BIOGRAPHICAL SKETCH

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NAME: Gardner, Christopher D.

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POSITION TITLE: Professor of Medicine (Research)

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Colgate University, Hamilton, NY	B.A.	06/81	Philosophy
University of California, Berkeley	Ph.D.	06/93	Nutrition Science
Stanford University, Stanford, California	Post. Doc.	08/97	CVD Epidemiology

A. Personal Statement

My research program includes more than a dozen dietary intervention trials involving >1,700 participants, with high dietary intervention adherence and high participant retention. These have included a feeding study that involved providing food for 120 adults for one month after assigning them to two different low fat diets (one convenience food-based and one a diet of higher overall nutritional quality) (Ann Int Med 2005), and the *A TO Z study* (JAMA 2007), which compared the 12-month weight loss effects observed among 311 overweight or obese women assigned to the Atkins, Zone, LEARN, or Ornish diets. Recently I was awarded NIH R01 funding for a 5-year weight loss dietary intervention study with 400 overweight/obese adults comparing a Low-Carb to a Low-Fat diet (2012-2017) and testing for the possibility of a multi-locus genotype predisposition to success on one diet vs. the other (i.e., personalized nutrition). Supplemental funding was received to increase the sample size to 600 participants and increase the number and types of assessments. As of May 2015, 609 adults have been enrolled in the 12-month protocol, making this the largest single site weight loss diet study that we are aware of. In this ongoing study I am working on a substudy investigating microbiota changes in response to weight loss with Dr. Sonnenburg, my Co-Principal Investigator on the currently proposed project. Although these data are not yet available for presentation due to ongoing sample collection, this has created the opportunity for the two of us to work together and coordinate our activities. This preliminary work and these interactions have led directly to the project and hypotheses proposed here, which are the obvious “next step” research questions to arise from our ongoing and previously completed research. My background and experience make me particularly well suited to lead this collaborative project with Drs. Elias and Sonnenburg.

B. Positions and Honors

Positions

1997-1999 Research Associate, Department of Medicine, Stanford University
1999-2001 Assistant Professor, Department of Epidemiology and Prevention, UC Davis
2001-2007 Assistant Professor, Department of Medicine, Stanford University
2007-2013 Associate Professor, Department of Medicine, Stanford University
2013-present Professor, Department of Medicine, Stanford University

Honors/Awards/Fellowships

1988 University of California Regents Fellowship
1989 Outstanding Teaching Assistant, Department of Nutritional Sciences
1994 AHA Fellow, 20th U.S. 10-day Seminar on Epidemiology & Prevention of CVD
1995-1997 American Heart Association Postdoctoral Training Grant Recipient
2005 Outstanding Teacher, SPRC, Department of Medicine
2010 Outstanding Teacher, SPRC, Department of Medicine
2012 Outstanding Student Advisor, Human Biology Program

C. Contributions to Science

WEIGHT LOSS DIETS: LOW-FAT VS. LOW-CARB – WHICH IS BEST FOR WHO?

After several decades of predominance as the standard dietary approach to weight loss, the traditional Low-Fat diet espoused by most health professionals was challenged by proponents of Low-Carb diets. In the last 15 years there have been dozens of Low-Fat vs. Low-Carb weight loss diet studies. One of the largest, longest and best designed of these trials was the *A TO Z Study* for which I was PI. As reported now in dozens of meta-analyses of these trials, the Low-Fat approach has not proven superior to Low-Carb. In fact, the Low-Carb arms of these trials are usually as or more successful than Low-Fat. However, as we found in the A TO Z study, the average differences in weight loss ***between*** diet groups are typically modest. What our group has found more interesting is the heterogeneity in response ***within*** each diet group. We have now published a series of secondary papers using A TO Z study data examining variations in adherence, interactions with baseline insulin resistance, and variable diet quality. All of this has led to an ongoing study for which I am PI with 609 participants assigned to Low-Carb or Low-Fat where we are reframing the main research question. Rather than looking for which diet is best, we are seeking to learn about which diet is better for which kind of individual, by exploring potentially predisposing genetic, metabolic, & microbiotic differences.

Gardner CD, Kiazand A, Alhassan S, Kim S, Stafford RS, Balise RR, Kraemer, King AC. Comparison of the Atkins, Zone , Ornish and LEARN diets for change in weight and related risk factors among overweight premenopausal women: A randomized clinical trial. *JAMA* 2007;297:969-77.

Gardner CD, Kim S, Bersamin A, Dopler-Nelson M, Otten J, Oelrich B, Cherin R. Micronutrient quality of weight-loss diets that focus on macronutrients: Results from the A TO Z study. *Am J Clin Nutr* 2010;92:304-12.

