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EXPLORING THE RELATIONSHIP BETWEEN SOCIAL SUPPORT, PHARMACY ACCESS AND MEDICATION ADHERENCE

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EXPLORING THE RELATIONSHIP BETWEEN SOCIAL SUPPORT, PHARMACY ACCESS AND MEDICATION ADHERENCE

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ABSTRACT

Barriers of medication adherence exist among people with coronary heart disease (CHD) and CHD risk factors, including, poor social support, poor pharmacy access and other patient, social/economic, therapy, condition, and health-care system/health-care team-related factors. However, there are few data on influence of these factors on medication adherence among people with CHD risk factors other than diabetes. Therefore, this dissertation aimed to investigate associations of medication adherence with social support (n=17,113) and pharmacy access (n=8,250) quantitatively using data from the REasons for Geographic and Racial Differences in Stroke (REGARDS) study (black and white adults with CHD or CHD risk factors ≥45 years of age assessed 2003-2007 and ≥52 years of age assessed 2013-2016, respectively) and to obtain patient perspectives on how patient, social/economic, therapy, condition, and health-care system/health-care team-related factors influence medication adherence, through in-depth qualitative interviews of patients recruited from University of Alabama at Birmingham clinics (n=18). In REGARDS, medication adherence was self-reported. Social support was defined as having a caregiver in case of sickness or disability, being partnered, number of: close friends, close relatives, other adults in household, and close friends or relatives seen at least monthly. Participants who saw >10 close friends or relatives at least monthly had higher prevalence of medication adherence (PR=1.06; 95% CI: 1.00, 1.11) than those who saw <3 monthly. There were no other significant associations between

social support measures and medication adherence. Pharmacy location data were obtained from National Council for Prescription Drug Programs. Pharmacy access was defined as straight-line distances from REGARDS participants' residences to nearest pharmacy and number of pharmacies within 1.61, 8.1, 16.1 and 24.1 km radii from participants' residences. Pharmacy access measures were not associated with medication adherence. Four themes emerged from the qualitative data: perceived need for medication, beliefs about medications, influence of relationships with people and organizations and influence of pharmacy access and utilization on medication adherence. These occurred simultaneously and within context of patient, social/economic, therapy, condition and health-care system/health-care team-related factors. In conclusion, multidimensional interventions targeted at these factors, including social support, may help improve medication adherence among people with CHD and CHD risk factors.

Keywords: geographic/spatial factors, medication adherence, qualitative research, coronary heart disease, diabetes, hypertension

DEDICATION

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ASSOCIATION OF DISTANCE TO NEAREST PHARMACY AND PHARMACY DENSITY WITH MEDICATION ADHERENCE AMONG INDIVIDUALS TREATED FOR CORONARY HEART DISEASE RISK FACTORS

INTRODUCTION

The American Heart Association Heart Disease and Stroke Statistics (2017) showed that heart disease (coronary heart disease (CHD), hypertension and stroke) is the leading cause of death in the United States.[1] One in 7 deaths are attributed to CHD and it results in estimated costs of $199.6 billion annually.[1] For people with CHD and risk factors for CHD (those with diabetes, hypertension and dyslipidemia), medications can reduce the risk of CHD events and mortality. However, only 50 to 66% of patients are adherent to these medications.[2] The World Health Organization groups factors which influence medication adherence into patient, social/economic, therapy, condition and health-care system/health-care team related factors.[3-6] Poor social support, a social/economic factor, and lack of pharmacy access, a health-care system/health-care team related factor, are potential barriers of medication adherence. Furthermore, they are interrelated with other social/economic and health-care system/health-care team related factors as well as with patient, therapy and condition related factors. In this dissertation, I studied the relationships of social support, pharmacy access, and other factors with medication adherence among individuals with CHD and CHD risk factors.

Social Support and Medication Adherence

Social support is provided through relationships and interconnectedness which allow social network members to influence each other's behaviors through daily

interactions and feedback mechanisms.[5] In larger social networks with more social support such as where people have more relatives and close friends who they see often, there may be more practical assistance with and encouragement for self-care. However, within such networks, people may receive more recommendations against adherence.[5] Evidence regarding the relationship between social support and medication adherence is mixed. In one small study, social network size was not associated with adherence after acute coronary syndrome[7] and in a systematic review of small scale studies, social support was not associated with adherence among patients with a variety of conditions;[8] however, some studies have found an association between social support and medication adherence.[9-12]

Types of Social Support

Different types of social support exist, including functional support, structural support, and informational support. [13-15] Functional social support is defined as practical help provided by or received through an individual's social network including providing transportation to doctor's visits, care during illness and financial help. [13-15] Structural social support is defined as the number and types of connections within an individual's social network. [13-15] This includes size of social networks (number of people in an individual's social network), living arrangement (number of people in an individual's household) and marital status.[13-15] Informational support is defined as knowledge provided to an individual through their social network such as providing reading material about a recent diagnosis and providing advice about medication or medical conditions.[13-15]

Racial Differences between Social Support and Medication Adherence

There are racial differences in the way social networks operate and the way social support is received. In comparison to whites in the United States, blacks in the United States depend more on informal social networks to facilitate chronic disease management.[16-19] For example, black households may have more members compared to white households and this affords blacks different opportunities for social support compared to whites.[16, 20] Prior research also shows that medication adherence varies by race; blacks generally have lower medication adherence compared to whites.[3, 21]

Gender Differences between Social Support and Medication Adherence

The receipt of social support also differs by gender. While women were more likely to report receiving support from relatives, friends and peers; support for men tended to come from their partners.[22-24] Additionally, one prior study showed that illness-related diabetes social support was associated with a higher prevalence of medication adherence among women. However, among men, social support was not associated with medication adherence.[25]

Pharmacy Access and Medication Adherence

There are limited data assessing the independent association between geographic factors and medication adherence using geo-spatial analysis. In a literature review, Kirby and Kaneda provide extensive evidence to show that neighborhood disadvantage in the form of physical, service and social barriers affects health care access.[14] They note that traveling inconveniences and expenses in neighborhoods with bad roads and poor public

transportation systems, lack of safety in neighborhoods with poor policing and the availability of few health care providers in such environments, result in poor access to health care.[14] Further, disadvantaged neighborhoods may not have the necessary resources to maintain social organizations which would facilitate social network sharing of information about affordable health services and safe ways to access them.[14, 15] The ease of transportation and pharmacy location may influence pharmacy access.[5, 26] Evidence is mixed regarding distance as a barrier to health care access.[27] However, people who report transportation barriers also report barriers to pharmacy access.[27]

Racial Differences between Pharmacy Access and Medication Adherence

Racial differences exist in neighborhood residence; specifically, poorer neighborhoods have a higher proportion of blacks compared to whites.[28, 29] Additionally, prior studies have found that blacks had greater transportation barriers in accessing health-care compared to whites.[28, 29] Qato and colleagues also found that there were fewer pharmacies in segregated minority communities in comparison with segregated white and integrated communities in Chicago between 2000 and 2012.[30] Yet, other prior studies showed no racial differences in distance to pharmacies and other medical institutions.[31, 32]

Rural/Urban Differences between Pharmacy Access and Medication Adherence

Some prior studies also show that traveling time and distance act as greater barriers to health care access in rural areas compared to urban.[13, 32-34] However, in other studies, use of health-care services, transportation barriers and delays in care did not differ between urban and rural residents.[35, 36]

Implications for Current Research

Potential barriers to medication adherence among people with CHD and CHD risk factors make it difficult for them to achieve the intended goal of reducing the risk of CHD events and mortality. To date, little is known about how social support influences medication adherence in people with CHD risk factors other than diabetes. Therefore, we sought to evaluate the association of social support measures with medication adherence and whether this association varies by race and gender. Secondly, given the mixed but limited empirical data on the association of pharmacy access based on geography with medication adherence, we also sought to investigate the association between pharmacy access measures and medication adherence and whether this association varies by race and rural/urban residence. There is a lack of qualitative studies focusing on barriers to medication adherence in participants with CHD risk factors other than hypertension and a need for further studies of social/economic, therapy and condition related factors influencing medication adherence among people who use medications for CHD and CHD risk factors. Therefore, we further sought to explore patient perspectives on how patient, social/economic, therapy, condition, health-care system/health-care team related factors influence medication use among people who use medications for CHD and CHD risk factors. Investigating potential medication adherence barriers both quantitatively and qualitatively among people at high risk for CHD may provide important information to supplement current and future adherence interventions and influence policies regarding pharmacy access and the location of pharmacies. The ultimate goal is to reduce the risk of future CHD events and mortality by improving adherence to cardiovascular medications.

ASSOCIATION OF FUNCTIONAL AND STRUCTURAL SOCIAL SUPPORT WITH MEDICATION ADHERENCE AMONG INDIVIDUALS TREATED FOR CORONARY HEART DISEASE RISK FACTORS: FINDINGS FROM THE REASONS FOR GEOGRAPHIC AND RACIAL DIFFERENCES IN STROKE (REGARDS) STUDY

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ABSTRACT

Background

Functional social support has a stronger association with medical treatment adherence than structural social support in several populations and disease conditions. Using a contemporary U.S. population of adults treated with medications for coronary heart disease (CHD) risk factors, the association between social support and medication adherence was examined.

Methods

We included 17,113 black and white men and women with CHD or CHD risk factors aged ≥45 years recruited 2003-2007 from the REasons for Geographic and Racial Differences in Stroke (REGARDS) study. Participants reported their perceived social support (structural social support: being partnered, number of close friends, number of close relatives, and number of other adults in household; functional social support: having a caregiver in case of sickness or disability; combination of structural and functional social support: number of close friends or relatives seen at least monthly). Medication adherence was assessed using a 4-item scale. Multi-variable adjusted Poisson regression models were used to calculate prevalence ratios (PR) for the association between social support and medication adherence.

Results

Prevalence of medication adherence was 68.9%. Participants who saw >10 close friends or relatives at least monthly had higher prevalence of medication adherence (PR=1.06; 95% CI: 1.00, 1.11) than those who saw ≤3 per month. Having a caregiver in case of sickness or disability, being partnered, number of close friends, number of close relatives, and number of other adults in household were not associated with medication adherence after adjusting for covariates.

Conclusions

Seeing multiple friends and relatives was associated with better medication adherence among individuals with CHD risk factors. Increasing social support with combined structural and functional components may help support medication adherence.

INTRODUCTION

Medications can reduce the risk of coronary heart disease (CHD) events and mortality among people with known CHD and/or CHD risk factors such as diabetes, hypertension, and dyslipidemia [1-3]. However, a meta-analysis indicated that only 50 to 66% of patients were adherent to cardiovascular medications [4]. Some evidence suggests that social support promotes medication adherence in chronic disease management [5-10]. Social networks provide social support via a series of relationships and interconnectedness through which members influence each other's behaviors by their daily interactions and feedback mechanisms [11]. These networks may increase treatment adherence through support received from relatives and friends as well as assistance provided for self-care activities [9]. However, social network members may discourage others from using certain medications, thereby reducing adherence [11].

Social support has been conceptualized as consisting of functional support, structural support, and informational support [6, 12, 13]. Functional social support includes practical help provided by an individual's social network (e.g., providing transportation to doctor's visits, saying encouraging words, providing care during illness) [6, 12, 13]. Structural social support refers to the number and types of connection within an individual's social network (e.g., social network size, living arrangement, marital status) [6, 12, 13]. Informational support is the knowledge provided to an individual through their social network (e.g., providing reading material about a recent diagnosis)

[6, 12, 13]. In two prior meta-analyses, functional social support was more strongly associated with treatment adherence than structural social support [6, 14]. It is unclear whether functional and structural social support affect medication adherence specifically among those with CHD risk factors other than diabetes.

In addition, how social networks operate and how social support is received may vary by race and gender. Prior studies have found that black households may have more members compared to white households to mitigate costs due to low income [12, 15, 16], blacks depend more on informal social networks for chronic disease management than whites [12, 17-19], and blacks generally have lower medication adherence compared to whites [20-24]. Moreover, differences by gender have been reported with men being more likely to report more support from their partners while women were more likely to receive support from their friends, relatives, and peers [25-27].

The aim of the present study is to investigate the associations between perceived functional and structural social support and medication adherence in a large population of black and white men and women treated with medications for CHD risk factors. Additionally, we examined whether the associations between perceived social support and medication adherence varied by race and, separately, by gender.

METHODS

Study Population

The REasons for Geographic and Racial Differences in Stroke (REGARDS) study is a cohort of 30,239 English-speaking, community-dwelling, black and white adults age 45 and older who lived in the 48 contiguous U.S. at enrollment between 2003-2007 [28].

The REGARDS study was designed to investigate racial and regional variations in stroke mortality, and oversampled black individuals and people living in the U.S. stroke buckle (coastal regions of North Carolina, South Carolina and Georgia) and the rest of the stroke belt (remaining areas of North Carolina, South Carolina and Georgia and Alabama, Arkansas, Louisiana, Mississippi, and Tennessee) [28]. The Institutional Review Boards at participating centers approved the study protocol, and all participants provided written informed consent [28].

Data Collection

Information about socio-demographic factors, cardiovascular disease risk factors, cigarette smoking, physical activity, use of medications, and psychosocial factors including perceived social support, depressive symptoms, and stress was obtained via computer assisted telephone interviews [28, 29]. Trained health professionals conducted an in-home visit to obtain systolic and diastolic blood pressure, weight and height measurements and blood and spot urine samples [29]. Fasting was requested for 10-12 hours before the in-home visit [28]. Blood and urine samples were shipped overnight with ice packs to a central laboratory at the University of Vermont and lipid profiles and glucose were obtained from laboratory assays performed on blood samples [28, 29]. Prescription and nonprescription medication use in the two weeks prior to the in-home visit was recorded by pill bottle review [28].

Sample Selection

For the current analyses, participants were included if they had medication-treated diabetes (use of anti-diabetes medications), hypertension (use of antihypertensive medication), or dyslipidemia (use of lipid lowering medications) and/or prevalent CHD (self-reported history or electrocardiogram [ECG] evidence of a prior myocardial infarction [MI] or self-reported coronary artery bypass graft, coronary angioplasty, or coronary stenting) and use of CHD-related medications (nitrates, nitroglycerin, clopidogrel or use of aspirin to reduce risk of MI or stroke). Participants were excluded because of data anomalies (n=56), missing data on social support components (n=1,985), or medication adherence (n=517), if they were missing data on conditions of interest (diabetes, hypertension, dyslipidemia and/or prevalent CHD) or use of medications for the conditions (n=5,242) and did not have the conditions of interest or use medications for these conditions (n = 5,326) (Figure 1). After exclusions, the sample size was 17,113 participants. Participants excluded because of missing data were more likely to be younger (64.0 years vs 66.2 years), black (41.7% vs 44.6%), have health insurance (9.1% vs 5.1%), take fewer medications (4.2 vs 7.1), have a higher mean PCS score (47.4 vs 44.7) and less likely to be female (51.5% vs 53.8%), to have prevalent CHD (18.3% vs 28.9%) and be obese (36.6% vs 44.3%) compared to those included in the study (Supplemental Table 1). Participants excluded because they did not have conditions of interest or use of medications for the conditions were more likely to be younger (61.9 years vs 66.2 years), female (64.6% vs 53.8%), have health insurance (8.1% vs 5.1%), take fewer medications (3.5 vs 7.1), have a higher mean PCS score (50.4 vs 44.7) and less likely to be black (31.2% vs 44.6%), to have prevalent CHD (7.0% vs 28.9%) and to

be obese (22.0% vs 44.3%) compared to those included in the study (Supplemental Table 1).

Exposures

Six survey items were used to measure perceived social support. Each social support component was considered as a separate exposure variable. Consistent with prior literature [6, 12, 13], social support was further divided into three types: functional support, structural support and a combination of functional and structural support.

Functional support

One item was used to measure functional support.

1. Care during illness or disability status

Participants were asked, “If you had a serious illness or became disabled, do you have someone who would be able to provide care for you on an on going basis?” This item was dichotomized as (care during illness or disability vs no one to care during illness or disability).

Structural support

Four items were used to measure structural support.

1. Partnered status

   This was based on whether participants were married or in a marriage-like relationship vs divorced, widowed, separated, never been married. This was dichotomized as partnered vs not partnered respectively.
2. Number of close friends.

Participants were asked, “How many close friends do you have? That is, people that you feel at ease with, can talk to about private matters, and can call on for help?” This was categorized based on quartiles as 0-2 close friends, 3-4 close friends, 5-6 close friends, and >6 close friends.

3. Number of close relatives

   Participants were asked, “How many relatives do you have that you feel close to?” This was categorized based on quartiles as 0-3 close relatives, 4-5 close relatives, 6-10 close relatives, and >10 close relatives.

4. Number of other adults in household

   Participants were asked, “Not counting yourself, how many adults, age 18 or older currently live in the same household with you?” Because of limited variation in this item, it was divided into tertiles as 0 other adults in household, 1 other adult in household, and >1 other adult in household.

Combination of functional and structural support

One item included a combination of functional and structural support.

1. Frequency of contacts

Participants were asked “How many of these friends or relatives do you see at least once a month?” This was categorized based on quartiles as seeing 0-3 close friends or relatives at least monthly, seeing 4-5 close friends or relatives at least monthly, seeing 6-10 close friends or relatives at least monthly, and seeing >10 close friends or relatives at least monthly.

Outcome

Medication adherence was assessed using a four-item scale (30). Participants responded yes or no to the following questions: 1) “Do you ever forget to take your medicines?”; 2) “Are you careless at times about taking your medicine?”; 3) “When you feel better, do you sometimes stop taking your medicine?” and 4) “Sometimes if you feel worse when you start taking the medicine, do you stop taking it?” The outcome was categorized as low adherence (at least one “yes” response) and high adherence (no “yes” responses), consistent with prior literature [30] (Supplemental Table 2).

Covariates

Access to medications results from interaction between individuals and the health system, thus the Andersen and Aday conceptual model was selected to guide the analysis. This model proposed that individual and contextual characteristics determine how and if an individual uses health services; these characteristics are categorized into predisposing, enabling, and need factors [31].

Pre-disposing factors

The pre-disposing factors included in the analyses were age (continuous), race (black vs. white), gender (male vs. female), region of residence (Stroke Buckle vs. Stroke Belt vs. Non-Belt), annual household income (<$20,000 vs. ≥$20,000) and education (high school graduate or less vs. some college or college graduate).

Enabling factors

The enabling factors available for these analyses were insurance status (yes vs. no), rural status based on Rural Urban Commuting Area [RUCA] Codes [32], (rural vs. not rural) and percentage of individuals in a zip code living below the federal poverty line (continuous).

Need Factors

The need factors were cumulative number of medications (continuous), depressive symptoms based on the Center for Epidemiologic Studies–Depression Scale [CES-D] (CES-D score <4 vs. ≥4), physical functioning based on the Short Form 12 Physical Component Summary [PCS] score [33] (continuous), mental health based on the Short Form 12 Mental Health Component Summary (MCS) score [33] (continuous), Cohen's perceived stress scale [34] score (continuous), general health (excellent/very good vs good vs fair/poor), obesity status based on BMI (kg/m^2) estimated from measured height and weight during the in-home visit (obese vs not obese), physical activity (none vs. 1-3 times per week vs. ≥4 times per week) and Framingham CHD risk score: risk of coronary death or MI over 10 years among those free of CHD at baseline [35, 36] [(<10% vs 10-20% vs >20%) vs prevalent CHD].

Statistical Analysis

Participant characteristics and social support components were compared by medication adherence status (low versus high adherence) using descriptive statistics. Multivariable-adjusted Poisson regression models with robust variance estimation were

used to calculate prevalence ratios (PRs) for high medication adherence for each measure of social support as follows: 1. care during illness or disability vs no one to care during illness or disability; 2. partnered vs not partnered; 3. quartiles for number of close friends with 0-2 close friends as the reference; 4. quartiles for number of close relatives with 0-3 close relatives as the reference; 5. quartiles for number of close friends or relatives seen at least monthly with seeing 0-3 close friends or relatives at least monthly as the reference, and 6. tertiles for number of other adults in household with 0 other adults in household as the reference.

