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Center to Reduce CVD Disparities: Genes, Clinics, and Communities
University of North Carolina at Chapel Hill
Project Period: 08/15/2010 – 04/30/2016
Principal Investigator: Alice Ammerman, DrPH

FINAL PROGRESS REPORT

The Heart Healthy Lenoir (HHL) Project was a community-based research project conducted in Lenoir County, NC, a rural, low income county in the "stroke belt" of eastern NC. The project was a collaboration between the University of North Carolina at Chapel Hill, East Carolina University, and a broad coalition of community partners. The primary aim was to create long-term, sustainable approaches to reducing cardiovascular disease risk disparities. Following a year of in-depth formative research, three coordinated studies were conducted:

Study 1: The Lifestyle Study tested a lifestyle intervention to improve nutrition, physical activity and weight management, including policy and environmental change.

Study 2: The Hypertension Control Study tested the effect of a clinic-based intervention on lowering blood pressure.

Study 3: The Genomics Study examined genetic factors associated with cardiovascular disease risk and treatment success.

For all study activities, we took an approach that considered the multi-level social determinants of health and the potential social and community capital that support sustainable positive and healthful changes. This final report includes a summary of progress made toward the achievement of study aims, a list of significant results, and a list of publications.

Administrative Core

The administrative home of the research project was the Center for Health Promotion and Disease Prevention at the University of North Carolina. The purpose of the Administrative Core was to provide the organizational infrastructure and support for the research conducted in Lenoir County, NC, and to promote research collaboration with the other Centers for Population Health and Health Disparities (CPHHD) across the country. Our Center collaborated with investigators from other Centers to prepare multiple manuscripts, of which we have listed below the ones that have been published to date.

Publications

Cooper, L.A., Ortega, A.N., Ammerman, A.S., Buchwald, D., Paskett, E.D., Powell, L.H., … Williams, D.R. (2015). Calling for a bold new vision of health disparities intervention research. *American Journal of Public Health*, 105(S3), S374-S376. PMC4455513.

Glik DC, Sharif MZ, Tucker KL, Tejada SA, Prelip ML, Ammerman AS, Keyserling TC. Community engagement to support cardiovascular disease prevention in disparities populations: three case studies. Submitted to *Journal of Community Health* on 12/04/14; in press on 9/10/15.

Hohl, S.D., Thompson, B., Krok-Schoen, J.L., Weier, R.C., Martin, M., Bone, L... Paskett, E.D. (2016). Characterizing Community Health Workers on Research Teams: Results From the Centers for Population Health and Health Disparities. *American Journal of Public Health*, E1-E7. In Press.

Okamoto, J.; Centers for Population Health and Health Disparities Evaluation Working Group. (2015). Scientific collaboration and team science: a social network analysis of the centers for population health and health disparities. *Translational Behavioral Medicine: Practice Policy, Research,* 5(1), 12-23. PMC4332906.

Study 1
Community-Based Lifestyle Intervention to Reduce CVD Risk and Disparities in Risk (Lifestyle Study)
Principal Investigator: Thomas C. Keyserling, MD

Summary of Progress Toward Achievement of Study Aims

Phase I-Assessment and Preparation Phase (Years: start to 1.5): Using the Socio-Ecological Model (SEM) as a framework, we used a community-based participatory research approach and qualitative methods to assess individual, interpersonal, organizational, community, and policy factors relevant to CVD risk reduction in Lenoir County, NC. We then used these findings, informed by behavior change theory, to develop a community-based lifestyle intervention to reduce CVD risk in this community.

Aim 1: Assess perceived barriers, facilitators, and values among community members who may benefit from lifestyle change. (SEM: individual and interpersonal).
During the formative research phase, we assessed individuals' interactions with community-level assets and barriers related to healthful lifestyle changes. We conducted face-to-face interviews with 22 community members, inquiring specifically about their eating and physical activity behaviors, knowledge of heart disease risks, and awareness of community resources to facilitate healthy lifestyle choices. Participants were English speaking, over 18 years, and lived in Lenoir County. In an effort to ensure that interviewers were familiar with the community context, in-depth interviews were conducted by trained study staff recruited from Lenoir County. Interviews lasted approximately 60 minutes, were conducted in a private location, were audio-taped and transcribed verbatim.

Five themes (Jilcott Pitts, et al., 2013) emerged related to community level assets and barriers for healthier nutrition and PA. In terms of assets, community members highlighted availability, culture, and community resources for supporting healthier lifestyles. In terms of barriers, participants discussed location and cost as key factors impacting their choices about use of community resources.

Aim 2: Evaluate existing community characteristics, resources, programs, and policies that may facilitate or impede lifestyle change to reduce CVD risk. (SEM: organizational and community)

To better understand community-level assets and barriers, as well as the potential role of local organizations in addressing CVD risk and disparities, we conducted in-depth interviews with staff from eight community agencies and businesses, including the health department, hospital, cooperative extension, parks and recreation, faith community, a primary care practice, a pharmacy, and a farmer. We also conducted food venue audits (stores and restaurants) in three regions of Lenoir County, as well as park audits. In general, small grocery and convenience stores had the fewer healthy options, followed by dollar stores and supermarkets, which had the most healthy options. Park audits indicated lower quality parks in lower-income census block groups. Formative research also included development of a community resource guide, which was informed by targeted Internet searches and six community audits of defined geographic catchment zones in Lenoir County. The community resource guide listed local nutrition and physical activity resources that HHL participants could use to support healthful behavior changes.

Aim 3: Assess level of interest and concerns of the local business community (restaurants and grocery stores) relevant to offering more healthful menu and grocery options. (SEM: organizational and community)

In order to expand the reach of the overall HHL Project, we collaborated with the study's Community Advisory Committee (CAC), comprised of 20 local community leaders and health professionals, to engage the community in lifestyle promoting activities. Together, we decided that working with restaurants afforded an opportunity to reach many residents when they were primed to make decisions about food consumption. Then, with input and assistance from the local Chamber of Commerce, especially in regard to engaging local restaurants, we developed the protocol for a pilot and follow-up study. The intervention included table tents outlining 10 heart healthy eating tips, coupons promoting healthy menu items, an information brochure, and link to the study website. Pre and post intervention surveys were completed by restaurant managers and customers completed a brief "intercept" survey. Managers (n = 10) had a favorable response to the intervention format, reported the table tents and coupons were well received, and several noted improved nutrition knowledge. Overall, 4214 coupons were distributed with 1244 (30%) redeemed, most commonly for low sugar beverages. Of 300 customers surveyed, 126 (42%) noticed the table tents and of these, 115 (91%) considered the nutrition information helpful, 42 (33%) indicated the information influenced menu items purchased, and 91 (72%) reported the information will influence what they order at the restaurant in the future. The intervention was well-received by restaurant managers and positively influenced menu item selection by many customers. A paper describing this effort has been submitted to the *American Journal of Health Education* for review.

Aim 4: Assess activity and interest related to local sustainable food systems that may increase access to healthy foods and facilitate economic opportunities among food producers and distributors. (SEM: organizational and community)

We implemented two Photovoice efforts, one with adults and the other with youth, to better understand the barriers and facilitators of heathy eating. While the major focus was on food available through restaurants and in homes, participants discussed their interest in promoting more gardening, particularly on the land along the river which can no longer be used for building due to prior flooding. Several gardens have been initiated in this area by various community organizations. We also offered support and encouragement to community efforts related to "Common Ground of Eastern North Carolina." This effort established Kinston's first community garden in an effort to "create opportunities for youth of limited resources to engage in personal and social change through sustainable agriculture and environmental stewardship". We assisted Tammy Kelly, Director of the Lenoir County Cooperative Extension Program, with writing a grant to a local foundation and implementing a project which piloted the development of a CSA program providing subsidized boxes of fresh, locally grown produce to lower income participants. In response to requests from school board leadership in Lenoir County, one of UNC's Nutrition Department doctoral students, Linden Thayer, became very involved with a community launched effort to develop gardening opportunities for children in the public schools.

Aim 5: Assess level of interest and political will among local decision makers regarding policy change in support of healthier lifestyles. (SEM: policy)

To learn more about winnable obesity-prevention policies in the Lenoir County context, we used the Centers for Disease Control and Prevention "Common Community Measures for Obesity

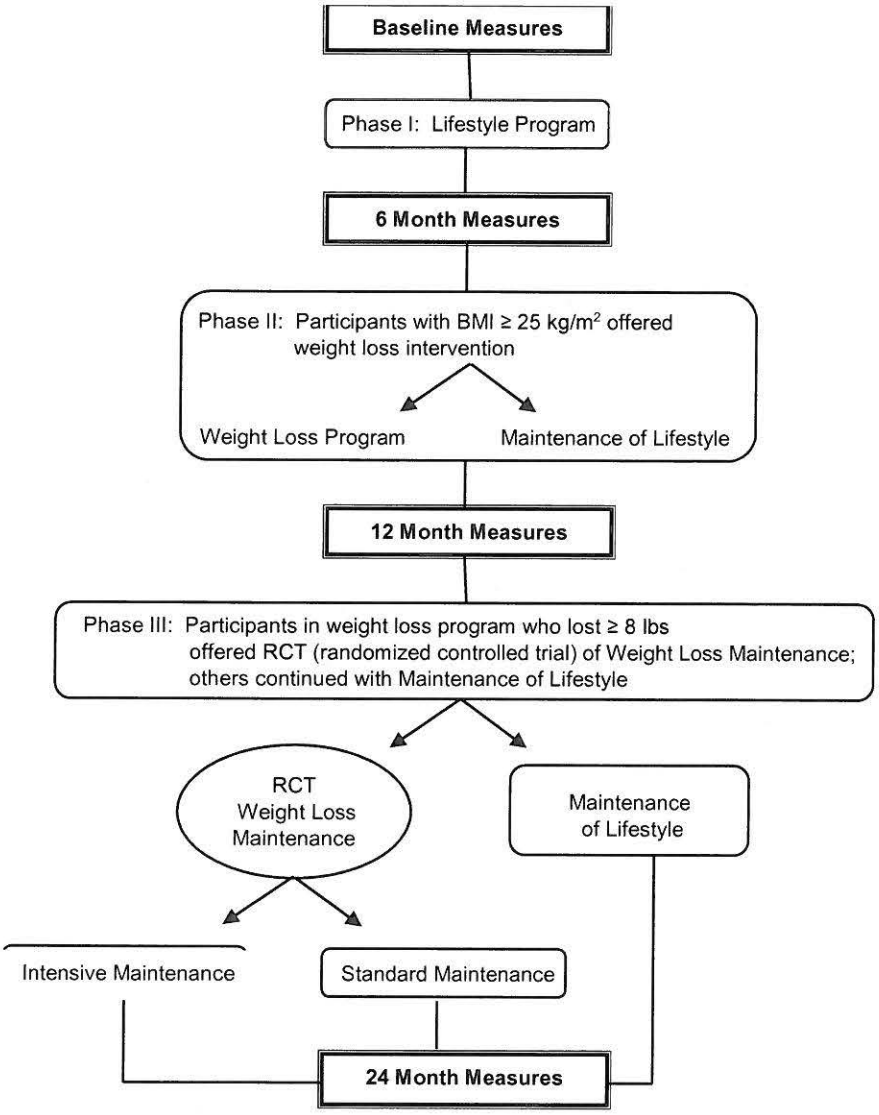
Prevention" (COCOMO), a list of 24 recommended and evidence-based strategies and accompanying measures to guide communities in identifying and implementing obesity-prevention policies. Using the COCOMO strategies, we facilitated discussion among our CAC members regarding obesity-prevention policies. In brief, CAC members scored each listed COCOMO recommended strategy based upon how realistic it was for the Lenoir County community context, existing infrastructure support, leadership support, and available resources. Responses were aggregated, and we announced the "biggest loser" (the least winnable strategy), and the "biggest winner" (the most winnable, or feasible, policy change strategy) to CAC members, who were then prompted to discuss facilitators and barriers to the identified policy change strategies.

The most winnable, or feasible, policies identified by CAC members were the following: Communities should: provide incentives for production, distribution, and procurement of food from local farms; enhance personal / traffic safety in areas where persons could be physically active; increase opportunities for extracurricular physical activity; increase support for breastfeeding; and enhance infrastructure supporting bicycling and walking. The least winnable policies were the following: Communities should: limit advertisements of less healthy foods and beverages; restrict availability of less healthy foods and beverages in public service venues; support locating schools within easy walking distance of residential areas; and zone for mixed use development (Jilcott Pitts, et al., 2012).

Aim 6: Develop protocol and intervention materials for Implementation Phase.
Using the results from the formative phase of the research and in coordination with the Community Advisory Committee, we designed a three-phase lifestyle intervention that was culturally appropriate and tailored to the needs of the Lenoir community. Next we describe the main study progress and results.

Phase II Implementation and Experimental Phase (Years: 1.0 to 4):
The Lifestyle Study included 3 phases, as depicted in Figure 1. Phase I, lasting 6 months and given to all participants, focused on improving diet quality and increasing PA. In Phase II, also 6 months in length, participants with a body mass index (BMI) ≥ 25 kg/m^2 were invited to take part in a weight loss intervention. Those who did not and those with a BMI < 25 kg/m^2 received a maintenance of lifestyle intervention. Phase III, lasting a year, included a randomized controlled trial (RCT) comparing a more intensive to less intensive maintenance of weight loss intervention for those who lost ≥ 8 pounds in Phase II and a maintenance of lifestyle intervention for the other participants. We did not include a control group in Phases I and II because we had previously shown lifestyle and weight loss interventions given in similar formats to low SES participants were effective when evaluated in randomized trials and we wanted to offer a lifestyle and weight loss interventions to as many community members as possible. Additionally, our CAC strongly encouraged a study design in which all participants received "active treatment."

Figure 1. Lifestyle Study Overview



When the proposal was drafted in 2009, our dietary focus was primarily to improve carbohydrate quality by suggesting increased fruit and vegetables, more whole grains, and more legumes. However, to be consistent with the evolving literature on the importance of fat quality in reducing CVD risk (Jakobsen MU, et al., 2009; Lichtenstein AH, et al., 2006; Mozaffarian D, et al., 2010; Oh K, et al., 2005; Siri-Tarino PW, et al., 2010; Sofi F, et al., 2010; Sofi F, et al., 2008; Mozaffarian D, et al., 2006), the intervention was further revised for this study to include a major focus on improving fat quality. With this modification, the intervention dietary pattern closely resembled that tested in the nut intervention arm of the PREDIMED study; thus, we call it the "Med-South diet," given the focus on the Southeastern US. As shown Table 1, 9 of the 13 major

recommendations advocated by the PREDIMED diet (Estruch R, et al., 2013) were almost identical to those in the Med-South diet.

Table 1. PREDIMED Diet goals compared to Med-South Diet goals[a]

Food	PREDIMED Diet goal	Med-South Diet goal
1--Vegetable Oil	Olive oil group: ≥ 4 tbsp/day extra virgin olive oil	2-6 servings/day of foods high in healthy fats (nuts, fish, full fat salad dressings and spreads, other foods prepared with olive or vegetable oils, and vegetables with high fat content such as avocado)
2--Tree nuts and peanuts	*Nut group: ≥ 3 servings/wk*	*≥ 3 servings/wk*
3--Fresh fruits	*≥ 3 servings/day*	*≥ 7 servings for fruits and vegetables/day*
4--Vegetables	*≥ 3 servings/day*	
5--Fish (especially fatty fish), seafood	≥ 3 servings/wk	≥ 1 servings/wk
6--Legumes	*≥ 3 servings/wk*	*≥ 3 servings/wk*
7--Sofrito[b]	≥ 2 servings/wk	No recommendation
8--White meat	*Instead of red meat*	*Consume poultry often*
9--Wine with meals (optional, only for habitual drinkers)	*≥7 glasses/wk*	*Do not recommend starting wine consumption, but provide information on effects of alcohol for heart health, suggesting 1 serving a day for females and up to 2 for males*
10--Soda drinks	*<1 drink/day*	*<1 drink/day*
11--Commercial bakery goods, sweets, and pastries	*<3 servings/wk*	*<3 servings/wk*
12--Spread fats	<1 serving/day	Up to several servings/day of *trans* fat free spreads
13--Red and processed meats	*<1 serving/day*	*≤ 1 serving/day*

Abbreviations: PREDIMED, Prevención con Dieta Mediterránea; tbsp, tablespoon; wk, week.
[a] Rows in italics indicate identical or nearly identical dietary recommendations

Baseline characteristics of participants are shown in Table 2. The mean age was 56 years (range 18 to 92), 260 (77%) were female, 219 (65%) were African American, 124 (37%) were employed full-time, 251 (74%) had health insurance, 210 (62%) had an annual household income of $\leq$ $40,000 per year, 291 (86%) had hypertension, and the mean BMI was 36 kg/m^2. On average, African American participants were younger, less educated, had lower household income, and (except for HDL-C) had more CVD risk factors.