Alhassan S, Kim S, Bersamin A, King AC**, Gardner CD.** Dietary adherence and weight loss success among overweight women: Results from the A TO Z weight loss study. *Intl J Obes* 2008;32(6):985-991.

McClain AD, Otten JJ, Hekler EB, **Gardner CD.** Adherence to a low-fat vs. low-carbohydrate diet differs by insulin resistance status. *Diabetes Obes Metab* 2013;15(1):87-90.

GARLIC – EXAMINATION OF POTENTIAL BLOOD CHOLESTEROL LOWERING EFFECTS

Decades ago, separate from the established effect on vampires, there was a mechanistic plausibility and a small number of trials suggesting that garlic consumption had a hypercholesterolemic effect. As a young investigator I contributed to the set of these trials that were generally underpowered, of short duration, and limited in design in various ways. We concluded in our null finding, as had many other published studies, that a larger more rigorously designed trial was needed. Working with two of the nation's leading authorities on garlic chemistry, we designed and conducted a rigorous NIH-funded trial. Two top selling supplements – an aged garlic extract and a dried powdered garlic – were compared with raw garlic. In the trial, 192 moderately hypercholesterolemic adults consumed one of the three types of garlic 6 days/week for 6 months. We published a separate methodological paper on the stability of the sulfur compounds, the putative active agents, in the three forms of garlic over the three years of the study. The trial results were null; this time definitively null. This one trial did not answer the general question as to whether garlic has (any) health benefits. But the dose, duration, study population, chemical characterization, adherence, retention and other study components were all appropriately and rigorously applied to test garlic's potential as a cholesterol lowering agent. Many of the previously and frequently cited limitations of past trials were addressed. We concluded that garlic was great from a culinary perspective, but not for lowering blood cholesterol in the doses and forms typically consumed.

Gardner CD, Chatterjee LC, Carlson JJ. Effect of garlic on serum cholesterol levels. In: Bidlack WR, Omaye ST, Mesking MS, Topham DKW, editors. Phytochemicals as bioactive agents. Lancaster, PA: Technomics Publishing Co. Inc., 2000. p. 199-212.

Gardner CD, Chatterjee L, Carlson J. Effect of garlic supplementation on plasma cholesterol in hypercholesterolemic adults. *Atherosclerosis* 2001;154:213-20.

Lawson LD, **Gardner CD**. Composition, stability, and bioavailability of garlic products being used in a clinical trial. *J Agric Food Chem* 2005;10:53 (16):6254-61.

Gardner CD, Lawson LD, Block E, Chatterjee LM, Kiazand A, Balise RR, Kraemer HC. The effect of raw garlic vs. commercial garlic supplements on plasma lipids in moderately hypercholesterolemic adults: A randomized clinical trial. *Arch Int Med* 2007;167:346-53.

NUTRITION INTERVENTION STUDIES – CHALLENGES & VALUE OF INCORPORATING WHOLE FOODS

One of my major contributions to nutrition science has been my long-term efforts to improve the design and conduct of rigorous intervention trials that involve whole foods, in contrast to studying isolated nutrients. Foods are much more challenging to study. Isolated nutrient studies generally involve using dietary supplements and placebos and do not require modification of habitual dietary habits; these studies can essentially be designed similar to a drug trial. In contrast, randomized trials that involve getting participants to consume certain foods, food groups, or food patterns must take into consideration: 1) the potential variability of specific nutrients of interest in the foods being consumed from one source to another, or even from one day to the next, 2) the parallel dietary changes that occur when a study subject eats more of a particular food (e.g., what other foods are displaced and consumed in lower amounts), 3) variability in adherence to adopting changes in habitual food intake, and 4) challenges of accurately assessing adherence. Despite the inherent challenges of working with whole foods relative to isolated nutrients in nutrition intervention trials, my main interest in this field is in helping the general population choose healthier foods to consume, and therefore I find the challenges worthwhile and necessary to take on.

Gardner CD, Coulston A, Chatterjee L, Rigby A, Spiller G, Farquhar JW. Effects of a plant-based diet on plasma lipids in hypercholesterolemic adults: A Randomized Trial. *Ann Int Med* 2005;142:725-33.

Gardner CD, Lawson LD, Block E, Chatterjee LM, Kiazand A, Balise RR, Kraemer HC. The effect of raw garlic vs. commercial garlic supplements on plasma lipids in moderately hypercholesterolemic adults: A randomized clinical trial. *Arch Int Med* 2007;167:346-53.

