Interventional Bioremediation of Microbiota In Metabolic Syndrome

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Study Product: Fecal Microbiota (FM)

Protocol Number: CTSI# 22791

IND Number: 16346

Trial Registration: NCT02730962

Version / Date: Version 4 /19 May 2016

CONFIDENTIAL

Version History

Version #	Version Date	Significant Changes from Previous Version
Version 1	09 Jan 2015	Original Protocol Version
Version 2	09 Jun 2015	Added secondary hypothesis and objective to test antibiotic conditioning versus placebo. Added two exclusion criteria regarding renal insufficiency and immune deficiencies.
Version 3	01 February 2016	Added procedures for lean donor group. Clarified dietary measures. Added procedures for oral glucose tolerance testing, resting metabolic rate, optional 6 hour clamp, FitBit data, and tools for participants to record adverse events. Expanded table of contents to include sub-section headings.
Version 4	04 May 2016	Increased number of participant visits from 13 to 15 to account for time needed between body composition and insulin clamp assessments. Specified that hepatic MRI and fMRI will be optional procedures. Clarified stool sample collection procedures. Added safety monitoring details.

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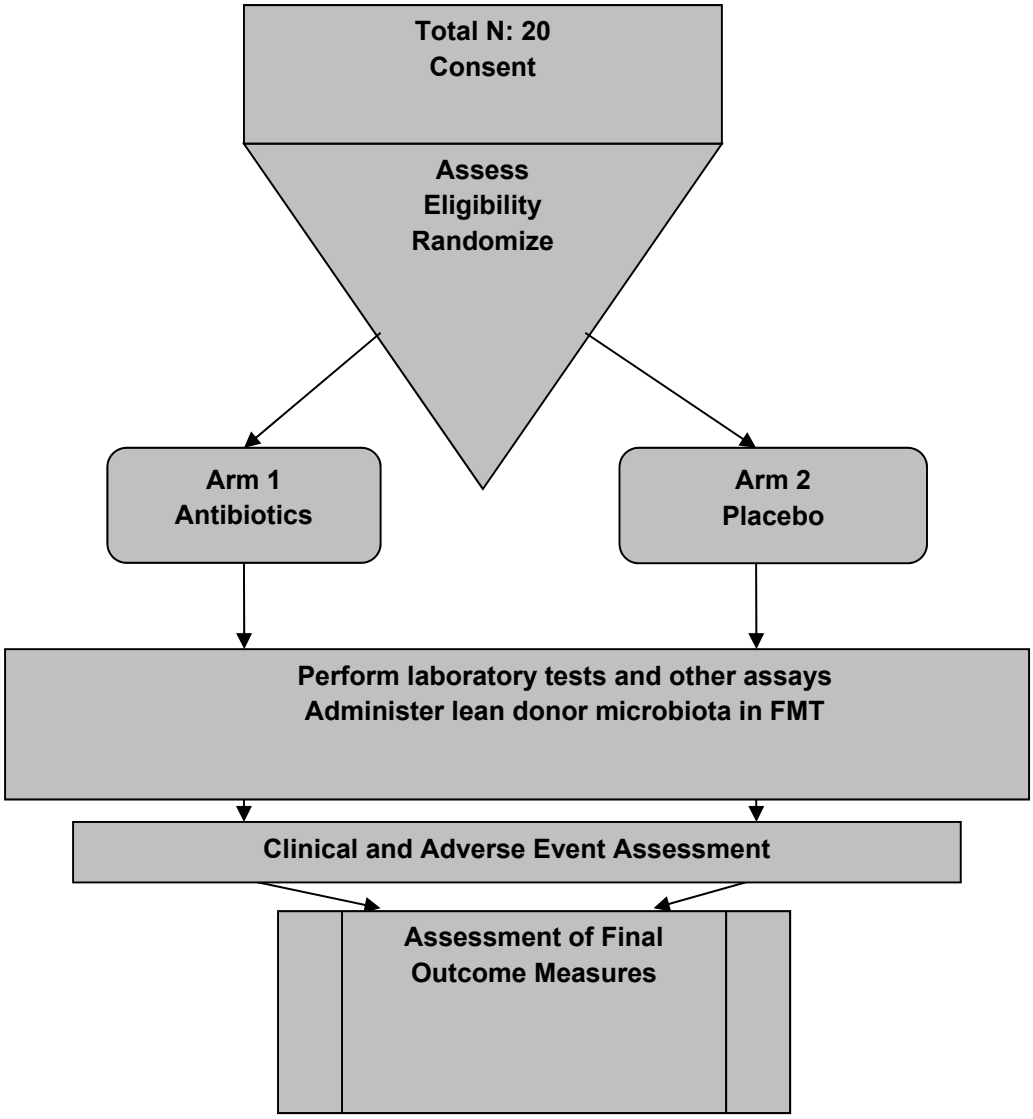
List of Abbreviations

AE	Adverse Event
ALT	Alanine Aminotransferase
AST	Aspartate Aminotransferase
BMI	Body Mass Index
CDI	Clostridium difficile Infection
CFR	Code of Federal Regulations
CRF	Case Report Form
CTCAE	Common Terminology Criteria for Adverse Events
DHQ	Diet History Questionnaire
DNA	Deoxyribonucleic Acid
ET	Early Termination
FDA	Food and Drug Administration
FFM	Fat Free Mass
FMT	Fecal Microbiota Transplant
FWA	Federal-wide Assurance
GIR	Glucose Infusion Rate
HIPAA	Health Insurance Portability and Accountability Act
HIV	Human Immunodeficiency Virus
IBD	Inflammatory Bowel Diseases
IBS	Irritable Bowel Syndrome
ICH	International Conference on Harmonization
ICMJE	International Committee of Medical Journal Editors
IDS	Investigational Drug Service
IND	Investigational New Drug
IRB	Institutional Review Board
ITT	Intent to Treat
MOGTT	Modified Oral Glucose Tolerance Test
NCI	National Cancer Institute
NDSR	Nutrient Data System for Research
PEG	Polyethylene Glycol
PICRUSt	Phylogenetic Investigation of Communities by Reconstruction of Unobserved States
PO	Per Os (by mouth)
RMR	Resting Metabolic Rate
SAE	Serious Adverse Event
UPIRTSO	Unanticipated Problems Involving Risks to Subjects or Others
TID	Ter in Die (three times a day)
US	United States

Protocol Summary

Title:	Interventional Bioremediation of Microbiota In Metabolic Syndrome
Phase:	1
Population:	20 pre-diabetic, obese or overweight males and females. Subjects will be recruited from the Twin Cities metropolitan area and will participate as outpatients in this clinical study.
Number of Sites:	1 (University of Minnesota)
Study Duration:	48 months
Subject Participation Duration:	Approximately 8 months
Agent or Intervention:	Distal gut microbiota prepared from fecal material by filtration and frozen. Subjects are randomized to antibiotic conditioning or placebo prior to receiving lean donor microbiota in a fecal microbiota transplantation procedure.
Objectives:	The primary objective of this study is to measure changes in insulin sensitivity using the insulin clamp technique associated with FMT in pre-diabetic subjects.
Endpoints:	The primary endpoint is the change in insulin sensitivity measured by standard euglycemic insulin clamp. Comparison will be made between the baseline measurement ~ 4 weeks prior to FMT and final measurement ~ 6 weeks post-FMT.

SCHEMA


Total N: 20
Consent
Assess
Eligibility
Randomize
Arm 1
Antibiotics
Arm 2
Placebo
Perform laboratory tests and other assays
Administer lean donor microbiota in FMT
Clinical and Adverse Event Assessment
Assessment of Final
Outcome Measures

1. Background Information and Scientific Rationale

1.1. Hypotheses

Primary Hypothesis: We propose that replacement of dysfunctional or disrupted (dysbiotic) microbiota in overweight or obese pre-diabetic subjects with microbiota obtained from lean donors will lead to greater improvement in insulin sensitivity. Furthermore, we anticipate that lean microbiota engraftment will result in a change in dietary intake and functional brain imaging will demonstrate altered responsiveness toward calorie-rich food images in homeostatic and hedonistic areas of the brain.

Secondary Hypothesis: We anticipate that optimal engraftment of the donor microbial community will require an antibiotic conditioning regimen. Thus, half of our subjects will be treated with antibiotics prior to FMT, and the other half will receive placebo. All subjects will undergo FMT using lean donor microbiota. We will measure similarity of recipient microbiota to donor in terms of taxonomic phylotypes and functional (metabolic) potential.

1.2. Background

Metabolic syndrome is a chronic disorder of energy utilization and storage in humans. Its multiple complications including obesity, diabetes, vascular disease, osteoarthritis, sleep apnea, liver disease, increased cancer risk, and many others, constitute the largest single health problem in the US and increasingly the world. A core problem underlying obesity and diabetes is the imbalance between energy intake/harvest and expenditure/distribution, which has simplistically been viewed as a mere issue of diet and exercise. Weight-loss programs based on diet and exercise alone typically achieve only short-term improvements, and typically fail to reach their target goals despite considerable investment of effort and resources. The failure is often blamed on the patient, but likely results from other factors that remain poorly understood in this complex disease.

While genetic predisposition plays a role in individual susceptibility to metabolic syndrome, environmental factors are undoubtedly involved since the pace of the obesity epidemic over the past several decades cannot possibly be explained by genetic selection. Recently, a number of seminal studies, done in both animals and humans, recognized the important role of gut microbiota in whole-body energy metabolism, and a compelling case now exists that altered gut microbiota is one of the elusive environmental influences driving the ongoing obesity epidemic (Cox and Blaser, 2013; Musso et al., 2011; Tremaroli and Backhed, 2012; Turnbaugh and Gordon, 2009). The composition and metabolic potential of gut microbiota in obese individuals is characteristically different from that in lean individuals. Specifically, microbiota from obese individuals contains less taxonomic diversity and is deficient in its potential to digest complex polysaccharides (Ridaura et al., 2013; Shen et al., 2013). In a landmark study of twins discordant for obesity, microbiota from obese siblings induced weight gain in germ-free animals irrespective of recipient diet composition (Ridaura et al., 2013). In contrast, microbiota from lean siblings inhibited this weight gain, but only on a diet rich in complex polysaccharides (i.e. high in whole grains, fruits, and vegetables). This result may explain why diet alone typically fails in individuals lacking the appropriate gut microbiota.

The human body represents a complex synergistic platform for microorganisms, which have co-evolved with their host and exist in highly organized and specialized microbial communities. The gastrointestinal tract contains 99% of these microbes, with numbers approaching 10^{11}/mg in the luminal contents of the colon. Collectively, these microbes outnumber the number of host cells by a factor of ten to one, and contain >100-fold more genes. Scientifically, the gut microbiota is now recognized as an organ integral to human physiology, and interacts intimately with the host metabolism and the immune system (Backhed et al., 2005). Since the vast majority of commensal gut microorganisms cannot be cultured in vitro using classical microbiological techniques, the entire field of host-microbiota interactions could not develop until emergence of culture-independent technologies that use metagenomics, metatranscriptomics, metabolomics (and other 'omics') technologies armed with computational methods able to analyze massive amounts of data. Over the last several years major initiatives, such as the NIH-sponsored Human Microbiome Project (HMP), started to define the "normal" bacterial constituents of the gut microbiome (HMP normal = healthy 18-40 year old individuals in several large American cities). Strikingly, when compared to certain ancestral populations, such as those from rural communities in Malawi (Africa) and remote villages of Amerindians in the Amazon forest, the Western gut microbiome (even the lean individuals from the HMP database) is substantially less diverse (Yatsunenko et al., 2012). Indeed, there has been increasing concern that changes in societal lifestyles, including pervasive use of antibiotics and increased consumption of calorie-rich processed foods, has resulted in population-wide ecological disruptions within our own bodies (Blaser, 2006). A common theme in comparing Western siblings discordant for obesity or comparing Western versus ancestral community microbiome is the decreased potential to digest complex polysaccharides. At first glance, this is counterintuitive since loss of digestive capacity should result in decreased energy harvest. However, microbial metabolites have the potential for extensive signaling within the host, and impact appetite, intestinal motility, metabolic rate, and energy storage.

Over the recent years short chain fatty acids (SCFAs), the principal end-product of bacterial fermentation of polysaccharides (and include Formic acid, Acetic acid, Propionic acid, Isobutyric acid, Butyric acid, Isovaleric acid, and Pentanoic acid), have received the most attention as potential microbial products that can regulate host metabolism over the last several years. They signal via the G-protein coupled free fatty acid receptors (FFARs), which are expressed widely in humans, including in the enteroendocrine system, liver, brain, sympathetic nervous system, muscle, adipose tissue, immune cells, and pancreatic beta cells (Fig 1).

SCFAs promote intestinal gluconeogenesis, in part, via a gut-brain neural circuit, which is sensed by the liver and leads to decreased circulating glucose by inhibiting liver gluconeogenesis (De Vadder et al., 2014). Moreover, SCFAs improve gut barrier function by enhancing secretion of gut peptides by the colonic L cells and by providing energy to the colonocytes. An improved gut barrier lowers the circulating endotoxin levels and the associated inflammatory state characteristic of metabolic syndrome. In addition, SCFAs participate in gut peptide mediated appetite suppression, adipose tissue signaling (e.g., increased leptin production), and pancreatic β-cell function (Shen et al., 2013). However, it is also virtually certain that other products of microbial metabolism are involved in human energy metabolism. In fact, ~ 10% of circulating small molecules in the body are derived from microbial metabolism (Wikoff et al., 2009)! Secondary bile acids, produced in the distal gut, are known

to be involved in host lipid metabolism and immune function (Stepanov et al., 2013). Gut microbiota are also involved in setting the tone of the endocannabinoid system, which plays an important role in food intake (Cani et al., 2007; Muccioli et al., 2010). Collectively, there is compelling evidence that altered gut microbiota activity of individuals with metabolic syndrome can impact all aspects of energy metabolism: energy intake, harvest, expenditure, storage, and distribution. Physiologically, *insulin resistance* and increased circulating levels of glucose, which ultimately manifest as type 2 diabetes, are one of the central features in metabolic syndrome.

No serious study of human obesity and metabolic syndrome can ignore the central role of eating behavior, which is dictated both by metabolic requirements and multiple psychological, social, and environmental influences. With the development of functional MRI (fMRI) technology, researchers have been able to visualize a network of brain areas that are activated in response to nutrient ingestion, food cues, anorexigenic and orexigenic gut peptides, and hormones such as insulin and leptin (De Silva et al., 2012). Certain areas of the brain, such as the hypothalamus, regulate food intake based on homeostatic signals, e.g., glucose levels and hormone signaling, and are dependent on central insulin sensitivity. However, several other regions, including the ventral and dorsal striatum, insula, anterior cingulated cortex, amygdala, orbitofronal cortex, ventral pallidum, and medial prefrontal cortex, incorporate hedonistic calculus into the overall food intake control. Collectively, multiple studies demonstrate that obesity is associated with both altered responsiveness in homeostatic brain regions, and altered responsiveness in the hedonistic regions characterized by hyperactive reward to high calorie food cues and reduced consummative food reward. Furthermore, activity in both homeostatic and hedonistic brain centers is regulated in part by satiety-related gut hormones, which are modulated by products of microbial metabolism (Shen et al., 2013).

Most of our current understanding in this highly complex field is built on association studies. While these studies have offered some insights, the next step towards making causal connections requires direct interventional approaches. However, we are a long way from understanding rules of microbial community assembly and function within the human host. While probiotics may have some potential in altering the gut microbial community structure, microorganisms contained in probiotics are often limited in number, not adapted to the human host, do not become established (fail to engraft), and their effects are generally negligible, indirect, and unpredictable.

Currently, the most effective known way to substantially alter the gut microbiota is to perform fecal microbiota transplantation (FMT). A promising pilot study on FMT analogous to one we propose here was reported by Vrieze and colleagues in 2012 (Vrieze et al., 2012). Male subjects with metabolic syndrome (9 per group) received their own fecal microbiota or fecal microbiota from lean male donors via a duodenal tube following bowel lavage. The allogenic (non-self) treatment group was found to have increased fecal microbial diversity, increased prevalence of a butyrate-producing bacterium, *Roseburia intestinalis*, and increased peripheral insulin sensitivity 6 weeks after the procedure, while the autologous (self) treatment group experienced no changes.

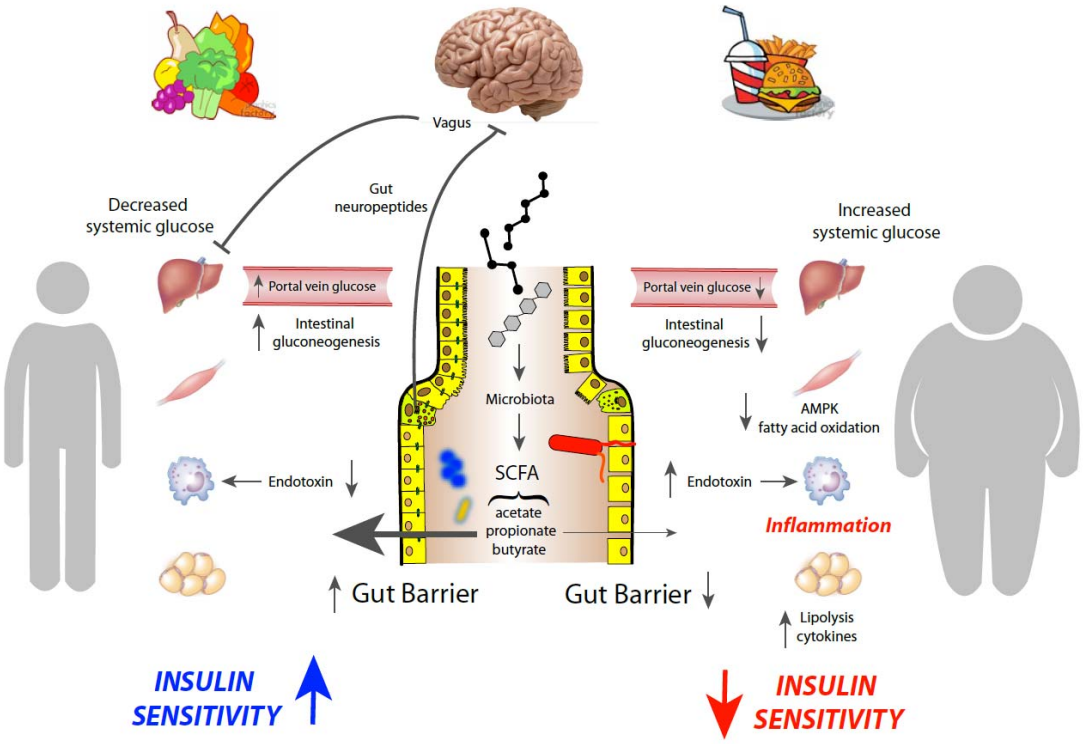


Figure 1. Microbiota, food, and brain function in the pathogenesis of insulin resistance and development of diabetes. Metabolically capable microbiota, illustrated on the left side of the figure, digest complex polysaccharides reaching the distal gut and produce end products, such as short chain fatty acids, which strengthen the gut barrier function. In contrast, less capable microbiota, illustrated on the right side of the figure, is not able to perform this function well, which leads to disrupted gut barrier function. Microbiota in individuals with metabolic syndrome also contains higher proportion of Proteobacteria (Gram-negative facultative anaerobes), which tend to translocate more readily through the gut causing "metabolic endotoxemia". Short chain fatty acids have pleiotropic effects within the intestine and throughout the host, which is illustrated by various target organs such as liver, muscle, the immune system, and adipose tissue. Butyrate and propionate promote intestinal gluconeogenesis, which leads to increased portal vein glucose concentration and decreased liver gluconeogenesis, which ultimately leads to lower systemic glucose levels. Short chain fatty acids also promote secretion of satiety-related gut neuropeptides by the enterochromaffin cells, which alter the brain responsiveness to food stimuli. All combined, optimized diet and microbiota are both necessary to achieve best insulin sensitivity and prevent or treat metabolic syndrome.

Over the past number of years we have developed a clinical fecal microbiota transplant program for treatment of patients with refractory *Clostridium difficile* infection (CDI). The vast majority of these patients have multiply recurrent *C. difficile* infection syndrome (R-CDI), a condition characterized by virtual certainty of infection relapse if anti-CDI antibiotics, e.g., vancomycin or fidaxomicin, are discontinued. We and others have shown that fecal microbial community structure in these patients is markedly disrupted with marked decrease in overall microbial

diversity, commonly complete loss of the entire Bacteroidetes phylum, and major relative expansion of the Proteobacteria, and specifically members of the family *Enterbacteraceae*. FMT results in prompt recovery of normal (donor-like) fecal microbial community structure, which is associated with rapid resolution of this clinical syndrome.

In our program we developed standardized protocols of rigorous donor screening and testing, consistent laboratory preparation of donor microbiota, and microbiota cryopreservation. We will draw on this well-developed infrastructure to conduct this trial. The most important difference, however, is that subjects entering this trial will not have had antibiotic-disrupted microbiota as our classical CDI patients. Our CDI patients are offered FMT only after failure of all standard antibiotic regimens, which equals to a massive amount of antibiotic exposure in multiple cycles over an average period of a year (Hamilton et al., 2012). Therefore, it is not surprising that we observe prompt restoration of the normal fecal microbial community structure that closely resembles the donor microbiota.

