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A Longitudinal Examination of the Sociality of Cardiovascular Disease and its Most Common Risk Factor, Hypertension

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Citation	Parker, Brenda. "A Longitudinal Examination of the Sociality of Cardiovascular Disease and its Most Common Risk Factor, Hypertension." Dissertation, Georgia State University, 2022. https://doi.org/10.57709/28403490
DOI	https://doi.org/10.57709/28403490
Download date	2026-03-09 03:38:34
Link to Item	https://hdl.handle.net/20.500.14694/14283

ABSTRACT

A LONGITUDINAL EXAMINATION OF THE SOCIALITY
OF CARDIOVASCULAR DISEASE AND ITS MOST COMMON RISK FACTOR,
HYPERTENSION

By

BRENDA MARIE PARKER

FEBRUARY 23, 2022

Cardiovascular disease (CVD) is the leading cause of morbidity and mortality in the US, placing considerable economic and clinical burden on the nation. Hypertension (HTN) is the most common modifiable risk factor associated with CVD. Racial disparities in HTN incidence and prevalence make its burden all the heavier on minority populations.

Significant investments have failed to improve HTN incidence and prevalence. Studies have looked to non-medical factors, including social capital (SC) constructs, to explain this phenomenon. However, most studies are cross-sectional or over limited follow-up periods, unable to examine relationships between the timing or duration of SC and CVD-related outcomes. Three studies were conducted to address this gap.

The first study addresses the first research question: How has SC been defined, classified, and measured in the existing CVD literature? Across 74 studies included in the review, SC was largely defined as social networks and social support. The most common keywords were social support and risk factors and most studied CVD outcomes included mortality, myocardial infarction, and hypertension.

The second study uses a nationally representative longitudinal sample to answer the second research question: What is the association between life course social isolation and HTN in early middle adulthood? The findings suggested that social isolation in young or early middle adulthood significantly increases the odds of HTN, as does moving into social isolation in adulthood and the accumulation of social isolation across adolescence, young, and early middle adulthood.

The last study uses the same data source to answer the last research question: Do racial differences in the prevalence of HTN in early middle adulthood change when social connections are considered? The results showed that marriage/cohabitation in early middle adulthood mediated a significantly moderate portion of the non-Hispanic Black/White disparity in HTN prevalence. Similar mediation effects were found when considered across both adulthood life stages for marriage/cohabitation, close friendships, regular religious attendance, and volunteering.

The findings of this dissertation highlight opportunities to further examine the relationship between SC constructs and CVD-related measures and suggest that interventions to increase SC may reduce the overall incidence, and racial differences associated with, HTN in early middle adulthood.

A LONGITUDINAL EXAMINATION OF THE SOCIALITY OF CARDIOVASCULAR DISEASE AND ITS MOST COMMON RISK FACTOR, HYPERTENSION

by

BRENDA MARIE PARKER

DOCTOR OF PHARMACY, UNIVERSITY OF GEORGIA
MASTER OF PUBLIC HEALTH, EMORY UNIVERSITY

A Dissertation Submitted to the Graduate Faculty
of Georgia State University in Partial Fulfillment
of the
Requirements for the Degree

DOCTOR OF PHILOSOPHY IN PUBLIC HEALTH

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APPROVAL PAGE

A LONGITUDINAL EXAMINATION OF THE SOCIALITY
OF CARDIOVASCULAR DISEASE AND ITS MOST COMMON RISK FACTOR,
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FEBRUARY 23, 2022

To my husband,

the ever-present cheerleader who constantly encourages me to go after all that my heart desires,

and my children,

who sacrificed their mommy many nights and weekends so that she may achieve her goal.

Acknowledgments

As a working professional and dedicated wife / mother, the decision to return to graduate school was not one made alone. Little did I realize that the journey and destination would be no less an effort supported by so many. For the many, I am forever grateful.

Firstly, Dr. Xiangming Fang – my faculty advisor, dissertation committee chair, and friend: Thank you for the gift of your time and mentorship, which have directly impacted my personal and professional life in so many meaningful ways.

Secondly, Dr. Douglas Roblin, Dr. Laura Salazar, and Dr. Shannon Self-Brown: Thank you for the continued support and encouragement throughout this journey from each of you, three of the smartest and kindest individuals with whom I have had the privilege of learning.

Thirdly, Dr. Drew Bradlyn and Dr. Ali Rahimi – Thank you for your shared dedication to scientific inquiry and making the world a better place, one patient at a time.

Lastly, Jesus Christ, my Lord and Savior – To Him be all the glory.