Gardner CD, Messina M, Kiazand A, Morris JL, Varady AN, Franke AA. Effect of two types of soy milk and dairy milk on plasma lipids in hypercholesterolemic adults: A randomized trial. *J Am Coll Nutr* 2007;26:669-77.

Mummah S, Oelrich B, Hope J, Vu Q, Gardner CD. Effect of raw milk on lactose intolerance: a randomized controlled pilot study. *Ann Fam Med* 2014;12:134-41.

NOVEL RISK FACTORS – EXPLORATION FOR USE AS STUDY OUTCOMES

My primary scientific interest is identifying dietary modifications that lead to optimal health. In the last 100 years nutrition science has undergone a transition from addressing concerns about acute deficiency diseases to chronic diseases associated with overconsumption of unhealthy foods. A significant challenge in studying chronic diseases is the long follow-up periods necessary to document incident cases. In the nutrition field this has often been addressed by studying chronic disease ***risk factors*** that can be modified by dietary changes over the course of weeks or months, such as blood cholesterol concentrations as a risk factor for cardiovascular disease. However, there is more to optimal health than low blood cholesterol. A significant portion of my research career has involved exploring alternative and novel risk factors as study outcomes. To date those have included small dense LDL particles, HDL subfractions, Metabolic Syndrome, and inflammatory markers. Similarly, the current study proposes looking at the impact of dietary manipulations on microbial diversity as a potential component of optimal health.

Gardner CD, Fortmann SP, Krauss RM. Association of small low-density lipoprotein particles with the incidence of coronary artery disease in men and women. *JAMA*,1996;276(11):875-81.

Gardner CD, Tribble DL, Young DR, Ahn DK, Fortmann SP. Associations of HDL, HDL(2), and HDL(3) cholesterol and apolipoproteins A-I and B with lifestyle factors in healthy women and men: The Stanford Five Project. *Prev Med*, 2000;31(4):346-56.

Alhassan S, Kiazand A, Balise RR, King AC, Reaven GM, **Gardner CD**. Metabolic syndrome: Do definitions identify similar individuals among overweight premenopausal women? *Metabolism* 2008;57:49-56.

Dewell A, Marvasti F, Harris W, Tsao P, **Gardner CD.** Low and high dose plant and marine (n-3) fatty acids do not affect plasma inflammatory markers in adults with metabolic syndrome. *J Nutr* 2011;141:2166-71.

SOY AND PHYTOESTROGENS – POTENTIAL CARDIOVASCULAR AND PROSTATE BENEFITS

Soy beans are relatively unique among other plant foods for several reasons: more optimal distribution of amino acids, more protein and fat than any other bean, source of the omega-3 fat linolenic acid, and one of the most significant dietary sources of phytoestrogens. Claims of health benefits have been controversial. In designing and conducting trials to test for potential benefits it has been clear that soy studies require an assessment of the levels of the various components, which can vary from one soy food to another, and from one crop to the next. I had the opportunity to design and conduct two studies involving soy supplements or soy foods, with or without phytoestrogens, that tested potential effects on blood cholesterol. The effects observed were modest at best. This finding is consistent with several other trials conducted at approximately the same time as ours, but different than some previous trials that reported a benefit and which led to an FDA approved health claim about the benefit of soy protein. I also had the opportunity to work with and endocrinologist and a urologist at Stanford regarding soy phytoestrogen uptake in the prostate of men diagnosed with prostate cancer. This has led to some initially promising findings that suggest the potential benefits for the prostate in men is probably greater than for blood cholesterol lowering in the general population.

Tham DM, **Gardner CD**, Haskell WL. Clinical review 97: Potential health benefits of dietary phytoestrogens: a review of the clinical, epidemiological, and mechanistic evidence. *J Clin Endocrin Metab*, 1998;83(7):2223-35.

Gardner CD, Newell KA, Haskell W. Effect of Phytoestrogen supplementation on plasma cholesterol in hypercholesterolemic, postmenopausal women. *Am J Clin Nutr,*2001;73:728-35.

Gardner CD, Messina M, Kiazand A, Morris JL, Varady AN, Franke AA. Effect of two types of soy milk and dairy milk on plasma lipids in hypercholesterolemic adults: A randomized trial. *J Am Coll Nutr* 2007;26:669-77.

Gardner CD, Oelrich B, Liu J, Feldman D, Franke AA, Brooks JD. Prostastic soy isoflavone concentrations exceed serum levels after dietary supplementation. *Prostate* 2009;69:719-26.

