C-Reactive Protein (hsCRP), Diet, and Physical Activity (PA) in Rural Women

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Abstract

Purpose: The purpose of this study was to evaluate the effect of dietary fruit and vegetable intake and physical activity (PA) levels on inflammatory marker high sensitivity C-reactive protein (hsCRP) among rural women 35-65 years of age.

Sample: Rural, non-smoking women (N = 99) in two states.

Method: Cohort analysis from a primary study with randomized-controlled trial (RCT).

Results: The dependent variable was calculated as: (a) the log-transformed (log) hsCRP *difference*, post minus pre values and (b) post log hsCRP. There was no difference between the intervention groups on log difference hsCRP (t (97) = -.88, *p* = .38); however, those women in the experimental group had half the level of log hsCRP. There was a significant difference in log hsCRP *difference*by activity level (F (2, 90) = 3.67, p = .03) indicating higher activity reduced hsCRP. Those women with a moderate activity level in the experimental group had the lowest hsCRP levels. The log hsCRP *difference* was not significantly different when evaluated for those who increased or did not increase their fruit and vegetable intake (p = .35). When analyzed by body mass level there was a significant difference in log hsCRP *difference* (F = 2.96, 7, 47, p = .001). A multiple regression with three variables accounted for 12% of the variance in log hsCRP.

C**onclusion:** Cardiovascular health of rural women is an area of great concern but limited research. The results of this study indicate increased levels of PA and fruit and vegetable intake by rural women are associated with decreased levels of hsCRP and thus with improved cardiovascular health. This study can contribute to the body of knowledge concerning the role of diet and physical activity on cardiovascular health in rural female populations.

***Keywords*:** Rural, C-reactive Protein, Diet, Physical Activity, Female Cardiovascular Disease, CVD

C-Reactive Protein (hsCRP), Diet, and Physical Activity (PA) in Rural Women

Health in rural areas is supported by a collaborative effort from public and private entities, community members, and healthcare providers. Nursing has multiple roles in the community, particularly in rural areas. Nurse researchers use information from community health assessments, the literature, and practice to develop questions and studies that will eventually guide nursing interventions to strengthen the health of the community. Data is becoming increasingly important in the development of evidence-based practice and nurses are in a unique position to use data to help guide health care interventions. In rural communities nurses can influence health care delivery, policy, and environmental issues in multiple arenas such as clinics, hospitals, schools, and public health. The rural environment is challenging in the provision of both prevention and intervention in cardiovascular disease. One author (Graves, 2009) suggests that there is a need to meld community, innovation, evidence-based practice and technology in framing cardiovascular health in rural populations. The aim of this study was to further the evidence of the effects of dietary fruit and vegetable intake and PA levels on hsCRP particular to a target population of rural midlife women. In addition an analysis of the factors that predicted a portion of the variance of hsCRP was conducted. Transtheoretical (Velicer, Rossie, Prochaska, & Diclemente, 1996) and Moos Socio-ecologic models (Moos, 1979) were used to develop interventions for the parent study described in the methods section. This report contributes to the body of knowledge concerning the role of diet and physical activity on measures of hsCRP in a rural female population.

C-reactive Protein (hsCRP)

Research is being conducted on the benefits and importance of a healthy diet and physical activity (PA). Health care researchers have shown that a healthy lifestyle reduces risk of chronic diseases. C-reactive protein (CRP) is a biomarker of inflammation (Ridker & Rifai, 2006); and an independent predictor of vascular and chronic diseases (Bilhorn, Luo, Lee, & Wong, 2012); this measure contributes to an individual's burden of heart disease. Awareness can be a strong motivator for women to make change. Much like knowing your numbers around cholesterol and blood pressure, CRP may add another link to cardiovascular disease (CVD) burden reduction.

C-reactive protein and specifically hsCRP measure the same molecule in the blood as mg/L to different degrees of sensitivity (Ridker & Rifai, 2006). Levels of less than one equate to a low vascular risk, one to three is moderate, and greater than three is high. Previously there was a belief that a persistent CRP value greater than 10 mg/L, related to systemic inflammation from other origins, was not pertinent to CVD. Evidence now suggests otherwise, according to Ridker and Rifai (2006) those with values greater than 10 mg/L are at a very high vascular risk even if the point of origin is not cardiac.

Risk factors of heart disease such as age, smoking, diabetes, high blood pressure and dyslipidemia are widely known. These factors are part of the Framingham Coronary Heart Disease Risk assessment (Framingham) (Wilson et al., 1998). The Framingham calculates risk of CHD within a 10-year period for those without known heart disease; but does not predict other CVD risks (Wilson et al., 1998). Other factors that may influence CVD risk that are not included in risk calculations are obesity, inactivity, and dietary intake. Another tool currently used in the medical field is the Reynolds Risk Score (Cook et al., 2012). This measurement includes hsCRP as a factor along with family history of premature myocardial infarction. Hemoglobin A1c

(HA1c) is included as a factor in the Reynolds measure for diabetics only. Cook et al. (2012), compared Reynolds Risk score to the Framingham based model. The Reynolds score, which included hsCRP measures, was shown to be a better discriminator for predicting CVD risk in a sample of 1,722 cases (Cook et al., 2012).