First a crude model was analyzed for each exposure variable. Then, sequential adjustments were made using three models for each exposure variable based on the Andersen and Aday conceptual model [31]. The crude model was adjusted for pre-disposing factors (age, race, gender region of residence, annual household income and education) to create model 1. Model 2 was created by further adjusting model 1 for enabling factors (insurance status, rural status and percentage of individuals in a zip code living below the federal poverty line). Model 2 was further adjusted for need factors (cumulative number of medications, depressive symptoms, MCS score, perceived stress scale score, general health, obesity status, physical activity, and CHD risk category) to create model 3. Race and gender were tested separately to determine whether they were effect modifiers of the associations between high medication adherence and each of the six exposures using cross-product (interaction) terms. Multivariable-adjusted Poisson regression models with robust variance estimation as above were used to estimate PRs for high medication adherence separately for each race and gender. Multiple imputation by

chained equations with ten datasets was used to account for missing covariate data [37]. The data was analyzed using SAS, version 9.4, SAS Institute, Cary, NC.

RESULTS

Among the 17,113 participants, the prevalence of high medication adherence was 68.9%. Participants with high medication adherence were more likely to be rural residents (20.5% vs 18.5%), to have higher mean PCS (45.0 vs 43.9) and MCS scores (54.6 vs 53.0), fewer depressive symptoms (10.3% vs 14.3%), and less perceived stress (3.0 vs 3.6) compared to participants with low medication adherence (Table 1).

Black participants were more likely to have >1 other adult in the household compared to white participants ($p < 0.001$) (Supplemental Table 3). Women were less likely to have someone to care for them during illness or disability ($p < 0.001$) or to be partnered ($p < 0.001$) and were more likely to have no other adults in the household ($p < 0.001$), compared to men (Supplemental Table 4). The associations between the social support components and medication adherence were similar between groups defined by race and gender (P-values for interaction >0.10 for all exposure-effect modifier combinations) (Supplemental Table 5 and 6).

DISCUSSION

In this study of adults with CHD risk factors (diabetes, hypertension, dyslipidemia and/or prevalent CHD), the number of close friends or relatives seen at least monthly, a combination of functional and structural support, was modestly associated with higher medication adherence. The other measures of perceived social support assessed in this

study, were not associated with medication adherence, once factors known to influence health services utilization were accounted for. However, overall, the prevalence of high medication adherence was notable (68.9%) given the high-risk status of this population.

Two meta-analyses indicated that functional social support had a stronger association with treatment adherence (medication adherence and adherence to other self-care activities) compared to structural social support in adults and children with a range of conditions including hypertension [6, 14]. The current study added new data which suggests that the combination of functional and structural social support via interactions with close friends or relatives may have a greater impact on medication adherence compared to other measures of functional or structural social support. Collectively, these results suggest that the quality of relationships may have a greater impact on medication adherence compared to the number of individuals in one's social network [6]. The mechanisms behind this are unclear; it has been proposed that functional support received from relatives or friends as well as assistance provided for self-care activities facilitates medication adherence [9]. This functional support further aids individuals to cope and to be motivated and optimistic about different aspects of self-management of their chronic conditions [6, 9, 38]. As a result of supportive interactions that lead to better coping, suggested interventions to improve medication adherence include encouraging social network members to assist non-adherent members with prescription refills and pill reminders [11].

The current study may have had limited power to detect clinically important variations by race and gender in the associations between social support and medication adherence. Prior studies have found differences in the associations between social support

and chronic disease self-management activities by race and gender. One study found that among women, diabetes-specific social support was associated with an increased prevalence of medication adherence among people with diabetes; however, among men, social support was not associated with medication adherence [39]. In another study, Rees and colleagues found that the association between social support and diabetes self-management activities differed by race [40]. However, medication adherence was not assessed in this study.

The strengths of the current study include the availability of data on a four-item medication adherence scale, social support components, health-related and socio-economic variables on a large population of black and white men and women from the 48 contiguous US states.

The current study has several potential limitations. This was a cross-sectional study; therefore, it was not possible to determine the temporality sequence between social support components and medication adherence. The cross-sectional nature of the study further limits our ability to make causal inferences regarding whether social support directly influences medication adherence. Since social support and medication adherence were both self-reported, it is possible that misclassification may have resulted. However, the four-item medication adherence scale used in the current analysis has been widely used, including in prior studies using the REGARDS data to evaluate anti-hypertensive medication [41] and statin [42] adherence. We relied on the participants' perceptions of social support; we did not have information about whether unexpected support may have been provided in times of need. Further, the reporting of both social support and medication adherence may be affected by social desirability bias. Additionally, only one

measure of functional support was available; therefore, this limits the ability to make further conclusions regarding the association between functional support and medication adherence. Some covariates relied also on self-report, which could have increased the potential for misclassification. Although a variety of confounders were accounted for, there was potential for residual confounding.

Conclusions

The results of the current study indicate that among people with CHD risk factors, frequent contact with close friends or relatives (which comprises a combination of functional and structural social support) had a small association with medication adherence. Enhancing combined functional and structural social support for people with CHD risk factors such as diabetes, hypertension, dyslipidemia and prevalent CHD may help improve their medication adherence.

Data Availability Statement

This study uses data from REasons for Geographic and Racial Differences in Stroke (REGARDS) cohort. In order to abide by its obligations with NIH/NINDS and the Institutional Review Board of the University of Alabama at Birmingham, REGARDS facilitates data sharing through formal data use agreements. Any investigator is welcome to access the REGARDS data through this process. Any investigator interested in accessing the data may complete a manuscript proposal as per NIH requirements to obtain de-identified data. Requests for data access may be sent to regardsadmin@uab.edu

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Conflicts of Interest

I have read the journal's policy and the authors of this manuscript have the following competing interests: F.L.M receives funding from the American Heart Association Predoctoral Fellowship, A.P.C. receives funding from Amgen for unrelated work, R.W.D receives funding from Amgen and Amarin for unrelated work, M.W.L. has no relationships to disclose, M.M.S receives funding from Amgen and diaDexus for unrelated work, E.B.L receives funding from Amgen for unrelated work and has consulted for Amgen and Novartis. This does not alter our adherence to PLOS ONE policies on sharing data and materials.

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Table 1. Characteristics of REGARDS[a] participants by medication adherence status

	Medication Adherence		
Characteristics	**Low adherence**	**High adherence**	**p**
	n = 5,323	n = 11,790	
Predisposing factors			
Age, years, mean ± SD	65.3 ± 9.0	66.7 ± 9.0	<0.0001
Black, n (%)	2,404 (45.2)	5,223 (44.3)	0.29
Women, n (%)	2,948 (55.4)	6,254 (53.0)	0.005
Region, n (%)			<0.0001
Stroke belt[b]	1,915 (36.0)	4,078 (34.6)	
Stroke buckle[c]	1,026 (19.3)	2,646 (22.4)	
Non-stroke belt or buckle	2,382 (44.8)	5,066 (43.0)	
Annual household income <$20,000, n (%)	1,073 (22.8)	2,294 (22.0)	0.26
Education ≤ High school, n (%)	2,233 (42.0)	4,809 (40.8)	0.15
Enabling factors			
No health insurance, n (%)	285 (5.4)	585 (5.0)	0.28
Percentage of individuals in a zip code living below the federal poverty line, mean ± SD	17.0 ± 9.5	17.0 ± 9.3	0.92
Rural residence, n (%)	893 (18.5)	2,187 (20.5)	0.004
Need factors			
CHD[a] risk categories[d], n (%)			0.08
< 10%	2,271 (42.7)	5,142 (43.6)	
10-20%	921 (17.3)	2,132 (18.1)	
>20%	521 (9.8)	1,175 (10.0)	
Prevalent CHD[ae]	1,610 (30.3)	3,341 (28.3)	
Physical activity[f], n (%)			<0.0001

None	2,021 (38.5)	4,212 (36.1)	
1-3 times per week	1,918 (36.5)	4,073 (34.9)	
4+ times per week	1,316 (25.0)	3,376 (29.0)	
Cumulative number of medications ± SD	7.2 ± 4.0	7.0 ± 3.9	0.0009
General Health[f], n (%)			<0.0001
Excellent/Very Good	1,831 (34.5)	4,711 (40.0)	
Good	2,140 (40.3)	4,491 (38.2)	
Fair/Poor	1,343 (25.3)	2,565 (21.8)	
Obesity prevalence, n (%)	2,500 (47.4)	5,016 (42.8)	<0.0001
Depressive symptoms, CES-D score ≥ 4, n (%)	758 (14.3)	1,203 (10.3)	<0.0001
Physical Component Summary Score, mean ± SD	43.9 ± 11.0	45.0 ± 10.9	<0.0001
Mental Component Summary Score, mean ± SD	53.0 ± 9.1	54.6 ± 8.2	<0.0001
Perceived Stress Scale Score, mean ± SD	3.6 ± 3.0	3.0 ± 2.9	<0.0001

[a]Abbreviations: REGARDS, Reasons for Geographic and Racial Differences in Stroke; CHD, coronary heart disease

[b]Defined as the states of Alabama, Arkansas, Louisiana, Mississippi, Tennessee and the noncoastal regions of North Carolina, South Carolina and Georgia.

[c]Defined as the coastal regions of North Carolina, South Carolina and Georgia

[d]Framingham CHD hard event risk score: risk of coronary death or MI over 10 years (among those free of CHD at baseline)

[e]Self-reported history or electrocardiogram (ECG) evidence of a prior myocardial infarction MI or self-reported coronary artery bypass graft, coronary angioplasty, or coronary stenting

[f]The frequencies and percentages may not add up to the total sample size due to missing data.

Table 2. Social support components by medication adherence status

	Medication Adherence		
	Low adherence	**High adherence**	**p**
Functional support			
Care during illness or disability, n (%)	4,491 (84.4)	10,274 (87.1)	<0.0001
Structural support			
Partnered, n (%)	3,239 (60.8)	7,168 (60.8)	0.95
Close Friends (Quartiles)			<0.0001
0-2 close friends, n (%)	1,531 (28.8)	3,080 (26.1)	
3-4 close friends, n (%)	1,493 (28.1)	3,189 (27.1)	
5-6 close friends, n (%)	1,101 (20.7)	2,643 (22.4)	
>6 close friends, n (%)	1,198 (22.5)	2,878 (24.4)	
Close Relatives (Quartiles)			0.0002
0-3 close relatives, n (%)	2,012 (37.8)	4,057 (34.4)	
4-5 close relatives, n (%)	1,141 (21.4)	2,566 (21.8)	
6-10 close relatives, n (%)	1,357 (25.5)	3,243 (27.5)	
>10 close relatives, n (%)	813 (15.3)	1,924 (16.3)	
Other adults in household (Tertiles)			0.0004
0 other adults in household, n (%)	1,417 (26.6)	3,246 (27.5)	
1 other adult in household, n (%)	2,957 (55.6)	6,725 (57.0)	
>1 other adult in household, n (%)	949 (17.8)	1,819 (15.4)	
Functional and structural support			

Frequency of Contacts (Quartiles)			<0.0001
Seeing 0-3 close friends or relatives at least monthly, n (%)	1,957 (36.8)	3,812 (32.3)	
Seeing 4-5 close friends or relatives at least monthly, n (%)	1,025 (19.3)	2,320 (19.7)	
Seeing 6-10 close friends or relatives at least monthly, n (%)	1,402 (26.3)	3,239 (27.5)	
Seeing >10 close friends or relatives at least monthly, n (%)	939 (17.6)	2,419 (20.5)	

Table 3. Adjusted Models with prevalence ratios and 95% confidence intervals of high medication adherence by social support components

	Crude Model	**Model 1[a]**	**Model 2[b]**	**Model 3[c]**
	PR 95% CI	**PR 95% CI**	**PR 95% CI**	**PR 95% CI**
Functional support				
Care during illness or disability vs no one to care during illness or disability	1.08 (1.02, 1.14)	1.08 (1.02, 1.14)	1.08 (1.02, 1.14)	1.05 (0.99, 1.11)
Structural support				
Partnered vs not partnered	1.00 (0.96, 1.04)	1.00 (0.96, 1.04)	1.00 (0.96, 1.04)	0.99 (0.95, 1.04)
Close Friends (Quartiles)				
0-2 close friends	Ref	Ref	Ref	Ref
3-4 close friends	1.02 (0.97, 1.07)	1.02 (0.97, 1.07)	1.01 (0.97, 1.07)	1.01 (0.96, 1.06)
5-6 close friends	1.06 (1.00, 1.11)	1.05 (1.00, 1.11)	1.05 (1.00, 1.11)	1.03 (0.98, 1.09)
>6 close friends	1.06 (1.00, 1.11)	1.05 (0.99, 1.10)	1.05 (0.99, 1.10)	1.02 (0.97, 1.08)
Close Relatives (Quartiles)				
0-3 close relatives	Ref	Ref	Ref	Ref
4-5 close relatives	1.04 (0.99, 1.09)	1.04 (0.99, 1.09)	1.04 (0.99, 1.09)	1.02 (0.97, 1.07)
6-10 close relatives	1.06 (1.01, 1.10)	1.05 (1.00, 1.10)	1.05 (1.00, 1.10)	1.03 (0.98, 1.08)
>10 close relatives	1.05 (1.00, 1.11)	1.04 (0.99, 1.10)	1.04 (0.98, 1.10)	1.02 (0.96, 1.07)
Other adults in household (Tertiles)				
0 other adults in	Ref	Ref	Ref	Ref

household				
1 other adult in household	1.00 (0.96, 1.04)	1.00 (0.96, 1.05)	1.00 (0.96, 1.05)	1.00 (0.96, 1.05)
>1 other adult in household	0.94 (0.89, 1.00)	0.96 (0.91, 1.02)	0.97 (0.91, 1.03)	0.97 (0.92, 1.03)
Functional and structural support				
Frequency of Contacts				
Seeing 0-3 close friends or relatives at least monthly	Ref	Ref	Ref	Ref
Seeing 4-5 close friends or relatives at least monthly	1.05 (1.00, 1.10)	1.05 (1.00, 1.10)	1.05 (1.00, 1.10)	1.03 (0.98, 1.09)
Seeing 6-10 close friends or relatives at least monthly	1.06 (1.01, 1.11)	1.06 (1.01, 1.11)	1.06 (1.01, 1.11)	1.03 (0.99, 1.08)
Seeing >10 close friends or relatives at least monthly	1.09 (1.04, 1.15)	1.09 (1.03, 1.14)	1.09 (1.03, 1.14)	1.06 (1.00, 1.11)

[a]Model 1(Pre-disposing factors): age (continuous), race (categorical), gender (categorical), region of residence (categorical), annual household income (categorical) and education (categorical).

[b]Model 2 (Enabling factors): model 1 covariates, insurance status (categorical), rural status (categorical), percentage of individuals in a zip code living below the federal poverty line (continuous).

[c]Model 3 (Need factors): model 2 covariates, cumulative number of medications (continuous), depressive symptoms, (CES-D) score (categorical), physical component summary score (continuous), mental component summary score (continuous), perceived stress scale score (continuous), general health (categorical), obesity status (categorical), physical activity (categorical), coronary heart disease risk category (categorical)

Supplemental Table 1. Characteristics of REGARDS[a] participants by sample inclusion/exclusion status

	Sample			
Characteristics	**Included**	**Excluded**		**p**
		Missing data	**No conditions of interest**	
	n = 17,113	n = 7,744	n = 5,326	
Predisposing factors				
Age, years, mean ± SD	66.2 ± 9.1	64.0 (9.5)	61.6 (9.6)	<0.0001
Black, n (%)	7,627 (44.6)	3,226 (41.7)	1,661 (31.2)	<0.0001
Women, n (%)	9,202 (53.8)	3,990 (51.5)	3,440 (64.6)	<0.0001
Region, n (%)				0.0004
Stroke belt[b]	5,993 (35.0)	2,666 (34.4)	1,788 (33.6)	
Stroke buckle[c]	3,672 (21.5)	1,590 (20.5)	1,045 (19.6)	
Non-stroke belt or buckle	7,448 (43.5)	3,488 (45.0)	2,493 (46.8)	
Annual household income <$20,000, n (%)	3,367 (22.2)	1,437 (21.6)	674 (14.5)	<0.0001
Education ≤ High school, n (%)	7,042 (41.2)	3,056 (39.5)	1,498 (28.1)	<0.0001
Enabling factors				
No health insurance, n (%)	870 (5.1)	705 (9.1)	430 (8.1)	<0.0001
Percentage of individuals in a zip code living below the federal poverty line, mean ± SD	17.0 ± 9.3	17.1 (9.4)	15.0 (9.2)	<0.0001
Rural residence, n (%)	3,080 (19.9)	1,423 (20.3)	862 (18.0)	0.006
Need factors				
CHD[a] risk categories[d], n (%)				<0.0001
< 10%	7,413 (43.3)	3,542 (45.7)	4,353 (81.8)	
10-20%	3,053 (17.8)	1,773 (22.9)	507 (9.5)	
>20%	1,696 (9.9)	1,011 (13.1)	90 (1.7)	
Prevalent CHD[ae]	4,951 (28.9)	1,418 (18.3)	374 (7.0)	

Physical activity[f], n (%)				<0.0001
None	6,233 (36.9)	2,541 (33.6)	1,466 (28.0)	
1-3 times per week	5,991 (35.4)	2,703 (35.7)	2,001 (38.1)	
4+ times per week	4,692 (27.7)	2,327 (30.7)	1,779 (33.9)	
Cumulative number of medications ± SD	7.1 ± 4.0	4.2 (3.8)	3.5 (3.5)	<0.0001
General Health[f], n (%)				<0.0001
Excellent/Very Good	6,542 (38.3)	3,809 (49.4)	3,620 (68.0)	
Good	6,631 (38.8)	2,633 (34.1)	1,311 (24.6)	
Fair/Poor	3,908 (22.9)	1,275 (16.5)	391 (7.4)	
Obesity prevalence, n (%)	7,516 (44.3)	2,815 (36.6)	1,168 (22.0)	<0.0001
Depressive symptoms, CES-D score ≥ 4, n (%)	1,961 (11.5)	910 (11.8)	478 (9.1)	<0.0001
Physical Component Summary Score, mean ± SD	44.7 ± 10.9	47.4 (10.2)	50.4 (8.6)	<0.0001
Mental Component Summary Score, mean ± SD	54.1 ± 8.5	53.7 (8.7)	54.2 (7.9)	0.0007
Perceived Stress Scale Score, mean ± SD	3.2 ± 3.0	3.3 (3.0)	3.1 (2.7)	0.0005

[a]Abbreviations: REGARDS, Reasons for Geographic and Racial Differences in Stroke; CHD, coronary heart disease

[b]Defined as the states of Alabama, Arkansas, Louisiana, Mississippi, Tennessee and the noncoastal regions of North Carolina, South Carolina and Georgia.

[c]Defined as the coastal regions of North Carolina, South Carolina and Georgia

[d]Framingham CHD hard event risk score: risk of coronary death or MI over 10 years (among those free of CHD at baseline)

[e]Self-reported history or electrocardiogram (ECG) evidence of a prior myocardial infarction MI or self-reported coronary artery bypass graft, coronary angioplasty, or coronary stenting

[f]The frequencies and percentages may not add up to the total sample size due to missing data.