In contrast to the experience with FMT in treating CDI, several groups have done pilot studies with FMT in treatment of ulcerative colitis. Angelberger and colleagues used metronidazole for 5-10 days prior to FMT, and saw evidence of stable engraftment only in one recipient (Angelberger et al., 2013). Interestingly, this recipient also had the best clinical response. Engraftment was either transient or minimal in the other 4 subjects in the study. Rossen and colleagues have recently reported results from a phase 2 trial of FMT, where one group received their own (autochthonous) microbiota, and the other group received healthy donor microbiota via nasoduodenal infusion (Rossen et al., 2015). There was some evidence of engraftment in the recipients of allochthonous microbiota, although basic microbial community structure signatures were comparable in responders of both groups. The clinical response rates were comparable between recipients of autochthonous and allochthonous microbiota. The methodological differences in terms of recipient characteristics and microbiome analysis between the two studies make it impossible to comment on the value of metronidazole pre-treatment. However, a single antibiotic that has previously been found to have no beneficial effect in ulcerative colitis and targeting arguably the most desirable constituents of microbiota highlights the need for greater exploration of this point.

Taking the results of these previous trials together, we hypothesize that an antibiotic conditioning regimen will be essential in this protocol to achieve optimal engraftment. In order to test this hypothesis, half of the subjects in this study will be treated with a cocktail of antibiotics prior to FMT and the other half will be given placebo.

1.3. Scientific Rationale

Distal gut microbiota participate in all aspects of energy metabolism, including energy intake, harvest, distribution, and expenditure. Products of microbial fermentation, such as SCFAs, have the potential to interact with multiple signaling pathways in the host. Individuals who are obese or have diabetes have altered composition of distal gut microbiota. Replacing this microbiota with that isolated from lean individuals has the potential to have beneficial effects on energy metabolism.

The goal in this study is to achieve an ecologically stable state of gut microbiota that is metabolically more capable to digest complex polysaccharides, produce short chain fatty acids, and less capable in breaching the gut barrier. We hypothesize that in order to achieve that we will need to suppress the native microbiota and open up ecological niches in the intestine for optimal engraftment of new microbial constituents.

The role of conditioning antibiotics prior to FMT has not been systematically investigated. We hypothesize that antibiotic conditioning is critical for successful engraftment of the donor microbial community. We will now directly test how antibiotic conditioning contributes to donor microbiota engraftment – half of our subjects will receive antibiotics and half will receive placebo. All subjects will undergo FMT using lean donor microbiota.

1.4. Potential Risks and Benefits

FMT has emerged in the recent years primarily as a response to the *C. difficile* epidemic. Multiple case series collected from across the US, Canada, Europe, Australia have been consistent in the overall efficacy of this procedure, regardless of technical details such as route of administration. A small, randomized trial was reported in 2013 using FMT in the treatment of recurrent CDI, in comparison with standard antibiotic therapy. Thus far, the experience has been impressive for clinical efficacy, and few reported side effects. A multicenter experience reported by Kelly and colleagues on using FMT in 80 immunosuppressed patients suffering from recurrent CDI did not uncover infectious disease risks in this theoretically most vulnerable population. However, we recognize the unknown elements of complex microbiota, even when prepared from absolutely asymptomatic, healthy donors. We cannot exclude the possibility of a potential pathobiont, silent in the donor, causing an infection in the new recipient. In addition, we cannot exclude a possibility that a particular microbial community may in result in some untoward metabolic or immunologic consequence in a new host, even though it was apparently working well in the original donor. On the other hand, it should be emphasized that these microbiota preparations are derived from healthy human donors. By definition, each microbial community was already tested for decades in at least one human subject (the donor). This cannot be said of any synthetic microbial preparation.

The choice of antibiotics proposed in this study was guided by known effects of chosen drugs, our experience with patients suffering from recurrent *C. difficile* infections, and the literature on microbiota differences in patients with obesity and diabetes. The colon microbiota is dominated by obligate anaerobes, primarily members of two bacterial phyla – Bacteroidetes and Firmicutes. Microbiota in obese individuals have greater fraction of genes contributed by Actinobacteria and Firmicutes, while microbiota from lean individuals is enriched for genes contributed by Bacteroidetes (Qin et al., 2012; Turnbaugh et al., 2009). Proteobacteria are generally increased in proportion in microbiota of diabetics and constitute the dominant bacteria that can penetrate the gut barrier and enter the blood stream (Amar et al., 2011; Tilg and Moschen, 2014). The antibiotics used in this study, clindamycin and vancomycin, target the majority of obligate gut anaerobes. Two antibiotics that have distinct mechanisms of action are likely to cause greater disruptive effects on the native microbial communities. Neomycin was chosen to target Gram-negative bacteria, members of the Proteobacteria phylum, which are likely to breach the gut barrier and may be pathogenic in metabolic syndrome by causing systemic endotoxemia.

1.4.1. Potential Risks

Antibiotic Conditioning: There are risks associated with antibiotic medications, including allergic reactions to the drugs and development of drug-resistant bacteria. Subjects with known allergies to antibiotics used in this trial will not be recruited into the study. The risk of forcing emergence of drug resistance in the native microbiota of the subjects is purely theoretical and has not been clearly documented in the literature. FMT further mitigates this theoretical risk because normal microbiota will likely outcompete microorganisms that express antibiotic resistance genes in absence of continued antibiotic pressure given associated metabolic costs. Subjects may, however, develop transient non-*C. difficile* antibiotic-associated diarrhea.

The risk of developing *Clostridium difficile* infection during the antibiotic treatment is essentially nil because vancomycin is one of the antibiotics. Vancomycin is an approved treatment for *Clostridium difficile.* Resistance to vancomycin has not yet been described in the literature and at most is extremely rare. The subjects are further very unlikely to get *Clostridium difficile* infection after completing antibiotics because they will receive FMT, using lean microbiota. This microbiota is routinely being used in treatment of multiply recurrent *C. difficile* infections in our program (> 250 patients treated since 2008, ~ 98% success rate).

Clindamycin is well absorbed systemically. The administration of it will be limited to only 5 days, and there will be a 2-day washout period prior to FMT. This is the only antibiotic that is highly bioavailable following oral administration in our protocol, and may increase the risk of a vaginal fungal infection. If this happens, we will evaluate the patient and treat in accordance with standard guidelines, e.g., oral fluconazole.

Neomycin has poor oral bioavailability (~ 3%) and has been specifically approved for clinical use for suppression of bacteria in the bowel, e.g., preoperative bowel preparation (up to 12 grams 24 to 48 hours prior to surgery) and treatment of hepatic encephalopathy (4 grams daily in chronic use). However, this drug has a black box warning regarding potential nephrotoxicity and ototoxicity. Therefore, neomycin administration will be limited to one day only (2 days prior to the FMT). In addition, renal insufficiency is an exclusion criterion (Creatinine ≤ 1.25 mg/dL).

FMT: The risks of FMT are largely mitigated by extensive donor screening and testing described in IND 15071, which is cross-referenced for the purpose of material preparation. However, given the complexity of gut microbiota and many unknowns in microbiota-host interactions, some risks remain intrinsic to the procedure.

1. <u>*Potential infectious risk.*</u> Gut microbiota are generally non-pathogenic since their well-being depends on the well-being of the host. However, many enteric pathogens have originated in gut microbiota, including *C. difficile*. Some hosts are asymptomatic carriers of such pathogens, necessitating formal testing. Some pathogens causing chronic infections, e.g., hepatitis viruses, can be shed in the fecal material.

2. *Metabolic risk.* The premise of this application is that gut microbiota participate in all aspects of energy metabolism. All donors in our Program are lean. Any single feature of metabolic syndrome (BMI, hypertension, abnormal lipid panel, abnormal fasting glucose, abnormal liver function tests) excludes donor candidates from participation. However, clinical donor indicators may not be perfectly predictive of metabolic potential of his or her microbiota, and it is possible that an opposite from desired effect could result from the intervention.

3. *Risk of gastrointestinal symptoms.* Gut microbiota constitute an integral part of the gastrointestinal tract. They can potentially play a role in a variety of gastrointestinal disorders, including irritable bowel syndrome (IBS) and inflammatory bowel disease (IBD). FMT can trigger exacerbations of existing IBD. However, FMT has also been reported to be successful in treatment of both IBS and IBD. A number of clinical trials are ongoing in testing the idea that FMT can be a treatment for IBD. Patients with R-CDI and underlying IBD have clearly benefited from FMT in our own FMT program. Trials are also anticipated for IBS in some institutions. Nevertheless, at this time there is at least a small theoretical risk of FMT triggering a gastrointestinal disorder, whether inflammatory, motility, or sensory constitutes a small theoretical risk. This risk is mitigated by ensuring that the donor has no gastrointestinal problems of any kind.

   Common side effects associated with FMT include: fever, abdominal cramping, diarrhea, constipation, nausea, and bloating.

4. *Risk of autoimmunity.* Gut microbiota play critical roles in the development of the immune system. Their role in the function of a mature immune system is unknown. There is a theoretical risk that some form of immune disorder can be triggered by a new composition of gut microbiota in a recipient. This theoretical risk is mitigated by ensuring that the donor has no immunologic problems, including allergic disorders, serological evidence of autoimmunity, or autoimmune disorders.

5. *Risk of colorectal cancer.* Gut microbiota may participate in pathogenesis of colon cancer, although the causal link between specific composition of microbiota and colon cancer development has not been demonstrated. This theoretical risk is mitigating by ensuring that the donor has no first-degree relatives of gastrointestinal malignancy and that the donor has gone undergone screening for colorectal cancer according to current guidelines from the American Society of Gastrointestinal Endoscopy and the American Gastroenterological Association.

6. *Risk of colonoscopy.* The FMT will be done by colonoscopic route of administration. Colonoscopy is the most common screening procedure for colon polyps and cancer in the US. It is a low risk procedure, although it does involve a small risk of allergic reaction to sedative medications, perforation, or bleeding.

1.4.2. Known Potential Benefits

Metabolic syndrome and obesity are very complex disorders. We are not expecting this trial to result in a cure. We hope it will constitute an important step toward understanding the mechanisms of these disorders and contributions of the gut microbiota to their pathophysiology. The potential benefits, therefore, are primarily societal in terms of enhancing understanding and ultimately finding better ways to treat these disorders.

Some subjects may benefit indirectly from participating in the study. The subjects will undergo a colonoscopy, which has the potential to identify polyps or earlier diagnosis of colon cancer.

1.4.3. Risk/Benefit Ratio

Overall the risk of participating in this study is small. The benefit is primarily societal. Direct health benefits to participants could result from findings at the colonoscopy, e.g., identification and removal of adenomatous polyps, and the possibility of metabolic benefit if the study hypothesis is correct.

2. STUDY OBJECTIVES

2.1. Primary Objective

The primary objective of this study is to measure changes in insulin sensitivity, using the insulin clamp technique, associated with FMT in pre-diabetic subjects and whether those changes differ by antibiotic vs. placebo conditioning.

2.2. Secondary Objectives

1. Evaluate the safety, tolerability, and feasibility of colonoscopic FMT, including antibiotic or placebo conditioning, in pre-diabetic subjects.
2. Determine whether antibiotic conditioning regimen prior to FMT increases engraftment of donor microbiota compared to placebo conditioning.

2.3. Exploratory Objectives

1. Evaluate fecal, plasma, and urine metabolomic profiles before and after FMT
2. Evaluate effects of FMT on the activity of homeostatic and hedonistic brain centers using fMRI.
3. Estimate whether FMT results in altered eating behavior using food frequency questionnaires and dietary recalls.
4. Measure changes in circulating liver enzyme levels (AST, ALT, Alkaline Phosphatase) following FMT.

3. STUDY DESIGN

This is a randomized, double-blind, pilot study of prediabetic patients using colonoscopic FMT with the aim of improving insulin sensitivity in the active antibiotic treatment arm. The patients will be randomized in 1:1 ratio to receive antibiotic conditioning or placebo prior to FMT. In the FMT procedure, both groups will receive microbiota prepared from lean donors (as described in our IND 15071). This is a double-blind study: neither the subject, nor the study physician administering the antibiotics, will know whether the subject received antibiotics or placebo. All subjects will have their luminal colon contents purged with a colonoscopy prep prior to FMT.

Subjects will be recruited at the University Academic Health Center, targeting outpatient endocrinology and liver disease outpatient clinics.

3.1. Study Outcome Measures

The subjects will be coming to clinic as described in the Schedule of Events Table in the Appendices.

3.1.1. Primary Outcome Measures

Primary outcome measures in this study include:

1. Insulin sensitivity measured by standard euglycemic insulin clamp. We will compare post-FMT insulin sensitivity measurements between subjects that received antibiotic versus placebo conditioning.
2. Difference between the baseline measurement ~ 4 weeks prior to FMT and final measurement ~ 6 weeks post-FMT within each group (antibiotic and placebo conditioned).

3.1.2. Secondary Outcome Measures

Secondary outcome measures in this study include:

1. Changes in fecal bacterial composition (pre- vs. post-FMT) associated with antibiotic vs. placebo conditioning, assessed by laboratory analysis.
2. Changes in fecal bacterial composition associated with FMT overall (pooling antibiotic and placebo conditioning groups) by laboratory analysis.
3. Adverse event rates overall and within antibiotic vs. placebo conditioning groups, assessed by review of adverse event diary card, specific questioning, and, as appropriate, examination.

3.1.3. Exploratory Outcome Measures

Exploratory outcome measures in this study include:

1. Evaluate effects of FMT on the activity of homeostatic and hedonistic brain centers using fMRI.
2. Change in liver fat content pre- vs. post-FMT using MRI.
3. Change in total energy and macro- and micronutrient intake pre- vs. post-FMT using FFQs and 3-day diet records.
4. Changes in resting metabolic rate and body composition pre- vs. post-FMT using indirect calorimetry.
5. Changes in circulating liver enzyme levels (AST, ALT, alkaline phosphatase) pre- vs. post-FMT assessed by clinical laboratory analysis.

4. STUDY ENROLLMENT AND WITHDRAWAL

4.1. Inclusion Criteria

Subjects will be eligible to participate in the study if all of the following conditions exist:

1. Provide informed consent
2. Ambulatory and community dwelling
3. Age 18 - 70 years of age
4. Able and willing to comply with the study schedule and procedures
5. Pre-diabetic with fasting blood glucose > 100 mg/dL and/or blood glucose 140-200 mg/dL 2-hours after ingestion of 75 gm glucose and/or Hemoglobin A1C > 5.7-6.5 percent

4.2. Exclusion Criteria

Subjects will be excluded from participation in the study if any of the following conditions exist:

1. Serious, concomitant illness that, in the opinion of the Investigator, would interfere with evaluation of safety or efficacy, or put the subject at risk of harm from study participation.
2. Known inflammatory bowel disease (Crohn's disease, ulcerative colitis, lymphocytic colitis).
3. Current abnormal liver tests that may be attributed to a cause other than non-alcoholic liver disease. NOTE: These exclusionary conditions may include viral hepatitis, alcoholic liver disease, hemochromatosis, Wilson's disease, medication-induced liver test abnormalities, celiac disease.
4. Renal insufficiency, defined as creatinine ≤ 1.25 mg/dL
5. Significant alcohol use, defined as > 20 g/day in females and > 30 g/day in males for a period of 3 months within one year prior to screening.
6. Underlying chronic gastrointestinal disease that can cause diarrhea, including short bowel syndrome, diarrhea-predominant irritable bowel syndrome, malabsorption, celiac disease.
7. History of partial or complete colectomy.
8. History of malabsorptive bariatric surgery.
9. Use of insulin or hypoglycemic medications.
10. History of anaphylactic food allergies, e.g., peanuts, seafood.
11. Food intolerances and allergies, including gluten sensitivity, lactose intolerance, and intolerance of high fiber dietary content.
12. Symptomatic problems associated with intestinal gas and bloating.
13. Irritable bowel syndrome, including diarrhea-dominant, constipation-dominant, and mixed.
14. Functional GI disorder.

15. Unable to tolerate a colonoscopy.
16. Presence of an indwelling intravenous line.
17. Infection requiring antibiotics other than the conditioning antibiotics during the study period.
18. Inability to take vancomycin, neomycin, and clindamycin antibiotics prior to FMT due to known hypersensitivity or intolerance.
19. Major genetic immune dysfunction (e.g., common variable immune deficiency).
20. Acquired immune deficiencies due to infections such as HIV.
21. Immunosuppressive medications including one of the following: systemic corticosteroids, calcineurin inhibitors, thipurines, methotrexate, biologics (e.g., anti-tumor necrosis factor drugs), cancer chemotherapy.
22. Planned use of oral probiotics while on study.
23. Planned or ongoing chemotherapy for malignancy.
24. Planned antibiotic therapy within the period of the study, e.g., perioperative antibiotics.
25. Pregnant or lactating. Female participants of child-bearing age and their partners will be counseled on contraceptive measures to prevent pregnancy during the study period.
26. History of drug or alcohol abuse in the past 2 years.
27. Currently participating in another clinical study.
28. Legally incompetent and unable to understand the study's purpose, significance and consequences, and to make decisions accordingly.
29. Presence of metal implants, such as surgical clips or pacemakers, which will preclude performance of MRI tests.
30. Inability to undergo MRI testing for any reason, e.g., claustrophobia.

4.3. Treatment Assignment Procedures

This is a randomized, double-blind study. Subjects are randomized in a 1:1 ratio to receive antibiotics or placebo prior to FMT with lean donor microbiota.

4.3.1. Randomization Procedures

Lean donor fecal microbiota suitable for FMT will be prepared from all study subjects in accordance with the laboratory protocols outlined in IND 15071. The study statistician will prepare a randomization schedule. Randomization of subjects will occur at the University of Minnesota Investigational Drug Service (IDS). Randomly permuted blocks will be used for creating the randomization schedule.

4.3.2. Un-Blinding Procedures

In the unlikely event it becomes necessary to break the blind for an individual subject the treatment assignment for that subject only will be revealed. A broken blind must be clearly justified and explained by a comment on the appropriate case report form (CRF).

4.4. Withdrawal

4.4.1. Reasons for Withdrawal

A study subject will be discontinued from further study agent/interventions in the study for:

- Completion of the study;
- Request by subject to terminate participation;
- Requirement for prohibited concomitant medication or treatment;
- Unable to comply with requirements of the protocol;
- Lost to follow-up;
- At the request of the institutional review board (IRB);
- The subject's well-being, based on the opinion of the investigator.

Subjects who are discontinued from further study agent/interventions will be followed for safety until completion of the normal visit schedule. Subjects will be contacted by phone within one week after the course of antibiotics ± FMT procedure, and again at one month and two months after the procedure.

4.4.2. Handling of Withdrawal

Subjects will be encouraged to complete the study; however, they may voluntarily withdraw at any time. The sponsor-investigator will provide a written explanation of the reason for withdrawal in a source document and the reason will be recorded on a case report form. Subjects will be asked for permission to continue scheduled evaluations, and complete an end-of-study evaluation. Medical care that may be required for management of adverse events in the course of the study will be charged to the medical insurance of the participant. Subjects who drop out of the study will not be replaced.

4.5. Termination of the Study

If the sponsor-investigator or appropriate regulatory officials discover conditions arising during the study that indicate that the study should be halted, this action may be taken after appropriate consultation between the sponsor-investigator, study statistician, and independent medical monitor. Conditions that may warrant termination of the study include, but are not limited to, the following:

- The discovery of an unexpected, serious, or unacceptable risk to the subjects enrolled in the study,
- A decision on the part of the sponsor-investigator to suspend or discontinue testing, evaluation, or development of the product.

5. INVESTIGATIONAL AGENTS

5.1. Antibiotics/Placebo

Subjects will be randomized 1:1 to receiving antibiotics or placebo prior to FMT. The antibiotics will be purchased commercially by the University of Minnesota's Investigational

Drug Service (IDS). IDS will prepare the placebo to be identical in appearance to the three antibiotics.

Subjects assigned to the antibiotic group will receive the following three antibiotics:

- Vancomycin 500 mg PO TID for 7 days,
- Neomycin 1000 mg PO TID for 1 day, and
- Clindamycin 300 mg PO TID for 5 days

5.2. FMT

Single donor lots of minimally manipulated microbial material derived from feces of qualified lean donors will be prepared as described in IND 15071. Product is intended for homologous function and localized use as replacement of missing components to restore normal microbial ecology and function of the distal gut. Lean donor eligibility qualifications are identical to those described in IND 15071. The fecal microbiota product will be formulated, packaged, and labeled as described in IND 15071. Only frozen product will be used. It will be stored as described in IND 15071. The cryobags will be thawed in a $4 \pm 2^{o}C$ ice bath over 15 minutes and they may remain in the ice bath for up to 3 hours prior to administration into study subjects.

5.3. Administration

Antibiotics/Placebo:

The antibiotics/placebo will be dispensed by IDS in a blinded fashion and administered by the study investigator.

FMT:

The fecal microbiota will be administered via colonoscopy as described in IND 15071. The fecal material suspension will be injected, via colonoscopy, into the terminal ileum and/or cecum. Following the FMT, subjects will remain supine for 30 minutes and vital signs will be measured per colonoscopy recovery routine.