American Heart Association (AHA) guidelines (Mosca et al., 2011) currently recommend hsCRP assessment only in women at a moderate or high level of risk of CVD. High risk CHD is now defined as ≥10 points on the Framingham instrument. During the time of data collection for this study, moderate risk was defined as < 20 points and high as ≥20 on the Framingham. The 2011 guidelines (Mosca et al., 2011. p. 1247) assert that a Framingham score of ≥ 10 points in women indicates high risk for all CVD, not just CHD. Studies have not yet provided evidence of linkage between reduced hsCRP and clinical outcomes (Mosca et al., 2011). Through an exhaustive literature search, several studies were noted to have looked at the relationship of hsCRP to diet and PA among various populations but this is the first to investigate the relationship in rural women. Along with current guidelines of cholesterol and lipid panels, hsCRP provides a more specific measure of CVD risks.

Cardiovascular disease was estimated to cause about 1 death per minute in US women in 2007 (Mosca et al., 2011. p. 1244). The rate of coronary heart disease (CHD) mortality among women 35 – 54 years of age is increasing, possibly due to an increase in obesity (Mosca et al., 2011). There is a lack of literature specific to CVD and CHD in rural women. Many of the studies of CVD risk that are available are from single rural locations or regions and are not female specific (Fahs et al., 2012). In this study, CVD was assessed to be a major risk of women living in two rural counties, one in NY and the other in VA. The largest town in the NY county was coded as ten, an isolated small rural area, on the Rural-Urban Commuting Area (RUCA)

scale which ranges from one to ten (Atav & Darling, 2012). The largest town in the VA County had a RUCA of seven. Both counties had a Rural Urban Continuum Code (RUCC) of six where the range is one to nine and the higher the code the more rural the county (U.S. Department of Agriculture & Economic Research Service, n.d.-a, n.d.-b) . Both RUCA and RUCC are measurement systems used to identify rural areas (U.S. Department of Agriculture & Economic Research Service, n.d.-a, n.d.-b)

Background

Physical Activity (PA) and C-reactive protein (hsCRP)

Physical inactivity is a major risk factor leading to heart disease (Snell & Mitchell, 1999). A literature review found studies relating PA and hsCRP (Akbartabartoori, Lean, & Hankey, 2008; Albert, Glynn, & Ridker, 2004; Aronson et al., 2004; Boekholdt et al., 2006; Borodulin, Laatikainen, Salomaa, & Jousilahti, 2006; Church et al., 2002; Colbert et al., 2004; Davis et al., 2008; Dvorakova-Lorenzova et al., 2006; Ford, 2002; Geffken et al., 2001; Huffman et al., 2006; Jae et al., 2007; LaMonte, Ainsworth, & Durstine, 2005; McFarlin et al., 2006; Milani, Lavie, & Mehra, 2004; Mora, Cook, Buring, Ridker, & Lee, 2007; Murphy, Murtagh, Boreham, Hare, & Nevill, 2006; Okita et al., 2004; Olson, Dengel, Leon, & Schmitz, 2007; Panton et al., 2007; Pitsavos, Panagiotakos, Chrysohoou, Kavouras, & Stefanadis, 2005; Stamatakis, Hillsdon, & Primatesta, 2007; Stewart et al., 2007; Vigorito et al., 2007; Woolf et al., 2008). Four studies (Davis et al., 2008; Huffman et al., 2006; Murphy et al., 2006; Panton et al., 2007) report that PA did not reduce hsCRP. A short term, low level intervention (Davis et al., 2008) was less likely to reduce hsCRP than studies with exercise interventions of longer than 6 weeks (Okita et al., 2004; Stewart et al., 2007; Vigorito et al., 2007). More research is necessary to be able to predict hsCRP response to variations in PA.

Diet and C-reactive Protein (hsCRP)

Fruits and vegetables are excellent sources of antioxidants, vitamins, and fiber. Dietary recommendations for adults are between 2 - 4 servings of fruit and 3 - 5 servings of vegetables per day. Specific fruit intake and hsCRP were reviewed. Strawberries consumption has been found to decrease hsCRP (Sesso, Gaziano, Jenkins, & Buring, 2007), but not at a statistically significant level (p = 0.35). In a study of cherry consumption, after 28 days, hsCRP had decreased by 25%, (p < 0.05) (Kelley, Rasooly, Jacob, Kader, & Mackey, 2006). The relationship between fruit and vegetable consumption and hsCRP was examined (Gao, Bermudez, & Tucker, 2004) and the results showed that hsCRP had a significant inverse relationship with fruits and vegetables independent of other effects, (p trend - 0.010) A more complete review of the literature regarding specific dietary elements and CRP is available (Pribulick, 2009).

The purpose of the current study was to evaluate the effect of dietary fruit and vegetable intake and PA levels on hsCRP among rural women ages 35-65 years of age. In addition, factors such as stage of change (SOC), Framingham Coronary Heart Risk Score (Framingham), BMI, and county were analyzed to account for the amount of variance of hsCRP

Methodology

Design

This study was conducted as an analysis of a cohort of non-smokers from the primary study (Fahs et al., 2012) *Promoting Heart Health in Rural Women* (PHH), funded by a grant through the National Institute of Health (NIH) as a R15 study 1R15NR009218-01A. The primary study was an experimental, design with convenience sampling and random assignment to group that has been described in detail elsewhere and summarized below (Fahs et al., 2012; Pribulick,

Willams, & Fahs, 2010). Two rural communities, one in upstate NY and another in VA, were chosen as sites based on previous studies completed in those states. Human subject protocol approval was granted for the parent study from two universities and the protocol for this cohort analysis was also approved. The PHH study lasted 14 months for each subject. It included demographic, stage of change (SOC), dietary intake, physical activity, CHD risk assessment and anthropometric data. A convenience sample was randomized to group: a) Staged Matched Nurse and Community Intervention (SMN+CI) or b) Community Intervention (CI) only. The theoretical framework included the Transtheoretical and Moos Socio-ecological models and interventions are described in detail elsewhere (Fahs et al., 2012). Of the 117 rural women completing the PHH study, a cohort of non-smoking women was created for the purposes of this study (Pribulick, 2009).

