data, we found that, contrary to the original hypothesis, participants who received free, weekly deliveries of fresh produce did not display an overall increase in Healthy Eating Index (HEI) Score over time. Despite this finding, the majority of participants in the intervention group reported they perceived that their intake of fruits and vegetables had increased over the 3-month intervention period. Buyuktuncer and colleagues reported similar findings in their pilot fruit and vegetable prescription program. While no significant difference was observed in the consumption of fruits and vegetables before and after the intervention run by Buyuktuncer and colleagues, 62.7% of participants reported that they perceived their fruit and vegetable intake had increased as a result of the intervention.[38]

Furthermore, participants in the control group, who did not receive free fresh produce, did show an overall increase in Healthy Eating Index Score over time. This trend may be partially explained by the long term positive impacts nutrition education has been shown to have on patients’ dietary behaviors coupled with the minimal presence of food insecurity.[61] With no participants in the control group reporting food insecurity at baseline, and one reporting it at 3-months follow up, control group participants may overall have had a decreased perceived barrier of financial burden associated with healthy eating habits, making it more likely that they make these changes.[33] Additionally, HEI score reflects a much larger array of dietary choices

and patterns than fruit and vegetable intake.[58,62] Indeed, assessment of the total cups of fruits and vegetables consumed between groups revealed negligible changes in intake over time for both groups, but other dietary components, such as seafood, total saturated-, and polyunsaturated- fat intake, changed more favorably over time within the control group versus the intervention group, which may have contributed to the increase in median HEI score for the control group (Data not shown).

While at face value these DHQ survey responses appear to indicate that the intervention had no effect on fruit and vegetable intake, other parameters of the DHQ survey results indicate that the survey may not have been self-administered correctly. For example, multiple DHQ surveys indicated participants consumed less than 800 calories per day, based upon the answers that participants provided throughout the survey (Data not shown). Despite this, due to the small sample size of this sub-analysis, all participants who completed their surveys were included in the data analysis. The inaccurately completed DHQ surveys may be due in part to response burden, which is the amount of effort required of a respondent to complete a questionnaire or survey.[63] Longer surveys are typically associated with increased response burden and concomitant reductions in survey participation or completion, and the DHQ survey used in the present study is estimated to take 1-hour to complete.[63,64]

Although not a primary objective of this study, food insecurity was an important variable to monitor throughout this study, as it varied substantially between groups at both time points and over time. Since the Hunger Vital Sign Food Insecurity Screen asks respondents about their food situation at home over the last 12 months, changes in responses can be attributed to the time passed between baseline and 3-month follow up. Notably, food insecurity prevalence in the intervention group, but not in the control group, decreased over time. Unfortunately, there was a small increase in prevalence in food insecurity among the control group, with one participant reporting food insecurity at 3-months from baseline where they were food secure at baseline.

Other studies, such as Brighter Bites and a Head Start farm to family pilot program, showed similar reductions in food insecurity in groups receiving fresh produce.[49,50] However, unlike these two studies, this study occurred during a global pandemic which altered important factors related to food security, such as food availability and financial stability.

Studies which work with free-living adults are subject to be influenced by personal, work, and societal forces affecting their daily lives. In the case of this research study, the COVID-19 pandemic has contributed to disruptions to the health, wellbeing, and the structure and flow of individuals' daily lives worldwide, and is an important confounder to consider when interpreting the results of the present research. Unique stressors created by the COVID-19 pandemic that may have influenced the findings of this research include fear or stress related to visiting the grocery store, increased food scarcity, disruption in typical daily structure, such as inability to leave home to go to one's place of work, inability to dine in at restaurants, lack of stable income, and restricted avenues to engage in stress-reducing activities outside the home.[65,66] More research is needed to understand the psychosocial effects of the COVID19 pandemic and how this relates to overall health and health-related behaviors.

A. Limitations

As demonstrated by the substantial difference between screened eligible patients and patients actively enrolled, study recruitment (ongoing) was slow and resulted in too small sample size available for formal data analysis. Furthermore, despite block randomization to reduce disparities between groups, the intervention group had a substantially higher prevalence of food insecurity compared to the control group at baseline, which likely reflects the small number of subjects recruited and would be expected to even out with increased enrollment. This may confound the magnitude of improvement seen in cardiovascular risk factors (i.e. lipid profile, blood pressure) of the intervention group over time and the degree of difference between groups at 6-month follow-up. This study, like many human research trials conducted in 2020,

was affected by the COVID19 pandemic. For the protection and safety of study participants, no participants included in this data analysis had an in-clinic follow up visit at 3-months from baseline. This further limits the capacity to quantitatively assess the impact the intervention had on cardiovascular disease risk, as it was not possible to collect these anthropometric and plasma concentration data points immediately post-intervention. Finally, the small sample size precluded adequate assessment of racial or minority status (i.e. 80% Non-Hispanic White, mean age 56.30 ± 11.63 years), and these results are not generalizable to the United States adult population or to the subpopulation at increased risk for cardiovascular disease.

VIII. CONCLUDING REMARKS

The present thesis sought to determine the effect increased access to fruits and vegetables through a Food Rx program had on sustained dietary changes, as measured by the Healthy Eating Index (HEI) Score, and the effect this would have on perceived changes in dietary intake of- and cooking habits involving- fruits and vegetables. For the very limited number of subjects that could be studied at the time of this report, the results did not support the original hypothesis that receipt of fruits and vegetables would lead to improvements in HEI scores. However, the results did support the hypothesis that receipt of fruits and vegetables would lead to perceived increases in fruit and vegetable intake and use in cooking or meal preparation habits. This thesis presents the findings of a small subpopulation analysis from a larger study and are only appropriate for informing members of the research team for the Food Rx pilot study at the OHSU Knight Cardiovascular Institute. These findings are not generalizable to the United States adult population or those at increased risk for cardiovascular disease. More research is needed to determine the role fruit and vegetable prescription programs may play in reducing the risk of cardiovascular disease.

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