The rationale for choosing colonoscopic route of administration includes:

- Our program has the greatest experience with this route of administration, including data on microbiota engraftment in patients treated for recurrent CDI.
- Some of the conditions discovered by colonoscopy constitute important metadata, i.e., covariant data important in the compositional microbiota analysis, which is one of the primary endpoints in our study. For example, presence or absence of diverticulosis may affect composition of microbiota in the new host.

- Colonoscopy ensures that the patient has purged the colon of all residual luminal contents, which presumably may include antibiotics that can affect implantation of fecal microorganisms.
- Some of the conditions discovered by colonoscopy may be exclusion criteria in this study, e.g., inflammatory bowel disease.

5.4. Maintaining Blind for Investigational Agent

The sponsor-investigator will not have access to the antibiotic or placebo during their preparation at the IDS.

5.5. Accountability/Final Disposition for the Investigational Agent

Molecular and Cellular Therapeutics, the manufacturer, will maintain product records for the manufacturing process through delivery of the product to the sponsor-investigator. The Molecular and Cellular Therapeutics facility will maintain product accountability records from receipt through dispensing the product to the sponsor-investigator. The sponsor-investigator will record administration of the product to each subject.

5.6. Ancillary Supplies Description

The following ancillary supplies are for the FMT procedure. As part of the standard colon cleansing preparation, MoviPrep (PEG-based purgative for colonoscopy or another FDA-colonoscopic preparation in case the subject is intolerant of MoviPrep) will be dispensed by IDS and administered by the study investigator to the subject. Sedative medications will be administered by the study investigator for standard colonoscopy prep and procedure.

6. STUDY PROCEDURES / EVALUATION SCHEDULE

6.1. Clinical/Laboratory Evaluations and Study Schedule

Consent will be obtained before any clinical evaluations are performed. There is one screening visit and 15 visits planned over the approximately 8 month study duration for each subject. The study will last until every evaluable subject has completed the Safety Follow-Up Visit. (See Schedule of Events in the Appendices).

6.2. Initial Screening Visit (Day -40)

The study will be explained to potential subjects qualified from initial recruitment referrals. Consent will be obtained at this time that will go over all the procedures and studies involved. During this visit the medical history will be collected and inclusion/exclusion criteria will be thoroughly reviewed. The following procedures will occur after the consent form is signed:

- Medical history, including medications over the previous 12 months, and demographics
- Thorough review of the study, including involved procedures
- Review of methods used to record and measure food consumption during the study, to be conducted by dietitian.

- Three-day diet record is initiated following this visit, to be completed prior to visit 1 (baseline).
- Complete physical examination
- Vital signs (heart rate, temperature, blood pressure, respiration rate)
- Height and weight
- Measurement of serum creatinine, unless a recent (< 1 month) result is available
- Possible repeat of fasting glucose, HgbA1C, or hepatic panel testing if recent (< 6 months) results are not available
-

6.3. Visit 1 - Baseline (Day -31, +/- 5 days)

The following procedures are conducted during this visit.

- Fasting blood collection for research measurements including metabolomics and flow cytometry
- Modified 2-hour oral glucose tolerance test
- Urine collection for metabolomics
- Urine pregnancy test for women of childbearing potential
- Feces collected for research measurements, including microbial and metabolomics composition
- Dietitian assessment to review 3-day diet record, with directions to repeat prior to Visit 4
- NCI Diet History Questionnaire II (DHQ II) to assess the baseline diet of subjects prior to entry into the study
- Subjects receive Fitbit and instructions on use
- Subjects receive adverse events diary card and instructions on completion
- Subjects receive thermometer
- Clinical labs including liver function tests, fasting lipid panel, CRP level
- Adverse events
- Concomitant medications

6.4. Visit 2 (Day -25, +/- 5 days)

- Fecal and urine samples are collected
- Urine pregnancy test for women of childbearing potential
- Weight
- Vital signs (heart rate, temperature, blood pressure, respiration rate)
- fMRI (optional)
- Hepatic MRI (optional)
- iDXA
- Download Fitbit data
- Adverse events
- Concomitant medications

6.5. Visit 3 (Day -18, +/- 5 days)

- Fecal and urine samples are collected
- Clinical labs including hepatic panel, fasting lipid panel, CRP level, blood glucose
- Urine pregnancy test for women of childbearing potential
- Weight
- Resting metabolic rate assessment
- 6-hour insulin clamp (option for 3-hour clamp if participant does not consent for 6-hour procedure)
- Clinical labs
- Download Fitbit data
- Adverse events
- Concomitant medications

6.6. Visit 4 (Day -14, +/- 2 days)

The following procedures are conducted during this visit.

- Weight
- Dietitian visit to review 3-day diet record, with directions to repeat prior to Visit 5.
- Download Fitbit data
- Urine pregnancy test for women of childbearing potential
- Randomly assigned treatment (either antibiotics or placebo) are dispensed to the subject to take home. The antibiotic regimen is described in the following list. There is a two day washout of neomycin and clindamycin before FMT.
  - vancomycin 500 mg PO three times daily x 7 days (Day -8 – Day -2),
  - neomycin 1000 mg PO three times daily x 1 day (Day -2),
  - clindamycin 300 mg PO three times daily x 5 days (Day -8 to Day -3).
- Adverse events
- Concomitant medications

6.7. Visit 5 (Day -7, +/- 4 days)

The following procedures are conducted during this visit.

- Brief physical examination
- Vital signs (heart rate, temperature, blood pressure, respiration rate)
- Weight
- Dietitian visit to review 3-day diet record, with directions to repeat at least 24 hours prior to visit 6.
- Colonoscopy prep instructions are reviewed and prep supplies are picked up. NOTE: Colonoscopy prep supplies will be dispensed by the study coordinator.
- Urine pregnancy test for women of childbearing potential
- Fasting blood collection for metabolomics and flow cytometry
- Fecal and urine samples are collected
- Download Fitbit data
- Adverse events
- Concomitant medications

6.8. Colonoscopy Prep

Preparation for colonoscopy is done on Day -1, the day before the FMT procedure. This is not a study visit.

6.9. Visit 6 (Day 0) – FMT

The following procedures are conducted during this visit.

- Urine pregnancy test for women of childbearing potential
- Clinical labs including hepatic panel, fasting lipid panel, CRP level, blood glucose
- Three-day diet record results from previous week submitted to dietitian, with instructions to repeat between visits 7 and 8.
- Colonoscopy
- Fecal microbiota transplant
- Adverse events
- Concomitant medications

6.10. Visit 7 (Day 2, Phone/Home Visit)

- Urine collection for metabolomics
- Fecal sample collected for research measurements, including microbial and metabolomic composition
- Adverse events
- Concomitant medications

6.11. Visit 8 (Day 9, +/- 1 Day; ~ 1 week post FMT)

The following procedures are conducted during this visit.

- Brief physical examination
- Vital signs (heart rate, temperature, blood pressure, respiration rate)
- Weight
- Fasting blood collection for metabolomics and flow cytometry
- Clinical labs including hepatic panel, fasting lipid panel, CRP level, blood glucose
- Urine collection for metabolomics
- Fecal sample collected for research measurements, including microbial and metabolomic composition
- Dietitian visit to review 3-day diet record, with directions to repeat prior to visit 9.
- Download Fitbit data
- Adverse events
- Concomitant medications

6.12. Visit 9 (Day 16, +/- 2 Days, Phone/Home Visit; ~ 2 weeks post FMT)

- Urine collection for metabolomics
- Fecal sample collected for research measurements, including microbial and metabolomic composition
- Dietitian to review 3-day diet record, with directions to repeat prior to visit 10.
- Adverse eventsConcomitant medications

6.13. Visit 10 (Day 23, +/- 2 days, Phone/Home Visit)

- Urine collection for metabolomics
- Fecal sample collected for research measurements, including microbial and metabolomic composition
- Adverse events
- Concomitant medications

6.14. Visit 11 (Day 30, +/- 2 Days; ~ 4 weeks post FMT)

The following procedures are conducted during this visit.

- Brief physical examination
- Vital signs (heart rate, temperature, blood pressure, respiration rate)
- Weight
- Fasting blood collection for metabolomics and flow cytometry
- Modified 2-hour oral glucose tolerance test
- Urine collection for metabolomics
- Dietitian visit to review 3-day diet record, with directions to repeat prior to visit 14
- Download Fitbit data
- Fecal sample collected for research measurements, including microbial and metabolomic composition
- Clinical labs including liver function tests, fasting lipid panel, CRP level, creatinine level, blood glucose
- Adverse events
- Concomitant medications

6.15. Visit 12 (Day 34, +/- 5 Days)

- Weight
- Urine pregnancy test for women of childbearing potential
- Vital signs (heart rate, temperature, blood pressure, respiration rate)
- fMRI (optional)
- Hepatic MRI (optional)
- iDXA
- Download Fitbit data
- Adverse events
- Concomitant medications

6.16. Visit 13 (Day 41, +/- 5 Days)

- Urine pregnancy test for women of childbearing potential
- Weight
- Resting metabolic rate assessment
- 6-hour insulin clamp (option for 3-hour clamp if participant does not consent for 6-hour procedure)
- Clinical labs including hepatic panel, fasting lipid panel, CRP level
- Download Fitbit data
- Adverse events

- Concomitant medications

6.17. Visit 14 (Day 45, +/- 1 Week) or Early Termination

The following procedures are conducted during this visit.

- Complete physical examination
- Vital signs (heart rate, temperature, blood pressure, respiration rate)
- Weight
- Fasting blood collection for metabolomics and flow cytometry
- Clinical labs including fasting lipid panel, blood glucose
- Urine collection for metabolomics
- Dietitian visit to review 3-day diet record.
- NCI DHQ II to assess mean dietary intake from baseline to approximately 5 weeks post-intervention.
- Fecal sample collected for research measurements, including microbial and metabolomic composition.
- Download Fitbit data
- Retrieve Fitbit from subject
- Adverse events
- Concomitant medications

6.18. Visit 15 (Day 180 +/-1 Week) Safety Follow-Up

- Complete physical examination
- Vital signs (heart rate, temperature, blood pressure, respiration rate)
- Weight
- Fasting blood collection for metabolomics and flow cytometry
- Clinical labs including fasting lipid panel, blood glucose
- Modified 2-hour oral glucose tolerance test
- Urine collection for metabolomics
- Fecal sample collected for research measurements, including microbial and metabolomic composition
- NCI DHQ II to assess mean dietary intake post-intervention
- Adverse events
- Concomitant medications

6.19. Unscheduled Visits

If at any time an unscheduled visit, including phone calls, should occur throughout the duration of the study, the following procedures will be completed.

- Adverse Events
- Concomitant medications
- Ask for any concerns about study procedures
- Physical examination and review of medical history as needed
- Order any lab tests as clinically indicated

6.20. Lean Donor Clinical/Laboratory Evaluations

Eligible donors will be enrolled from the Fecal Microbiota Donor Screening program. These individuals are ideal as they are already pre-screened, have no chronic diseases, and are already familiar with the process of stool collection. Consent will be obtained before any clinical evaluations are performed. Donors will undergo clinical/laboratory testing per the FMT Donor Screening protocol (as described in our IND 15071). Donors will also undergo additional clinical/laboratory evaluations to establish baseline measurements for comparison to subjects enrolled in the study. The following procedures will be collected over the course of two visits (within a 10 day period):

- Thorough review of the study, including involved procedures
- Medical history, including medications over the previous 12 months, and demographics
- Complete physical examination
- Vital signs (heart rate, temperature, blood pressure, respiration rate)
- Height and weight
- Possible repeat of fasting glucose, HgbA1C, or oral 2-hour glucose tolerance test if recent (< 6 months) results are not available
- Urine pregnancy test for women of childbearing potential
- Fasting blood collection for metabolomics and flow cytometry
- Clinical labs including fasting lipid panel
- Urine collection for metabolomics
- Dietitian assessment
- NCI DHQ II to assess baseline of diet of the donor
- Resting metabolic rate assessment
- Insulin clamp
- Modified 2-hour oral glucose tolerance test
- iDXA
- Adverse events
- Concomitant medications

The donors will come in for as many donation visits as is necessary to obtain sufficient material for the study. Donor material will be collected and processed via the protocol for the FMT Donor Screening program.

6.21. Specimen Preparation, Handling, and Storage for Metabolomics

Subjects will collect a first morning urine sample in a sterile container. The subjects will be provided all the supplies for urine collection, including 50 mL containers and coolers for transport.

Blood will be collected in the clinic in Vacutainer Blood Collection Tubes containing approximately 1.8 mg K_2EDTA per mL of blood as anticoagulant. The tubes will be inverted carefully 10 times to mix blood and anticoagulant, and kept at room temperature until centrifugation, which will be done within 15 minutes of collection.

Centrifugation will be carried out for 10 minutes at 13 RCF (relative centrifugal force) at room temperature. The top layer will be collected and frozen at -80^{o}C.

Participants will provide and store fecal samples at home 1 day prior to a scheduled visit or will provide a sample at the study site on the day of the visit. Participants collecting samples at home will be provided with all necessary supplies and will be instructed to store samples in a freezer prior to bringing to the study site. Fecal samples will be collected in a toilet hat and split upon receiving from participant. A 1.5 gram sample from the center of the specimen will be mixed with RNAprotect® solution and frozen in liquid nitrogen within 15 minutes of collection. The remainder of fecal specimens collected on-site as well as a portion of fecal specimens collected at home will be transferred into sterile containers. Specimens will be put in the freezer until transfer to the investigator's lab.

The investigator's lab will store all of the stool samples as well as the urine and blood samples collected for metabolomics. This laboratory is located at:

Medical Biosciences Building
University of Minnesota
2101 6th Street SE
Minneapolis, MN 55414

6.22. Modified 2-Hour Oral Glucose Tolerance Test (MOGTT)

An IV catheter will be inserted into an antecubital vein for blood sampling and kept patent with a continuous infusion of saline. Blood samples to determine plasma glucose, insulin, and C-peptide concentrations will be collected 10 and 5 min immediately before ingesting a 75-gram glucose load and at 10, 20, 30, 60, 90, and 120 min after glucose ingestion. The total areas under the curve for glucose, insulin, and C-peptide concentrations will be calculated by using the trapezoid method. Insulin sensitivity will be assessed by using the oral glucose insulin sensitivity index (Mari et al., 2001). Indices of β-cell function will be estimated from plasma glucose and C-peptide concentrations by using the oral minimal model of C-peptide secretion and kinetics (Mari et al., 2001; Breda et al., 2002). This model calculates the insulin secretion rate as a function of time and the following indices of β-cell responsivity: (i) dynamic responsivity index ($\Phi_d(10^9)$), which is an index of insulin secretion in response to the rate of change in glucose concentration; (ii) static responsivity index ($\Phi_s(10^9 min^{-1})$), which is an index of insulin secretion in response to a given glucose concentration; and (iii) overall responsivity index (Φ_o ($10^9 min^{-1}$)), which is a global sensitivity to glucose index of postprandial insulin secretion. The MOGTT will be performed a Visits 1, 11, and 15.

6.23. Insulin Sensitivity Assessment with 6-Hour Hyperinsulinemic-Euglycemic Clamp

Subjects will be admitted to the clinical research unit at Visit 3 and Visit 13. After subjects have fasted overnight, a catheter will be inserted into a hand or forearm vein to obtain blood samples, and into an antecubital vein of the contralateral arm to infuse stable isotope glucose tracer, dextrose and insulin. At 0700 h a one-stage

hyperinsulinemic-euglycemic clamp procedure with stable-isotopically labeled glucose tracer will be initiated to determine insulin sensitivity. After baseline blood samples are obtained, a primed-constant infusion of [6,6-$^{2}H_2$]glucose (22 μmol/kg prime and 0.22 μmol.kg^{-1}.min^{-1} constant infusion) will be started at t=0 min and continued throughout the clamp procedure. At 1000 h, after the basal period is completed, a one-stage euglycemic, hyperinsulinemic clamp will be initiated and continued for 3 h. Euglycemia will be achieved by a variable rate infusion of 20% dextrose enriched to approximately 2.5% with [6,6-$^{2}H_2$]glucose to minimize changes in glucose isotopic enrichment. Insulin will be infused at a rate of 40 mU.m^{2}.min^{-1} for 3 h (initiated with a two-step priming dose of 200 mU.m^{2}.min^{-1} for 5 min followed by 100 mU.m^{2}.min^{-1} for 5 min). The infusion of [$^{2}H_2$]glucose will be stopped completely at the start of the insulin infusion. Plasma samples will be taken before beginning the isotope infusion to obtain baseline measurements of substrate enrichment. Plasma samples will be taken every 10 min during the last 30 min of the basal period and the insulin clamp to determine glucose concentrations and kinetics, and plasma insulin concentrations. Plasma samples will be obtained every 10 min at the end of the basal period and throughout the entire clamp period to monitor plasma glucose concentration.

6.24. Insulin Sensitivity Assessment with 3-Hour Hyperinsulinemic-Euglycemic Clamp

The 3-hour insulin clamp will be performed at Visit 3 and Visit 13 if a participant does not consent for the 6-hour procedure. After an overnight fast, two peripheral IVs will be placed (1 in each arm), with one IV used for infusion, and one IV used for blood sampling. Starting at time 0, insulin will be infused at 1.0 mU/kg FFM/min, along with a potassium infusion (KPO4 at 50 ml/hr) and dextrose infusion (Dextrose 20%, titrated to maintain the blood glucose at 85-95 mg/dl). Serum blood glucose will be measured every 10 minutes (Analox, United Kingdom) and insulin will be measured every 30 minutes.

6.25. Dietary Follow-up

Dietary intake data will be collected throughout the study to estimate total energy intake and composition of macro- and micronutrient intake. Two methods of dietary assessment will be used: food frequency questionnaires (FFQs) and 3-day diet records. The National Cancer Institute's Diet History Questionnaire II (DHQ II) is a freely available FFQ and has a food list consisting of 134 food items and 8 dietary supplement questions (see Appendix 2). A web-based version of the DHQ II will be completed by subjects at visits 1 (Day -31), 14 (Day +45), and 15 (Day +180). Three-day diet records will be completed by subjects at 8 time points (immediately prior to visits 1 (baseline), 4, 5, 6, 8, 9, 11, and 14). A research dietitian trained and certified in the University of Minnesota's Nutrient Data System for Research (NDSR) dietary interviewing and assessment protocols will instruct subjects on methods for accurate assessment and recording of dietary intake, and will follow up with subjects at each of the above listed time points and additionally as needed. DHQ II data will be analyzed with Diet*Calc software developed by the NCI. Analysis of 3-day diet records will be performed using NDSR data output.

6.26. Resting Metabolic Rate Assessment

Resting metabolic rate (RMR) will be assessed via indirect calorimetry using a ParvoMedics True One 2400 metabolic cart with a canopy hood. The procedure will be conducted at the CTSI by trained technicians, and each assessment is approximately 60 minutes in duration. This will be done during the insulin clamp at Visit 3 and Visit 13.

6.27. Fitbit Data Collection

Subjects will be provided a Fitbit at Visit 1, set up their account with the assistance of the Study Coordinator to ensure proper privacy settings, and be given instructions on use. Fitbit data that is automatically collected includes, but is not limited to: steps taken, distance, calories burned, active minutes, and data on sleep habits, including time slept, quality of sleep, and number of times an individual wakes in the night. Additional manual entry of health data can be entered into the Fitbit Dashboard, including: weight, blood pressure, heart rate, diet, exercise, and water consumption. Fitbit data will be downloaded in person with the Study Coordinator at visits 2, 3, 4, 5, 8, 11, 12, 13, and 14, and stored on University of Minnesota secure servers.

Fitbit is HIPAA compliant and offers personalized privacy settings. The study team will assist the subjects with privacy settings to ensure their data is secure and not made available to the public.

6.28. Hepatic Magnetic Resonance Imaging

Hepatic MRI imaging will be an optional procedure in this study. A hepatic proton density fat fraction by using the Siemens Prisma 3T Magnetic Resonance Imaging (MRI) scanner will be performed. This technique has been validated to determine percentage of hepatic steatosis and correlates with findings on liver biopsy (Reeder and Sirlin, 2010). The MRI will be performed at Visit 2 and Visit 12.

6.29. Functional Magnetic Resonance Imaging

fMRI imaging will be an optional procedure in this study. Subjects will be scanned using the Siemens Prisma 3T MRI scanner. After automated scout and shimming procedures, high resolution T1-weighted structural scans will be collected. The fMRI images, i.e., BOLD signal, will be acquired using echo planar (T2*-weighted) sequences (repetition time [TR] = 710ms, echo time = 30 ms, flig angle 52, slice thickness = 2 mm; 72 sequential axial slices, oriented along the anterior-posterior commissure line). Note: the exact scanner parameters may change depending on protocol optimization. In addition to the functional imaging scans, structural imaging scans will be collected for localization, slice selection, and image registration purposes. Three visual tasks will be presented over separate scanning runs: (1) low-calorie foods, (2) high-calorie foods, and (3) nonedible food-related utensils, as described previously (Killgore et al., 2003). The fMRI will be performed at Visit 2 and Visit 12.