Complete List of Published Work in MyBibliography:
http://www.ncbi.nlm.nih.gov/sites/myncbi/christopher.gardner.1/bibliograpahy/41157640/public/?sort=date&direction=descending

D. Research Support

1R01DK091831 Gardner (PI) 09/01/2012 – 08/31/2017
NIH/NIDDK
Do Genotype Patterns Predict Weight Loss Success for Low Carb vs. Low Fat Diets?
In a previous weight loss study we conducted, post-hoc analyses suggested there are multi-locus genotype patterns that predispose some individuals to be more successful with weight loss on a Low-Carb diet, and some on a Low-Fat diet. The objective of this follow-up study is to determine if genotype can predict differential weight loss success on Low-Carb vs. Low-Fat diets among 400 adults randomly assigned to one of the two diets for a year.
Role : PI

Nutrition Science Initiative (NuSI) Gardner (PI) 09/01/2013 - 08/31/2016
Diet X Genotype Plus NuSI
Funding has been obtained to expand the NIH/NIDDK study described above in the following ways: 1) increase the sample size by 200 (all minority participants), 2) Add measurements to the study, including microbiome and fat biopsies, and 3) explore approaches and strategies for increasing adherence, improving assessment of adherence, and making the delivery of the intervention more cost effective.
Role: PI

1R01 DK091831-01A1 Engleman (PI) 08/1/2012 – 05/31/2016
National Institutes of Health
Defining Adaptive Immune Mechanisms of Insulin Resistance
The objective of this project is to more clearly define immune targets and the mechanisms contributing to adaptive immune regulation of insulin resistance. The results of these experiments have the potential to yield new diagnostic or therapeutic modalities to manage this important disease.
Role: Co-Investigator

U01DK098245 Sun Kim (PI) 06/01/2013 - 05/31/2018
National Institutes of Health
Vitamin D to Prevent Type 2 Diabetes
The purpose of the Vitamin D and Type 2 Diabetes study (D2d study) is to assess whether, in participants with pre-diabetes, oral daily vitamin D_3 supplementation reduces the rate of progression from pre-diabetes to clinical diabetes. The D2d study is a multicenter, randomized (1:1), double-masked, placebo-controlled, parallel-group, primary prevention clinical trial with 2 arms (oral daily vitamin D vs. placebo) in participants at high risk for diabetes (with pre-diabetes) who will be followed for an average of 3 years after randomization for incident diabetes.
Role: Co-I of Stanford site

1R01HL117736-01A1 Prochaska (PI) 04/15/2014-03/31/2019
National Institutes of Health
Technology Innovations for Supporting Health Among Alaska Native People
This study aims to identify effective and cost-effective interventions for tobacco use and other risk behaviors for cardiovascular disease among Alaska Native people in rural villages. In a randomized controlled trial, the study will compare interventions using telemedicine to promote the American Heart Association's identified ideal health behaviors (nonsmoking and physical activity) relative to ideal health factors (managing cholesterol and blood pressure).
Role: Co-Investigator

Recently Completed Research Support (last 3 years)

Contract #200-2-12-52155 Lyn Steffen (PI) 09/01/2012 - 08/26/2015
Centers for Disease Control
Sodium Intake and Excretion
The purpose of this study is to collected detailed sodium consumption data from a combination of individual dietary assessment and 24-hour urine collection from 450 individuals. The Stanford site will be responsible for recruiting 150 participants with specific targets for Asians, Hispanics/Latinos and Caucasians.
Role: PI of Stanford site, multi-site trial

71252 Basu (PI) 09/01/2013-08/31/2014
Robert Wood Johnson Foundation
Improving Healthy Eating Through Changes in Supplemental Nutrition Assistance Program (SNAP) Policies
The major goals of this project are to use simulation models to study how changes to vegetable subsidy programs may impact chronic disease rates among low-income children.
Role: Co-Investigator

R21 AT004475 Gardner (PI) 09/30/2009 – 08/31/2012
NIH/NCCAM
Effects of GSH +/- Arginine on Inflammatory Markers Among Adults with CVD Risk
The major purpose of this study is to examine the effects of an antioxidant dietary supplement (glutathione) with or without an amino acid dietary supplement (arginine) on markers of inflammation among adults with elevated cardiovascular disease risk factors.
Role: PI

R21 AT005123 Meyer (PI) 05/01/2010 – 04/30/2012
NIH/NCCAM
Dietary Maneuvers to Limit Production of Colon-Derived Uremic Solutes
Identify dietary treatments which reduce the production of certain urinary organic waste solutes linked to dialysis. The project will administer two dietary maneuvers (plant foods and extrinsic fiber) and investigate production of p-cresol sulfate and indoxyl sulfate in hemodialysis patients.
Role: Co-Investigator