

THESIS

RELATIONSHIPS BETWEEN PLASMA CYTOKINES, LEUKOCYTE TELOMERE  
LENGTH, SERUM LIPID PROFILE, AND NUTRIENT INTAKE IN HEALTHY ADULTS  
FOLLOWING A 4-WEEK DIETARY INTERVENTION STUDY

Submitted by

Gregory James Harbison

Department of Environmental and Radiological Health Sciences

In partial fulfillment of the requirements

For the Degree of Master of Science

Colorado State University

Summer 2016

Master's committee:

Advisor: Elizabeth P. Ryan

Susan M. Bailey  
Ronald B. Tjalkens  
Tiffany L. Weir

Copyright by Gregory James Harbison 2016

All Rights Reserved

## ABSTRACT

### RELATIONSHIPS BETWEEN PLASMA CYTOKINES, LEUKOCYTE TELOMERE LENGTH, SERUM LIPID PROFILE, AND NUTRIENT INTAKE IN HEALTHY ADULTS FOLLOWING A 4-WEEK DIETARY INTERVENTION STUDY

Colorectal cancer is the third most commonly diagnosed cancer worldwide and the fourth leading cause of cancer-related death. The etiology of colorectal cancer is predominately attributed to modifiable lifestyle factors that promote chronic inflammation, and only 20% of colorectal cases are credited to hereditary syndromes. Specifically, recent nutritional studies have suggested that diet modification is a promising lifestyle intervention for reducing systemic inflammation and promoting colorectal cancer prevention and remission. In particular, rice and navy beans have been identified as two foods with anti-inflammatory and anti-neoplastic properties that warrant evaluation for chemoprevention through dietary supplementation in humans. In this study, plasma cytokines (IL-2, IL-4, IL-6, IL-8, IL-10, TNF, and VEGF) and leukocyte telomere length were measured at baseline, two weeks, and four weeks in individuals with and without a history of colorectal cancer who consumed a diet supplemented with rice bran, navy beans, or a placebo-control for 28 days. Serum lipid profile and nutrient intake were also measured. At baseline, the three diet intervention groups had no significant differences in cytokine concentration, telomere length, or lipid profile. At the end of the study, individuals with a history of colorectal cancer who consumed the navy bean supplemented diet had significantly higher plasma TNF and VEGF concentrations than individuals consuming the control diet. Otherwise, at the end of the study, no significant differences in cytokine concentration or

telomere length between groups existed. Additionally, compared to males, females with a history of colorectal cancer had significantly longer telomeres at baseline but not at four weeks. Females with a history of colorectal cancer also had significantly lower IL-4, IL-6, and IL-10 at baseline, but no significant difference was found at four weeks. Linear correlation analysis on repeated measures that adjusted for sex, age, and total energy intake showed significant correlations between several study variables. Telomere length was inversely correlated with age, serum triglyceride level, carbohydrate intake, and saturated fat intake. IL-2 and IL-4 concentrations were inversely correlated with  $\alpha$ -Tocopherol intake. IL-8 was inversely correlated with vitamin B3 intake. VEGF was positively correlated with vitamin B9 intake. Total serum cholesterol was positively correlated with saturated fat intake and inversely correlated with  $\beta$ -Carotene intake. Serum LDL was inversely correlated with  $\beta$ -Carotene intake, and serum HDL was positively correlated with intake of saturated fat and linolenic acid. Triglyceride level was inversely correlated with intake of  $\beta$ -Carotene and fiber and was positively correlated with selenium intake. Finally, comparison of two experimental methods for telomere length measurement showed positive but inconclusive correlations.

## ACKNOWLEDGEMENTS

This research was supported by the National Cancer Institute and was completed as part of the Beans/Bran Enriching Nutritional Eating For Intestinal Health Trial (BENEFIT). I thank Dr. Elizabeth Ryan and Dr. Susan Bailey for granting me this research opportunity and for providing insight and mentorship that greatly assisted this thesis. Thank you for your patience and support throughout this project. Similarly, I am grateful for the assistance and support I received from all current and former members of Dr. Ryan's lab including Erica Borresen, Genevieve Forster, Dustin Brown, Andrew Goodyear, Cadie Tillotson, Job Mapesa, Irfan Ghazi, and Sangeeta Rao. I also am thankful for the expertise and guidance provided by the members of Dr. Bailey's lab including Lynn Taylor, David Maranon, Brock Sishc, Miles McKenna, Christine Battaglia, and Chris Nelson. Additionally, this research would not have been achievable without support and equipment from the respective laboratories of Dr. Ronald Tjalkens, Dr. Tiffany Weir, Dr. Gerrit Bouma, and Dr. Christopher Bell. I also extend my gratitude to the University of Colorado Cancer Center Summer Research Fellowship for organizing the initial summer research project that prompted this thesis. Furthermore, I would like to acknowledge the individuals who volunteered to participate in the BENEFIT study. Without them, this project would not have been possible. Finally, I wish to thank my parents and my family for their encouragement, and I wish to express my whole-hearted appreciation to Kathy Demmon for her unwavering support and love.

## TABLE OF CONTENTS

ABSTRACT.....	ii
ACKNOWLEDGEMENTS.....	iv
LIST OF TABLES.....	vii
LIST OF FIGURES.....	xii
INTRODUCTION.....	1
CHAPTER 1: BACKGROUND.....	3
1.1 Colorectal cancer, inflammation, and cytokines.....	3
1.2 Colorectal cancer and telomere length.....	8
1.3 Colorectal cancer and diet.....	10
CHAPTER 2: MATERIALS AND METHODS.....	12
2.1 Study samples.....	12
2.2 Blood collection and processing.....	14
2.3 Cytokine immunoassay.....	14
2.4 Telomere length measurement by interphase quantitative fluorescence in situ hybridization (IQ-FISH).....	16
2.5 Telomere length measurement by singleplex qPCR.....	18
2.6 Telomere length measurement by monochrome multiplex qPCR.....	22
2.7 Nutrient data collection.....	23
2.8 Statistical analysis.....	24
2.8.1 Descriptive statistics.....	24
2.8.2 Normality testing.....	24
2.8.3 Cytokine statistical analysis.....	25
2.8.4 Analysis of longitudinal, between diet group, and between cohort differences.....	28
2.8.5 Linear correlation analysis.....	28
CHAPTER 3: RESULTS.....	30
3.1 Differences in plasma cytokine levels within and between diet groups.....	30
3.2 Differences in leukocyte telomere length within and between diet groups.....	45
3.3 Differences in lipid levels within and between diet groups.....	49
3.3.1 Study participants without a history of colorectal cancer.....	49
3.3.2 Study participants with a history of colorectal cancer.....	51
3.4 Differences in nutrient intake within diet groups.....	53
3.4.1 Study participants without a history of colorectal cancer.....	53
3.4.2 Study participants with a history of colorectal cancer.....	53
3.5 Differences in nutrient intake between diet groups.....	55
3.5.1 Study participants without a history of colorectal cancer.....	55
3.5.2 Study participants with a history of colorectal cancer.....	55
3.6 Differences in telomere length and cytokine concentration between sexes.....	72
3.7 Differences in lipid levels between sexes.....	74
3.8 Differences in nutrient intake between sexes.....	76
3.9 Linear repeated measures correlations.....	80
3.10 Differences in study variable between cohorts.....	95

3.11 Correlations between experimental methods for telomere length measurement.....	100
CHAPTER 4: DISCUSSION AND CONCLUSIONS.....	101
4.1 No positive effect on plasma cytokine concentrations or leukocyte telomere length after dietary supplementation with rice bran or navy beans.....	101
4.1.1 Relative increase in TNF and VEGF concentrations within navy bean diet group .....,.....	101
4.1.2 Study limitations and potential factors influencing results.....	103
4.2 Multiple individual dietary factors correlate with plasma cytokine level, leukocyte telomere length, and serum lipid concentrations.....	110
4.2.1 Cytokine correlations .....	110
4.2.1a IL-2 and IL-4 both inversely correlated with $\alpha$ -Tocopherol intake.....	111
4.2.1b IL-8 inversely correlated with vitamin B3 intake .....	112
4.2.1c VEGF positively correlated with vitamin B9 intake.....	113
4.2.2 Telomere length correlations.....	114
4.2.2a Telomere length inversely correlated with triglycerides.....	115
4.2.2b Telomere length inversely correlated with carbohydrate and saturated fat intake.....	115
4.2.3 Lipid profile correlations.....	116
4.2.3a Total cholesterol, LDL, and triglycerides inversely correlated with $\beta$ -Carotene intake .....	116
4.2.3b HDL positively correlated with linolenic acid intake; total cholesterol and HDL positively correlated with saturated fat intake.....	117
4.2.3c Triglycerides inversely correlated with fiber intake and positively correlated with selenium intake.....	117
4.2.4 Dietary patterns associated with healthy lifestyles.....	118
4.3 Correlation between qPCR and IQ-FISH methods for telomere length measurement is non-robust.....	119
4.3.1 Variability in telomere length of controls as measured by IQ-FISH .....	119
4.3.2 Significant but non-robust correlation between IQ-FISH and qPCR methods for telomere length measurement.....	121
4.3.3 Benefits and disadvantages for IQ-FISH and qPCR methods of telomere length measurement.....	122
CHAPTER 5: FUTURE DIRECTIONS.....	124
REFERENCES.....	125
APPENDIX I: Descriptive statistics of study participants without a history of CRC.....	140
APPENDIX II: Descriptive statistics of study participants with a history of CRC.....	143

## LIST OF TABLES

TABLE 1: Differences in age, weight, and body mass index between diet groups and between time points for study participants without a history of colorectal cancer .....	33
TABLE 2: Differences in plasma interleukin-2 and interleukin-4 between diet groups and between time points for study participants without a history of colorectal cancer.....	34
TABLE 3: Differences in plasma interleukin-6 and interleukin-8 between diet groups and between time points for study participants without a history of colorectal cancer.....	35
TABLE 4: Differences in plasma interleukin-10 and tumor necrosis factor between diet groups and between time points for study participants without a history of colorectal cancer.....	36
TABLE 5: Differences in age, weight, and body mass index between diet groups and between time points for study participants with a history of colorectal cancer.....	37
TABLE 6: Differences in plasma interleukin-2 between diet groups and between time points for study participants with a history of colorectal cancer.....	38
TABLE 7: Differences in plasma interleukin-4 between diet groups and between time points for study participants with a history of colorectal cancer.....	39
TABLE 8: Differences in plasma interleukin-6 between diet groups and between time points for study participants with a history of colorectal cancer.....	40
TABLE 9: Differences in plasma interleukin-8 between diet groups and between time points for study participants with a history of colorectal cancer.....	41
TABLE 10: Differences in plasma interleukin-10 between diet groups and between time points for study participants with a history of colorectal cancer.....	42
TABLE 11: Differences in plasma tumor necrosis factor between diet groups and between time points for study participants with a history of colorectal cancer.....	43
TABLE 12: Differences in plasma vascular endothelial growth factor between diet groups and between time points for study participants with a history of colorectal cancer.....	47
TABLE 13: Differences in leukocyte telomere length as measured by multiplex qPCR and IQ-FISH between diet groups and between time points for study participants with a history of colorectal cancer.....	48
TABLE 14: Differences in leukocyte telomere length as measured by singleplex qPCR between diet groups and between time points for study participants with a history of colorectal cancer.....	50
TABLE 15: Differences in serum lipids between diet groups and between time points for study participants with a history of colorectal cancer.....	51
TABLE 16: Differences in serum levels of total cholesterol, low-density lipoprotein, high-density lipoprotein, and triglycerides between diet groups and between time points for study participants with a history of colorectal cancer.....	52
TABLE 17: Differences in vitamin A, vitamin C, zinc, and calcium intake between diet groups and between time points for study participants without a history of colorectal cancer.....	58

TABLE 18: Differences in potassium, sodium, and iron intake between diet groups and between time points for study participants without a history of colorectal cancer.....	59
TABLE 19: Differences in calorie, protein, and carbohydrate intake between diet groups and between time points for study participants without a history of colorectal cancer.....	60
TABLE 20: Differences in fat, saturated fat, and fiber intake between diet groups and between time points for study participants without a history of colorectal cancer.....	61
TABLE 21: Differences in vitamin A, $\beta$ -Carotene, and vitamin C intake between diet groups and between time points for study participants with a history of colorectal cancer.....	62
TABLE 22: Differences in vitamin D, vitamin E, and $\alpha$ -Tocopherol intake between diet groups and between time points for study participants with a history of colorectal cancer.....	63
TABLE 23: Differences in vitamin B1 (thiamin), vitamin B2 (riboflavin), and vitamin B3 (niacin) intake between diet groups and between time points for study participants with a history of colorectal cancer.....	64
TABLE 24: Differences in vitamin B6 (pyridoxine), vitamin B9 (folate), and vitamin B12 (cobalamin) intake between diet groups and between time points for study participants with a history of colorectal cancer.....	65
TABLE 25: Differences in zinc, calcium, potassium, and sodium intake between diet groups and between time points for study participants with a history of colorectal cancer.....	66
TABLE 26: Differences in iron, magnesium, and selenium intake between diet groups and between time points for study participants with a history of colorectal cancer.....	67
TABLE 27: Differences in calorie, protein, carbohydrate, and fat intake between diet groups and between time points for study participants with a history of colorectal cancer.....	68
TABLE 28: Differences in saturated fat, oleic acid, linoleic acid, and linolenic intake between diet groups and between time points for study participants with a history of colorectal cancer.....	69
TABLE 29: Differences in fiber intake between diet groups and between time points for study participants with a history of colorectal cancer.....	70
TABLE 30: Differences in leukocyte telomere length between sexes for study participants with a history of colorectal cancer.....	72
TABLE 31: Differences in plasma cytokine concentrations between sexes for study participants with a history of colorectal cancer.....	73
TABLE 32: Differences in age, weight, BMI, and cholesterol between sexes for study participants with a history of colorectal cancer.....	75
TABLE 33: Differences in serum triglyceride levels between sexes for study participants with a history of colorectal cancer.....	75
TABLE 34: Differences in vitamin intake between sexes for study participants with a history of colorectal cancer.....	77

TABLE 35: Differences in vitamin B2 and vitamin B3 intake between sexes for study participants with a history of colorectal cancer.....	77
TABLE 36: Differences in intake of minerals, macronutrients, fatty acids, and fiber between sexes for study participants with a history of colorectal cancer.....	78
TABLE 37: Differences in intake of sodium, selenium, calories, protein, and total fat between sexes for study participants with a history of colorectal cancer.....	79
TABLE 38: Linear correlations between weight, BMI, serum lipids, and leukocyte telomere length .....	85
TABLE 39: Linear correlations for IL-2, IL-4, and IL-6 concentrations with weight, BMI, serum lipids, and leukocyte telomere length .....	85
TABLE 40: Linear correlations for IL-8, IL-10, TNF, and VEGF concentrations with weight, BMI, serum lipids, and leukocyte telomere length.....	86
TABLE 41: Linear correlations for vitamin intake with weight, BMI, serum lipids, and leukocyte telomere length .....	87
TABLE 42: Linear correlations B vitamin intake with weight, BMI, serum lipids, and leukocyte telomere length .....	88
TABLE 43: Linear correlations mineral intake with weight, BMI, serum lipids, and leukocyte telomere length .....	89
TABLE 44: Linear correlations total protein, carbohydrate, fat, saturated fat, oleic acid, linoleic acid, and linolenic acid intake with weight, BMI, serum lipids, and leukocyte telomere length .....	90
TABLE 45: Linear correlations for vitamin intake with plasma cytokine concentrations.....	91
TABLE 46: Linear correlations for B vitamin intake with plasma cytokine concentrations.....	92
TABLE 47: Linear correlations for mineral intake with plasma cytokine concentrations.....	93
TABLE 48: Linear correlations for macronutrient, fatty acid, and fiber intake with plasma cytokine concentrations.....	94
TABLE 49: Comparison of age, weight, body mass index, total cholesterol, low-density lipoprotein, and high-density lipoprotein of study participants without a history of colorectal cancer to participants with a history of colorectal cancer.....	95
TABLE 50: Comparison of serum triglyceride level of study participants without a history of colorectal cancer to participants with a history of colorectal cancer.....	96
TABLE 51: Comparison of plasma cytokine concentrations of study participants without a history of colorectal cancer to participants with a history of colorectal cancer.....	97
TABLE 52: Comparison of sodium, calorie, protein, and total fat intake of study participants without a history of colorectal cancer to participants with a history of colorectal cancer.....	98
TABLE 53: Comparison of dietary intake variables of study participants without a history of colorectal cancer to participants with a history of colorectal cancer.....	99
TABLE 54: Linear correlations between multiplex qPCR telomere length and respective batches of IQ-FISH telomere length.....	100
TABLE 55: Descriptive statistics by time point of age, weight, BMI, and lipid profile for study participants without a history of colorectal cancer .....	140
TABLE 56: Descriptive statistics by time point of IL-2, IL-4, IL-6, IL-8, IL-10, and TNF for study participants without a history of colorectal cancer.....	141
TABLE 57: Descriptive statistics by time point of dietary intake components for study participants without a history of colorectal cancer.....	142

TABLE 58: Descriptive statistics by time point of age, weight, BMI, and lipid profile for study participants with a history of colorectal cancer.....	143
TABLE 59: Descriptive statistics by time point and diet group of age, weight, BMI, and lipid profile for study participants with a history of colorectal cancer.....	144
TABLE 60: Descriptive statistics by time point and sex of age, weight, BMI, and lipid profile for study participants with a history of colorectal cancer.....	145
TABLE 61: Descriptive statistics by time point of IL-2, IL-4, IL-6, IL-8, IL-10, TNF, and VEGF for study participants with a history of colorectal cancer.....	146
TABLE 62: Descriptive statistics by time point and diet group of IL-2 and IL-4 for study participants with a history of colorectal cancer.....	147
TABLE 63: Descriptive statistics by time point and diet group of IL-6 and IL-8 for study participants with a history of colorectal cancer.....	148
TABLE 64: Descriptive statistics by time point and diet group of IL-10 and TNF for study participants with a history of colorectal cancer.....	149
TABLE 65: Descriptive statistics by time point and diet group of VEGF for study participants with a history of colorectal cancer.....	150
TABLE 66: Descriptive statistics by time point and sex of IL-2, IL-4, IL-6, IL-8, IL-10, TNF, and VEGF for study participants with a history of colorectal cancer.....	151
TABLE 67: Descriptive statistics by time point telomere length for study participants with a history of colorectal cancer.....	152
TABLE 68: Descriptive statistics by time point and diet group of telomere length for study participants with a history of colorectal cancer.....	153
TABLE 69: Descriptive statistics by time point and sex of telomere length for study participants with a history of colorectal cancer.....	154
TABLE 70: Descriptive statistics by time point of vitamin intake for study participants with a history of colorectal cancer.....	155
TABLE 71: Descriptive statistics by time point and diet group of vitamin A, $\beta$ -Carotene, vitamin C, vitamin D, and $\alpha$ -Tocopherol intake for study participants with a history of colorectal cancer.....	156
TABLE 72: Descriptive statistics by time point and diet group of B vitamin intake for study participants with a history of colorectal cancer.....	157
TABLE 73: Descriptive statistics by time point and sex of vitamin intake for study participants with a history of colorectal cancer.....	158
TABLE 74: Descriptive statistics by time point of mineral intake for study participants with a history of colorectal cancer.....	159
TABLE 75: Descriptive statistics by time point and diet group of mineral intake for study participants with a history of colorectal cancer.....	160
TABLE 76: Descriptive statistics by time point and sex of mineral intake for study participants with a history of colorectal cancer.....	161
TABLE 77: Descriptive statistics by time point of calories, protein, carbohydrate, fat, saturated fat, fatty acid, and fiber intake for study participants with a history of colorectal cancer.....	161
TABLE 78: Descriptive statistics by time point and diet group of calories, protein, carbohydrate, fat, and saturated fat intake for study participants with a history of colorectal cancer.....	162

TABLE 79: Descriptive statistics by time point and diet group of fatty acid and fiber intake for study participants with a history of colorectal cancer.....	163
TABLE 80: Descriptive statistics by time point and sex of calories, protein, carbohydrate, fat, saturated fat, fatty acid, and fiber intake for study participants with a history of colorectal cancer.....	164

## LIST OF FIGURES

FIGURE 1: Study participant randomization flow chart.....	13
FIGURE 2: Graphs of plasma concentrations of IL-2, IL-4, IL-6, IL-8, and IL-10 for study participants with a history of colorectal cancer.....	31
FIGURE 3: Graphs of plasma concentrations of TNF and VEGF for study participants with a history of colorectal cancer.....	32
FIGURE 4: Graph of multiplex qPCR telomere length for study participants with a history of colorectal cancer .....	46
FIGURE 5: Correlation graphs of significant lipid associations for study participants with a history of colorectal cancer.....	82
FIGURE 6: Correlation graphs of significant cytokine associations for study participants with a history of colorectal cancer.....	83
FIGURE 7: Correlation graphs of significant telomere length associations for study participants with a history of colorectal cancer.....	84

## INTRODUCTION

Colorectal cancer is the third most commonly diagnosed cancer worldwide and the fourth leading cause of cancer-related death.[1] The distribution of colorectal cancer varies by location, with higher prevalence and incidence in more developed nations, and within the United States, the lifetime risk of developing colorectal cancer is 1 in 20.[1-3] Numerous studies have associated the risk of colorectal cancer development with several modifiable lifestyle factors, and by some estimates, approximately half of all colorectal cancer in the United States may be preventable through maintaining an appropriate diet, physical activity level, and body weight.[1, 4] Fortunately, due to increased screening and improved methods of treatment, the mortality rate of colorectal cancer has progressively declined over the last several decades, and today, the 5-year relative survival rate for early stage colorectal cancers is approximately 90%.[2] As a result, there are over 1 million people in the United States with a past medical history of colorectal cancer, and recent observational studies of this population have suggested the modification of high-risk lifestyle factors as a promising intervention for the prevention of colorectal cancer recurrence.[5-7]

The etiology of colorectal cancer is predominately attributed to modifiable lifestyle factors with only 20% of cases credited to hereditary syndromes, such as familial adenomatous polyposis, and the most significant lifestyle factors related to colorectal cancer occurrence include physical inactivity, obesity, smoking behavior, alcohol use, and poor dietary habits.[8-15] These factors all have a shared tendency to induce chronic inflammation, which is strongly implicated in the development and progression of colorectal cancer and multiple other pathologies.[16, 17]

The significance of inflammation in the development and promotion of colorectal cancer is strongly supported by data demonstrating the protective effect of long-term aspirin and non-steroidal anti-inflammatory drug (NSAID) use.[18-21] However, the chronic use of these drugs is often problematic; they are known to cause adverse effects, such as gastrointestinal ulcers or bleeding, and their use is not appropriate for individuals with contraindicating conditions, such as liver disease or coagulopathies.[22, 23] Consequently, non-pharmaceutical alternatives for reducing inflammation, such as through diet and physical activity interventions, have arisen as promising approaches for the prevention of colorectal cancer incidence and recurrence.[7, 24-28]

In this study, the potential for a 28-day dietary intervention program to modulate blood biomarkers of inflammation and aging in a population of healthy individuals with and without a history of colorectal cancer was investigated. Specifically, the effect of a rice bran or navy bean supplemented diet on the concentration of seven distinct circulating plasma cytokines and on leukocyte telomere length was explored. The primary hypothesis of this investigation was that individuals who consumed a rice bran or navy bean supplemented diet for 28 days would have lower levels of inflammatory plasma cytokines and display slower rates of leukocyte telomere degradation compared to individuals who consumed a control diet. As a secondary component, potential correlations between plasma cytokine concentrations, leukocyte telomere length, serum lipid profile, and nutrient intake were examined with the supposition that poor dietary habits would be associated with dyslipidemia, increased inflammatory cytokine levels, and relatively shorter leukocyte telomeres. Lastly, a final goal of this study was to compare and assess the degree of correlation between two distinct experimental methods for telomere length estimation: fluorescence in situ hybridization and quantitative polymerase chain reaction.

## CHAPTER 1: BACKGROUND

### 1.1 Colorectal cancer, inflammation, and cytokines

Chronic inflammation results from the dysfunction of acute inflammatory processes. In healthy individuals, acute inflammatory responses to cellular injury caused by infectious, chemical, or mechanical stimuli occur rapidly and are mediated by immune cells, cytokines, cell-adhesion molecules, complement peptides, and other specialized molecules through the induction of vasodilation, vascular permeability, chemotaxis, and phagocytosis.[29] In the setting of persistent, systemic inflammatory stimulation, such as with regular cigarette smoking or red meat consumption, acute inflammatory processes designed to protect against cellular insult progress into chronic inflammation and self-harm.[30-33]

The association between inflammation and cancer development is well established, and prolonged immune activation has been shown to increase the likelihood of carcinogenesis through multiple mechanisms including the accumulation of chromosomal mutations via reactive oxygen species (ROS), the promotion of angiogenesis by proliferative growth factors, and the inhibition of apoptosis through oncogenic signaling molecules.[9, 16, 34-40]

Inflammatory processes are driven by cytokines, a large class of low molecular weight glycoproteins produced by both immune and non-immune cells in order to regulate the immune system.[17, 29] Cytokines play a vital role in mediating immunity, inflammation, and hematopoiesis by activating genes for growth, differentiation, and cell activity, and there is substantial evidence to show their utilization by tumors for progression and survival.[41, 42] Furthermore, individual cytokines are often pleiotropic, and thus able to exert multiple effects depending on cell or tissue type.[43] As a result, the cytokine network possesses many

redundancies, synergisms, and antagonisms, which enable coordinated regulation of amplitude and duration of immune responses.[43] Finally, the synthesis and secretion of cytokines is often brief and self-limiting, and due to their potency, small changes in circulating cytokine concentrations can produce dramatic effects.[43]

Chronic systemic inflammation secondary to environmental risk factors is overwhelmingly implicated in the development and progression of colorectal cancer.[9, 39, 40] Interleukin-6 (IL-6) and tumor necrosis factor (TNF) are two particularly inflammatory cytokines that play key roles in the initiation and progression of inflammation-associated cancers.[17, 44] Both cytokines are potent inducers of reactive oxygen species, which have been shown to increase genomic instability and promote carcinogenesis.[39, 45] Additionally, IL-6 and TNF regulate the proliferation, survival, invasion, and metastasis of cancer cells through induction of pro-tumorigenic transcription factors such as Signal Transducer and Activator of Transcription 3 (STAT3) and Nuclear Factor- $\kappa$ B (NF- $\kappa$ B), respectively.[17, 44, 46-50] Accordingly, higher systemic concentrations of IL-6 and TNF are associated with both colorectal cancer occurrence and severity.[51-58]

Other cytokines with significant effects on chronic inflammation and colorectal carcinogenesis include interleukin-8 (IL-8), vascular endothelial growth factor (VEGF), interleukin-2 (IL-2), interleukin-10 (IL-10), and interleukin-4 (IL-4).

IL-8 is a potent chemotactic factor for neutrophils and plays a significant role in angiogenesis.[59, 60] IL-8 directly regulates angiogenesis through promoting endothelial cell proliferation and inhibiting apoptosis via surface receptor binding.[61] This process also enhances the activity of proteinases involved in the breakdown of the extracellular matrix.[61] Additionally, IL-8 indirectly promotes angiogenic processes by activating vascular endothelial

growth factor.[62-64] IL-8 is primarily produced and secreted by macrophages through NF- $\kappa$ B pathways activated by pro-inflammatory cytokines such as TNF, and within tumor microenvironments, macrophage overexpression of IL-8 contributes to invasion and metastasis.[65-67] Consequently, high concentrations of IL-8 are strongly associated with colorectal carcinoma occurrence, development, prognosis, and recurrence.[68-73]

VEGF is a platelet-derived growth factor capable of highly specific mitogenic activity on endothelial cells.[74] VEGF expression is directly stimulated by STAT3 activity, and similar to IL-8, binding between VEGF and receptors on the vascular endothelium promotes endothelial cell proliferation and expression of molecules required for reorganization of the extracellular matrix.[74-76] These processes initiate angiogenesis, and thus are vital for normal growth and wound healing. However, they also perform an essential function in solid tumor development and progression, and higher concentrations of serum VEGF are associated with colorectal cancer occurrence, severity, and recurrence.[71, 77-81]

IL-2 occupies a critical role in regulating inflammatory immune responses, and it has both dual and complementary functions through its ability to both provoke and inhibit inflammatory immune processes.[82] IL-2 displays pro-inflammatory properties through its ability to stimulate T cell proliferation and survival, promote CD8<sup>+</sup> T cell and natural killer (NK) cell cytolytic activity, and control naïve CD4<sup>+</sup> T cell differentiation into T helper 1 (T<sub>h</sub>1) cells.[83-88] Additionally, IL-2 possesses anti-inflammatory functions by modulating systemic inflammation through maintaining peripheral levels of T<sub>reg</sub> cells, a subset of T cells with immunosuppressive properties, and inhibiting differentiation of T helper 17 cells (T<sub>h</sub>17), a subset of T cells that secrete pro-inflammatory cytokines such as IL-6.[89-92] Both T<sub>reg</sub> and T<sub>h</sub>17 cells are abundant in the intestine, and their dysregulation is associated with several autoimmune and

inflammatory diseases such as inflammatory bowel disease.[45, 92, 93] However, given the contrasting regulatory functions of IL-2, the implications of high serum IL-2 are not well understood. While at least one study has found an association between high plasma IL-2 and reduced colorectal cancer recurrence, multiple other studies have failed to reproduce similar findings, and a robust association between IL-2 and colorectal cancer risk has not been established.[83, 94-96]

IL-10 is an anti-inflammatory cytokine that exerts significant immunosuppressive effects through its ability to suppress the secretion of inflammatory cytokines by T<sub>h</sub>1 cells, T<sub>h</sub>17 cells, and macrophages and to prevent antigen presentation by dendritic cells, macrophages, and B-cells.[97-100] IL-10 is secreted by nearly all leukocytes, as well as tumor cells, and it limits immune responses and promotes homeostasis by activating STAT3 signaling pathways that selectively prevent cytokine expression.[101-103] Depending on the context, IL-10 has both pro-tumorigenic and anti-tumorigenic abilities. Through curtailing chronic inflammatory processes, IL-10 exhibits a capacity for preventing tumor initiation and progression in healthy tissues, and several *in vitro* and animal models support this concept.[104-108] However, in the presence of established tumors, IL-10 can encourage proliferation and metastasis by suppressing anti-cancer immune responses.[104, 109, 110] In this regard, several observational studies have found a positive correlation between elevated serum IL-10 concentration and colorectal cancer severity and prognosis.[96, 111-113]

IL-4 is generally labeled as an anti-inflammatory cytokine given its capacity to inhibit macrophages and suppress secretion of pro-inflammatory cytokines such as TNF via activation of Signal Transducer and Activator of Transcription 6 (STAT6) pathways.[114-116] Early *in vitro* studies on IL-4 demonstrated a growth inhibitory effect on colorectal cancer cells, and IL-4

was initially investigated as a possible stimulatory target for cancer immunotherapy.[117, 118] However, later studies implicated IL-4 as a tumor promoter through demonstrating its ability to inhibit apoptosis and stimulate angiogenesis in mature cancer cells.[119-121] Recently, IL-4 has been observed to be secreted by and prevent the death of colorectal cancer stem-like cells, a small population of self-regenerating and treatment-resistant cells that support the initiation and progression of colorectal tumors.[122-124] Accordingly, elevated serum IL-4 concentration in colorectal cancer patients has been associated with poor disease prognosis.[55] However, the association of serum IL-4 concentration with colorectal cancer initiation or recurrence has not been strongly established, and several studies have not observed a significant correlation between serum IL-4 and colorectal cancer risk.[125-127]

Overall, dual and contradicting effects that are dependent on the duration, magnitude, and setting of the immune response characterize inflammation in relation to colorectal cancer. A properly regulated inflammatory response protects against malignancy and is critical for the maintenance of host tissue integrity. However, when this process is prolonged or impaired, such as during chronic, low-grade insult by environmental stimuli, the likelihood of carcinogenesis is amplified. Additionally, an immune response can have drastically different consequences depending on its local surroundings. This is evidenced within the tumor microenvironment, where an anti-inflammatory or wound healing immune mechanism may be hijacked to promote tumor proliferation and invasion. Thus, the interpretation of immunological data is not a straightforward endeavor, and at this time, definitive conclusions regarding the exact effect of a specific cytokine level in an individual are impractical and unrealistic. Nevertheless, the investigation of serum cytokine levels is a worthwhile and accessible enterprise as it provides

greater comprehension and understanding of inflammation's role in disease and has led to the development of numerous immunotherapies.[128, 129]

## **1.2 Colorectal cancer and telomere length**

Telomeres cap the ends of human chromosomes and play critical roles in maintaining genome stability.[130, 131] The specialized nucleoprotein structure of telomeres prevents loss of genetic material after each cycle of replication and protects against recombination with other chromosomes.[132] Composed of tandem nucleotide repeats (5'-TTAGGG-3') and an array of associated proteins, human telomeres progressively shorten with every cell division. This erosion is a result of the end-replication problem in eukaryotes, where conventional DNA polymerases are unable to synthesize in the 3'-5' direction.[130, 133] Due to this mechanism, telomere degradation is strongly correlated with increased age.[134] However, there is considerable inter-individual variation of telomere length based upon hereditary and environmental factors. Similar to inflammation, telomere length is influenced by a host of lifestyle factors, including physical inactivity, obesity, smoking behavior, alcohol use, and diet.[135-139]

Colorectal cancer risk has been associated with telomere dysfunction in colon epithelial cells and circulating leukocytes, with both long and short telomeres implicated in colorectal cancer occurrence.[140-144] However, a recent study suggested this bimodal association is a result of the age of onset of colorectal cancer; young individuals with longer telomeres and older individuals with shorter telomeres were both found to be at increased risk of colorectal cancer development.[145] Given that the majority of colorectal cancer occurs in older individuals, telomere length shortening is most consistently linked to colorectal cancer incidence and progression.[146, 147] Thus, shorter leukocyte and colonic telomere length have been proposed

as potential biomarkers for assessing colorectal cancer risk, diagnosis, and progression.[143, 148-151]

Additionally, telomere erosion in colonic epithelial cells can play a pivotal role in the early stages of colorectal carcinogenesis through triggering chromosomal instability.[152-154] This effect is quite significant given chromosomal instability is observed in 65-70% of sporadic colorectal cancer cases.[155] Typically, when telomeres in healthy cells reach a critically short length, termed the Hayflick limit, replicative senescence and apoptosis occur, and through this process, tumorigenesis is inhibited.[156-158] However, if severe telomere dysfunction precedes activation of cell cycle arrest, or tumor suppressive mechanisms such as p53 are compromised, continued mitosis causes progressive telomere degradation and results in the complete loss of one or more telomeres.[152, 155] Genomic instability subsequently ensues through chromosomal aberrations caused by end-to-end fusions and a succession of breakage-fusion-bridge cycles.[159] This process produces gross chromosomal instability and thus demonstrates the direct mechanistic effect that telomere length degradation within colon cells can play in the initiation of colorectal cancer.[152, 160, 161]

Conversely, shorter leukocyte telomere length has not been directly implicated in the promotion of colorectal cancer. Leukocyte telomere length is indicative of an individual's relative degree of biological aging, and considerable evidence suggests a strong correlation between chronic systemic inflammation and shortened telomere length.[162, 163] Correspondingly, leukocyte telomere length has been associated with increased risk of inflammation-associated colorectal cancer, and significant leukocyte telomere attrition in colorectal cancer patients is frequently accompanied by immune dysregulation and decreased probability of long-term survival.[140, 144, 162-164] As a result, leukocyte telomere length has

been implicated as a potential biomarker for the likelihood of colorectal cancer development and prognosis.[143, 148]

### **1.3 Colorectal cancer and diet**

The effect of poor diet on increased colorectal cancer risk is well demonstrated, and in particular, the Western diet, with high levels of consumption of refined carbohydrates and processed meat, is linked with increased cancer risk.[165] Given this finding, it is no surprise that multiple studies have demonstrated the effectiveness of diet modulation and supplementation in the reduction of chronic inflammation and colorectal cancer risk.[166-176]

Specifically, there is strong evidence to support decreased risk of colorectal cancer with the consumption of unrefined grains and legumes.[177-183] The chemoprevention ability of grains and legumes is primarily attributed to these foods' high dietary fiber content.[183-185] The phytochemical and antioxidant content of grains and legumes may also play a role in the prevention of colorectal cancer but this association is less established.[186-190]

Dietary fiber refers to a diverse group of plant carbohydrates that resist digestion and absorption in the small intestine and undergo fermentation into short-chain fatty acids in the colon.[191, 192] Dietary fiber helps prevent colonic tissue injury from chronic inflammation by serving as a nutrition source for the microorganisms that protect intestinal epithelial cells.[193] Additionally, fermentation of dietary fiber results in decreased colonic inflammation through the inhibitory effects of short-chain fatty acids on chemokines such as interleukin-8 and on pro-inflammatory cytokines such as tumor necrosis factor.[194-196] An inverse association between a high-fiber diet and peripheral systemic inflammation has also been demonstrated.[197, 198]

The high phytochemical and antioxidant content of grains and legumes also contributes to their anti-inflammatory and anti-neoplastic properties. For example, rice bran, the outer layer of the rice grain (*Oryza* spp.), possesses several bioactive components, such as  $\gamma$ -oryzanol, ferulic acid, tocopherols/tocotrienols, and tricin, that are known to have antioxidant and anti-inflammatory effects.[199, 200] Similarly, common beans (*Phaseolus vulgaris* L.) have high concentrations of bioactive phenolic compounds, such as catechin, ferulic acid, *p*-Coumaric acid, kaempferol,  $\beta$ -Carotene, and  $\gamma$ -Tocopherol, which exhibit anti-inflammatory properties.[201]

In relation to colorectal cancer, recent nutritional studies have identified rice bran and navy beans as foods with potential for chemoprevention.[199, 202-204] Animal studies have also demonstrated the ability of these foods to decrease both local and systemic biomarkers of inflammation and improve colonic health.[205-208] Given the evidence for these foods' anti-inflammatory and anti-neoplastic effects, this study evaluated their ability to modulate markers of inflammation in a population of healthy adults with and without a history of colorectal cancer.

## CHAPTER 2: MATERIALS AND METHODS

### 2.1 Study samples

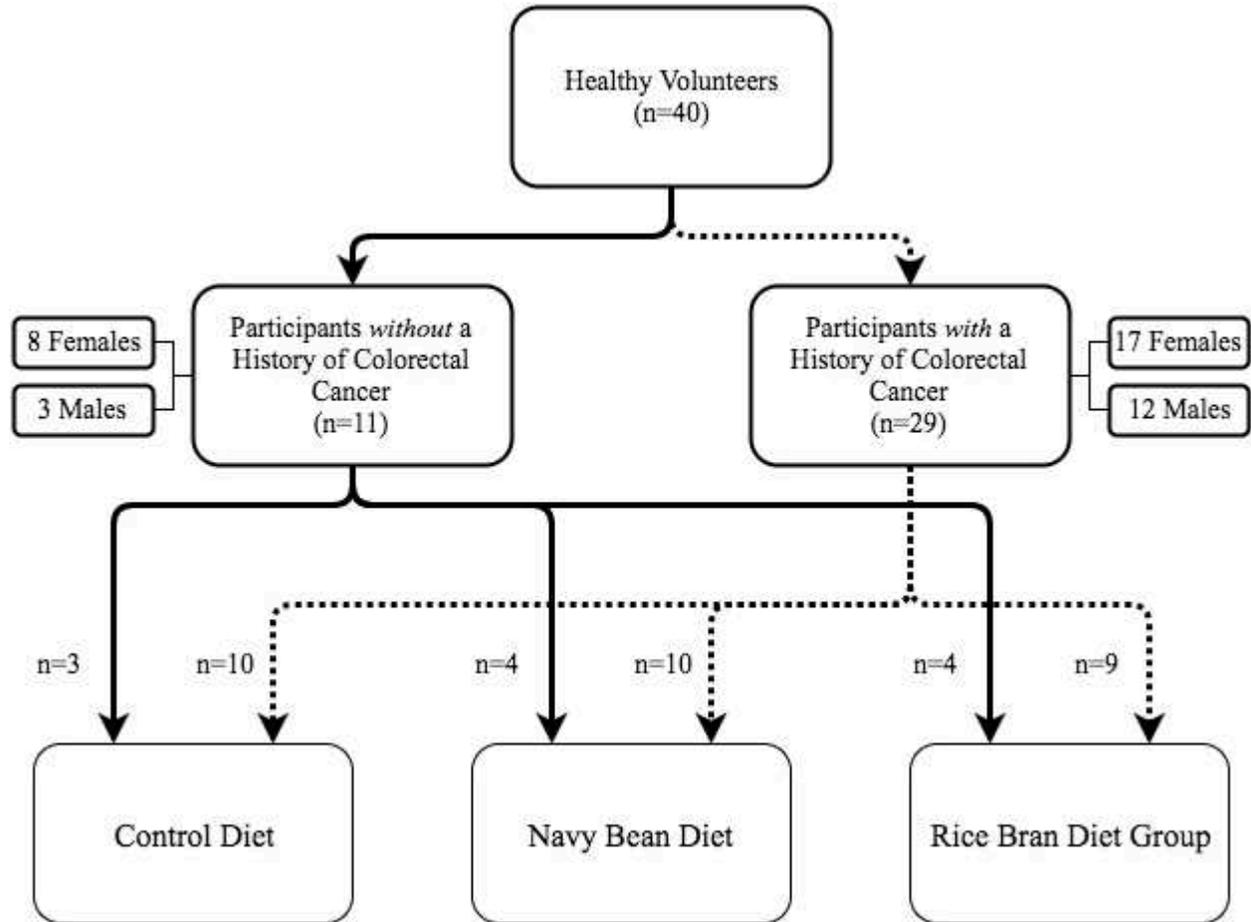
A total of 40 healthy individuals were evaluated in this study, and within this population, two cohorts were separately classified based upon whether or not they possessed a past medical history of colorectal cancer. The cohort of individuals with a history of colorectal cancer was comprised of seventeen females and twelve males, and the cohort without a history of colorectal cancer consisted of eight females and three males.

Each study participant was randomly assigned to either a control, navy bean, or rice bran dietary intervention group, and during the 28 day study, participants consumed one meal and one snack specially designed to provide a daily dietary treatment of either 35 g of navy bean powder, 30 g of rice bran, or a placebo control. Other than substituting one meal and one snack per day, participants were not asked to modify their previous dietary habits.

For the cohort of individuals with a history of colorectal cancer, ten individuals were assigned to a control diet, ten individuals were assigned to a navy bean diet, and nine individuals were assigned to a rice bran diet. For the eleven total individuals without a history of colorectal cancer, three individuals were in the control group, four individuals were in the navy bean group, and three individuals were in the rice bran group.

Study participants with a history of colorectal cancer were confirmed to have not undergone chemotherapy or radiation therapy within the last four months and all volunteers in the study had no history of any other form of cancer. Participants also did not have a history of gallstones, food allergies, or significant dietary restrictions. Additionally, all study participants

denied any current tobacco use or the use within the last month of any prescription antibiotics. Finally, no females in the study were pregnant or breast-feeding.



**Figure 1:** Study participant randomization flow chart. All individuals were healthy volunteers who participated in a 28-day dietary intervention trial. Participants were randomized by age, BMI, and total daily caloric intake into a control, navy bean (35 g/day), and rice bran (30 g/day) supplementation treatment group. Each individual consumed one meal and one snack per day that contained the dietary treatment. Otherwise, participants' diets were not restricted in any other manner and were allowed to consume any other foods they desired. Each participant completed a three-day food journal at three separate periods during the 28-day study in order to estimate average daily nutritional intake.

## **2.2 Blood collection and processing**

Whole blood samples were collected from all study participants by a licensed phlebotomist on day 0, day 14, and day 28 of the study. Prior to blood collection, all participants fasted for at least eight hours to eliminate any effects of recent food intake on serum lipid profile. While lipid levels were measured in an outside clinical laboratory, all other blood component analysis was performed at Colorado State University within the respective laboratories of Dr. Elizabeth Ryan or Dr. Susan Bailey.

After collection, plasma samples were isolated by centrifugation with EDTA and stored at -80°C in Mr. Frosty Freezing Containers filled with isopropyl alcohol. Samples were thawed on ice immediately prior to the cytokine immunoassay, and all samples analyzed had not previously been thawed since collection.

Leukocytes were isolated by centrifugation using Cell Preparation Tubes (CPT) (BD Biosciences) with sodium citrate. Leukocyte samples were rinsed in 1X phosphate buffered saline (PBS), suspended in cell freezing media (10% DMSO: 90% FBS), and cryopreserved in liquid nitrogen vapor. Prior to telomere length measurement, leukocytes were thawed, rinsed in 1X PBS, counted, and split into separate fractions for telomere length measurement by both quantitative polymerase chain reaction and interphase fluorescence in situ hybridization.

## **2.3 Cytokine immunoassay**

The cytokines IL-2, IL-4, IL-6, IL-8, IL-10, and TNF were measured in the plasma of a total of eleven individuals without a history of colorectal cancer and 23 individuals with a history of colorectal cancer. VEGF concentrations were also obtained from 23 participants with a history of colorectal cancer but VEGF measurements from individuals without a history of colorectal

cancer were excluded from analysis as the quality control for this analyte fell outside of the acceptable range for quality assay performance. Quality controls for all other analytes were within acceptable range.

Plasma cytokine levels were measured using the Milliplex® MAP Human Cytokine/Chemokine Magnetic Bead Panel Immunoassay. Non-diluted plasma samples were prepared for analysis in a 96 well plate following the specific protocol provided by Millipore. Analytes were quantified using a MagPix analytical test instrument, which utilizes xMAP technology (Luminex Corp., Austin, TX) and xPONENT software (Luminex). The xMAP technology uses fluorescent magnetic beads coated with analyte specific capture antibodies to simultaneously measure multiple analytes in a sample. After the beads have captured the analyte, a biotinylated detection antibody binds to the complex. Streptavidin PE binds as a reporter molecule. Inside the Luminex instrument, magnetic beads are held in a monolayer by a magnet and two LEDs are used to excite the internal bead dye and the reporter molecule. Fluorescence intensity is measured by an internal charge coupled device camera, and mean fluorescence intensity (MFI) is recorded per well. Minimum bead count for acceptable fluorescence was set at 50 beads per well. Cytokine concentrations (pg/mL) were based on a six point standard curve generated for each cytokine. A weighted 5-parameter logistic (5-PL) equation was fitted to MFI values for a 1:5 dilution series ranging from 3.2 – 10,000 pg/mL. The coefficient of determination ( $R^2$ ) for each standard curve ranged from 0.9902 to 0.9999 with an average of 0.9978. Each plasma sample was measured in duplicate. Duplicate MFI's were averaged and an individual sample concentration (pg/mL) was determined using the 5-PL equation.

The 5-PL equation is:

$$y = a + \frac{b - a}{\left[1 + \left(\frac{x}{c}\right)^d\right]^f}$$

where:

a= MFI for minimal asymptote

b= MFI for maximum asymptote

c= concentration at inflection point (concentration at 50% maximum MFI)

d= slope factor

f= asymmetry factor

## 2.4 Interphase quantitative fluorescence in situ hybridization (IQ-FISH)

Telomere length was also quantified using Interphase Quantitative Fluorescence In Situ Hybridization (IQ-FISH). The preferred approach for measuring telomeres by FISH is on metaphase chromosomes. However, this technique requires actively dividing cells and was not suitable for the available cryopreserved samples. Additionally, leukocytes have varying mitotic indices between cell type, and after multiple passages, cultured leukocyte samples would likely have different cell population ratios than freshly drawn samples.

IQ-FISH is a technique used for the visualization of interphase nuclei and was used to estimate relative telomere length of fixed leukocytes.[209] After leukocyte isolation and separation of cells into respective qPCR and IQ-FISH fractions, the IQ-FISH fraction was fixed in 3:1 methanol and stored at -20°C. At time of hybridization, leukocytes fixed in methanol:acetic acid were dropped on StarFrost® microscope slides and cell density was checked by microscope. Fixed cell suspensions were treated with 200 µl of 100 mg/ml RNase A, 150 nM NaCl, and 15 mM sodium citrate at 37°C for 1 hour and 15 minutes. Slides were rinsed twice in 1X PBS for 5 min each, dehydrated through a graded ethanol series (75%, 80%, 100%) for 2 min each, denatured in 70% formamide/2X saline-sodium citrate (SSC) for 2.5 min at 37°C, and dehydrated again through a graded ethanol series (75%, 80%, 100%) for 2 min each, before probe hybridization. The probe hybridization mixture per slide consisted of 36 µL

formamide, 12  $\mu\text{L}$  0.05M Tris-HCl, 2.5  $\mu\text{L}$  0.1 M KCl, 0.6  $\mu\text{L}$  0.1M  $\text{MgCl}_2$  and 0.15  $\mu\text{L}$  PNA probe. Fifty microliters of probe hybridization mix were applied to each sample and incubated in the dark at 37° C for 24 hours.

After probe hybridization, slides were treated with a series of washes consisting of 50% formamide/2XSSC, 2X SSC, and 2X SSC with 0.1% Tergitol type NP40 detergent. After drying, slides were counterstained with 50 $\mu\text{l}$  DAPI, which is specific for AT rich sequences that dominate in non-telomeric DNA. Counter-stained slides were cover slipped and stored at -20°C until image analysis.

Two-dimensional (2-D) image acquisition was performed on all available samples. A minimum of 50 images was obtained per respective fluorophore excitation camera filter (DAPI and TRITC) for 2-dimensional (2-D) image analysis. Three-dimensional (3-D) image acquisition was also performed on selected samples for analysis of variations between Cy3 and TRITC filter excitation spectrums. In 3-D image acquisition, 26 Z-axis images were taken in 0.2  $\mu\text{m}$  segments with both DAPI and Cy3 filters. These images were then reconstructed to form a 2-D image. Conversion of 2-D image pixels to relative numerical values for telomere fluorescence intensity (TFI) was performed using TELOMETER, an ImageJ software plug-in designed for interphase FISH on telomeres.

Telomere length was measured by IQ-FISH in a total of twenty individuals with a history of colorectal cancer, and for each individual, telomere length was measured at day 0, day 14, and day 28 of the study. The twenty individuals were randomly separated into three parallel batches due to limits within the number of samples that could be processed at a single time. The Raji cell line, a cultured line of human B-lymphocytes, and the LY-S cell line, a cultured line of mouse lymphoma cells, were selected as internal controls for inter-batch comparison.

Ultimately, inter-batch comparison of telomere length measured by IQ-FISH was complicated by variability in results that was dependent on whether sample mean fluorescence intensities were normalized to the Raji or LY-S control cell lines. For the Raji control cell line, mean fluorescence intensities were highest in batch one (33.53) followed by batch two (25.11) and then batch three (19.87). A similar trend was observed for the LY-S control cell line where mean fluorescence intensities were highest in batch one (32.47) followed by batch two (30.96) and then batch three (14.32). However, when normalized to the Raji cell line, the average mean fluorescence intensities for individuals in batches one, two, and three were 1.69, 2.21, and 1.67, respectively. Whereas, when normalized to the LY-S cell line, the average mean fluorescence intensities for individuals in batches one, two, and three were 1.75, 1.79, and 2.03, respectively. Therefore, depending on which control cell line results were normalized to, the batch with the longest average telomere length could be either batch three or batch two. Given these conflicting results, it was decided to only analyze IQ-FISH telomere length measurements as separate, non-comparable batches. Unfortunately, this significantly limited the sample sizes for the IQ-FISH telomere length data and thus negatively impacted the utility of this data.

## **2.5 Telomere length measurement by singleplex qPCR**

Singleplex quantitative polymerase chain reaction (qPCR) was used to calculate the relative leukocyte telomere length of twenty-two study participants with a history of colorectal cancer, and for each individual, telomere length was measured using singleplex qPCR at day 0, day 14, and day 28 of the study. The twenty-two individuals were randomly separated into two groups due to limits within the number of samples that could fit on a single qPCR plate, and the Raji cell line was used as a normalizing factor for inter-plate telomere length comparison.

The singleplex qPCR method estimates the average telomere length per individual by quantifying the ratio of telomere repeat copy number (T) to single copy housekeeping gene (S) in a sample.[210] The *36B4* gene, which encodes an acidic ribosomal phosphoprotein, was used as the housekeeping gene, and the telomere and *36B4* reactions were performed in separate wells with the same amount of sample DNA (20 ng). Reaction efficiencies were determined by the slope of a standard curve of 1.68-fold serially diluted Raji cell line DNA ranging from 100 ng to 7.47 ng total DNA. Additionally, reaction efficiency was estimated in each individual reaction well using LinRegPCR (version 12.18). LinRegPCR is a software program that estimates individual PCR reaction efficiencies using the slope of the log-linear phase of the reaction's amplification curve, and the program has been shown to reduce variability in qPCR results.[211] The relative starting concentration ( $N_0$ ) of each sample was calculated by LinRegPCR via the threshold level of the PCR amplification curve ( $N_q$ ) and the cycle threshold ( $C_q$ ) using the formula:

$$N_0 = \frac{N_q}{(\text{Mean efficiency of amplicon group})^{C_q}}$$

Individual telomere length was estimated by the ratio:  $\frac{N_0 (tel1/2)}{N_0 (36B4)}$  for each individual sample, and relative telomere length was determined by dividing each sample by the average telomere length of all individuals on a single plate. Finally, inter-plate comparison was attempted by normalizing each sample's relative telomere length to the relative telomere length of the Raji control cell line, which was measured on each plate.

DNA was isolated from leukocyte samples using the commercially available QIAGEN<sup>®</sup> DNeasy<sup>®</sup> Blood & Tissue Kit. Isolated genomic DNA was quantified using the spectrophotometer function of a Biotek<sup>™</sup> Cytation3 multi-mode microplate reader with the

assistance of Gen5™ Data Collection and Analysis Software. DNA purity was assessed by the A260/280 ratio with samples not within 1.8-2.0 excluded from analysis. Prior to qPCR, DNA was stored at -20 C in Tris-EDTA buffer (10 mM Tris-HCl, 0.5 mM EDTA; pH 9.0).

DNA was amplified in 20µl singleplex qPCR reactions on a 384-well plate using a Roche LightCycler® 480 Real-Time PCR System. Each 20 µL sample contained 8 µL LightCycler® 480 SYBR® Green I Master Mix (2x), 2 µL of telomere or 36B4 primers (1 µL reverse, 1 µL forward), 20 ng DNA, and PCR grade water. All samples were run in triplicate. Primers were obtained from Integrated DNA Technologies, Inc. (IDT). Telomere and 36B4 primer pairs used for singleplex qPCR had the following respective sequences:

tel1 5'-GGT TTT TGA GGG TGA GGG TGA GGG TGA GGG T-3'

tel2 5'-TCC CGA CTA TCC CTA TCC CTA TCC CTA TCC CTA TCC CTA-3'

36B4F 5'-CAG CAA GTG GGA AGG TGT AAT CC-3'

36B4R 5'-CCC ATT CTA TCA TCA ACG GGT ACA A-3'

The thermal cycling profile was: 10 min at 95°C, followed by 45 cycles of 95°C for 10 sec, 54°C for 1 min, and a melt dissociation curve.

Based off a standard curve of serially diluted Raji cell line DNA, reaction efficiencies for the 36B4 reaction were 98.5% for plate one and 100.7% for plate two, with a coefficient of determination,  $R^2$ , of 0.995 for both plates. When analyzed on a per-well basis using LinRegPCR software, the average reaction efficiency for the 36B4 primer set was 90.0% for plate one and 92.1% for plate two. For the tel1/tel2 primer pair, reaction efficiencies based off a Raji cell line standard curve were 66.7% for plate one and 65.0% for plate two, with an  $R^2$  value of 0.875 and 0.830, respectively. Using LinRegPCR, reaction efficiencies for the tel1/tel2 primer set were 66.7% for plate one and 65.0% for plate two.

For the 36B4 primer set, coefficient of variation values for the cycle thresholds of triplicate individual samples ranged from 0.02% to 0.51% with a mean value of 0.20%. The coefficient of variation for the cycle thresholds of triplicate individual samples amplified with tel1/tel2 ranged from 0.01% to 1.98% with a mean value of 0.83%. For the Raji cell line, which was used as a control for normalization between the two plates, the coefficient of variation for the cycle thresholds of the triplicate samples amplified with 36B4 primers was 0.04% and 0.06%. For the tel1/tel2 primer set, Raji cell line triplicate samples had a coefficient of variation of 7.43% for plate one and 3.49% for plate two. Finally, the estimated individual telomere lengths of the Raji control samples had a coefficient of variation of 68.8%. For both plates, graphs of the derivative melt dissociation curve for the 36B4 primer set showed a single peak with an approximate melting temperature of 80.5°C.

Ultimately, telomere length measured by singleplex qPCR was determined to be unreliable due to non-specific product amplification. Not only were efficiencies of the tel1/tel2 reactions markedly less than 90%, but also 165 out of 198 distinct samples had tel1/tel2 melt dissociation curves with two peaks (one at approximately 80.0°C and another at 82.5°C). Additionally, melt dissociation curves of the no template control reactions for the tel1/tel2 primer set showed a small, broad elevation in derivative fluorescence ranging from approximately 78.0°C to 80.0°C. Non-specific product formation was likely a result of primer-dimerization given the shorter product (80.0°C) was very close to the estimated salt-adjusted melting temperature of the tel2 primer (78.8°C).[212] Due to the non-specific product amplification by the tel1/tel2 primers, a separate protocol for telomere length measurement by qPCR was performed.

## 2.6 Telomere length measurement by monochrome multiplex qPCR

Relative leukocyte telomere length was estimated in twenty-seven study participants with a history of colorectal cancer using a monochrome multiplex qPCR method, and for each individual, telomere length was measured using multiplex qPCR at day 0 and day 28 of the study. This experiment was performed by Lynn Taylor of Dr. Bailey's lab. The multiplex qPCR method for telomere length measurement is similar in concept and protocol to the singleplex method except that all reactions occur within a single well and a different set of telomere and housekeeping gene primers are used.[213]

Sample DNA was isolated by the same protocol as the singleplex method. Each multiplex qPCR reaction had a total volume of 25  $\mu$ L and consisted of 1X GoTaq qPCR Master Mix (Promega), 900 nM telg and telc telomere primers, 400 nM albu and albd albumin primers, and 10 ng genomic DNA. The telomere and albumin primers used for multiplex qPCR were:

telg 5'-ACA CTA AGG TTT GGG TTT GGG TTT GGG TTA GTG T-3'

telc 5'-TGT TAG GTA TCC CTA TCC CTA TCC CTA TCC CTA TCC CTA ACA-3'

albu 5'-CGG CGG CGG GCG GCG CGG GCT GGG CGG AAA TGC TGC ACA GAA TCC TTG-3'

albd 5'-GCC CGG CCC GCC GCG CCC GTC CCG CCG GAA AAG CAT GGT CGC CTG TT-3'

DNA was amplified in a BioRad CFX96/C1000 Thermal Cycling System with the following two-stage thermal cycling profile: Stage 1: 15 min at 95°C; Stage 2: 2 cycles of 15 s at 94°C, 15 s at 49°C; and Stage 3: 32 cycles of 15 s at 94°C, 10 s at 62°C, 15 s at 74°C with signal acquisition, 10 s at 84°C, 15 s at 88°C with signal acquisition. Reaction efficiencies were assessed using standard curves created from a 3-fold serial dilution of human genomic DNA ranging from 50 ng to 0.62 ng. Similar to the singleplex qPCR method, individual telomere length was estimated by calculating the ratio of the telomere and housekeeping gene starting

quantities  $\frac{N_0(telc/g)}{N_0(albu/d)}$  for each individual sample. However, instead of LinRegPCR, another similar software program, CFX Manager™ Software, was used. Relative telomere length was determined by dividing each sample by the average telomere length of the triplicate human genomic DNA that was used as a control on each plate.

For the albu/albd primers, reaction efficiencies based off the respective standard curves for plates one, two, and three were 100.1%, 95.2%, and 97.3%, with R<sup>2</sup> values of 0.999, 0.997, and 0.998. For the telg/telc primers, reaction efficiencies for plates one, two, and three were 112.9%, 107.7%, and 105.5%, with R<sup>2</sup> values of 0.998, 0.998, and 0.995.

The coefficient of variation for the cycle thresholds of triplicate individual samples amplified with the albu/albd primers ranged from 0.05% to 0.81% with a mean value of 0.30%. For the telg/telc primer set, coefficient of variation for triplicate cycle threshold values ranged from 0.08% to 1.48% with a mean value of 0.54%.

In contrast to the Raji cell line DNA used for the singleplex method, the human genomic DNA standard was found to have consistent individual telomere lengths across all three plates. The coefficient of variation between all three plates was 5.06%. Additionally, melt dissociation curves for the multiplex telomere data indicated a single peak for both the telg/telc and the albu/albd primer pairs. No amplification was observed in the no template controls.

## **2.7 Nutrient data collection**

Each participant's daily nutrient intake was estimated through using individual, self-reported total food and beverage consumption habits. Each participant recorded a dietary food journal of their consumption behavior over a three-day span at three separate time points of the study. These food journals were then analyzed using a diet analysis software program,

Nutritionist Pro™, to obtain estimates of each individual's nutrient consumption. Specifically, data was obtained for total daily intake of several minerals (calcium, iron, magnesium, potassium, selenium, sodium, and zinc), vitamins (A,  $\beta$ -carotene, B1, B2, B3, B6, B9, B12, C, D, E, and  $\alpha$ -Tocopherol), macronutrients (carbohydrates, protein, total fat, and saturated fat), unsaturated fatty acids (oleic, linoleic, and linolenic) and fiber. This data was then used for correlation analysis with telomere length and cytokine concentrations.

## **2.8 Statistical analysis**

### *2.8.1 Descriptive statistics*

All statistical analysis was performed with cloud-based SAS University Edition software through the use of VMWare Fusion virtualization software. Descriptive statistics for all study variables are reported separately for the two study cohorts: participants with a history of colorectal cancer and participants without a history of colorectal cancer. Additionally, descriptive statistics within each dietary intervention group and by sex are reported for participants with a history of colorectal cancer.

### *2.8.2 Normality testing*

The distribution of each variable within the two study cohorts was assessed for normality using the Shapiro-Wilk (S-W) and Anderson-Darling (A-D) tests. Of these tests, the S-W test is considered to provide better statistical power and to be more appropriate for small sample sizes ( $n < 30$ ).<sup>[214]</sup> However, the A-D test, a non-parametric, goodness-of-fit test, is an acceptable and frequently used test of normality.<sup>[215]</sup> For variables that failed either of these tests, a natural

logarithm transformation was performed prior to statistical analysis. Additionally, distribution and probability plots were created to visually assess for normality prior to data analysis.

### 2.8.3 *Cytokine statistical analysis*

Immunological data acquisition and analysis is often restricted by the levels of detection (LOD) of the immunoassay's standard curve. In general, serum cytokine concentrations are relatively low and transient. Therefore, it is not uncommon to have cytokine MFI values that fall below the lowest level of detection (LLOD) of the standard curve. In this situation, population data is "left-censored", meaning the exact value of some observations are missing but known to fall within a range between zero and the LLOD. Several methods are available and frequently used to deal with left-censored immunological data, the most common of which are deletion, substitution, extrapolation, regression, and multiple imputation.[216, 217] These five approaches were applied and compared in this study.

The first approach, list-wise deletion, ignored all samples with concentrations below the LLOD (3.2 pg/ml). Linear regression analysis by time point and diet group was performed on a strict data set comprised of concentration values falling between the standard curve range of 3.2 pg/ml to 10,000 pg/ml. Benefits of this approach include its simplicity and the overall confidence in observed values.[218] However, deletion reduces statistical power and can produce significantly biased results. For these reasons, the deletion method is not well suited for small sample sizes with missing data.

The second approach applied a substitution method to values below the LLOD. Missing observations were substituted with a fixed value of LOD/2 (1.6 pg/ml) prior to linear regression analysis. Benefits of substitution include its simplicity and the ability for complete case analysis.

However, substitution limits population variability and can result in weakened estimates of correlation and covariance.

The third approach extrapolated missing values using the standard curve's 5-PL equation. Extrapolation allows for complete case data analysis and unlike substitution, does not artificially decrease variability. However, extrapolation is rather imprecise due to the near horizontal slope at the lower end of the sigmoidal 5-PL where small changes in MFI can result in drastic differences in estimated sample concentration.

The fourth technique employed Tobit regression, a form of censored regression analysis, to estimate linear relationships of censored cytokine data by time point and diet group. The Tobit regression estimates a linear regression model for the observed data and assumes the same distribution of errors for censored values. The Tobit model is described by the relationship between the observed, censored variable,  $y$ , in terms of the latent variable,  $y^*$ , and the censoring threshold,  $c$ , as:

$$y = \begin{cases} y^* & \text{when } y^* > c \\ c & \text{when } y^* \leq c \end{cases}$$

The latent variable,  $y^*$ , is considered the true value and is defined by the linear relationship with an independent variable  $x$  in the equation:

$$y^* = \beta x + u$$

The regression coefficient,  $\beta$ , and the error term,  $u$ , are determined by maximum likelihood estimation (MLE) based off their linear relationship with the observed data. Specifically, MLE selects the value of  $\beta$  and  $u$  that would result in the highest probability of producing the observed values. Tobit regression is an effective and well-established method for handling censored data.[219] However, the Tobit model assumes a normal distribution and

constant variance across observations, which are rarely satisfied by immunological data.[220, 221]

The final approach utilized multiple imputation (MI) to account for missing values. This technique assumes a similar distribution within censored values as in observed data and uses MLE to create a complete data set by estimating each missing value.[222] This process is repeated several times to create multiple data sets that are then each analyzed separately. Analysis results from each imputed data set are then combined. MI has consistently been demonstrated to produce unbiased results with missing data.[216, 219, 223] However, MI is not effective for data with small sample sizes or with high percentages of censoring as the distribution of observed values is more likely to not reflect the distribution of censored values.[221, 224, 225] Furthermore, similar to Tobit regression, MI assumes the data is normally distributed.

For several analytes, the concentration estimated from the MFI via the 5-PL standard curve fell outside the lowest level of detection (3.2 pg/ml). For individuals without a history of colorectal cancer (n=11), the primary analytes that were either undetectable or required extrapolation beyond the limits of the standard curve were IL-2 (n=4), IL-4 (n=5), IL-6 (n=6), and IL-10 (n=5). A similar trend was seen in individuals with a history of colorectal cancer (n=23) with IL-2 (n=9), IL-4 (n=12), IL-6 (n=11), and IL-10 (n=9).

Across all three plates, values for each respective cytokine's standard curve and quality controls were consistent and precise, which allowed for direct inter-plate comparison. For IL-2, the coefficient of variation of controls and standards ranged from 0.30% to 9.11% with an average of 2.85%. For IL-4, IL-6, and IL-8, the coefficients of variation of controls ranged from 0.18% to 9.44% with an average of 3.38%, from 0.15% to 11.5% with an average of 4.36%, and

from 0.16% to 7.61% with an average of 2.77%, respectively. Similar trends were seen in the consistency of the controls and standards for IL-10, TNF, and VEGF, where each averaged a coefficient of variation of 2.87%, 2.67%, and 2.36%.

#### 2.8.4 *Analysis of longitudinal, between diet group, and between cohort differences*

For both cohorts, differences in study variables between the three dietary intervention groups and across the three time points of data collection were assessed for statistical significance using one-way analysis of variance (ANOVA). Additionally, both linear regression and a two-way ANOVA was performed on the cohort with a history of colorectal cancer to assess for differences between sexes as well as for the effect of sex and diet and the effect of sex and time point on the dependent study variables. Lastly, differences in dependent variables between the two cohorts were analyzed by linear regression.

Differences in non-transformed variables are reported in the respective unit for that variable. For transformed variables, relative differences between diet groups, time points, or cohorts are reported as a ratio of geometric means (RoGM). RoGM was obtained after back transformation of the difference of the transformed means of each variable. That is, if  $X_1$  and  $X_2$  are the means of two natural log-transformed data sets, then:

$$RoGM = \frac{e^{X_1}}{e^{X_2}} = e^{(X_1 - X_2)}$$

#### 2.8.5 *Linear correlation analysis*

Correlation between variables was estimated using a repeated measure within subjects correlation model. This model accounts for the lack of independence among the repeated measurements by removing the variation between subjects, and it estimates whether a change in

one variable in an individual is associated with a similar change in another variable for that same individual. In the overwhelming majority of correlations, an unstructured covariance matrix was used for modeling covariation between measurements within a single subject. This covariance matrix assumes no pattern on the covariances, and it is recommended structure for longitudinal data from randomized clinical trials.[226] However, when this model did not fit the data, a compound symmetry structure was specified for the covariance matrix.

