



---

All Theses and Dissertations

---

2010-08-02

# Effects of Duration of Proton Pump Inhibitor (PPI) Therapy on Markers of Bone Health in Men and Postmenopausal Women

Zarina Maria Pabin

*Brigham Young University - Provo*

Follow this and additional works at: <https://scholarsarchive.byu.edu/etd>



Part of the [Food Science Commons](#), and the [Nutrition Commons](#)

---

## BYU ScholarsArchive Citation

Pabin, Zarina Maria, "Effects of Duration of Proton Pump Inhibitor (PPI) Therapy on Markers of Bone Health in Men and Postmenopausal Women" (2010). *All Theses and Dissertations*. 2580.

<https://scholarsarchive.byu.edu/etd/2580>

This Thesis is brought to you for free and open access by BYU ScholarsArchive. It has been accepted for inclusion in All Theses and Dissertations by an authorized administrator of BYU ScholarsArchive. For more information, please contact [scholarsarchive@byu.edu](mailto:scholarsarchive@byu.edu), [ellen\\_amatangelo@byu.edu](mailto:ellen_amatangelo@byu.edu).

Effects of Duration of Proton Pump Inhibitor (PPI)

Therapy on Markers of Bone Health in

Men and Post-Menopausal Women

Zarina M. Pabin

A thesis submitted to the faculty of  
Brigham Young University  
in partial fulfillment of the requirements for the degree of

Master of Science

Robert T. Davidson, Chair  
Rickelle Richards  
N. Paul Johnston

Department of Nutrition, Dietetics, and Food Science

Brigham Young University

December 2010

Copyright © 2010 Zarina M. Pabin

All Right Reserved

## ABSTRACT

### Effects of Duration of Proton Pump Inhibitor (PPI) Therapy on Markers of Bone Health in Men and Post-Menopausal Women

Zarina M. Pabin

Department of Nutrition, Dietetics, and Food Science

Master of Science

This observational study compared bone health biomarkers, bone mineral density (BMD), dietary habits, and physical activity levels of men (n=31) and non-estrogen supplementing post-menopausal women (n=23) divided according to duration of proton pump inhibitor (PPI) therapy; more than 5 years (n=16), less than 5 years (n=15), and no PPI therapy (n=23). The shortest duration of PPI therapy was 2 months and the longest duration of PPI therapy was 25 years with a mean duration of 7.5 years. No significant differences were found between measures of spine BMD, urinary deoxypyridinoline (bone resorption), urinary calcium and magnesium, serum osteocalcin (bone formation), serum parathyroid hormone, serum magnesium, serum 25 hydroxyvitamin D<sub>3</sub>, dietary and supplement intake, or physical activity levels. However, mean hip BMD was higher in females than in males in participants who took PPI therapy for any duration. In the no PPI therapy group, hip BMD was not significantly different between genders. These results suggest that there may be no measurable or clinically significant negative effects of long term PPI therapy on bone health. However, men may be at higher risk of hip fracture when taking long-term PPI therapy than women.

Keywords: Proton pump inhibitor, PPI, bone, fracture

## ACKNOWLEDGEMENTS

Thank you to Dr. Davidson for believing in me and allowing me to own this project. Thank you to Dr. Susan Fullmer for her wisdom in writing and teaching. Thank you to Brian Newell for keeping me on my toes with his healthy curiosity and reliability as a research assistant. Thank you to Dr. Kay Franz for sharing her brilliance and being an outstanding example of professionalism. Thank you to Melanie Peine for her example of personal strength and perseverance as well as help in organizing all the necessary paperwork to keep me on track. Thank you to my other committee members, Dr. Richards and Dr. Johnston, for their support and advice on this project. A special thank you to everyone who has touched my life during my time at Brigham Young University. Go Cougars!

## TABLE OF CONTENTS

TITLE PAGE.....	i
ACKNOWLEDGEMENTS.....	ii
ABSTRACT.....	iii
TABLE OF CONTENTS.....	iv
CHAPTER 1 - INTRODUCTION	
STATEMENT OF THE PROBLEM.....	1
PURPOSE.....	2
OBJECTIVES AND HYPOTHESES.....	3
LIMITATIONS.....	5
DEFINITION OF TERMS.....	6
CHAPTER 2 – LITERATURE REVIEW	
OSTEOPOROSIS.....	8
BONE STRUCTURE.....	11
BONE MODELING/REMODELING.....	12
FACTORS AFFECTING BONE MINERAL DENSITY.....	14
MEASURING BONE MINERAL DENSITY.....	26

OSTEOCALCIN.....	26
PYRIDINIUM CROSSLINKS.....	27
GERD.....	27
HELICOBACTER PYLORI.....	31
HYPOCHLORHYDRIA AND ACHLORHYDRIA.....	32
CALCIUM ABSORPTION.....	34
MAGNESIUM ABSORPTION.....	35
IMPORTANT CONSIDERATIONS FOR FUTURE STUDIES.....	36
LIMITATIONS OF PREVIOUS RESEARCH.....	37
SUMMARY.....	37
CHAPTER 3 – MATERIALS AND METHODS.....	38
CHAPTER 4 – RESULTS AND DISCUSSION.....	44
CONCLUSION.....	50
REFERENCES.....	51
APPENDIX A – PRE-STUDY FORMS AND DOCUMENTS.....	59
PROSPECTUS.....	60
IRB APPROVAL LETTER.....	64
RECRUITING FLIER.....	65

SCREENING QUESTIONS.....	66
APPENDIX B – STUDY FORMS AND DOCUMENTS.....	67
CONSENT FORM.....	68
PARTICIPANT STUDY INSTRUCTIONS.....	71
DIET HISTORY QUESTIONNAIRE.....	73
SUPPLEMENTARY PHYSICAL ACTIVITY QUESTIONS.....	109
APPENDIX C – RAW DATA.....	110
EXPLANATION OF RAW DATA.....	111
RAW DATA TABLES.....	116

## CHAPTER 1

### INTRODUCTION

#### STATEMENT OF THE PROBLEM

Gastroesophageal reflux disease (GERD), more commonly known as heartburn, refers to symptoms and damage to the lining of the esophagus due to reflux of acidic gastric contents most often due to inappropriate relaxation of the lower esophageal sphincter (1,2). It has been estimated that the worldwide prevalence of GERD has doubled in the past thirty years with population based studies indicating up to 25% of adults experiencing heartburn at least once monthly and 5% of adults experiencing heartburn daily (1,2). Both men and women appear to be equally affected by GERD with some studies showing a higher prevalence in women than men (3,4).

Alongside lifestyle modifications to manage GERD, most patients require the use of medications to control symptoms (5). The most commonly prescribed medications are histamine-2 (H2) blockers [Tagamet® (cimetidine), Zantac® (ranitidine), Pepcid® (famotidine), Axid®(nizatidine)] and proton pump inhibitors (PPI) [Prevacid® (lansoprazole), Prilosec® (omeprazole), Protonix® (pantoprazole), Aciphex® (rabeprazole), Nexium® (esomeprazole)]. The goal of these medications is to reduce symptoms of GERD through decreasing hydrochloric acid production in the stomach (5). In 2002, the sales of PPI's reached more than \$10 billion, second only to the sales of statins and in 2004, Nexium® became the third highest selling prescription drug in the United States (6,7).

Three of four recently published large case-control studies have reported an independent correlation between long-term PPI use and risk of hip or spine fracture, with one study showing



PPI's only associated with a limited increase in fracture risk (8-11). The mechanism of this association is proposed as being chronically decreased calcium absorption because of acid suppression and consequential hyperparathyroidism, such that individuals who are meeting the recommendations for dietary calcium intake may not be absorbing enough calcium to maintain bone mass (12). A recently published literature review has indicated that calcium carbonate (the most common form of supplemental calcium), appears to be more difficult to absorb in an environment with an elevated pH than other supplemental forms (13). Current recommendations suggest calcium citrate as the ideal calcium supplement, due to its increased solubility, for people with achlorhydria or those taking either H2 blockers or PPI's (14).

The prevalence, incidence, and cost of osteoporosis and associated fractures are increasing, particularly in women. Alongside the graying of the general population and the widespread use of PPI therapy in the aging population, determining the impact of long-term PPI therapy on bone health is a worthy research cause. Research in this area is likely to support the emerging practice of prescribing PPI therapy in the minimum effective dose to avoid long-term complications of GERD while not compromising bone health (2,5).

### Purpose

The purpose of this project was to determine if there was a significant difference between the spine and hip bone mineral density (BMD), calcium status, magnesium status, or markers of bone metabolism of men and post-menopausal women who have taken long-term proton pump inhibitor (PPI) therapy for more than 5 years and the same parameters of men and post-menopausal women who have taken PPI therapy for less than 5 years or who have never taken PPI therapy.

## Objectives and Hypotheses

Objective 1: To compare the spine and hip BMD of men and post-menopausal women who have taken PPI therapy for more than five years to the spine and hip BMD of men and post-menopausal women who have taken PPI therapy for less than five years or have never taken PPI therapy.

Null hypothesis: There is no difference between the spine or hip BMD of men and post-menopausal women who have taken PPI therapy for more than 5 years and the spine or hip BMD of men and post-menopausal women who have taken PPI therapy for less than 5 years or have never taken PPI therapy.

Alternative hypothesis: There is a difference between the spine or hip BMD of men and post-menopausal women who have taken PPI therapy for more than 5 years and the spine or hip BMD of men and post-menopausal women who have taken PPI therapy for less than 5 years or have never taken PPI therapy. PPI users have lower bone mass than non-PPI users.

Objective 2: To compare the biomarkers of calcium status, magnesium status, and bone metabolism of men and post-menopausal women who have taken PPI therapy for more than five years to the biomarkers of calcium status, magnesium status, and bone metabolism of men and post-menopausal women who have taken PPI therapy for less than five years or never taken PPI therapy.

Null hypothesis: There is no difference between the biomarkers of calcium status, magnesium status, or bone metabolism of men and post-menopausal women who have taken PPI therapy for more than five years and the biomarkers of calcium status, magnesium status, and bone metabolism of men and post-menopausal women who have taken PPI therapy for less than five years or never taken PPI therapy.

Alternative hypothesis: There is a difference between the biomarkers of calcium status, magnesium status, or bone metabolism of men and post-menopausal women who have taken PPI therapy for more than five years and the biomarkers of calcium status, magnesium status, and bone metabolism of men and post-menopausal women who have taken PPI therapy for less than five years or never taken PPI therapy. PPI users biomarker levels favor bone resorption over bone formation while non-PPI users favor neither bone resorption nor bone formation.

Objective 3: To compare the physical activity levels and dietary intakes of energy, carbohydrate, protein, fat, calcium, magnesium, and vitamin D of men and post-menopausal women who have taken PPI therapy for more than five years to the dietary intakes of energy, carbohydrate, protein, fat, calcium, magnesium, and vitamin D of men and post-menopausal women who have taken PPI therapy for less than five years or never taken PPI therapy.

Null hypothesis: There is no difference between the physical activity levels or dietary intakes of energy, carbohydrate, protein, fat, calcium, magnesium, or vitamin D of men and post-menopausal women who have taken PPI therapy for more than 5 years and the physical activity levels or dietary intakes of energy, carbohydrate, protein, fat, calcium, magnesium, or vitamin D of men and post-menopausal women who have taken PPI therapy for less than five years or never taken PPI therapy.

Alternative hypothesis: There is a difference between physical activity levels or the dietary intakes of energy, carbohydrate, protein, fat, calcium, magnesium, or vitamin D of men and post-menopausal women who have taken PPI therapy for more than 5 years and the physical activity levels or the dietary intakes of energy, carbohydrate, protein, fat, calcium, magnesium, or vitamin D of men and post-menopausal women who have taken PPI therapy for less than five years or never taken PPI therapy.

## Limitations

This study is purely observational. No statements of causal inferences can be made about participants in our study or the general population. Any limitations in methods are discussed in Chapter 3 – Materials and Methods.

## DEFINITION OF TERMS

**Bone mineral content (BMC):** the mineral (calcium, phosphorus, magnesium) content within an area of bone expressed in grams.

**Bone mineral density (BMD):** a measure of fracture risk calculated from the BMC (g) and the area of the bone ( $\text{cm}^2$ ) to yield an areal measure of BMD ( $\text{g}/\text{cm}^2$ ). Can be expressed as a volumetric BMD in  $\text{g}/\text{cm}^3$ .

**Hormone replacement therapy (HRT):** pharmacologic therapy used to prevent or treat osteoporosis with the intention of mimicking the effects of estrogen or modifying the process of bone remodeling to reduce bone loss.

**Interleukin-1, 6, 11:** peptides, released by activated monocytes and lymphocytes, that assist in the coordination of bone remodeling.

**Menarche:** the first menstrual period, usually occurring at puberty.

**Menopause:** the cessation of menses.

**Menses:** the first portion of the uterine cycle, the portion in which the endometrial lining sloughs away.

**Monocyte colony-stimulating factor (M-CSF):** a peptide that stimulates the production of monocytes.

**Osteocalcin (Bone Gla Protein):** a non-collagenous protein produced by osteoblasts commonly used as a measure of bone formation.

**Osteoprotegerin (OPG):** a receptor found on the surface of osteoblasts involved in the regulation of bone remodeling.

**Peak bone mass:** the maximal bone mass attained during childhood, adolescence, and young adulthood.

**Primary amenorrhea:** the absence of menstruation by the age of 16 in a girl who has secondary sex characteristics.

**Receptor for activation of nuclear factor kappa B (RANK):** a receptor found on the surface of osteoclasts that participates in the regulation of bone remodeling through binding of RANKL and OPG.

**Receptor for activation of nuclear factor kappa B ligand (RANK-L):** a receptor found on the surface of osteoblasts involved in the regulation of bone remodeling.

**Secondary amenorrhea:** the absence of the menstrual period for greater than 3 months after menarche.

## CHAPTER 2

### LITERATURE REVIEW

#### Osteoporosis

Osteoporosis is a disease characterized by low bone mass and deterioration of bone structure that causes bone fragility and increased risk of fracture (15). The terms primary, age-related, or post-menopausal osteoporosis (used interchangeably) refer to the cumulative bone loss that occurs with aging (15). Primary osteoporosis is the most common type of osteoporosis and is a considerable public health concern (15). Secondary osteoporosis refers to osteoporosis produced as a byproduct of another disease or condition and is less common (15). According to the National Health and Nutrition Examination Survey (NHANES III, 1988-1994), 56% (approximately 30.3 million) of women 50 years or older in the United States have low bone mass (formerly referred to as osteopenia) and 16% of these (approximately 4.8 million) have osteoporosis (16-18). While osteoporosis is not currently as considerable a public health concern for men as for women, according to the same survey, 18% (approximately 7.3 million) of men 50 years or older in the United States have low bone mass with 2% (approximately 150,000) having osteoporosis (16,17). By the year 2020, the number of women and men over the age of 50 with osteoporosis is expected to reach 10.5 million and 3.3 million, respectively, as a result of the expected growth and aging of the overall population (15).

General diet and lifestyle guidelines for the prevention and treatment of osteoporosis include obtaining adequate intakes of dietary calcium, phosphorus, and vitamin D, performing regular weight-bearing exercise, and avoiding tobacco products and alcohol abuse (19). Adherence to these behavioral guidelines is especially important between birth and young adulthood to ensure attainment of peak bone mass. Following the attainment of peak bone mass and with subsequent aging, bone mass slowly declines in both men and women at a rate of 1-

1.5% per year (15). Women, however, also experience an estrogen deficiency attributed rapid bone loss of ~2% annually beginning 2-3 years prior to the last menses and ending 3-5 years after menopause (20). Rate of bone loss then returns to the slow steady rate of 1-1.5% per year experienced prior to menopause (15,20). Men do not experience the same drastic effects on bone due to the hormonal changes of menopause, however, men reach the same fracture risk level as women but at an older age (21).

Irrespective of known strategies to prevent and treat osteoporosis, osteoporosis causes 1.5 million fractures in the United States alone, with the largest portion being vertebral (700,000), followed by hip (300,000), wrist (250,000), and fractures at other sites (300,000) (22). The health implications for those diagnosed with an osteoporotic fracture vary based on the site and severity of the fracture and include severe pain, decreased functional capacity, and increased risk of mortality within 1 year following the fracture (15,17). While most fractures occur in women, the consequences of fracture are more severe in men with some research showing men having almost twice the mortality from hip fractures as women (21,23).

## Costs

In 2002, estimated direct medical costs to the United States healthcare system for treatment of osteoporotic fractures, largely borne by society through Medicare, ranged from \$12.2-\$17.9 billion (15). These costs routinely include medications and in-patient and long-term nursing home care stays related to orthopedic surgery. Costs are expected to exceed \$60 billion by the year 2030 due to increased incidence of osteoporosis (22).

## Pharmacologic Treatment of Osteoporosis

Current drug treatments used to supplement dietary and lifestyle modifications in the prevention and treatment of osteoporosis in post-menopausal women include hormone



replacement therapy (HRT) (Prempro®) which mimics the protective effects of endogenous estrogen on bone, raloxifene (Evista®) which modifies the sensitivity of estrogen receptors on bone, bisphosphonates (Fosamax®, Boniva®, Actonel®) which act by inhibiting the activity of osteoclasts (bone resorption), and calcitonin, and teriparatide [a form of parathyroid hormone (PTH)], which both stimulate bone formation (19,20,23,24). All of these agents are effective at improving bone mineral density in post-menopausal women at clinically significant sites with no apparent adverse side effects aside from upper gastrointestinal disorders from bisphosphonate use (20). These upper gastrointestinal irritations sometimes results in concurrent prescribing of PPI's alongside bisphosphonates. The long-term safety of many of these bone building medications has not yet been fully researched and some recent population studies have associated the use of HRT with increased risk of heart attack and stroke (20,25). Also, although effective at increasing bone mineral density and decreasing fracture risk in both men and women, non-compliance to oral bisphosphonate therapy is common (23,26).

### Treatment of Fracture

Treatment for an osteoporotic fracture begins by stabilizing and repairing the fracture (27). Hip and wrist fractures are commonly repaired through hip replacement surgery or surgical repositioning and casting, respectively (15). For surgical treatment of vertebral fractures, two techniques used to repair vertebral fractures are vertebroplasty and kyphoplasty (15). Both techniques involve injecting bone cement into the body of the vertebrae in an attempt to reestablish structure and reduce pain (27). Both techniques also carry risk of the cement leaking into the blood stream and causing significant complications, including, but not limited, to pulmonary emboli (27). Aside from complications resulting from surgical repair of an osteoporotic fracture, additional resources are required following surgery to minimize pain, improve function and mobility, reduce fracture risk, motivate the patient to continue medication/exercise interventions, address psychosocial consequences of fracture, and monitor

bone health (27). Non-surgical treatment of fractures aimed at reducing the incidence of additional fractures and preserving current bone mass, include bracing, pharmacological pain control, and functional rehabilitation programs including fall prevention training and spinal biomechanics education (23,28).

### Bone Structure

Bones provide mobility, support, leverage, and protection for the body as well as serving as a reservoir for calcium and phosphorus and participating in acid-base balance (15,29,30). Nearly 70% of the weight of a bone is composed of strong but brittle hydroxyapatite crystals  $[Ca_{10}(PO_4)_6(OH)_2]$  which collectively are capable of withstanding large compressive forces but poorly tolerate bending, torsion, or other sudden impacts (30). The remaining ~30% of the weight of the bone is composed of flexible collagen fibers collectively capable of withstanding bending, torsion, and tensile forces (30). The microarchitectural arrangement of the bone matrix of strong hydroxyapatite crystals surrounding flexible collagen fibers gives bone its dynamic biomechanical properties, allowing the bearing of chronic compressive loads required by body weight with resiliency to high tensile forces typical of movement, both without structural failure (30).

There are two types of adult bone; 1) cortical or compact bone, found in the diaphyseal walls of long bones and on the surface of cuboid and flat bones and 2) trabecular or cancellous bone, found in the epiphyseal and metaphyseal ends of long bones and on the interior of cuboid and flat bones contain the same basic materials but are arranged in distinctly different ways (31,32). Cortical bone matrix contains numerous small, tightly packed cylindrical units called osteons, each composed of multiple concentric rings of bone matrix called lamellae (32). The hollow center of each osteon is called a Haversian canal and houses the blood and nerve supply (32). The spaces between the lamellae are called lacunae and these spaces house mature bone

cells called osteocytes (32). Tiny channels called canaliculi connect the Haversian canals to the lacunae, allowing nerve communication and exchange of materials between osteocytes and the blood (30). Cortical bone provides strength to withstand typical longitudinal compressive forces due to gravity (15).

Conversely, the matrix of trabecular bone is organized into a lattice-like structure with lacunae containing osteocytes nestled within the struts of the structure. The large spaces separating individual trabeculae allow for exchange of materials between the lacunae and the blood (32). The principal function of trabecular bone is to act in a spring-like fashion to disperse mechanical loads thus allowing adaptation to dynamic or unusual loads in addition to compressive loads without structural damage (33). Trabecular bone is also the major site of age-related changes to bone mass due to increased surface area available for resorption (19,29,33). This decreases the thickness and number of trabeculae, significantly compromising the structural integrity of bone and leading to increased risk of fracture (33).

### Bone Modeling/Remodeling

Normal growth and maintenance of bone is achieved through the coordinated actions of the two primary bone cell types; osteoblasts (bone formation) and osteoclasts (bone resorption) (34). Osteoblasts and osteoclasts form organized units called basic multicellular units (BMUs) or bone remodeling units (BRUs) that participate in the processes of bone modeling and remodeling (15,34). Modeling refers to bone formation and resorption in different sites within the same bone, such as occurs during growth (15). Remodeling refers to the process of bone formation and resorption at the same site within a bone and is the dominant process following the attainment of peak bone mass after age 25-30 years with complete replacement of the skeleton occurring approximately every 10 years (15).

The four major bone cell types include osteoblasts, osteocytes, lining cells, and

osteoclasts. Osteoblasts form bone by secretion of collagen matrix (31). Osteocytes, mature osteoblasts buried within the matrix, are the most numerous cell in bone and function to maintain the bone matrix via their long branches which connect them to other osteocytes as well as bone lining cells (30,35). Lining cells, are flat cells derived from osteoblasts that cover the periosteum and rapidly release calcium from the bone in response to low blood calcium, protect bone from bone dissolving chemicals in the blood, and contain receptors for hormones and other factors that control bone turnover (36). Osteoclasts, derived from monocytes, secrete acids and enzymes that dissolve bone matrix as part of routine bone turnover (30,35,37).

While some remodeling may be targeted to repair specific microdamaged sites, a large portion of remodeling likely occurs randomly (29). The process of remodeling consists of four distinct phases termed activation, resorption, reversal, and formation (29). Activation refers to recruitment of osteoclastic precursors from circulation that permeate the bone lining cell layer and merge together forming preosteoclasts (29). Next, the preosteoclasts form a “bone-resorbing compartment” by binding to the bone matrix on the surface of trabeculae and on the endosteal and intracortical surfaces of cortical bone (15,29,38). The resorption phase begins with pumping of protons into the “bone-resorbing compartment” by specific proton pumps within the osteoclast membrane, lowering the pH to ~4.0 (29). Theoretically, proton pump inhibitor (PPI) therapy may be beneficial to bone health by decreasing bone resorption through inhibiting the action of these proton pumps, the vacuolar type H<sup>+</sup>-ATPases, responsible for maintaining the acidic environment on the ruffled border of the osteoclasts (8). While some research supports this theory, closer examination is needed to demonstrate its validity (39-43). Next, numerous enzymes that are most active at a low pH are secreted from osteoclast lysosomes that digest the bone matrix within the “bone-resorbing compartment” (29). Following osteoclast apoptosis, the reversal phase begins with recruitment of preosteoblasts into the resorption cavity (29). The signaling mechanism by which this occurs is not clear although various theories have emerged including the secretion of chemoattractant growth factors by osteoclasts that attract osteoblastic

precursors and strain-regulated activation of osteoblasts (29). The formation phase involves the synthesis and mineralization of collagen matrix by osteoblasts (29). Eventually, as bone formation continues, osteoblasts become buried within the matrix as osteocytes (29).

Under normal conditions, remodeling results in maintenance of the adult skeleton by replacing damaged and old bone tissue with new tissue through the coupling of bone resorption and bone formation (44). Both androgens and estrogens have been shown to positively influence bone remodeling by increasing the lifespan of osteoblasts and decreasing the lifespan of osteoclasts (45). Loss of androgens or estrogens increases the rate of bone resorption without an appropriate compensatory increase in bone formation, resulting in net bone loss (45). In estrogen deficiency, deeper resorption sites on the surface of trabeculae and on the endosteal and intracortical surfaces of cortical bone occur without equivalent bone formation to refill the site of resorption leading most notably to a reduction in trabecular number and thickness, compromising bone structure and strength (15,29,38). While this bone loss can be postponed through the use of hormone replacement therapy (HRT), results from the Women's Health Initiative study have warned of potential adverse health effects of long-term HRT leading many women to opt out of hormonal treatment (25). Normal healthy men do not experience a comparable rapid loss of androgens, however, bone loss still occurs at a steady rate, putting them at risk of fractures later in life (21).

### Factors Affecting Bone Mineral Density (BMD)

#### Peak bone mass

Skeletal mass increases longitudinally from birth to adulthood with a particularly rapid rate of growth during adolescence (29). The precise ages of the attainment of peak bone mass at various body sites have yet to be determined but popular scientific opinion generally supports peak bone mass being reached by age 30 (29). Decline in bone mass begins as early as age 30

and continues as age advances with an increased rate experienced by women at menopause (29). Thus, maximizing peak bone mass during growth and young adulthood through known osteogenic strategies including adequate intakes of calcium, phosphorus, and vitamin D, and participation in regular physical activity is essential to withstand the gradual loss of bone that occurs with aging.

Suboptimal attainment of peak bone mass may be associated with a premature increase in bone fragility and increased risk for fractures later in life (29). Young female athletes are at an especially high risk of failure to attain peak bone mass due to the prevalence of both primary and secondary amenorrhea in this population (46). Androgen deficiency during adolescence can also lead to poor attainment of peak bone mass in males (45). During puberty, men develop longer and larger bones, and adult men typically have greater bone mineral density than women (45).

## Hormones

While estrogens and androgens exert marked beneficial effects on bone remodeling, superseding this influence are multiple other hormonal mechanisms including those of systemic hormones such as PTH, calcitonin, 1,25-dihydroxyvitamin D<sub>3</sub> (1,25(OH)<sub>2</sub>D<sub>3</sub> - calcitriol), and local factors such as Receptor for Activation of Nuclear factor Kappa B Ligand (RANKL), and various monocyte derivatives including interleukins (IL), colony stimulating factors (CSF), and prostaglandins (PG) (29,36).

Parathyroid Hormone. Especially important is the release of PTH from the parathyroid glands in response to low blood calcium (47). PTH release results in increased blood calcium by increasing calcium reabsorption in the kidney, increasing bone resorption, and indirectly increasing absorption of dietary calcium in the intestine through increased production of 1,25(OH)<sub>2</sub>D<sub>3</sub> (47). PTH increases bone resorption by binding to osteoblast membrane receptors

and causing a decrease in the expression of osteoprotegerin (OPG) on the surface of the osteoblast, an increase in expression of RANKL on the surface of the osteoblast, and increased production of IL-6 (a potent stimulator of bone resorption) by the osteoblast (47). Binding of RANKL, found anchored to the surface of osteoblasts or in a free form, to its receptor, RANK, on the surface of osteoclastic precursors causes an increase in differentiation of osteoclasts which increases mobilization of calcium from bone (37,47). Without the influence of PTH, binding of OPG from osteoblasts to RANK on osteoclast precursors inhibits the differentiation of osteoclasts and inhibits bone resorption (47).

Calcitonin. Released from the C-cells of the thyroid gland in response to high blood calcium, calcitonin, favors bone mineralization through inhibition of osteoclasts (36,47). Thyroid hormones, however, favor bone resorption through stimulation of osteoclasts. Thus defects in parathyroid and/or thyroid metabolism can significantly alter the process of bone remodeling.

Vitamin D. Aside from its role in increasing intestinal absorption of calcium, 1,25(OH)<sub>2</sub>D<sub>3</sub> also promotes differentiation of osteoblast and osteoclast precursors through favoring expression of RANKL on the surface of osteoblasts (as opposed to OPG) (37). This process is also proposed to be mediated through increased production of IL-6, similar to the effects of PTH (36,37). However, recent studies showing inhibition of bone resorption by administration of 1,25(OH)<sub>2</sub>D<sub>3</sub> to OPG knockout mice (simulating the increased bone resorption occurring during osteoporosis), challenge this long-standing theory (48). In these studies, 1,25(OH)<sub>2</sub>D<sub>3</sub> appears to inhibit bone resorption through effects on osteoclast differentiation via interference with the RANKL/RANK pathway (48). 1,25(OH)<sub>2</sub>D<sub>3</sub> has also been shown to increase the production of monocyte-CSF (M-CSF) which is the only cytokine aside from RANKL that is required for the differentiation of osteoclasts from their monocyte lineage (36,37). Therefore, 1,25(OH)<sub>2</sub>D<sub>3</sub> may have variable effects on bone remodeling dependent on the presence or absence of excess

osteoclastic activity (48). Regardless, the presence of vitamin D receptors (VDR) on the surface of osteoblasts, leads many to assume a role of vitamin D beyond increasing calcium absorption (49). Also being explored more recently are the roles of numerous genetic VDR variations which have been found to be associated with differences in fracture risk due to phenotypic effects on adult height, bone size, and BMD (50-52).