Table 2. Baseline characteristics: overall, by race, and by intervention group[a]

Characteristics	Overall	Race[b]		Participant Selected Intervention Group[c]		
		African American	White	Lifestyle	Weight loss, group	Weight loss, combination
	n=339	n=219	n=117	n=160	n=57	n=81
Demographics						
Age, mean (SE)	56 (0.6)	54 (0.8)	58 (1.0)	57 (1.0)	53 (1.3)	55 (1.1)
Female sex	260 (77)	181 (83)	76 (65)	110 (69)	52 (91)	72 (89)
Race						
African American				101 (63)	41 (72)	62 (79)
White				58 (37)	16 (28)	17 (21)
Education, y						
≤ 8 (middle school or less)	16 (5)	11 (5)	5 (4)	11 (7)	1 (2)	2 (3)
9-11 (some high school)	45 (13)	35 (16)	9 (8)	27 (17)	5 (9)	9 (11)
12 (high school graduate)	128 (38)	94 (43)	34 (29)	60 (37)	20 (35)	33 (41)
13-15 (some college)	79 (23)	45 (21)	33 (28)	35 (22)	15 (26)	18 (22)
16 (college graduate)	49 (14)	26 (12)	22 (19)	17 (11)	11 (19)	13 (16)
> 16 (graduate school)	22 (7)	8 (4)	14 (12)	10 (6)	5 (9)	6 (7)
Education: high school or less	189 (56)	140 (64)	48 (41)	98 (61)	26 (46)	44 (54)
Marital status						
Married or living with partner	159 (47)	82 (37)	76 (65)	69 (43)	23 (40)	41 (51)
Other	180 (53)	137 (63)	41 (35)	91 (57)	34 (60)	40 (49)
Currently have health insurance	251 (74)	156 (71)	92 (79)	117 (73)	45 (79)	58 (72)
Current employment						
Working full time	124 (37)	82 (37)	40 (34)	46 (29)	29 (51)	38 (47)
Working part time	42 (12)	31 (14)	10 (8)	23 (14)	4 (7)	10 (12)
Do not work due to health reasons	69 (20)	43 (20)	26 (22)	37 (23)	9 (16)	16 (20)
Retired	53 (16)	26 (12)	27 (23)	29 (18)	7 (12)	8 (10)
Other	51 (15)	37 (17)	14 (12)	25 (16)	8 (14)	9 (11)
Annual household income						
< $10,000	62 (20)	50 (26)	11 (10)	40 (29)	6 (11)	9 (11)
$10,000 to < $20,000	64 (21)	45 (23)	19 (17)	29 (21)	11 (21)	18 (23)

$20,000 to < $40,000	84 (28)	60 (31)	23 (21)	32 (24)	14 (26)	27 (35)
$40,000 to < $60,000	33 (11)	15 (8)	18 (17)	11 (8)	8 (15)	9 (11)
$60,000 to < $80,000	27 (9)	13 (7)	14 (13)	11 (8)	11 (21)	5 (6)
≥ $80,000	34 (11)	10 (5)	24 (22)	13 (10)	3 (6)	10 (13)
CVD and risk factors for CVD						
Known coronary heart disease	49 (14)	30 (14)	19 (16)	29 (18)	5 (9)	5 (6)
Known CVD	62 (18)	37 (17)	25 (21)	34 (21)	7 (12)	8 (10)
Hypertension	291 (86)	195 (89)	95 (81)	143 (89)	47 (82)	66 (81)
Cholesterol category						
High (≥ 240 mg/dL)	187 (56)	110 (51)	76 (65)	88 (56)	31 (55)	47 (59)
Borderline (200-239 mg/dL)	46 (14)	33 (15)	12 (10)	16 (10)	11 (19)	13 (16)
Desirable (< 200 mg/dL)	102 (30)	72 (33)	29 (25)	54 (34)	15 (26)	20 (25)
Diabetes	124 (37)	89 (41)	34 (29)	62 (39)	21 (37)	27 (33)
Current cigarette smoker	54 (16)	37 (17)	17 (14)	36 (22)	4 (7)	5 (6)
Packs of cigarettes smoked per day, mean (SE) for current smokers	0.7 (0.1)	0.6 (0.1)	0.9 (0.1)	0.7 (0.1)	0.6 (0.2)	0.6 (0.3)
Taking BP lowering medication	260 (77)	176 (80)	83 (71)	129 (81)	43 (75)	60 (74)
Lifestyle mean (SE)						
DRA total score	27.8 (0.3)	28.0 (0.5)	27.6 (0.4)	27.8 (0.5)	27.2 (0.7)	27.6 (0.6)
Fat quality screener score	15.5 (0.2)	15.4 (0.2)	15.07 (0.3)	15.4 (0.2)	15.3 (0.3)	15.4 (0.3)
Fruit and vegetable, servings per day	3.4 (0.1)	3.4 (0.1)	3.5 (0.2)	3.5 (0.2)	3.0 (0.3)	3.5 (0.2)
Carotenoid index[e], mean (SE)	40.7 (1.3)	41.9 (1.6)	38.2 (2.5)	41.1 (2.0)	42.1 (3.5)	39.1 (2.4)
Walking time, min/wk[f]	91 (11.3)	100 (16.2)	73 (11.8)	110 (18.8)	97 (26.5)	55 (13.3)
Activity time, min/wk[g]	149 (14.0)	150 (18.2)	143 (21.5)	160 (22.7)	148 (29.1)	135 (25.7)
Physiologic mean (SE)						
Weight, kg	98.1 (1.4)	100 (1.7)	94 (2.3)	93.8 (2.0)	101.3 (3.3)	106.4 (2.6)
BMI	36 (0.5)	37 (0.6)	34 (0.8)	34 (0.7)	38 (1.1)	40 (1.0)
Systolic BP, mm Hg	135 (1.2)	136 (1.6)	132 (1.8)	138 (1.8)	130 (2.6)	133 (2.3)

Diastolic BP, mm Hg	82 (0.7)	83 (0.9)	80 (1.0)	83 (1.0)	82 (1.4)	81 (1.3)
HbA_{1c}, % of total Hb	6.6 (0.1)	6.7 (0.1)	6.2 (0.1)	6.5 (0.1)	6.9 (0.3)	6.5 (0.2)
Total cholesterol, mg/dL	193 (2.3)	191 (2.8)	196 (4.0)	191 (3.1)	198 (6.0)	189 (4.7)
HDL cholesterol, mg/dL	54 (0.8)	57 (1.0)	50 (1.4)	55 (1.2)	53 (1.8)	53 (1.5)

Abbreviations: BMI, body mass index(calculated as weight in kilograms divided by height in meters squared); BP, blood pressure; CVD, cardiovascular disease; DRA, Dietary Risk Assessment; HDL-C, high-density lipoprotein; HbA_{1c}, hemoglobin A_{1c}; SE, standard error.
Note: SI unit conversion factors: To convert all types of cholesterol to millimoles per liter, multiply by 0.0259.
[a] Unless otherwise noted, data are reported as number (percentage) of participants.
[b] 3 categorized as other race.
[c] Participants selected intervention group at 6 month follow-up visit; if they did not attend this visit they were assigned to lifestyle group.
[d] Framingham risk scores calculated as percent chance of developing angina, having a myocardial infarction, or dying of coronary heart disease over a 10 year time frame.
[e] Carotenoid index, calculated as the sum of α-carotene, β-carotene,β-cryptoxanthin, and zeaxanthin. Data presented are for nonsmokers (n=261). A higher index indicates greater fruit and vegetable consumption. Statistical tests performed on log-transformed data.
[f] Includes walking for transportation and exercise.
[g] Includes walking and other moderate and vigorous activity.

Aim 1: Assess effect of intervention on diet quality at 6 month follow-up.
Objective: Compared to baseline, participation in the lifestyle intervention will result in an increase of fruit and vegetable intake of at least 1.25 servings per day as estimated by blood carotenoids and the increase will be similar between racial groups and by literacy levels.

The change in fruit and vegetable intake at 6 months, as depicted in Table 3, was modest. By brief questionnaire, the increase was 1/3 of an additional serving per day. Also, the measured carotenoid index actually decreased slightly at 6 month. As noted, when this proposal was written in 2009, the primary aim of the intervention was to increase fruit and vegetable consumption. However, to be consistent with the evolving literature on the importance of fat quality in reducing CVD risk, the intervention was further revised for this study to include a major focus on improving fat quality. With this change and initial focus of the intervention on improving fat quality, one might expect less of an impact on fruit and vegetable consumption.

Table 3. Change from baseline to 6 and 12 months and from 6 months to 12 months[a]

	Phase 1		Phase 2			
	Baseline to 6 months		6 months to 12 months		Baseline to 12 months	
	(6 months minus baseline)		(12 months minus 6 months)		(12 months minus baseline)	
Outcome	n	Mean, 95% CI	n	Mean, 95% CI	n	Mean, 95% CI
Dietary						
DRA total score						
All	235	4.3 (3.7 to 5.0)***	219	-0.7 (-1.3 to -0.1)*	227	3.3 (2.5 to 4.0)***
Subgroup by race[b]						
--African American	155	4.6 (3.7 to 5.5)***	151	-0.2 (-1.0 to 0.6)	156	4.0 (3.1 to 4.9)***
--White	77	3.9 (2.9 to 5.0)***	66	-1.9 (-2.7 to -1.1)***	69	1.7 (0.4 to 3.0)**
Subgroup by intervention[c]						
--Lifestyle			93	0.0 (-1.0 to 0.9)	102	1.7 (0.7 to 2.8)***
--Wt loss, group			51	-0.3 (-1.5 to 0.9)	51	5.1 (3.8 to 6.4)***
--Wt loss, combination			75	-1.7 (-2.8 to -0.7)***	74	4.1 (2.7 to 5.6)***
Fat quality screener score						
All	229	1.4 (1.0 to 1.7)***	218	-0.1 (-0.5 to 0.2)	225	1.0 (06 to 1.3)***
--African American	150	1.4 (0.9 to 1.8)***	150	0.1 (-0.3 to 0.5)	154	1.2 (0.8 to 1.7)***
--White	76	1.3 (0.7 to 2.0)***	66	-0.6 (-1.2 to -0.1)*	69	0.4 (-0.2 to 1.0)
--Lifestyle			93	0.2 (-0.4 to 0.8)	102	0.7 (0.1 to 1.2)*
--Wt loss, group			51	-0.1 (-0.8 to 0.5)	48	1.3 (0.6 to 2.0)***
--Wt loss, combination			74	-0.6 (-1.1 to -0.1)*	75	1.2 (0.6 to 1.8)***
Fruit and vegetable servings per day						
All	249	0.3 (0.1 to 0.5)**	221	0.4 (0.2 to 0.5)***	253	0.5 (0.3 to 0.8)***
--African American	168	0.2 (0.0 to 0.5)	153	0.5 (0.2 to 0.7)***	178	0.5 (0.2 to 0.9)**
--White	78	0.3 (0.0 to 0.7)*	66	0.0 (-0.3 to 0.3)	73	0.5 (0.1 to 0.9)**
--Lifestyle			95	0.1 (-0.2 to 0.4)	127	0.1 (-0.2 to 0.5)
--Wt loss, group			51	0.5 (0.1 to 0.9)*	51	1.0 (0.5 to 1.5)***
--Wt loss, combination			75	0.6 (0.2 to 0.9)***	75	0.9 (0.4 to 1.3)***
Carotenoid index[d]						
All	169	-0.9 (-3.3 to 1.5)	105	3.7 (0.4 to 6.9)	117	3.1 (-0.4 to 6.7)*

--African American	118	-0.2 (-2.8 to 2.5)	77	3.1 (-0.8 to 7.1)	88	3.0 (-1.4 to 7.5)
--White	49	-3.5 (-8.7 to 1.8)	27	5.6 (-0.4 to 11.7)*	28	3.4 (-2.0 to 8.9)
--Lifestyle			33	5.6 (-0.2 to 11.9)	40	3.1 (-3.2 to 9.5)
--Wt loss, group			29	1.9 (-3.5 to 7.3)	31	3.7 (-3.0 to 10.4)
--Wt loss, combination			43	3.2 (-2.0 to 8.4)	46	2.7 (-2.9 to 8.3)
Physical Activity						
Walking time, min/wk[e]						
All	249	64 (19 to 109)**	221	7 (-49 to 63)	253	71 (28 to 113)***
--African American	168	65 (5 to 125)*	153	16 ((-59 to 91)	178	68 (13 to 123)*
--White	78	66 (4 to 128)*	66	-14 (-88 to 61)	73	82 (23 to 142)**
--Lifestyle			95	29 (-56 to 113)	127	60 (-10 to 130)
--Wt loss, group			51	-21 (-164 to 123)	51	66 (-27 to 158)
--Wt loss, combination			75	-2 (-81 to 77)	75	93 (45 to 141)***
Activity time, min/wk[f]						
All	249	97 (36 to 158)**	221	-26 (-96 to 44)	253	83 (30 to 136)**
--African American	168	106 (28 to 184)**	153	-19 (-115 to 77)	178	75 (14 to 136)*
--White	78	88(-13 to 188)	66	-42 (-115 to 32)	73	110 (2 to 218)*
--Lifestyle			95	3 (-84 to 90)	127	67 (-24 to 158)
--Wt loss, group			51	-90 (-310 to 131)	51	108 (9 to 208)*
--Wt loss, combination			75	-19 (-105 to 66)	75	93 (35 to 151)**
Blood Pressure Medication and Physiologic						
Taking BP lowering medication, %						
All	249	2.0% (-0.3 to 4.4)	221	-0.5% (-2.8 to 1.9)	253	0.0% (-3.3 to 3.3)
--African American	167	1.2% (-1.7 to 4.1)	153	0.0% (-3.1 to 3.1)	178	-0.6% (-4.5 to 3.4)
--White	78	3.8% (-0.4 to 8.1)	66	-1.5% (-4.5 to 1.4)	73	1.4% (-4.6 to 7.4)
--Lifestyle			95	-1.0% (-3.1 to 1.0)	127	-0.8% (-5.4 to 3.8)
--Wt loss, group			51	-2.0% (-8.6 to 4.7)	51	-2.0% (-10.5 to 6.6)
--Wt loss, combination			75	1.3% (-3.2 to 5.8)	75	2.7% (-2.5 to 7.9)
Systolic BP, mm Hg						
All	249	-6.4 (-8.7 to -4.1)***	220	0.0 (-2.5 to 2.6)	251	-6.1 (-9.0 to -3.3)***

--African American	168	-6.8 (-9.7 to -3.8)***	152	-0.9 (-4.0 to 2.1)	176	-6.9 (-10.5 to -3.3)***
--White	78	-5.6 (-9.4 to -1.8)**	66	2.5 (-2.5 to 7.4)	73	-4.2 (-8.8 to 0.3)
--Lifestyle			95	-2.2 (-6.2 to 1.8)	126	-8.3 (-12.6 to -3.9)***
--Wt loss, group			50	3.3 (-1.0 to 7.6)	50	-3.6 (-7.8 to 0.5)
--Wt loss, combination			75	0.7 (-3.8 to 5.3)	75	-4.3 (-9.7 to 1.1)
Diastolic BP, mm Hg						
All	249	-3.7 (-4.9 to -2.5)***	220	-1.5 (-2.9 to -0.1)*	251	-5.0 (-6.4 to -3.6)***
--African American	168	-3.5 (-5.1 to -2.0)***	152	-2.3 (-4.0 to -0.5)**	176	-5.2 (-7.0 to -3.4)***
--White	78	-4 (-6.1 to -2.3)***	66	0.7 (-1.8 to 3.2)	73	-4.2 (-6.4 to -1.9)***
--Lifestyle			95	-2.2 (-4.4 to 0.1)	126	-5.4 (-7.5 to -3.2)***
--Wt loss, group			50	1.2 (-1.0 to 3.4)	50	-4.2 (-6.9 to -1.6)**
--Wt loss, combination			75	-2.5 (-5.1 to 0.1)	75	-4.5 (-7.2 to -2.3)***
Weight, kg						
All	248	-0.7 (-1.2 to -0.3)**	219	-1.1 (-1.7 to -0.5)***	250	-1.7 (-2.5 to 1.0)***
--African American	167	-0.8 (-1.4 to -0.3)**	151	-0.9 (-1.6 to -0.3)**	175	-1.7 (-2.6 to -0.8)***
--White	78	-0.4 (-1.3 to 0.5)	66	-1.4 (-2.3 to -0.3)*	73	-1.6 (-3.1 to -0.2)*
--Lifestyle			94	-0.3 (-1.3 to 0.6)	125	-0.9 (-2.1 to 0.2)
--Wt loss, group			50	-1.3 (-2.4 to -0.2)*	50	-3.1 (-4.9 to -1.3)***
--Wt loss, combination			75	-1.9 (-2.8 to -1.0)***	75	-2.1 (-3.2 to -1.0)***
Weight, ≥ 5% weight loss, %						
All	248	9% (6 to 13)	219	18% (13 to 23)	250	23% (18 to 28)
--African American	167	12% (7 to 17)	151	18% (12 to 24)	175	23% (17 to 30)
--White	78	4% (0 to 8)	66	18% (9 to 28)	73	22% (12 to 31)
--Lifestyle			94	14% (7 to 21)	125	19% (12 to 26)
--Wt loss, group			50	22% (10 to 34	50	34% (21 to 47)
--Wt loss, combination			75	21% (12 to 31)	75	23% (13 to 32)

Abbreviations: BP, blood pressure; CI, confidence interval; DRA, dietary risk assessment.
Note: Boldface indicates statistical significance $^{*}p \le 0.05$; $^{**}p \le 0.01$; $^{***}p \le 0.001$

[a] Data are means except where noted.