6.30. iDXA Dual X-ray Absortiometry

Body composition and body fat distribution will be assessed by dual-energy X-ray absorptiometry (DXA) in the total body-scanning mode with an iDXA apparatus (GE

Healthcare Lunar IDXA enCore software version 16) at the Delaware Clinical Research Unit (DCRU). The Lunar iDXA has demonstrated excellent precision for total body measurements of body composition, total body fat, and percent total body fat. The iDXA procedure will be performed at Visit 2 and Visit 12.

6.31. Subject Compensation

Subjects will be compensated for their time and travel costs for study visits. Compensation amounts are specified in the study's consent form.

7. SAFETY AND ADVERSE EVENTS

7.1. Definitions

Adverse Event (AE)

An adverse event (AE) is any symptom, sign, illness or experience that develops or worsens in severity during the course of the study. Intercurrent illnesses or injuries will be regarded as adverse events. Abnormal results of study procedures are considered to be AEs if the abnormality:

- Results in study withdrawal
- Is associated with a serious adverse event (SAE)
- Is associated with clinical signs or symptoms
- Leads to additional treatment or to further diagnostic tests
- Is considered by the Investigator to be of clinical significance.

Adverse Reaction

An adverse reaction is any adverse event caused by the investigational agent. Adverse reactions are a subset of suspected adverse reactions.

Suspected Adverse Reaction

A suspected adverse reaction is an adverse event for which there is a reasonable possibility that the investigational agent caused the adverse event.

Serious Adverse Event (SAE)

A serious adverse event (SAE) is any adverse event that is:

- Fatal
- Life-threatening
- Requires or prolongs a hospital stay
- Results in persistent or significant disability or incapacity
- A congenital anomaly or birth defect

Important medical events are events that may not be immediately life-threatening, but are clearly of major clinical significance and may be SAEs. They may jeopardize the subject, and may require intervention to prevent one or the other serious outcomes noted above.

Hospitalization

Hospitalization shall include any initial admission (even if less than 24 hours) to a healthcare facility as a result of a precipitating clinical adverse event; to include transfer within the hospital

to an intensive care unit. Hospitalization or prolongation of hospitalization in the absence of a precipitating, clinical adverse event (e.g., for a preexisting condition not associated with a new adverse event or with a worsening of the preexisting condition; admission for a protocol-specified procedure) is not, in itself, a serious adverse effect.

Expected Adverse Event
Expected adverse events are those that are known to be associated with or have the potential to arise as a consequence of participation in the study.

Unexpected Adverse Event
An adverse event or suspected adverse reaction is considered unexpected if it is not listed in the Protocol at the specificity or severity that has been observed.

Unanticipated Problems Involving Risk to Subjects or Others (UPIRTSO)
An adverse event that in the opinion of the Principal Investigator is unexpected and related to the investigational agent.

Assessment of Severity
The sponsor-investigator will make an assessment of severity for each AE and SAE reported during the study. The assessment will be based on the sponsor-investigator's clinical judgment. The severity of each AE recorded will be assigned a severity based on Common Terminology Criteria for Adverse Events (CTCAE) grading.

Assessment of Causality
The sponsor-investigator will estimate the relationship between the investigational agent and the occurrence of each AE or SAE by using his best clinical judgment. Other elements, such as the history of the underlying disease, concomitant therapy, other risk factors, and the temporal relationship of the event to administration of the investigational agent, will be considered and investigated.

An SAE may be recorded when the sponsor-investigator has minimal information to include in the initial report. The sponsor-investigator may change his opinion of the causality in light of follow-up information, with subsequent amendment of the SAE report.

Categories	*Definition*
Definitely related	This relationship suggests that a definite causal relationship exists between the administration of the investigational agent and the AE, and other conditions (concurrent illness, progression/expression of disease state, or concurrent medication reaction) do not appear to explain the event.
Probably related	This relationship suggests that a reasonable temporal sequence of the event with

	investigational agent administration exists and, based upon the known or previously reported adverse reactions, or judgment based on the investigator's clinical experience, the association of the event with the investigational agent seems likely.
Possibly related	This relationship suggests that treatment with the investigational agent may have caused or contributed to the AE (i.e., the event follows a reasonable temporal sequence from the time of investigational agent administration and/or follows a known response pattern to the investigational agent but could also have been produced by other factors.)
Not related	This relationship suggests that there is no association between the investigational agent and the reported event.

7.2. Recording of Adverse Events

At each contact with the subject, the investigator will seek information on adverse events by specific questioning, reviewing the adverse events diary card, and, as appropriate, by examination. Information on all adverse events will be recorded immediately in the source document, and also in the appropriate adverse event module of the case report form (CRF). All clearly related signs, symptoms, and abnormal diagnostic procedures results will be recorded in the source document, though should be grouped under one diagnosis.

The clinical course of each event will be followed until resolution, stabilization, or until it has been determined that the study treatment or participation is not the cause. Serious adverse events will be collected for the six month period following study product administration. Serious adverse events that are still ongoing at the end of the study period will be followed up to determine the final outcome. Any serious adverse event that occurs after the study period and is considered to be possibly related to the study treatment or study participation will be recorded and reported immediately.

The study's medical monitor will review adverse events data every 6 months.

Expected adverse events include:

- Events associated with venipunctures.
  - Discomfort and slight bruising.
- Events associated with colonoscopy.
  - Diarrhea during the preparation
  - Discomfort during the colonoscopy procedure
  - Inability to drive for 24 hours following the colonoscopy due to administration of sedative medications

- Events associated to insulin clamp, mitigated by physician supervision and sugar administration.
  - Low blood sugar
  - Sweating
  - Weakness
- Events associated with MRI scanning.
  - Discomfort associated with laying still
  - Dizziness, mild nausea, headache associated with loud noises and sensations of flashing lights in the scanner

Possible, although unlikely, adverse events that may be encountered include:

- Events associated with venipunctures.
  - Bruising
  - Bleeding
  - Lightheadedness, fainting
  - Infection at the venipuncture site
  - Nausea
  - Anxiety
  - Swelling at the venipuncture site
- Events associated with antibiotic administration.
  - Nausea, abdominal discomfort.
  - Diarrhea
  - Allergic reaction
- Events associated with colonoscopy.
  - Nausea during the preparation to the examination
  - Bleeding from the colon, particularly at sites of biopsies or incidental polyp removal
  - Tear in the colon wall
- Events associated with MRI scanning.
  - Severe anxiety or claustrophobia associated with being in a confined space

7.3. Reporting of Serious Adverse Events

7.3.1. IRB Notification by Sponsor-Investigator

Reports of all serious adverse events (including follow-up information) must be submitted to the IRB within the reporting timeline requirements, if the SAE falls under the UPIRTSO guidelines. Copies of each report and documentation of IRB notification and receipt will be kept in the Clinical Investigator's binder.

7.3.2. FDA Notification by Sponsor-Investigator

The study sponsor-investigator shall notify the FDA by telephone or by facsimile (preferred) transmission of any unexpected fatal or life-threatening experience associated with the use of the investigational agent as soon as possible but no later than 7 calendar days from the sponsor-investigator's original receipt of the information.

If a previous adverse event that was not initially deemed reportable is later found to fit the criteria for reporting, the study sponsor-investigator will submit the adverse event in a written report to the FDA as soon as possible, but no later than 15 calendar days from the time the determination is made.

7.3.3. UPIRTSO Events

Upon first learning of a UPIRTSO event, investigators are required to submit a report of the applicable event(s) to the IRB within the required reporting timeline.

8. CLINICAL MANAGEMENT OF EVENTS

8.1. Adverse Event Management

If an adverse event occurs that requires clinical management, the subject will be evaluated at an Unscheduled Study Visit with a physical exam. Tests and treatments that may be clinically indicated will be ordered.

8.2. Temporary Interruption of Study Product in an Individual Subject

Subjects will receive one administration of the fecal microbiota. No temporary interruption of study product in an individual subject will occur.

9. CLINICAL SITE MONITORING PLAN

Independent monitoring of the clinical study for compliance will be conducted periodically (i.e., at a minimum of annually) by qualified staff of the University of Minnesota's CTSI in accordance with the established monitoring plan.

10. STATISTICAL CONSIDERATIONS

10.1. Study Hypotheses

The central hypothesis for this study is that implantation of microbiota from lean donors without any features of metabolic syndrome will improve insulin sensitivity in pre-diabetic subjects. Fecal microbiota transplant will increase the fecal microbial diversity and enhance the ability of gut microbiota to produce mediators, such as short-chain fatty acids. These mediators have the potential to alter subject appetite and food cravings, metabolic rate, and responsiveness to insulin. We further hypothesize that antibiotic conditioning regimen will increase engraftment of donor phylotypes by FMT over a placebo conditioning regimen.

10.2. Sample Size Considerations

This feasibility study plans to enroll 24 subjects who will be randomly assigned to receive antibiotic conditioning or placebo using a 1:1 ratio. We anticipate that 4 subjects may drop out from the study for various reasons, including inability to comply with the rigorous study visit schedule or new medical problems unrelated to the study, e.g., use of antibiotics for an infection. Study enrollment is intentionally limited to prevent unnecessary risk in this population until the study feasibility has been determined. This pilot study is similar in size to an earlier report by Vrieze and colleagues where 18 subjects with metabolic syndrome were randomized to receive lean or their own fecal microbiota (placebo) via duodenal tube lavage, with improvement in peripheral insulin sensitivity documented at 6 weeks (Vrieze et al., 2012). Some of the differences in the

present study include (1) randomization to antibiotic conditioning versus placebo prior to FMT (2) colonoscopic administration of fecal microbiota rather than nasoduodenal infusion, and (3) longer follow-up of subjects.

We will compare post-FMT insulin sensitivity between the two groups (antibiotic versus placebo conditioned) using a two-sample t-test: 10 subjects/arm should yield a detectable difference of 3.51 units in Glucose Infusion Rate (GIR) (80% power) and 4.05 units in GIR (90% power). In addition, we will use paired t-tests to test whether post-FMT insulin sensitivity increased within each group by comparing pre- and post-FMT insulin tests for each subject.

An intent to treat (ITT) population will include all patients randomized and analyzed according to the treatment assigned. Evaluation of the safety profile will be primarily descriptive in nature including frequency, type, and severity of adverse events by treatment arms. Descriptive analyses of baseline characteristics and outcomes across the two treatment groups will include means and standard deviations for continuous variables and frequencies for categorical variables. Exploratory analyses will use an ANCOVA style regression for comparing the difference between the treatment arms for continuous measures while adjusting for the baseline measure. For continuous measures with outliers or skewed distributions, a Wilcoxon rank-sum test will be used to compare the treatment arms. A binomial exact test will be used to compare the difference in proportions between the two arms.

Comparison of donor microbiota engraftment efficiency will be performed using a number of assays, including an estimate of percent engraftment using SourceTracker software (Knights et al., 2011), which is based on a Bayesian approach to estimate microbial community origins, quantification of donor-specific operational taxonomic units, functional analysis of pre- and post-FMT microbial communities using PICRUSt software (Phylogenetic Investigation of Communities by Reconstruction of Unobserved States) (Langille et al., 2013), and pre- and post-FMT fecal metabolome analysis. The combination of these analytical methods should determine superiority of one protocol over another in achieving greater similarity of post-FMT microbiota to donor material, although given the exploratory nature of this work and its rapidly evolving methodology it is difficult to make meaningful power calculations at this stage on the engraftment objective. Nevertheless, failure to distinguish antibiotic versus placebo conditioning prior to FMT using these methods will be sufficient to determine that our chosen antibiotic conditioning regimen is not beneficial to enhancement of microbiota engraftment.

10.3. Randomization

Randomization will occur in a 1:1 ratio in the IDS pharmacy between antibiotics and placebo formulations.

10.4. Blinding

Both the treatment personnel and the subject will be blinded. To maintain blinding, the drug packaging will be identical between the two groups.

10.5. Planned Interim Analyses

No interim analyses are planned for this study.

10.6. Safety Review

To minimize risk, cumulative safety data will be reviewed by the sponsor-investigator and an independent medical monitor at a minimum of every six months or more frequently should an urgent situation arise. This safety monitoring will include careful assessment and appropriate reporting of adverse events as noted above, using adverse events source documents and records kept in the study's web-based data entry system. Medical monitoring will include a regular assessment of the number and type of serious adverse events. Study enrollment and dosing will be stopped and an ad hoc review will be performed if any of the following occurs:

1. Death of an enrolled subject when the cause is considered to be "related" to FM;
2. Occurrence of a life-threatening allergic/hypersensitivity reaction (anaphylaxis), manifested by bronchospasm with or without urticaria or angioedema;
3. An overall pattern of symptomatic, clinical, or laboratory events that the sponsor-investigator, scientific liaisons, regulatory affairs manager and statistician consider associated with study product and that may appear minor in terms of individual events but that, collectively, may represent a serious potential concern for safety;
4. Any SAE that is possibly, probably, or definitely related to study product administration;
5. Two or more subjects experience the same CTCAE Grade 3 or higher adverse event that is possibly, probably, or definitely related to study product administration.

10.7. Final Analysis Plan

An ITT population will include all patients randomized and analyzed according to the treatment assigned. Evaluation of the safety profile will be primarily descriptive in nature including frequency, type, and severity of adverse events by treatment arms. Descriptive analyses of baseline characteristics and outcomes across the two treatment groups will include means and standard deviations for continuous variables and frequencies for categorical variables. Exploratory analyses will use an ANCOVA style regression for comparing the difference between the treatment arms for continuous measures while adjusting for the baseline measure. For continuous measures with outliers or skewed distributions, a Wilcoxon rank-sum test will be used to compare the treatment arms. A binomial exact test will be used to compare the difference in proportions between the two treatment arms.

11. DATA HANDLING / RECORD KEEPING / SOURCE DOCUMENTS

11.1. Data Capture Methods

Clinical data (including AEs and concomitant medications) and clinical laboratory data will be entered into an internet data entry system provided by the Clinical and Translational Science Institute. The data system includes password protection and

internal quality checks to identify data that appear inconsistent, incomplete, or inaccurate. Clinical data will be entered directly from the source documents.

11.2. Types of Data

Data for this study will include safety, laboratory and outcome measures.

11.3. Study Records Retention

Per University of Minnesota policy all documents concerning the use of human subjects in research will be maintained for at least 3 years from completion of IRB-related work and at least 6 years for HIPAA. No record will be destroyed without the written consent of the sponsor-investigator.

The sponsor-investigator will permit authorized representatives of the University of Minnesota and regulatory agencies to examine (and when required by applicable law, copy) clinical records for the purposes of clinical site monitoring, quality assurance reviews, audits, and evaluation of the study safety and progress.

11.4. Source Documents

A source document is defined as the location where study-related data are initially recorded. Source documents for this study will include hard copy paper and/or electronic forms, laboratory printouts, and medical records onto or into which data will first be recorded.

11.5. Protocol Deviations

A protocol deviation is any noncompliance with the clinical trial protocol. The noncompliance may be either on the part of the subject, the investigator, or the study site staff. As a result of deviations, corrective actions are to be developed by the site and implemented promptly.

When a deviation from the protocol is necessary for an individual subject, the Investigator must complete a description of the deviation from the protocol and justification on the Protocol Deviation Form. It will not be considered a protocol deviation if a subject is unable to provide a stool sample at any visit that requires a stool sample.

12. QUALITY CONTROL AND QUALITY ASSURANCE

The investigative site will document any internal reviews of the conduct of the protocol.

13. ETHICS/PROTECTION OF HUMAN SUBJECTS

13.1. Ethical Standard

The investigator(s) will ensure that this study is conducted in conformity with the principles of The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research of The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (April 18, 1979) and codified in 45 CFR 46, 21 CFR 312, and/or ICH E6; 62 Federal Regulations 25691 (1997). The University

of Minnesota holds a current federal-wide assurance (FWA) issued by OHRP for federally funded research.

13.2. Institutional Review Board

The Human Subjects Protection Program at the University of Minnesota will be asked to review and approve this protocol, associated consent documents, and recruitment materials. Approval of any amendments to the protocol or consent materials will also be requested before they are implemented.

14. INFORMED CONSENT PROCESS

The informed consent process will be initiated before a volunteer agrees to participate in the study and will continue throughout the individual's study participation. The subject will sign the informed consent document before any procedures are undertaken for the study. A copy of the signed informed consent document will be given to the subject for his/her records. The consent will explain that subjects may withdraw consent at any time throughout the course of the trial. Extensive explanation and discussion of risks and possible benefits of this investigation will be provided to the subjects in understandable language. Adequate time will be provided to ensure that the subject has time to consider and discuss participation in the protocol.

The consent form will describe, in detail, the study interventions / products / procedures and risks / benefits associated with participation in the study. The rights and welfare of the subjects will be protected by emphasizing that their access to and the quality of medical care will not be adversely affected if they decline to participate in this study.

14.1. Subject Confidentiality

Subject confidentiality is strictly held in trust by the participating investigator, his staff, and their agents. This confidentiality includes documentation, investigation data, subject's clinical information, and all other information generated during participation in the study.

No information concerning the study or the data generated from the study will be released to any unauthorized third party without prior written approval of the sponsor and the subject.

The study monitor or other authorized representatives of governmental regulatory agencies may inspect all documents and records required to be maintained by the investigator, including but not limited to, medical records (office, clinic, or hospital) and pharmacy records for the subjects in this study. The clinical study site will permit access to such records.

14.2. Principal Investigator Responsibility When Subject Withdraws or is Discontinued

If a subject terminates the study early, and is willing, the tests and procedures that would occur at Visit 14 (Early Termination) will be done.

14.3. Future Use of Stored Specimens

Blood samples collected during the study will be sent to and processed by hospital laboratory personnel at University of Minnesota Medical Center, Fairview. Blood will be discarded.

Fecal and urine samples will be stored by the investigator's laboratory for the purpose of purifying DNA for metagenomic analysis. Fecal and urine samples will not be anonymized and will not be shared with other investigators. The specimens may be stored in the investigator's laboratory for up to 5 years. No human genetic testing will be performed on these samples.

Subjects may withdraw consent for fecal and urine sample storage. If a subject withdraws consent samples will be destroyed. Any data from fecal samples obtained prior to withdrawal of consent will be used in study results analysis.

Subjects will be asked to agree to re-contact for future research on stored samples.

15. PUBLICATION POLICY

The International Committee of Medical Journal Editors (ICMJE) member journals has adopted a trials-registration policy as a condition for publication. This policy requires that all clinical trials be registered in a public trials registry such as ClinicalTrials.gov, which is sponsored by the National Library of Medicine. This protocol is registered on ClinicalTrials.gov as NCT02730962.

16. LITERATURE REFERENCES

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17.Appendix 1: Schedule of Events

Pre-FMT								Post-FMT									
Procedures	Screening	Baseline	Visit 2	Visit 3	Visit 4	Visit 5	Visit 6	Visit 7	Visit 8	Visit 9	Visit 10	Visit 11	Visit 12	Visit 13	Visit 14 F1	Visit 15
	-40 days	Day -31 ± 5 days	Day -25 ± 5 days	Day -18 ± 5 days	Day -14 ± 2 days	Day -7 ± 4 days	Day 0	Day 2	Day 9 ± 1 day	Day 16 ± 2 days	Day 23 ± 2 days	Day 30 ± 2 days	Day 34 ± 5 days	Day 41 ± 5 days	Day 45 ± 1 week	Day 180 ± 1 week
Obtain Consent	X															
Medical History	X															
Physical exam	X					X			X			X			X	X
Vitals	X		X	X	X	X			X			X			X	X
Height	X															
Weight	X	X	X	X	X	X			X			X	X	X	X	X
Clinical Labs	X F2	X F3		X			X		X			X		X	X	X
Urine Pregnancy test F4		X			X	X	X							X		
Fasting Blood for Metabolo-mics		X				X			X			X			X	X
Urine sample collection		X	X	X		X		X	X	X	X	X			X	X
Provide stool sample		X	X	X		X		X	X	X	X	X			X	X
Food frequency questionn-aire		X													X	X

Pre-FMT								Post-FMT									
Procedures	Screening	Baseline	Visit 2	Visit 3	Visit 4	Visit 5	Visit 6	Visit 7	Visit 8	Visit 9	Visit 10	Visit 11	Visit 12	Visit 13	Visit 14 F1	Visit 15
	-40 days	Day -31 ± 5 days	Day -25 ± 5 days	Day -18 ± 5 days	Day -14 ± 2 days	Day -7 ± 4 days	Day 0	Day 2	Day 9 ± 1 day	Day 16 ± 2 days	Day 23 ± 2 days	Day 30 ± 2 days	Day 34 ± 5 days	Day 41 ± 5 days	Day 45 ± 1 week	Day 180 ± 1 week
Provide food diary	X	X			X	X	X		X			X				
Review food diary		X			X	X	X		X	X		X			X	
Fitbit			X	X	X	X			X			X	X	X	X	
Insulin Clamp F5				X										X		
MOGTT		X										X				X
RMR				X										X		
fMRI			X										X			
Hepatic MRI			X										X			
iDXA			X										X			
Start antibiotics or placebo					X											
Colono-scopy F6							X									
Fecal microbiota transplant (FMT)							X									
Adverse Events/ Con meds		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X

F1. This visit will also be performed if early termination.
F2. Possible repeat of fasting glucose, HgbA1C, or oral 2-hour glucose tolerance test if recent (< 6 months) results are not available. Creatinine if results not available within one month.
F3. Clinical labs include: LFTs (including AST, ALT, alk phos), fasting lipid panel, CRP at Baseline Visit and Visit 11. Creatinine at Visit 11.
F4. For woman of child bearing potential only.
F5. 6--hour insulin clamp. Subjects may opt for a shorter 3-hour clamp.
F6. Colonoscopy prep will take place the day before FMT.