Author's Statement Page

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Brenda Marie Parker

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Chapter I: Literature Review and Statement of Purpose

Introduction

Cardiovascular disease (CVD) is the leading cause of death in the United States, accounting for nearly one-third of total deaths across the country.[1] The economic impact of CVD is no less burdensome, with annual direct (medical) and indirect (lost future productivity) costs estimated to exceed $363 billion.[1] An umbrella term that comprises several conditions, including coronary heart disease (CHD), heart failure (HF) and stroke, the impact of CVD is largely preventable, up to 75%, by addressing modifiable risk factors such as hypertension (HTN) and high cholesterol.[2]

In addition to the implementation of interventions to address modifiable risk factors, there have been increased efforts to understand the non-medical factors, or social determinants, that account for 80-90% of health outcomes in the United States.[3] The relationship between socioeconomic determinants and CVD have been widely studied in the literature; the most studied, education and income, demonstrating a direct association in many analyses.[4] The impact of neighborhoods and neighborhood disadvantage has been shown to have a significant effect on the development of CVD and related events.[5-8] Social relationships, or the network and support provided through such interactions, have been less studied in the context of CVD risk and outcomes, providing opportunities to expand this body of literature.

The theoretical underpinnings of this dissertation are founded in two conceptual models – social capital theory and life course theory. The integration of these theories facilitates meaningful examinations of the relationship between aspects of social capital and CVD over an individual's

life course. A brief literature review of these theories is presented in the proceeding section, including the rationale for their intersection from independent theories, their relationship to CVD health, and both the availability and limitations in this area of research. The statement of purpose at the end of the chapter provides a compelling description of how this dissertation and the analyses contained within will enhance the field of public health.

Conceptual Models

Social Capital Theory

Social capital theory is complex, in part, because it is not a singular theory. Rather, it reflects contemporary authors' varied disciplines and subsequent approaches to this concept. It is generally recognized that social capital theory, and its nuances, primarily stems from three individuals: Pierre Bourdieu, James Coleman, and Robert Putnam. There have been extensive examinations of these individuals and their approaches to social capital; another such review is unnecessary and outside the scope of this paper.[9] Nonetheless, a brief review of each perspective and important concepts of each is provided and summarized in Table 1.

The modern day understanding of social capital was first introduced in the mid-to-late 1980's by Pierre Bourdieu, a French sociologist. Bourdieu described capital as a construct composed of three primary forms: economic, cultural, and social. Of these, economic capital reflected the accumulation of resources for monetary gain while cultural and social capital accumulated to provide non-monetary benefits. Social capital, as Bourdieu defined it, was 'the aggregate of the actual or potential resources which are linked to possession of a durable network of more or less

institutionalized relationships of mutual acquaintance and recognition…which provides each of its members with the backing of the collectively-owned capital'.[10] At the core of his conceptualization of social capital was the benefit the individual receives from continuous, intentional investments in relationships. The magnitude of the benefit accrued through social capital, however, is limited by social position or status as reflected by the economic, cultural, and symbolic power of the individuals within the networks constructed by the individual.

In the late 1980's and early 1990's, James Coleman, an American sociologist, introduced a similar social capital framework to that of Bourdieu's, whereby the individual is the beneficiary of social capital. Coleman's definition of social capital described it as a 'variety of entities with two elements in common: they all consist of some aspect of social structure, and they facilitate certain actions…within the structure', reflecting his viewpoint that social capital is the confluence of 'two broad intellectual streams'.[11] His approach combined the purposive nature of economic theory with the relational structure within sociological theory such that the relations between individuals result in productive activity. Through introducing three forms of social capital – reciprocity, information channels, and social norms – Coleman provided the necessary framework for the cognitive dimension of social capital. In a similar manner, his focus on family ties, built upon Bourdieu's network construct, shaped one of the two domains, bonding capital, within the structural dimension of social capital.

Robert Putnam, an American political scientist, is the name most often associated with social capital theory, due, in large part, to the publicity of his 1995 journal article and 2000 book. In his publications, he lamented the decay of social capital in America since the 1960's, evidenced by

an observed decrease in voter turnout, church attendance, and Boy Scout troop leaders.[12,13] Putnam believed that social capital was a public good for community consumption rather a private good to be the sole possession of the individual, defining it as 'features of social organization such as networks, norms, and social trust that facilitate coordination and cooperation for mutual benefit'.[14] While Coleman introduced bonding capital through his focus on family and closed networks, Putnam expanded the structural dimension of social capital to include bridging capital, which reflects the ties in which individuals invest outside of the exclusive relationships created by families and similar social structures to connect with others less like themselves.