[b] 3 categorized as other race.

[c] Participants selected intervention group at 6 month follow-up visit; if they did not attend this visit they were assigned to lifestyle group.

[d] Carotenoid index, calculated as the sum of α-carotene, β-carotene,β-cryptoxanthin, and zeaxanthin. Data presented are for nonsmokers and available only through 12 month follow-up visit. A higher index indicates greater fruit and vegetable consumption. Statistical tests performed on log-transformed data.

[e] Includes walking for transportation and exercise.

[f] Includes walking and other moderate and vigorous activity.

Aim 2: Assess the following outcomes at 6 month follow-up: diet quality as measured by questionnaire, physical activity as measured by questionnaire and accelerometer, blood pressure, blood lipids, A1c, weight, and health related quality of life.

These outcomes are also depicted in Table 3. At 6 month follow-up, there was significant improvement in self-reported diet quality, dietary fat quality, and physical activity. In addition, there was substantial improvement in measured blood pressure and, although Phase I did not focus on weight loss, there was modest weight change of -0.7 kg (-1.2 to -0.3) on average. At 6 months, there was minimal change in A1c of 0.01% ((-0.1, 0.1) but among those with diabetes, there was a slight reduction of -0.1% (-0.4, 0.2). Blood lipids were not measured at 6 month follow-up.

Aim 3: Assess use of community resources relevant to lifestyle change

Of 249 participants completing the acceptability survey at 6 month follow-up, 114 (47%) indicated the community resource guide was very helpful and 70 (29%) reported it was somewhat helpful in making dietary changes. In addition, 86 (42%) reported the guide was very helpful and 67 (33%) reported the guide was somewhat helpful for increasing physical activity.

Aim 4: Re-assess above outcomes at 12, 18, and 24 months to determine if changes at 6 months are maintained, enhance, or attenuated overtime.

These outcomes are reported in Table 3 and 4. Overall, most of the self-reported dietary changes were maintained through 12 months, but more so for the weight loss groups, especially for fruit and vegetable intake. From 6 to 12 months, the carotenoid index increased significantly for whites and from baseline to 12 months, there was a statistically significant increase in the carotenoid index score for all participants. The increase in PA reported from baseline to 6 months was generally maintained at 12 months, though less so for the group-based weight loss participants. Change in BP noted at 6 months was also maintained. At 12 months, among all participants there was a significant change in HDL-C of -2 mg/dL (-2.8 to -0.4) and a non-significant change in total cholesterol of -3 mg/dL (-7.0 to 0.7). A1c was little changed for all participants, -0.07 (-0.20, 0.06), with perhaps a clinically significant trend in reduction, -0.3% (0.63, 0.02), for those with diabetes.

Table 4. Change from 12 months to 24 months and from baseline to 24 months[a]

	Phase 3			
	12 months to 24 months (24 months minus 12 months)		Baseline to 24 months (24 months minus baseline)	
Outcome	n	Mean, 95% CI	n	Mean, 95% CI
Dietary				
DRA total score				
All	236	-0.3 (-0.8 to 0.2)	226	2.9 (2.3 to 3.6)***
Subgroup by race[b]				
--African American	168	-0.7 (-1.3 to 0.0)*	158	3.0 (2.2 to 3.8)***
--White	66	0.6 (-0.2 to 1.4)	66	2.8 (1.6 to 4.0)***
Subgroup by intervention[c]				
--Lifestyle	116	-0.1 (-0.8 to 0.6)	105	1.8 (0.9 to 2.7)***
--Wt loss, group	48	-1.1 (-2.1 to -0.2)*	50	4.0 (2.7 to 5.4)***
--Wt loss, combination	72	0.0 (-0.9 to 1.0)	71	3.9 (2.6 to 5.2)***
Fat quality screener score				
All	236	-0.4 (-0.7 to 0)*	224	0.7 (0.3 to 1.0)***
--African American	168	-0.6 (-1.0 to -0.1)**	156	0.7 (0.2 to 1.1)**
--White	66	0.1 (-0.5 to 0.6)	66	0.6 (-0.2 to 1.5)
--Lifestyle	116	-0.7 (-1.3 to -0.2)**	105	0.1 (-0.5 to 0.7)
--Wt loss, group	48	-0.2 (-0.9 to 0.5)	47	1.2 (0.4 to 2.0)**
--Wt loss, combination	72	0.1 (-0.5 to 0.6)	72	1.1 (0.5 to 1.7)***
Fruit and vegetable servings per day				
All	237	-0.2 (-0.4 to 0.1)	250	0.4 (0.2 to 0.6)***
--African American	169	-0.2 (-0.5 to 0.1)	177	0.3 (0.1 to 0.6)*
--White	66	0.0 (-0.4 to 0.3)	71	0.5 (0.1 to 0.8)**
--Lifestyle	117	0.1 (-0.2 to 0.4)	127	0.2 (-0.1 to 0.5)
--Wt loss, group	48	-0.1 (-0.6 to 0.3)	51	0.9 (0.4 to 1.4)***
--Wt loss, combination	72	-0.5 (-0.9 to -0.1)**	72	0.3 (-0.1 to 0.8)
Physical Activity				
Walking time, min/wk[d]				

All	237	-52 (-89 to -15)**	250	22 (-13 to 56)
--African American	169	-49 (-95 to -3)*	177	21 (-25 to 67)
--White	66	-63 (-123 to -2)*	71	27 (-12 to 65)
--Lifestyle	117	-55 (-111 to 2)	127	8 (-50 to 65)
--Wt loss, group	48	-81 (-163 to 0)*	51	-4 (-69 to 60)
--Wt loss, combination	72	-29 (-84 to 27)	72	65 (22 to 108)**
Activity time, min/wk[e]				
All	237	-40 (-91 to 11)	250	48 (-7 to 103)
--African American	169	-25 (-89 to 40)	177	54 (-17 to 124)
--White	66	-82 (-164 to -0.5)*	71	39 (-46 to 124)
--Lifestyle	117	-17 (-106 to 73)	127	51 (-46 to 149)
--Wt loss, group	48	-116 (-208 to -24)**	51	12 (-70 to 95)
--Wt loss, combination	72	-27 (-84 to 29)	72	68 (7 to 129)*
Blood Pressure Medication and Physiologic				
Taking BP lowering medication, %				
All	237	0.4% (-2.3 to 3.2)	250	0.8% (-3.0 to 4.6)
--African American	169	1.2%(-1.6 to 4.0)	177	1.1% (-3.3 to 5.6)
--White	66	0.0% (-5.9 to 5.9)	77	1.4% (-5.9 to 8.7)
--Lifestyle	117	2.6% (-1.1 to 6.3)	127	1.6% (-4.2 to 7.3)
--Wt loss, group	48	2.1% (-5.0 to 9.1)	72	2.0% (-6.6 to 10.5)
--Wt loss, combination	72	-4.2% (-8.8 to 0.4)	54	-1.4% (-7.5 to 4.7)
Systolic BP, mm Hg				
All	235	-1.3 (-3.9 to 1.3)	250	-7.2 (-9.9 to -4.6)***
--African American	167	-2.0 (-5.3 to 1.2)	177	-8.4 (-11.8 to -5.1)***
--White	66	0.9 (-3.3 to 5.2)	71	-4.1 (-8.5 to 0.4)
--Lifestyle	116	-1.2 (-4.9 to 2.5)	127	-8.8 (-12.9 to -4.8)***
--Wt loss, group	47	0.4 (-3.9 to 4.8)	51	-3.9 (-8.4 to 0.6)
--Wt loss, combination	72	-2.4 (-7.8 to 2.9)	72	-6.8 (-11.8 to -1.9)**
Diastolic BP, mm Hg				
All	235	-1.9 (-3.4 to -0.5)	250	-6.7 (-8.3 to -5.1)***

--African American	167	-2.4 (-4.2 to 0.5)**	177	-7.2 (-9.2 to -5.1)***
--White	66	-1.0 (-3.0 to 1.0)	71	-5.4 (-7.6 to -3.3)***
--Lifestyle	116	-1.9 (-4.0 to 0.2)	127	-6.8 (-9.1 to -4.4)***
--Wt loss, group	47	-3.1 (-5.8 to -0.4)*	51	-7.7 (-10.7 to -4.6)***
--Wt loss, combination	72	-1.3 (-3.9 to 1.3)	72	-6.0 (-8.8 to -3.2)***
Weight, kg				
All	232	0.1 (-0.6 to 0.8)	247	-1.6 (-2.5 to -0.7)***
--African American	164	-0.1 (-1.0 to .08)	174	-1.8 (-2.8 to -0.8)***
--White	66	0.6 (-0.6 to 1.7)	71	-1.0 (-2.9 to 0.8)
--Lifestyle	113	-0.9 (-2.0 to 0.1)	124	-1.7 (-2.9 to -0.5)**
--Wt loss, group	47	1.2 (-0.4 to 2.8)	51	-2.1 (-4.3 to 0.0)*
--Wt loss, combination	72	1.0 (-0.2 to 2.2)	72	-1.1 (-2.7 to 0.4)
Weight, ≥ 5% weight loss, %				
All	232	12% (8 to 16)	247	23% (18 to 28)
--African American	164	12% (7 to 17)	174	24% (18 to 31)
--White	66	12% (4 to 20)	71	18% (9 to 27)
--Lifestyle	113	16% (9 to 23)	124	23% (16 to 31)
--Wt loss, group	47	11% (2 to 20)	51	25% (13 to 38)
--Wt loss, combination	72	7% (1 to 13)	72	21% (11 to 30)

Abbreviations: BP, blood pressure; CI, confidence interval; DRA, dietary risk assessment.
Note: Boldface indicates statistical significance $^{*}p \le 0.05$; $^{**}p \le 0.01$; $^{***}p \le 0.001$
[a] Data are means except where noted.
[b] 3 categorized as other race.
[c] Participants selected intervention group at 6 month follow-up visit; if they did not attend this visit they were assigned to lifestyle group.
[d] Includes walking for transportation and exercise.
[e] Includes walking and other moderate and vigorous activity.

From baseline to 12 months, weight change was -0.9 kg (-2.1 to 0.2) for the maintenance of lifestyle intervention, with 24 (19%) losing ≥ 5% body weight; -3.1 kg (-4.9 to -1.3) for the group-based weight loss intervention, with 17 (34%) losing ≥ 5% body weight; and -2.1 kg (-3.2 to -1.0) for the combination weight loss intervention, with 17 (23%) ≥ 5% body weight. During Phase II, outcomes were similar for African Americans and Whites. At the completion of Phase II, 46 participants in the group-based and 70 in the combination weight loss intervention completed an acceptability survey. Among group participants, 37 (80%) reported they were very satisfied and 6 (13%) reported they were satisfied with the intervention. For combination participants, 51 (71%) reported they were very satisfied and 12 (17%) reported they were satisfied with the intervention.

Phase III outcomes are shown in Table 4. Of the 30 participants who lost ≥ 8 pounds at 12 month follow-up, 27 (90%) agreed to take part in the maintenance of weight loss RCT, while 258 received the maintenance lifestyle intervention (Figure 3). Among those in the RCT, compared to baseline, weight change was -7.0 kg at 12 and -5.9 kg at 24 months for the 15 participants in the intensive intervention and -6.9 kg and -2.4 kg, respectively for the 12 participants in the less intensive intervention. Those losing ≥ 5% body weight at 24 months included 7 (47%) of those receiving the more intensive and 3 (25%) of those receiving the less intensive intervention.

Change in outcomes from 12 to 24 and baseline to 24 months for all returnees are shown in Table 4. In general, during the 2nd year of the intervention, there was minor attenuation in self-reported dietary behaviors, more pronounced attenuation of PA, and minimal attenuation in BP reduction. Compared to baseline, weight change was -1.7 kg (-2.9 to -0.5) for the lifestyle only intervention with 29 (23%) losing ≥ 5% body weight, -2.1 kg (-4.3 to 0.0) for the group weight loss intervention with 13 (25%) losing ≥ 5% body weight, and -1.1 kg (-2.7 to 0.4) for the combination weight loss intervention with 15 (21%) ≥ 5% body weight. During Phase III, outcomes were similar for African Americans and Whites. Of note, 24 month weight change, stratified by diabetes status at baseline was -3.67 (-5.19, -2.14), compared to -0.40 (-1.42, 0.62) for those with diabetes.

Aim 5: Assess policy and environmental change (including levels of economic/entrepreneurial activity) using the RE-AIM Framework and CDC Common Community Measures for Obesity Prevention (COCOMO).

As described in the formative phase, under the leadership of Dr. Stephanie Jilcott Pitts, we conducted a survey of community leaders concerning their knowledge and attitudes regarding obesity prevention policy and published a paper on our findings. As stated above, the most winnable, or feasible, policies identified by CAC members were the following: Communities should: provide incentives for production, distribution, and procurement of food from local farms; enhance personal / traffic safety in areas where persons could be physically active; increase opportunities for extracurricular physical activity; increase support for breastfeeding; and enhance infrastructure supporting bicycling and walking. We used this to guide future intervention efforts including the pilot study of a subsidized CSA which promoted the use of local produce and the farmer's market. To support the efforts of local businesses, we initiated the restaurant program, also discussed above in this report. We also tested recipes that translated the Mediterranean diet into southern food culture, including heart healthy BBQ and hush puppies. While we succeeded in generating substantial interest among participants in the annual BBQ festival, we were not able to assess whether either individuals or restaurant owners have adopted any of these recipes for their own use.

Randomized Controlled Trial-Primary aim: Assess difference in weight loss from baseline between 2 intervention arms after a one year maintenance of weight loss intervention.
Hypothesis: Those in the intensive maintenance of weight loss intervention will weigh at least 2 kg less than those in the standard intervention.

These outcomes are shown above for Aim 4. Overall, the embedded randomized controlled trial was inadequately powered to conduct statistical testing (see discussion of major study findings below). However, the observed trend in differences between maintenance intensities was greater than 2 kg.

Secondary Aim 1: Assess the following outcomes at 12, 18, and 24 month follow-up from baseline: weight, diet quality, physical activity, blood pressure, blood lipids, and health related quality of life.

This is reported above in aggregate, but not for RCT sample participants, given small sample size.

Secondary Aim 2: Conduct an economic analysis, reporting a) costs associated with each phase of the intervention and b) costs associated with a unit reduction in body weight after the intensive weight loss program and after the maintenance of weight loss program.

The RCT was underpowered for this purpose. We did not conduct this analysis for the larger sample because we felt without randomization to establish weight change in a control group, there would be little prospects of publication.

Phase III— Analysis, Report Writing, and Dissemination, Phase. (Years: 2.5 to 5):
Aim 1: Complete analysis and report writing of major findings.

To date, all Phase I manuscripts have been published.

Phase II manuscripts currently under review include:

Keyserling TC, Samuel-Hodge CD, Jilcott Pitts S, Garcia BA, Johnston LF, Gizlice Z, Miller CL, Braxton DF, Evenson KR, Smith JC, Davis GB, Quenum EL, Majette Elliott NT, Gross MD, Ammerman AS. A Community-Based Lifestyle and Weight Loss Intervention Promoting a Mediterranean-Style Diet Pattern evaluated in the Stroke Belt of North Carolina: the Heart Healthy Lenoir Program. Submitted to *BMC Public Health* on 2/9/16.