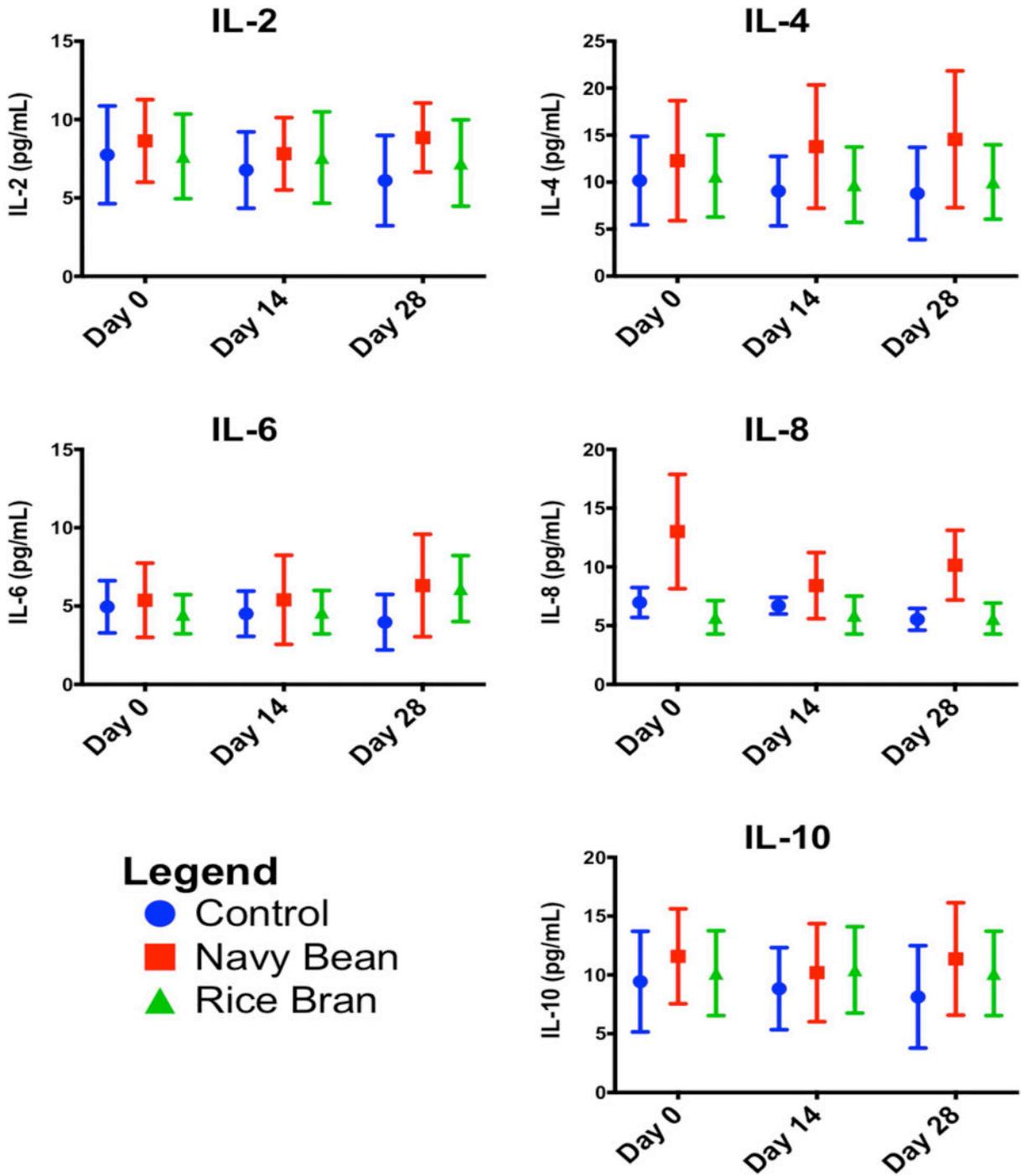
## CHAPTER 3: RESULTS

### 3.1 Differences in plasma cytokine levels within and between diet groups

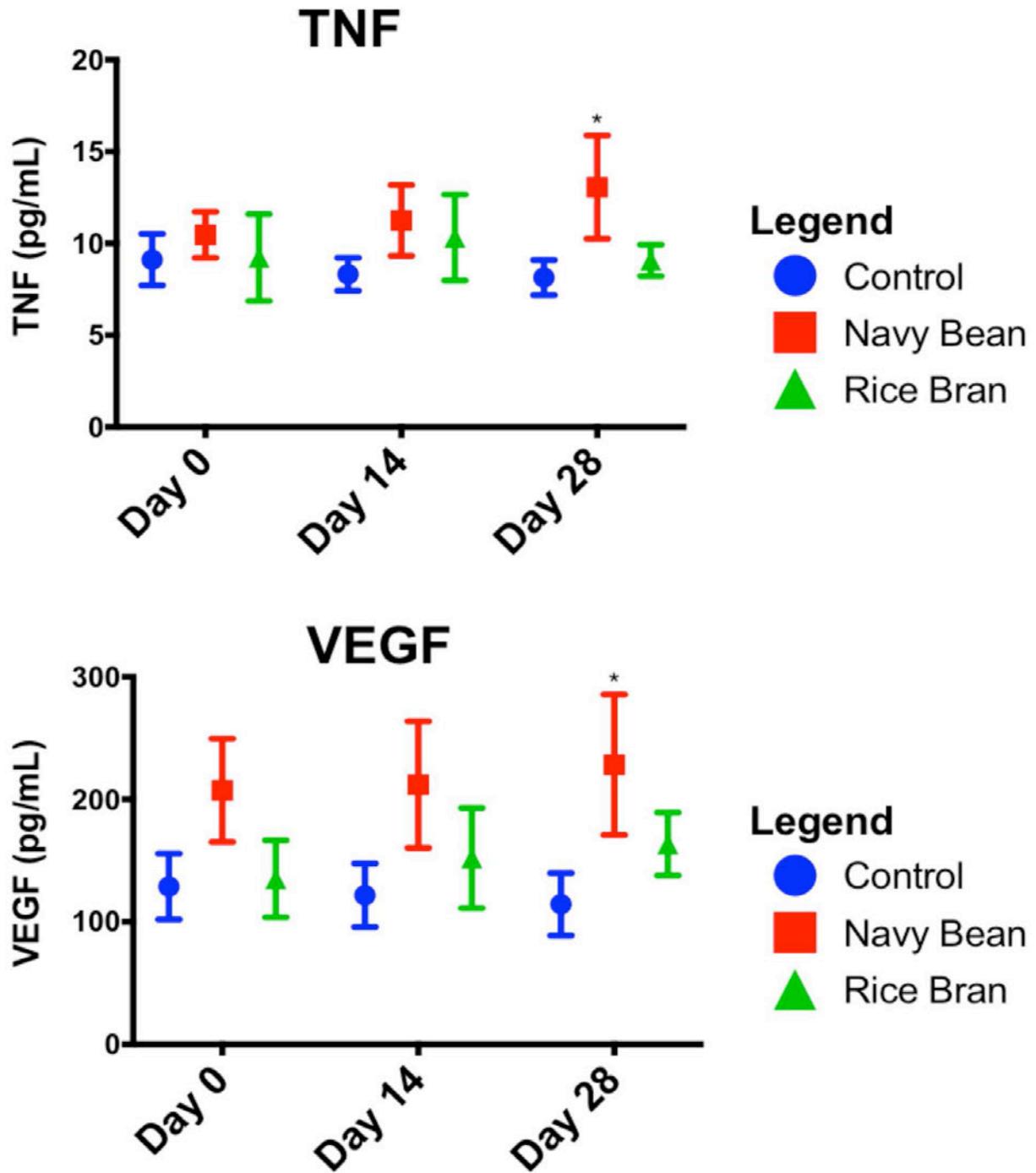
In regards to cytokine concentration, for participants without a history of colorectal cancer, no significant differences were seen between diet group or time point for any cytokine. Similarly, no significant differences were found between diet groups or time point for IL-2, IL-4, IL-6, IL-8, and IL-10 in participants with a history of colorectal cancer.

At day 28, the navy bean group within the history of colorectal cancer cohort had significantly higher TNF concentrations compared to the control group (RoGM=1.53; 95% CI=[1.02, 2.31]; p=0.041). Within these two groups, no values were below the limits of detection of the standard curve, so censored data analysis was not required.

VEGF concentration in the navy bean group at day 28 was also significantly greater than the control group when analyzed using the Tobit regression approach for censored data (RoGM=3.63; 95% CI=[1.09, 12.05]; p=0.036) but non-significantly greater when using the other approaches for handling censored data: substitution (RoGM=3.89; 95% CI=[0.91, 16.62]; p=0.065), extrapolation (RoGM=12.01; 95% CI=[0.62, 232.43]; p=0.096), and multiple imputation (RoGM=1.45; 95% CI=[0.83, 2.53]; p=0.183). Given that the Tobit regression approach has been shown to be the most unbiased method for handling censored data and that only one VEGF value was below the lowest level of detection in regards to the comparison of the navy bean and control groups at day 28, the obtained significant result is considered the most reliable of all approaches used for the censored data analysis.[216]



**Figure 2:** Graphs showing mean plasma concentration  $\pm$  standard error of the mean for IL-2, IL-4, IL-6, IL-8, and IL-10. No significant differences were found between diet groups or time points.



**Figure 3:** Graphs showing mean plasma concentration  $\pm$  standard error of the mean for TNF and VEGF. At day 28, both TNF and VEGF concentration in the navy bean diet group were significantly higher than in the control groups. No significant change in TNF or VEGF concentration was found within diet groups between time points.

**Table 1:** Differences in age, weight, and body mass index between diet groups (left) and between time points (right) for study participants without a history of colorectal cancer. Variables shown above: age (top), weight (middle), and body mass index (BMI; bottom). The control group (n=3) was observed to have a significantly higher average weight than both the navy bean (n=4) and rice bran (n=4) groups at all time points. However, this was not observed when comparing BMI. The control group was observed to have a significantly greater BMI than the rice bran group at day 0. Otherwise, no significant difference was observed in BMI at other time points.

Parameter Estimates for Study Participants without a History of Colorectal Cancer: One-Way Analysis of Variance of Age by Diet Group							
Time Point	Parameter	Comparison groups	Diff. of Arithmetic Means (years)	Standard Error	95% Confidence Limits	p-value	Type III p-value
Day 0	Diet	Navy Bean Control	-4.83	12.23	-33.04 23.38	0.703	0.882
		Rice Bran Control	0.42	12.23	-27.79 28.63	0.974	
		Navy Bean Rice Bran	-5.25	11.33	-31.37 20.87	0.655	
Day 14	Diet	Navy Bean Control	-4.83	12.23	-33.04 23.38	0.703	0.882
		Rice Bran Control	0.42	12.23	-27.79 28.63	0.974	
		Navy Bean Rice Bran	-5.25	11.33	-31.37 20.87	0.655	
Day 28	Diet	Navy Bean Control	-4.83	12.23	-33.04 23.38	0.703	0.882
		Rice Bran Control	0.42	12.23	-27.79 28.63	0.974	
		Navy Bean Rice Bran	-5.25	11.33	-31.37 20.87	0.655	

Parameter Estimates for Study Participants without a History of Colorectal Cancer: One-Way Analysis of Variance of Age by Time Point							
Diet	Parameter	Comparison groups	Diff. of Arithmetic Means (years)	Standard Error	95% Confidence Limits	p-value	Type III p-value
Control	Time	Day 14 Day 0	0.00	17.75	-43.42 43.42	1.000	1.000
		Day 28 Day 0	0.00	17.75	-43.42 43.42	1.000	
		Day 28 Day 14	0.00	17.75	-43.42 43.42	1.000	
Navy Bean	Time	Day 14 Day 0	0.00	7.97	-18.03 18.03	1.000	1.000
		Day 28 Day 0	0.00	7.97	-18.03 18.03	1.000	
		Day 28 Day 14	0.00	7.97	-18.03 18.03	1.000	
Rice Bran	Time	Day 14 Day 0	0.00	11.01	-24.90 24.90	1.000	1.000
		Day 28 Day 0	0.00	11.01	-24.90 24.90	1.000	
		Day 28 Day 14	0.00	11.01	-24.90 24.90	1.000	

Parameter Estimates for Study Participants without a History of Colorectal Cancer: One-Way Analysis of Variance of Weight by Diet Group							
Time Point	Parameter	Comparison groups	Diff. of Arithmetic Means (kg)	Standard Error	95% Confidence Limits	p-value	Type III p-value
Day 0	Diet	Navy Bean Control	-19.19	6.72	-35.62 -2.75	0.029	0.036
		Rice Bran Control	-21.36	6.72	-37.80 -4.93	0.019	
		Navy Bean Rice Bran	2.18	6.72	-14.26 18.61	0.757	
Day 14	Diet	Navy Bean Control	-19.14	6.44	-34.90 -3.38	0.025	0.032
		Rice Bran Control	-20.96	6.44	-36.72 -5.19	0.017	
		Navy Bean Rice Bran	1.82	6.44	-13.95 17.58	0.787	
Day 28	Diet	Navy Bean Control	-18.48	6.59	-34.59 -2.36	0.031	0.042
		Rice Bran Control	-19.69	6.59	-35.80 -3.57	0.024	
		Navy Bean Rice Bran	1.21	6.59	-14.91 17.33	0.860	

Parameter Estimates for Study Participants without a History of Colorectal Cancer: One-Way Analysis of Variance of Weight by Time Point							
Diet	Parameter	Comparison groups	Diff. of Arithmetic Means (kg)	Standard Error	95% Confidence Limits	p-value	Type III p-value
Control	Time	Day 14 Day 0	-0.21	10.38	-25.61 25.18	0.984	0.941
		Day 28 Day 0	-1.21	10.38	-26.61 24.19	0.911	
		Day 28 Day 14	-1.00	10.38	-26.39 24.40	0.927	
Navy Bean	Time	Day 14 Day 0	-0.17	3.65	-9.11 8.78	0.965	0.930
		Day 28 Day 0	-0.50	3.65	-9.44 8.44	0.896	
		Day 28 Day 14	-0.33	3.65	-9.28 8.61	0.930	
Rice Bran	Time	Day 14 Day 0	0.19	2.99	-7.11 7.50	0.951	0.920
		Day 28 Day 0	0.47	2.99	-6.84 7.77	0.881	
		Day 28 Day 14	0.27	2.99	-7.03 7.58	0.930	

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Body Mass Index by Diet Group							
Time Point	Parameter	Comparison groups	Diff. of Arithmetic Means (kg/m <sup>2</sup> )	Standard Error	95% Confidence Limits	p-value	Type III p-value
Day 0	Diet	Navy Bean Control	-5.29	3.04	-12.30 1.72	0.120	0.114
		Rice Bran Control	-7.14	3.04	-14.15 -0.13	0.047	
		Navy Bean Rice Bran	1.85	2.81	-4.64 8.34	0.529	
Day 14	Diet	Navy Bean Control	-4.83	3.62	-13.69 4.03	0.230	0.252
		Rice Bran Control	-6.53	3.62	-15.39 2.33	0.121	
		Navy Bean Rice Bran	1.70	3.62	-7.16 10.56	0.655	
Day 28	Diet	Navy Bean Control	-4.60	3.67	-13.58 4.38	0.257	0.294
		Rice Bran Control	-6.13	3.67	-15.11 2.84	0.146	
		Navy Bean Rice Bran	1.53	3.67	-7.44 10.51	0.691	

Parameter Estimates for Study Participants without a History of Colorectal Cancer: One-Way Analysis of Variance of Body Mass Index by Time Point							
Diet	Parameter	Comparison groups	Diff. of Arithmetic Means (kg/m <sup>2</sup> )	Standard Error	95% Confidence Limits	p-value	Type III p-value
Control	Time	Day 14 Day 0	-0.10	5.54	-13.66 13.46	0.986	0.960
		Day 28 Day 0	-0.43	5.54	-14.00 13.13	0.940	
		Day 28 Day 14	-0.33	5.54	-13.90 13.23	0.954	
Navy Bean	Time	Day 14 Day 0	0.36	2.33	-5.16 5.87	0.882	0.922
		Day 28 Day 0	0.26	2.33	-5.26 5.77	0.915	
		Day 28 Day 14	-0.10	2.49	-5.99 5.79	0.969	
Rice Bran	Time	Day 14 Day 0	0.51	1.42	-2.84 3.86	0.730	0.798
		Day 28 Day 0	0.58	1.42	-2.78 3.93	0.697	
		Day 28 Day 14	0.07	1.51	-3.52 3.65	0.966	

**Table 2:** Differences in plasma interleukin-2 and interleukin-4 between diet groups (left) and between time points (right) for study participants without a history of colorectal cancer. Variables shown above: IL-2 with substituted censored values (top), IL-2 with extrapolated censored values (second from top), IL-4 with substituted censored values (second from bottom), and IL-4 with extrapolated censored values (bottom). No significant differences were observed in the displayed variables between treatment groups or time points.

Parameter Estimates for Study Participants without a History of Colorectal Cancer: One-Way Analysis of Variance of Interleukin-2 (Substitution) by Diet Group									
Time Point	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Day 0	Diet	Navy Bean	Control	1.88	3.15	0.13	26.50	0.596	0.752
		Rice Bran	Control	2.38	3.15	0.17	33.44	0.472	
		Navy Bean	Rice Bran	0.79	2.89	0.07	9.16	0.832	
Day 14		Navy Bean	Control	1.98	2.98	0.16	24.44	0.549	0.523
		Rice Bran	Control	3.64	2.98	0.29	45.04	0.270	
		Navy Bean	Rice Bran	0.54	2.74	0.05	5.57	0.562	
Day 28		Navy Bean	Control	2.19	2.95	0.18	26.63	0.489	0.518
		Rice Bran	Control	3.65	2.95	0.30	44.24	0.266	
		Navy Bean	Rice Bran	0.60	2.72	0.06	6.07	0.626	

Parameter Estimates for Study Participants without a History of Colorectal Cancer: One-Way Analysis of Variance of Interleukin-2 (Substitution) by Time Point									
Diet	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Control	Time	Day 14	Day 0	0.73	1.53	0.26	2.05	0.479	0.630
		Day 28	Day 0	0.71	1.53	0.25	2.00	0.451	
		Day 28	Day 14	0.98	1.53	0.35	2.76	0.960	
Navy Bean		Day 14	Day 0	0.76	1.70	0.23	2.53	0.622	0.744
		Day 28	Day 0	0.83	1.70	0.25	2.75	0.731	
		Day 28	Day 14	1.09	1.70	0.33	3.61	0.880	
Rice Bran		Day 14	Day 0	1.11	4.75	0.03	37.84	0.946	0.964
		Day 28	Day 0	1.09	4.75	0.03	37.04	0.957	
		Day 28	Day 14	0.98	4.75	0.03	33.25	0.989	

Parameter Estimates for Study Participants without a History of Colorectal Cancer: One-Way Analysis of Variance of Interleukin-2 (Extrapolation) by Diet Group									
Time Point	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Day 0	Diet	Navy Bean	Control	2.87	21.54	0.002	3411.0	0.740	0.919
		Rice Bran	Control	1.02	21.54	0.001	1210.5	0.995	
		Navy Bean	Rice Bran	2.82	17.15	0.004	1977.8	0.725	
Day 14		Navy Bean	Control	3.49	19.89	0.004	3448.4	0.687	0.916
		Rice Bran	Control	1.81	19.89	0.002	1786.7	0.848	
		Navy Bean	Rice Bran	1.93	15.93	0.003	1142.9	0.818	
Day 28		Navy Bean	Control	18.19	20.82	0.017	19968.0	0.367	0.638
		Rice Bran	Control	8.49	20.82	0.008	9325.4	0.501	
		Navy Bean	Rice Bran	2.14	16.62	0.003	1398.7	0.793	

Parameter Estimates for Study Participants without a History of Colorectal Cancer: One-Way Analysis of Variance of Interleukin-2 (Extrapolation) by Time Point									
Diet	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Control	Time	Day 14	Day 0	0.63	15.25	0.00	493.66	0.870	0.647
		Day 28	Day 0	0.13	15.25	0.00	102.92	0.484	
		Day 28	Day 14	0.21	15.25	0.00	163.89	0.586	
Navy Bean		Day 14	Day 0	0.76	10.11	0.00	143.05	0.909	0.940
		Day 28	Day 0	0.83	10.11	0.00	155.32	0.937	
		Day 28	Day 14	1.09	10.11	0.01	203.61	0.972	
Rice Bran		Day 14	Day 0	1.11	31.72	0.00	2772.83	0.976	0.984
		Day 28	Day 0	1.09	31.72	0.00	2713.62	0.981	
		Day 28	Day 14	0.98	31.72	0.00	2436.51	0.995	

Parameter Estimates for Study Participants without a History of Colorectal Cancer: One-Way Analysis of Variance of Interleukin-4 (Substitution) by Diet Group									
Time Point	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Day 0	Diet	Navy Bean	Control	0.96	4.55	0.029	31.7	0.981	0.981
		Rice Bran	Control	0.77	4.55	0.023	25.4	0.867	
		Navy Bean	Rice Bran	1.25	4.07	0.049	31.8	0.877	
Day 14		Navy Bean	Control	0.77	4.57	0.023	25.6	0.869	0.973
		Rice Bran	Control	1.05	4.57	0.032	35.0	0.974	
		Navy Bean	Rice Bran	0.73	4.08	0.029	18.8	0.831	
Day 28		Navy Bean	Control	0.85	4.59	0.025	28.4	0.915	0.989
		Rice Bran	Control	1.03	4.59	0.031	34.5	0.987	
		Navy Bean	Rice Bran	0.83	4.10	0.032	21.4	0.895	

Parameter Estimates for Study Participants without a History of Colorectal Cancer: One-Way Analysis of Variance of Interleukin-4 (Substitution) by Time Point									
Diet	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Control	Time	Day 14	Day 0	0.73	3.25	0.04	12.96	0.795	0.863
		Day 28	Day 0	0.73	3.25	0.04	12.98	0.795	
		Day 28	Day 14	1.00	3.25	0.06	17.88	1.000	
Navy Bean		Day 14	Day 0	0.58	2.43	0.08	4.34	0.556	0.700
		Day 28	Day 0	0.64	2.43	0.09	4.76	0.625	
		Day 28	Day 14	1.10	2.43	0.15	8.20	0.919	
Rice Bran		Day 14	Day 0	0.99	7.01	0.01	81.25	0.997	0.991
		Day 28	Day 0	0.97	7.01	0.01	79.21	0.987	
		Day 28	Day 14	0.97	7.01	0.01	79.87	0.990	

Parameter Estimates for Study Participants without a History of Colorectal Cancer: One-Way Analysis of Variance of Interleukin-4 (Extrapolation) by Diet Group									
Time Point	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Day 0	Diet	Navy Bean	Control	1.47	31.37	0.001	4154.23	0.914	0.666
		Rice Bran	Control	0.09	31.37	0.000	262.41	0.510	
		Navy Bean	Rice Bran	15.83	24.29	0.010	24794.07	0.412	
Day 14		Navy Bean	Control	1.09	28.50	0.000	2471.83	0.980	0.752
		Rice Bran	Control	0.13	28.50	0.000	287.67	0.555	
		Navy Bean	Rice Bran	8.59	22.23	0.007	10972.05	0.508	
Day 28		Navy Bean	Control	1.49	26.24	0.001	2783.81	0.906	0.904
		Rice Bran	Control	0.39	26.24	0.000	730.25	0.781	
		Navy Bean	Rice Bran	3.81	20.59	0.004	4080.07	0.670	

Parameter Estimates for Study Participants without a History of Colorectal Cancer: One-Way Analysis of Variance of Interleukin-4 (Extrapolation) by Time Point									
Diet	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Control	Time	Day 14	Day 0	0.73	31.86	0.00	3458.40	0.929	0.953
		Day 28	Day 0	0.73	31.86	0.00	3461.18	0.929	
		Day 28	Day 14	1.00	31.86	0.00	4770.34	1.000	
Navy Bean		Day 14	Day 0	0.54	12.06	0.00	150.38	0.809	0.872
		Day 28	Day 0	0.73	12.06	0.00	205.10	0.904	
		Day 28	Day 14	1.36	12.06	0.00	381.05	0.904	
Rice Bran		Day 14	Day 0	0.99	39.64	0.00	4088.46	0.998	0.845
		Day 28	Day 0	3.05	39.64	0.00	12568.79	0.769	
		Day 28	Day 14	3.07	39.64	0.00	12674.35	0.767	

**Table 3:** Differences in plasma interleukin-6 and interleukin-8 between diet groups (left) and between time points (right) for study participants without a history of colorectal cancer. Variables shown above: IL-6 with substituted censored values (top), IL-6 with extrapolated censored values (second from top), IL-8 with substituted censored values (second from bottom), and IL-8 with extrapolated censored values (bottom). No significant differences were observed in the displayed variables between treatment groups or time points.

Parameter Estimates for Study Participants without a History of Colorectal Cancer: One-Way Analysis of Variance of Interleukin-6 (Substitution) by Diet Group									
Time Point	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Day 0	Diet	Navy Bean	Control	0.89	3.69	0.04	18.07	0.930	0.993
		Rice Bran	Control	1.02	3.69	0.05	20.77	0.987	
		Navy Bean	Rice Bran	0.87	3.35	0.05	14.14	0.911	
Day 14	Diet	Navy Bean	Control	0.62	3.47	0.03	10.89	0.708	0.837
		Rice Bran	Control	1.22	3.47	0.07	21.51	0.878	
		Navy Bean	Rice Bran	0.51	3.17	0.04	7.23	0.571	
Day 28	Diet	Navy Bean	Control	1.28	3.65	0.06	25.30	0.855	0.886
		Rice Bran	Control	1.87	3.65	0.09	37.11	0.641	
		Navy Bean	Rice Bran	0.68	3.32	0.04	10.82	0.758	

Parameter Estimates for Study Participants without a History of Colorectal Cancer: One-Way Analysis of Variance of Interleukin-6 (Substitution) by Time Point									
Diet	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Control	Time	Day 14	Day 0	0.83	2.28	0.11	6.24	0.827	0.637
		Day 28	Day 0	0.53	2.28	0.07	4.01	0.474	
		Day 28	Day 14	0.64	2.28	0.09	4.84	0.611	
		Day 14	Day 0	0.57	1.83	0.15	2.25	0.383	
		Day 28	Day 0	0.76	1.83	0.20	2.99	0.667	
		Day 28	Day 14	1.33	1.83	0.34	5.21	0.648	
Navy Bean	Time	Day 14	Day 0	0.99	5.74	0.02	51.42	0.994	0.566
		Day 28	Day 0	0.98	5.74	0.02	50.81	0.989	
		Day 28	Day 14	0.99	5.74	0.02	51.47	0.995	

Parameter Estimates for Study Participants without a History of Colorectal Cancer: One-Way Analysis of Variance of Interleukin-6 (Extrapolation) by Diet Group									
Time Point	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Day 0	Diet	Navy Bean	Control	0.75	12.88	0.00	273.17	0.915	0.330
		Rice Bran	Control	0.03	12.88	0.00	10.88	0.207	
		Navy Bean	Rice Bran	25.11	10.65	0.11	5876.31	0.210	
Day 14	Diet	Navy Bean	Control	0.56	10.63	0.00	131.41	0.815	0.251
		Rice Bran	Control	0.02	10.63	0.00	5.09	0.144	
		Navy Bean	Rice Bran	25.83	8.92	0.17	4017.95	0.176	
Day 28	Diet	Navy Bean	Control	0.81	21.45	0.00	956.31	0.948	0.990
		Rice Bran	Control	0.65	21.45	0.00	760.58	0.891	
		Navy Bean	Rice Bran	1.26	17.09	0.00	874.90	0.938	

Parameter Estimates for Study Participants without a History of Colorectal Cancer: One-Way Analysis of Variance of Interleukin-6 (Extrapolation) by Time Point									
Diet	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Control	Time	Day 14	Day 0	1.36	6.56	0.01	135.26	0.876	0.503
		Day 28	Day 0	0.15	6.56	0.00	14.81	0.350	
		Day 28	Day 14	0.11	6.56	0.00	10.91	0.284	
		Day 14	Day 0	1.02	4.79	0.03	35.15	0.992	
		Day 28	Day 0	0.16	4.79	0.00	5.55	0.273	
		Day 28	Day 14	0.16	4.79	0.00	5.47	0.269	
Navy Bean	Time	Day 14	Day 0	0.99	32.74	0.00	2640.36	0.997	0.511
		Day 28	Day 0	3.20	32.74	0.00	8570.70	0.746	
		Day 28	Day 14	3.25	32.74	0.00	8683.59	0.744	

Parameter Estimates for Study Participants without a History of Colorectal Cancer: One-Way Analysis of Variance of Interleukin-8 (Substitution) by Diet Group									
Time Point	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Day 0	Diet	Navy Bean	Control	0.56	2.90	0.05	6.55	0.604	0.865
		Rice Bran	Control	0.69	2.90	0.06	8.00	0.734	
		Navy Bean	Rice Bran	0.82	2.68	0.08	7.95	0.845	
Day 14	Diet	Navy Bean	Control	0.65	2.56	0.08	5.69	0.662	0.900
		Rice Bran	Control	0.84	2.56	0.10	7.28	0.854	
		Navy Bean	Rice Bran	0.78	2.38	0.11	5.79	0.783	
Day 28	Diet	Navy Bean	Control	0.97	2.50	0.12	7.99	0.971	0.494
		Rice Bran	Control	2.49	2.50	0.30	20.63	0.348	
		Navy Bean	Rice Bran	0.39	2.34	0.05	2.74	0.296	

Parameter Estimates for Study Participants without a History of Colorectal Cancer: One-Way Analysis of Variance of Interleukin-8 (Substitution) by Time Point									
Diet	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Control	Time	Day 14	Day 0	1.06	2.05	0.18	6.11	0.939	0.588
		Day 28	Day 0	0.55	2.05	0.09	3.16	0.432	
		Day 28	Day 14	0.52	2.05	0.09	2.98	0.393	
		Day 14	Day 0	1.23	1.68	0.38	3.98	0.700	
		Day 28	Day 0	0.94	1.68	0.29	3.04	0.907	
		Day 28	Day 14	0.76	1.68	0.24	2.47	0.617	
Navy Bean	Time	Day 14	Day 0	1.29	3.61	0.07	23.52	0.848	0.741
		Day 28	Day 0	1.99	3.61	0.11	36.26	0.606	
		Day 28	Day 14	1.54	3.61	0.08	28.13	0.744	

Parameter Estimates for Study Participants without a History of Colorectal Cancer: One-Way Analysis of Variance of Interleukin-8 (Extrapolation) by Diet Group									
Time Point	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Day 0	Diet	Navy Bean	Control	0.66	3.03	0.05	8.49	0.718	0.893
		Rice Bran	Control	0.60	3.03	0.05	7.73	0.658	
		Navy Bean	Rice Bran	1.10	2.79	0.10	11.69	0.929	
Day 14	Diet	Navy Bean	Control	0.65	2.42	0.08	5.03	0.643	0.867
		Rice Bran	Control	0.94	2.42	0.12	7.20	0.942	
		Navy Bean	Rice Bran	0.70	2.27	0.11	4.62	0.672	
Day 28	Diet	Navy Bean	Control	1.16	2.45	0.15	9.20	0.872	0.505
		Rice Bran	Control	2.66	2.45	0.34	21.03	0.308	
		Navy Bean	Rice Bran	0.44	2.30	0.06	2.97	0.349	

Parameter Estimates for Study Participants without a History of Colorectal Cancer: One-Way Analysis of Variance of Interleukin-8 (Extrapolation) by Time Point									
Diet	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Control	Time	Day 14	Day 0	1.06	2.12	0.17	6.66	0.942	0.575
		Day 28	Day 0	0.51	2.12	0.08	3.23	0.410	
		Day 28	Day 14	0.49	2.12	0.08	3.06	0.374	
		Day 14	Day 0	1.05	1.47	0.44	2.50	0.908	
		Day 28	Day 0	0.90	1.47	0.38	2.16	0.799	
		Day 28	Day 14	0.86	1.47	0.36	2.07	0.712	
Navy Bean	Time	Day 14	Day 0	1.65	3.70	0.09	31.85	0.711	0.690
		Day 28	Day 0	2.27	3.70	0.12	43.88	0.546	
		Day 28	Day 14	1.38	3.70	0.07	26.62	0.812	

**Table 4:** Differences in plasma interleukin-10 and tumor necrosis factor between diet groups (left) and between time points (right) for study participants without a history of colorectal cancer. Variables shown above: IL-10 with substituted censored values (top), IL-10 with extrapolated censored values (second from top), TNF with substituted censored values (second from bottom), and TNF with extrapolated censored values (bottom). No significant differences were observed in the displayed variables between treatment groups or time points.

Parameter Estimates for Study Participants without a History of Colorectal Cancer: One-Way Analysis of Variance of Interleukin-10 (Substitution) by Diet Group									
Time Point	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Day 0	Diet	Navy Bean	Control	1.43	3.98	0.06	34.57	0.802	0.963
		Rice Bran	Control	1.10	3.98	0.05	26.66	0.946	
		Navy Bean	Rice Bran	1.30	3.59	0.07	24.76	0.844	
Day 14		Navy Bean	Control	1.13	3.49	0.06	20.15	0.925	0.963
		Rice Bran	Control	0.82	3.49	0.05	14.69	0.880	
		Navy Bean	Rice Bran	1.37	3.18	0.10	19.76	0.792	
Day 28	Navy Bean	Control	1.75	3.76	0.08	37.10	0.684	0.834	
	Rice Bran	Control	2.22	3.76	0.10	47.07	0.564		
	Navy Bean	Rice Bran	0.79	3.41	0.05	13.33	0.851		

Parameter Estimates for Study Participants without a History of Colorectal Cancer: One-Way Analysis of Variance of Interleukin-10 (Substitution) by Time Point									
Diet	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Control	Time	Day 14	Day 0	1.33	2.32	0.17	10.45	0.744	0.584
		Day 28	Day 0	0.63	2.32	0.08	4.93	0.602	
		Day 28	Day 14	0.47	2.32	0.06	3.70	0.406	
		Day 14	Day 0	1.05	1.84	0.27	4.16	0.934	
		Day 28	Day 0	0.77	1.84	0.19	3.04	0.678	
		Day 28	Day 14	0.73	1.84	0.19	2.89	0.619	
Navy Bean	Time	Day 14	Day 0	1.05	1.84	0.27	4.16	0.934	0.743
		Day 28	Day 0	0.77	1.84	0.19	3.04	0.678	
		Day 28	Day 14	0.73	1.84	0.19	2.89	0.619	
		Day 14	Day 0	0.996	6.08	0.02	59.10	0.998	
		Day 28	Day 0	1.27	6.08	0.02	75.18	0.898	
		Day 28	Day 14	1.27	6.08	0.02	75.46	0.897	
Rice Bran	Time	Day 14	Day 0	0.996	6.08	0.02	59.10	0.998	0.931
		Day 28	Day 0	1.27	6.08	0.02	75.18	0.898	
		Day 28	Day 14	1.27	6.08	0.02	75.46	0.897	

Parameter Estimates for Study Participants without a History of Colorectal Cancer: One-Way Analysis of Variance of Interleukin-10 (Extrapolation) by Diet Group									
Time Point	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Day 0	Diet	Navy Bean	Control	0.33	19.08	0.00	299.81	0.720	0.416
		Rice Bran	Control	0.02	19.08	0.00	18.27	0.223	
		Navy Bean	Rice Bran	16.41	15.33	0.03	8895.35	0.336	
Day 14		Navy Bean	Control	1.13	10.42	0.01	251.26	0.960	0.426
		Rice Bran	Control	0.08	10.42	0.00	16.85	0.303	
		Navy Bean	Rice Bran	14.91	8.76	0.10	2222.40	0.248	
Day 28	Navy Bean	Control	2.17	24.36	0.00	3416.36	0.815	0.938	
	Rice Bran	Control	0.77	24.36	0.00	1218.49	0.938		
	Navy Bean	Rice Bran	2.80	19.22	0.00	2560.11	0.736		

Parameter Estimates for Study Participants without a History of Colorectal Cancer: One-Way Analysis of Variance of Interleukin-10 (Extrapolation) by Time Point									
Diet	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Control	Time	Day 14	Day 0	1.11	6.48	0.01	107.05	0.958	0.511
		Day 28	Day 0	0.12	6.48	0.00	11.47	0.297	
		Day 28	Day 14	0.11	6.48	0.00	10.35	0.277	
		Day 14	Day 0	3.75	7.64	0.04	372.19	0.532	
		Day 28	Day 0	0.77	7.64	0.01	76.53	0.901	
		Day 28	Day 14	0.21	7.64	0.00	20.43	0.457	
Navy Bean	Time	Day 14	Day 0	3.75	7.64	0.04	372.19	0.532	0.630
		Day 28	Day 0	0.77	7.64	0.01	76.53	0.901	
		Day 28	Day 14	0.21	7.64	0.00	20.43	0.457	
		Day 14	Day 0	4.12	35.30	0.00	13076.59	0.700	
		Day 28	Day 0	4.51	35.30	0.00	14301.08	0.683	
		Day 28	Day 14	1.09	35.30	0.00	3469.64	0.981	
Rice Bran	Time	Day 14	Day 0	4.12	35.30	0.00	13076.59	0.700	0.788
		Day 28	Day 0	4.51	35.30	0.00	14301.08	0.683	
		Day 28	Day 14	1.09	35.30	0.00	3469.64	0.981	

Parameter Estimates for Study Participants without a History of Colorectal Cancer: One-Way Analysis of Variance of Tumor Necrosis Factor (Substitution) by Diet Group									
Time Point	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Day 0	Diet	Navy Bean	Control	1.34	2.06	0.26	7.09	0.692	0.800
		Rice Bran	Control	0.86	2.06	0.16	4.54	0.841	
		Navy Bean	Rice Bran	1.56	1.95	0.34	7.28	0.523	
Day 14		Navy Bean	Control	1.13	2.01	0.23	5.64	0.868	0.978
		Rice Bran	Control	1.00	2.01	0.20	4.98	0.995	
		Navy Bean	Rice Bran	1.13	1.91	0.26	5.03	0.852	
Day 28	Navy Bean	Control	1.82	1.75	0.50	6.63	0.315	0.479	
	Rice Bran	Control	1.93	1.75	0.53	7.02	0.275		
	Navy Bean	Rice Bran	0.94	1.68	0.29	3.12	0.915		

Parameter Estimates for Study Participants without a History of Colorectal Cancer: One-Way Analysis of Variance of Tumor Necrosis Factor (Substitution) by Time Point									
Diet	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Control	Time	Day 14	Day 0	0.97	1.35	0.47	2.03	0.934	0.412
		Day 28	Day 0	0.60	1.35	0.29	1.26	0.142	
		Day 28	Day 14	0.62	1.35	0.30	1.29	0.160	
		Day 14	Day 0	0.82	1.19	0.55	1.22	0.282	
		Day 28	Day 0	0.82	1.19	0.55	1.22	0.279	
		Day 28	Day 14	0.999	1.19	0.67	1.49	0.994	
Navy Bean	Time	Day 14	Day 0	0.82	1.19	0.55	1.22	0.282	0.518
		Day 28	Day 0	0.82	1.19	0.55	1.22	0.279	
		Day 28	Day 14	0.999	1.19	0.67	1.49	0.994	
		Day 14	Day 0	1.13	2.62	0.13	9.98	0.904	
		Day 28	Day 0	1.35	2.62	0.15	11.95	0.763	
		Day 28	Day 14	1.20	2.62	0.14	10.61	0.856	
Rice Bran	Time	Day 14	Day 0	1.13	2.62	0.13	9.98	0.904	0.841
		Day 28	Day 0	1.35	2.62	0.15	11.95	0.763	
		Day 28	Day 14	1.20	2.62	0.14	10.61	0.856	

Parameter Estimates for Study Participants without a History of Colorectal Cancer: One-Way Analysis of Variance of Tumor Necrosis Factor (Extrapolation) by Diet Group									
Time Point	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Day 0	Diet	Navy Bean	Control	1.34	1.98	0.28	6.50	0.676	0.824
		Rice Bran	Control	0.92	1.98	0.19	4.43	0.903	
		Navy Bean	Rice Bran	1.47	1.88	0.34	6.30	0.562	
Day 14		Navy Bean	Control	1.13	1.82	0.28	4.50	0.847	0.967
		Rice Bran	Control	1.82	1.82	0.29	4.64	0.809	
		Navy Bean	Rice Bran	0.97	1.74	0.27	3.50	0.958	
Day 28	Navy Bean	Control	1.82	1.75	0.50	6.63	0.315	0.479	
	Rice Bran	Control	1.93	1.75	0.53	7.02	0.275		
	Navy Bean	Rice Bran	0.94	1.68	0.29	3.12	0.915		

Parameter Estimates for Study Participants without a History of Colorectal Cancer: One-Way Analysis of Variance of Tumor Necrosis Factor (Extrapolation) by Time Point									
Diet	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Control	Time	Day 14	Day 0	0.97	1.35	0.47	2.03	0.934	0.412
		Day 28	Day 0	0.60	1.35	0.29	1.26	0.142	
		Day 28	Day 14	0.62	1.35	0.30	1.29	0.160	
		Day 14	Day 0	0.82	1.19	0.55	1.22	0.282	
		Day 28	Day 0	0.82	1.19	0.55	1.22	0.279	
		Day 28	Day 14	0.999	1.19	0.67	1.49	0.994	
Navy Bean	Time	Day 14	Day 0	0.82	1.19	0.55	1.22	0.282	0.518
		Day 28	Day 0	0.82	1.19	0.55	1.22	0.279	
		Day 28	Day 14	0.999	1.19	0.67	1.49	0.994	
		Day 14	Day 0	1.23	2.44	0.16	9.24	0.819	
		Day 28	Day 0	1.27	2.44	0.17	9.49	0.797	
		Day 28	Day 14	1.03	2.44	0.14	7.69	0.978	
Rice Bran	Time	Day 14	Day 0	1.23	2.44	0.16	9.24	0.819	0.865
		Day 28	Day 0	1.27	2.44	0.17	9.49	0.797	
		Day 28	Day 14	1.03	2.44	0.14	7.69	0.978	

**Table 5:** Differences in age, weight, and body mass index between diet groups (left) and between time points (right) for study participants with a history of colorectal cancer. Variables shown above: age (top), weight (middle), and body mass index (BMI; bottom). No significant differences were observed between time point or diet group.

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Age by Diet Group									
Time Point	Parameter	Comparison groups		Diff. of Arithmetic Means (years)	Standard Error	95% Confidence Limits		p-value	Type III p-value
Day 0	Diet	Navy Bean	Control	-5.60	5.15	-16.19	4.99	0.287	0.561
		Rice Bran	Control	-2.73	5.29	-13.61	8.15	0.610	
		Navy Bean	Rice Bran	-2.87	5.29	-13.75	8.01	0.593	
Day 14		Navy Bean	Control	-5.60	5.15	-16.19	4.99	0.287	0.561
		Rice Bran	Control	-2.73	5.29	-13.61	8.15	0.610	
		Navy Bean	Rice Bran	-2.87	5.29	-13.75	8.01	0.593	
Day 28		Navy Bean	Control	-5.70	5.17	-16.33	4.93	0.280	0.552
		Rice Bran	Control	-2.83	5.31	-13.75	8.09	0.598	
		Navy Bean	Rice Bran	-2.87	5.31	-13.79	8.05	0.594	

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Age by Time Point									
Diet	Parameter	Comparison groups		Diff. of Arithmetic Means (years)	Standard Error	95% Confidence Limits		p-value	Type III p-value
Control	Time	Day 14	Day 0	0.00	6.20	-12.73	12.73	1.000	1.000
		Day 28	Day 0	0.10	6.20	-12.63	12.83	0.987	
		Day 28	Day 14	0.10	6.20	-12.63	12.83	0.987	
Navy Bean		Day 14	Day 0	0.00	5.32	-10.92	10.92	1.000	1.000
		Day 28	Day 0	0.00	5.32	-10.92	10.92	1.000	
		Day 28	Day 14	0.00	5.32	-10.92	10.92	1.000	
Rice Bran		Day 14	Day 0	0.00	3.54	-7.31	7.31	1.000	1.000
		Day 28	Day 0	0.00	3.54	-7.31	7.31	1.000	
		Day 28	Day 14	0.00	3.54	-7.31	7.31	1.000	

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Weight by Diet Group									
Time Point	Parameter	Comparison groups		Diff. of Arithmetic Means (kg)	Standard Error	95% Confidence Limits		p-value	Type III p-value
Day 0	Diet	Navy Bean	Control	2.35	8.11	-14.33	19.02	0.775	0.708
		Rice Bran	Control	6.89	8.34	-10.25	24.02	0.416	
		Navy Bean	Rice Bran	-4.54	8.34	-21.68	12.59	0.591	
Day 14		Navy Bean	Control	2.66	8.11	-14.01	19.33	0.746	0.773
		Rice Bran	Control	6.01	8.33	-11.12	23.14	0.477	
		Navy Bean	Rice Bran	-3.35	8.33	-20.48	13.78	0.691	
Day 28		Navy Bean	Control	2.94	8.19	-13.89	19.77	0.723	0.720
		Rice Bran	Control	6.86	8.41	-10.43	24.15	0.422	
		Navy Bean	Rice Bran	-3.92	8.41	-21.22	13.37	0.645	

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Weight by Time Point									
Diet	Parameter	Comparison groups		Diff. of Arithmetic Means (kg)	Standard Error	95% Confidence Limits		p-value	Type III p-value
Control	Time	Day 14	Day 0	-0.34	7.54	-15.82	15.13	0.964	0.997
		Day 28	Day 0	-0.54	7.54	-16.01	14.93	0.943	
		Day 28	Day 14	-0.20	7.54	-15.67	15.27	0.979	
Navy Bean		Day 14	Day 0	-0.03	9.05	-18.61	18.55	0.998	1.000
		Day 28	Day 0	0.05	9.05	-18.53	18.63	0.996	
		Day 28	Day 14	0.08	9.05	-18.50	18.66	0.993	
Rice Bran		Day 14	Day 0	-1.22	8.10	-17.94	15.49	0.881	0.989
		Day 28	Day 0	-0.57	8.10	-17.28	16.15	0.945	
		Day 28	Day 14	0.65	8.10	-16.06	17.37	0.936	

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Body Mass Index by Diet Group									
Time Point	Parameter	Comparison groups		Diff. of Arithmetic Means (kg/m <sup>2</sup> )	Standard Error	95% Confidence Limits		p-value	Type III p-value
Day 0	Diet	Navy Bean	Control	1.22	2.61	-4.14	6.58	0.644	0.837
		Rice Bran	Control	1.48	2.68	-4.02	6.99	0.584	
		Navy Bean	Rice Bran	-0.26	2.68	-5.77	5.24	0.922	
Day 14		Navy Bean	Control	1.32	2.62	-4.06	6.70	0.619	0.858
		Rice Bran	Control	1.21	2.69	-4.33	6.74	0.658	
		Navy Bean	Rice Bran	0.11	2.69	-5.42	5.65	0.966	
Day 28		Navy Bean	Control	1.40	2.67	-4.09	6.89	0.605	0.827
		Rice Bran	Control	1.49	2.75	-4.16	7.13	0.592	
		Navy Bean	Rice Bran	-0.09	2.75	-5.73	5.56	0.974	

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Body Mass Index by Time Point									
Diet	Parameter	Comparison groups		Diff. of Arithmetic Means (kg/m <sup>2</sup> )	Standard Error	95% Confidence Limits		p-value	Type III p-value
Control	Time	Day 14	Day 0	-0.11	1.45	-3.08	2.86	0.940	0.994
		Day 28	Day 0	-0.16	1.45	-3.13	2.81	0.913	
		Day 28	Day 14	-0.05	1.45	-3.02	2.92	0.973	
Navy Bean		Day 14	Day 0	-0.01	3.62	-7.43	7.41	0.998	1.000
		Day 28	Day 0	0.02	3.62	-7.40	7.44	0.996	
		Day 28	Day 14	0.03	3.62	-7.39	7.45	0.993	
Rice Bran		Day 14	Day 0	-0.39	2.46	-5.47	4.69	0.876	0.987
		Day 28	Day 0	-0.16	2.46	-5.23	4.92	0.950	
		Day 28	Day 14	0.23	2.46	-4.84	5.31	0.925	

**Table 6:** Differences in plasma interleukin-2 between diet groups (left) and between time points (right) for study participants with a history of colorectal cancer (n=23). Many study participants had IL-2 levels that were below the lowest level of detection of the cytokine immunoassay (39.1% at day 0, 43.4% at day 14, and 43.4% at day 28). Shown above are analyses of four different IL-2 data sets that each utilized a different approach for managing left-censored data. These approaches are: substitution with a fixed value (top), extrapolation using the 5-parametric logistic standard curve equation (second from top), Tobit regression (second from bottom), and multiple imputation (bottom). For all approaches, no significant difference was observed in plasma IL-2 level between diet group or time point.

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Interleukin-2 (Substitution) by Diet Group								
Time Point	Parameter	Comparison groups	Ratio of Geometric Means	Standard Error	95% Confidence Limits	p-value	Type III p-value	
Day 0	Diet	Navy Bean Control	1.49	1.75	0.46	4.82	0.483	0.740
		Rice Bran Control	1.01	1.68	0.34	2.99	0.980	
		Navy Bean Rice Bran	1.47	1.78	0.44	4.90	0.508	
Day 14		Navy Bean Control	1.51	1.75	0.47	4.88	0.468	0.752
		Rice Bran Control	1.09	1.68	0.37	3.20	0.873	
		Navy Bean Rice Bran	1.39	1.78	0.42	4.62	0.571	
Day 28	Navy Bean Control	2.10	1.72	0.68	6.47	0.186	0.405	
	Rice Bran Control	1.28	1.65	0.45	3.62	0.626		
	Navy Bean Rice Bran	1.64	1.74	0.52	5.20	0.383		

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Interleukin-2 (Substitution) by Time Point								
Diet	Parameter	Comparison groups	Ratio of Geometric Means	Standard Error	95% Confidence Limits	p-value	Type III p-value	
Control	Time	Day 14 Day 0	0.90	1.67	0.31	2.58	0.831	0.859
		Day 28 Day 0	0.76	1.67	0.26	2.17	0.589	
		Day 28 Day 14	0.84	1.67	0.29	2.43	0.742	
Navy Bean		Day 14 Day 0	0.91	1.64	0.32	2.60	0.847	0.951
		Day 28 Day 0	1.06	1.64	0.37	3.03	0.908	
		Day 28 Day 14	1.17	1.64	0.41	3.34	0.758	
Rice Bran	Day 14 Day 0	0.96	1.76	0.29	3.13	0.945	0.996	
	Day 28 Day 0	0.95	1.76	0.29	3.11	0.934		
	Day 28 Day 14	0.99	1.76	0.30	3.23	0.989		

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Interleukin-2 (Extrapolation) by Diet Group								
Time Point	Parameter	Comparison groups	Ratio of Geometric Means	Standard Error	95% Confidence Limits	p-value	Type III p-value	
Day 0	Diet	Navy Bean Control	9.08	5.23	0.29	286.37	0.197	0.217
		Rice Bran Control	0.44	4.60	0.02	10.66	0.599	
		Navy Bean Rice Bran	20.52	5.45	0.60	704.78	0.090	
Day 14		Navy Bean Control	8.94	4.83	0.33	239.01	0.180	0.289
		Rice Bran Control	0.80	4.27	0.04	16.46	0.877	
		Navy Bean Rice Bran	11.23	5.02	0.39	325.83	0.150	
Day 28	Navy Bean Control	4.28	5.55	0.12	152.94	0.406	0.604	
	Rice Bran Control	0.81	4.86	0.03	21.76	0.893		
	Navy Bean Rice Bran	5.32	5.79	0.14	207.31	0.353		

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Interleukin-2 (Extrapolation) by Time Point								
Diet	Parameter	Comparison groups	Ratio of Geometric Means	Standard Error	95% Confidence Limits	p-value	Type III p-value	
Control	Time	Day 14 Day 0	0.86	4.81	0.03	22.01	0.925	0.995
		Day 28 Day 0	0.88	4.81	0.03	22.40	0.934	
		Day 28 Day 14	1.02	4.81	0.04	26.01	0.991	
Navy Bean		Day 14 Day 0	0.85	2.74	0.10	7.25	0.872	0.655
		Day 28 Day 0	0.41	2.74	0.05	3.54	0.394	
		Day 28 Day 14	0.49	2.74	0.06	4.17	0.487	
Rice Bran	Day 14 Day 0	1.55	6.11	0.04	66.83	0.812	0.959	
	Day 28 Day 0	1.60	6.11	0.04	68.89	0.799		
	Day 28 Day 14	1.03	6.11	0.02	44.49	0.987		

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Interleukin-2 (Tobit Regression) by Diet Group								
Time Point	Parameter	Comparison groups	Ratio of Geometric Means	Standard Error	95% Confidence Limits	p-value	Type III p-value	
Day 0	Diet	Navy Bean Control	1.56	1.82	0.48	5.03	0.461	0.719
		Rice Bran Control	1.01	1.77	0.33	3.08	0.985	
		Navy Bean Rice Bran	1.54	1.86	0.46	5.17	0.486	
Day 14		Navy Bean Control	1.66	1.90	0.47	5.83	0.430	0.718
		Rice Bran Control	1.12	1.83	0.34	3.67	0.854	
		Navy Bean Rice Bran	1.48	1.92	0.41	5.31	0.544	
Day 28	Navy Bean Control	2.36	1.85	0.71	7.90	0.163	0.374	
	Rice Bran Control	1.37	1.79	0.44	4.28	0.594		
	Navy Bean Rice Bran	1.73	1.86	0.51	5.84	0.377		

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Interleukin-2 (Tobit Regression) by Time Point								
Diet	Parameter	Comparison groups	Ratio of Geometric Means	Standard Error	95% Confidence Limits	p-value	Type III p-value	
Control	Time	Day 14 Day 0	0.84	1.98	0.22	3.21	0.796	0.850
		Day 28 Day 0	0.68	1.99	0.17	2.61	0.569	
		Day 28 Day 14	0.81	2.01	0.20	3.17	0.758	
Navy Bean		Day 14 Day 0	0.90	1.50	0.41	2.00	0.805	0.924
		Day 28 Day 0	1.06	1.50	0.48	2.35	0.883	
		Day 28 Day 14	1.17	1.50	0.53	2.60	0.693	
Rice Bran	Day 14 Day 0	0.95	2.07	0.23	3.99	0.948	0.997	
	Day 28 Day 0	0.94	2.08	0.23	3.95	0.938		
	Day 28 Day 14	0.99	2.08	0.24	4.15	0.990		

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Interleukin-2 (Multiple Imputation) by Diet Group								
Time Point	Parameter	Comparison groups	Ratio of Geometric Means	Standard Error	95% Confidence Limits	p-value	Type III p-value	
Day 0	Diet	Navy Bean Control	1.31	1.68	0.48	3.61	0.599	0.838
		Rice Bran Control	1.22	1.66	0.45	3.30	0.697	
		Navy Bean Rice Bran	1.08	1.70	0.38	3.03	0.889	
Day 14		Navy Bean Control	1.22	1.57	0.50	2.98	0.657	0.876
		Rice Bran Control	1.02	1.52	0.45	2.32	0.967	
		Navy Bean Rice Bran	1.20	1.59	0.49	2.98	0.690	
Day 28	Navy Bean Control	2.20	1.79	0.69	6.98	0.178	0.314	
	Rice Bran Control	1.67	1.71	0.58	4.83	0.337		
	Navy Bean Rice Bran	1.31	1.71	0.46	3.75	0.609		

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Interleukin-2 (Multiple Imputation) by Time Point								
Diet	Parameter	Comparison groups	Ratio of Geometric Means	Standard Error	95% Confidence Limits	p-value	Type III p-value	
Control	Time	Day 14 Day 0	0.99	1.71	0.34	2.85	0.987	0.551
		Day 28 Day 0	0.62	1.80	0.19	2.02	0.421	
		Day 28 Day 14	0.63	1.76	0.20	1.92	0.408	
Navy Bean		Day 14 Day 0	0.92	1.54	0.40	2.14	0.855	0.951
		Day 28 Day 0	1.04	1.54	0.45	2.41	0.927	
		Day 28 Day 14	1.12	1.54	0.48	2.62	0.785	
Rice Bran	Day 14 Day 0	0.83	1.60	0.33	2.07	0.687	0.898	
	Day 28 Day 0	0.85	1.60	0.34	2.13	0.731		
	Day 28 Day 14	1.03	1.57	0.43	2.49	0.950		

**Table 7:** Differences in plasma interleukin-4 between diet groups (left) and between time points (right) for study participants with a history of colorectal cancer (n=23). Many study participants had IL-4 levels that were below the lowest level of detection of the cytokine immunoassay (47.8% at day 0, 47.8% at day 14, and 47.8% at day 28). Shown above are analyses of four different IL-4 data sets that each utilized a different approach for managing left-censored data. These approaches are: substitution with a fixed value (top), extrapolation using the 5-parametric logistic standard curve equation (second from top), Tobit regression (second from bottom), and multiple imputation (bottom). For all approaches, no significant difference was observed in plasma IL-4 level between diet group or time point.

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Interleukin-4 (Substitution) by Diet Group									
Time Point	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Day 0	Diet	Navy Bean	Control	1.10	2.05	0.25	4.94	0.894	0.983
		Rice Bran	Control	1.12	1.94	0.28	4.47	0.865	
		Navy Bean	Rice Bran	0.98	2.09	0.21	4.57	0.982	
Day 14		Navy Bean	Control	1.52	1.98	0.37	6.34	0.545	0.821
		Rice Bran	Control	1.09	1.88	0.29	4.07	0.890	
		Navy Bean	Rice Bran	1.39	2.01	0.32	6.01	0.640	
Day 28	Navy Bean	Control	1.78	1.98	0.43	7.46	0.408	0.702	
	Rice Bran	Control	1.32	1.88	0.35	4.92	0.668		
	Navy Bean	Rice Bran	1.36	2.02	0.31	5.87	0.669		

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Interleukin-4 (Substitution) by Time Point									
Diet	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Control	Time	Day 14	Day 0	0.97	1.82	0.28	3.34	0.960	0.948
		Day 28	Day 0	0.83	1.82	0.24	2.87	0.763	
		Day 28	Day 14	0.86	1.82	0.25	2.96	0.802	
Navy Bean		Day 14	Day 0	1.34	2.27	0.23	7.68	0.726	0.917
		Day 28	Day 0	1.35	2.27	0.24	7.73	0.720	
		Day 28	Day 14	1.01	2.27	0.18	5.77	0.994	
Rice Bran	Day 14	Day 0	0.94	1.92	0.24	3.67	0.931	0.996	
	Day 28	Day 0	0.98	1.92	0.25	3.80	0.973		
	Day 28	Day 14	1.04	1.92	0.27	4.02	0.958		

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Interleukin-4 (Extrapolation) by Diet Group									
Time Point	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Day 0	Diet	Navy Bean	Control	4.62	6.96	0.08	264.59	0.440	0.653
		Rice Bran	Control	0.82	5.99	0.02	34.38	0.914	
		Navy Bean	Rice Bran	5.61	7.31	0.09	355.45	0.396	
Day 14		Navy Bean	Control	4.85	6.94	0.09	275.36	0.425	0.629
		Rice Bran	Control	0.80	5.96	0.02	33.00	0.900	
		Navy Bean	Rice Bran	6.09	7.27	0.10	382.14	0.374	
Day 28	Navy Bean	Control	7.67	6.73	0.14	409.88	0.298	0.502	
	Rice Bran	Control	0.97	5.80	0.02	38.07	0.987		
	Navy Bean	Rice Bran	7.89	7.06	0.13	465.03	0.303		

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Interleukin-4 (Extrapolation) by Time Point									
Diet	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Control	Time	Day 14	Day 0	0.98	5.80	0.03	36.69	0.989	0.993
		Day 28	Day 0	0.83	5.80	0.02	31.11	0.915	
		Day 28	Day 14	0.85	5.80	0.02	31.87	0.926	
Navy Bean		Day 14	Day 0	1.02	5.79	0.02	43.35	0.989	0.980
		Day 28	Day 0	1.38	5.79	0.03	58.19	0.858	
		Day 28	Day 14	1.34	5.79	0.03	56.78	0.869	
Rice Bran	Day 14	Day 0	0.94	7.27	0.02	58.50	0.977	1.000	
	Day 28	Day 0	0.98	7.27	0.02	60.58	0.991		
	Day 28	Day 14	1.04	7.27	0.02	64.14	0.986		

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Interleukin-4 (Tobit Regression) by Diet Group									
Time Point	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Day 0	Diet	Navy Bean	Control	1.18	2.81	0.16	8.99	0.871	0.977
		Rice Bran	Control	1.21	2.60	0.19	7.85	0.843	
		Navy Bean	Rice Bran	0.98	2.86	0.12	7.69	0.984	
Day 14		Navy Bean	Control	1.83	2.43	0.32	10.43	0.497	0.785
		Rice Bran	Control	1.15	2.31	0.22	5.95	0.865	
		Navy Bean	Rice Bran	1.59	2.47	0.27	9.29	0.610	
Day 28	Navy Bean	Control	2.24	2.46	0.38	13.07	0.371	0.670	
	Rice Bran	Control	1.46	2.33	0.28	7.68	0.657		
	Navy Bean	Rice Bran	1.54	2.48	0.26	9.13	0.638		

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Interleukin-4 (Tobit Regression) by Time Point									
Diet	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Control	Time	Day 14	Day 0	0.96	2.49	0.16	5.76	0.966	0.964
		Day 28	Day 0	0.79	2.50	0.13	4.79	0.801	
		Day 28	Day 14	0.82	2.50	0.14	4.98	0.834	
Navy Bean		Day 14	Day 0	1.51	2.61	0.23	9.84	0.669	0.885
		Day 28	Day 0	1.52	2.60	0.23	9.91	0.663	
		Day 28	Day 14	1.01	2.55	0.16	6.30	0.994	
Rice Bran	Day 14	Day 0	0.93	2.42	0.16	5.29	0.938	0.997	
	Day 28	Day 0	0.97	2.42	0.17	5.51	0.976		
	Day 28	Day 14	1.04	2.42	0.18	5.91	0.962		

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Interleukin-4 (Multiple Imputation) by Diet Group									
Time Point	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Day 0	Diet	Navy Bean	Control	0.86	1.93	0.24	3.12	0.814	0.895
		Rice Bran	Control	1.09	1.86	0.32	3.68	0.887	
		Navy Bean	Rice Bran	0.78	2.00	0.20	3.07	0.726	
Day 14		Navy Bean	Control	1.20	1.79	0.38	3.75	0.754	0.932
		Rice Bran	Control	1.04	1.70	0.37	2.97	0.935	
		Navy Bean	Rice Bran	1.15	1.80	0.36	3.65	0.814	
Day 28	Navy Bean	Control	1.73	1.90	0.49	6.13	0.395	0.643	
	Rice Bran	Control	1.44	1.82	0.44	4.68	0.546		
	Navy Bean	Rice Bran	1.20	1.88	0.35	4.17	0.769		

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Interleukin-4 (Multiple Imputation) by Time Point									
Diet	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Control	Time	Day 14	Day 0	0.89	1.70	0.31	2.52	0.823	0.676
		Day 28	Day 0	0.64	1.72	0.22	1.86	0.415	
		Day 28	Day 14	0.72	1.70	0.26	2.05	0.542	
Navy Bean		Day 14	Day 0	1.24	2.19	0.27	5.76	0.780	0.913
		Day 28	Day 0	1.30	2.19	0.28	6.07	0.739	
		Day 28	Day 14	1.04	2.15	0.23	4.67	0.954	
Rice Bran	Day 14	Day 0	0.85	1.75	0.28	2.55	0.771	0.934	
	Day 28	Day 0	0.85	1.75	0.28	2.53	0.765		
	Day 28	Day 14	1.00	1.71	0.35	2.85	0.996		

**Table 8:** Differences in plasma interleukin-6 between diet groups (left) and between time points (right) for study participants with a history of colorectal cancer (n=23). Many study participants had IL-6 levels that were below the lowest level of detection of the cytokine immunoassay (47.8% at day 0, 52.1% at day 14, and 52.1% at day 28). Shown above are analyses of four different IL-6 data sets that each utilized a different approach for managing left-censored data. These approaches are: substitution with a fixed value (top), extrapolation using the 5-parametric logistic standard curve equation (second from top), Tobit regression (second from bottom), and multiple imputation (bottom). For all approaches, no significant difference was observed in plasma IL-6 level between diet group or time point.

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Interleukin-6 (Substitution) by Diet Group									
Time Point	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Day 0	Diet	Navy Bean	Control	1.03	1.59	0.39	2.71	0.952	0.991
		Rice Bran	Control	0.97	1.53	0.40	2.36	0.938	
		Navy Bean	Rice Bran	1.06	1.61	0.39	2.87	0.898	
Day 14		Navy Bean	Control	1.05	1.60	0.39	2.80	0.920	0.990
		Rice Bran	Control	1.06	1.54	0.43	2.62	0.898	
		Navy Bean	Rice Bran	0.99	1.62	0.36	2.72	0.986	
Day 28		Navy Bean	Control	1.53	1.64	0.55	4.30	0.396	0.577
		Rice Bran	Control	1.53	1.58	0.59	3.95	0.364	
		Navy Bean	Rice Bran	1.00	1.66	0.35	2.89	0.993	

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Interleukin-6 (Substitution) by Time Point									
Diet	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Control	Time	Day 14	Day 0	0.92	1.50	0.40	2.10	0.828	0.766
		Day 28	Day 0	0.75	1.50	0.33	1.72	0.481	
		Day 28	Day 14	0.82	1.50	0.36	1.88	0.624	
Navy Bean		Day 14	Day 0	0.93	1.75	0.28	3.09	0.904	0.949
		Day 28	Day 0	1.12	1.75	0.34	3.70	0.846	
		Day 28	Day 14	1.20	1.75	0.36	3.97	0.753	
Rice Bran		Day 14	Day 0	1.00	1.57	0.39	2.57	0.997	0.913
		Day 28	Day 0	1.18	1.57	0.46	3.03	0.714	
		Day 28	Day 14	1.18	1.57	0.46	3.03	0.717	

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Interleukin-6 (Extrapolation) by Diet Group									
Time Point	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Day 0	Diet	Navy Bean	Control	3.20	3.13	0.30	34.59	0.521	0.542
		Rice Bran	Control	1.01	2.87	0.11	9.12	0.989	
		Navy Bean	Rice Bran	3.15	3.22	0.27	36.16	0.338	
Day 14		Navy Bean	Control	3.80	3.26	0.32	44.65	0.271	0.534
		Rice Bran	Control	1.50	2.97	0.15	14.53	0.714	
		Navy Bean	Rice Bran	2.54	3.35	0.20	31.64	0.451	
Day 28		Navy Bean	Control	4.14	3.94	0.24	72.16	0.312	0.590
		Rice Bran	Control	1.58	3.54	0.11	22.10	0.720	
		Navy Bean	Rice Bran	2.61	4.07	0.14	48.88	0.502	

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Interleukin-6 (Extrapolation) by Time Point									
Diet	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Control	Time	Day 14	Day 0	0.86	3.50	0.07	11.46	0.908	0.901
		Day 28	Day 0	0.57	3.50	0.04	7.62	0.662	
		Day 28	Day 14	0.66	3.50	0.05	8.81	0.747	
Navy Bean		Day 14	Day 0	1.03	1.94	0.25	4.21	0.967	0.864
		Day 28	Day 0	0.74	1.94	0.18	3.05	0.661	
		Day 28	Day 14	0.72	1.94	0.18	2.96	0.632	
Rice Bran		Day 14	Day 0	1.28	3.64	0.09	18.79	0.852	0.962
		Day 28	Day 0	0.90	3.64	0.06	13.19	0.934	
		Day 28	Day 14	0.70	3.64	0.05	10.33	0.787	

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Interleukin-6 (Tobit Regression) by Diet Group									
Time Point	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Day 0	Diet	Navy Bean	Control	1.03	1.68	0.38	2.85	0.947	0.990
		Rice Bran	Control	0.96	1.61	0.38	2.45	0.932	
		Navy Bean	Rice Bran	1.08	1.70	0.38	3.06	0.888	
Day 14		Navy Bean	Control	1.07	1.78	0.35	3.31	0.908	0.988
		Rice Bran	Control	1.08	1.70	0.38	3.07	0.884	
		Navy Bean	Rice Bran	0.99	1.80	0.31	3.12	0.986	
Day 28		Navy Bean	Control	1.87	1.90	0.53	6.60	0.331	0.524
		Rice Bran	Control	1.82	1.83	0.56	5.93	0.319	
		Navy Bean	Rice Bran	1.03	1.87	0.30	3.49	0.967	

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Interleukin-6 (Tobit Regression) by Time Point									
Diet	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Control	Time	Day 14	Day 0	0.88	1.68	0.32	2.45	0.812	0.730
		Day 28	Day 0	0.66	1.72	0.23	1.90	0.436	
		Day 28	Day 14	0.74	1.73	0.25	2.17	0.585	
Navy Bean		Day 14	Day 0	0.92	1.90	0.26	3.23	0.896	0.936
		Day 28	Day 0	1.15	1.87	0.34	3.95	0.822	
		Day 28	Day 14	1.25	1.88	0.36	4.31	0.720	
Rice Bran		Day 14	Day 0	1.00	1.69	0.36	2.81	0.997	0.905
		Day 28	Day 0	1.22	1.69	0.44	3.41	0.698	
		Day 28	Day 14	1.22	1.69	0.44	3.40	0.701	

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Interleukin-6 (Multiple Imputation) by Diet Group									
Time Point	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Day 0	Diet	Navy Bean	Control	1.04	1.63	0.40	2.73	0.936	0.856
		Rice Bran	Control	1.16	1.58	0.47	2.85	0.749	
		Navy Bean	Rice Bran	0.90	1.62	0.35	2.33	0.825	
Day 14		Navy Bean	Control	1.03	1.52	0.45	2.34	0.950	0.909
		Rice Bran	Control	1.04	1.52	0.46	2.38	0.919	
		Navy Bean	Rice Bran	0.98	1.58	0.40	2.43	0.972	
Day 28		Navy Bean	Control	2.02	1.80	0.63	6.52	0.234	0.229
		Rice Bran	Control	2.37	1.80	0.71	7.89	0.153	
		Navy Bean	Rice Bran	0.85	1.71	0.30	2.45	0.767	

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Interleukin-6 (Multiple Imputation) by Time Point									
Diet	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Control	Time	Day 14	Day 0	0.99	1.60	0.39	2.48	0.981	0.404
		Day 28	Day 0	0.56	1.75	0.18	1.72	0.300	
		Day 28	Day 14	0.56	1.72	0.19	1.68	0.295	
Navy Bean		Day 14	Day 0	0.98	1.73	0.33	2.86	0.965	0.910
		Day 28	Day 0	1.08	1.73	0.37	3.18	0.889	
		Day 28	Day 14	1.11	1.69	0.40	3.08	0.847	
Rice Bran		Day 14	Day 0	0.89	1.56	0.36	2.19	0.798	0.720
		Day 28	Day 0	1.14	1.47	0.53	2.44	0.739	
		Day 28	Day 14	1.28	1.52	0.55	2.95	0.562	



**Table 10:** Differences in plasma interleukin-10 between diet groups (left) and between time points (right) for study participants with a history of colorectal cancer (n=23). Many study participants had IL-10 levels that were below the lowest level of detection of the cytokine immunoassay (39.1% at day 0, 34.8% at day 14, and 43.5% at day 28). Shown above are analyses of four different IL-10 data sets that each utilized a different approach for managing left-censored data. These approaches are: substitution with a fixed value (top), extrapolation using the 5-parametric logistic standard curve equation (second from top), Tobit regression (second from bottom), and multiple imputation (bottom). For all approaches, no significant difference was observed in plasma IL-10 level between diet group or time point.