The initial cohort in this study included 99 non-smoking rural women between the ages of 35 and 65 years of age. The upstate NY sample was larger consisting of 72 women (99% Caucasian); whereas the Virginia participants numbered 27 including 7 African American and 2 Hispanic women. Participants in the PHH study who self-reported smoking or had cotinine levels indicating active smoking were excluded since research has shown that smoking in and of itself may lead to secondary increases in CRP levels (Ridker & Rifai, 2006, p. 4). Six participants had fasting labs and anthropometric measures at completion but did not submit the final questionnaire. Therefore, up to 93 subjects could be used in the analysis specific to dietary intake and PA. Some measures such as the Yale Physical Activity Survey (YPAS) required coding of “do not know” as missing data, thus reducing the potential sample for those measures of activity.

The mean age in this sample was 51.57 with a standard deviation (*SD*) of 7.89; SMN+CI mean age = 52.69 (7.65) and CI = 50.46 (8.04) years. The Stage matched nurse intervention group (SMN+CI) for this study had a sample of 49 women with n = 50 for the CI. There were no statistically significant difference between groups, SMN+CI and CI on age. The mean body mass index (BMI) for the SMN+CI group was 30.90 kg/m^2, *SD* = 5.60 kg/m^2, and for the CI group, 30.52 kg/m^2, *SD* = 7.25 kg/m^2. There was no statistically significant difference on BMI pre-intervention by group

Instruments

For the purposes of this study, the following instruments were used:

(a) University of Rhode Island Stages of Change Instruments for 5-A-Day and Physical Activity, (b) NIH/NCI Fruit and Vegetable by Meal Screener, (c) Yale Physical Activity Survey (YPAS), (d) hsCRP, (e) anthropometric measure of BMI and (f) Framingham Coronary Heart Risk score (Framingham). Instruments to measure stage of change (SOC) have been developed for use in studies that utilize the Transtheoretical model. These tools ask about the current engagement in the behavior and how long the individual has been engaged in the behavior as well as intent and anticipated timeframe for future behavior (Velicer et al., 1996). Instruments for SOC for dietary intake of fruits and vegetables, exercise, smoking, and weight loss are available online at http://www.uri.edu/research/cprc/measures.htm (Cancer Prevention Research Center [CPRC], n.d.). The NIH/NCI Fruit and Vegetable by Meal Screener was first developed in the early 1990's to track fruit and vegetable changes among specific populations (National Cancer Institute, 2008). The tool assesses portion size and frequency of fruit and vegetable intake over a 24-hour period. Thompson and colleagues assessed fruit and vegetable tools to find a moderate validity among three instruments: (a) Food Frequency Questionnaire, (b) By-Meal

screener, and (c) All-Day screener (Thompson et al., 2002). The NIH/NCI By-Meal screener measures fruit and vegetable intake in this study.

A self-report tool that was originally developed to measure physical activity among older populations, the YPAS, has been used and compared in many studies. The YPAS and the International Physical Activity Questionnaire were compared for reliability and validity (Kolbe-Alexander, Lambert, Harkins, & Ekelund, 2006). Reliability for YPAS ranged from r = .44 to .80 for men and r = .59 to .99 for women. The results were comparable for reliability and criterion validity. There are several tools available to measure activity. However, the YPAS was chosen because the design focus was on a group of women that included older adults and the YPAS included questions on activities that many rural women participate in such as gardening. This instrument has also been used in samples that include African American women (Young, Jee, & Appel, 2001). The instrument has not been previously tested specifically in a rural sample. The three subscales of the YPAS are: (a) Total Time Summary Index (TTSI) which measures self-reported activity in hours per week, (b) Energy Expenditure Summary Index (EESI) is reported as kilocalories for the week, and (c) Activity Dimensions Summary Score (ADSS) which includes weekly amounts of time spent in vigorous and leisurely walking, moving about, standing, and sitting.

The Framingham is an algorithm for calculating coronary heart disease risk in the next 10 years. A score of over 20 points indicates high risk of having a heart attack in the next 10 years (Wilson et al., 1998). The measure used in this study was specifically designed for women and incorporates measures such as blood pressure, cholesterol, and smoking status. The Framingham score sheet for women and other versions for this tool can be viewed at the Framingham

webpage (The National Heart Lung and Blood Institute [NHLBI] & Boston University, n.d.). Women in this study had Framingham scores of 20 points or less.

The anthropometric measure for this study was BMI. Weights were taken on the same commercial scale placed on a hard surface for each participant; height was measured against a rigid scale, calibrated in inches fixed to the wall. Cut points for BMI were classified into (a) normal, BMI of less than 25 kg/m^2, (b) overweight 25 - $\leq$ 30 kg/m^2, and (c) obese > 30 kg/m^2 (Association of Women's Health Obstetric and Neonatal Nurses., 2003).