Jilcott Pitts S, Keyserling TC, Johnson L, McGuirt JT, Gizlice Z, Evenson KR, Whitt OR, Garcia BA, Ammerman, AS. Examining the association between intervention-related changes in diet, physical activity, and weight as moderated by the food and physical activity environments among rural, Southern adults. Submitted to *Journal Rural Health* on 2/26/16.

Phase II manuscripts currently under development:

Thayer LM, Pimentel DC, Smith JC, Garcia BA, Sylvester LL, Kelly T, Johnston LF, Smith TW, Ammerman AS, Keyserling TC. Eating Well While Dining Out in Rural North Carolina: A Restaurant-Based Intervention to Help Customers Select Heart Healthy Menu Items.

Manuscript reporting major outcomes for those with and without diabetes.

Manuscript reporting detailed description of lifestyle change through 6 month follow-up.

Manuscript reporting detailed description of weight loss and correlates of weight loss through 24 month follow-up.

Aim 2: Prepare intervention components for dissemination.

Our current plan is to prepare Phase I of the lifestyle intervention, the component that includes 4 counseling session with primary focus on improving dietary pattern and increasing physical activity, for dissemination. Our rationale is that this component of the intervention was very well received, yielded major positive changes in self-reported lifestyle behaviors, and was associated with a reduction in blood pressure and a modest reduction in weight (though Phase I does not focus on weight loss). Further, the dietary content is very similar to that tested in the nut arm of the PREDIMED RCT, which was associated with a 30% reduction in CVD events among participants with and without diabetes. Our rationale is that the dietary intervention was very well received, that the advocated pattern appears to be one that can be maintained over time, and that the pattern is highly concordant with emergent evidence about diet and CVD risk reduction. On the other hand, we do not plan to disseminate the weight loss program. Though this intervention was also well received, the sustained weight loss at 24 months differed little between those electing to take part in the weight program and those who took part in this program. The bottom line is that we think more research is needed before the weight loss program should be disseminated.

To have the broadest reach, our plan is to disseminate this lifestyle program in a web-based format. Consistent with our strong focus group findings, the program is given by a counselor using materials on the web, either in person or remotely by phone using technology that allows the counselor to take control of the participant's computer or tablet to guide the counseling. We believe this very structured program could be given by a variety of health counselors in clinical or public health settings. Further, we also believe the format could be used by peer counselors.

Significant Results

In this study to evaluate a lifestyle and weight loss intervention that promoted a Mediterranean style eating pattern adapted for the southeastern US, participants reported substantial improvements in dietary behaviors (improved fat quality and fruit and vegetable intake) at 6 month follow-up that were generally maintained through 24 months, with increases in fruit and vegetable consumption corroborated by the objective measure of blood carotenoids at 12 month follow-up. A major difference between the diet pattern tested in this study and most previous dietary intervention trials conducted in the US, including several we have conducted in low-income populations (Keyserling, et al., 2008; Ammerman AS, et al., 1992; Ammerman AS, et al., 2003; Keyserling, et al., 1997; Keyserling, et al., 1999; Rosamond, et al., 2000; Ammerman A, et al., 2002), was the recommendation to increase consumption of foods containing high quality fats (no restriction on total fat intake), with a focus on increasing fat intake from nuts and vegetable oils. We believe this recommendation to consume more healthful fats was well received because we encouraged consumption of many foods that historically have been an important part of the southern diet, but previously discouraged by dietary guidelines focusing on fat restriction. Perhaps this appealing aspect of the Med-South diet contributed to the maintenance of dietary change through 24 months.

Though a sub-set of weight loss participants achieved and maintained meaningful weight loss, overall, the weight loss component of this trial did not achieve study goals. First, we expected 60% of participants to take part in the weight loss program, but only 138 (40% of enrollees and 55% of those returning and eligible at 6 month follow-up) elected to do so. Second, for weight loss participants, the average weight loss at the conclusion of the weight loss intervention (baseline to 12 months) of 2.5 kg was less than observed in our previous weight loss intervention trials. Because fewer participants elected to take part in the weight loss intervention and weight loss was less than expected, the embedded RCT of weight loss maintenance was substantially underpowered. Possible reasons for less weight loss than

expected include the non-selected sample (in our prior weight loss studies, participants were screened for motivation to lose weight) and an older population with more co-morbidities. An unexpected positive finding was that 20% of African American participants who returned for follow-up at the conclusion of Phase I, which was not a weight loss intervention, lost ≥ 5% of body weight.

Though the US Preventive Services Task Force (US Preventive Services Task Force, 2015) recommends clinicians should offer and refer all adults with BMI ≥ 30 kg/m^2 to an intensive weight loss program, most published weight loss studies conducted in primary care and community settings (Booth, et al., 2014; Gudzune, et al., 2015; Hartmann-Boyce, et al., 2014) have included selected samples, often younger, with lower BMI, and with less co-morbidity than those seen in routine practice. In contrast, we offered our weight loss intervention to a non-selected, high risk, older, and largely minority sample. With the caveat that our weight change was compared to baseline and not a control group, our achieved weight loss, though modest, was greater than reported in a recent meta-analysis by Booth (Booth, et al., 2014) assessing behavioral weight loss programs in primary care settings with pooled results across 15 RCTs of -1.4 kg (-2.1 to -0.6). Furthermore, in a recent review (Harvey, Ogden, 2014) of weight loss studies conducted in disadvantaged populations, only 20% lost more than 5% of body weight at follow-up, which is less than we achieved in this study. However, overall weight loss was modest, especially at 24 month follow-up, highlighting the need for more effective weight loss interventions for high risk populations, as enrolled in this study.

This study has several limitations. The overall design (excluding the embedded RCT) was a pre-post comparison study with no control group. Thus, observed changes could be due to secular trends or other factors. Many outcomes were self-reported, which may be exaggerated due to social desirability reporting bias. Also, we present many comparisons and some p-values may be significant by chance. Further, our sample size was relatively small for some of the subgroup outcomes reported. Finally, the generalizability of our findings may be limited to samples similar to those enrolled in this study.

In this study promoting a Mediterranean style dietary pattern as a major component of a lifestyle and weight loss intervention to reduce CVD risk, the large majority of participants reported substantial improvement in dietary intake and a meaningful percentage lost weight and maintained weight loss. Importantly, as lifestyle and weight loss changes were similar for African American and white participants, this type of culturally tailored intervention has the potential to reduce both CVD risk and disparities in CVD rates. Future research should include RCTs enrolling similar high risk populations that assess change in CVD risk factors and ultimately change in CVD events.

Publications

Jilcott Pitts, S.B., Keyserling, T.C., Johnston, L.F., Smith, T.W., McGuirt, J.T., Evenson, K.R., ... Ammerman, A.S. (2015). Associations between neighborhood-level factors related to a healthful lifestyle and dietary intake, physical activity, and support for obesity prevention polices among rural adults. *Journal of Community Health*, 40(2), 276-84. PMC4320021.

Jilcott Pitts, S. B., Vu, M. B., Garcia, B. A., McGuirt, J. T., Braxton, D., Hengel, C. E., ... Ammerman, A. S. (2013). A community assessment to inform a multi-level intervention to reduce CVD risk and risk disparities in a rural community. *Family & Community Health*, 36(2), 135–146. PMC4155752.

Jilcott Pitts, S. B., Whetstone, L. M., Wilkerson, J. R., Smith, T. W., & Ammerman, A. S. (2012). A Community-Driven Approach to Identifying "Winnable" Policies Using the Centers for Disease Control and Prevention's Common Community Measures for Obesity Prevention. *Preventing Chronic Disease*, *9*, E79. PMC3392084.

Kowitt, S., Woods-Jaeger, B., Lomas, J., Taggart, T., Thayer, L., Sutton, S., Lightfoot, A. (2015) Using Photovoice to Understand Barriers to and Facilitators of Cardiovascular Health Among African American Adults and Adolescents, North Carolina, 2011–2012. *Preventing Chronic Disease*, 12. PMC4591620.

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Study 2: Reducing Disparities in Hypertension with a Practice-Based Enhanced Care Program (Hypertension Control Study)

Background: This Heart Healthy Lenoir project implemented several modes of Community Based Participatory Research (CBPR) to understand sources of disparities in care and outcomes in Lenoir County. Patients, community members, practice providers and staff were involved in helping the research teams from East Carolina University and UNC Chapel Hill to conceptualize research design, outcomes, and methods of disseminating the results of our study aims. Our aims are detailed below and key background, results and conclusions are included by aim. The intervention was delivered at multiple levels and was guided by the Socioecological Model (Ref), but also by addressing key drivers of practice change (Margolis 2010). Activities that support the Key drivers are those that the study team guided practices to implement such that changes could be made and altered as needed to be sustained. The Key driver approach is firmly rooted in the Chronic Care Model (Wagner 1996).

Aim 1. Formative Phase Work (Year 1):

Use Community-Based Participatory Research principles to understand sources of disparities and inadequate care in Lenoir County, refine a practice-based approach to improving hypertension care, and make community connections to support ongoing links between the practices and community to sustain optimal hypertension care.

1a. Assess patient facilitators and barriers to hypertension care and preferences for a hypertension management program.

1b. Identify practice level strategies to enhance hypertension management by addressing current system barriers and building on practice assets.

To address this aim, semi-structured individual interviews with patients, providers, and practice staff were performed to assess patient- and practice-level facilitators and barriers to achieving optimal blood pressure control. This dialogue allowed the researcher team to develop a blood pressure management intervention with the practices. In-depth interviews were conducted with 41 adults with hypertension, purposely sampled to include diversity of sex, race, literacy, and blood pressure control, and with key office staff at 5 of the primary care practices included in the formative year. Interviews explored barriers to controlling blood pressure, the practice's role in controlling blood pressure, opinions on the using teams in care delivery, thoughts of using home BP measurements to help in clinical decision making and self management support and to get their ideas on how to engage a phone based health coach in the care of regional patients with uncontrolled HTN.

Eligible patient participants were English-speaking patients aged 18 years or older, diagnosed and managed with hypertension who were attending 1 of 5 primary care practices in rural eastern North Carolina. Six to 10 patients per practice were invited to participate in the focus groups.

To complement patient perspectives, providers and staff of each practice participated in an in-depth interview. The interviews within each practice were conducted in 2 groups; 1 with practice leadership (management, lead nurses, providers) and the other with practice staff

(front office personnel, billing staff, and other clinical staff) to maximize diversity of perspectives and minimize single-source bias. Face-to-face semi-structured interviews explored domains of overall health concerns, barriers to optimal blood pressure control, and perceptions of improving primary care delivery for hypertensive patients. We asked opinions about the use of care delivery teams and provided examples of how team-based care has been used effectively in other settings to stimulate discussions on how this approach could be incorporated into the intervention. Where applicable we offered examples of effective office level QI strategies for people to comment on their relevance in their settings (Walsh Medical Care 2006). Trained community members conducted interviews and attempted to match interviewer with interviewee by race, which occurred 90.2% of the time. Interviews lasted approximately 60 minutes and were audio-taped and transcribed.

Aim 1 Key results:

Of the 41 patients who participated in the interviews, 41% reported their blood pressure was at the right level less than half the time. When patients were asked, "What makes it hard to keep your blood pressure under control?", 2 main barriers were identified. First, patients said it was challenging to take medications regularly. Approximately 36% said they had missed a pill at least once in the past week. For some, remembering to take medications as scheduled was difficult. Some patients could not afford their medications. Others mentioned that they were "tired" of having to take medicine. This was influenced by the number and frequency of pills. As one patient said, "*You know, what's hard . . . to me really is sometimes I get tired [of taking medicine]. And I do know that I do need to take it. And sometimes I might not take it every day at the same time.*" (Female patient, age 59, uncontrolled blood pressure)

A second barrier for patients centered on their diet. They said that an unhealthy diet that used too much salt and overeating affected blood pressure levels. Patients appeared to recognize the link between nutrition and blood pressure, but they admitted that making behavior changes was challenging. For example, as one patient stated, *"Sometimes you might overeat something you know you're not supposed to be eating like fried foods. Drinking a little bit too much, and too much salt. Food got enough salt in it already. Gotta learn how to eat it with other seasoning."* (Male patient, age 59, uncontrolled blood pressure)

Both provider and practice staff interviews showed agreement that patients' inadequate adherence with medications affected their blood pressure. Providers recognized that patients did not take their medications because of cost or that they skipped doses to save money.

There was consensus among patients, providers, and office staff that inadequate medication adherence and poor eating habits were important barriers to blood pressure control. However, from the provider and staff perspective, the larger barrier was patients' lack of understanding of the importance of hypertension control. Practice staff reported that some patients held certain beliefs that may affect their treatment adherence. If the patients felt well, they did not make controlling their blood pressure as a high priority. As one provider explained, "*I think patients really focus on symptoms, and when they don't have symptoms, they are not sick. . . . If they feel very well with a blood pressure of 180 over 100, it's very hard for me to sell the blood pressure medication, especially if it's expensive and they had to pay for it. So I wish that high blood pressure would cause pain, because then patients would*

be buying." (Provider)

Another key barrier mentioned by providers and practice staff was patients' belief that little could be done to prevent hypertension and its consequences. Providers and staff noted that some patients considered hypertension a problem that *"runs in the family"* or is *"genetic"* and were convinced that high blood pressure was inevitable. Practice staff shared, *"We ask them their family history. They give their history and say 'I'm sure I'm gonna have it too.' They do think that, no matter what they do, they're gonna get it cause their momma had it, their daddy had it, their grandma had it."* (Practice staff)

Patients identified several strategies that doctors or nurses could use to help them control blood pressure. At the top of the list were regular office visits. They valued the periodic checkups during which providers could make adjustments in prescribed medications. For example, 1 patient explained how providers could help: *"The nurse practitioner at (the practice) saw a need to change it, and I've always wanted like a diuretic for the fluid because I feel like that would help me. . . . She saw the need to add that right in with my blood pressure medicine. That's good if a doctor would monitor (my medications), see the need if it's not working or you need to change, and change you over on that."* (Female patient, age 60, uncontrolled blood pressure).

Patients saw an important role for providers with antihypertensive medication management. They felt their doctors or nurses could help with medication adherence by prescribing medications that were "correct" for high blood pressure or "suited each individual." Accessibility of refills and cost were also important factors related to adherence. More results are included in our Aim 1 publication (Donahue et al Preventing Chronic Disease 2014).

Aim 2. Implementation Phase:

Evaluate the effect of the intervention on lowering blood pressure in a cohort of patients with hypertension

2a. Primary: Evaluate effectiveness of the intervention on average blood pressure for all patients in the cohort and by race.
Hypothesis: A practice-based intervention to improve blood pressure control will reduce mean blood pressure overall and by race at 1 year and sustain that improvement at 2 years.

2b. Primary: Evaluate the differential effect of the intervention by race (African American vs. White).
Hypothesis: African American patients will have greater improvement in mean blood pressure compared to White patients.

2c. Secondary: Evaluate the differential effect of the intervention by health literacy (inadequate or marginal literacy vs. adequate literacy).
Hypothesis: Patients with low health literacy will have greater improvement as those with higher health literacy.

Background/Methods: We conducted a prospective cohort study involving 525 adults with Hypertension (HTN) across 6 primary care practices in a geographically defined area in the rural Southeastern US (a sixth practice was brought on after the formative year). The practices

included 3 private practices, a hospital-owned practice, and 2 community health centers. The practices varied in size from single provider practices to multispecialty group practices. Study recruitment occurred from October 2011 to October 2012 with follow-up completed in October 2014. We used a non-randomized observational trial design to maximize feasibility and acceptability for conducting this research in busy rural primary care practices un-accustomed to participating in research and to facilitate broad community participation- important to addressing health disparities.

We identified and recruited English-speaking patients from participating practices with an established HTN diagnosis and at least 1 visit in the last year with an office measurement of SBP ≥150 mmHg in order to enhance the probability of finding patients with uncontrolled HTN at the baseline study visit (≥ 140/ ≥ 90). Patients were invited to participate via community advertising, point of care hand-outs, "robo calls" and a letter signed by the primary care practice lead. Eligible participants provided written informed consent for study participation.

We used a participatory approach to intervention development, which engaged the providers and staff of the participating practices. Briefly, our multi-component intervention included strategies at both the practice/organization level (e.g., design team calls, regional dinner meetings, practice facilitation, and review of electronic health record [EHR] data) and at the patient level (i.e., telephone coaching, home BP monitoring) for patients with uncontrolled HTN who were in the cohort. The telephone coaching part of our intervention was informed by components of Bosworth's Take Care of Your Blood Pressure study (Bosworth PEC 2008).