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Interleukin-10 (Substitution) by Diet Group									
Time Point	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Day 0	Diet	Navy Bean	Control	1.61	1.88	0.43	6.02	0.457	0.738
		Rice Bran	Control	1.09	1.79	0.32	3.66	0.886	
		Navy Bean	Rice Bran	1.48	1.91	0.39	5.71	0.548	
Day 14		Navy Bean	Control	1.31	1.86	0.36	4.77	0.668	0.908
		Rice Bran	Control	1.08	1.77	0.33	3.55	0.896	
		Navy Bean	Rice Bran	1.21	1.89	0.32	4.57	0.762	
Day 28	Navy Bean	Control	1.87	1.89	0.50	7.06	0.337	0.615	
	Rice Bran	Control	1.40	1.80	0.41	4.77	0.572		
	Navy Bean	Rice Bran	1.33	1.92	0.34	5.20	0.663		

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Interleukin-10 (Substitution) by Time Point									
Diet	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Control	Time	Day 14	Day 0	1.03	1.73	0.33	3.19	0.960	0.852
		Day 28	Day 0	0.78	1.73	0.25	2.40	0.646	
		Day 28	Day 14	0.75	1.73	0.24	2.34	0.611	
Navy Bean		Day 14	Day 0	0.83	1.84	0.23	3.07	0.771	0.957
		Day 28	Day 0	0.90	1.84	0.24	3.30	0.863	
		Day 28	Day 14	1.08	1.84	0.29	3.95	0.906	
Rice Bran	Day 14	Day 0	1.02	1.93	0.26	4.00	0.977	0.999	
	Day 28	Day 0	1.00	1.93	0.25	3.91	0.998		
	Day 28	Day 14	0.98	1.93	0.25	3.84	0.975		

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Interleukin-10 (Extrapolation) by Diet Group									
Time Point	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Day 0	Diet	Navy Bean	Control	5.50	4.58	0.23	131.55	0.276	0.348
		Rice Bran	Control	0.57	4.07	0.03	10.59	0.690	
		Navy Bean	Rice Bran	9.70	4.76	0.37	251.03	0.161	
Day 14		Navy Bean	Control	5.36	5.20	0.17	167.30	0.321	0.283
		Rice Bran	Control	0.34	4.58	0.01	8.00	0.481	
		Navy Bean	Rice Bran	15.98	5.42	0.47	543.04	0.117	
Day 28	Navy Bean	Control	4.08	6.33	0.09	191.53	0.455	0.577	
	Rice Bran	Control	0.56	5.48	0.02	19.57	0.739		
	Navy Bean	Rice Bran	7.25	6.63	0.14	374.56	0.308		

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Interleukin-10 (Extrapolation) by Time Point									
Diet	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Control	Time	Day 14	Day 0	0.81	4.47	0.04	17.72	0.886	0.875
		Day 28	Day 0	0.47	4.47	0.02	10.35	0.619	
		Day 28	Day 14	0.58	4.47	0.03	12.85	0.723	
Navy Bean		Day 14	Day 0	0.79	2.90	0.08	7.62	0.824	0.596
		Day 28	Day 0	0.35	2.90	0.04	3.38	0.339	
		Day 28	Day 14	0.44	2.90	0.05	4.31	0.458	
Rice Bran	Day 14	Day 0	0.48	6.93	0.01	26.69	0.706	0.905	
	Day 28	Day 0	0.47	6.93	0.01	26.14	0.698		
	Day 28	Day 14	0.98	6.93	0.02	54.84	0.992		

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Interleukin-10 (Tobit Regression) by Diet Group									
Time Point	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Day 0	Diet	Navy Bean	Control	1.75	2.01	0.45	6.88	0.423	0.703
		Rice Bran	Control	1.09	1.94	0.30	4.00	0.897	
		Navy Bean	Rice Bran	1.61	2.05	0.39	6.59	0.511	
Day 14		Navy Bean	Control	1.36	1.92	0.38	4.89	0.641	0.892
		Rice Bran	Control	1.07	1.86	0.31	3.61	0.919	
		Navy Bean	Rice Bran	1.27	1.98	0.33	4.85	0.723	
Day 28	Navy Bean	Control	2.29	2.16	0.50	10.41	0.283	0.558	
	Rice Bran	Control	1.54	2.07	0.37	6.45	0.552		
	Navy Bean	Rice Bran	1.49	2.17	0.32	6.81	0.611		

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Interleukin-10 (Tobit Regression) by Time Point									
Diet	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Control	Time	Day 14	Day 0	1.06	1.95	0.29	3.93	0.925	0.813
		Day 28	Day 0	0.71	1.99	0.18	2.71	0.611	
		Day 28	Day 14	0.66	1.98	0.17	2.52	0.546	
Navy Bean		Day 14	Day 0	0.83	1.73	0.28	2.44	0.734	0.943
		Day 28	Day 0	0.89	1.73	0.30	2.63	0.840	
		Day 28	Day 14	1.08	1.73	0.37	3.17	0.890	
Rice Bran	Day 14	Day 0	1.02	2.42	0.18	5.80	0.979	1.000	
	Day 28	Day 0	1.00	2.42	0.18	5.66	0.998		
	Day 28	Day 14	0.98	2.42	0.17	5.53	0.978		

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Interleukin-10 (Multiple Imputation) by Diet Group									
Time Point	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Day 0	Diet	Navy Bean	Control	1.25	1.75	0.42	3.73	0.692	0.901
		Rice Bran	Control	1.17	1.71	0.41	3.35	0.766	
		Navy Bean	Rice Bran	1.06	1.77	0.35	3.24	0.913	
Day 14		Navy Bean	Control	1.24	1.73	0.42	3.62	0.695	0.892
		Rice Bran	Control	1.19	1.66	0.44	3.22	0.726	
		Navy Bean	Rice Bran	1.04	1.73	0.35	3.05	0.946	
Day 28	Navy Bean	Control	1.58	1.73	0.54	4.61	0.407	0.672	
	Rice Bran	Control	1.37	1.67	0.50	3.77	0.536		
	Navy Bean	Rice Bran	1.15	1.76	0.38	3.48	0.810		

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Interleukin-10 (Multiple Imputation) by Time Point									
Diet	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Control	Time	Day 14	Day 0	0.86	1.63	0.33	2.25	0.760	0.783
		Day 28	Day 0	0.73	1.65	0.27	1.94	0.524	
		Day 28	Day 14	0.84	1.64	0.32	2.22	0.732	
Navy Bean		Day 14	Day 0	0.85	1.76	0.28	2.59	0.781	0.951
		Day 28	Day 0	0.92	1.75	0.30	2.76	0.878	
		Day 28	Day 14	1.07	1.75	0.36	3.22	0.899	
Rice Bran	Day 14	Day 0	0.88	1.77	0.29	2.68	0.816	0.936	
	Day 28	Day 0	0.85	1.78	0.28	2.63	0.780		
	Day 28	Day 14	0.97	1.73	0.33	2.84	0.959		

**Table 11:** Differences in plasma tumor necrosis factor between diet groups (left) and between time points (right) for study participants with a history of colorectal cancer (n=23). Only 2 study participants had TNF levels that were below the lowest level of detection of the cytokine immunoassay (8.7% at day 0, 0% at day 14, and 0% at day 28). Shown above are analyses of four different TNF data sets that each utilized a different approach for managing left-censored data. These approaches are: substitution with a fixed value (top), extrapolation using the 5-parametric logistic standard curve equation (second from top), Tobit regression (second from bottom), and multiple imputation (bottom). In all four approaches, at day 28, the navy bean group was observed to have significantly higher plasma TNF levels than the control group.

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Tumor Necrosis Factor (Substitution) by Diet Group									
Time Point	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Day 0	Diet	Navy Bean	Control	1.30	1.40	0.64	2.63	0.452	0.647
		Rice Bran	Control	0.95	1.37	0.50	1.83	0.874	
		Navy Bean	Rice Bran	1.36	1.42	0.66	2.82	0.382	
Day 14		Navy Bean	Control	1.34	1.23	0.87	2.06	0.179	0.392
		Rice Bran	Control	1.16	1.21	0.77	1.72	0.459	
		Navy Bean	Rice Bran	1.16	1.24	0.74	1.80	0.505	
Day 28	Navy Bean	Control	1.53	1.22	1.02	2.31	0.041	0.115	
	Rice Bran	Control	1.15	1.20	0.79	1.67	0.460		
	Navy Bean	Rice Bran	1.34	1.22	0.88	2.04	0.161		

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Tumor Necrosis Factor (Substitution) by Time Point									
Diet	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Control	Time	Day 14	Day 0	1.02	1.26	0.63	1.65	0.936	0.991
		Day 28	Day 0	0.99	1.26	0.61	1.60	0.955	
		Day 28	Day 14	0.97	1.26	0.60	1.57	0.892	
Navy Bean		Day 14	Day 0	1.05	1.25	0.65	1.69	0.834	0.784
		Day 28	Day 0	1.17	1.25	0.72	1.89	0.503	
		Day 28	Day 14	1.11	1.25	0.69	1.80	0.642	
Rice Bran	Day 14	Day 0	1.24	1.31	0.71	2.16	0.435	0.703	
	Day 28	Day 0	1.19	1.31	0.68	2.08	0.526		
	Day 28	Day 14	0.96	1.31	0.55	1.68	0.881		

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Tumor Necrosis Factor (Extrapolation) by Diet Group									
Time Point	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Day 0	Diet	Navy Bean	Control	1.20	1.30	0.70	2.08	0.491	0.675
		Rice Bran	Control	0.95	1.27	0.58	1.58	0.845	
		Navy Bean	Rice Bran	1.26	1.31	0.72	2.21	0.599	
Day 14		Navy Bean	Control	1.34	1.23	0.87	2.06	0.179	0.392
		Rice Bran	Control	1.16	1.21	0.77	1.72	0.459	
		Navy Bean	Rice Bran	1.16	1.24	0.74	1.80	0.505	
Day 28	Navy Bean	Control	1.53	1.22	1.02	2.31	0.041	0.115	
	Rice Bran	Control	1.15	1.20	0.79	1.67	0.460		
	Navy Bean	Rice Bran	1.34	1.22	0.88	2.04	0.161		

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Tumor Necrosis Factor (Extrapolation) by Time Point									
Diet	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Control	Time	Day 14	Day 0	0.94	1.21	0.63	1.41	0.768	0.896
		Day 28	Day 0	0.91	1.21	0.61	1.37	0.648	
		Day 28	Day 14	0.97	1.21	0.65	1.45	0.871	
Navy Bean		Day 14	Day 0	1.05	1.25	0.65	1.69	0.834	0.784
		Day 28	Day 0	1.17	1.25	0.72	1.89	0.503	
		Day 28	Day 14	1.11	1.25	0.69	1.80	0.642	
Rice Bran	Day 14	Day 0	1.14	1.26	0.71	1.85	0.566	0.837	
	Day 28	Day 0	1.10	1.26	0.68	1.77	0.688		
	Day 28	Day 14	0.96	1.26	0.59	1.55	0.861		

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Tumor Necrosis Factor (Tobit Regression) by Diet Group									
Time Point	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Day 0	Diet	Navy Bean	Control	1.23	1.30	0.73	2.05	0.436	0.625
		Rice Bran	Control	0.96	1.28	0.59	1.54	0.857	
		Navy Bean	Rice Bran	1.28	1.31	0.76	2.18	0.357	
Day 14		Navy Bean	Control	1.34	1.21	0.91	1.95	0.136	0.323
		Rice Bran	Control	1.16	1.20	0.81	1.64	0.418	
		Navy Bean	Rice Bran	1.16	1.22	0.78	1.71	0.466	
Day 28	Navy Bean	Control	1.53	1.20	1.07	2.20	0.019	0.062	
	Rice Bran	Control	1.15	1.18	0.82	1.59	0.419		
	Navy Bean	Rice Bran	1.34	1.21	0.93	1.93	0.118		

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Tumor Necrosis Factor (Tobit Regression) by Time Point									
Diet	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Control	Time	Day 14	Day 0	0.96	1.21	0.66	1.39	0.820	0.924
		Day 28	Day 0	0.93	1.21	0.64	1.35	0.693	
		Day 28	Day 14	0.97	1.21	0.67	1.41	0.866	
Navy Bean		Day 14	Day 0	1.05	1.23	0.70	1.57	0.816	0.743
		Day 28	Day 0	1.17	1.23	0.78	1.75	0.452	
		Day 28	Day 14	1.11	1.23	0.74	1.66	0.603	
Rice Bran	Day 14	Day 0	1.16	1.25	0.75	1.79	0.506	0.791	
	Day 28	Day 0	1.11	1.25	0.72	1.72	0.631		
	Day 28	Day 14	0.96	1.25	0.62	1.48	0.853		

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Tumor Necrosis Factor (Multiple Imputation) by Diet Group									
Time Point	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Day 0	Diet	Navy Bean	Control	1.06	1.24	0.68	1.67	0.771	0.914
		Rice Bran	Control	0.97	1.23	0.63	1.49	0.889	
		Navy Bean	Rice Bran	1.10	1.25	0.69	1.74	0.681	
Day 14		Navy Bean	Control	1.34	1.23	0.87	2.06	0.179	0.392
		Rice Bran	Control	1.16	1.21	0.77	1.72	0.459	
		Navy Bean	Rice Bran	1.16	1.24	0.74	1.80	0.505	
Day 28	Navy Bean	Control	1.53	1.22	1.02	2.31	0.041	0.115	
	Rice Bran	Control	1.15	1.20	0.79	1.67	0.460		
	Navy Bean	Rice Bran	1.34	1.22	0.88	2.04	0.161		

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Tumor Necrosis Factor (Multiple Imputation) by Time Point									
Diet	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Control	Time	Day 14	Day 0	0.84	1.19	0.58	1.20	0.322	0.456
		Day 28	Day 0	0.81	1.19	0.56	1.17	0.245	
		Day 28	Day 14	0.97	1.19	0.68	1.38	0.854	
Navy Bean		Day 14	Day 0	1.05	1.25	0.65	1.69	0.834	0.784
		Day 28	Day 0	1.17	1.25	0.72	1.89	0.503	
		Day 28	Day 14	1.11	1.25	0.69	1.80	0.642	
Rice Bran	Day 14	Day 0	0.99	1.24	0.64	1.55	0.981	0.971	
	Day 28	Day 0	0.96	1.24	0.61	1.49	0.831		
	Day 28	Day 14	0.96	1.23	0.63	1.47	0.845		

**Table 12:** Differences in plasma vascular endothelial growth factor between diet groups (left) and between time points (right) for study participants with a history of colorectal cancer (n=23). Only a few study participants had VEGF levels that were below the lowest level of detection of the cytokine immunoassay (4.3% at day 0, 8.7% at day 14, and 8.7% at day 28). Shown above are analyses of four different VEGF data sets that each utilized a different approach for managing left-censored data. These approaches are: substitution with a fixed value (top), extrapolation using the 5-parametric logistic standard curve equation (second from top), Tobit regression (second from bottom), and multiple imputation (bottom). For the Tobit regression approach, at day 28, the navy bean group was observed to have significantly higher plasma VEGF level than the control group. This was not observed within the other data sets for VEGF.

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Vascular Endothelial Growth Factor (Substitution) by Diet Group									
Time Point	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Day 0	Diet	Navy Bean	Control	2.35	1.75	0.73	7.52	0.143	0.330
		Rice Bran	Control	1.49	1.67	0.51	4.37	0.446	
		Navy Bean	Rice Bran	1.57	1.77	0.48	5.19	0.439	
Day 14	Diet	Navy Bean	Control	3.44	2.04	0.77	15.31	0.099	0.220
		Rice Bran	Control	2.25	1.93	0.57	8.90	0.233	
		Navy Bean	Rice Bran	1.53	2.08	0.33	7.06	0.568	
Day 28	Diet	Navy Bean	Control	3.89	2.01	0.91	16.62	0.065	0.122
		Rice Bran	Control	2.96	1.90	0.77	11.29	0.107	
		Navy Bean	Rice Bran	1.31	2.04	0.30	5.83	0.705	

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Vascular Endothelial Growth Factor (Substitution) by Time Point									
Diet	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Control	Time	Day 14	Day 0	0.70	2.41	0.11	4.28	0.684	0.869
		Day 28	Day 0	0.64	2.41	0.10	3.97	0.623	
		Day 28	Day 14	0.93	2.41	0.15	5.70	0.932	
Navy Bean	Time	Day 14	Day 0	1.02	1.36	0.53	1.97	0.945	0.976
		Day 28	Day 0	1.07	1.36	0.55	2.07	0.832	
		Day 28	Day 14	1.05	1.36	0.54	2.02	0.886	
Rice Bran	Time	Day 14	Day 0	1.05	1.31	0.60	1.85	0.862	0.641
		Day 28	Day 0	1.28	1.31	0.73	2.25	0.378	
		Day 28	Day 14	1.22	1.31	0.69	2.15	0.478	

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Vascular Endothelial Growth Factor (Extrapolation) by Diet Group									
Time Point	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Day 0	Diet	Navy Bean	Control	4.12	2.96	0.43	39.74	0.207	0.405
		Rice Bran	Control	2.62	2.72	0.32	21.19	0.347	
		Navy Bean	Rice Bran	1.57	3.04	0.15	16.02	0.689	
Day 14	Diet	Navy Bean	Control	10.64	4.21	0.53	213.19	0.116	0.208
		Rice Bran	Control	6.95	3.76	0.44	110.24	0.159	
		Navy Bean	Rice Bran	1.53	4.36	0.07	33.04	0.776	
Day 28	Diet	Navy Bean	Control	12.01	4.14	0.62	232.43	0.096	0.153
		Rice Bran	Control	9.13	3.70	0.59	140.29	0.107	
		Navy Bean	Rice Bran	1.31	4.29	0.06	27.38	0.853	

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Vascular Endothelial Growth Factor (Extrapolation) by Time Point									
Diet	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Control	Time	Day 14	Day 0	0.40	6.34	0.01	17.91	0.621	0.834
		Day 28	Day 0	0.37	6.34	0.01	16.60	0.592	
		Day 28	Day 14	0.93	6.34	0.02	41.92	0.967	
Navy Bean	Time	Day 14	Day 0	1.02	1.36	0.53	1.97	0.945	0.976
		Day 28	Day 0	1.07	1.36	0.55	2.07	0.832	
		Day 28	Day 14	1.05	1.36	0.54	2.02	0.886	
Rice Bran	Time	Day 14	Day 0	1.05	1.31	0.60	1.85	0.862	0.641
		Day 28	Day 0	1.28	1.31	0.73	2.25	0.378	
		Day 28	Day 14	1.22	1.31	0.69	2.15	0.478	

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Vascular Endothelial Growth Factor (Tobit Regression) by Diet Group									
Time Point	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Day 0	Diet	Navy Bean	Control	2.23	1.62	0.87	5.71	0.096	0.249
		Rice Bran	Control	1.42	1.56	0.59	3.38	0.432	
		Navy Bean	Rice Bran	1.57	1.64	0.60	4.12	0.358	
Day 14	Diet	Navy Bean	Control	3.22	1.89	0.93	11.17	0.065	0.160
		Rice Bran	Control	2.11	1.80	0.67	6.63	0.204	
		Navy Bean	Rice Bran	1.53	1.91	0.43	5.44	0.511	
Day 28	Diet	Navy Bean	Control	3.63	1.85	1.09	12.10	0.036	0.070
		Rice Bran	Control	2.76	1.76	0.91	8.39	0.074	
		Navy Bean	Rice Bran	1.31	1.87	0.38	4.49	0.663	

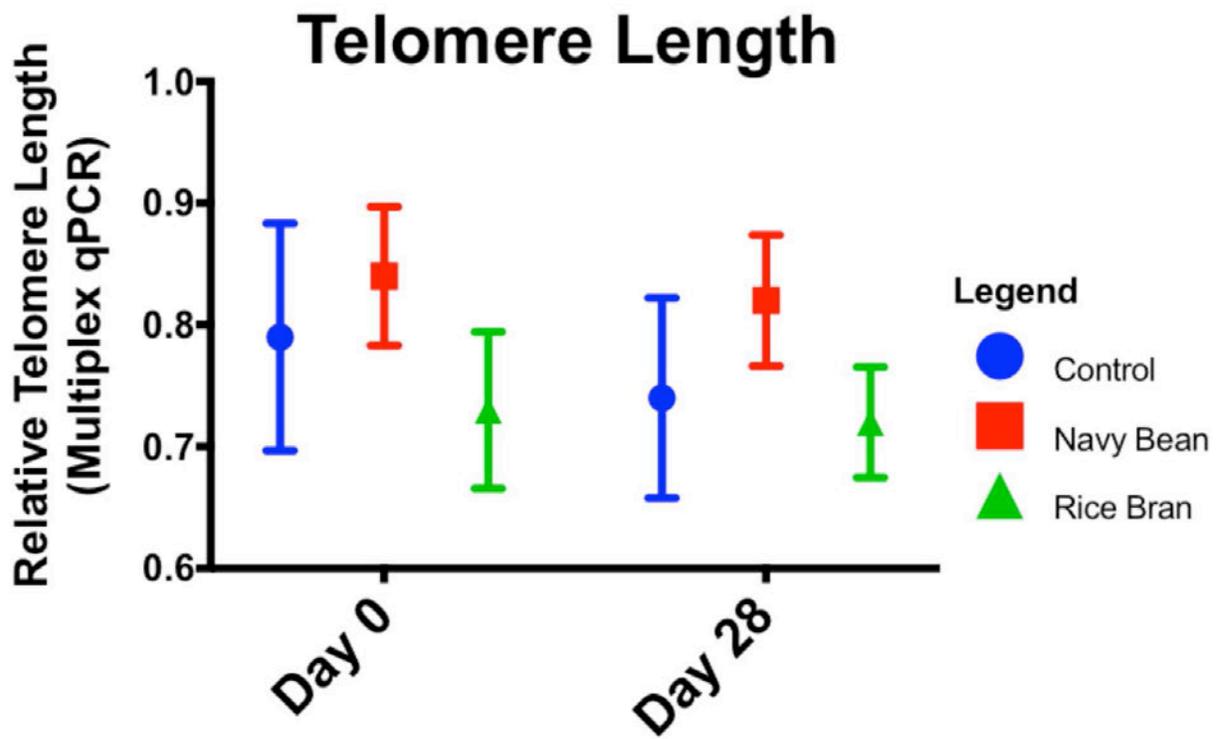
Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Vascular Endothelial Growth Factor (Tobit Regression) by Time Point									
Diet	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Control	Time	Day 14	Day 0	0.69	2.38	0.13	3.74	0.663	0.853
		Day 28	Day 0	0.63	2.38	0.12	3.46	0.598	
		Day 28	Day 14	0.92	2.39	0.17	5.09	0.928	
Navy Bean	Time	Day 14	Day 0	1.02	1.33	0.59	1.78	0.939	0.971
		Day 28	Day 0	1.07	1.33	0.62	1.86	0.813	
		Day 28	Day 14	1.05	1.33	0.60	1.82	0.873	
Rice Bran	Time	Day 14	Day 0	1.05	1.29	0.64	1.73	0.850	0.595
		Day 28	Day 0	1.28	1.29	0.78	2.11	0.336	
		Day 28	Day 14	1.22	1.29	0.74	2.01	0.439	

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Vascular Endothelial Growth Factor (Multiple Imputation) by Diet Group									
Time Point	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Day 0	Diet	Navy Bean	Control	1.44	1.33	0.79	2.63	0.219	0.285
		Rice Bran	Control	0.92	1.30	0.53	1.60	0.746	
		Navy Bean	Rice Bran	1.57	1.33	0.86	2.87	0.132	
Day 14	Diet	Navy Bean	Control	1.25	1.33	0.69	2.27	0.436	0.323
		Rice Bran	Control	0.82	1.30	0.47	1.42	0.457	
		Navy Bean	Rice Bran	1.53	1.32	0.86	2.73	0.139	
Day 28	Diet	Navy Bean	Control	1.45	1.30	0.83	2.53	0.183	0.380
		Rice Bran	Control	1.10	1.28	0.65	1.85	0.705	
		Navy Bean	Rice Bran	1.31	1.29	0.76	2.26	0.304	

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Vascular Endothelial Growth Factor (Multiple Imputation) by Time Point									
Diet	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Control	Time	Day 14	Day 0	1.17	1.25	0.73	1.88	0.485	0.78
		Day 28	Day 0	1.06	1.25	0.66	1.71	0.785	
		Day 28	Day 14	0.91	1.26	0.56	1.48	0.679	
Navy Bean	Time	Day 14	Day 0	1.02	1.36	0.53	1.97	0.945	0.98
		Day 28	Day 0	1.07	1.36	0.55	2.07	0.832	
		Day 28	Day 14	1.05	1.36	0.54	2.02	0.886	
Rice Bran	Time	Day 14	Day 0	1.05	1.31	0.60	1.85	0.862	0.64
		Day 28	Day 0	1.28	1.31	0.73	2.25	0.378	
		Day 28	Day 14	1.22	1.31	0.69	2.15	0.478	

### **3.2 Differences in leukocyte telomere length within and between diet groups**

For individuals with a history of colorectal cancer and regardless of the method used for telomere length measurement, no significant differences were observed in leukocyte telomere length between diet groups or within diet groups over time. However, from day 0 to day 28, the rice bran and navy bean groups were both found to have a smaller, although non-significant, decrease in multiplex qPCR telomere length when compared to the control group. That is, less telomere shortening was observed in the intervention groups.



**Figure 4:** Graph of relative telomere length for control, navy bean, and rice bran diet groups at day 0 and day 28. Relative telomere length was estimated by multiplex qPCR. No significant difference was found between diet groups or time points.

**Table 13:** Differences in leukocyte telomere length as measured by multiplex qPCR and IQ-FISH between diet groups (left) and between time points (right) for study participants with a history of colorectal cancer. Shown above are analyses of telomere length measured by multiplex quantitative polymerase chain reaction (top) and telomere length measured by interphase fluorescence in situ hybridization (FISH). Due to variability within the experimental control used for FISH, each batch of samples was analyzed separately: batch 1 (second from top; n=6), batch 2 (second from bottom; n=7), and batch 3 (bottom; n=8). No significant differences were observed between diet groups or time point for telomere length measured by multiplex qPCR and interphase FISH. RTL = relative telomere length; MFI = mean fluorescence intensity.

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Multiplex qPCR Telomere Length by Diet Group								
Time Point	Parameter	Comparison groups	Diff. of Arithmetic Means (RTL)	Standard Error	95% Confidence Limits	p-value	Type III p-value	
Day 0	Diet	Navy Bean	Control	0.0506	0.099	-0.155	0.256	0.615
		Rice Bran	Control	-0.0621	0.109	-0.288	0.163	0.575
		Navy Bean	Rice Bran	0.1127	0.107	-0.108	0.333	0.301
Navy Bean		Control	0.0864	0.090	-0.099	0.272	0.345	
Rice Bran		Control	-0.0178	0.099	-0.222	0.186	0.859	
Navy Bean		Rice Bran	0.1042	0.099	-0.100	0.308	0.303	
Day 28							0.579	
							0.505	

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Multiplex qPCR Telomere Length by Time Point										
Diet	Parameter	Comparison groups	Diff. of Arithmetic Means (RTL)	Standard Error	95% Confidence Limits	p-value	Type III p-value			
Control	Time	Day 28	Day 0	-0.0509	0.124	-0.312	0.210	0.686	0.686	
		Navy Bean	Day 28	Day 0	-0.0151	0.077	-0.178	0.147	0.847	0.847
		Rice Bran	Day 28	Day 0	-0.0066	0.081	-0.183	0.170	0.936	0.936

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Interphase FISH Telomere Length (Batch 1) by Diet Group								
Time Point	Parameter	Comparison groups	Diff. of Arithmetic Means (MFI)	Standard Error	95% Confidence Limits	p-value	Type III p-value	
Day 0	Diet	Navy Bean	Control	21.67	8.92	-6.73	50.07	0.094
		Rice Bran	Control	-0.33	11.29	-36.26	35.59	0.978
		Navy Bean	Rice Bran	22.00	11.97	-16.10	60.10	0.163
Navy Bean		Control	13.00	11.35	-23.13	49.13	0.335	
Rice Bran		Control	12.00	14.36	-33.70	57.70	0.465	
Navy Bean		Rice Bran	1.00	15.23	-47.47	49.47	0.952	
Day 14							0.534	
Day 28	Diet	Navy Bean	Control	5.00	13.23	-37.10	47.10	0.731
		Rice Bran	Control	15.00	16.73	-38.25	68.25	0.436
		Navy Bean	Rice Bran	-10.00	17.75	-66.48	46.48	0.613

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Interphase FISH Telomere Length (Batch 1) by Time Point									
Diet	Parameter	Comparison groups	Diff. of Arithmetic Means (MFI)	Standard Error	95% Confidence Limits	p-value	Type III p-value		
Control	Time	Day 14	Day 0	9.67	10.42	-15.82	35.16	0.389	
		Day 28	Day 0	9.67	10.42	-15.82	35.16	0.389	
		Day 28	Day 14	0.00	10.42	-25.49	25.49	1.000	
		Day 14	Day 0	1.00	11.60	-35.93	37.93	0.937	
		Day 28	Day 0	-7.00	11.60	-43.93	29.93	0.589	
		Day 28	Day 14	-8.00	11.60	-44.93	28.93	0.540	
Navy Bean								0.728	
Rice Bran									

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Interphase FISH Telomere Length (Batch 2) by Diet Group								
Time Point	Parameter	Comparison groups	Ratio of Geometric Means	Standard Error	95% Confidence Limits	p-value	Type III p-value	
Day 0	Diet	Navy Bean	Control	0.97	1.12	0.70	1.35	0.839
		Rice Bran	Control	0.98	1.14	0.68	1.40	0.869
		Navy Bean	Rice Bran	1.00	1.12	0.72	1.38	0.983
Navy Bean		Control	1.16	1.12	0.85	1.60	0.260	
Rice Bran		Control	0.86	1.13	0.61	1.22	0.298	
Navy Bean		Rice Bran	1.35	1.12	0.98	1.85	0.059	
Day 14							0.134	
Day 28	Diet	Navy Bean	Control	1.15	1.27	0.58	2.25	0.604
		Rice Bran	Control	1.00	1.30	0.48	2.09	0.996
		Navy Bean	Rice Bran	1.15	1.27	0.59	2.25	0.600

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Interphase FISH Telomere Length (Batch 2) by Time Point									
Diet	Parameter	Comparison groups	Ratio of Geometric Means	Standard Error	95% Confidence Limits	p-value	Type III p-value		
Control	Time	Day 14	Day 0	0.97	1.33	0.39	2.43	0.926	
		Day 28	Day 0	0.82	1.33	0.33	2.06	0.546	
		Day 28	Day 14	0.85	1.33	0.34	2.12	0.604	
		Day 14	Day 0	1.16	1.08	0.96	1.40	0.105	
		Day 28	Day 0	0.97	1.08	0.80	1.17	0.678	
		Day 28	Day 14	0.84	1.08	0.69	1.01	0.058	
Navy Bean								0.091	
Rice Bran								0.638	

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Interphase FISH Telomere Length (Batch 3) by Diet Group								
Time Point	Parameter	Comparison groups	Diff. of Arithmetic Means (MFI)	Standard Error	95% Confidence Limits	p-value	Type III p-value	
Day 0	Diet	Navy Bean	Control	5.25	9.07	-18.08	28.58	0.588
		Rice Bran	Control	-1.08	6.20	-17.02	14.85	0.868
		Navy Bean	Rice Bran	6.33	9.37	-17.76	30.43	0.529
Navy Bean		Control	-4.75	8.33	-26.16	16.66	0.593	
Rice Bran		Control	0.58	5.69	-14.04	15.21	0.922	
Navy Bean		Rice Bran	-5.33	8.60	-27.44	16.78	0.562	
Day 14							0.823	
Day 28	Diet	Navy Bean	Control	13.00	11.05	-15.39	41.39	0.292
		Rice Bran	Control	14.00	7.55	-5.40	33.40	0.123
		Navy Bean	Rice Bran	-1.00	11.41	-30.32	28.32	0.934

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Interphase FISH Telomere Length (Batch 3) by Time Point									
Diet	Parameter	Comparison groups	Diff. of Arithmetic Means (MFI)	Standard Error	95% Confidence Limits	p-value	Type III p-value		
Control	Time	Day 14	Day 0	-5.00	6.03	-18.63	8.63	0.428	
		Day 28	Day 0	-6.75	6.03	-20.38	6.88	0.292	
		Day 28	Day 14	-1.75	6.03	-15.38	11.88	0.778	
		Day 14	Day 0	-15.00					
		Day 28	Day 0	1.00					
		Day 28	Day 14	16.00					
Navy Bean									
Rice Bran								0.302	

**Table 14:** Differences in leukocyte telomere length measured by singleplex qPCR diet groups (left) and between time points (right) for study participants with a history of colorectal cancer. Shown above are data analyses from plate 1 (top), plate 2 (middle), and both plates combined (bottom). The experimental plates were normalized to a control cell line. However, given the variability observed within the control telomere length measured by FISH, the singleplex qPCR plates were analyzed separately as well as combined. No significant differences were observed between diet group or time point for telomere length measured by singleplex qPCR.

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Singleplex qPCR Telomere Length (Plate 1) by Diet Group									
Time Point	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Day 0	Diet	Navy Bean	Control	0.406	1.875	0.098	1.684	0.186	0.395
		Rice Bran	Control	0.676	1.875	0.163	2.804	0.549	
		Navy Bean	Rice Bran	0.601	1.875	0.145	2.490	0.438	
Day 14		Navy Bean	Control	0.576	1.658	0.184	1.807	0.304	0.533
		Rice Bran	Control	0.904	1.658	0.288	2.835	0.846	
		Navy Bean	Rice Bran	0.637	1.658	0.203	2.000	0.396	
Day 28	Navy Bean	Control	0.563	1.766	0.155	2.037	0.338	0.507	
	Rice Bran	Control	1.041	1.766	0.288	3.768	0.945		
	Navy Bean	Rice Bran	0.540	1.766	0.149	1.957	0.307		

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Singleplex qPCR Telomere Length (Plate 1) by Time Point									
Diet	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Control	Time	Day 14	Day 0	1.11	1.53	0.42	2.91	0.820	0.926
		Day 28	Day 0	0.93	1.53	0.35	2.46	0.877	
		Day 28	Day 14	0.85	1.53	0.32	2.23	0.704	
Navy Bean		Day 14	Day 0	1.57	1.81	0.41	6.00	0.469	0.756
		Day 28	Day 0	1.29	1.81	0.34	4.95	0.675	
		Day 28	Day 14	0.83	1.81	0.22	3.16	0.754	
Rice Bran	Day 14	Day 0	1.48	1.94	0.33	6.60	0.570	0.809	
	Day 28	Day 0	1.44	1.94	0.32	6.43	0.597		
	Day 28	Day 14	0.97	1.94	0.22	4.35	0.969		

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Singleplex qPCR Telomere Length (Plate 2) by Diet Group									
Time Point	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Day 0	Diet	Navy Bean	Control	2.87	2.11	0.49	16.82	0.201	0.407
		Rice Bran	Control	1.16	1.92	0.25	5.44	0.825	
		Navy Bean	Rice Bran	2.47	2.26	0.36	17.01	0.304	
Day 14		Navy Bean	Control	1.76	1.90	0.38	8.05	0.408	0.621
		Rice Bran	Control	1.53	1.75	0.41	5.76	0.474	
		Navy Bean	Rice Bran	1.15	2.02	0.22	6.05	0.847	
Day 28	Navy Bean	Control	2.80	1.96	0.57	13.74	0.171	0.362	
	Rice Bran	Control	1.47	1.80	0.37	5.90	0.533		
	Navy Bean	Rice Bran	1.90	2.08	0.33	10.81	0.410		

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Singleplex qPCR Telomere Length (Plate 2) by Time Point									
Diet	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Control	Time	Day 14	Day 0	1.58	1.80	0.44	5.71	0.451	0.714
		Day 28	Day 0	1.46	1.80	0.40	5.27	0.533	
		Day 28	Day 14	0.92	1.80	0.26	3.33	0.893	
Navy Bean		Day 14	Day 0	0.97	1.99	0.11	8.72	0.968	0.837
		Day 28	Day 0	1.42	1.99	0.16	12.78	0.645	
		Day 28	Day 14	1.47	1.99	0.16	13.17	0.618	
Rice Bran	Day 14	Day 0	2.08	1.68	0.59	7.42	0.207	0.378	
	Day 28	Day 0	1.85	1.68	0.52	6.58	0.282		
	Day 28	Day 14	0.89	1.68	0.25	3.16	0.824		

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Singleplex qPCR Telomere Length (Plates 1 & 2) by Diet Group									
Time Point	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Day 0	Diet	Navy Bean	Control	0.92	1.62	0.33	2.52	0.857	0.981
		Rice Bran	Control	0.93	1.59	0.36	2.46	0.886	
		Navy Bean	Rice Bran	0.98	1.66	0.34	2.85	0.968	
Day 14		Navy Bean	Control	0.91	1.46	0.41	2.00	0.798	0.792
		Rice Bran	Control	1.19	1.44	0.56	2.53	0.644	
		Navy Bean	Rice Bran	0.76	1.49	0.33	1.77	0.510	
Day 28	Navy Bean	Control	1.02	1.54	0.41	2.53	0.962	0.850	
	Rice Bran	Control	1.25	1.51	0.52	2.98	0.597		
	Navy Bean	Rice Bran	0.82	1.58	0.31	2.13	0.664		

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Singleplex qPCR Telomere Length (Plates 1 & 2) by Time Point									
Diet	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Control	Time	Day 14	Day 0	1.35	1.46	0.62	2.94	0.434	0.729
		Day 28	Day 0	1.20	1.46	0.55	2.61	0.638	
		Day 28	Day 14	0.89	1.46	0.41	1.93	0.754	
Navy Bean		Day 14	Day 0	1.34	1.71	0.43	4.18	0.597	0.825
		Day 28	Day 0	1.34	1.71	0.43	4.18	0.597	
		Day 28	Day 14	1.00	1.71	0.32	3.13	0.999	
Rice Bran	Day 14	Day 0	1.71	1.50	0.73	4.02	0.203	0.375	
	Day 28	Day 0	1.60	1.50	0.68	3.76	0.263		
	Day 28	Day 14	0.94	1.50	0.40	2.20	0.871		

### **3.3 Differences in lipid levels within and between diet groups**

#### *3.3.1 Study participants without a history of colorectal cancer*

Within each respective diet group, no significant differences were observed between serum levels of total cholesterol, LDL, HDL, and triglycerides measured at day 0, day 14, and day 28 for study participants who did not have a history of colorectal cancer.

In regards to inter-group comparison of lipid levels, the only significant difference between diets was found at day 28, where the navy bean diet group possessed a significantly higher level of HDL compared to the rice bran group ( $\mu_{NB}-\mu_{RB}=56.75$  mg/dL; 95% CI [37.89, 75.61];  $p<0.0001$ ). This difference was not significant at day 0 or day 14 of the study. In comparison to the control group, no significant differences were found with either the rice bran or navy bean group at all time points of sample collection.

**Table 15:** Differences in serum lipids between diet groups (left) and between time points (right) for study participants without a history of colorectal cancer. Variables shown above: total cholesterol (top), low-density lipoprotein (LDL; second from top), high-density lipoprotein (HDL; second from bottom), and triglycerides (bottom). At day 28, the navy bean group (n=4) was observed to have significantly higher levels of HDL than the rice bran group (n=4). Otherwise, no significant differences were observed in the displayed variables between treatment groups or time points.

Parameter Estimates for Study Participants without a History of Colorectal Cancer: One-Way Analysis of Variance of Total Cholesterol by Diet Group									
Time Point	Parameter	Comparison groups		Diff. of Arithmetic Means (mg/dL)	Standard Error	95% Confidence Limits	p-value	Type III p-value	
Day 0		Navy Bean	Control	-1.75	36.75	-86.50	83.00	0.963	0.935
		Rice Bran	Control	10.00	36.75	-74.75	94.75	0.792	
		Navy Bean	Rice Bran	-11.75	34.03	-90.22	66.72	0.739	
Day 14	Diet	Navy Bean	Control	19.75	32.92	-56.17	95.67	0.565	0.682
		Rice Bran	Control	29.25	32.92	-46.67	105.17	0.400	
		Navy Bean	Rice Bran	-9.50	30.48	-79.79	60.79	0.763	
Day 28		Navy Bean	Control	9.75	37.53	-76.81	96.31	0.802	0.934
		Rice Bran	Control	13.75	37.53	-72.81	100.31	0.724	
		Navy Bean	Rice Bran	-4.00	34.75	-84.13	76.13	0.911	

Parameter Estimates for Study Participants without a History of Colorectal Cancer: One-Way Analysis of Variance of Total Cholesterol by Time Point									
Diet	Parameter	Comparison groups		Diff. of Arithmetic Means (mg/dL)	Standard Error	95% Confidence Limits	p-value	Type III p-value	
Control		Day 14	Day 0	0.50	22.59	-50.60	51.60	0.983	0.954
		Day 28	Day 0	-1.50	22.59	-52.60	49.60	0.949	
		Day 28	Day 14	-2.00	22.59	-53.10	49.10	0.931	
Navy Bean	Time	Day 14	Day 0	-1.75	41.06	-94.63	91.13	0.967	0.884
		Day 28	Day 0	-9.25	41.06	-102.13	83.63	0.827	
		Day 28	Day 14	-7.50	41.06	-100.38	85.38	0.859	
Rice Bran		Day 14	Day 0	-21.00	38.27	-114.65	72.65	0.603	0.730
		Day 28	Day 0	-13.00	38.27	-106.65	80.65	0.746	
		Day 28	Day 14	8.00	38.27	-85.65	101.65	0.841	

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Low-density Lipoprotein by Diet Group									
Time Point	Parameter	Comparison groups		Diff. of Arithmetic Means (mg/dL)	Standard Error	95% Confidence Limits	p-value	Type III p-value	
Day 0		Navy Bean	Control	-9.25	28.68	-75.37	56.87	0.755	0.795
		Rice Bran	Control	9.00	28.68	-57.12	75.12	0.762	
		Navy Bean	Rice Bran	-18.25	26.55	-79.47	42.97	0.511	
Day 14	Diet	Navy Bean	Control	6.25	25.02	-51.45	63.95	0.809	0.770
		Rice Bran	Control	17.75	25.02	-39.95	75.45	0.498	
		Navy Bean	Rice Bran	-11.50	23.17	-64.92	41.92	0.633	
Day 28		Navy Bean	Control	1.42	30.26	-68.37	71.20	0.964	0.988
		Rice Bran	Control	4.42	30.26	-65.37	74.20	0.888	
		Navy Bean	Rice Bran	-3.00	28.02	-67.61	61.61	0.917	

Parameter Estimates for Study Participants without a History of Colorectal Cancer: One-Way Analysis of Variance of Low-density Lipoprotein by Time Point									
Diet	Parameter	Comparison groups		Diff. of Arithmetic Means (mg/dL)	Standard Error	95% Confidence Limits	p-value	Type III p-value	
Control		Day 14	Day 0	-13.00	34.35	-97.04	71.04	0.718	0.811
		Day 28	Day 0	-10.67	34.35	-94.71	73.37	0.767	
		Day 28	Day 14	2.33	34.35	-81.71	86.37	0.948	
Navy Bean	Time	Day 14	Day 0	2.50	14.86	-31.11	36.11	0.870	0.913
		Day 28	Day 0	0.00	14.86	-33.61	33.61	1.000	
		Day 28	Day 14	-2.50	14.86	-36.11	31.11	0.870	
Rice Bran		Day 14	Day 0	-4.25	31.48	-75.45	66.95	0.896	0.757
		Day 28	Day 0	-15.25	31.48	-86.45	55.95	0.640	
		Day 28	Day 14	-11.00	31.48	-82.20	60.20	0.735	

Parameter Estimates for Study Participants without a History of Colorectal Cancer: One-Way Analysis of Variance of High-density Lipoprotein by Diet Group									
Time Point	Parameter	Comparison groups		Diff. of Arithmetic Means (mg/dL)	Standard Error	95% Confidence Limits	p-value	Type III p-value	
Day 0		Navy Bean	Control	14.17	10.90	-10.96	39.29	0.230	0.457
		Rice Bran	Control	9.92	10.90	-15.21	35.04	0.389	
		Navy Bean	Rice Bran	4.25	10.09	-19.01	27.51	0.685	
Day 14	Diet	Navy Bean	Control	13.75	8.95	-6.89	34.39	0.163	0.274
		Rice Bran	Control	14.00	8.95	-6.64	34.64	0.156	
		Navy Bean	Rice Bran	-0.25	8.29	-19.36	18.86	0.977	
Day 28		Navy Bean	Control	11.42	12.49	-17.39	40.22	0.388	0.551
		Rice Bran	Control	13.42	12.49	-15.39	42.22	0.314	
		Navy Bean	Rice Bran	56.75	8.18	37.89	75.61	0.0001	

Parameter Estimates for Study Participants without a History of Colorectal Cancer: One-Way Analysis of Variance of High-density Lipoprotein by Time Point									
Diet	Parameter	Comparison groups		Diff. of Arithmetic Means (mg/dL)	Standard Error	95% Confidence Limits	p-value	Type III p-value	
Control		Day 14	Day 0	-3.33	10.68	-29.48	22.81	0.766	0.843
		Day 28	Day 0	-1.00	10.68	-27.14	25.14	0.929	
		Day 28	Day 14	2.33	10.68	-23.81	28.48	0.834	
Navy Bean	Time	Day 14	Day 0	-3.75	6.91	-19.37	11.87	0.600	0.734
		Day 28	Day 0	-3.75	6.91	-19.37	11.87	0.600	
		Day 28	Day 14	0.00	6.91	-15.62	15.62	1.000	
Rice Bran		Day 14	Day 0	0.75	12.87	-28.36	29.86	0.955	0.900
		Day 28	Day 0	2.50	12.87	-26.61	31.61	0.850	
		Day 28	Day 14	1.75	12.87	-27.36	30.86	0.895	

Parameter Estimates for Study Participants without a History of Colorectal Cancer: One-Way Analysis of Variance of Triglycerides by Diet Group									
Time Point	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits	p-value	Type III p-value	
Day 0		Navy Bean	Control	0.79	1.46	0.33	1.89	0.549	0.646
		Rice Bran	Control	0.70	1.46	0.29	1.67	0.367	
		Navy Bean	Rice Bran	1.13	1.42	0.50	2.55	0.730	
Day 14	Diet	Navy Bean	Control	1.08	1.49	0.43	2.69	0.853	0.916
		Rice Bran	Control	0.92	1.49	0.37	2.30	0.847	
		Navy Bean	Rice Bran	1.17	1.44	0.50	2.72	0.684	
Day 28		Navy Bean	Control	0.88	1.43	0.39	2.02	0.741	0.916
		Rice Bran	Control	0.87	1.43	0.38	1.98	0.701	
		Navy Bean	Rice Bran	1.02	1.39	0.47	2.19	0.954	

Parameter Estimates for Study Participants without a History of Colorectal Cancer: One-Way Analysis of Variance of Triglycerides by Time Point									
Diet	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits	p-value	Type III p-value	
Control		Day 14	Day 0	0.81	1.68	0.23	2.88	0.700	0.800
		Day 28	Day 0	1.00	1.68	0.28	3.55	0.997	
		Day 28	Day 14	1.23	1.68	0.35	4.38	0.703	
Navy Bean	Time	Day 14	Day 0	1.11	1.38	0.54	2.30	0.754	0.822
		Day 28	Day 0	1.12	1.38	0.54	2.32	0.734	
		Day 28	Day 14	1.01	1.38	0.49	2.09	0.979	
Rice Bran		Day 14	Day 0	1.08	1.35	0.55	2.12	0.808	0.644
		Day 28	Day 0	1.24	1.35	0.63	2.44	0.482	
		Day 28	Day 14	1.15	1.35	0.59	2.27	0.641	

### 3.3.2 *Study participants with a history of colorectal cancer*

Within each respective diet group, no significant changes were found between serum levels of total cholesterol, LDL, HDL, and triglycerides measured at day 0, day 14, and day 28 for study participants with a history of colorectal cancer. Significant differences were observed between the diet groups.

For the colorectal cancer cohort, initial total cholesterol for individuals within the rice bran dietary group was significantly greater than individuals assigned to a control diet ( $\mu_{RB} - \mu_{Ctrl} = 42.00$  mg/dL; 95% CI [1.38, 82.62];  $p=0.043$ ). This difference was also present at day 14 of the study ( $\mu_{RB} - \mu_{Ctrl} = 45.92$  mg/dL; 95% CI [7.74, 84.10];  $p=0.020$ ) but was no longer observed to be significant at day 28 ( $\mu_{RB} - \mu_{Ctrl} = 38.01$  mg/dL; 95% CI [-0.07, 76.09];  $p=0.0504$ ). This same group of individuals was also found to have a significantly higher LDL level than the control group at all time points of the study (Day 0:  $\mu_{RB} - \mu_{Ctrl} = 37.29$  mg/dL; 95% CI [3.72, 70.86];  $p=0.031$ ; Day 14:  $\mu_{RB} - \mu_{Ctrl} = 42.07$  mg/dL; 95% CI [11.07, 73.06];  $p=0.010$ ; Day 28:  $\mu_{RB} - \mu_{Ctrl} = 35.00$  mg/dL; 95% CI [1.50, 68.50];  $p=0.041$ ). No significant differences between the navy bean diet group and the control diet group were discovered in total cholesterol, LDL, HDL, and triglycerides. Similarly, no significant difference was observed between the rice bran and control groups for triglycerides and HDL.

**Table 16:** Differences in serum levels of total cholesterol, low-density lipoprotein, high-density lipoprotein, and triglycerides between diet groups (left) and between time points (right) for study participants with a history of colorectal cancer. Variables shown above: total cholesterol (top), low-density lipoprotein (LDL; second from top), high-density lipoprotein (HDL; second from bottom), and triglycerides (bottom). Total cholesterol of the rice bran group (n=9) was observed to be significantly greater than the control group (n=10) at day 0 and day 14. Similarly, LDL of the rice bran group was observed to be significantly greater than the control group at all time points.

Parameter Estimates for Study Participants without a History of Colorectal Cancer: One-Way Analysis of Variance of Total Cholesterol by Diet Group									
Time Point	Parameter	Comparison groups		Diff. of Arithmetic Means (mg/dL)	Standard Error	95% Confidence Limits	p-value	Type III p-value	
Day 0		Navy Bran	Control	-1.75	36.75	-86.50	83.00	0.963	0.935
		Rice Bran	Control	10.00	36.75	-74.75	94.75	0.792	
		Navy Bran	Rice Bran	-11.75	34.03	-90.22	66.72	0.739	
Day 14	Diet	Navy Bran	Control	19.75	32.92	-56.17	95.67	0.565	0.682
		Rice Bran	Control	29.25	32.92	-46.67	105.17	0.400	
		Navy Bran	Rice Bran	-9.50	30.48	-79.79	60.79	0.763	
Day 28		Navy Bran	Control	9.75	37.53	-76.81	96.31	0.802	0.934
		Rice Bran	Control	13.75	37.53	-72.81	100.31	0.724	
		Navy Bran	Rice Bran	-4.00	34.75	-84.13	76.13	0.911	

Parameter Estimates for Study Participants without a History of Colorectal Cancer: One-Way Analysis of Variance of Total Cholesterol by Time Point									
Diet	Parameter	Comparison groups		Diff. of Arithmetic Means (mg/dL)	Standard Error	95% Confidence Limits	p-value	Type III p-value	
Control		Day 14	Day 0	0.50	22.59	-50.60	51.60	0.983	0.954
		Day 28	Day 0	-1.50	22.59	-52.60	49.60	0.949	
		Day 28	Day 14	-2.00	22.59	-53.10	49.10	0.931	
Navy Bran	Time	Day 14	Day 0	-1.75	41.06	-94.63	91.13	0.967	0.884
		Day 28	Day 0	-9.25	41.06	-102.13	83.63	0.827	
		Day 28	Day 14	-7.50	41.06	-100.38	85.38	0.859	
Rice Bran		Day 14	Day 0	-21.00	38.27	-114.65	72.65	0.603	0.730
		Day 28	Day 0	-13.00	38.27	-106.65	80.65	0.746	
		Day 28	Day 14	8.00	38.27	-85.65	101.65	0.841	

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Low-density Lipoprotein by Diet Group									
Time Point	Parameter	Comparison groups		Diff. of Arithmetic Means (mg/dL)	Standard Error	95% Confidence Limits	p-value	Type III p-value	
Day 0		Navy Bran	Control	-9.25	28.68	-75.37	56.87	0.755	0.795
		Rice Bran	Control	9.00	28.68	-57.12	75.12	0.762	
		Navy Bran	Rice Bran	-18.25	26.55	-79.47	42.97	0.511	
Day 14	Diet	Navy Bran	Control	6.25	25.02	-51.45	63.95	0.809	0.770
		Rice Bran	Control	17.75	25.02	-39.95	75.45	0.498	
		Navy Bran	Rice Bran	-11.50	23.17	-64.92	41.92	0.633	
Day 28		Navy Bran	Control	1.42	30.26	-68.37	71.20	0.964	0.988
		Rice Bran	Control	4.42	30.26	-65.37	74.20	0.888	
		Navy Bran	Rice Bran	-3.00	28.02	-67.61	61.61	0.917	

Parameter Estimates for Study Participants without a History of Colorectal Cancer: One-Way Analysis of Variance of Low-density Lipoprotein by Time Point									
Diet	Parameter	Comparison groups		Diff. of Arithmetic Means (mg/dL)	Standard Error	95% Confidence Limits	p-value	Type III p-value	
Control		Day 14	Day 0	-13.00	34.35	-97.04	71.04	0.718	0.811
		Day 28	Day 0	-10.67	34.35	-94.71	73.37	0.767	
		Day 28	Day 14	2.33	34.35	-81.71	86.37	0.948	
Navy Bran	Time	Day 14	Day 0	2.50	14.86	-31.11	36.11	0.870	0.913
		Day 28	Day 0	0.00	14.86	-33.61	33.61	1.000	
		Day 28	Day 14	-2.50	14.86	-36.11	31.11	0.870	
Rice Bran		Day 14	Day 0	-4.25	31.48	-75.45	66.95	0.896	0.757
		Day 28	Day 0	-15.25	31.48	-86.45	55.95	0.640	
		Day 28	Day 14	-11.00	31.48	-82.20	60.20	0.735	

Parameter Estimates for Study Participants without a History of Colorectal Cancer: One-Way Analysis of Variance of High-density Lipoprotein by Diet Group									
Time Point	Parameter	Comparison groups		Diff. of Arithmetic Means (mg/dL)	Standard Error	95% Confidence Limits	p-value	Type III p-value	
Day 0		Navy Bran	Control	14.17	10.90	-10.96	39.29	0.230	0.457
		Rice Bran	Control	9.92	10.90	-15.21	35.04	0.389	
		Navy Bran	Rice Bran	4.25	10.09	-19.01	27.51	0.685	
Day 14	Diet	Navy Bran	Control	13.75	8.95	-6.89	34.39	0.163	0.274
		Rice Bran	Control	14.00	8.95	-6.64	34.64	0.156	
		Navy Bran	Rice Bran	-0.25	8.29	-19.36	18.86	0.977	
Day 28		Navy Bran	Control	11.42	12.49	-17.39	40.22	0.388	0.551
		Rice Bran	Control	13.42	12.49	-15.39	42.22	0.314	
		Navy Bran	Rice Bran	56.75	8.18	37.89	75.61	0.0001	

Parameter Estimates for Study Participants without a History of Colorectal Cancer: One-Way Analysis of Variance of High-density Lipoprotein by Time Point									
Diet	Parameter	Comparison groups		Diff. of Arithmetic Means (mg/dL)	Standard Error	95% Confidence Limits	p-value	Type III p-value	
Control		Day 14	Day 0	-3.33	10.68	-29.48	22.81	0.766	0.843
		Day 28	Day 0	-1.00	10.68	-27.14	25.14	0.929	
		Day 28	Day 14	2.33	10.68	-23.81	28.48	0.834	
Navy Bran	Time	Day 14	Day 0	-3.75	6.91	-19.37	11.87	0.600	0.734
		Day 28	Day 0	-3.75	6.91	-19.37	11.87	0.600	
		Day 28	Day 14	0.00	6.91	-15.62	15.62	1.000	
Rice Bran		Day 14	Day 0	0.75	12.87	-28.36	29.86	0.955	0.900
		Day 28	Day 0	2.50	12.87	-26.61	31.61	0.850	
		Day 28	Day 14	1.75	12.87	-27.36	30.86	0.895	

Parameter Estimates for Study Participants without a History of Colorectal Cancer: One-Way Analysis of Variance of Triglycerides by Diet Group									
Time Point	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits	p-value	Type III p-value	
Day 0		Navy Bran	Control	0.79	1.46	0.33	1.89	0.549	0.646
		Rice Bran	Control	0.70	1.46	0.29	1.67	0.367	
		Navy Bran	Rice Bran	1.13	1.42	0.50	2.55	0.730	
Day 14	Diet	Navy Bran	Control	1.08	1.49	0.43	2.69	0.853	0.916
		Rice Bran	Control	0.92	1.49	0.37	2.30	0.847	
		Navy Bran	Rice Bran	1.17	1.44	0.50	2.72	0.684	
Day 28		Navy Bran	Control	0.88	1.43	0.39	2.02	0.741	0.916
		Rice Bran	Control	0.87	1.43	0.38	1.98	0.701	
		Navy Bran	Rice Bran	1.02	1.39	0.47	2.19	0.954	

Parameter Estimates for Study Participants without a History of Colorectal Cancer: One-Way Analysis of Variance of Triglycerides by Time Point									
Diet	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits	p-value	Type III p-value	
Control		Day 14	Day 0	0.81	1.68	0.23	2.88	0.700	0.800
		Day 28	Day 0	1.00	1.68	0.28	3.55	0.997	
		Day 28	Day 14	1.23	1.68	0.35	4.38	0.703	
Navy Bran	Time	Day 14	Day 0	1.11	1.38	0.54	2.30	0.754	0.822
		Day 28	Day 0	1.12	1.38	0.54	2.32	0.734	
		Day 28	Day 14	1.01	1.38	0.49	2.09	0.979	
Rice Bran		Day 14	Day 0	1.08	1.35	0.55	2.12	0.808	0.644
		Day 28	Day 0	1.24	1.35	0.63	2.44	0.482	
		Day 28	Day 14	1.15	1.35	0.59	2.27	0.641	

### 3.4 Differences in nutrient intake within diet groups

#### 3.4.1 Study participants without a history of colorectal cancer

Within diet groups, individuals without a history of colorectal cancer were only found to have a few significant changes in nutrient intake over the course of the study. For the rice bran diet, vitamin A was found to be significantly decreased at day 28 compared to day 0 (RoGM=0.44; 95% CI=[0.29, 0.67]; p=0.002). A similar decrease was found in vitamin A intake from day 14 to day 28 (RoGM=0.64; 95% CI=[0.42, 0.97]; p=0.038). Within the navy bean diet group, protein intake was found to have significantly decreased at day 28 compared to day 0 ( $\mu_{d28}-\mu_{d0}=-23.80$  g; 95% CI=[-44.68, -2.91]; p=0.031).

#### 3.4.2 Study participants with a history of colorectal cancer

When compared to their initial intake, individuals with a history of colorectal cancer who consumed a rice bran or navy bean supplemented diet were observed to have significant increases in several vitamins and minerals.

By day 14, the rice bran group was found to have significantly greater levels of intake of vitamin A (RoGM=1.72; 95% CI=[1.03, 2.88]; p=0.040),  $\beta$ -carotene (RoGM=3.25; 95% CI=[1.39, 8.12]; p=0.014), vitamin C (RoGM=1.75; 95% CI=[1.00, 3.06]; p=0.049),  $\alpha$ -Tocopherol (RoGM=1.54 95% CI=[1.19, 1.99]; p=0.002), vitamin B1 (RoGM=1.82; 95% CI=[1.50, 2.20]; p=<0.0001), vitamin B3 ( $\mu_{d14}-\mu_{d0}=9.32$   $\mu$ g; 95% CI=[4.28, 14.36]; p=0.001), vitamin B6 (RoGM=1.07; 95% CI=[1.74, 2.27]; p=<0.0001), potassium (RoGM=1.29; 95% CI=[1.09, 1.52]; p=0.004), and fiber (RoGM=1.36; 95% CI=[1.06, 1.73]; p=0.017) when compared to the start of the study. Similar differences in intake for the rice bran group were found between day 28 and day 0: vitamin A (RoGM=1.96; 95% CI=[1.17, 3.29]; p=0.013),  $\beta$ -

carotene (RoGM=3.68; 95% CI=[1.47, 9.18]; p=0.007), vitamin C (RoGM=1.98; 95% CI=[1.13, 3.45]; p=0.019),  $\alpha$ -Tocopherol (RoGM=1.63; 95% CI=[1.26, 2.10]; p=0.001), vitamin B1 (RoGM=1.90; 95% CI=[1.56, 2.30]; p=<0.0001), vitamin B3 ( $\mu_{d28} - \mu_{d0} = 8.19 \mu\text{g}$ ; 95% CI=[3.15, 13.22]; p=0.003), vitamin B6 (RoGM=2.05; 95% CI=[1.79, 2.34]; p=<0.0001), potassium (RoGM=1.41; 95% CI=[1.19, 1.66]; p=0.0003), and fiber (RoGM=1.41; 95% CI=[1.10, 1.80]; p=0.008).

For the navy bean diet group, significant differences were found between day 14 and day 0 for vitamin A (RoGM=1.87; 95% CI=[1.13, 3.09]; p=0.016),  $\beta$ -carotene (RoGM=3.27; 95% CI=[1.35, 7.87]; p=0.010), zinc (RoGM=1.57; 95% CI=[1.11, 2.22]; p=0.013), potassium (RoGM=1.66; 95% CI=[1.35, 2.05]; p=<0.0001), and fiber (RoGM=1.59; 95% CI=[1.18, 2.13]; p=0.003). The same variables were significantly greater at day 28 compared to day 0: vitamin A (RoGM=2.18; 95% CI=[1.32, 3.60]; p=0.040),  $\beta$ -carotene (RoGM=3.81; 95% CI=[1.58, 9.19]; p=0.004), zinc (RoGM=1.58; 95% CI=[1.12, 2.23]; p=0.012), potassium (RoGM=1.79; 95% CI=[1.45, 2.20]; p=<0.0001), and fiber (RoGM=1.81; 95% CI=[1.35, 2.43]; p=0.0003). Additionally, significant increases in the intake of vitamin B9 (RoGM=1.44; 95% CI=[1.00, 2.06]; p=0.0499) and linolenic acid (RoGM=1.64; 95% CI=[1.05, 2.54]; p=0.030) was found between day 28 and day 0 for the navy bean diet.

Within the control diet, the only variable found to have a significant change from day 0 was saturated fat. At day 14, saturated fat intake was significantly greater than at day 0 (RoGM=1.27; 95% CI=[1.00, 1.62]; p=0.0498). However, at day 28, no significant difference in saturated fat was found from day 0 for the control diet group (RoGM=1.21; 95% CI=[0.95, 1.54]; p=0.116).

### **3.5 Differences in nutrient intake between diet groups**

#### *3.5.1 Study participants without a history of colorectal cancer*

Within individuals without a history of colorectal cancer, only a few significant differences were found between diet groups. At day 0, vitamin A intake was observed to be significantly higher in the rice bran group compared to the control group (RoGM=2.05; 95% CI=[1.45, 2.90]; p=0.001). A similar relationship was found in the difference of vitamin A intake at day 0 between the navy bean and rice bran groups (RoGM=0.49; 95% CI=[0.36, 0.68]; p=0.001). However, no significant relationship in vitamin A intake was found between any group at day 14 or day 28.

In regards to the rice bran and control groups, the only significant relationships other than vitamin A intake were found at day 14 within calcium (RoGM=1.33; 95% CI=[1.02, 1.73]; p=0.036) and fiber (RoGM=1.48, 95% CI=[1.97, 2.04]; p=0.023) intakes.

Lastly, at day 0, iron intake was observed to be significantly lower in the navy bean group compared to the control (RoGM=0.70; 95% CI=[0.54, 0.90]; p=0.011) and rice bran (RoGM=0.69; 95% CI=[0.54, 0.87]; p=0.006) groups.

#### *3.5.2 Study participants with a history of colorectal cancer*

At day 0, the only significant differences in nutrient intake between diet groups existed between the navy bean and control diets. Within the navy bean group, intakes of vitamin D (RoGM=0.25; 95% CI=[0.08, 0.78]; p=0.019), vitamin B2 ( $\mu_{\text{NB}} - \mu_{\text{Ctrl}} = -0.46 \mu\text{g}$ ; 95% CI=[-0.87, -0.05]; p=0.030), and potassium (RoGM=0.72; 95% CI=[0.55, 0.96]; p=0.027) were each significantly less than the corresponding intake within the control group.

By day 14, several more significant differences were observed between the navy bean and control group. Along with the sustained differences in vitamin D (RoGM=0.57; 95% CI=[0.34, 0.94]; p=0.030) and vitamin B2 ( $\mu_{NB} - \mu_{Ctrl} = -0.41$   $\mu\text{g}$ ; 95% CI=[-0.65, -0.18]; p=0.001) at day 14, previously unseen significant differences were found between the navy bean and control group in respect to intake of vitamin B12 (RoGM=0.58; 95% CI=[0.39, 0.87]; p=0.011), fat ( $\mu_{NB} - \mu_{Ctrl} = -18.77$   $\mu\text{g}$ ; 95% CI=[-37.10, -0.44]; p=0.045), and linolenic acid (RoGM=1.56; 95% CI=[1.08, 2.25]; p=0.019). Additionally, potassium intake at day 14 within the navy bean group was observed to be significantly higher than in the control group (RoGM=1.19; 95% CI=[1.01, 1.40]; p=0.036); this is an opposite relationship as that found at day 0.

At day 28, differences between the respective intakes of vitamin D, vitamin B2, vitamin B12, fat, and linolenic acid within the navy bean and control diet were no longer significant. The only significant relationships at day 28 were found within intake of vitamin B2 ( $\mu_{NB} - \mu_{Ctrl} = -0.34$   $\mu\text{g}$ ; 95% CI=[-0.61, -0.08]; p=0.013), potassium (RoGM=1.22; 95% CI=[1.01, 1.48]; p=0.041), and fiber (RoGM=1.41; 95% CI=[1.13, 1.72]; p=0.003).

Between the rice bran and control diets, at day 14, significantly greater levels of intake were observed in the rice bran group for vitamin B1 (RoGM=1.69; 95% CI=[1.30, 2.19]; p=0.0003), vitamin B3 ( $\mu_{RB} - \mu_{Ctrl} = 10.17$   $\mu\text{g}$ ; 95% CI=[5.43, 14.92]; p=0.0002), vitamin B6 (RoGM=1.77; 95% CI=[1.47, 2.13]; p=<0.0001), and fiber (RoGM=1.22; 95% CI=[1.01, 1.48]; p=0.041). Similar relationships were found at day 28: vitamin B1 (RoGM=1.37; 95% CI=[1.10, 1.70]; p=0.007), vitamin B3 ( $\mu_{RB} - \mu_{Ctrl} = 7.62$   $\mu\text{g}$ ; 95% CI=[2.52, 12.72]; p=0.005), vitamin B6 (RoGM=1.73; 95% CI=[1.36, 2.19]; p=<0.0001), and fiber (RoGM=1.41; 95% CI=[1.13, 1.75]; p=0.003).

Comparison of the navy bean and rice bran groups at day 14 revealed significantly less intake within the navy bean group of  $\alpha$ -Tocopherol (RoGM=0.70; 95% CI=[0.51, 0.98]; p=0.036), vitamin B1 (RoGM=0.50; 95% CI=[0.39, 0.65]; p<0.0001), vitamin B2 ( $\mu_{NB} - \mu_{RB} = -0.29$   $\mu$ g; 95% CI=[-0.53, -0.05]; p=0.022), vitamin B3 ( $\mu_{NB} - \mu_{RB} = -12.03$   $\mu$ g; 95% CI=[-16.78, -7.29]; p<0.0001), vitamin B6 (RoGM=0.49; 95% CI=[0.41, 0.59]; p<0.0001), vitamin B12 (RoGM=0.64; 95% CI=[0.42, 0.97]; p=0.036), oleic acid (RoGM=0.69; 95% CI=[0.49, 0.96]; p=0.031), linoleic acid (RoGM=0.61; 95% CI=[0.40, 0.93]; p=0.024), and linolenic acid (RoGM=0.56; 95% CI=[0.39, 0.80]; p=0.003). However, at day 28, the only significant differences between the navy bean and rice bran diets were found in vitamin B1 (RoGM=0.59; 95% CI=[0.47, 0.73]; p<0.0001), vitamin B3 ( $\mu_{NB} - \mu_{RB} = -9.00$   $\mu$ g; 95% CI=[-14.10, -3.90]; p=0.001), and vitamin B6 (RoGM=0.52; 95% CI=[0.41, 0.66]; p<0.0001). The significant differences between the navy bean and rice bran diets that were found in  $\alpha$ -Tocopherol, vitamin B2, vitamin B12, oleic acid, linoleic acid, and linolenic acid at day 14 were not significant at day 28.

**Table 17:** Differences in vitamin A, vitamin C, zinc, and calcium intake between diet groups (left) and between time points (right) for study participants without a history of colorectal cancer. Variables shown above: vitamin A intake (top), vitamin C intake (second from top), zinc intake (second from bottom), and calcium intake (bottom). At day 0, vitamin A intake within the rice bran treatment group (n=4) was significantly greater than both the navy bean (n=4) and control (n=3) treatment groups. Over the duration of the study, vitamin A intake within the rice bran group decreased by day 28 was significantly less than at day 0 and day 14. Additionally, at day 14, calcium intake within the rice bran group significantly greater than the control group. Otherwise, no significant differences were observed in the displayed variables between treatment groups or time points.