18. Appendix 2: Diet History Questionnaire II

The NCI Diet History Questionnaire II is included on the following pages.

This is a sample form. Do not use for scanning.

NATIONAL INSTITUTES OF HEALTH

Diet History Questionnaire II

GENERAL INSTRUCTIONS

- **Answer each question as best you can. Estimate if you are not sure. A guess is better than leaving a blank.**
- **Use only a black ball-point pen. Do not use a pencil or felt-tip pen. Do not fold, staple, or tear the pages.**
- **Put an X in the box next to your answer.**
- **If you make any changes, cross out the incorrect answer and put an X in the box next to the correct answer. Also draw a circle around the correct answer.**
- **If you mark NEVER, NO, or DON'T KNOW for a question, please follow any arrows or instructions that direct you to the next question.**

BEFORE TURNING THE PAGE, PLEASE COMPLETE THE FOLLOWING QUESTIONS.

Today's date:

MONTH	DAY		YEAR
☐ Jan	|___|___|		☐ 2010
☐ Feb	☐0	☐0	☐ 2011
☐ Mar	☐1	☐1	☐ 2012
☐ Apr	☐2	☐2	☐ 2013
☐ May	☐3	☐3	☐ 2014
☐ Jun		☐4	☐ 2015
☐ Jul		☐5	☐ 2016
☐ Aug		☐6	☐ 2017
☐ Sep		☐7	☐ 2018
☐ Oct		☐8	☐ 2019
☐ Nov		☐9	☐ 2020
☐ Dec			

In what month were you born?

☐ Jan
☐ Feb
☐ Mar
☐ Apr
☐ May
☐ Jun
☐ Jul
☐ Aug
☐ Sep
☐ Oct
☐ Nov
☐ Dec

In what year were you born?

19 |___|___|

☐0	☐0
☐1	☐1
☐2	☐2
☐3	☐3
☐4	☐4
☐5	☐5
☐6	☐6
☐7	☐7
☐8	☐8
☐9	☐9

Are you male or female?

☐Male
☐Female

BAR CODE LABEL OR SUBJECT ID HERE

|___|___|___|___|___|___|___|___|

1. Over the past month, how often did you drink **carrot juice**?

☐ NEVER (GO TO QUESTION 2)

☐ 1 time in past month
☐ 2–3 times in past month
☐ 1–2 times per week
☐ 3–4 times per week
☐ 5–6 times per week
☐ 1 time per day
☐ 2–3 times per day
☐ 4–5 times per day
☐ 6 or more times per day

1a. Each time you drank **carrot juice**, how much did you usually drink?

☐ Less than ½ cup (4 ounces)
☐ ½ to 1¼ cups (4 to 10 ounces)
☐ More than 1¼ cups (10 ounces)

2. Over the past month, how often did you drink **tomato juice** or **other vegetable juice**? *(Please do not include carrot juice.)*

☐ NEVER (GO TO QUESTION 3)

☐ 1 time in past month
☐ 2–3 times in past month
☐ 1–2 times per week
☐ 3–4 times per week
☐ 5–6 times per week
☐ 1 time per day
☐ 2–3 times per day
☐ 4–5 times per day
☐ 6 or more times per day

2a. Each time you drank **tomato juice** or **other vegetable juice**, how much did you usually drink?

☐ Less than ¾ cup (6 ounces)
☐ ¾ to 1¼ cups (6 to 10 ounces)
☐ More than 1¼ cups (10 ounces)

3. Over the past month, how often did you drink **orange juice** or **grapefruit juice?**

☐ NEVER (GO TO QUESTION 4)

☐ 1 time in past month
☐ 2–3 times in past month
☐ 1–2 times per week
☐ 3–4 times per week
☐ 5–6 times per week
☐ 1 time per day
☐ 2–3 times per day
☐ 4–5 times per day
☐ 6 or more times per day

3a. Each time you drank **orange juice** or **grapefruit juice**, how much did you usually drink?

☐ Less than ¾ cup (6 ounces)
☐ ¾ to 1¼ cups (6 to 10 ounces)
☐ More than 1¼ cups (10 ounces)

Question 4 appears in the next column

3b. How often was the orange juice or grapefruit juice you drank **calcium-fortified**?

☐ Almost never or never
☐ About ¼ of the time
☐ About ½ of the time
☐ About ¾ of the time
☐ Almost always or always

4. Over the past month, how often did you drink **other 100% fruit juice** or **100% fruit juice mixtures** (such as apple, grape, pineapple, or others)?

☐ NEVER (GO TO QUESTION 5)

☐ 1 time in past month
☐ 2–3 times in past month
☐ 1–2 times per week
☐ 3–4 times per week
☐ 5–6 times per week
☐ 1 time per day
☐ 2–3 times per day
☐ 4–5 times per day
☐ 6 or more times per day

4a. Each time you drank **other 100% fruit juice** or **100% fruit juice mixtures**, how much did you usually drink?

☐ Less than ¾ cup (6 ounces)
☐ ¾ to 1½ cups (6 to 12 ounces)
☐ More than 1½ cups (12 ounces)

4b. How often were the other 100% fruit juice or 100% fruit juice mixtures you drank **calcium-fortified**?

☐ Almost never or never
☐ About ¼ of the time
☐ About ½ of the time
☐ About ¾ of the time
☐ Almost always or always

5. How often did you drink **other fruit drinks** (such as cranberry cocktail, Hi-C, lemonade, or Kool-Aid, diet or regular)?

☐ NEVER (GO TO QUESTION 6)

☐ 1 time in past month
☐ 2–3 times in past month
☐ 1–2 times per week
☐ 3–4 times per week
☐ 5–6 times per week
☐ 1 time per day
☐ 2–3 times per day
☐ 4–5 times per day
☐ 6 or more times per day

Question 6 appears on the next page

Over the <u>past month</u>…

5a. Each time you drank **fruit drinks**, how much did you usually drink?

- ☐ Less than 1 cup (8 ounces)
- ☐ 1 to 2 cups (8 to 16 ounces)
- ☐ More than 2 cups (16 ounces)

5b. How often were your fruit drinks **diet** or **sugar-free**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

6. How often did you drink **milk as a beverage** (NOT in coffee, NOT in cereal)? *(Please do not include chocolate milk and hot chocolate.)*

- ☐ NEVER (GO TO QUESTION 7)

- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1–2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2–3 times per day
- ☐ 4–5 times per day
- ☐ 6 or more times per day

6a. Each time you drank **milk as a beverage**, how much did you usually drink?

- ☐ Less than 1 cup (8 ounces)
- ☐ 1 to 1½ cups (8 to 12 ounces)
- ☐ More than 1½ cups (12 ounces)

6b. What kind of **milk** did you usually drink?

- ☐ Whole milk
- ☐ 2% fat milk
- ☐ 1 % fat milk
- ☐ Skim, nonfat, or ½% fat milk
- ☐ Soy milk
- ☐ Rice milk
- ☐ Other

7. How often did you drink **chocolate milk** (including hot chocolate)?

- ☐ NEVER (GO TO QUESTION 8)

- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1–2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2–3 times per day
- ☐ 4–5 times per day
- ☐ 6 or more times per day

Question 8 appears in the next column

7a. Each time you drank **chocolate milk**, how much did you usually drink?

- ☐ Less than 1 cup (8 ounces)
- ☐ 1 to 1½ cups (8 to 12 ounces)
- ☐ More than 1½ cups (12 ounces)

7b. How often was the chocolate milk **reduced-fat** or **fat-free**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

8. How often did you drink **meal replacement** or **high-protein beverages** (such as Instant Breakfast, Ensure, Slimfast, Sustacal or others)?

- ☐ NEVER (GO TO QUESTION 9)

- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1–2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2–3 times per day
- ☐ 4–5 times per day
- ☐ 6 or more times per day

8a. Each time you drank **meal replacement** or **high-protein beverages**, how much did you usually drink?

- ☐ Less than 1 cup (8 ounces)
- ☐ 1 to 1½ cups (8 to 12 ounces)
- ☐ More than 1½ cups (12 ounces)

9. How often did you drink **soda** or **pop**?

- ☐ NEVER (GO TO QUESTION 10)

- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1–2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2–3 times per day
- ☐ 4–5 times per day
- ☐ 6 or more times per day

9a. Each time you drank **soda** or **pop,** how much did you usually drink?

- ☐ Less than 12 ounces or less than 1 can or bottle
- ☐ 12 to 16 ounces or 1 can or bottle
- ☐ More than 16 ounces or more than 1 can or bottle

Question 10 appears on the next page

Over the <u>past month</u>…

9b. How often were these sodas or pop **diet** or **sugar-free**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

9c. How often were these sodas or pop **caffeine-free**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

10. How often did you drink **sports drinks** (such as Propel, PowerAde, or Gatorade)?

☐ NEVER (GO TO QUESTION 11)

- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1–2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2–3 times per day
- ☐ 4–5 times per day
- ☐ 6 or more times per day

10a. Each time you drank **sports drinks**, how much did you usually drink?

- ☐ Less than 12 ounces or less than 1 bottle
- ☐ 12 to 24 ounces or 1 to 2 bottles
- ☐ More than 24 ounces or more than 2 bottles

11. How often did you drink **energy drinks** (such as Red Bull or Jolt)?

☐ NEVER (GO TO QUESTION 12)

- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1–2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2–3 times per day
- ☐ 4–5 times per day
- ☐ 6 or more times per day

11a. Each time you drank **energy drinks**, how much did you usually drink?

- ☐ Less than 8 ounces or less than 1 cup
- ☐ 8 to 16 ounces or 1 to 2 cups
- ☐ More than 16 ounces or more than 2 cups

Question 12 appears in the next column

12. How often did you drink **beer**?

☐ NEVER (GO TO QUESTION 13)

- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1–2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2–3 times per day
- ☐ 4–5 times per day
- ☐ 6 or more times per day

12a. Each time you drank **beer**, how much did you usually drink?

- ☐ Less than a 12-ounce can or bottle
- ☐ 1 to 3 12-ounce cans or bottles
- ☐ More than 3 12-ounce cans or bottles

13. How often did you drink **water** (including tap, bottled, and carbonated water)?

☐ NEVER (GO TO QUESTION 14)

- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1–2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2–3 times per day
- ☐ 4–5 times per day
- ☐ 6 or more times per day

13a. Each time you drank **water**, how much did you usually drink?

- ☐ Less than 12 ounces or less than 1 bottle
- ☐ 12 to 24 ounces or 1 to 2 bottles
- ☐ More than 24 ounces or more than 2 bottles

13b. How often was the water you drank **tap water**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

Question 14 appears on the next page

Over the <u>past month</u>…

13c. How often was the water you drank **bottled, sweetened water** (with low or no-calorie sweetener, including carbonated water)?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

13d. How often was the water you drank **bottled, unsweetened water** (including carbonated water)?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

14. How often did you drink **wine** or **wine coolers**?

- ☐ NEVER (GO TO QUESTION 15)
- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1–2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2–3 times per day
- ☐ 4–5 times per day
- ☐ 6 or more times per day

14a. Each time you drank **wine** or **wine coolers**, how much did you usually drink?

- ☐ Less than 5 ounces or less than 1 glass
- ☐ 5 to 12 ounces or 1 to 2 glasses
- ☐ More than 12 ounces or more than 2 glasses

15. How often did you drink **liquor** or **mixed drinks**?

- ☐ NEVER (GO TO QUESTION 16)
- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1–2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2–3 times per day
- ☐ 4–5 times per day
- ☐ 6 or more times per day

15a. Each time you drank **liquor** or **mixed drinks**, how much did you usually drink?

- ☐ Less than 1 shot of liquor
- ☐ 1 to 3 shots of liquor
- ☐ More than 3 shots of liquor

Question 16 appears in the next column

16. How often did you eat **oatmeal, grits,** or **other cooked cereal?**

- ☐ NEVER (GO TO QUESTION 17)
- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

16a. Each time you ate **oatmeal, grits,** or **other cooked cereal,** how much did you usually eat?

- ☐ Less than ¾ cup
- ☐ ¾ to 1¼ cups
- ☐ More than 1¼ cups

16b. How often was **butter** or **margarine** added to your oatmeal, grits or other cooked cereal?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

17. How often did you eat **cold cereal**?

- ☐ NEVER (GO TO QUESTION 18)
- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

17a. Each time you ate **cold cereal**, how much did you usually eat?

- ☐ Less than 1 cup
- ☐ 1 to 2½ cups
- ☐ More than 2½ cups

17b. How often was the cold cereal you ate **Total Raisin Bran**, **Total Cereal**, or **Product 19**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

Question 18 appears on the next page

Over the <u>past month</u>…

17c. How often was the cold cereal you ate **All Bran**, **Fiber One**, **100% Bran**, or **All-Bran Bran Buds**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

17d. How often was the cold cereal you ate **some other bran** or **fiber cereal** (such as Cheerios, Shredded Wheat, Raisin Bran, Bran Flakes, Grape-Nuts, Granola, Wheaties, or Healthy Choice)?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

17e. How often was the cold cereal you ate any **other type of cold cereal** (such as Corn Flakes, Rice Krispies, Frosted Flakes, Special K, Froot Loops, Cap'n Crunch, or others)?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

17f. Was **milk** added to your cold cereal?

- ☐ NO (GO TO QUESTION 18)
- ☐ YES

17g. What kind of **milk** was usually added?

- ☐ Whole milk
- ☐ 2% fat milk
- ☐ 1% fat milk
- ☐ Skim, nonfat, or ½% fat milk
- ☐ Soy milk
- ☐ Rice milk
- ☐ Other

17h. Each time **milk was added to your cold cereal**, how much was usually added?

- ☐ Less than ½ cup
- ☐ ½ to 1 cup
- ☐ More than 1 cup

Question 18 appears in the next column

18. How often did you eat **applesauce**?

- ☐ NEVER (GO TO QUESTION 19)
- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

18a. Each time you ate **applesauce**, how much did you usually eat?

- ☐ Less than ½ cup
- ☐ ½ to 1 cup
- ☐ More than 1 cup

19. How often did you eat **apples**?

- ☐ NEVER (GO TO QUESTION 20)
- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

19a. Each time you ate **apples**, how many did you usually eat?

- ☐ Less than 1 apple
- ☐ 1 apple
- ☐ More than 1 apple

20. How often did you eat **pears** (fresh, canned, or frozen)?

- ☐ NEVER (GO TO QUESTION 21)
- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

20a. Each time you ate **pears**, how many did you usually eat?

- ☐ Less than 1 pear
- ☐ 1 pear
- ☐ More than 1 pear

21. How often did you eat **bananas?**

- ☐ NEVER (GO TO QUESTION 22)
- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

Question 22 appears on the next page

Over the <u>past month</u>…

21a. Each time you ate **bananas**, how many did you usually eat?

- ☐ Less than 1 banana
- ☐ 1 banana
- ☐ More than 1 banana

22. How often did you eat **dried fruit** (such as prunes or raisins)? *(Please do not include dried apricots.)*

- ☐ NEVER (GO TO QUESTION 23)
- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

22a. Each time you ate **dried fruit**, how much did you usually eat?

- ☐ Less than 2 tablespoons
- ☐ 2 to 5 tablespoons
- ☐ More than 5 tablespoons

23. How often did you eat **peaches, nectarines,** or **plums**?

- ☐ NEVER (GO TO QUESTION 24)
- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

23a. Each time you ate **peaches, nectarines,** or **plums,** how much did you usually eat?

- ☐ Less than 1 fruit or less than ½ cup
- ☐ 1 to 2 fruits or ½ to ¾ cup
- ☐ More than 2 fruits or more than ¾ cup

Question 24 appears in the next column

24. How often did you eat **grapes**?

- ☐ NEVER (GO TO QUESTION 25)
- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

24a. Each time you ate **grapes**, how much did you usually eat?

- ☐ Less than ½ cup or less than 10 grapes
- ☐ ½ to 1 cup or 10 to 30 grapes
- ☐ More than 1 cup or more than 30 grapes

25. How often did you eat **cantaloupe**?

- ☐ NEVER (GO TO QUESTION 26)
- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

25a. Each time you ate **cantaloupe**, how much did you usually eat?

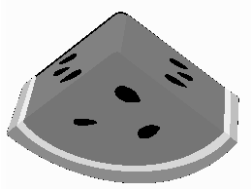
- ☐ Less than ¼ melon or less than ½ cup
- ☐ ¼ melon or ½ to 1 cup
- ☐ More than ¼ melon or more than 1 cup

26. How often did you eat **melon, other than cantaloupe** (such as watermelon or honeydew)?

- ☐ NEVER (GO TO QUESTION 27)
- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

26a. Each time you ate **melon other than cantaloupe**, how much did you usually eat?

- ☐ Less than ½ cup or 1 small wedge
- ☐ ½ to 2 cups or 1 medium wedge
- ☐ More than 2 cups or 1 large wedge



Question 27 appears on the next page

Over the <u>past month</u>…

27. How often did you eat **strawberries**?

- ☐ NEVER (GO TO QUESTION 28)
- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

27a. Each time you ate **strawberries**, how much did you usually eat?

- ☐ Less than ¼ cup or less than 3 berries
- ☐ ¼ to ¾ cup or 3 to 8 berries
- ☐ More than ¾ cup or more than 8 berries

28. How often did you eat **oranges, tangerines,** or **clementines**?

- ☐ NEVER (GO TO QUESTION 29)
- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

28a. Each time you ate **oranges, tangerines,** or **clementines,** how many did you usually eat?

- ☐ Less than 1 fruit
- ☐ 1 fruit
- ☐ More than 1 fruit

29. How often did you eat **grapefruit**?

- ☐ NEVER (GO TO QUESTION 30)
- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

29a. Each time you ate **grapefruit**, how much did you usually eat?

- ☐ Less than ½ grapefruit
- ☐ ½ grapefruit
- ☐ More than ½ grapefruit

Question 30 appears in the next column

30. How often did you eat **pineapple**?

- ☐ NEVER (GO TO QUESTION 31)
- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

30a. Each time you ate **pineapple**, how much did you usually eat?

- ☐ Less than ¼ cup or less than 1 medium slice
- ☐ ¼ to ¾ cup or 1 medium slice
- ☐ More than ¾ cup or more than 1 medium slice

31. How often did you eat **other kinds of fruit**?

- ☐ NEVER (GO TO QUESTION 32)
- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

31a. Each time you ate **other kinds of fruit**, how much did you usually eat?

- ☐ Less than ¼ cup
- ☐ ¼ to ¾ cup
- ☐ More than ¾ cup

32. How often did you eat **COOKED greens** (such as spinach, turnip, collard, mustard, chard, or kale)?

- ☐ NEVER (GO TO QUESTION 33)
- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

32a. Each time you ate **COOKED greens**, how much did you usually eat?

- ☐ Less than ½ cup
- ☐ ½ to 1 cup
- ☐ More than 1 cup

33. How often did you eat **RAW greens** (such as spinach, turnip, collard, mustard, chard, or kale)? (*We will ask about lettuce later.)*

- ☐ NEVER (GO TO QUESTION 34)
- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

Question 34 appears on the next page

Over the <u>past month</u>…

33a. Each time you ate **RAW greens**, how much did you usually eat?

- ☐ Less than ½ cup
- ☐ ½ to 1 cup
- ☐ More than 1 cup

34. How often did you eat **coleslaw**?

- ☐ NEVER (GO TO QUESTION 35)
- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

34a. Each time you ate **coleslaw**, how much did you usually eat?

- ☐ Less than ¼ cup
- ☐ ¼ to ¾ cup
- ☐ More than ¾ cup

35. How often did you eat **sauerkraut** or **cabbage** (other than coleslaw)?

- ☐ NEVER (GO TO QUESTION 36)
- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

35a. Each time you ate **sauerkraut** or **cabbage**, how much did you usually eat?

- ☐ Less than ¼ cup
- ☐ ¼ to 1 cup
- ☐ More than 1 cup

36. How often did you eat **carrots** (fresh, canned, or frozen)?

- ☐ NEVER (GO TO QUESTION 37)
- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

36a. Each time you ate **carrots**, how much did you usually eat?

- ☐ Less than ¼ cup or less than 2 baby carrots
- ☐ ¼ to ½ cup or 2 to 5 baby carrots
- ☐ More than ½ cup or more than 5 baby carrots

Question 37 appears in the next column

37. How often did you eat **string beans** or **green beans** (fresh, canned, or frozen)?

- ☐ NEVER (GO TO QUESTION 38)
- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

37a. Each time you ate **string beans** or **green beans**, how much did you usually eat?

- ☐ Less than ½ cup
- ☐ ½ to 1 cup
- ☐ More than 1 cup

38. How often did you eat **peas** (fresh, canned, or frozen)?

- ☐ NEVER (GO TO QUESTION 39)
- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

38a. Each time you ate **peas**, how much did you usually eat?

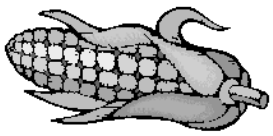
- ☐ Less than ¼ cup
- ☐ ¼ to ¾ cup
- ☐ More than ¾ cup

39. How often did you eat **corn**?

- ☐ NEVER (GO TO QUESTION 40)
- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

39a. Each time you ate **corn**, how much did you usually eat?