Plasma Indicator

C-reactive protein (hsCRP) was measured once for each woman at the beginning and end of their 14-month participation. All fasting blood samples obtained were processed through a local hospital with hsCRP sent to Quest Diagnostic Laboratory for analysis. One milliliter of serum was required (personal communication United Health Services and Quest Diagnostics, 2008). C-reactive protein was measured in milligrams per liter. In any given sample population hsCRP levels can have a large variance. One way to correct for positively skewed data is to log transform the values (Field, 2005). Log transformation reduces positively skewed data by condensing the right tail of the distribution (Field, 2005, p. 80). For this reason the study utilizes a log transformation to report hsCRP. For the purposes of study hsCRP was reported in two ways: (a) the hsCRP value was log-transformed and (b) a log hsCRP *difference* was calculated by subtracting the post-intervention log transformed hsCRP from the pre-intervention value. The difference in log is measuring the ratio of the reported values and not the difference. Dependent variables for hsCRP in this study are either log transformed or log hsCRP difference. The hsCRP pre-intervention in this sample ranged from a minimum of .20 mg/L to a maximum of 36.70 mg/L, *SD* = 5.43 mg/L. After log transformation, the range was -1.61 to 3.60 with a mean of .58,

SD = 1.21. Original hsCRP units reported as mg/L become log (mg) – log (L) after transformation; for ease of reading in this report transformed hsCRP continue to be noted as mg/L.

Results

Stage of change for both PA and diet was categorized into two groups: (a) preparation or lower and (b) action or higher since cells using the original five categories had too few subjects (see Figure 1).

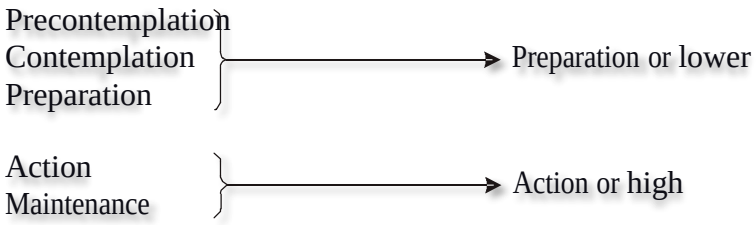

Figure 1: Stage of Change (SOC) categorized into two groups

The Mann-Whitney U test (Green & Salkind, 2004), to evaluate differences in the medians of populations, for PA was not statistically significant, z = -1.55, p = .12. Those subjects making no change or who had lower SOC scores in the area of PA had an average rank of log hsCRP of 52.12 among the 93 subjects, while those making a positive change had an average rank of 43.31. In this sample, a positive change in PA stage correlates with lower CRP.

A Mann-Whitney U test was also conducted on log hsCRP and dietary SOC. The test results were not significant, z = -1.21, p = .23. Those subjects making no change or who had lower SOC dietary scores had an average rank of hsCRP of 50.37, while those making a positive change had an average rank of 43.59. As with PA, positive change in dietary SOC correlates with a lower hsCRP and thus overall lower cardiovascular risk factors.

Intervention in Diet and Physical Activity (PA) and hsCRP

An independent-samples t-test was conducted to evaluate whether behavioral lifestyle intervention related to diet and PA would reduce hsCRP measurements in rural women. The t-test compared group of SMN+CI and CI on the log hsCRP difference, at an interval level of measurement. A t-test on the difference was conducted, and was not significant, t (97) = -.88, p = .38. The mean log hsCRP *difference* of the SMN+CI group was -.05 mg/L, *SD* = .84 and .11 mg/L, *SD* = .94 for the CI group. The SMN+CI group has a healthier hsCRP level, half that of the CI group demonstrating that though there was not a statistical difference, hsCRP change was in the direction predicted.

Physical Activity (PA) Levels Yale Physical Activity Scale and hsCRP.

For the relationship between levels of PA and hsCRP for the entire sample, correlation coefficients were computed among the three YPAS subscales: TTSI, EESI, and ADSS. There was a weak negative significant relationship between the ADSS and the log hsCRP difference, r (80) = -.24, p = .04. To further understand this relationship, a frequency was run on ADSS to find the cut points for three groups which were labeled: (a) low, (b) moderate; and (c) high levels of activity. A one-way analysis of variance (ANOVA) was conducted to evaluate the effect of levels of PA, as described above, on the log hsCRP *difference*. The ANOVA was significant, F (2, 90) = 3.67, p = .03. Follow-up Dunnett's T3 tests were conducted to evaluate pairwise differences among the means, since the population variances among the three groups were unequal; SD ranged from .61 (± .37) to .93 (± .87). There was a significant difference in the means between the moderate level of activity and the high level of activity, mean difference (*MD*) .52, p = .04. This indicates that an increase in PA reduced hsCRP measures in rural women. Correlations were also run on the ADSS ratio, calculated as post-intervention score

minus pre-intervention score, providing the log hsCRP *difference*. There was a weak, inverse, statistically significant correlation between the variables, $r\ (80) = -.24$, $p = .04$. Physical activity levels increased hsCRP decreased, as desired.

To further ascertain the effects of increasing PA on hsCRP, each of the subscales from the YPAS were recoded into new variables showing the change between pre and post-intervention activity. Each YPAS subscale was recoded into two groups: (a) those with an increase for the subscale versus (b) no change or a decrease. An independent-sample t-test was conducted with log transformed hsCRP post-intervention. In each of the three YPAS subscales, the group with increased PA had lower, more positive hsCRP means, implying a trend of reduced risk of heart disease; however, none of the tests reached significance (see Table 1).