Currently, serum 25(OH)2D3 concentrations are measured to assess the adequacy of dietary vitamin D (53). Serum levels of 25(OH)2D3 below 27.5 nmol/L are considered to indicate vitamin D deficiency (54). Serum levels of 25(OH)2D3 decline with age even with dietary supplementation (55). Vitamin D deficiency is associated with increased incidence of hip fractures, most likely due to impaired calcium absorption and other effects at the cellular level as mentioned above (55).

Local Factors. Many local factors also influence bone remodeling by manipulation of the expression of RANKL and OPG. IL-11 and prostaglandin E2 (PGE2) increase the expression of RANKL on the surface of osteoblasts, thus increasing the number of active osteoclasts and promoting bone resorption (37). IL-1 can also stimulate osteoclastogenesis directly or indirectly through increasing IL-6, M-CSF and IL-11 (37). Both tumor necrosis factor alpha (TNF- $\alpha$ ) and transforming growth factor beta (TGF- $\beta$ ) initiate osteoclast formation independently of the RANKL pathway, likely through increased production of IL-6 by osteoblasts (37).

Other Hormones. Growth hormone/IGF-1 (Insulin-like growth factor) and cortisol also affect bone remodeling; growth hormone/IGF-1 favoring bone formation through enhancing osteoblast function and cortisol, favoring bone resorption, by promoting osteoblast apoptosis, increasing osteoclast activity, and decreasing intestinal calcium absorption (36,37). In addition to IGF-1, bone morphogenic proteins (BMP) released from osteoblasts stimulate further synthesis of



osteoblasts as do various fibroblast growth factors (FGF) (37). Glucocorticoids can also inhibit the synthesis of IL-1, IL-6, and prostaglandins, all of which enhance bone resorption (37). In fact, glucocorticoid induced osteoporosis (GIO) is the most common form of medication induced secondary osteoporosis (15). While not typically categorized as a hormone, vitamin A can directly oppose the action of vitamin D via stimulation of osteoclastogenesis via the shared retinoic acid receptor (RXR) nuclear binding site (36).

Estrogens. The influence of estrogens on attainment of peak bone mass and maintenance of bone mass is substantial. Men develop longer and larger bones in adolescence than women likely due to the absence of the stimulating effect of estrogen on epiphyseal closure and its inhibitory effect on periosteal apposition (45). While detailed mechanisms are not complete, estrogen receptors have been found to be present on osteoblasts, osteocytes, lining cells, osteoblastic precursor cells, osteoclastic precursor cells, and multiple other cells and factors associated with bone metabolism (37). Estrogen, specifically the  $17\beta$ -estradiol form, exerts an overall protective effect on bone via multiple potential mechanisms. Estrogen inhibits the synthesis of osteoclastic precursors [through decreasing monocyte colony-stimulating factor (M-CSF), increasing the ratio of OPG to RANKL on the surface of osteoblasts, and decreasing the expression of the IL-1 receptors on osteoclasts and osteoclastic precursors], inhibits the synthesis of osteoclasts (by decreasing IL-6 concentrations), induces osteoclast apoptosis, and may also enhance osteoblast survival (20,36,37,47). Estrogen also influences extraskelatal processes related to calcium homeostasis such as intestinal calcium absorption, serum concentrations of  $1,25(\text{OH})_2\text{D}_3$ , renal calcium reabsorption, and the secretion of PTH (37).

Mounting in vivo research suggests multiple other protective functions of estrogen on bone including promoting the proliferation and viability of osteoblasts through control of osteoblast apoptosis, promoting the production and mineralization of bone matrix through regulation of the expression of proteins such as alkaline phosphatase, osteocalcin, and type I

collagen, promoting growth factor/cytokine expression and responsiveness which are required for the normal coupling of osteoclastic action with osteoblastic action, regulating factors affecting bone resorption including a possible suppression of PTH action in addition to decreasing IL-6 (as mentioned above), and enhancing osteoblast receptor expression and signal transduction, promoting bone formation (37). Interestingly, several in vivo studies also suggest that estrogens may regulate the process of mechanosensory stimulation or that mechanical strain and estrogen action share common signaling pathways (37).

The protective effects of estrogen on bone are also evidenced by human studies that show substantial increases in BMD when exercise programs are combined with HRT or from HRT alone and the successful use of HRT to treat osteoporosis (24,56,57). In addition, detrimental effects on bone have been observed following discontinuance of HRT in post-menopausal women, reporting BMD declines between 2.3% and 6.2% in the first year (58). Tremollieres et al (59) reported a transient acceleration of bone loss at the spine in women discontinuing HRT similar to that experienced in untreated women in the first 2 years following menopause.

Androgens. Research supports the independent benefit of androgens on bone health in both men and women with effects of deficiency more pronounced in men (37). It has been estimated that 30-50 percent of elderly men are deficient in sex steroids due to an increase in sex hormone binding globulin (SHBG) which binds both androgens and estrogens rendering them inactive (15). Case control studies also report a higher than normal prevalence of hypogonadism in men with spine or hip fracture (45). Further demonstrating the influence of androgens on bone health in females, animal research has shown osteopenia in intact female rats with blockage of androgen receptors (37).

Androgen deficiency induces bone loss in men similar to that found in women with estrogen deficiency, especially at trabecular bone sites (45). Androgens exert their effects on bone via androgen receptors or indirectly via estrogen receptors following conversion to

estrogens (45). Androgen receptors have been found in osteoblasts, osteocytes, and in mononuclear cells and endothelial cells of blood vessels within bone marrow (60). Like estrogens, androgens have been shown to promote bone maintenance through decreasing osteoblast and osteocyte apoptosis, increasing TGF- $\beta$  and IGF-1 (factors involved with bone formation), and decreasing IL-6 production (a factor involved with bone resorption)(37,45). Whether androgens increase OPG (a factor involved in bone formation) as estrogens has yet to be determined (45). The most dramatic impact of androgens in males is their effect during growth on bone size, particularly increasing cortical thickness, via their stimulatory effect on periosteal apposition (37). The effects of androgens during other life stages has not been as well studied as that of estrogens (37).

#### Dietary Calcium Intake

It is essential that abundant calcium be available for hormonal control of bone remodeling to occur normally. Since plasma calcium is tightly controlled, adequate dietary calcium intake is necessary to minimize bone resorption stimulated by low plasma calcium. While the recommended AI (adequate intake) of calcium for men and women aged 51-70 years is 1200 mg/day, evidence from NHANES (1971-2000) suggests that while dietary calcium intake from food sources in this age group has increased over the last 3 decades, intakes by women are currently only ~50% of these recommendations and intakes by men are only ~65% (61,62). Although calcium supplementation (including calcium containing antacids, multivitamins, and calcium alone) is prevalent in older men and women, most epidemiologic surveys include questions about the mere presence of current or past dietary supplementation, providing little data as to the consistency of the intake of dietary supplements (63,64). Therefore, supplemental calcium may only contribute minimally if at all to total dietary calcium intake in this population

unless strict adherence is observed, such as occurs during research. Further, the estimated dietary intake of calcium is so low that supplemental calcium, even if taken on a regular basis, may not bring total intake up to the AI.

### Dietary Vitamin D Intake

Under the stimulation of PTH, vitamin D acts to maintain normal plasma calcium levels by increasing calcium absorption from dietary sources, which becomes increasingly important as age advances (65). The current AI for vitamin D for men and women aged 51-70 years is 400 IU/day (10 µg) (61). According to NHANES 1999-2000, the intake of vitamin D from both food and supplemental sources in persons aged 51 and over is ~95% of the recommended value (66). However, this intake data does vary by race and circulating vitamin D can also be compromised by the absence of adequate sun exposure (66). Also, recent controversy regarding the need to increase vitamin D recommendations to 1000 IU/day (25 µg) to maintain circulating vitamin D at levels associated with health benefits may render these intakes inadequate in the coming years. The effects of variations in VDR's also supports the theory that individual requirements for vitamin D may vary (50-52).

### Dietary Phosphorus Intake

Dietary phosphorus deficiency occurs very rarely due to the abundance of phosphorus containing foods in the diet with half of the needed intake coming from all types of animal products (65). Efficient intestinal absorption and renal conservation of phosphorus also protect very well against deficiency (65). Hypophosphatemia and phosphorus deficiency are rarely seen among healthy non-hospitalized people (67). However, depletion of phosphorus can occur from megadoses of aluminum hydroxide containing antacids, which bind dietary phosphorus in the gut, preventing its absorption (65).

## Dietary Magnesium Intake

While magnesium has not been shown to have as definitive a role in bone health as other nutrients, most of the magnesium in the human body is found in bones alongside calcium and phosphorus (15). Adequate dietary magnesium appears to enhance bone quality through improving bone density (15). A dietary deficiency of magnesium can lead to hypocalcemia through interference with PTH secretion (54). Under normal circumstances, magnesium acts similarly to calcium in inhibiting PTH secretion and conversely, its absence, increases PTH which stimulates bone resorption (68). Magnesium deficiency is also associated with reduced synthesis of 1,25(OH)<sub>2</sub>D<sub>3</sub> in humans (68). Studies done in rats with intakes ranging from no magnesium to levels set to reflect the dietary deficiency of Americans, have shown bone loss, decrease in osteoblasts, and increases in osteoclasts as well as low levels of PTH and 1,25(OH)<sub>2</sub>D<sub>3</sub>, decreased levels of OPG, and increased levels of RANKL, all factors favoring bone resorption (68).

Both men and women in the United States consume less than the recommended level of magnesium with median intakes of 220 mg/day for women and 320 mg/day for men with recommended intakes being 320 mg/day for women, and 420 mg/day for men (54). Numerous epidemiological studies conducted with subjects of all ages, mostly cross sectional, have linked dietary magnesium deficiency with osteoporosis (68,69). However, few studies have examined the magnesium status of people with osteoporosis and the results of these studies are not consistent (70-75). Also, epidemiological studies are somewhat limited as they identify population trends and are often difficult to apply to individuals.

## Physical activity

Intermittent mechanical stresses on bone provided by physical activity in childhood and adolescence are essential for the proper development of bone structure and optimization of peak bone mass (31). Based on epidemiological evidence correlating physical activity with overall better health, both public and private health organizations recommend that moderate physical activity continue throughout the life cycle. Weight bearing exercise is proposed to provide the greatest site-specific osteogenic effects according to Wolff's law of biomechanics stating that bone tissue will adapt its structure to the mechanical demands placed upon it (34). Although less commonly than appendicular sites such as the wrist and hip, this principle has been suggested to apply equally to the lumbar spine (76). Marked decreases in bone density during periods of immobility or in zero gravity situations such as space travel also support Wolff's law (77). Common aerobic activities such as walking, running, jumping, and aerobics are well known to place an osteogenic load at the hips in post-menopausal women, but their effects on lumbar spine BMD are inconsistent (78,79). Also, any exercise that strengthens postural muscles and/or increases flexibility can improve balance and thus lower the risk of falls which can lead to fractures (80).

While multiple socioeconomic and psychological factors influence individual physical activity level, general functional ability and overall physical activity levels tend to decrease over time. A reduced physical activity level supports decline in bone mass and density due to the absence of mechanical loads or strains to stimulate bone formation. With most evidence suggesting that low physical activity levels persist among older adults in the United States, identification of exercises that can modify measurable health outcomes such as bone density may provide motivation for increases in physical activity in these high risk populations (81,82).

Sometimes overlooked among the most potent factors in the pathogenesis of osteoporotic fracture including low bone density and poor bone quality, is the propensity to fall which can be remedied by regular balance training (19,83). Strengthening of the core muscles of the lower

back and abdomen to prevent falls has been suggested as an important step in fracture prevention in older adults (83). While little research exists showing a definitive reduction in the occurrence of fracture due to balance training, the enhanced sense of control and increases in postural balance are likely protective against falls (84-86). Interestingly, recent animal research provides evidence that exercise may be able to effectively reduce fracture risk by inducing favorable changes in bone geometry without dramatic effects on bone mass (80).

### Smoking and Alcohol Consumption

Both tobacco smoking and alcohol consumption are associated with increased risk for fracture at all sites in both men and postmenopausal women (15,87-90). Smoking has been shown to be detrimental to bone health in a variety of ways including direct toxic effects on bone cells, impairing calcium absorption, and interfering with the normal metabolism of vitamin D and other hormones important for bone health including estrogen (15). Current smoking places a person at higher risk of bone fracture than does former smoking (15). One recent study found that women who smoked were more likely to have a particular gene mutation that negatively affects bone health (87).

Alcohol abuse has well established negative effects on bone health (15). Alcohol inhibits bone remodeling through interfering with the effect of vitamin D and may also increase calcium and magnesium loss (15). While some studies suggest moderate alcohol intake increases bone density (particularly in women), it does not seem to lower overall fracture risk (15). Excessive alcohol consumption increases the risk of fracture most likely due to the increased risk of falling (15).

## Genetics

Multiple hereditary factors greatly influence peak bone mass and quality of bone structure which collectively form the largest determinants of the timing of fracture risk (29,33). In fact, it has been indicated that between 50-90% of peak bone density is attributable to genetic factors (15). Additionally, women with a family history of osteoporosis in first degree relatives tend to have lower bone density than women with no family history of osteoporosis (20). Both low body weight/size and weight loss have also been associated with reductions in overall BMD in post-menopausal women due to the reduced loads (15,31).

## Gender and Race

Asian and white women in the United States have been found to be at higher risk for osteoporosis due to lower BMD than other racial or ethnic groups (15). While men experience the same gradual decline in bone mass as women, they do not experience the accelerated bone loss accompanying menopause and generally attain higher peak bone mass due to longer and larger bones (45). This higher bone mass has been argued to be an artifact of the areal bone mineral density measure given by dual x-ray absorptiometry (DXA) and may not translate to a higher bone strength (45).



## Measuring BMD

Currently, the gold standard for assessment of BMD is dual x-ray absorptiometry (DXA). DXA detects bone mineral content (BMC), expressed in grams (g), and the area of the bone, expressed in square centimeters (cm<sup>2</sup>) by measuring the attenuation of x-rays passed through various body sites (91,92). A two-dimensional BMD value, expressed in (g/cm<sup>2</sup>) is calculated based on these measures (92). Since DXA cannot detect the depth of the bone being measured, the BMD value obtained represents an “areal” density in units of g/cm<sup>2</sup> rather than a true volumetric density in units of g/cm<sup>3</sup> (91). A BMD score is interpreted by either the number of standard deviations from the mean of age-matched controls (Z-score), or the number of standard deviations from the young normal mean (T-score) (93). The World Health Organization (WHO) reference standards for diagnosis of osteoporosis and low bone mass for women are T-scores of -2.5 or less and between -1.0 and -2.5, respectively, and are derived from the NHANES III femur bone density data for 20-29 year old white, females (18,93). A T-score -2.5 or less with an accompanying fracture is classified as severe osteoporosis (92). For assessing the BMD of postmenopausal women, the preferred method is the T-score (18). The validity of applying these standards to men is questionable, however, it is the commonly used method of diagnosing osteoporosis in men (23).

## Osteocalcin (Bone Gla protein)

Osteocalcin is a vitamin K dependent, noncollagenous protein secreted almost exclusively by osteoblasts that is incorporated into normal bone matrix (53,94). Approximately thirty percent of the total osteocalcin produced by osteoblasts is released into the blood where it is measured as an indicator of bone turnover (53). Serum osteocalcin is the most commonly marker of bone formation during pharmacological treatment of patients with osteoporosis but its release during bone resorption has not been ruled out (53,94).

## Pyridinium Crosslinks

Deoxypyridinoline (DPX) is a crosslinked protein found in type 1 collagen that makes up nearly 90% of the bone matrix providing tensile strength to the bone (53). DPX is released into the bloodstream and excreted in the urine in response to bone resorption (53). By measuring at least one measure of bone formation, osteocalcin, and at least one measure of bone resorption, DPX, it is possible to draw strong conclusions about overall bone turnover (95).

## Gastroesophageal Reflux Disease (GERD)

Gastroesophageal reflux disease (GERD), more commonly known as heartburn, refers to symptoms and damage to the lining of the esophagus due to reflux of acidic gastric contents into the esophagus most often due to inappropriate relaxation of the lower esophageal sphincter (LES) (1,2). It has been estimated that the worldwide prevalence of GERD has doubled in the past thirty years, with population-based studies indicating up to 25% of adults experiencing heartburn at least once per month and 5% of adults experiencing heartburn daily (1,2). Both men and women appear to be equally affected by GERD with some studies showing a higher prevalence in women than men (3,4,96).

Alongside lifestyle modifications to manage GERD, most patients require the use of medications to control symptoms (5). The most commonly prescribed medications are histamine-2 (H2) blockers [Tagamet® (cimetidine), Zantac® (ranitidine), Pepcid® (famotidine), Axid®(nizatidine)] and proton pump inhibitors (PPI) [Prevacid® (lansoprazole), Prilosec® (omeprazole), Protonix® (pantoprazole), Aciphex® (rabeprazole), Nexium® (esomeprazole)]. The goal of these medications is to reduce symptoms of GERD through decreasing hydrochloric acid production in the stomach (5). In 2002, the sales of PPI's reached more than \$10 billion,

second only to the sales of statins and in 2004, Nexium® became the third highest selling prescription drug in the United States (6,7).

In 2002, the annual direct cost for diagnosing and managing GERD in the United States was estimated at \$9.3 billion, more than any other digestive disease (97). Long-term effects of uncontrolled GERD include esophageal strictures and/or ulcers, Barrett's esophagus (benign changes in esophageal mucosal cells), and esophageal adenocarcinoma (2).

### Risk Factors for GERD

Risk factors associated with GERD include being overweight or obese, consumption of alcohol, smoking, family history of upper gastrointestinal symptoms, diet, and lifestyle (3).

While often recommended as a reasonable treatment for GERD as well as other health benefits, it remains unclear whether weight loss in people who are overweight or obese will decrease symptoms of GERD (3,99). The relationship between obesity and GERD may be due to the increased incidence of hiatal hernia in this population and to other mechanical and physiological factors predisposing obese people to GERD (99). Alcohol and cigarette smoking both increase the risk of GERD through exacerbation of already existing problems with LES pressure (3). Tobacco smoking may increase the frequency of GERD events through the stimulatory effects of nicotine (3). Alcohol has been shown to reduce the strength of peristalsis waves in the esophagus, impair the clearance of acid contents from the stomach, and reduce saliva output in normal subjects, all which would increase the likelihood of GERD events in persons with GERD (3).

## Treatment of GERD

Lifestyle modifications are the first line of treatment for GERD. The American College of Gastroenterology recommends elevating the head of the bed (HOB), decreased fat, chocolate, alcohol, peppermint, and coffee intake, smoking cessation, and avoiding laying down for 3 hours following a meal (100). While there is physiologic evidence suggesting that these modifications will improve symptoms of GERD and some have been associated with improvements in GERD in case-control studies, most patients require further treatment with H<sub>2</sub> receptor antagonists (H<sub>2</sub>RA) or proton pump inhibitors (PPI) (100-102). H<sub>2</sub>RA are generally used for initial therapy or temporary management of GERD, while the majority of PPI use is for long-term management of GERD that remains uncontrolled with H<sub>2</sub>RA therapy (5).

## Gastric Acid Production and Secretion

Parietal cells produce and secrete hydrochloric acid (HCl) into the stomach. This process is tightly regulated by neural, hormonal, paracrine, and intracellular pathways to adjust the pH of the stomach to the needs of the body to maintain normal digestive and absorptive properties (98). Lower than normal acid production can interfere with the absorption of iron, calcium, and vitamin B<sub>12</sub>, and is associated with gastrointestinal infections, bacterial overgrowth, and gastric cancer (98). Excess acid production can cause ulcerations of the esophagus, stomach, and proximal small intestine (98).

Secretion of gastric acid begins with the sight, taste, smell, or thought of food stimulating mucous cells, chief cells, parietal cells, and G cells to produce mucous, digestive enzymes, HCl, and gastrin respectively (30). Gastrin released into the bloodstream stimulates acid secretion primarily by stimulating enterochromaffin-like (ECL) cells to release histamine as well as direct stimulation of parietal cells (98). Histamine binds to histamine H<sub>2</sub> receptors on surrounding parietal cells that are coupled to generation of cAMP and the resulting acid secretion (98).

Acetylcholine also directly stimulates parietal cells and plays a role in suppression of somatostatin, the primary inhibitor of ECL and parietal cells (98). Other inhibitors include cholecystokinin (CCK), atrial natriuretic peptide (ANP), both of which exert their effects through increasing somatostatin, and nitric oxide (98).

Increased concentrations of calcium or cAMP inside the parietal cell triggers the translocation of the inactive H<sup>+</sup>K<sup>+</sup> -ATPase proton pump from cytoplasmic tubulovesicles to the apical plasma membrane where it is activated and becomes subject to the action of PPI's (98). A proton is pumped out of the parietal cells into the canaliculus in exchange for a potassium ion (98). An apical chloride channel pumps the needed chloride ion out to combine with the hydrogen ions to produce HCl (98). An apical potassium channel provides the means for maintaining a potassium gradient to drive the H<sup>+</sup>K<sup>+</sup> -ATPase (98).

### H2 Receptor Antagonists

H2RA's block the receptors for histamine that stimulate gastric acid production (12). However, as described above, there are more potent stimulators of gastric acid secretion making H2RA therapy less effective than PPI therapy which suppresses the final step in gastric secretion at the level of the H<sup>+</sup>K<sup>+</sup> -ATPase pump (12). Of the few studies that have examined chronic H2RA therapy and BMD, the results are inconsistent and suggest that taking the less potent H2RA's may be detrimental to bone health but requires a longer duration of therapy than the more potent PPI's to show decreases in BMD or increases in fracture (10,103,104).

### Proton Pump Inhibitors

PPI's inhibit gastric acid secretion by targeting the H<sup>+</sup>K<sup>+</sup> ATPase pump of the parietal cell (105). PPI's are weak bases that accumulate in compartments with a pH less than 4 (105).

These include the resorption lacunae of osteoclasts and the canaliculus of a stimulated parietal cell (105). In these spaces, PPI's are converted to tetracyclic sulfenamides which form stable disulfide bonds with cysteines on the surface of the H<sup>+</sup>K<sup>+</sup> ATPase pump and reduce its activity (98,105). The potential anti-resorptive effect of these drugs at the level of the osteoclast was discussed previously.

Most PPI's are only available by prescription, with the exception of Prilosec (omeprazole) which became available over the counter in 2002 as Prilosec OTC (12). Typical doses of PPI's range from 10-40 mg daily. Despite emerging evidence about the possible detrimental effect of PPI's on BMD, no warnings about chronic use are contained in the patient educational information available on the website for the American College of Gastroenterology.

### Surgery

Surgical management of GERD is performed in only 10-20% of all GERD patients and is only resorted to when there is failure or patient refusal pharmacological therapy (5,106). Anti-reflux surgery to decrease the size of the opening between the stomach and esophagus (laparoscopic Nissen fundoplication) and other similar procedures are successful at relieving the major symptoms of GERD but can also bring on new and persistent symptoms that require other pharmacologic treatment (5,106). Also, due to transitional nature of the area of the esophagus, there is a typical need for repeat surgery within 5 years (106).

### Helicobacter Pylori

Helicobacter pylori (H. pylori) is a bacteria that infects the gastric mucosa and causes prolonged and often chronic gastroduodenal inflammation that can alter both the structure and function of the stomach and proximal duodenum leading to gastric or duodenal cancer, ulcers, and atrophic gastritis (107). Atrophic gastritis can lead to malabsorption of iron, and other

divalent cations such as calcium, and magnesium, as well as vitamin B12 via decreased acid and intrinsic factor secretion (107).

Depending on where the infection is located within the stomach, the acid secretion can be either suppressed or elevated. Most patients with *H. pylori* infection present with general inflammation of the stomach and show suppressed acid secretion due to atrophy of the parietal cells, antibodies to *H. pylori* and products secreted by *H. pylori* that directly interfere with the H<sup>+</sup>,K<sup>+</sup> -ATPase pumps, and other products secreted by *H. pylori* that indirectly inhibit acid secretion by affecting gene expression of anti-secretory cytokines and other proteins (98). Patients with an infection located in the antrum or lower region of the stomach show elevated levels of acid secretion due to hypergastrinemia. These patients are at highest risk of developing duodenal ulcers or gastroesophageal reflux disease (98).

While infections of *H. pylori* are much less common in the United States than in the last 50 years, treatment is aimed at reducing gastric acidity since *H. pylori* thrives in an acidic environment (107). The most common treatments include prolonged PPI therapy in combination with antibiotics (107). Due to the seriousness of the cancerous conditions that are likely if *H. pylori* is left untreated, patients with *H. pylori* are likely to be compliant to long term PPI therapy.

### Hypochlorhydria and Achlorhydria

The most common cause of achlorhydria in the older population is progressive atrophic gastritis which can occur as a result of *H. pylori* infection, autoimmune conditions such as pernicious anemia, or more commonly non-autoimmune or environmental factors (108). While hypochlorhydria and achlorhydria are typical in the older population and have been theorized to significantly impact nutrient absorption by affecting both the basal and maximal acid outputs, the only vitamin with clinically significant malabsorption is vitamin B12 due to the impaired

secretion of intrinsic factor by the atrophied gastric cells (55,109).

Hypochlorhydria has been shown to result in weaker bones in animal studies attributed to different rates of calcium absorption (110). Mixed results have been obtained on the effects of hypochlorhydria on calcium absorption in humans with most studies showing some level of decrease in calcium absorption with acid suppression therapy (111-115). One study showed no difference in calcium absorption from insoluble calcium carbonate or soluble calcium citrate with intragastric pH of 7 or 3 (116). These studies, however, were performed on a short term basis only and may not accurately reflect changes in calcium absorption from prolonged PPI therapy.

Most studies support that calcium carbonate is the most difficult form of calcium to absorb but is the most commonly available form of supplemental calcium. The general recommendation for a healthy population with normal gastric acid secretion is to take calcium supplements with food to improve percent absorption (110). This recommendation stems from the theory that since calcium salts need high amounts of acid for dissolution, and acid output is highest postprandially, that with meals is the best time to maximize absorption. Some authors suggest that in hypochlorhydric patients, this higher acid output may not occur and the acid that is present is simply used to digest the other food and does not increase dissolution of calcium salts (109). These authors suggest maximizing calcium absorption in these patients by supplementing small doses of the most soluble calcium salt available in combination with vitamin D given several times per day on an empty stomach with water or acid juice or perhaps as effervescent tablets (109). However, increasing doses of medicines or supplements has been associated with a decrease in compliance.



## Calcium Absorption

Calcium in foods and dietary supplements is present as part of fairly insoluble salts. Ionized calcium ( $\text{Ca}^{+2}$ ) must be released from these salts to be absorbed. The acidic pH within the stomach is responsible for solubilizing the ionized calcium within about 1 hour of ingestion. However, calcium and divalent cations, once solubilized from their dietary sources, tend to form complexes with other minerals or molecules within the more alkaline pH of the small intestine (54,117). The formation of these complexes and competition with other divalent cations for absorption leads to a relatively low percent absorption of calcium. Percent absorption of calcium is at or below 25% for most adults and is highest (as much as 60%) in periods of rapid growth such as infancy and the second and third trimesters of pregnancy (61). Both the percent calcium absorption as well as the compensatory increase in calcium absorption when faced with low calcium intake tend to decrease with age (55). It has also been estimated that calcium absorption declines by as much as 0.2% per year following age 40 with an additional 2.2% loss accompanying menopause in women (61,118). This decline in calcium absorption with age is directly related to the decrease in circulating  $1,25(\text{OH})_2\text{D}_3$  and a subsequent decline in intestinal vitamin D receptors (118,119). Circulating  $1,25(\text{OH})_2\text{D}_3$  levels decrease with age due to a decline in kidney function, decreased synthesis of vitamin D in the skin related to lower sun exposure, and a general decline in intestinal absorption of vitamin D (55,118).

Calcium is absorbed into the blood by active transport (transcellular pathway) and passive diffusion (paracellular pathway) (54,61). The predominant mechanism of absorption by active transport is regulated primarily by the circulating level of  $1,25(\text{OH})_2\text{D}_3$  and occurs mainly in the duodenum and proximal jejunum (54). This mechanism is predominant during times of low or moderate calcium intake (61). Most calcium absorption occurs in the ileum due to the relatively longer period of time calcium is present in this part of the intestine (54).

The mechanism by which  $1,25(\text{OH})_2\text{D}_3$  acts to increase calcium absorption begins with low blood calcium triggering the production of PTH which then stimulates the action of the renal

enzyme 25-hydroxyvitamin D 1 alpha-hydroxylase which results in production of the active 1,25(OH)<sub>2</sub>D<sub>3</sub> from the inactive 25-dihydroxyvitamin D<sub>3</sub> synthesized in the skin (54). This 1,25(OH)<sub>2</sub>D<sub>3</sub> acts to increase calcium absorption by binding to vitamin D receptors (VDR) in the cytoplasm of the enterocyte and translocating to the nucleus to increase the gene expression of the brush-border calcium channel TRPV6, the cytosolic mobile calcium buffer calbindin D, and the basolateral membrane Ca<sup>2+</sup> ATPase exporter pump (54,67). TRPV6 allows for increased influx of calcium from the lumen of the intestines (54). Calbindin D facilitates absorbed calcium for export into the blood by acting as a chaperone protein to increase substrate availability to the Ca<sup>2+</sup> ATPase exporter pump on the basolateral membrane (54).