The social capital framework developed through the intersection of these independent, yet complementary theories is illustrated in Figure 1. As previously mentioned, two primary dimensions of social capital have taken shape over time: cognitive, which describes the norms, values, attitudes, and beliefs that lead individuals to engage in cooperative action for mutual benefit, and structural, manifests in the roles, rules, precedents, procedures, and networks that facilitate said cooperative action and the resulting mutual benefit.[15] There are two primary mechanisms through which the cognitive dimension of social capital is manifested: reciprocity, a cyclical phenomenon by which individuals both expect others to return the invest they have made in them and are compelled to return the investments made in them by the investors, and trust or trustworthiness, characteristics of an individual that convey to others a sense of good will.[16] Within the structural dimension, there are three mechanisms by which social capital takes shape: bonding, where connections are within groups, bridging, where connections are between groups, and linking, where connections are across societal gradients.[17] In summary, cognitive

social capital refers to how individuals *feel* about their social relations while structural social capital refers to the connections people *have* within a social context.

Life Course Theory

Life course theory, like social capital theory, has its roots in sociology as a framework that is used to examine the human experience across its continuum. It is a broad field of study based on the assumption that life happens in a sequence of defined events and roles over time, shaped by age, social structures, and historical change.[18,19] There are basic concepts in life course theory by which life may be influenced over its course, including cohorts, life events, trajectories, transitions, and turning points.[20] In addition, there are key principles of life course theory which underly the assumption that lives are lived in an ordered fashion and shaped by external pathways: agency, life span development, linked lives, time and place, and timing.[19,21] Some overlap exists in these concepts and themes, which have been further defined below (Table 2).

There are several theoretical models by which life course theory is applied to chronic disease epidemiology. These models can generally be grouped into one of two categories: timing of causation and causal pathways (Figure 2). The critical and sensitive period models posit that exposure during a specific window of time conveys an increased risk of disease. In the critical period, or latency, model, exposure during a period of biological development can have adverse or protective effects on disease risk or outcome, whereas, the sensitive period model speculates that the risk of disease is stronger when the exposure is during periods of behavioral development than it would be had the exposure occurred during some other period of time.[22] Accumulation of risk and chain of risk models describe the causal pathways by which repeated

exposures over the life course may confer disease risk and/or outcome. In the accumulation of risk model, different exposures have a cumulative effect, independently or clustered, on disease risk and/or outcome, where the chain of risk model describes the effect on disease risk and/or outcome as a result of sequential exposures that may be additive or multiplicative in nature.[23]

Social Capital and Life Course Models in the Context of Cardiovascular Disease

Social capital and life course models have been applied with varying methodologies to help explain CVD incidence, prevalence, and adverse health outcomes. Studies seeking to describe the direct relationship between social capital and CVD have found positive associations at individual- and community-levels, across both cognitive and structural dimensions.[24-27] Indirectly, social capital has been studied to understand racial disparities in the prevalence of CVD risk factors, showing that it explains both the mechanism and magnitude of the relationship.[28,29] Studies which have applied life course theory to understand the impact of social determinants, including social capital, over a lifetime on cardiovascular outcomes have shown that timing and duration of exposure are significantly related to adverse CVD-related outcomes.[8,30,31] The findings of these studies confirm the significant impact social capital, directly and indirectly, has on cardiovascular health, the importance of a life course perspective in CVD epidemiology, and the utility of research that accounts for both to identify means that improve health outcomes. Few studies have examined the direct and indirect association of social capital constructs, over the life course, with HTN in early middle adulthood, leaving an evidentiary void of which this dissertation aims to fill.

Statement of Purpose

The aim of this research dissertation is twofold: one, to identify how social capital is defined, classified, and understood within the existing CVD literature, and two, to examine mechanisms by which social capital intersects with HTN, the most common CVD risk factor, across the life course. Three analyses are proposed to accomplish these aims, with a summary of each provided below.

An analysis of the literature, titled ‘Social Capital and Cardiovascular Disease: A Scoping Review to Understand Key Concepts and Identify Research Opportunities’ , will use emerging research methods to answer the following research question: How has social capital been characterized and measured in the literature related to cardiovascular disease? The scoping review is intended to describe the characterization of social capital in CVD research and identify methods commonly used to examine the relationship between the two, reporting and mapping these findings to inform future research in this area.

The subsequent data analyses seek to understand the relationship between social capital and HTN, directly and indirectly.

- The first analysis, titled ‘An Examination of the Longitudinal Relationship between Social Isolation and Hypertension’, is intended to examine the relationship between social isolation patterns and HTN at various life stages – adolescence, young adulthood, and early middle adulthood.
- The second analysis, titled ‘Race/Ethnicity, Hypertension, and Social Connections: A Mediation Analysis’, explores the potential mechanisms by which adulthood social

connectedness may mediate the relationship between race/ethnicity and HTN in early middle adulthood.

The findings of these analyses may inform cross-sector interventions to address social capital at various stages of life wherein social capital confers the greatest protection against adverse cardiovascular outcomes. To our knowledge, these analyses are the first to leverage a large dataset representing over 20,000 adolescents followed for five waves in the examination of the relationship between life course social capital and HTN in early middle adulthood.