Parameter Estimates for Study Participants without a History of Colorectal Cancer: One-Way Analysis of Variance of Vitamin A Intake by Diet Group									
Time Point	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Day 0		Navy Bean	Control	1.01	1.16	0.71	1.42	0.961	0.001
		Rice Bran	Control	2.05	1.16	1.45	2.90	0.001	
		Navy Bean	Rice Bran	0.49	1.15	0.36	0.68	0.001	
Day 14	Diet	Navy Bean	Control	1.70	1.47	0.68	4.24	0.211	0.296
		Rice Bran	Control	1.77	1.43	0.76	4.17	0.156	
		Navy Bean	Rice Bran	0.96	1.43	0.41	2.25	0.910	
Day 28		Navy Bean	Control	1.31	1.33	0.67	2.54	0.372	0.581
		Rice Bran	Control	1.02	1.30	0.55	1.90	0.944	
		Navy Bean	Rice Bran	1.28	1.30	0.69	2.39	0.376	

Parameter Estimates for Study Participants without a History of Colorectal Cancer: One-Way Analysis of Variance of Vitamin A Intake by Time Point									
Diet	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Control		Day 14	Day 0	0.80	1.43	0.33	1.93	0.563	0.701
		Day 28	Day 0	0.89	1.43	0.37	2.13	0.752	
		Day 28	Day 14	1.11	1.43	0.46	2.66	0.788	
Navy Bean	Time	Day 14	Day 0	1.36	1.32	0.70	2.61	0.309	0.511
		Day 28	Day 0	1.15	1.32	0.60	2.22	0.623	
		Day 28	Day 14	0.85	1.34	0.42	1.71	0.602	
Rice Bran		Day 14	Day 0	0.69	1.21	0.46	1.06	0.082	0.041
		Day 28	Day 0	0.44	1.21	0.29	0.67	0.002	
		Day 28	Day 14	0.64	1.21	0.42	0.97	0.038	

Parameter Estimates for Study Participants without a History of Colorectal Cancer: One-Way Analysis of Variance of Vitamin C Intake by Diet Group									
Time Point	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Day 0		Navy Bean	Control	1.07	1.30	0.59	1.95	0.798	0.957
		Rice Bran	Control	1.01	1.30	0.55	1.84	0.972	
		Navy Bean	Rice Bran	1.06	1.27	0.61	1.85	0.812	
Day 14	Diet	Navy Bean	Control	0.79	1.36	0.38	1.64	0.473	0.504
		Rice Bran	Control	1.13	1.33	0.57	2.22	0.692	
		Navy Bean	Rice Bran	0.70	1.33	0.36	1.39	0.261	
Day 28		Navy Bean	Control	1.81	1.40	0.82	4.00	0.122	0.250
		Rice Bran	Control	1.16	1.37	0.55	2.44	0.648	
		Navy Bean	Rice Bran	1.55	1.37	0.74	3.27	0.203	

Parameter Estimates for Study Participants without a History of Colorectal Cancer: One-Way Analysis of Variance of Vitamin C Intake by Time Point									
Diet	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Control		Day 14	Day 0	0.84	1.29	0.45	1.58	0.524	0.479
		Day 28	Day 0	0.74	1.29	0.39	1.39	0.282	
		Day 28	Day 14	0.88	1.29	0.47	1.65	0.631	
Navy Bean	Time	Day 14	Day 0	0.62	1.34	0.31	1.23	0.144	0.228
		Day 28	Day 0	1.24	1.34	0.63	2.47	0.479	
		Day 28	Day 14	2.00	1.36	0.96	4.17	0.060	
Rice Bran		Day 14	Day 0	0.94	1.33	0.49	1.79	0.824	0.714
		Day 28	Day 0	0.85	1.33	0.44	1.62	0.580	
		Day 28	Day 14	0.91	1.33	0.47	1.74	0.738	

Parameter Estimates for Study Participants without a History of Colorectal Cancer: One-Way Analysis of Variance of Zinc Intake by Diet Group									
Time Point	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Day 0		Navy Bean	Control	0.87	1.14	0.65	1.17	0.303	0.5641
		Rice Bran	Control	0.94	1.14	0.70	1.26	0.623	
		Navy Bean	Rice Bran	0.93	1.12	0.71	1.22	0.543	
Day 14	Diet	Navy Bean	Control	1.05	1.25	0.63	1.77	0.826	0.974
		Rice Bran	Control	1.03	1.23	0.63	1.67	0.891	
		Navy Bean	Rice Bran	1.02	1.23	0.63	1.66	0.921	
Day 28		Navy Bean	Control	0.90	1.29	0.49	1.65	0.686	0.706
		Rice Bran	Control	0.81	1.27	0.46	1.44	0.421	
		Navy Bean	Rice Bran	1.10	1.27	0.62	1.95	0.698	

Parameter Estimates for Study Participants without a History of Colorectal Cancer: One-Way Analysis of Variance of Zinc Intake by Time Point									
Diet	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Control		Day 14	Day 0	0.80	1.29	0.43	1.49	0.410	0.589
		Day 28	Day 0	0.86	1.29	0.46	1.60	0.568	
		Day 28	Day 14	1.07	1.29	0.58	2.01	0.788	
Navy Bean	Time	Day 14	Day 0	0.96	1.17	0.66	1.40	0.828	0.638
		Day 28	Day 0	0.88	1.17	0.61	1.29	0.464	
		Day 28	Day 14	0.92	1.19	0.61	1.37	0.624	
Rice Bran		Day 14	Day 0	0.88	1.19	0.59	1.30	0.466	0.319
		Day 28	Day 0	0.74	1.19	0.50	1.10	0.122	
		Day 28	Day 14	0.85	1.19	0.57	1.26	0.368	

Parameter Estimates for Study Participants without a History of Colorectal Cancer: One-Way Analysis of Variance of Calcium Intake by Diet Group									
Time Point	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Day 0		Navy Bean	Control	0.88	1.14	0.64	1.20	0.362	0.189
		Rice Bran	Control	1.13	1.14	0.83	1.54	0.387	
		Navy Bean	Rice Bran	0.78	1.13	0.58	1.03	0.08	
Day 14	Diet	Navy Bean	Control	1.23	1.13	0.93	1.62	0.129	0.092
		Rice Bran	Control	1.33	1.12	1.02	1.73	0.036	
		Navy Bean	Rice Bran	0.92	1.12	0.71	1.20	0.480	
Day 28		Navy Bean	Control	0.79	1.13	0.59	1.05	0.089	0.211
		Rice Bran	Control	0.88	1.12	0.67	1.14	0.278	
		Navy Bean	Rice Bran	0.90	1.12	0.69	1.17	0.380	

Parameter Estimates for Study Participants without a History of Colorectal Cancer: One-Way Analysis of Variance of Calcium Intake by Time Point									
Diet	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Control		Day 14	Day 0	0.82	1.12	0.62	1.09	0.142	0.253
		Day 28	Day 0	1.07	1.12	0.81	1.42	0.557	
		Day 28	Day 14	1.31	1.12	0.98	1.73	0.060	
Navy Bean	Time	Day 14	Day 0	1.15	1.14	0.85	1.56	0.316	0.450
		Day 28	Day 0	0.96	1.14	0.71	1.31	0.788	
		Day 28	Day 14	0.84	1.15	0.61	1.16	0.244	
Rice Bran		Day 14	Day 0	0.97	1.12	0.75	1.25	0.785	0.378
		Day 28	Day 0	0.83	1.12	0.64	1.07	0.138	
		Day 28	Day 14	0.86	1.12	0.67	1.11	0.212	

**Table 18:** Differences in potassium, sodium, and iron intake between diet groups (left) and between time points (right) for study participants without a history of colorectal cancer. Variables shown above: potassium intake (top), sodium intake (middle), and iron intake (bottom). At day 0, iron intake within the navy bean treatment group (n=4) was significantly less than both the rice bran (n=4) and control (n=3) treatment groups. Otherwise, no significant differences were observed in the displayed variables between treatment groups or time points.

Parameter Estimates for Study Participants without a History of Colorectal Cancer: One-Way Analysis of Variance of Vitamin A Intake by Diet Group									
Time Point	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Day 0	Diet	Navy Bean	Control	1.01	1.16	0.71	1.42	0.961	0.001
		Rice Bran	Control	2.05	1.16	1.45	2.90	0.001	
		Navy Bean	Rice Bran	0.49	1.15	0.36	0.68	0.001	
Day 14	Diet	Navy Bean	Control	1.70	1.47	0.68	4.24	0.211	0.296
		Rice Bran	Control	1.77	1.43	0.76	4.17	0.156	
		Navy Bean	Rice Bran	0.96	1.43	0.41	2.25	0.910	
Day 28	Diet	Navy Bean	Control	1.31	1.33	0.67	2.54	0.372	0.581
		Rice Bran	Control	1.02	1.30	0.55	1.90	0.944	
		Navy Bean	Rice Bran	1.28	1.30	0.69	2.39	0.376	

Parameter Estimates for Study Participants without a History of Colorectal Cancer: One-Way Analysis of Variance of Vitamin A Intake by Time Point									
Diet	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Control	Time	Day 14	Day 0	0.80	1.43	0.33	1.93	0.563	0.701
		Day 28	Day 0	0.89	1.43	0.37	2.13	0.752	
		Day 28	Day 14	1.11	1.43	0.46	2.66	0.788	
Navy Bean	Time	Day 14	Day 0	1.36	1.32	0.70	2.61	0.309	0.511
		Day 28	Day 0	1.15	1.32	0.60	2.22	0.623	
		Day 28	Day 14	0.85	1.34	0.42	1.71	0.602	
Rice Bran	Time	Day 14	Day 0	0.69	1.21	0.46	1.06	0.082	0.041
		Day 28	Day 0	0.44	1.21	0.29	0.67	0.002	
		Day 28	Day 14	0.64	1.21	0.42	0.97	0.038	

Parameter Estimates for Study Participants without a History of Colorectal Cancer: One-Way Analysis of Variance of Vitamin C Intake by Diet Group									
Time Point	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Day 0	Diet	Navy Bean	Control	1.07	1.30	0.59	1.95	0.798	0.957
		Rice Bran	Control	1.01	1.30	0.55	1.84	0.972	
		Navy Bean	Rice Bran	1.06	1.27	0.61	1.85	0.812	
Day 14	Diet	Navy Bean	Control	0.79	1.36	0.38	1.64	0.473	0.504
		Rice Bran	Control	1.13	1.33	0.57	2.22	0.692	
		Navy Bean	Rice Bran	0.70	1.33	0.36	1.39	0.261	
Day 28	Diet	Navy Bean	Control	1.81	1.40	0.82	4.00	0.122	0.250
		Rice Bran	Control	1.16	1.37	0.55	2.44	0.648	
		Navy Bean	Rice Bran	1.55	1.37	0.74	3.27	0.203	

Parameter Estimates for Study Participants without a History of Colorectal Cancer: One-Way Analysis of Variance of Vitamin C Intake by Time Point									
Diet	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Control	Time	Day 14	Day 0	0.84	1.29	0.45	1.58	0.524	0.479
		Day 28	Day 0	0.74	1.29	0.39	1.39	0.282	
		Day 28	Day 14	0.88	1.29	0.47	1.65	0.631	
Navy Bean	Time	Day 14	Day 0	0.62	1.34	0.31	1.23	0.144	0.228
		Day 28	Day 0	1.24	1.34	0.63	2.47	0.479	
		Day 28	Day 14	2.00	1.36	0.96	4.17	0.060	
Rice Bran	Time	Day 14	Day 0	0.94	1.33	0.49	1.79	0.824	0.714
		Day 28	Day 0	0.85	1.33	0.44	1.62	0.580	
		Day 28	Day 14	0.91	1.33	0.47	1.74	0.738	

Parameter Estimates for Study Participants without a History of Colorectal Cancer: One-Way Analysis of Variance of Zinc Intake by Diet Group									
Time Point	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Day 0	Diet	Navy Bean	Control	0.87	1.14	0.65	1.17	0.303	0.5641
		Rice Bran	Control	0.94	1.14	0.70	1.26	0.623	
		Navy Bean	Rice Bran	0.93	1.12	0.71	1.22	0.543	
Day 14	Diet	Navy Bean	Control	1.05	1.25	0.63	1.77	0.826	0.974
		Rice Bran	Control	1.03	1.23	0.63	1.67	0.891	
		Navy Bean	Rice Bran	1.02	1.23	0.63	1.66	0.921	
Day 28	Diet	Navy Bean	Control	0.90	1.29	0.49	1.65	0.686	0.706
		Rice Bran	Control	0.81	1.27	0.46	1.44	0.421	
		Navy Bean	Rice Bran	1.10	1.27	0.62	1.95	0.698	

Parameter Estimates for Study Participants without a History of Colorectal Cancer: One-Way Analysis of Variance of Zinc Intake by Time Point									
Diet	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Control	Time	Day 14	Day 0	0.80	1.29	0.43	1.49	0.410	0.589
		Day 28	Day 0	0.86	1.29	0.46	1.60	0.568	
		Day 28	Day 14	1.07	1.29	0.58	2.01	0.788	
Navy Bean	Time	Day 14	Day 0	0.96	1.17	0.66	1.40	0.828	0.638
		Day 28	Day 0	0.88	1.17	0.61	1.29	0.464	
		Day 28	Day 14	0.92	1.19	0.61	1.37	0.624	
Rice Bran	Time	Day 14	Day 0	0.88	1.19	0.59	1.30	0.466	0.319
		Day 28	Day 0	0.74	1.19	0.50	1.10	0.122	
		Day 28	Day 14	0.85	1.19	0.57	1.26	0.368	

Parameter Estimates for Study Participants without a History of Colorectal Cancer: One-Way Analysis of Variance of Calcium Intake by Diet Group									
Time Point	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Day 0	Diet	Navy Bean	Control	0.88	1.14	0.64	1.20	0.362	0.189
		Rice Bran	Control	1.13	1.14	0.83	1.54	0.387	
		Navy Bean	Rice Bran	0.78	1.13	0.58	1.03	0.08	
Day 14	Diet	Navy Bean	Control	1.23	1.13	0.93	1.62	0.129	0.092
		Rice Bran	Control	1.33	1.12	1.02	1.73	0.036	
		Navy Bean	Rice Bran	0.92	1.12	0.71	1.20	0.480	
Day 28	Diet	Navy Bean	Control	0.79	1.13	0.59	1.05	0.089	0.211
		Rice Bran	Control	0.88	1.12	0.67	1.14	0.278	
		Navy Bean	Rice Bran	0.90	1.12	0.69	1.17	0.380	

Parameter Estimates for Study Participants without a History of Colorectal Cancer: One-Way Analysis of Variance of Calcium Intake by Time Point									
Diet	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Control	Time	Day 14	Day 0	0.82	1.12	0.62	1.09	0.142	0.253
		Day 28	Day 0	1.07	1.12	0.81	1.42	0.557	
		Day 28	Day 14	1.31	1.12	0.98	1.73	0.060	
Navy Bean	Time	Day 14	Day 0	1.15	1.14	0.85	1.56	0.316	0.450
		Day 28	Day 0	0.96	1.14	0.71	1.31	0.788	
		Day 28	Day 14	0.84	1.15	0.61	1.16	0.244	
Rice Bran	Time	Day 14	Day 0	0.97	1.12	0.75	1.25	0.785	0.378
		Day 28	Day 0	0.83	1.12	0.64	1.07	0.138	
		Day 28	Day 14	0.86	1.12	0.67	1.11	0.212	

**Table 19:** Differences in calorie, protein, and carbohydrate intake between diet groups (left) and between time points (right) for study participants without a history of colorectal cancer. Variables shown above: calorie intake (top), protein intake (middle), and carbohydrate intake (bottom). Within the navy bean treatment group (n=4), protein intake was significantly lower at day 28 than at day 14. Otherwise, no significant differences were observed in the displayed variables between treatment groups or time points.

Parameter Estimates for Study Participants without a History of Colorectal Cancer: One-Way Analysis of Variance of Calorie Intake by Diet Group									
Time Point	Parameter	Comparison groups		Diff. of Arithmetic Means (cal)	Standard Error	95% Confidence Limits		p-value	Type III p-value
Day 0	Diet	Navy Bean	Control	-130.1	158.7	-496.0	235.8	0.436	0.190
		Rice Bran	Control	176.3	158.7	-189.6	542.2	0.299	
		Navy Bean	Rice Bran	-306.4	146.9	-645.2	32.4	0.07	
Day 14		Navy Bean	Control	-48.2	309.0	-778.8	682.4	0.880	0.959
		Rice Bran	Control	37.6	289.0	-645.8	721.0	0.900	
		Navy Bean	Rice Bran	-85.8	289.0	-769.2	597.6	0.775	
Day 28	Navy Bean	Control	-367.4	229.9	-911.0	176.1	0.154	0.291	
	Rice Bran	Control	-122.5	215.0	-631.0	385.9	0.587		
	Navy Bean	Rice Bran	-244.9	215.0	-753.4	263.6	0.292		

Parameter Estimates for Study Participants without a History of Colorectal Cancer: One-Way Analysis of Variance of Calorie Intake by Time Point									
Diet	Parameter	Comparison groups		Diff. of Arithmetic Means (cal)	Standard Error	95% Confidence Limits		p-value	Type III p-value
Control	Time	Day 14	Day 0	26.0	246.6	-577.5	629.4	0.920	0.880
		Day 28	Day 0	58.5	246.6	-545.0	661.9	0.821	
		Day 28	Day 14	32.5	246.6	-570.9	635.9	0.899	
Navy Bean		Day 14	Day 0	107.9	184.4	-328.1	543.9	0.577	0.377
		Day 28	Day 0	-178.8	184.4	-614.8	257.1	0.364	
		Day 28	Day 14	-286.7	197.1	-752.8	179.4	0.189	
Rice Bran	Day 14	Day 0	-112.8	229.4	-631.7	406.2	0.635	0.516	
	Day 28	Day 0	-240.4	229.4	-759.3	278.6	0.322		
	Day 28	Day 14	-127.6	229.4	-646.5	391.3	0.592		

Parameter Estimates for Study Participants without a History of Colorectal Cancer: One-Way Analysis of Variance of Protein Intake by Diet Group									
Time Point	Parameter	Comparison groups		Diff. of Arithmetic Means (g)	Standard Error	95% Confidence Limits		p-value	Type III p-value
Day 0	Diet	Navy Bean	Control	-4.05	7.85	-22.16	14.06	0.620	0.728
		Rice Bran	Control	1.73	7.85	-16.38	19.85	0.831	
		Navy Bean	Rice Bran	-5.78	7.27	-22.55	10.99	0.449	
Day 14		Navy Bean	Control	5.41	12.27	-23.60	34.42	0.673	0.892
		Rice Bran	Control	4.60	11.48	-22.54	31.74	0.701	
		Navy Bean	Rice Bran	0.81	11.48	-26.33	27.95	0.945	
Day 28	Navy Bean	Control	-14.40	10.15	-38.40	9.60	0.199	0.406	
	Rice Bran	Control	-8.81	9.49	-31.26	13.64	0.384		
	Navy Bean	Rice Bran	-5.59	9.49	-28.04	16.85	0.574		

Parameter Estimates for Study Participants without a History of Colorectal Cancer: One-Way Analysis of Variance of Protein Intake by Time Point									
Diet	Parameter	Comparison groups		Diff. of Arithmetic Means (g)	Standard Error	95% Confidence Limits		p-value	Type III p-value
Control	Time	Day 14	Day 0	2.26	10.85	-24.28	28.81	0.842	0.816
		Day 28	Day 0	-1.72	10.85	-28.27	24.83	0.879	
		Day 28	Day 14	-3.98	10.85	-30.53	22.56	0.726	
Navy Bean		Day 14	Day 0	11.73	8.26	-7.81	31.26	0.199	0.139
		Day 28	Day 0	-12.07	8.26	-31.61	7.46	0.187	
		Day 28	Day 14	-23.80	8.83	-44.68	-2.91	0.031	
Rice Bran	Day 14	Day 0	5.13	9.52	-16.40	26.65	0.603	0.311	
	Day 28	Day 0	-12.26	9.52	-33.79	9.27	0.230		
	Day 28	Day 14	-17.39	9.52	-38.91	4.14	0.101		

Parameter Estimates for Study Participants without a History of Colorectal Cancer: One-Way Analysis of Variance of Carbohydrate Intake by Diet Group									
Time Point	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Day 0	Diet	Navy Bean	Control	0.95	1.10	0.75	1.19	0.596	0.333
		Rice Bran	Control	1.09	1.10	0.87	1.38	0.390	
		Navy Bean	Rice Bran	0.86	1.10	0.70	1.07	0.153	
Day 14		Navy Bean	Control	0.97	1.17	0.68	1.40	0.867	0.959
		Rice Bran	Control	0.96	1.15	0.68	1.35	0.781	
		Navy Bean	Rice Bran	1.02	1.15	0.72	1.43	0.920	
Day 28	Navy Bean	Control	0.80	1.19	0.53	1.21	0.237	0.436	
	Rice Bran	Control	0.95	1.18	0.65	1.40	0.767		
	Navy Bean	Rice Bran	0.84	1.18	0.57	1.24	0.319		

Parameter Estimates for Study Participants without a History of Colorectal Cancer: One-Way Analysis of Variance of Carbohydrate Intake by Time Point									
Diet	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Control	Time	Day 14	Day 0	1.08	1.17	0.74	1.58	0.620	0.709
		Day 28	Day 0	1.10	1.17	0.75	1.60	0.568	
		Day 28	Day 14	1.01	1.17	0.69	1.48	0.938	
Navy Bean		Day 14	Day 0	1.11	1.15	0.79	1.56	0.473	0.446
		Day 28	Day 0	0.93	1.15	0.66	1.30	0.604	
		Day 28	Day 14	0.83	1.17	0.58	1.19	0.263	
Rice Bran	Day 14	Day 0	0.95	1.12	0.73	1.24	0.669	0.778	
	Day 28	Day 0	0.95	1.12	0.73	1.24	0.692		
	Day 28	Day 14	1.004	1.12	0.77	1.31	0.974		

**Table 20:** Differences in fat, saturated fat, and fiber intake between diet groups (left) and between time points (right) for study participants without a history of colorectal cancer. Variables shown above: total fat intake (top), saturated fat intake (middle), and fiber intake (bottom). At day 14, fiber intake within the rice bran treatment group (n=4) was significantly greater than the control group (n=3). Otherwise, no significant differences were observed in the displayed variables between treatment groups or time points. A natural logarithm was performed on all data shown above, and a ratio of geometric means was obtained after back transformation. Confidence intervals and standard errors displayed are for the ratio of the respective comparison group means (left group : right group).

Parameter Estimates for Study Participants without a History of Colorectal Cancer: One-Way Analysis of Variance of Calorie Intake by Diet Group									
Time Point	Parameter	Comparison groups		Diff. of Arithmetic Means (cal)	Standard Error	95% Confidence Limits	p-value	Type III p-value	
Day 0	Diet	Navy Bean	Control	-130.1	158.7	-496.0	235.8	0.436	0.190
		Rice Bran	Control	176.3	158.7	-189.6	542.2	0.299	
		Navy Bean	Rice Bran	-306.4	146.9	-645.2	32.4	0.07	
Day 14	Diet	Navy Bean	Control	-48.2	309.0	-778.8	682.4	0.880	0.959
		Rice Bran	Control	37.6	289.0	-645.8	721.0	0.900	
		Navy Bean	Rice Bran	-85.8	289.0	-769.2	597.6	0.775	
Day 28	Diet	Navy Bean	Control	-367.4	229.9	-911.0	176.1	0.154	0.291
		Rice Bran	Control	-122.5	215.0	-631.0	385.9	0.587	
		Navy Bean	Rice Bran	-244.9	215.0	-753.4	263.6	0.292	

Parameter Estimates for Study Participants without a History of Colorectal Cancer: One-Way Analysis of Variance of Calorie Intake by Time Point									
Diet	Parameter	Comparison groups		Diff. of Arithmetic Means (cal)	Standard Error	95% Confidence Limits	p-value	Type III p-value	
Control	Time	Day 14	Day 0	26.0	246.6	-577.5	629.4	0.920	0.880
		Day 28	Day 0	58.5	246.6	-545.0	661.9	0.821	
		Day 28	Day 14	32.5	246.6	-570.9	635.9	0.899	
Navy Bean	Time	Day 14	Day 0	107.9	184.4	-328.1	543.9	0.577	0.377
		Day 28	Day 0	-178.8	184.4	-614.8	257.1	0.364	
		Day 28	Day 14	-286.7	197.1	-752.8	179.4	0.189	
Rice Bran	Time	Day 14	Day 0	-112.8	229.4	-631.7	406.2	0.635	0.516
		Day 28	Day 0	-240.4	229.4	-759.3	278.6	0.322	
		Day 28	Day 14	-127.6	229.4	-646.5	391.3	0.592	

Parameter Estimates for Study Participants without a History of Colorectal Cancer: One-Way Analysis of Variance of Protein Intake by Diet Group									
Time Point	Parameter	Comparison groups		Diff. of Arithmetic Means (g)	Standard Error	95% Confidence Limits	p-value	Type III p-value	
Day 0	Diet	Navy Bean	Control	-4.05	7.85	-22.16	14.06	0.620	0.728
		Rice Bran	Control	1.73	7.85	-16.38	19.85	0.831	
		Navy Bean	Rice Bran	-5.78	7.27	-22.55	10.99	0.449	
Day 14	Diet	Navy Bean	Control	5.41	12.27	-23.60	34.42	0.673	0.892
		Rice Bran	Control	4.60	11.48	-22.54	31.74	0.701	
		Navy Bean	Rice Bran	0.81	11.48	-26.33	27.95	0.945	
Day 28	Diet	Navy Bean	Control	-14.40	10.15	-38.40	9.60	0.199	0.406
		Rice Bran	Control	-8.81	9.49	-31.26	13.64	0.384	
		Navy Bean	Rice Bran	-5.59	9.49	-28.04	16.85	0.574	

Parameter Estimates for Study Participants without a History of Colorectal Cancer: One-Way Analysis of Variance of Protein Intake by Time Point									
Diet	Parameter	Comparison groups		Diff. of Arithmetic Means (g)	Standard Error	95% Confidence Limits	p-value	Type III p-value	
Control	Time	Day 14	Day 0	2.26	10.85	-24.28	28.81	0.842	0.816
		Day 28	Day 0	-1.72	10.85	-28.27	24.83	0.879	
		Day 28	Day 14	-3.98	10.85	-30.53	22.56	0.726	
Navy Bean	Time	Day 14	Day 0	11.73	8.26	-7.81	31.26	0.199	0.139
		Day 28	Day 0	-12.07	8.26	-31.61	7.46	0.187	
		Day 28	Day 14	-23.80	8.83	-44.68	-2.91	0.031	
Rice Bran	Time	Day 14	Day 0	5.13	9.52	-16.40	26.65	0.603	0.311
		Day 28	Day 0	-12.26	9.52	-33.79	9.27	0.230	
		Day 28	Day 14	-17.39	9.52	-38.91	4.14	0.101	

Parameter Estimates for Study Participants without a History of Colorectal Cancer: One-Way Analysis of Variance of Carbohydrate Intake by Diet Group									
Time Point	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits	p-value	Type III p-value	
Day 0	Diet	Navy Bean	Control	0.95	1.10	0.75	1.19	0.596	0.333
		Rice Bran	Control	1.09	1.10	0.87	1.38	0.390	
		Navy Bean	Rice Bran	0.86	1.10	0.70	1.07	0.153	
Day 14	Diet	Navy Bean	Control	0.97	1.17	0.68	1.40	0.867	0.959
		Rice Bran	Control	0.96	1.15	0.68	1.35	0.781	
		Navy Bean	Rice Bran	1.02	1.15	0.72	1.43	0.920	
Day 28	Diet	Navy Bean	Control	0.80	1.19	0.53	1.21	0.237	0.436
		Rice Bran	Control	0.95	1.18	0.65	1.40	0.767	
		Navy Bean	Rice Bran	0.84	1.18	0.57	1.24	0.319	

Parameter Estimates for Study Participants without a History of Colorectal Cancer: One-Way Analysis of Variance of Carbohydrate Intake by Time Point									
Diet	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits	p-value	Type III p-value	
Control	Time	Day 14	Day 0	1.08	1.17	0.74	1.58	0.620	0.709
		Day 28	Day 0	1.10	1.17	0.75	1.60	0.568	
		Day 28	Day 14	1.01	1.17	0.69	1.48	0.938	
Navy Bean	Time	Day 14	Day 0	1.11	1.15	0.79	1.56	0.473	0.446
		Day 28	Day 0	0.93	1.15	0.66	1.30	0.604	
		Day 28	Day 14	0.83	1.17	0.58	1.19	0.263	
Rice Bran	Time	Day 14	Day 0	0.95	1.12	0.73	1.24	0.669	0.778
		Day 28	Day 0	0.95	1.12	0.73	1.24	0.692	
		Day 28	Day 14	1.004	1.12	0.77	1.31	0.974	

**Table 21:** Differences in vitamin A,  $\beta$ -Carotene, and vitamin C intake between diet groups (left) and between time points (right) for study participants with a history of colorectal cancer (n=29). Variables shown above: vitamin A intake (top),  $\beta$ -carotene intake (middle), and vitamin C intake (bottom). Within both the navy bean (n=10) and rice bran (n=9) groups, vitamin A and  $\beta$ -carotene intake were both significantly greater at day 28 and day 14 than at day 0. Additionally, within the rice bran group, vitamin C intake was observed to be significantly great at day 28 and day 14 than at day 0.

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Vitamin E Intake by Diet Group								
Time Point	Parameter	Comparison groups	Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Day 0	Diet	Navy Bean Control	1.17	2.48	0.18	7.69	0.864	0.974
		Rice Bran Control	0.96	2.55	0.14	6.67	0.966	
		Navy Bean Rice Bran	1.22	2.48	0.19	8.01	0.830	
Day 14	Diet	Navy Bean Control	0.99	1.41	0.49	2.03	0.985	0.562
		Rice Bran Control	1.40	1.43	0.67	2.91	0.356	
		Navy Bean Rice Bran	0.71	1.43	0.34	1.48	0.347	
Day 28	Diet	Navy Bean Control	1.77	1.65	0.63	4.95	0.266	0.301
		Rice Bran Control	2.19	1.67	0.76	6.29	0.141	
		Navy Bean Rice Bran	0.81	1.67	0.28	2.33	0.683	

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Vitamin E Intake by Time Point									
Diet	Parameter	Comparison groups	Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value	
Control	Time	Day 14 Day 0	0.92	1.92	0.24	3.55	0.905	0.990	
		Day 28 Day 0	0.92	1.92	0.24	3.53	0.899		
		Day 28 Day 14	1.00	1.85	0.28	3.54	0.994		
		Day 14 Day 0	0.78	1.95	0.20	3.10	0.720		
		Day 28 Day 0	1.39	1.95	0.35	5.49	0.627		
		Day 28 Day 14	1.77	1.92	0.46	6.74	0.388		
Navy Bean	Time	Day 14 Day 0	0.78	1.95	0.20	3.10	0.720	0.683	
		Day 28 Day 0	1.39	1.95	0.35	5.49	0.627		
		Day 28 Day 14	1.77	1.92	0.46	6.74	0.388		
		Day 14 Day 0	1.34	1.62	0.50	3.64	0.545		
		Day 28 Day 0	2.09	1.62	0.77	5.66	0.139		
		Day 28 Day 14	1.56	1.60	0.59	4.09	0.354		
Rice Bran	Time	Day 14 Day 0	1.34	1.62	0.50	3.64	0.545	0.319	
		Day 28 Day 0	2.09	1.62	0.77	5.66	0.139		
		Day 28 Day 14	1.56	1.60	0.59	4.09	0.354		

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of $\alpha$ -Tocopherol Intake by Diet Group								
Time Point	Parameter	Comparison groups	Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Day 0	Diet	Navy Bean Control	0.55	1.44	0.26	1.18	0.118	0.263
		Rice Bran Control	0.64	1.45	0.29	1.38	0.239	
		Navy Bean Rice Bran	0.87	1.44	0.41	1.85	0.705	
Day 14	Diet	Navy Bean Control	0.93	1.17	0.67	1.27	0.626	0.089
		Rice Bran Control	1.32	1.17	0.95	1.82	0.095	
		Navy Bean Rice Bran	0.70	1.17	0.51	0.98	0.036	
Day 28	Diet	Navy Bean Control	1.04	1.18	0.75	1.46	0.798	0.163
		Rice Bran Control	1.36	1.18	0.96	1.91	0.078	
		Navy Bean Rice Bran	0.77	1.18	0.54	1.08	0.126	

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of $\alpha$ -Tocopherol Intake by Time Point									
Diet	Parameter	Comparison groups	Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value	
Control	Time	Day 14 Day 0	0.75	1.33	0.42	1.33	0.397	0.534	
		Day 28 Day 0	0.76	1.33	0.43	1.37	0.350		
		Day 28 Day 14	1.03	1.30	0.59	1.77	0.924		
		Day 14 Day 0	1.25	1.30	0.73	2.14	0.409		
		Day 28 Day 0	1.44	1.30	0.84	2.47	0.177		
		Day 28 Day 14	1.15	1.29	0.68	1.95	0.578		
Navy Bean	Time	Day 14 Day 0	1.25	1.30	0.73	2.14	0.409	0.392	
		Day 28 Day 0	1.44	1.30	0.84	2.47	0.177		
		Day 28 Day 14	1.15	1.29	0.68	1.95	0.578		
		Day 14 Day 0	1.54	1.13	1.19	1.99	0.002		
		Day 28 Day 0	1.63	1.13	1.26	2.10	0.001		
		Day 28 Day 14	1.06	1.13	0.83	1.36	0.639		
Rice Bran	Time	Day 14 Day 0	1.54	1.13	1.19	1.99	0.002	0.001	
		Day 28 Day 0	1.63	1.13	1.26	2.10	0.001		
		Day 28 Day 14	1.06	1.13	0.83	1.36	0.639		

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Vitamin B1 Intake by Diet Group								
Time Point	Parameter	Comparison groups	Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Day 0	Diet	Navy Bean Control	0.65	1.28	0.39	1.08	0.091	0.225
		Rice Bran Control	0.75	1.29	0.45	1.27	0.270	
		Navy Bean Rice Bran	0.86	1.28	0.52	1.43	0.553	
Day 14	Diet	Navy Bean Control	0.85	1.13	0.66	1.09	0.182	<.0001
		Rice Bran Control	1.69	1.13	1.30	2.19	0.0003	
		Navy Bean Rice Bran	0.50	1.13	0.39	0.65	<.0001	
Day 28	Diet	Navy Bean Control	0.80	1.11	0.65	0.99	0.043	0.000
		Rice Bran Control	1.37	1.11	1.10	1.70	0.007	
		Navy Bean Rice Bran	0.59	1.11	0.47	0.73	<.0001	

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Vitamin B1 Intake by Time Point									
Diet	Parameter	Comparison groups	Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value	
Control	Time	Day 14 Day 0	0.81	1.24	0.52	1.26	0.334	0.427	
		Day 28 Day 0	1.04	1.24	0.67	1.62	0.848		
		Day 28 Day 14	1.29	1.22	0.85	1.95	0.223		
		Day 14 Day 0	1.05	1.17	0.77	1.45	0.737		
		Day 28 Day 0	1.29	1.17	0.94	1.77	0.115		
		Day 28 Day 14	1.22	1.16	0.90	1.66	0.197		
Navy Bean	Time	Day 14 Day 0	1.05	1.17	0.77	1.45	0.737	0.239	
		Day 28 Day 0	1.29	1.17	0.94	1.77	0.115		
		Day 28 Day 14	1.22	1.16	0.90	1.66	0.197		
		Day 14 Day 0	1.82	1.10	1.50	2.21	<.0001		
		Day 28 Day 0	1.90	1.10	1.56	2.30	<.0001		
		Day 28 Day 14	1.04	1.10	0.86	1.26	0.649		
Rice Bran	Time	Day 14 Day 0	1.82	1.10	1.50	2.21	<.0001	<.0001	
		Day 28 Day 0	1.90	1.10	1.56	2.30	<.0001		
		Day 28 Day 14	1.04	1.10	0.86	1.26	0.649		

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Vitamin B2 Intake by Diet Group								
Time Point	Parameter	Comparison groups	Diff. of Arithmetic Means ( $\mu$ g)	Standard Error	95% Confidence Limits		p-value	Type III p-value
Day 0	Diet	Navy Bean Control	-0.46	0.20	-0.87	-0.05	0.030	0.087
		Rice Bran Control	-0.19	0.20	-0.61	0.23	0.366	
		Navy Bean Rice Bran	-0.27	0.20	-0.68	0.14	0.185	
Day 14	Diet	Navy Bean Control	-0.41	0.12	-0.65	-0.18	0.001	0.004
		Rice Bran Control	-0.12	0.12	-0.37	0.12	0.304	
		Navy Bean Rice Bran	-0.29	0.12	-0.53	-0.05	0.022	
Day 28	Diet	Navy Bean Control	-0.34	0.13	-0.61	-0.08	0.013	0.041
		Rice Bran Control	-0.12	0.13	-0.39	0.15	0.381	
		Navy Bean Rice Bran	-0.22	0.13	-0.50	0.05	0.102	

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Vitamin B2 Intake by Time Point									
Diet	Parameter	Comparison groups	Diff. of Arithmetic Means ( $\mu$ g)	Standard Error	95% Confidence Limits		p-value	Type III p-value	
Control	Time	Day 14 Day 0	0.00	0.17	-0.36	0.36	0.998	0.827	
		Day 28 Day 0	0.09	0.17	-0.27	0.45	0.611		
		Day 28 Day 14	0.09	0.16	-0.25	0.43	0.591		
		Day 14 Day 0	0.04	0.16	-0.28	0.37	0.777		
		Day 28 Day 0	0.21	0.16	-0.12	0.53	0.201		
		Day 28 Day 14	0.16	0.15	-0.15	0.47	0.302		
Navy Bean	Time	Day 14 Day 0	0.04	0.16	-0.28	0.37	0.777	0.391	
		Day 28 Day 0	0.21	0.16	-0.12	0.53	0.201		
		Day 28 Day 14	0.16	0.15	-0.15	0.47	0.302		
		Day 14 Day 0	0.06	0.11	-0.16	0.29	0.556		
		Day 28 Day 0	0.16	0.11	-0.06	0.38	0.150		
		Day 28 Day 14	0.10	0.10	-0.12	0.31	0.367		
Rice Bran	Time	Day 14 Day 0	0.06	0.11	-0.16	0.29	0.556	0.338	
		Day 28 Day 0	0.16	0.11	-0.06	0.38	0.150		
		Day 28 Day 14	0.10	0.10	-0.12	0.31	0.367		

**Table 22:** Differences in vitamin D, vitamin E, and  $\alpha$ -Tocopherol intake between diet groups (left) and between time points (right) for study participants with a history of colorectal cancer (n=29). Variables shown above: vitamin D intake (top), vitamin A intake (middle), and  $\alpha$ -Tocopherol intake (bottom). At day 0 and day 14, the navy bean group (n=10) was observed to have a significantly lower intake of vitamin D than the control group (n=10). At day 28 and day 14, the rice bran group (n=9) had significantly greater intake of  $\alpha$ -Tocopherol than at day 0.

*Parameter Estimates for Study Participants with a History of Colorectal Cancer:  
One-Way Analysis of Variance of Vitamin D Intake by Diet Group*

Time Point	Parameter	Comparison groups	Ratio of Geometric Means	Standard Error	95% Confidence Limits	p-value	Type III p-value	
Day 0	Diet	Navy Bean Control	0.25	1.74	0.08	0.78	0.019	0.053
		Rice Bran Control	0.64	1.77	0.20	2.09	0.441	
		Navy Bean Rice Bran	0.39	1.74	0.12	1.22	0.100	
Day 14		Navy Bean Control	0.57	1.28	0.34	0.94	0.030	0.073
		Rice Bran Control	0.89	1.29	0.53	1.49	0.640	
		Navy Bean Rice Bran	0.64	1.29	0.38	1.08	0.091	
Day 28	Navy Bean Control	0.67	1.38	0.35	1.30	0.226	0.474	
	Rice Bran Control	0.83	1.39	0.42	1.63	0.567		
	Navy Bean Rice Bran	0.81	1.39	0.41	1.60	0.537		

*Parameter Estimates for Study Participants with a History of Colorectal Cancer:  
One-Way Analysis of Variance of Vitamin D Intake by Time Point*

Diet	Parameter	Comparison groups	Ratio of Geometric Means	Standard Error	95% Confidence Limits	p-value	Type III p-value	
Control	Time	Day 14 Day 0	0.79	1.38	0.41	1.52	0.464	0.421
		Day 28 Day 0	0.65	1.38	0.34	1.26	0.193	
		Day 28 Day 14	0.83	1.35	0.45	1.54	0.533	
Navy Bean		Day 14 Day 0	1.82	1.57	0.72	4.63	0.197	0.347
		Day 28 Day 0	1.78	1.57	0.70	4.52	0.215	
		Day 28 Day 14	0.98	1.56	0.39	2.42	0.957	
Rice Bran	Day 14 Day 0	1.10	1.45	0.51	2.36	0.806	0.764	
	Day 28 Day 0	0.84	1.45	0.39	1.81	0.651		
	Day 28 Day 14	0.77	1.43	0.37	1.62	0.473		

*Parameter Estimates for Study Participants with a History of Colorectal Cancer:  
One-Way Analysis of Variance of Vitamin E Intake by Diet Group*

Time Point	Parameter	Comparison groups	Ratio of Geometric Means	Standard Error	95% Confidence Limits	p-value	Type III p-value	
Day 0	Diet	Navy Bean Control	1.17	2.48	0.18	7.69	0.864	0.974
		Rice Bran Control	0.96	2.55	0.14	6.67	0.966	
		Navy Bean Rice Bran	1.22	2.48	0.19	8.01	0.830	
Day 14		Navy Bean Control	0.99	1.41	0.49	2.03	0.985	0.562
		Rice Bran Control	1.40	1.43	0.67	2.91	0.356	
		Navy Bean Rice Bran	0.71	1.43	0.34	1.48	0.347	
Day 28	Navy Bean Control	1.77	1.65	0.63	4.95	0.266	0.301	
	Rice Bran Control	2.19	1.67	0.76	6.29	0.141		
	Navy Bean Rice Bran	0.81	1.67	0.28	2.33	0.683		

*Parameter Estimates for Study Participants with a History of Colorectal Cancer:  
One-Way Analysis of Variance of Vitamin E Intake by Time Point*

Diet	Parameter	Comparison groups	Ratio of Geometric Means	Standard Error	95% Confidence Limits	p-value	Type III p-value	
Control	Time	Day 14 Day 0	0.92	1.92	0.24	3.55	0.905	0.990
		Day 28 Day 0	0.92	1.92	0.24	3.53	0.899	
		Day 28 Day 14	1.00	1.85	0.28	3.54	0.994	
Navy Bean		Day 14 Day 0	0.78	1.95	0.20	3.10	0.720	0.683
		Day 28 Day 0	1.39	1.95	0.35	5.49	0.627	
		Day 28 Day 14	1.77	1.92	0.46	6.74	0.388	
Rice Bran	Day 14 Day 0	1.34	1.62	0.50	3.64	0.545	0.319	
	Day 28 Day 0	2.09	1.62	0.77	5.66	0.139		
	Day 28 Day 14	1.56	1.60	0.59	4.09	0.354		

*Parameter Estimates for Study Participants with a History of Colorectal Cancer:  
One-Way Analysis of Variance of  $\alpha$ -Tocopherol Intake by Diet Group*

Time Point	Parameter	Comparison groups	Ratio of Geometric Means	Standard Error	95% Confidence Limits	p-value	Type III p-value	
Day 0	Diet	Navy Bean Control	0.55	1.44	0.26	1.18	0.118	0.263
		Rice Bran Control	0.64	1.45	0.29	1.38	0.239	
		Navy Bean Rice Bran	0.87	1.44	0.41	1.85	0.705	
Day 14		Navy Bean Control	0.93	1.17	0.67	1.27	0.626	0.089
		Rice Bran Control	1.32	1.17	0.95	1.82	0.095	
		Navy Bean Rice Bran	0.70	1.17	0.51	0.98	0.036	
Day 28	Navy Bean Control	1.04	1.18	0.75	1.46	0.798	0.163	
	Rice Bran Control	1.36	1.18	0.96	1.91	0.078		
	Navy Bean Rice Bran	0.77	1.18	0.54	1.08	0.126		

*Parameter Estimates for Study Participants with a History of Colorectal Cancer:  
One-Way Analysis of Variance of  $\alpha$ -Tocopherol Intake by Time Point*

Diet	Parameter	Comparison groups	Ratio of Geometric Means	Standard Error	95% Confidence Limits	p-value	Type III p-value	
Control	Time	Day 14 Day 0	0.75	1.33	0.42	1.33	0.307	0.534
		Day 28 Day 0	0.76	1.33	0.43	1.37	0.350	
		Day 28 Day 14	1.03	1.30	0.59	1.77	0.924	
Navy Bean		Day 14 Day 0	1.25	1.30	0.73	2.14	0.409	0.392
		Day 28 Day 0	1.44	1.30	0.84	2.47	0.177	
		Day 28 Day 14	1.15	1.29	0.68	1.95	0.578	
Rice Bran	Day 14 Day 0	1.54	1.13	1.19	1.99	0.002	0.001	
	Day 28 Day 0	1.63	1.13	1.26	2.10	0.001		
	Day 28 Day 14	1.06	1.13	0.83	1.36	0.639		



**Table 24:** Differences in intake of vitamin B6 (pyridoxine), vitamin B9 (folate), and vitamin B12 (cobalamin) between diet groups (left) and between time points (right) for study participants with a history of colorectal cancer (n=29). Variables shown above: vitamin B6 intake (top), vitamin B9 intake (middle), and vitamin B12 intake (bottom). In regards to vitamin B6 intake, at day 14 and day 28, the rice bran group (n=9) was observed to have a significantly greater intake than both the control (n=10) and navy bean (n=10) groups. Accordingly, vitamin B6 intake for the rice bran group at day 28 and day 14 was significantly greater compared to day 0. For vitamin B12 intake, at day 14, the navy bean group was observed to have a significantly lower intake than both the control and rice bran groups. Otherwise, no significant differences were observed in the displayed variables between treatment groups or time points.

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Vitamin B6 Intake by Diet Group								
Time Point	Parameter	Comparison groups	Ratio of Geometric Means	Standard Error	95% Confidence Limits	p-value	Type III p-value	
Day 0	Diet	Navy Bean Control	0.79	1.24	0.51	1.23	0.280	0.509
		Rice Bran Control	0.95	1.25	0.60	1.50	0.828	
		Navy Bean Rice Bran	0.83	1.24	0.53	1.29	0.388	
Day 14	Diet	Navy Bean Control	0.87	1.09	0.72	1.04	0.110	<.0001
		Rice Bran Control	1.77	1.09	1.47	2.13	<.0001	
		Navy Bean Rice Bran	0.49	1.09	0.41	0.59	<.0001	
Day 28	Diet	Navy Bean Control	0.89	1.12	0.71	1.12	0.320	<.0001
		Rice Bran Control	1.73	1.12	1.36	2.19	<.0001	
		Navy Bean Rice Bran	0.52	1.12	0.41	0.66	<.0001	

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Vitamin B6 Intake by Time Point								
Diet	Parameter	Comparison groups	Ratio of Geometric Means	Standard Error	95% Confidence Limits	p-value	Type III p-value	
Control	Time	Day 14 Day 0	1.07	1.18	0.76	1.51	0.687	0.761
		Day 28 Day 0	1.13	1.18	0.80	1.60	0.465	
		Day 28 Day 14	1.06	1.17	0.76	1.46	0.726	
Navy Bean	Time	Day 14 Day 0	1.17	1.18	0.84	1.65	0.339	0.337
		Day 28 Day 0	1.28	1.18	0.91	1.80	0.148	
		Day 28 Day 14	1.09	1.17	0.78	1.52	0.601	
Rice Bran	Time	Day 14 Day 0	1.99	1.07	1.74	2.27	<.0001	<.0001
		Day 28 Day 0	2.05	1.07	1.79	2.34	<.0001	
		Day 28 Day 14	1.03	1.06	0.91	1.17	0.629	

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Vitamin B9 Intake by Diet Group								
Time Point	Parameter	Comparison groups	Ratio of Geometric Means	Standard Error	95% Confidence Limits	p-value	Type III p-value	
Day 0	Diet	Navy Bean Control	0.66	1.29	0.39	1.12	0.118	0.282
		Rice Bran Control	0.77	1.30	0.45	1.33	0.337	
		Navy Bean Rice Bran	0.85	1.29	0.50	1.45	0.542	
Day 14	Diet	Navy Bean Control	0.92	1.15	0.69	1.22	0.537	0.327
		Rice Bran Control	1.14	1.15	0.85	1.52	0.370	
		Navy Bean Rice Bran	0.81	1.15	0.60	1.08	0.140	
Day 28	Diet	Navy Bean Control	0.92	1.16	0.68	1.26	0.593	0.863
		Rice Bran Control	0.95	1.17	0.69	1.31	0.760	
		Navy Bean Rice Bran	0.97	1.17	0.70	1.33	0.829	

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Vitamin B9 Intake by Time Point								
Diet	Parameter	Comparison groups	Ratio of Geometric Means	Standard Error	95% Confidence Limits	p-value	Type III p-value	
Control	Time	Day 14 Day 0	0.89	1.25	0.56	1.42	0.612	0.777
		Day 28 Day 0	1.03	1.25	0.65	1.64	0.900	
		Day 28 Day 14	1.16	1.24	0.74	1.79	0.503	
Navy Bean	Time	Day 14 Day 0	1.24	1.19	0.86	1.78	0.236	0.140
		Day 28 Day 0	1.44	1.19	1.00	2.06	0.0499	
		Day 28 Day 14	1.16	1.19	0.82	1.65	0.393	
Rice Bran	Time	Day 14 Day 0	1.31	1.15	0.98	1.75	0.070	0.142
		Day 28 Day 0	1.27	1.15	0.95	1.70	0.106	
		Day 28 Day 14	0.97	1.15	0.73	1.29	0.822	

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Vitamin B12 Intake by Diet Group								
Time Point	Parameter	Comparison groups	Ratio of Geometric Means	Standard Error	95% Confidence Limits	p-value	Type III p-value	
Day 0	Diet	Navy Bean Control	0.57	1.38	0.29	1.10	0.092	0.228
		Rice Bran Control	0.79	1.39	0.40	1.56	0.479	
		Navy Bean Rice Bran	0.72	1.38	0.37	1.40	0.317	
Day 14	Diet	Navy Bean Control	0.58	1.22	0.39	0.87	0.011	0.025
		Rice Bran Control	0.91	1.22	0.60	1.38	0.652	
		Navy Bean Rice Bran	0.64	1.22	0.42	0.97	0.036	
Day 28	Diet	Navy Bean Control	0.69	1.25	0.44	1.08	0.100	0.233
		Rice Bran Control	0.90	1.25	0.57	1.43	0.645	
		Navy Bean Rice Bran	0.76	1.25	0.48	1.21	0.243	

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Vitamin B12 Intake by Time Point								
Diet	Parameter	Comparison groups	Ratio of Geometric Means	Standard Error	95% Confidence Limits	p-value	Type III p-value	
Control	Time	Day 14 Day 0	1.19	1.24	0.76	1.87	0.424	0.619
		Day 28 Day 0	1.00	1.24	0.63	1.56	0.987	
		Day 28 Day 14	0.83	1.23	0.55	1.28	0.387	
Navy Bean	Time	Day 14 Day 0	1.22	1.32	0.69	2.16	0.474	0.728
		Day 28 Day 0	1.20	1.32	0.68	2.13	0.509	
		Day 28 Day 14	0.98	1.31	0.57	1.71	0.953	
Rice Bran	Time	Day 14 Day 0	1.38	1.28	0.82	2.31	0.209	0.438
		Day 28 Day 0	1.14	1.28	0.68	1.90	0.613	
		Day 28 Day 14	0.82	1.27	0.50	1.36	0.430	

**Table 25:** Differences in intake of zinc, calcium, potassium, and sodium between diet groups (left) and between time points (right) for study participants with a history of colorectal cancer (n=29). Variables shown above: zinc intake (top), calcium intake (second from top), potassium intake (second from bottom), and sodium intake (bottom). In regards to zinc intake, at day 14 and day 28, the navy bean group (n=10) was observed to have a significantly greater intake than at day 0, and no significant differences were observed between diet groups. For potassium intake, the navy bean group was observed to have a significantly greater intake than the control group (n=10) at all time points. Additionally, both the navy bean and rice bran groups had significantly greater potassium intake at day 14 and day 28 compared to day 0. Accordingly, vitamin B6 intake for the rice bran group at day 28 and day 14 was significantly greater compared to day 0. Otherwise, no significant differences were observed in the displayed variables between treatment groups or time points.

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Zinc Intake by Diet Group								
Time Point	Parameter	Comparison groups	Ratio of Geometric Means	Standard Error	95% Confidence Limits	p-value	Type III p-value	
Day 0	Diet	Navy Bean Control	0.67	1.24	0.43	1.05	0.081	0.192
		Rice Bran Control	0.89	1.25	0.56	1.41	0.599	
		Navy Bean Rice Bran	0.76	1.24	0.48	1.19	0.214	
Day 14		Navy Bean Control	0.89	1.17	0.65	1.22	0.458	0.642
		Rice Bran Control	1.02	1.17	0.74	1.42	0.893	
		Navy Bean Rice Bran	0.87	1.17	0.63	1.21	0.392	
Day 28	Navy Bean Control	0.94	1.13	0.74	1.20	0.623	0.799	
	Rice Bran Control	1.02	1.13	0.79	1.31	0.879		
	Navy Bean Rice Bran	0.92	1.13	0.72	1.19	0.529		

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Calcium Intake by Diet Group								
Time Point	Parameter	Comparison groups	Ratio of Geometric Means	Standard Error	95% Confidence Limits	p-value	Type III p-value	
Day 0	Diet	Navy Bean Control	0.68	1.27	0.41	1.13	0.132	0.305
		Rice Bran Control	0.78	1.28	0.46	1.31	0.327	
		Navy Bean Rice Bran	0.88	1.27	0.53	1.45	0.599	
Day 14		Navy Bean Control	0.77	1.14	0.58	1.01	0.062	0.142
		Rice Bran Control	0.81	1.15	0.61	1.08	0.144	
		Navy Bean Rice Bran	0.95	1.15	0.71	1.26	0.695	
Day 28	Navy Bean Control	0.81	1.14	0.61	1.07	0.132	0.264	
	Rice Bran Control	0.97	1.15	0.73	1.29	0.829		
	Navy Bean Rice Bran	0.84	1.15	0.63	1.11	0.206		

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Potassium Intake by Diet Group								
Time Point	Parameter	Comparison groups	Ratio of Geometric Means	Standard Error	95% Confidence Limits	p-value	Type III p-value	
Day 0	Diet	Navy Bean Control	0.72	1.15	0.55	0.96	0.027	0.080
		Rice Bran Control	0.86	1.15	0.65	1.15	0.302	
		Navy Bean Rice Bran	0.84	1.15	0.63	1.11	0.212	
Day 14		Navy Bean Control	1.19	1.08	1.01	1.40	0.036	0.105
		Rice Bran Control	1.10	1.08	0.93	1.30	0.244	
		Navy Bean Rice Bran	1.08	1.08	0.91	1.28	0.344	
Day 28	Navy Bean Control	1.22	1.10	1.01	1.48	0.041	0.109	
	Rice Bran Control	1.15	1.10	0.94	1.40	0.161		
	Navy Bean Rice Bran	1.06	1.10	0.87	1.30	0.519		

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Sodium Intake by Diet Group								
Time Point	Parameter	Comparison groups	Diff. of Arithmetic Means (mg)	Standard Error	95% Confidence Limits	p-value	Type III p-value	
Day 0	Diet	Navy Bean Control	130.40	406.80	-713.25	974.04	0.752	0.563
		Rice Bran Control	441.57	418.59	-426.53	1309.67	0.303	
		Navy Bean Rice Bran	-311.17	406.80	-1154.82	532.47	0.452	
Day 14		Navy Bean Control	-321.69	370.94	-1084.17	440.79	0.394	0.685
		Rice Bran Control	-119.87	381.11	-903.24	663.51	0.756	
		Navy Bean Rice Bran	-201.83	381.11	-985.20	581.55	0.601	
Day 28	Navy Bean Control	-278.15	291.80	-877.95	321.64	0.349	0.256	
	Rice Bran Control	228.16	299.79	-388.07	844.39	0.454		
	Navy Bean Rice Bran	-506.31	299.79	-1122.55	109.92	0.103		

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Zinc Intake by Time Point								
Diet	Parameter	Comparison groups	Ratio of Geometric Means	Standard Error	95% Confidence Limits	p-value	Type III p-value	
Control	Time	Day 14 Day 0	1.18	1.20	0.82	1.71	0.364	0.648
		Day 28 Day 0	1.12	1.20	0.78	1.63	0.520	
		Day 28 Day 14	0.95	1.18	0.67	1.35	0.775	
Navy Bean		Day 14 Day 0	1.57	1.18	1.11	2.22	0.012	0.018
		Day 28 Day 0	1.58	1.18	1.12	2.23	0.012	
		Day 28 Day 14	1.01	1.18	0.72	1.41	0.961	
Rice Bran	Day 14 Day 0	1.36	1.16	0.99	1.86	0.054	0.121	
	Day 28 Day 0	1.29	1.16	0.94	1.77	0.105		
	Day 28 Day 14	0.95	1.16	0.70	1.29	0.728		

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Calcium Intake by Time Point								
Diet	Parameter	Comparison groups	Ratio of Geometric Means	Standard Error	95% Confidence Limits	p-value	Type III p-value	
Control	Time	Day 14 Day 0	1.06	1.18	0.75	1.49	0.751	0.948
		Day 28 Day 0	1.02	1.18	0.72	1.44	0.907	
		Day 28 Day 14	0.97	1.17	0.70	1.34	0.832	
Navy Bean		Day 14 Day 0	1.18	1.19	0.83	1.68	0.334	0.496
		Day 28 Day 0	1.21	1.19	0.85	1.72	0.280	
		Day 28 Day 14	1.02	1.18	0.72	1.44	0.904	
Rice Bran	Day 14 Day 0	1.10	1.21	0.75	1.62	0.619	0.447	
	Day 28 Day 0	1.27	1.21	0.86	1.87	0.215		
	Day 28 Day 14	1.16	1.20	0.79	1.68	0.434		

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Potassium Intake by Time Point								
Diet	Parameter	Comparison groups	Ratio of Geometric Means	Standard Error	95% Confidence Limits	p-value	Type III p-value	
Control	Time	Day 14 Day 0	1.01	1.13	0.78	1.31	0.944	0.877
		Day 28 Day 0	1.06	1.13	0.82	1.38	0.648	
		Day 28 Day 14	1.05	1.13	0.82	1.34	0.681	
Navy Bean		Day 14 Day 0	1.66	1.11	1.35	2.05	<0.001	<0.001
		Day 28 Day 0	1.79	1.11	1.45	2.20	<0.001	
		Day 28 Day 14	1.08	1.10	0.88	1.32	0.462	
Rice Bran	Day 14 Day 0	1.29	1.08	1.09	1.52	0.004	0.001	
	Day 28 Day 0	1.41	1.08	1.19	1.66	0.0003		
	Day 28 Day 14	1.09	1.08	0.93	1.29	0.260		

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Sodium Intake by Time Point								
Diet	Parameter	Comparison groups	Diff. of Arithmetic Means (mg)	Standard Error	95% Confidence Limits	p-value	Type III p-value	
Control	Time	Day 14 Day 0	193.19	385.05	-599.84	986.23	0.620	0.855
		Day 28 Day 0	26.29	385.05	-766.74	819.33	0.946	
		Day 28 Day 14	-166.90	363.03	-914.58	580.78	0.650	
Navy Bean		Day 14 Day 0	-258.89	366.50	-1012.24	494.45	0.486	0.577
		Day 28 Day 0	-382.26	366.50	-1135.61	371.09	0.307	
		Day 28 Day 14	-123.37	356.72	-856.62	609.89	0.732	
Rice Bran	Day 14 Day 0	-368.24	341.48	-1074.65	338.17	0.292	0.567	
	Day 28 Day 0	-187.12	341.48	-893.52	519.29	0.589		
	Day 28 Day 14	181.12	331.28	-504.19	866.44	0.590		

**Table 26:** Differences in intake of iron, magnesium, and selenium between diet groups (left) and between time points (right) for study participants with a history of colorectal cancer (n=29). Variables shown above: iron intake (top), magnesium intake (middle), and selenium intake (bottom). In regards to iron intake, at day 14 and day 28, the rice bran group (n=9) was observed to have a significantly greater intake than the control (n=10) and navy bean (n=10) groups, and within the rice bran group, iron intake was significantly greater at day 28 and day 14 than at day 0. The navy bean group was also observed to have a significantly greater potassium intake at day 28 and day 14 than at day 0. For magnesium, at day 14 and day 28, the rice bran group had significantly greater intake than both the control and navy bean groups. At day 14 and day 28, both the navy bean and rice bran groups had significantly greater potassium intake compared to their respective intake at day 0. Finally, at day 14, the navy bean group was observed to have a significantly lower selenium intake than both the control and rice bran groups. Otherwise, no significant differences were observed in the displayed variables between treatment groups or time points.

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Iron Intake by Diet Group									
Time Point	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Day 0	Diet	Navy Bean	Control	0.58	1.28	0.35	0.97	0.040	0.115
		Rice Bran	Control	0.75	1.29	0.44	1.27	0.271	
		Navy Bean	Rice Bran	0.78	1.28	0.47	1.29	0.317	
Day 14	Diet	Navy Bean	Control	0.94	1.10	0.77	1.15	0.513	0.002
		Rice Bran	Control	1.36	1.11	1.11	1.67	0.005	
		Navy Bean	Rice Bran	0.69	1.11	0.56	0.85	0.001	
Day 28	Diet	Navy Bean	Control	0.95	1.13	0.75	1.22	0.681	0.027
		Rice Bran	Control	1.32	1.13	1.03	1.70	0.031	
		Navy Bean	Rice Bran	0.72	1.13	0.56	0.93	0.012	

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Iron Intake by Time Point									
Diet	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Control	Time	Day 14	Day 0	0.87	1.23	0.57	1.32	0.496	0.789
		Day 28	Day 0	0.93	1.23	0.61	1.42	0.721	
		Day 28	Day 14	1.07	1.21	0.72	1.59	0.729	
Navy Bean	Time	Day 14	Day 0	1.39	1.16	1.02	1.90	0.036	0.026
		Day 28	Day 0	1.51	1.16	1.11	2.06	0.010	
		Day 28	Day 14	1.09	1.16	0.81	1.47	0.573	
Rice Bran	Time	Day 14	Day 0	1.57	1.12	1.24	2.00	0.001	0.001
		Day 28	Day 0	1.64	1.12	1.29	2.08	0.0003	
		Day 28	Day 14	1.04	1.12	0.82	1.31	0.730	

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Magnesium Intake by Diet Group									
Time Point	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Day 0	Diet	Navy Bean	Control	0.70	1.30	0.41	1.20	0.182	0.390
		Rice Bran	Control	0.88	1.31	0.50	1.55	0.624	
		Navy Bean	Rice Bran	0.80	1.30	0.46	1.37	0.394	
Day 14	Diet	Navy Bean	Control	1.12	1.12	0.88	1.42	0.360	0.001
		Rice Bran	Control	1.66	1.13	1.30	2.12	0.0003	
		Navy Bean	Rice Bran	0.67	1.13	0.53	0.86	0.003	
Day 28	Diet	Navy Bean	Control	1.20	1.09	1.00	1.44	0.051	0.0003
		Rice Bran	Control	1.53	1.10	1.27	1.85	<0.001	
		Navy Bean	Rice Bran	0.78	1.10	0.65	0.94	0.012	

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Magnesium Intake by Time Point									
Diet	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value	Type III p-value
Control	Time	Day 14	Day 0	0.94	1.21	0.64	1.38	0.725	0.928
		Day 28	Day 0	0.99	1.21	0.67	1.45	0.946	
		Day 28	Day 14	1.06	1.19	0.73	1.52	0.763	
Navy Bean	Time	Day 14	Day 0	1.50	1.21	1.00	2.23	0.048	0.031
		Day 28	Day 0	1.70	1.21	1.14	2.53	0.012	
		Day 28	Day 14	1.13	1.21	0.77	1.67	0.513	
Rice Bran	Time	Day 14	Day 0	1.77	1.08	1.51	2.08	<0.001	<0.001
		Day 28	Day 0	1.73	1.08	1.47	2.03	<0.001	
		Day 28	Day 14	0.97	1.08	0.83	1.14	0.733	

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Selenium Intake by Diet Group									
Time Point	Parameter	Comparison groups		Diff. of Arithmetic Means (mg)	Standard Error	95% Confidence Limits		p-value	Type III p-value
Day 0	Diet	Navy Bean	Control	-18.63	18.66	-57.33	20.07	0.329	0.431
		Rice Bran	Control	4.41	19.20	-35.42	44.24	0.821	
		Navy Bean	Rice Bran	-23.04	18.66	-61.74	15.66	0.230	
Day 14	Diet	Navy Bean	Control	-29.41	12.52	-55.14	-3.67	0.027	0.016
		Rice Bran	Control	8.61	12.86	-17.82	35.05	0.509	
		Navy Bean	Rice Bran	-38.02	12.86	-64.46	-11.58	0.007	
Day 28	Diet	Navy Bean	Control	-18.20	11.39	-41.61	5.20	0.122	0.272
		Rice Bran	Control	-4.74	11.70	-28.79	19.31	0.689	
		Navy Bean	Rice Bran	-13.46	11.70	-37.51	10.58	0.260	

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Selenium Intake by Time Point									
Diet	Parameter	Comparison groups		Diff. of Arithmetic Means (mg)	Standard Error	95% Confidence Limits		p-value	Type III p-value
Control	Time	Day 14	Day 0	6.94	14.79	-23.52	37.40	0.643	0.895
		Day 28	Day 0	3.24	14.79	-27.22	33.70	0.828	
		Day 28	Day 14	-3.70	13.94	-32.42	25.02	0.793	
Navy Bean	Time	Day 14	Day 0	-3.83	11.50	-27.47	19.80	0.741	0.800
		Day 28	Day 0	3.67	11.50	-19.96	27.30	0.752	
		Day 28	Day 14	7.51	11.19	-15.49	30.51	0.508	
Rice Bran	Time	Day 14	Day 0	11.15	17.28	-24.61	46.90	0.525	0.594
		Day 28	Day 0	-5.91	17.28	-41.66	29.85	0.736	
		Day 28	Day 14	-17.05	16.77	-51.74	17.63	0.320	

**Table 27:** Differences in calorie, protein, carbohydrate, and fat intake between diet groups (left) and between time points (right) for study participants with a history of colorectal cancer (n=29). Variables shown above: calorie intake (top), protein intake (second from top), carbohydrate intake (second from bottom), and fat intake (bottom). The only significant difference observed within these variables was in regards to the lower fat intake of the navy bean group (n=10) compared to the control group (n=10) at day 14. Otherwise, no significant differences were observed in the displayed variables between treatment groups or time points.