The primary aim (2a, 2b) was to evaluate the effectiveness of the intervention on average SBP at 12- and 24-months for all patients in the cohort and by race (AAs versus white). Seven participants were excluded from the race-stratified analysis because they were categorized as "other" race. We also examined in the proportion of the sample with controlled BP control (BP<140/90) overall and by race at baseline, 12 and 24 months. Our sample size calculation was based on detecting a difference in mean SBP of 3.5mmHg between AAs and whites using a one-sided 0.05 t-test, assuming a baseline mean disparity in SBP between AAs and whites of approximately 5mmHg.

We used descriptive statistics to summarize the sample characteristics overall and by race and compared participant characteristics by race using Chi-Square tests for categorical variables and t-tests for continuous variables. The overall effect of the intervention on reducing SBP at 12 and 24 months was tested using a paired t-test. We compared mean changes in SBP between AAs and whites using simple linear regression and multivariable regression controlling for age, gender, co-enrollment in the lifestyle study, and other covariates that were imbalanced between the races (educational level, diabetes, and weight). We did not adjust for household income as it was highly correlated with educational level and was not reported by 15% of study participants.

We conducted above analyses under intent-to-treat principle by imputing missing SBP data using last observation carried forward approach, as well as conducting the analyses on only participants with non-missing outcome data for the time period of interest. As results were qualitatively the same, we report outcomes for returnees only. We also conducted longitudinal analyses using generalized linear mixed models that included a random intercept to account for within subject correlation over time and race and time as fixed effects to examine changes over time and to assess changes in SBP at 12 and 24 months. Because the results were similar to results obtained using paired-t-tests and linear regressions at single time points, we do not present the results from longitudinal models.

Key results:

Aim 2a/b

525 participants were enrolled from six local practices; 306 of the 525 were African American, 212 Caucasian. Baseline participant characteristics are provided in Table 5 below.

Table 5 Participant Characteristics:

Participant Characteristics Bivariate Analyses	Overall N = 525†	Black/African American N = 306	White/Caucasian N= 212	*p value*
Age, mean (range)	58 (20-93)	57 (25-93)	60 (22-91)	0.02
Female sex	356 (68)	218 (71)	134 (63)	0.05
Education: high school or less	382 (73)	246 (80)	132 (62)	P<0.001
Low health literacy (STOFHLA score = 0-22)	111 (23)	85 (30)	25 (12)	P<0.001
Currently have health insurance	394 (75)	218 (71)	170 (80)	0.02
Employment: Working full or part time	199 (38)	120 (39)	74 (35)	0.32
Household Income ≤ 40K	350 (78)	224 (88)	121 (66)	P<0.001
Self-rated health good-excellent	322 (61)	187 (61)	130 (61)	0.96
CVD and risk factors for CVD				
Cardiovascular disease (CVD)	122 (23)	69 (23)	52 (25)	0.60
Diabetes	227 (43)	154 (50)	70 (33)	P<0.001
Current cigarette smoker	118 (23)	69 (23)	47 (22)	0.54
Systolic BP, mm Hg, mean (SE)	139 (1.0)	140 (1.3)	137 (1.4)	0.25
Diastolic BP, mm Hg, mean (SE)	82 (0.6)	83 (0.8)	80 (0.8)	0.01
SBP ≥ 140 mm Hg	231 (44)	138 (45)	89 (42)	.48
Med count class mean (SE)	1.9 (.01)	2.1 (0.1)	1.6 (0.1)	P<0.001
Low (Morisky score <6)	187 (40)	128 (42)	58 (34)	0.05
Lifestyle study participant	200 (38)	130 (42)	72 (34)	0.07
Weight, kg	98 (1.2)	102 (1.5)	93 (1.8)	P<.001
BMI	36 (0.4)	37 (0.6)	34 (0.6)	P<.001
Number of comorbidities mean (SE)‡	3.5 (0.1)	3.4 (0.1)	3.7 (0.2)	0.04

Effect of Intervention on Mean Change in SBP at 12 and 24 months.
At 12 months compared to baseline, mean SBP was 6mmHg lower for the overall sample in unadjusted analyses (Table 6). Both AAs (-5.0mmHg) and whites (-7.8mmHg) had a significant decrease in mean SBP (both p-values <0.001), but the unadjusted difference in the changes in SBP between the races was not statistically significant (-2.7mmHg; p=0.26). After multivariable adjustment, the difference in the changes in mean SBP between race groups remained small and statistically non-significant.

Table 6: Mean Change in SBP at 12 months, Overall and By Race

Outcome	n	Baseline	12 Months	Change in SBP: 12 months minus baseline (95% CI)	Difference in SBP Change: AAs minus Whites (95% CI)	Adjusted* Difference in SBP Change: AAs minus Whites (95% CI)	Adjusted† Difference in SBP Change: AAs minus Whites (95% CI)	Adjusted‡ Difference in SBP Change: AAs minus Whites (95% CI)
				Systolic blood pressure, mmHg (95% CI)				
Overall	408	139 (137.1 to 140.1)	133 (131.0 to 134.6)	-6.0 (-8.0 to -4.1) P=0.001				
Blacks	257	139 (137.2 to 141.7)	134 (132.1 to 136.7)	-5.0 (-7.6 to -2.5) P=0.001	-2.7 (-7.5 to 2.0) P=0.26	-1.7 (-6.5 to 3.0) P=0.47	-2.1 (-6.8 to 2.6) P=0.38	-3.4 (-7.7 to 0.9) P=0.12
Whites	151	138 (135.2 to 140.5)	130 (127.4 to 132.8)	-7.8 (-10.6 to -4.9) P<0.001				

*Model adjusts for: age and sex.
†Model adjusts for: age, sex, and co-enrollment in lifestyle study.
‡Model adjusts for: age, sex, co-enrollment lifestyle study, education level, diabetes, weight, and health insurance.

Table 7 presents the differences in mean SBP from baseline to 24 months overall and by race. Mean SBP decreased by 6.4mmHg overall from baseline to 24 months. Similar to the baseline to 12 month comparisons, mean SBP decreased in both AAs and whites, but the unadjusted AA-white differences in mean SBP change was small and not statistically significant (-1.3mmHg; p=0.61). The adjusted differences in mean SBP change by race remained non-significant after multivariable adjustment.

We also conducted a longitudinal analysis, examining SBP changes from 0- 6, 6-12, 12-18, and 18-24 months (data not shown). This analysis demonstrated that the greatest reduction in SBP occurred during the first 12 months (p<0.01 for both 0-6mo. and 6-12 mo. time periods) and the trend was similar in AAs and whites.

Table 7: Mean Change in SBP at 24 months, Overall and By Race

Outcome	n	Baseline	24 Months	Change in SBP: 24 months minus baseline (95% CI)	Difference in SBP Change: AAs minus Whites (95% CI)	Adjusted* Difference in SBP Change: AAs minus Whites (95% CI)	Adjusted† Difference in SBP Change: AAs Minus Whites (95% CI)	Adjusted‡ Difference in SBP Change: AAs minus Whites (95% CI)
				Systolic blood pressure, mmHg (95% CI)				
Overall	383	139 (137.4 to 141.0)	133 (131.2 to 134.5)	-6.4 (-8.3 to -4.4) P<0.001				
-Blacks	246	140 (137.4 to 141.9)	134 (131.5 to 135.9)	-6.0 (-8.5 to -3.3) P<0.001	-1.3 (-6.1 to 3.6) P=0.61	-0.001 (-4.8 to 4.8) P=0.99	-0.47 (-5.3 to 4.4) P=0.85	-2.0 (-6.1 to 2.1) P=0.33
-Whites	137	138 (135.5 to 141.2)	131 (128.9 to 133.5)	-7.2 (-10.0 to -4.3) P<0.001				

*Model adjusts for: age and sex.

†Model adjusts for: age, sex, and co-enrollment in lifestyle study.

‡Model adjusts for: age, sex, co-enrollment lifestyle study, education level, diabetes, weight, and health insurance.

Effect of Intervention on BP Control (<140/90mmHg) at 12 and 24 months

At baseline, 55% of the overall sample had controlled BP (54% AAs and 56% whites). At 12 months, 70% of the overall sample had controlled BP. Of those who were uncontrolled at baseline (N=183), 56% of them were controlled at 12 months and this significantly differed by race (62% of whites vs. 52% of AAs; p<0.0001). At 24 months, 54% of the overall sample had controlled BP. Of those who were uncontrolled at baseline (N=175), 59% of them had controlled BP at 24 months and this was significantly different by race (56% of whites vs. 61% of AAs; p<0.0001)

Dissemination: Lessons learned and methods to implement effective practice facilitation have been of interest to many. We have used our experience and protocols to develop a course as part of the Practice Facilitation Certification at the University of Buffalo (Halladay 2016). This course was implemented via webinar on May 4, 2016.

Conclusion/summary. A multi-component QI intervention delivered in rural primary care practices was effective at lowering mean SBP at 12 and 24 months in AA and white patients with uncontrolled HTN, but it did not reduce racial disparities SBP. We did not have a significant difference in mean SBP by race at baseline (mean SBP in AAs 140mmHg; mean SBP in whites 137mmHg; p=0.25). At 12 months, both AAs (-5.0mmHg) and whites (-7.8mmHg) had a significant decrease in mean SBP (both p-values <0.001), but the difference in the mean changes in SBP between the races was not statistically significant in unadjusted or adjusted models. At 24 months, mean SBP decreased in both AAs (-6.0mmHg) and whites (-7.2mmHg), but the unadjusted AA-white differences in mean SBP change was not statistically significant in unadjusted or adjusted analyses.

Our study demonstrates that we can reduce mean SBP and improve BP control among AA and white patients with a history of uncontrolled BP from a rural underserved community through a

systematic practice-based QI intervention targeting patients, providers, and staff. However, a different approach may be necessary to narrow racial disparities in BP when they exist. Surprisingly we did not have a significant racial disparity in SBP at baseline.

Aim 2c. Literacy group comparisons: We also evaluated the differential effect of the intervention by health literacy, using the S-TOHFLA assessment tool (Baker PEC 1999). The study group was the same as the 525 included in the race comparisons aim and 493 subjects completed the S-TOHFLA (Aim 2c study group).

Descriptive/ Bivariate comparisons: Overall sample: Table 8 includes the descriptive statistics of the patient cohort. Among the 525 participants included in the HHL study, 493 completed the S-TOHFLA assessment and thus were included these analyses. Among these, 23% received a score of < or = to 22 and were categorize as having low health literacy. Fifty-eight percent of the subjects were African Americans and 31% were males. The mean age was 57 years. The mean BMI and Systolic BP were 36.2 kg/m^2 and 138.2 mm Hg respectively. **Literacy group comparisons:** the low literacy group subjects were older (64.8 vs. 54.7, P<.00001), and had a higher proportion of males (41% vs. 28%, p <.01) and African Americans than the higher literacy group. Mean weight and body mass index was greater in those with higher literacy while mean systolic BP was 144 mm Hg at baseline for those in low literacy compared to 138 mm Hg for those in the higher literacy groups (p<.001).A higher percentage of the low literacy group reported having health insurance. Of note, in this study any coverage, including receiving Medicaid, was considered insured. Only 6% of the low literacy group had household incomes of 40 K or greater. The low literacy group also had a higher mean number of medical co-morbidities.

Among the 493 in the sample, 389 completed both baseline and 12 month study visits and 355 completed baseline and 24 month study visits. After examining the differences in baseline characteristics between those that attended the 12 and 24 month visits and those that did not attend these visits, we found attendees at the 12 month visit were more likely than non-attendees to be older and included a higher percentage of African American patients (p<.05). At 24 months attendees were likewise older and included a higher percentage of AA's, but in addition, included a higher percentage of participants in the low literacy group compared to non-attendees.

Background/Methods – health literacy specific intervention components.

Using participatory methods, we worked to adapt and create strategies that were feasible, evidenced informed, locally relevant and, where applicable, understandable to people of all levels of health literacy. Such strategies included: use of home BP monitoring (HBPM), having patients and their clinical teams discuss HBPM data at the point of care, abstracting and discussing population level HTN control performance data and discussing techniques to improve HTN control.

During the intervention phase, clinical staff learned to motivate patients to change their health behaviors, use techniques to better clarify if patients are truly understanding their instructions, address a limited number of items per patient visit and engage in patient goal setting. We also conducted didactic teaching presentations on health literacy and engaged in role playing exercises at regional dinner meetings. These meetings allowed clinical staff to practice motivational interviewing and teach back techniques.

As noted above the participants in the nested cohort of patients with uncontrolled HTN were invited to participate with a phone coach. This evidence-based phone coaching curricula was delivered by two trained phone coaches via 12 monthly phone calls that lasted 15-20 minutes each. The coaches helped participants set care goals, reviewed accurate BP measurement techniques, and BP target values on each phone call. The investigators worked with practice representatives to choose patient facing self-management support materials that were mailed to each participant prior to each phone coaching session. The research team carefully selected these materials such that they were more picture based, included simple language, addressed a limited number of items, and included "white space" for easier review (Galesic 2009, Garcia-Retamero 2009). The resources included text at the 6th to 8th grade reading level (Kincaid 1975).

Analyses and results: Mean changes in SBP were compared using multivariable regression including a priori planned adjustment for age, BMI, race, and co-enrollment in the lifestyle study. Models were additionally adjusted for other covariates found to be statistically significant at the $p<.05$ level in our bivariate analyses; restricting the inclusion of these co-variates to those not targeted for change by our intervention. The final model included the following co-variates: insurance status, household income, gender, estimated glomerular filtration rate, number of medical co-morbidities, number of classes of anti-hypertensive medications at baseline, subjective social status, and presence of diabetes mellitus.

The 493 participants whom completed the S-TOHFLA assessment were included in these analyses. Among these, 23% received a score of ≤ 22 were categorized as having low health literacy. Fifty-eight percent of the subjects were African Americans and 31% were males. The mean age was 57 (range 20-92) years. The mean BMI and Systolic BP were 36.2 kg/m^2 (SD 9.5) and 138.2 mm Hg (SD 22) respectively. **Literacy group comparisons:** The low literacy group subjects compared to those with higher literacy were older (64.8 vs. 54.7 yrs, P<.00001), had a higher proportion of males (41% vs. 28%, p <.01) and African American. The mean systolic BP was 144 mm Hg (SD 23) at baseline for those in low literacy compared to 138 mm Hg (SD 21) for those in the higher literacy groups (p<.001). A higher percentage of the low literacy group reported having health insurance (including Medicaid). Mean weight and BMI was greater in those with higher literacy. Only 6% of the low literacy group had household incomes of ≥40 K. The low literacy group also had a higher mean number of medical co-morbidities.