Table 1: T-test in Comparing Increased Physical Activity (PA) by Yale Subscales

Log Post hsCRP t-test	No Change or Lower PA Mean (SD) n	Increase PA Mean (SD) n
TTSI t = .915, df = 91, p = .36	.71 (1.01) 43	.49 (1.28) 50
EESI t = .483, df = 91, p = .63	.66 (1.18) 40	.54 (1.16) 53
ADSS t=.311, df=91, p = .76	.64 (1.28) 36	.57 (1.09) 57

EESI = Energy Expenditure Summary Index in Kcal per week, TTSI = Total Time, ADSS = total daily activity duration score

Table 2 shows descriptive statistics for low, moderate and high activity levels on the activity dimension measure of ADSS, YPAS subscale for both the intervention (SMN+CI) and control (CI) group. Group differences in moderate activity level on mean log hsCRP in the SMN+CI and CI groups were large and can also be seen in Figure 2.

Table 2: Activity Dimensions Summary Score Levels for Group and Mean Log hsCRP

Activity level	Group	Mean	SD	N
Low	SMN+CI	1.38	.98	16
	CI	.72	1.25	16
	Total	1.05	1.15	32
Moderate	SMN+CI	-.25	.91	11
	CI	1.23	1.02	6
	Total	.29	1.19	17
High	SMN+CI	.20	.81	21
	CI	.55	1.27	23
	Total	.38	1.08	44
Total	SMN+CI	.49	1.10	48
	CI	.71	1.23	45
	Total	.60	1.18	93

SMN+CI = Stage Matched Nursing and Community Intervention; CI = Community Intervention

In addition, a Factorial ANOVA was computed with the categories of low, moderate or high activity and intervention group; SMN+CI or CI. Activity Dimension Summary Score was chosen for one independent variable because this subscale best represents PA overall. Log transformed hsCRP post data were used as the dependent variable.

The ANOVA was significant, F (2, 87) = 3.8, p = .03. The lowest estimated marginal means post log hsCRP were seen in the SMN+CI group with the moderate activity level (see Figure 2).

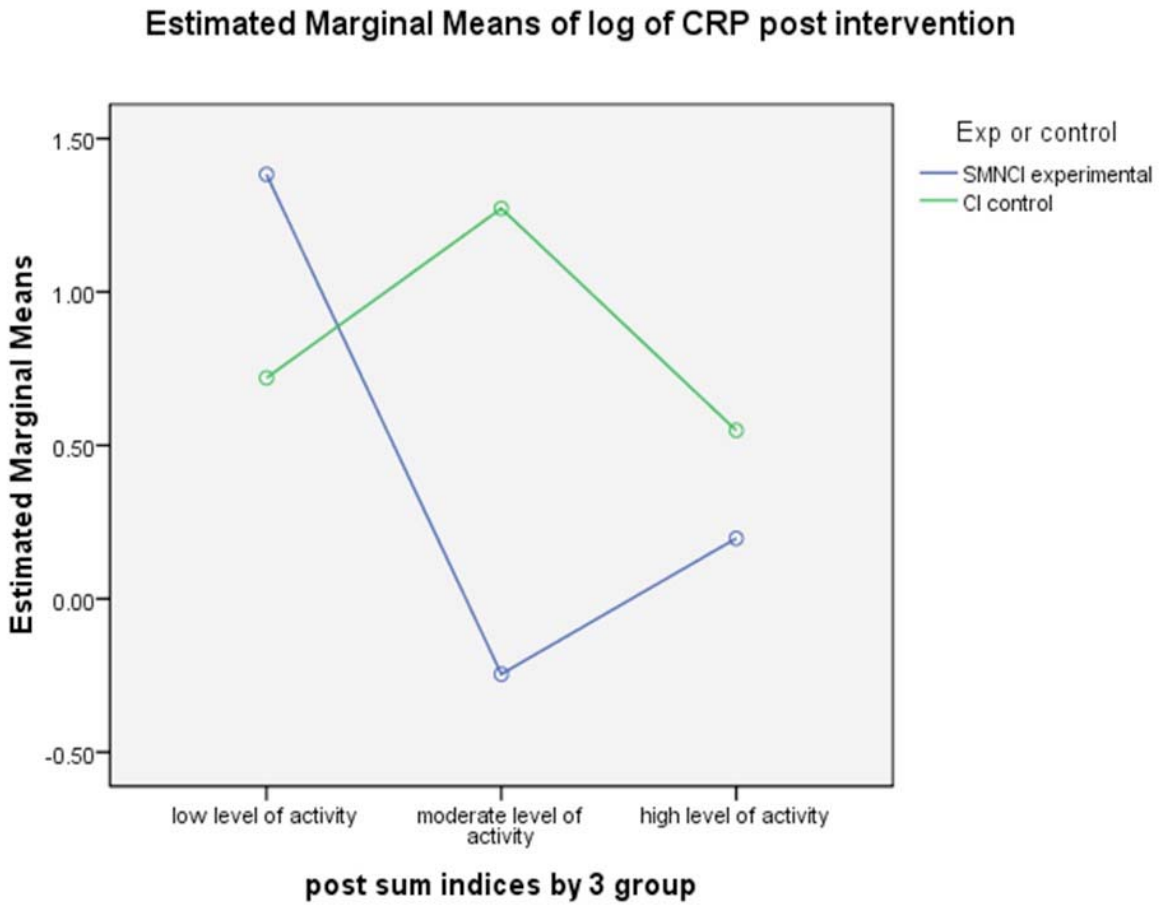

Figure 2: Group Activity Dimension Summary Scores with Post hsCRP

Figure 2 shows a large dip in post hsCRP means for the SMN+CI group who were categorized as having a moderate level of activity as measured on the sum of indices on the Activity Dimension Summary Score (ADSS) of the Yale Physical Activity Scale (YPAS).