The paracellular mechanism of passive diffusion that predominates with high calcium intakes allows the movement of calcium between mucosal cells depending on the concentration gradient between the luminal side of the enterocyte and the serosal side of the enterocyte and is not regulated by hormones (54,61). Some evidence suggests that another absorption process involving the transport of calcium through the enterocyte via endosomal and lysosomal vesicles and exit from the cell via exocytosis may exist (54). However, little is known about the contribution of this process to overall calcium absorption or how it is regulated (54).

### Magnesium Absorption

As with calcium, magnesium absorption occurs through two different pathways, a saturable active transcellular pathway and a nonsaturable paracellular passive transport pathway (54). The paracellular mechanism accounts for approximately 90% of intestinal magnesium absorption with the remaining absorption theorized to be through a magnesium-specific transport protein/channel that is not yet well defined (67). In healthy individuals, magnesium is absorbed along the entire gastrointestinal tract with an absorption percentage of 30% to 50% and absorption is inversely proportional to intake (54).

Unlike calcium absorption, the role of hormones in the regulation of magnesium absorption at the intestine is less clear and the regulation of magnesium homeostasis is largely dependent on the filtration and reabsorption of magnesium in the kidney tubules (54,67). Calcium and magnesium have similar absorption patterns with magnesium's active transport process seeming to be saturable at much lower concentrations than that of calcium. This is why the passive pathway is so much more dominant in magnesium absorption than it is in calcium absorption. While the mechanism remains unknown, vitamin D appears to enhance magnesium absorption (54).

Since magnesium exists in food in its elemental form, gastric acid is not required for solubilization as it is with calcium. While the absorption of magnesium salts from dietary supplements may be affected by decreased gastric acid secretion, supplements do not currently contribute significantly to the dietary intake of magnesium in the United States.

#### Important Considerations for Future Studies

While the primary reason for taking PPI's is to prevent symptoms of GERD, PPI's are also taken to prevent inflammation and ulcers associated with the use of nonsteroidal anti-inflammatory drugs (NSAIDS). This introduces another population who may be affected by chronic PPI therapy and could be studied without the confounding factors relating to the underlying condition of GERD (8). More attention should also be focused on examining the validity of the protective effect of PPI therapy on bone health through decreasing bone resorption by inhibiting the acidifying action of osteoclasts. While this mechanism may be unlikely, as proton pump inhibitors likely only affect cells within the stomach, it merits further investigation.

### Limitations of Previous Research

To our knowledge, only one other study has been published examining BMD in patients taking long term PPI therapy (120) and no studies have been published examining biochemical markers of bone turnover in patients on long term PPI therapy. Yu *et al* (120) concluded that long term PPI therapy in combination with low calcium intake was associated with a modest increase in hip fracture. Previous research associating PPI use with higher risk of bone fracture is limited to retrospective studies examining medical records (8-11).

### Summary

This purpose of this study was to determine the effect of long term PPI therapy on BMD and related bone biomarkers in men and post-menopausal women not on HRT who represent the population most affected by osteoporosis. The study was designed to more closely examine the biochemical effects of PPI therapy on biomarkers of bone health following the results of population studies showing an independent correlation between BMD, fracture risk, and duration of PPI therapy.

## CHAPTER 3

### MATERIALS AND METHODS

#### Research Design

This observational study compared bone health markers in men and post-menopausal women who had been taking PPI therapy for more than 5 years, less than 5 years, or never taken PPI therapy.

#### Subjects

Twenty-five women and 31 men (n=56) were recruited by posting fliers on BYU campus, in waiting areas at local medical offices, and by mailing fliers to BYU Alumni. Women qualified for the study if they were at least five years post-menopausal and had not been on HRT for at least five years. Additional exclusion criteria for both men and women included known osteoporosis, history of osteoporosis medications, current smoking, current excessive alcohol intake, large bone fracture within the last 10 years, and/or presence of diseases or use of medications that affect bone metabolism. Two female participants dropped out after the blood draw. Data from 54 participants (23 female, 31 male) were used in the final analysis. Of the 31 males in our study, 25 were PPI users and 6 were not. Of the females in our study, 6 were PPI users and 17 were not. Total PPI users = 31, total non-PPI users = 23. Participants were further divided into three groups based on duration of PPI therapy, no PPI therapy, PPI therapy of greater than or equal to 5 years, and PPI therapy of greater than 5 years (See Table 1). Of the non-PPI users 6 were males and 17 were females. In the greater than or equal to 5 years PPI therapy group, 12 were males and 3 were females. In the greater than 5 years PPI therapy group, 13 were male and 3 were female.

Table 1: Characteristics of groups divided according to gender and duration of PPI therapy

Gender	Duration of PPI Therapy		
	None	≤ 5 years	> 5 years
Male	6	12	13
Female	17	3	3
Total	23	15	16
Mean Age	62 years	63.4 years	63.2 years

### Food Frequency Questionnaire

The online version of the Diet History Questionnaire (DHQ) version 2007 was used to assess dietary habits and Diet Calc (1.4.3) was used to analyze the dietary intake data. Participants were allowed to perform this test either in paper and pencil format or the web-based format either away from the laboratory or within the laboratory depending on their preference. Supplemental questions were added to determine physical activity level. Food frequency questionnaires (FFQ) are widely used in population based research and the strength of these tools increases with the number of respondents. FFQ's are useful in identifying trends in dietary intake, however, their use in smaller studies is limited by the number of respondents and relies heavily on accurate recollection of study participants. Long-term dietary intake of bone health related nutrients is more relevant to our study than short-term dietary intake so the FFQ was chosen as the tool for assessing dietary intake.

## Physical Activity Level

Current and past levels of aerobic activity and resistance training were assessed using a questionnaire created by our research team. Participants were designated as “active” for *current* aerobic activity if they self-reported a minimum of 30 minutes per day at least 3 days per week of aerobic activity over the last 6 months. Participants were designated as “active” for *current* resistance training if they self-reported a minimum of 2 days per week of resistance training over the last 6 months. Participants were designated as “active” for *past* aerobic activity if they self-reported a consistent participation in aerobic activities for a minimum of 30 minutes per day at least 3 days per week over the last 20 years. Participants were designated as “active” for *past* resistance training if they self-reported a consistent participation in resistance training a minimum of 2 days per week over the last 20 years. Physical activity levels was designated as “inactive” for current aerobic activity, current resistance training, past aerobic activity, or past resistance training if participant self-reported any activity level less than described above.

## Anthropometric Data

### Height

Height was measured to the nearest 0.5 inch using a professional grade stadiometer, Model PE-WM-60-76-BRG2 (Perspective Enterprises, Portage, MI). Subjects were measured standing with head, shoulder blades, buttocks, gastrocnemius muscles, and calcaneus bones touching the wall and weight distributed evenly between both feet. Participants were measured without shoes.

## Weight

Weight was measured to the nearest 0.25 pound (lb) using an electronic scale (Tanita 310). Subjects were weighed wearing their underwear and one layer of clothing with no shoes.

## Waist-to-hip Ratio

Waist-to-hip ratio was measured to the nearest 0.25 inch using a tension controlled tape measure. All measures were performed by the same researcher.

## Body Composition and Bone Density

Body composition and bone density were assessed using DXA (Lunar, GE Prodigy). Body composition was measured using a total body scan. Bone density was measured at the lumbar spine (L1-L4) and the hips. Technician coefficient of variation for lumbar spine BMD and hip BMD was established using recommended protocol at 0.5% (92).

## Blood and Urine Samples

Serum samples were spun down and frozen to -20 degrees Fahrenheit immediately following the blood draw by BYU Student Health Center laboratory staff and transported and frozen to -80 degrees Fahrenheit within one week of collection by a member of our research staff. Urinary samples were processed according to standard protocol and frozen within one week of collection to -80 degrees Fahrenheit. Urine sample jugs were inverted three times and samples for freezing were obtained from the middle of the specimen.



## Osteocalcin and Deoxypyridinoline (DPX)

Serum osteocalcin and urinary DPX were measured using LabCorp standard protocol. Since osteocalcin levels peak at night and are lowest in the morning, serum samples were drawn between 8 and 11 AM for consistency. Urinary DPX samples were collected from the first morning voids, also between the hours of 8-11 AM.

## Other Laboratory Values

Serum parathyroid hormone, serum magnesium, serum 25(OH)2D3, serum osteocalcin, 24-hour urinary calcium, 24 hour urinary magnesium, and urinary DPX to creatinine ratio were all measured using LabCorp standard protocol using the samples described above.

## Statistical Analysis

Statistical comparisons were done using ANOVA to compare the three groups of less than 5 years PPI therapy, more than 5 years PPI therapy, and no PPI therapy to each other on measures of hip and spine BMC, hip and spine BMD, serum parathyroid hormone, serum magnesium, serum 25(OH)2D3, serum osteocalcin, 24-hour urinary calcium, 24 hour urinary magnesium, and serum DPX to urinary creatinine ratio. The decision to divide the groups at 5 years was made to be consistent with other research examining the effects of long-term PPI therapy. Since the groups contained both genders, differences between genders were investigated by utilizing an interaction between gender and duration to see if there was any difference in how the genders responded to the duration of PPI therapy.

Stepwise regression was performed on all covariates affecting any outcome variables to determine if any were significant. This was done to rule out the effects of any of the covariates on the outcome variables. Covariates considered were age, waist:hip ratio; use of thyroid medication; use of a multivitamin; BMI; output from body composition analysis including tissue,

fat, lean, and fat-free mass; body weight; current or past aerobic or resistance exercise; total dietary intake (including supplements) of phosphorus, sodium, potassium, vitamin A, vitamin C, calcium, magnesium, vitamin D, and caffeine; and presence of osteoporosis or osteopenia at hip or spine.

## CHAPTER 4

### RESULTS

Lean and fat free mass were both significant at a p-value of  $<0.0001$  for covariates affecting BMD which was expected. Diagnosis of osteoporosis or osteopenia was significant for urinary calcium and DPX:creatinine ratio which was also expected. No other covariates were found to be significant. ANOVA results showed no significant differences between groups of varying durations of PPI therapy on hip or spine BMD or any other bone health biomarkers (Table 2). Because our groups were imbalanced in numbers of men and women (Table 1), we investigated differences in gender through investigating the interaction between gender and duration to determine if the effect of duration of PPI therapy was affected by gender. The effect of the interaction between gender and duration was significant at a p-value of 0.04 for hip BMD, implying that the duration of PPI therapy affected the men and women in our study differently. Hip BMD was higher in females than males at both duration levels of PPI therapy but was not significantly different between groups who took no PPI therapy (Graph 1 and Table 3). Furthermore, the T-score associated with the mean BMD of males at both durations of PPI therapy was categorized as osteopenia while the same of females was classified as normal. Mean age of all participants was 63 years.

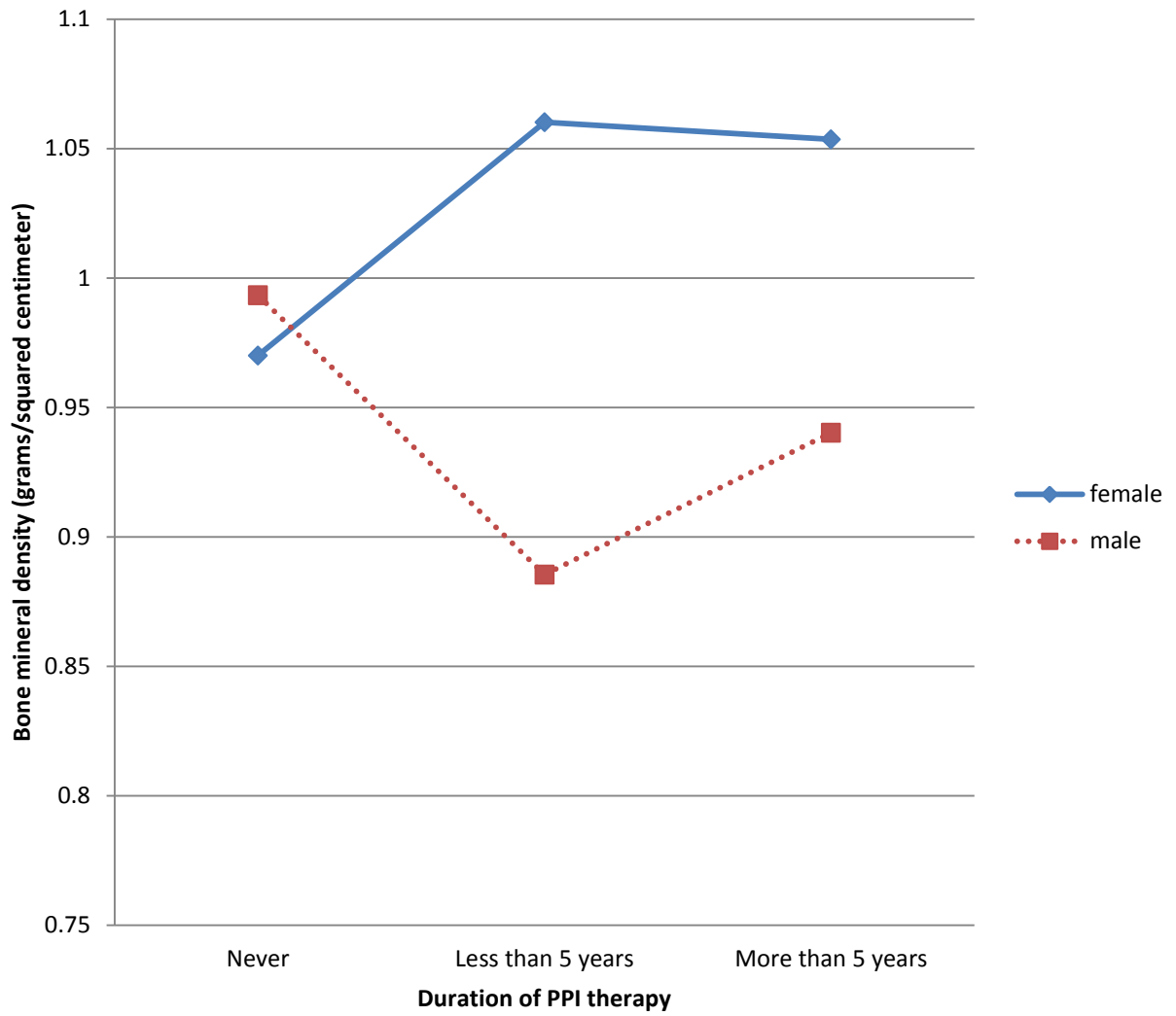
**Table 2: Outcome variables with means and standard errors**

Group	Gender		Duration of PPI Therapy		
	Male n = 31	Female n = 23	None n = 23	≤ 5 years n = 15	> 5 years n = 16
<b>Hip BMD</b>					
Mean (g/cm <sup>2</sup> )	0.940 (0.02)	1.026 (0.04)	0.979 (0.03)	0.973 (0.03)	0.997 (0.03)
<b>Spine BMD</b>					
Mean (g/cm <sup>2</sup> )	1.203 (0.03)	1.196 (0.04)	1.136 (0.03)	1.253 (0.04)	1.209 (0.04)
<b>Serum Osteocalcin</b>					
Normal Range = 9.4 – 47.4 ng/ml					
Mean (ng/ml)	23.40 (1.87)	28.38 (2.55)	23.60 (2.25)	29.21 (2.92)	24.87 (2.63)
<b>Urinary DPX:Creatinine Ratio</b>					
Normal Range = 2.3 – 7.4 nmol DPX : mmol Creatinine					
Mean	10.16 (1.55)	11.00 (1.93)	10.48 (1.47)	10.02 (1.80)	11.24 (1.88)
<b>Serum 25 dihydroxyvitamin D<sub>3</sub></b>					
Normal range = 32 – 100 ng/ml					
Mean (ng/ml)	27.59 (2.11)	25.55 (2.79)	24.61 (2.32)	29.65 (2.80)	25.46 (2.65)
<b>24 Hour Urinary Calcium</b>					
Normal Range = 100 – 300 mg/24 hours					
Mean (mg/24 hours)	188.18 (23.93)	163.87 (28.72)	204.10 (26.06)	151.54 (34.28)	172.43 (30.87)
<b>Serum Parathyroid Hormone</b>					
Normal Range = 15 – 65 pg/ml					
Mean (pg/ml)	45.09 (5.07)	41.39 (6.69)	49.28 (4.32)	39.30 (5.18)	41.13 (5.05)
<b>Serum Magnesium</b>					
Normal Range = 1.6 – 2.6 mg/dl					
Mean (mg/dl)	2.07 (0.03)	2.06 (0.04)	2.07 (0.03)	2.03 (0.04)	2.09 (0.04)
<b>24 Hour Urinary Magnesium</b>					
Normal Range = 12-293 mg/24hours					
Mean (mg/24 hours)	106.55 (7.77)	78.26 (10.31)	115.40 (9.50)	82.10 (11.91)	79.72 (10.92)

**Table 3: Mean hip BMD, standard errors, and T-score classifications of males and females according to duration of PPI therapy**

Gender	Duration of PPI Therapy		
	None	≤ 5 years	> 5 years
Males (g/cm <sup>2</sup> )	0.993 (0.040)	0.885 (0.038)	0.940 (0.031)
T-score Classification	Normal	Osteopenia	Osteopenia
Females (g/cm <sup>2</sup> )	0.965 (0.036)	1.060 (0.060)	1.054 (0.064)
T-score Classification	Normal	Normal	Normal

**Graph 1: Hip BMD by gender and varying durations of PPI therapy**



## DISCUSSION

According to our results, the effects of gender and duration of PPI therapy on hip bone mineral density were dependent on one another without being statistically significant when considered independently. This suggests that men and women may respond differently to long-term PPI therapy; however, not in the way one would expect. In general, females have a lower bone mass than males at any age. However, in our study, women had a higher bone mineral density at the hip than men when on PPI therapy for a longer duration. Furthermore, the T-score associated with the mean BMD of males at both durations of PPI therapy was categorized as osteopenia while the same of females was classified as normal. Osteopenia is a known independent risk factor for osteoporotic fracture in both genders (15). These results suggest that men are more likely to increase their fracture risk by taking PPI therapy for long durations than women.

By measuring at least one measure of bone formation, osteocalcin, and at least one measure of bone resorption, DPX, it is possible to draw strong conclusions about overall bone turnover (95). While no participants had an osteocalcin outside of normal, all participants had an above normal DPX:Creatinine ratio suggesting a higher level of bone resorption with a normal amount of bone formation. These results are consistent with the mechanism resulting in age-related osteoporosis of increased bone resorption without an appropriate increase in bone formation.

By measuring PTH, vitamin D, serum calcium, urinary calcium, serum magnesium, and urinary magnesium simultaneously, we obtained a fairly complete biochemical picture of overall calcium and magnesium balance. While some participant values were outside the normal range, especially for vitamin D, no significant differences were found between groups relating to calcium or magnesium balance.

Given these results, the reasons for the previously demonstrated associations between long-term PPI therapy and increased risk of bone fracture (8-11) may be related to another

independent or otherwise unrelated cause. Regardless of any calcium or other nutrient supplementation, our BMD results indicate that even in the face of sub-par calcium (<1200 mg/day) and vitamin D (<400 IU/day) intake, long-term PPI therapy did not have obvious adverse effects on bone health. Our results do suggest that male PPI users may be at a higher risk of fracture when compared with female PPI users due to a premature decline in bone mass, the cause of which has yet to be determined.

To significantly affect bone status, calcium and vitamin D nutriture would need to be decreased for a long period of time. In this study, we did not examine long-term calcium or vitamin D status. Long durations of PPI therapy can impair absorption of calcium supplements, which are increasingly being used to help meet the elevated calcium requirements of people over age 50. Physicians should consider the solubility of the various forms of supplemental calcium when recommending calcium supplementation to long-term PPI users. While we did not collect details about calcium supplementation such as dosage, frequency, or type, it is interesting to note that more male PPI users were supplementing calcium than female PPI users. With lower bone mass in the male PPI users, perhaps the calcium supplements were not being absorbed as well and true calcium intake was lower than the food frequency questionnaire would have been able to identify. Future research should focus on tracking changes in BMD in calcium supplemented and non-calcium supplemented PPI users to determine if the effectiveness of the calcium supplementation is impaired due to the acid suppression.

One recently published study directly compared BMD and risk of fracture at the spine and hip and use of PPI's and H2RA's in men and women already enrolled in two larger studies related to osteoporosis and bone fracture. They discovered that men taking either class of medications had lower cross-sectional bone mass. Also, they found an increased risk of nonspine fracture in women, but only in men who were not taking calcium supplements(120). These results spark more research questions in the area of possibly increased calcium needs and the role of calcium supplementation in long term PPI users.



## Conclusion

The results of this study support the theory of a protective effect of PPI's on bone health, although the mechanism may not be directly related to the PPI's. Long-term PPI therapy did not appear to inhibit calcium absorption enough to bring about any detrimental changes in bone mineral density in the men and post-menopausal women in our study. However, male PPI users were at a higher risk of fracture at the hip than female PPI users.

While the number of participants in each group was imbalanced and significantly decreases the power of our findings, future studies in this area should focus on assessing total calcium intake from all sources and help to determine if there is a higher need for calcium for long-term PPI users to avoid any medication induced bone losses.

## REFERENCES

1. Fass R. GERD/Dyspepsia. Philadelphia, Pennsylvania: Hanley and Belfus, Inc, 2004.
2. Moayyedi P, Talley NJ. Gastro-oesophageal reflux disease. *Lancet* 2006;367:2086-2100.
3. Dore MP, Maragkoudakis E, Fraley K, et al. Diet, Lifestyle and Gender in Gastro-Esophageal Reflux Disease. *Dig Dis Sci* 2008;53:2027-2032.
4. Jacobson BC, Ferris TG, Shea TL, Mahlis EM, Lee TH, Wang TC. Who is using chronic acid suppression therapy and why? *Am J Gastroenterol* 2003;98:51-58.
5. Heidelbaugh JJ, Nostrant TT, Kim C, Harrison RV. Management of gastroesophageal reflux disease. *Am Fam Physician* 2003;68(7):1311,-1318, 1321-1322.
6. Raghunath AS, Morain CO, Mcloughlin RC. Review article: the long-term use of proton-pump inhibitors. *Aliment Pharmacol Ther* 2005;22(Suppl. 1):55-63.
7. Class S. HEALTH CARE IN FOCUS: The pharmaceutical industry is seeking a new prescription for success as it faces pricing pressures, challenges from generics, and consumer disenchantment. *Chem Eng News* 2004;82(49):18-29.
8. Roux C, Briot K, Gossec L, et al. Increase in vertebral fracture risk in postmenopausal women using omeprazole. *Calcif Tissue Int* 2009;84:13--19.
9. Yang Y, Lewis JD, Epstein S, Metz DC. Long-term proton pump inhibitor therapy and risk of hip fracture. *JAMA* 2006;296:2947-2953.
10. Vestergaard P, Rejnmark L, Mosekilde L. Proton pump inhibitors, histamine H2 receptor antagonists, and other antacid medications and the risk of fracture. *Calcif Tissue Int* 2006;79:76-83.
11. Targownik LE, Lix LM, Metge CJ, Prior HJ, Leung S, Leslie WD. Use of proton pump inhibitors and risk of osteoporosis related fractures. *CMAJ* 2008;179:319-326.
12. Wright MJ, Proctor DD, Insogna KL, Kerstetter JE. Proton pump-inhibiting drugs, calcium homeostasis, and bone health. *Nutr Rev* 2008;66:103-8.
13. Tahir R, Patel PN. Role of Proton Pump Inhibitors in Calcium Absorption, Bone Resorption, and Risk of Hip Fracture. *J Pharm Technol* 2007;23:275-280.
14. Straub DA. Calcium supplementation in clinical practice: a review of forms, doses, and indications. *Nutr Clin Pract* 2007;22:286-296.
15. US Department of Health and Human Services (DHHS). *Bone Health and Osteoporosis: A Report of the Surgeon General*. Rockville, MD: US Department of Health and Human Services, Office of the Surgeon General, 2004.

16. United States Census Bureau. Census 2000 Summary File 1 (SF 1) 100-Percent Data. 2000.
17. Center for Disease Control (CDC). *National Health and Nutrition Examination Survey: Osteoporosis*. 2006;2006.
18. International Society for Clinical Densitometry (ISCD). *Official Positions of the International Society for Clinical Densitometry*. 2006.
19. National Osteoporosis Foundation (NOF). *Physician's Guide to Prevention and Treatment of Osteoporosis*. 1999.
20. The North American Menopause Society. Management of osteoporosis in postmenopausal women: 2006 position statement of the North American Menopause Society. *The Journal of The North American Menopause Society* 2006;13:340-367.
21. Kaufman JM, Goemaere S. Osteoporosis in men. *Best Pract Res Clin Endocrinol Metab* 2008;22:787-812.
22. National Osteoporosis Foundation (NOF). *8 Common Myths About Osteoporosis*. 2006.
23. Sweet MG, Sweet JM, Jeremiah MP, Galazka SS. Diagnosis and treatment of osteoporosis. *Am Fam Physician* 2009;79:193-200.
24. National Osteoporosis Foundation (NOF). *Medications to Prevent and Treat Osteoporosis*. 2006.
25. National Heart, Lung, and Blood Institute. Facts about Menopausal Hormone Therapy. 2007:24.
26. Siris ES, Harris ST, Rosen CJ, et al. Adherence to bisphosphonate therapy and fracture rates in osteoporotic women: relationship to vertebral and nonvertebral fractures from 2 US claims databases. *Mayo Clin Proc* 2006;81:1013-22.
27. National Osteoporosis Foundation (NOF). *Osteoporosis Clinical Updates: Rehabilitation of patients with osteoporosis-related fractures*. 2007.
28. Kim DH. Osteoporotic compression fractures of the spine; current options and considerations for treatment. *The Spine Journal* 2006;6:479-487.
29. The American Society for Bone and Mineral Research. *Primer on the Metabolic Bone Diseases and Disorders of Mineral Metabolism*. Washington, D.C.: American Society for Bone and Mineral Research, 2006.
30. Martini FH. *Fundamentals of Anatomy and Physiology*. Upper Saddle River, New Jersey: Prentice Hall, 2001.
31. Borer KT. Physical activity in the prevention and amelioration of osteoporosis in women : interaction of mechanical, hormonal and dietary factors. *Sports Med* 2005;35:779-830.

32. Stalheim-Smith A, Fitch GK. Understanding Human Anatomy and Physiology. St. Paul, MN: West Publishing Company, 1993.
33. Seeman E. Bone Quality - The Material and Structural Basis of Bone Strength and Fragility. *N Engl J Med* 2006;354:2250-2261.
34. McDonnell P. Vertebral Osteoporosis and Trabecular Bone Quality. *Annals of Biomedical Engineering* 2007;35:170-189.
35. Ott S. Bone Cells. 2003;2007.
36. Ott S. Bone Physiology. 2006;2007.
37. Marcus R, Feldman David, Kelsey Jennifer. Osteoporosis: Volume 1. 2001.
38. Parfitt A. Misconceptions (2): Turnover Is Always Higher in Cancellous Than in Cortical Bone. *Bone* 2002;30:807-809.
39. Farina C, Gagliardi S. Selective Inhibition of Osteoclast Vacuolar H<sup>+</sup>-ATPase. *Curr Pharm Des* 2002;8:2033-2048.
40. Baron R, Neff L, Louvard D, Courtoy PJ. Cell-mediated extracellular acidification and bone resorption: evidence for a low pH in resorbing lacunae and localization of a 100-kD lysosomal membrane protein at the osteoclast ruffled border. *J Cell Biol* 1985;101:2210-2222.
41. Vistentin L, Dodds RA, Valente M, et al. A selective inhibitor of the osteoclastic V-H<sup>+</sup>-ATPase prevents bone loss in both thyroparathyroidectomized and ovariectomized rats. *J Clin Inv* 2000;106(2):309-318.
42. Mizunashi K, Furukawa Y, Katano K, Abe K. Effect of omeprazole, an inhibitor of H<sup>+</sup> -K<sup>+</sup> -ATPase, on bone resorption in humans. *Calcif Tissue Int* 1993;53:21-25.
43. Tuukkanen J, Vaananen HK. Omeprazole, a specific inhibitor of H<sup>+</sup> -K<sup>+</sup> -ATPase inhibits bone resorption in vitro. *Calcif Tissue Int* 1986;38:123-125.
44. Suominen H. Muscle training for bone strength. *Aging Clinical and Experimental Research* 2006;18:85-93.
45. Vanderschueren D, Vandendput L, Boonen S, Lindberg MK, Bouillon R, Ohlsson C. Androgens and bone. *Endocr Rev* 2004;25:389-425.
46. Nichols JF. Prevalence of the Female Athlete Triad Syndrome Among High School Athletes. *Arch Pediatr Adolesc Med* 2006;160:137-142.
47. Griffin, James E., Ojeda, Sergio R. Textbook of Endocrine Physiology. 2004.
48. Takasu H. c-Fos protein as a target of anti-osteoclastogenic action of vitamin D, and synthesis of new analogs. *The Journal of Clinical Investigation* 2006;116:528-535.