Supplemental Table 2. Social support components by race

	Race		
	Blacks n = 7,627	**Whites n=9,486**	**p**
Functional support			
Care during illness or disability, n (%)	6,554 (85.9)	8,211 (86.6)	0.24
Structural support			
Partnered, n (%)	3,664 (48.0)	6,743 (71.1)	<0.0001
Close Friends (Quartiles)			<0.0001
0-2 close friends, n (%)	2,628 (34.5)	1,983 (20.9)	
3-4 close friends, n (%)	2,303 (30.2)	2,379 (25.1)	
5-6 close friends, n (%)	1,406 (18.4)	2,338 (24.7)	
>6 close friends, n (%)	1,290 (16.9)	2,786 (29.4)	
Close Relatives (Quartiles)			0.05
0-3 close relatives, n (%)	2,777 (36.4)	3,292 (34.7)	
4-5 close relatives, n (%)	1,643 (21.5)	2,064 (21.8)	
6-10 close relatives, n (%)	2,040 (26.8)	2,560 (27.0)	
>10 close relatives, n (%)	1,167 (15.3)	1,570 (16.6)	
Other adults in household (Tertiles)			<0.0001
0 other adults in household, n (%)	2,346 (30.8)	2,317 (24.4)	
1 other adult in household, n (%)	3,651 (47.9)	6,031 (63.6)	
>1 other adult in household, n (%)	1,630 (21.4)	1,138 (12.0)	
Functional and structural support			
Frequency of Contacts			<0.0001
Seeing 0-3 close friends or relatives at least monthly, n (%)	2,848 (37.3)	2,921 (30.8)	
Seeing 4-5 close friends or relatives at least monthly, n (%)	1,525 (20.0)	1,820 (19.2)	
Seeing 6-10 close friends or relatives at least monthly, n (%)	2,007 (26.3)	2,634 (27.8)	
Seeing >10 close friends or relatives at least monthly, n (%)	1,247 (16.4)	2,111 (22.3)	

Supplemental Table 3. Social support components by gender

	Gender		
	Women n=9,202	**Men n=7,911**	**p**
Functional support			
Care during illness or disability, n (%)	7,634 (83.0)	7,131 (90.1)	<0.0001
Structural support			
Partnered, n (%)	4,044 (44.0)	6,363 (80.4)	<0.0001
Close Friends (Quartiles)			<0.0001
0-2 close friends, n (%)	2,625 (28.5)	1,986 (25.1)	
3-4 close friends, n (%)	2,793 (30.4)	1,889 (23.9)	
5-6 close friends, n (%)	2,007 (21.8)	1,737 (22.0)	
>6 close friends, n (%)	1,777 (19.3)	2,299 (29.1)	
Close Relatives (Quartiles)			<0.0001
0-3 close relatives, n (%)	3,457 (37.6)	2,612 (33.0)	
4-5 close relatives, n (%)	2,098 (22.8)	1,609 (20.3)	
6-10 close relatives, n (%)	2,381 (25.9)	2,219 (28.1)	
>10 close relatives, n (%)	1,266 (13.8)	1,471 (18.6)	
Other adults in household (Tertiles)			<0.0001
0 other adults in household, n (%)	3,388 (36.8)	1,275 (16.1)	
1 other adult in household, n (%)	4,378 (47.6)	5,304 (67.1)	
>1 other adult in household, n (%)	1,436 (15.6)	1,332 (16.8)	
Functional and structural support			
Frequency of Contacts (Quartiles)			<0.0001
Seeing 0-3 close friends or relatives at least monthly, n (%)	3,104 (33.7)	2,665 (33.7)	
Seeing 4-5 close friends or relatives at least monthly, n (%)	1,845 (20.1)	1,500 (19.0)	
Seeing 6-10 close friends or relatives at least monthly, n (%)	2,573 (28.0)	2,068 (26.1)	
Seeing >10 close friends or relatives at least monthly, n (%)	1,680 (18.3)	1,678 (21.2)	

Supplemental Table 4. Adjusted Models with prevalence ratios and 95% confidence intervals of high medication adherence by social support components among blacks and whites

	Blacks				**Whites**				
	Crude Model	**Model 1[a]**	**Model 2[b]**	**Model 3[c]**	**Crude Model**	**Model 1[a]**	**Model 2[b]**	**Model 3[c]**	
	PR 95% CI	**PR 95% CI**	**PR 95% CI**	**PR 95% CI**	**PR 95% CI**	**PR 95% CI**	**PR 95% CI**	**PR 95% CI**	**p[d]**
Functional support									
Care during illness or disability vs none	1.11 (1.02, 1.20)	1.11 (1.02, 1.20)	1.11 (1.02, 1.20)	1.07 (0.99, 1.17)	1.05 (0.98, 1.13)	1.06 (0.98, 1.14)	1.06 (0.98, 1.14)	1.03 (0.96, 1.11)	0.36
Structural support									
Partnered vs not partnered	0.99 (0.94, 1.05)	0.98 (0.92, 1.04)	0.98 (0.92, 1.04)	0.98 (0.92, 1.04)	1.00 (0.95, 1.06)	1.02 (0.96, 1.09)	1.02 (0.96, 1.08)	1.01 (0.95, 1.08)	0.74
Close Friends (Quartiles)									0.39
0-2 close friends	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	
3-4 close friends	1.01 (0.94, 1.08)	1.00 (0.94, 1.08)	1.00 (0.94, 1.08)	1.01 (0.96, 1.06)	1.04 (0.96, 1.11)	1.04 (0.96, 1.11)	1.04 (0.96, 1.11)	1.02 (0.95, 1.10)	
5-6 close friends	1.03 (0.95, 1.11)	1.02 (0.94, 1.10)	1.02 (0.94, 1.10)	1.03 (0.98, 1.09)	1.08 (1.01, 1.16)	1.08 (1.01, 1.16)	1.08 (1.01, 1.16)	1.06 (0.98, 1.14)	
>6 close friends	1.03 (0.95, 1.12)	1.01 (0.93, 1.10)	1.01 (0.94, 1.10)	1.02 (0.96, 1.07)	1.08 (1.01, 1.16)	1.08 (1.00, 1.15)	1.08 (1.00, 1.15)	1.05 (0.97, 1.12)	
Close Relatives (Quartiles)									0.74

0-3 close relatives	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	
4-5 close relatives	1.02 (0.95, 1.11)	1.02 (0.95, 1.10)	1.02 (0.95, 1.10)	1.01 (0.94, 1.09)	1.05 (0.98, 1.12)	1.05 (0.98, 1.12)	1.05 (0.98, 1.12)	1.03 (0.97, 1.10)	
6-10 close relatives	1.03 (0.96, 1.11)	1.02 (0.96, 1.10)	1.02 (0.96, 1.10)	1.01 (0.94, 1.08)	1.04 (0.97, 1.12)	1.07 (1.01, 1.14)	1.07 (1.00, 1.14)	1.05 (0.99, 1.12)	
>10 close relatives	1.06 (0.98, 1.15)	1.05 (0.97, 1.14)	1.05 (0.97, 1.14)	1.02 (0.94, 1.11)	1.07 (1.01, 1.14)	1.03 (0.96, 1.11)	1.03 (0.96, 1.11)	1.01 (0.94, 1.09)	
Other adults in household (Tertiles)									0.50
0 other adults in household	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	
1 other adult in household	0.99 (0.93, 1.05)	0.99 (0.92, 1.05)	1.00 (0.92, 1.05)	1.00 (0.95, 1.04)	1.00 (0.95, 1.06)	1.02 (0.95, 1.08)	1.02 (0.95, 1.08)	1.01 (0.95, 1.08)	
>1 other adult in household	0.97 (0.90, 1.05)	0.98 (0.91, 1.06)	0.97 (0.91, 1.03)	0.97 (0.92, 1.03)	0.91 (0.83, 0.99)	0.94 (0.86, 1.03)	0.94 (0.86, 1.03)	0.95 (0.86, 1.04)	
Functional and structural support									
Frequency of Contacts (Quartiles)									0.52
Seeing 0-3 close friends or relatives at least monthly	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	
Seeing 4-5 close friends or relatives at least monthly	1.03 (0.95, 1.11)	1.03 (0.96, 1.11)	1.03 (0.96, 1.11)	1.02 (0.94, 1.10)	1.07 (0.99, 1.15)	1.06 (0.99, 1.14)	1.06 (0.99, 1.14)	1.05 (0.98, 1.12)	

Seeing 6-10 close friends or relatives at least monthly	1.07 (0.99, 1.14)	1.07 (0.99, 1.14)	1.07 (0.99, 1.14)	1.04 (0.97, 1.12)	1.05 (0.98, 1.12)	1.05 (0.98, 1.12)	1.05 (0.98, 1.12)	1.03 (0.96, 1.10)	
Seeing >10 close friends or relatives at least monthly	1.07 (0.99, 1.16)	1.07 (0.98, 1.15)	1.07 (0.98, 1.16)	1.03 (0.95, 1.12)	1.10 (1.03, 1.18)	1.10 (1.03, 1.18)	1.10 (1.03, 1.18)	1.07 (1.00, 1.15)	

[a]Model 1 (Pre-disposing factors): age (continuous), gender (categorical), region of residence (categorical), annual household income (categorical) and education (categorical).

[b]Model 2 (Enabling factors): model 1 covariates, insurance status (categorical), rural status (categorical), percentage of individuals in a zip code living below the federal poverty line (continuous).

[c]Model 3 (Need factors): model 2 covariates, cumulative number of medications (continuous), depressive symptoms, (CES-D) score (categorical), physical component summary score (continuous), mental component summary score (continuous), perceived stress scale score (continuous), general health (categorical), obesity status (categorical), physical activity (categorical), coronary heart disease risk category (categorical).

[d]P-value for interaction (Model 3)

Supplemental Table 5. Adjusted Models with odds ratios and 95% confidence intervals of high medication adherence by social support components among women and men

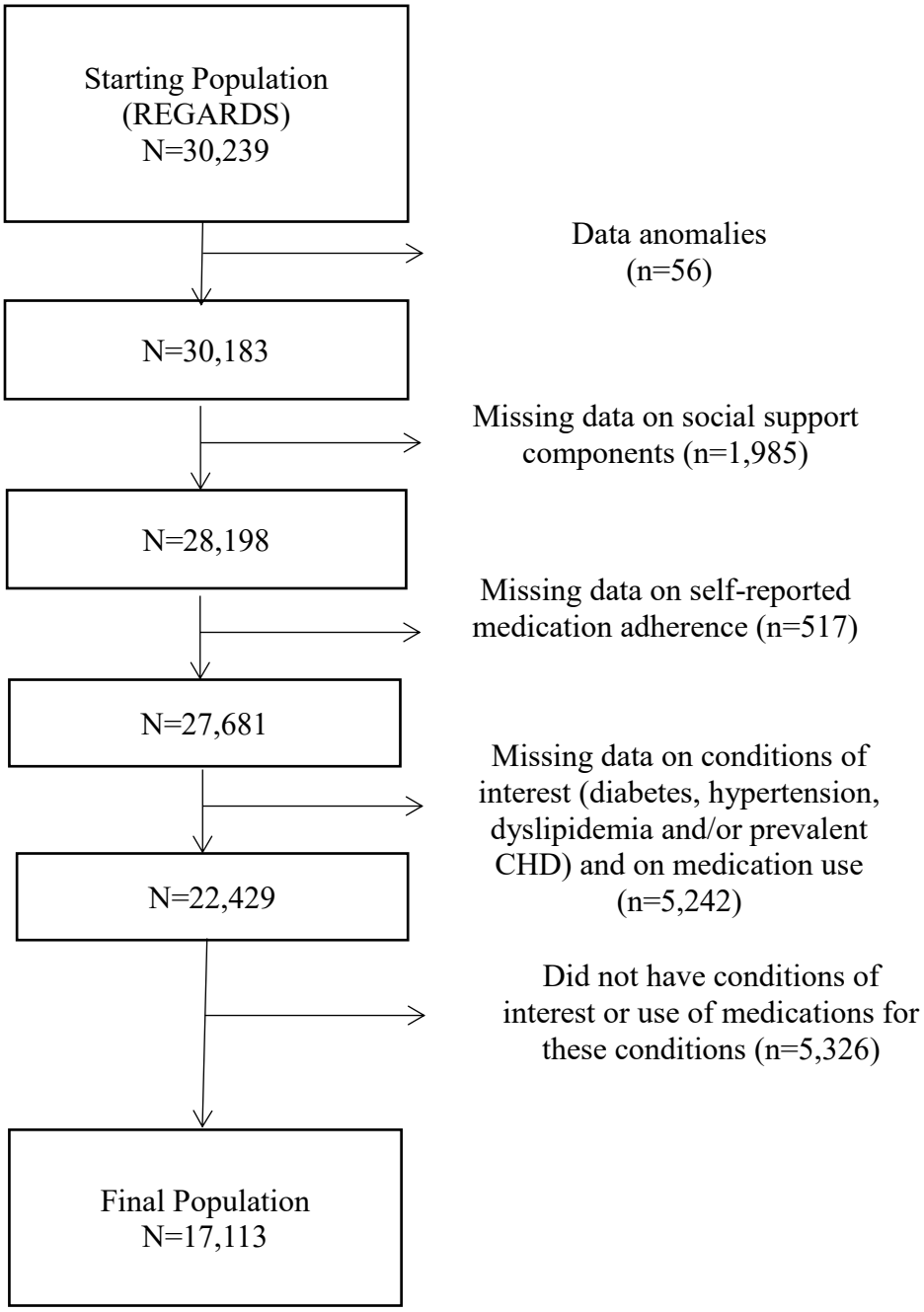
	Women				**Men**				
	Crude Model	**Model 1[a]**	**Model 2[b]**	**Model 3[c]**	**Crude Model**	**Model 1[a]**	**Model 2[b]**	**Model 3[c]**	
	PR 95% CI	**PR 95% CI**	**PR 95% CI**	**PR 95% CI**	**PR 95% CI**	**PR 95% CI**	**PR 95% CI**	**PR 95% CI**	**p[d]**
Functional support									
Care during illness or disability vs none	1.09 (1.02, 1.16)	1.09 (1.02, 1.17)	1.09 (1.02, 1.17)	1.07 (1.00, 1.15)	1.05 (0.96, 1.15)	1.05 (0.96, 1.15)	1.05 (0.96, 1.15)	1.01 (0.92, 1.11)	0.51
Structural support									
Partnered vs not partnered	0.99 (0.94, 1.04)	1.00 (0.95, 1.06)	1.00 (0.95, 1.06)	1.01 (0.95, 1.08)	0.99 (0.92, 1.06)	1.00 (0.93, 1.07)	0.99 (0.93, 1.06)	0.98 (0.91, 1.05)	0.71
Close Friends (Quartiles)									0.79
0-2 close friends	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	
3-4 close friends	1.03 (0.97, 1.11)	1.04 (0.96, 1.11)	1.04 (0.96, 1.11)	1.02 (0.95,1.09)	1.00 (0.93, 1.08)	1.00 (0.93, 1.08)	1.00 (0.93, 1.08)	0.99 (0.91, 1.07)	
5-6 close friends	1.06 (0.99, 1.13)	1.08 (1.01, 1.16)	1.08 (1.01, 1.16)	1.03 (0.96, 1.11)	1.05 (0.98, 1.14)	1.06 (0.98, 1.14)	1.06 (0.98, 1.14)	1.03 (0.96, 1.12)	
>6 close friends	1.06 (0.99, 1.14)	1.08 (1.00, 1.15)	1.08 (1.00, 1.15)	1.03 (0.95, 1.11)	1.04 (0.97, 1.12)	1.04 (0.97, 1.12)	1.04 (0.97, 1.12)	1.01 (0.94, 1.09)	
Close Relatives (Quartiles)									0.99
0-3 close	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	

relatives									
4-5 close relatives	1.05 (0.98, 1.12)	1.05 (0.98, 1.12)	1.05 (0.98, 1.12)	1.04 (0.97, 1.11)	1.02 (0.95, 1.10)	1.02 (0.95, 1.10)	1.02 (0.95, 1.10)	1.00 (0.93, 1.08)	
6-10 close relatives	1.04 (0.98, 1.11)	1.03 (0.97, 1.10)	1.03 (0.97, 1.10)	1.02 (0.95, 1.08)	1.07 (1.00, 1.14)	1.06 (1.00, 1.14)	1.06 (0.99, 1.14)	1.05 (0.98, 1.12)	
>10 close relatives	1.05 (0.98, 1.14)	1.04 (0.97, 1.13)	1.04 (0.97, 1.13)	1.02 (0.94, 1.10)	1.04 (0.97, 1.13)	1.04 (0.96, 1.12)	1.04 (0.96, 1.12)	1.01 (0.94, 1.09)	
Other adults in household (Tertiles)									0.83
0 other adults in household	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	
1 other adult in household	0.98 (0.93, 1.04)	1.00 (0.94, 1.06)	1.00 (0.94, 1.06)	1.00 (0.95, 1.06)	1.00 (0.93, 1.08)	1.01 (0.94, 1.09)	1.01 (0.93, 1.09)	0.99 (0.92, 1.07)	
>1 other adult in household	0.95 (0.88, 1.02)	0.98 (0.91, 1.06)	0.98 (0.91, 1.06)	0.99 (0.92, 1.07)	0.93 (0.85, 1.02)	0.95 (0.86, 1.04)	0.95 (0.86, 1.04)	0.95 (0.86, 1.04)	
Functional and structural support									
Frequency of Contacts (Quartiles)									0.54
Seeing 0-3 close friends or relatives at least monthly	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	
Seeing 4-5 close friends or relatives at least monthly	1.03 (0.96, 1.10)	1.02 (0.95, 1.10)	1.02 (0.95, 1.10)	1.01 (0.94, 1.08)	1.08 (1.00, 1.16)	1.08 (1.00, 1.16)	1.08 (1.00, 1.16)	1.06 (0.99, 1.15)	

Seeing 6-10 close friends or relative at least monthly	1.06 (0.99, 1.13)	1.05 (0.99, 1.12)	1.05 (0.99, 1.12)	1.03 (0.97, 1.10)	1.06 (0.98, 1.13)	1.06 (0.99, 1.13)	1.06 (0.99, 1.13)	1.04 (0.97, 1.11)	
Seeing >10 close friends or relatives at least monthly	1.12 (1.04, 1.20)	1.11 (1.03, 1.19)	1.11 (1.03, 1.19)	1.08 (1.00, 1.16)	1.06 (0.99, 1.14)	1.07 (0.99, 1.15)	1.07 (0.99, 1.15)	1.04 (0.96, 1.12)	

[a]Model 1 (Pre-disposing factors): age (continuous), race (categorical), region of residence (categorical), annual household income (categorical) and education (categorical).
[b]Model 2 (Enabling factors): model 1 covariates, insurance status (categorical), rural status (categorical), percentage of individuals in a zip code living below the federal poverty line (continuous).
[c]Model 3 (Need factors): model 2 covariates, cumulative number of medications (continuous), depressive symptoms, (CES-D) score (categorical), physical component summary score (continuous), mental component summary score (continuous), perceived stress scale score (continuous), general health (categorical), obesity status (categorical), physical activity (categorical), coronary heart disease risk category (categorical).
[d]P-value for interaction (Model 3)

Figure 1. Flow Chart with Exclusion Criteria



ASSOCIATION OF DISTANCE TO NEAREST PHARMACY AND PHARMACY DENSITY WITH MEDICATION ADHERENCE AMONG INDIVIDUALS TREATED FOR CORONARY HEART DISEASE RISK FACTORS

by

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ABSTRACT

Poor pharmacy access may act as a barrier to medication adherence among people with coronary heart disease (CHD) risk factors. We investigated the association between pharmacy access and medication adherence among black and white adults aged ≥52 years (n=8,250) from the REasons for Geographic and Racial Differences in Stroke (REGARDS) Study second in-home visit (data collected in 2013-2016), including those who used medications for diabetes, hypertension, dyslipidemia, or prevalent CHD. Data on pharmacy locations were obtained from the National Council for Prescription Drug Programs. Pharmacy access [quartiles of straight-line distances from participants' residences to the nearest pharmacy and quartiles of number of pharmacies in 1.61 km (1 mile), 8.05 km (5 mile), 16.1 km (10 mile) and 24.1 km (15 mile) buffers was assessed using geospatial analysis. Self-reported medication adherence was assessed using a validated 4-item scale. Multi-variable adjusted Poisson regression models were used to calculate prevalence ratios for the association between pharmacy access and self-reported medication adherence. The prevalence of high medication adherence was 70.4%. After adjusting for covariates, distance from participants' residences to nearest pharmacy, as well as number of pharmacies across all 4 buffer sizes, were not associated with medication adherence. We also did not find any evidence for interaction of population density or race with pharmacy access. In conclusion, in this population with CHD and

CHD risk factors, lack of access to pharmacies based on geography was not a barrier to medication adherence.