Intake of Fruits and Vegetables and hsCRP.

Mean intake of fruit and vegetable servings increased in the SMN+CI and CI group; with the largest mean intake in the SMN+CI group post-intervention (see Table 3).

Table 3: Fruit and Vegetable Servings, Pre and Post-intervention by Group

Group	Fruit & Vegetable Intake Pre-intervention (N)	Mean	SD	Fruit & Vegetable Intake Post-intervention (N)	Mean	SD
SMN+CI	49	7.90	3.01	48	10.04	3.44
CI	50	8.60	3.43	45	8.95	3.30

SMN+CI = Stage Matched Nursing and Community Intervention, CI = community intervention

Correlation coefficients were computed with dietary intake of fruits and vegetables pre and post-intervention. There was a weak, negative significant relationship between dietary intake of fruits and vegetables post-intervention and log hsCRP *difference* (r (93) = -.21, p = .05). There was a significant difference in the SOC for diet reported in the parent study (Fahs et al., 2012) therefore it was not surprising to find this inverse relationship. As dietary intake of fruits and vegetables increase, the log hsCRP *difference* decreases by a proportionate amount.

To answer the question "What is the effect of an increase in fruits and/or vegetable intake on hsCRP?" a new variable was computed representing the difference of fruits and vegetables pre-intervention from fruits and vegetables post-intervention. This new variable was then

recoded into two groups: (a) those that increased their diet in fruits and vegetables and (b) those that had not changed or decreased their diet in fruits and vegetable. Those that increased fruit and vegetable servings (n = 71) had a mean increase of 2.39 portion servings (*SD* = 2.23), while those in the second group (n = 22), had a mean decrease of 1.77 servings (*SD* = 1.28). The mean log post hsCRP for those that increased their fruit and vegetable consumption was .44 mg/dl compared to those that had no increase in fruit and vegetables at 1.09. The t-test reported was for equal variances assumed and was significant, (t = 2.33, *df* = 91, *p* = .02). Next an independent-sample t-test was conducted using the log hsCRP *difference,* and the new variable of increase or no change in servings of fruits and vegetables (t = .95, df= 91, p = .35). In this configuration, there was no significant difference between those that increased or decreased their intake of fruits and vegetables.

BMI and hsCRP.

Three correlation coefficients were examined to assess the relationship between BMI and hsCRP (see Table 4). Each relationship between BMI and hsCRP was statistically significant. Consistent with the literature as BMI goes up, hsCRP correspondingly rises.

Table 4: Correlation of BMI and C-reactive protein (hsCRP) and log transformed hsCRP

N = 99	Pearson Correlation r	Sig. (2 tailed) p
Pre hsCRP and BMI	.31	.002
Post hsCRP and BMI	.21	.03
Log hsCRP post and BMI post intervention	.43	.00

Body mass index post-intervention was then classified into three groups: (a) normal, (b) overweight, and (c) obese. An ANOVA was conducted to evaluate the relationship between BMI and log hsCRP post-intervention. The ANOVA was significant, F (2, 96) = 7.47, p = .001. The strength of relationship between BMI and hsCRP, as assessed by the Partial Eta Squared, was moderate, with BMI accounting for 14% of the variance of hsCRP. Follow-up tests to evaluate pairwise differences among the means of the three groups were then conducted. Given that the variances among the groups ranged from .96 to 1.68 homogeneity was not assumed and the Dunnett's T3 test was chosen. There was a significant difference in the means between the overweight group and the obese group. The obese group had a significantly higher hsCRP level. A higher BMI is associated with a higher hsCRP level.

All factors and hsCRP.

A multiple backward regression analysis was conducted to evaluate how well the following variables measured post-intervention predicted log hsCRP *difference*: (a) age, (b) sum of fruit and vegetables (c) ADSS (d) TTSI (e) SOC for physical activity (f) SOC diet (g) BMI (h) Framingham, (i) county and (j) group. Both the ADSS and TTSI are subscales of activity as measured on the YPAS. A backward regression placed all variables in the model. Each variable was measured against a removal criterion which determined whether the variable added significance; if no significance was added, the predictor was removed. This test was repeated until only the variables that give significance to predicting the dependent variable were in the model (Field, 2005). Three variables remained in the model; sum of fruits and vegetables, ADSS, and the Framingham. The ANOVA revealed the overall model was significant (R = .35) (F (3, 88) = 4.03, p = .01). This finding represents a linear relationship; the three independent variables significantly predicted the dependent variable, log hsCRP *difference*. The model summary

showed R^2 = .12, adjusted R^2 = .09. The R value looks at the correlation between the predicted and observed values of the dependent variable hsCRP. The R^2 explains that 12% of the variance in hsCRP is predicted by the three independent variables. Table 5 reports the regression model coefficients.

Table 5: Regression Model Coefficients for Three Predictor Variables on hsCRP Difference

Variables	Mean (SD)	Beta Unstandardized (Standardized)	t	p	Zero Order	Partial	Tolerance
Sum F & V	9.52 (3.42)	-.54 (-.21)	-2.07	.04	-.21	-.22	.99
ADSS	46.86 (21.84)	-.01 (-.23)	-2.21	.03	-.20	-.23	.95
Framingham	4.16 (3.58)	-.05 (-.22)	-2.08	.04	-.15	-.22	.95

Sum F & V = number of portion servings for fruits and vegetables per day, ADSS = total daily activity duration score

The role of the inflammatory marker hsCRP is likely to become more prominent in the diagnosis and treatment of cardiovascular disease as research findings begin to guide practice. Several studies have examined the influence of multiple variables on hsCRP levels; however, none have specifically looked at hsCRP in rural US women up to this point. Recommendations for primary prevention measures with regards to heart disease in low to moderate risk patients include lifestyle changes such as improving diet and physical activity. The findings of this study

add to the body of knowledge concerning the influence of behavioral modifications, higher levels of intake of fruits and vegetables, and increased PA and how these factors can influence hsCRP.