- ☐ Less than 1 ear or less than ½ cup
- ☐ 1 ear or ½ to 1 cup
- ☐ More than 1 ear or more than 1 cup



Question 40 appears on the next page

Over the <u>past month</u>…

40. How often did you eat **broccoli** (fresh or frozen)?

☐ NEVER (GO TO QUESTION 41)

☐ 1 time in past month
☐ 2–3 times in past month
☐ 1 time per week
☐ 2 times per week
☐ 3–4 times per week
☐ 5–6 times per week
☐ 1 time per day
☐ 2 or more times per day

40a. Each time you ate **broccoli**, how much did you usually eat?

☐ Less than ¼ cup
☐ ¼ to 1 cup
☐ More than 1 cup

41. How often did you eat **cauliflower** or **Brussels sprouts** (fresh or frozen)?

☐ NEVER (GO TO QUESTION 42)

☐ 1 time in past month
☐ 2–3 times in past month
☐ 1 time per week
☐ 2 times per week
☐ 3–4 times per week
☐ 5–6 times per week
☐ 1 time per day
☐ 2 or more times per day

41a. Each time you ate **cauliflower** or **Brussels sprouts**, how much did you usually eat?

☐ Less than ¼ cup
☐ ¼ to ½ cup
☐ More than ½ cup

42. How often did you eat **asparagus** (fresh or frozen)?

☐ NEVER (GO TO QUESTION 43)

☐ 1 time in past month
☐ 2–3 times in past month
☐ 1 time per week
☐ 2 times per week
☐ 3–4 times per week
☐ 5–6 times per week
☐ 1 time per day
☐ 2 or more times per day

42a. Each time you ate **asparagus**, how much did you usually eat?

☐ Less than ⅓ cup or less than 4 spears
☐ ⅓ to ⅔ cup or 4 to 7 spears
☐ More than ⅔ cup or more than 7 spears

Question 43 appears in the next column

43. How often did you eat **winter squash** (such as pumpkin, butternut, or acorn)?

☐ NEVER (GO TO QUESTION 44)

☐ 1 time in past month
☐ 2–3 times in past month
☐ 1 time per week
☐ 2 times per week
☐ 3–4 times per week
☐ 5–6 times per week
☐ 1 time per day
☐ 2 or more times per day

43a. Each time you ate **winter squash**, how much did you usually eat?

☐ Less than ½ cup
☐ ½ to ¾ cup
☐ More than ¾ cup

44. How often did you eat **mixed vegetables**?

☐ NEVER (GO TO QUESTION 45)

☐ 1 time in past month
☐ 2–3 times in past month
☐ 1 time per week
☐ 2 times per week
☐ 3–4 times per week
☐ 5–6 times per week
☐ 1 time per day
☐ 2 or more times per day

44a. Each time you ate **mixed vegetables**, how much did you usually eat?

☐ Less than ½ cup
☐ ½ to 1 cup
☐ More than 1 cup

45. How often did you eat **onions**?

☐ NEVER (GO TO QUESTION 46)

☐ 1 time in past month
☐ 2–3 times in past month
☐ 1 time per week
☐ 2 times per week
☐ 3–4 times per week
☐ 5–6 times per week
☐ 1 time per day
☐ 2 or more times per day

45a. Each time you ate **onions**, how much did you usually eat?

☐ Less than 1 slice or less than 1 tablespoon
☐ 1 slice or 1 to 4 tablespoons
☐ More than 1 slice or more than 4 tablespoons

Question 46 appears on the next page

Over the past month…

46. Now think about all the **cooked vegetables** you ate in the past month and how they were prepared. How often were your vegetables **COOKED WITH** some sort of **fat**, including oil spray? *(Please do not include potatoes.)*

- ☐ NEVER (GO TO QUESTION 47)
- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

46a. Which fats were usually added to your vegetables **DURING COOKING**? *(Please do not include potatoes. **Mark all that apply.**)*

- ☐ Margarine (including low-fat)
- ☐ Butter (including low-fat)
- ☐ Lard, fatback, or bacon fat
- ☐ Olive oil
- ☐ Corn oil
- ☐ Canola or rapeseed oil
- ☐ Oil spray, such as Pam or others
- ☐ Other kinds of oils
- ☐ None of the above

47. Now, thinking again about all the **cooked vegetables** you ate in the past month, how often was some sort of fat, sauce, or dressing added **AFTER COOKING OR AT THE TABLE**? *(Please do not include potatoes.)*

- ☐ NEVER (GO TO QUESTION 48)
- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1–2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 times per day
- ☐ 3 or more times per day

Question 48 appears in the next column

47a. Which fats, sauces, or dressings were usually added **AFTER COOKING OR AT THE TABLE**? *(Please do not include potatoes. **Mark all that apply.**)*

- ☐ Margarine (including low-fat)
- ☐ Butter (including low-fat)
- ☐ Lard, fatback, or bacon fat
- ☐ Salad dressing
- ☐ Cheese sauce
- ☐ White sauce
- ☐ Other

47b. If margarine, butter, lard, fatback, or bacon fat was added to your cooked vegetables **AFTER COOKING OR AT THE TABLE**, how much did you usually add?

- ☐ Did not usually add these
- ☐ Less than 1 teaspoon
- ☐ 1 to 3 teaspoons
- ☐ More than 3 teaspoons

47c. If salad dressing, cheese sauce, or white sauce was added to your cooked vegetables **AFTER COOKING OR AT THE TABLE**, how much did you usually add?

- ☐ Did not usually add these
- ☐ Less than 1 tablespoon
- ☐ 1 to 3 tablespoons
- ☐ More than 3 tablespoons

48. How often did you eat **sweet peppers** (green, red, or yellow)?

- ☐ NEVER (GO TO QUESTION 49)
- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

48a. Each time you ate **sweet peppers**, how much did you usually eat?

- ☐ Less than ⅛ pepper
- ☐ ⅛ to ¼ pepper
- ☐ More than ¼ pepper

Question 49 appears on the next page

Over the <u>past month</u>…

49. How often did you eat **fresh tomatoes** (including those in salads)?

- ☐ NEVER (GO TO QUESTION 50)
- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

49a. Each time you ate **fresh tomatoes**, how much did you usually eat?

- ☐ Less than ¼ tomato
- ☐ ¼ to ½ tomato
- ☐ More than ½ tomato

50. How often did you eat **lettuce salads** (with or without other vegetables)?

- ☐ NEVER (GO TO QUESTION 51)
- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

50a. Each time you ate **lettuce salads**, how much did you usually eat?

- ☐ Less than ¼ cup
- ☐ ¼ to 1¼ cups
- ☐ More than 1¼ cups

50b. How often did the lettuce salads you ate include **dark green lettuce**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

51. How often did you eat **salad dressing** (including low-fat) **on salads**?

- ☐ NEVER (GO TO QUESTION 52)
- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

51a. Each time you ate **salad dressing on salads**, how much did you usually eat?

- ☐ Less than 2 tablespoons
- ☐ 2 to 4 tablespoons
- ☐ More than 4 tablespoons

Question 52 appears in the next column

52. How often did you eat **sweet potatoes** or **yams**?

- ☐ NEVER (GO TO QUESTION 53)
- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

52a. Each time you ate **sweet potatoes** or **yams**, how much did you usually eat?

- ☐ 1 small potato or less than ¼ cup
- ☐ 1 medium potato or ¼ to ¾ cup
- ☐ 1 large potato or more than ¾ cup

53. How often did you eat **French fries**, **home fries**, **hash browned potatoes**, or **tater tots**?

- ☐ NEVER (GO TO QUESTION 54)
- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

53a. Each time you ate **French fries**, **home fries**, **hash browned potatoes**, or **tater tots** how much did you usually eat?

- ☐ Less than 10 fries or less than ½ cup
- ☐ 10 to 25 fries or ½ to 1 cup
- ☐ More than 25 fries or more than 1 cup

54. How often did you eat **potato salad**?

- ☐ NEVER (GO TO QUESTION 55)
- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

54a. Each time you ate **potato salad**, how much did you usually eat?

- ☐ Less than ½ cup
- ☐ ½ to 1 cup
- ☐ More than 1 cup

55. How often did you eat **baked, boiled,** or **mashed potatoes**?

- ☐ NEVER (GO TO QUESTION 56)
- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

Question 56 appears on the next page

Over the <u>past month</u>…

55a. Each time you ate **baked, boiled,** or **mashed potatoes**, how much did you usually eat?

- ☐ 1 small potato or less than ½ cup
- ☐ 1 medium potato or ½ to 1 cup
- ☐ 1 large potato or more than 1 cup

55b. How often was **sour cream** (including low-fat) added to your potatoes, **EITHER IN COOKING OR AT THE TABLE**?

- ☐ Almost never or never (GO TO QUESTION 55d)
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

55c. Each time **sour cream** was added to your potatoes, how much was usually added?

- ☐ Less than 1 tablespoon
- ☐ 1 to 3 tablespoons
- ☐ More than 3 tablespoons

55d. How often was **margarine** (including low-fat) added to your potatoes, **EITHER IN COOKING OR AT THE TABLE**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

55e. How often was **butter** (including low-fat) added to your potatoes, **EITHER IN COOKING OR AT THE TABLE**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

55f. Each time **margarine** or **butter** was added to your potatoes, how much was usually added?

- ☐ Never added
- ☐ Less than 1 teaspoon
- ☐ 1 to 3 teaspoons
- ☐ More than 3 teaspoons

55g. How often was **cheese** or **cheese sauce** added to your potatoes, **EITHER IN COOKING OR AT THE TABLE**?

- ☐ Almost never or never (GO TO QUESTION 56)
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

55h. Each time **cheese** or **cheese sauce** was added to your potatoes, how much was usually added?

- ☐ Less than 1 tablespoon
- ☐ 1 to 3 tablespoons
- ☐ More than 3 tablespoons

56. How often did you eat **salsa**?

- ☐ NEVER (GO TO QUESTION 57)
- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

56a. Each time you ate **salsa**, how much did you usually eat?

- ☐ Less than 1 tablespoon
- ☐ 1 to 5 tablespoons
- ☐ More than 5 tablespoons

57. How often did you eat **catsup**?

- ☐ NEVER (GO TO QUESTION 58)
- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

57a. Each time you ate **catsup**, how much did you usually eat?

- ☐ Less than 1 teaspoon
- ☐ 1 to 6 teaspoons
- ☐ More than 6 teaspoons

58. How often did you eat **stuffing, dressing,** or **dumplings**?

- ☐ NEVER (GO TO QUESTION 59)
- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

Question 56 appears in the next column

Question 59 appears on the next page

Over the past month…

58a. Each time you ate **stuffing, dressing,** or **dumplings**, how much did you usually eat?

- ☐ Less than ½ cup
- ☐ ½ to 1 cup
- ☐ More than 1 cup

59. How often did you eat **chili**?

- ☐ NEVER (GO TO QUESTION 60)
- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

59a. Each time you ate **chili**, how much did you usually eat?

- ☐ Less than ½ cup
- ☐ ½ to 1¾ cups
- ☐ More than 1¾ cups

60. How often did you eat **Mexican foods** (such as tacos, tostados, burritos, tamales, fajitas, enchiladas, quesadillas, and chimichangas)?

- ☐ NEVER (GO TO QUESTION 61)
- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

60a. Each time you ate **Mexican foods**, how much did you usually eat?

- ☐ Less than 1 taco, burrito, etc.
- ☐ 1 to 2 tacos, burritos, etc.
- ☐ More than 2 tacos, burritos, etc.

61. How often did you eat **cooked dried beans** (such as baked beans, pintos, kidney, blackeyed peas, lima, lentils, soybeans, or refried beans)? *(Please do not include bean soups or chili.)*

- ☐ NEVER (GO TO QUESTION 62)
- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

61a. Each time you ate **beans**, how much did you usually eat?

- ☐ Less than ½ cup
- ☐ ½ to 1 cup
- ☐ More than 1 cup

Question 62 appears in the next column

61b. How often were the beans you ate **refried beans**, **beans prepared with any type of fat**, or **with meat added**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

62. How often did you eat **other kinds of vegetables**?

- ☐ NEVER (GO TO QUESTION 63)
- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

62a. Each time you ate **other kinds of vegetables**, how much did you usually eat?

- ☐ Less than ¼ cup
- ☐ ¼ to ½ cup
- ☐ More than ½ cup

63. How often did you eat **rice** or **other cooked grains** (such as bulgur, cracked wheat, or millet)?

- ☐ NEVER (GO TO QUESTION 64)
- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

63a. Each time you ate **rice** or **other cooked grains**, how much did you usually eat?

- ☐ Less than ½ cup
- ☐ ½ to 1½ cups
- ☐ More than 1½ cups

63b. How often was **butter**, **margarine**, or **oil** added to your rice or other cooked grains **IN COOKING OR AT THE TABLE**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

Question 64 appears on the next page

Over the <u>past month</u>…

64. How often did you eat **pancakes, waffles,** or **French toast**?

- ☐ NEVER (GO TO QUESTION 65)
- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

64a. Each time you ate **pancakes, waffles,** or **French toast**, how much did you usually eat?

- ☐ Less than 1 medium piece
- ☐ 1 to 3 medium pieces
- ☐ More than 3 medium pieces

64b. How often was **margarine** (including low-fat) added to your pancakes, waffles, or French toast **AFTER COOKING OR AT THE TABLE**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

64c. How often was **butter** (including low-fat) added to your pancakes, waffles, or French toast **AFTER COOKING OR AT THE TABLE**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

64d. Each time **margarine** or **butter** was added to your pancakes, waffles, or French toast, how much was usually added?

- ☐ Never added
- ☐ Less than 1 teaspoon
- ☐ 1 to 3 teaspoons
- ☐ More than 3 teaspoons

64e. How often was **syrup** added to your pancakes, waffles, or French toast?

- ☐ Almost never or never (GO TO QUESTION 65)
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

Question 65 appears in the next column

64f. Each time **syrup** was added to your pancakes, waffles, or French toast, how much was usually added?

- ☐ Less than 1 tablespoon
- ☐ 1 to 4 tablespoons
- ☐ More than 4 tablespoons

65. How often did you eat **lasagna, stuffed shells, stuffed manicotti, ravioli,** or **tortellini**? *(Please do not include spaghetti or other pasta.)*

- ☐ NEVER (GO TO QUESTION 66)
- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

65a. Each time you ate **lasagna**, **stuffed shells**, **stuffed manicotti**, **ravioli**, or **tortellini**, how much did you usually eat?

- ☐ Less than 1 cup
- ☐ 1 to 2 cups
- ☐ More than 2 cups

66. How often did you eat **macaroni and cheese**?

- ☐ NEVER (GO TO QUESTION 67)
- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

66a. Each time you ate **macaroni and cheese**, how much did you usually eat?

- ☐ Less than 1 cup
- ☐ 1 to 1½ cups
- ☐ More than 1½ cups

67. How often did you eat **pasta salad** or **macaroni salad**?

- ☐ NEVER (GO TO QUESTION 68)
- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

Question 68 appears on the next page

Over the <u>past month</u>…

67a. Each time you ate **pasta salad** or **macaroni salad**, how much did you usually eat?

- ☐ Less than ½ cup
- ☐ ½ to 1 cup
- ☐ More than 1 cup

68. Other than the pastas listed in Questions 65, 66, and 67, how often did you eat **pasta, spaghetti**, or **other noodles**?

- ☐ NEVER (GO TO QUESTION 69)

- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

68a. Each time you ate **pasta, spaghetti**, **or other noodles**, how much did you usually eat?

- ☐ Less than 1 cup
- ☐ 1 to 3 cups
- ☐ More than 3 cups

68b. How often did you eat your pasta, spaghetti, or other noodles with **tomato sauce** or **spaghetti sauce made WITH meat**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

68c. How often did you eat your pasta, spaghetti, or other noodles with **tomato sauce** or **spaghetti sauce made WITHOUT meat**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

68d. How often did you eat your pasta, spaghetti, or other noodles with **margarine, butter, oil,** or **cream sauce**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

Question 69 appears in the next column

69. How often did you eat **bagels** or **English muffins**?

- ☐ NEVER (GO TO INTRODUCTION TO QUESTION 70)

- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

69a. How often were the bagels or English muffins you ate **whole wheat**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

69b. Each time you ate **bagels** or **English muffins**, how many did you usually eat?

- ☐ Less than 1 bagel or English muffin
- ☐ 1 bagel or English muffin
- ☐ More than 1 bagel or English muffin

69c. How often was **margarine** (including low-fat) added to your bagels or English muffins?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

69d. How often was **butter** (including low-fat) added to your bagels or English muffins?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

69e. Each time **margarine** or **butter** was added to your bagels or English muffins, how much was usually added?

- ☐ Never added
- ☐ Less than 1 teaspoon
- ☐ 1 to 2 teaspoons
- ☐ More than 2 teaspoons

Introduction to Question 70 appears on the next page

Over the <u>past month</u>…

69f. How often was **cream cheese** (including low-fat) spread on your bagels or English muffins?

- ☐ Almost never or never (GO TO INTRODUCTION TO QUESTION 70)
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

69g. Each time **cream cheese** was added to your bagels or English muffins, how much was usually added?

- ☐ Less than 1 tablespoon
- ☐ 1 to 2 tablespoons
- ☐ More than 2 tablespoons

The next questions ask about your intake of breads other than bagels or English muffins. First, we will ask about bread you ate as part of sandwiches only. Then we will ask about all other bread you ate.

70. How often did you eat **breads** or **rolls AS PART OF SANDWICHES** (including burger and hot dog rolls)?
(Please do not include fast food sandwiches.)

- ☐ NEVER (GO TO QUESTION 71)

- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

70a. Each time you ate **breads** or **rolls AS PART OF SANDWICHES**, how many did you usually eat?

- ☐ 1 slice or ½ roll
- ☐ 2 slices or 1 roll
- ☐ More than 2 slices or more than 1 roll

70b. How often were the breads or rolls that you used for your sandwiches **white bread** (including burger and hot dog rolls)?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

Question 71 appears in the next column

70c. How often was **mayonnaise** or **mayonnaise-type dressing** (including low-fat) added to the breads or rolls used for your sandwiches?

- ☐ Almost never or never (GO TO QUESTION 70e)
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

70d. Each time **mayonnaise** or **mayonnaise-type dressing** was added to the breads or rolls used for your sandwiches, how much was usually added?

- ☐ Less than 1 teaspoon
- ☐ 1 to 3 teaspoons
- ☐ More than 3 teaspoons

70e. How often was **margarine** (including low-fat) added to the breads or rolls used for your sandwiches?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

70f. How often was **butter** (including low-fat) added to the breads or rolls used for your sandwiches?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

70g. Each time **margarine** or **butter** was added to the breads or rolls used for your sandwiches, how much was usually added?

- ☐ Never added
- ☐ Less than 1 teaspoon
- ☐ 1 to 2 teaspoons
- ☐ More than 2 teaspoons

71. How often did you eat **breads** or **dinner rolls**, **NOT AS PART OF SANDWICHES**?

- ☐ NEVER (GO TO QUESTION 72)

- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

Question 72 appears on the next page

Over the <u>past month</u>…

71a. Each time you ate **breads** or **dinner rolls, NOT AS PART OF SANDWICHES**, how much did you usually eat?

- ☐ 1 slice or 1 dinner roll
- ☐ 2 slices or 2 dinner rolls
- ☐ More than 2 slices or 2 dinner rolls

71b. How often were the breads or rolls you ate **white bread**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

71c. How often was **margarine** (including low-fat) added to your breads or rolls?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

71d. How often was **butter** (including low-fat) added to your breads or rolls?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

71e. Each time **margarine** or **butter** was added to your breads or rolls, how much was usually added?

- ☐ Never added
- ☐ Less than 1 teaspoon
- ☐ 1 to 2 teaspoons
- ☐ More than 2 teaspoons

71f. How often was **cream cheese** (including low-fat) added to your breads or rolls?

- ☐ Almost never or never (GO TO QUESTION 72)
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

Question 72 appears in the next column

71g. Each time **cream cheese** was added to your breads or rolls, how much was usually added?

- ☐ Less than 1 tablespoon
- ☐ 1 to 2 tablespoons
- ☐ More than 2 tablespoons

72. How often did you eat **jam, jelly,** or **honey** on bagels, muffins, bread, rolls, or crackers?

- ☐ NEVER (GO TO QUESTION 73)
- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

72a. Each time you ate **jam, jelly,** or **honey**, how much did you usually eat?

- ☐ Less than 1 teaspoon
- ☐ 1 to 3 teaspoons
- ☐ More than 3 teaspoons

73. How often did you eat **peanut butter** or **other nut butter**?

- ☐ NEVER (GO TO QUESTION 74)
- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

73a. Each time you ate **peanut butter** or **other nut butter**, how much did you usually eat?

- ☐ Less than 1 tablespoon
- ☐ 1 to 2 tablespoons
- ☐ More than 2 tablespoons

74. How often did you eat **roast beef** or **steak IN SANDWICHES**?

- ☐ NEVER (GO TO QUESTION 75)
- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

74a. Each time you ate **roast beef** or **steak IN SANDWICHES**, how much did you usually eat?