INTRODUCTION

Although medications are available which can reduce coronary heart disease (CHD) risk and mortality, 50-66% of patients are adherent to such medications.[1] Access to medications is essential for following treatment plans and medication management.[2] Transportation-related expenses, poor public transportation, and few health care providers in disadvantaged neighborhoods can contribute to poor health care access overall.[3] However, one study conducted among a Medicaid population in Illinois, found no significant association between medication adherence and distance to the nearest pharmacy among adults with diabetes.[4] Blacks tend to have lower medication adherence compared to whites,[5-9] perhaps in part because blacks tend to have greater transportation barriers in accessing health-care compared to whites.[10,11] Yet, in the study conducted among the Medicaid population in Illinois, there was no difference in distance to pharmacies for black and white participants.[4] Some prior studies conducted both nationally and among participants in select states, also showed that travel time acts as a greater barrier to health care access in rural areas compared to urban areas. [12-14] In the current study, we investigated the association of pharmacy access, determined from geospatial analysis, with medication adherence, determined using self-reported data among participants in the REasons for Geographic And Racial Differences in Stroke

(REGARDS) Study, focusing on those participants with diabetes, hypertension, dyslipidemia or prevalent CHD. We also investigated whether the association between medication adherence and pharmacy access measures varied by race or population density.

METHODS

The REGARDS study enrolled 30,239 English-speaking, black and white adults from the 48 contiguous US states who were aged 45 years and older at baseline (2003-2007).[15] The REGARDS Study was designed to investigate differences in stroke mortality by race and region, and oversampled black adults and those living in the stroke buckle (coastal regions of North Carolina, South Carolina and Georgia) and the rest of the stroke belt (remaining areas of North Carolina, South Carolina and Georgia and Alabama, Arkansas, Louisiana, Mississippi, and Tennessee).[15] Participants completed a baseline in-home examination that included questionnaires, physical measurements, and collection of blood and urine specimens.[16] In 2013-2016, a second in-home examination was completed for 16,150 participants (excluding 56 participants with data anomalies, 6,590 who died and 7,443 who were lost to follow-up or declined the second examination).[16] The Institutional Review Boards at participating centers approved the REGARDS study protocol, and all participants provided written informed consent.[15,16]

The current analyses included participants from the second in-home examination who had medication-treated CHD risk factors and/or medication-treated prevalent CHD. CHD risk factors included diabetes (use of anti-diabetes medications), hypertension (use of antihypertensive medication), and dyslipidemia (use of lipid lowering medications). Prevalent CHD (self-reported history or electrocardiogram evidence of a prior myocardial

infarction [MI] or self-reported coronary artery bypass graft, coronary angioplasty, or coronary stenting) medications included nitrates, nitroglycerin, PY12 receptor antagonists or aspirin use to reduce risk of MI or stroke. Participants were excluded because of missing residential latitude or longitude (n=233), missing medication adherence (n=4,986), missing population density due to missing population counts in some zip codes (n=231), if they were missing data on or did not have at least one of the conditions of interest (diabetes, hypertension, dyslipidemia and/or prevalent CHD) (n=1,812) and did not use medications for these conditions (n = 638) (Figure 1). The final sample size after exclusions was 8,250 participants.

Socio-demographic factors, geocoded residential data, cardiovascular disease risk factors, physical activity, depressive symptoms, and stress were obtained via computer assisted telephone interview.[16] Systolic and diastolic blood pressure, weight and height measurements and blood and spot urine samples were obtained by trained health professionals during the second in-home visit.[17] Participants were asked to fast for 10-12 hours before the in-home visit.[15] Samples of blood and urine were sent to a central laboratory at the University of Vermont via overnight shipping; laboratory assays were performed on blood samples to obtain lipid profiles and glucose.[15,17] Medication use during the two weeks before the second in-home visit was recorded based on pill bottle review.[15] Data on perceived neighborhood characteristics (social cohesion, safety from crime, neighborhood problems), perceived social support and life-space,[18] a validated measure of mobility in the environment, were obtained from a self-administered questionnaire during the second examination.

Pharmacy location data was obtained from the National Council for Prescription Drug Programs (NCPDP) on US community pharmacies for the year, 2015.[19] Each licensed pharmacy has an NCPDP number for claims processing. The data provide information about active US community pharmacies including mailing addresses, which were validated by the NCPDP.[19] Pharmacy addresses were geocoded using ArcGIS Business Analyst Desktop version 10.5.1 with ESRI 2016 Business Analyst Data. We used a minimum match score of 90; 95% (n=75,191) of the addresses matched, 1% (n=823) tied and 3% (n=3,303) were unmatched. We also lowered the minimum match score to 80; 96%; (n=75,943) matched, 1% (n=885) tied and 3% (n=2,489) were unmatched. Since the percentages of matched, tied and unmatched addresses did not change after lowering the minimum match score, we kept the data from the minimum match score of 90 and included the matched and tied addresses (n = 76,014). After excluding pharmacies outside of the 48 contiguous US states and the District of Columbia (n=160), the final pharmacy count was 75,854. We calculated population density as a measure of rural/urban residence,[20] by dividing the population in each zip code by the corresponding land area using the 2010 Zip Code Tabulated Area (ZCTA)[21] and population data for 2010 from the US Census Bureau.[22] Since a measure of rural/urban residence was considered a priori to be a potential effect modifier of the association between pharmacy access measures and medication adherence, rurality based on Rural Urban Commuting Area [RUCA] Codes[23] was not used because of uneven frequency distributions.

We used ArcGIS version 10.2.0 to obtain the exposure, pharmacy access measures. These were defined as quartiles of straight-line distances from participants'

residences to the nearest pharmacy and number of pharmacies in 1.61 km (1 mile), 8.05 km (5 mile), 16.1 km (10 mile) and 24.1 km (15 mile) buffers (Figure 2). We used straight-line distances in lieu of travel distance or travel time because of the high correlation ($r^2 > 0.9$) found between the two measures from a study within the US.[24] Further, the use of street networks needed for the calculation of travel distance for the continental US require computer intensive resources which are not available to the authors. Additionally, the cost of purchasing the street networks is exorbitant.

The outcome, medication adherence was assessed at the second REGARDS examination using a 4-item validated scale[25] and based on the questions: 1) Do you ever forget to take your medicines? 2) Are you careless at times about taking your medicine? 3) When you feel better, do you sometimes stop taking your medicine? 4) Sometimes if you feel worse when you start taking the medicine, do you stop taking it? The response choices were "yes" or "no." This variable was categorized as low adherence (1-4 "yes" responses) and high adherence (0 "yes" responses).[26]

Because accessing pharmacies and medications involves the interaction of people with the health system, we used the Andersen and Aday conceptual model, which describes how predisposing, enabling, and need characteristics of individuals and their environments influence use of health services, as a guide for the selection of covariates for adjustment.[27] Pre-disposing characteristics included age (continuous), race (black vs. white), sex (male vs. female), region of residence (Stroke Buckle vs. Stroke Belt vs. Non-Belt), annual household income (<$20,000 vs. ≥$20,000) and education (high school graduate or less vs. some college or college graduate)]. Enabling factors included insurance status (yes vs. no), rural/urban residence based on quartiles of population

density, composite life-space score (continuous),[18] social cohesion score (continuous; lower values indicate greater social cohesion), safety from crime score (continuous; lower values indicate greater safety from crime), neighborhood problems score (continuous; lower values indicate fewer neighborhood problems),[28] emotional/informational support (continuous), tangible support (continuous) and affectionate support (continuous).[29] Need factors included depressive symptoms based on the Center for Epidemiologic Studies Depression Scale (CES-D score <10 vs. ≥10), physical functioning based on the Short Form 12 Physical Component Summary (PCS) score[30] (continuous), mental health based on the Short Form 12 Mental Health Component Summary (MCS) score[30] (continuous), Cohen's perceived stress scale[31] score (continuous), self-reported general health (excellent/very good vs good vs fair/poor), obesity status based on BMI (kg/m^2) estimated from measured height and weight during the second in-home visit (obese vs not obese), physical activity (none vs. 1-3 times per week vs. ≥4 times per week) and Framingham CHD risk score [risk of coronary death or MI over 10 years among those free of CHD at the second examination[32,33] (<10%, 10-20%, >20%, vs prevalent CHD].

Participant characteristics were compared by medication adherence status (low versus high adherence) using descriptive statistics. Multivariable adjusted Poisson regression models with robust variance estimation were used to calculate prevalence ratios (PRs) for high medication adherence separately for each pharmacy access measure: quartiles of straight-line distances from participants' residences to the pharmacies and quartiles of number of pharmacies in the 1.61, 8.05, 16.1 and 24.1 km buffers. We first constructed a crude model for each exposure variable. Sequential adjustments were then made using three models for each exposure variable based on the Andersen and Aday

conceptual model,[27] adjusting for pre-disposing factors (age, race, sex, region of residence, annual household income and education) in model 1, further adjusting for enabling factors (insurance status, population density, composite life-space score, social cohesion, safety from crime, neighborhood problems, emotional/informational support, tangible support and affectionate support) in model 2, and finally adding need factors (depressive symptoms, PCS score, MCS score, perceived stress scale score, self-reported general health, obesity status, physical activity, and CHD risk category) to obtain model 3.

We examined whether the associations varied by race and, separately, population density by including a cross-product (interaction) term with each of the four pharmacy access measures in fully adjusted Poisson regression models. Multivariable-adjusted Poisson regression models with robust variance estimation were used to estimate PRs for high medication adherence separately for each race. We also conducted a sensitivity analysis among participants who had diabetes, hypertension, dyslipidemia and/or prevalent CHD irrespective of medication use, using multivariable-adjusted Poisson regression models with robust variance estimation. Multiple imputation by chained equations with ten datasets was used to account for missing covariate data.[34] The data was analyzed using SAS, version 9.4, SAS Institute, Cary, NC.

RESULTS

The prevalence of high medication adherence was 70.4%. Participants with high medication adherence were more likely to live in neighborhoods with higher social cohesion (35.4% vs 29.4%), more safety from crime (61.2% vs 55.1%) and fewer

problems (36.3% vs 29.5%) and have excellent/very good self-reported health (46.1% vs 36.4%) compared to participants with low medication adherence (Table 1). Distance from participants' residences to nearest pharmacy and number of pharmacies in 1.61, 8.05, 16.1 and 24.1 km buffers were not associated with medication adherence (Table 2). Results of the sensitivity analysis which included all participants with conditions of interest irrespective of medication use were similar (Supplemental Table 1).

Black participants were more likely to live closer to the nearest pharmacy (1.81 km vs 3.02 km) and have higher mean number of pharmacies in the 1.61 (3.32 vs 2.17), 8.05 (65.8 vs 30.7), 16.1 (202.9 vs 85.0) and 24.1 (349.6 vs 146.2) km buffers compared to whites (Supplemental Table 2). Participants in the highest quartile of population density were more likely to have shorter distances to nearest pharmacy (0.87 km vs 5.29 km) and higher mean number of pharmacies in the 1.61, 8.05, 16.1 and 24.1 km buffers [(6.01 vs 0.95), (119.2 vs 5.09), (368.7 vs 11.2) and (638.6 vs 22.1)] respectively, compared to those in the lowest quartile (Supplemental Table 3). There was no evidence for interaction of race (Supplemental Table 4) or population density (not shown) with pharmacy access (P-values for interaction for all exposure-effect modifier combinations > 0.10).

DISCUSSION

In the current study of black and white US adults from across the 48 contiguous US states, pharmacy access measures (distance and density) were not associated with self-reported medication adherence. This finding is consistent with prior regional studies. In a study using claims data from the Illinois Department of Healthcare and Family, no significant association between medication adherence and straight-line distance to

pharmacies was observed among non-elderly adults with diabetes using angiotensin converting enzyme inhibitors or angiotensin II receptor blockers.[4] Similarly, Schectman and colleagues found no association between travel distance to pharmacy and medication adherence in an indigent rural population who obtained anti-hypertension, lipid-lowering or oral anti-diabetes medication from an internal medicine practice.[35]

While prior results and those of the current study suggest that pharmacy access based on geography does not influence medication adherence among people who take medications for CHD risk factors or prevalent CHD, it is possible that distance to pharmacies[14] and number of pharmacies within the different buffers may not be adequate measures of access to medications. It may be that pharmacy access along with other barriers such as, type of health insurance and not having a usual source of care may together influence medication adherence. In contrast, one study found that distance did act as a barrier to care among adults aged 65 and over who received clinical preventive services such as mammography and cervical cancer screening for women, prostate-specific antigen test and digital rectal examination for men, fecal occult blood testing, sigmoidoscopy, influenza vaccination and pneumococcal vaccination within specific time periods;[36] this may be due to the older age of the population and the focus on healthcare access to specific preventive services rather than medication adherence.

We did not find any differences in the association between pharmacy access and medication adherence by race or population density, a continuous measure related to the previously studied dichotomy of rural/urban residence. Two prior studies found that there were no significant differences in distance to pharmacies and other medical institutions between blacks and whites.[4,37] However, in two other studies, blacks had greater

transportation barriers in accessing health care compared to whites.[10,11] In a study by Qato and colleagues, conducted between 2000 and 2012, segregated minority communities had fewer pharmacies compared to segregated white and integrated communities in Chicago.[38] Further, there was a disproportionately larger number of pharmacy deserts in segregated black communities compared to segregated white communities in 2012.[38] Some prior studies have also found that distance acts as a greater barrier to health care access in rural areas compared to urban.[12-14,37] However, health services utilization, transportation barriers and having delayed care did not differ between urban and rural residents.[39,40] Nevertheless, medication adherence was not considered in any of the studies assessing both race and racial/urban differences.

The REGARDS study has extensive data on cardiovascular disease (CVD) as well as a validated self-reported measure of medication adherence[5] and geographic data that were linked to Geographic Information System (GIS) sources to assess pharmacy access among a large, racially and geographically diverse population with data based on continuous follow-up. However, the results of the current study should also be considered in light of its limitations. Approximately 25% of the REGARDS participants were lost to follow-up at the time of the second home visit; however the annual retention rate was 97% which is comparable to other cohort studies.[16] Further, a previous study conducted by Mondesir and colleagues using REGARDS data from the first home visit showed that the prevalence of high medication adherence was approximately 68.9%;[41] this is similar to that of the current study. In addition, medication adherence was a global measure and based on self-report; it may have been affected by social desirability bias and may have resulted in misclassification. The geo-spatial analysis was based only on the physical

location of pharmacies relative to participants' homes; therefore, we may have underestimated access among participants using mail order pharmacies or accessing pharmacies near a place of employment or other frequently visited location. Further there was no information available on filling prescriptions and failure to fill prescriptions (primary non-adherence) which may more sensitive to pharmacy access and warrants further study. In addition, we only used pharmacy data from 2015; changes in pharmacy availability such as closures and openings during the period of the REGARDS second home exam (2013-2016) may have introduced misclassification bias. While straight-line distance is highly correlated with travel distance and travel time, there are exceptions in areas with lakes, rivers and mountains where the physical features cannot be crossed. This may have resulted in misclassification. However, for nonemergency medical care such as with the pharmacy, differences in travel time less than 30 minutes do not influence physical access, according to a study by Lee and colleagues.[42] Some covariates were self-reported which may have increased misclassification. In conclusion, in this population with prevalent CHD and/or CHD risk factors, lack of access to pharmacies based on geography was not detected a barrier to medication adherence.

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Conflicts of Interest

F.L.M has no relationships to disclose. T.N.C. has no relationships to disclose. A.P.B. is supported by K01HL133468 and R01HL139837 from the NHLBI and receives funding from Novartis and Amarin Pharmaceuticals for unrelated work. D.M.Q. receives funding from the Robert Wood Johnson Foundation and Blue Cross Blue Shield Association and serves as a consultant for Public Citizen's Health Research Group. G.S.L. is supported by AG049970-01A1 from the NIA. A.P.C. receives funding from Amgen for unrelated

work, M.M.S receives funding from Amgen for unrelated work, E.B.L receives funding from Amgen for unrelated work and has served on Amgen advisory boards and as a consultant for a Novartis-sponsored research project.

Author Contributions

F.L.M. conceived and designed the study, analyzed and interpreted the data, had full access to the data and takes responsibility for the integrity of the data and the accuracy of the data analysis and wrote the manuscript. T.N.C. contributed to the design of the study, provided expertise on geo-spatial analysis and revised the manuscript for intellectually important content. A.P.B. provided expertise on pharmacy access, medication use and revised the manuscript for intellectually important content. D.M.Q. provided expertise on pharmacy access and revised the manuscript for intellectually important content. G.S.L. provided expertise on pharmacy access and revised the manuscript for intellectually important content. A.P.C. provided expertise on CHD and CHD risk factors and revised the manuscript for intellectually important content. M.M.S. provided expertise on CHD and CHD risk factors and revised the manuscript for intellectually important content. E.B.L. contributed to the conception and design of the study, provided statistical expertise and revised the manuscript for intellectually important content.

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Table 1. Characteristics of REGARDS[a] participants by medication adherence status

	Medication Adherence		
	Low adherence	**High adherence**	**p**
	n = 2,443	n = 5,807	
Predisposing factors			
Age, years, mean ± SD	71.7 ± 8.4	73.0 ± 8.5	<0.0001
Black, n (%)	1,014 (41.5)	2,396 (41.3)	0.84
Women, n (%)	1,516 (62.1)	3,497 (60.2)	0.12
Region, n (%)			0.01
Stroke belt[b]	917 (37.5)	2,009 (34.6)	
Stroke buckle[c]	552 (22.6)	1,452 (25.0)	
Non-stroke belt or buckle	974 (39.9)	2,346 (40.4)	
Annual household income <$20,000[f], n (%)	366 (17.7)	799 (16.3)	0.14
Education ≤ High school[f], n (%)	851 (34.9)	1,998 (34.4)	0.69
Enabling factors			
No health insurance[f], n (%)	37 (1.5)	47 (0.8)	0.004
Population density quartiles			0.43
Quartile 1	628 (25.7)	1,517 (26.1)	
Quartile 2	626 (25.6)	1,462 (25.2)	
Quartile 3	616 (25.2)	1,388 (23.9)	
Quartile 4	573 (23.5)	1,440 (24.8)	
Lifespace score, median (IQR)	81 (59-100)	82 (60-100)	0.28
Social cohesion score[f]			<0.0001
Tertile 1 (1-10)	515 (29.4)	1,504 (35.4)	
Tertile 2 (11-13)	659 (37.6)	1,557 (36.7)	
Tertile 3 (14-25)	579 (33.0)	1,185 (27.9)	
Safety from crime score[f]			<0.0001
Tertile 1 (1-3)	965 (55.1)	2,600 (61.2)	
Tertile 2 (4)	385 (22.0)	844 (19.9)	
Tertile 3 (5-9)	401 (22.9)	808 (19.0)	
Neighborhood problems score[f]			<0.0001
Tertile 1 (1-7)	516 (29.5)	1,545 (36.3)	
Tertile 2 (8-10)	637 (36.4)	1,450 (34.1)	
Tertile 3 (11-24)	598 (34.2)	1,256 (29.6)	
Emotional/informational support, mean ± SD	16.5 ± 3.6	17.1 ± 3.4	<0.0001
Tangible support, mean ± SD	3.50 ± 1.38	3.62 ± 1.39	0.004
Affectionate support, mean ± SD	4.38 ± 0.95	4.48 ± 0.91	0.0002
Need factors			
CHD[a] risk categories[d], n (%)			0.15

< 10%	1,134 (46.4)	2,803 (48.3)	
10-20%	379 (15.5)	943 (16.2)	
>20%	196 (8.0)	415 (7.2)	
Prevalent CHD[ae]	734 (30.1)	1,646 (28.4)	
Physical activity[f], n (%)			<0.0001
None	1,141 (47.4)	2,406 (42.1)	
1-3 times per week	812 (33.7)	1,991 (34.9)	
4+ times per week	455 (18.9)	1,315 (23.0)	
General Health[f], n (%)			<0.0001
Excellent/Very Good	884 (36.4)	2,658 (46.1)	
Good	1,001 (41.3)	2,213 (38.4)	
Fair/Poor	541 (22.3)	899 (15.6)	
Obesity prevalence[f], n (%)	1,098 (45.2)	2,361 (40.9)	0.0003
Depressive symptoms, CES-D score ≥ 10[f], n (%)	427 (17.7)	588 (10.2)	<0.0001
Physical Component Summary Score, mean ± SD	42.0 ± 11.5	44.5 ± 10.8	<0.0001
Mental Component Summary Score, mean ± SD	54.0 ± 8.9	55.8 ± 7.5	<0.0001
Perceived Stress Scale Score, mean ± SD	3.7 ± 3.0	3.0 ± 2.8	<0.0001

[a]Abbreviations: REGARDS, Reasons for Geographic and Racial Differences in Stroke; CHD, coronary heart disease

[b]Defined as the states of Alabama, Arkansas, Louisiana, Mississippi, Tennessee and the noncoastal regions of North Carolina, South Carolina and Georgia.