Table 8: Baseline Participant Characteristics	**Overall**	**Low Literacy**	**Higher Literacy**	*P* value
Characteristics	N = 493	N = 111	N = 382	
Demographics, N (%) unless noted otherwise as standard deviation (SD) or (range)				
Age, mean (range)	57.0 (20-92)	64.8 (30-92)	54.7 (20-83)	P<0.001
Male gender	153 (31%)	46 (41%)	107 (28%)	0.01
African American	284 (58%)	85 (77%)	199 (52%)	P<0.001
Highest grade completed, mean (SD)	12.2 (2.4)	10.8 (2.7)	12.6 (2.1)	P<0.001
Currently have health insurance	366 (74%)	93 (84%)	273 (72%)	0.01
Working full or part time	196 (40%)	25 (23%)	171 (45%)	P<0.001
Household income ≥ 40K	96 (19%)	5 (6%)	91 (27%)	P<0.001

CVD and risk factors for CVD, N (%)				
Diabetes (self report or $HbA_{1c} \geq 6.5$)	211 (43%)	62 (56%)	149 (39%)	P<0.01
Current cigarette smoker (every day or somedays)	112 (23%)	21 (19%)	91 (24%)	0.28
Taking BP lowering medication	438 (89%)	107 (96%)	331 (87%)	P<0.01
Physiologic, mean (SD) unless noted otherwise				
Weight, lbs, (SD)	217 (57.5)	205 (53.8)	220 (58.1)	0.02
BMI (SD)	36 (9.5)	35 (8.8)	37 (9.7)	0.04
Systolic BP, mm Hg (SD)	138.2 (21.6)	144.3 (22.8)	136.5 (20.9)	P<0.001
Diastolic BP, mm Hg (SD)	82.0 (12.9)	79.9 (12.9)	82.6 (12.8)	0.03
Systolic BP $\geq$ 140 mm Hg	216 (44%)	63 (57%)	153 (40%)	P<0.01
Total cholesterol, mg/dL (SD)	190.3 (41.0)	190.4 (42.9)	190.2 (40.5)	0.58
HDL-C, mg/dL, (SD)	51.9 (15.4)	54.4 (16.3)	51.2 (15.0)	0.06
GFR, mL/min/1.73m^2 (SD)	86.9 (22.8)	78.9 (22.7)	89.2 (22.4)	P<.001
Number of comorbidities (SD)	2.49 (1.9)	2.80 (1.8)	2.40 (1.9)	0.02
Lifestyle study participant	193 (39%)	34 (31%)	159 (42%)	0.05
STOFHLA score = 0-36 (SD)	28.2 (9.7)	12.3 (7.2)	32.8 (3.4)	n/a
Self-rated health good-excellent, N (%)	307 (62%)	73 (66%	234 (61%)	0.45
Comm_Standing (SD)	6.5 (2.3)	6.7 (2.6)	6.5 (2.2)	0.54
US_Standing (SD)	5.5 (2.1)	6.0 (2.5)	5.3 (2.0)	P<0.01
Med_Class_Count (SD)	1.9 (1.3)	2.1 (1.2)	1.8 (1.3)	0.04
Anti-hypertensive medication adherence				
Morisky score (SD)	5.7 (1.4)	5.9 (1.4)	5.7 (1.4)	0.04
Low Morisky score = < 6	177 (36%)	36 (34%)	141 (43%)	0.12
HTN Knowledge score (0-13) (SD)	7.8 (2.8)	6.8 (2.4)	8.1 (2.9)	P<.001
Number of side effects (SD)	2.5 (2.6)	2.3 (2.5)	2.6 (2.6)	0.40
Mental Health Inventory (SD)	72.7 (19.7)	74.7 (18.0)	72.1 (20.1)	0.36
Prescription medications cost/month (SD)	$57 (79.5)	$57 (74.8)	$57 (80.9)	0.89
Patient Activation Measure (SD)	63.1 (15.5)	58.0 (11.5)	64.6 (16.1)	P<0.001

Abbreviations: BMI, body mass index(calculated as weight in kilograms divided by height in meters squared); BP, blood pressure; CVD, cardiovascular disease; HDL-C, high-density lipoprotein; GFR, glomerular filtration rate; HbA_{1c}, hemoglobin A_{1c}; HTN, hypertension; SD, standard deviation; STOFHLA, Short Test of Functional Health Literacy in Adults.
SI unit conversion factors: To convert all types of cholesterol to millimoles per liter, multiply by 0.0259

Participant Characteristics/bivariate analyses:

Table 9 reveals the crude and adjusted mean SBP for the two literacy groups comparing baseline with 12 months and baseline with 24 months. At 12 months compared to baseline,

mean SBP was reduced by 5.6 mm Hg (p<0.00001) for the overall sample in unadjusted analyses. Both the low and the higher literacy groups had statistically significant decreases in mean SBP (6.6 mmHg and 5.3 mmHg, respectively), but the unadjusted difference by literacy group was not statistically significant (Δ 1.3 mm Hg, P=.067). After multi variable adjustment, the difference in mean SBP reductions between the literacy groups remained small and statistically non-significant.

At 24 month analyses, the mean SBP decreased by 5.5 mm Hg overall (p<0.0001). Those in the lower literacy group had an 8.1 mm Hg mean SBP reduction (p=.004), while the higher literacy group's mean SBP reduced by 4.6 mm Hg; the unadjusted between group difference was small and not significantly different (Δ 3.5 mm Hg, p = 0.25) and multivariate adjustment did not result in substantive differences. Therefore, despite within group improvements, the results did not demonstrate a statistically significant narrowing of SBP disparities between the 2 groups at either time point.

Table 9. Crude and Adjusted Change in Mean Systolic Blood Pressure (SBP) by Literacy Level

Baseline to 12 Months.

Outcome	n	Baseline SBP mm Hg (SD)	12 Month SBP (SD)	Mean change within groups: p value	Crude: difference between groups: p-value	Model 1 adjusted[a] difference between groups: p-value	Model 2 adjusted[b] difference between groups: p-value
Overall	377	138.2 (1.1)	132.6 (1.1)	-5.6 p<0.00001			
Low Literacy	89	143.7 (2.3)	137.1 (2.4)	-6.6 p =.02	Δ 1.3 p=0.67	Δ 2.4 p=0.41	Δ 0.7 p=0.83
Higher Literacy	288	136.4 (1.2)	131.2 (1.2)	-5.3 p<0.0001			

[a]Model adjusts for age
[b]Model adjusts for age, co-participation in the lifestyle study, HTN med_class_count, US standing

Baseline to 24 Months.

Outcome	n		24 Month SBP (SD)			Model 1 Adjusted[c] difference between groups: p-value	Model 2 Adjusted[d] difference between groups: p-value
Overall	355	138.3 (1.1)	132.8 (1.0)	-5.5 p<0.0001			
Low Literacy	90	143.7 (2.3)	135.6 (2.2)	-8.1 P=0.004	Δ 3.5 p=0.25	Δ 0.2 p = 0.94	Δ 0.34 p=0.92
High Literacy	265	136.4 (1.2)	131.8 (1.2)	-4.6 p=0.0006			

[c]Model adjusts for age
[d]Model adjusts for age, US_standing
low literacy = STOHFLA score of 0-22, higher literacy = STOHFLA score of 23-36
All analyses on respective visit attendees only

Conclusion/Summary: Our results suggest that a practice based multi-level intervention designed using the principles of health literacy can equally help lower SBP in patients with low and higher health literacy for up to 2 years. Although SBP reduction was not differentially greater in the low literacy group, a result which would have supported our hypothesis and demonstrated a narrowing of disparities, importantly disparities in mean change in SBP over time was not widened, a phenomenon which has been unexpectedly found in other studies (Green 2008, Sobel 2009).

We credit the success of our intervention to the multi-level approach that guided clinical staff, patients and the health coaches to improve how they communicate with each other.

Aim 3. Practice level Cost analysis.

Evaluate the cost of implementing and sustaining a community supported practice-based intervention for improving blood pressure control from the health care system perspective.

As part of this practice based QI effort, we performed an activity based costing analysis to describe the practice level costs incurred to develop, implement and maintain key tasks. We asked about staff and supply costs, but the vast majority of costs were those incurred by staff focusing their time on the needs of the project and to implement practice changes.

We interviewed 20 practice stakeholders and phone based health coaches during 2012-2014. We calculated the time invested by individuals to perform each task within each study phase and applied national hourly wages to generate cost estimates.

Our descriptive analyses focused on four of the most engaged practices. Activities included time to abstract HTN control data, participate in project meetings, identify patients with uncontrolled HTN, create standardized work, and to provide additional health coaching for patients with uncontrolled HTN.

The tables below describe the costs by phase (development, implementation and maintenance) to engage in the HHL study activities.

Table 10: Practice Level Staff Costs[a] and Staffing Models Used among Four of the Most Engaged HHL Practices - Development Phase Tasks

Developmental Phase Year – One Time Costs Only

	Total cost of each task and # of practice staff involved per Task[b] (# staff noted in parenthesis)			
	Practice 1	Practice 2	Practice 3	Practice 4
Task 1. Initial generation of lists of patients with hypertension and uncontrolled hypertension by race and ethnicity by informatics staff:	$ 382 (2)	$ 910 (1)	$ 1,074 (2)	$ 910 (1)
Task 2. 1 hour on site practice provider/staff meeting - designing and tailoring intervention (visit planners, phone coaching content, etc.)	$ 306 (10)	$188 (5)	$171 (4)	$139 (5)
Task 3. On-site instruction on accurate BP measurement	$ 191 (11)	$214 (7)	$172 (4)	$234 (7)
Total Costs in Development Phase	**$ 879**	**$ 1,312**	**$1,417**	**$1,283**

Staffing Models Used for Each Task

Task 1. Practice 1: Informatics staff (1 offsite informatics staff and 1 onsite administrator with informatics skills)
Practice 2: Informatics staff (trained administrator)
Practice 3: Informatics staff (1 offsite informatics staff and 1 onsite administrator with informatics skills)
Practice 4: Informatics staff (trained administrator)

Task 2. Practice 1: members = 1PM, 1NP, 1MD,1RN, 2LPN, 2 MA, 2 office support staff
Practice 2 = 1NP,1RN, 1 lab/technologist, 1 MA, 1 office support staff
Practice 3 = 1 MD, 1 PA, 1 office manager, 1 office support staff
Practice 4 = 1MD, 2 MA, 2 office support staff

Task 3. Practice 1: members = 1 NMW, 6 CMA, 1 LPN, 3 MA,
Practice 2 = 1NP,1RN, 1 technician, 1 MA, 1 CNA, 1MD
Practice 3 = 1 MD, 1 PA, 1 office manager, 1 CMA
Practice 4 = 1MD, 1NP, 3 MA, 2 RN

[a] All costs are generated using 2010 mean salaries without benefits of key practice staff required for each activity
[b] Numbers of staff required for each activity is based upon actual experience of the project and research team consensus.

Table 11: Practice Level Staff Costs[a] and Staffing Models Used among Four of the Most Engaged HHL Practices – Implementation Phase Tasks

First Year of Implementation

	Total cost of each task and # of practice staff involved per Task[b] (# staff noted in parenthesis)			
	Practice 1	Practice 2	Practice 3	Practice 4
Task 4. Hypertension control rates/performance data abstractions: monthly (all patients seen in a month) and yearly (unique patients yearly data pulled every 6 months) by Informatics staff:	$346 (2)	$218 (1)	$182.1 (2)	$218 (1)
Task 5. Practice staff attendance at 4 quarterly dinner meetings per year[a]	$2,449 (10)	$1,702 (5)	n/a	$1,001 (4)
Task 6. Participation staff in 4 separate one hour on site coaching visits[a]	$ 1,225 (10)	$851 (5)	n/a	$500 (4)
Task 7. Participation in 10 monthly calls by lead provider and/or administrator	$,1361 (2)	$419 (1)	n/a	$836 (1)
Total Costs in implementation years	**$5,381**	**$3,190**		**$3,027**
Task 8. Special cost in ONLY first year of implementation phase that was required to identify patients at the point of care with uncontrolled HTN as EHR abstractions performed by IT staff inaccurately underestimated this population.	$1,450 (4)	$5,907 (1)	n/a	$472 (1)
Thus total costs in year one of implementation only	**$6,831**	**$9,097**	[b]	**$3,499**

Staffing Models Used for Each Task

Task 4. All Practices: Same informatics staff as in table 1 task 1.

Task 5. Quarterly meetings - estimate of average number of attendees per meeting Practice 1: 1PM, 1NP,1MD,1RN,2LPN,2MA,2 administrative support staff Practice 2: 1NP,1RN, 1 MA, 1 lab/technologist, 1 office support staff Practice 3: n/a Practice 4: 1MD, 1MA, 2 office support staff
Task 6. On site coaching visits - estimates of average attendance): Practice 1: members = 1PM, 1NP,1MD,1RN,2LPN,2MA,2 administrative support staff Practice 2: 1NP,1RN, 1 MA, 1 lab/technologist, 1 office support staff Practice 3: n/a Practice 4: 1MD, 1MA, 2 office support staff
Task 7. Monthly Design team Calls Practice 1: 1 MD, 1 PM Practice 2: 1NP Practice 3: n/a Practice 4: 1 MD
Task 8. Special Costs to identify patient patients with uncontrolled HTN Practice 1: staff member: LPN (identify patients (1 min for 200 patients) and providers (review lists for acceptability – 20 minutes per week for 6 months) Practice 2: office manager faxed visit lists and entered visit BP's on to these lists for study staff to then reach out to those with uncontrolled HTN. Took 1.5 hrs/day for 5 months, then 30 min per day for 7 months. Practice 3: practice did not participate substantially in this part, full turnover of providers Practice 4: Medical assistant scanned daily BP's for 15 min per day to find eligible folks to send to research staff

[a] Numbers of staff required for each activity is based upon actual experience of the project and research team consensus where repetitive activities occurred with slight variations in practice staff attendance at each activity

[b] Total cost not available for practice. The practice was engaged during the early phases, but did not sustain engagement long term

Table 12: Staff and Coaching Costs for Phone Coaching Services for patients with Uncontrolled HTN and cost estimates to provide services for future incident cases

Costs for Phone Coaching Services by Task					
					Cost per new patient[a] – incident cases during maintenance period.
	Practice 1 (871 pts)	Practice 2 (660 pts)	Practice 3 (445 pts)	Practice 4 (177 pts)	
Task 9. MD/NP/PA time to review coaching report summaries based upon # patients with uncontrolled HTN	$ 9,964	$ 5,518	$ 3,952	$ 1,480	$ 12
Task 10. MA time to process coaching summary reports for provider review and signature	$ 3,345	$ 2,534	$1,708	$680.	$ 4
Total Practice Staff Costs	**$ 13,309**	**$ 8,052**	**$5,660**	**2,160**	**$ 16**
Task 11. Paying per hour for Vendor sponsored phone coaching services. Phone coach	$ 30,311	$ 22,968	$15,486	$ 6,160	$ 35
Task 12. Paying per hour for Vendor sponsored phone coaching service. Administrative support for phone coach	$8,013	$ 6,072	$ 4,094	$ 1,628	$9
Total Health Coaching Costs	**$ 38,324**	**$ 29,040**	**$ 19,508**	**$ 22,407**	**$ 44**

[a] We created a "primary care provider" salary based upon averaging the hourly salaries of family medicine and internal medicine providers using the 2010 bureau of labor statistics data

Conclusion/Summary: Our results highlight the need for practices to invest in human resources in order to improve the identification and management of patients with hypertension.

Not unexpectedly, as our practices had little prior experience population level data abstraction procedures, substantial time investments were required of the IT and clinical staff members in the Developmental phase of the project (Table 10).

The majority of the practice staff costs were those devoted to attending on-site and regional meetings. Providing patient level health coaching was one of the greatest expenses and ideally could be reduced by having higher numbers of patients with controlled BP's.

Despite practice and staffing differences between the four most engaged practices, the developmental phase cost were similar, ranging $879 - $1,417 (Table 11). Implementation costs varied more widely as practices took different approaches to identify patients with uncontrolled

hypertension. Practice specific phone health coaching costs ranged from $19,508 to over $38,000 (Table 12).

The time required to implement new hypertension care activities and to offer health coaching to those with uncontrolled HTN is not inconsequential, but likely consistent with other efforts to improve care processes and patient outcomes in primary care practice.

This study adds to the growing literature on practice level costs of engaging in systems change. Understanding these costs and balancing these against practice incentives may be helpful as stakeholders make decisions regarding engaging in HTN QI.

Publications

Cené, C.W., Halladay, J.R., Gizlice, Z., Roedersheimer, K., Hinderliter, A., Cummings, D.M., ... DeWalt, D.A. (2015) Associations between subjective social status and physical and mental health functioning among patients with hypertension. *Journal of Health Psychology.* PMC Journal -In Process.

Cummings, D.M., Wu, J.R., Cene, C., Halladay, J., Donahue, K.E., Hinderliter, A. ...DeWalt, D. (2015). Perceived Social Standing, Medication Nonadherence, and Systolic Blood Pressure in the Rural South. *Journal of Rural Health.* PMC Journal –In Process.

Donahue, K. E., Vu, M. B., Halladay, J. R., Miller, C., Garcia, B. A., Cummings, D. M., ... DeWalt, D. (2014). Patient and Practice Perspectives on Strategies for Controlling Blood Pressure, North Carolina, 2010–2012. *Preventing Chronic Disease*, 11, E69. PMC4008946.

Donahue, K., Tillman, J., Halladay, J., Cene, C., Hinderliter, A., Cummings, D., . . . DeWalt, D. (2016). Lessons Learned from Implementing Health Coaching in the Heart Healthy Lenoir Hypertension Study. Progress in Community Health Partnerships: Research, Education, and Action. – In Process.

Halladay, J., Tillman, J., Hinderliter, A., Cummings, D., Donahue, D., Cene, C., . . . DeWalt, D. (2016). Practice level costs of office based hypertension performance improvement. The Heart Healthy Lenoir Study. *Journal of Healthcare Management.* – In Process

Halladay, J. R., Donahue, K. E., Hinderliter, A. L., Cummings, D. M., Cene, C. W., Miller, C. L., ... DeWalt, D. (2013). The heart healthy lenoir project-an intervention to reduce disparities in hypertension control: study protocol. *BMC Health Services Research*, 13, 441. PMC4015615.