- ☐ Less than 1 slice or less than 2 ounces
- ☐ 1 to 2 slices or 2 to 4 ounces
- ☐ More than 2 slices or more than 4 ounces

Question 75 appears on the next page

Over the <u>past month</u>…

75. How often did you eat **turkey** or **chicken COLD CUTS** (such as loaf, luncheon meat, turkey ham, turkey salami, or turkey pastrami)? *(We will ask about other turkey or chicken later.)*

- ☐ NEVER (GO TO QUESTION 76)

- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

75a. Each time you ate **turkey or chicken COLD CUTS**, how much did you usually eat?

- ☐ Less than 1 slice
- ☐ 1 to 3 slices
- ☐ More than 3 slices

76. How often did you eat **luncheon** or **deli-style ham**? *(We will ask about other ham later.)*

- ☐ NEVER (GO TO QUESTION 77)

- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

76a. Each time you ate **luncheon** or **deli-style ham**, how much did you usually eat?

- ☐ Less than 1 slice
- ☐ 1 to 3 slices
- ☐ More than 3 slices

76b. How often was the luncheon or deli-style ham you ate **light**, **low-fat**, or **fat-free**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

77. How often did you eat **other cold cuts** or **luncheon meats** (such as bologna, salami, corned beef, pastrami, or others, including low-fat)? *(Please do not include ham, turkey, or chicken cold cuts.)*

- ☐ NEVER (GO TO QUESTION 78)

- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

Question 78 appears in the next column

77a. Each time you ate **other cold cuts** or **luncheon meats**, how much did you usually eat?

- ☐ Less than 1 slice
- ☐ 1 to 3 slices
- ☐ More than 3 slices

77b. How often were the other cold cuts or luncheon meats you ate **light, low-fat**, or **fat-free**? *(Please do not include ham, turkey, or chicken cold cuts.)*

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

78. How often did you eat **canned tuna** (including in salads, sandwiches, or casseroles)?

- ☐ NEVER (GO TO QUESTION 79)

- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

78a. Each time you ate **canned tuna**, how much did you usually eat?

- ☐ Less than ¼ cup or less than 2 ounces
- ☐ ¼ to ½ cup or 2 to 3 ounces
- ☐ More than ½ cup or more than 3 ounces

78b. How often was the canned tuna you ate **water-packed**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

78c. How often was the canned tuna you ate **prepared with mayonnaise** or **other dressing** (including low-fat)?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

Question 79 appears on the next page

Over the <u>past month</u>…

79. How often did you eat **GROUND chicken** or **turkey**? *(We will ask about other chicken and turkey later.)*

- ☐ NEVER (GO TO QUESTION 80)

- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

79a. Each time you ate **GROUND chicken** or **turkey**, how much did you usually eat?

- ☐ Less than 2 ounces or less than ½ cup
- ☐ 2 to 4 ounces or ½ to 1 cup
- ☐ More than 4 ounces or more than 1 cup

80. How often did you eat **beef hamburgers** or **cheeseburgers** from a **FAST FOOD** or **OTHER RESTAURANT**?

- ☐ NEVER (GO TO QUESTION 81)

- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

80a. Each time you ate **beef hamburgers** or **cheeseburgers** from a **FAST FOOD** or **OTHER RESTAURANT**, what size did you usually eat?

- ☐ Small hamburger (such as a regular Burger King or McDonald's Hamburger)
- ☐ Medium (such as McDonald's or Burger King Double Burger or Cheeseburger)
- ☐ Large (such as Burger King Whopper or Double Whopper or a McDonald's Double Quarter Pounder)

80b. Each time you ate **beef hamburgers** or **cheeseburgers** from a **FAST FOOD** or **OTHER RESTAURANT**, how much did you usually eat?

- ☐ Less than 1 burger
- ☐ 1 burger
- ☐ More than 1 burger

80c. How often did you have **cheeseburgers** rather than **hamburgers**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

Question 81 appears in the next column

81. How often did you eat **beef hamburgers** or **cheeseburgers** that were **NOT FROM A FAST FOOD** or **OTHER RESTAURANT**?

- ☐ NEVER (GO TO QUESTION 82)

- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

81a. Each time you ate **beef hamburgers** or **cheeseburgers** that were **NOT FROM A FAST FOOD** or **OTHER RESTAURANT**, how much did you usually eat?

- ☐ Less than 1 patty or less than 2 ounces
- ☐ 1 patty or 2 to 4 ounces
- ☐ More than 1 patty or more than 4 ounces

81b. How often were these beef hamburgers or cheeseburgers made with **lean ground beef**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

82. How often did you eat **ground beef in mixtures** (such as meatballs, casseroles, chili, or meatloaf)?

- ☐ NEVER (GO TO QUESTION 83)

- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

82a. Each time you ate **ground beef in mixtures**, how much did you usually eat?

- ☐ Less than 3 ounces or less than ½ cup
- ☐ 3 to 8 ounces or ½ to 1 cup
- ☐ More than 8 ounces or more than 1 cup

83. How often did you eat **hot dogs** or **frankfurters**? *(Please do not include sausages or vegetarian hot dogs.)*

- ☐ NEVER (GO TO QUESTION 84)

- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

Question 84 appears on the next page

Over the <u>past month</u>…

83a. Each time you ate **hot dogs** or **frankfurters**, how many did you usually eat?

- ☐ Less than 1 hot dog
- ☐ 1 to 2 hot dogs
- ☐ More than 2 hot dogs

83b. How often were the hot dogs or frankfurters you ate **light** or **low-fat**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

84. How often did you eat **beef mixtures** (such as beef stew, beef pot pie, beef and noodles, or beef and vegetables)?

- ☐ NEVER (GO TO QUESTION 85)

- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

84a. Each time you ate **beef mixtures**, how much did you usually eat?

- ☐ Less than 1 cup
- ☐ 1 to 2 cups
- ☐ More than 2 cups

85. How often did you eat **roast beef** or **pot roast**? *(Please do not include roast beef or pot roast in sandwiches.)*

- ☐ NEVER (GO TO QUESTION 86)

- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

85a. Each time you ate **roast beef** or **pot roast**, how much did you usually eat?

- ☐ Less than 2 ounces
- ☐ 2 to 5 ounces
- ☐ More than 5 ounces

Question 86 appears in the next column

86. How often did you eat **steak** (beef)? (*Please do not include steak in sandwiches*)

- ☐ NEVER (GO TO QUESTION 87)

- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

86a. Each time you ate **steak** (beef), how much did you usually eat?

- ☐ Less than 3 ounces
- ☐ 3 to 7 ounces
- ☐ More than 7 ounces

86b. How often was the steak you ate **lean steak**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

87. How often did you eat **pork** or **beef spareribs**?

- ☐ NEVER (GO TO QUESTION 88)

- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

87a. Each time you ate **pork** or **beef spareribs**, how much did you usually eat?

- ☐ Less than 4 ribs
- ☐ 4 to 12 ribs
- ☐ More than 12 ribs

88. How often did you eat **roast turkey, turkey cutlets,** or **turkey nuggets** (including in sandwiches)?

- ☐ NEVER (GO TO QUESTION 89)

- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

88a. Each time you ate **roast turkey, turkey cutlets,** or **turkey nuggets**, how much did you usually eat? *(Please note: 4 to 8 turkey nuggets = 3 ounces.)*

- ☐ Less than 2 ounces
- ☐ 2 to 4 ounces
- ☐ More than 4 ounces

Question 89 appears on the next page

Over the past month…

89. How often did you eat **chicken mixtures** (such as salads, sandwiches, casseroles, stews, or other mixtures)?

- ☐ NEVER (GO TO QUESTION 90)
- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

89a. Each time you ate **chicken mixtures**, how much did you usually eat?

- ☐ Less than ½ cup
- ☐ ½ to 1½ cups
- ☐ More than 1½ cups

90. How often did you eat **baked, broiled, roasted, stewed,** or **fried chicken** (including nuggets)? *(Please do not include chicken in mixtures.)*

- ☐ NEVER (GO TO QUESTION 91)
- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

90a. Each time you ate **baked, broiled, roasted, stewed,** or **fried chicken** (including nuggets), how much did you usually eat?

- ☐ Less than 2 drumsticks or wings, less than 1 breast or thigh, or less than 4 nuggets
- ☐ 2 drumsticks or wings, 1 breast or thigh, or 4 to 8 nuggets
- ☐ More than 2 drumsticks or wings, more than 1 breast or thigh, or more than 8 nuggets

90b. How often was the chicken you ate **fried chicken** (including deep fried) or **chicken nuggets**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

90c. How often was the chicken you ate **WHITE meat**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

Question 91 appears in the next column

90d. How often did you eat chicken **WITH skin**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

91. How often did you eat **baked ham** or **ham steak**?

- ☐ NEVER (GO TO QUESTION 92)
- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

91a. Each time you ate **baked ham** or **ham steak**, how much did you usually eat?

- ☐ Less than 1 ounce
- ☐ 1 to 3 ounces
- ☐ More than 3 ounces

92. How often did you eat **pork** (including chops, roasts, and in mixed dishes)? *(Please do not include ham, ham steak, or sausage.)*

- ☐ NEVER (GO TO QUESTION 93)
- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

92a. Each time you ate **pork**, how much did you usually eat?

- ☐ Less than 2 ounces or less than 1 chop
- ☐ 2 to 5 ounces or 1 chop
- ☐ More than 5 ounces or more than 1 chop

93. How often did you eat **gravy** on meat, chicken, potatoes, rice, etc.?

- ☐ NEVER (GO TO QUESTION 94)
- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

93a. Each time you ate **gravy** on meat, chicken, potatoes, rice, etc., how much did you usually eat?

- ☐ Less than ⅛ cup
- ☐ ⅛ to ½ cup
- ☐ More than ½ cup

Question 94 appears on the next page

Over the <u>past month</u>…

94. How often did you eat **liver** (all kinds) or **liverwurst**?

☐ NEVER (GO TO QUESTION 95)

☐ 1 time in past month
☐ 2–3 times in past month
☐ 1 time per week
☐ 2 times per week
☐ 3–4 times per week
☐ 5–6 times per week
☐ 1 time per day
☐ 2 or more times per day

94a. Each time you ate **liver** or **liverwurst**, how much did you usually eat?

☐ Less than 1 ounce
☐ 1 to 4 ounces
☐ More than 4 ounces

95. How often did you eat **bacon** (including low-fat)?

☐ NEVER (GO TO QUESTION 96)

☐ 1 time in past month
☐ 2–3 times in past month
☐ 1 time per week
☐ 2 times per week
☐ 3–4 times per week
☐ 5–6 times per week
☐ 1 time per day
☐ 2 or more times per day

95a. Each time you ate **bacon**, how much did you usually eat?

☐ Fewer than 2 slices
☐ 2 to 3 slices
☐ More than 3 slices

95b. How often was the bacon you ate **light, low-fat,** or **lean**?

☐ Almost never or never
☐ About ¼ of the time
☐ About ½ of the time
☐ About ¾ of the time
☐ Almost always or always

96. How often did you eat **sausage** (including low-fat)?

☐ NEVER (GO TO QUESTION 97)

☐ 1 time in past month
☐ 2–3 times in past month
☐ 1 time per week
☐ 2 times per week
☐ 3–4 times per week
☐ 5–6 times per week
☐ 1 time per day
☐ 2 or more times per day

96a. Each time you ate **sausage**, how much did you usually eat?

☐ Less than 1 patty or 2 links
☐ 1 to 3 patties or 2 to 5 links
☐ More than 3 patties or 5 links

Question 97 appears in the next column

96b. How often was the sausage you ate **light, low-fat**, or **lean**?

☐ Almost never or never
☐ About ¼ of the time
☐ About ½ of the time
☐ About ¾ of the time
☐ Almost always or always

97. How often did you eat **fried shellfish** (such as crab, lobster, shrimp)?

☐ NEVER (GO TO QUESTION 98)

☐ 1 time in past month
☐ 2–3 times in past month
☐ 1 time per week
☐ 2 times per week
☐ 3–4 times per week
☐ 5–6 times per week
☐ 1 time per day
☐ 2 or more times per day

97a. Each time you ate **fried shellfish**, how much did you usually eat?

☐ Less than 2 ounces
☐ 2 to 4 ounces
☐ More than 4 ounces

98. How often did you eat **shellfish** (such as crab, lobster, shrimp) **that was NOT FRIED**?

☐ NEVER (GO TO QUESTION 99)

☐ 1 time in past month
☐ 2–3 times in past month
☐ 1 time per week
☐ 2 times per week
☐ 3–4 times per week
☐ 5–6 times per week
☐ 1 time per day
☐ 2 or more times per day

98a. Each time you ate **shellfish that was NOT FRIED**, how much did you usually eat?

☐ Less than 1 ounce
☐ 1 to 4 ounces
☐ More than 4 ounces

99. How often did you eat **salmon, fresh tuna or trout**?

☐ NEVER (GO TO QUESTION 100)

☐ 1 time in past month
☐ 2–3 times in past month
☐ 1 time per week
☐ 2 times per week
☐ 3–4 times per week
☐ 5–6 times per week
☐ 1 time per day
☐ 2 or more times per day

99a. Each time you ate **salmon, fresh tuna or trout**, how much did you usually eat?

☐ Less than 2 ounces
☐ 2 to 6 ounces
☐ More than 6 ounces

Question 100 appears on the next page

Over the <u>past month</u>…

100. How often did you eat **fish sticks** or other **fried fish** (not including shellfish)?

- ☐ NEVER (GO TO QUESTION 101)
- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

100a. Each time you ate **fish sticks** or **other fried fish**, how much did you usually eat?

- ☐ Less than 2 ounces or less than 1 fillet
- ☐ 2 to 7 ounces or 1 fillet
- ☐ More than 7 ounces or more than 1 fillet

101. How often did you eat **other fish that was NOT FRIED** (not including shellfish)?

- ☐ NEVER (GO TO INTRODUCTION TO QUESTION 102)
- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

101a. Each time you ate **other fish that was NOT FRIED**, how much did you usually eat?

- ☐ Less than 2 ounces or less than 1 fillet
- ☐ 2 to 5 ounces or 1 fillet
- ☐ More than 5 ounces or more than 1 fillet

Now think about all the meat, poultry, and fish you ate in the <u>past month</u> and how they were prepared.

102. How often was **oil, butter, margarine**, **or other fat** used to **FRY, SAUTE, BASTE, OR MARINATE** any meat, poultry, or fish you ate? *(Please do not include deep frying.)*

- ☐ NEVER (GO TO QUESTION 103)
- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

Question 103 appears in the next column

102a. Which of the following **fats** were regularly used to prepare your meat, poultry, or fish? ***(Mark all that apply.)***

- ☐ Margarine (including low-fat)
- ☐ Butter (including low-fat)
- ☐ Lard, fatback, or bacon fat
- ☐ Olive oil
- ☐ Corn oil
- ☐ Canola or rapeseed oil
- ☐ Oil spray (such as Pam or others)
- ☐ Other kinds of oils
- ☐ None of the above

103. How often did you eat **tofu, soy burgers,** or **soy meat-substitutes**?

- ☐ NEVER (GO TO QUESTION 104)
- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

103a. Each time you ate **tofu, soy burgers,** or **soy meat-substitutes**, how much did you usually eat?

- ☐ Less than ¼ cup or less than 2 ounces
- ☐ ¼ to ½ cup or 2 to 4 ounces
- ☐ More than ½ cup or more than 4 ounces

104. How often did you eat **soups**?

- ☐ NEVER (GO TO QUESTION 105)
- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

104a. Each time you ate **soup**, how much did you usually eat?

- ☐ Less than 1 cup
- ☐ 1 to 2 cups
- ☐ More than 2 cups

104b. How often were the soups you ate **bean soups**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

Question 105 appears on the next page

Over the past month…

104c. How often were the soups you ate **cream soups** (including chowders)?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

104d. How often were the soups you ate **tomato** or **vegetable soups**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

104e. How often were the soups you ate **broth soups** (including chicken) **with** or **without noodles** or **rice**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

105. How often did you eat **pizza**?

- ☐ NEVER (GO TO QUESTION 106)

- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

105a. Each time you ate **pizza**, how much did you usually eat?

- ☐ Less than 1 slice or less than 1 mini pizza
- ☐ 1 to 3 slices or 1 mini pizza
- ☐ More than 3 slices or more than 1 mini pizza

105b. How often did you eat pizza with **pepperoni, sausage**, or **other meat**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

Question 106 appears in the next column

106. How often did you eat **crackers**?

- ☐ NEVER (GO TO QUESTION 107)

- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

106a. Each time you ate **crackers**, how many did you usually eat?

- ☐ Fewer than 4 crackers
- ☐ 4 to 10 crackers
- ☐ More than 10 crackers

107. How often did you eat **corn bread** or **corn muffins**?

- ☐ NEVER (GO TO QUESTION 108)

- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

107a. Each time you ate **corn bread** or **corn muffins,** how much did you usually eat?

- ☐ Less than 1 piece or muffin
- ☐ 1 to 2 pieces or muffins
- ☐ More than 2 pieces or muffins

108. How often did you eat **biscuits**?

- ☐ NEVER (GO TO QUESTION 109)

- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

108a. Each time you ate **biscuits**, how many did you usually eat?

- ☐ Fewer than 1 biscuit
- ☐ 1 to 2 biscuits
- ☐ More than 2 biscuits

109. How often did you eat **potato chips** (including low-fat, fat-free, or low-salt)?

- ☐ NEVER (GO TO QUESTION 110)

- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

Question 110 appears on the next page

Over the <u>past month</u>…

109a. Each time you ate **potato chips**, how much did you usually eat?

- ☐ Fewer than 10 chips or less than 1 cup
- ☐ 10 to 25 chips or 1 to 2 cups
- ☐ More than 25 chips or more than 2 cups

109b. How often were the potato chips you ate **fat-free**? *(Please do not include reduced-fat chips.)*

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

110. How often did you eat **corn chips or tortilla chips** (including low-fat, fat-free, or low-salt)?

- ☐ NEVER (GO TO QUESTION 111)
- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

110a. Each time you ate **corn chips**, how much did you usually eat?

- ☐ Fewer than 10 chips or less than 1 cup
- ☐ 10 to 25 chips or 1 to 1½ cups
- ☐ More than 25 chips or more than 1½ cups

110b. How often were the corn chips or tortilla chips you ate **fat-free**? *(Please do not include reduced-fat chips.)*

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

111. How often did you eat **popcorn** (including low-fat)?

- ☐ NEVER (GO TO QUESTION 112)
- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

Question 112 appears in the next column

111a. Each time you ate **popcorn**, how much did you usually eat?

- ☐ Less than 2 cups, popped
- ☐ 2 to 5 cups, popped
- ☐ More than 5 cups, popped

112. How often did you eat **pretzels**?

- ☐ NEVER (GO TO QUESTION 113)
- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

112a. Each time you ate **pretzels**, how many did you usually eat?

- ☐ Fewer than 5 average twists
- ☐ 5 to 20 average twists
- ☐ More than 20 average twists

113. How often did you eat **peanuts, walnuts, seeds,** or **other nuts**?

- ☐ NEVER (GO TO QUESTION 114)
- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

113a. Each time you ate **peanuts, walnuts, seeds,** or **other nuts**, how much did you usually eat?

- ☐ Less than ¼ cup
- ☐ ¼ to ½ cup
- ☐ More than ½ cup

114. How often did you eat **energy, high-protein**, or **breakfast bars** (such as Power Bars, Balance, Clif, or others)?

- ☐ NEVER (GO TO QUESTION 115)
- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

114a. Each time you ate **energy, high-protein**, or **breakfast bars**, how much did you usually eat?

- ☐ Less than 1 bar
- ☐ 1 bar
- ☐ More than 1 bar

Question 115 appears on the next page

Over the <u>past month</u>…

115. How often did you eat **yogurt** (NOT including frozen yogurt)?

☐ NEVER (GO TO QUESTION 116)

☐ 1 time in past month
☐ 2–3 times in past month
☐ 1 time per week
☐ 2 times per week
☐ 3–4 times per week
☐ 5–6 times per week
☐ 1 time per day
☐ 2 or more times per day

115a. Each time you ate **yogurt**, how much did you usually eat?

☐ Less than ½ cup or less than 1 container
☐ ½ to 1 cup or 1 container
☐ More than 1 cup or more than 1 container

115b. How often was the **yogurt** you ate **low-fat** or **fat-free**?

☐ Almost never or never
☐ About ¼ of the time
☐ About ½ of the time
☐ About ¾ of the time
☐ Almost always or always

116. How often did you eat **cottage cheese** (including low-fat)?

☐ NEVER (GO TO QUESTION 117)

☐ 1 time in past month
☐ 2–3 times in past month
☐ 1 time per week
☐ 2 times per week
☐ 3–4 times per week
☐ 5–6 times per week
☐ 1 time per day
☐ 2 or more times per day

116a. Each time you ate **cottage cheese**, how much did you usually eat?

☐ Less than ¼ cup
☐ ¼ to 1 cup
☐ More than 1 cup

117. How often did you eat **cheese** (including low-fat; including on cheeseburgers or in sandwiches or subs)?

☐ NEVER (GO TO QUESTION 118)

☐ 1 time in past month
☐ 2–3 times in past month
☐ 1 time per week
☐ 2 times per week
☐ 3–4 times per week
☐ 5–6 times per week
☐ 1 time per day
☐ 2 or more times per day

Question 118 appears in the next column

117a. Each time you ate **cheese**, how much did you usually eat?