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Calorie Intake by Diet Group								
Time Point	Parameter	Comparison groups	Diff. of Arithmetic Means (g)	Standard Error	95% Confidence Limits	p-value	Type III p-value	
Day 0	Diet	Navy Bean Control	-176.87	278.06	-753.54	399.80	0.531	0.961
		Rice Bran Control	-150.89	286.12	-744.28	442.49	0.603	
		Navy Bean Rice Bran	-25.98	278.06	-602.64	550.69	0.926	
Day 14	Diet	Navy Bean Control	-177.44	192.52	-573.17	218.29	0.365	0.559
		Rice Bran Control	-182.36	197.79	-588.93	224.22	0.365	
		Navy Bean Rice Bran	4.92	197.79	-401.66	411.49	0.980	
Day 28	Diet	Navy Bean Control	-96.65	207.59	-523.36	330.06	0.645	0.636
		Rice Bran Control	128.06	213.28	-310.34	566.46	0.553	
		Navy Bean Rice Bran	-224.71	213.28	-663.11	213.69	0.302	

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Protein Intake by Diet Group								
Time Point	Parameter	Comparison groups	Diff. of Arithmetic Means (g)	Standard Error	95% Confidence Limits	p-value	Type III p-value	
Day 0	Diet	Navy Bean Control	-7.55	11.45	-31.28	16.19	0.516	0.788
		Rice Bran Control	-6.17	11.78	-30.59	18.26	0.606	
		Navy Bean Rice Bran	-1.38	11.45	-25.12	22.35	0.905	
Day 14	Diet	Navy Bean Control	-11.34	8.67	-29.15	6.47	0.202	0.371
		Rice Bran Control	-1.08	8.90	-19.38	17.22	0.904	
		Navy Bean Rice Bran	-10.26	8.90	-28.56	8.04	0.260	
Day 28	Diet	Navy Bean Control	-4.16	8.26	-21.14	12.83	0.619	0.570
		Rice Bran Control	4.94	8.49	-12.51	22.38	0.566	
		Navy Bean Rice Bran	-9.09	8.49	-26.54	8.36	0.294	

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Carbohydrate Intake by Diet Group								
Time Point	Parameter	Comparison groups	Ratio of Geometric Means	Standard Error	95% Confidence Limits	p-value	Type III p-value	
Day 0	Diet	Navy Bean Control	0.98	1.17	0.70	1.35	0.882	0.910
		Rice Bran Control	0.93	1.18	0.67	1.31	0.673	
		Navy Bean Rice Bran	1.05	1.17	0.76	1.45	0.774	
Day 14	Diet	Navy Bean Control	1.03	1.11	0.84	1.27	0.763	0.486
		Rice Bran Control	0.91	1.11	0.73	1.13	0.386	
		Navy Bean Rice Bran	1.13	1.11	0.91	1.40	0.249	
Day 28	Diet	Navy Bean Control	1.09	1.11	0.88	1.35	0.396	0.476
		Rice Bran Control	1.13	1.11	0.91	1.41	0.243	
		Navy Bean Rice Bran	0.96	1.11	0.78	1.20	0.727	

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Fat Intake by Diet Group								
Time Point	Parameter	Comparison groups	Diff. of Arithmetic Means (g)	Standard Error	95% Confidence Limits	p-value	Type III p-value	
Day 0	Diet	Navy Bean Control	-14.31	14.04	-43.43	14.80	0.319	0.601
		Rice Bran Control	-6.92	14.45	-36.88	23.03	0.636	
		Navy Bean Rice Bran	-7.39	14.04	-36.50	21.72	0.604	
Day 14	Diet	Navy Bean Control	-18.77	8.92	-37.10	-0.44	0.045	0.123
		Rice Bran Control	-6.68	9.16	-25.52	12.15	0.472	
		Navy Bean Rice Bran	-12.08	9.16	-30.92	6.75	0.199	
Day 28	Diet	Navy Bean Control	-12.46	10.60	-34.25	9.32	0.250	0.330
		Rice Bran Control	2.95	10.89	-19.43	25.33	0.789	
		Navy Bean Rice Bran	-15.41	10.89	-37.80	6.97	0.169	

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Calorie Intake by Time Point								
Diet	Parameter	Comparison groups	Diff. of Arithmetic Means (g)	Standard Error	95% Confidence Limits	p-value	Type III p-value	
Control	Time	Day 14 Day 0	-30.99	273.56	-594.40	532.43	0.911	0.952
		Day 28 Day 0	-82.95	273.56	-646.36	480.47	0.764	
		Day 28 Day 14	-51.96	257.92	-583.15	479.23	0.842	
Navy Bean	Time	Day 14 Day 0	-31.55	215.41	-474.34	411.24	0.885	0.955
		Day 28 Day 0	-2.73	215.41	-445.52	440.06	0.990	
		Day 28 Day 14	28.83	209.67	-402.15	459.81	0.892	
Rice Bran	Time	Day 14 Day 0	-62.45	192.10	-459.83	334.94	0.748	0.472
		Day 28 Day 0	196.00	192.10	-201.38	593.39	0.318	
		Day 28 Day 14	258.45	186.36	-127.07	643.97	0.179	

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Protein Intake by Time Point								
Diet	Parameter	Comparison groups	Diff. of Arithmetic Means (g)	Standard Error	95% Confidence Limits	p-value	Type III p-value	
Control	Time	Day 14 Day 0	2.94	10.82	-19.34	25.22	0.788	0.868
		Day 28 Day 0	-2.49	10.82	-24.77	19.79	0.820	
		Day 28 Day 14	-5.43	10.20	-26.44	15.57	0.599	
Navy Bean	Time	Day 14 Day 0	-0.85	9.40	-20.17	18.48	0.929	0.982
		Day 28 Day 0	0.90	9.40	-18.43	20.23	0.925	
		Day 28 Day 14	1.75	9.15	-17.06	20.56	0.850	
Rice Bran	Time	Day 14 Day 0	8.03	8.45	-9.45	25.50	0.352	0.538
		Day 28 Day 0	8.61	8.45	-8.86	26.09	0.319	
		Day 28 Day 14	0.59	8.19	-16.37	17.54	0.944	

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Carbohydrate Intake by Time Point								
Diet	Parameter	Comparison groups	Ratio of Geometric Means	Standard Error	95% Confidence Limits	p-value	Type III p-value	
Control	Time	Day 14 Day 0	0.98	1.15	0.73	1.30	0.868	0.975
		Day 28 Day 0	0.97	1.15	0.73	1.29	0.831	
		Day 28 Day 14	0.99	1.14	0.76	1.30	0.960	
Navy Bean	Time	Day 14 Day 0	1.03	1.11	0.83	1.28	0.766	0.728
		Day 28 Day 0	1.09	1.11	0.88	1.35	0.437	
		Day 28 Day 14	1.05	1.11	0.85	1.30	0.620	
Rice Bran	Time	Day 14 Day 0	0.95	1.13	0.73	1.24	0.717	0.216
		Day 28 Day 0	1.18	1.13	0.91	1.53	0.204	
		Day 28 Day 14	1.24	1.13	0.96	1.59	0.098	

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Fat Intake by Time Point								
Diet	Parameter	Comparison groups	Diff. of Arithmetic Means (g)	Standard Error	95% Confidence Limits	p-value	Type III p-value	
Control	Time	Day 14 Day 0	-0.06	13.95	-28.79	28.68	0.997	0.893
		Day 28 Day 0	-5.57	13.95	-34.31	23.16	0.693	
		Day 28 Day 14	-5.51	13.15	-32.60	21.58	0.679	
Navy Bean	Time	Day 14 Day 0	-4.51	9.59	-24.23	15.20	0.642	0.884
		Day 28 Day 0	-3.72	9.59	-23.43	15.99	0.701	
		Day 28 Day 14	0.79	9.33	-18.39	19.98	0.933	
Rice Bran	Time	Day 14 Day 0	0.18	10.31	-21.14	21.51	0.986	0.891
		Day 28 Day 0	4.30	10.31	-17.02	25.63	0.680	
		Day 28 Day 14	4.12	10.00	-16.56	24.81	0.684	

**Table 28:** Differences in saturated fat, oleic acid, linoleic acid, and linolenic acid intake between diet groups (left) and between time points (right) for study participants with a history of colorectal cancer (n=29). Variables shown above: saturated fat intake (top), oleic acid intake (second from top), linoleic acid intake (second from bottom), and linolenic acid intake (bottom). At day 14, the rice bran group (n=9) was observed to have a significantly greater intake of oleic acid, linoleic acid, and linolenic acid compared to the navy bean group (n=10). Similarly, the rice bran group had a significantly greater linolenic acid intake compared to control group (n=10) at day 14. However, no significant differences in fatty acid intake were observed between groups at day 0 or day 28. Within groups, the navy bean group was found to have a significantly greater intake of linolenic acid at day 28 compared to day 0, and the control group was found to have a significantly greater intake of saturated fat at day 14 compared to day 0. Otherwise, no significant differences were observed in the displayed variables between treatment groups or time points.

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Saturated Fat Intake by Diet Group								
Time Point	Parameter	Comparison groups	Ratio of Geometric Means	Standard Error	95% Confidence Limits	p-value	Type III p-value	
Day 0		Navy Bean Control	0.98	1.21	0.65	1.46	0.911	0.819
		Rice Bran Control	1.10	1.22	0.73	1.67	0.638	
		Navy Bean Rice Bran	0.89	1.21	0.59	1.33	0.552	
Day 14	Diet	Navy Bean Control	0.79	1.13	0.61	1.02	0.073	0.159
		Rice Bran Control	0.96	1.14	0.74	1.25	0.753	
		Navy Bean Rice Bran	0.82	1.14	0.63	1.07	0.146	
Day 28		Navy Bean Control	0.80	1.17	0.58	1.10	0.164	0.243
		Rice Bran Control	1.02	1.17	0.74	1.42	0.884	
		Navy Bean Rice Bran	0.78	1.17	0.56	1.09	0.135	

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Saturated Fat Intake by Time Point								
Diet	Parameter	Comparison groups	Ratio of Geometric Means	Standard Error	95% Confidence Limits	p-value	Type III p-value	
Control		Day 14 Day 0	1.27	1.12	1.00	1.62	0.0498	0.122
		Day 28 Day 0	1.21	1.12	0.95	1.54	0.116	
		Day 28 Day 14	0.95	1.12	0.76	1.19	0.649	
Navy Bean	Time	Day 14 Day 0	1.03	1.19	0.72	1.46	0.875	0.972
		Day 28 Day 0	0.99	1.19	0.69	1.41	0.949	
		Day 28 Day 14	0.96	1.18	0.68	1.36	0.819	
Rice Bran		Day 14 Day 0	1.11	1.21	0.75	1.65	0.594	0.803
		Day 28 Day 0	1.13	1.21	0.76	1.68	0.545	
		Day 28 Day 14	1.01	1.21	0.69	1.49	0.941	

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Oleic Acid Intake by Diet Group								
Time Point	Parameter	Comparison groups	Diff. of Geometric Means (g)	Standard Error	95% Confidence Limits	p-value	Type III p-value	
Day 0		Navy Bean Control	0.82	1.31	0.46	1.44	0.464	0.705
		Rice Bran Control	0.99	1.32	0.55	1.77	0.966	
		Navy Bean Rice Bran	0.83	1.31	0.47	1.46	0.491	
Day 14	Diet	Navy Bean Control	0.72	1.17	0.52	1.00	0.052	0.058
		Rice Bran Control	1.05	1.18	0.75	1.47	0.763	
		Navy Bean Rice Bran	0.69	1.18	0.49	0.96	0.031	
Day 28		Navy Bean Control	0.84	1.21	0.56	1.24	0.362	0.490
		Rice Bran Control	1.05	1.22	0.70	1.57	0.821	
		Navy Bean Rice Bran	0.80	1.22	0.53	1.20	0.268	

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Oleic Acid Intake by Time Point								
Diet	Parameter	Comparison groups	Diff. of Geometric Means (g)	Standard Error	95% Confidence Limits	p-value	Type III p-value	
Control		Day 14 Day 0	1.14	1.27	0.69	1.86	0.600	0.839
		Day 28 Day 0	1.02	1.27	0.62	1.67	0.942	
		Day 28 Day 14	0.90	1.25	0.56	1.43	0.631	
Navy Bean	Time	Day 14 Day 0	1.01	1.25	0.64	1.58	0.967	0.979
		Day 28 Day 0	1.04	1.25	0.67	1.64	0.847	
		Day 28 Day 14	1.03	1.24	0.67	1.60	0.876	
Rice Bran		Day 14 Day 0	1.21	1.18	0.86	1.70	0.264	0.520
		Day 28 Day 0	1.08	1.18	0.77	1.52	0.655	
		Day 28 Day 14	0.89	1.17	0.64	1.24	0.483	

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Linoleic Acid Intake by Diet Group								
Time Point	Parameter	Comparison groups	Ratio of Geometric Means	Standard Error	95% Confidence Limits	p-value	Type III p-value	
Day 0		Navy Bean Control	0.70	1.44	0.33	1.49	0.333	0.439
		Rice Bran Control	1.09	1.46	0.50	2.38	0.824	
		Navy Bean Rice Bran	0.64	1.44	0.30	1.37	0.235	
Day 14	Diet	Navy Bean Control	0.82	1.22	0.54	1.24	0.334	0.074
		Rice Bran Control	1.34	1.23	0.88	2.05	0.162	
		Navy Bean Rice Bran	0.61	1.23	0.40	0.93	0.024	
Day 28		Navy Bean Control	0.90	1.22	0.60	1.36	0.609	0.542
		Rice Bran Control	1.14	1.23	0.74	1.74	0.544	
		Navy Bean Rice Bran	0.79	1.23	0.52	1.21	0.274	

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Linoleic Acid Intake by Time Point								
Diet	Parameter	Comparison groups	Ratio of Geometric Means	Standard Error	95% Confidence Limits	p-value	Type III p-value	
Control		Day 14 Day 0	0.87	1.37	0.46	1.67	0.671	0.907
		Day 28 Day 0	0.90	1.37	0.47	1.72	0.743	
		Day 28 Day 14	1.03	1.34	0.56	1.89	0.918	
Navy Bean	Time	Day 14 Day 0	1.03	1.32	0.58	1.83	0.912	0.838
		Day 28 Day 0	1.17	1.32	0.66	2.07	0.582	
		Day 28 Day 14	1.13	1.31	0.65	1.97	0.651	
Rice Bran		Day 14 Day 0	1.08	1.18	0.77	1.52	0.644	0.688
		Day 28 Day 0	0.94	1.18	0.67	1.32	0.710	
		Day 28 Day 14	0.87	1.17	0.63	1.21	0.393	

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Linolenic Acid Intake by Diet Group								
Time Point	Parameter	Comparison groups	Ratio of Geometric Means	Standard Error	95% Confidence Limits	p-value	Type III p-value	
Day 0		Navy Bean Control	0.63	1.43	0.30	1.33	0.217	0.277
		Rice Bran Control	1.10	1.45	0.51	2.35	0.806	
		Navy Bean Rice Bran	0.58	1.43	0.28	1.22	0.141	
Day 14	Diet	Navy Bean Control	0.87	1.19	0.61	1.24	0.427	0.008
		Rice Bran Control	1.56	1.20	1.08	2.25	0.019	
		Navy Bean Rice Bran	0.56	1.20	0.39	0.80	0.003	
Day 28		Navy Bean Control	1.07	1.20	0.73	1.55	0.728	0.828
		Rice Bran Control	1.12	1.21	0.76	1.65	0.544	
		Navy Bean Rice Bran	0.95	1.21	0.65	1.40	0.788	

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Linolenic Acid Intake by Time Point								
Diet	Parameter	Comparison groups	Ratio of Geometric Means	Standard Error	95% Confidence Limits	p-value	Type III p-value	
Control		Day 14 Day 0	0.89	1.36	0.48	1.67	0.712	0.923
		Day 28 Day 0	0.97	1.36	0.52	1.82	0.929	
		Day 28 Day 14	1.09	1.33	0.60	1.97	0.766	
Navy Bean	Time	Day 14 Day 0	1.22	1.24	0.79	1.90	0.356	0.087
		Day 28 Day 0	1.64	1.24	1.05	2.54	0.030	
		Day 28 Day 14	1.34	1.23	0.87	2.05	0.175	
Rice Bran		Day 14 Day 0	1.27	1.23	0.82	1.96	0.264	0.411
		Day 28 Day 0	1.00	1.23	0.65	1.54	0.988	
		Day 28 Day 14	0.78	1.23	0.52	1.19	0.243	

**Table 29:** Differences in fiber intake between diet groups (left) and between time points (right) for study participants with a history of colorectal cancer (n=29). The rice bran (n=9) and navy bean (n=10) groups both displayed a significantly greater fiber intake at day 28 and day 14 compared to day 0. Additionally, at day 28, these groups were both found to have significantly greater fiber intake compared to the control group (n=10), and at day 14, the fiber intake in the rice bran group was also significantly greater than the control group.

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Fiber Intake by Diet Group								
Time Point	Parameter	Comparison groups	Ratio of Geometric Means	Standard Error	95% Confidence Limits	p-value	Type III p-value	
Day 0	Diet	Navy Bean Control	0.68	1.24	0.43	1.07	0.095	0.223
		Rice Bran Control	0.89	1.25	0.56	1.41	0.594	
		Navy Bean Rice Bran	0.77	1.24	0.49	1.21	0.247	
Day 14	Diet	Navy Bean Control	1.10	1.09	0.92	1.33	0.285	0.120
		Rice Bran Control	1.22	1.10	1.01	1.48	0.041	
		Navy Bean Rice Bran	0.90	1.10	0.75	1.09	0.288	
Day 28	Diet	Navy Bean Control	1.39	1.11	1.13	1.72	0.003	0.004
		Rice Bran Control	1.41	1.11	1.13	1.75	0.003	
		Navy Bean Rice Bran	0.99	1.11	0.80	1.23	0.929	

Parameter Estimates for Study Participants with a History of Colorectal Cancer: One-Way Analysis of Variance of Fiber Intake by Time Point								
Diet	Parameter	Comparison groups	Ratio of Geometric Means	Standard Error	95% Confidence Limits	p-value	Type III p-value	
Control	Time	Day 14 Day 0	0.98	1.18	0.70	1.38	0.922	0.723
		Day 28 Day 0	0.89	1.18	0.63	1.24	0.475	
		Day 28 Day 14	0.90	1.17	0.66	1.24	0.513	
Navy Bean	Time	Day 14 Day 0	1.59	1.15	1.18	2.13	0.003	0.001
		Day 28 Day 0	1.81	1.15	1.35	2.43	0.0003	
		Day 28 Day 14	1.14	1.15	0.86	1.52	0.356	
Rice Bran	Time	Day 14 Day 0	1.36	1.13	1.06	1.73	0.017	0.016
		Day 28 Day 0	1.41	1.13	1.10	1.80	0.008	
		Day 28 Day 14	1.04	1.12	0.82	1.32	0.733	

### 3.6 Differences in telomere length and cytokine concentrations between sexes

Relative telomere length as measured by multiplex qPCR was found to be significantly longer in females than males at day 0 ( $\mu_f - \mu_m = 0.34$ ; 95% CI=[0.06, 0.61];  $p=0.020$ ) but not at day 28 ( $\mu_f - \mu_m = 0.27$ ; 95% CI=[0.0.1, 0.53];  $p=0.185$ ). No significant differences were observed between sexes in telomere length as measured by singleplex qPCR or IQ-FISH.

Analysis of plasma cytokine concentrations from the substitution data set indicated that at day 0, females had significantly lower levels of IL-4 (RoGM=0.29; 95% CI=[0.10, 0.81];  $p=0.020$ ), IL-6 (RoGM=0.43; 95% CI=[0.23, 0.82];  $p=0.013$ ), and IL-10 (RoGM=0.36; 95% CI=[0.14, 0.90];  $p=0.031$ ) when compared to males. These differences were also significant at day 14: IL-4 (RoGM=0.34; 95% CI=[0.12, 0.92];  $p=0.035$ ), IL-6 (RoGM=0.38; 95% CI=[0.20, 0.72];  $p=0.004$ ), and IL-10 (RoGM=0.32; 95% CI=[0.13, 0.75];  $p=0.011$ ). Additionally, at day 14, females were found to have significantly lower levels of IL-8 (RoGM=0.46; 95% CI=[0.29, 0.74];  $p=0.003$ ). No significant difference was observed between sexes for any cytokines at day 28.

Within the extrapolated data set, at day 0, females were only found to have significantly lower levels of IL-10 (RoGM=0.06; 95% CI=[0.01, 0.58];  $p=0.018$ ) compared to males. At day 14, IL-10 was still significantly lower in females than in males (RoGM=0.06; 95% CI=[0.005, 0.83];  $p=0.037$ ). Additionally, at day 14, females had significantly lower levels of IL-4 (RoGM=0.05; 95% CI=[0.003, 0.98];  $p=0.049$ ), IL-6 (RoGM=0.12; 95% CI=[0.02, 0.65];  $p=0.017$ ), and IL-8 (RoGM=0.50; 95% CI=[0.34, 0.75];  $p=0.002$ ) compared to males. At day 28, similar to the substitution data set, no significant differences in plasma cytokine concentrations from the extrapolated data set were observed between males and females.

**Table 30:** Differences in leukocyte telomere length between sexes for study participants with a history of colorectal cancer (n=27). Telomere length measured by multiplex qPCR is the most reliable estimate in this report. At day 0, females (n=15) had significantly longer telomeres than males (n=12). However, no significant difference in telomere length was found between sexes at day 28.

<i>Linear Regression Analysis between Sexes for Study Participants with a History of Colorectal Cancer: Multiplex qPCR Leukocyte Telomere Length</i>								
	Time Point	Comparison groups		Diff. of Arithmetic Means (RTL)	Standard Error	95% Confidence Limits		p-value
Multiplex qPCR Telomere Length	Day 0	Female	Male	0.166	0.078	0.005	0.328	0.044
	Day 28	Female	Male	0.103	0.076	-0.053	0.259	0.185

**Table 31:** Differences in plasma cytokine concentrations between sexes for study participants with a history of colorectal cancer (n=29). At day 0, when using the substitution method for handling censored data, females had lower IL-4, IL-6, and IL-10 concentrations. When using the extrapolation method, females did not have significantly lower IL-4 concentrations at day 0 but did have significantly lower IL-6 and IL-10 concentrations at day 0. At day 28, no significant differences in cytokine concentrations were found between sexes when using both the extrapolation and substitution methods for handling censored data.

<i>Linear Regression Analysis between Sexes for Study Participants with a History of Colorectal Cancer: Plasma Cytokine Concentrations</i>								
	Time Point	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value
Interleukin-2 (Substitution)	Day 0	Female	Male	0.52	1.52	0.22	1.26	0.139
	Day 14	Female	Male	0.50	1.52	0.21	1.19	0.110
	Day 28	Female	Male	0.70	1.54	0.28	1.73	0.422
Interleukin-2 (Extrapolation)	Day 0	Female	Male	0.19	3.83	0.01	3.12	0.232
	Day 14	Female	Male	0.10	3.33	0.01	1.19	0.066
	Day 28	Female	Male	0.62	3.92	0.04	10.65	0.732
Interleukin-4 (Substitution)	Day 0	Female	Male	0.29	1.63	0.10	0.81	0.020
	Day 14	Female	Male	0.34	1.62	0.12	0.92	0.035
	Day 28	Female	Male	0.37	1.65	0.13	1.05	0.061
Interleukin-4 (Extrapolation)	Day 0	Female	Male	0.13	4.39	0.01	2.90	0.188
	Day 14	Female	Male	0.05	4.07	0.003	0.98	0.049
	Day 28	Female	Male	0.17	4.43	0.01	3.80	0.250
Interleukin-6 (Substitution)	Day 0	Female	Male	0.43	1.37	0.23	0.82	0.013
	Day 14	Female	Male	0.38	1.35	0.20	0.72	0.004
	Day 28	Female	Male	0.57	1.46	0.26	1.24	0.147
Interleukin-6 (Extrapolation)	Day 0	Female	Male	0.29	2.40	0.05	1.76	0.167
	Day 14	Female	Male	0.12	2.28	0.02	0.65	0.017
	Day 28	Female	Male	0.42	2.94	0.04	3.92	0.425
Interleukin-8 (Substitution)	Day 0	Female	Male	0.56	1.41	0.28	1.15	0.110
	Day 14	Female	Male	0.46	1.25	0.29	0.74	0.003
	Day 28	Female	Male	0.69	1.32	0.39	1.25	0.209
Interleukin-8 (Extrapolation)	Day 0	Female	Male	0.40	1.91	0.10	1.53	0.170
	Day 14	Female	Male	0.50	1.21	0.34	0.75	0.002
	Day 28	Female	Male	0.58	1.39	0.29	1.15	0.115
Interleukin-10 (Substitution)	Day 0	Female	Male	0.36	1.56	0.14	0.90	0.031
	Day 14	Female	Male	0.32	1.51	0.13	0.75	0.011
	Day 28	Female	Male	0.53	1.63	0.19	1.46	0.205
Interleukin-10 (Extrapolation)	Day 0	Female	Male	0.06	2.97	0.01	0.58	0.018
	Day 14	Female	Male	0.06	3.42	0.005	0.83	0.037
	Day 28	Female	Male	0.36	4.31	0.02	7.41	0.487
Tumor Necrosis Factor (Substitution)	Day 0	Female	Male	0.71	1.30	0.41	1.21	0.192
	Day 14	Female	Male	0.75	1.17	0.54	1.04	0.078
	Day 28	Female	Male	0.98	1.19	0.69	1.40	0.930
Tumor Necrosis Factor (Extrapolation)	Day 0	Female	Male	0.78	1.22	0.51	1.19	0.232
	Day 14	Female	Male	0.75	1.17	0.54	1.04	0.078
	Day 28	Female	Male	0.98	1.19	0.69	1.40	0.930
Vascular Endothelial Growth Factor (Substitution)	Day 0	Female	Male	1.14	1.58	0.44	2.95	0.782
	Day 14	Female	Male	0.84	1.82	0.24	2.94	0.781
	Day 28	Female	Male	1.30	1.82	0.37	4.54	0.663
Vascular Endothelial Growth Factor (Extrapolation)	Day 0	Female	Male	1.89	2.40	0.31	11.64	0.475
	Day 14	Female	Male	0.95	3.36	0.08	11.77	0.966
	Day 28	Female	Male	1.47	3.36	0.12	18.23	0.756

### 3.7 Differences in lipid levels between sexes

Females were found to have significantly higher levels of HDL and significantly lower levels of triglycerides at all three time points. No significant differences were found between females and males for total cholesterol or LDL.

On average, females had triglyceride levels approximately 40% lower than males: day 0 (RoGM=0.60; 95% CI=[0.41, 0.88]; p=0.010), day 14 (RoGM=0.65; 95% CI=[0.44, 0.96]; p=0.033), and day 28 (RoGM=0.61; 95% CI=[0.41, 0.91]; p=0.016). In regards to HDL, females had ~34% higher serum HDL levels compared to males: day 0 ( $\mu_f - \mu_m = 18.59$  mg/dL; 95% CI=[9.44, 27.75]; p=0.0003), day 14 ( $\mu_f - \mu_m = 19.20$  mg/dL; 95% CI=[10.24, 28.16]; p=0.0002), and day 28 ( $\mu_f - \mu_m = 17.77$  mg/dL; 95% CI=[8.85, 26.70]; p=0.0004).

**Table 32:** Differences in age, weight, BMI, and cholesterol between sexes for study participants with a history of colorectal cancer (n=29). Compared to males (n=12), females (n=17) had significantly higher serum HDL and significantly lower serum triglycerides at all time points.

<i>Linear Regression Analysis between Sexes for Study Participants with a History of Colorectal Cancer: Age, Weight, BMI, and Serum Lipid Levels</i>								
	Time Point	Comparison groups		Diff. of Arithmetic Means	Standard Error	95% Confidence Limits		p-value
Age (years)	Day 0	Female	Male	-0.93	4.35	-9.87	8.00	0.832
	Day 14	Female	Male	-0.93	4.35	-9.87	8.00	0.832
	Day 28	Female	Male	-1.01	4.37	-9.99	7.96	0.818
Weight (kg)	Day 0	Female	Male	-20.13	5.59	-31.60	-8.65	0.001
	Day 14	Female	Male	-19.94	5.59	-31.40	-8.48	0.001
	Day 28	Female	Male	-19.37	5.76	-31.19	-7.56	0.002
BMI (kg/m <sup>2</sup> )	Day 0	Female	Male	-2.59	2.11	-6.92	1.75	0.231
	Day 14	Female	Male	-2.52	2.13	-6.88	1.84	0.245
	Day 28	Female	Male	-2.31	2.18	-6.79	2.17	0.299
Total Cholesterol (mg/dL)	Day 0	Female	Male	23.63	16.63	-10.49	57.75	0.167
	Day 14	Female	Male	24.95	15.91	-7.70	57.61	0.129
	Day 28	Female	Male	26.55	15.25	-4.74	57.85	0.093
LDL (mg/dL)	Day 0	Female	Male	20.66	13.88	-7.81	49.14	0.148
	Day 14	Female	Male	17.62	13.42	-9.91	45.16	0.200
	Day 28	Female	Male	23.57	13.50	-4.13	51.27	0.092
HDL (mg/dL)	Day 0	Female	Male	18.59	4.46	9.44	27.75	0.0003
	Day 14	Female	Male	19.20	4.37	10.24	28.16	0.0002
	Day 28	Female	Male	17.77	4.35	8.85	26.70	0.0004

**Table 33:** Difference in serum triglyceride levels between sexes for study participants with a history of colorectal cancer (n=29). Compared to males (n=12), females (n=17) had significantly lower serum triglycerides at all time points. Triglyceride data was not distributed normally, and a natural logarithm transformation was performed prior to analysis. A back transformation was performed on the difference of the cohorts' transformed mean to obtain a ratio of the geometric means.

<i>Linear Regression Analysis between Sexes for Study Participants with a History of Colorectal Cancer: Serum Triglyceride Levels</i>								
	Parameter	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value
Triglycerides	Day 0	Female	Male	0.60	1.20	0.41	0.88	0.010
	Day 14	Female	Male	0.65	1.21	0.44	0.96	0.033
	Day 28	Female	Male	0.61	1.21	0.41	0.91	0.016

### 3.8 Differences in nutrient intake between sexes

Females and males were found to have marked differences in intake of several different vitamins, minerals, and macronutrients. At both day 0, females were found to have significantly lower levels of intake of vitamin B2 ( $\mu_f - \mu_m = -0.62$ ; 95% CI=[-1.16, -0.08];  $p=0.026$ ), zinc (RoGM=0.623; 95% CI=[0.557, 0.698];  $p=0.008$ ), sodium ( $\mu_f - \mu_m = -650.1$  mg; 95% CI=[-1292.1, -8.2];  $p=0.047$ ), selenium ( $\mu_f - \mu_m = -40.7$  mg; 95% CI=[-68.0, -13.3];  $p=0.028$ ), carbohydrates (RoGM=0.77; 95% CI=[0.61, 0.98];  $p=0.036$ ), protein ( $\mu_f - \mu_m = -28.1$  g; 95% CI=[-43.2, -12.9];  $p=0.001$ ), calories ( $\mu_f - \mu_m = -589.4$ ; 95% CI=[-986.3, -192.5];  $p=0.005$ ), fat ( $\mu_f - \mu_m = -22.3$  g; 95% CI=[-44.4, -0.2];  $p=0.048$ ), saturated fat (RoGM=0.76; 95% CI=[0.59, 0.98];  $p=0.038$ ), and linoleic acid (RoGM=0.55; 95% CI=[0.31, 0.99];  $p=0.047$ ). These same nutrients were also significantly were also consumed less by females at day 28: vitamin B2 ( $\mu_f - \mu_m = -0.51$ ; 95% CI=[-0.95, -0.07];  $p=0.024$ ), zinc (RoGM=0.803; 95% CI=[0.79, 0.82];  $p=0.022$ ), sodium ( $\mu_f - \mu_m = -696.8$  mg; 95% CI=[-1140.4, -253.2];  $p=0.003$ ), selenium ( $\mu_f - \mu_m = -20.9$  mg; 95% CI=[-39.5, -2.4];  $p=0.028$ ), carbohydrates (RoGM=0.82; 95% CI=[0.70, 0.96];  $p=0.017$ ), protein ( $\mu_f - \mu_m = -17.4$  g; 95% CI=[-30.0, -4.8];  $p=0.009$ ), calories ( $\mu_f - \mu_m = -523.8$ ; 95% CI=[-818.3, -229.3];  $p=0.001$ ), fat ( $\mu_f - \mu_m = -20.9$  g; 95% CI=[-37.8, -4.1];  $p=0.017$ ), saturated fat (RoGM=0.76; 95% CI=[0.59, 0.98];  $p=0.038$ ), and linoleic acid (RoGM=0.71; 95% CI=[0.51, 0.98];  $p=0.038$ ). Additionally, at day 28, iron intake in females was significantly less than in males (RoGM=0.77; 95% CI=[0.63, 0.95];  $p=0.017$ ). No significant differences between females and males were observed in the intake of any nutrients at day 14.

**Table 34:** Differences in vitamin intake between sexes for study participants with a history of colorectal cancer (n=29). No significant differences between males and females were found in intake of the vitamins listed above. All displayed variables were not distributed normally, and a natural logarithm transformation was performed prior to analysis. A back transformation was performed on the difference of the cohorts' transformed mean to obtain a ratio of the geometric means.

<i>Linear Regression Analysis between Sexes for Study Participants with a History of Colorectal Cancer: Vitamin Intake</i>								
	Time Point	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value
Vitamin A	Day 0	Female	Male	1.01	1.34	0.55	1.85	0.969
	Day 14	Female	Male	1.13	1.22	0.75	1.69	0.545
	Day 28	Female	Male	0.87	1.15	0.65	1.16	0.321
β-Carotene	Day 0	Female	Male	1.58	1.73	0.51	4.93	0.414
	Day 14	Female	Male	1.46	1.33	0.81	2.63	0.202
	Day 28	Female	Male	0.97	1.23	0.64	1.48	0.890
Vitamin C	Day 0	Female	Male	1.38	1.41	0.68	2.80	0.352
	Day 14	Female	Male	1.05	1.24	0.68	1.63	0.809
	Day 28	Female	Male	0.84	1.19	0.59	1.19	0.311
Vitamin D	Day 0	Female	Male	0.59	1.65	0.21	1.66	0.302
	Day 14	Female	Male	0.84	1.25	0.53	1.32	0.430
	Day 28	Female	Male	0.61	1.29	0.36	1.04	0.068
Vitamin E	Day 0	Female	Male	1.64	2.07	0.36	7.42	0.505
	Day 14	Female	Male	0.71	1.33	0.40	1.28	0.244
	Day 28	Female	Male	0.65	1.53	0.27	1.56	0.326
α-Tocopherol	Day 0	Female	Male	0.89	1.37	0.47	1.70	0.711
	Day 14	Female	Male	0.96	1.15	0.72	1.28	0.784
	Day 28	Female	Male	0.86	1.15	0.64	1.15	0.288
Vitamin B1	Day 0	Female	Male	0.78	1.23	0.51	1.20	0.245
	Day 14	Female	Male	0.79	1.16	0.59	1.07	0.126
	Day 28	Female	Male	0.85	1.12	0.67	1.08	0.178
Vitamin B6	Day 0	Female	Male	0.76	1.18	0.53	1.08	0.115
	Day 14	Female	Male	0.88	1.15	0.67	1.16	0.357
	Day 28	Female	Male	0.89	1.15	0.66	1.19	0.407
Vitamin B9	Day 0	Female	Male	0.85	1.24	0.54	1.32	0.445
	Day 14	Female	Male	0.94	1.12	0.74	1.19	0.594
	Day 28	Female	Male	0.79	1.12	0.62	1.00	0.051
Vitamin B12	Day 0	Female	Male	0.64	1.30	0.37	1.09	0.097
	Day 14	Female	Male	0.81	1.20	0.56	1.19	0.273
	Day 28	Female	Male	0.83	1.21	0.57	1.23	0.340

**Table 35:** Differences in vitamin B2 and vitamin B3 intake between sexes for study participants with a history of colorectal cancer (n=29). At day 0 and day 28, females (n=17) were found to have significantly lower intake of vitamin B2 than males. No other significant differences in vitamin intake were found between males and females.

<i>Linear Regression Analysis between Sexes for Study Participants with a History of Colorectal Cancer: Vitamin B2 and Vitamin B3 Intake</i>								
	Time Point	Comparison groups		Diff. of Arithmetic Means	Standard Error	95% Confidence Limits		p-value
Vitamin B2 (mg)	Day 0	Female	Male	-0.62	0.26	-1.16	-0.08	0.026
	Day 14	Female	Male	-0.29	0.18	-0.67	0.08	0.120
	Day 28	Female	Male	-0.51	0.21	-0.95	-0.07	0.024
Vitamin B3 (mg)	Day 0	Female	Male	-4.10	3.43	-11.20	2.99	0.244
	Day 14	Female	Male	-4.87	2.59	-10.18	0.44	0.071
	Day 28	Female	Male	-4.62	2.35	-9.44	0.20	0.059

**Table 36:** Differences in intake of minerals, macronutrients, fatty acids, and fiber between sexes for study participants with a history of colorectal cancer (n=29). At day 0 and day 28, females had significantly lower intake of zinc, carbohydrates, saturated fat, and linoleic acid. Additionally, at day 28, females had significantly lower intake of iron compared to males. All displayed variables were not distributed normally, and a natural logarithm transformation was performed prior to analysis. A back transformation was performed on the difference of the cohorts' transformed mean to obtain a ratio of the geometric means.

<i>Linear Regression Analysis between Sexes for Study Participants with a History of Colorectal Cancer: Mineral, Macronutrient, Fatty Acid, and Fiber Intake</i>								
Time Point	Time Point	Comparison groups		Ratio of Geometric Means	Standard Error	95% Confidence Limits		p-value
Zinc	Day 0	Female	Male	0.623	1.28	0.557	0.698	0.008
	Day 14	Female	Male	0.781	1.36	0.748	0.817	0.051
	Day 28	Female	Male	0.803	1.35	0.786	0.820	0.022
Calcium	Day 0	Female	Male	0.68	1.21	0.46	1.00	0.051
	Day 14	Female	Male	0.91	1.13	0.71	1.16	0.446
	Day 28	Female	Male	0.82	1.12	0.65	1.03	0.088
Potassium	Day 0	Female	Male	0.89	1.13	0.69	1.14	0.328
	Day 14	Female	Male	1.00	1.07	0.86	1.16	0.989
	Day 28	Female	Male	0.91	1.08	0.77	1.07	0.239
Iron	Day 0	Female	Male	0.79	1.24	0.51	1.23	0.279
	Day 14	Female	Male	0.87	1.10	0.71	1.06	0.159
	Day 28	Female	Male	0.77	1.11	0.63	0.95	0.017
Magnesium	Day 0	Female	Male	0.75	1.24	0.48	1.16	0.179
	Day 14	Female	Male	1.00	1.14	0.77	1.30	0.984
	Day 28	Female	Male	0.90	1.10	0.74	1.10	0.308
Carbohydrates	Day 0	Female	Male	0.77	1.12	0.61	0.98	0.036
	Day 14	Female	Male	0.87	1.09	0.73	1.03	0.101
	Day 28	Female	Male	0.82	1.08	0.70	0.96	0.017
Saturated Fat	Day 0	Female	Male	0.60	1.13	0.47	0.77	0.0003
	Day 14	Female	Male	0.92	1.12	0.73	1.16	0.468
	Day 28	Female	Male	0.76	1.13	0.59	0.98	0.038
Oleic Acid	Day 0	Female	Male	0.68	1.23	0.44	1.05	0.076
	Day 14	Female	Male	0.91	1.16	0.68	1.22	0.517
	Day 28	Female	Male	0.79	1.17	0.57	1.08	0.135
Linoleic Acid	Day 0	Female	Male	0.55	1.33	0.31	0.99	0.047
	Day 14	Female	Male	0.72	1.19	0.51	1.03	0.068
	Day 28	Female	Male	0.71	1.17	0.51	0.98	0.038
Linolenic Acid	Day 0	Female	Male	0.71	1.35	0.38	1.31	0.256
	Day 14	Female	Male	1.00	1.19	0.70	1.42	0.986
	Day 28	Female	Male	0.87	1.16	0.64	1.18	0.344
Fiber	Day 0	Female	Male	1.03	1.21	0.69	1.52	0.892
	Day 14	Female	Male	1.08	1.08	0.91	1.27	0.367
	Day 28	Female	Male	0.93	1.11	0.75	1.15	0.484

**Table 37:** Differences in intake of sodium, selenium, calories, protein, and total fat between sexes for study participants with a history of colorectal cancer (n=29). At day 0 and day 28, females had significantly lower intake of sodium, selenium, calories, protein, and total fat.

<i>Linear Regression Analysis between Sexes for Study Participants with a History of Colorectal Cancer: Sodium, Selenium, Calories, Protein, and Total Fat Intake</i>								
Time Point	Time Point	Comparison groups		Diff. of Arithmetic Means (mg)	Standard Error	95% Confidence Limits		p-value
Sodium (mg)	Day 0	Female	Male	-650.130	310.308	-1292.051	-8.209	0.047
	Day 14	Female	Male	-570.479	291.386	-1168.353	27.396	0.061
	Day 28	Female	Male	-696.789	216.196	-1140.386	-253.192	0.003
Selenium (mg)	Day 0	Female	Male	-40.652	13.244	-68.049	-13.256	0.005
	Day 14	Female	Male	-18.206	11.641	-42.092	5.680	0.129
	Day 28	Female	Male	-20.942	9.046	-39.503	-2.381	0.028
Calories	Day 0	Female	Male	-589.403	191.849	-986.274	-192.533	0.005
	Day 14	Female	Male	-303.952	151.863	-615.548	7.644	0.055
	Day 28	Female	Male	-523.795	143.516	-818.266	-229.325	0.001
Protein (g)	Day 0	Female	Male	-28.060	7.335	-43.233	-12.887	0.001
	Day 14	Female	Male	-13.842	6.955	-28.112	0.429	0.057
	Day 28	Female	Male	-17.369	6.133	-29.954	-4.785	0.009
Fat (g)	Day 0	Female	Male	-22.290	10.684	-44.391	-0.188	0.048
	Day 14	Female	Male	-9.685	7.777	-25.642	6.272	0.224
	Day 28	Female	Male	-20.927	8.216	-37.785	-4.068	0.017

### 3.9 Linear repeated measures correlations

Linear associations between study variables were evaluated using a repeated measure correlation model with adjustment for the influences of age, sex, and total energy intake. Overall, significant correlations observed in the present study were consistent with prior studies.

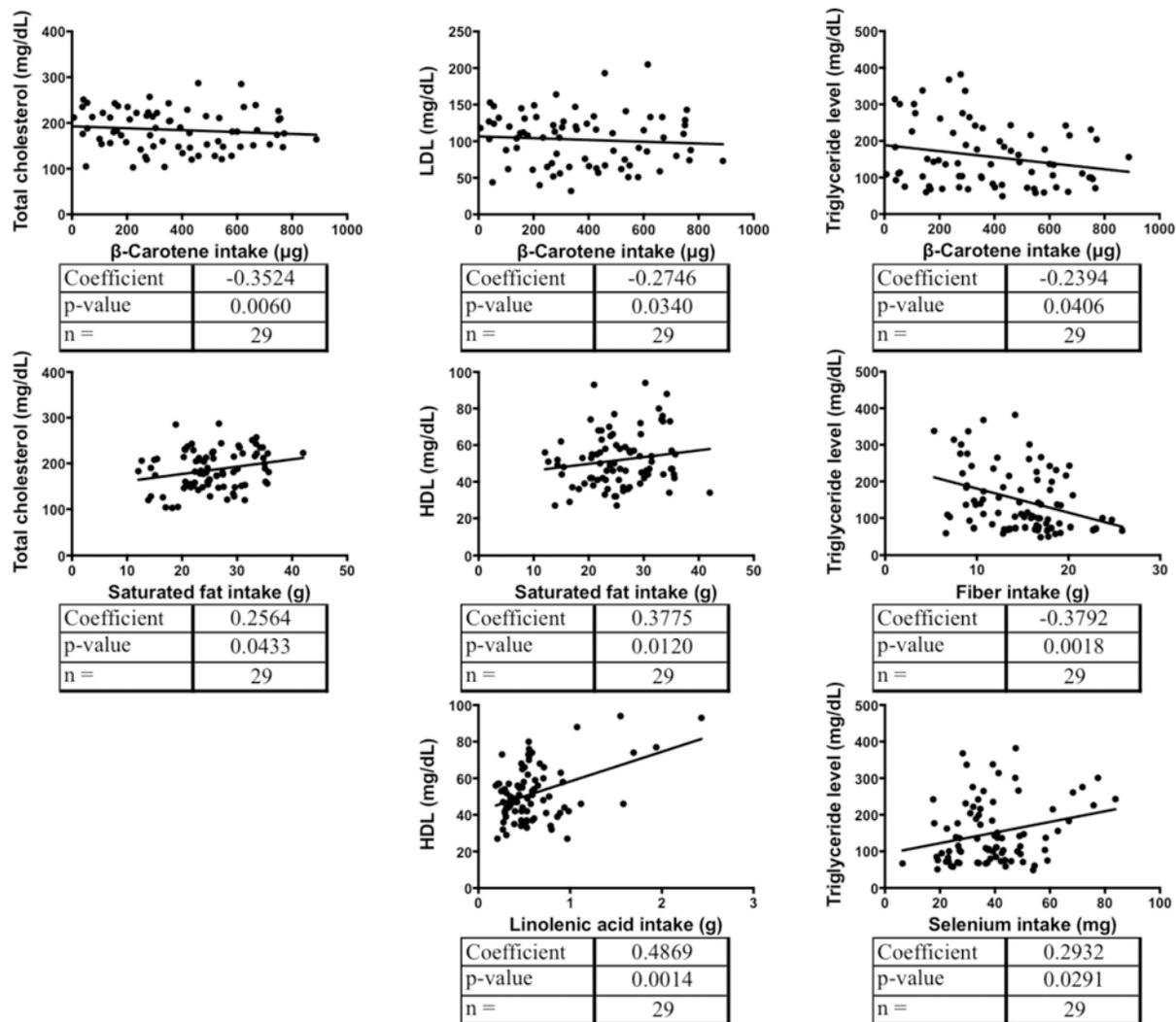
BMI was positively correlated with triglyceride level ( $r=0.3439$ ;  $p=0.0107$ ) and saturated fat intake ( $r=0.3700$ ;  $p=0.0023$ ) and negatively correlated with  $\beta$ -Carotene intake ( $r=-0.2965$ ;  $p=0.0124$ ) and vitamin C intake ( $r=-0.3086$ ;  $p=0.0095$ ).

In regards to lipid profile, total serum cholesterol was positively correlated with saturated fat intake ( $r=0.2564$ ;  $p=0.0433$ ) and negatively correlated with  $\beta$ -Carotene intake ( $r=-0.3524$ ;  $p=0.0060$ ). Similarly, LDL cholesterol was negatively correlated with  $\beta$ -Carotene intake ( $r=-0.2746$ ;  $p=0.0340$ ). HDL cholesterol was positively correlated with saturated fat intake ( $r=0.3775$ ;  $p=0.0120$ ) and linolenic acid intake ( $r=0.4969$ ;  $p=0.0014$ ). Triglyceride level was positively correlated with selenium intake ( $r=0.2932$ ;  $p=0.0291$ ) and negatively correlated with  $\beta$ -Carotene intake ( $r=-0.2394$ ;  $p=0.0406$ ), fiber intake ( $r=-0.3792$ ;  $p=0.0018$ ), and leukocyte telomere length ( $r=-0.2992$ ;  $p=0.0499$ ).

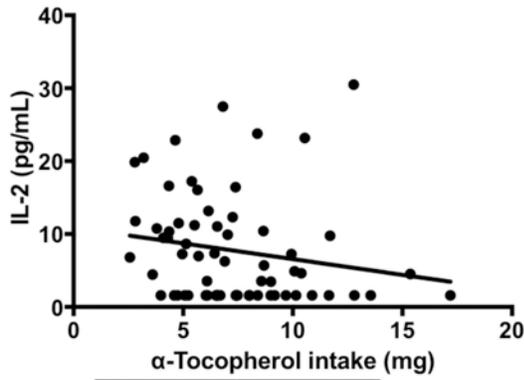
Several plasma cytokines were significantly correlated with various dietary factors. Plasma IL-2 concentration was negatively correlated with  $\alpha$ -Tocopherol intake for both the substitution ( $r=-0.3773$ ;  $p=0.0151$ ) and extrapolation ( $r=-0.3731$ ;  $p=0.0177$ ) data sets. Similarly, plasma IL-4 concentration was negatively correlated with  $\alpha$ -Tocopherol intake for both the substitution ( $r=-0.4381$ ;  $p=0.0042$ ) and extrapolation ( $r=-0.4111$ ;  $p=0.0087$ ) data sets. Plasma IL-8 concentration was negatively correlated with vitamin B3 intake for both the substitution ( $r=-0.2889$ ;  $p=0.0365$ ) and extrapolation ( $r=-0.2933$ ;  $p=0.0478$ ) data sets. Plasma VEGF concentration was positively correlated with vitamin B9 intake for both the substitution

( $r=0.2928$ ;  $p=0.0322$ ) and extrapolation ( $r=0.3071$ ;  $p=0.0229$ ) data sets. No significant correlations were found for IL-6, IL-10, or TNF.

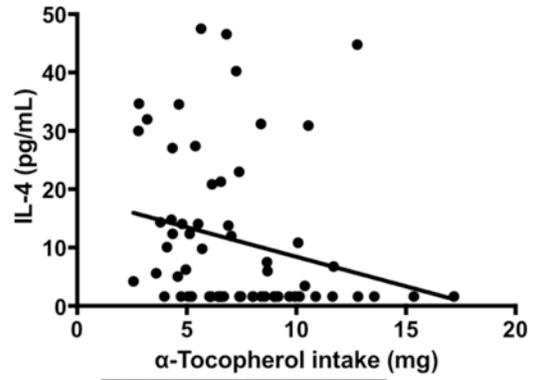
As expected, telomere length was significantly correlated with age after adjusting for sex ( $r=-0.6162$ ;  $p<0.0001$ ). Additionally, telomere length was negatively correlated with triglyceride level ( $r=-0.2992$ ;  $p=0.0499$ ), carbohydrate intake ( $r=-0.3348$ ;  $p=0.0185$ ), and saturated fat intake ( $r=-0.4125$ ;  $p=0.0028$ ).



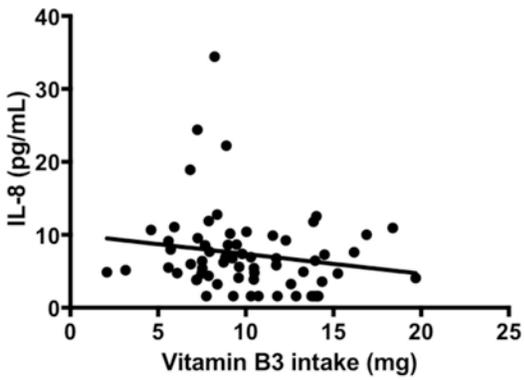
**Figure 5:** Graphs showing significant correlations for lipid profile for participants with a history of colorectal cancer. Each graph shows data points at all three time points. The coefficient of correlation was determined by a repeat measures statistical method using an unstructured correlation matrix. The graphs are meant for display purposes and do not directly represent the coefficient of correlation obtained with the repeated measures statistical test.



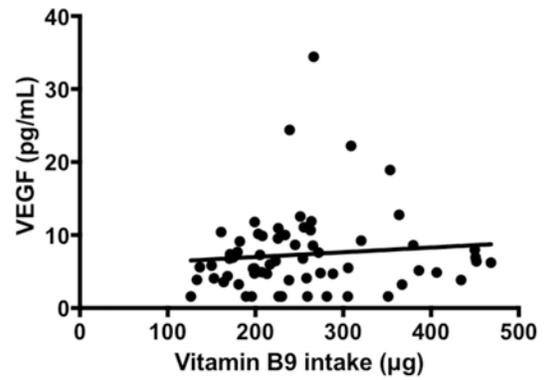
Coefficient	-0.3773
p-value	0.0151
n =	23



Coefficient	-0.4381
p-value	0.0042
n =	23

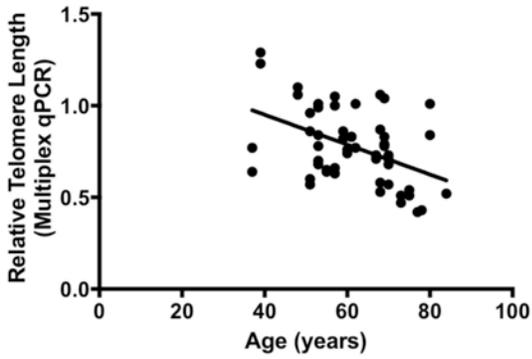


Coefficient	-0.2889
p-value	0.0365
n =	23

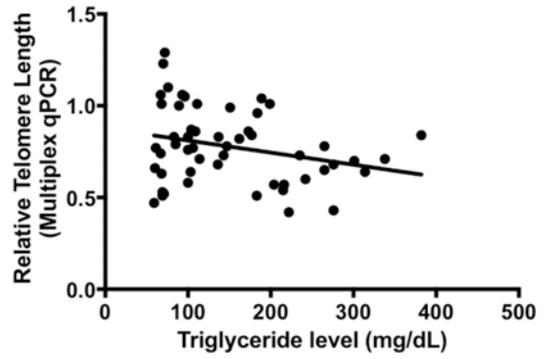


Coefficient	0.3071
p-value	0.0229
n =	23

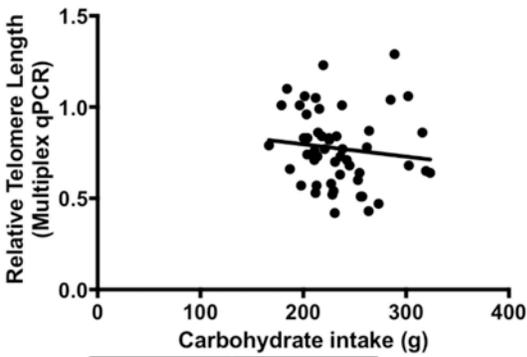
**Figure 6: Figure 7:** Graphs showing significant correlations for telomere length for participants with a history of colorectal cancer. Each graph shows data points at all three time points. The coefficient of correlation was determined by a repeat measures statistical method using an unstructured correlation matrix. The graphs are meant for display purposes and do not directly represent the coefficient of correlation obtained with the repeated measures statistical test.



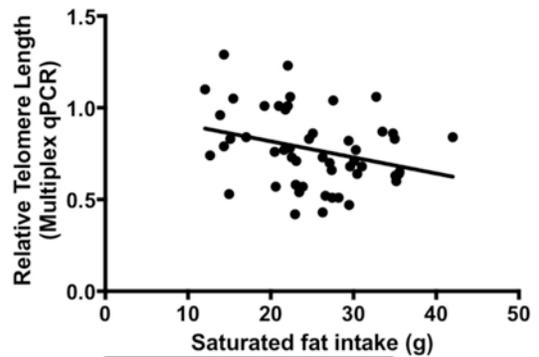
Coefficient	-0.6162
p-value	<.0001
n =	27



Coefficient	-0.2992
p-value	0.0499
n =	27



Coefficient	-0.3348
p-value	0.0185
n =	27
n =	23



Coefficient	-0.4125
p-value	0.0028
n =	27
n =	23

**Figure 8:** Graphs showing significant correlations for telomere length for participants with a history of colorectal cancer. Each graph shows data points at all three time points. The coefficient of correlation was determined by a repeat measures statistical method using an unstructured correlation matrix. The graphs are meant for display purposes and do not directly represent the coefficient of correlation obtained with the repeated measures statistical test.

**Table 38:** Linear correlations between weight, BMI, serum lipids, and leukocyte telomere length. Correlation analysis was performed on repeated measures of each variable, and age and sex were used as covariates. Telomere length was inversely correlated with triglyceride level.

<i>Repeated Measure Correlations for Study Participants with a History of Colorectal Cancer: Weight, BMI, Serum Lipids, and Leukocyte Telomere Length (Multiplex qPCR)</i>							
		Weight	BMI	Total Cholesterol	LDL	HDL	Triglycerides
Weight (Cov: Age & Sex)	Coefficient		0.9609	0.1878	0.0804	-0.2925	0.3439
	p-value		<.0001	0.1367	0.5107	0.0128	0.0107
	n =		29	29	29	29	29
BMI (Cov: Age & Sex)	Coefficient	0.9609		0.2344	0.1238	-0.1635	0.3905
	p-value	<.0001		0.0518	0.2966	0.1895	0.0010
	n =	29		29	29	29	29
Total Cholesterol (Cov: Age & Sex)	Coefficient	0.1878	0.2344		0.9316	0.1867	0.4226
	p-value	0.1367	0.0518		<.0001	0.1004	0.0007
	n =	29	29		29	29	29
LDL (Cov: Age & Sex)	Coefficient	0.0804	0.1238	0.9316		0.0606	0.1997
	p-value	0.5107	0.2966	<.0001		0.5874	0.0927
	n =	29	29	29		29	29
HDL (Cov: Age & Sex)	Coefficient	-0.2925	-0.1635	0.1867	0.0606		-0.5343
	p-value	0.0128	0.1895	0.1004	0.5874		0.0002
	n =	29	29	29	29		29
Triglycerides (Cov: Age & Sex)	Coefficient	0.3438	0.3905	0.4225	0.1997	-0.5343	
	p-value	0.0107	0.0010	0.0007	0.0927	0.0002	
	n =	29	29	29	29	29	
Multiplex qPCR Telomere Length (Cov: Age & Sex)	Coefficient	-0.2798	-0.1052	-0.0804	-0.0267	0.1437	-0.2992
	p-value	0.0841	0.4522	0.6128	0.8725	0.4180	0.0499
	n =	25	25	25	25	25	25

**Table 39:** Linear correlations for IL-2, IL-4, and IL-6 concentrations with weight, BMI, serum lipids, and leukocyte telomere length. Correlation analysis was performed on repeated measures of each variable, and age and sex were used as covariates.

<i>Repeated Measure Correlations for Study Participants with a History of Colorectal Cancer: Weight, BMI, Serum Lipids, and Leukocyte Telomere Length (Multiplex qPCR) vs. Plasma IL-2, IL-4, and IL-6</i>							
		Interleukin-2 (Substitution)	Interleukin-2 (Extrapolation)	Interleukin-4 (Substitution)	Interleukin-4 (Extrapolation)	Interleukin-6 (Substitution)	Interleukin-6 (Extrapolation)
Weight (Cov: Age & Sex)	Coefficient	-0.3548	-0.2648	0.1670	0.1786	-0.1363	-0.0397
	p-value	0.0611	0.1369	0.1812	0.1533	0.4867	0.8355
	n =	23	23	23	23	23	23
BMI (Cov: Age & Sex)	Coefficient	-0.2118	-0.0373	0.0397	-0.0960	-0.0263	0.0489
	p-value	0.2194	0.8248	0.7873	0.5735	0.8795	0.7734
	n =	23	23	23	23	23	23
Total Cholesterol (Cov: Age & Sex)	Coefficient	0.1359	0.2451	0.1000	0.1831	0.0282	0.1388
	p-value	0.3640	0.1042	0.5048	0.2242	0.8507	0.3560
	n =	23	23	23	23	23	23
LDL (Cov: Age & Sex)	Coefficient	0.1275	0.2355	0.0639	0.1681	-0.0616	0.1733
	p-value	0.3713	0.0691	0.6542	0.2418	0.6655	0.2277
	n =	23	23	23	23	23	23
HDL (Cov: Age & Sex)	Coefficient	-0.0129	-0.1270	-0.0108	-0.1410	-0.0577	0.0673
	p-value	0.9359	0.4069	0.9467	0.3576	0.7200	0.6788
	n =	23	23	23	23	23	23
Triglycerides (Cov: Age & Sex)	Coefficient	0.0176	-0.0499	0.0257	0.0283	0.1641	-0.1613
	p-value	0.8881	0.6793	0.8374	0.8170	0.1788	0.1909
	n =	23	23	23	23	23	23
Multiplex qPCR Telomere Length (Cov: Age & Sex)	Coefficient	0.0790	0.0931	0.0727	0.0513	0.1779	0.0726
	p-value	0.6510	0.5745	0.6831	0.7650	0.3408	0.6564
	n =	20	20	20	20	20	20

**Table 40:** Linear correlations for IL-8, IL-10, TNF, and VEGF concentrations with weight, BMI, serum lipids, and leukocyte telomere length. Correlation analysis was performed on repeated measures of each variable, and age and sex were used as covariates.

<i>Repeated Measure Correlations for Study Participants with a History of Colorectal Cancer: Weight, BMI, Serum Lipids, and Leukocyte Telomere Length (Multiplex qPCR) vs. Plasma IL-8, IL-10, TNF, and VEGF</i>									
		Interleukin-8 (Substitution)	Interleukin-8 (Extrapolation)	Interleukin-10 (Substitution)	Interleukin-10 (Extrapolation)	Tumor Necrosis Factor (Substitution)	Tumor Necrosis Factor (Extrapolation)	Vascular Endothelial Growth Factor (Substitution)	Vascular Endothelial Growth Factor (Extrapolation)
Weight (Cov: Age & Sex)	Coefficient	0.0453	-0.0617	-0.2688	-0.2060	0.0576	0.0831	-0.1252	-0.1940
	p-value	0.8203	0.7540	0.1597	0.2514	0.7739	0.6786	0.5249	0.3027
	n =	23	23	23	23	23	23	23	23
BMI (Cov: Age & Sex)	Coefficient	0.2467	0.1280	-0.0469	0.0856	0.1474	0.1516	0.0517	0.0094
	p-value	0.1570	0.4606	0.7868	0.6147	0.4020	0.3893	0.7658	0.9547
	n =	23	23	23	23	23	23	23	23
Total Cholesterol (Cov: Age & Sex)	Coefficient	0.2644	0.1026	0.2939	0.2268	0.2426	0.2824	0.1146	0.1069
	p-value	0.0785	0.4941	0.0507	0.1332	0.1057	0.0598	0.4432	0.4738
	n =	23	23	23	23	23	23	23	23
LDL (Cov: Age & Sex)	Coefficient	0.2339	0.1276	0.2265	0.2820	0.1860	0.2171	0.1783	0.1856
	p-value	0.1030	0.3725	0.0802	0.0517	0.1931	0.1291	0.2117	0.1934
	n =	23	23	23	23	23	23	23	23
HDL (Cov: Age & Sex)	Coefficient	-0.1471	0.0463	-0.0275	-0.1620	0.0969	0.0470	-0.1044	-0.1208
	p-value	0.3562	0.7744	0.8651	0.2954	0.5455	0.7690	0.5039	0.4215
	n =	23	23	23	23	23	23	23	23
Triglycerides (Cov: Age & Sex)	Coefficient	0.1817	-0.0702	0.0672	-0.0274	0.0209	0.0577	-0.0325	-0.0576
	p-value	0.1321	0.5554	0.5937	0.8248	0.8604	0.6279	0.7863	0.6294
	n =	23	23	23	23	23	23	23	23
Multiplex qPCR Telomere Length (Cov: Age & Sex)	Coefficient	0.2679	0.2045	0.3139	0.1349	0.0673	0.0811	0.2938	0.2699
	p-value	0.1073	0.1533	0.0773	0.4377	0.6569	0.6096	0.0726	0.0983
	n =	20	20	20	20	20	20	20	20

**Table 41:** Linear correlations vitamin intake with weight, BMI, serum lipids, and leukocyte telomere length. Correlation analysis was performed on repeated measures of each variable, and age and sex were used as covariates. Additionally, all dietary intakes were adjusted for total calorie intake.  $\beta$ -Carotene was significantly inversely correlated with weight, BMI, total cholesterol, LDL, and triglycerides. Vitamin C was inversely correlated with BMI.

<i>Repeated Measure Correlations for Study Participants with a History of Colorectal Cancer: Weight, BMI, Serum Lipids, and Leukocyte Telomere Length (Multiplex qPCR) vs. Vitamin Intake</i>							
		Vitamin A	$\beta$ -Carotene	Vitamin C	Vitamin D	Vitamin E	$\alpha$ -Tocopherol
Weight (Cov: Age & Sex)	Coefficient	-0.1396	-0.3401	-0.2325	0.0744	-0.1580	-0.1925
	p-value	0.2994	0.0124	0.0852	0.5792	0.2358	0.1530
	n =	29	29	29	29	29	29
BMI (Cov: Age & Sex)	Coefficient	-0.1443	-0.2965	-0.3086	0.0058	-0.1609	-0.0951
	p-value	0.2109	0.0124	0.0095	0.9591	0.1617	0.4071
	n =	29	29	29	29	29	29
Total Cholesterol (Cov: Age & Sex)	Coefficient	-0.2458	-0.3524	-0.0297	-0.0483	-0.1581	-0.0569
	p-value	0.0515	0.0060	0.8108	0.6981	0.2053	0.6474
	n =	29	29	29	29	29	29
LDL (Cov: Age & Sex)	Coefficient	-0.1497	-0.2746	0.0309	-0.0871	-0.1178	0.0490
	p-value	0.2434	0.0340	0.8089	0.4979	0.3575	0.7023
	n =	29	29	29	29	29	29
HDL (Cov: Age & Sex)	Coefficient	-0.1866	-0.2340	-0.1450	0.1156	-0.0765	-0.2404
	p-value	0.2008	0.1037	0.1888	0.4381	0.5979	0.1006
	n =	29	29	29	29	29	29
Triglycerides (Cov: Age & Sex)	Coefficient	-0.2539	-0.2394	-0.0678	-0.1148	-0.1383	-0.1029
	p-value	0.1082	0.0406	0.5498	0.3174	0.2254	0.3638
	n =	29	29	29	29	29	29
Multiplex qPCR Telomere Length (Cov: Age & Sex)	Coefficient	-0.0925	-0.0087	-0.0052	-0.2142	0.0017	0.2037
	p-value	0.5087	0.9463	0.9695	0.1489	0.9890	0.1780
	n =	27	27	27	27	27	27

**Table 42:** Linear correlations for B vitamin intake with weight, BMI, serum lipids, and leukocyte telomere length. Correlation analysis was performed on repeated measures of each variable, and age and sex were used as covariates. Additionally, all dietary intakes were adjusted for total calorie intake.

<i>Repeated Measure Correlations for Study Participants with a History of Colorectal Cancer: Weight, BMI, Serum Lipids, and Leukocyte Telomere Length (Multiplex qPCR) vs. B Vitamin Intake</i>							
		Vitamin B1	Vitamin B2	Vitamin B3	Vitamin B6	Vitamin B9	Vitamin B12
Weight (Cov: Age & Sex)	Coefficient	0.1133	0.0624	0.1758	0.0035	-0.2048	0.0176
	p-value	0.4005	0.6420	0.1561	0.9791	0.1290	0.8957
	n =	29	29	29	29	29	29
BMI (Cov: Age & Sex)	Coefficient	0.0226	-0.0231	0.1879	-0.0584	-0.2262	-0.0295
	p-value	0.8434	0.8395	0.1037	0.6096	0.0525	0.7956
	n =	29	29	29	29	29	29
Total Cholesterol (Cov: Age & Sex)	Coefficient	0.1774	0.2164	0.1906	0.2208	-0.0278	0.2294
	p-value	0.1237	0.0865	0.1371	0.0821	0.8231	0.0699
	n =	29	29	29	29	29	29
LDL (Cov: Age & Sex)	Coefficient	0.1891	0.2366	0.1878	0.1528	0.0755	0.1939
	p-value	0.1045	0.0690	0.1414	0.1875	0.5556	0.1346
	n =	29	29	29	29	29	29
HDL (Cov: Age & Sex)	Coefficient	0.2561	0.2228	-0.1027	0.0360	-0.0747	0.1577
	p-value	0.0862	0.1346	0.4337	0.8072	0.6115	0.2893
	n =	29	29	29	29	29	29
Triglycerides (Cov: Age & Sex)	Coefficient	-0.0758	-0.1379	0.0490	-0.0633	-0.1926	0.0171
	p-value	0.5034	0.2320	0.6940	0.5782	0.0942	0.8797
	n =	29	29	29	29	29	29
Multiplex qPCR Telomere Length (Cov: Age & Sex)	Coefficient	-0.0260	-0.1746	-0.0019	-0.1394	0.1229	-0.1296
	p-value	0.8675	0.2191	0.9902	0.3795	0.4083	0.3840
	n =	27	27	27	27	27	27

**Table 43:** Linear correlations for mineral intake with weight, BMI, serum lipids, and leukocyte telomere length. Correlation analysis was performed on repeated measures of each variable, and age and sex were used as covariates. Additionally, all dietary intakes were adjusted for total calorie intake. Selenium intake was inversely correlated with serum triglyceride level.

<i>Repeated Measure Correlations for Study Participants with a History of Colorectal Cancer: Weight, BMI, Serum Lipids, and Leukocyte Telomere Length (Multiplex qPCR) vs. Mineral Intake</i>								
		Zinc	Calcium	Potassium	Sodium	Iron	Magnesium	Selenium
Weight (Cov: Age & Sex)	Coefficient	0.0244	0.0268	-0.0055	0.0126	-0.0866	0.1148	-0.0048
	p-value	0.8489	0.8416	0.9675	0.9080	0.5189	0.3952	0.9665
	n =	29	29	29	29	29	29	29
BMI (Cov: Age & Sex)	Coefficient	0.1186	-0.0665	-0.0678	0.0018	-0.0562	0.1500	0.0630
	p-value	0.3019	0.5607	0.5540	0.9868	0.6226	0.1943	0.6243
	n =	29	29	29	29	29	29	29
Total Cholesterol (Cov: Age & Sex)	Coefficient	0.1486	0.0020	0.1091	-0.0244	0.1970	0.1009	0.1522
	p-value	0.2252	0.9873	0.3813	0.8232	0.1174	0.4045	0.2298
	n =	29	29	29	29	29	29	29
LDL (Cov: Age & Sex)	Coefficient	0.0827	-0.0227	0.2338	-0.0216	-0.0118	0.0700	0.0262
	p-value	0.5043	0.8593	0.0716	0.8433	0.9236	0.5747	0.8204
	n =	29	29	29	29	29	29	29
HDL (Cov: Age & Sex)	Coefficient	-0.0252	0.1444	-0.1194	-0.0100	0.0579	0.1825	-0.1560
	p-value	0.8682	0.3301	0.4162	0.9271	0.6953	0.2185	0.2398
	n =	29	29	29	29	29	29	29
Triglycerides (Cov: Age & Sex)	Coefficient	0.1402	-0.1144	-0.1566	0.0002	-0.1121	-0.0698	0.2932
	p-value	0.3039	0.3203	0.1881	0.9983	0.3301	0.5414	0.0291
	n =	29	29	29	29	29	29	29
Multiplex qPCR Telomere Length (Cov: Age & Sex)	Coefficient	0.0096	-0.2550	-0.1178	-0.2085	-0.0386	-0.0168	0.0061
	p-value	0.9649	0.0616	0.3803	0.2724	0.7973	0.9154	0.9717
	n =	27	27	27	27	27	27	27

**Table 44:** Linear correlations for total protein, carbohydrate, fat, saturated fat, oleic acid, linoleic acid, and linolenic acid intake with weight, BMI, serum lipids, and leukocyte telomere length. Correlation analysis was performed on repeated measures of each variable, and age and sex were used as covariates. Additionally, all dietary intakes were adjusted for total calorie intake. Saturated fat intake was positively correlated with weight, BMI, total cholesterol, and HDL and was negatively correlated with telomere length. Carbohydrate was also negatively correlated with telomere length. Linolenic acid intake was positively correlated with HDL, and fiber intake was negatively correlated with triglyceride level.