[c]Defined as the coastal regions of North Carolina, South Carolina and Georgia

[d]Framingham CHD hard event risk score: risk of coronary death or MI over 10 years (among those free of CHD at baseline)

[e]Self-reported history or electrocardiogram evidence of a prior myocardial infarction MI or self-reported coronary artery bypass graft, coronary angioplasty, or coronary stenting

[f]The frequencies and percentages may not add up to the total sample size due to missing data.

Table 2. Prevalence ratios and 95% confidence intervals for the association of pharmacy access with high medication adherence among REGARDS participants receiving pharmacologic therapy for CHD or CHD risk factors

	Crude Model	**Model 1[a]**	**Model 2[b]**	**Model 3[c]**
	PR 95% CI	**PR 95% CI**	**PR 95% CI**	**PR 95% CI**
Distance to nearest pharmacy (Quartiles)				
< 0.73 km	Ref	Ref	Ref	Ref
0.73-1.28 km	1.03 (0.96, 1.10)	1.03 (0.96, 1.11)	1.03 (0.96, 1.11)	1.04 (0.96, 1.12)
1.29- 2.52 km	1.01 (0.94, 1.09)	1.01 (0.94, 1.09)	1.01 (0.93, 1.09)	1.01 (0.94, 1.09)
>2.52 km	0.99 (0.92, 1.07)	1.00 (0.93, 1.08)	0.99 (0.91, 1.07)	0.99 (0.91, 1.08)
Pharmacies in 1.61 km buffer (Quartiles)				
0 pharmacies	Ref	Ref	Ref	Ref
1-2 pharmacies	1.00 (1.07, 1.06)	0.99 (0.93, 1.06)	1.00 (0.94, 1.07)	1.00 (0.94, 1.07)
3 pharmacies	1.02 (0.93, 1.12)	1.02 (0.93, 1.12)	1.02 (0.93, 1.13)	1.02 (0.93, 1.12)
>3 pharmacies	1.01 (0.95, 1.08)	1.01 (0.94, 1.08)	1.02 (0.94, 1.09)	1.01 (0.94, 1.09)
Pharmacies in 8.05 km buffer (Quartiles)				
0-7 pharmacies	Ref	Ref	Ref	Ref
8-26 pharmacies	0.98 (0.92, 1.06)	0.98 (0.91, 1.06)	0.99 (0.91, 1.08)	0.98 (0.90, 1.07)
27-53 pharmacies	0.98 (0.91, 1.06)	0.98 (0.91, 1.06)	1.00 (0.90, 1.11)	0.99 (0.89, 1.10)
>54 pharmacies	1.02 (0.95, 1.09)	1.01 (0.93, 1.10)	1.02 (0.90, 1.16)	1.01 (0.89, 1.15)
Pharmacies in 16.1 km buffer (Quartiles)				

0-17 pharmacies	Ref	Ref	Ref	Ref
18-70 pharmacies	0.99 (0.92, 1.07)	0.99 (0.92, 1.07)	1.00 (0.91, 1.11)	0.99 (0.90, 1.10)
71-151 pharmacies	0.98 (0.91, 1.06)	0.98 (0.91, 1.06)	1.01 (0.90, 1.14)	1.00 (0.89, 1.13)
>151 pharmacies	1.03 (0.95, 1.10)	1.03 (0.95, 1.13)	1.06 (0.92, 1.22)	1.05 (0.91, 1.21)
Pharmacies in 24.1 km buffer (Quartiles)				
0-30 pharmacies	Ref	Ref	Ref	Ref
31-103 pharmacies	0.98 (0.91, 1.05)	0.99 (0.92, 1.07)	1.00 (0.92, 1.10)	0.99 (0.91, 1.09)
104-252 pharmacies	1.02 (0.91, 1.05)	0.99 (0.92, 1.06)	1.00 (0.90, 1.12)	1.00 (0.90, 1.11)
>252 pharmacies	1.02 (0.95, 1.10)	1.03 (0.94, 1.12)	1.04 (0.92, 1.19)	1.04 (0.91, 1.19)

[a]Model 1(Pre-disposing factors): age (continuous), race (categorical), gender (categorical), region of residence (categorical), annual household income (categorical) and education (categorical).

[b]Model 2 (Enabling factors): model 1 covariates, insurance status (categorical), population density (categorical), lifespace score (continuous), emotional/informational support (continuous), tangible support (continuous), affectionate support (continuous).

[c]Model 3 (Need factors): model 2 covariates, depressive symptoms, (CES-D) score (categorical), physical component summary score (continuous), mental component summary score (continuous), perceived stress scale score (continuous), general health (categorical), obesity status (categorical), physical activity (categorical), coronary heart disease risk category (categorical)

Supplemental Table 1. Prevalence ratios and 95% confidence intervals for the association of pharmacy access with high medication adherence among REGARDS participants with CHD or CHD risk factors

	Crude Model	Model 1[a]	Model 2[b]	Model 3[c]
	PR 95% CI	**PR 95% CI**	**PR 95% CI**	**PR 95% CI**
Distance to nearest pharmacy (Quartiles)				
< 0.73 km	Ref	Ref	Ref	Ref
0.73-1.28 km	1.02 (0.95, 1.09)	1.02 (0.95, 1.10)	1.02 (0.95, 1.11)	1.02 (0.96, 1.10)
1.29- 2.53 km	1.01 (0.94, 1.08)	1.01 (0.94, 1.08)	1.01 (0.94, 1.08)	1.01 (0.94, 1.09)
>2.53 km	0.99 (0.93, 1.07)	1.00 (0.93, 1.07)	0.98 (0.91, 1.07)	0.99 (0.91, 1.07)
Pharmacies in 1.61 km buffer (Quartiles)				
0 pharmacies	Ref	Ref	Ref	Ref
1-2 pharmacies	0.99 (0.93, 1.06)	0.99 (0.93, 1.06)	1.00 (0.94, 1.07)	1.00 (0.94, 1.07)
3 pharmacies	1.01 (0.92, 1.10)	1.01 (0.93, 1.11)	1.02 (0.93, 1.12)	1.02 (0.93, 1.12)
>3 pharmacies	1.01 (0.95, 1.08)	1.01 (0.95, 1.08)	1.02 (0.95, 1.09)	1.01 (0.94, 1.09)
Pharmacies in 8.05 km buffer (Quartiles)				
0-7 pharmacies	Ref	Ref	Ref	Ref
8-26 pharmacies	0.99 (0.92, 1.06)	0.99 (0.92, 1.06)	1.00 (0.92, 1.08)	0.99 (0.91, 1.07)
27-53 pharmacies	0.99 (0.92, 1.06)	0.99 (0.92, 1.06)	1.00 (0.90, 1.11)	0.99 (0.90, 1.10)
>54 pharmacies	1.01 (0.95, 1.09)	1.01 (0.94, 1.10)	1.03 (0.92, 1.16)	1.02 (0.91, 1.15)
Pharmacies in 16.1 km buffer (Quartiles)				
0-17 pharmacies	Ref	Ref	Ref	Ref
18-70 pharmacies	1.00 (0.93, 1.07)	0.99 (0.93, 1.07)	1.00 (0.91, 1.10)	1.00 (0.91, 1.09)

71-150 pharmacies	0.99 (0.92, 1.06)	0.99 (0.92, 1.07)	1.03 (0.91, 1.15)	1.02 (0.91, 1.14)
>150 pharmacies	1.03 (0.96, 1.10)	1.04 (0.96, 1.13)	1.08 (0.95, 1.24)	1.07 (0.94, 1.23)
Pharmacies in 24.1 km buffer (Quartiles)				
0-30 pharmacies	Ref	Ref	Ref	Ref
31-102 pharmacies	1.00 (0.93, 1.07)	0.99 (0.93, 1.06)	1.00 (0.92, 1.09)	0.99 (0.91, 1.08)
103-251 pharmacies	0.98 (0.92, 1.05)	0.99 (0.92, 1.06)	1.00 (0.91, 1.11)	1.00 (0.90, 1.11)
>251 pharmacies	1.02 (0.95, 1.09)	1.03 (0.95, 1.12)	1.06 (0.93, 1.20)	1.05 (0.93, 1.19)

[a]Model 1(Pre-disposing factors): age (continuous), race (categorical), gender (categorical), region of residence (categorical), annual household income (categorical) and education (categorical).

[b]Model 2 (Enabling factors): model 1 covariates, insurance status (categorical), population density (categorical), lifespace score (continuous), emotional/informational support (continuous), tangible support (continuous), affectionate support (continuous).

[c]Model 3 (Need factors): model 2 covariates, depressive symptoms, (CES-D) score (categorical), physical component summary score (continuous), mental component summary score (continuous), perceived stress scale score (continuous), general health (categorical), obesity status (categorical), physical activity (categorical), coronary heart disease risk category (categorical)

Supplemental Table 2. Pharmacy access measures by race

	Race		
	Blacks n = 3,410	**Whites n = 4,840**	**p**
Distance to nearest pharmacy, km mean ± SD	1.81 ± 2.52	3.02 ± 3.83	<0.0001
Number of pharmacies within buffers			
1.61 km buffer, mean ± SD	3.32 ± 7.34	2.17 ± 4.41	<0.0001
8.05 km buffer, mean ± SD	65.8 ± 108.0	30.7 ± 56.6	<0.0001
16.1 km buffer, mean ± SD	202.9 ± 296.8	85.0 ± 156.0	<0.0001
24.1 km buffer, mean ± SD	349.6 ± 500.7	146.2 ± 257.3	<0.0001

Supplemental Table 3. Pharmacy access measures by population density

	Population density				
	Quartile 1 n = 2,145	**Quartile 2 n = 2,088**	**Quartile 3 n = 2,004**	**Quartile 4 n = 2,013**	**p**
Distance to nearest pharmacy, km mean ± SD	5.29 ± 5.27	2.33 ± 2.12	1.40 ± 0.89	0.87 ± 0.56	<0.0001
Number of pharmacies within buffers					
1.61 km buffer, mean ± SD	0.95 ± 1.70	1.56 ± 2.36	2.21 ± 2.67	6.01 ± 10.4	<0.0001
8.05 km buffer, mean ± SD	5.09 ± 6.43	20.0 ± 14.5	40.2 ± 19.5	119.2 ± 142.0	<0.0001
16.1 km buffer, mean ± SD	11.2 ± 13.4	50.9 ± 36.6	115.1 ± 63.4	368.7 ± 370.5	<0.0001
24.1 km buffer, mean ± SD	22.1 ± 25.7	82.8 ± 63.6	196.5 ± 132.3	638.6 ± 605.0	<0.0001

Supplemental Table 4. Adjusted Models with prevalence ratios and 95% confidence intervals of high medication adherence by quartiles of pharmacy access measures among blacks and whites

	Blacks				**Whites**				
	Crude Model	**Model 1[a]**	**Model 2[b]**	**Model 3[c]**	**Crude Model**	**Model 1[a]**	**Model 2[b]**	**Model 3[c]**	
	PR 95% CI	**PR 95% CI**	**PR 95% CI**	**PR 95% CI**	**PR 95% CI**	**PR 95% CI**	**PR 95% CI**	**PR 95% CI**	**p[d]**
Distance to nearest pharmacy (Quartiles)									0.80
< 0.73 km	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	
0.73-1.28 km	1.01 (0.91, 1.12)	1.02 (0.91, 1.13)	1.02 (0.91, 1.13)	1.02 (0.91, 1.13)	1.04 (0.94, 1.15)	1.05 (0.95, 1.16)	1.05 (0.95, 1.16)	1.06 (0.95, 1.17)	
1.29- 2.52 km	1.01 (0.91, 1.12)	1.02 (0.91, 1.14)	1.02 (0.91, 1.14)	1.02 (0.91, 1.14)	1.01 (0.91, 1.12)	1.01 (0.92, 1.12)	1.01 (0.91, 1.12)	1.01 (0.92, 1.12)	
>2.52 km	1.02 (0.99, 1.15)	1.03 (0.90, 1.18)	1.01 (0.88, 1.17)	1.00 (0.87, 1.16)	0.99 (0.90, 1.08)	0.99 (0.90, 1.09)	0.98 (0.88, 1.09)	0.99 (0.89, 1.10)	
Pharmacies in 1.61 km buffer (Quartiles)									0.43
0 pharmacies	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	
1-2 pharmacies	1.00 (0.90, 1.10)	0.99 (0.90, 1.10)	1.00 (0.90, 1.11)	1.01 (0.90, 1.12)	1.00 (0.91, 1.08)	0.99 (0.91, 1.08)	1.00 (0.91, 1.09)	1.00 (0.92, 1.10)	
3 pharmacies	1.03 (0.90, 1.18)	1.03 (0.89, 1.18)	1.03 (0.89, 1.19)	1.04 (0.90, 1.20)	1.00 (0.88, 1.14)	1.00 (0.88, 1.14)	1.01 (0.89, 1.15)	1.00 (0.88, 1.14)	
>3 pharmacies	0.98 (0.89, 1.09)	0.97 (0.86, 1.08)	0.98 (0.87, 1.10)	0.98 (0.87, 1.11)	1.04 (0.95, 1.13)	1.04 (0.95, 1.13)	1.04 (0.95, 1.15)	1.04 (0.94, 1.14)	
Pharmacies in 8.05 km buffer (Quartiles)									0.80
0-7 pharmacies	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	
8-26	0.94	0.94	0.95	0.95	1.01	1.00	1.01	0.99	

pharmacies	(0.81, 1.08)	(0.81, 1.08)	(0.80, 1.13)	(0.80, 1.13)	(0.92, 1.10)	(0.92, 1.09)	(0.91, 1.12)	(0.90, 1.10)	
27-53 pharmacies	0.96 (0.84, 1.09)	0.96 (0.83, 1.09)	0.98 (0.80, 1.19)	0.98 (0.80, 1.19)	0.99 (0.90, 1.09)	0.99 (0.90, 1.09)	1.00 (0.88, 1.14)	0.99 (0.87, 1.13)	
>54 pharmacies	1.00 (0.88, 1.14)	0.98 (0.84, 1.13)	1.01 (0.81, 1.26)	1.01 (0.81, 1.26)	1.02 (0.92, 1.12)	1.02 (0.92, 1.13)	1.02 (0.87, 1.21)	1.01 (0.86, 1.19)	
Pharmacies in 16.1 km buffer (Quartiles)									0.67
0-17 pharmacies	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	
18-70 pharmacies	0.96 (0.83, 1.10)	0.94 (0.82, 1.09)	0.93 (0.76, 1.15)	0.94 (0.76, 1.15)	1.01 (0.93, 1.10)	1.01 (0.93, 1.10)	1.03 (0.92, 1.15)	1.01 (0.91, 1.13)	
71-151 pharmacies	0.96 (0.85, 1.08)	0.95 (0.84, 1.08)	0.94 (0.76, 1.18)	0.94 (0.75, 1.18)	1.00 (0.91, 1.10)	1.00 (0.91, 1.10)	1.04 (0.90, 1.21)	1.03 (0.89, 1.20)	
>151 pharmacies	1.00 (0.89, 1.13)	0.99 (0.85, 1.14)	0.99 (0.77, 1.26)	0.99 (0.77, 1.26)	1.04 (0.94, 1.15)	1.05 (0.94, 1.18)	1.09 (0.91, 1.31)	1.08 (0.90, 1.30)	
Pharmacies in 24.1 km buffer (Quartiles)									
0-30 pharmacies	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	0.93
31-103 pharmacies	0.99 (0.87, 1.14)	1.00 (0.85, 1.12)	0.99 (0.83, 1.19)	0.99 (0.83, 1.19)	0.99 (0.91, 1.08)	0.99 (0.91, 1.08)	1.00 (0.90, 1.12)	0.99 (0.89, 1.10)	
104-252 pharmacies	0.96 (0.84, 1.08)	0.96 (0.84, 1.09)	0.98 (0.80, 1.19)	0.97 (0.80, 1.18)	1.00 (0.91, 1.10)	1.01 (0.92, 1.11)	1.02 (0.90, 1.17)	1.02 (0.90, 1.17)	
>252 pharmacies	1.03 (0.92, 1.16)	1.02 (0.88, 1.19)	1.05 (0.83, 1.31)	1.04 (0.83, 1.31)	1.01 (0.91, 1.12)	1.02 (0.92, 1.14)	1.03 (0.87, 1.22)	1.03 (0.87, 1.22)	

[a]Model 1(Pre-disposing factors): age (continuous), gender (categorical), region of residence (categorical), annual household income (categorical) and education (categorical).

[b]Model 2 (Enabling factors): model 1 covariates, insurance status (categorical), population density (categorical), lifespace score (continuous), emotional/informational support (continuous), tangible support (continuous), affectionate support (continuous).