☐ Less than ½ ounce or less than 1 slice
☐ ½ to 1½ ounces or 1 slice
☐ More than 1½ ounces or more than 1 slice

117b. How often was the cheese you ate **low-fat or fat-free**?

☐ Almost never or never
☐ About ¼ of the time
☐ About ½ of the time
☐ About ¾ of the time
☐ Almost always or always

118. How often did you eat **frozen yogurt, sorbet,** or **ices** (including low-fat or fat-free)?

☐ NEVER (GO TO QUESTION 119)

☐ 1 time in past month
☐ 2–3 times in past month
☐ 1 time per week
☐ 2 times per week
☐ 3–4 times per week
☐ 5–6 times per week
☐ 1 time per day
☐ 2 or more times per day

118a. Each time you ate **frozen yogurt, sorbet,** or **ices**, how much did you usually eat?

☐ Less than ½ cup or less than 1 scoop
☐ ½ to 1 cup or 1 to 2 scoops
☐ More than 1 cup or more than 2 scoops

119. How often did you eat **ice cream, ice cream bars,** or **sherbet** (including low-fat or fat-free)?

☐ NEVER (GO TO QUESTION 120)

☐ 1 time in past month
☐ 2–3 times in past month
☐ 1 time per week
☐ 2 times per week
☐ 3–4 times per week
☐ 5–6 times per week
☐ 1 time per day
☐ 2 or more times per day

119a. Each time you ate **ice cream, ice cream bars,** or **sherbet**, how much did you usually eat?

☐ Less than ½ cup or less than 1 scoop
☐ ½ to 1½ cups or 1 to 2 scoops
☐ More than 1½ cups or more than 2 scoops

119b. How often was the ice cream you ate **light, low-fat,** or **fat-free ice cream** or **sherbet**?

☐ Almost never or never
☐ About ¼ of the time
☐ About ½ of the time
☐ About ¾ of the time
☐ Almost always or always

Question 120 appears on the next page

Over the <u>past month</u>…

120. How often did you eat **cake** (including low-fat or fat-free)?

- ☐ NEVER (GO TO QUESTION 121)
- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

120a. Each time you ate **cake**, how much did you usually eat?

- ☐ Less than 1 medium piece
- ☐ 1 medium piece
- ☐ More than 1 medium piece

121. How often did you eat **cookies** or **brownies** (including low-fat or fat-free)?

- ☐ NEVER (GO TO QUESTION 122)
- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

121a. Each time you ate **cookies** or **brownies**, how much did you usually eat?

- ☐ Less than 2 cookies or 1 small brownie
- ☐ 2 to 4 cookies or 1 medium brownie
- ☐ More than 4 cookies or 1 large brownie

122. How often did you eat **doughnuts**, **sweet rolls**, **Danish**, or **pop-tarts**?

- ☐ NEVER (GO TO QUESTION 123)
- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

122a. Each time you ate **doughnuts, sweet rolls, Danish,** or **pop-tarts**, how much did you usually eat?

- ☐ Less than 1 piece
- ☐ 1 to 2 pieces
- ☐ More than 2 pieces

Question 123 appears in the next column

123. How often did you eat **sweet muffins** or **dessert breads** (including low-fat or fat-free)?

- ☐ NEVER (GO TO QUESTION 124)
- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

123a. Each time you ate **sweet muffins or dessert breads**, how much did you usually eat?

- ☐ Less than 1 medium piece
- ☐ 1 medium piece
- ☐ More than 1 medium piece

124. How often did you eat **fruit crisp, cobbler,** or **strudel**?

- ☐ NEVER (GO TO QUESTION 125)
- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

124a. Each time you ate **fruit crisp, cobbler,** or **strudel,** how much did you usually eat?

- ☐ Less than ½ cup
- ☐ ½ to 1 cup
- ☐ More than 1 cup

125. How often did you eat **pie**?

- ☐ NEVER (GO TO QUESTION 126)
- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

125a. Each time you ate **pie**, how much did you usually eat?

- ☐ Less than ⅛ of a pie
- ☐ About ⅛ of a pie
- ☐ More than ⅛ of a pie

Question 126 appears on the next page

Over the <u>past month</u>…

The next four questions ask about the kinds of pie you ate. Please read all four questions before answering.

125b. How often were the pies you ate **fruit pie** (such as apple, blueberry, others)?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

125c. How often were the pies you ate **cream, pudding, custard,** or **meringue pie**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

125d. How often were the pies you ate **pumpkin** or **sweet potato pie**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

125e. How often were the pies you ate **pecan pie**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

126. How often did you eat **chocolate candy**?

- ☐ NEVER (GO TO QUESTION 127)

- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

126a. Each time you ate **chocolate candy**, how much did you usually eat?

- ☐ Less than 1 average bar or less than 1 ounce
- ☐ 1 average bar or 1 to 2 ounces
- ☐ More than 1 average bar or more than 2 ounces

Question 127 appears in the next column

127. How often did you eat **other candy**?

- ☐ NEVER (GO TO QUESTION 128)

- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

127a. Each time you ate **other candy**, how much did you usually eat?

- ☐ Fewer than 2 pieces
- ☐ 2 to 9 pieces
- ☐ More than 9 pieces

128. How often did you eat **eggs, egg whites,** or **egg substitutes** (NOT counting eggs in baked goods and desserts)? *(Please include eggs in salads, quiche, and soufflés.)*

- ☐ NEVER (GO TO QUESTION 129)

- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

128a. Each time you ate **eggs**, how many did you usually eat?

- ☐ 1 egg
- ☐ 2 eggs
- ☐ 3 or more eggs

128b. How often were the eggs you ate **egg substitutes** or **egg whites only**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

128c. How often were the eggs you ate **regular whole eggs**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

128d. How often were the eggs you ate **cooked in oil, butter,** or **margarine**?

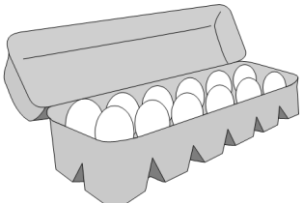
- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

Question 129 appears on the next page

Over the <u>past month</u>…

128e. How often were the eggs you ate part of **egg salad**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always



129. How many cups of **coffee**, caffeinated or decaffeinated, did you drink (including coffee drinks such as Latte, Mocha, Frappuccino, etc.)?

- ☐ NONE (GO TO QUESTION 130)
- ☐ Less than 1 cup in past month
- ☐ 1–3 cups in past month
- ☐ 1 cup per week
- ☐ 2–4 cups per week
- ☐ 5–6 cups per week
- ☐ 1 cup per day
- ☐ 2–3 cups per day
- ☐ 4–5 cups per day
- ☐ 6 or more cups per day

129a. How often was the coffee you drank **decaffeinated**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

130. How many glasses, cans, or bottles of **COLD** or **ICED tea,** caffeinated or decaffeinated, did you drink?

- ☐ NONE (GO TO QUESTION 131)
- ☐ Less than 1 glass, can or bottle in past month
- ☐ 1–3 glasses, cans or bottles in past month
- ☐ 1 glass, can or bottle per week
- ☐ 2–4 glasses, cans or bottles per week
- ☐ 5–6 glasses, cans or bottles per week
- ☐ 1 glass, can or bottle per day
- ☐ 2–3 glasses, cans or bottles per day
- ☐ 4–5 glasses, cans or bottles per day
- ☐ 6 or more glasses, cans or bottles per day

Question 131 appears in the next column

130a. How often was the cold or iced tea you drank **decaffeinated** or **herbal**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

130b. How often was the cold or iced tea you drank **presweetened with either sugar or artificial sweeteners** (such as Splenda, Equal, Sweet'N Low or others)?

- ☐ Almost never or never (GO TO QUESTION 131)
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

130c. What kind of **sweetener** was added to your presweetened cold or iced tea most of the time?

- ☐ Sugar or honey
- ☐ Artificial sweeteners (such as Splenda, Equal, Sweet 'N Low or others)

131. How many cups of **HOT tea**, caffeinated or decaffeinated, did you drink?

- ☐ NONE (GO TO QUESTION 132)
- ☐ Less than 1 cup in past month
- ☐ 1–3 cups in past month
- ☐ 1 cup per week
- ☐ 2–4 cups per week
- ☐ 5–6 cups per week
- ☐ 1 cup per day
- ☐ 2–3 cups per day
- ☐ 4–5 cups per day
- ☐ 6 or more cups per day

131a. How often was the hot tea you drank **decaffeinated** or **herbal**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

Question 132 appears on the next page

Over the past month…

132. Over the past month, did you add **sugar, honey or other sweeteners** to your tea or coffee (hot or iced)?

- ☐ NO (GO TO QUESTION 133)
- ☐ YES

132a. How often did you add **sugar** or **honey** to your coffee or tea (hot or iced)?

- ☐ Almost never or never (GO TO QUESTION 132c)
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

132b. Each time **sugar** or **honey** was added to your coffee or tea, how much was usually added?

- ☐ Less than 1 teaspoon
- ☐ 1 to 3 teaspoons
- ☐ More than 3 teaspoons

132c. How often did you add **artificial sweetener** (such as Splenda, Equal, Sweet'N Low or others) to your coffee or tea?

- ☐ Almost never or never (GO TO QUESTION 133)
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

132d. What kind of **artificial sweetener** did you usually use?

- ☐ Equal or aspartame
- ☐ Sweet'N Low or saccharin
- ☐ Splenda or sucralose
- ☐ Herbal extracts or other kind

132e. Each time **artificial sweetener** was added to your coffee or tea, how much was usually added?

- ☐ Less than 1 packet or less than 1 teaspoon
- ☐ 1 packet or 1 teaspoon
- ☐ More than 1 packet or more than 1 teaspoon

Question 133 appears in the next column

133. Over the past month, did you add **whiteners** (such as cream, milk, or non-dairy creamer) to your tea or coffee?

- ☐ NO (GO TO QUESTION 134)
- ☐ YES

133a. How often was **non-dairy creamer** added to your coffee or tea?

- ☐ Almost never or never (GO TO QUESTION 133d)
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

133b. Each time **non-dairy creamer** was added to your coffee or tea, how much was usually used?

- ☐ Less than 1 teaspoon
- ☐ 1 to 3 teaspoons
- ☐ More than 3 teaspoons

133c. What kind of **non-dairy creamer** did you usually use?

- ☐ Regular powdered
- ☐ Low-fat or fat-free powdered
- ☐ Regular liquid
- ☐ Low-fat or fat-free liquid

133d. How often was **cream** or **half and half** added to your coffee or tea?

- ☐ Almost never or never (GO TO QUESTION 133f)
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

133e. Each time **cream** or **half and half** was added to your coffee or tea, how much was usually added?

- ☐ Less than 1 tablespoon
- ☐ 1 to 2 tablespoons
- ☐ More than 2 tablespoons

133f. How often was **milk** added to your coffee or tea?

- ☐ Almost never or never (GO TO QUESTION 134)
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

Question 134 appears on the next page

Over the past month…

133g. Each time **milk** was added to your coffee or tea, how much was usually added?

- ☐ Less than 1 tablespoon
- ☐ 1 to 3 tablespoons
- ☐ More than 3 tablespoons

133h. What kind of **milk** was usually added to your coffee or tea?

- ☐ Whole milk
- ☐ 2% milk
- ☐ 1% milk
- ☐ Skim, nonfat, or ½% milk
- ☐ Evaporated or condensed (canned) milk
- ☐ Soy milk
- ☐ Rice milk
- ☐ Other

134. How often was **sugar** or **honey** added to foods you ate? *(Please do not include sugar in coffee, tea, other beverages, or baked goods.)*

- ☐ NEVER (GO TO INTRODUCTION TO QUESTION 135)

- ☐ 1 time in past month
- ☐ 2–3 times in past month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

134a. Each time **sugar** or **honey** was added to foods you ate, how much was usually added?

- ☐ Less than 1 teaspoon
- ☐ 1 to 3 teaspoons
- ☐ More than 3 teaspoons

The following questions are about the kinds of margarine, mayonnaise, sour cream, cream cheese, and salad dressing that you ate. If possible, please check the labels of these foods to help you answer.

135. Over the past month, did you eat **margarine**?

- ☐ NO (GO TO QUESTION 136)
- ☐ YES

135a. How often was the margarine you ate **light**, **low-fat**, or **fat-free** (stick or tub)?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

Question 136 appears in the next column

136. Over the past month, did you eat **butter**?

- ☐ NO (GO TO QUESTION 137)
- ☐ YES

136a. How often was the butter you ate **light** or **low-fat**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

137. Over the past month, did you eat **mayonnaise** or **mayonnaise-type dressing**?

- ☐ NO (GO TO QUESTION 138)
- ☐ YES

137a. How often was the mayonnaise you ate **light, low-fat or fat-free**?

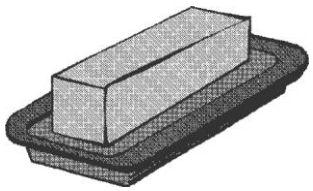
- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

138. Over the past month, did you eat **sour cream**?

- ☐ NO (GO TO QUESTION 139)
- ☐ YES

138a. How often was the sour cream you ate **light, low-fat,** or **fat-free**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always



Question 139 appears on the next page

Over the past month…

139. Over the past month, did you eat **cream cheese**?

- ☐ NO (GO TO QUESTION 140)
- ☐ YES

139a. How often was the cream cheese you ate **light, low-fat,** or **fat-free**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

140. Over the past month, did you eat **salad dressing**?

- ☐ NO (GO TO INTRODUCTION TO QUESTION 141)
- ☐ YES

140a. How often was the salad dressing you ate **light,** low-**fat** or **fat-free**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

The following two questions ask you to summarize your usual intake of vegetables and fruits. Please do not include salads, potatoes, or juices.

141. Over the past month, how many servings of **vegetables** (not including salad or potatoes) did you eat per week or per day?

- ☐ Less than 1 per week
- ☐ 1–2 per week
- ☐ 3–4 per week
- ☐ 5–6 per week
- ☐ 1 per day
- ☐ 2 per day
- ☐ 3 per day
- ☐ 4 per day
- ☐ 5 or more per day

142. Over the past month, how many servings of **fruit** (not including juices) did you eat per week or per day?

- ☐ Less than 1 per week
- ☐ 1–2 per week
- ☐ 3–4 per week
- ☐ 5–6 per week
- ☐ 1 per day
- ☐ 2 per day
- ☐ 3 per day
- ☐ 4 per day
- ☐ 5 or more per day

143. Over the past month, which of the following foods did you eat **AT LEAST THREE TIMES?** ***(Mark all that apply.)***

- ☐ Avocado, guacamole
- ☐ Cheesecake
- ☐ Chocolate, fudge, or butterscotch toppings or syrups
- ☐ Chow mein noodles
- ☐ Croissants
- ☐ Dried apricots
- ☐ Egg rolls
- ☐ Granola bars
- ☐ Hot peppers
- ☐ Jell-O, gelatin
- ☐ Mangoes
- ☐ Milkshakes or ice-cream sodas
- ☐ Olives
- ☐ Oysters
- ☐ Pickles or pickled vegetables or fruit
- ☐ Plantains
- ☐ Pork neck bones, hock, head, feet
- ☐ Pudding or custard
- ☐ Veal, venison, lamb
- ☐ Whipped cream, regular
- ☐ Whipped cream, substitute
- ☐ NONE

144. For **ALL** of the past month, have you followed any type of **vegetarian diet**?

- ☐ NO (GO TO INTRODUCTION TO QUESTION 145)
- ☐ YES

144a. Which of the following foods did you **TOTALLY EXCLUDE** from your diet? ***(Mark all that apply.)***

- ☐ Meat (beef, pork, lamb, etc.)
- ☐ Poultry (chicken, turkey, duck)
- ☐ Fish and seafood
- ☐ Eggs
- ☐ Dairy products (milk, cheese, etc.)

Introduction to Question 145 appears on the next page

The next questions are about your use of vitamin pills or other supplements.

145. Over the past month, did you take any **multivitamins**, such as One-a-Day-, Theragran-, Centrum-, or Prenatal-type multivitamins (as pills, liquids, or packets)?

☐ NO (GO TO INTRODUCTION TO QUESTION 147)

☐ YES

146. How often did you take **One-a-day-, Theragran-, Centrum- or Prenatal-type** multivitamins?

☐ 1–3 days in past month
☐ 1–3 days per week
☐ 4–6 days per week
☐ Every day

146a. Did your **multivitamin** usually contain **minerals** (such as iron, zinc, etc.)?

☐ NO
☐ YES
☐ Don't know

146b. Over the past month, did you take any **vitamins**, **minerals**, or **other herbal supplements** other than your multivitamin?

☐ NO

Thank you *very much* for completing this questionnaire! Because we want to be able to use all the information you have provided, we would greatly appreciate it if you would please take a moment to review each page making sure that you:

- **Did not skip any pages and**
- **Crossed out the incorrect answer and circled the correct answer if you made any changes.**

☐ YES (GO TO INTRODUCTION TO QUESTION 147

Introduction to Question 147 appears in the next column

These last questions are about the vitamins, minerals, or herbal supplements you took that are NOT part of a One-a-day-, Theragran-, or Centrum-type of multivitamin.

Over the past month…

147. How often did you take **Antacids such as Tums or Rolaids**?

☐ NEVER (GO TO QUESTION 148)

☐ 1–3 days per month
☐ 1–3 days per week
☐ 4–6 days per week
☐ Every day

147a. When you took **Antacids such as Tums or Rolaids**, about how many tablets or lozenges did you take in one day?

☐ Less than 1
☐ 1
☐ 2
☐ 3
☐ 4 or more
☐ Don't know

147b. Was your antacid usually "extra strength"?

☐ NO
☐ YES
☐ Don't know

148. How often did you take **Calcium** (with or without Vitamin D) (**NOT** as part of a multivitamin in Question 146 or antacid in Question 147)?

☐ NEVER (GO TO QUESTION 149)

☐ 1–3 days per month
☐ 1–3 days per week
☐ 4–6 days per week
☐ Every day

148a. When you took **Calcium** , about how much elemental calcium did you take in one day? *(If possible, please check the label for elemental calcium.)*

☐ Less than 500 mg
☐ 500–599 mg
☐ 600–999 mg
☐ 1,000 mg or more
☐ Don't know

148b. Did your **Calcium** usually contain **Vitamin D**?

☐ NO
☐ YES
☐ Don't know

Question 149 appears on the next page

Over the past month…

148c. Did your **Calcium** usually contain **Magnesium**?

- ☐ NO
- ☐ YES
- ☐ Don't know

148d. Did your **Calcium** usually contain **Zinc**?

- ☐ NO
- ☐ YES
- ☐ Don't know

149. How often did you take **Iron** (**NOT** as part of a multivitamin in Question 146)?

- ☐ NEVER
- ☐ 1–3 days per month
- ☐ 1–3 days per week
- ☐ 4–6 days per week
- ☐ Every day

150. How often did you take **Vitamin C** (**NOT** as part of a multivitamin in Question 146)?

- ☐ NEVER (GO TO QUESTION 151)
- ☐ 1–3 days per month
- ☐ 1–3 days per week
- ☐ 4–6 days per week
- ☐ Every day

150a. When you took **Vitamin C**, about how much did you take in one day?

- ☐ Less than 500 mg
- ☐ 500–999 mg
- ☐ 1,000–1,499 mg
- ☐ 1,500–1,999 mg
- ☐ 2,000 mg or more
- ☐ Don't know

151. How often did you take **Vitamin E** (**NOT** as part of a multivitamin in Question 146)?

- ☐ NEVER (GO TO INTRODUCTION TO QUESTION 152)
- ☐ 1–3 days per month
- ☐ 1–3 days per week
- ☐ 4–6 days per week
- ☐ Every day

Introduction to Question 152 appears in the next column

151a. When you took **Vitamin E**, about how much did you take in one day?

- ☐ Less than 400 IU
- ☐ 400–799 IU
- ☐ 800–999 IU
- ☐ 1,000 IU or more
- ☐ Don't know

The last two questions ask you about other supplements you took more than once per week.

152. Please mark any of the following **single supplements** you took more than once per week (**NOT** as part of a multivitamin in Question 147):

- ☐ B-6
- ☐ B-complex
- ☐ B-12
- ☐ Beta-carotene
- ☐ Folic acid/folate
- ☐ Magnesium
- ☐ Occu-vite/Eye health
- ☐ Potassium
- ☐ Selenium
- ☐ Vitamin A
- ☐ Vitamin D
- ☐ Zinc

153. Please mark any of the following **herbal, botanical, or other supplements** you took more than once per week.

- ☐ Chondroitin
- ☐ Coenzyme Q-10
- ☐ Echinacea
- ☐ Energy supplements
- ☐ Fish oil/omega 3's
- ☐ Flaxseed/oil
- ☐ Garlic
- ☐ Ginger
- ☐ Ginkgo biloba
- ☐ Ginseng
- ☐ Glucosamine/ chondroitin
- ☐ Peppermint
- ☐ Probiotics
- ☐ Saw palmetto
- ☐ Soy supplement
- ☐ Sports supplements
- ☐ St. John's wort
- ☐ Other

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