Responses to Unanswered Questions During the 2021 Early-Stage Investigator Lecture
Dietary Patterns To Prevent Cardiovascular Disease

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1. **Is there a theoretical mechanism of decreased sodium leading to lower inflammatory markers, such as upregulation of glucocorticoids?**

   We hypothesized that it may be secondary to pro-inflammatory effects of increased aldosterone.

2. **What is known about vegetarian diet and its relationship to CVD? Does the lower cholesterol composition of the diet help reduce cardiovascular events? Are there additional benefits from eliminating meats?**

   Vegetarian diets are associated with lower blood pressure. However, we found that in real-world settings—specifically our recent DIGO trial, which involved DASH groceries—that if you truly increase consumption of fruit and vegetables, sodium reduction is somewhat unavoidable. How foods are processed plays an important role here and should be considered when weighing the relative health of a specific food (beyond its animal versus plant source). French fries are a fine example. There is good evidence that plant-based eating reduces cholesterol and cholesterol reduction was a feature of DASH. However, in the DASH trial, this did not appear to be a driver of the difference in cardiac biomarkers. Beyond individual health, important concerns about the environmental impacts (sustainability) of animal-based diets have been raised, which warrant consideration as well.

3. **Thinking about translation, there is not a clear and feasible guidance about "low sodium diet," so how can we communicate and develop a guide that is friendly, adoptable, and efficacious implementable including in the public school system where the diet is extremely high in salt and sugars.**

   This is an important point. I recently worked with a resident (Ruey Hu) on an analysis of NHANES that showed that a one-size-fits-all daily recommendation for sodium can be misleading for populations that consume fewer calories of food (e.g., older adults, women). Sodium density seems to be a more important driver of blood pressure than total sodium. This makes population guides challenging. Also, I've seen health certifications of snack food that were below a sodium threshold to also be problematic, since intended use of the product may be in addition to a principal meal (idea–is it healthy to snack on foods with sodium even if it is a small fraction of daily value?). I really think something should be done on the population level to reduce sodium levels in all food products. Also, some regulatory standards in net sodium provided in meal plans (relevant for students as well as infirm and older adults) are really needed. I think for meal plan/population meal preparation we may be more effective upstream—preparing more universally healthy options versus a healthy and unhealthy option.

4. **Where are the main reductions in a low-sodium diet? Is it focused mainly on a reduction in the use of table salt or in the reduction of sodium from sources other than salt such as processed and canned foods?**

   This really depends on where you live. In the United States, ~75% of the sodium we are exposed to is already in foods. In some countries (for example, China) sodium is often added at the time of preparation. My patients often say they don't have salt shakers at home, but don't realize that one of the principal sources of sodium are bread and rolls (not just soups, snacks, and processed meats). Eating at home (versus restaurants) is another great way to reduce sodium intake.

5. **In SOTRUE, potassium was fixed at a higher level than what the United States typically consumes. In DASH, the two experimental diets had much higher potassium levels than the control diet. Can you comment on the potential/hypothesized role of potassium in your observed effects in SOTRUE?**

   In SOTRUE we wanted to isolate the effect of sodium in the meal plans and were worried potassium could differ between the two meal plans. It turned out that the culinary team was able to create our sodium contrast through added salt to various entrees. However, it is a good point. We were happy to see that both typical and low sodium plans reduced blood pressure.

6. **You mentioned that the DASH diet is not well known among the public. Can you think of best ways we can promote awareness among the public particularly in health care providers?**

   I think reimbursement for ambulatory nutrition services could help. Health providers are very pressed for time, but dietary discussions should be coupled with BP screening. I think there needs to be greater transparency in labeling. I thought the NYC initiative to place salt shakers next to high sodium entrees was a great idea—it was met with a lot of resistance, but people should be able to know that what they are being served is harmful.

7. **Can you talk about benefits of the DASH-Sodium trial in racial subgroups? Are there any comparison studies available?**

   The effects of DASH and DASH-Sodium have been studied across Black and White adults and were found to be even greater in Black adults. There is a paucity of data for other racial/ethnic groups. In NHANES, we found that Asian Americans may consume the most sodium and it might be beneficial for more data among these groups as well. There was an interesting paper by Howard et al (Association of Clinical and Social Factors With Excess Hypertension Risk in Black Compared With White US Adults. JAMA. 2018;320(13):1338-1348. doi:10.1001/jama.2018.13467) that identified diet as one of the primary mediators of disparities in hypertension across racial groups. It will be important to address inequities in access to healthy food to see the benefits of DASH realized among Black populations.

8. **It's interesting that SNAP does not improve diet quality with $30 per week but the 5 Plus Nuts and Beans study was able to with the same amount of money.**

   Well, the data by Zhang et al did not look at SNAP versus no SNAP so it's hard to confirm this statement. However, SNAP does not restrict dollars toward fruits and vegetables. This "Harvest

Basket" concept is a subject of much debate. Some believe we should restrict SNAP to select foods, but I am concerned about removing client autonomy of choice and how that would impact their personal dignity (not be given the option to make decisions for themselves). Also, 5 Plus showed changes in behavior, but not blood pressure. We need a definitive study that establishes the right dose of groceries needed to improve health.

9. **How do we explain benefits/no benefits of the DASH diet in non-sodium sensitive individuals? Can we assume these non-sensitive individuals are safe to not modify their diets?**

   There is an important and recent paper on this topic (He J, Huang JF, Li C, et al. Hypertension. Sodium Sensitivity, Sodium Resistance, and Incidence of Hypertension: A Longitudinal Follow-Up Study of Dietary Sodium Intervention. 2021 Apr 26. doi:10.1161/HYPERTENSIONAHA.120.16758 [Epub ahead of print] PMID:33896191.). In this paper, participants with sodium-resistance were at higher risk of cardiovascular disease events. I worry about phenotype misclassification (blood pressure is associated with a fair degree of measurement error) and that giving a green light to dietary indiscretion among this high-risk group would not be safe.

10. **Can you talk about any research related to the DASH Sodium trial in the vegetarian south Asian population?**

    I am not familiar with research in this area but would love to learn more. It is an important population, underrepresented in research.

11. **Great, I was going to ask how we can eat more sustainable (no meat, no fish) and still be healthy. Thus, there has been a growing interest and adoption in plant-based diets, including for sports competition. When is the NIH going to develop funding to sponsor plant-based studies to keep up with the current—already progressing—plant-based diet behavior**?

    Good question. I believe the Office of Nutrition Research has released their strategic priorities for the coming years.

12. **Do these findings confirm that limiting saturated fats is always the best choice?**

    Macronutrients were less important drivers of the differences we noted in the cardiac biomarkers.

13. **Was there a difference in the outcomes of the DASH diet in women versus men?**

    I believe effects of DASH were similar for both men and women.

14. **Are there any websites with links to recipes and meals used for each diet that could be helpful resources?**

    This is a good question. There are a number of websites with DASH recipes. Here is one published by the Mayo Clinic: https://www.mayoclinic.org/healthy-lifestyle/recipes/dash-diet-recipes/rcs-20077146.

    The book, "The DASH Diet for Hypertension," by some of the author investigators (Thomas Moore, Mark Jenkins, Laura Svetkey) published in 2011, also includes a number of the original recipes.