49. Masuyama R. Vitamin D receptor in chondrocytes promotes osteoclastogenesis and regulates FGF23 production in osteoblasts. *The Journal of Clinical Investigation* 2006;116:3150-3159.
50. Fang Y. Vitamin D Receptor Gene Haplotype Is Associated with Body Height and Bone Size. *The Journal of Clinical Endocrinology and Metabolism* 2007;92:1491-1501.
51. Uitterlinden A. The Association between Common Vitamin D Receptor Gene Variations and Osteoporosis: A Participant-Level Meta-Analysis. *Annals of Internal Medicine* 2006;145:255-264.
52. Whitt K. The effects of vitamin D receptor polymorphisms on bone mineral density in men and women. *The FASEB Journal* 2007;21:366.
53. Pagana KD, Pagana TJ. *Mosby's Manual of Diagnostic and Laboratory Tests*. St Louis, Missouri: Mosby's Inc, 2006.
54. Stipanuk MH. *Biochemical, Physiological, Molecular Aspects of Human Nutrition*. Philadelphia, PA: Saunders, Elsevier, 2006.
55. Bhutto A, Morley JE. The clinical significance of gastrointestinal changes with aging. *Curr Opin Clin Nutr Metab Care* 2008;11:651-660.
56. Notelovitz M. Estrogen therapy and variable-resistance weight training increase bone mineral in surgically menopausal women. *J Bone Miner Res* 1991;6:583-590.
57. Villareal DT. Effects of exercise training added to ongoing hormone replacement therapy on bone mineral density in frail elderly women. *J Am Geriatr Soc* 2003;51:985-990.
58. Simon JA. Skeletal Consequences of Hormone Therapy Discontinuance: A Systematic Review. *Obstetrical and Gynecological Survey* 2006;61:115-124.
59. Tremollieres FA. Withdrawal of Hormone Replacement Therapy is Associated with Significant Vertebral Bone Loss in Postmenopausal Women. *Osteoporos Int* 2001;12:385-390.
60. Abu EO, Horner A, Kusec V, Triffitt JT, Compston JE. The localization of androgen receptors in human bone. *J Clin Endocrinol Metab* 1997;82:3493-7.
61. Institute of Medicine (IOM). *Dietary Reference Intakes for Calcium, Phosphorus, Magnesium, Vitamin D, and Fluoride*. Washington, DC: National Academy Press, 1997.
62. Briefel RR. Secular Trends in Dietary Intake in the United States. *Annu Rev Nutr* 2004;24:401-431.
63. Radimer K. Dietary Supplement Use by US Adults: Data from the National Health and Nutrition Examination Survey, 1999-2000. *American Journal of Epidemiology* 2004;160:339-349.
64. Thompson J. The compliance paradox: What we need to know about "real-world" dietary

supplement use in the United States. *Alternative Therapies* 2007;13:48-55.

65. Stipanuk M. *Biochemical, Physiological, Molecular Aspects of Human Nutrition*. St. Louis, Missouri: Saunders Elsevier, 2006.

66. Moore C. Vitamin D intakes by children and adults in the United States differ among ethnic groups. *Journal of Nutrition* 2005;135:2478-2485.

67. Shils M. *Modern Nutrition in Health and Disease*. Philadelphia, PA: Lippincott Williams & Wilkins, 2006.

68. Rude RK, Singer FR, Gruber HE. Skeletal and hormonal effects of magnesium deficiency. *J Am Coll Nutr* 2009;28(2):131-141.

69. Ryder KM, Shorr RI, Bush AJ, et al. Magnesium intake from food and supplements is associated with bone mineral density in healthy older white subjects. *J Am Geriatr Soc* 2005;53:1875-1880.

70. Gur A, Colpan L, Nas K, et al. The role of trace minerals in the pathogenesis of postmenopausal osteoporosis and a new effect of calcitonin. *J Bone Min Metab* 2002;20:39-43.

71. Brodowski J. Levels of ionized magnesium in women with various stages of postmenopausal osteoporosis progression evaluated on the densitometric examinations. *Przegl Lek* 2000;57:714-716.

72. Kantorovich V, Adams J, Gaines J, et al. Genetic heterogeneity in familial renal magnesium wasting. *J Clin Endocrinol Met* 2002;87:612-617.

73. Reginster J, Maertens de Noordhout B, Albert A, Dupont-Onkelinx A, Franchimont P. Serum and erythrocyte magnesium in osteoporotic and osteoarthritic postmenopausal women. *Magnesium* 1985;4:208.

74. Cohen L, Kitzes A. Bone magnesium, crystallinity index and state of body magnesium in subjects with senile osteoporosis, maturity-onset diabetes and women treated with contraceptive preparations. *Magnesium* 1983;2:70-75.

75. Cohen L, Laor A, Kitzes R. Magnesium malabsorption in postmenopausal osteoporosis. *Magnesium* 1983;2:139-143.

76. Revel M. One year psoas training can prevent lumbar bone loss in postmenopausal women: a randomized controlled trial. *Calcif Tissue Int* 1993;53:307-311.

77. LeBlanc AD. Skeletal responses to space flight and the bed rest analog: A review. *J Musculoskelet Neuronal Interact* 2007;7:33-47.

78. Kohrt WM. Effects of exercise involving predominantly either JRF or GRF on bone mineral density in older women. *J Bone Miner Res* 1997;12:1253-1261.

79. Nelson ME. Effects of high-intensity strength training on multiple risk factors for osteoporotic fractures. *JAMA* 1994;272:1909-1914.
80. Turner CH. Designing Exercise Regimens to Increase Bone Strength. *Exerc Spor Sci Rev* 2003;31:45-50.
81. US Department of Health and Human Services (DHHS). *Physical Activity and Health: A Report of the Surgeon General*. Atlanta, GA: US Department of Health and Human Services, Centers for Disease Control and Prevention, 1996.
82. French M. Factors the influence adherence to calcium recommendations. *Canadian Journal of Dietetics Practice* 2005;66:25-29.
83. Kannus P. Non-pharmacological Means to Prevent Fractures Among Older Adults. *Annals of Medicine* 2005;37:303-310.
84. Carter N. Results of a 10 week community based strength and balance training programme to reduce fall risk factors: a randomised controlled trial in 65-75 year old women with osteoporosis. *Br J Sports Med* 2001;35:348-351.
85. Yaggie JA. Effects of balance training on selected skills. *Journal of Strength and Conditioning Research* 2006;20:422-428.
86. Turner L. Physical Activity and Osteoporotic Fracture Among Older Women. *Journal of Athletic Training* 1998;33:207-210.
87. Giampietro PF, McCarty C, Mukesh B, et al. The role of cigarette smoking and statins in the development of postmenopausal osteoporosis: a pilot study utilizing the Marshfield Clinic Personalized Medicine Cohort. *Osteoporos Int* 2010;21:467-77.
88. Hollenbach KA, Barrett-Connor E, Edelstein SL, Holbrook T. Cigarette smoking and bone mineral density in older men and women. *Am J Public Health* 1993;83:1265-1270.
89. Trimpou P, Landin-Wilhelmsen K, Odén A, Rosengren A, Wilhelmsen L. Male risk factors for hip fracture—a 30-year follow-up study in 7,495 men. *Osteoporos Int* 2010;21:409-416.
90. Ward KD, Klesges RC. A meta-analysis of the effects of cigarette smoking on bone mineral density. *Calcif Tissue Int* 2001;68:259-270.
91. Ott S. *Bone Mineral Apparent Density*. 2003.
92. Bonnick SL, Lewis LA. *Bone Densitometry for Technologists*. Totowa, New Jersey: Humana Press, 2006.
93. New SA. Exercise, bone and nutrition. *Proc Nutr Soc* 2001;60:265-74.
94. Bikle DD. Biochemical markers in the assessment of bone disease. *Am J Med* 1997;103:427-36.

95. Miller PD. Practical Clinical Application of Biochemical Markers of Bone Turnover. *Journal of Clinical Densitometry* 1999;2:323-342.
96. Nilsson M, Johnsen R, Ye W, Hveem K, Lagergren J. Prevalence of gastro-oesophageal reflux symptoms and the influence of age and sex. *Scand J Gastroenterol* 2004;39:1040-5.
97. Sandler RS, Everhart JE, Donowitz M, et al. The burden of selected digestive diseases in the United States. *Gastroenterology* 2002;122:1500-1511.
98. Schubert ML. Gastric secretion. *Curr Opin Gastroenterol* 2007;23:595-601.
99. Anand G, Katz PO. Gastroesophageal reflux disease and obesity. *Rev Gastroenterol Disord* 2008;8:233-9.
100. Kaltenbach T, Crockett S, Gerson LB. Are lifestyle measures effective in patients with gastroesophageal reflux disease? An evidence-based approach. *Arch Intern Med* 2006;166:965-71.
101. DeVault KR, Castell DO. Updated guidelines for the diagnosis and treatment of gastroesophageal reflux disease. *Am J Gastroenterol* 2005;100:190-200.
102. Nowak M, Büttner P, Harrison S, Daniell K, Raasch B, Speare R. Effectiveness of lifestyle measures in the treatment of gastroesophageal reflux disease - a case series. *Ther Clin Risk Manag* 2006;2:329-34.
103. Adachi Y, Shiota E, Matsumata T, Iso Y, Yoh R, Kitano S. Bone mineral density in patients taking H<sub>2</sub>-receptor antagonist. *Calcif Tissue Int* 1998;62:283-285.
104. Yang Y, Lewis JD, Epstein S, Metz DC. Long-term proton pump inhibitor therapy and risk of hip fracture. *JAMA* 2006;296:2947-53.
105. Wright M, Proctor D, Insogna K, Kerstetter J. Proton pump-inhibiting drugs, calcium homeostasis, and bone health. *Nutrition Reviews* 2008;66:103-108.
106. Rice TW, Blackstone EH. Surgical management of gastroesophageal reflux disease. *Gastroenterol Clin N Am* 2008;37:901-919.
107. Graham DY, Lu H, Yamoaka Y. Therapy for helicobacter pylori infection can be improved: sequential therapy and beyond. *Drugs* 2008;68(6):725-736.
108. Saltzman JR, Russell RM. The aging gut: nutritional issues. *Gastroenterol Clin North Am* 1998;27:309-324.
109. Sipponen P, Harkonen M. Hypochlorhydric stomach: a risk condition for calcium malabsorption and osteoporosis. *Scand J Gastroenterol* 2010;45(2):133-138.
110. Tahir R, Patel PN. Role of proton pump inhibitors in calcium absorption, bone resorption, and risk of hip fracture. *J Pharm Technol* 2007;23:275-80.



111. Ivanovich P, Fellows H, Rich C. The absorption of calcium carbonate. *Ann Intern Med* 1967;66:917-923.
112. Recker R. Calcium absorption and achlorhydria. *N Engl J Med* 1985;313:70-73.
113. Graziani G, Badalamenti S, Como G. Calcium and phosphate plasma levels in dialysis patients after dietary Ca-P overload. Role of gastric acid secretion. *Nephron* 2002;91:474-479.
114. Serfaty-Lacrosniere C, Wood RJ, Voytko D, et al. Hypochlorhydria from short-term omeprazole treatment does not inhibit intestinal absorption of calcium, phosphorus, magnesium or zinc from food in humans. *J Am Coll Nutr* 1995;14(4):364-368.
115. O'Connell MB, Madden DM, Murray AM, Heaney RP, Kerzner LJ. Effects of proton pump inhibitors on calcium carbonate absorption in women: a randomized crossover trial. *Am J Med* 2005;118:778-781.
116. Bo-Linn GW, Davis GR, Buddrus DJ, Morawski SG, Santa Ana C, Fordtran J. An evaluation of the importance of gastric acid secretion in the absorption of dietary calcium. *J Clin Invest* 1984;73:640-647.
117. Groff JL, Gropper SS. *Advanced Nutrition and Human Metabolism*. Belmont, CA: Wadsworth/Thomson Learning, 2000.
118. Chiu KM. Efficacy of calcium supplements on bone mass in postmenopausal women. *J Gerontol* 1999;54A:M275-280.
119. Lanske B, Razzaque MS. Vitamin D and aging: old concepts and new insights. *J Nutr Biochem* 2007;18:771-777.
120. Yu EW, Blackwell T, Ensrud KE, et al. Acid-suppressive medications and risk of bone loss and fracture in older adults. *Calcif Tissue Int* 2008;83:251-259.

APPENDIX A  
PRE-STUDY FORMS AND DOCUMENTS

1. PROSPECTUS
2. IRB APPROVAL LETTER
3. RECRUITING FLIER
4. SCREENING QUESTIONS

DEPARTMENT OF NUTRITION, DIETETICS, AND FOOD SCIENCE  
MASTER OF SCIENCE THESIS PROSPECTUS

**Zarina Pabin, RD**

PO BOX 7010

Provo, UT 84604

November 16, 2007

**Proposed Title**

Effects of Long-Term Proton Pump Inhibitor Therapy on Bone Mineral Density and Biomarkers of Calcium, Magnesium, Iron, Zinc and Vitamin B<sub>12</sub> Status in Post-Menopausal Women\*

\*Note: For my thesis project I will not be measuring all the listed biomarkers due to funding constraints. I plan to measure bone mineral density and at least the markers for calcium.

**Statement of the Problem**

GERD refers to symptoms and damage to the lining of the esophagus that occur due to reflux of acidic gastric contents into the esophagus (1). It has been estimated that the worldwide prevalence of GERD has doubled in the past thirty years with approximately 25% of people reporting having heartburn at least once per month (1,2). In 2002, the annual direct cost for managing GERD in the United States was estimated to exceed \$9 billion dollars (2). Long-term effects of uncontrolled GERD include esophageal strictures and/or ulcers, Barrett's esophagus (benign changes in esophageal mucosal cells), and esophageal adenocarcinoma (2).

The most commonly prescribed medications for the management of GERD are histamine-2 (H<sub>2</sub>) blockers (Tagamet®, Zantac®, Pepcid®, Axid®) and PPI's (Prevacid®, Prilosec®, Protonix®, Aciphex®, Nexium®). The goal of these medications is to reduce symptoms of GERD through decreasing hydrochloric acid production in the stomach (3). H<sub>2</sub> blockers are generally used for initial therapy or temporary management of GERD, while the majority of PPI use is for long-term management of GERD that remains uncontrolled with H<sub>2</sub> blockers (3). In 2002, the sales of PPI's reached more than \$10 billion, second only to the sales of statins and in 2004, Nexium® became the third highest selling drug in the United States (4,5).

It is widely accepted that optimal absorption of minerals, particularly the divalent cations calcium, magnesium, iron, and zinc, requires the acidic environment of the stomach to release the mineral from food and/or supplements and convert it to its ionized form (6,7). It is also proposed that the absorption mechanisms requiring ionization become more predominant during times of suboptimal intake (6,8) which is typical of calcium and magnesium intakes in post-menopausal women (9-11). Vitamin B<sub>12</sub> also requires gastric acid for optimal absorption and current literature supports the practice of routinely testing patients who are taking long term PPI therapy for vitamin B<sub>12</sub> deficiency (12,13).

**Justification of the Problem**

Post-menopausal women are already at particularly high risk for osteoporosis and subsequent fractures due to the accelerated bone loss experienced at menopause (14). In 2006, a large case-control study conducted with over 192,000 subjects over the age of 50, found an

association between long-term PPI therapy and increased risk of hip fracture after controlling for an extensive list of confounding factors including BMI, smoking history, alcoholism, diseases affecting bone metabolism, and prior history of fracture (15). Most previous research into the effects of PPI's on mineral absorption has examined patients on PPI therapy for relatively short periods of time (the longest lasting 4 years) with mixed results (8,16-25). Coupled with the increased use and longer durations of PPI therapy seen in the last decade, current literature suggests further research into the long-term effects of these medications on mineral status (13).

## **Methods/Procedures**

### **Participants**

We plan to recruit 100 women who are at least five years post-menopausal of whom 50 have taken long term PPI therapy either continuously or intermittently for at least ten years and 50 have never been on PPI therapy. Exclusion criteria for all participants includes use of hormone replacement therapy (HRT) in the last five years, history of osteoporosis medication use, and/or presence of diseases or use of medications that affect bone metabolism. We will begin recruiting via fliers on BYU campus and extend written letters of invitation to local medical offices asking permission for fliers to be displayed in their waiting areas as needed to achieve recruiting goals. A website will be utilized to assist with recruitment, screening, and answer frequently asked questions. Our study will also be registered with [clinicaltrials.gov](http://clinicaltrials.gov). Written consent will be obtained from all qualifying participants prior to any procedures being performed.

### **Blood Draw**

A licensed phlebotomist at the BYU Student Health Center (SHC) will perform blood draws of 26 ml (~3 Tablespoons) per participant. Samples will be analyzed for biomarkers of bone formation, bone resorption, parathyroid hormone, vitamin D, magnesium, iron, zinc, and vitamin B<sub>12</sub> status. A written report of results will be available to participants upon request.

### **Urine Collection**

Participants will be asked to collect 2 consecutive 24-hour urine collections for laboratory analysis of markers of calcium and magnesium status. All necessary materials and instructions will be provided to the participants by researchers or research assistants directly involved in the project. Specimens will be returned to the BYU Student Health Center and analyzed in the NDFS department.

### **Diet Survey**

To estimate the adequacy of participant intake of calcium, magnesium, iron, zinc, and vitamin B<sub>12</sub>, an electronic version of the National Institutes of Health Diet History Questionnaire (DHQ) will be administered to each participant. The estimated time to complete the survey is 40-60 minutes. Participants will be mailed a report of the results of the survey and given the opportunity to review it with a Registered Dietitian.

### Dual X-Ray Absorptiometry (DXA) Scan

DXA scans will be performed on each participant assessing bone mineral content (BMC) and bone mineral density (BMD) at the hip and spine and body composition by one of two qualified technicians. A written report of results will be immediately available to participants.

### Data Analysis

T-tests will be performed on single measures of BMC, BMD, and all biomarkers using SAS software Version 9.1.

### **Delimitations of the Problem**

Our study is purely observational and no causal relationships can be inferred from the results to our study participants or to the general population.

### **References**

1. Fass R. GERD/Dyspepsia. Philadelphia, Pennsylvania: Hanley and Belfus, Inc, 2004.
2. Moayyedi P, Talley NJ. Gastro-oesophageal reflux disease. *Lancet* 2006;367:2086-2100.
3. Heidelbaugh JJ, Nostrant TT, Kim C, Harrison RV. Management of gastroesophageal reflux disease. *Am Fam Physician* 2003;68(7):1311,-1318, 1321-1322.
4. Raghunath AS, Morain CO, Mcloughlin RC. Review article: the long-term use of proton-pump inhibitors. *Aliment Pharmacol Ther* 2005;22(Suppl. 1):55-63.
5. Class S. HEALTH CARE IN FOCUS: The pharmaceutical industry is seeking a new prescription for success as it faces pricing pressures, challenges from generics, and consumer disenchantment. *Chem Eng News* 2004;82(49):18-29.
6. Shils M. *Modern Nutrition in Health and Disease*. Philadelphia, PA: Lippincott Williams & Wilkins, 2006.
7. O'Connell MB, Madden DM, Murray AM, Heaney RP, Kerzner LJ. Effects of proton pump inhibitors on calcium carbonate absorption in women: a randomized crossover trial. *Am J Med* 2005;118:778-781.
8. Sharma VR, Brannon MA, Carlross EA. Effect of omeprazole on oral iron replacement in patients with iron deficiency anemia. *South Med J* 2004;97(9):887-889.
9. Institute of Medicine (IOM). *Dietary Reference Intakes for Calcium, Phosphorus, Magnesium, Vitamin D, and Fluoride*. Washington, DC: National Academy Press, 1997.
10. Briefel RR. Secular Trends in Dietary Intake in the United States. *Annu Rev Nutr* 2004;24:401-431.
11. Ford ES, Mokdad AH. Dietary magnesium intake in a national sample of U.S. adults. *J Nutr* 2003;133:2879-2882.
12. Laine L, Ahnen D, McClain C, Solcia E, Walsh JH. Review article: potential gastrointestinal effects of long-term acid suppression with proton pump inhibitors. *Aliment Pharmacol Ther* 2000;14:651-668.
13. Jensen RT. Consequences of long-term proton pump blockade: insights from studies of patients with gastrinomas. *Basic Clin Pharmacol Toxicol* 2006;98:4-19.
14. The North American Menopause Society. Management of osteoporosis in postmenopausal women: 2006 position statement of the North American Menopause Society. *The Journal of The North American Menopause Society* 2006;13:340-367.

15. Yang Y, Lewis JD, Epstein S, Metz DC. Long-term proton pump inhibitor therapy and risk of hip fracture. *JAMA* 2006;296:2947-2953.
16. Bjornsson E, Mattsson N, Simren M, Agerforz P, Abrahamsson H, Kilander A. Iron and vitamin B12 status in patients on long-term treatment with proton pump inhibitors. *Gastroenterology* 2004;126(4, Suppl 2):A433.
17. Koop H, Bachem MG. Serum iron, ferritin, and vitamin B12 during prolonged omeprazole therapy. *J Clin Gastroenterology* 1992;14:288-292.
18. Vestergaard P, Rejnmark L, Mosekilde L. Proton pump inhibitors, histamine H2 receptor antagonists, and other antacid medications and the risk of fracture. *Calcif Tissue Int* 2006;79:76-83.
19. Skikne BS, Lynch SR, Cook JD. Role of gastric acid in food iron absorption. *Gastroenterology* 1981;81(6):1068-1071.
20. Sturniolo GC, Montino MC, Rossetto L, et al. Inhibition of gastric acid secretion reduces zinc absorption in man. *J Am Coll Nutr* 1991;10(4):372-375.
21. Ozutemiz AO, Aydin HH, Isler M, Celik HA, Batur Y. Effect of omeprazole on plasma zinc levels after oral zinc administration. *Indian J Gastroenterol* 2002;21(6):216-218.
22. Force RW, Meeker AD, Cady PS, Culbertson VL, Force WS, Kelley CM. Ambulatory care increased vitamin B12 requirement association with chronic acid suppression therapy. *Ann Pharmacother* 2003;37(4):490-493.
23. Valuck RJ, Ruscini JM. A case-control study on adverse effects: H2 blocker or proton pump inhibitor use and risk of vitamin B12 deficiency in older adults. *J Clin Epidemiol* 2004;57:422-428.
24. Serfaty-Lacrosniere C, Wood RJ, Voytko D, et al. Hypochlorhydria from short-term omeprazole treatment does not inhibit intestinal absorption of calcium, phosphorus, magnesium or zinc from food in humans. *J Am Coll Nutr* 1995;14(4):364-368.
25. Hamdan II. In vitro study of the interaction between omeprazole and the metal ions Zn(II), Cu(II), and Co(II). *Pharmazie* 2001;56(11):877-881.

INSTITUTIONAL REVIEW BOARD FOR  
HUMAN SUBJECTS



January 14, 2008

Robert Davidson  
S243 ESC  
Campus Mail

Re: Effects of Long-Term Proton Pump Inhibitor Therapy (>10 years) on Bone Mineral Density and Biomarkers of Calcium, Magnesium, Iron, Zinc, and Vitamin B12 Status in Post-Menopausal Women

Dear Dr. Davidson,

This is to inform you that Brigham Young University's IRB has approved the above research study.

The approval period is from **1/14/2008 to 12/5/2008**. **Your study number is F08-0009. Please be sure to reference this number in any correspondence with the IRB.**

Continued approval is conditional upon your compliance with the following requirements:

- A copy of the **Informed Consent Document**, approved as of **1/14/2008** is enclosed. No other consent form should be used. It must be signed by each subject prior to initiation of any protocol procedures. In addition, each subject must be given a copy of the signed consent form.
- All protocol amendments and changes to approved research must be submitted to the IRB and not be implemented until approved by the IRB.
- **The enclosed recruitment advertisement has been approved.** Advertisements, letters, Internet postings and any other media for subject recruitment must be submitted to IRB and approved prior to use.
- A few months before this date we will send out a continuing review form. There will only be two reminders. Please fill this form out in a timely manner to ensure that there is not a lapse in your approval.

If you have any questions, please do not hesitate to call me.

Sincerely,

A handwritten signature in black ink, appearing to read "Sandee Muñoz".

Christopher Dromey, PhD, Chair  
Sandee M.P. Muñoz, Administrator  
Institutional Review Board for Human Subjects  
CD/se  
Enclosures

BRIGHAM YOUNG UNIVERSITY · A-285 ASB · PROVO, UTAH 84602

(801) 422-3841 / FAX: (801) 422-0620

# Have you been taking any of these medications for 10 years or more?

**Prevacid®**

(Lansoprazole)

**Prilosec®**

(Omeprazole)

**Protonix®**

(Pantoprazole)

**Aciphex®**

(Rabeprazole)

**Nexium®**

(Esomeprazole)

Researchers in the *Nutrition, Dietetics, and Food Science Department* at BYU need female volunteers who:

- Are at least 5 years post-menopausal
- Do not have osteoporosis
- Have not taken hormone replacement therapy for at least 5 years
- Either have been taking proton pump inhibitors for 10 years or more

-OR-

Have never taken proton pump inhibitors

Study participation includes FREE:

- ★ Bone density testing (using low dose x-rays)
- ★ Dietary analysis with a Registered Dietitian
- ★ Body composition testing (percent body fat)
- ★ Blood and urine analysis for markers of bone health (blood draw and urine collection required)

\* All study related testing will require a maximum of 4 hours of your time spread over 3 visits

**Interested? Please visit [www.byuppiproject.com](http://www.byuppiproject.com) or call 877.4.BYU.PPI (877.429.8774)**



## Research Participant Screening Questions

1. Name: \_\_\_\_\_
2. Phone number: \_\_\_\_\_
3. What is your age? \_\_\_\_\_
4. What is your gender? \_\_\_\_\_
5. Are you currently or have you taken hormone replacement therapy or estrogens [e.g., Prempro® (conjugated/medroxyprogesterone)], in the past 5 years?
 

YES	NO
-----	----
6. Have you ever taken or are you currently taking any osteoporosis medications? [e.g., Fosamax® (alendronate), Boniva® (ibandronate), Actonel® (risedronate), Evista® (raloxifene)]
 

YES	NO
-----	----

If so, please list the months and years of treatment \_\_\_\_\_
7. Have you experienced a bone fracture in the last 10 years?
 

YES	NO
-----	----
8. Do you currently smoke?
 

YES	NO
-----	----
9. Have you ever smoked?
 

YES	NO
-----	----

If so, please list the months and years of smoking \_\_\_\_\_
10. Do you consume more than 1 alcoholic drink per day?
 

YES	NO
-----	----

(Each of the following count as one drink: 12 fluid ounces of regular beer, 5 fluid ounces of wine, or 1.5 fluid ounces of 80-proof distilled spirits)

Please list all medications, including dietary supplements you currently take at least once per week including dosage and frequency.

Supplement

Dose

Frequency

## APPENDIX B

### STUDY FORMS AND DOCUMENTS

#### 1. CONSENT FORMS

#### 2. PARTICIPANT STUDY INSTRUCTIONS

#### 3. DIET HISTORY QUESTIONNAIRE

#### 4. SUPPLEMENTARY PHYSICAL ACTIVITY QUESTIONS

## Consent to be a Research Participant

### Introduction

This research study is being conducted in the Nutrition, Dietetics, and Food Science (NDFS) Department at Brigham Young University (BYU) to determine the effect of ten years or more of proton pump inhibitor (PPI) therapy used to treat gastroesophageal reflux disease (GERD) on bone mineral density (BMD), and biomarkers of calcium, magnesium, iron, zinc, and vitamin B<sub>12</sub>. The researchers conducting this study are Robert Davidson, PhD, Assistant Professor in the NDFS Department at BYU, Kay B Franz, Professor in the NDFS Department at BYU, and Zarina Pabin, RD, a graduate student in the NDFS Department at BYU.

### Procedures

You will be asked to complete the following procedures during your participation in the study.

1. Blood draw (26 mL or approximately 3 Tablespoons) performed by a licensed phlebotomist at the BYU Student Health Center used to measure biomarkers of calcium, magnesium, iron, zinc, and vitamin B<sub>12</sub>.
2. Two consecutive 24-hour urine collections, instructions and specimen return will take approximately 30-45 minutes.
3. Bone mineral content (BMC), bone mineral density (BMD), body composition, and weight using dual x-ray absorptiometry (DXA), height using a stadiometer, waist and hip circumference using a tape measure, and completion of a food frequency questionnaire, visit will take approximately 90-120 minutes.

DXA is a painless procedure that estimates bone density and body composition [fat mass, and lean mass (organ and muscle)] by measuring the attenuation of two low-dose x-ray beams as they pass through the body. The total radiation dose expected from the duration of the study is 19.1 mrem [compared to a mammogram (45 mrem), dental x-ray (6 mrem) or a round trip transcontinental flight (6 mrem)]. The average radiation dose from natural background sources in the environment is estimated to be about 300 mrem/year. With the exception of pregnant women, there are no known risks associated with a DXA scan.

Lab analysis will be performed at the BYU Student Health Center and all other procedures will take place in the NDFS Department at BYU.

\*It is asked that you complete each of the following no later than May 15, 2007.

1. Go to BYU Student Health Center between the hours of 8 AM-11 AM, Monday-Friday to participate in the blood draw and to receive your urine collection materials.
2. Return urine collection to BYU Student Health Center between the hours of 8 AM-5 PM, Monday-Friday.
3. Make an appointment to receive your DXA scan and complete your food frequency questionnaire in the Nutrition, Dietetics, and Food Science Department by logging on to the following website: [www.byuppiproject.com](http://www.byuppiproject.com) using your participant identification number and password.

Page 1 of 3 \_\_\_\_\_ initials

## **Risks/Discomforts**

There are minimal risks associated with participation in this study. You may experience physical discomfort during the blood draw. The x-ray dose associated with the DXA scan you will receive has been outlined in the procedures above and will not affect your ability to receive radiation in the near future from other diagnostic tools.