Tillman, J. (2013). Health Coaching Interventions with a Heart-Healthy Lenoir Project Client. (Donahue, et al., 2016)*Global Advances in Health and Medicine,* 2(3), 83-6. PMC3833539.

Study 3
CVD Genetic Predispositions and Genomic Signatures (Genomics Study)
Principal Investigator: Jonathan Schisler, PhD

Summary of Progress Toward Achievement of Study Aims

AIM #1: DETERMINE THE PREVALENCE OF GENOMIC RISK SIGNATURES IN HIGH-RISK COMMUNITY POPULATIONS USING GENOME-WIDE ASSOCIATION STUDIES (GWAS).

In concordance with Study 1 and 2 of the proposal, this project consisted of three primary phases: Assessment and Preparation Phase (Y1), Implementation and Experimental Phase (Y2-Y4), and Analysis and Dissemination Phase (Y5-Y6). All three specific aims of our research plan are were dependent on the completion of the genotyping from all enrolled study subjects (completed in Y4) as well as the study subjects' success in the study (Y5).

Biological material transport and processing

The majority of the recruitment of study subjects started in September 2011. Blood samples were transported bi-weekly back to the Bioprocessing Core (BPC) at the University of North Carolina for DNA extraction. They were processed upon arrival to extract DNA, subsequently analyzed for quality control metrics and stored until enrollment is closed and all sample processing is completed. The majority of the DNA purifications were completed in December 2012 with a total of 549 samples. Of these 549 samples, 512 samples were submitted for genotyping in January 2013. The genotyping data was completed in April of 2013. The remainder of samples (approximately 30-45) were submitted in Y5 and can be used for additional candidate SNP confirmations.

SNP analysis

A workflow was established to identify problematic single nucleotide polymorphisms (SNPs) and potential problematic samples and subsequent optimization of genotyping calls based on the Cohorts for Heart and Aging Research in Genomic Epidemiology (CHARGE) Consortium. The results of our genotyping processing and final data structure is presented.

Genetic data quality control

Table 13. SNP call rate per study subject (n = 512)

Minimum	98.51%
Maximum	99.97%
Mean	99.84%
Std. Deviation	0.08810%
Std. Error of Mean	0.00389%
Coefficient of variation	0.09%

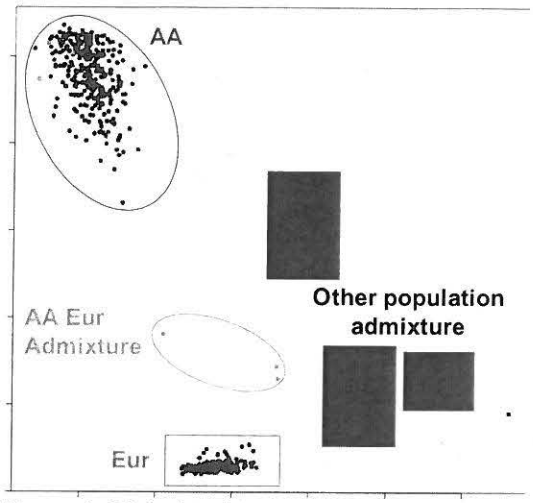

Figure 3. PCA plot of the samples based on numerical conversion of genotype to (-1, 0, 1). From the graph below, we can see clearly several aspects: a) persons of African descent in the upper left, persons of European descent in the bottom middle, c) a few persons who have varying degrees of apparent admixture between African and European, d) a few persons who have influences from other population groups.

The samples from other populations or from admixture are identified below and are outliers from either the African American (AA) or European/Caucasian (Eur or CAU) populations as plotted in **Figure 3**:

- 1970-073_07-121-1: green point directly between the two clusters (admixture of European and African populations)
- 1972-04H_01-121-1 & 1969-04C_01-011-1: two other green points (admixture of European and African and potentially other influences)
- 1969-02F_01-066-1: outlier in lower middle right (other population admixture)
- 1969-06F_07-079-1: outlier in lower extreme right (other population admixture)
- 1971-06A_01-125-1: outlier in lower right (other population admixture)
- 1971-01G_01-109-1: outlier in upper middle (other population admixture)
- 259689_07-154-1: was removed prior to this analysis (an extreme outlier)

Only one sample had a call rate below 99% (1972-06H_02-186-1, 98.8% Call rate). However, the genotypes appear to be of high quality and therefore we recommend that this sample be kept. In a separate issue, this sample may not be appropriate for Copy Number (CN) analysis. Sample 259689_07-154-1 showed adequate QC related to call rate and het rate (Call Rate = 99.4%, Het Rate is normal); however, it is still suspicious due to the extreme differences in its genotypic profile compared with other samples. Also, the numerical designation suggests a unique origin compared to other samples. Whether the differences are due to the sample being from a radically different population group, or due to specimen capture biases, this sample was removed from the study.

The following are results of the improvements from performing both automated data-driven clustering and manually driven clustering to improve specific SNPs. **Figure 4** and **Tables 14 & 15** summarize both overall quality of the samples and the impact of our efforts.

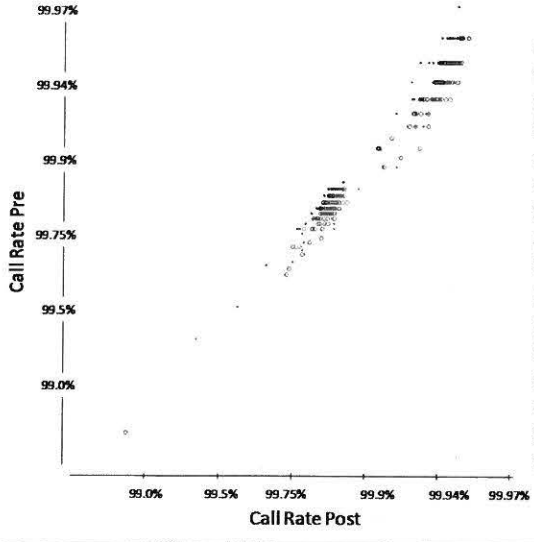

Figure 4. Summary of sample call rates prior to and post data-driven and custom analysis of SNPs:
- ○ African ancestry
- • European ancestry

Samples in magenta experienced an increase in Call Rate (65%) due to the data-driven custom analysis. Persons of African ancestry benefited more from custom clustering than persons of European descent.

Table 14. Improvement in calls for autosomal SNPs. A Low Call rate is a SNP with a Call Rate < 90%. A Better CR SNP is a SNP with a call rate between 90% and 95%. A High CR SNP is a SNP with a Call Rate > 95%. A SNP violates HWE assumptions (HWE viol) if the p-value associated with a HWE test normalized to 100 subjects is less than 0.001.

	African	Eur	All		African	Eur	All
State	pre	pre	pre		post	post	post
Low Call Rate (CR)	278	339	231		96	130	75
No variation	174,925	223,929	151,856		172,528	223,357	149,130
Better CR	805	779	666		293	458	209
Better CR-HWE viol	71	55	44		70	75	49
High CR	756,526	707,550	779,595		759,556	708,615	782,845
High CR-HWE viol	186	139	399		248	156	483
Autosomal SNPs of higher quali	757,331	708,329	780,261		759,849	709,073	783,054
Total autosomal SNPs	932,791	932,791	932,791		932,791	932,791	932,791

Table 15. Improvement in calls overall, includes non-autosomal SNPs

	African	Eur	African	Eur
State	pre	pre	post	post
Low Call Rate (CR)	304	392	278	329
No variation	180,281	231,030	178,001	230,585
Better Call Rate	936	998	400	607
High Call Rate	776,657	725,758	779,499	726,657
Total SNPs	958,178	958,178	958,178	958,178

From **Table 14**, we see that overall, nearly 2800 SNPs were improved in a significant way: higher call rates, fewer SNPs with no variation in one or the other population group while holding the SNPs that violate HWE nearly the same. For example, we see that in the African population, the number of SNPs that had no variation as measured decreased by nearly 2400 (1.4%) and that the number of SNPs that had high call rates while meeting HWE assumptions increased by over 3000. While the European population group did not post as impressive a gain in quality, they still had > 1000 SNPs with high call rates that met HWE that did not previously.

From **Table 15**, we see that combining both African and European results, SNPs with low call rates were reduced, SNPs with no variation dropped, and the number of SNPs with call rates > 95% increased by over 3700. SNPs with the intermediate ("Better") call rate dropped primarily because more SNPs were improved to the High Call Rate group than were improved from the Low Call Rate or No Variation group to the Better Call Rate group. So even the drop in this class indicates the greater gain.

Identification of cardiovascular disease (CVD) genomic risk markers

We identified 649 and 93 markers associated with CVD in CAU and AA populations, respectively. These SNPs data were derived from published scientific literature, CVD pathway analysis, and whole-genome analysis data sets. The rationally selected marker set offers

comprehensive coverage of genes in pathways underpinning primary and secondary vascular disease processes such as blood pressure, insulin resistance, metabolic disorders, dyslipidemia, and inflammation. Given the primary independent physiological variable that improved across both studies, we focused on the baseline systolic blood pressure and the associations to previously established blood pressure risk SNPs (31 and 20 SNPs in CAU and AA, respectively). In our unadjusted model we did not identify any significant associations with SBP and the AA SNPs previously associated with blood pressure in larger GWAS; however, we did see significant associations ($p < 1E\text{-}5$) with 3 of the 31 SNPs in our Caucasian population (rs1378942, rs1458038, and rs17367504). This likely reflects the lack of larger GWAS in African Americans, the difficulty of association studies in ad-mixed populations, and the lack of "healthy control" datasets. We are now running adjusted models (age, gender, BMI) as well as independent association studies from our own dataset; however, the unexpected lower mean SBP across both studies may limit the ability to detect baseline associations. Hence, our approach in Aim 2 where we look for associations with the responsiveness to the intervention appears to be more applicable in identifying risk SNPs.

Return of results

A subset of these data are also being used to study the effects of genomic risk knowledge on motivation toward health behavior, a project synthesized in Y4 as a natural extension of Aim 1. Research suggests improvements in motivation toward behavior change when individuals receive genetic counseling based on one gene and even better outcomes when individuals receive genetic counseling based on two genes. Not surprisingly, less is known about the impact of receiving genetic information in minority populations, particularly in the Stroke Belt. We are determining if genomic-risk knowledge will increase motivation towards CVD risk reduction health behaviors as compared to prior personal knowledge of risk and whether this is moderated by risk status in a subset of the genotyped participants (150 African-Americans). For inclusion of genotyping data in this study we further filtered the CVD markers to meet the following requirements:

1. identification through an adequately powered GWAS with CVD associations at the genome-wide significance level ($p \leq 5x10^{-8}$);
2. replicated associations;
3. present in African ancestry.

This yielded a 19 allele marker panel used to calculate genetic risk represented as an additive model versus a multiplicative model. Additive models have been used in previously by our group and others and are thought to be a more effective method of risk communication. Briefly, participants received a score (ranging from 0 – 38 based on the 19 total alleles) and participants were categorized into "high" (upper quartile), "average" (middle two quartiles), and "low" (lowest quartile) genetic risk for developing CVD. Participant's risk category was conveyed verbally, with visual aids, and in a written summary given to the participants. The data collection completed in March of 2016 and the analysis to be completed in the next month.

As a result, we hope our approach will allow us to adapt CVD genomic risk intervention materials tailored to African-Americans in Lenoir Count and using a randomized controlled

design, determine the effect of conveying CVD genomic risk via culturally and literacy appropriate materials on the motivation toward changing diet and physical activity behaviors, psychosocial factors, and self-reported change in diet and physical activity behaviors the following outcomes relative to no genomic risk communication.

AIM #2: DEVELOP AND EVALUATE NOVEL GENOMIC MODELS INCORPORATING HIGH-RISK FEATURES IN THIS POPULATION TO DESIGN PATIENT- AND GENOMIC-SPECIFIC INTERVENTIONS.

We used the genotype data from 347 study participants to identify genetic-based factors that may contribute to increased cardiovascular disease (CVD) risk, with a particular focus on hypertension. To identify potential SNPs associated with a change in systolic blood pressure (ΔSBP) one-year post-intervention (-8.71 mmHg ± 1.81 and -4.58 mmHg ± 1.71 in CAU and AA groups, respectively) we used the 585,865 quality SNPs used for our analyses (outlined in Aim #1). We then developed a multi-variable linear model accounting for ΔSBP-associated covariates, including age, gender, BMI, smoking status, and age-interaction terms, to identify significant SNP associations separately in the African American (AA) and Caucasian (CAU) cohort:

$\Delta SBP_{12\text{-month}}$ ~ Age + Gender + Smoking + Gender*Age + Smoking*Age + SNP + SNP*Age.

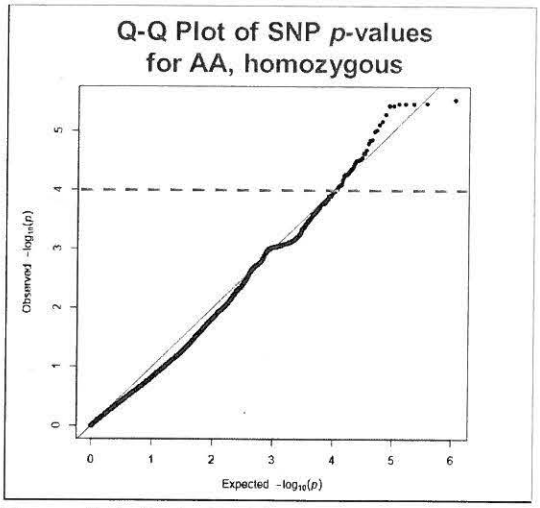

Figure 5. Q-Q plot for AA population reveals a skew in the *p*-values for both the homozygous SNP term. This could indicate that there is an association that may be difficult to assess by this study due to a reduced statistical power. We further investigated the loci in this skewed area of the plot (above dotted blue line) by filtering for *p*-values < 0.0001.

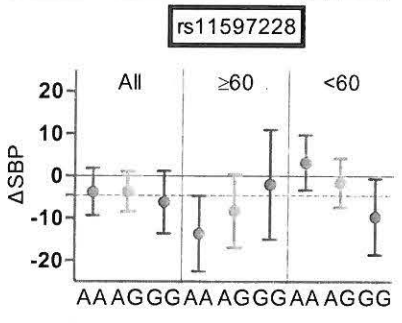

Figure 6. Using SNP rs11597228 as an example, we are able to demonstrate the effect of the age interaction term on ΔSBP by partitioning the AA cohort into old (≥60 years of age) and young (<60 years of age) age group. While the major "A" allele associates with a reduction in SBP in the old age group, the minor "G" allele associates with SBP reduction in the young age group. Dotted line demarks average ΔSBP in AA HTN group (-4.58 mmHg).

In the AA cohort the resulting Q-Q plots identified a skewed region that we filtered for *p*-values < 0.0001 resulting in the identification of 46 SNPs for both the homozygous SNP term (**Figure 5**) and the interaction term, Age, associated with SBP change at one-year post-intervention. Interestingly, we identified 7 SNPs mapped to 3 separate loci linked to 6 candidate genes (*CELF2*, *SFTA1P*, *CHST9*, *AQP4*, *CPVL*, and *CHN2*) that may be involved in CVD risk and inflammation. **Figure 6** depicts the result at the *CELF2/SFTA1P* locus where the SNP*age interaction is clear. **Table 16** lists the primary hits identified in the AA cohort. In the CAU cohort we identified 66 SNPs at with the same criteria,

however we only had single locus hits and given the smaller cohort size, we have focused primarily on the AA cohort.

The identification of SNPs associated with the success of a hypertension intervention suggests that genetic factors in combination with age may contribute to an individual's success in lowering SBP. Further investigation is required to determine the role of these SNPs in the ability of individuals to respond to the HHL intervention in regards to lowering SBP, such that more precise treatment recommendations may be made in the future as part of personalized care delivery. Likewise, SNPs associated with either a lack of, or increase in SBP may signal clinicians to advise alternative treatments for such patients.

Table 16. Many SNPs appeared to be randomly distributed throughout the genome with several notable exceptions, including 7 SNPs listed in the table below which are linked to three separate loci and six candidate genes. The rs identification number (SNP ID), the genes in the region of the SNP loci, the major and minor allele on the forward strand, minor allele frequency (MAF), and the p-values for the indicated modeling variables is provided.