[c]Model 3 (Need factors): model 2 covariates, depressive symptoms, (CES-D) score (categorical), physical component summary score (continuous), mental component summary score (continuous), perceived stress scale score (continuous), general health (categorical), obesity status (categorical), physical activity (categorical), coronary heart disease risk category (categorical)

[d]P-value for interaction (Model 3)

Figure 1. Flow Chart with Exclusion Criteria

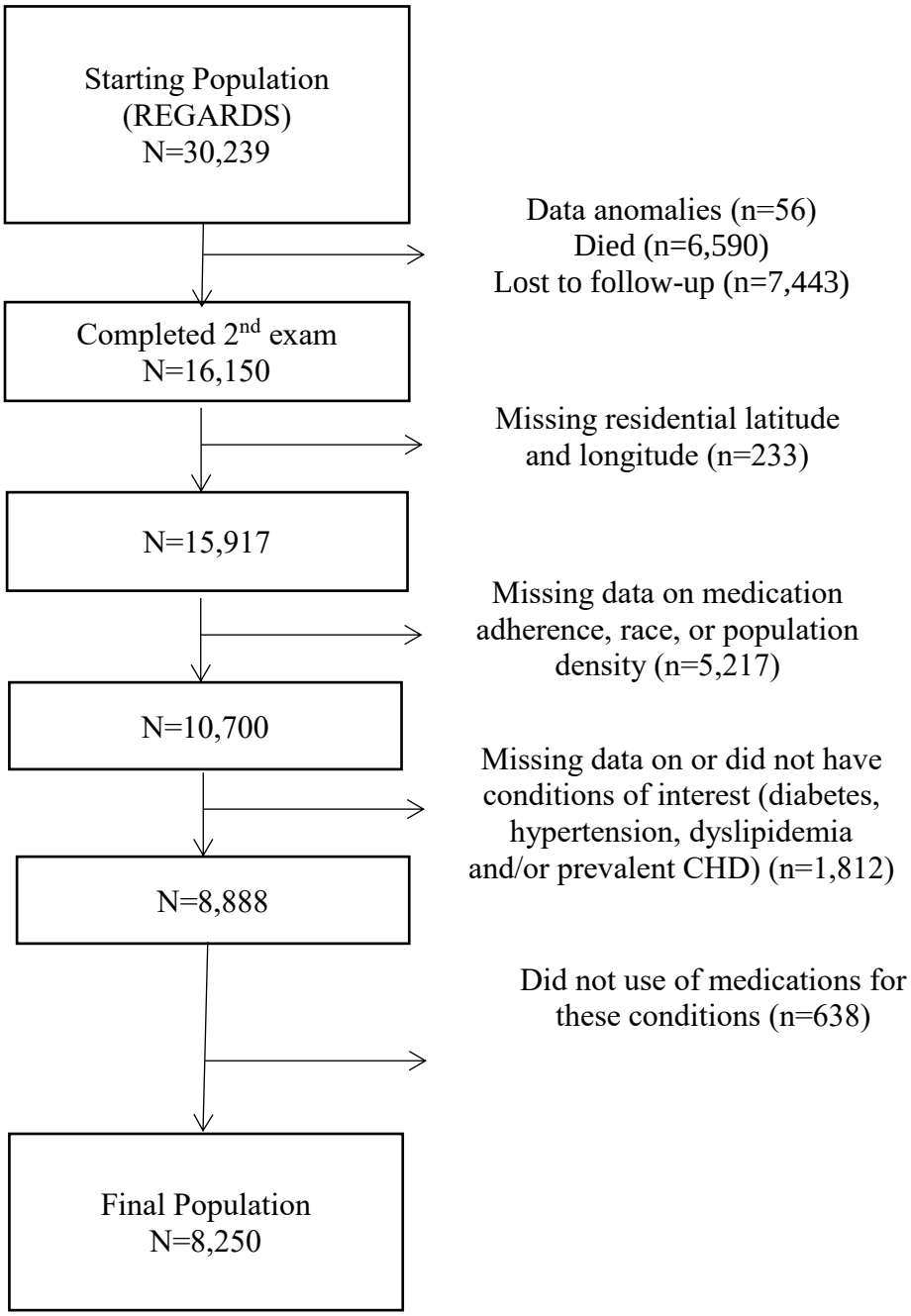

Figure 1. Exclusion criteria applied to obtain final analytical sample

Figure 2. Measuring pharmacy access

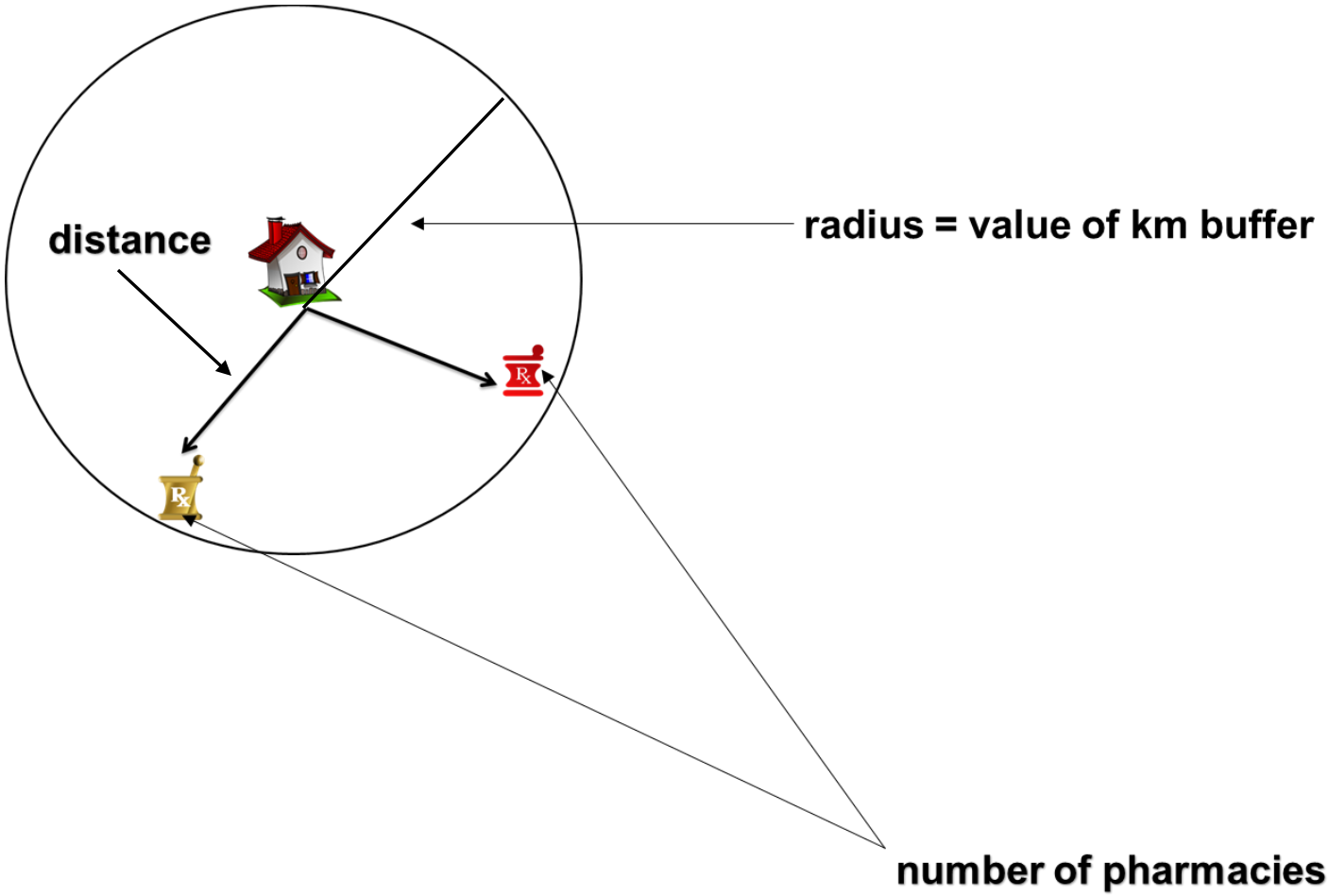

Figure 2. Measuring pharmacy access as straight-line distances between participants' residences and pharmacies and counting number of pharmacies within different km buffers where the radius of the circle represents the value of the mile buffer (e.g. 1.61 km)

PATIENT PERSPECTIVES ON FACTORS INFLUENCING MEDICATION ADHERENCE AMONG PEOPLE WITH CORONARY HEART DISEASE (CHD) AND CHD RISK FACTORS

by

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ABSTRACT

Few qualitative studies have explored factors influencing medication adherence among people with coronary heart disease (CHD) or CHD risk factors. We explored how patient (e.g. self-efficacy), social/economic (e.g. social support and cost of medications), therapy (e.g. side effects), condition (e.g. comorbidities), and healthcare system/healthcare team (e.g. support from healthcare providers and pharmacy access) related factors influence medication adherence, within the context of the World Health Organization Multidimensional Adherence Model. We conducted 18 in-depth qualitative interviews from April to July 2018 with ambulatory care patients (8 black males, 5 black females, 2 white males, and 3 white females) from the University of Alabama at Birmingham health system who were using medications for diabetes, hypertension, dyslipidemia and/or prevalent CHD. Interviews were audio-recorded and transcribed verbatim. We used thematic analysis to code the transcripts. Four main themes emerged from the data: perceived need for medication, beliefs about medications, influence of relationships with people and organizations on medication use, and influence of pharmacy access and utilization on medication adherence. These occurred within the contexts of the patient, social/economic, therapy, condition, and healthcare system/healthcare team. This underscores the need for multidimensional interventions aimed at improving medication adherence and overall health of patients with CHD and CHD risk factors.

INTRODUCTION

According to the American Heart Association Heart Disease and Stroke Statistics – 2017 update, heart disease which includes coronary heart disease (CHD) and hypertension is the leading cause of death in the US (Benjamin et al., 2017). It accounts for 1 in 7 deaths and estimated direct and indirect costs of $199.6 billion annually as of 2012 to 2013 (Benjamin et al., 2017). Medications which reduce the risk of CHD events and mortality are taken as prescribed by only 50-66% of patients with CHD and CHD risk factors (Naderi et al., 2012).

The World Health Organization Multidimensional Adherence Model (WHO-MAM) emphasizes 5 dimensions which interact to influence medication adherence: patient, social/economic, therapy, condition, and healthcare system/healthcare team related factors (Berben et al., 2012). Patient-related factors include self-efficacy, perceived health, beliefs about the efficacy of medications and knowledge of medications (Berben et al., 2012). Social/economic factors include social support and family functioning (Berben et al., 2012). Therapy related factors include side effects and dose complexity (Berben et al., 2012). Condition related factors include comorbidities (Berben et al., 2012). Healthcare system/healthcare team related factors include support from healthcare providers, negative interactions with providers and pharmacy access (Berben et al., 2012).

One systematic review of quantitative studies using the WHO-MAM found that patient-related barriers to anti-hypertensive medication use were studied more frequently than social/economic, therapy and condition related factors (AlGhurair et al., 2012).The findings from other prior quantitative studies indicated that factors within all dimensions of the WHO-MAM influenced medication adherence among people with cardiovascular disease (CVD), diabetes, heart failure and those who took antihyperlipidemic medications (Dunbar-Jacob et al., 2003; Gellad et al., 2011; Sung et al., 1998; J.-R. Wu et al., 2008a). Similarly, qualitative studies conducted separately among people with hypertension, heart failure and following percutaneous coronary intervention (PCI) also revealed the multidimensional nature of medication adherence (Johnson et al., 1999; Pettersen et al., 2018; J. R. Wu et al., 2008b).

However, few qualitative studies have focused on barriers to medication adherence in participants with CHD risk factors other than hypertension. There is a need for additional data on factors influencing medication adherence in people with not only hypertension but also, diabetes, dyslipidemia and prevalent CHD. Therefore, it is important to obtain patient perspectives on both barriers and facilitators of medication adherence among people with different CHD risk factors. This data may provide evidence for the development of interventions to improve medication adherence among people with CHD and CHD risk factors. Coupled with this is the need for further studies of social/economic, therapy and condition-related factors which influence medication adherence in this population. Therefore, we explored how patient, social/economic, therapy, condition, healthcare system/healthcare team related factors influence

medication use among people who use medications for diabetes, hypertension, dyslipidemia and prevalent CHD guided by the WHO-MAM conceptual model.

METHODS

Ethics Statement

The Institutional Review Board at the University of Alabama at Birmingham (UAB) approved the study protocol, and all participants provided written informed consent.

Sampling and Recruitment

Patients who used prescribed medications for diabetes, hypertension, dyslipidemia and/or prevalent CHD were recruited from the University of Alabama at Birmingham Health System between April and July 2018. We used purposive sampling (Mack et al., 2005; Tongco, 2007), while considering data saturation, to recruit equal numbers of men and women who self-identified as black or white and who were aged ≥ 45 years. Purposive sampling was employed to reflect the demographic distribution of the Reasons for Geographic and Racial Differences in Stroke (REGARDS) study, an on-going cohort study of black and white men and women, which has been used to quantitatively study barriers to medication adherence (Mondesir et al., 2018). The details of the REGARDS study methodology are described elsewhere (Howard et al., 2005).

One member of the study team (FLM) recruited participants and collected data. The electronic medical record for ambulatory care patients of two physicians at the Endocrinology and Cardiology clinics in the UAB Health System was initially screened

for potential participants. After identifying potential participants, they were further screened by phone and invited to participate if eligible. Twenty-two participants were recruited; however, one did not participate due to scheduling difficulties, one was unwilling to sign the consent form, and two could not be re-contacted to schedule the study visit. Participants were given a $20 Visa gift card incentive.

Data Collection

Study visits were scheduled to coincide with regular clinic visits. Participants completed a brief demographic questionnaire and participated in individual face to face in-depth interviews which lasted about 40 minutes on average. A semi-structured interview field guide with open-ended questions was used to assess how patient, social/economic, therapy, condition, and healthcare system/healthcare team related factors influence medication use. Interviews were audio-recorded and transcribed verbatim.

Data Analysis

We employed thematic analysis approach (Braun & Clarke, 2006) to analyze and code the transcripts. Broad and fine codes were initially created by one researcher (FLM) using an a priori list of codes based on the WHO-MAM model, the interview guide, and a first examination of the data. These broad codes were discussed with two other members of the study team (GM and RM). Based on this discussion, the codes were modified and then discussed with the rest of the investigative team. Three researchers (FLM, GM and

RM) coded the transcripts using NVivo version 12, a computer-assisted qualitative data analysis software package.

The coding process was iterative. This facilitated discussions, changes and clarifications during the coding process and resulted in the development of additional codes. One transcript was initially triple coded to establish agreement on coding definitions. Discrepancies were resolved through discussion by coding team members. A second transcript was also triple coded after resolving discrepancies. This further increased reliability and substantiated codebook definitions. For the remaining transcripts, each coder focusing on a specific set of codes. We used the WHO-MAM model to structure an initial analytical report of the results based on the emerging themes and sub-themes from the data. This document was shared with other members of the research team; this generated more ideas and comments, which were incorporated into the report.

RESULTS

Participants were 57.7 years old on average (SD = 8.0), predominantly black (72.2%) and male (55.6%) (Table 1). All participants had health insurance and prescription drug coverage (Table 1). Participants described many factors which influenced their medication use both positively and negatively. Four main themes emerged from the data: perceived need for medication, beliefs about medications, influence of relationships with people and organizations on medication use, and influence of pharmacy access and utilization on medication adherence. These perceptions were

discussed both separately and in combination with each other. The results are presented by themes and categorized based on the context of the WHO-MAM.

Perceived Need for Medications

Patient Related Factors

Many participants indicated that their perceptions of their current health status influenced their medication adherence.

> "Doing fairly well managing my conditions and taking my medicine as much as I can, as often as I can. I try to stay on task. Haven't gotten any bad reports from the doctor, so I'm managing very well." (Male, Black, 40-49 years age group)

Some participants noted that they were independent when it came to taking their medications.

> "Basically, nobody says anything, because I think they know how I am…I don't need anything to remind me." (Female, Black, 60-69 years age group)

However, patients also shared perspectives on patient related factors that were barriers to medication adherence. A few participants shared the perspective that when they were younger, they did not see a need to take their medications as prescribed. They felt that being young would protect them from experiencing the brunt of their illnesses.

> "I say when you're younger, you don't think that you really need medicine because you're thinking that, "Oh, I'm young. My body should compensate for what I need," but as I grew older and realize that when I got my blood pressure taken, and it was high, I'm like, "Maybe I need to take my medicine." I'm much

more conscious than when I was younger to take my meds…" (Female, Black, 50-59 years age group)

Some participants noted that there were times when they were too busy to take their medications, or they were so busy that they forgot to take their medications.

"But when I get busy, if I'm on a project, I'm outside, I try to take it before I go outside. But there's sometimes when I get trapped at work, and I'll end up working 16 hours, and of course I don't have the medicine. Other than my insulin, I have it with me all the time..." (Female, Black, 60-69 years age group)

Additionally, a few participants shared their perceptions about how taking medications worsened their health problems.

"When I first started with blood pressure medicine I think it was a trigger for other problems…I really believe it induced diabetes. I don't know why, I just feel like I don't trust pharmaceuticals..." (Female, Black, 60-69 years age group)

Reluctance to take medications also appeared to be a barrier in taking medications for one participant.

"I don't necessarily believe that you forget, because it's your health. I just think you just get lazy…And you don't wanna do it…And you know, that one time is not gonna do that much to you." (Male, Black, 60-69 years age group)

One black woman cited going to bed as a reason for missed medication doses. "Sometimes I missed my night meds because I go to sleep and I missed taking them because I don't get back up. If I, say for example, if I'm tired from work and I go to sleep intending to take my medicine, wake up at 9:00 or 10:00, but I'll sleep through, so I'll get up the next morning and just take my next dose." (Female, Black, 60-69 years age group)

Social/Economic Factors

Social: Participants shared perspectives on social and economic factors that improved their medication adherence, based on their perceived need for medications. Some participants felt the importance of taking medications so that they could be around for family.

> "I want to live, so wanting to have life and to interact with them [family members] and particularly my grandchildren now. I take it [medications] on a regular basis." (Female, White, 70-79 years age group)

Additionally, some participants took their medications because they did not want to be a burden to the family members by being sick.

> "It makes me want to take my medication like I'm supposed to because the last thing I want to do is have them [family members] come visit me in the hospital...Like I said my whole goal is to be as healthy as possible so I can spend more quality time with them and not having them come and checking on me because I'm sick or not doing well." (Male, Black, 40-49 years age group)

Economic: All the participants reported that they had health insurance coverage for prescribed medications and that most of them were able to afford their medication copays.

> "Well, I didn't miss it because I knowed I had to take it. We had some money set aside to get the medicine, and then [name of pharmacy1] would call us and remind us when it's time to get some more…" (Male, Black, 60-69 years age group)

However, a few black participants cited financial difficulties from time to time in relation to obtaining their medications.

> "There are some financial difficulties. I just weigh them. Like mortgage always has to be paid, but sometimes you can pay on them, you don't have to pay the full amount. So my insulin, I need it, so I have to buy it. There's no discussing or should I or shouldn't I…" (Female, Black, 40-49 years age group)

Therapy Related Factors

A few participants reported therapy related factors which sometimes made it more difficult to take their medications in the context of perceived need for medications. A white woman in the age range, 40-49 shared her challenges and ways of overcoming them:

> "So, when a new medication is introduced, especially with my diagnoses, we are brought in to consult with the pharmacist every time to see if there's going to be any interference with the current medication that I'm on, and if there's side effects, what can I expect, because typically when you see that little teeny tiny print that says, "Two percent or a half of percent will have these issues." Nine times out of 10 I'm in that two or the .5 percent." (Female, White, 40-49 years age group)

A black woman in the age range, 60-69 reported that the size of pills made it hard for her to take her medications as prescribed:

> "…if it's hard to swallow, if it tastes bad or make me feel bad, then I won't take it…"

Condition Related Factors

A few participants noted that they missed their medications on a few occasions because they were too sick to take them despite perceived need.

> "the only problem I have sometimes, is …if I got a real bad chest pain, I can't get my nitroglycerin top off sometimes because that's about what I'm doing to calm down, so I can get it off…Because that pain get so sharp, don't let you do nothing. I have to stop everything I'm doing. And then when it relaxes, when it lets up a little bit, then I can unscrew it." (Male, Black, 60-69 years age group)

Health-care System/Health-care Team Related Factors

Many participants reported that the receipt of advice and information from pharmacists in relation to their medications promoted their medication adherence within the context of having a perceived need for the medications.

> "If I have a cold and I know that the medicine I take, I can't take anything over the counter with it, so I got to be very careful because you don't want any interaction with your medicine. I call the pharmacist and I ask him, I say, "You know, I got this cold I picked up. What you think would be the best thing for me to take that it won't affect the medicine that I'm taking already?" He'll tell me, and everything works out." (Male, Black, 50-59 years age group)

Participants noted a range in the frequency of their pharmacy visits that was based on how frequently they need their medications.

"We try to keep it on a three-month schedule. There's some medications that I have to pick up once a month. So, we're at the pharmacy maybe twice a month." (Female, White, 40-49 years age group)

Similarly, participants cited a range of wait times in the context of having a perceived need for the medications.