<i>Repeated Measure Correlations for Study Participants with a History of Colorectal Cancer: Weight, BMI, Serum Lipids, and Leukocyte Telomere Length (Multiplex qPCR) vs. Protein, Carbohydrate, and Fat Intake</i>									
		Protein	Carbohydrate	Fat	Saturated Fat	Oleic Acid	Linoleic Acid	Linolenic Acid	Fiber
Weight (Cov: Age & Sex)	Coefficient	-0.0768	-0.0608	0.2073	0.3732	-0.0523	-0.1879	-0.1388	-0.1309
	p-value	0.5141	0.6507	0.0655	0.0070	0.6967	0.1612	0.3013	0.3318
	n =	29	29	29	29	29	29	29	29
BMI (Cov: Age & Sex)	Coefficient	-0.2445	-0.1521	-0.2502	0.3700	0.0844	-0.0316	-0.0819	-0.1445
	p-value	0.1163	0.1870	0.1335	0.0023	0.4615	0.7811	0.4739	0.2109
	n =	29	29	29	29	29	29	29	29
Total Cholesterol (Cov: Age & Sex)	Coefficient	0.0883	0.0335	-0.2170	0.2564	0.1738	0.1526	0.1850	-0.0183
	p-value	0.5484	0.7877	0.1129	0.0433	0.1666	0.2239	0.1411	0.8831
	n =	29	29	29	29	29	29	29	29
LDL (Cov: Age & Sex)	Coefficient	-0.0846	0.1637	-0.1932	0.0690	0.1409	0.1615	0.1083	0.1043
	p-value	0.5681	0.2040	0.0824	0.5905	0.2745	0.2119	0.3995	0.4160
	n =	29	29	29	29	29	29	29	29
HDL (Cov: Age & Sex)	Coefficient	-0.2303	-0.2894	-0.1318	0.3775	-0.0054	-0.0329	0.4869	0.1090
	p-value	0.0540	0.0504	0.2754	0.0120	0.9706	0.8241	0.0014	0.4593
	n =	29	29	29	29	29	29	29	29
Triglycerides (Cov: Age & Sex)	Coefficient	0.2529	-0.1012	0.0073	0.1639	0.0339	0.0174	-0.1274	-0.3792
	p-value	0.2305	0.4017	0.9720	0.1645	0.7686	0.8776	0.2619	0.0018
	n =	29	29	29	29	29	29	29	29
Multiplex qPCR Telomere Length (Cov: Age & Sex)	Coefficient	-0.3030	-0.3348	0.2851	-0.4125	-0.1355	-0.1266	0.0113	0.0597
	p-value	0.2030	0.0185	0.1880	0.0028	0.3925	0.4907	0.9432	0.6483
	n =	27	27	27	27	27	27	27	27

**Table 45:** Linear correlations for vitamin intake with plasma cytokine concentrations. Correlation analysis was performed on repeated measures of each variable, and age and sex were used as covariates. Additionally, all dietary intakes were adjusted for total calorie intake.  $\alpha$ -Tocopherol intake was negatively correlated with IL-2 and IL-4.

<i>Repeated Measure Correlations for Study Participants with a History of Colorectal Cancer: Plasma Cytokine Concentrations vs. Vitamin Intake</i>							
		Vitamin A	$\beta$ -Carotene	Vitamin C	Vitamin D	Vitamin E	$\alpha$ -Tocopherol
Interleukin-2 (Substitution) (Cov: Age & Sex)	Coefficient	-0.1591	-0.1796	-0.1523	-0.1979	-0.0164	-0.3773
	p-value	0.2418	0.1860	0.3007	0.1327	0.9085	0.0151
	n =	23	23	23	23	23	23
Interleukin-2 (Extrapolation) (Cov: Age & Sex)	Coefficient	-0.1283	-0.1821	-0.0318	-0.1496	-0.0095	-0.3731
	p-value	0.3451	0.1954	0.8302	0.2611	0.9486	0.0177
	n =	23	23	23	23	23	23
Interleukin-4 (Substitution) (Cov: Age & Sex)	Coefficient	-0.2048	-0.2489	-0.1742	-0.1997	-0.0903	-0.4381
	p-value	0.1370	0.0661	0.2472	0.1368	0.5173	0.0042
	n =	23	23	23	23	23	23
Interleukin-4 (Extrapolation) (Cov: Age & Sex)	Coefficient	-0.1401	-0.1612	-0.0549	-0.1128	0.0237	-0.4111
	p-value	0.3077	0.2554	0.7152	0.4012	0.8728	0.0087
	n =	23	23	23	23	23	23
Interleukin-6 (Substitution) (Cov: Age & Sex)	Coefficient	-0.2263	-0.2495	-0.1105	-0.1356	-0.1171	-0.2463
	p-value	0.0900	0.0640	0.4448	0.2972	0.4075	0.0986
	n =	23	23	23	23	23	23
Interleukin-6 (Extrapolation) (Cov: Age & Sex)	Coefficient	-0.0097	-0.1038	-0.0108	-0.0391	-0.0058	-0.2530
	p-value	0.9436	0.4590	0.9422	0.7700	0.9681	0.1086
	n =	23	23	23	23	23	23
Interleukin-8 (Substitution) (Cov: Age & Sex)	Coefficient	-0.1499	-0.1482	-0.0244	-0.2448	-0.0969	-0.2426
	p-value	0.2547	0.2730	0.8621	0.0566	0.5000	0.1074
	n =	23	23	23	23	23	23
Interleukin-8 (Extrapolation) (Cov: Age & Sex)	Coefficient	-0.0991	-0.1161	0.0194	-0.1484	-0.1095	-0.2253
	p-value	0.4504	0.3887	0.8905	0.2427	0.4452	0.1346
	n =	23	23	23	23	23	23
Interleukin-10 (Substitution) (Cov: Age & Sex)	Coefficient	-0.1709	-0.1975	-0.1136	-0.2583	-0.1257	-0.2020
	p-value	0.2152	0.1444	0.4456	0.0524	0.3752	0.2026
	n =	23	23	23	23	23	23
Interleukin-10 (Extrapolation) (Cov: Age & Sex)	Coefficient	-0.0688	-0.1475	-0.0157	-0.1620	-0.1282	-0.2375
	p-value	0.6275	0.3092	0.9200	0.2408	0.3965	0.1073
	n =	23	23	23	23	23	23
TNF (Substitution) (Cov: Age & Sex)	Coefficient	-0.0802	-0.1398	0.0089	-0.0736	-0.1385	-0.2091
	p-value	0.5384	0.3071	0.9495	0.5728	0.3377	0.1642
	n =	23	23	23	23	23	23
TNF (Extrapolation) (Cov: Age & Sex)	Coefficient	-0.0614	-0.1155	0.0433	-0.1048	-0.0953	-0.1953
	p-value	0.6373	0.3988	0.7593	0.4254	0.5092	0.1936
	n =	23	23	23	23	23	23
VEGF (Substitution) (Cov: Age & Sex)	Coefficient	0.1022	0.0774	-0.0040	-0.0951	-0.1315	0.2085
	p-value	0.4352	0.5722	0.9775	0.4584	0.3647	0.1748
	n =	23	23	23	23	23	23
VEGF (Extrapolation) (Cov: Age & Sex)	Coefficient	0.1291	0.1034	-0.0044	-0.0351	-0.0905	0.2368
	p-value	0.3225	0.4508	0.9754	0.7855	0.5339	0.1133
	n =	23	23	23	23	23	23

**Table 46:** Linear correlations for B vitamin intake with plasma cytokine concentrations. Correlation analysis was performed on repeated measures of each variable, and age and sex were used as covariates. Additionally, all dietary intakes were adjusted for total calorie intake. Vitamin B3 (niacin) intake was negatively correlated with IL-8 concentration. Vitamin B9 (folate) was positively correlated with VEGF concentration.

<i>Repeated Measure Correlations for Study Participants with a History of Colorectal Cancer: Plasma Cytokine Concentrations vs. B Vitamin Intake</i>							
		Vitamin B1	Vitamin B2	Vitamin B3	Vitamin B6	Vitamin B9	Vitamin B12
Interleukin-2 (Substitution) (Cov: Age & Sex)	Coefficient	-0.0304	0.0233	0.0146	-0.0087	-0.0812	0.1612
	p-value	0.8116	0.8677	0.9222	0.9473	0.5572	0.2530
	n =	23	23	23	23	23	23
Interleukin-2 (Extrapolation) (Cov: Age & Sex)	Coefficient	-0.0357	0.0138	-0.1419	-0.0834	-0.0730	0.1841
	p-value	0.7762	0.9196	0.3059	0.5215	0.5977	0.1772
	n =	23	23	23	23	23	23
Interleukin-4 (Substitution) (Cov: Age & Sex)	Coefficient	0.0012	0.0078	0.0387	-0.0011	-0.0830	0.2320
	p-value	0.9925	0.9559	0.7918	0.9936	0.5495	0.1017
	n =	23	23	23	23	23	23
Interleukin-4 (Extrapolation) (Cov: Age & Sex)	Coefficient	-0.0557	0.0571	-0.0598	-0.0471	-0.0953	0.1720
	p-value	0.6603	0.6792	0.6630	0.7194	0.4925	0.2079
	n =	23	23	23	23	23	23
Interleukin-6 (Substitution) (Cov: Age & Sex)	Coefficient	0.0135	-0.0405	0.0832	0.0439	0.0411	0.1049
	p-value	0.9150	0.7683	0.5751	0.7375	0.7629	0.4475
	n =	23	23	23	23	23	23
Interleukin-6 (Extrapolation) (Cov: Age & Sex)	Coefficient	0.0020	0.0047	-0.0822	-0.0350	0.1002	0.1068
	p-value	0.9876	0.9729	0.5638	0.7897	0.4748	0.4389
	n =	23	23	23	23	23	23
Interleukin-8 (Substitution) (Cov: Age & Sex)	Coefficient	-0.2090	-0.1823	-0.2889	-0.2016	-0.1303	0.0228
	p-value	0.0944	0.1809	0.0365	0.1162	0.3398	0.8659
	n =	23	23	23	23	23	23
Interleukin-8 (Extrapolation) (Cov: Age & Sex)	Coefficient	-0.1922	-0.1839	-0.2933	-0.1762	-0.1071	0.0841
	p-value	0.1225	0.1750	0.0478	0.1679	0.4306	0.5334
	n =	23	23	23	23	23	23
Interleukin-10 (Substitution) (Cov: Age & Sex)	Coefficient	0.0977	0.0283	0.1079	0.0709	0.0437	0.1522
	p-value	0.4548	0.8441	0.4707	0.6015	0.7605	0.2916
	n =	23	23	23	23	23	23
Interleukin-10 (Extrapolation) (Cov: Age & Sex)	Coefficient	-0.0616	0.0025	-0.1902	-0.1183	-0.0490	0.1495
	p-value	0.6372	0.9860	0.1716	0.3821	0.7351	0.2938
	n =	23	23	23	23	23	23
TNF (Substitution) (Cov: Age & Sex)	Coefficient	-0.0687	-0.1882	-0.1601	-0.0900	-0.0068	0.0684
	p-value	0.5707	0.1498	0.2870	0.4711	0.9598	0.5982
	n =	23	23	23	23	23	23
TNF (Extrapolation) (Cov: Age & Sex)	Coefficient	-0.0688	-0.2286	-0.1411	-0.0773	0.0206	0.0314
	p-value	0.5697	0.0791	0.3487	0.5346	0.8776	0.8087
	n =	23	23	23	23	23	23
VEGF (Substitution) (Cov: Age & Sex)	Coefficient	0.0350	-0.2114	0.0039	0.1975	0.2928	-0.1360
	p-value	0.7752	0.1111	0.9791	0.1266	0.0322	0.3022
	n =	23	23	23	23	23	23
VEGF (Extrapolation) (Cov: Age & Sex)	Coefficient	0.0660	-0.1880	-0.0243	0.2327	0.3071	-0.1161
	p-value	0.5889	0.1542	0.8647	0.0698	0.0229	0.3758
	n =	23	23	23	23	23	23

**Table 47:** Linear correlations for mineral intake with plasma cytokine concentrations. Correlation analysis was performed on repeated measures of each variable, and age and sex were used as covariates. Additionally, all dietary intakes were adjusted for total calorie intake.

<i>Repeated Measure Correlations for Study Participants with a History of Colorectal Cancer: Plasma Cytokine Concentrations vs. Mineral Intake</i>								
		Zinc	Calcium	Potassium	Sodium	Iron	Magnesium	Selenium
Interleukin-2 (Substitution) (Cov: Age & Sex)	Coefficient	-0.0553	-0.0268	-0.0127	0.0424	-0.0123	-0.1358	0.0490
	p-value	0.6938	0.8556	0.9264	0.9302	0.9306	0.3517	0.7289
	n =	23	23	23	23	23	23	23
Interleukin-2 (Extrapolation) (Cov: Age & Sex)	Coefficient	-0.0327	0.0269	-0.0563	-0.0848	-0.0684	-0.1980	-0.0649
	p-value	0.7961	0.8497	0.6737	0.4860	0.6236	0.1728	0.6425
	n =	23	23	23	23	23	23	23
Interleukin-4 (Substitution) (Cov: Age & Sex)	Coefficient	-0.0358	-0.0315	-0.0060	0.0010	-0.0286	-0.1448	0.0279
	p-value	0.7885	0.8305	0.9661	0.9939	0.8402	0.3316	0.8427
	n =	23	23	23	23	23	23	23
Interleukin-4 (Extrapolation) (Cov: Age & Sex)	Coefficient	-0.0129	-0.0127	0.0059	0.0156	-0.0430	-0.1600	-0.0163
	p-value	0.9200	0.9296	0.9650	0.8998	0.7586	0.2758	0.9068
	n =	23	23	23	23	23	23	23
Interleukin-6 (Substitution) (Cov: Age & Sex)	Coefficient	-0.0669	-0.0387	0.0310	0.0213	-0.0517	-0.1007	-0.0030
	p-value	0.6317	0.7874	0.8240	0.9329	0.7094	0.4879	0.9829
	n =	23	23	23	23	23	23	23
Interleukin-6 (Extrapolation) (Cov: Age & Sex)	Coefficient	-0.1431	0.1238	-0.0028	0.0163	-0.0593	-0.1502	-0.1073
	p-value	0.2576	0.3890	0.9833	0.8917	0.6737	0.3058	0.4432
	n =	23	23	23	23	23	23	23
Interleukin-8 (Substitution) (Cov: Age & Sex)	Coefficient	0.0033	-0.1911	-0.0774	0.0230	-0.2310	-0.1516	-0.0663
	p-value	0.9825	0.1839	0.5746	0.8930	0.1028	0.2623	0.6385
	n =	23	23	23	23	23	23	23
Interleukin-8 (Extrapolation) (Cov: Age & Sex)	Coefficient	-0.0636	-0.0932	-0.0874	0.0230	-0.1803	-0.2585	-0.1085
	p-value	0.6633	0.5151	0.5219	0.9549	0.1990	0.0702	0.4422
	n =	23	23	23	23	23	23	23
Interleukin-10 (Substitution) (Cov: Age & Sex)	Coefficient	-0.0092	-0.0256	-0.0049	0.0403	0.0795	-0.0510	0.0569
	p-value	0.9470	0.8656	0.9723	0.8903	0.5868	0.7356	0.6875
	n =	23	23	23	23	23	23	23
Interleukin-10 (Extrapolation) (Cov: Age & Sex)	Coefficient	-0.0691	0.0399	-0.0277	-0.0343	-0.0964	-0.2418	-0.0807
	p-value	0.5904	0.7894	0.8432	0.9094	0.5111	0.1133	0.5633
	n =	23	23	23	23	23	23	23
TNF (Substitution) (Cov: Age & Sex)	Coefficient	0.0733	-0.0953	-0.0468	0.0343	-0.1197	-0.1791	0.1516
	p-value	0.6417	0.4910	0.7228	0.8754	0.3789	0.1939	0.2864
	n =	23	23	23	23	23	23	23
TNF (Extrapolation) (Cov: Age & Sex)	Coefficient	0.0886	-0.1412	-0.0133	0.0487	-0.1096	-0.1692	0.1388
	p-value	0.5758	0.3036	0.9196	0.9034	0.4188	0.2185	0.3289
	n =	23	23	23	23	23	23	23
VEGF (Substitution) (Cov: Age & Sex)	Coefficient	-0.1077	0.0505	0.1944	0.0411	0.2099	0.2574	-0.0050
	p-value	0.4185	0.7170	0.1358	0.7317	0.1247	0.0694	0.9719
	n =	23	23	23	23	23	23	23
VEGF (Extrapolation) (Cov: Age & Sex)	Coefficient	-0.0926	0.1044	0.1843	0.0463	0.2499	0.2178	-0.0390
	p-value	0.4505	0.4449	0.1538	0.6975	0.0639	0.0982	0.7827
	n =	23	23	23	23	23	23	23

**Table 48:** Linear correlations for macronutrient, fatty acid, and fiber intake with plasma cytokine concentrations. Correlation analysis was performed on repeated measures of each variable, and age and sex were used as covariates. Additionally, all dietary intakes were adjusted for total calorie intake.

<i>Repeated Measure Correlations for Study Participants with a History of Colorectal Cancer: Plasma Cytokine Concentrations vs. Calorie, Protein, Carbohydrate, Fat, and Fiber Intake</i>									
		Protein	Carbohydrate	Fat	Saturated Fat	Oleic Acid	Linoleic Acid	Linolenic Acid	Fiber
Interleukin-2 (Substitution) (Cov: Age & Sex)	Coefficient	-0.2556	0.1073	-0.1610	-0.0112	-0.1606	-0.0945	0.0025	-0.0712
	p-value	0.2559	0.4424	0.5441	0.9389	0.2881	0.4823	0.9839	0.6124
	n =	23	23	23	23	23	23	23	23
Interleukin-2 (Extrapolation) (Cov: Age & Sex)	Coefficient	-0.1087	0.1582	-0.0566	0.0213	-0.2007	-0.1446	-0.0218	-0.0638
	p-value	0.3737	0.2521	0.6687	0.8778	0.1692	0.2694	0.8606	0.6465
	n =	23	23	23	23	23	23	23	23
Interleukin-4 (Substitution) (Cov: Age & Sex)	Coefficient	-0.2670	0.0888	-0.1873	0.0416	-0.0788	-0.0700	-0.0109	-0.0997
	p-value	0.2255	0.5290	0.4727	0.7749	0.6002	0.5964	0.9310	0.4861
	n =	23	23	23	23	23	23	23	23
Interleukin-4 (Extrapolation) (Cov: Age & Sex)	Coefficient	0.0408	0.1260	0.0701	0.0445	-0.1623	-0.1411	-0.0225	-0.0371
	p-value	0.7425	0.3638	0.6046	0.7492	0.2681	0.2824	0.8570	0.7917
	n =	23	23	23	23	23	23	23	23
Interleukin-6 (Substitution) (Cov: Age & Sex)	Coefficient	-0.3086	0.0458	-0.1082	-0.0201	0.0214	0.0288	-0.0304	-0.1755
	p-value	0.1638	0.7394	0.6856	0.8894	0.8840	0.8233	0.8034	0.2080
	n =	23	23	23	23	23	23	23	23
Interleukin-6 (Extrapolation) (Cov: Age & Sex)	Coefficient	-0.0768	0.0665	-0.4330	0.0055	-0.0463	-0.0688	0.0617	0.0692
	p-value	0.5236	0.6300	0.0635	0.9691	0.7506	0.5998	0.6219	0.6233
	n =	23	23	23	23	23	23	23	23
Interleukin-8 (Substitution) (Cov: Age & Sex)	Coefficient	-0.3888	0.0889	-0.1715	-0.0052	-0.0188	-0.1637	-0.2139	-0.2401
	p-value	0.0772	0.5240	0.5214	0.9713	0.9003	0.2050	0.0807	0.0865
	n =	23	23	23	23	23	23	23	23
Interleukin-8 (Extrapolation) (Cov: Age & Sex)	Coefficient	0.0739	0.1376	-0.2572	-0.0346	-0.0257	-0.1528	-0.1303	-0.1352
	p-value	0.6603	0.3223	0.3271	0.8086	0.8618	0.2349	0.2815	0.3313
	n =	23	23	23	23	23	23	23	23
Interleukin-10 (Substitution) (Cov: Age & Sex)	Coefficient	-0.3741	0.0825	-0.1561	-0.0805	-0.0519	0.0323	0.0421	-0.0348
	p-value	0.0837	0.5648	0.5563	0.5967	0.7385	0.8132	0.7404	0.8109
	n =	23	23	23	23	23	23	23	23
Interleukin-10 (Extrapolation) (Cov: Age & Sex)	Coefficient	-0.0829	0.1211	-0.0086	0.0895	-0.1264	-0.1518	-0.0564	-0.0904
	p-value	0.4979	0.4017	0.9486	0.5339	0.4097	0.2647	0.6602	0.5365
	n =	23	23	23	23	23	23	23	23
TNF (Substitution) (Cov: Age & Sex)	Coefficient	-0.1806	0.0007	-0.2316	-0.0173	-0.0714	-0.1773	0.0291	0.0049
	p-value	0.4383	0.9961	0.3841	0.8996	0.6082	0.1587	0.8106	0.9709
	n =	23	23	23	23	23	23	23	23
TNF (Extrapolation) (Cov: Age & Sex)	Coefficient	-0.1800	0.0260	-0.2585	-0.0551	-0.1033	-0.1899	0.0143	0.0380
	p-value	0.4401	0.8485	0.3289	0.6854	0.4526	0.1307	0.9061	0.7782
	n =	23	23	23	23	23	23	23	23
VEGF (Substitution) (Cov: Age & Sex)	Coefficient	-0.3021	0.1226	-0.4342	-0.2482	0.0332	0.1714	0.1340	0.2416
	p-value	0.1724	0.3139	0.0738	0.0692	0.8121	0.1950	0.2753	0.0720
	n =	23	23	23	23	23	23	23	23
VEGF (Extrapolation) (Cov: Age & Sex)	Coefficient	-0.1511	0.1162	-0.1704	-0.2355	0.0310	0.1994	0.1722	0.2623
	p-value	0.2689	0.3375	0.2426	0.0816	0.8199	0.1203	0.1574	0.0542
	n =	23	23	23	23	23	23	23	23

### 3.10 Differences in study variables between cohorts

When comparing demographics, lipid levels, and cytokine concentration, the only significant differences found between study participants with a history of colorectal cancer and participants without a history of cancer were in participant's age and in triglyceride level at day 14. Individuals with a history of colorectal cancer were found to be significantly older than those without a history of cancer ( $\mu_w - \mu_{w/o} = 20.9$  years; 95% CI=[12.1, 29.7];  $p < 0.0001$ ). In regards to triglyceride level, individuals with a history of colorectal cancer were observed to have significantly greater levels of triglycerides compared to individuals without a history of colorectal cancer (RoGM=1.55; 95% CI=[1.06, 2.27];  $p=0.024$ ). This difference was not significant at day 0 (RoGM=1.42; 95% CI=[0.98, 2.07];  $p=0.065$ ) or at day 28 (RoGM=1.33; 95% CI=[0.91, 1.93];  $p=0.134$ ). No significant differences were found in BMI, weight, total cholesterol, HDL, LDL, or any cytokine.

The only other significant differences between the two study cohorts were observed within nutrient intake. At day 0, individuals with a history of colorectal cancer were found to have significantly lower intakes of vitamin A (RoGM=0.51; 95% CI=[0.32, 0.81];  $p=0.006$ ), zinc (RoGM=0.73; 95% CI=[0.55, 0.98];  $p=0.038$ ), potassium (RoGM=0.72; 95% CI=[0.59, 0.87];  $p=0.0017$ ), and iron (RoGM=0.70; 95% CI=[0.50, 0.99];  $p=0.041$ ). These differences were not significant at day 14: vitamin A (RoGM=0.86; 95% CI=[0.59, 1.26];  $p=0.4359$ ), zinc (RoGM=1.14; 95% CI=[0.90, 1.44];  $p=0.277$ ), potassium (RoGM=1.02; 95% CI=[0.89, 1.17];  $p=0.7349$ ), and iron (RoGM=0.97; 95% CI=[0.78, 1.19];  $p=0.740$ ). At day 28, the difference in potassium intake between the two cohorts was switched, and individuals with a history of colorectal cancer were found to have significantly higher intake than the other cohort (RoGM=1.21; 95% CI=[1.03, 1.42];  $p=0.0203$ ). Otherwise, intakes of vitamin A (RoGM=1.18;

95% CI=[0.90, 1.55]; p=0.219), zinc (RoGM=1.18; 95% CI=[0.97, 1.44]; p=0.095), and iron (RoGM=1.01; 95% CI=[0.81, 1.26]; p=0.928) at day 28 were not significantly different between the two cohorts.

**Table 49:** Comparison of age, weight, body mass index, total cholesterol, low-density lipoprotein, and high-density lipoprotein of study participants without a history of colorectal cancer (n=11) to participants with a history of colorectal cancer (n=29). Participants with a history of CRC were significantly older than participants without a history of CRC. Otherwise, no significant differences were observed between the two cohorts. All variables displayed above were normally distributed with similar variances between cohorts.

<i>Linear Regression Analysis between Cohorts: Comparison of Age, Weight, BMI, and Serum Lipid Levels between Study Participants With and Without a History of Colorectal Cancer</i>								
	Time Point	CRC Cohort Mean	No CRC Cohort Mean	Difference of Means	Standard Error	95% Confidence Limits		p-value
Age (years)	Day 0	61.6	40.7	20.9	4.3	12.1	29.7	<.0001
	Day 14	61.6	40.7	20.9	4.3	12.1	29.7	<.0001
	Day 28	61.7	40.7	20.9	4.4	12.1	29.8	<.0001
Weight (kg)	Day 0	80.2	70.8	9.4	6.4	-3.5	22.3	0.148
	Day 14	79.7	70.8	9.0	6.3	-3.9	21.8	0.165
	Day 28	79.9	70.4	9.5	6.4	-3.5	22.4	0.146
BMI (kg/m <sup>2</sup> )	Day 0	28.1	24.5	3.6	1.9	-0.3	7.5	0.068
	Day 14	28.0	25.2	2.8	2.1	-1.5	7.1	0.190
	Day 28	28.0	25.1	3.0	2.1	-1.3	7.3	0.170
Total Cholesterol (mg/dL)	Day 0	186.5	190.0	-3.5	15.8	-35.4	28.4	0.826
	Day 14	186.8	183.8	3.0	15.1	-27.5	33.5	0.845
	Day 28	188.5	182.5	5.9	15.1	-24.6	36.4	0.696
LDL (mg/dL)	Day 0	105.9	117.9	-12.0	13.0	-38.4	14.3	0.361
	Day 14	104.4	113.7	-9.3	12.3	-34.1	15.5	0.452
	Day 28	107.1	109.5	-2.4	13.0	-28.7	23.9	0.855
HDL (mg/dL)	Day 0	52.5	53.1	-0.6	5.2	-11.1	9.9	0.908
	Day 14	51.2	51.1	0.1	5.1	-10.1	10.3	0.987
	Day 28	51.6	52.4	-0.8	5.2	-11.4	9.8	0.883

**Table 50:** Comparison of serum triglyceride level of study participants without a history of colorectal cancer (n=11) to participants with a history of colorectal cancer (n=29). No significant difference was observed between the two cohorts. Serum triglycerides within the cohort of participants with a history CRC were not normally distributed, and a natural logarithm transformation of both cohorts was performed prior to analysis. A back transformation was performed on the difference of the cohorts' transformed mean to obtain a ratio of the geometric means.

<i>Linear Regression Analysis between Cohorts: Comparison of Serum Triglyceride Level between Study Participants With and Without a History of Colorectal Cancer</i>								
	Time Point	CRC Cohort Mean	No CRC Cohort Mean	Difference of Means	Standard Error	95% Confidence Limits		p-value
Triglycerides (mg/dL)	Day 0	143.07	96.73	1.42	1.20	0.98	2.07	0.065
	Day 14	157.76	97.36	1.55	1.21	1.06	2.27	0.024
	Day 28	150.86	106.18	1.33	1.20	0.91	1.93	0.134

**Table 51:** Comparison of plasma cytokine concentrations of study participants without a history of colorectal cancer (n=11) to participants with a history of colorectal cancer (n=29). Variables shown above include the substitution and extrapolation data set for the following cytokines: IL-2, IL-4, IL-6, IL-8, IL-10, and TNF. The quality controls of the VEGF immunoassay failed for the cohort of participants without a history of CRC, and therefore, VEGF was not compared between the two cohorts. No significant differences in cytokine concentrations were observed between the two cohorts. All cytokine data within both cohorts was not normally distributed, and a natural logarithm transformation was performed prior to analysis. A back transformation was performed on the difference of the cohorts' transformed mean to obtain a ratio of the geometric means.

<i>Linear Regression Analysis between Cohorts: Comparison of Plasma Cytokine Concentrations between Study Participants With and Without a History of Colorectal Cancer</i>								
(pg/mL)	Time Point	CRC Cohort Mean	No CRC Cohort Mean	Difference of Means	Standard Error	95% Confidence Limits		p-value
Interleukin-2 (Substitution)	Day 0	7.95	21.07	0.97	1.53	0.41	2.30	0.939
	Day 14	7.33	18.67	1.03	1.53	0.44	2.44	0.941
	Day 28	7.22	18.03	0.99	1.52	0.42	2.32	0.974
Interleukin-2 (Extrapolation)	Day 0	7.51	20.49	1.33	3.43	0.11	16.39	0.818
	Day 14	6.86	18.04	1.69	3.23	0.15	18.40	0.659
	Day 28	6.80	17.31	2.14	3.44	0.17	26.49	0.544
Interleukin-4 (Substitution)	Day 0	10.88	46.42	0.66	1.71	0.22	1.98	0.447
	Day 14	10.52	43.04	0.92	1.69	0.31	2.70	0.878
	Day 28	10.73	40.15	0.86	1.70	0.29	2.53	0.777
Interleukin-4 (Extrapolation)	Day 0	10.32	45.70	0.93	4.03	0.05	15.99	0.961
	Day 14	9.87	42.28	1.25	3.94	0.08	20.45	0.872
	Day 28	10.15	39.62	0.76	3.84	0.05	11.77	0.840
Interleukin-6 (Substitution)	Day 0	4.90	26.16	0.65	1.50	0.29	1.48	0.295
	Day 14	4.78	23.52	0.80	1.49	0.35	1.81	0.578
	Day 28	5.33	22.88	0.84	1.52	0.36	1.97	0.676
Interleukin-6 (Extrapolation)	Day 0	4.58	25.52	1.52	2.60	0.22	10.66	0.665
	Day 14	4.60	23.31	1.45	2.59	0.21	10.03	0.700
	Day 28	4.97	22.20	2.34	2.91	0.27	20.58	0.433
Interleukin-8 (Substitution)	Day 0	8.11	17.39	0.87	1.44	0.41	1.84	0.715
	Day 14	6.87	17.95	0.70	1.35	0.38	1.30	0.254
	Day 28	6.76	16.60	0.77	1.37	0.40	1.46	0.405
Interleukin-8 (Extrapolation)	Day 0	8.14	17.51	0.71	1.73	0.23	2.18	0.539
	Day 14	6.97	18.03	0.71	1.32	0.40	1.25	0.223
	Day 28	6.78	16.66	0.72	1.41	0.36	1.45	0.344
Interleukin-10 (Substitution)	Day 0	10.24	32.99	0.91	1.62	0.34	2.44	0.842
	Day 14	9.74	32.14	0.80	1.58	0.32	2.03	0.628
	Day 28	9.67	29.94	0.91	1.62	0.34	2.45	0.853
Interleukin-10 (Extrapolation)	Day 0	9.96	32.52	1.95	3.27	0.17	21.70	0.578
	Day 14	9.28	31.97	0.47	3.16	0.04	4.86	0.512
	Day 28	9.17	29.49	0.96	3.66	0.07	13.51	0.975
Tumor Necrosis Factor (Substitution)	Day 0	9.51	12.77	0.91	1.30	0.54	1.55	0.726
	Day 14	9.78	11.84	1.04	1.23	0.68	1.58	0.849
	Day 28	9.75	10.91	1.11	1.21	0.76	1.64	0.577
Tumor Necrosis Factor (Extrapolation)	Day 0	9.64	12.82	0.94	1.25	0.60	1.49	0.798
	Day 14	9.78	11.97	0.98	1.21	0.67	1.44	0.930
	Day 28	9.75	10.91	1.11	1.21	0.76	1.64	0.577

**Table 52:** Comparison of sodium, calorie, protein, and total fat intake of study participants without a history of colorectal cancer (n=11) to participants with a history of colorectal cancer (n=29). No significant differences were observed between the two cohorts for the displayed variables. All variables shown above were normally distributed with comparable variances between cohorts.

<i>Linear Regression Analysis between Cohorts: Comparison of Sodium, Calorie, Protein, and Fat Intake between Study Participants With and Without a History of Colorectal Cancer</i>								
	Time Point	CRC Cohort Mean	No CRC Cohort Mean	Difference of Means	Standard Error	95% Confidence Limits		p-value
Sodium (mg)	Day 0	2957.4	2849.5	108.0	275.2	-451.3	667.2	0.697
	Day 14	2814.3	3092.4	-278.2	316.8	-920.0	363.7	0.386
	Day 28	2770.4	2682.2	88.2	255.6	-429.8	606.2	0.732
Calorie	Day 0	1983.8	2006.1	-22.3	174.3	-376.5	331.8	0.899
	Day 14	1947.0	2015.9	-68.9	148.2	-369.2	231.5	0.645
	Day 28	2019.2	1888.6	130.6	155.0	-183.4	444.7	0.405
Protein (g)	Day 0	76.3	78.6	-2.4	7.2	-17.0	12.2	0.744
	Day 14	79.7	85.2	-5.5	6.7	-19.0	7.9	0.410
	Day 28	78.6	69.9	8.7	6.2	-4.0	21.3	0.173
Fat (g)	Day 0	76.4	78.6	-2.2	9.3	-21.1	16.7	0.815
	Day 14	75.2	72.2	3.0	7.3	-11.7	17.7	0.683
	Day 28	74.9	70.9	4.0	8.0	-12.1	20.1	0.618

**Table 53:** Comparison of dietary intake variables of study participants without a history of colorectal cancer (n=11) to participants with a history of colorectal cancer (n=29). Variables shown above include intake of vitamin A, vitamin C, zinc, calcium, potassium, iron, carbohydrate, saturated fat, and fiber. At day 0, vitamin A, zinc, potassium, and iron intake were significantly lower in participants with a history of CRC compared to those without a history of CRC. At day 28, potassium intake was found to be significantly higher in participants with a history of colorectal cancer. All displayed variables were not distributed normally, and a natural logarithm transformation was performed prior to analysis. A back transformation was performed on the difference of the cohorts' transformed mean to obtain a ratio of the geometric means.

<i>Linear Regression Analysis between Cohorts: Comparison of Nutrient Intake between Study Participants With and Without a History of Colorectal Cancer</i>								
	Time Point	CRC Cohort Mean	No CRC Cohort Mean	Difference of Means	Standard Error	95% Confidence Limits		p-value
Vitamin A (µg)	Day 0	828.3	1376.3	0.51	1.26	0.32	0.81	0.006
	Day 14	1149.0	1293.7	0.86	1.21	0.59	1.26	0.436
	Day 28	1198.8	996.0	1.18	1.14	0.90	1.55	0.219
Vitamin C (mg)	Day 0	102.2	130.1	0.60	1.30	0.35	1.03	0.062
	Day 14	127.2	105.3	1.11	1.21	0.76	1.63	0.586
	Day 28	143.4	123.2	1.14	1.18	0.81	1.60	0.433
Zinc (mg)	Day 0	7.8	9.9	0.73	1.16	0.55	0.98	0.038
	Day 14	10.3	8.8	1.14	1.12	0.90	1.44	0.277
	Day 28	9.8	8.4	1.18	1.10	0.97	1.44	0.095
Calcium (mg)	Day 0	966.5	1021.8	0.86	1.17	0.62	1.18	0.344
	Day 14	1016.4	1001.6	0.98	1.11	0.79	1.21	0.850
	Day 28	1055.4	967.2	1.05	1.11	0.86	1.30	0.604
Potassium (mg)	Day 0	2605.4	3511.2	0.72	1.10	0.59	0.87	0.002
	Day 14	3292.5	3204.4	1.02	1.07	0.89	1.17	0.735
	Day 28	3553.9	2923.5	1.21	1.08	1.03	1.42	0.020
Iron (mg)	Day 0	14.3	18.1	0.70	1.18	0.50	0.99	0.041
	Day 14	15.8	16.7	0.97	1.11	0.78	1.19	0.740
	Day 28	17.1	16.9	1.01	1.12	0.81	1.26	0.928
Carbohydrate (g)	Day 0	252.1	245.5	0.99	1.10	0.81	1.21	0.901
	Day 14	244.2	257.5	0.94	1.08	0.80	1.10	0.405
	Day 28	264.9	246.7	1.07	1.09	0.90	1.26	0.429
Saturated Fat (g)	Day 0	23.5	27.7	0.82	1.14	0.63	1.07	0.136
	Day 14	26.0	26.1	0.99	1.11	0.80	1.23	0.925
	Day 28	25.8	26.8	0.92	1.13	0.72	1.18	0.508
Fiber (g)	Day 0	24.7	30.2	0.75	1.16	0.56	1.01	0.056
	Day 14	29.3	30.4	0.97	1.08	0.82	1.14	0.679
	Day 28	30.4	27.9	1.08	1.10	0.88	1.31	0.459

### 3.11 Correlation between experimental methods for telomere length measurement

Due to variability within the control cell line used for inter-batch comparison of telomere lengths as measured by IQ-FISH, correlation analysis between telomere lengths as measured by IQ-FISH and qPCR was performed relative to each IQ-FISH batch. In regards to batch one of IQ-FISH, multiplex qPCR telomere length was positively but non-significantly linearly correlated ( $r=0.3253$ ;  $p=0.3357$ ). For batch two, multiplex qPCR telomere length was also positively but non-significantly linearly correlated ( $r=0.2607$ ;  $p=0.3205$ ). Finally, for batch three of IQ-FISH, multiplex qPCR telomere length was positively and significantly linearly correlated ( $r=0.4793$ ;  $p=0.0455$ ).

**Table 54:** Linear correlations between multiplex qPCR telomere length and respective batches of IQ-FISH telomere length. Telomere length as measured by multiplex qPCR was positively correlated with all three batches of IQ-FISH. However, the only significant correlation between the two experimental methods for telomere length was observed between multiplex qPCR telomere length and IQ-FISH batch 3. Adjusted repeated measures correlations over three time points using sex as a covariate was performed to determine overall association between the two methods.

<i>Repeated Measure Correlations for Study Participants with a History of Colorectal Cancer: Multiplex qPCR Telomere Length vs. IQ-FISH Telomere Length</i>				
		IQ-FISH Telomere Length Batch #1	IQ-FISH Telomere Length Batch #2	IQ-FISH Telomere Length Batch #3
Multiplex qPCR Telomere Length (Cov: Sex)	Coefficient	0.3253	0.2607	0.4793
	p-value	0.3357	0.3205	0.0455
	n =	6	7	8

## CHAPTER 4: DISCUSSION

### **4.1 No positive effect on plasma cytokine concentrations or leukocyte telomere length after dietary supplementation with rice bran or navy beans**

The primary hypothesis of this study was that individuals who consumed a navy bean or rice bran supplemented diet for 28 days would display decreased concentrations of pro-inflammatory cytokines, increased concentrations of anti-inflammatory cytokines, and slower rates of leukocyte telomere length degradation when compared to individuals consuming a control diet. Similarly, it was proposed that the navy bean and rice bran diet groups at day 28 would have decreased levels of pro-inflammatory cytokines compared to baseline values. These notions were based on the known anti-inflammatory effects of high dietary fiber intake, as well as the high concentration of phenolic compounds and other bioactive phytochemicals in both rice bran and navy beans.

#### *4.1.1 Relative increase in TNF and VEGF concentrations within navy bean diet group*

Contrary to predictions, no significant positive effect was found in plasma cytokine concentrations or leukocyte telomere length after dietary supplementation with rice bran or navy beans. In contrast, a pro-inflammatory response was observed as individuals with a history of colorectal cancer who consumed a navy bean supplemented diet were found to have significantly higher plasma concentrations of TNF and VEGF at day 28 than individuals who consumed a placebo-control diet. As consumption of cooked navy beans has previously been shown to reduce systemic levels of pro-inflammatory cytokines, the relative elevation in plasma TNF and VEGF

concentrations within the navy bean treatment group compared to the control group is unexpected and difficult to interpret.[208]

A potential cause of the pro-inflammatory effects observed with consumption of the navy bean diet is that the navy bean powder used in this study could have contained low levels of a mitogenic glycoprotein, phytohemagglutinin (PHA).[227] PHA is a lectin produced by legumes that is well known for its toxic effects.[227-239] Previous studies have found that the concentration of PHA in uncooked beans is very high and typically ranges from 1,000 to 10,000 ppm.[240] However, as PHA is heat-labile, it is undetectable in properly cooked beans when measured using an ELISA method with a sensitivity of 30 ppm.[241-244] Given that the navy bean powder in this study was obtained from a commercial source and was cooked in accordance with industry standards, it is less likely any hypothetical existence of PHA was a result of beans being improperly prepared. Therefore, if PHA was present in the navy bean powder used in this study, it is most likely to have been in concentrations below 30 ppm, which would correspond to a maximum daily intake of 1.05 milligrams per day per participant. As previous *in vitro* experiments have found that TNF and VEGF secretion by leukocytes is stimulated by PHA treatment, it is possible that the increase in plasma TNF and VEGF concentrations observed in this study was a result of sustained, low dose PHA exposure.[245-248] However, currently, the explicit effects of chronic ingestion of low residual PHA are unknown, and accounts of PHA consumption by humans are related to acute ingestion of raw or under-cooked beans.[249-251] Consequently, further evaluation of potential PHA content within the cooked navy bean powder used as a dietary treatment in this study is indicated in order to clarify if it is a possible cause of the significant difference in plasma TNF and VEGF concentrations between the navy bean and placebo-control diet groups.

#### *4.1.2 Study limitations and potential factors influencing results*

While no other significant outcomes were observed in regards to plasma cytokine concentrations or rate of leukocyte telomere shortening after dietary supplementation, the reasons for this are likely due to other influences rather than the inefficacy of rice bran and navy beans. Possible explanations for not obtaining results in accordance with the study's primary hypothesis include the short duration of the study, the relatively small sample size of the study, and the significant differences in cytokine concentrations and leukocyte telomere length between sexes. Other factors possibly involved include the chosen dosage of the rice bran and navy bean interventions and the cultivar of rice bran and navy beans used. Additionally, uncontrolled for inter-individual factors within the study population such as physical activity, psychosocial elements, socioeconomic status, and the use of immunomodulatory medications could conceivably have influenced the outcome of the study.

In comparison to other studies that have investigated the effects of dietary intervention on systemic cytokine concentrations, the duration of this study is relatively short, and as a result, the hypothesized effects of navy bean and rice bran supplementation may require a longer term of dietary intervention in order to be demonstrated. Prior high-fiber dietary intervention trials have shown significantly decreased plasma IL-6, TNF, and IL-8 concentrations within as short a period as 6 weeks, so it is possible that slightly prolonged intervention with rice bran or navy beans would have demonstrated favorable anti-inflammatory effects.[252] Nevertheless, the effects of dietary interventions are more consistently demonstrated with longer extents of intervention, and trials lasting over 6 months typically produce the most successful outcomes.[253-255]

Similarly, due to the short duration of the study, it is reasonable that no significant changes in telomere length were observed. The majority of longitudinal studies of leukocyte telomere length typically only detect significant changes after several years instead of weeks, with only one known study observing a significant change in as little as six months.[256-260] In general, because most circulating mature leukocytes are myeloid-derived cells that are terminally differentiated and lack the capability to replicate, leukocyte telomere length is primarily a reflection of the telomere length of hematopoietic stem cells.[261, 262] While hematopoietic stem cells possess low levels of telomerase activity, these levels are insufficient to prevent incremental telomere loss with each cellular replication, which in healthy adults is estimated to occur at a rate ranging from 0.6 to 2.2 times per year.[261, 263-265] Given these estimates, within a time frame of four weeks, only between 4.6% and 16.9% of hematopoietic stem cells would be expected to have replicated, which realistically indicates that a change in average peripheral leukocyte telomere length would be relatively small. Therefore, in order to fully evaluate the potential impact of rice bran or navy bean dietary supplementation on the rate of telomere length attrition, a longer time of dietary intervention is required.

If a sustained dietary intervention is not practical, another possible biomarker of interest for gauging the effect of short-term diet supplementation is the measurement of the activity of telomerase, the enzyme responsible for telomere elongation. One study interested in the effect of comprehensive lifestyle changes in men with a history of prostate cancer found significant increases in telomerase activity compared to a control group after only three months of intervention.[266] A subsequent follow up study of this population showed those with increased telomerase activity at three months had longer telomeres five years later.[256, 266] Therefore, at least for short-term lifestyle interventions, it may be more meaningful to measure differences in

telomerase activity over weeks with follow up measurement of telomere length months to years later.

Another possible explanation for not observing a significant effect of rice bran or navy bean supplementation on inflammatory cytokine concentrations or telomere length is the study's limited statistical power secondary to the small number of individuals within each cohort and diet group. This is an issue as a study with a low statistical power has a decreased likelihood of revealing a true effect. Therefore, it is possible that a repeated study with a large sample size could demonstrate the proposed systemic anti-inflammatory effects of navy bean and rice bran consumption. In this report, when using the variances associated with diet group cytokine concentration and telomere length data at day 28 from the cohort of individuals with a history of colorectal cancer, the estimated total sample size required to achieve an 80% chance of detecting a significant result ( $p < 0.05$ ) ranged from 51 to 615 depending on the respective variable used for calculation.[267] These estimates are noticeably larger than the sample sizes used in this study, where only a total of 34 participants had cytokine values measured and 27 participants had telomere length measured.

In addition to the small sample size, the presence of both males and females in this study is another possible confounding influence that may have prevented demonstration of the anti-inflammatory effects of rice bran and navy bean diets on cytokine concentration and leukocyte telomere length. Specifically, significant differences between males and females in leukocyte telomere length and IL-2, IL-4, IL-6, IL-8, and IL-10 concentrations lead to segmentation of the already small sample size and thus, effectively further reduced the statistical power of the study.

While a two-way ANOVA analysis interested in the effects of sex and diet group on cytokine concentration and telomere length did not suggest a significant interaction between sex

and diet group, there were perceptible differences in results when analysis was performed with the consideration of potential gender influences. For example, consider the noticeable effect that including sex has in the comparison of average leukocyte telomere length between the navy bean and control diets at day 0 and day 28. In a model that does not account for the influence of sex, the navy bean group (n=10) was observed to have an average relative telomere length compared to the control group (n=10) that was 6.4% longer at day 0 (p=0.6150) and 11.7% longer at day 28 (p=0.3450). In a two-way ANOVA model that accounted for the effect of sex, the navy bean group was estimated to have an average relative telomere length compared to the control group that was 30.4% longer at day 0 (p=0.108) and 36.7% longer at day 28 (p=0.060). While the interaction between the independent variables of diet and sex was non-significant, the marked difference in p-values at day 28 between the one-way and two-way ANOVA models does demonstrate how, in the setting of a small sample size, the variable of sex had an observable influence on study outcomes. In future studies with a substantially larger sample size, this effect would likely be minimized due to greater intra-gender variability within the sample population.

Another possible explanation for not confirming the study's hypothesis is that the chosen levels of rice bran and navy bean supplementation may not have been sufficient. In this study, intervention diets were supplemented with either 35 grams per day of navy bean powder or 30 grams per day of rice bran powder. These dosages are in alignment with the levels of dry bean or rice bran intake in other studies that have found significant associations with markers of positive health.[268, 269] Yet, overall, there is a lack of data on what amount of daily intake of rice bran or navy beans is necessary in order to observe their beneficial effects, and it is probable that a larger degree of supplementation would induce a greater effect on both cytokine concentrations and the relative rate of telomere length shortening.

Determining an effective and realistic degree of dietary supplementation is difficult. In regards to inflammatory cytokines, separate studies on mice have found that intake of 40 grams per kilogram of rice bran or 740 grams per kilogram of navy beans can each decrease plasma IL-6 levels.[205-207] Obviously, in humans, these levels of intake are not practical and are most likely not necessary to achieve significant reductions in systemic inflammation. In regards to humans, dietary intervention studies interested in the effects of rice bran on cholesterol have shown that intakes of 100 grams per day, 84 grams per day, and 60 grams per day can be well tolerated and are also effective at controlling dyslipidemia.[270-272] Similarly, high levels of bean intake were well tolerated by participants within the Polyp Prevention Trial, which found individuals in the highest two quartiles of dry bean intake (30.6-233.0 grams per day) had significantly lower levels of serum IL-6 as well as a reduction in risk of advanced colorectal adenoma recurrence.[253, 268] Given that these studies indicate that larger consumption of rice bran and navy beans is clearly possible, and in light of a lack of data on the amount of supplementation that constitutes an effective treatment, it is worth considering during future dietary interventions to assess the relative differences between tiered quantities of rice bran or navy bean supplementation. Similarly, it would likely be valuable to evaluate the effects of a combination treatment of both navy beans and rice bran.

The incredible diversity of both rice bran and navy bean varieties must also be considered when assessing the effect of these foods on inflammatory markers and telomere length. The sheer volume of rice and bean cultivars is evidenced in the over 130,000 varieties of *Oryza spp.* and over 16,000 varieties of *Phaseolus vulgaris* L. stored in bio-repositories worldwide.[273, 274] This remarkable genetic diversity results in discernable differences in each variety's nutritional composition and bioactive compound content.[275-280] As this study only

investigated the effects of one variety of each food type (a non-pigmented brown rice bran and a white navy bean), the possibility exists that other varieties of rice bran or beans may be more potent inducers of anti-inflammatory responses. Therefore, further research on the relative effects of dietary intervention with a diverse selection of rice bran or beans is warranted.

The influence of non-dietary lifestyle factors may also have had an influence on the results of this study. Unfortunately, this analysis did not control for elements that previous studies have indicated are associated with both plasma cytokine concentrations and leukocyte telomere length. In particular, physical inactivity [281-287], emotional stress [288, 289], depression [290-294], and low socioeconomic position [295-298] have each been separately correlated with both shorter telomere lengths and increased inflammatory markers. These studies suggest that the effects of dietary intervention with rice bran or navy beans cannot be fully elucidated without a full understanding of each individual's physical, emotional, and social status.

Another conceivable influence that was not evaluated in this study is the potential that participants may have taken immunomodulatory medications during the intervention trial. To this author's knowledge, the only enrollment criteria in relation to medication usage were that a participant may not have taken oral antibiotics or anti-hyperlipidemia agents within a month prior to the start of the trial and also must have been at least four months removed from any chemotherapy or radiation treatment. Therefore, it is possible that participants may have used other medications with immunoregulatory potential, such as non-steroidal anti-inflammatory drugs, glucocorticoids, cytostatic agents, and anti-TNF agents.

Given that there is moderate to strong evidence for NSAID use in the prevention of colorectal adenoma recurrence, it is reasonable that a participant may have used an NSAID

during the trial.[299-304] Currently, the effect of NSAIDs on systemic cytokine levels is not entirely understood and is likely dependent on the type, frequency, and amount of NSAID used. While a select number of studies have found that NSAID use, particularly aspirin use, is significantly associated with lower levels of IL-2, IL-6, and IL-10 and higher levels of TNF [305-308], a similar number of studies have found no observable associations between NSAIDs and plasma cytokine levels.[309-313] Additionally, prior studies have indicated that the effect of NSAID use on circulating cytokine levels can be synergistically or antagonistically altered by supplementation of dietary components, such as folic acid and omega-3 fatty acids.[314, 315] In relation to leukocyte telomere length, comprehensive studies on NSAID use are severely lacking. In the only known study, no significant association was found between leukocyte telomere length and the use of NSAIDs once per week in a population of 300 participants at risk for esophageal cancer.[316, 317] Overall, given the lack of conclusive evidence on NSAIDs' effect on plasma cytokine concentrations and leukocyte telomere length, it is unclear if accounting for NSAID use would have meaningfully impacted the results of this study.

Similar to NSAIDs, the potential use of immunomodulatory medications such as glucocorticoids, cytostatic agents, or anti-TNF agents was not evaluated in this analysis. Additionally, the etiology of participants' colorectal cancer was not considered. Given that 1-2% of all colorectal cancers are associated with a coexisting diagnosis of inflammatory bowel disease (IBD), the possibility exists that participants in the study possessed a history of colitis-associated colorectal cancer and therefore may have managed their IBD symptoms with routinely prescribed medications such as budesonide, methotrexate, or infliximab.[318-323] The potential use of steroids, cytostatic agents, and anti-TNF agents during the intervention trial is an issue because these medications are known to significantly augment cytokine signaling, synthesis, and

plasma concentrations.[247, 323-332] Furthermore, cytostatic agents, which directly inhibit nucleic acid synthesis, have been associated with decreased telomerase activity in peripheral leukocytes and therefore may influence the rate of telomere length shortening in long-term users.[333, 334]

## **4.2 Multiple individual dietary factors correlate with plasma cytokine level, leukocyte telomere length, and serum lipid concentrations**

A secondary objective of this study was to investigate potential correlations between plasma cytokine concentrations, leukocyte telomere length, serum lipid profile, and nutrient intake. Based on prior research, it was hypothesized that poor dietary habits would be associated with dyslipidemia, increased inflammatory cytokines, and shorter leukocyte telomere length. Overall, the significant correlations found in the present study were consistent with this hypothesis. Additionally, the significant correlations found support recommendations for maintaining a healthy diet.

### *4.2.1 Cytokine correlations*

For plasma cytokine concentrations, after adjusting for the influences of age, sex, and total energy intake, only a few significant correlations were found:  $\alpha$ -Tocopherol intake was inversely correlated with IL-2 and IL-4, vitamin B3 intake was inversely correlated with IL-8, and vitamin B9 intake was positively correlated with VEGF.

#### 4.2.1a IL-2 and IL-4 both inversely correlated with $\alpha$ -Tocopherol intake

The inverse association of  $\alpha$ -Tocopherol intake with plasma levels of IL-2 and IL-4 is consistent with findings of multiple *in vitro* and animal studies.[335-342] However, there is a lack of human clinical trial or observational data on the association of  $\alpha$ -Tocopherol intake and plasma IL-2 or IL-4 concentrations. Overall, the majority of published studies on  $\alpha$ -Tocopherol intake and cytokine concentrations in humans have focused on cytokines other than IL-2 and IL-4, and unlike the present study, these studies have found significant inverse associations between  $\alpha$ -Tocopherol intake and pro-inflammatory cytokines IL-6, IL-8, and TNF.[343-346]

$\alpha$ -Tocopherol is one of eight isoforms of vitamin E and is a fat-soluble antioxidant that potently prevents oxidation of phospholipid membranes and plasma lipoproteins.[347, 348] Lipid peroxidation caused by free radical driven chain reactions is attenuated by  $\alpha$ -Tocopherol due to peroxy radicals having a nearly 1,000 times greater affinity for  $\alpha$ -Tocopherol than for fatty acids.[348] Additionally, beyond a general antioxidant role,  $\alpha$ -Tocopherol directly modulates several signal transduction pathways through inhibition of various transcription factors, and high doses of  $\alpha$ -Tocopherol are associated with the up-regulation of anti-inflammatory peroxisome proliferator-activated receptor gamma (PPAR- $\gamma$ ) expression and down-regulation of pro-inflammatory NF- $\kappa$ B activity.[336, 349] As gene expression of both IL-2 and IL-4 is inhibited by PPAR- $\gamma$  and promoted by NF- $\kappa$ B,  $\alpha$ -Tocopherol is likely to influence plasma IL-2 and IL-4 concentrations through these pathways.[336, 337, 350, 351]

However, while  $\alpha$ -Tocopherol has vigorous anti-inflammatory effects that have been demonstrated mechanistically, *in vitro*, and observationally, there is a lack of evidence for the ability of  $\alpha$ -Tocopherol supplementation to reduce cancer risk.[352] A large dietary intervention study investigating  $\alpha$ -Tocopherol supplementation (50 mg per day) for a median of 6 years found

no reduced risk of colorectal cancer in a population of over 25,000 male smokers.[353, 354] A similar study found no reduced risk of colorectal cancer after  $\alpha$ -Tocopherol supplementation (400 IU per day) for over 5 years in a population of over 35,000 healthy males.[355] Therefore, while in the present study  $\alpha$ -Tocopherol is correlated with reduced IL-2 and IL-4, the evidence for a strong chemoprevention effect of  $\alpha$ -Tocopherol intake is currently lacking.

#### *4.2.1b IL-8 inversely correlated with vitamin B3 intake*

In regards to other cytokine correlations, the inverse association between IL-8 and vitamin B3 intake is consistent with previous *in vitro*, animal, and human clinical trial experiments.[356-361] Dietary vitamin B3, also known as niacin, is a water-soluble vitamin that is a precursor for the coenzymes nicotinamide adenine dinucleotide (NAD<sup>+</sup>/NADH) and nicotinamide adenine dinucleotide phosphate (NADP<sup>+</sup>/NADPH).[362] These coenzymes not only play vital roles in energy metabolism as electron carriers in oxidation-reduction reactions, but also are implicated in biomolecule synthesis, gene expression, calcium homeostasis, oxidative stress reduction, and apoptosis.[363] Furthermore, low cellular NAD<sup>+</sup> concentration activates a regulatory nuclear enzyme, poly(ADP-ribose) polymerase-1 (PARP-1), and PARP-1 stimulation leads to the promotion of several pro-inflammatory transcription factors, including NF- $\kappa$ B.[364] Given IL-8 production is primarily produced and secreted by macrophages through NF- $\kappa$ B pathways, the inverse association between dietary vitamin B3 intake and plasma IL-8 concentration in the present study is possibly a result of PARP-1 modulation by NAD<sup>+</sup>. [65, 67, 358]

The negative correlation with IL-8 concentration also indicates a conceivable protective effect for vitamin B3 in the progression of cancer. *In vitro* and observational studies on

colorectal cancer have found that IL-8 promotes tumor growth, metastasis, and angiogenesis, and several studies have identified IL-8 as a potential therapeutic target for colorectal cancer.[365, 366] However, direct interventional evidence for the ability of vitamin B3 to decrease IL-8 concentrations or colorectal cancer risk is lacking.[367] Therefore, while higher vitamin B3 intake is associated with lower plasma IL-8 concentration, more research is required in order to fully evaluate the potential chemoprevention effects of vitamin B3.

#### *4.2.1c VEGF positively correlated with vitamin B9 intake*

The final significant cytokine correlation found in this study was a positive association between vitamin B9 intake and plasma VEGF concentration. Vitamin B9, otherwise known as folate, is a water-soluble vitamin that is essential for multiple metabolic pathways through its function as a single-carbon donor in the *de novo* synthesis of thymidylates and purines and in the re-methylation of homocysteine to form methionine.[368] While all cell types require vitamin B9 in order to survive, the relative necessity of each cell varies with metabolic activity, and in the majority of somatic cells, vitamin B9 requirements are comparatively low compared to the requirements of fast growing cells.[369] In order to satisfy metabolic demands, fast growing cells, such as those found in tumors, preferentially express the high-affinity vitamin B9 transporter, Folate Receptor alpha (FR- $\alpha$ ).[369] Binding with FR- $\alpha$  by vitamin B9 not only leads to cellular uptake, but also activates several growth-promoting transcription factors, including STAT3.[370] Therefore, given VEGF expression is directly regulated by STAT3, the significant positive association between folate intake and VEGF in the present study may conceivably be a result of FR- $\alpha$  activation in fast growing cells.[76] As correlation analysis only assessed participants in this study that possessed a history of colorectal cancer, it is possible that higher

levels of folate intake are triggering increased VEGF expression by activation of the FR- $\alpha$ /STAT3 pathway in enduring malignant cell populations. However, further investigation is ultimately required to fully elucidate the mechanism behind the correlation between VEGF and vitamin B9.

The relationship of vitamin B9 intake and colorectal cancer risk is not entirely understood. In epidemiological studies, high vitamin B9 intake was initially indicated to lower colorectal cancer risk through presumably modulating mechanisms for DNA synthesis, repair, and integrity.[371-375] However, several meta-analyses of randomized clinical trials on vitamin B9 supplementation have found no association with colorectal cancer risk,[376-380] and there is some evidence that vitamin B9 supplementation can increase the risk of colorectal cancer and other cancers.[381-383] While the effects of intracellular vitamin B9 deficiency on actively dividing pre-neoplastic and neoplastic cells is well demonstrated by *in vitro* studies and is the basis for widely used anti-folate chemotherapeutics such as 5-fluorouracil, the impact of vitamin B9 intake in general populations is difficult to predict. It is likely that vitamin B9 inhibits tumor initiation in normal cells and promotes survival, proliferation, and angiogenesis in malignant cells.[384, 385]

#### 4.2.2 *Telomere length correlations*

In relation to leukocyte telomere length, after adjusting for age, sex, and total energy intake, telomere length was found to be significantly inversely associated with serum triglyceride level, carbohydrate intake, and saturated fat intake. Additionally, telomere length was found to be significantly associated with both age and sex, which is consistent with previous findings in

prior studies.[258, 386, 387] No other variables were significantly correlated with leukocyte telomere length.

#### *4.2.2a Telomere length inversely correlated with triglycerides*

Triglycerides are comprised of three fatty acid chains that are bonded to a three-carbon carbohydrate backbone via an ester bond, and circulating serum triglyceride levels are primarily driven by carbohydrate intake.[388] Additionally, high saturated fat intake, particularly medium chain saturated fatty acid intake, is strongly correlated with increased serum triglycerides as well as increased free serum saturated fatty acids.[389-391] Elevated levels of serum triglycerides and free saturated fatty acids are associated with pro-inflammatory processes through NF- $\kappa$ B activity and reactive oxygen species generation, and this increased oxidative stress thus promotes increased rates of telomere shortening.[392-396] In accordance with these mechanisms, observational studies have previously demonstrated significant associations between higher serum triglyceride level, saturated fat intake, and carbohydrate intake with shorter leukocyte telomere length.[397-401]

#### *4.2.2b Telomere length inversely correlated with carbohydrate and saturated fat intake*

In regards to colorectal cancer, while both high triglyceride level and shorter telomere length have each been independently and consistently correlated with risk of colorectal cancer incidence and recurrence, studies investigating the relationship between total saturated fat or carbohydrate intake and risk of colorectal cancer incidence or recurrence have been inconsistent with the majority of studies having found no significant association.[144, 402-419] Therefore, while reduced saturated fat and carbohydrate intake is associated with longer telomere length in

the present study, further research is required in order to determine if decreasing saturated fat or carbohydrate intake promotes colorectal cancer prevention.

#### *4.2.3 Lipid profile correlations*

Several dietary factors were found to be associated with serum lipids. Dietary components associated with positive influences on lipid parameters included  $\beta$ -Carotene, linolenic acid, and fiber. Conversely, saturated fat and selenium were associated with negative effects on lipid levels.

##### *4.2.3a Total cholesterol, LDL, and triglycerides inversely correlated with $\beta$ -Carotene intake*

$\beta$ -Carotene is a fat-soluble, pigmented antioxidant that was negatively correlated with serum levels of total cholesterol, LDL, and triglycerides in the present study. While prior studies have found that  $\beta$ -Carotene intake is strongly associated with decreased markers of plasma lipid oxidation, associations between  $\beta$ -Carotene intake and circulating concentrations of lipoproteins and triglycerides have been inconsistent.[420-427] The majority of studies in humans have found  $\beta$ -Carotene intake is associated with either no significant change or only a small decrease in total cholesterol and triglycerides.[420, 422, 424, 425] However, strong evidence for an anti-hyperlipidemic effect from  $\beta$ -Carotene intake was found in a recent study on rats where  $\beta$ -Carotene supplementation was associated with reduced serum levels of total cholesterol and non-HDL cholesterol and increased fecal total cholesterol content.[428] Given  $\beta$ -Carotene is a fat-soluble vitamin that is absorbed in the small intestine with other lipophilic molecules, including cholesterol and triglycerides, it was proposed that  $\beta$ -Carotene supplementation may reduce total serum cholesterol levels through preventing cholesterol absorption in the intestine.[428, 429]

Ultimately, a similar mechanism may be responsible for the inverse correlation between  $\beta$ -Carotene intake and lipids in the present study. However, further research is required in order to fully understand the mechanism behind the association.

#### *4.2.3b HDL positively correlated with linolenic acid intake; total cholesterol and HDL positively correlated with saturated fat intake*

The observed correlation between increased lipid levels (total cholesterol and HDL) and high saturated fat intake is well known and is consistent with previous studies.[430, 431] Current dietary recommendations call for substitution of saturated fats with polyunsaturated fats in order to improve lipid profile.[430] Linolenic acid is a polyunsaturated fatty acid that was positively correlated with serum HDL levels in the present study, and linolenic acid is found in two isoforms:  $\alpha$ -Linolenic acid and  $\gamma$ -Linolenic acid.  $\alpha$ -Linolenic acid is an  $\omega$ -3 fatty acid and  $\gamma$ -Linolenic acid is an  $\omega$ -6 fatty acid. In regards to previous studies, both  $\omega$ -3 fatty acids and  $\omega$ -6 fatty acids have been associated with improved lipid status, and specifically, there is strong evidence to support  $\omega$ -3 supplementation for increasing HDL cholesterol.[431-436] Therefore, in the context of prior studies and the significant correlations found in the present study, it is highly suggested to replace saturated fats with polyunsaturated fats in order to improve serum lipid profile and overall health.

#### *4.2.3c Triglycerides inversely correlated with fiber intake and positively correlated with selenium intake*

Finally, triglyceride levels were negatively correlated with fiber intake and positively correlated with selenium intake. In regards to fiber intake, the observed association is supported

by a recent meta-analysis of randomized control studies found a non-significant, negative association between triglycerides and dietary fiber.[437] In regards to selenium intake, the observed correlation is supported by a large scale cross-sectional study of over 5,000 adults with non-deficient selenium levels that found those with higher serum selenium had elevated serum triglyceride levels.[438] Therefore, given these findings and the correlations in the present study, clinical management of hypertriglyceridemia may benefit through consideration of total fiber and selenium intake.

#### *4.2.4 Dietary patterns associated with healthy lifestyles*

Recent studies indicate that dietary patterns characterized by predominately plant-based, minimally processed foods are most strongly associated with health promotion and disease prevention.[439] Given the strong influence of diet on health, the prevention of chronic disease requires the consideration of dietary patterns. In regards to the present study, the observed significant correlations support recommendations for dietary patterns designed to promote healthy living. Specifically, the correlations in this study indicate relatively higher intakes of antioxidants and fiber and lower intakes of carbohydrates and saturated fats are associated with improved markers of inflammation and aging. Therefore, it is important to consider these factors in maintaining health, and ideally, the sources of dietary components should be obtained from whole, plant-based foods.

### **4.3 Correlation between qPCR and IQ-FISH methods for telomere length measurement is non-robust**

A final objective of the study was to assess correlation between two different experimental methods for telomere length measurement, IQ-FISH and qPCR. Unfortunately, due to variation within the control cell line used for IQ-FISH, correlation between the two methods was only possible on a limited number of samples within each IQ-FISH batch. However, a significant positive correlation was found between IQ-FISH telomere lengths for batch 3 and the corresponding samples that were measured by multiplex qPCR.

#### *4.3.1 Variability in telomere length of controls as measured by IQ-FISH*

Inter-batch comparison of telomere length measured by IQ-FISH was complicated by the different effect that normalization to the Raji cell line produced relative to results obtained after normalization to the LY-S cell line. Normalization to the Raji cell line resulted in individuals in batch two having the relatively longest telomere length (2.21), followed by batch one (1.69) and then batch three (1.67). The average fluorescence intensity of the Raji cell line was highest in batch one and lowest in batch three. Normalization to the LY-S cell line produced results that indicated individuals in batch three had the relatively longest telomere length (2.03), followed by batch two (1.79) and then batch one (1.75). The average fluorescence intensity of the LY-S cell line was highest in batch one and lowest in batch three. Normalization of each experimental batch to the Raji or LY-S control produced different results, and this finding indicates inconsistency in the repeated measurements of either the Raji or LY-S cell lines. Given these conflicting trends, statistical analysis of telomere length measured by IQ-FISH was performed on

individual batches only, and IQ-FISH telomere lengths of individuals in different batches were not directly compared.

To evaluate the inconsistency demonstrated within the repeat telomere length measurements of the Raji and LY-S control cell lines, the same slides that were initially used for 2-D image acquisition were re-photographed using a different microscope that allowed for 26 Z-axis images in 0.2  $\mu\text{m}$  segments. These images were then compressed into a 2-D composite image and telomere length was re-estimated on 50 cells that had not previously been imaged. A mean fluorescence of these cells was used to re-measure telomere length within the control cell lines in order to evaluate if the relative fluorescence of the controls between the three experimental batches was consistent with the trends seen in the 2-D photographs.

Comparison of the 2-D and 3-D fluorescence intensities for the respective batches of the Raji and LY-S control lines showed that the LY-S cell line had a similar trend in both the 2-D and 3-D images whereas the Raji cell line had contradictory results in the 2-D and 3-D measurements. For the 3-D measurements, the average fluorescence of the LY-S cell line in batch one, batch two, and batch three were 99.40, 72.62, and 61.51, respectively; these results align with the 2-D images which identified batch one as the highest intensity, followed by batch two and then batch three. Additionally, the use of LY-S as a control for telomere length measurement is supported by other studies that have shown maintenance of telomere length within this cell line.[440]

For the Raji cell line, 3-D measurements revealed average fluorescence intensities of 165.65, 64.90, and 99.21 for batch one, batch two, and batch three, respectively; these findings contradict the 2-D images which showed batch three to have the lowest average intensity. A possible explanation for the inconsistency in the repeated telomere length measurements of the

Raji cell line may be caused by it being a carrier of the Epstein-Barr virus (EBV), which has been shown to promote telomere dysfunction and genomic instability.[441] EBV infection is associated with several illnesses and diseases, including Burkitt's lymphoma, Hodgkin's lymphoma, and infectious mononucleosis.[442-445] The Raji cell line is derived from a EBV-positive Burkitt's lymphoma, and in one study that utilized FISH on metaphase chromosomes, EBV-positive Burkitt's lymphoma cell lines, including Raji, were found to have an abnormal number of telomeres in 37.2% of samples.[441] Additionally, EBV-positive cells were observed to have significantly increased prevalence of dicentric chromosomes, fragments, and chromatid gaps compared to mitogen-induced B-lymphoblast cell lines.[441] Therefore, it is likely the inconsistency in interphase FISH fluorescence intensities of repeated measurements of the Raji cell line is a result of DNA damage associated with latent EBV infection and ultimately indicates that the Raji cell line is a poor control for repeat experiments of interphase FISH telomere length measurement. The telomere dysfunction effect of EBV is a likely contributor to the failure of the standard curves within the singleplex qPCR experiments.