Power Calculations for Parent and Cohort Study

With a completion of 117 subjects the power for ascertaining differences in fruit and vegetable intake in the parent study, PHH was .79, alpha = .05. Prior to completion of the parent study, the effect size for differences in hsCRP between groups with a nurse run intervention was unknown (Fahs et al., 2012). A calculation of the mean differences for log hsCRP between intervention groups indicated a small effect size (Pribulick, 2009). This information suggests that it would take a large sample of 158 subjects per group (N = 316) to detect a 1% change in hsCRP, at a power of .80. This study has a low calculated power of 13.3% to detect difference in hsCRP by group. The low power of the test may mask significant differences that were not detected by the analysis. Only replication with a larger sample will answer the question of whether a Type II error exists. The study found significant associations between log hsCRP and the factors of dietary intake and PA.

Stage of Change, Interventions, and Log hsCRP

Rural women in the higher SOC categories, action or maintenance, on both diet and physical activity had lower levels of hsCRP in this study. The Mann-Whitney U that ranked median log hsCRP did not indicate a significant difference by level of SOC for either diet or PA. Yet the mean log hsCRP post was lower for those in the action or higher level of SOC for both diet (M = .44, SD = 1.17) and PA (M =.43, SD = 1.16) than those in preparation or lower (M = .70, SD = 1.15 and M = .84, SD = 1.13) respectively. There is a clear need for future study with a larger sample to more fully test whether nurse interventions in PA and diet can significantly reduce hsCRP.

There are other factors that can affect hsCRP levels during the course of a 14 month study. For instance, four subjects in this cohort began cholesterol lowering therapy at some point after the study was underway. At the beginning of the study seven (14%) SMN+CI and five (10%) CI subjects reported being on cholesterol lowering drugs, all on a medication to reduce cholesterol had been on that drug for a minimum of one year. Cholesterol lowering medications have been shown to decrease hsCRP and to prevent vascular events with normal LDL cholesterol and elevated hsCRP (Ridker et al., 2008). At the end of the study, six (13%) SMN+CI and ten (22%) CI subjects reported being on cholesterol lowering drugs. A Chi-square did not show a difference between the SMN+CI and CI groups on pre or post use of cholesterol lowering medications, (X^2 = 1.905, df = 3, p = .59). The exact time the cholesterol lowering therapy began is not known. In addition, subjects were not asked to report what type of cholesterol medication they were on. Therefore it is not possible to know if or to what degree this situation could affect outcomes. There is also the possibility that the screening data influenced subjects to seek medical assistance given the knowledge of their lab results and Framingham 10-year coronary heart disease risk score.

The findings in this study are supported by several previous studies (Aronson et al., 2004; LaMonte et al., 2005; McFarlin et al., 2006) that also found that increased levels of physical activity were associated with lower hsCRP levels. Two studies found differences in hsCRP relationships with PA depending on gender (Albert et al., 2004; Borodulin et al., 2006). The Albert (2004) study reported no statistically significant relationship between levels of physical activity and hsCRP in women, p trend = .38 while most subgroups of physical activity in men remained significant. Borodulin et al. (2006) found a statistical significance in women but only a borderline significance in men. In this study, all subjects were women.

A 9-week lifestyle intervention program in the literature (Dvorakova-Lorenzova et al., 2006) focused on diet and physical activity was successful in 30% reduction of hsCRP levels, 4.31 ± 3.71 to 3.01 ±3.12 mg/L. The physical activity was supervised 1-hour training sessions plus three added sessions per week of cycling, jogging or brisk walking. Another program (Stewart et al., 2007) used a supervised, aerobic and resistance exercise program, three days per week for 12 weeks. Their groups included young and old, physically inactive participants who received the supervised exercise and a similar group who maintained their usual activity level as the control group. The experimental group, both young and old, had a significant decreased in hsCRP post training, $p < 0.01$. Although this study intervention did not reduce hsCRP at a significant level, the trend toward a reduction in the SMN+CI group, were the moderately active group had the lowest hsCRP (see Figure 2) is supported by the literature (Dvorakova-Lorenzova et al., 2006; Stewart et al., 2007). This also indicates that a large sample size may have been needed to see the small effect size in change in hsCRP. The above studies (Dvorakova-Lorenzova et al., 2006; Stewart et al., 2007) had supervised PA activity unlike this study. It may be that a more structured, supervised PA component would be more successful in reducing hsCRP.

A previous study (Gao et al., 2004) found an inverse dose-response between fruit and vegetable intake and CRP (p trend = .017) and is reflective of the current study which found significant inverse associations between these two variables. Gao et al. questioned whether the antioxidant components of fruits and vegetables were the contributing factor to the anti-inflammatory effect found. The role of fruits and vegetables in reducing hsCRP has been established. Future research should focus on having women eat adequate fruits and vegetables on a consistent basis as well explore the role of antioxidants in relation to hsCRP levels. A study of

total antioxidant capacity (TAC) of diet (Brighenti et al., 2005) included a stepwise multiple regression analysis of contributing food groups to the TAC. Fruit, vegetables, and nuts accounted for 5.6% of the TAC. Brighenti et al. hypothesized that the metabolism of hsCRP may be regulated by the TAC of the diet as opposed to any single antioxidant compound. This may also apply to the concept of increasing fruits and vegetables in the diet. There may be a greater dose-response if the dose consists of a variety of fruits and vegetables as opposed to a select few.