"There might be a wait when I get to the pharmacy, but I'm not waiting on them to fill my prescription. I'm just waiting to pick it up…I'm not there 30, 40 minutes waiting on them to put it together or fill it. Most of the time it's just there might be three or four customers ahead of me in line. I'll just wait my turn to pick up my stuff." (Male, Black, 40-49 years age group)

Beliefs about Medications

Patient Related Factors

Some participants believed that their medications "work", especially because taking it resulted in a feeling of wellness. As such, this led to better medication adherence as shared by a black man in the age range, 60-69:

"All the medications I take now are preventive and they are all working fine. Not any particular one, but all of them. Because I'm a diabetic, now I'm taking insulin, but my rate of care hasn't changed any." (Male, Black, 60-69 years age group)

A few participants noted that because of their faith in God, they knew that the medications will work. For these participants, they felt the need to take their medications as prescribed in order to carry out God's will.

"…they [church members] pray for us…They always talk about they want me to get healed, so yeah, they're very supportive…my pastor always says take your medicine. So, even though you've got prescribed medicine make sure you take it…" (Male, Black, 40-49 years age group)

A few participants felt that taking medications was important to be able to work, to maintain health, and to feel good leading to better adherence.

"My appetites have changed, my relationship to my medication, the whole protocol of taking care of myself really is front and center. It's very important to watch what I'm eating, watch my exercise, make sure that I'm doing the medicine, the insulin protocol correctly… So it's just something I realized how important it is to do, so I'm always doing that." (Male, White, 60-69 years age group)

One participant reported that she took medications to feel good and to be healthy:

"If you take your medicine, it will be much better for you because that way, nine times out of 10, you'll end up on the good side…I couldn't argue that with him, but they [doctors] tell you the good and the bad of taking the medicines versus not taking them. You really want to feel good, so it's within you. It's within me." (Female, Black, 50-59 years age group)

One participant shared that over time, he gained a better understanding of what his medications were and how they worked; this led to better medication adherence:

"So I've gotten, I guess, better educated about it all. And I've seen issues with people who've also had diabetes, and I've read about issues of people who've had diabetes and what the negative outcomes are. So that's been eye awakening." (Male, White, 60-69 years age group)

However, some participants expressed how it is “overwhelming” and difficult to take medications in the right way every time although they believe it is the right thing:

> “And I think some of it is, when you have a chronic illness, you want to do the right thing but it's just overwhelming to take all your medicines and do everything just right every day. It's just to me difficult…sometimes I'm immaculate with taking my medication, and I don't miss a dose. And then sometimes I just can't swallow another pill.” (Female, Black, 60-69 years age group)

Social/Economic Factors

In terms of social factors, a few participants received advice about medication use or illnesses from family members which influenced their beliefs.

> “Just like everybody else. They [family members] go and they'll call me and say, I read this article about diabetes. Have you asked your doctor about this? Or have you asked your doctor about this study?” (Female, Black, 60-69 years age group)

A few participants received information about medication use from friends, which positively influenced their beliefs about medications.

> “My best friend, she is on one of the same meds that I take. I ask her how did the medicine make her feel? She gave me her opinion on how it makes her feel. I said, "It's okay. I see now. I felt the same way…” (Female, Black, 50-59 years age group)

Some participants reported that being there for their family members served as motivation in addition to the belief in the efficacy of the medications; this promoted medication adherence.

> "I have a set of five-year-old twin boys who I want to be around for a long time with them. That's motivation enough for me… It's just a matter of when I look and I see my mom and my sister, it's just like I said, I want to be around to enjoy my family and friends for a long time." (Male, Black, 50-59 years age group)

Therapy Related Factors

One participant reported on the experiences of other people who had side effects from their medications. He noted that they stopped the medications for a short period of time but resumed because of their beliefs in the importance of taking their medication.

> "I've had people that have had bad experiences. Sometimes some of the insulin will disrupt their digestive system. Metformin I think is probably one of the most common that people take that they've said they experienced some digestive issues. That's one of the side effects of it, but it is what it is…They'll discontinue it maybe for like a couple hours or a day or so, but then they know that they have to take the medicine. It's not an option." (Male, Black, 50-59 years age group)

Condition Related Factors

A few participants noted that they missed their medications on a few occasions because they were too sick to take them. However, they did not believe that it happened often.

> "I'm sure there might have been a time or two, or maybe I had the flu and I didn't take the medicines, but it really doesn't seem to be a problem or that I can recall." (Male, White, 60-69 years age group)

Health-care System/Health-care Team Related Factors

Many participants cited that their beliefs regarding the efficacy of medications were the result of having a good relationship with and support of doctors in relation to their conditions and medications; this had a positive influence on their medication adherence.

> "Yes, [doctors] they have been very helpful in providing and suggesting the medications that I take and have always cared about how it has affected after I've started taking it, how it's affected the problem." (Female, White, 60-69 years age group)

Many participants also cited that receiving information from pharmacists positively influenced their beliefs about medications and improved medication adherence. "Oh I will speak to any pharmacy. I will pick up a telephone and just dial any pharmacist and ask them about a medication, so it doesn't matter…While I'm at work, I'll overhear a pharmacist talking to a patient about medicines, and I'll listen to that too. So I try to gather information from a lot of places" (Female, Black, 60-69 years age group)

How Relationships with Different People and Organizations Influence Medication Adherence

Patient Related Factors

One participant noted that his faith/trust in doctors made it easier for him to take his medications because the doctor said to do so.

> "Well, the doctor is the doctor, so if he tells me I need to take something that's telling me he's concerned about my health - my overall health." (Male, Black, 60-69 years age group)

Social/Economic Factors

Emotional support: Some participants reported receiving emotional support (receiving encouraging words, hope and care provided and having someone to listen) from family members which helped them cope with daily stresses and challenges of their conditions.

> "But they are constantly encouraging me and asking about my progress…They influence me by saying stuff, giving me compliments like, "You're really doing good." Or whatever. That's about the influence." (Female, Black, 60-69 years age group)

In addition to family members, some participants cited receiving emotional support from friends which helped them cope with the challenges of managing their conditions.

> "You been to the doctor? What they say about this? What they say about that? Okay, what are you changing? You working …out, doing exercising…Like I said, again, we [friends] check on each other. We make sure we're doing what we're supposed to do because several of them have high blood pressure or cholesterol issues. So, we're each other support group…No, we're pretty tough on each other, so we stay on top of each other, especially if we find out we're not doing what

we're supposed to do. So, it doesn't make it hard." (Male, Black, 40-49 years age group)

A few participants stated that they received emotional support from people other than family members or friends.

"…and they [co-workers] all bought cards and send me encouraging words while I was sick ….and it's like I wouldn't say we were like family, but you have close associates that you associate with while you're at work, but you don't associate with them away from work. It's like that." (Female, Black, 50-59 years age group)

Functional support: Many participants also reported receiving functional support (having someone to pick up medications, to provide reminders about medications, to provide financial help, to care for you, provide food or take you to the doctor when sick) from family members which promoted medication adherence.

"Everybody in my family will stay on me and make sure that I do take my medicines…Everybody will call, are you taking your medicine? …or did you take your medicine, do you have your medicine? Have you been to the doctor? What did the doctor say?" (Male, Black, 50-59 years age group)

Some participants also noted receiving functional support from friends which promoted medication adherence.

"But I had my friend, she would set my medicine out and stuff like that…You know, like set it up for the week. She'd be right there with me. So, that when things would happen to me where I couldn't set my medicine out, I'd have her to set it out…So I just had my friend help me. So we go over it, except now, if I don't feel like doing it, she'll do it for me and have it all ready…Well, most of the

time, I have my friend pick my medicine up. But other than that, the only thing too is, I can't get it if I'm working out of town or I'm running late, she'll get it..." (Male, Black, 50-59 years age group)

A few participants cited receiving functional support from people other than family members and friends which promoted their medication adherence.

"For a while, in the beginning, I had a girl that would give me my shot. She was a registered nurse. So when I got my insulin and stuff, I'd call her, and tell her, "[name of woman], I got my medicine." I'd say, "You want me to bring it to you, or you going to pick it up?..." (Female, Black, 60-69 years age group)

Informational support: A few participants reported that they received advice about medication use or illnesses from family members which promoted medication adherence.

"I told my daughter, "I think I'm going to try tumeric." She said, "Did you check with Dr. [name of doctor2] about taking tumeric?" I said, "No." She said, "Check with him first." She said, "If I remember right, that interferes with blood thinner." Sure enough, she was right, it does interfere with blood thinner." (Female, White, 70-79 years age group)

A few participants cited receiving advice about medication use or illnesses from friends.

"…a friend used to tell me, she says, "Tumeric will really help with inflammation." I said, "Sure, ankles bother me so much" "Why don't you try the tumeric?" (Female, White, 70-79 years age group)

A few participants reported receiving advice about medication use or illnesses from people other than family members and friends.

"My church. Yeah. We talk about medicines, but it's just like general session." (Female, Black, 50-59 years age group)

No social support: A few participants noted that they were not in receipt of social support in relation to their medication use but did not report this as having an impact on their medication adherence.

"…[siblings] they don't ask me too much about my medicine stuff…they don't say much about it because they know what my mom and grand mom went through so they got their own problems but I was the only one that was bothered with diabetes." (Male, Black, 60-69 years age group)

Some have roles which they feel are important to the function of their family. Therefore, they took their medications as stated by a black man in the age range, 60-69: "…I have two sisters and a mother that's 86 years old, I know I need to be around because they need me for certain things. Cut the grass or do some carpet work on the house, whatever they need I know that's my job." (Male, Black, 60-69 years age group)

Therapy Related Factors

One participant reported that she had side effects from a medication which were not adequately addressed by her doctors although she had a relationship with them. This had a negative influence on her medication adherence:

"I take Simvastatin or Zocor or something, one of the statin drugs. I think that was the beginning of my muscle problems, when I started to take that. So as a result, I

will not take that on a regular basis…With that medication…I have talked to the eye doctor, the GYN, the internal medicine, I've talked to everyone about it, and they kind of just brush it off. Like no big deal, why are you worried about that?...But then I got that letter from [name of public health institute] or somewhere that says, was the combination of the high dose of my Benazepril or whatever medication I was on, and the Simvastatin that was causing muscle atrophy, and nobody had shared that with me, and they just discounted it." (Female, Black, 60-69 years age group)

Condition Related Factors

One participant reported that she got sick through her relationship with her grandchildren and this had a negative influence on her medication adherence:

"I have a virus one time that I couldn't keep anything down, so it was a stomach virus that I got from one of my grandkids that brought it from school..." (Female, Black, 50-59 years age group)

Health-care System/Health-care Team Related Factors

Many participants cited that having a good relationship with their doctors helped to promote their medication adherence.

"Oh, I'm close to all of my providers. Yeah. I've got a doctor for probably every part of my body, but my cardiologist, my oncologist, one of my surgeons…I have a close relationship to. I can call them, and they'll call me ...Well, get back with me. I've got a good group that I can discuss things with, and I've used the patient

portal to ask questions as well just like I can send a question to my primary and she'll get back with me within 24 hours." (Female, Black, 50-59 years age group)

Additionally**,** many participants reported that having a good relationship with pharmacists helped to promote their medication adherence.

"They have my prescription history. If I have questions they can look back and ask me anything, answer questions for me. But yeah, I think it just makes it a lot simpler for me." (Female, Black, 40-49 years age group)

Clinical support from doctors was also reported as being beneficial in promoting medication adherence among interviewed participants.

"I have a good team of doctors that I like, and that's hard to find some doctors that you really have confidence in. Even when I had the surgery, everything just went smooth. My family doctor is a good doctor. My cardio doctor, and the surgeon that did the surgery is a good doctor." (Male, Black, 50-59 years age group)

However, some participants mentioned having negative interactions with their providers which in some cases negatively affected medication adherence.

"We've only had to terminate our relationship with one specialist, and it wasn't because they were not doing their job, it was because the head nurse was not doing their job…So, I had to terminate that relationship last year. Because she was calling in prescriptions that were not approved for me and sending me into a tailspin…And so we had to fire them. And that is the only bad experience I've had." (Female, White, 40-49 years age group)

Patient Related Factors

Participants' stories revealed that self-efficacy played a role in their decisions regarding obtaining and using their medications. A sense of self-confidence in achieving the goals of accessing and using the medications and feeling better because of those events was seen as leading to better adherence.

> "Most of the time, I usually pick up my own medicine. So, I pick it up even when I'm at work. Like I say, where I work at, I have access to just move out the city when I'm at work." (Male, Black, 50-59 years age group)

Social/Economic Factors

Social: Many participants also received functional support from family members in relation to pharmacy access and utilization.

> "…my husband…if I don't have time to run to the pharmacy and he's out and about, can you pick up my meds? …he helps in picking up medication, and at nighttime, if I'm exhausted or my muscles are tired, and I'm really sore, and I'm not moving very fast, he can grab stuff for me." (Female, White, 40-49 years age group)

Some participants received functional support from friends in relation to pharmacy access and utilization.

"If I need something when I first got out of the hospital…well, I had a prescription. That was such a rough time for me. I didn't even think about the prescriptions…My friends were there…" (Female, Black, 60-69 years age group)

A few participants received functional support from people other than family members and friends in relation to pharmacy access and utilization. People other than family members and friends picked up medications or provided reminders about taking medications.

"As far as them reminding me, now I have one church friend who will say, like last night, I didn't feel well, and she said, "Well, did you take your medicine?" I said, "Yeah, I've taken everything."… If I called them right now, and said, "I need you to go to [name of pharmacy1]. They got a prescription for me. Would you go pick it up?" They don't question…" (Female, Black, 60-69 years age group)

Economic: All the participants reported that they had health insurance coverage for prescribed medications and that most of them were able to afford their medication copays. For them, this positively influenced pharmacy access and utilization.

"…the insurance cover what they going to cover. Now, I usually get that money back after I do a refund form that I send back to the health provider. And I get sent money back on what the prescription costs." (Male, Black, 50-59 years age group)

However, one participant reported on the experiences of other people who had financial difficulties and had to make decisions about which medications to get.

> "I've talked with people who are diabetic and financially there have been times when they've had to make some decisions of what medicine to get or whatever, and it's not just with diabetes it's period." (Male, Black, 50-59 years age group)

Therapy Related Factors

One participant reported that although she only takes two medications, they are on different schedules. Therefore, she has to go to the pharmacy twice a month.

> "I do the two, pretty much those are the only two medicines that I'm on, and I can't get them both at the same time. So at least twice a month I'm having to do one or the other…Long acting is once a day in the morning. And fast acting is counting your carbs." (Female, Black, 60-69 years age group)

Condition Related Factors

One participant stated that there were times when she could not personally access the pharmacy because she was too sick. However, she had access to her medications through the help of family members.

> "…Unless I'm sick, like I was from October to, well, still having problems, where I can't get out, my daughter and my son will go get it…They'll help me…They don't even know what I have to have. I just call them and tell them. During that time, they checked, "Ma, you need anything else filled? You need this? You need that?" (Female, Black, 60-69 years age group)

Health-care System/Health-care Team Related Factors

Most participants noted that the ease of getting to the pharmacy (transportation availability, close distance and short time to pharmacy and lower number of pharmacies used) resulted in improved medication access. This, in turn, led to better medication adherence.

> "My pharmacist is about probably four to five minutes from my home. I used the pharmacist right there in my neighborhood, and this is literally less than five minutes from my house." (Female, Black, 50-59 years age group)

Most interviewed participants had no travel concerns in getting to the pharmacy.

> "Not in that small little town. No, I feel pretty safe and secure… Bad roads? We're lucky too. We live in the city, within the city limits. The neighborhood we live in the city maintains streets and all that stuff." (Female, White, 70-79 years age group)

A few black participants reported having some minor travel concerns in getting to the pharmacy. However, they did not report an effect on medication adherence.

> "…the way I would normally go to [name of pharmacy2], you have to go down this other long street, which is a straight shot. There are not lights or anything on [name of street2]. I just don't like it. They don't ever have to worry about me being on [name of street2] at night, because there are basically no lights on [name of street2]…So I would rather go all the way around [name of street1] and come back up the lighted area where I know there's a lot of traffic, because it's not going to be that much on [name of street2]..." (Female, Black, 60-69 years age group)

Participants noted a range in the frequency of their pharmacy visits but did not report an impact on medication adherence.

> "I probably go to the pharmacy about three times a month…It's just off schedule. Like now, coming here, I have something new. So I'll pick it up on this day and then I have something else and I pick up on another day. And I may need a cream or something. It's just different medication on different days." (Female, Black, 40-49 years age group)

Participants cited a range of wait times, but did not note a major impact on medication adherence.

> "Well when you punch it in, they got the recording now, if you need it within that same day they can have it ready for you like in four or five hours…If not it's about two or three days. Sometimes they'll get to it quicker…You can hit a button if you need it right away…In four or five hours, you can go pick it up." (Male, Black, 50-59 years age group)

Despite having physical pharmacy access, one participant reported that he did not have medication because he may have to wait for his insurance to pay for the medications. He shared this as follows:

> "See sometimes you run out and you go to the pharmacy and the insurance won't pay for the medication and then you have to wait until the insurance pays for the medication." (Male, Black, 60-69 years age group)

Similarly, one participant shared that a lack of insurance at some point in his life made it difficult for him to obtain his medications.

"…when I had a job that didn't carry insurance. These other two [other two medications] cost too much to get so I didn't have it…Till I got one that did have coverage that I could pay for…Yeah, I did without it [medications]." (Male, Black, 50-59 years age group)

For participants who used mail order pharmacies, the cheaper cost of this service compared to getting medications at physical pharmacy locations was cited as a reason for using mail order pharmacies. They noted that this led to improved medication access and adherence.

"The cost that I've gotta pay today. The mail order, I'll order and I'll save maybe five dollars…I have one drug like that. So if I mail order it, I know that's gonna save me so I can go ahead on and order two, three other drugs also, if I do that." (Male, Black, 60-69 years age group)

One participant who used mail order pharmacies cited the convenience of having the medications delivered to their homes as facilitating medication access and adherence.

"You don't have to get out and drive. They come right to your mailbox, and it's always refrigerated when it comes, very helpful." (Female, White, 60-69 years age group)

On the other hand, some participants who did not use mail order pharmacies shared the perspective that the service results in inconvenience because of the possibility of receiving the wrong medication. This medication would have to be mailed back and medication access and thus adherence would be negatively affected.

> "I always said to myself could they send you the wrong prescription and you have to send it back or the dose might not be right, so I'd rather go pick it up in person." (Male, Black, 50-59 years age group)

Some participants cited a lack of privacy as a reason for not using mail order pharmacies. They noted that sometimes mail is delivered to the wrong mailbox and by extension, their medications are easily accessible to others. For them, use of the mail order service could result in poor medication access and adherence.

> "I don't like the idea of medication coming in through the mail and someone…having a missed package or having someone rifle through our mailbox." (Female, White, 40-49 years age group)

DISCUSSION

In the current study, black and white men and women with CHD and CHD risk factors shared co-occurring perceptions and experiences on how their perceived need for medications, beliefs about medications, relationships with different people or organizations, and pharmacy access and utilization influence their medication use. These occurred in different dimensions, as described in the WHO-MAM model: patient, social/economic, therapy, condition and healthcare system/healthcare team dimensions.

The results of the current study are in line with the findings from a systematic review focused on barriers to medication adherence among people who took antihypertensive medications. This study found that patient-related factors (e.g. self-efficacy, patient's knowledge and beliefs about medication), condition-related factors (e.g. ability to open or close the medication bottle and perceived health), social/economic

factors (e.g. social support and cost of medications), therapy related barriers (e.g. medication side effects, medication efficacy and dose complexity), condition-related factors (e.g. severity of symptoms) and healthcare system/healthcare team related barriers (e.g. medication reimbursement and poor patient-provider relationships) were barriers to medication adherence (AlGhurair et al., 2012). Similar to the current study, the systematic review found that patient related factors such as patient's beliefs about nonadherence, social/economic barriers such as health literacy, therapy barriers such as having medical support for dealing with side effects and healthcare system/healthcare team factors such as distance from healthcare facilities were not important barriers to medication adherence (AlGhurair et al., 2012).