## **Compensation and Benefits**

Participants will not receive any monetary compensation for participation in this study and there is no financial cost to you as a participant. The potential benefits of participation in this study include dietary analysis, nutrition counseling with a Registered Dietitian, and useful information about your bone density, body composition, and nutritional status. Also, through your participation, researchers will learn more about the effects of long-term proton pump inhibitor therapy on nutritional status. This information may help healthcare professionals in optimizing the health of patients who require long-term proton pump inhibitor therapy for management of GERD.

## **Confidentiality**

Confidentiality will be maintained throughout the project and no individual identifying information will be disclosed. Participants will be assigned an arbitrary identification number for purposes of data collection and all study-related documents will be kept in a locked file cabinet and only available to researchers directly involved in the project. DXA information will be stored securely in password protected files on computers in the Nutrition Assessment Lab (S288) in the NDFS Department at BYU according to participant identification number. It is the intention of the investigators to report and publish the mean values and other statistical reports of all participants. Your personal information and the results of your tests will not be distributed without your written permission.

## **Participation**

Exclusion criteria for all participants includes use of hormone replacement therapy (HRT) in the last five years, history of osteoporosis medication use, and/or presence of diseases or use of medications that affect bone metabolism. Participation in this research study is voluntary. You have the right to withdraw from this study at anytime. If you choose to withdraw from the study, you have a right to receive reports of procedures completed up to the point of withdrawal (body composition, bone density).

## **Questions about the Research**

If you have questions regarding this research study, you may contact Zarina Pabin, RD at 877-4-BYU-PPI (877-429-8774), [zarina@byupproject.com](mailto:zarina@byupproject.com), or Robert Davidson, PhD at 801-422-1432, [robert\\_davidson@byu.edu](mailto:robert_davidson@byu.edu), S-243 ESC Brigham Young University - Provo, UT.

If you have questions regarding your rights as a participant in a research project, you may contact Dr. Renea Beckstrand, Chair of the Institutional Review Board (IRB), 422 SWKT, 801.422.3873, [renea\\_beckstrand@byu.edu](mailto:renea_beckstrand@byu.edu).

I, \_\_\_\_\_, have read, understood, and received a copy of the above consent form; the study and procedures have been explained to me and my questions have been answered to my satisfaction. I understand the inherent risks involved and I understand that I may withdraw at anytime without penalty. I desire of my own free will to participate in this study.

\_\_\_\_\_  
Participant Signature

\_\_\_\_\_  
Date

# BYU PPI Project Visit Instructions

## Visit #1 – Blood Draw, receive urine collection materials:

You **do not need to make an appointment** for this visit, but it does need to be completed between the hours of 8 AM - 11 AM, M-F.

**Where:** BYU Student Health Center (Northeast corner of 900 E and University Parkway in Provo)

**When:** M-F, 8 AM - 11 AM

(The BYU Student Health Center is **closed on Tuesdays from 10:45 AM – 12:15 PM** for university forums and devotionals)

**Duration:** 10-30 minutes

**Instructions:** Enter through the main entrance of the BYU Student Health Center and tell a receptionist you are there for a blood draw for the “Acid Reflux Study.” Proceed to the lab as instructed. Sign green consent form and return it to the lab technician. You may keep the white copy for yourself. Receive blood draw. Receive urine collection materials. Complete **2** consecutive 24-hour urine collections following the instruction sheet included with the collection bottles **and** collect a sample of your first morning void (urination) of another day in the small blue topped cup provided, see table below for guidelines. **Remember to keep your collections refrigerated.**

Day 1	Collection Day 1	Collection Day 2	Collection Day 3
<ul style="list-style-type: none"> <li>● Receive blood draw</li> <li>● Pick up urine collection materials from BYU Student Health Center</li> </ul>	<ul style="list-style-type: none"> <li>● Collect first void into small blue topped cup</li> <li>● Collect all consecutive voids for the rest of the day in the first large urine collection bottle (this will be your first 24-hour urine collection)</li> <li>● <b>Remember to refrigerate</b></li> </ul>	<p><u>(Include first void on Day 2 in <b>first</b> 24 hour urine collection)</u></p> <ul style="list-style-type: none"> <li>● Begin new collection with <b>second</b> void and collect all consecutive voids for the rest of the day in the second large urine collection bottle (this will be your second 24-hour urine collection)</li> <li>● <b>Remember to refrigerate</b></li> </ul>	<p><u>(Include first void on Day 3 in <b>second</b> 24 hour urine collection)</u></p> <ul style="list-style-type: none"> <li>● <b>Remember to refrigerate</b></li> </ul>

### **Visit #2 – Return completed urine collections:**

You **do not need to make an appointment** for this visit. You may visit the BYU Student Health Center anytime M-F between the hours of 8 AM - 5 PM.

**Where:** BYU Student Health Center

**When:** M-F, 8 AM - 5 PM

(The BYU Student Health Center is **closed on Tuesdays from 10:45 AM – 12:15 PM** for university forums and devotionals)

**Duration:** 10-15 minutes

**Instructions:** Return filled urine collection containers (3) to the BYU Student Health Center **within 24 hours of completed collection.**

### **Visit #3 – Food frequency questionnaire, height, weight, waist-hip ratio, DXA scan:**

You **will need to make an appointment** for this visit. Please schedule your appointment at [www.byuppiproject.com](http://www.byuppiproject.com) or call 1.877.4.BYU.PPI (1.877.429.8774).

**Where:** Nutrition, Dietetics, and Food Science Department at BYU – Eyring Science Center (ESC), Room S288

**When:** Schedule your appointment online using your participant ID (located at the top right of your consent form) and your last name, at [www.byuppiproject.com](http://www.byuppiproject.com) or call 1.877.4.BYU.PPI (1.877.429.8774) to schedule over the phone.

**Duration:** 90-120 minutes\*

**Instructions:** See included parking maps to locate visitor parking lots available for parking. Also see included maps to the Eyring Science Center (ESC) and proceed to room S288.

**\*Note:** If you would like to shorten the duration of this visit to approximately 60 minutes, you can complete the food frequency questionnaire at home by visiting our website at [www.byuppiproject.com](http://www.byuppiproject.com) and clicking on “Food Frequency Questionnaire”. **If you choose to complete the questionnaire online, please do so prior to scheduling your lab visit.** Your user ID for the food frequency questionnaire is your participant ID (located at the top right of your consent form) and your password is also your participant ID. If you have any questions or concerns, please call 1.877.4.BYU.PPI (1.877.429.8774).

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

NATIONAL INSTITUTES OF HEALTH

## *Diet History Questionnaire*



### 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
<input type="checkbox"/> Jan	<input type="text"/>	<input type="checkbox"/> 2007
<input type="checkbox"/> Feb	<input type="text"/>	<input type="checkbox"/> 2008
<input type="checkbox"/> Mar	<input type="checkbox"/> 0 <input type="checkbox"/> 0	<input type="checkbox"/> 2009
<input type="checkbox"/> Apr	<input type="checkbox"/> 1 <input type="checkbox"/> 1	<input type="checkbox"/> 2010
<input type="checkbox"/> May	<input type="checkbox"/> 2 <input type="checkbox"/> 2	<input type="checkbox"/> 2011
<input type="checkbox"/> Jun	<input type="checkbox"/> 3 <input type="checkbox"/> 3	
<input type="checkbox"/> Jul	<input type="checkbox"/> 4 <input type="checkbox"/> 4	
<input type="checkbox"/> Aug	<input type="checkbox"/> 5 <input type="checkbox"/> 5	
<input type="checkbox"/> Sep	<input type="checkbox"/> 6 <input type="checkbox"/> 6	
<input type="checkbox"/> Oct	<input type="checkbox"/> 7 <input type="checkbox"/> 7	
<input type="checkbox"/> Nov	<input type="checkbox"/> 8 <input type="checkbox"/> 8	
<input type="checkbox"/> Dec	<input type="checkbox"/> 9 <input type="checkbox"/> 9	

In what month were you born?

<input type="checkbox"/> Jan
<input type="checkbox"/> Feb
<input type="checkbox"/> Mar
<input type="checkbox"/> Apr
<input type="checkbox"/> May
<input type="checkbox"/> Jun
<input type="checkbox"/> Jul
<input type="checkbox"/> Aug
<input type="checkbox"/> Sep
<input type="checkbox"/> Oct
<input type="checkbox"/> Nov
<input type="checkbox"/> Dec

In what year were you born?

19 |  |

<input type="checkbox"/> 0	<input type="checkbox"/> 0
<input type="checkbox"/> 1	<input type="checkbox"/> 1
<input type="checkbox"/> 2	<input type="checkbox"/> 2
<input type="checkbox"/> 3	<input type="checkbox"/> 3
<input type="checkbox"/> 4	<input type="checkbox"/> 4
<input type="checkbox"/> 5	<input type="checkbox"/> 5
<input type="checkbox"/> 6	<input type="checkbox"/> 6
<input type="checkbox"/> 7	<input type="checkbox"/> 7
<input type="checkbox"/> 8	<input type="checkbox"/> 8
<input type="checkbox"/> 9	<input type="checkbox"/> 9

Are you male or female?

Male  
 Female

BAR CODE LABEL OR SUBJECT ID  
HERE

<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
----------------------	----------------------	----------------------	----------------------	----------------------	----------------------	----------------------	----------------------	----------------------	----------------------



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

1. Over the past 12 months, how often did you drink **tomato juice** or **vegetable juice**?

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

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

- Less than ¼ cup (6 ounces)
- ¼ to 1¼ cups (6 to 10 ounces)
- More than 1¼ cups (10 ounces)

2. Over the past 12 months, how often did you drink **orange juice** or **grapefruit juice**?

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

2a. Each time you drank **orange juice** or **grapefruit juice**, how much did you usually drink?

- Less than ¼ cup (6 ounces)
- ¼ to 1¼ cups (6 to 10 ounces)
- More than 1¼ cups (10 ounces)

3. Over the past 12 months, 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 4)
- 1 time per month or less     1 time per day
- 2–3 times per month         2–3 times per day
- 1–2 times per week          4–5 times per day
- 3–4 times per week          6 or more times per day
- 5–6 times per week

3a. Each time you drank **other fruit juice** or **fruit juice mixtures**, how much did you usually drink?

- Less than ¼ cup (6 ounces)
- ¼ to 1½ cups (6 to 12 ounces)
- More than 1½ cups (12 ounces)

**Over the past 12 months...**

4. 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 5)
- 1 time per month or less     1 time per day
- 2–3 times per month         2–3 times per day
- 1–2 times per week          4–5 times per day
- 3–4 times per week          6 or more times per day
- 5–6 times per week

4a. 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)

4b. How often were your fruit drinks **diet** or **sugar-free drinks**?

- 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 **milk as a beverage** (NOT in coffee, NOT in cereal)? (Please include chocolate milk and hot chocolate.)

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

5a. 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)

5b. 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

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

Over the past 12 months...

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

NEVER (GO TO QUESTION 7)

- |   |  |
|---|--|
| <input type="checkbox"/> 1 time per month or less | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 2-3 times per month      | <input type="checkbox"/> 2-3 times per day       |
| <input type="checkbox"/> 1-2 times per week       | <input type="checkbox"/> 4-5 times per day       |
| <input type="checkbox"/> 3-4 times per week       | <input type="checkbox"/> 6 or more times per day |
| <input type="checkbox"/> 5-6 times per week       |  |

6a. Each time you drank **meal replacement 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)

7. Over the past 12 months, did you drink **soft drinks, soda, or pop**?

NO (GO TO QUESTION 8)

YES

7a. How often did you drink **soft drinks, soda, or pop IN THE SUMMER**?

NEVER

- |   |  |
|---|--|
| <input type="checkbox"/> 1 time per month or less | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 2-3 times per month      | <input type="checkbox"/> 2-3 times per day       |
| <input type="checkbox"/> 1-2 times per week       | <input type="checkbox"/> 4-5 times per day       |
| <input type="checkbox"/> 3-4 times per week       | <input type="checkbox"/> 6 or more times per day |
| <input type="checkbox"/> 5-6 times per week       |  |

7b. How often did you drink **soft drinks, soda, or pop DURING THE REST OF THE YEAR**?

NEVER

- |   |  |
|---|--|
| <input type="checkbox"/> 1 time per month or less | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 2-3 times per month      | <input type="checkbox"/> 2-3 times per day       |
| <input type="checkbox"/> 1-2 times per week       | <input type="checkbox"/> 4-5 times per day       |
| <input type="checkbox"/> 3-4 times per week       | <input type="checkbox"/> 6 or more times per day |
| <input type="checkbox"/> 5-6 times per week       |  |

7c. Each time you drank **soft drinks, 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

7d. How often were these soft drinks, soda, 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

7e. How often were these soft drinks, soda, 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

8. Over the past 12 months, did you drink **beer**?

NO (GO TO QUESTION 9)

YES

8a. How often did you drink **beer IN THE SUMMER**?

NEVER

- |   |  |
|---|--|
| <input type="checkbox"/> 1 time per month or less | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 2-3 times per month      | <input type="checkbox"/> 2-3 times per day       |
| <input type="checkbox"/> 1-2 times per week       | <input type="checkbox"/> 4-5 times per day       |
| <input type="checkbox"/> 3-4 times per week       | <input type="checkbox"/> 6 or more times per day |
| <input type="checkbox"/> 5-6 times per week       |  |

8b. How often did you drink **beer DURING THE REST OF THE YEAR**?

NEVER

- |   |  |
|---|--|
| <input type="checkbox"/> 1 time per month or less | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 2-3 times per month      | <input type="checkbox"/> 2-3 times per day       |
| <input type="checkbox"/> 1-2 times per week       | <input type="checkbox"/> 4-5 times per day       |
| <input type="checkbox"/> 3-4 times per week       | <input type="checkbox"/> 6 or more times per day |
| <input type="checkbox"/> 5-6 times per week       |  |

8c. 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



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

Over the past 12 months...

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

- NEVER (GO TO QUESTION 10)
- 1 time per month or less       1 time per day
- 2-3 times per month       2-3 times per day
- 1-2 times per week       4-5 times per day
- 3-4 times per week       6 or more times per day
- 5-6 times per week

9a. 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

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

- NEVER (GO TO QUESTION 11)
- 1 time per month or less       1 time per day
- 2-3 times per month       2-3 times per day
- 1-2 times per week       4-5 times per day
- 3-4 times per week       6 or more times per day
- 5-6 times per week

10a. 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

11. Over the past 12 months, did you eat **oatmeal**, **grits**, or **other cooked cereal**?

- NO (GO TO QUESTION 12)
- YES

11a. How often did you eat **oatmeal**, **grits**, or **other cooked cereal** IN THE WINTER?

- NEVER
- 1-6 times per winter       2 times per week
- 7-11 times per winter       3-4 times per week
- 1 time per month       5-6 times per week
- 2-3 times per month       1 time per day
- 1 time per week       2 or more times per day

11b. How often did you eat **oatmeal**, **grits**, or **other cooked cereal** DURING THE REST OF THE YEAR?

- NEVER
- 1-6 times per year       2 times per week
- 7-11 times per year       3-4 times per week
- 1 time per month       5-6 times per week
- 2-3 times per month       1 time per day
- 1 time per week       2 or more times per day

11c. 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

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

- NEVER (GO TO QUESTION 13)
- 1-6 times per year       2 times per week
- 7-11 times per year       3-4 times per week
- 1 time per month       5-6 times per week
- 2-3 times per month       1 time per day
- 1 time per week       2 or more times per day

12a. Each time you ate **cold cereal**, how much did you usually eat?

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

12b. How often was the cold cereal you ate **Total**, **Product 19**, or **Right Start**?

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

12c. How often was the cold cereal you ate **All Bran**, **Fiber One**, **100% Bran**, or **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

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

Over the past 12 months...

12d. 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

12e. 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

12f. Was **milk** added to your cold cereal?

- NO (GO TO QUESTION 13)
- YES

12g. 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

12h. 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

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

- NEVER (GO TO QUESTION 14)
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per 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

13a. Each time you ate **applesauce**, how much did you usually eat?

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

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

- NEVER (GO TO QUESTION 15)
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per 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

14a. Each time you ate **apples**, how many did you usually eat?

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

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

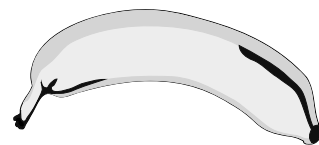
- NEVER (GO TO QUESTION 16)
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per month
- 1 time per week
- 2 times per week
- 3–4 times per week
- 5–6 times per week
- 1 time per day
- 2 or more times per day

15a. Each time you ate **pears**, how many did you usually eat?

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

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

- NEVER (GO TO QUESTION 17)
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per 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



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

Over the past 12 months...

16a. Each time you ate **bananas**, how many did you usually eat?

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

17. How often did you eat **dried fruit**, such as prunes or raisins (not including dried apricots)?

- NEVER (GO TO QUESTION 18)
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per 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 **dried fruit**, how much did you usually eat (not including dried apricots)?

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

18. Over the past 12 months, did you eat **peaches, nectarines, or plums**?

- NO (GO TO QUESTION 19)
- YES

18a. How often did you eat **fresh peaches, nectarines, or plums WHEN IN SEASON?**

- NEVER
- 1–6 times per season
- 7–11 times per season
- 1 time per month
- 2–3 times per 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

18b. How often did you eat **peaches, nectarines, or plums** (fresh, canned, or frozen) **DURING THE REST OF THE YEAR?**

- NEVER
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per 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

18c. 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

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

- NEVER (GO TO QUESTION 20)
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per 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 **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

20. Over the past 12 months, did you eat **cantaloupe**?

- NO (GO TO QUESTION 21)
- YES

20a. How often did you eat **fresh cantaloupe WHEN IN SEASON?**

- NEVER
- 1–6 times per season
- 7–11 times per season
- 1 time per month
- 2–3 times per 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

20b. How often did you eat **fresh or frozen cantaloupe DURING THE REST OF THE YEAR?**

- NEVER
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per 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

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

Over the past 12 months...

20c. 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

21. Over the past 12 months, did you eat **melon, other than cantaloupe** (such as watermelon or honeydew)?

- NO (GO TO QUESTION 22)
- YES

21a. How often did you eat **fresh melon, other than cantaloupe** (such as watermelon or honeydew) **WHEN IN SEASON?**

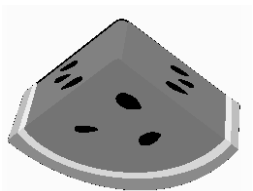
- NEVER
- 1–6 times per season
- 7–11 times per season
- 1 time per month
- 2–3 times per month
- 1 time per week
- 2 times per week
- 3–4 times per week
- 5–6 times per week
- 1 time per day
- 2 or more times per day

21b. How often did you eat **fresh or frozen melon, other than cantaloupe** (such as watermelon or honeydew) **DURING THE REST OF THE YEAR?**

- NEVER
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per 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

21c. 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 22 appears in the next column

22. Over the past 12 months, did you eat **strawberries?**

- NO (GO TO QUESTION 23)
- YES

22a. How often did you eat **fresh strawberries WHEN IN SEASON?**

- NEVER
- 1–6 times per season
- 7–11 times per season
- 1 time per month
- 2–3 times per 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

22b. How often did you eat **fresh or frozen strawberries DURING THE REST OF THE YEAR?**

- NEVER
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per 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

22c. 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

23. Over the past 12 months, did you eat **oranges, tangerines, or tangelos?**

- NO (GO TO QUESTION 24)
- YES

23a. How often did you eat **fresh oranges, tangerines, or tangelos WHEN IN SEASON?**

- NEVER
- 1–6 times per season
- 7–11 times per season
- 1 time per month
- 2–3 times per 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 24 appears on the next page

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

Over the past 12 months...

23b. How often did you eat **oranges, tangerines, or tangelos** (fresh or canned) **DURING THE REST OF THE YEAR?**

- NEVER
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per 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

23c. Each time you ate **oranges, tangerines, or tangelos**, how many did you usually eat?

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

24. Over the past 12 months, did you eat **grapefruit**?

- NO (GO TO QUESTION 25)
- YES

24a. How often did you eat **fresh grapefruit** **WHEN IN SEASON?**

- NEVER
- 1–6 times per season
- 7–11 times per season
- 1 time per month
- 2–3 times per 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

24b. How often did you eat **grapefruit** (fresh or canned) **DURING THE REST OF THE YEAR?**

- NEVER
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per 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

24c. Each time you ate **grapefruit**, how much did you usually eat?

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

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

- NEVER (GO TO QUESTION 26)
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per 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 **other kinds of fruit**, how much did you usually eat?

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

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

- NEVER (GO TO QUESTION 27)
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per 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 **COOKED greens**, how much did you usually eat?

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

27. 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 28)
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per 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 **RAW greens**, how much did you usually eat?

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

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

Over the past 12 months...

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

- NEVER (GO TO QUESTION 29)
- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

28a. Each time you ate **coleslaw**, how much did you usually eat?

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

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

- NEVER (GO TO QUESTION 30)
- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

29a. 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

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

- NEVER (GO TO QUESTION 31)
- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

30a. 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 31 appears in the next column

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

- NEVER (GO TO QUESTION 32)
- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

31a. 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

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

- NEVER (GO TO QUESTION 33)
- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

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

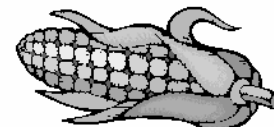
- Less than ¼ cup  
 ¼ to ¾ cup  
 More than ¾ cup

33. Over the past 12 months, did you eat **corn**?

- NO (GO TO QUESTION 34)  
 YES

33a. How often did you eat **fresh corn** **WHEN IN SEASON**?

- NEVER
- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per season  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per season | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month      | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month   | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week       | <input type="checkbox"/> 2 or more times per day |



Question 34 appears on the next page



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

**Over the past 12 months...**

33b. How often did you eat **corn** (fresh, canned, or frozen) **DURING THE REST OF THE YEAR**?

- NEVER
- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

33c. 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

34. Over the past 12 months, how often did you eat **broccoli** (fresh or frozen)?

- NEVER (GO TO QUESTION 35)
- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

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

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

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

- NEVER (GO TO QUESTION 36)
- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

35a. 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

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

- NEVER (GO TO QUESTION 37)
- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

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

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

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

- NEVER (GO TO QUESTION 38)
- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

37a. 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

38. Now think about all the **cooked vegetables** you ate in the past 12 months 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 39)
- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |



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

Over the past 12 months...

38a. Which fats were usually added to your vegetables **DURING COOKING**? (Please do not include potatoes. **Mark all that apply.**)

- |  |   |
|--|---|
| <input type="checkbox"/> Margarine (including low-fat) | <input type="checkbox"/> Corn oil                         |
| <input type="checkbox"/> Butter (including low-fat)    | <input type="checkbox"/> Canola or rapeseed oil           |
| <input type="checkbox"/> Lard, fatback, or bacon fat   | <input type="checkbox"/> Oil spray, such as Pam or others |
| <input type="checkbox"/> Olive oil                     | <input type="checkbox"/> Other kinds of oils              |
|  | <input type="checkbox"/> None of the above                |

39. Now, thinking again about all the **cooked vegetables** you ate in the past 12 months, 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 40)
- |  |  |
|--|--|
| <input type="checkbox"/> 1-6 times per year  | <input type="checkbox"/> 3-4 times per week      |
| <input type="checkbox"/> 7-11 times per year | <input type="checkbox"/> 5-6 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 2-3 times per month | <input type="checkbox"/> 2 times per day         |
| <input type="checkbox"/> 1-2 times per week  | <input type="checkbox"/> 3 or more times per day |

39a. Which fats, sauces, or dressings were usually added **AFTER COOKING OR AT THE TABLE**? (Please do not include potatoes. **Mark all that apply.**)

- |  |   |
|--|---|
| <input type="checkbox"/> Margarine (including low-fat) | <input type="checkbox"/> Salad dressing |
| <input type="checkbox"/> Butter (including low-fat)    | <input type="checkbox"/> Cheese sauce   |
| <input type="checkbox"/> Lard, fatback, or bacon fat   | <input type="checkbox"/> White sauce    |
|  | <input type="checkbox"/> Other          |

39b. 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

39c. 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

Question 40 appears in the next column

40. Over the past 12 months, how often did you eat **sweet peppers** (green, red, or yellow)?

- NEVER (GO TO QUESTION 41)
- |  |  |
|--|--|
| <input type="checkbox"/> 1-6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7-11 times per year | <input type="checkbox"/> 3-4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5-6 times per week      |
| <input type="checkbox"/> 2-3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

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

- Less than 1/8 pepper
- 1/8 to 1/4 pepper
- More than 1/4 pepper

41. Over the past 12 months, did you eat **fresh tomatoes** (including those in salads)?

- NO (GO TO QUESTION 42)
- YES

41a. How often did you eat **fresh tomatoes** (including those in salads) **WHEN IN SEASON**?

- NEVER
- |  |  |
|--|--|
| <input type="checkbox"/> 1-6 times per season  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7-11 times per season | <input type="checkbox"/> 3-4 times per week      |
| <input type="checkbox"/> 1 time per month      | <input type="checkbox"/> 5-6 times per week      |
| <input type="checkbox"/> 2-3 times per month   | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week       | <input type="checkbox"/> 2 or more times per day |

41b. How often did you eat **fresh tomatoes** (including those in salads) **DURING THE REST OF THE YEAR**?

- NEVER
- |  |  |
|--|--|
| <input type="checkbox"/> 1-6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7-11 times per year | <input type="checkbox"/> 3-4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5-6 times per week      |
| <input type="checkbox"/> 2-3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

41c. Each time you ate **fresh tomatoes**, how much did you usually eat?

- Less than 1/4 tomato
- 1/4 to 1/2 tomato
- More than 1/2 tomato

Question 42 appears on the next page

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

Over the past 12 months...

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

- NEVER (GO TO QUESTION 43)
- 1–6 times per year       2 times per week
- 7–11 times per year     3–4 times per week
- 1 time per month         5–6 times per week
- 2–3 times per month     1 time per day
- 1 time per week          2 or more times per day

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

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

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

- NEVER (GO TO QUESTION 44)
- 1–6 times per year       2 times per week
- 7–11 times per year     3–4 times per week
- 1 time per month         5–6 times per week
- 2–3 times per month     1 time per day
- 1 time per week          2 or more times per day

43a. 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

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

- NEVER (GO TO QUESTION 45)
- 1–6 times per year       2 times per week
- 7–11 times per year     3–4 times per week
- 1 time per month         5–6 times per week
- 2–3 times per month     1 time per day
- 1 time per week          2 or more times per day

44a. 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

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

- NEVER (GO TO QUESTION 46)
- 1–6 times per year       2 times per week
- 7–11 times per year     3–4 times per week
- 1 time per month         5–6 times per week
- 2–3 times per month     1 time per day
- 1 time per week          2 or more times per day

45a. 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

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

- NEVER (GO TO QUESTION 47)
- 1–6 times per year       2 times per week
- 7–11 times per year     3–4 times per week
- 1 time per month         5–6 times per week
- 2–3 times per month     1 time per day
- 1 time per week          2 or more times per day

46a. Each time you ate **potato salad**, how much did you usually eat?

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

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

- NEVER (GO TO QUESTION 48)
- 1–6 times per year       2 times per week
- 7–11 times per year     3–4 times per week
- 1 time per month         5–6 times per week
- 2–3 times per month     1 time per day
- 1 time per week          2 or more times per day

47a. 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

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

Over the past 12 months...

47b. 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 47d)
- About ¼ of the time
- About ½ of the time
- About ¾ of the time
- Almost always or always

47c. 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

47d. 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

47e. 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

47f. 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

47g. 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 48)
- About ¼ of the time
- About ½ of the time
- About ¾ of the time
- Almost always or always

47h. 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

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

- NEVER (GO TO QUESTION 49)
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per 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 **salsa**, how much did you usually eat?

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

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

- NEVER (GO TO QUESTION 50)
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per 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 **catsup**, how much did you usually eat?

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

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

- NEVER (GO TO QUESTION 51)
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per 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 **stuffing, dressing, or dumplings**, how much did you usually eat?

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

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

Over the past 12 months...

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

- NEVER (GO TO QUESTION 52)
- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

51a. Each time you ate **chili**, how much did you usually eat?

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

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

- NEVER (GO TO QUESTION 53)
- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

52a. 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.

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

- NEVER (GO TO QUESTION 54)
- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

53a. Each time you ate **beans**, how much did you usually eat?

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

53b. 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

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

- NEVER (GO TO QUESTION 55)
- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

54a. 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

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

- NEVER (GO TO QUESTION 56)
- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

55a. 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

55b. How often was **butter, margarine, or oil** added to your rice **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

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

Over the past 12 months...

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

- NEVER (GO TO QUESTION 57)
- 1–6 times per year       2 times per week
- 7–11 times per year     3–4 times per week
- 1 time per month         5–6 times per week
- 2–3 times per month     1 time per day
- 1 time per week          2 or more times per day

56a. 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

56b. 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

56c. 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

56d. 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

56e. How often was **syrup** added to your pancakes, waffles, or French toast?