SNP ID	Genes	Loci	Major / minor allele	MAF	Het SNP	Homo SNP	Het SNP×Age	Homo SNP×Age
rs2074784	*CPVL; CHN2*	**7**: 29111578-29122176	A/C	0.34	5.82E-01	**3.15E-05**	7.00E-01	**4.82E-05**
rs3735558	*CPVL; CHN2*	**7**: 29111578-29122176	A/C	0.35	9.31E-01	**3.06E-05**	8.50E-01	**4.71E-05**
rs4747873	*CELF2; SFTA1P*	**10**: 10660837-10707182	C/T	0.45	3.34E-02	**4.71E-05**	4.46E-02	**7.42E-05**
rs6602448	*CELF2; SFTA1P*	**10**: 10660837-10707182	A/G	0.37	6.62E-02	**9.65E-05**	7.46E-02	**8.67E-05**
rs11597228	*CELF2; SFTA1P*	**10**: 10660837-10707182	A/G	0.46	4.64E-03	**4.28E-05**	5.48E-03	**5.95E-05**
rs16942954	*CHST9; AQP4*	**18**: 24501350-24502493	A/G	0.047	9.00E-01	**3.46E-06**	9.67E-01	**3.84E-06**
rs16942955	*CHST9; AQP4*	**18**: 24501350-24502493	A/G	0.047	9.00E-01	**3.46E-06**	9.67E-01	**3.84E-06**

AIM #3: DETERMINE WHETHER GENOMIC SIGNATURES CAN BE USED TO PREDICT RESPONSIVENESS TO INTERVENTIONS THAT UNDERLIE CVD DISPARITIES.

Few Americans meet consumption recommendations for dark green and orange vegetables, which are strongly associated with reduced risk of chronic diseases (Kimmons, 2009). Vegetable sweetness and bitterness were found to be independent predictors of more or less preference for sampled vegetables and vegetable intake, respectively (Dinehart, 2006). Using structural equation modeling the authors found that one's ability to detect a bitter compound

called 6-n-propylthiouricil, or PROP, was significantly related to vegetable preference, which in turn is related to frequency of vegetable consumption. PROP and phenylthiocarbamide (PTC), which resemble bitter compounds found in vegetables, are ligands for the G-protein coupled receptor TAS2R38. More specifically, vegetables in the brassica family, such as collard greens, kale, broccoli, cabbage, and Brussels sprouts, contain glucosinolates and isothiocyanates (molecules resembling PROP), and are therefore detected by the TAS2R38. Three missense polymorphisms constituting two primary hapolotypes in the TAS2R38 gene lead to distinct bitter tasting phenotypes (below). Individuals with at least one PAV haplotype perceive PTC-like molecules in vegetables as tasting bitter, and therefore may develop an aversion to those types of vegetables, and even vegetables in general. Moreover, efforts to increase vegetable intake may have different outcomes depending on individuals' perceptions of the taste of vegetables.

Our study examined if the TAS2R38 diplotypes (**Figure 7**), associated with bitter taste perception in vegetables, affects: 1) the frequency of reported vegetable consumption prior to, and 2) the change in frequency of vegetable consumption after six months of either an enhanced or a minimal nutrition counseling intervention within the HHL study. SNP status was obtained from HHL participants either through DNA isolated from peripheral blood cells using the Infinium Human Omni Express Exome+ BeadChip (Illumina) and standard imputation methods for missing genotypes. Frequency of vegetable intake and covariates (age, gender, race, income) were available for 491 and 373 participants at baseline and at the six-month follow-up, respectively (**Table 17**). We found that bitter taste diplotype (PAV) was not associated with vegetable intake at baseline (p=0.90). After the dietary intervention we found a significant difference in frequency of vegetable intake from baseline to follow-up between groups defined by diplotype status (p<0.001); participants that were heterozygous or homozygous for the bitter taste haplotype consumed fewer vegetables suggesting that dietary intervention success regarding dark green vegetable intake may be influenced by underlying genetic differences in taste perceptions

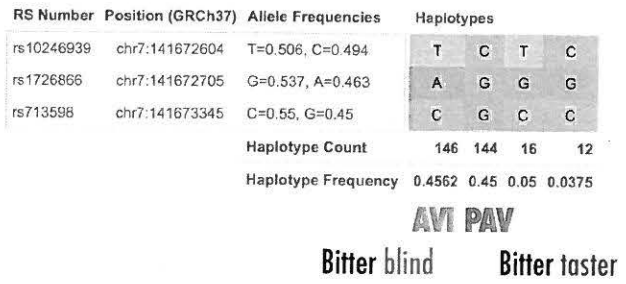

Figure 7. Combined hapmap (ASW and CEU) haplotypes associated with bitter taste at the TAS2R38 gene.

Table 17. Participant characteristics. Data from 107 participants were not available after 6 months, however, the percentages of participants in each intervention group and haplotype group remained similar.

	Baseline (n=497)		Accouting for 6-month dropout (n=390)	
Intervention intensity	Minimal	Enhanced	Minimal	Enhanced
Total participants	237	260	178	212
Diplotype				
AVI/AVI	59 (25%)	78 (30%)	42 (24%)	67 (32%)
AVI/PAV	110 (46%)	115 (44%)	84 (47%)	95 (45%)
PAV/PAV	68 (29%)	67 (26%)	52 (29%)	50 (24%)
Sex				
M	76 (32%)	61 (23%)	63 (35%)	44 (21%)
F	161 (68%)	199 (77%)	115 (65%)	168 (79%)
Race/ethnicity				
Black	110 (46%)	89 (34%)	84 (47%)	71 (33%)
White	127 (54%)	171 (66%)	94 (53%)	141 (67%)
Age				
18-29	3 (1%)	8 (3%)	1 (1%)	6 (3%)
30-44	33 (14%)	33 (13%)	13 (7%)	23 (11%)
45-65	135 (57%)	177 (68%)	107 (60%)	145 (68%)
>65	65 (27%)	42 (16%)	57 (32%)	38 (18%)
Total household income				
<$14,999	69 (29%)	80 (31%)	47 (26%)	60 (28%)
$15,000 – 29,000	53 (22%)	63 (24%)	40 (22%)	55 (26%)
$30,000 – 49,000	44 (19%)	45 (17%)	35 (20%)	37 (17%)
>$50,000	30 (13%)	48 (18%)	18 (10%)	43 (20%)
Education				
Grade 12 or less	170 (72%)	148 (57%)	123 (69%)	114 (54%)
2 years post high school	34 (14%)	47 (18%)	26 (15%)	37 (17%)
4 years post high school	21 (9%)	47 (18%)	20 (11%)	43 (20%)
5 or more years post high school	12 (5%)	18 (7%)	9 (5%)	18 (8%)
Smoking status				
Never smoke	179 (76%)	221 (85%)	35 (20%)	31 (15%)
Smoke some days or Smoke everyday	58 (24%)	39 (15%)	143 (80%)	181 (85%)

(**Figure 8**). Our results suggest that bitter taste genetic variation could be utilized in designing interventions to promote healthy eating.

This study demonstrates a proof of concept that genes associated with bitter taste perception can influence frequency of vegetable intake over time in a diverse study sample. The variability in frequency of

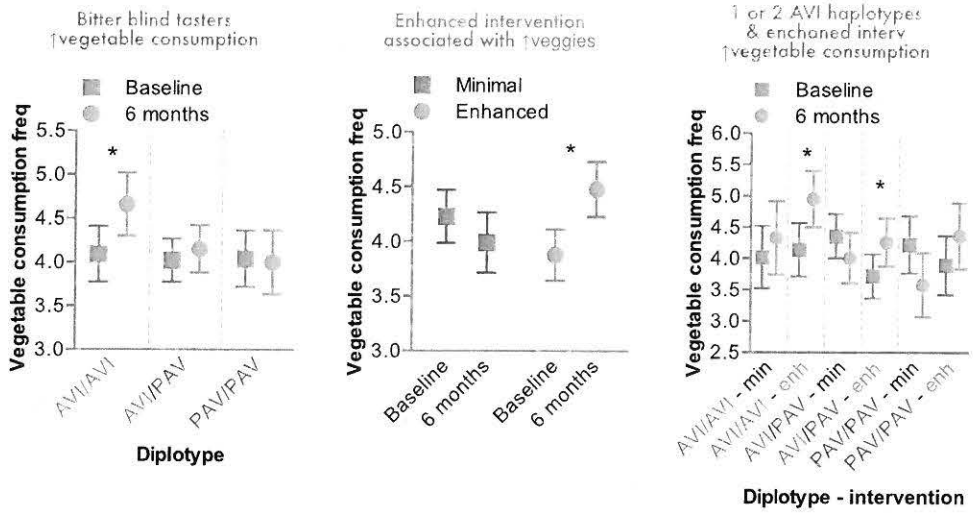

Figure 8. Vegetable consumption by diplotype represented by the mean ± 95% confidence intervals (CI). **Left**, there were no differences in baseline vegetable consumption. 2way ANOVA identified an interaction between the diplotypes and time ($p = 0.041$) and the bitter blind taster was the only diplotype that had an increase in vegetable consumption frequency after six months (*$p < 0.05$). **Middle**, 2way ANOVA identified an interaction between the intervention and time ($p < 0.001$) and only the enhanced intervention group had an increase in vegetable consumption frequency after six months (*$p < 0.05$). **Right**, 3way ANOVA did not identify an interaction between intervention group, haplotype, and time ($p = 0.52$). Only bitter blind or semi-bitter tasters increased vegetable intake after six months (*$p < 0.05$).

intake according to participants' haplotype could help explain why dietary change interventions report mixed results. Taste has a strong influence over peoples' dietary habits and should be considered when designing dietary change interventions.

We completed imputation of all three bitter taste receptor gene clusters (chromosomes 5, 7, and 12) within our dietary intervention cohort as well as a plasma carotenoid panel and are currently performing additional association analyses between these additional bitter taste receptor polymorphisms, carotenoid levels, and reported vegetable intake.

Publications & Presentations

Skinner, H.G., Calancie, L., Vu, M.B., Garcia, B., DeMarco, M., Patterson, C., ... Schisler, J. (2015) Using Community-Based Participatory Research Principles to Develop More Understandable Recruitment and Informed Consent Documents in Genomic Research. *Public Library of Science One*, 10(5). PMC4418607.

Kaitlin C. Lenhart, Kimberly Robasky, Wendell Jones, Jacqueline Halladay, Alice Ammerman, Cam Patterson, Jonathan C. Schisler. (2016) Genetic variation associated with blood pressure change among a cohort of African American's Adults in the Heart Healthy Lenoir trial. *Manuscript in preparation, abstract accepted and presented at the International Experimental Biology 2016 American Society for Investigative Pathology Meeting.*

Larissa Calancie, Kaitlin Lenhart, Thomas Keyserling, Ziya Gizlice, Cam Patterson, Alice Ammerman, Jonathan C. Schisler (2016). Implications of taste receptor polymorphisms in dietary interventions: TAS2R38 polymorphisms associate with changes in vegetable intake. *Manuscript in preparation, abstract accepted and presented at the International Experimental Biology 2016 American Society for Nutrition Meeting.*

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Halladay, Jacquie. University of Buffalo Practice Facilitation Certification Course (PFC 901). Learning Session "The Heart Healthy Lenoir Project - applied practice facilitation" Webinar May 4, 2016. Course Director, Dr. Chet Fox. Millard Fillmore College, Buffalo, NY. https://www.millardfillmorecollege.com/cstudio/class/pfc_901

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Program Director/Principal Investigator (Last, First, Middle): Keyserling, Thomas C.

Inclusion Enrollment Report

This report format should NOT be used for data collection from study participants.

Study Title: Community-Based Lifestyle Intervention to Reduce CVD Risk & Disparities in Risk

Total Enrollment: 339 **Protocol Number:** 10-0395

Grant Number: 5P50HL105184

PART A. TOTAL ENROLLMENT REPORT: Number of Subjects Enrolled to Date (Cumulative) by Ethnicity and Race

Ethnic Category	Sex/Gender			
	Females	Males	Unknown or Not Reported	Total
Hispanic or Latino	2	2	0	4 **
Not Hispanic or Latino	256	74	0	330
Unknown (individuals not reporting ethnicity)	2	3	0	5
Ethnic Category: Total of All Subjects*	260	79	0	339 *
Racial Categories				
American Indian/Alaska Native	1	0	0	1
Asian	0	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0	0
Black or African American	177	38	0	215
White	76	40	0	116
More Than One Race	4	1	0	5
Unknown or Not Reported	2	0	0	2
Racial Categories: Total of All Subjects*	260	79	0	339 *

PART B. HISPANIC ENROLLMENT REPORT: Number of Hispanics or Latinos Enrolled to Date (Cumulative)

Racial Categories	Females	Males	Unknown or Not Reported	Total
American Indian or Alaska Native	0	0	0	0
Asian	0	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0	0
Black or African American	0	0	0	0
White	0	2	0	2
More Than One Race	0	0	0	0
Unknown or Not Reported	2	0	0	2
Racial Categories: Total of Hispanics or Latinos**	2	2	0	4 **

* These totals must agree.
** These totals must agree.

Program Director/Principal Investigator (Last, First, Middle): Halladay, Jacqueline

Inclusion Enrollment Report

This report format should NOT be used for data collection from study participants.

Study Title: Reducing Disparities in Hypertension with a Practice-based Enhanced Care Program

Total Enrollment: 525 **Protocol Number:** 10-0395

Grant Number: 5P50HL105184

PART A. TOTAL ENROLLMENT REPORT: Number of Subjects Enrolled to Date (Cumulative) by Ethnicity and Race

Ethnic Category	Sex/Gender			
	Females	Males	Unknown or Not Reported	Total
Hispanic or Latino	4	5	0	9 **
Not Hispanic or Latino	348	160	0	508
Unknown (individuals not reporting ethnicity)	4	4	0	8
Ethnic Category: Total of All Subjects*	356	169	0	525 *
Racial Categories				
American Indian/Alaska Native	0	0	0	0
Asian	0	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0	0
Black or African American	213	87	0	300
White	134	75	0	209
More Than One Race	5	3	0	8
Unknown or Not Reported	4	4	0	8
Racial Categories: Total of All Subjects*	356	169	0	525 *

PART B. HISPANIC ENROLLMENT REPORT: Number of Hispanics or Latinos Enrolled to Date (Cumulative)

Racial Categories	Females	Males	Unknown or Not Reported	Total
American Indian or Alaska Native	0	0	0	0
Asian	0	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0	0
Black or African American	1	0	0	1
White	1	2	0	3
More Than One Race	0	1	0	1
Unknown or Not Reported	2	2	0	4
Racial Categories: Total of Hispanics or Latinos**	4	5	0	9 **

* These totals must agree.
** These totals must agree.

Program Director/Principal Investigator (Last, First, Middle): Schisler, Jonathan

Inclusion Enrollment Report

This report format should NOT be used for data collection from study participants.

Study Title: CVD Genetic Predispositions and Genomic Signatures

Total Enrollment: 560 **Protocol Number:** 10-0395

Grant Number: 5P50HL105184

PART A. TOTAL ENROLLMENT REPORT: Number of Subjects Enrolled to Date (Cumulative) by Ethnicity and Race

Ethnic Category	Sex/Gender			
	Females	Males	Unknown or Not Reported	Total
Hispanic or Latino	4	4	0	8 **
Not Hispanic or Latino	393	151	0	544
Unknown (individuals not reporting ethnicity)	5	3	0	8
Ethnic Category: Total of All Subjects*	402	158	0	560 *
Racial Categories				
American Indian/Alaska Native	1	0	0	1
Asian	0	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0	0
Black or African American	242	79	0	321
White	148	75	0	223
More Than One Race	5	2	0	7
Unknown or Not Reported	6	2	0	8
Racial Categories: Total of All Subjects*	402	158	0	560 *

PART B. HISPANIC ENROLLMENT REPORT: Number of Hispanics or Latinos Enrolled to Date (Cumulative)

Racial Categories	Females	Males	Unknown or Not Reported	Total
American Indian or Alaska Native	0	0	0	0
Asian	0	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0	0
Black or African American	0	0	0	0
White	0	2	0	2
More Than One Race	0	1	0	1
Unknown or Not Reported	4	1	0	5
Racial Categories: Total of Hispanics or Latinos**	4	4	0	8 **

* These totals must agree.
** These totals must agree.

Description of Data, Research Materials, Protocols, Software, or Other Information Resulting from Research that is Available to be Shared

We are preparing a final de-identified dataset for NIH in accordance with the NIH Policy on Releasing and Sharing Data and in full compliance with the 1996 Health Insurance Portability and Accountability Act (HIPAA). In addition, we generated genome-wide association data sets from our studies. As outlined by Best Practices from the CHARGE consortium, the genomic data will be uploaded appropriately to the NCBI repository (dbGAP and GEO) to be released upon publication or after a two-year embargo after the end of the study date.