In another systematic review of barriers to medication adherence among the elderly, patient-related factors included disease-related knowledge, health literacy and cognitive function (Gellad et al., 2011). Social/economic factors in this systematic review included cost of medications and therapy related factors included medication side effects and polypharmacy (Gellad et al., 2011). Condition-related factors included having comorbidities and healthcare system/healthcare team related factors included poor patient-provider relationships, lack of transportation to the pharmacy and not having health insurance coverage for medications (Gellad et al., 2011). There was one similarity with the results of the current study; poor patient-provider relationships emerged as an important barrier to medication adherence. Otherwise, many of the results were in contrast with that of the current study. These differences may be the result of the differing ages of the participants, as elderly patients may face many logistical barriers due to their age (Gellad et al., 2011) and health conditions.

In other quantitative studies of barriers to medication adherence among people with CVD, poorly controlled diabetes, advanced heart failure, and those who took antihyperlipidemic medications, common factors such as lack of social support, cost of medications, trouble swallowing medications, medication side effects and disease severity were associated with low medication adherence (Dunbar-Jacob et al., 2003; Gazmararian et al., 2006; Odegard & Gray, 2008; Sung et al., 1998; J.-R. Wu et al., 2008a). The barriers to medication adherence in people with CVD and CVD risk factors found in these studies were similar to those discussed by the participants in the current study. The results of these studies also indicated that certain factors that might be hypothesized to be associated with adherence were not associated with lower medication adherence; these factors included perceived health, perceived importance of treatment, remembering doses, difficulty swallowing medications, depression, patient-provider relationships and pharmacy utilization (Dunbar-Jacob et al., 2003; Gazmararian et al., 2006; Odegard & Gray, 2008; Sung et al., 1998; J.-R. Wu et al., 2008a). These are in contrast with the findings of the current study. These differences may be due to the quantitative nature of the prior studies compared to the qualitative nature of the current study; methods used to measure the barriers of medication adherence and medication adherence itself differ between the two types of studies.

Quantitative analyses conducted concurrently with the current study using the REGARDS data (black and white men and women aged 45 years and older in the 48 contiguous US states and the District of Columbia) found that seeing more than ten friends or relatives at least monthly was associated with high medication adherence (Mondesir et al., 2018). However, pharmacy access based on geography (in preparation)

was not associated with medication adherence among people with diabetes, hypertension, dyslipidemia and prevalent CHD. The results of the former study are similar to the current study findings, which indicated that relationships with family and friends improved medication adherence. Conversely, the results of the latter study differed from the current study results, which showed that ease of pharmacy access promoted medication adherence. It is possible that the distances from REGARDS participants' residences to pharmacies were not extreme enough to cause problems.

Despite some differences between the findings of prior quantitative studies and the current study, the combination of the results indicates that patient, social/economic, therapy, condition and healthcare system/healthcare team related factors interact to influence medication adherence through a complex process.

A qualitative study by Johnson et al., 1999, found that a perceived need for medications and a belief in the efficacy of medications facilitated medication adherence while inability to access medications, and forgetting were barriers to medication adherence among elderly patients with hypertension (Johnson et al., 1999). Another qualitative study conducted among patients with heart failure showed that facilitators of medication adherence were a desire to be healthy, having a knowledge of disease and symptoms, and having a good relationship with family members as well as health care providers (J. R. Wu et al., 2008b). Further, a recent qualitative study by Pettersen et al., 2018, found that lack of knowledge about disease severity, side effects of medications and poor informational support from providers acted as barriers to medication adherence among people who had their first PCI (Pettersen et al., 2018). The results of the current study are similar to that of prior qualitative studies focused on barriers and facilitators of

medication adherence. This indicates that while medication adherence is part of a complex process, that process may be similar across different CVD related conditions.

The findings from this study should be interpreted in light of its limitations. The findings are not representative of all black and white men and women aged 45 years and older with CHD and CHD risk factors who see providers at health care facilities near UAB. Importantly, all the study participants had health insurance and prescription drug coverage. As such, we may have lost the opportunity to identify themes specific to experiences of other populations with less access to care and medications. Further, we recruited patients who attended specialist clinics (Endocrinology and Cardiology). These patients may be more highly motivated as they complied with recommendations to seek specialist care. As such, our sample may have been enriched with people who were more likely to be adherent to their medications. There was also limited variability in participants' experiences with physical access to the pharmacy. Additionally, while the current study included participants with CHD and CHD risk factors, participants may have had other comorbidities, which may have influenced their medication adherence. Furthermore, the interview guide used in the current study had few specific questions on condition-related factors. Despite these limitations, the study also had strengths. It provides an in-depth understanding of how theoretically important factors can still influence medication adherence among people who not only have prescription drug coverage but also have no restrictions with physical access to the pharmacy. Few qualitative studies have focused on participants with multiple CHD risk factors. The use of one on one in-depth interviews overcame the social desirability bias which may have been inherent in focus groups. For example, it is possible that some participants in the

focus group setting would be less likely to admit that they did not take their medications, in the presence of others.

CONCLUSION

People's perceptions and experiences on how their need for medications, beliefs about medications, relationships with different people or organizations, and pharmacy access and utilization influence their medication use are important for understanding and addressing sub-optimal medication adherence in patients with CHD and CHD risk factors. We found that barriers and facilitators to adherence occur in the context of the patient, social/economic, therapy, condition and healthcare system/healthcare team. This underscores the need for multidimensional interventions aimed at improving medication adherence and overall health of patients with CHD and CHD risk factors.

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Conflicts of Interest

F.L.M has no relationships to disclose, E.B.L receives funding from Amgen for unrelated work and has served on Amgen advisory boards and as a consultant for a Novartis-sponsored research project, G.M has no relationships to disclose, R.M has no relationships to disclose, A.P.C receives funding from Amgen for unrelated work, M.M.S receives funding from Amgen for unrelated work, J.M.T. has no relationships to disclose.

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Table 1. Characteristics of the study participants (N =18).

Characteristics	
Age (mean ± SD)	57.7 ± 8.0
Black (n, %)	13 (72.2)
Women (n, %)	8 (44.4)
<College graduate (n, %)	11 (61.1)
Employed (n, %)	12 (66.7)
Health insurance (n, %)	18 (100)
Prescription drug coverage (n, %)	18 (100)
Area of residence (n, %)	
Urban	8 (44.4)
Suburban	9 (50.0)
Rural	1 (5.6)
Self-reported diabetes (n, %)	14 (77.8)
Self-reported hypertension (n, %)	12 (66.7)
Self-reported dyslipidemia (n, %)	11 (61.1)
Self-reported coronary heart disease (n, %)	8 (44.4)

SUMMARY

Medications taken for CHD and CHD risk factors can reduce the risk of CHD events and mortality. Yet, about half of patients are not adherent to these medications. This suggests the need for further research to better understand factors which influence medication adherence in order to develop interventions aimed at improving it. The goal of this dissertation was to investigate the association of medication adherence with social support and pharmacy access quantitatively using the REasons for Geographic and Racial Differences in Stroke (REGARDS) study and to obtain patient-centered perspectives on how patient, social/economic, therapy, condition, and health-care system/health-care team-related factors influence medication adherence qualitatively through in-depth interviews.

In a cross-sectional analysis of 17,116 people who took medications for diabetes, hypertension, dyslipidemia and prevalent CHD, we showed that seeing multiple friends and relatives, a measure of combined structural and functional support, was modestly associated with better medication adherence among individuals with CHD and CHD risk factors. However, other social support measures were not associated with medication adherence.

In a cross-sectional analysis of 8,250 people who took medications for diabetes, hypertension, dyslipidemia and prevalent CHD, we found pharmacy access based on geography was not associated with medication adherence.

Lastly, in a qualitative study of 18 participants, we found that their perceptions and experiences of how perceived need for medications, beliefs about medications, how relationships with different people or organizations, and how pharmacy access and utilization influence medication use, occur simultaneously. Moreover, they occur within the context of patient, social/economic, therapy, condition and health-care system/health-care team related factors.

In conclusion, this work highlights the importance of investigating barriers to medication adherence in people with CHD and CHD risk factors. Our data suggest that improving social support with combined structural and functional components may help promote medication adherence. In addition, lack of access to pharmacies based on geography does not appear to be a barrier to medication adherence. Finally, medication adherence barriers are multidimensional in nature. Further quantitative research is needed using other measures of medication adherence such as pharmacy claims data. Additionally, there is a need for more qualitative research conducted in other areas of Birmingham, Alabama and the rest of the US among people from different socio-economic backgrounds.

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APPENDIX A

INSTITUTIONAL REVIEW BOARD APPROVAL

THE UNIVERSITY OF ALABAMA AT BIRMINGHAM
Office of the Institutional Review Board for Human Use

470 Administration Building
701 20th Street South
Birmingham, AL 35294-0104
205.934.3789 | Fax 205.934.1301 | irb@uab.edu

APPROVAL LETTER

TO: Mondesir, Favel

FROM: University of Alabama at Birmingham Institutional Review Board
Federalwide Assurance # FWA00005960
IORG Registration # IRB00000196 (IRB 01)
IORG Registration # IRB00000726 (IRB 02)

DATE: 04-May-2018

RE: IRB-160421002
Exploring the Relationship of Social Networks, Pharmacy Access and Pharmacy Density with Cardiovascular Medication Adherence (Exploring the Relationship of Pharmacy Access and Pharmacy Density with Cardiovascular Medication Adherence)

The IRB reviewed and approved the Continuing Review submitted on 04-May-2018 for the above referenced project. The review was conducted in accordance with UAB's Assurance of Compliance approved by the Department of Health and Human Services.

Type of Review:	Expedited
Expedited Categories:	7
Determination:	Approved
Approval Date:	04-May-2018
Approval Period:	One Year
Expiration Date:	03-May-2019

The following apply to this project related to informed consent and/or assent:

- Waiver of Informed Consent
- Waiver of HIPAA

Documents Included in Review:

- Revised IPR.180503
- CURRENT CLEAN CONSENT.180503

CONSENT FORM

UAB IRB Approved 04-May-2018 until 03-May-2019

TITLE OF RESEARCH:	Exploring the relationship of social networks, pharmacy access and pharmacy density with cardiovascular medication adherence (Exploring the relationship of pharmacy access and pharmacy density with cardiovascular medication adherence)
IRB PROTOCOL NO.:	X160421002
INVESTIGATOR:	Favel Mondesir, MSPH
SPONSOR:	UAB Department of Epidemiology and an American Heart Association Predoctoral Fellowship

Purpose of the Research

We are asking you to take part in a research study. This research study will explore the relationship between cardiovascular medication use, social support and pharmacy access. For people with diabetes, hypertension, high cholesterol or who have heart disease, medications can help to decrease future heart disease events. However, the percentage of patients who use their medications is fairly low. I want to learn from people who take medications for these conditions about their opinions and ideas about how people's relationships with family and friends and their access to pharmacies are related to medication use. This study will enroll 20-30 participants from Kirklin Clinic.

Explanation of Procedures

If you decide to participate in the study you will be asked to complete a short questionnaire and to participate in an interview. The questionnaire will take about 5 minutes to fill out and the interview will take about 45 minutes. The questionnaire will ask questions about demographics. You may answer the questionnaire yourself, or it can be read to you and you can say your answers out loud and I will write them down. If you do not wish to answer any of the questions included in the questionnaire, you may skip them and move on to the next question.

During the interview, I will sit down with you in a comfortable private area at Kirklin Clinic or on the fourth floor of Lister Hill Library or over the phone if it is more convenient for you. The questions in the interview will focus on how your relationships with family and friends and your ability to access pharmacies are related to your use of medications for diabetes, hypertension, high cholesterol or heart disease. If you do not wish to answer any of the questions during the interview, you may say so and I will move on to the next question. I will be the only person present for the in person or phone interview unless you would like someone else to be there.

I will also ask for your permission to audio record this interview, so that your responses will be recorded accurately. I will also be writing some notes during the interview. You may choose not to have your interview audio-recorded. If you do not wish to be audio-recorded, I will write down your responses as accurately as possible.

I will also provide you with bottled water if it is an in person interview.

Risks and Discomforts

This study will involve minimal risk and discomfort. The probability of harm and discomfort will not be greater than your daily life encounters. Risks may include emotional discomfort from answering interview questions. Every precaution will be taken to ensure confidentiality of your responses. However, there is the potential for loss of confidentiality.

Benefits

You will not directly benefit from participating in this study but there may be potential benefits to patients in the future. Benefits will include the promotion of our understanding of how people's relationships with family and friends and their access to pharmacies affect cardiovascular medication use. Others may benefit in the future from the information we acquire from this study.

Alternatives

Your alternative is to not participate in this study.

Confidentiality

Information obtained about you for this study will be kept confidential to the extent required by law. However, research information that identifies you may be shared with the UAB Institutional Review Board (IRB) and others who are responsible for ensuring compliance with laws and regulations related to research, including the Office for Human Research Protections (OHRP). The information from the research may be published for scientific purposes; however, your identity or any identifying information will not be given out.

Every precaution will be taken to ensure confidentiality of your responses. The information recorded is confidential, your name is not being included on the forms, only a number will identify you, and no one else except Ms. Favel Mondesir, Dr. Emily Levitan and Dr. Janet Turan will have access to them. We are the members of the research team. However, the audio recordings will be sent to a company for transcription. The audio recordings will be destroyed two years after the study ends. I will take steps to keep information about you confidential, and to protect it from unauthorized disclosure, tampering, or damage. However, there is the potential for loss of confidentiality. Any information about you will have a number on it instead of your name. Only the researchers will know what your number is and we will lock that information up with a lock and key. It will not be shared with or given to anyone. Further, the data will be stored on password-protected computers. Direct quotes will be used in publications about the findings from this study and there is a possibility that they may be traced back to you.

Voluntary Participation and Withdrawal

Whether or not you take part in this study is your choice. There will be no penalty if you decide not to be in the study. If you decide not to be in the study, you will not lose any benefits you are otherwise owed. You are free to withdraw from this research study at any time. Your choice to leave the study will not affect your relationship with this institution.

If at any time during the interview you do not want to be recorded anymore or you want to stop completely or take a break from the interview, please feel free to let me know.

You may be removed from the study without your consent if I judge that is not in your best interests (for example, if you appear to be in distress), or if you are not following the study rules.

If you are a UAB student or employee, taking part in this research is not a part of your UAB class work or duties. You can refuse to enroll, or withdraw after enrolling at any time before the study is over, with no effect on your class standing, grades, or job at UAB. You will not be offered or receive any special consideration if you take part in this research.

Cost of Participation

There will be no cost to you for taking part in this study.

Payment for Participation in Research

You will receive a $20 gift card for your participation in this study.

Questions

If you have any questions, concerns, or complaints about the research or a research-related injury including available treatments, you may contact Ms. Favel Mondesir at (205) 934-7164 or Dr. Emily Levitan at (205) 975-7680. They will be glad to answer any of your questions.

If you have questions about your rights as a research participant, or concerns or complaints about the research, you may contact the UAB Office of the IRB (OIRB) at (205) 934-3789 or toll free at 1-855-860-3789. Regular hours for the OIRB are 8:00 a.m. to 5:00 p.m. CT, Monday through Friday. You may also call this number in the event the research staff cannot be reached or you wish to talk to someone else.

Legal Rights

You are not waiving any of your legal rights by signing this informed consent document.

Storage of Interview Transcripts for Future Use

As part of this study, we would like to keep transcripts of your interview for future research on cardiovascular medication use. The future research may be conducted by Ms. Favel Mondesir or by other researchers that obtain IRB approval for their research. The transcripts will be labeled with a study ID and any identifiers will be kept separate. Hard copies will be stored in a locked cabinet and electronic copies will be stored on a password protected computer. Results of any future research will not be given to you or your doctor.

You do not have to agree to allow transcripts of your interview to be kept for future research in order to be part of this study.

You may request at any time that transcripts of your interview be destroyed and not be used for future research. If you decide you want transcripts of your interview to be destroyed, you may contact Ms. Favel Mondesir at the University of Alabama at Birmingham at 205-934-7164. Once the request is received, and if transcripts of your interview have not already been used for other research, they will be destroyed. If you do not make such a request, transcripts of your interview will be stored indefinitely or until used.

Initial your choice below:

___ I agree to allow transcripts of my interview be kept and used for future research on cardiovascular medication use.

___ I do not agree to allow transcripts of my interview to be kept and used for future research.

Signatures

Your signature below indicates that you have read (or been read) the information provided above and agree to participate in this study. You will receive a copy of this signed and dated consent form.

Signature of Participant	Date
Signature of Person Obtaining Consent	Date

University of Alabama at Birmingham
AUTHORIZATION FOR USE/DISCLOSURE OF
PROTECTED HEALTH INFORMATION (PHI) FOR RESEARCH

Participant Name: _____
Research Protocol: Exploring the relationship of social networks, pharmacy access and pharmacy density with cardiovascular medication adherence

UAB IRB Protocol Number: X160421002
Principal Investigator: Favel Mondesir, PhD student
Sponsor: UAB Department of Epidemiology and an American Heart Association Predoctoral Fellowship

What is the purpose of this form? You are being asked to sign this form so that UAB may use and release your protected health information for research. Participation in research is voluntary. If you choose to participate in the research, you must sign this form so that your protected health information may be used for the research.

Why do the researchers want my protected health information? The researchers want to use your protected health information as part of the research protocol listed above and as described to you in the informed consent.

What protected health information do the researchers want to use? All medical information, including but not limited to information and/or records of any diagnosis or treatment of disease or condition, which may include sexually transmitted diseases (e.g., HIV, etc.) or communicable diseases, drug/alcohol dependency, etc.; all personal identifiers, including but not limited to your name, social security number, medical record number, date of birth, dates of service, etc.; any past, present, and future history, examinations, laboratory results, imaging studies and reports and treatments of whatever kind, including but not limited to drug/alcohol treatment, psychiatric/psychological treatment; financial/billing information, including but not limited to copies of your medical bills, and any other information related to or collected for use in the research protocol, regardless of whether the information was collected for research or non-research (e.g., treatment) purposes.

Who will disclose, use and/or receive my protected health information? All Individuals/entities listed in the informed consent documents, including but not limited to, the physicians, nurses and staff and others performing services related to the research (whether at UAB or elsewhere); other operating units of UAB, HSF, UAB Highlands, Children's of Alabama, Eye Foundation Hospital, and the Jefferson County Department of Health, as necessary for their operations; the IRB and its staff; the sponsor of the research and its employees and agents, including any CRO; and any outside regulatory agencies, such as the Food and Drug Administration, providing oversight or performing other legal and/or regulatory functions for which access to participant information is required.

How will my protected health information be protected once it is given to others? Your protected health information that is given to the study sponsor will remain private to the extent possible, even though the study sponsor is not required to follow the federal privacy laws. However, once your information is given to other organizations that are not required to follow federal privacy laws, we cannot assure that the information will remain protected.

How long will this Authorization last? Your authorization for the uses and disclosures described in this Authorization does not have an expiration date.

Can I cancel this Authorization? You may cancel this Authorization at any time by notifying the Principal Investigator, in writing, referencing the research protocol and IRB Protocol Number. If you cancel this Authorization, the study doctor and staff will not use any new health information for research. However, researchers may continue to use the protected health information that was provided before you cancelled your authorization.

Can I see my protected health information? You have a right to request to see your protected health information. However, to ensure the scientific integrity of the research, you will not be able to review the research information until after the research protocol has been completed.

Signature of participant: _____ Date: _____