- Almost never or never (GO TO QUESTION 57)
- About ¼ of the time
- About ½ of the time
- About ¾ of the time
- Almost always or always

Question 57 appears in the next column

56f. 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

57. 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 58)
- 1–6 times per year       2 times per week
- 7–11 times per year     3–4 times per week
- 1 time per month         5–6 times per week
- 2–3 times per month     1 time per day
- 1 time per week          2 or more times per day

57a. 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

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

- NEVER (GO TO QUESTION 59)
- 1–6 times per year       2 times per week
- 7–11 times per year     3–4 times per week
- 1 time per month         5–6 times per week
- 2–3 times per month     1 time per day
- 1 time per week          2 or more times per day

58a. 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

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

- NEVER (GO TO QUESTION 60)
- 1–6 times per year       2 times per week
- 7–11 times per year     3–4 times per week
- 1 time per month         5–6 times per week
- 2–3 times per month     1 time per day
- 1 time per week          2 or more times per day

Question 60 appears on the next page

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

Over the past 12 months...

59a. 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

60. Other than the pastas listed in Questions 57, 58, and 59, how often did you eat **pasta, spaghetti, or other noodles**?

NEVER (GO TO QUESTION 61)

- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

60a. 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

60b. 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

60c. 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

60d. 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 61 appears in the next column

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

NEVER (GO TO INTRODUCTION TO QUESTION 62)

- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

61a. 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

61b. 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

61c. 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

61d. 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

61e. How often was **cream cheese** (including low-fat) spread on your bagels or English muffins?

- Almost never or never (GO TO INTRODUCTION TO QUESTION 62)
- About ¼ of the time
- About ½ of the time
- About ¾ of the time
- Almost always or always

Introduction to Question 62 appears on the next page

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

Over the past 12 months...

61f. 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.

62. How often did you eat **breads** or **rolls AS PART OF SANDWICHES** (including burger and hot dog rolls)?

- NEVER (GO TO QUESTION 63)
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per 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 **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

62b. 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

62c. How often was **mayonnaise** or **mayonnaise-type dressing** (including low-fat) added to your sandwich bread or rolls?

- Almost never or never (GO TO QUESTION 62e)
- About ¼ of the time
- About ½ of the time
- About ¾ of the time
- Almost always or always

Question 62e appears in the next column

Question 63 appears in the next column

62d. Each time **mayonnaise** or **mayonnaise-type dressing** was added to your sandwich breads or rolls, how much was usually added?

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

62e. How often was **margarine** (including low-fat) added to your sandwich bread 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

62f. How often was **butter** (including low-fat) added to your sandwich bread 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

62g. Each time **margarine** or **butter** was added to your sandwich breads or rolls, how much was usually added?

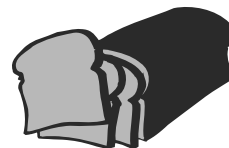
- Never added
- Less than 1 teaspoon
- 1 to 2 teaspoons
- More than 2 teaspoons

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

- NEVER (GO TO QUESTION 64)
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per 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 **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



Question 64 appears on the next page



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

Over the past 12 months...

63b. 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

63c. 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

63d. 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

63e. Each time **margarine** or **butter** was added to your breads or rolls, how much was usually added?

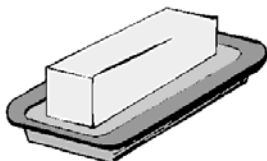
- Never added
- Less than 1 teaspoon
- 1 to 2 teaspoons
- More than 2 teaspoons

63f. How often was **cream cheese** (including low-fat) added to your breads or rolls?

- Almost never or never (GO TO QUESTION 64)
- About ¼ of the time
- About ½ of the time
- About ¾ of the time
- Almost always or always

63g. 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



Question 64 appears in the next column

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

- NEVER (GO TO QUESTION 65)
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per 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 **jam, jelly, or honey**, how much did you usually eat?

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

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

- NEVER (GO TO QUESTION 66)
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per 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 **peanut butter** or **other nut butter**, how much did you usually eat?

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

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

- NEVER (GO TO QUESTION 67)
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per 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 **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 67 appears on the next page

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

Over the past 12 months...

67. 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 68)
- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

67a. 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

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

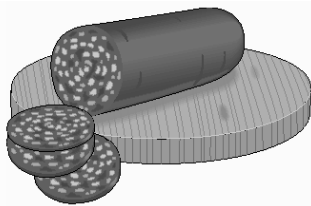
- NEVER (GO TO QUESTION 69)
- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

68a. 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

68b. 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



Question 69 appears in the next column

69. 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 70)
- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

69a. 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

69b. How often were the other cold cuts or luncheon meats you ate **light, low-fat, or fat-free cold cuts or luncheon meats**? *(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

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

- NEVER (GO TO QUESTION 71)
- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

70a. 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

70b. How often was the canned tuna you ate **water-packed tuna**?

- 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 on the next page

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

Over the past 12 months...

70c. 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

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

- NEVER (GO TO QUESTION 72)
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per 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

71a. 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

72. How often did you eat **beef hamburgers or cheeseburgers?**

- NEVER (GO TO QUESTION 73)
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per 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 **beef hamburgers or cheeseburgers**, 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

72b. How often were the beef hamburgers or cheeseburgers you ate 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

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

- NEVER (GO TO QUESTION 74)
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per 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 **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

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

- NEVER (GO TO QUESTION 75)
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per 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 **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

74b. How often were the hot dogs or frankfurters you ate **light or low-fat hot dogs?**

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



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

Over the past 12 months...

75. 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 76)
- 1–6 times per year       2 times per week
- 7–11 times per year     3–4 times per week
- 1 time per month         5–6 times per week
- 2–3 times per month     1 time per day
- 1 time per week          2 or more times per day

75a. Each time you ate **beef stew, beef pot pie, beef and noodles, or beef and vegetables**, how much did you usually eat?

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

76. 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 77)
- 1–6 times per year       2 times per week
- 7–11 times per year     3–4 times per week
- 1 time per month         5–6 times per week
- 2–3 times per month     1 time per day
- 1 time per week          2 or more times per day

76a. Each time you ate **roast beef or pot roast** (including in mixtures), how much did you usually eat?

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

77. How often did you eat **steak** (beef)? (Do not include steak in sandwiches)

- NEVER (GO TO QUESTION 78)
- 1–6 times per year       2 times per week
- 7–11 times per year     3–4 times per week
- 1 time per month         5–6 times per week
- 2–3 times per month     1 time per day
- 1 time per week          2 or more times per day

77a. Each time you ate **steak** (beef), how much did you usually eat?

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

Question 78 appears in the next column

77b. 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

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

- NEVER (GO TO QUESTION 79)
- 1–6 times per year       2 times per week
- 7–11 times per year     3–4 times per week
- 1 time per month         5–6 times per week
- 2–3 times per month     1 time per day
- 1 time per week          2 or more times per day

78a. 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

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

- NEVER (GO TO QUESTION 80)
- 1–6 times per year       2 times per week
- 7–11 times per year     3–4 times per week
- 1 time per month         5–6 times per week
- 2–3 times per month     1 time per day
- 1 time per week          2 or more times per day

79a. 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

80. How often did you eat **chicken** as part of **salads, sandwiches, casseroles, stews, or other mixtures**?

- NEVER (GO TO QUESTION 81)
- 1–6 times per year       2 times per week
- 7–11 times per year     3–4 times per week
- 1 time per month         5–6 times per week
- 2–3 times per month     1 time per day
- 1 time per week          2 or more times per day

Question 81 appears on the next page

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

Over the past 12 months...

80a. Each time you ate **chicken** as part of **salads, sandwiches, casseroles, stews, or other mixtures**, how much did you usually eat?

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

81. 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 82)
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per 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 **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

81b. 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

81c. 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

81d. 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

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

- NEVER (GO TO QUESTION 83)
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per 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 **baked ham or ham steak**, how much did you usually eat?

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

83. 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 84)
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per 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

83a. 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

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

- NEVER (GO TO QUESTION 85)
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per 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 **gravy** on meat, chicken, potatoes, rice, etc., how much did you usually eat?

- Less than ⅓ cup
- ⅓ to ½ cup
- More than ½ cup

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

Over the past 12 months...

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

- NEVER (GO TO QUESTION 86)
- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

85a. 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

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

- NEVER (GO TO QUESTION 87)
- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

86a. Each time you ate **bacon**, how much did you usually eat?

- Fewer than 2 slices  
 2 to 3 slices  
 More than 3 slices

86b. How often was the bacon you ate **light, low-fat, or lean bacon**?

- Almost never or never  
 About  $\frac{1}{4}$  of the time  
 About  $\frac{1}{2}$  of the time  
 About  $\frac{3}{4}$  of the time  
 Almost always or always

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

- NEVER (GO TO QUESTION 88)
- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

87a. 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

87b. How often was the sausage you ate **light, low-fat, or lean sausage**?

- Almost never or never  
 About  $\frac{1}{4}$  of the time  
 About  $\frac{1}{2}$  of the time  
 About  $\frac{3}{4}$  of the time  
 Almost always or always

88. How often did you eat **fish sticks** or **fried fish** (including fried seafood or shellfish)?

- NEVER (GO TO QUESTION 89)
- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

88a. Each time you ate **fish sticks** or **fried fish**, how much did you usually eat?

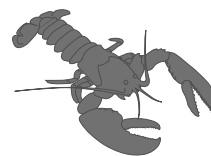
- Less than 2 ounces or less than 1 fillet  
 2 to 7 ounces or 1 fillet  
 More than 7 ounces or more than 1 fillet

89. How often did you eat **fish** or **seafood that was NOT FRIED** (including shellfish)?

- NEVER (GO TO INTRODUCTION TO QUESTION 90)
- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

89a. Each time you ate **fish** or **seafood 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



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

Over the past 12 months...

Now think about all the meat, poultry, and fish you ate in the past 12 months and how they were prepared.

90. 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 91)
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per 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. 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

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

- NEVER (GO TO QUESTION 92)
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per 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 **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

Question 92 appears in the next column

92. Over the past 12 months, did you eat **soups**?

NO (GO TO QUESTION 93)

YES

92a. How often did you eat **soup DURING THE WINTER**?

- NEVER
- 1–6 times per winter
- 7–11 times per winter
- 1 time per month
- 2–3 times per 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

92b. How often did you eat **soup DURING THE REST OF THE YEAR**?

- NEVER
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per 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

92c. Each time you ate **soup**, how much did you usually eat?

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

92d. 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

92e. 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

Question 93 appears on the next page

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

Over the past 12 months...

92f. 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

92g. 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

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

- NEVER (GO TO QUESTION 94)
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per 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 **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

93b. 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

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

- NEVER (GO TO QUESTION 95)
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per 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 **crackers**, how many did you usually eat?

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

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

- NEVER (GO TO QUESTION 96)
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per 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 **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

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

- NEVER (GO TO QUESTION 97)
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per 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 **biscuits**, how many did you usually eat?

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

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

- NEVER (GO TO QUESTION 98)
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per 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



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

Over the past 12 months...

97a. Each time you ate **potato chips, tortilla chips, or corn 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

97b. How often were the chips you ate **Wow chips** or other **chips made with fat substitute** (Olean or Olestra)?

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

97c. How often were the chips you ate other **low-fat** or **fat-free chips**?

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

98. How often did you eat **popcorn** (including low-fat)?

- NEVER (GO TO QUESTION 99)
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per 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 **popcorn**, how much did you usually eat?

- Less than 2 cups, popped
- 2 to 5 cups, popped
- More than 5 cups, popped

99. How often did you eat **pretzels**?

- NEVER (GO TO QUESTION 100)
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per 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 **pretzels**, how many did you usually eat?

- Fewer than 5 average twists
- 5 to 20 average twists
- More than 20 average twists

100. How often did you eat **peanuts, walnuts, seeds, or other nuts**?

- NEVER (GO TO QUESTION 101)
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per 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 **peanuts, walnuts, seeds, or other nuts**, how much did you usually eat?

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

101. How often did you eat **energy, high-protein, or breakfast bars** such as **Power Bars, Balance, Clif, or others**?

- NEVER (GO TO QUESTION 102)
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per 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 **energy, high-protein, or breakfast bars**, how much did you usually eat?

- Less than 1 bar
- 1 bar
- More than 1 bar

102. How often did you eat **yogurt** (NOT including frozen yogurt)?

- NEVER (GO TO QUESTION 103)
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per 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

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

Over the past 12 months...

102a. 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

103. How often did you eat **cottage cheese** (including low-fat)?

- NEVER (GO TO QUESTION 104)
- 1–6 times per year       2 times per week
- 7–11 times per year     3–4 times per week
- 1 time per month         5–6 times per week
- 2–3 times per month     1 time per day
- 1 time per week          2 or more times per day

103a. Each time you ate **cottage cheese**, how much did you usually eat?

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

104. How often did you eat **cheese** (including low-fat; including on cheeseburgers or in sandwiches or subs)?

- NEVER (GO TO QUESTION 105)
- 1–6 times per year       2 times per week
- 7–11 times per year     3–4 times per week
- 1 time per month         5–6 times per week
- 2–3 times per month     1 time per day
- 1 time per week          2 or more times per day

104a. 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

104b. How often was the cheese you ate **light or low-fat cheese**?

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

104c. How often was the cheese you ate **fat-free cheese**?

- 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 **frozen yogurt, sorbet, or ices** (including low-fat or fat-free)?

- NEVER (GO TO QUESTION 106)
- 1–6 times per year       2 times per week
- 7–11 times per year     3–4 times per week
- 1 time per month         5–6 times per week
- 2–3 times per month     1 time per day
- 1 time per week          2 or more times per day

105a. 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

106. How often did you eat **ice cream, ice cream bars, or sherbet** (including low-fat or fat-free)?

- NEVER (GO TO QUESTION 107)
- 1–6 times per year       2 times per week
- 7–11 times per year     3–4 times per week
- 1 time per month         5–6 times per week
- 2–3 times per month     1 time per day
- 1 time per week          2 or more times per day

106a. 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

106b. 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

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

Over the past 12 months...

107. How often did you eat **cake** (including low-fat or fat-free)?

- NEVER (GO TO QUESTION 108)
- 1–6 times per year       2 times per week
- 7–11 times per year     3–4 times per week
- 1 time per month         5–6 times per week
- 2–3 times per month     1 time per day
- 1 time per week          2 or more times per day

107a. Each time you ate **cake**, how much did you usually eat?

- Less than 1 medium piece
- 1 medium piece
- More than 1 medium piece

107b. How often was the cake you ate **light, low-fat, or fat-free cake**?

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

108. How often did you eat **cookies or brownies** (including low-fat or fat-free)?

- NEVER (GO TO QUESTION 109)
- 1–6 times per year       2 times per week
- 7–11 times per year     3–4 times per week
- 1 time per month         5–6 times per week
- 2–3 times per month     1 time per day
- 1 time per week          2 or more times per day

108a. 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

108b. How often were the cookies or brownies you ate **light, low-fat, or fat-free cookies or brownies**?

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

109. How often did you eat **doughnuts, sweet rolls, Danish, or pop-tarts**?

- NEVER (GO TO QUESTION 110)
- 1–6 times per year       2 times per week
- 7–11 times per year     3–4 times per week
- 1 time per month         5–6 times per week
- 2–3 times per month     1 time per day
- 1 time per week          2 or more times per day

109a. 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

110. How often did you eat **sweet muffins or dessert breads** (including low-fat or fat-free)?

- NEVER (GO TO QUESTION 111)
- 1–6 times per year       2 times per week
- 7–11 times per year     3–4 times per week
- 1 time per month         5–6 times per week
- 2–3 times per month     1 time per day
- 1 time per week          2 or more times per day

110a. 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

110b. How often were the sweet muffins or dessert breads you ate **light, low-fat, or fat-free sweet muffins or dessert breads**?

- 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 **fruit crisp, cobbler, or strudel**?

- NEVER (GO TO QUESTION 112)
- 1–6 times per year       2 times per week
- 7–11 times per year     3–4 times per week
- 1 time per month         5–6 times per week
- 2–3 times per month     1 time per day
- 1 time per week          2 or more times per day

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

Over the past 12 months...

111a. 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

112. How often did you eat **pie**?

- NEVER (GO TO QUESTION 113)
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per 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 **pie**, how much did you usually eat?

- Less than ⅛ of a pie
- About ⅛ of a pie
- More than ⅛ of a pie

**The next four questions ask about the kinds of pie you ate. Please read all four questions before answering.**

112b. 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

112c. 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

112d. 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

112e. 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

113. How often did you eat **chocolate candy**?

- NEVER (GO TO QUESTION 114)
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per 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 **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

114. How often did you eat **other candy**?

- NEVER (GO TO QUESTION 115)
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per 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 **other candy**, how much did you usually eat?

- Fewer than 2 pieces
- 2 to 9 pieces
- More than 9 pieces

115. 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 116)
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per 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

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

Over the past 12 months...

115a. Each time you ate **eggs**, how many did you usually eat?

- 1 egg
- 2 eggs
- 3 or more eggs

115b. How often were the eggs you ate **egg substitutes**?

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

115c. How often were the eggs you ate **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

115d. How often were the eggs you ate **regular whole eggs**?

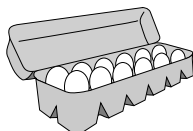
- Almost never or never
- About ¼ of the time
- About ½ of the time
- About ¾ of the time
- Almost always or always

115e. 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

115f. 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



Question 116 appears in the next column

116. How many cups of **coffee**, caffeinated or decaffeinated, did you drink?

- NEVER (GO TO QUESTION 117)
- Less than 1 cup per month
- 1–3 cups per 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

116a. 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

117. How many glasses of **ICED tea**, caffeinated or decaffeinated, did you drink?

- NEVER (GO TO QUESTION 118)
- Less than 1 cup per month
- 1–3 cups per 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

117a. How often was the iced tea you drank **decaffeinated or herbal tea**?

- 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 many cups of **HOT tea**, caffeinated or decaffeinated, did you drink?

- NEVER (GO TO QUESTION 119)
- Less than 1 cup per month
- 1–3 cups per 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

118a. How often was the hot tea you drank **decaffeinated or herbal tea**?

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

Question 119 appears on the next page

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

Over the past 12 months...

119. How often did you add **sugar** or **honey** to your coffee or tea?

- NEVER (GO TO QUESTION 120)
- Less than 1 time per month
- 1–3 times per month
- 1 time per week
- 2–4 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

119a. 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

120. How often did you add **artificial sweetener** to your coffee or tea?

- NEVER (GO TO QUESTION 121)
- Less than 1 time per month
- 1–3 times per month
- 1 time per week
- 2–4 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

120a. What kind of **artificial sweetener** did you usually use?

- Equal or aspartame
- Sweet N Low or saccharin

121. How often was **non-dairy creamer** added to your coffee or tea?

- NEVER (GO TO QUESTION 122)
- Less than 1 time per month
- 1–3 times per month
- 1 time per week
- 2–4 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

121a. 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

121b. 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

122. How often was **cream** or **half and half** added to your coffee or tea?

- NEVER (GO TO QUESTION 123)
- Less than 1 time per month
- 1–3 times per month
- 1 time per week
- 2–4 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

122a. 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

123. How often was **milk** added to your coffee or tea?

- NEVER (GO TO QUESTION 124)
- Less than 1 time per month
- 1–3 times per month
- 1 time per week
- 2–4 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

123a. 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

123b. 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

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

Over the past 12 months...

124. 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 125)
- 1–6 times per year
- 7–11 times per year
- 1 time per month
- 2–3 times per 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 **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 eat. If possible, please check the labels of these foods to help you answer.

125. Over the past 12 months, did you eat **margarine**?

- NO (GO TO QUESTION 126)
- YES

125a. How often was the margarine you ate **regular-fat margarine** (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

125b. How often was the margarine you ate **light** or **low-fat margarine** (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 126 appears in the next column

125c. How often was the margarine you ate **fat-free margarine**?

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

126. Over the past 12 months, did you eat **butter**?

- NO (GO TO QUESTION 127)
- YES

126a. How often was the butter you ate **light** or **low-fat butter**?

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

127. Over the past 12 months, did you eat **mayonnaise** or **mayonnaise-type dressing**?

- NO (GO TO QUESTION 128)
- YES

127a. How often was the mayonnaise you ate **regular-fat mayonnaise**?

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

127b. How often was the mayonnaise you ate **light** or **low-fat mayonnaise**?

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

Question 128 appears on the next page

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

Over the past 12 months...

127c. How often was the mayonnaise you ate **fat-free mayonnaise**?

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

128. Over the past 12 months, did you eat **sour cream**?

NO (GO TO QUESTION 129)

YES

128a. How often was the sour cream you ate **regular-fat sour cream**?

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

128b. How often was the sour cream you ate **light, low-fat, or fat-free sour cream**?

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

129. Over the past 12 months, did you eat **cream cheese**?

NO (GO TO QUESTION 130)

YES

129a. How often was the cream cheese you ate **regular-fat cream cheese**?

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

129b. How often was the cream cheese you ate **light, low-fat, or fat-free cream cheese**?

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

130. Over the past 12 months, did you eat **salad dressing**?

NO (GO TO INTRODUCTION TO QUESTION 131)

YES

130a. How often was the salad dressing you ate **regular-fat salad dressing** (including oil and vinegar dressing)?

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

130b. How often was the salad dressing you ate **light or low-fat salad dressing**?

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

130c. How often was the salad dressing you ate **fat-free salad dressing**?

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

**The following two questions ask you to summarize your usual intake of vegetables and fruits. Please do not include salads, potatoes, or juices.**

131. Over the past 12 months, how many servings of **vegetables** (not including salad or potatoes) did you eat per week or per day?

- |   |  |
|---|--|
| <input type="checkbox"/> Less than 1 per week | <input type="checkbox"/> 2 per day         |
| <input type="checkbox"/> 1-2 per week         | <input type="checkbox"/> 3 per day         |
| <input type="checkbox"/> 3-4 per week         | <input type="checkbox"/> 4 per day         |
| <input type="checkbox"/> 5-6 per week         | <input type="checkbox"/> 5 or more per day |
| <input type="checkbox"/> 1 per day            |  |



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

**Over the past 12 months...**

132. Over the past 12 months, how many servings of **fruit** (not including juices) did you eat per week or per day?

- |   |  |
|---|--|
| <input type="checkbox"/> Less than 1 per week | <input type="checkbox"/> 2 per day         |
| <input type="checkbox"/> 1–2 per week         | <input type="checkbox"/> 3 per day         |
| <input type="checkbox"/> 3–4 per week         | <input type="checkbox"/> 4 per day         |
| <input type="checkbox"/> 5–6 per week         | <input type="checkbox"/> 5 or more per day |
| <input type="checkbox"/> 1 per day            |  |

133. Over the past month, which of the following foods did you eat **AT LEAST THREE TIMES?** *(Mark all that apply.)*

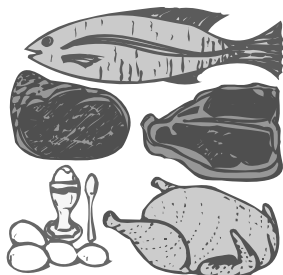
- |   |   |
|---|---|
| <input type="checkbox"/> Avocado, guacamole                                   | <input type="checkbox"/> Olives                                 |
| <input type="checkbox"/> Cheesecake   | <input type="checkbox"/> Oysters                                |
| <input type="checkbox"/> Chocolate, fudge, or butterscotch toppings or syrups | <input type="checkbox"/> Pickles or pickled vegetables or fruit |
| <input type="checkbox"/> Chow mein noodles                                    | <input type="checkbox"/> Plantains                              |
| <input type="checkbox"/> Croissants   | <input type="checkbox"/> Pork neckbones, hock, head, feet       |
| <input type="checkbox"/> Dried apricots                                       | <input type="checkbox"/> Pudding or custard                     |
| <input type="checkbox"/> Egg rolls  | <input type="checkbox"/> Veal, venison, lamb                    |
| <input type="checkbox"/> Granola bars   | <input type="checkbox"/> Whipped cream, regular                 |
| <input type="checkbox"/> Hot peppers  | <input type="checkbox"/> Whipped cream, substitute              |
| <input type="checkbox"/> Jello, gelatin                                       |   |
| <input type="checkbox"/> Milkshakes or ice-cream sodas                        | <input type="checkbox"/> NONE                                   |

134. For **ALL** of the past 12 months, have you followed any type of **vegetarian diet**?

- NO (GO TO INTRODUCTION TO QUESTION 135)
- YES

134a. 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.)



**The next questions are about your use of fiber supplements or vitamin pills.**

135. Over the past 12 months, did you take any of the following types of **fiber or fiber supplements** on a regular basis (more than once per week for at least 6 of the last 12 months)? *(Mark all that apply.)*

- NO, didn't take any fiber supplements on a regular basis (GO TO QUESTION 136)
- YES, psyllium products (such as Metamucil, Fiberall, Serutan, Perdiem, Correctol)
- YES, methylcellulose/cellulose products (such as Citrucel, Unifiber)
- YES, Fibercon
- YES, Bran (such as wheat bran, oat bran, or bran wafers)

136. Over the past 12 months, did you take any **multivitamins**, such as One-a-Day-, Theragran-, or Centrum-type multivitamins (as pills, liquids, or packets)?

- NO (GO TO INTRODUCTION TO QUESTION 138)
- YES

137. How often did you take **One-a-day-, Theragran-, or Centrum-type** multivitamins?

- Less than 1 day per month
- 1–3 days per month
- 1–3 days per week
- 4–6 days per week
- Every day

137a. Does your **multivitamin** usually contain **minerals** (such as iron, zinc, etc.)?

- NO
- YES
- Don't know

137b. For how many years have you taken **multivitamins**?

- Less than 1 year
- 1–4 years
- 5–9 years
- 10 or more years



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

Over the past 12 months...

137c. Over the past 12 months, 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 138)

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.

Please include vitamins taken as part of an antioxidant supplement.

138. How often did you take **Beta-carotene** (NOT as part of a multivitamin in Question 137)?

NEVER (GO TO QUESTION 139)

- Less than 1 day per month
- 1–3 days per month
- 1–3 days per week
- 4–6 days per week
- Every day

138a. When you took **Beta-carotene**, about how much did you take in one day?

- Less than 10,000 IU
- 10,000–14,999 IU
- 15,000–19,999 IU
- 20,000–24,999 IU
- 25,000 IU or more
- Don't know

138b. For how many years have you taken **Beta-carotene**?

- Less than 1 year
- 1–4 years
- 5–9 years
- 10 or more years

Question 139 appears in the next column

139. How often did you take **Vitamin A** (NOT as part of a multivitamin in Question 137)?

NEVER (GO TO QUESTION 140)

- Less than 1 day per month
- 1–3 days per month
- 1–3 days per week
- 4–6 days per week
- Every day

139a. When you took **Vitamin A**, about how much did you take in one day?

- Less than 8,000 IU
- 8,000–9,999 IU
- 10,000–14,999 IU
- 15,000–24,999 IU
- 25,000 IU or more
- Don't know

139b. For how many years have you taken **Vitamin A**?

- Less than 1 year
- 1–4 years
- 5–9 years
- 10 or more years

140. How often did you take **Vitamin C** (NOT as part of a multivitamin in Question 137)?

NEVER (GO TO QUESTION 141)

- Less than 1 day per month
- 1–3 days per month
- 1–3 days per week
- 4–6 days per week
- Every day

140a. 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

140b. For how many years have you taken **Vitamin C**?

- Less than 1 year
- 1–4 years
- 5–9 years
- 10 or more years

Question 141 appears on the next page

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

**Over the past 12 months...**

141. How often did you take **Vitamin E** (**NOT** as part of a multivitamin in Question 137)?

- NEVER (GO TO QUESTION 142)
- Less than 1 day per month
- 1–3 days per month
- 1–3 days per week
- 4–6 days per week
- Every day

141a. 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

141b. For how many years have you taken **Vitamin E**?

- Less than 1 year
- 1–4 years
- 5–9 years
- 10 or more years

142. How often did you take **Calcium** or **Calcium-containing antacids** (**NOT** as part of a multivitamin in Question 137)?

- NEVER (GO TO QUESTION 143)
- Less than 1 day per month
- 1–3 days per month
- 1–3 days per week
- 4–6 days per week
- Every day

142a. When you took **Calcium** or **Calcium-containing antacids**, 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

142b. For how many years have you taken **Calcium** or **Calcium-containing antacids**?

- Less than 1 year
- 1–4 years
- 5–9 years
- 10 or more years

**The last two questions ask you about other supplements you took more than once per week.**

143. Please mark any of the following **single supplements** you took more than once per week (**NOT** as part of a multivitamin in Question 137):

- |   |  |
|---|--|
| <input type="checkbox"/> B-6            | <input type="checkbox"/> Folic acid/folate       |
| <input type="checkbox"/> B-complex      | <input type="checkbox"/> Glucosamine             |
| <input type="checkbox"/> Brewer's yeast | <input type="checkbox"/> Hydroxytryptophan (HTP) |
| <input type="checkbox"/> Cod liver oil  | <input type="checkbox"/> Iron                    |
| <input type="checkbox"/> Coenzyme Q     | <input type="checkbox"/> Niacin                  |
| <input type="checkbox"/> Fish oil       | <input type="checkbox"/> Selenium                |
| (Omega-3 fatty acids)                   | <input type="checkbox"/> Zinc                    |

144. Please mark any of the following **herbal** or **botanical supplements** you took more than once per week.

- |   |  |
|---|--|
| <input type="checkbox"/> Aloe Vera            | <input type="checkbox"/> Ginger                      |
| <input type="checkbox"/> Astragalus           | <input type="checkbox"/> Ginkgo biloba               |
| <input type="checkbox"/> Bilberry             | <input type="checkbox"/> Ginseng (American or Asian) |
| <input type="checkbox"/> Cascara sagrada      | <input type="checkbox"/> Goldenseal                  |
| <input type="checkbox"/> Cat's claw           | <input type="checkbox"/> Grapeseed extract           |
| <input type="checkbox"/> Cayenne              | <input type="checkbox"/> Kava, kava                  |
| <input type="checkbox"/> Cranberry            | <input type="checkbox"/> Milk thistle                |
| <input type="checkbox"/> Dong Kuai (Tangkwei) | <input type="checkbox"/> Saw palmetto                |
| <input type="checkbox"/> Echinacea            | <input type="checkbox"/> Siberian ginseng            |
| <input type="checkbox"/> Evening primrose oil | <input type="checkbox"/> St. John's wort             |
| <input type="checkbox"/> Feverfew             | <input type="checkbox"/> Valerian                    |
| <input type="checkbox"/> Garlic               | <input type="checkbox"/> Other                       |

**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.**

### Supplemental Physical Activity Questions

The following questions are to determine your level of physical activity, as bone density is affected by physical activity.