#### *4.3.2 Significant but non-Robust correlation between IQ-FISH and qPCR methods for telomere length measurement*

No other prior studies are known to have correlated the methods of IQ-FISH and qPCR for telomere length measurement. A previous study has compared telomere length measurement by flow-FISH and qPCR, and in that study, FISH and qPCR correlated significantly in healthy individuals ( $r=0.33$ ;  $p<0.0001$ ) but not in patients with bone marrow failure or idiopathic pulmonary fibrosis ( $r=0.1$ ;  $p=0.08$ ).[446] In the present study, correlation results are inconclusive as a segment of the participants showed a significant correlation in telomere length measurement

while the majority of the participant telomere lengths did not significantly correlate between the two methods. These findings are severely limited by the issue of sample size due to inability to directly compare inter-batch IQ-FISH measurements. Ultimately, in order to fully evaluate the correlation between the two methods, repeated measurements with a larger sample size is required. However, the preliminary results in this study do suggest a modest but limited correlation between the two methods.

#### *4.3.3 Benefits and disadvantages for IQ-FISH and qPCR methods for telomere length measurement*

The methods for telomere length measurement used in this study each have inherent benefits and disadvantages that should be considered when designing future experiments. The benefits of the qPCR method include its low cost and amenability for high through-put experimental designs. However, a major disadvantage of the qPCR method is a lack of ability to compare results from different studies. The current method estimates a relative telomere length that is not comparable to results from other studies. This makes telomere lengths estimated by qPCR less useful for meta-analyses or retrospective review papers. While a procedure for absolute telomere length measurement by qPCR has been published, it has not been widely used and many researchers have reported difficulty with optimizing the standard curve require for this method.[447, 448]

In regards to interphase FISH, the advantages for this method include its ability to measure telomere length by FISH on non-actively dividing cells. However, this characteristic can also be a disadvantage as single telomeres are not able to be measured with FISH on interphase

cells. Additionally, other disadvantages includes that the FISH method requires a good deal of time to complete and the supplies and equipment required can be cost prohibitive.

## CHAPTER 5: FUTURE DIRECTIONS

The data and analysis in this thesis were completed as an ancillary component of a pilot dietary intervention trial interested in elucidating anti-inflammatory and anti-carcinogenic properties of whole grains and legumes. While an explicit demonstration of the proposed anti-inflammatory and anti-aging effects of rice bran and navy beans was not observed in the present study, the findings and considerations in this thesis are intended to provide a basis for designing and optimizing a more expansive and integrated dietary intervention program. Ultimately, more novel research remains to be completed and more previously published findings need to be replicated in order to fully clarify and validate the health promoting effects of rice bran and beans.

Indeed, in relation to cancer prevention, increased consumption of whole grains and legumes is an attainable lifestyle modification that is very likely to improve incidence and survivorship rates. However, the effects of whole grain and legume consumption must be considered in the context of other lifestyle factors or else the beneficial impact of these foods will be marginalized. Therefore, a multifaceted approach for cancer prevention that incorporates dietary as well as other advantageous lifestyle changes is recommended.

## REFERENCES

1. Ferlay J, S.I., Ervik M, Dikshit R, Eser S, Mathers C, Rebelo M, Parkin DM, Forman D, Bray, F. . *GLOBOCAN 2012 v1.1: Estimated cancer incidence, mortality, and prevalence worldwide in 2012*. 2012; Available from: <http://globocan.iarc.fr/Default.aspx>
2. *United States Cancer Statistics: 1999–2011 Incidence and Mortality Web-based Report*. 2014, Department of Health and Human Services, Centers for Disease Control and Prevention, and National Cancer Institute: Atlanta.
3. *Cancer Facts & Figures*. 2013, American Cancer Society: Atlanta.
4. Van Blarigan, E.L. and J.A. Meyerhardt, *Role of physical activity and diet after colorectal cancer diagnosis*. J Clin Oncol, 2015. **33**(16): p. 1825-34.
5. Meyerhardt, J.A., et al., *Dietary glycemic load and cancer recurrence and survival in patients with stage III colon cancer: findings from CALGB 89803*. J Natl Cancer Inst, 2012. **104**(22): p. 1702-11.
6. Meyerhardt, J.A., et al., *Association of dietary patterns with cancer recurrence and survival in patients with stage III colon cancer*. JAMA, 2007. **298**(7): p. 754-64.
7. Davies, N.J., L. Batehup, and R. Thomas, *The role of diet and physical activity in breast, colorectal, and prostate cancer survivorship: a review of the literature*. Br J Cancer, 2011. **105 Suppl 1**: p. S52-73.
8. *Colorectal Cancer*. 2014, American Cancer Society.
9. Terzic, J., et al., *Inflammation and colon cancer*. Gastroenterology, 2010. **138**(6): p. 2101-2114 e5.
10. Oyesanmi, O., et al., *Alcohol consumption and cancer risk: understanding possible causal mechanisms for breast and colorectal cancers*. Evid Rep Technol Assess (Full Rep), 2010(197): p. 1-151.
11. Kruk, J. and U. Czerniak, *Physical activity and its relation to cancer risk: updating the evidence*. Asian Pac J Cancer Prev, 2013. **14**(7): p. 3993-4003.
12. Jarosz, M., W. Sekula, and E. Rychlik, *Trends in dietary patterns, alcohol intake, tobacco smoking, and colorectal cancer in Polish population in 1960-2008*. Biomed Res Int, 2013. **2013**: p. 183204.
13. Johnson, C.M., et al., *Meta-analyses of colorectal cancer risk factors*. Cancer Causes Control, 2013. **24**(6): p. 1207-22.
14. Rustgi, A.K., *The genetics of hereditary colon cancer*. Genes Dev, 2007. **21**(20): p. 2525-38.
15. McClellan, J.L., et al., *Intestinal inflammatory cytokine response in relation to tumorigenesis in the Apc(Min/+) mouse*. Cytokine, 2012. **57**(1): p. 113-9.
16. Coussens, L.M. and Z. Werb, *Inflammation and cancer*. Nature, 2002. **420**(6917): p. 860-7.
17. Grivennikov, S.I., F.R. Greten, and M. Karin, *Immunity, inflammation, and cancer*. Cell, 2010. **140**(6): p. 883-99.
18. Chan, A.T., et al., *Long-term use of aspirin and nonsteroidal anti-inflammatory drugs and risk of colorectal cancer*. JAMA, 2005. **294**(8): p. 914-23.
19. Thun, M.J., M.M. Namboodiri, and C.W. Heath, Jr., *Aspirin use and reduced risk of fatal colon cancer*. N Engl J Med, 1991. **325**(23): p. 1593-6.
20. Nan, H., et al., *Association of aspirin and NSAID use with risk of colorectal cancer according to genetic variants*. JAMA, 2015. **313**(11): p. 1133-42.
21. Johnson, C.C., et al., *Influence of NSAID Use Among Colorectal Cancer Survivors on Cancer Outcomes*. Am J Clin Oncol, 2014.
22. Roderick, P.J., H.C. Wilkes, and T.W. Meade, *The gastrointestinal toxicity of aspirin: an overview of randomised controlled trials*. Br J Clin Pharmacol, 1993. **35**(3): p. 219-26.
23. Sostres, C., C.J. Gargallo, and A. Lanás, *Nonsteroidal anti-inflammatory drugs and upper and lower gastrointestinal mucosal damage*. Arthritis Res Ther, 2013. **15 Suppl 3**: p. S3.
24. Denlinger, C.S. and P.F. Engstrom, *Colorectal cancer survivorship: movement matters*. Cancer Prev Res (Phila), 2011. **4**(4): p. 502-11.
25. Sheflin, A.M., et al., *Pilot dietary intervention with heat-stabilized rice bran modulates stool microbiota and metabolites in healthy adults*. Nutrients, 2015. **7**(2): p. 1282-300.
26. Ho, J.W., et al., *Study protocol for "Moving Bright, Eating Smart"- A phase 2 clinical trial on the acceptability and feasibility of a diet and physical activity intervention to prevent recurrence in colorectal cancer survivors*. BMC Public Health, 2013. **13**: p. 487.
27. Grimmett, C., et al., *Diet and physical activity intervention in colorectal cancer survivors: a feasibility study*. Eur J Oncol Nurs, 2015. **19**(1): p. 1-6.
28. Davies, A.A., et al., *Nutritional interventions and outcome in patients with cancer or preinvasive lesions: systematic review*. J Natl Cancer Inst, 2006. **98**(14): p. 961-73.
29. Elgert, K.D., *Immunology: Understanding the immune system*. 2 ed. 2009: Wiley-Blackwell.
30. Samraj, A.N., et al., *A red meat-derived glycan promotes inflammation and cancer progression*. Proc Natl Acad Sci U S A, 2015. **112**(2): p. 542-7.
31. Nathan, C. and A. Ding, *Nonresolving inflammation*. Cell, 2010. **140**(6): p. 871-82.
32. Amon, R., et al., *Glycans in immune recognition and response*. Carbohydr Res, 2014. **389**: p. 115-22.

33. Diez-Pina, J.M., et al., *Tumor necrosis factor alpha as a marker of systemic and local inflammation in "healthy" smokers*. Int J Gen Med, 2009. **2**: p. 9-14.
34. Poullis, A., et al., *Bowel inflammation as measured by fecal calprotectin: a link between lifestyle factors and colorectal cancer risk*. Cancer Epidemiol Biomarkers Prev, 2004. **13**(2): p. 279-84.
35. Hussain, S.P. and C.C. Harris, *Inflammation and cancer: an ancient link with novel potentials*. Int J Cancer, 2007. **121**(11): p. 2373-80.
36. Yehuda-Shnaidman, E. and B. Schwartz, *Mechanisms linking obesity, inflammation and altered metabolism to colon carcinogenesis*. Obes Rev, 2012. **13**(12): p. 1083-95.
37. Gilroy, D. and R. De Maeyer, *New insights into the resolution of inflammation*. Semin Immunol, 2015. **27**(3): p. 161-8.
38. Headland, S.E. and L.V. Norling, *The resolution of inflammation: Principles and challenges*. Semin Immunol, 2015. **27**(3): p. 149-60.
39. Itzkowitz, S.H. and X. Yio, *Inflammation and cancer IV. Colorectal cancer in inflammatory bowel disease: the role of inflammation*. Am J Physiol Gastrointest Liver Physiol, 2004. **287**(1): p. G7-17.
40. Mariani, F., P. Sena, and L. Roncucci, *Inflammatory pathways in the early steps of colorectal cancer development*. World J Gastroenterol, 2014. **20**(29): p. 9716-31.
41. Lippitz, B.E., *Cytokine patterns in patients with cancer: a systematic review*. Lancet Oncol, 2013. **14**(6): p. e218-28.
42. Evans, C.H., *Cytokines: molecular keys to homeostasis, development, and pathophysiology*. J Cell Biochem, 1993. **53**(4): p. 277-9.
43. Vilcek, J., *The cytokines: an overview*. The Cytokine Handbook, ed. M.T.a.A.W.T. Lotze. Vol. 1. 2003: Academic Press.
44. Bromberg, J. and T.C. Wang, *Inflammation and cancer: IL-6 and STAT3 complete the link*. Cancer Cell, 2009. **15**(2): p. 79-80.
45. West, N.R., et al., *Emerging cytokine networks in colorectal cancer*. Nat Rev Immunol, 2015. **15**(10): p. 615-29.
46. Yu, H., M. Kortylewski, and D. Pardoll, *Crosstalk between cancer and immune cells: role of STAT3 in the tumour microenvironment*. Nat Rev Immunol, 2007. **7**(1): p. 41-51.
47. Landskron, G., et al., *Chronic inflammation and cytokines in the tumor microenvironment*. J Immunol Res, 2014. **2014**: p. 149185.
48. De Simone, V., et al., *Th17-type cytokines, IL-6 and TNF-alpha synergistically activate STAT3 and NF-kB to promote colorectal cancer cell growth*. Oncogene, 2015. **34**(27): p. 3493-503.
49. Waldner, M.J., S. Foersch, and M.F. Neurath, *Interleukin-6--a key regulator of colorectal cancer development*. Int J Biol Sci, 2012. **8**(9): p. 1248-53.
50. Taniguchi, K. and M. Karin, *IL-6 and related cytokines as the critical lynchpins between inflammation and cancer*. Semin Immunol, 2014. **26**(1): p. 54-74.
51. Chung, Y.C. and Y.F. Chang, *Significance of inflammatory cytokines in the progression of colorectal cancer*. Hepatogastroenterology, 2003. **50**(54): p. 1910-3.
52. Knupfer, H. and R. Preiss, *Serum interleukin-6 levels in colorectal cancer patients--a summary of published results*. Int J Colorectal Dis, 2010. **25**(2): p. 135-40.
53. Stanilov, N., et al., *Colorectal cancer severity and survival in correlation with tumour necrosis factor-alpha*. Biotechnol Biotechnol Equip, 2014. **28**(5): p. 911-917.
54. Grimm, M., et al., *Tumor necrosis factor-alpha is associated with positive lymph node status in patients with recurrence of colorectal cancer--indications for anti-TNF-alpha agents in cancer treatment*. Anal Cell Pathol (Amst), 2010. **33**(3): p. 151-63.
55. Sharma, R., et al., *Systemic inflammatory response predicts prognosis in patients with advanced-stage colorectal cancer*. Clin Colorectal Cancer, 2008. **7**(5): p. 331-7.
56. Li, X., et al., *Colorectal cancer progression is associated with accumulation of Th17 lymphocytes in tumor tissues and increased serum levels of interleukin-6*. Tohoku J Exp Med, 2014. **233**(3): p. 175-82.
57. Abe Vicente, M., et al., *The influence of nutritional status and disease on adiponectin and TNF-alpha; levels in colorectal cancer patients*. Nutr Hosp, 2014. **30**(1): p. 140-6.
58. Kim, Y.W., et al., *Association of serum and intratumoral cytokine profiles with tumor stage and neutrophil lymphocyte ratio in colorectal cancer*. Anticancer Res, 2014. **34**(7): p. 3481-7.
59. Baggiolini, M., A. Walz, and S.L. Kunkel, *Neutrophil-activating peptide-1/interleukin 8, a novel cytokine that activates neutrophils*. J Clin Invest, 1989. **84**(4): p. 1045-9.
60. Belperio, J.A., et al., *CXC chemokines in angiogenesis*. J Leukoc Biol, 2000. **68**(1): p. 1-8.
61. Li, A., et al., *IL-8 directly enhanced endothelial cell survival, proliferation, and matrix metalloproteinases production and regulated angiogenesis*. J Immunol, 2003. **170**(6): p. 3369-76.
62. Martin, D., R. Galisteo, and J.S. Gutkind, *CXCL8/IL8 stimulates vascular endothelial growth factor (VEGF) expression and the autocrine activation of VEGFR2 in endothelial cells by activating NFkappaB through the CBM (Carma3/Bcl10/Malt1) complex*. J Biol Chem, 2009. **284**(10): p. 6038-42.
63. Zarogoulidis, P., et al., *Interleukin-8 and interleukin-17 for cancer*. Cancer Invest, 2014. **32**(5): p. 197-205.
64. Petreaca, M.L., et al., *Transactivation of vascular endothelial growth factor receptor-2 by interleukin-8 (IL-8/CXCL8) is required for IL-8/CXCL8-induced endothelial permeability*. Mol Biol Cell, 2007. **18**(12): p. 5014-23.

65. Wang, S., et al., *NF-kappaB signaling pathway, inflammation and colorectal cancer*. Cell Mol Immunol, 2009. **6**(5): p. 327-34.
66. Quatromoni, J.G. and E. Eruslanov, *Tumor-associated macrophages: function, phenotype, and link to prognosis in human lung cancer*. Am J Transl Res, 2012. **4**(4): p. 376-89.
67. Lowe, J.M., et al., *p53 and NF-kappaB coregulate proinflammatory gene responses in human macrophages*. Cancer Res, 2014. **74**(8): p. 2182-92.
68. Ning, Y. and H.J. Lenz, *Targeting IL-8 in colorectal cancer*. Expert Opin Ther Targets, 2012. **16**(5): p. 491-7.
69. Terada, H., T. Urano, and H. Konno, *Association of interleukin-8 and plasminogen activator system in the progression of colorectal cancer*. Eur Surg Res, 2005. **37**(3): p. 166-72.
70. Jin, W.J., et al., *Diagnostic value of interleukin-8 in colorectal cancer: a case-control study and meta-analysis*. World J Gastroenterol, 2014. **20**(43): p. 16334-42.
71. Kemik, O., et al., *The relationship among acute-phase response proteins, cytokines and hormones in cachectic patients with colon cancer*. World J Surg Oncol, 2010. **8**: p. 85.
72. Nastase, A., et al., *Expression of interleukin-8 as an independent prognostic factor for sporadic colon cancer dissemination*. J Med Life, 2014. **7**(2): p. 215-9.
73. Comstock, S.S., et al., *Association of serum cytokines with colorectal polyp number and type in adult males*. Eur J Cancer Prev, 2015.
74. Gabrilovich, D.I., and M.D. Mikhail, *Vascular Endothelial Growth Factor*, in *The Cytokine Handbook*, M.T.a.A.W.T. Lotze, Editor., Academic Press.
75. Hoeben, A., et al., *Vascular endothelial growth factor and angiogenesis*. Pharmacol Rev, 2004. **56**(4): p. 549-80.
76. Niu, G., et al., *Constitutive Stat3 activity up-regulates VEGF expression and tumor angiogenesis*. Oncogene, 2002. **21**(13): p. 2000-8.
77. Tonnesen, M.G., X. Feng, and R.A. Clark, *Angiogenesis in wound healing*. J Invest Dermatol Symp Proc, 2000. **5**(1): p. 40-6.
78. Colotta, F., et al., *Cancer-related inflammation, the seventh hallmark of cancer: links to genetic instability*. Carcinogenesis, 2009. **30**(7): p. 1073-81.
79. Ciechomska, I.A., C.G. Goemans, and A.M. Tolkovsky, *Molecular links between autophagy and apoptosis*. Methods Mol Biol, 2008. **445**: p. 175-93.
80. Fujisaki, K., et al., *Circulating vascular endothelial growth factor in patients with colorectal cancer*. Am J Gastroenterol, 1998. **93**(2): p. 249-52.
81. Alabi, A.A., et al., *Preoperative serum vascular endothelial growth factor-a is a marker for subsequent recurrence in colorectal cancer patients*. Dis Colon Rectum, 2009. **52**(5): p. 993-9.
82. Hoyer, K.K., et al., *Interleukin-2 in the development and control of inflammatory disease*. Immunol Rev, 2008. **226**: p. 19-28.
83. Liao, W., J.X. Lin, and W.J. Leonard, *Interleukin-2 at the crossroads of effector responses, tolerance, and immunotherapy*. Immunity, 2013. **38**(1): p. 13-25.
84. Siegel, J.P., et al., *The IL-2 receptor beta chain (p70): role in mediating signals for LAK, NK, and proliferative activities*. Science, 1987. **238**(4823): p. 75-8.
85. Mingari, M.C., et al., *Human interleukin-2 promotes proliferation of activated B cells via surface receptors similar to those of activated T cells*. Nature, 1984. **312**(5995): p. 641-3.
86. Liao, W., et al., *Modulation of cytokine receptors by IL-2 broadly regulates differentiation into helper T cell lineages*. Nat Immunol, 2011. **12**(6): p. 551-9.
87. Malek, T.R., *The main function of IL-2 is to promote the development of T regulatory cells*. J Leukoc Biol, 2003. **74**(6): p. 961-5.
88. Berger, A., *Th1 and Th2 responses: what are they?* BMJ, 2000. **321**(7258): p. 424.
89. Laurence, A., et al., *Interleukin-2 signaling via STAT5 constrains T helper 17 cell generation*. Immunity, 2007. **26**(3): p. 371-81.
90. Yang, X.P., et al., *Opposing regulation of the locus encoding IL-17 through direct, reciprocal actions of STAT3 and STAT5*. Nat Immunol, 2011. **12**(3): p. 247-54.
91. Banchereau, J., V. Pascual, and A. O'Garra, *From IL-2 to IL-37: the expanding spectrum of anti-inflammatory cytokines*. Nat Immunol, 2012. **13**(10): p. 925-31.
92. Littman, D.R. and A.Y. Rudensky, *Th17 and regulatory T cells in mediating and restraining inflammation*. Cell, 2010. **140**(6): p. 845-58.
93. Muzes, G., B. Molnar, and F. Sipos, *Regulatory T cells in inflammatory bowel diseases and colorectal cancer*. World J Gastroenterol, 2012. **18**(40): p. 5688-94.
94. Caporale, A., et al., *Locoregional IL-2 therapy in the treatment of colon cancer. Cell-induced lesions of a murine model*. Anticancer Res, 2007. **27**(2): p. 985-9.
95. Grande, C., et al., *Interleukin-2 for the treatment of solid tumors other than melanoma and renal cell carcinoma*. Anticancer Drugs, 2006. **17**(1): p. 1-12.
96. Bobe, G., et al., *Serum cytokine concentrations, flavonol intake and colorectal adenoma recurrence in the Polyp Prevention Trial*. Br J Cancer, 2010. **103**(9): p. 1453-61.

97. Cope, A., et al., *The Th1 life cycle: molecular control of IFN-gamma to IL-10 switching*. Trends Immunol, 2011. **32**(6): p. 278-86.
98. Huber, S., et al., *Th17 cells express interleukin-10 receptor and are controlled by Foxp3(-) and Foxp3+ regulatory CD4+ T cells in an interleukin-10-dependent manner*. Immunity, 2011. **34**(4): p. 554-65.
99. Fiorentino, D.F., et al., *IL-10 inhibits cytokine production by activated macrophages*. J Immunol, 1991. **147**(11): p. 3815-22.
100. Fiorentino, D.F., et al., *IL-10 acts on the antigen-presenting cell to inhibit cytokine production by Th1 cells*. J Immunol, 1991. **146**(10): p. 3444-51.
101. Hutchins, A.P., D. Diez, and D. Miranda-Saavedra, *The IL-10/STAT3-mediated anti-inflammatory response: recent developments and future challenges*. Brief Funct Genomics, 2013. **12**(6): p. 489-98.
102. Murray, P.J., *The primary mechanism of the IL-10-regulated antiinflammatory response is to selectively inhibit transcription*. Proc Natl Acad Sci U S A, 2005. **102**(24): p. 8686-91.
103. Niemand, C., et al., *Activation of STAT3 by IL-6 and IL-10 in primary human macrophages is differentially modulated by suppressor of cytokine signaling 3*. J Immunol, 2003. **170**(6): p. 3263-72.
104. Oft, M., *IL-10: master switch from tumor-promoting inflammation to antitumor immunity*. Cancer Immunol Res, 2014. **2**(3): p. 194-9.
105. Kuhn, R., et al., *Interleukin-10-deficient mice develop chronic enterocolitis*. Cell, 1993. **75**(2): p. 263-74.
106. Hale, L.P. and P.K. Greer, *A novel murine model of inflammatory bowel disease and inflammation-associated colon cancer with ulcerative colitis-like features*. PLoS One, 2012. **7**(7): p. e41797.
107. Poutahidis, T., et al., *Rapid reversal of interleukin-6-dependent epithelial invasion in a mouse model of microbially induced colon carcinoma*. Carcinogenesis, 2007. **28**(12): p. 2614-23.
108. Mumm, J.B., et al., *IL-10 elicits IFN-gamma-dependent tumor immune surveillance*. Cancer Cell, 2011. **20**(6): p. 781-96.
109. Mocellin, S., F.M. Marincola, and H.A. Young, *Interleukin-10 and the immune response against cancer: a counterpoint*. J Leukoc Biol, 2005. **78**(5): p. 1043-51.
110. Trifunovic, J., et al., *Pathologic patterns of interleukin 10 expression--a review*. Biochem Med (Zagreb), 2015. **25**(1): p. 36-48.
111. O'Hara, R.J., et al., *Advanced colorectal cancer is associated with impaired interleukin 12 and enhanced interleukin 10 production*. Clin Cancer Res, 1998. **4**(8): p. 1943-8.
112. Galizia, G., et al., *Prognostic significance of circulating IL-10 and IL-6 serum levels in colon cancer patients undergoing surgery*. Clin Immunol, 2002. **102**(2): p. 169-78.
113. Stanilov, N., et al., *Advanced Colorectal Cancer Is Associated With Enhanced IL-23 and IL-10 Serum Levels*. Labmedicine, 2010. **41**(3): p. 159-163.
114. Rocken, M., M. Racke, and E.M. Shevach, *IL-4-induced immune deviation as antigen-specific therapy for inflammatory autoimmune disease*. Immunol Today, 1996. **17**(5): p. 225-31.
115. Rogy, M.A., et al., *Transfer of interleukin-4 and interleukin-10 in patients with severe inflammatory bowel disease of the rectum*. Hum Gene Ther, 2000. **11**(12): p. 1731-41.
116. Li, B.H., et al., *Stat6 activity-related Th2 cytokine profile and tumor growth advantage of human colorectal cancer cells in vitro and in vivo*. Cell Signal, 2012. **24**(3): p. 718-25.
117. Lahm, H., et al., *Growth inhibition of human colorectal-carcinoma cells by interleukin-4 and expression of functional interleukin-4 receptors*. Int J Cancer, 1994. **59**(3): p. 440-7.
118. Toi, M., R. Bicknell, and A.L. Harris, *Inhibition of colon and breast carcinoma cell growth by interleukin-4*. Cancer Res, 1992. **52**(2): p. 275-9.
119. Todaro, M., et al., *Apoptosis resistance in epithelial tumors is mediated by tumor-cell-derived interleukin-4*. Cell Death Differ, 2008. **15**(4): p. 762-72.
120. Li, Z., et al., *Endogenous interleukin-4 promotes tumor development by increasing tumor cell resistance to apoptosis*. Cancer Res, 2008. **68**(21): p. 8687-94.
121. Conticello, C., et al., *IL-4 protects tumor cells from anti-CD95 and chemotherapeutic agents via up-regulation of antiapoptotic proteins*. J Immunol, 2004. **172**(9): p. 5467-77.
122. Francipane, M.G., et al., *Crucial role of interleukin-4 in the survival of colon cancer stem cells*. Cancer Res, 2008. **68**(11): p. 4022-5.
123. Puglisi, M.A., et al., *Colon cancer stem cells: controversies and perspectives*. World J Gastroenterol, 2013. **19**(20): p. 2997-3006.
124. Di Stefano, A.B., et al., *Survivin is regulated by interleukin-4 in colon cancer stem cells*. J Cell Physiol, 2010. **225**(2): p. 555-61.
125. Choi, J.W., et al., *Proteomic and cytokine plasma biomarkers for predicting progression from colorectal adenoma to carcinoma in human patients*. Proteomics, 2013. **13**(15): p. 2361-74.
126. Kantola, T., et al., *Stage-dependent alterations of the serum cytokine pattern in colorectal carcinoma*. Br J Cancer, 2012. **107**(10): p. 1729-36.
127. Kang, M., et al., *Association of plasma endotoxin, inflammatory cytokines and risk of colorectal adenomas*. BMC Cancer, 2013. **13**: p. 91.

128. Amedei, A., D. Prisco, and D.E. MM, *The use of cytokines and chemokines in the cancer immunotherapy*. Recent Pat Anticancer Drug Discov, 2013. **8**(2): p. 126-42.
129. Pellegrini, M., T.W. Mak, and P.S. Ohashi, *Fighting cancers from within: augmenting tumor immunity with cytokine therapy*. Trends Pharmacol Sci, 2010. **31**(8): p. 356-63.
130. Blackburn, E.H., *Structure and function of telomeres*. Nature, 1991. **350**(6319): p. 569-73.
131. Hackett, J.A., D.M. Feldser, and C.W. Greider, *Telomere dysfunction increases mutation rate and genomic instability*. Cell, 2001. **106**(3): p. 275-86.
132. Flint, J., et al., *The relationship between chromosome structure and function at a human telomeric region*. Nat Genet, 1997. **15**(3): p. 252-7.
133. Oeseburg, H., et al., *Telomere biology in healthy aging and disease*. Pflugers Arch, 2010. **459**(2): p. 259-68.
134. Muezzinler, A., A.K. Zaineddin, and H. Brenner, *A systematic review of leukocyte telomere length and age in adults*. Ageing Res Rev, 2013. **12**(2): p. 509-19.
135. Cherkas, L.F., et al., *The association between physical activity in leisure time and leukocyte telomere length*. Arch Intern Med, 2008. **168**(2): p. 154-8.
136. Valdes, A.M., et al., *Obesity, cigarette smoking, and telomere length in women*. Lancet, 2005. **366**(9486): p. 662-4.
137. Muezzinler, A., A.K. Zaineddin, and H. Brenner, *Body mass index and leukocyte telomere length in adults: a systematic review and meta-analysis*. Obes Rev, 2014. **15**(3): p. 192-201.
138. Norat, T., et al., *Meat, fish, and colorectal cancer risk: the European Prospective Investigation into cancer and nutrition*. J Natl Cancer Inst, 2005. **97**(12): p. 906-16.
139. O'Callaghan, N.J., et al., *Colonocyte telomere shortening is greater with dietary red meat than white meat and is attenuated by resistant starch*. Clin Nutr, 2012. **31**(1): p. 60-4.
140. Qin, Q., et al., *Telomere length in peripheral blood leukocytes is associated with risk of colorectal cancer in Chinese population*. PLoS One, 2014. **9**(2): p. e88135.
141. Zee, R.Y., et al., *Mean telomere length and risk of incident colorectal carcinoma: a prospective, nested case-control approach*. Cancer Epidemiol Biomarkers Prev, 2009. **18**(8): p. 2280-2.
142. Cui, Y., et al., *Association of leukocyte telomere length with colorectal cancer risk: nested case-control findings from the Shanghai Women's Health Study*. Cancer Epidemiol Biomarkers Prev, 2012. **21**(10): p. 1807-13.
143. Haghighi, M.M., et al., *Telomere shortening: a biological marker of sporadic colorectal cancer with normal expression of p53 and mismatch repair proteins*. Genet Test Mol Biomarkers, 2014. **18**(4): p. 236-44.
144. Chen, Y., et al., *Short leukocyte telomere length predicts poor prognosis and indicates altered immune functions in colorectal cancer patients*. Ann Oncol, 2014. **25**(4): p. 869-76.
145. Boardman, L.A., et al., *The association of telomere length with colorectal cancer differs by the age of cancer onset*. Clin Transl Gastroenterol, 2014. **5**: p. e52.
146. Baichoo, E. and L.A. Boardman, *Toward a molecular classification of colorectal cancer: the role of telomere length*. Front Oncol, 2014. **4**: p. 158.
147. Feng, T.B., et al., *Reduced telomere length in colorectal carcinomas*. Asian Pac J Cancer Prev, 2012. **13**(2): p. 443-6.
148. Riegert-Johnson, D.L., et al., *Shorter peripheral blood telomeres are a potential biomarker for patients with advanced colorectal adenomas*. Int J Biol Markers, 2012. **27**(4): p. e375-80.
149. Valls-Bautista, C., et al., *In colon cancer, normal colon tissue and blood cells have altered telomere lengths*. J Surg Oncol, 2015. **111**(7): p. 899-904.
150. Garcia-Aranda, C., et al., *Correlations of telomere length, telomerase activity, and telomeric-repeat binding factor 1 expression in colorectal carcinoma*. Cancer, 2006. **106**(3): p. 541-51.
151. Zhang, C., et al., *The Association between Telomere Length and Cancer Prognosis: Evidence from a Meta-Analysis*. PLoS One, 2015. **10**(7): p. e0133174.
152. Rampazzo, E., et al., *Relationship between telomere shortening, genetic instability, and site of tumour origin in colorectal cancers*. Br J Cancer, 2010. **102**(8): p. 1300-5.
153. Meeker, A.K., et al., *Telomere length abnormalities occur early in the initiation of epithelial carcinogenesis*. Clin Cancer Res, 2004. **10**(10): p. 3317-26.
154. Engelhardt, M., et al., *Telomerase and telomere length in the development and progression of premalignant lesions to colorectal cancer*. Clin Cancer Res, 1997. **3**(11): p. 1931-41.
155. Pino, M.S. and D.C. Chung, *The chromosomal instability pathway in colon cancer*. Gastroenterology, 2010. **138**(6): p. 2059-72.
156. Hayflick, L., *The Limited in Vitro Lifetime of Human Diploid Cell Strains*. Exp Cell Res, 1965. **37**: p. 614-36.
157. Frenck, R.W., Jr., E.H. Blackburn, and K.M. Shannon, *The rate of telomere sequence loss in human leukocytes varies with age*. Proc Natl Acad Sci U S A, 1998. **95**(10): p. 5607-10.
158. Saretzki, G., et al., *Telomere shortening triggers a p53-dependent cell cycle arrest via accumulation of G-rich single stranded DNA fragments*. Oncogene, 1999. **18**(37): p. 5148-58.
159. Bailey, S.M. and J.P. Murnane, *Telomeres, chromosome instability and cancer*. Nucleic Acids Res, 2006. **34**(8): p. 2408-17.
160. Roger, L., et al., *Extensive telomere erosion in the initiation of colorectal adenomas and its association with chromosomal instability*. J Natl Cancer Inst, 2013. **105**(16): p. 1202-11.
161. Bertorelle, R., et al., *Telomeres, telomerase and colorectal cancer*. World J Gastroenterol, 2014. **20**(8): p. 1940-50.

162. O'Donovan, A., et al., *Cumulative inflammatory load is associated with short leukocyte telomere length in the Health, Aging and Body Composition Study*. PLoS One, 2011. **6**(5): p. e19687.
163. Jurk, D., et al., *Chronic inflammation induces telomere dysfunction and accelerates ageing in mice*. Nat Commun, 2014. **2**: p. 4172.
164. Risques, R.A., et al., *Ulcerative colitis is a disease of accelerated colon aging: evidence from telomere attrition and DNA damage*. Gastroenterology, 2008. **135**(2): p. 410-8.
165. Chan, A.T. and E.L. Giovannucci, *Primary prevention of colorectal cancer*. Gastroenterology, 2010. **138**(6): p. 2029-2043 e10.
166. Donaldson, M.S., *Nutrition and cancer: a review of the evidence for an anti-cancer diet*. Nutr J, 2004. **3**: p. 19.
167. Glade, M.J., *Food, nutrition, and the prevention of cancer: a global perspective*. American Institute for Cancer Research/World Cancer Research Fund, American Institute for Cancer Research, 1997. Nutrition, 1999. **15**(6): p. 523-6.
168. Ahmed, F.E., *Effect of diet, life style, and other environmental/chemopreventive factors on colorectal cancer development, and assessment of the risks*. J Environ Sci Health C Environ Carcinog Ecotoxicol Rev, 2004. **22**(2): p. 91-147.
169. Willett, W.C., *Diet, nutrition, and avoidable cancer*. Environ Health Perspect, 1995. **103 Suppl 8**: p. 165-70.
170. Johnson, I.T., *New approaches to the role of diet in the prevention of cancers of the alimentary tract*. Mutat Res, 2004. **551**(1-2): p. 9-28.
171. Bak, Y.K., J.W. Lampe, and M.K. Sung, *Effects of dietary supplementation of glucosamine sulfate on intestinal inflammation in a mouse model of experimental colitis*. J Gastroenterol Hepatol, 2014. **29**(5): p. 957-63.
172. Pandurangan, A.K. and N.M. Esa, *Dietary non-nutritive factors in targeting of regulatory molecules in colorectal cancer: an update*. Asian Pac J Cancer Prev, 2013. **14**(10): p. 5543-52.
173. Cai, F., et al., *Interaction of omega-3 polyunsaturated fatty acids with radiation therapy in two different colorectal cancer cell lines*. Clin Nutr, 2014. **33**(1): p. 164-70.
174. Higgins, J.A. and I.L. Brown, *Resistant starch: a promising dietary agent for the prevention/treatment of inflammatory bowel disease and bowel cancer*. Curr Opin Gastroenterol, 2013. **29**(2): p. 190-4.
175. Silva Jde, A., et al., *Fish oil supplement alters markers of inflammatory and nutritional status in colorectal cancer patients*. Nutr Cancer, 2012. **64**(2): p. 267-73.
176. Bi, X., et al., *Black raspberries inhibit intestinal tumorigenesis in *apc1638+/-* and *Muc2-/-* mouse models of colorectal cancer*. Cancer Prev Res (Phila), 2010. **3**(11): p. 1443-50.
177. Park, Y., et al., *Dietary fiber intake and risk of colorectal cancer: a pooled analysis of prospective cohort studies*. JAMA, 2005. **294**(22): p. 2849-57.
178. Aune, D., et al., *Dietary fibre, whole grains, and risk of colorectal cancer: systematic review and dose-response meta-analysis of prospective studies*. BMJ, 2011. **343**: p. d6617.
179. Park, Y., et al., *Dietary fiber intake and mortality in the NIH-AARP diet and health study*. Arch Intern Med, 2011. **171**(12): p. 1061-8.
180. Tantamango, Y.M., et al., *Association between dietary fiber and incident cases of colon polyps: the adventist health study*. Gastrointest Cancer Res, 2011. **4**(5-6): p. 161-7.
181. Schatzkin, A., et al., *Prospective study of dietary fiber, whole grain foods, and small intestinal cancer*. Gastroenterology, 2008. **135**(4): p. 1163-7.
182. Schatzkin, A., et al., *Dietary fiber and whole-grain consumption in relation to colorectal cancer in the NIH-AARP Diet and Health Study*. Am J Clin Nutr, 2007. **85**(5): p. 1353-60.
183. Kunzmann, A.T., et al., *Dietary fiber intake and risk of colorectal cancer and incident and recurrent adenoma in the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial*. Am J Clin Nutr, 2015. **102**(4): p. 881-90.
184. Murphy, N., et al., *Dietary fibre intake and risks of cancers of the colon and rectum in the European prospective investigation into cancer and nutrition (EPIC)*. PLoS One, 2012. **7**(6): p. e39361.
185. Kushi, L.H., K.A. Meyer, and D.R. Jacobs, Jr., *Cereals, legumes, and chronic disease risk reduction: evidence from epidemiologic studies*. Am J Clin Nutr, 1999. **70**(3 Suppl): p. 451S-458S.
186. Sanchez-Chino, X., et al., *Nutrient and nonnutrient components of legumes, and its chemopreventive activity: a review*. Nutr Cancer, 2015. **67**(3): p. 401-10.
187. Tapiero, H., et al., *Polyunsaturated fatty acids (PUFA) and eicosanoids in human health and pathologies*. Biomed Pharmacother, 2002. **56**(5): p. 215-22.
188. Johnson, I.T. and E.K. Lund, *Review article: nutrition, obesity and colorectal cancer*. Aliment Pharmacol Ther, 2007. **26**(2): p. 161-81.
189. Adom, K.K. and R.H. Liu, *Antioxidant activity of grains*. J Agric Food Chem, 2002. **50**(21): p. 6182-7.
190. Slavin, J.L., *Mechanisms for the impact of whole grain foods on cancer risk*. J Am Coll Nutr, 2000. **19**(3 Suppl): p. 300S-307S.
191. Papathanasopoulos, A. and M. Camilleri, *Dietary fiber supplements: effects in obesity and metabolic syndrome and relationship to gastrointestinal functions*. Gastroenterology, 2010. **138**(1): p. 65-72 e1-2.
192. Chemists, A.A.o.C., *The definition of dietary fiber*. Cereal Foods World, 2001. **46**: p. 112-129.
193. Zeng, H., D.L. Lazarova, and M. Bordonaro, *Mechanisms linking dietary fiber, gut microbiota and colon cancer prevention*. World J Gastrointest Oncol, 2014. **6**(2): p. 41-51.

194. Cox, M.A., et al., *Short-chain fatty acids act as antiinflammatory mediators by regulating prostaglandin E(2) and cytokines*. World J Gastroenterol, 2009. **15**(44): p. 5549-57.
195. Vinolo, M.A., et al., *Suppressive effect of short-chain fatty acids on production of proinflammatory mediators by neutrophils*. J Nutr Biochem, 2011. **22**(9): p. 849-55.
196. Luhrs, H., et al., *Butyrate inhibits NF-kappaB activation in lamina propria macrophages of patients with ulcerative colitis*. Scand J Gastroenterol, 2002. **37**(4): p. 458-66.
197. Ma, Y., et al., *Association between dietary fiber and markers of systemic inflammation in the Women's Health Initiative Observational Study*. Nutrition, 2008. **24**(10): p. 941-9.
198. Miller, S.J., et al., *Dietary fibre linked to decreased inflammation in overweight minority youth*. Pediatr Obes, 2015.
199. Henderson, A.J., et al., *Chemopreventive properties of dietary rice bran: current status and future prospects*. Adv Nutr, 2012. **3**(5): p. 643-53.
200. Sohail, M., et al., *Rice Bran Nutraceuticals: A Comprehensive Review*. Crit Rev Food Sci Nutr, 2016: p. 0.
201. Chen, P.X., et al., *Characterization of free, conjugated and bound phenolics and lipophilic antioxidants in regular- and non-darkening cranberry beans (Phaseolus vulgaris L.)*. Food Chem, 2015. **185**: p. 298-308.
202. Reynoso-Camacho, R., Ramos-Gomez, M., Loarca-Pina, G., *Bioactive components in common beans (Phaseolus vulgaris L.)*, in *Advances in agricultural and food biotechnology*, R.G. Guevara-González, Torres-Pacheco, I., Editor. 2006, Research Signpost: Trivandrum, India. p. 217-236.
203. Webber, D.M., et al., *Phenolic profile and antioxidant activity of extracts prepared from fermented heat-stabilized defatted rice bran*. J Food Sci, 2014. **79**(11): p. H2383-91.
204. Stefenon, C.A., et al., *Phenolic composition and antioxidant activity in sparkling wines: modulation by the ageing on lees*. Food Chem, 2014. **145**: p. 292-9.
205. Bobe, G., et al., *Dietary cooked navy beans and their fractions attenuate colon carcinogenesis in azoxymethane-induced ob/ob mice*. Nutr Cancer, 2008. **60**(3): p. 373-81.
206. Mentor-Marcel, R.A., et al., *Inflammation-associated serum and colon markers as indicators of dietary attenuation of colon carcinogenesis in ob/ob mice*. Cancer Prev Res (Phila), 2009. **2**(1): p. 60-9.
207. Komiyama, Y., et al., *New prebiotics from rice bran ameliorate inflammation in murine colitis models through the modulation of intestinal homeostasis and the mucosal immune system*. Scand J Gastroenterol, 2011. **46**(1): p. 40-52.
208. Zhang, C., et al., *Cooked navy and black bean diets improve biomarkers of colon health and reduce inflammation during colitis*. Br J Nutr, 2014. **111**(9): p. 1549-63.
209. Lansdorp, P.M., et al., *Heterogeneity in telomere length of human chromosomes*. Hum Mol Genet, 1996. **5**(5): p. 685-91.
210. Cawthon, R.M., *Telomere measurement by quantitative PCR*. Nucleic Acids Res, 2002. **30**(10): p. e47.
211. Ruijter, J.M., et al., *Amplification efficiency: linking baseline and bias in the analysis of quantitative PCR data*. Nucleic Acids Res, 2009. **37**(6): p. e45.
212. Kibbe, W.A., *OligoCalc: an online oligonucleotide properties calculator*. Nucleic Acids Res, 2007. **35**(Web Server issue): p. W43-6.
213. Cawthon, R.M., *Telomere length measurement by a novel monochrome multiplex quantitative PCR method*. Nucleic Acids Res, 2009. **37**(3): p. e21.
214. Ghasemi, A. and S. Zahediasl, *Normality tests for statistical analysis: a guide for non-statisticians*. Int J Endocrinol Metab, 2012. **10**(2): p. 486-9.
215. Oztuna, D., Elhan, A.H., Ersoz, T., *Investigation of Four Different Normality Tests in Terms of Type I Error Rate and Power under Different Distributions*. Turk J Med Sci, 2006. **36**(3): p. 171-176.
216. Uh, H.W., et al., *Evaluation of regression methods when immunological measurements are constrained by detection limits*. BMC Immunol, 2008. **9**: p. 59.
217. Andersen, A., et al., *Censored correlated cytokine concentrations: multivariate Tobit regression using clustered variance estimation*. Stat Med, 2013. **32**(16): p. 2859-74.
218. Humphries, M., *Missing data and how to deal: An overview of missing data [PDF document]*. 2013, University of Texas Population Research Center.
219. Lotz, A., Kendzia, B., Gawyrch, K., Lehnert, M., Bruning, T., Pesch, B., *Statistical methods for the evaluation of left-censored data*. GMS Med Inform Biom Epidemiol, 2013. **9**(2): p. Doc05.
220. Arabmazar, A., Schmidt, P., *Investigation of the robustness of the tobit estimator to non-normality*. Econometrica 1982. **50**(4): p. 1055-1063.
221. Ballenberger, N., et al., *Novel statistical approaches for non-normal censored immunological data: analysis of cytokine and gene expression data*. PLoS One, 2012. **7**(10): p. e46423.
222. Lubin, J.H., et al., *Epidemiologic evaluation of measurement data in the presence of detection limits*. Environ Health Perspect, 2004. **112**(17): p. 1691-6.
223. Baccarelli, A., et al., *Handling of dioxin measurement data in the presence of non-detectable values: overview of available methods and their application in the Seveso chloracne study*. Chemosphere, 2005. **60**(7): p. 898-906.
224. Helsel, D.R., *More than obvious: better methods for interpreting nondetect data*. Environ Sci Technol, 2005. **39**(20): p. 419A-423A.
225. Chen, H., et al., *A distribution-based multiple imputation method for handling bivariate pesticide data with values below the limit of detection*. Environ Health Perspect, 2011. **119**(3): p. 351-6.

226. Lu, K. and D.V. Mehrotra, *Specification of covariance structure in longitudinal data analysis for randomized clinical trials*. Stat Med, 2010. **29**(4): p. 474-88.
227. Nowell, P.C., *Phytohemagglutinin: an initiator of mitosis in cultures of normal human leukocytes*. Cancer Res, 1960. **20**: p. 462-6.
228. Pusztai, A., et al., *Nutritional evaluation of kidney beans (Phaseolus vulgaris): chemical composition, lectin content and nutritional value of selected cultivars*. J Sci Food Agric, 1979. **30**(9): p. 843-8.
229. Jaffe, W.G. and C.L. Lette, *Heat-labile growth-inhibiting factors in beans (Phaseolus vulgaris)*. J Nutr, 1968. **94**(2): p. 203-10.
230. Gupta, Y.P., *Anti-nutritional and toxic factors in food legumes: a review*. Plant Foods Hum Nutr, 1987. **37**(3): p. 201-28.
231. King, T.P., A. Pusztai, and E.M. Clarke, *Kidney bean (Phaseolus vulgaris) lectin-induced lesions in rat small intestine. 3. Ultrastructural studies*. J Comp Pathol, 1982. **92**(3): p. 357-73.
232. King, T.P., A. Pusztai, and E.M. Clarke, *Kidney bean (Phaseolus vulgaris) lectin-induced lesions in the small intestine: 1. Light microscope studies*. J Comp Pathol, 1980. **90**(4): p. 585-95.
233. Wilson, A.B., et al., *Kidney bean (Phaseolus vulgaris) lectin-induced lesions in rat small intestine: 2. Microbiological studies*. J Comp Pathol, 1980. **90**(4): p. 597-602.
234. Pusztai, A., E.M. Clarke, and T.P. King, *The nutritional toxicity of Phaseolus vulgaris lectins*. Proc Nutr Soc, 1979. **38**(1): p. 115-20.
235. Evans, R.J., et al., *Isolation and properties of protein fractions from navy beans (Phaseolus vulgaris) which inhibit growth of rats*. Biochim Biophys Acta, 1973. **303**(1): p. 175-84.
236. Jayne-Williams, D.J. and C.D. Burgess, *Further observations on the toxicity of navy beans (Phaseolus vulgaris) for Japanese quail (Coturnix coturnix japonica)*. J Appl Bacteriol, 1974. **37**(1): p. 149-69.
237. Pieri, C., et al., *The response of human lymphocytes to phytohemagglutinin is impaired at different levels during aging*. Ann N Y Acad Sci, 1992. **673**: p. 110-9.
238. McPherson, L.L., *The effect of the consumption of red kidney beans (Phaseolus vulgaris) on the growth of rats and the implications for human populations*. J R Soc Health, 1990. **110**(6): p. 222-6.
239. Pusztai, A., T.P. King, and E.M. Clarke, *Recent advances in the study of the nutritional toxicity of kidney bean (Phaseolus vulgaris) lectins in rats*. Toxicol, 1982. **20**(1): p. 195-7.
240. Champion, B., R.P. Glahn, A. Tava, D. Perrone, E. Doria, F. Sparvoli, R. Cecotti, V. Dani and E. Nielsen, *Genetic reduction of antinutrients in common bean (Phaseolus vulgaris L.) seed, increases nutrients and in vitro iron bioavailability without depressing main agronomic traits*. Field Crops Res, 2013. **141**(1): p. 27-37.
241. Boniglia, C.a.E.S., *Measurement by ELISA of active lectin in dietary supplements containing kidney bean protein*. Food Chem Toxicol, 2003. **68**(4): p. 1283-1286.
242. Vincenzi, S., et al., *Quantitative determination of dietary lectin activities by enzyme-linked immunosorbent assay using specific glycoproteins immobilized on microtiter plates*. J Agric Food Chem, 2002. **50**(22): p. 6266-70.
243. Bressani, R., *Research needs to up-grade the nutritional quality of common beans (Phaseolus vulgaris)*. Qual Plant Plant Foods Hum Nutr, 1983. **32**: p. 101-110.
244. Nciri, N., et al., *Toxicity Assessment of Common Beans (Phaseolus vulgaris L.) Widely Consumed by Tunisian Population*. J Med Food, 2015. **18**(9): p. 1049-64.
245. Hajjighasemi, F.a.A.M., *Propranolol effect on proliferation and vascular endothelial growth factor secretion in human immunocompetent cells*. Clin Immunol Immunopathol 2010. **2**(2): p. 22-27.
246. Hajjighasemi, F., *Profile of VEGF secretion in human peripheral blood mononuclear cells in vitro*. Res J Biol Sci, 2013. **8**(6): p. 210-214.
247. Ai, W., et al., *Optimal method to stimulate cytokine production and its use in immunotoxicity assessment*. Int J Environ Res Public Health, 2013. **10**(9): p. 3834-42.
248. De Groote, D., et al., *Direct stimulation of cytokines (IL-1 beta, TNF-alpha, IL-6, IL-2, IFN-gamma and GM-CSF) in whole blood. I. Comparison with isolated PBMC stimulation*. Cytokine, 1992. **4**(3): p. 239-48.
249. Rodhouse, J.C., et al., *Red kidney bean poisoning in the UK: an analysis of 50 suspected incidents between 1976 and 1989*. Epidemiol Infect, 1990. **105**(3): p. 485-91.
250. Al-Khaldi, S., *Bad Bug Book, Foodborne Pathogenic Microorganisms and Natural Toxins*. Second Edition ed. Phytohaemagglutinin (kidney bean lectin). 2012: United States Food and Drug Administration.
251. Lajolo, F.M. and M.I. Genovese, *Nutritional significance of lectins and enzyme inhibitors from legumes*. J Agric Food Chem, 2002. **50**(22): p. 6592-8.
252. Xie, L.M., et al., *Effects of fermentable dietary fiber supplementation on oxidative and inflammatory status in hemodialysis patients*. Int J Clin Exp Med, 2015. **8**(1): p. 1363-9.
253. Bobe, G., et al., *Interleukin-6 as a potential indicator for prevention of high-risk adenoma recurrence by dietary flavonols in the polyp prevention trial*. Cancer Prev Res (Phila), 2010. **3**(6): p. 764-75.
254. Buyken, A.E., et al., *Association between carbohydrate quality and inflammatory markers: systematic review of observational and interventional studies*. Am J Clin Nutr, 2014. **99**(4): p. 813-33.
255. Chuang, S.C., et al., *The intake of grain fibers modulates cytokine levels in blood*. Biomarkers, 2011. **16**(6): p. 504-10.

256. Ornish, D., et al., *Effect of comprehensive lifestyle changes on telomerase activity and telomere length in men with biopsy-proven low-risk prostate cancer: 5-year follow-up of a descriptive pilot study*. *Lancet Oncol*, 2013. **14**(11): p. 1112-20.
257. Lee, J., et al., *The relationship between telomere length and mortality in chronic obstructive pulmonary disease (COPD)*. *PLoS One*, 2012. **7**(4): p. e35567.
258. Chen, W., et al., *Longitudinal versus cross-sectional evaluations of leukocyte telomere length dynamics: age-dependent telomere shortening is the rule*. *J Gerontol A Biol Sci Med Sci*, 2011. **66**(3): p. 312-9.
259. Svenson, U., et al., *Blood cell telomere length is a dynamic feature*. *PLoS One*, 2011. **6**(6): p. e21485.
260. Bendix, L., et al., *Longitudinal changes in leukocyte telomere length and mortality in humans*. *J Gerontol A Biol Sci Med Sci*, 2014. **69**(2): p. 231-9.
261. Aviv, A., *Leukocyte telomere length: the telomere tale continues*. *Am J Clin Nutr*, 2009. **89**(6): p. 1721-2.
262. Weng, N., *Interplay between telomere length and telomerase in human leukocyte differentiation and aging*. *J Leukoc Biol*, 2001. **70**(6): p. 861-7.
263. Sidorov, I., et al., *Leukocyte telomere dynamics and human hematopoietic stem cell kinetics during somatic growth*. *Exp Hematol*, 2009. **37**(4): p. 514-24.
264. Kimura, M., et al., *Synchrony of telomere length among hematopoietic cells*. *Exp Hematol*, 2010. **38**(10): p. 854-9.
265. Shepherd, B.E., et al., *Estimating human hematopoietic stem cell kinetics using granulocyte telomere lengths*. *Exp Hematol*, 2004. **32**(11): p. 1040-50.
266. Ornish, D., et al., *Increased telomerase activity and comprehensive lifestyle changes: a pilot study*. *Lancet Oncol*, 2008. **9**(11): p. 1048-57.
267. Wu, P.S., M. Lin, and S.C. Chow, *On sample size estimation and re-estimation adjusting for variability in confirmatory trials*. *J Biopharm Stat*, 2016. **26**(1): p. 44-54.
268. Lanza, E., et al., *High dry bean intake and reduced risk of advanced colorectal adenoma recurrence among participants in the polyp prevention trial*. *J Nutr*, 2006. **136**(7): p. 1896-903.
269. Sanders, T.A. and S. Reddy, *The influence of rice bran on plasma lipids and lipoproteins in human volunteers*. *Eur J Clin Nutr*, 1992. **46**(3): p. 167-72.
270. Hegsted, M., M.M. Windhauser, S.K. Morris, and S.B. Lester, *Stabilized rice bran and oat bran lower cholesterol in humans*. *Nutr Res*, 1993. **13**(4): p. 387-398.
271. Gerhardt, A.L. and N.B. Gallo, *Full-fat rice bran and oat bran similarly reduce hypercholesterolemia in humans*. *J Nutr*, 1998. **128**(5): p. 865-9.
272. Kestin, M., et al., *Comparative effects of three cereal brans on plasma lipids, blood pressure, and glucose metabolism in mildly hypercholesterolemic men*. *Am J Clin Nutr*, 1990. **52**(4): p. 661-6.
273. Leung, H., et al., *Allele mining and enhanced genetic recombination for rice breeding*. *Rice (N Y)*, 2015. **8**(1): p. 34.
274. Kisha, T. *Common Bean (Phaseolus vulgaris L.) Germplasm Collection*. 2013; Available from: <http://iapreview.ars.usda.gov/Main/Docs.htm?docid=9065>.
275. Hongu, N., et al., *Pigmented rice bran and plant sterol combination reduces serum lipids in overweight and obese adults*. *J Am Coll Nutr*, 2014. **33**(3): p. 231-8.
276. Belobrajdic, D.P. and A.R. Bird, *The potential role of phytochemicals in wholegrain cereals for the prevention of type-2 diabetes*. *Nutr J*, 2013. **12**: p. 62.
277. Wang, Q., et al., *Supplementation of black rice pigment fraction improves antioxidant and anti-inflammatory status in patients with coronary heart disease*. *Asia Pac J Clin Nutr*, 2007. **16 Suppl 1**: p. 295-301.
278. Oomah, B.D., A. Corbe, and P. Balasubramanian, *Antioxidant and anti-inflammatory activities of bean (Phaseolus vulgaris L.) hulls*. *J Agric Food Chem*, 2010. **58**(14): p. 8225-30.
279. Mojica, L. and E.G. de Mejia, *Characterization and Comparison of Protein and Peptide Profiles and their Biological Activities of Improved Common Bean Cultivars (Phaseolus vulgaris L.) from Mexico and Brazil*. *Plant Foods Hum Nutr*, 2015. **70**(2): p. 105-12.
280. Forster, G.M., et al., *Rice varietal differences in bioactive bran components for inhibition of colorectal cancer cell growth*. *Food Chem*, 2013. **141**(2): p. 1545-52.
281. Soares-Miranda, L., et al., *Physical Activity, Physical Fitness, and Leukocyte Telomere Length: The Cardiovascular Health Study*. *Med Sci Sports Exerc*, 2015. **47**(12): p. 2525-34.
282. Sassenroth, D., et al., *Sports and Exercise at Different Ages and Leukocyte Telomere Length in Later Life--Data from the Berlin Aging Study II (BASE-II)*. *PLoS One*, 2015. **10**(12): p. e0142131.
283. Borghini, A., et al., *Chronic and acute effects of endurance training on telomere length*. *Mutagenesis*, 2015. **30**(5): p. 711-6.
284. Tartibian, B., et al., *A randomized controlled study examining the effect of exercise on inflammatory cytokine levels in post-menopausal women*. *Post Reprod Health*, 2015. **21**(1): p. 9-15.
285. Jahromi, A.S., et al., *Effects of Endurance Training on the Serum Levels of Tumour Necrosis Factor-alpha and Interferon-gamma in Sedentary Men*. *Immune Netw*, 2014. **14**(5): p. 255-9.
286. Nishida, Y., et al., *Objectively measured physical activity and inflammatory cytokine levels in middle-aged Japanese people*. *Prev Med*, 2014. **64**: p. 81-7.
287. Karch, I., et al., *The effect of physical activity on serum levels of selected biomarkers of atherosclerosis*. *Kardiol Pol*, 2013. **71**(1): p. 55-60.

288. Mathur, M.B., et al., *Perceived stress and telomere length: A systematic review, meta-analysis, and methodologic considerations for advancing the field*. *Brain Behav Immun*, 2016.
289. Sribanditmongkol, V., et al., *Effect of perceived stress on cytokine production in healthy college students*. *West J Nurs Res*, 2015. **37**(4): p. 481-93.
290. Lin, P.Y., Y.C. Huang, and C.F. Hung, *Shortened telomere length in patients with depression: A meta-analytic study*. *J Psychiatr Res*, 2016. **76**: p. 84-93.
291. Schmidt, F.M., et al., *Cytokine levels in depressed and non-depressed subjects, and masking effects of obesity*. *J Psychiatr Res*, 2014. **55**: p. 29-34.
292. Marini, S., et al., *Inflammatory markers and suicidal attempts in depressed patients: A review*. *Int J Immunopathol Pharmacol*, 2016.
293. Oliveira Miranda, D., et al., *Proinflammatory cytokines correlate with depression and anxiety in colorectal cancer patients*. *Biomed Res Int*, 2014. **2014**: p. 739650.
294. Young, J.J., D. Bruno, and N. Pomara, *A review of the relationship between proinflammatory cytokines and major depressive disorder*. *J Affect Disord*, 2014. **169**: p. 15-20.
295. Park, M., et al., *Where You Live May Make You Old: The Association between Perceived Poor Neighborhood Quality and Leukocyte Telomere Length*. *PLoS One*, 2015. **10**(6): p. e0128460.
296. Needham, B.L., et al., *Neighborhood characteristics and leukocyte telomere length: the Multi-Ethnic Study of Atherosclerosis*. *Health Place*, 2014. **28**: p. 167-72.
297. Carroll, J.E., S. Cohen, and A.L. Marsland, *Early childhood socioeconomic status is associated with circulating interleukin-6 among mid-life adults*. *Brain Behav Immun*, 2011. **25**(7): p. 1468-74.
298. Koster, A., et al., *Association of inflammatory markers with socioeconomic status*. *J Gerontol A Biol Sci Med Sci*, 2006. **61**(3): p. 284-90.
299. Wang, Y., F.C. Zhang, and Y.J. Wang, *The efficacy and safety of non-steroidal anti-inflammatory drugs in preventing the recurrence of colorectal adenoma: a meta-analysis and systematic review of randomized trials*. *Colorectal Dis*, 2015. **17**(3): p. 188-96.
300. Pommegaard, H.C., et al., *Aspirin, Calcitriol, and Calcium Do Not Prevent Adenoma Recurrence in a Randomized Controlled Trial*. *Gastroenterology*, 2016. **150**(1): p. 114-122 e4.
301. Benamouzig, R., et al., *Prevention by daily soluble aspirin of colorectal adenoma recurrence: 4-year results of the APACC randomised trial*. *Gut*, 2012. **61**(2): p. 255-61.
302. Baron, J.A., et al., *A randomized trial of aspirin to prevent colorectal adenomas*. *N Engl J Med*, 2003. **348**(10): p. 891-9.
303. Bertagnolli, M.M., et al., *Celecoxib for the prevention of sporadic colorectal adenomas*. *N Engl J Med*, 2006. **355**(9): p. 873-84.
304. Arber, N., et al., *Celecoxib for the prevention of colorectal adenomatous polyps*. *N Engl J Med*, 2006. **355**(9): p. 885-95.
305. Ikonomidis, I., et al., *Increased proinflammatory cytokines in patients with chronic stable angina and their reduction by aspirin*. *Circulation*, 1999. **100**(8): p. 793-8.
306. Il'yasova, D., et al., *Circulating levels of inflammatory markers and cancer risk in the health aging and body composition cohort*. *Cancer Epidemiol Biomarkers Prev*, 2005. **14**(10): p. 2413-8.
307. Clendenen, T.V., et al., *Factors associated with inflammation markers, a cross-sectional analysis*. *Cytokine*, 2011. **56**(3): p. 769-78.
308. Solheim, S., et al., *Influence of aspirin on inflammatory markers in patients after acute myocardial infarction*. *Am J Cardiol*, 2003. **92**(7): p. 843-5.
309. Azar, R.R., et al., *Effects of aspirin (325 mg/day) on serum high-sensitivity C-reactive protein, cytokines, and adhesion molecules in healthy volunteers*. *Am J Cardiol*, 2003. **92**(2): p. 236-9.
310. Hovens, M.M., et al., *Effects of aspirin on serum C-reactive protein and interleukin-6 levels in patients with type 2 diabetes without cardiovascular disease: a randomized placebo-controlled crossover trial*. *Diabetes Obes Metab*, 2008. **10**(8): p. 668-74.
311. Lang Kuhs, K.A., et al., *Association between Regular Aspirin Use and Circulating Markers of Inflammation: A Study within the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial*. *Cancer Epidemiol Biomarkers Prev*, 2015. **24**(5): p. 825-32.
312. Navarro, S.L., et al., *Factors Associated with Multiple Biomarkers of Systemic Inflammation*. *Cancer Epidemiol Biomarkers Prev*, 2016. **25**(3): p. 521-31.
313. Vaucher, J., et al., *Cytokines and hs-CRP levels in individuals treated with low-dose aspirin for cardiovascular prevention: a population-based study (CoLaus Study)*. *Cytokine*, 2014. **66**(2): p. 95-100.
314. Ho, G.Y., et al., *Antagonistic effects of aspirin and folic acid on inflammation markers and subsequent risk of recurrent colorectal adenomas*. *J Natl Cancer Inst*, 2009. **101**(23): p. 1650-4.
315. Block, R.C., et al., *The Effects of EPA+DHA and Aspirin on Inflammatory Cytokines and Angiogenesis Factors*. *World J Cardiovasc Dis*, 2012. **2**(1): p. 14-19.
316. Risques, R.A., et al., *Leukocyte telomere length predicts cancer risk in Barrett's esophagus*. *Cancer Epidemiol Biomarkers Prev*, 2007. **16**(12): p. 2649-55.

317. Hardikar, S., et al., *Obesity and inflammation markers in relation to leukocyte telomere length in a cross-sectional study of persons with Barrett's esophagus*. BMC Obes, 2015. **2**: p. 32.
318. Munkholm, P., *Review article: the incidence and prevalence of colorectal cancer in inflammatory bowel disease*. Aliment Pharmacol Ther, 2003. **18 Suppl 2**: p. 1-5.
319. Lakatos, P.L. and L. Lakatos, *Risk for colorectal cancer in ulcerative colitis: changes, causes and management strategies*. World J Gastroenterol, 2008. **14(25)**: p. 3937-47.
320. Prantera, C. and S. Marconi, *Glucocorticosteroids in the treatment of inflammatory bowel disease and approaches to minimizing systemic activity*. Therap Adv Gastroenterol, 2013. **6(2)**: p. 137-56.
321. Chapman, C.G. and D.T. Rubin, *The potential for medical therapy to reduce the risk of colorectal cancer and optimize surveillance in inflammatory bowel disease*. Gastrointest Endosc Clin N Am, 2014. **24(3)**: p. 353-65.
322. Swaminath, A., R. Taunk, and G. Lawlor, *Use of methotrexate in inflammatory bowel disease in 2014: A User's Guide*. World J Gastrointest Pharmacol Ther, 2014. **5(3)**: p. 113-21.
323. Scharl, M., S.R. Vavricka, and G. Rogler, *Review: new anti-cytokines for IBD: what is in the pipeline?* Curr Drug Targets, 2013. **14(12)**: p. 1405-20.
324. Almawi, W.Y., et al., *Regulation of cytokine and cytokine receptor expression by glucocorticoids*. J Leukoc Biol, 1996. **60(5)**: p. 563-72.
325. Liu, Z., et al., *Evaluating the effects of immunosuppressants on human immunity using cytokine profiles of whole blood*. Cytokine, 2009. **45(2)**: p. 141-7.
326. Rogatsky, I. and L.B. Ivashkiv, *Glucocorticoid modulation of cytokine signaling*. Tissue Antigens, 2006. **68(1)**: p. 1-12.
327. Remmelts, H.H., et al., *Dexamethasone downregulates the systemic cytokine response in patients with community-acquired pneumonia*. Clin Vaccine Immunol, 2012. **19(9)**: p. 1532-8.
328. Barrera, P., et al., *Effects of antirheumatic agents on cytokines*. Semin Arthritis Rheum, 1996. **25(4)**: p. 234-53.
329. Yao, X., et al., *Targeting interleukin-6 in inflammatory autoimmune diseases and cancers*. Pharmacol Ther, 2014. **141(2)**: p. 125-39.
330. Ringheanu, M., et al., *Effects of infliximab on apoptosis and reverse signaling of monocytes from healthy individuals and patients with Crohn's disease*. Inflamm Bowel Dis, 2004. **10(6)**: p. 801-10.
331. Neurath, M.F., et al., *Methotrexate specifically modulates cytokine production by T cells and macrophages in murine collagen-induced arthritis (CIA): a mechanism for methotrexate-mediated immunosuppression*. Clin Exp Immunol, 1999. **115(1)**: p. 42-55.
332. Cutolo, M., et al., *Anti-inflammatory mechanisms of methotrexate in rheumatoid arthritis*. Ann Rheum Dis, 2001. **60(8)**: p. 729-35.
333. Getliffe, K.M., et al., *Lymphocyte telomere dynamics and telomerase activity in inflammatory bowel disease: effect of drugs and smoking*. Aliment Pharmacol Ther, 2005. **21(2)**: p. 121-31.
334. Nielsen, O.H., B. Vainer, and J. Rask-Madsen, *Review article: the treatment of inflammatory bowel disease with 6-mercaptopurine or azathioprine*. Aliment Pharmacol Ther, 2001. **15(11)**: p. 1699-708.
335. Hushmehdy, S., et al., *Select phytochemicals suppress human T-lymphocytes and mouse splenocytes suggesting their use in autoimmunity and transplantation*. Nutr Res, 2009. **29(8)**: p. 568-78.
336. Hsieh, C.C. and B.F. Lin, *Opposite effects of low and high dose supplementation of vitamin E on survival of MRL/lpr mice*. Nutrition, 2005. **21(9)**: p. 940-8.
337. Li-Weber, M., et al., *Vitamin E inhibits IL-4 gene expression in peripheral blood T cells*. Eur J Immunol, 2002. **32(9)**: p. 2401-8.
338. Wang, Y., D.S. Huang, and R.R. Watson, *Vitamin E supplementation modulates cytokine production by thymocytes during murine AIDS*. Immunol Res, 1993. **12(4)**: p. 358-66.
339. Okamoto, N., et al., *Effects of alpha tocopherol and probucol supplements on allergen-induced airway inflammation and hyperresponsiveness in a mouse model of allergic asthma*. Int Arch Allergy Immunol, 2006. **141(2)**: p. 172-80.
340. Abdala-Valencia, H., et al., *alpha-Tocopherol supplementation of allergic female mice inhibits development of CD11c+CD11b+ dendritic cells in utero and allergic inflammation in neonates*. Am J Physiol Lung Cell Mol Physiol, 2014. **307(6)**: p. L482-96.
341. Novoselova, E.G., et al., *Naturally occurring antioxidant nutrients reduce inflammatory response in mice*. Eur J Pharmacol, 2009. **615(1-3)**: p. 234-40.
342. Zhang, X., et al., *Dietary RRR-alpha-tocopherol succinate attenuates lipopolysaccharide-induced inflammatory cytokines secretion in broiler chicks*. Br J Nutr, 2010. **104(12)**: p. 1796-805.
343. Devaraj, S. and I. Jialal, *Alpha tocopherol supplementation decreases serum C-reactive protein and monocyte interleukin-6 levels in normal volunteers and type 2 diabetic patients*. Free Radic Biol Med, 2000. **29(8)**: p. 790-2.
344. van Tits, L.J., et al., *alpha-tocopherol supplementation decreases production of superoxide and cytokines by leukocytes ex vivo in both normolipidemic and hypertriglyceridemic individuals*. Am J Clin Nutr, 2000. **71(2)**: p. 458-64.
345. Jamal, M., et al., *Effect of ascorbic acid and alpha-tocopherol supplementations on serum leptin, tumor necrosis factor alpha, and serum amyloid A levels in individuals with type 2 diabetes mellitus*. Avicenna J Phytomed, 2015. **5(6)**: p. 531-9.
346. Upritchard, J.E., W.H. Sutherland, and J.I. Mann, *Effect of supplementation with tomato juice, vitamin E, and vitamin C on LDL oxidation and products of inflammatory activity in type 2 diabetes*. Diabetes Care, 2000. **23(6)**: p. 733-8.