Inoue, Komoda, Uchida, and Node (2008), considered the effects of a single tropical fruit, Camu-Camu. Camu-Camu is found in the Amazon, contains high vitamin C, and is juiced for dietary consumption. The Camu-Camu group had a significant reduction in hsCRP from baseline whereas the vitamin C group had no change. Though the sample size was small, the impressive findings were based on one fruit with high antioxidant properties. Yet this is a fruit seldom reported in the American diet and it is unlikely women in this study had access to Camu-Camu juice.

Not surprisingly, BMI and hsCRP were highly correlated. Past studies have also shown strong correlations between BMI and hsCRP (Colbert et al., 2004; Dvorakova-Lorenzova et al., 2006). However, more work is needed on the effect lowering BMI may have on hsCRP and whether or how much of a genetic component influences hsCRP levels.

Limitations

Standard guidelines used for hsCRP as a risk marker specify that measurements of hsCRP be performed twice; the average number being used to evaluate risk (Ridker & Rifai, 2006). The primary study only obtained lab samples once at the beginning and completion of the study. This is a limitation; however the log transformation changed the shape of the distribution and mitigated the effects of the outliers. A second limitation is that information regarding chronic

conditions was not collected. Certain chronic conditions such as rheumatoid arthritis would predispose participants to an elevated hsCRP level. Randomization into SMN+CI and CI groups was designed to correct for this type of limitation.

Stage of change for both diet and physical activity was collapsed into two levels, preparation and below or action and above, since there were not enough subjects to run analysis by the five levels of SOC. A larger sample size would permit analysis by each of the five levels of SOC. The primary study included a calculated 21% attrition (Fahs et al., 2012). For the purposes of this study, the SMN+CI group numbered 49 participants and 50 for the CI. Six participants did not return their final questionnaires, thus analysis of self-report data such as PA and dietary intake had maximum of 93 subjects. Another limitation is the self-report data used in the evaluation with SOC, YPAS, and the NIH/NCI fruit and vegetable screener. A participant's answers may reflect what they feel is expected of them or a genuine miscalculation instead of factual data. However, all instruments had previously been calculated for validity and reliability.

Hormone replacement therapy (HRT) has been shown to increase hsCRP levels according to Ledue and Rifai (as cited in Ridker & Rifai, 2006, p. 354). Seven women at the beginning of the study answered affirmatively to taking HRT compared to five women at the completion of the study. C-reactive protein values at the beginning of the study for those women on HRT (M = 3.1, SD = 3.62) were not significantly different from those not on hormone replacement therapy, (M = 3.70, SD = 5.58) t = .46, df = 97, p = .67. However the influence of HRT on hsCRP was not analyzed as part of this study.

Application of the Research to Practice

This research can be useful in generating programs related to diet and physical activity specific to producing a change in hsCRP levels. However, nurses need to be aware that rural

communities often do not have accessible and acceptable facilities for recreational activities especially during seasons with inclement weather. Sidewalks are often in disrepair, if they exist at all and rural roads may not be safe for walking. Although there are no recommended guidelines to reduce hsCRP through exercise, this study, along with others support the notion that moderate levels of activity are associated with lower hsCRP levels.

Since a relationship between intake of fruits and vegetables and decreased hsCRP was shown in this study, guidelines to increase intake of fruits and vegetables should be implemented in attempts to reduce hsCRP. Although rural areas may have agricultural capabilities not all rural citizens have the space, inclination, resources, or skill to produce their own fruit and vegetables. Often access to food stores is problematic and with rising costs and lack of public transportation, "food deserts" can exist in rural as well as urban areas. Unstable environmental and economic forces are negatively influencing food cost and accessibility. The findings of this study indicate it is important to improve PA and dietary intake of fruits and vegetables to reduce hsCRP levels and thus have a positive influence on heart health for rural women. Some of the challenges mentioned above need to be taken into consideration when developing programs designed to improve healthy living behaviors in rural communities.

This study indicates that women who have higher levels of PA and diets richer in fruits and vegetables have better hsCRP. However, the nurse intervention program, SMN+CI tested against the CI did not significantly reduce hsCRP and a possible Type II error may exist since the power calculated for this cohort study was low. The possibility exists that if women are informed of their CRP, and told how to reduce this biomarker, they can be motivated to make changes to their diet and PA

This study contributes to the research on hsCRP among rural women. Collectively with other research, future designs can be more focused and tightly defined. The more evidence produced on diet and PA to reduce hsCRP over multiple studies, the more likely the research will influence not only practice but also policy development. Research contributes to policy by bringing forth evidence based on scientific theory, yet policy is not always based on research findings. Policy development takes place not only at the federal level but also within professional organizational structures such as the American Nurses Association and Rural Nurse Organization, health focused organization such as the American Heart Association; or hospital or community health agencies, particularly with the advent of medical homes and the push for data driven practice with the Affordable Care Act. This study adds information on hsCRP, lifestyle modifications, PA levels, and dietary intake of fruits and vegetables that may contribute to future research, practice and policy considerations; particularly for rural women.

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