1. Are you currently involved in a regular exercise program? YES NO
2. If yes, what exercise activities are you involved in? (Check all that apply)  
 Biking     Karate     Kickboxing     Walking     Yoga  
 Jogging     Pilates     Swimming     Weight Training     Other \_\_\_\_\_
3. Over the last 20 years, have you participated in any of the following exercise activities? (Check all that apply)  
 Biking     Karate     Kickboxing     Walking     Yoga  
 Jogging     Pilates     Swimming     Weight Training     Other \_\_\_\_\_

If yes, please list the months and years of participation

\_\_\_\_\_

## APPENDIX C

### RAW DATA

#### 1. EXPLANATION OF RAW DATA

#### 2. RAW DATA TABLES

## EXPLANATION OF RAW DATA

PARTICIPANT ID:	Arbitrary identification number assigned for tracking purposes only
GENDER:	Identifies participant gender (M = Male, F = Female)
PPI USE:	Identifies participant as a “0” if they are NOT a PPI user and as a “1” if they are a PPI user
TREATMENT:	Identifies participant as a “control” if they are NOT a PPI user and as a “case” if they are a PPI user
PPI DOSE:	Dosage of PPI in milligrams
PPI DURATION:	Duration of PPI therapy in months
BIRTHDATE:	Participant birthdate in MM/DD/YY format
AGE:	Identifies participant age at time of data collection
HEIGHT:	Participant height in inches
WAIST:	Participant waist circumference in inches
HIP:	Participant hip circumference in inches
W:H RATIO:	Ratio of WAIST:HIP categories as listed above (no units)
THYROID:	Identifies participant as a “0” if they do NOT currently use prescription thyroid medication and as a “1” if they currently use prescription thyroid medication
H2RA:	Identifies participant as a “0” if they do NOT currently use Histamine-2 Receptor Antagonist (H2RA) medication and as a “1” if they currently use H2RA’s
CALCIUM (SUPPL):	Identifies participants as a “0” if they do NOT currently use calcium supplements and as a “1” if they currently use calcium supplements
VIT D (SUPPL):	Identifies participants as a “0” if they do NOT currently use vitamin D supplements and as a “1” if they currently use vitamin D supplements
MVI:	Identifies participants as a “0” if they do NOT currently use a multivitamin and as a “1” if they currently use a multivitamin
MAGNESIUM (SUPPL):	Identifies participants as a “0” if they do NOT currently use magnesium supplements and as a “1” if they currently use magnesium supplements

VIT A (SUPPL):	Identifies participants as a “0” if they do NOT currently use vitamin A supplements and as a “1” if they currently use vitamin A supplements
VIT C (SUPPL):	Identifies participants as a “0” if they do NOT currently use vitamin C supplements and as a “1” if they currently use vitamin C supplements
POTASSIUM (SUPPL):	Identifies participants as a “0” if they do NOT currently use potassium supplements and as a “1” if they currently use potassium supplements
DPX:	Lab value for urinary deoxypyridinoline in nmol
CREATININE:	Lab value for urinary creatinine in mg/dl
DPX:CREATININE RATIO:	Ratio of DPX:CREATININE categories as listed above (no units)
MG, URINE:	Lab value for urinary magnesium in mg/dl
DAY 1 – 24 HOUR URINE VOLUME:	Total volume of 24 hour urine collections in ml
24 HOUR MAGNESIUM, URINE:	Calculation of (MG, URINE)* (DAY 1 – 24 HOUR URINE VOLUME)/100 = mg magnesium per 24 hours
CA, URINE:	Lab value for urinary calcium in mg/dl
24 HOUR CALCIUM, URINE:	Calculation of (CA, URINE)* (DAY 1 – 24 HOUR URINE VOLUME)/100 = mg calcium per 24 hours
OSTEOCALCIN, SERUM:	Lab value for serum osteocalcin in ng/ml
25-HYDROXY VIT D:	Lab value for 25 hydroxy vitamin D in ng/ml
MG, SERUM:	Lab value for serum magnesium in mg/dl
PTH:	Lab value for parathyroid hormone in pg/ml
L1-L4 BMD:	Bone mineral density score for L1-L4 in grams/cm <sup>2</sup>
LEFT HIP BMD:	Bone mineral density score for left hip in grams/cm <sup>2</sup>
RIGHT HIP BMD:	Bone mineral density score for right hip in grams/cm <sup>2</sup>
MEAN HIP BMD:	Mean bone mineral density score averaging LEFT HIP BMD and RIGHT HIP BMD in grams/cm <sup>2</sup>
TISSUE:	Grams of tissue as reported from DXA full body scan reports

FAT:	Grams of fat as reported from DXA full body scan reports
LEAN:	Grams of lean as reported from DXA full body scan reports
BMC:	Grams of bone mineral content as reported from DXA full body scan reports
FAT FREE:	Grams of fat free mass as reported from DXA full body scan reports
ANDROID:	Percent android fat as reported from DXA full body scan reports
GYNOID:	Percent gynoid fat as reported from DXA full body scan reports
TOTAL BODY FAT:	Percent total fat as reported from DXA full body scan reports
A/G RATIO:	Ratio of ANDROID:GYNOID categories as listed above (no units)
BMI:	Body mass index (BMI) as reported from DXA full body scan reports
TOTAL MASS:	Total body mass in kilograms as reported from DXA full body scan reports
FOOD ENERGY:	Output from DHQ for daily energy intake in calories
PROTEIN:	Output from DHQ for daily protein intake in grams
TOTAL FAT:	Output from DHQ for daily fat intake in grams
CARBOHYDRATE:	Output from DHQ for daily carbohydrate intake in grams
VITAMIN A IU:	Output from DHQ for daily vitamin A intake in international units
VITAMIN A RE:	Output from DHQ for daily vitamin A intake in retinol equivalents
TOTAL VITAMIN A ACTIVITY:	Output from DHQ for daily vitamin A intake in retinol activity equivalents
VITAMIN C:	Output from DHQ for daily vitamin C intake in milligrams
CALCIUM:	Output from DHQ for daily calcium intake in milligrams
PHOSPHORUS:	Output from DHQ for daily phosphorus intake in milligrams
MAGNESIUM:	Output from DHQ for daily magnesium intake in milligrams
SODIUM:	Output from DHQ for daily sodium intake in milligrams
POTASSIUM:	Output from DHQ for daily potassium intake in milligrams
CAFFEINE:	Output from DHQ for daily caffeine intake in milligrams



VITAMIN D (CALCIFEROL):	Output from DHQ for daily vitamin D intake in micrograms
VITAMIN D (IU):	Output from DHQ for daily vitamin D intake in international units
SUPP VITAMIN A:	Output from DHQ for daily supplemental vitamin A intake in retinol activity equivalents
SUPP VITAMIN C:	Output from DHQ for daily supplemental vitamin C intake in milligrams
SUPP CALCIUM:	Output from DHQ for daily supplemental calcium intake in milligrams
SUPP MAGNESIUM:	Output from DHQ for daily supplemental magnesium intake in milligrams
SUPP VITAMIN D:	Output from DHQ for daily supplemental vitamin D intake in international units
AEROBIC CURRENT:	Identifies participants as a “0” if they are NOT currently participating in an aerobic exercise program for a minimum of 30 minutes per day, 3 days per week and as “1” if they are currently participating in an aerobic exercise program for a minimum of 30 minutes per day, 3 days per week.
RESISTANCE CURRENT:	Identifies participants as a “0” if they are NOT currently participating in a resistance training program for a minimum of 2 days per week and as “1” if they are currently participating in a resistance training program for a minimum of 2 days per week.
AEROBIC PAST:	Identifies participants as a “0” if they have NOT participated in any aerobic exercise programs consistently over the last 20 years and as “1” if they have participated in any aerobic exercise programs consistently over the last 20 years.
RESISTANCE PAST:	Identifies participants as a “0” if they have NOT participated in any resistance training programs consistently over the last 20 years and as “1” if they have participated in any resistance training programs consistently over the last 20 years.
TOTAL VITAMIN A:	Calculated total vitamin A intake in retinol activity equivalents (TOTAL VITAMIN A ACTIVITY + SUPP VITAMIN A)
TOTAL VITAMIN C:	Calculated total vitamin C intake in milligrams (VITAMIN C + SUPP VITAMIN C)
TOTAL CALCIUM:	Calculated total calcium intake in milligrams (CALCIUM + SUPP CALCIUM)

TOTAL MAGNESIUM: Calculated total magnesium intake in milligrams (MAGNESIUM + SUPP MAGNESIUM)

TOTAL VITAMIN D: Calculated total vitamin D intake in international units (VITAMIN D CALCIFEROL + SUPP VITAMIN D)

SPINE: Category of T-score from lumbar spine DXA scans (Normal, Osteopenia, Osteoporosis)

HIP: Category of T-score from hip DXA scans (Normal, Osteopenia, Osteoporosis)

SPINE HIP: Worst category from SPINE and HIP above (Osteoporosis < Osteopenia < Normal)

PPI Project Raw Data

Participant ID	Gender	PPI Use	treatment	PPI Dose	PPI Duration	Birthdate	age	Height	Waist
				mg	months	MM/DD/YY	years	inches	inches
143778	F	0	control	0	0	05/05/33	76.00	64.5	34
156191	F	0	control	0	0	10/19/38	70.00	64	31.25
186859	F	0	control	0	0	06/24/27	82.00	62.5	39.25
194554	F	0	control	0	0	03/26/28	81.00	60.75	33.75
200004	M	1	case	20	12	06/01/44	65.00	70.75	52.25
216549	M	1	case	20	120	11/20/52	56.00	72	45
230453	F	0	control	0	0	02/05/48	61.00	67.25	31.75
230499	M	1	case	40	30	09/13/57	52.00	68.75	42
255516	M	1	case	20	180	05/15/47	62.00	68.25	38.5
312030	F	0	control	0	0	09/02/53	56.00	60.75	35.75
339596	F	0	control	0	0	10/10/51	58.00	61	26.5
352370	F	0	control	0	0	10/01/48	61.00	61	34.75
358284	F	0	control	0	0	03/07/43	66.00	62.5	31.75
376015	F	0	control	0	0	04/09/37	72.00	62.25	29.5
398933	F	0	control	0	0	03/15/50	59.00	66.25	47
432753	M	0	control	0	0	02/11/47	62.00	71.25	41.75
464561	M	1	case	20	144	12/21/45	63.00	68.5	45.25
509383	M	0	control	0	0	01/01/47	62.00	69	36.75
569482	M	1	case	20	120	08/02/60	49.00	74	42.5
587755	F	0	control	0	0	02/24/47	62.00	61.25	33.25
609593	M	1	case	20	4	08/19/62	47.00	70.5	34
640807	M	1	case	30	96	09/11/37	72.00	65.5	43
646395	M	0	control	0	0	02/01/62	47.00	66.5	31
647641	M	1	case	20	60	11/07/54	54.00	76.5	42.75
698799	F	0	control	0	0	03/23/52	57.00	63.25	39.75
708771	F	0	control	0	0	02/09/57	52.00	62.25	28.5
712709	F	0	control	0	0	04/10/54	55.00	63	33.5
717551	M	0	control	0	0	02/20/52	57.00	66.5	40
720105	F	1	case	40	48	02/27/52	57.00	64.5	44.5
747737	F	1	case	20	60	05/14/38	71.00	62.25	38.5
758002	M	0	control	0	0	05/08/53	56.00	68.5	42.25
760342	F	0	control	0	0	06/11/35	74.00	60.5	34
765918	M	1	case	40	156	06/15/38	71.00	65.5	39.5
775008	M	1	case	20	180	01/03/66	43.00	75.25	42
777907	M	1	case	20	72	03/29/44	65.00	69.5	43.75
784819	M	1	case	30	18	05/24/35	74.00	71.5	33.25
788789	M	1	case	30	120	03/21/52	57.00	68.25	46
806492	M	1	case	20	120	11/25/34	74.00	64.75	40.25
812964	M	1	case	20	84	02/26/37	72.00	72.75	44
833746	M	1	case	20	60	12/07/21	87.00	66.75	42.75
835846	M	1	case	40	2	10/13/53	56.00	72.5	37
836130	M	1	case	40	60	11/17/48	60.00	71	36.5
839855	F	1	case	20	24	10/12/30	79.00	64.5	42
853838	M	1	case	20	72	06/19/39	70.00	66	42.5
865646	F	1	case	40	84	12/08/49	59.00	64	31.5
875236	F	0	control	0	0	10/03/50	59.00	63	35.25
875636	M	1	case	40	36	09/01/59	50.00	72	52.25
920971	M	1	case	40	36	02/22/39	70.00	68	43.5
925821	M	0	control	0	0	06/08/68	41.00	70.75	31.75

PPI Project Raw Data

Participant ID	Gender	PPI Use	treatment	PPI Dose	PPI Duration	Birthdate	age	Height	Waist
				mg	months	MM/DD/YY	years	inches	inches
950103	M	1	case	40	60	12/06/44	64.00	76	48.75
980834	F	1	case	20	120	08/24/47	62.00	60.25	44
985282	M	1	case	10	60	03/18/44	65.00	65	43.75
992966	M	1	case	30	300	03/25/45	64.00	70.25	41.25
998751	F	1	case	40	240	06/20/36	73.00	64	35.5

PPI Project Raw Data

Participant ID	Hips	W:H	Thyroid	H2RA	Calcium	Vit D	MVI	Magnesium	Vit A
	inches		(Rx)		(Suppl)	(Suppl)		(Suppl)	(Suppl)
143778	42.5	0.80	0	0	0	0	0	0	0
156191	39	0.80	0	0	0	0	0	0	0
186859	39.25	1.00	0	0	0	0	0	0	0
194554	40.5	0.83	1	0	0	0	0	0	0
200004	51	1.02	0	0	0	0	1	0	0
216549	46.25	0.97	0	0	0	0	0	0	0
230453	40.25	0.79	0	0	1	0	1	1	0
230499	42.5	0.99	0	0	0	0	0	0	0
255516	43.75	0.88	0	0	0	0	1	0	0
312030	41.5	0.86	1	1	0	0	1	0	0
339596	37.5	0.71	0	0	1	0	1	1	1
352370	45.75	0.76	0	0	0	0	1	0	0
358284	42.5	0.75	0	0	0	0	0	0	0
376015	38.25	0.77	0	0	0	0	1	0	0
398933	56.5	0.83	0	0	0	0	1	0	0
432753	44	0.95	0	0	0	0	1	0	0
464561	45.25	1.00	0	0	0	0	1	0	0
509383	38	0.97	0	0	0	0	0	0	0
569482	45.5	0.93	0	0	0	0	0	0	0
587755	41.75	0.80	1	0	1	0	1	0	0
609593	40.25	0.84	0	0	0	0	0	0	0
640807	42	1.02	0	0	1	0	0	0	0
646395	37.25	0.83	0	0	1	1	1	0	0
647641	44.5	0.96	0	0	0	0	1	0	0
698799	43	0.92	0	0	0	0	0	0	0
708771	36.5	0.78	0	0	0	1	0	1	0
712709	42	0.80	0	0	0	0	0	0	0
717551	44	0.91	0	1	0	0	1	0	0
720105	48.5	0.92	0	0	0	0	0	0	0
747737	45.5	0.85	1	0	0	0	1	0	0
758002	41.5	1.02	0	0	0	0	0	0	0
760342	38.5	0.88	0	0	1	0	1	0	0
765918	41.25	0.96	0	0	0	0	0	0	0
775008	44	0.95	0	0	0	0	0	0	0
777907	42.25	1.04	0	0	0	0	0	0	0
784819	39.5	0.84	0	0	1	1	0	0	0
788789	44.25	c	0	0	0	1	1	0	0
806492	38.25	1.05	1	0	0	0	0	0	0
812964	46	0.96	0	1	0	0	1	0	0
833746	43.25	0.99	0	0	0	0	0	0	0
835846	42	0.88	0	0	0	0	0	0	0
836130	41	0.89	0	0	0	0	1	0	0
839855	48.5	0.87	0	0	0	0	1	0	0
853838	42.75	0.99	0	0	0	0	0	0	0
865646	45.25	0.70	0	0	1	0	1	0	0
875236	41.5	0.85	0	0	1	0	0	0	0
875636	52	1.00	0	0	0	0	1	0	0
920971	46.5	0.94	0	0	0	0	1	0	0
925821	37.25	0.85	0	0	0	0	0	0	0

PPI Project Raw Data

Participant ID	Hips	W:H	Thyroid	H2RA	Calcium	Vit D	MVI	Magnesium	Vit A
	inches		(Rx)		(Suppl)	(Suppl)		(Suppl)	(Suppl)
950103	47.75	1.02	0	0	0	0	1	0	0
980834	51	0.86	0	0	0	0	0	0	0
985282	44.25	0.99	0	0	1	0	1	0	0
992966	45.5	0.91	0	0	0	0	1	0	0
998751	42	0.85	0	0	0	0	1	0	0

PPI Project Raw Data

Participant ID	Vit C (Suppl)	Potassium (Suppl)	DPX (nmol)	Creatinine (mg/dl)	DPX/Creatinine Ratio (0mol DPX/mmol Cr)	Mg, urine (mg/dl)
143778	0	0	143	44.9	36	2.7
156191	0	0	121	111.4	12.3	8.3
186859	0	0	23.1	22	11.9	1.1
194554	0	0	14.3	31.5	5.1	5.5
200004	0	0	80.7	127.2	7.2	8.6
216549	0	0	60.2	127.8	5.3	7.6
230453	1	0	22	74.4	3.3	10.1
230499	0	0	36.7	129.3	3.2	6.6
255516	0	0	103	105.1	11.1	8.6
312030	0	0	42.1	28.4	16.8	6.7
339596	0	0	65.1	73.3	10	8.7
352370	0	0	22.1	58.5	4.3	5.3
358284	0	0	38.5	47.3	9.2	2.8
376015	0	0	121	32	42.7	3.7
398933	0	0	46	62.8	8.3	7.8
432753	0	0	59.8	171.1	3.9	6.7
464561	0	0	114	162.5	7.9	8.9
509383	0	0	40.7	107.2	4.3	6.6
569482	0	0	61.3	175	4	10.3
587755	0	0	13.5	35.3	4.3	6.7
609593	0	0	38.5	91.3	4.8	5.5
640807	0	0	41.9	95.2	5	5.7
646395	0	0	50.4	85.1	6.7	13.2
647641	0	0	118	273.3	4.9	6.3
698799	0	0	35.5	65.2	6.2	4.1
708771	0	0	32.3	73.4	5	14.2
712709	0	0	124	90.5	15.5	3.6
717551	1	0	41.2	79.7	5.8	9
720105	0	0	73.3	161	5.1	5.5
747737	0	0	28	69	4.6	8.7
758002	0	0	83.2	183.5	5.1	17
760342	1	0	37.4	39.3	10.8	7.4
765918	0	0	130	96.6	15.2	4.2
775008	0	0	42.9	136.2	3.6	6.6
777907	0	0	33.6	94.1	4	2.8
784819	0	0	70.1	93.3	8.5	14
788789	0	0	63.1	123	5.8	9.5
806492	0	0	87.8	158.9	6.2	11.2
812964	0	0	23.7	73.2	3.7	3.4
833746	0	0	86.5	59.9	16.3	3.3
835846	0	0	143	186.6	8.7	10
836130	1	0	87.8	164.4	6	10.1
839855	0	0	82.5	55.1	16.9	1.9
853838	0	0	99.8	118.8	9.5	2.9
865646	0	0	95.8	62.7	17.3	6.1
875236	0	0	26	38.1	7.7	2.6
875636	1	0	118	118.3	11.3	3.1
920971	0	0	66.6	146.1	5.2	9.4
925821	0	0	34.3	56	6.9	4.5

PPI Project Raw Data

Participant ID	Vit C (Suppl)	Potassium (Suppl)	DPX (nmol)	Creatinine (mg/dl)	DPX/Creatinine Ratio (0mol DPX/mmol Cr)	Mg, urine (mg/dl)
950103	0	0	123	135.1	10.3	5.9
980834	0	0	62.4	112.1	6.3	8.9
985282	0	1	23.5	128	2.1	6.1
992966	0	0	65.3	82.2	9	7.1
998751	0	0	94.5	83.8	12.7	8.1



PPI Project Raw Data

Participant ID	Day 1 – 24 hr urine volume (ml)	24 hr Mg, urine (mg/24 hr)	Ca, urine (mg/dl)	24 hr Ca, urine (mg/24 hr)
143778	2200	59.4	7.5	165
156191	640	53.12	16.8	107.52
186859			1.6	
194554	1750	96.25	2.7	47.25
200004	1575	135.45	9	141.75
216549	1800	136.8	16.4	295.2
230453	1200	121.2	18.8	225.6
230499	1450	95.7	22.5	326.25
255516	1575	135.45	7.5	118.125
312030	1600	107.2	7.9	126.4
339596	1000	87	20.3	203
352370	1500	79.5	14.3	214.5
358284			0.9	
376015	2150	79.55	3.7	79.55
398933	2500	195	25.7	642.5
432753	1250	83.75	15	187.5
464561	1325	117.925	30.9	409.425
509383	1100	72.6	12.1	133.1
569482	1250	128.75	17	212.5
587755			13.5	
609593	1875	103.125	17.9	335.625
640807	1500	85.5	3.3	49.5
646395	1500	198	21.1	316.5
647641	1000	63	7.1	71
698799	1575	64.575	7.3	114.975
708771	575	81.65	18.8	108.1
712709	1175	42.3	17.9	210.325
717551	1525	137.25	6.9	105.225
720105	1050	57.75	13.6	142.8
747737	1625	141.375	7.3	118.625
758002	1100	187	19	209
760342	2100	155.4	7.7	161.7
765918	1350	56.7	12.7	171.45
775008	1150	75.9	9.3	106.95
777907	1825	51.1	4.9	89.425
784819	1375	192.5	4.9	67.375
788789	1325	125.875	33.6	445.2
806492	725	81.2	11.5	83.375
812964	800	27.2	9.5	76
833746	1400	46.2	0.7	9.8
835846			32	
836130	925	93.425	16.3	150.775
839855	1375	26.125	10.6	145.75
853838	1075	31.175	14.5	155.875
865646	1500	91.5	13	195
875236	2525	65.65	3.7	93.425
875636			15.7	
920971	1450	136.3	20.5	297.25
925821	2925	131.625	12.9	377.325

PPI Project Raw Data

<b>Participant ID</b>	<b>Day 1 – 24 hr urine volume</b>	<b>24 hr Mg, urine</b>	<b>Ca, urine</b>	<b>24 hr Ca, urine</b>
	<b>(ml)</b>	<b>(mg/24 hr)</b>	<b>(mg/dl)</b>	<b>(mg/24 hr)</b>
950103	1575	92.925	11.9	187.425
980834	700	62.3	22.4	156.8
985282	1150	70.15	7.5	86.25
992966	2250	159.75	12.4	279
998751	725	58.725	4.8	34.8

PPI Project Raw Data

Participant ID	Osteocalcin, serum (ng/ml)	25-hydroxy Vit D (ng/ml)	Mg, serum (mg/dl)	PTH (pg/ml)	L1-L4_BMD g/cm <sup>2</sup>
143778	18.6	22.8	2.2	36	1.381
156191	19.1	12.3	1.9	81	0.931
186859	27.9	18.1	2.1	37	0.969
194554	20.7	18.4	2.2	39	0.901
200004	23.9	26	1.9	94	1.514
216549	37.4	40.7	2.1	33	1.266
230453	36.6	28	2.2	56	0.979
230499	32.6	17.7	2.2	43	1.016
255516	32.6	21	1.8	29	1.223
312030	24.2	31.4	2	23	1.111
339596	36.1	42.7	2.3	34	1.051
352370	27.9	10	2	40	1.046
358284	19.5	22.9	2	45	0.959
376015	44.1	24.6	2	86	0.769
398933	15.4	16.5	2	95	1.117
432753	23	17.9	2.1	36	1.359
464561	22	13.3	1.9	31	1.220
509383	19.5	16.6	2	62	1.088
569482	16.6	15.4	2.1	27	1.218
587755	31.5	34.5	2.1	41	1.059
609593	21.4	24.2	2.2	42	1.015
640807	18.7	25.2	2.1	47	0.898
646395	19.4	49.7	2.1	25	0.981
647641	28.1	43.9	2.1	24	1.228
698799	26.9	14	2.2	48	1.094
708771	30.5	44	1.9	27	1.075
712709	24.1	30.6	2.2	40	1.102
717551		20.9	2.1	50	1.071
720105		24.1	1.9	45	1.317
747737	31.2	34.7	1.9	55	1.280
758002	30.9	16.9	1.9	41	1.265
760342	11.7	27.2	2.2	21	1.292
765918	13.1	14.6	2	36	1.255
775008	30	22.1	2	20	1.460
777907	13.8	10.9	2.1	31	1.575
784819	60.9	58	2.1	49	1.116
788789	24.2	24.6	1.9	18	1.392
806492	23.2	61.8	2	19	1.610
812964	34.2	35.7	2.4	129	1.169
833746	12	34	2.1	69	1.376
835846	22	32	2.1	20	1.436
836130	24.4	22.1	2.1	37	1.191
839855	42.5	23.1	1.9	54	1.609
853838	23	21.5	2.2	28	1.455
865646	16.7	32.4	2.3	48	1.093
875236	28.1	20.2	2	37	1.037
875636	18.8	19.6	1.8	37	0.931
920971		45.5	2.1	49	1.338
925821	13.2	31.1	2.1	41	1.249

PPI Project Raw Data

Participant ID	Osteocalcin, serum (ng/ml)	25-hydroxy Vit D (ng/ml)	Mg, serum (mg/dl)	PTH (pg/ml)	L1-L4_BMD g/cm <sup>2</sup>
950103	31.6	28.6	1.8	39	1.156
980834	20.8	11.2	2.2	75	1.000
985282	8	25.6	2.1	17	1.226
992966	12.1	19.4	2.5	45	1.363
998751	34.7	25.9	1.8	40	1.335

PPI Project Raw Data

Participant ID	Left_Hip_BMD	Right_Hip_BMD	Mean_Hip_BMD	Tissue	Fat	Lean	BMC
	g/cm <sup>2</sup>	g/cm <sup>2</sup>	g/cm <sup>2</sup>	g	g	g	g
143778	1.207	0.459		68,480	29,396	39,084	2,902
156191	0.598	0.059	0.593	53,997	18,606	35,391	1,781
186859	0.745	0.727	0.736	62,581	25,888	36,693	2,052
194554	0.687	2.413		55,499	22,148	33,351	1,710
200004	1.115	1.088	1.102	129,649	54,878	74,771	4,289
216549	1.201	1.240	1.220	116,746	47,746	69,001	4,114
230453	0.753	0.763	0.758	64,014	25,086	38,928	2,151
230499	0.819	0.826	0.822	91,251	29,554	61,697	3,106
255516	1.035	1.002	1.019	81,850	26,758	55,092	3,195
312030	0.857	0.918	0.888	62,977	31,549	31,428	2,412
339596	0.884	0.901	0.892	46,514	15,279	31,235	1,951
352370	0.859	0.861	0.860	67,537	33,120	34,417	2,343
358284	0.866	0.882	0.874	65,604	27,381	38,223	2,086
376015	0.646	0.600	0.623	52,476	14,743	37,732	1,758
398933	0.873	0.864	0.868	121,512	57,599	63,913	2,548
432753	1.120	1.046	1.083	91,129	33,526	57,603	4,002
464561	0.830	0.949	0.889	95,677	32,497	63,181	3,074
509383	0.855	0.888	0.871	68,609	18,383	50,226	2,684
569482	0.991	0.975	0.983	93,938	31,517	62,422	3,409
587755	0.732	0.690	0.711	60,229	21,199	39,030	2,035
609593	0.942	0.947	0.944	69,355	12,679	56,677	2,927
640807	0.823	0.794	0.809	80,451	24,916	55,535	2,416
646395	0.938	0.919	0.928	60,460	14,051	46,409	2,438
647641	1.259	1.259	1.259	102,404	30,275	72,130	4,017
698799	1.000	0.942	0.971	79,340	34,250	45,090	2,522
708771	0.852	0.846	0.858	51,305	14,454	36,851	2,234
712709	0.928	0.887	0.908	62,976	24,097	38,879	2,306
717551	0.986	0.920	0.953	77,191	22,308	54,883	2,619
720105	1.044	1.034	1.039	88,258	39,852	48,406	2,542
747737	0.940	0.954	0.947	75,875	37,851	38,025	2,936
758002	1.232	1.259	1.245	90,342	22,970	67,372	3,701
760342	1.068	1.056	1.062	59,133	25,403	33,731	2,372
765918	0.955	0.947	0.951	74,498	22,865	51,633	2,959
775008	1.177	1.132	1.155	97,570	28,115	69,454	4,217
777907	1.137	1.095	1.116	91,350	29,222	62,128	3,600
784819	0.803	0.804	0.822	65,868	10,818	55,050	3,105
788789	1.046	1.005	1.025	94,176	35,358	58,818	3,523
806492	1.059	1.013	1.036	68,936	19,519	49,417	2,905
812964	1.044	1.071	1.058	92,653	35,786	56,867	3,257
833746				75,217	28,329	46,887	2,664
835846	1.224	1.152	1.188	81,195	20,143	61,052	3,851
836130	0.948	0.874	0.911	73,844	21,120	52,724	2,991
839855	1.284	1.320	1.302	87,375	42,344	45,031	3,386
853838	0.787	0.794	0.791	83,339	27,723	55,617	2,829
865646	0.951	0.894	0.922	65,885	28,314	37,571	2,399
875236	0.879	0.875	0.877	65,729	27,608	38,120	2,433
875636	0.896	0.933	0.914	132,138	52,530	79,608	3,088
920971	0.825	0.802	0.814	95,544	31,578	63,966	2,991
925821	1.117	1.089	1.103	71,743	10,598	61,146	3,276