347. Traber, M.G. and J.F. Stevens, *Vitamins C and E: beneficial effects from a mechanistic perspective*. Free Radic Biol Med, 2011. **51**(5): p. 1000-13.
348. Buettner, G.R., *The pecking order of free radicals and antioxidants: lipid peroxidation, alpha-tocopherol, and ascorbate*. Arch Biochem Biophys, 1993. **300**(2): p. 535-43.
349. Calfee-Mason, K.G., B.T. Spear, and H.P. Glauert, *Effects of vitamin E on the NF-kappaB pathway in rats treated with the peroxisome proliferator, ciprofibrate*. Toxicol Appl Pharmacol, 2004. **199**(1): p. 1-9.
350. Chung, S.W., B.Y. Kang, and T.S. Kim, *Inhibition of interleukin-4 production in CD4+ T cells by peroxisome proliferator-activated receptor-gamma (PPAR-gamma) ligands: involvement of physical association between PPAR-gamma and the nuclear factor of activated T cells transcription factor*. Mol Pharmacol, 2003. **64**(5): p. 1169-79.
351. Yang, X.Y., et al., *Activation of human T lymphocytes is inhibited by peroxisome proliferator-activated receptor gamma (PPARgamma) agonists. PPARgamma co-association with transcription factor NFAT*. J Biol Chem, 2000. **275**(7): p. 4541-4.
352. Stone, W.L., et al., *The role of antioxidants and pro-oxidants in colon cancer*. World J Gastrointest Oncol, 2014. **6**(3): p. 55-66.
353. Virtamo, J., et al., *Effects of alpha-tocopherol and beta-carotene supplementation on cancer incidence and mortality: 18-year postintervention follow-up of the Alpha-tocopherol, Beta-carotene Cancer Prevention Study*. Int J Cancer, 2014. **135**(1): p. 178-85.
354. Albanes, D., et al., *Effects of supplemental alpha-tocopherol and beta-carotene on colorectal cancer: results from a controlled trial (Finland)*. Cancer Causes Control, 2000. **11**(3): p. 197-205.
355. Lippman, S.M., et al., *Effect of selenium and vitamin E on risk of prostate cancer and other cancers: the Selenium and Vitamin E Cancer Prevention Trial (SELECT)*. JAMA, 2009. **301**(1): p. 39-51.
356. Ungerstedt, J.S., et al., *Nicotinamide inhibits endotoxin-induced monocyte tissue factor expression*. J Thromb Haemost, 2003. **1**(12): p. 2554-60.
357. Lappas, M. and M. Permezel, *The anti-inflammatory and antioxidative effects of nicotinamide, a vitamin B(3) derivative, are elicited by FoxO3 in human gestational tissues: implications for preterm birth*. J Nutr Biochem, 2011. **22**(12): p. 1195-201.
358. Ferreira, R.G., et al., *Neutrophil recruitment is inhibited by nicotinamide in experimental pleurisy in mice*. Eur J Pharmacol, 2012. **685**(1-3): p. 198-204.
359. Ganji, S.H., M.L. Kashyap, and V.S. Kamanna, *Niacin inhibits fat accumulation, oxidative stress, and inflammatory cytokine IL-8 in cultured hepatocytes: Impact on non-alcoholic fatty liver disease*. Metabolism, 2015. **64**(9): p. 982-90.
360. Premkumar, V.G., et al., *Serum cytokine levels of interleukin-1beta, -6, -8, tumour necrosis factor-alpha and vascular endothelial growth factor in breast cancer patients treated with tamoxifen and supplemented with co-enzyme Q(10), riboflavin and niacin*. Basic Clin Pharmacol Toxicol, 2007. **100**(6): p. 387-91.
361. Grange, P.A., et al., *Nicotinamide inhibits Propionibacterium acnes-induced IL-8 production in keratinocytes through the NF-kappaB and MAPK pathways*. J Dermatol Sci, 2009. **56**(2): p. 106-12.
362. Sauve, A.A., *NAD+ and vitamin B3: from metabolism to therapies*. J Pharmacol Exp Ther, 2008. **324**(3): p. 883-93.
363. Ying, W., *NAD+/NADH and NADP+/NADPH in cellular functions and cell death: regulation and biological consequences*. Antioxid Redox Signal, 2008. **10**(2): p. 179-206.
364. Kauppinen, T.M., L. Gan, and R.A. Swanson, *Poly(ADP-ribose) polymerase-1-induced NAD(+) depletion promotes nuclear factor-kappaB transcriptional activity by preventing p65 de-acetylation*. Biochim Biophys Acta, 2013. **1833**(8): p. 1985-91.
365. Ning, Y., et al., *Interleukin-8 is associated with proliferation, migration, angiogenesis and chemosensitivity in vitro and in vivo in colon cancer cell line models*. Int J Cancer, 2011. **128**(9): p. 2038-49.
366. Balasoiu, M., et al., *Serum and tumor microenvironment IL-8 values in different stages of colorectal cancer*. Rom J Morphol Embryol, 2014. **55**(2 Suppl): p. 575-8.
367. Kabat, G.C., et al., *Dietary intake of selected B vitamins in relation to risk of major cancers in women*. Br J Cancer, 2008. **99**(5): p. 816-21.
368. Locasale, J.W., *Serine, glycine and one-carbon units: cancer metabolism in full circle*. Nat Rev Cancer, 2013. **13**(8): p. 572-83.
369. Xia, W. and P.S. Low, *Folate-targeted therapies for cancer*. J Med Chem, 2010. **53**(19): p. 6811-24.
370. Hansen, M.F., et al., *Folic acid mediates activation of the pro-oncogene STAT3 via the Folate Receptor alpha*. Cell Signal, 2015. **27**(7): p. 1356-68.
371. Giovannucci, E., *Epidemiologic studies of folate and colorectal neoplasia: a review*. J Nutr, 2002. **132**(8 Suppl): p. 2350S-2355S.
372. Sanjoaquin, M.A., et al., *Folate intake and colorectal cancer risk: a meta-analytical approach*. Int J Cancer, 2005. **113**(5): p. 825-8.
373. Le Marchand, L., et al., *Plasma levels of B vitamins and colorectal cancer risk: the multiethnic cohort study*. Cancer Epidemiol Biomarkers Prev, 2009. **18**(8): p. 2195-201.
374. Liu, Y., et al., *Vitamin and multiple-vitamin supplement intake and incidence of colorectal cancer: a meta-analysis of cohort studies*. Med Oncol, 2015. **32**(1): p. 434.
375. Kim, Y.I., *Role of folate in colon cancer development and progression*. J Nutr, 2003. **133**(11 Suppl 1): p. 3731S-3739S.

376. Ibrahim, E.M. and J.M. Zekri, *Folic acid supplementation for the prevention of recurrence of colorectal adenomas: metaanalysis of interventional trials*. Med Oncol, 2010. **27**(3): p. 915-8.
377. Figueiredo, J.C., et al., *Folic acid and prevention of colorectal adenomas: a combined analysis of randomized clinical trials*. Int J Cancer, 2011. **129**(1): p. 192-203.
378. Qin, T., et al., *Folic acid supplements and colorectal cancer risk: meta-analysis of randomized controlled trials*. Sci Rep, 2015. **5**: p. 12044.
379. Carroll, C., et al., *Meta-analysis: folic acid in the chemoprevention of colorectal adenomas and colorectal cancer*. Aliment Pharmacol Ther, 2010. **31**(7): p. 708-18.
380. Kim, Y.I., *Folic acid supplementation and cancer risk: point*. Cancer Epidemiol Biomarkers Prev, 2008. **17**(9): p. 2220-5.
381. Fife, J., et al., *Folic acid supplementation and colorectal cancer risk: a meta-analysis*. Colorectal Dis, 2011. **13**(2): p. 132-7.
382. Cole, B.F., et al., *Folic acid for the prevention of colorectal adenomas: a randomized clinical trial*. JAMA, 2007. **297**(21): p. 2351-9.
383. Wien, T.N., et al., *Cancer risk with folic acid supplements: a systematic review and meta-analysis*. BMJ Open, 2012. **2**(1): p. e000653.
384. Novakovic, P., et al., *Effects of folate deficiency on gene expression in the apoptosis and cancer pathways in colon cancer cells*. Carcinogenesis, 2006. **27**(5): p. 916-24.
385. Porcelli, L., et al., *The impact of folate status on the efficacy of colorectal cancer treatment*. Curr Drug Metab, 2011. **12**(10): p. 975-84.
386. Cassidy, A., et al., *Associations between diet, lifestyle factors, and telomere length in women*. Am J Clin Nutr, 2010. **91**(5): p. 1273-80.
387. Gardner, M., et al., *Gender and telomere length: systematic review and meta-analysis*. Exp Gerontol, 2014. **51**: p. 15-27.
388. Parks, E.J., *Effect of dietary carbohydrate on triglyceride metabolism in humans*. J Nutr, 2001. **131**(10): p. 2772S-2774S.
389. Grundy, S.M. and M.A. Denke, *Dietary influences on serum lipids and lipoproteins*. J Lipid Res, 1990. **31**(7): p. 1149-72.
390. Burdge, G.C. and P.C. Calder, *Introduction to fatty acids and lipids*. World Rev Nutr Diet, 2015. **112**: p. 1-16.
391. Zak, A., et al., *[Composition of the nonesterified fatty acids and lipid peroxidation in metabolic syndrome]*. Cas Lek Cesk, 2007. **146**(5): p. 484-91.
392. Leamy, A.K., R.A. Egnatchik, and J.D. Young, *Molecular mechanisms and the role of saturated fatty acids in the progression of non-alcoholic fatty liver disease*. Prog Lipid Res, 2013. **52**(1): p. 165-74.
393. Zhang, K., *Integration of ER stress, oxidative stress and the inflammatory response in health and disease*. Int J Clin Exp Med, 2010. **3**(1): p. 33-40.
394. Schonfeld, P. and L. Wojtczak, *Fatty acids as modulators of the cellular production of reactive oxygen species*. Free Radic Biol Med, 2008. **45**(3): p. 231-41.
395. Tripathy, D., et al., *Elevation of free fatty acids induces inflammation and impairs vascular reactivity in healthy subjects*. Diabetes, 2003. **52**(12): p. 2882-7.
396. Welty, F.K., *How do elevated triglycerides and low HDL-cholesterol affect inflammation and atherothrombosis?* Curr Cardiol Rep, 2013. **15**(9): p. 400.
397. Harte, A.L., et al., *Telomere length attrition, a marker of biological senescence, is inversely correlated with triglycerides and cholesterol in South Asian males with type 2 diabetes mellitus*. Exp Diabetes Res, 2012. **2012**: p. 895185.
398. Revesz, D., et al., *Telomere length as a marker of cellular aging is associated with prevalence and progression of metabolic syndrome*. J Clin Endocrinol Metab, 2014. **99**(12): p. 4607-15.
399. Song, Y., et al., *Intake of small-to-medium-chain saturated fatty acids is associated with peripheral leukocyte telomere length in postmenopausal women*. J Nutr, 2013. **143**(6): p. 907-14.
400. Garcia-Calzon, S., et al., *Dietary total antioxidant capacity is associated with leukocyte telomere length in a children and adolescent population*. Clin Nutr, 2015. **34**(4): p. 694-9.
401. Garcia-Calzon, S., et al., *Dietary inflammatory index and telomere length in subjects with a high cardiovascular disease risk from the PREDIMED-NAVARRA study: cross-sectional and longitudinal analyses over 5 y*. Am J Clin Nutr, 2015. **102**(4): p. 897-904.
402. You, J., et al., *Metabolic syndrome contributes to an increased recurrence risk of non-metastatic colorectal cancer*. Oncotarget, 2015. **6**(23): p. 19880-90.
403. Nkondjock, A., et al., *Specific fatty acids and human colorectal cancer: an overview*. Cancer Detect Prev, 2003. **27**(1): p. 55-66.
404. Astorg, P., *[Dietary fatty acids and colorectal and prostate cancers: epidemiological studies]*. Bull Cancer, 2005. **92**(7): p. 670-84.
405. Hodge, A.M., et al., *Dietary and biomarker estimates of fatty acids and risk of colorectal cancer*. Int J Cancer, 2015. **137**(5): p. 1224-34.

406. Jung, Y.S., et al., *Associations Between Parameters of Glucose and Lipid Metabolism and Risk of Colorectal Neoplasm*. *Dig Dis Sci*, 2015. **60**(10): p. 2996-3004.
407. Yang, M.H., et al., *The association of serum lipids with colorectal adenomas*. *Am J Gastroenterol*, 2013. **108**(5): p. 833-41.
408. Zhang, X., et al., *Lipid levels in serum and cancerous tissues of colorectal cancer patients*. *World J Gastroenterol*, 2014. **20**(26): p. 8646-52.
409. Chun, Y.J., et al., *Associations of colorectal cancer incidence with nutrient and food group intakes in Korean adults: a case-control study*. *Clin Nutr Res*, 2015. **4**(2): p. 110-23.
410. Zhong, X., et al., *Dietary fat, fatty acid intakes and colorectal cancer risk in Chinese adults: a case-control study*. *Eur J Cancer Prev*, 2013. **22**(5): p. 438-47.
411. Aune, D., et al., *Carbohydrates, glycemic index, glycemic load, and colorectal cancer risk: a systematic review and meta-analysis of cohort studies*. *Cancer Causes Control*, 2012. **23**(4): p. 521-35.
412. Terry, P.D., et al., *Glycemic load, carbohydrate intake, and risk of colorectal cancer in women: a prospective cohort study*. *J Natl Cancer Inst*, 2003. **95**(12): p. 914-6.
413. Tayyem, R.F., et al., *Macro- and micronutrients consumption and the risk for colorectal cancer among Jordanians*. *Nutrients*, 2015. **7**(3): p. 1769-86.
414. Tayyem, R.F., et al., *Consumption of Whole Grains, Refined Cereals, and Legumes and Its Association With Colorectal Cancer Among Jordanians*. *Integr Cancer Ther*, 2015.
415. Coleman, H.G., et al., *Aspects of dietary carbohydrate intake are not related to risk of colorectal polyps in the Tennessee Colorectal Polyp Study*. *Cancer Causes Control*, 2015. **26**(8): p. 1197-202.
416. Kuriki, K., et al., *Risk of colorectal cancer is linked to erythrocyte compositions of fatty acids as biomarkers for dietary intakes of fish, fat, and fatty acids*. *Cancer Epidemiol Biomarkers Prev*, 2006. **15**(10): p. 1791-8.
417. Okuno, M., et al., *Abnormalities in fatty acids in plasma, erythrocytes and adipose tissue in Japanese patients with colorectal cancer*. *In Vivo*, 2013. **27**(2): p. 203-10.
418. Ghadimi, R., et al., *Serum concentrations of fatty acids and colorectal adenoma risk: a case-control study in Japan*. *Asian Pac J Cancer Prev*, 2008. **9**(1): p. 111-8.
419. Sun, Z., et al., *Association of total energy intake and macronutrient consumption with colorectal cancer risk: results from a large population-based case-control study in Newfoundland and Labrador and Ontario, Canada*. *Nutr J*, 2012. **11**: p. 18.
420. Cocate, P.G., et al., *Carotenoid consumption is related to lower lipid oxidation and DNA damage in middle-aged men*. *Br J Nutr*, 2015. **114**(2): p. 257-64.
421. Ciccone, M.M., et al., *Dietary intake of carotenoids and their antioxidant and anti-inflammatory effects in cardiovascular care*. *Mediators Inflamm*, 2013. **2013**: p. 782137.
422. Nierenberg, D.W., G.T. Bayrd, and T.A. Stukel, *Lack of effect of chronic administration of oral beta-carotene on serum cholesterol and triglyceride concentrations*. *Am J Clin Nutr*, 1991. **53**(3): p. 652-4.
423. Cartmel, B., et al., *Changes in cholesterol and triglyceride concentrations in the Vanguard population of the Carotene and Retinol Efficacy Trial (CARET)*. *Eur J Clin Nutr*, 2005. **59**(10): p. 1173-80.
424. Wang, Y., et al., *Dietary carotenoids are associated with cardiovascular disease risk biomarkers mediated by serum carotenoid concentrations*. *J Nutr*, 2014. **144**(7): p. 1067-74.
425. Wallstrom, P., et al., *Serum concentrations of beta-carotene and alpha-tocopherol are associated with diet, smoking, and general and central adiposity*. *Am J Clin Nutr*, 2001. **73**(4): p. 777-85.
426. Ascherio, A., et al., *Correlations of vitamin A and E intakes with the plasma concentrations of carotenoids and tocopherols among American men and women*. *J Nutr*, 1992. **122**(9): p. 1792-801.
427. Ribaya-Mercado, J.D., J.M. Ordovas, and R.M. Russell, *Effect of beta-carotene supplementation on the concentrations and distribution of carotenoids, vitamin E, vitamin A, and cholesterol in plasma lipoprotein and non-lipoprotein fractions in healthy older women*. *J Am Coll Nutr*, 1995. **14**(6): p. 614-20.
428. Silva, L.S., et al., *Diet supplementation with beta-carotene improves the serum lipid profile in rats fed a cholesterol-enriched diet*. *J Physiol Biochem*, 2013. **69**(4): p. 811-20.
429. Ros, E., *Intestinal absorption of triglyceride and cholesterol. Dietary and pharmacological inhibition to reduce cardiovascular risk*. *Atherosclerosis*, 2000. **151**(2): p. 357-79.
430. Kris-Etherton, P.M. and J.A. Fleming, *Emerging nutrition science on fatty acids and cardiovascular disease: nutritionists' perspectives*. *Adv Nutr*, 2015. **6**(3): p. 326S-375S.
431. Mensink, R.P., et al., *Effects of dietary fatty acids and carbohydrates on the ratio of serum total to HDL cholesterol and on serum lipids and apolipoproteins: a meta-analysis of 60 controlled trials*. *Am J Clin Nutr*, 2003. **77**(5): p. 1146-55.
432. Burillo, E., et al., *Omega-3 fatty acids and HDL. How do they work in the prevention of cardiovascular disease?* *Curr Vasc Pharmacol*, 2012. **10**(4): p. 432-41.
433. Pan, A., et al., *alpha-Linolenic acid and risk of cardiovascular disease: a systematic review and meta-analysis*. *Am J Clin Nutr*, 2012. **96**(6): p. 1262-73.
434. Vrablik, M., et al., *Omega-3 fatty acids and cardiovascular disease risk: do we understand the relationship?* *Physiol Res*, 2009. **58 Suppl 1**: p. S19-26.

435. Harris, W.S., et al., *Omega-6 fatty acids and risk for cardiovascular disease: a science advisory from the American Heart Association Nutrition Subcommittee of the Council on Nutrition, Physical Activity, and Metabolism; Council on Cardiovascular Nursing; and Council on Epidemiology and Prevention*. *Circulation*, 2009. **119**(6): p. 902-7.
436. Siguel, E., *A new relationship between total/high density lipoprotein cholesterol and polyunsaturated fatty acids*. *Lipids*, 1996. **31 Suppl**: p. S51-6.
437. Hollaender, P.L., A.B. Ross, and M. Kristensen, *Whole-grain and blood lipid changes in apparently healthy adults: a systematic review and meta-analysis of randomized controlled studies*. *Am J Clin Nutr*, 2015. **102**(3): p. 556-72.
438. Bleys, J., et al., *Serum selenium and serum lipids in US adults*. *Am J Clin Nutr*, 2008. **88**(2): p. 416-23.
439. Katz, D.L. and S. Meller, *Can we say what diet is best for health?* *Annu Rev Public Health*, 2014. **35**: p. 83-103.
440. McIlrath, J., et al., *Telomere length abnormalities in mammalian radiosensitive cells*. *Cancer Res*, 2001. **61**(3): p. 912-5.
441. Kamranvar, S.A., et al., *Epstein-Barr virus promotes genomic instability in Burkitt's lymphoma*. *Oncogene*, 2007. **26**(35): p. 5115-23.
442. Henle, W. and G. Henle, *The relation of the Epstein-Barr virus to Burkitt's lymphoma*. *Zentralbl Bakteriolog Orig A*, 1972. **220**(1): p. 40-6.
443. Henle, W. and G. Henle, *Epstein-Barr virus-related serology in Hodgkin's disease*. *Natl Cancer Inst Monogr*, 1973. **36**: p. 79-84.
444. Henle, W. and G. Henle, *The Epstein-Barr Virus (EBV) in Burkitt's lymphoma and nasopharyngeal carcinoma*. *Ann Clin Lab Sci*, 1974. **4**(2): p. 109-14.
445. Dunmire, S.K., K.A. Hogquist, and H.H. Balfour, *Infectious Mononucleosis*. *Curr Top Microbiol Immunol*, 2015. **390**(Pt 1): p. 211-40.
446. Gutierrez-Rodrigues, F., et al., *Direct comparison of flow-FISH and qPCR as diagnostic tests for telomere length measurement in humans*. *PLoS One*, 2014. **9**(11): p. e113747.
447. O'Callaghan, N.J. and M. Fenech, *A quantitative PCR method for measuring absolute telomere length*. *Biol Proced Online*, 2011. **13**: p. 3.
448. Montpetit, A.J., et al., *Telomere length: a review of methods for measurement*. *Nurs Res*, 2014. **63**(4): p. 289-99.

## APPENDIX I

### 6. Descriptive Statistics for Study Participants without a History of Colorectal Cancer

**Table 55:** Descriptive statistics by time point of age (years), weight (kg), body mass index (kg/m<sup>2</sup>), and serum lipids (mg/dL) for study participants (n=11) without a history of colorectal cancer. P-values less than 0.05 are indicated with a double-underline.

<i>Descriptive Statistics for Study Participants without a History of Colorectal Cancer: Age, Weight, BMI, and Serum Lipids</i>												
Variable	Time Point	Number of Observations	Mean	S.D.	Max.	Q3	Median	Q1	Min.	Skewness	Kurtosis	S.W. p-value
Age (years)	Day 0	11	40.7	14.6	67	54	36	26	24	0.54	-0.96	0.256
	Day 14	11	40.7	14.6	67	54	36	26	24	0.54	-0.96	0.256
	Day 28	11	40.7	14.6	67	54	36	26	24	0.54	-0.96	0.256
Weight (kg)	Day 0	9	70.8	12.4	97.2	71.3	66.8	62.7	59.5	1.46	1.61	0.055
	Day 14	9	70.8	12.2	96.3	71.3	66.8	63.4	59.4	1.46	1.49	0.052
	Day 28	9	70.4	11.8	94.9	69.7	66.9	63.7	59.7	1.44	1.30	<u>0.036</u>
BMI (kg/m <sup>2</sup> )	Day 0	11	24.5	4.7	35.6	26.5	23.0	20.7	20.2	1.51	2.23	<u>0.042</u>
	Day 14	9	25.2	4.8	35.3	26.1	23.8	21.9	20.2	1.22	1.38	0.229
	Day 28	9	25.1	4.8	34.8	26.3	23.8	21.4	20.2	1.11	0.97	0.265
Total Cholesterol (mg/dL)	Day 0	11	190.0	43.4	256.0	228.0	167.0	156.0	137.0	0.50	-1.49	0.089
	Day 14	11	183.8	40.4	269.0	216.0	177.0	147.0	137.0	0.85	0.32	0.354
	Day 28	11	182.5	44.3	257.0	225.0	162.0	142.0	136.0	0.52	-1.46	0.093
LDL (mg/dL)	Day 0	11	117.9	34.6	179.0	135.0	112.0	89.0	82.0	0.90	-0.38	0.067
	Day 14	11	113.7	30.3	183.0	128.0	106.0	96.0	76.0	1.10	1.73	0.347
	Day 28	11	109.5	35.5	176.0	136.0	94.0	82.0	72.0	0.76	-0.71	0.113
HDL (mg/dL)	Day 0	11	53.1	14.1	80.0	65.0	51.0	42.0	35.0	0.51	-0.64	0.415
	Day 14	11	51.1	12.3	78.0	55.0	53.0	41.0	33.0	0.70	1.33	0.581
	Day 28	11	52.4	15.8	86.0	61.0	48.0	42.0	33.0	0.91	0.60	0.429
Triglycerides (mg/dL)	Day 0	11	96.7	49.6	212.0	132.0	80.0	56.0	48.0	1.33	1.73	0.074
	Day 14	11	97.4	48.2	181.0	154.0	72.0	64.0	51.0	0.81	-1.14	<u>0.017</u>
	Day 28	11	106.2	42.5	177.0	128.0	123.0	59.0	57.0	0.21	-1.30	0.156



**Table 57:** Descriptive statistics by time point of dietary intake data for study participants (n=11) without a history of colorectal cancer. P-values less than 0.05 are indicated with a double-underline.

<i>Descriptive Statistics for Study Participants without a History of Colorectal Cancer: Vitamin, Mineral, Macronutrient, and Fiber Intake</i>												
Variable	Time Point	Number of Observations	Mean	S.D.	Max.	Q3	Median	Q1	Min.	Skewness	Kurtosis	S.W. p-value
Vitamin A (µg)	Day 0	11	1376.3	594.4	2552.1	1911.4	1089.9	922.0	820.0	1.01	-0.22	0.059
	Day 14	10	1293.7	648.1	2531.8	1401.9	1217.5	806.0	497.2	0.99	0.33	0.203
	Day 28	10	996.0	323.5	1669.0	1146.1	978.2	760.3	518.1	0.71	1.05	0.692
Vitamin C (mg)	Day 0	11	130.1	46.7	250.0	157.5	107.3	96.7	89.4	1.91	4.15	<u>0.007</u>
	Day 14	10	105.3	40.1	184.0	130.0	89.4	83.1	54.4	0.95	0.21	0.291
	Day 28	10	123.2	56.5	240.8	160.5	107.9	75.3	63.2	0.98	0.55	0.266
Zinc (mg)	Day 0	11	9.9	1.6	13.2	11.5	9.5	8.4	8.0	0.91	0.07	0.264
	Day 14	10	8.8	2.1	12.8	10.1	9.1	6.9	6.1	0.36	-0.16	0.639
	Day 28	10	8.4	2.8	14.9	9.6	7.0	6.6	6.0	1.66	2.29	<u>0.010</u>
Calcium (mg)	Day 0	11	1021.8	197.2	1441.9	1081.2	1002.9	922.4	669.2	0.55	1.76	0.607
	Day 14	10	1001.6	168.7	1221.4	1152.6	1032.3	896.5	683.4	-0.60	-0.29	0.785
	Day 28	10	967.2	161.3	1256.3	1036.8	934.3	883.9	768.1	0.72	-0.23	0.369
Potassium (mg)	Day 0	11	3511.2	580.8	4434.7	3961.7	3530.1	2847.6	2662.9	-0.04	-0.93	0.739
	Day 14	10	3204.4	524.2	4010.4	3718.9	3104.9	2784.9	2553.3	0.47	-1.20	0.349
	Day 28	10	2923.5	594.6	3847.3	3373.1	2897.5	2599.5	1916.3	-0.01	-0.40	0.975
Sodium (mg)	Day 0	11	2849.5	584.7	3807.2	3355.5	2688.4	2457.2	1842.4	0.19	-0.42	0.732
	Day 14	10	3092.4	1010.8	5007.5	3333.1	2741.5	2469.5	2099.6	1.32	0.55	<u>0.016</u>
	Day 28	10	2682.2	794.9	4413.0	2915.9	2823.8	2081.9	1508.9	0.81	1.89	0.331
Iron (mg)	Day 0	11	18.1	4.1	24.4	21.6	16.9	14.7	12.4	0.22	-1.27	0.676
	Day 14	10	16.7	5.9	29.8	20.0	16.9	11.9	10.3	1.14	1.60	0.162
	Day 28	10	16.9	5.8	28.4	17.8	15.6	12.4	11.2	1.24	0.60	0.054
Calories	Day 0	11	2006.1	231.1	2390.8	2189.8	2026.5	1797.3	1629.5	-0.08	-0.79	0.937
	Day 14	10	2015.9	335.8	2641.7	2218.9	1940.6	1709.2	1640.5	0.68	-0.55	0.382
	Day 28	10	1888.6	291.8	2419.9	2099.1	1802.7	1698.4	1481.9	0.75	-0.21	0.365
Protein (g)	Day 0	11	78.6	9.6	94.9	83.9	78.4	74.9	60.1	-0.11	0.70	0.790
	Day 14	10	85.2	13.5	102.6	96.2	86.5	72.2	67.5	-0.07	-1.83	0.211
	Day 28	10	69.9	12.5	95.7	77.6	70.3	59.0	55.6	0.82	0.54	0.276
Carbohydrate (g)	Day 0	11	245.5	31.8	280.8	278.1	249.4	219.0	196.8	-0.42	-1.24	0.149
	Day 14	10	257.5	42.9	317.5	300.0	244.6	217.8	203.0	0.15	-1.68	0.207
	Day 28	10	246.7	52.2	338.1	277.3	240.3	210.5	164.1	0.40	-0.06	0.852
Fat (g)	Day 0	11	78.6	18.2	107.0	93.5	78.9	67.4	51.0	-0.07	-0.84	0.812
	Day 14	10	72.2	16.4	103.8	77.9	71.4	61.4	50.5	0.52	0.26	0.749
	Day 28	10	70.9	13.0	89.1	82.4	69.5	60.4	54.2	0.02	-1.74	0.265
Saturated Fat (g)	Day 0	11	27.7	7.8	41.3	36.2	25.7	23.1	17.9	0.75	-0.57	0.117
	Day 14	10	26.1	7.8	40.1	28.9	24.4	19.6	16.7	0.94	0.00	0.150
	Day 28	10	26.8	5.8	35.6	30.0	27.3	21.0	19.5	0.28	-1.06	0.381
Fiber (g)	Day 0	11	30.2	6.4	40.2	36.6	31.3	24.5	21.1	0.18	-1.36	0.458
	Day 14	10	30.4	7.2	42.9	37.4	28.6	24.5	22.1	0.51	-1.12	0.345
	Day 28	10	27.9	6.5	39.8	32.7	27.5	24.1	18.4	0.18	-0.07	0.890

## APPENDIX II

### 7. Descriptive Statistics of Study Participants with a History of Colorectal Cancer

**Table 58:** Descriptive statistics by time point of age (years), weight (kg), body mass index (kg/m<sup>2</sup>), and serum lipids (mg/dL) for study participants (n=29) with a history of colorectal cancer. P-values less than 0.05 are indicated with a double-underline.

<i>Descriptive Statistics for Study Participants with a History of Colorectal Cancer: Age, Weight, BMI, and Serum Lipids</i>													
Variable	Time Point	Number of Observations	Mean	S.D.	Max.	Q3	Median	Q1	Min.	Skewness	Kurtosis	S.W. p-value	A.D. p-value
Age (years)	Day 0	29	61.6	11.3	84	69	61	53	37	-0.17	-0.15	0.905	0.250
	Day 14	29	61.6	11.3	84	69	61	53	37	-0.17	-0.15	0.905	0.250
	Day 28	29	61.7	11.4	84	69	61	53	37	-0.15	-0.17	0.899	0.250
Weight (kg)	Day 0	29	80.2	17.7	117.9	91.2	80.1	65.8	43.4	0.02	-0.33	0.871	0.250
	Day 14	29	79.7	17.7	118.1	89.9	80.2	65.5	42.3	0.01	-0.26	0.927	0.250
	Day 28	29	79.9	17.9	120.2	89.4	80.4	65.4	42.9	0.07	-0.21	0.918	0.250
BMI (kg/m <sup>2</sup> )	Day 0	29	28.1	5.7	46.1	31.5	26.2	24.7	18.1	0.98	2.22	0.055	0.128
	Day 14	29	28.0	5.7	46.1	31.3	26.3	24.6	17.6	0.99	2.39	0.086	0.222
	Day 28	29	28.0	5.8	46.9	31.4	26.5	24.7	17.9	1.07	2.64	0.057	0.211
Total Cholesterol (mg/dL)	Day 0	29	186.5	44.9	275.0	213.0	183.0	154.0	105.0	0.05	-0.90	0.653	0.250
	Day 14	29	186.8	43.3	287.0	222.0	181.0	154.0	103.0	0.11	-0.44	0.565	0.250
	Day 28	29	188.5	41.9	285.0	222.0	189.0	151.0	104.0	0.13	-0.23	0.960	0.250
LDL (mg/dL)	Day 0	29	105.9	37.6	192.0	133.0	111.0	65.0	44.0	0.08	-0.71	0.193	0.133
	Day 14	29	104.4	36.0	193.0	129.0	105.0	73.0	40.0	0.28	-0.24	0.765	0.250
	Day 28	29	107.1	37.1	205.0	127.0	111.0	83.0	32.0	0.30	0.60	0.839	0.250
HDL (mg/dL)	Day 0	29	52.5	14.9	93.0	57.0	49.0	44.0	27.0	0.87	0.75	0.171	0.126
	Day 14	29	51.2	14.9	88.0	58.0	47.0	41.0	29.0	0.70	0.02	0.190	0.246
	Day 28	29	51.6	14.4	94.0	58.0	50.0	42.0	27.0	0.86	1.29	0.223	0.250
Triglycerides (mg/dL)	Day 0	29	143.1	81.9	338.0	183.0	111.0	76.0	49.0	1.08	0.19	<u>0.002</u>	<u>0.005</u>
	Day 14	29	157.8	88.8	368.0	231.0	136.0	85.0	51.0	0.89	-0.28	<u>0.004</u>	<u>0.005</u>
	Day 28	29	150.9	83.4	382.0	204.0	135.0	83.0	58.0	0.89	0.38	<u>0.011</u>	<u>0.024</u>



**Table 60:** Descriptive statistics by sex of age (years), weight (kg), BMI (kg/m<sup>2</sup>), total cholesterol (mg/dL), LDL (mg/dL), HDL (mg/dL), and triglycerides (mg/dL) for individuals with a history of colorectal cancer. Female (F) and male (M) values displayed in adjacent columns. P-values less than 0.05 are indicated with a double-underline.

<i>Descriptive Statistics by Sex for Study Participants with a History of Colorectal Cancer: Age, Weight, BMI, and Serum Lipids</i>																									
Variable	Time Point	Number of Observations		Mean		S.D.		Max.		Q3		Median		Q1		Min.		Skewness		Kurtosis		S.W. p-value		A.D. p-value	
		F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M
Age (years)	Day 0	17	12	61.2	62.2	10.2	13.3	84.0	80.0	68.0	74.0	61.0	62.0	57.0	52.0	39.0	37.0	-0.04	-0.33	1.22	-0.84	0.76	0.43	0.25	0.25
	Day 14	17	12	61.2	62.2	10.2	13.3	84.0	80.0	68.0	74.0	61.0	62.0	57.0	52.0	39.0	37.0	-0.04	-0.33	1.22	-0.84	0.76	0.43	0.25	0.25
	Day 28	17	12	61.2	62.3	10.2	13.4	84.0	80.0	68.0	74.0	61.0	62.0	57.0	52.0	39.0	37.0	-0.04	-0.31	1.22	-0.85	0.76	0.43	0.25	0.25
Weight (kg)	Day 0	17	12	71.9	92.0	17.3	10.3	118	107	80.1	101	67.6	91.2	63.0	85.7	43.4	74.6	0.99	-0.13	2.13	-0.70	0.15	0.64	0.12	0.25
	Day 14	17	12	71.5	91.4	17.4	10.0	118	105	80.2	100	67.3	90.1	62.1	85.4	42.3	74.4	1.01	-0.17	2.28	-0.77	0.17	0.59	0.15	0.25
	Day 28	17	12	71.9	91.3	18.0	10.1	120	105	80.4	99.8	67.1	89.2	62.1	85.3	42.9	74.6	1.07	-0.04	2.20	-0.88	0.16	0.48	0.16	0.25
BMI (kg/m <sup>2</sup> )	Day 0	17	12	27.1	29.7	6.8	3.3	46.1	34.5	31.3	32.2	25.6	30.2	22.6	26.7	18.1	24.7	1.48	-0.18	2.81	-1.36	<u>0.02</u>	0.44	<u>0.03</u>	0.25
	Day 14	17	12	26.9	29.5	6.8	3.3	46.1	34.4	30.6	32.0	25.5	29.7	22.4	26.6	17.6	24.6	1.48	-0.10	2.89	-1.32	<u>0.04</u>	0.58	<u>0.05</u>	0.25
	Day 28	17	12	27.1	29.4	7.0	3.3	46.9	34.7	31.4	31.9	25.4	29.4	22.4	26.6	17.9	24.7	1.48	0.05	2.86	-1.18	<u>0.03</u>	0.69	<u>0.05</u>	0.25
Total Cholesterol (mg/dL)	Day 0	17	12	196	173	42.4	46.5	275	244	235	213	199	168	158	132	128	105	0.16	0.11	-0.93	-1.24	0.79	0.66	0.25	0.25
	Day 14	17	12	197	172	41.7	43.0	287	235	226	213	204	173	160	140	134	103	0.35	-0.10	-0.49	-1.14	0.43	0.71	0.25	0.25
	Day 28	17	12	199	173	41.3	39.2	285	223	229	208	190	175	160	138	147	104	0.36	-0.35	-0.59	-0.94	0.35	0.48	0.25	0.25
LDL (mg/dL)	Day 0	17	12	114	93.8	36.6	37.2	192	148	133	126	118	97.0	78.0	61.0	61.0	44.0	0.08	0.15	-0.25	-1.49	0.30	0.29	0.25	0.25
	Day 14	17	12	112	94.1	36.1	34.9	193	149	132	122	117	89.5	80.0	66.0	59.0	40.0	0.40	0.11	0.04	-0.98	0.52	0.89	0.25	0.25
	Day 28	17	12	117	93.3	38.2	32.0	205	143	133	115	120	96.5	87.0	75.0	56.0	32.0	0.44	-0.46	0.44	-0.19	0.60	0.95	0.25	0.25
HDL (mg/dL)	Day 0	17	12	60.2	41.6	13.9	8.0	93.0	57.0	68.0	46.5	56.0	41.5	49.0	36.5	44.0	27.0	0.92	0.11	0.25	0.33	0.12	1.00	0.16	0.25
	Day 14	17	12	59.1	39.9	13.3	8.4	88.0	55.0	66.0	44.5	55.0	38.5	46.0	33.0	44.0	29.0	0.72	0.73	-0.40	-0.37	0.12	0.30	0.18	0.25
	Day 28	17	12	58.9	41.2	12.5	9.9	94.0	66.0	63.0	45.0	56.0	39.0	50.0	35.5	42.0	27.0	1.44	1.39	2.68	3.06	<u>0.04</u>	0.11	0.06	0.11
Triglycerides (mg/dL)	Day 0	17	12	111	189	54.0	94.3	265	338	137	272	100	184	69.0	107	49.0	69.0	1.51	0.33	3.00	-1.38	<u>0.02</u>	0.25	0.06	0.25
	Day 14	17	12	133	193	86.5	83.2	368	337	156	264	99.0	160	76.0	137	51.0	73.0	1.61	0.43	2.07	-1.06	<u>0.001</u>	0.36	<u>0.01</u>	0.23
	Day 28	17	12	120	194	65.2	89.6	276	382	162	250	100	191	70.0	125	58.0	59.0	1.14	0.51	0.36	0.40	<u>0.01</u>	0.95	<u>0.01</u>	0.25









**Table 65:** Descriptive statistics by time point and dietary intervention treatment of vascular endothelial growth factor for study participants with a history of colorectal cancer. All cytokine values measured in picograms per milliliter. Three different approaches (deletion, substitution, and extrapolation) were used for managing left-censored data. P-values less than 0.05 are indicated with a double-underline.

<i>Descriptive Statistics by Dietary Intervention Treatment for Study Participants with a History of Colorectal Cancer: Plasma VEGF Concentrations</i>														
Variable	Diet Group	Time Point	Number of Observations	Mean	S.D.	Max.	Q3	Median	Q1	Min.	Skewness	Kurtosis	S.W. p-value	A.D. p-value
Vascular Endothelial Growth Factor (Deletion) (pg/mL)	Control	Day 0	8	144.72	69.54	258.36	185.76	155.75	80.61	55.17	0.25	-0.74	0.724	0.250
		Day 14	7	142.41	26.37	180.61	170.65	138.76	122.92	103.73	0.16	-0.43	0.791	0.250
		Day 28	7	160.27	58.64	234.31	194.01	178.83	129.42	55.17	-0.83	0.75	0.636	0.250
	Navy Bean	Day 0	6	207.36	103.36	374.98	264.66	186.91	151.33	79.36	0.68	0.40	0.855	0.250
		Day 14	6	212.04	126.52	462.44	187.91	182.00	152.45	105.45	2.10	4.88	<u>0.010</u>	<u>0.010</u>
		Day 28	6	228.27	140.39	492.91	242.84	195.96	157.89	84.06	1.63	3.42	0.157	0.122
	Rice Bran	Day 0	8	135.10	88.93	345.57	132.05	115.96	92.01	55.17	2.34	6.13	0.002	0.005
		Day 14	8	152.05	115.40	400.91	196.26	102.74	81.15	55.17	1.73	2.91	<u>0.030</u>	<u>0.039</u>
		Day 28	8	163.51	72.56	313.79	190.05	148.86	122.51	71.48	1.26	2.40	0.352	0.250
Vascular Endothelial Growth Factor (Substitution) (pg/mL)	Control	Day 0	9	128.82	80.66	258.36	165.03	150.30	71.56	1.60	0.01	-0.61	0.948	0.250
		Day 14	9	121.74	77.79	234.31	170.65	137.17	103.73	1.60	-0.58	-0.22	0.335	0.250
		Day 28	9	114.39	76.67	194.01	178.83	136.59	55.17	1.60	-0.63	-1.21	0.092	0.129
	Navy Bean	Day 0	6	207.36	103.36	374.98	264.66	186.91	151.33	79.36	0.68	0.40	0.855	0.250
		Day 14	6	212.04	126.52	462.44	187.91	182.00	152.45	105.45	2.10	4.88	<u>0.010</u>	<u>0.010</u>
		Day 28	6	228.27	140.39	492.91	242.84	195.96	157.89	84.06	1.63	3.42	0.157	0.122
	Rice Bran	Day 0	8	135.10	88.93	345.57	132.05	115.96	92.01	55.17	2.34	6.13	0.002	0.005
		Day 14	8	152.05	115.40	400.91	196.26	102.74	81.15	55.17	1.73	2.91	<u>0.030</u>	<u>0.039</u>
		Day 28	8	163.51	72.56	313.79	190.05	148.86	122.51	71.48	1.26	2.40	0.352	0.250
Vascular Endothelial Growth Factor (Extrapolation) (pg/mL)	Control	Day 0	9	128.64	80.98	258.36	165.03	150.30	71.56	0.01	-0.01	-0.59	0.951	0.250
		Day 14	9	121.38	78.41	234.31	170.65	137.17	103.73	0.01	-0.60	-0.21	0.322	0.250
		Day 28	9	114.04	77.25	194.01	178.83	136.59	55.17	0.01	-0.65	-1.19	0.091	0.126
	Navy Bean	Day 0	6	207.36	103.36	374.98	264.66	186.91	151.33	79.36	0.68	0.40	0.855	0.250
		Day 14	6	212.04	126.52	462.44	187.91	182.00	152.45	105.45	2.10	4.88	<u>0.010</u>	<u>0.010</u>
		Day 28	6	228.27	140.39	492.91	242.84	195.96	157.89	84.06	1.63	3.42	0.157	0.122
	Rice Bran	Day 0	8	135.10	88.93	345.57	132.05	115.96	92.01	55.17	2.34	6.13	0.002	0.005
		Day 14	8	152.05	115.40	400.91	196.26	102.74	81.15	55.17	1.73	2.91	<u>0.030</u>	<u>0.039</u>
		Day 28	8	163.51	72.56	313.79	190.05	148.86	122.51	71.48	1.26	2.40	0.352	0.250



**Table 67:** Descriptive statistics by time point of telomere length measured by multiplex qPCR, interphase FISH, and singleplex qPCR for study participants with a history of colorectal cancer. All telomere length measurements listed are relative estimates and do not possess units. Additionally, due to variability in telomere length of control samples, individual batches of interphase FISH are unable to be directly compared and are therefore listed separately. Similarly, variability was observed within control samples for singleplex qPCR telomere length measurements. For singleplex qPCR telomere measurements, descriptive statistics are shown for each individual plate as well as for the pooled set of samples after normalization to a control. P-values less than 0.05 are indicated with a double-underline.

<i>Descriptive Statistics for Study Participants with a History of Colorectal Cancer: Leukocyte Telomere Length</i>													
Variable	Time Point	Number of Observations	Mean	S.D.	Max.	Q3	Median	Q1	Min.	Skewness	Kurtosis	S.W. p-value	A.D. p-value
Multiplex qPCR Telomere Length	Day 0	26	0.79	0.21	1.29	0.99	0.76	0.64	0.42	0.39	-0.34	0.657	0.250
	Day 28	27	0.76	0.20	1.23	0.86	0.77	0.58	0.43	0.41	-0.18	0.565	0.250
FISH Telomere Length (Batch 1)	Day 0	6	42.50	13.55	60.00	54.00	41.50	35.00	23.00	-0.13	-0.84	0.927	0.250
	Day 14	6	51.33	11.88	65.00	59.00	54.00	44.00	32.00	-0.79	0.15	0.783	0.250
	Day 28	6	49.17	12.66	62.00	60.00	52.50	38.00	30.00	-0.73	-1.01	0.445	0.250
FISH Telomere Length (Batch 2)	Day 0	7	49.57	5.26	56.00	56.00	49.00	45.00	43.00	0.19	-1.78	0.396	0.250
	Day 14	7	50.43	8.28	58.00	58.00	55.00	41.00	41.00	-0.34	-2.65	0.017	0.024
	Day 28	7	44.71	9.62	55.00	53.00	50.00	34.00	31.00	-0.51	-1.78	0.232	0.230
FISH Telomere Length (Batch 3)	Day 0	8	31.00	7.17	38.00	37.00	33.00	25.50	19.00	-0.85	-0.65	0.182	0.225
	Day 14	8	25.38	6.55	37.00	30.00	24.00	20.00	18.00	0.71	-0.33	0.629	0.250
	Day 28	8	30.88	11.13	51.00	36.50	31.50	21.50	17.00	0.57	0.05	0.660	0.250
Singleplex qPCR Telomere Length (Plate 1)	Day 0	12	0.89	0.69	2.19	1.22	0.72	0.42	0.15	1.03	0.19	0.074	0.106
	Day 14	12	1.10	0.71	2.38	1.62	0.85	0.62	0.23	0.84	-0.52	0.120	0.096
	Day 28	12	1.01	0.68	2.09	1.71	0.71	0.44	0.17	0.44	-1.59	0.084	0.066
Singleplex qPCR Telomere Length (Plate 2)	Day 0	10	0.64	0.58	1.87	0.77	0.48	0.21	0.11	1.42	1.11	0.023	0.024
	Day 14	10	0.89	0.68	2.39	1.28	0.57	0.42	0.24	1.33	1.41	0.058	0.072
	Day 28	10	0.93	0.70	2.14	1.19	0.84	0.33	0.20	0.92	-0.26	0.085	0.116
Singleplex qPCR Telomere Length (Plates 1 & 2)	Day 0	22	22.69	18.50	66.03	29.78	16.95	8.74	3.69	1.16	0.33	0.003	0.005
	Day 14	22	29.53	20.46	84.62	45.26	21.52	15.56	5.91	1.16	0.86	0.010	0.007
	Day 28	22	28.92	20.80	75.78	42.12	24.34	11.81	4.37	0.91	0.08	0.020	0.029



**Table 69:** Descriptive statistics by time point and sex of telomere length measured by multiplex qPCR, interphase FISH, and singleplex qPCR for study participants with a history of colorectal cancer. All telomere length measurements listed are relative estimates and do not possess units. Additionally, due to variability in telomere length of control samples, individual batches of interphase FISH are unable to be directly compared and are therefore listed separately. Similarly, variability was observed within control samples for singleplex qPCR telomere length measurements. For singleplex qPCR telomere measurements, descriptive statistics are shown for each individual plate as well as for the pooled set of samples after normalization to a control. Female (F) and male (M) values displayed in adjacent columns. P-values less than 0.05 are indicated with a double-underline.

Descriptive Statistics by Sex for Study Participants with a History of Colorectal Cancer: Leukocyte Telomere Length																											
Variable	Time Point	Number of Observations		Mean		S.D.		Max.		Q3		Median		Q1		Min.		Skewness		Kurtosis		S.W. p-value		A.D. p-value			
		F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M		
Multiplex qPCR Telomere Length	Day 0	14	12	0.87	0.70	0.20	0.19	1.29	1.01	1.01	0.83	0.83	0.67	0.74	0.56	0.53	0.42	0.44	0.53	-0.03	-0.72	0.93	0.17	0.25	0.14		
	Day 28	15	12	0.81	0.71	0.21	0.18	1.23	1.05	1.01	0.84	0.79	0.73	0.63	0.55	0.52	0.43	0.48	0.16	-0.36	-0.38	0.65	0.87	0.25	0.25		
FISH Telomere Length (Batch 1)	Day 0	4	2	43.50	40.50	16.78	7.78	60.00	46.00	57.00	46.00	45.50	40.50	30.00	35.00	23.00	35.00	-0.46	.	-2.38	.	0.68	1.00	0.25	0.23		
	Day 14	4	2	48.00	58.00	13.78	1.41	65.00	59.00	58.00	59.00	47.50	58.00	38.00	57.00	32.00	57.00	0.20	.	0.29	.	0.99	1.00	0.25	0.23		
	Day 28	4	2	46.00	55.50	14.61	6.36	62.00	60.00	58.00	60.00	46.00	55.50	34.00	51.00	30.00	51.00	0.00	.	-3.30	.	0.71	1.00	0.25	0.23		
FISH Telomere Length (Batch 2)	Day 0	4	3	50.25	48.67	6.75	3.51	56.00	52.00	56.00	52.00	51.00	49.00	44.50	45.00	43.00	45.00	-0.17	-0.42	-5.04	.	0.15	0.84	0.15	0.25		
	Day 14	4	3	49.75	51.33	9.00	9.07	58.00	58.00	57.50	58.00	50.00	55.00	42.00	41.00	41.00	41.00	-0.03	-1.52	-5.69	.	0.12	0.32	0.13	0.22		
	Day 28	4	3	48.00	40.33	9.56	9.50	55.00	50.00	54.00	50.00	51.50	40.00	42.00	31.00	34.00	31.00	-1.73	0.16	3.07	.	0.13	0.94	0.11	0.25		
FISH Telomere Length (Batch 3)	Day 0	4	4	34.00	28.00	3.92	8.98	38.00	38.00	37.00	35.50	34.50	27.50	31.00	20.50	29.00	19.00	-0.60	0.17	-0.77	-4.03	0.85	0.51	0.25	0.25		
	Day 14	4	4	29.50	21.25	6.61	3.30	37.00	25.00	34.00	24.00	30.00	21.00	25.00	18.50	21.00	18.00	-0.44	0.23	1.17	-3.87	0.90	0.51	0.25	0.25		
	Day 28	4	4	32.75	29.00	6.55	15.38	37.00	51.00	36.50	39.50	35.50	24.00	29.00	18.50	23.00	17.00	-1.91	1.50	3.69	2.07	0.03	0.26	0.04	0.22		
Singleplex qPCR Telomere Length (Plate 1)	Day 0	6	6	0.96	0.82	0.68	0.75	2.19	2.14	1.26	1.18	0.75	0.67	0.49	0.15	0.35	0.15	1.43	1.17	1.88	1.20	0.23	0.31	0.23	0.25		
	Day 14	6	6	1.13	1.06	0.60	0.86	2.23	2.38	1.43	1.82	0.89	0.76	0.76	0.40	0.61	0.23	1.50	0.88	1.87	-0.90	0.13	0.30	0.12	0.25		
	Day 28	6	6	1.11	0.91	0.74	0.67	2.09	1.84	1.81	1.60	0.94	0.71	0.47	0.40	0.42	0.17	0.38	0.61	-2.30	-1.47	0.16	0.39	0.18	0.25		
Singleplex qPCR Telomere Length (Plate 2)	Day 0	6	4	0.74	0.50	0.74	0.23	1.87	0.77	1.48	0.66	0.40	0.51	0.18	0.34	0.11	0.21	0.97	-0.18	-1.21	1.13	0.09	0.92	0.09	0.25		
	Day 14	6	4	1.08	0.62	0.80	0.37	2.39	1.13	1.50	0.88	0.89	0.55	0.42	0.36	0.36	0.24	0.89	0.96	-0.20	1.28	0.24	0.74	0.25	0.25		
	Day 28	6	4	1.08	0.70	0.83	0.45	2.14	1.19	2.07	1.09	0.84	0.66	0.42	0.31	0.20	0.30	0.59	0.18	-1.79	-4.93	0.17	0.22	0.16	0.21		
Singleplex qPCR Telomere Length (Plates 1 & 2)	Day 0	12	10	25.28	19.59	21.22	15.11	66.03	54.23	42.10	27.41	16.95	17.89	9.91	7.34	4.05	3.69	1.00	1.33	-0.45	2.38	0.03	0.14	0.02	0.23		
	Day 14	12	10	33.44	24.83	22.26	18.06	84.62	60.40	49.19	39.79	22.50	19.53	16.78	10.01	12.90	5.91	1.24	1.00	1.00	-0.01	0.03	0.15	0.04	0.14		
	Day 28	12	10	33.25	23.72	24.09	15.67	75.78	46.71	49.49	40.57	29.56	18.11	12.69	10.43	6.92	4.37	0.76	0.37	-0.64	-1.75	0.10	0.13	0.14	0.12		

**Table 70:** Descriptive statistics by time point of vitamin A ( $\mu\text{g}$ ),  $\beta$ -Carotene ( $\mu\text{g}$ ), vitamin C (mg), vitamin D ( $\mu\text{g}$ ), vitamin E (mg),  $\alpha$ -Tocopherol (mg), vitamin B1 (mg), vitamin B2 (mg), vitamin B3 (mg), vitamin B6 (mg), vitamin B9 ( $\mu\text{g}$ ), and vitamin B12 ( $\mu\text{g}$ ) for study participants (n=29) with a history of colorectal cancer. P-values less than 0.05 are indicated with a double-underline.

<i>Descriptive Statistics for Study Participants with a History of Colorectal Cancer: Vitamin Intake</i>													
Variable	Time Point	Number of Observations	Mean	S.D.	Max.	Q3	Median	Q1	Min.	Skewness	Kurtosis	S.W. p-value	A.D. p-value
Vitamin A ( $\mu\text{g}$ )	Day 0	25	828.3	622.8	2592.3	1044.2	612.6	413.0	161.4	1.59	2.42	<u>0.001</u>	<u>0.005</u>
	Day 14	29	1149.0	726.2	4037.5	1144.6	981.2	829.9	321.4	2.58	8.55	<u>8.7E-06</u>	<u>0.005</u>
	Day 28	29	1198.8	442.7	2280.7	1513.8	1074.2	945.0	466.5	0.69	0.05	0.207	0.130
$\beta$ -Carotene ( $\mu\text{g}$ )	Day 0	25	2586.2	3714.7	15149.7	2483.5	1023.0	504.6	35.9	2.57	6.55	<u>1.2E-06</u>	<u>0.005</u>
	Day 14	29	3767.2	3565.6	18525.2	3731.1	2845.8	2077.3	521.1	2.91	10.31	<u>1.3E-06</u>	<u>0.005</u>
	Day 28	29	3617.8	1832.9	7829.5	3973.9	3280.5	2527.2	698.9	0.88	0.06	<u>0.019</u>	<u>0.009</u>
Vitamin C (mg)	Day 0	25	102.2	88.9	427.4	136.8	86.2	49.6	8.4	2.29	6.83	<u>0.001</u>	<u>0.005</u>
	Day 14	29	127.2	71.4	338.3	181.8	119.8	73.9	36.9	1.08	1.10	<u>0.013</u>	<u>0.024</u>
	Day 28	29	143.4	76.1	406.0	178.2	118.4	91.6	68.6	1.73	3.73	<u>0.0003</u>	<u>0.005</u>
Vitamin D ( $\mu\text{g}$ )	Day 0	25	4.46	3.50	14.21	5.79	3.98	1.56	0.03	1.07	1.00	<u>0.032</u>	0.067
	Day 14	29	4.00	2.26	10.24	5.09	3.45	2.16	1.08	0.95	0.60	<u>0.046</u>	0.084
	Day 28	29	3.67	2.60	12.62	4.35	3.38	1.81	0.61	1.78	4.27	<u>0.001</u>	<u>0.006</u>
Vitamin E (mg)	Day 0	25	1.87	2.98	10.96	1.88	0.55	0.11	0.02	2.20	4.43	<u>1.8E-06</u>	<u>0.005</u>
	Day 14	29	0.69	0.67	3.29	0.67	0.51	0.37	0.08	2.64	7.85	<u>1.1E-06</u>	<u>0.005</u>
	Day 28	29	1.25	1.67	8.11	1.22	0.72	0.41	0.02	3.12	10.74	<u>1.3E-07</u>	<u>0.005</u>
$\alpha$ -Tocopherol (mg)	Day 0	25	8.17	9.67	49.68	8.77	5.58	3.33	1.96	3.62	14.98	<u>1.8E-07</u>	<u>0.005</u>
	Day 14	29	7.01	2.72	15.65	8.86	6.76	4.88	3.63	1.18	2.01	<u>0.010</u>	0.055
	Day 28	29	7.55	2.69	14.19	9.13	7.77	5.28	3.19	0.44	-0.05	0.474	0.250
Vitamin B1 (mg)	Day 0	25	1.27	0.86	4.79	1.42	1.12	0.84	0.35	3.09	12.03	<u>4.5E-06</u>	<u>0.005</u>
	Day 14	29	1.37	0.52	2.61	1.69	1.31	1.00	0.50	0.52	-0.30	0.515	0.250
	Day 28	29	1.58	0.48	2.57	1.91	1.61	1.14	0.86	0.19	-0.98	0.258	0.250
Vitamin B2 (mg)	Day 0	25	1.80	0.71	3.36	1.96	1.74	1.34	0.49	0.57	0.25	0.263	0.135
	Day 14	29	1.80	0.50	3.04	2.01	1.77	1.49	0.59	0.35	1.12	0.371	0.165
	Day 28	29	2.04	0.61	3.41	2.46	1.89	1.67	0.93	0.31	-0.47	0.826	0.250
Vitamin B3 (mg)	Day 0	25	18.05	8.59	39.06	21.87	16.20	14.48	3.81	0.58	0.54	0.201	0.115
	Day 14	29	20.14	7.17	32.58	25.28	20.86	14.36	6.37	-0.07	-1.00	0.474	0.250
	Day 28	29	20.93	6.54	36.70	25.72	21.50	14.85	10.61	0.20	-0.40	0.403	0.250
Vitamin B6 (mg)	Day 0	25	1.42	0.53	2.25	1.85	1.36	1.04	0.44	-0.08	-1.00	0.415	0.250
	Day 14	29	1.88	0.67	3.10	2.50	1.70	1.39	0.77	0.47	-1.04	<u>0.031</u>	<u>0.015</u>
	Day 28	29	2.00	0.73	3.58	2.51	1.86	1.47	0.88	0.47	-0.59	0.165	0.141
Vitamin B9 ( $\mu\text{g}$ )	Day 0	25	313.9	176.8	948.4	406.6	262.2	210.3	89.9	1.93	5.99	<u>0.001</u>	<u>0.017</u>
	Day 14	29	325.2	94.2	551.2	356.6	332.6	255.2	148.9	0.26	0.02	0.859	0.250
	Day 28	29	359.5	119.3	625.5	436.4	332.3	273.9	193.0	0.64	-0.44	0.113	0.143
Vitamin B12 ( $\mu\text{g}$ )	Day 0	25	2.91	1.45	5.71	3.64	2.91	1.85	0.35	0.16	-0.53	<u>0.766</u>	0.250
	Day 14	29	3.49	1.67	7.97	4.12	3.09	2.37	0.88	1.06	1.08	<u>0.045</u>	<u>0.054</u>
	Day 28	29	3.08	1.46	6.28	4.00	2.96	1.82	0.83	0.64	-0.35	0.101	0.132







**Table 74:** Descriptive statistics by time point of zinc, calcium, potassium, sodium, iron, magnesium, and selenium for study participants (n=29) with a history of colorectal cancer. All mineral intakes were measured in milligrams. P-values less than 0.05 are indicated with a double-underline.

<i>Descriptive Statistics for Study Participants with a History of Colorectal Cancer: Mineral Intake</i>													
Variable	Time Point	Number of Observations	Mean	S.D.	Max.	Q3	Median	Q1	Min.	Skewness	Kurtosis	S.W. p-value	A.D. p-value
Zinc (mg)	Day 0	25	7.8	3.2	15.5	9.4	7.6	5.7	2.2	0.37	0.14	0.930	0.250
	Day 14	29	10.3	3.7	22.1	11.6	9.9	8.2	4.7	1.41	2.98	<u>0.006</u>	<u>0.011</u>
	Day 28	29	9.8	2.6	16.0	11.0	9.8	8.1	5.8	0.80	0.44	0.083	0.137
Calcium (mg)	Day 0	25	966.5	448.8	2072.8	1333.5	876.1	628.5	264.2	0.58	-0.16	0.299	0.242
	Day 14	29	1016.4	333.5	1935.7	1198.2	886.2	797.0	524.9	0.96	0.68	<u>0.032</u>	<u>0.020</u>
	Day 28	29	1055.4	339.6	2050.0	1110.1	1033.0	888.7	538.0	1.20	2.12	<u>0.014</u>	<u>0.026</u>
Potassium (mg)	Day 0	25	2605.4	849.1	4668.5	2928.5	2384.1	1943.9	1516.3	1.13	0.55	<u>0.008</u>	<u>0.006</u>
	Day 14	29	3292.5	591.1	4633.8	3595.2	3353.3	3062.1	2206.2	-0.02	0.04	0.462	0.250
	Day 28	29	3553.9	747.3	4914.0	4184.6	3471.4	3090.7	2257.3	0.01	-0.89	0.441	0.250
Sodium (mg)	Day 0	25	2957.4	822.8	4210.9	3578.6	3221.6	2634.4	970.8	-0.82	0.06	0.106	0.071
	Day 14	29	2814.3	811.0	4307.8	3355.2	2827.6	2327.8	1062.9	0.05	-0.28	0.831	0.250
	Day 28	29	2770.4	662.6	4227.7	3207.0	2787.4	2229.0	1291.3	0.21	-0.09	0.715	0.250
Iron (mg)	Day 0	25	14.3	9.3	50.7	17.5	12.4	9.5	4.3	2.67	9.67	<u>4.E-05</u>	<u>0.005</u>
	Day 14	29	15.8	4.0	25.8	18.1	15.0	13.4	7.2	0.29	0.47	0.955	0.250
	Day 28	29	17.1	5.5	32.6	19.4	16.1	12.8	10.4	1.24	1.42	<u>0.007</u>	<u>0.018</u>
Magnesium (mg)	Day 0	25	330.2	186.8	792.7	343.8	304.0	218.7	107.1	1.40	1.63	<u>0.001</u>	<u>0.005</u>
	Day 14	29	409.4	136.3	757.8	515.9	358.3	322.3	203.6	0.63	-0.08	0.179	0.137
	Day 28	29	422.9	106.7	683.6	512.7	416.9	349.1	239.3	0.29	-0.25	0.652	0.250
Selenium (mg)	Day 0	25	74.7	38.2	184.8	87.9	71.2	46.8	9.9	1.03	1.74	0.139	0.175
	Day 14	29	79.5	31.7	146.6	101.6	75.7	56.6	28.0	0.45	-0.53	0.344	0.250
	Day 28	29	75.5	25.8	140.1	89.2	74.5	55.8	36.8	0.67	0.54	0.144	0.250







**Table 79:** Descriptive statistics by time point and dietary treatment group of oleic acid, linoleic acid, linolenic acid, and fiber intake for study participants (n=29) with a history of colorectal cancer. All macronutrient intakes were measured in grams. P-values less than 0.05 are indicated with a double-underline.

Descriptive Statistics by Dietary Intervention Treatment for Study Participants with a History of Colorectal Cancer: Fatty Acid and Fiber Intake														
Variable	Diet Group	Time Point	Number of Observations	Mean	S.D.	Max.	Q3	Median	Q1	Min.	Skewness	Kurtosis	S.W. p-value	A.D. p-value
Oleic Acid (g)	Control	Day 0	8	22.4	18.8	63.2	27.6	18.0	9.0	6.5	1.74	3.18	<u>0.037</u>	0.055
		Day 14	10	20.5	7.1	32.8	26.1	18.8	14.3	13.2	0.67	-0.96	0.207	0.250
		Day 28	10	18.6	7.5	34.4	23.5	14.9	12.8	11.3	1.10	0.48	0.080	0.085
	Navy Bean	Day 0	9	15.6	7.3	27.6	19.4	14.5	9.6	5.4	0.44	-0.62	0.808	0.250
		Day 14	10	15.5	7.4	29.4	21.1	13.7	9.4	7.9	0.89	-0.38	0.167	0.196
		Day 28	10	15.9	6.6	29.3	18.5	15.6	10.6	5.4	0.54	1.04	0.802	0.250
	Rice Bran	Day 0	8	17.7	5.6	25.6	23.0	16.2	13.1	11.1	0.44	-1.54	0.353	0.250
		Day 14	9	20.9	5.0	32.5	23.1	19.7	17.4	16.1	1.66	3.26	0.063	0.109
		Day 28	9	19.8	7.7	30.4	25.9	20.9	12.1	9.3	-0.24	-1.42	0.382	0.250
Linoleic Acid (g)	Control	Day 0	8	13.4	10.3	31.3	19.9	12.2	4.8	1.9	0.79	-0.30	0.420	0.250
		Day 14	10	9.8	6.5	26.3	10.2	8.3	5.9	3.5	2.06	5.11	<u>0.009</u>	<u>0.017</u>
		Day 28	10	9.5	4.7	21.3	10.3	8.7	7.4	4.1	1.94	5.03	<u>0.016</u>	<u>0.020</u>
	Navy Bean	Day 0	9	8.6	5.8	19.5	11.8	8.9	3.3	2.1	0.63	-0.02	0.416	0.250
		Day 14	10	7.7	4.3	17.3	8.7	6.2	4.5	4.4	1.64	1.99	<u>0.007</u>	<u>0.008</u>
		Day 28	10	8.7	3.8	14.9	11.8	9.0	5.6	2.6	-0.01	-0.61	0.988	0.250
	Rice Bran	Day 0	8	11.3	4.8	19.4	14.9	10.0	7.6	5.9	0.78	-0.59	0.425	0.250
		Day 14	9	11.5	2.5	16.0	12.9	10.8	9.3	8.8	0.68	-0.68	0.368	0.250
		Day 28	9	10.4	3.7	16.2	11.9	10.1	7.2	5.6	0.33	-0.90	0.653	0.250
Linolenic Acid (g)	Control	Day 0	8	1.54	1.42	4.21	2.32	1.00	0.62	0.23	1.28	0.52	0.059	0.052
		Day 14	10	1.02	0.48	1.93	1.44	0.74	0.65	0.61	0.88	-0.73	<u>0.024</u>	<u>0.022</u>
		Day 28	10	1.11	0.57	2.58	1.24	0.97	0.83	0.50	2.16	5.81	<u>0.006</u>	<u>0.010</u>
	Navy Bean	Day 0	9	0.78	0.54	2.08	0.89	0.67	0.41	0.27	2.00	4.86	<u>0.015</u>	<u>0.027</u>
		Day 14	10	0.84	0.29	1.58	0.91	0.74	0.70	0.56	2.12	5.05	<u>0.004</u>	<u>0.005</u>
		Day 28	10	1.18	0.47	1.73	1.58	1.30	0.81	0.44	-0.36	-1.62	0.201	0.208
	Rice Bran	Day 0	8	1.33	0.85	2.94	1.79	1.02	0.74	0.61	1.35	0.59	<u>0.033</u>	<u>0.034</u>
		Day 14	9	1.58	0.78	3.38	1.69	1.40	1.07	0.88	1.83	3.56	<u>0.023</u>	<u>0.036</u>
		Day 28	9	1.18	0.32	1.71	1.37	1.28	0.87	0.77	0.07	-0.89	0.457	0.250
Fiber (g)	Control	Day 0	8	30.2	17.9	66.4	40.9	22.3	17.0	15.1	1.35	1.30	0.061	0.079
		Day 14	10	26.5	5.4	35.6	32.0	25.9	21.4	20.5	0.51	-1.06	0.313	0.250
		Day 28	10	24.3	6.9	39.5	25.6	23.0	18.8	16.8	1.36	1.84	0.118	0.127
	Navy Bean	Day 0	9	19.9	10.0	39.8	23.5	15.6	12.3	10.7	1.22	0.53	0.080	0.093
		Day 14	10	29.4	7.2	43.5	32.2	27.8	24.1	21.2	1.10	0.38	0.154	0.139
		Day 28	10	33.4	6.8	42.0	41.3	31.5	30.3	24.0	0.04	-1.38	0.170	0.214
	Rice Bran	Day 0	8	24.6	8.0	37.6	30.2	24.1	17.4	15.6	0.36	-1.11	0.474	0.250
		Day 14	9	32.2	5.6	43.4	33.7	32.8	27.5	24.0	0.61	1.20	0.461	0.250
		Day 28	9	33.7	6.9	41.8	38.8	37.1	29.5	22.4	-0.54	-1.25	0.302	0.250