PPI Project Raw Data

<b>Participant ID</b>	<b>Left_Hip_BMD</b>	<b>Right_Hip_BMD</b>	<b>Mean_Hip_BMD</b>	<b>Tissue</b>	<b>Fat</b>	<b>Lean</b>	<b>BMC</b>
	<b>g/cm<sup>2</sup></b>	<b>g/cm<sup>2</sup></b>	<b>g/cm<sup>2</sup></b>	<b>g</b>	<b>g</b>	<b>g</b>	<b>g</b>
950103	0.847	0.906	0.877	117,602	41,884	75,717	4,302
980834	0.792	0.836	0.814	79,885	43,030	36,855	1,952
985282	0.998	0.968	0.983	75,513	21,960	53,553	2,764
992966	1.236	1.138	1.187	102,783	34,627	68,156	3,823
998751	1.176	1.188	1.182	65,442	30,681	34,761	2,801

PPI Project Raw Data

Participant ID	Fat_Free	Android	Gynoid	Total_Body_Fat	A/G_Ratio	BMI	Total_Mass
	g	%	%	%			kg
143778	41,985	44.00	49.20	42.90	0.89	27.20	71.40
156191	37,172	41.50	43.60	34.50	0.95	21.60	55.80
186859	38,745	49.10	45.60	41.40	1.08	26.00	64.60
194554	35,060	38.40	50.60	39.90	0.76	25.00	57.20
200004	79,060	54.40	43.50	42.30	1.25	41.70	133.90
216549	73,115	56.00	39.30	40.90	1.43	36.30	120.90
230453	41,079	37.00	49.30	39.20	0.75	23.20	66.20
230499	64,803	44.20	36.20	32.40	1.22	31.00	94.40
255516	58,287	39.10	39.30	32.70	1.00	28.30	85.00
312030	33,840	56.30	55.40	50.10	1.02	28.00	65.40
339596	33,186	35.20	43.80	32.80	0.80	20.40	48.50
352370	36,760	54.70	57.90	49.00	0.94	29.50	69.90
358284	40,309	44.90	51.40	41.70	0.87	27.30	67.70
376015	39,490	21.30	41.60	28.10	0.51	21.90	54.20
398933	66,460	50.10	56.50	47.40	0.89	45.60	124.10
432753	61,605	45.20	38.10	36.80	1.18	29.30	95.10
464561	66,254	45.90	34.50	34.00	1.33	33.00	98.80
509383	52,910	34.40	33.30	26.80	1.03	23.30	71.30
569482	65,831	46.10	37.20	33.60	1.24	27.70	97.30
587755	41,065	33.80	44.30	35.20	0.76	26.30	62.30
609593	59,604	22.60	26.50	18.30	0.85	22.60	72.30
640807	57,951	44.70	28.30	30.00	1.58	30.00	82.90
646395	48,847	32.40	30.30	23.20	1.07	22.00	62.90
647641	76,146	39.10	31.90	29.60	1.23	28.20	106.40
698799	47,612	53.00	42.50	43.20	1.25	31.60	81.90
708771	39,085	24.70	38.40	28.20	0.64	21.60	53.50
712709	41,185	45.20	43.10	38.30	1.05	25.80	65.30
717551	57,502	40.70	29.50	28.90	1.38	28.10	79.80
720105	50,949	55.40	43.10	45.20	1.28	34.50	90.80
747737	40,961	53.20	55.40	49.90	0.96	32.30	78.80
758002	71,073	37.50	26.20	25.40	1.43	31.00	94.00
760342	36,103	49.00	47.00	43.00	1.04	26.20	61.50
765918	54,591	41.60	31.20	30.70	1.33	28.20	77.50
775008	73,672	38.20	31.50	28.80	1.21	27.80	101.80
777907	65,727	42.80	29.90	32.00	1.43	30.50	94.90
784819	58,156	19.50	22.70	16.40	0.86	20.90	69.00
788789	62,341	49.30	40.40	37.50	1.22	33.00	97.70
806492	52,321	36.30	32.70	28.30	1.11	26.70	71.80
812964	60,124	49.60	38.40	38.60	1.29	28.30	95.90
833746	49,551	49.00	38.00	37.70	1.29	28.10	77.90
835846	64,903	34.10	25.30	24.80	1.35	25.20	85.00
836130	55,715	42.40	29.50	28.60	1.44	23.60	76.80
839855	48,418	54.70	54.50	48.50	1.00	34.10	90.80
853838	58,446	48.30	34.10	33.30	1.41	30.70	86.20
865646	39,970	45.80	52.10	43.00	0.88	26.20	68.30
875236	40,553	39.80	53.40	42.00	0.74	26.90	68.20
875636	82,696	50.60	42.50	39.80	1.19	40.60	135.20
920971	66,958	43.20	35.40	33.10	1.22	33.10	98.50
925821	64,421	21.70	18.40	14.80	1.18	22.90	75.00

PPI Project Raw Data

Participant ID	Fat_Free	Android	Gynoid	Total_Body_Fat	A/G_Ratio	BMI	Total_Mass
	g	%	%	%			kg
950103	80,019	46.00	38.00	35.60	1.21	33.00	121.90
980834	38,807	61.30	56.00	53.90	1.09	35.80	81.80
985282	56,317	39.70	29.90	29.10	1.33	28.80	78.30
992966	71,979	45.20	37.60	33.70	1.20	33.40	106.60
998751	37,563	49.30	55.10	46.90	0.89	26.20	68.20



PPI Project Raw Data

Participant ID	Food energy	Protein	Total fat	Carbohydrate	Vitamin A IU	Vitamin A RE
	kcal	g	g	g	IU (CSFII)	mcg RE (CSFII)
143778	2341.25	105.79	96.38	276.58	27787.19	2971.95
156191	1063.82	43.23	35.1	153.25	8062.3	929.05
186859	1871.02	85.38	72.4	231.71	12251.46	1725.67
194554	1048.37	33.04	37.46	156.34	21785.77	2450.67
200004	2743.37	100.78	114.41	345.83	5405.1	1016.68
216549	2142.09	90.61	71.22	292.96	7341.36	1370.2
230453	937.25	32.29	42.6	120.73	4926.06	521.36
230499	2369.35	83.64	93.09	312.96	7104.28	1121.84
255516	1888.75	59.24	59.07	295.04	5999.8	1164.76
312030	1610.36	75.54	48.52	226.12	11488.02	1922.38
339596	1213.16	48.02	41.77	170.45	4077.66	870.97
352370	1081.36	58.34	33.72	138.1	3265.86	792.05
358284	566.91	22.92	18.58	81.99	5790.52	677.32
376015	918.97	33.44	31.75	131.88	7151.94	820.67
398933	2075.07	77.99	83.69	261.58	7106.06	1280.81
432753	1755.52	75.54	76.51	206.48	12575.81	1701.56
464561	3187.45	118.11	105.7	457.46	11982.44	2066.82
509383	1954.82	88.13	65.47	267.89	26069.99	3073.22
569482	2630.53	92.32	117.78	316.2	9695.95	1403.61
587755	2008.57	106.27	54.01	291.35	23404.87	2711.32
609593	2328.08	91.41	89.25	305.29	19192.2	2311.79
640807	1449.4	53.52	58.1	186.79	4703.18	727.77
646395	1959.96	73.29	72.39	262.51	10414.75	1411.36
647641	3139.05	124.24	127.81	392.97	24318.38	3471.3
698799	1258.4	38.16	43.59	190.77	9514.65	1081.23
708771	1047.83	19.66	45.66	148.47	33025.95	3355.05
712709	2450.61	130.64	91.18	289.53	23994.52	2836.1
717551	3288.18	124.98	114.9	460.16	23617.29	2855.09
720105	707.43	33.06	22.38	98.47	4859.99	616.04
747737	1755.49	74.27	46.62	277.99	7112.67	1188.22
758002	1771.6	49.43	50.15	294.89	13893.47	1644.1
760342	778.05	32.43	35.74	90.28	7735.92	850.94
765918	1504.19	39.55	38.88	257.26	3803.94	506.31
775008	2828.67	107.3	100.12	387.61	11257.99	1790.63
777907	2334.54	131.8	119.69	187.72	4366.21	647.01
784819	2588.15	102.24	88.61	365.47	10972.28	1764.63
788789	2419.38	92.46	93.08	320.86	6140.04	1253.65
806492	1310.09	46.15	43.55	193.85	3975	670.87
812964	1859.25	63.64	64.34	270.51	10665.01	1333.98
833746	1966.49	64.87	86.79	246.93	5529.5	894.82
835846	2163.16	69.75	87.26	287.69	8377.97	1190.28
836130	1290.48	52.88	41.61	184.03	9115.87	1250.61
839855	1226.56	45.68	46.06	170.4	4141.49	738.03
853838	1625.41	63.22	74.37	181.07	5933.99	815.96
865646	2627.17	108.52	87.09	368.72	15915.91	1986.51
875236	2183.89	97.01	63.56	324.14	14395.44	1850.04
875636	700.03	35.93	29.07	77.23	4432.91	720.39
920971	1571.78	66.87	61.27	195.83	6297.61	1033.18
925821	2187.74	88.3	87.79	274.12	9075.38	1612.68

PPI Project Raw Data

<b>Participant ID</b>	<b>Food energy</b>	<b>Protein</b>	<b>Total fat</b>	<b>Carbohydrate</b>	<b>Vitamin A IU</b>	<b>Vitamin A RE</b>
	<b>kcal</b>	<b>g</b>	<b>g</b>	<b>g</b>	<b>IU (CSFII)</b>	<b>mcg RE (CSFII)</b>
950103	4555.5	169.17	191.41	558.58	11723.57	2431.29
980834	2021.37	92.85	64.97	279.36	12752.26	1766.18
985282	2165.38	85.65	94.15	256.64	11862.56	1617.69
992966	2336.11	97.06	94.43	293.53	11819.38	1632.5
998751	1995.61	71.78	77.13	272.22	12128.23	1556.95

PPI Project Raw Data

Participant ID	Total Vitamin A Activity	Vitamin C	Calcium	Phosphorus	Magnesium
	mcg RAE (NDS-R)	mg	mg	mg	mg
143778	1449.26	217.42	822.92	1434	360.79
156191	485.13	167.22	517.33	735.16	181.32
186859	1208.78	255.48	1392.51	1579.64	321.35
194554	1096.97	108.3	447.37	658.91	259.17
200004	868.98	81	1111.21	1800.85	446.75
216549	1119.45	132.69	1815.48	1977.12	307.31
230453	252.28	117.27	288.13	663.14	249.13
230499	797.69	127.45	877.01	1382.84	310.12
255516	894.7	226.27	797.25	1172.37	363.13
312030	1403.39	144	1634.6	1594.23	444.09
339596	655.93	34.89	976.92	1141.76	235.76
352370	657.6	47.7	942.18	1063.18	233.85
358284	358.58	37.53	322.74	421.26	92.43
376015	427.25	101.69	409.81	588.75	152.89
398933	1065.08	79.64	1370.78	1526.01	349.19
432753	1028.7	101.14	762.45	1354.04	389.48
464561	1659.36	157.81	2519.51	2540.19	500.97
509383	1500.97	122.71	1093.24	1604.8	372.13
569482	1011.72	122.56	1021.97	1574	353.85
587755	1339.04	321.87	1155.06	1744.72	531.01
609593	1213.92	142.39	1018.95	1518.47	364.98
640807	526.59	56.27	491.28	899.75	225.01
646395	811.69	116.78	756.15	1245.71	265.93
647641	2163.6	260.65	1801.99	2321.88	568.78
698799	535.68	152.35	368	760.46	274.45
708771	1425.6	50.41	266.49	378.24	160.65
712709	1489.25	177.63	1095.7	1861.55	392.71
717551	1589.61	312.53	1479.03	2381.37	592.03
720105	321.2	56.37	283.43	514.36	120.58
747737	919.38	86.85	1706.27	1833.38	383
758002	815.73	133.49	565.54	961.57	281.78
760342	435.55	159.93	364.23	529.59	149.24
765918	342.41	69.07	463.24	807.07	161.44
775008	1320.38	104.34	1760.61	2113.28	378.75
777907	511.67	178.37	946.77	1702.27	291.27
784819	1168.92	104.79	1597.13	2077.7	479.39
788789	952.51	153.74	1192.41	1645.86	411.17
806492	517.62	75.04	956.12	1042.46	226.71
812964	753.53	109.95	779.62	1138.23	282.75
833746	608.28	86.15	688.63	1224.58	337.55
835846	803.09	70.63	822.96	1272.56	266.2
836130	802.64	83.97	980.94	1126.73	233.78
839855	567.39	100.59	865.15	1036.07	228.13
853838	572.17	60	530.39	928.2	185.29
865646	1196.56	220.78	1115.79	1729.51	436.89
875236	1051.48	169.92	1283.92	1804.99	428.29
875636	557.33	71.85	426.3	599.9	113.1
920971	787.17	134.59	1278.53	1429.77	229.52
925821	1252.75	102.81	1804.08	1951.95	402.95

PPI Project Raw Data

<b>Participant ID</b>	<b>Total Vitamin A Activity</b>	<b>Vitamin C</b>	<b>Calcium</b>	<b>Phosphorus</b>	<b>Magnesium</b>
	<b>mcg RAE (NDS-R)</b>	<b>mg</b>	<b>mg</b>	<b>mg</b>	<b>mg</b>
950103	2102.88	168.16	2842.46	3209.53	593.03
980834	1196.35	155.12	1101.07	1498.67	379.67
985282	954.58	92.25	875.76	1442.26	321.08
992966	1062.84	198.47	1132.29	1833.1	472.77
998751	842.94	206.82	807.37	1357.96	379.43

PPI Project Raw Data

Participant ID	Sodium	Potassium	Caffeine	Vitamin D (calciferol)	Vitamin D (IU)
	mg	mg	mg	mcg (NDS-R)	IU
143778	4193.58	4239.38	1.38	3.74	149.6
156191	1588.41	2205.5	1.62	3.31	132.4
186859	2960.23	4048.53	3.55	7.72	308.8
194554	1180.58	2186.55	6.11	3.29	131.6
200004	4499.03	3159.69	4.81	8	320
216549	3340.47	3523.21	7.47	12.59	503.6
230453	1072.89	1829.53	0.13	0.2	8
230499	3661.41	3074.3	3.8	6.48	259.2
255516	2208.81	3087.95	14.31	4.46	178.4
312030	2514.05	3738.73	12.04	13.56	542.4
339596	1743.44	1939.63	1.44	6.3	252
352370	1637.96	1865.37	6.78	7	280
358284	876.26	1068.51	9.22	1.27	50.8
376015	1441.54	1806.46	0.04	1.1	44
398933	2758.25	3182.37	34.46	11.13	445.2
432753	2559.34	2774.02	4.26	6.72	268.8
464561	4414.64	5110.46	23.29	15.85	634
509383	3345.71	3361.07	1.3	5.07	202.8
569482	3562.14	3778.58	2.7	4.58	183.2
587755	4251.09	5533.15	107.02	11.01	440.4
609593	3349.51	3557.15	6.26	6.06	242.4
640807	2289.35	1821.67	3.38	2.61	104.4
646395	3346.26	2742.25	2.13	4.45	178
647641	5220.3	4764.27	14.39	13.04	521.6
698799	1895.34	2159.69	0.3	0.74	29.6
708771	1270.94	1681.22	3.41	0.76	30.4
712709	5072.67	4067.62	1.58	5.07	202.8
717551	5478.18	5665.64	6.36	7.94	317.6
720105	1293.98	1318.42	0.51	1.58	63.2
747737	2334.14	3775.85	8.66	9.35	374
758002	2675.78	2425.65	4.22	2.01	80.4
760342	2533.85	1913.45	1.6	0.9	36
765918	1696.99	1604.05	207.37	1.76	70.4
775008	4601.74	3936.02	8.91	9.08	363.2
777907	4897.74	3400.02	31.41	5.32	212.8
784819	3470.88	4256.01	9.68	8.6	344
788789	3110.08	3621.93	13.83	8.63	345.2
806492	1691.75	2206.98	6.62	4.61	184.4
812964	2839.7	2734.31	4.62	3.57	142.8
833746	2811.47	2456.53	15.29	2.73	109.2
835846	3278.28	2352.12	22.54	4.04	161.6
836130	2256.11	2522.31	5.5	6.04	241.6
839855	1545.94	2192.11	5.22	4.06	162.4
853838	2458.22	1793.83	82.68	3.2	128
865646	4255.18	4572.34	3.78	4.53	181.2
875236	3482.7	4525.45	4.61	6.96	278.4
875636	1660.27	1332.58	0.74	2.56	102.4
920971	2439.19	2811.26	5.58	7.11	284.4
925821	3322.28	3455.64	15.32	10.06	402.4

PPI Project Raw Data

<b>Participant ID</b>	<b>Sodium</b>	<b>Potassium</b>	<b>Caffeine</b>	<b>Vitamin D (calciferol)</b>	<b>Vitamin D (IU)</b>
	<b>mg</b>	<b>mg</b>	<b>mg</b>	<b>mcg (NDS-R)</b>	<b>IU</b>
950103	6566.66	6124.53	65.42	22.34	893.6
980834	3584.97	3942.02	7.7	8.19	327.6
985282	3711.28	2954.08	3.26	4.24	169.6
992966	4472.7	3656.39	8.22	4.62	184.8
998751	2797.46	3323.46	7.38	3.29	131.6

PPI Project Raw Data

Participant ID	Supp – Vitamin A mcg RAE	Supp – Vitamin C mg	Supp - Calcium mg	Supp – Magnesium mg
143778	496.1	80.02	33.18	0
156191	0	0	0	0
186859	0	0	0	0
194554	3571.43	42.86	428.57	71.43
200004	3571.43	42.86	0	71.43
216549	0	0	0	0
230453	0	757.14	428.57	0
230499	0	0	16.43	0
255516	3571.43	42.86	8.21	71.43
312030	3571.43	42.86	0	71.43
339596	1428.57	160	142.86	28.57
352370	1428.57	17.14	0	28.57
358284	0	0	0	0
376015	0	0	0	0
398933	331.83	3.98	0	6.64
432753	3571.43	42.86	0	0
464561	82.14	17.41	4.11	1.64
509383	0	0	0	0
569482	0	0	0	0
587755	3571.43	42.86	0	71.43
609593	0	109.22	66.37	0
640807	3571.43	51.07	171.43	71.43
646395	3571.43	109.22	714.29	71.43
647641	3571.43	59.28	0	71.43
698799	0	0	0	0
708771	0	0	0	0
712709	0	0	0	0
717551	3571.43	42.86	0	71.43
720105	0	0	714.29	0
747737	3571.43	42.86	0	71.43
758002	0	0	0	0
760342	3571.43	1114.29	714.29	71.43
765918	0	0	0	0
775008	82.14	0.99	0	0
777907	3571.43	42.86	0	71.43
784819	3571.43	42.86	714.29	71.43
788789	3571.43	42.86	0	71.43
806492	7142.86	757.14	357.14	71.43
812964	3571.43	42.86	0	71.43
833746	3571.43	42.86	285.71	71.43
835846	0	16.43	8.21	0
836130	331.83	37.16	0	6.64
839855	3571.43	221.43	0	71.43
853838	0	0	0	0
865646	3571.43	85.71	714.29	71.43
875236	0	0	142.86	0
875636	9285.71	757.14	357.14	71.43
920971	82.14	0.99	0	1.64
925821	1428.57	50	0	28.57

PPI Project Raw Data

<b>Participant ID</b>	<b>Supp – Vitamin A</b>	<b>Supp – Vitamin C</b>	<b>Supp - Calcium</b>	<b>Supp – Magnesium</b>
	<b>mcg RAE</b>	<b>mg</b>	<b>mg</b>	<b>mg</b>
950103	3571.43	51.07	8.21	71.43
980834	0	0	4.11	0
985282	3571.43	42.86	71.43	71.43
992966	3571.43	42.86	0	71.43
998751	3571.43	42.86	0	71.43



PPI Project Raw Data

Participant ID	Supp – Vitamin D IU	Aerobic_current	Resistance_current	Aerobic_past
143778	26.55	0	0	0
156191	0	0	0	0
186859	0	1	0	1
194554	285.71	1	0	1
200004	285.71	1	1	1
216549	0	0	0	0
230453	0	1	0	1
230499	0	0	0	1
255516	285.71	1	0	1
312030	285.71	0	0	1
339596	114.29	1	0	1
352370	114.29	1	0	1
358284	0	1	1	1
376015	0	1	1	0
398933	26.55	0	0	0
432753	285.71	1	1	1
464561	6.57	0	0	0
509383	0	1	0	1
569482	0	0	0	0
587755	285.71	1	0	1
609593	0	1	0	1
640807	285.71	0	0	0
646395	285.71	1	0	0
647641	285.71	1	1	1
698799	0	1	0	0
708771	0	0	0	1
712709	0	1	1	1
717551	285.71	1	0	1
720105	0	1	0	1
747737	285.71	1	0	1
758002	0	0	0	0
760342	285.71	1	0	1
765918	0	1	0	1
775008	6.57	0	0	1
777907	285.71	1	0	1
784819	285.71	1	1	1
788789	285.71	0	0	0
806492	285.71	1	0	1
812964	285.71	0	0	1
833746	285.71	1	0	1
835846	0	0	0	0
836130	26.55	1	0	1
839855	285.71	1	1	1
853838	0	0	0	0
865646	285.71	1	0	1
875236	0	1	0	1
875636	285.71	0	0	0
920971	6.57	1	0	0
925821	114.29	1	0	1

PPI Project Raw Data

Participant ID	Supp – Vitamin D	Aerobic_current	Resistance_current	Aerobic_past
	IU			
950103	285.71	0	0	0
980834	0	0	0	1
985282	285.71	1	0	0
992966	285.71	1	1	1
998751	285.71	0	0	1

PPI Project Raw Data

Participant ID	Resistance_past	Total Vitamin A (RAE)	Total Vitamin C mg	Total Calcium mg	Total Magnesium mg
143778	0	1945.36	297.44	856.1	360.79
156191	0	485.13	167.22	517.33	181.32
186859	0	1208.78	255.48	1392.51	321.35
194554	0	4668.4	151.16	875.94	330.6
200004	1	4440.41	123.86	1111.21	518.18
216549	0	1119.45	132.69	1815.48	307.31
230453	0	252.28	874.41	716.7	249.13
230499	0	797.69	127.45	893.44	310.12
255516	1	4466.13	269.13	805.46	434.56
312030	0	4974.82	186.86	1634.6	515.52
339596	0	2084.5	194.89	1119.78	264.33
352370	0	2086.17	64.84	942.18	262.42
358284	0	358.58	37.53	322.74	92.43
376015	0	427.25	101.69	409.81	152.89
398933	0	1396.91	83.62	1370.78	355.83
432753	1	4600.13	144	762.45	389.48
464561	0	1741.5	175.22	2523.62	502.61
509383	0	1500.97	122.71	1093.24	372.13
569482	0	1011.72	122.56	1021.97	353.85
587755	0	4910.47	364.73	1155.06	602.44
609593	0	1213.92	251.61	1085.32	364.98
640807	0	4098.02	107.34	662.71	296.44
646395	0	4383.12	226	1470.44	337.36
647641	1	5735.03	319.93	1801.99	640.21
698799	0	535.68	152.35	368	274.45
708771	0	1425.6	50.41	266.49	160.65
712709	1	1489.25	177.63	1095.7	392.71
717551	0	5161.04	355.39	1479.03	663.46
720105	0	321.2	56.37	997.72	120.58
747737	0	4490.81	129.71	1706.27	454.43
758002	0	815.73	133.49	565.54	281.78
760342	0	4006.98	1274.22	1078.52	220.67
765918	0	342.41	69.07	463.24	161.44
775008	0	1402.52	105.33	1760.61	378.75
777907	0	4083.1	221.23	946.77	362.7
784819	1	4740.35	147.65	2311.42	550.82
788789	0	4523.94	196.6	1192.41	482.6
806492	0	7660.48	832.18	1313.26	298.14
812964	0	4324.96	152.81	779.62	354.18
833746	0	4179.71	129.01	974.34	408.98
835846	0	803.09	87.06	831.17	266.2
836130	0	1134.47	121.13	980.94	240.42
839855	0	4138.82	322.02	865.15	299.56
853838	0	572.17	60	530.39	185.29
865646	0	4767.99	306.49	1830.08	508.32
875236	0	1051.48	169.92	1426.78	428.29
875636	0	9843.04	828.99	783.44	184.53
920971	0	869.31	135.58	1278.53	231.16
925821	1	2681.32	152.81	1804.08	431.52

PPI Project Raw Data

Participant ID	Resistance_past	Total Vitamin A (RAE)	Total Vitamin C mg	Total Calcium mg	Total Magnesium mg
950103	0	5674.31	219.23	2850.67	664.46
980834	0	1196.35	155.12	1105.18	379.67
985282	0	4526.01	135.11	947.19	392.51
992966	1	4634.27	241.33	1132.29	544.2
998751	0	4414.37	249.68	807.37	450.86

PPI Project Raw Data

Participant ID	Total Vitamin D IU	Spine	Hip	spine_hip
143778	176.15	Normal	Osteoporosis	Osteoporosis
156191	132.4	Osteopenia	Osteoporosis	Osteoporosis
186859	308.8	Osteopenia	Osteopenia	Osteopenia
194554	417.31	Osteopenia	Normal	Osteopenia
200004	605.71	Normal	Normal	Normal
216549	503.6	Normal	Normal	Normal
230453	8	Osteopenia	Osteopenia	Osteopenia
230499	259.2	Osteopenia	Osteopenia	Osteopenia
255516	464.11	Normal	Normal	Normal
312030	828.11	Normal	Osteopenia	Osteopenia
339596	366.29	Osteopenia	Normal	Osteopenia
352370	394.29	Osteopenia	Osteopenia	Osteopenia
358284	50.8	Osteopenia	Osteopenia	Osteopenia
376015	44	Osteoporosis	Osteoporosis	Osteoporosis
398933	471.75	Normal	Osteopenia	Osteopenia
432753	554.51	Normal	Normal	Normal
464561	640.57	Normal	Osteopenia	Osteopenia
509383	202.8	Osteopenia	Osteopenia	Osteopenia
569482	183.2	Normal	Normal	Normal
587755	726.11	Osteopenia	Osteoporosis	Osteoporosis
609593	242.4	Osteopenia	Osteopenia	Osteopenia
640807	390.11	Osteoporosis	Osteopenia	Osteoporosis
646395	463.71	Osteopenia	Osteopenia	Osteopenia
647641	807.31	Normal	Normal	Normal
698799	29.6	Normal	Normal	Normal
708771	30.4	Normal	Osteopenia	Osteopenia
712709	202.8	Normal	Normal	Normal
717551	603.31	Osteopenia	Osteopenia	Osteopenia
720105	63.2	Normal	Normal	Normal
747737	659.71	Normal	Normal	Normal
758002	80.4	Normal	Normal	Normal
760342	321.71	Normal	Normal	Normal
765918	70.4	Normal	Osteopenia	Osteopenia
775008	369.77	Normal	Normal	Normal
777907	498.51	Normal	Normal	Normal
784819	629.71	Normal	Osteopenia	Osteopenia
788789	630.91	Normal	Normal	Normal
806492	470.11	Normal	Normal	Normal
812964	428.51	Normal	Normal	Normal
833746	394.91	Normal	NA	Normal
835846	161.6	Normal	Normal	Normal
836130	268.15	Normal	Osteopenia	Osteopenia
839855	448.11	Normal	Normal	Normal
853838	128	Normal	Osteopenia	Osteopenia
865646	466.91	Normal	Normal	Normal
875236	278.4	Osteopenia	Osteopenia	Osteopenia
875636	388.11	Osteoporosis	Osteopenia	Osteoporosis
920971	290.97	Normal	Osteopenia	Osteopenia
925821	516.69	Normal	Normal	Normal

PPI Project Raw Data

Participant ID	Total Vitamin D	Spine	Hip	spine_hip
	IU			
950103	1179.31	Normal	Osteopenia	Osteopenia
980834	327.6	Osteopenia	Osteopenia	Osteopenia
985282	455.31	Normal	Normal	Normal
992966	470.51	Normal	Normal	Normal
998751	417.31	Normal	Normal	Normal