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Figures and Tables

Figure 1. Social Capital Framework

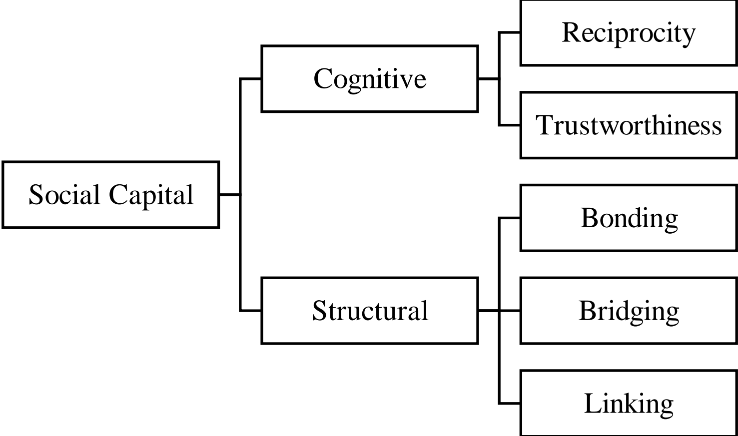

Figure 2. Life Course Theory Framework

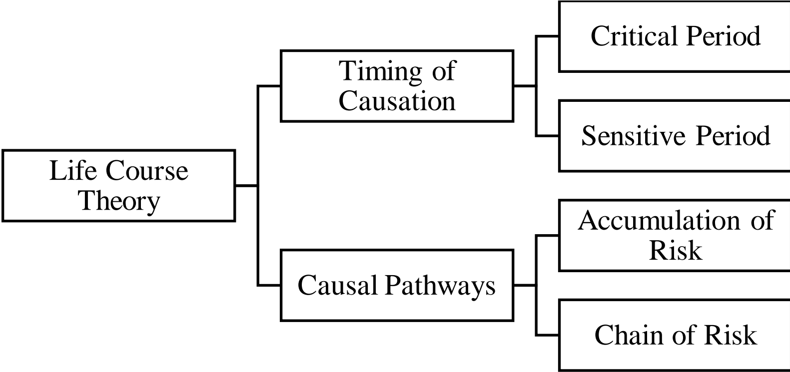

Table 1. Summary of Social Capital Theories

	Level of Analysis	Beneficiary	Key Concepts
Bourdieu	Individual Social Class	Upper class	Status or Power Network size
Coleman	Individual Family Community	Individual	Reciprocity Information Channels Norms
Putnam	Community Country	Public	Networks Reciprocity Trust/Trustworthiness

Table 2. Life Course Theory Concepts and Themes

Concept[20]	*Cohort:* a group of individuals born during the same period, sharing similar social and cultural experiences in the same order at the same age
	Life Event: an abrupt, significant occurrence with serious and long-lasting effects
	Trajectory: pathway characterized by long-term patterns of stability
	Transition: a change in role or status that is a distinct departure from the previous one
	Turning Point: a major change in trajectory
Theme[19,21]	*Agency:* individual decisions and choices impact the life course
	Life Span Development: individuals develop in biologically, socially, and psychologically meaningful ways beyond childhood
	Linked Lives: the interaction between individual social worlds – family, friends, and co-workers
	Time and Place: birth year and historical changes that impact the life course
	Timing: the incidence, duration, and sequence of roles, and relevant expectations and beliefs based on age

Chapter II. Social Capital and Cardiovascular Disease: A Scoping Review to Understand Key Concepts and Identify Research Opportunities

Introduction

Social and economic factors have been identified as the most significant modifiable determinants of health and disease.[1] While economic factors like income and education have been extensively studied, there has been a growing body of literature over the past two decades examining the relationship between social capital, a comprehensive social factor construct, and health. Some studies have found a positive correlation between the two variables, while others have found weak, or, worse, negative effects of social capital on health and health-related outcomes.[2-5] Studies that have examined the relationship of social capital with cardiovascular disease (CVD), specifically, have more consistently found positive associations; however, the varying definitions and measures of social capital limit the strength of associations and confound the reliability of findings.[6-13]

Cognitive and structural social capital are the primary dimensions that have taken shape over time. Cognitive structural capital describes the norms, values, attitudes, and beliefs that lead individuals to engage in cooperative action for mutual benefit, while structural social capital manifests in the roles, rules, precedents, procedures, and networks that facilitate said cooperative action and the resulting mutual benefit.[14] Cognitive social capital largely functions through two mechanisms: reciprocity, a cyclical phenomenon by which individuals both expect others to return the invest they have made in them and are compelled to return the investments made in them by the investors, and trust or trustworthiness, characteristics of an individual that convey to

others a sense of good will.[15] Structural social capital accumulates through network interactions and ties under the frameworks of bonding, where connections are within groups, bridging, where connections are between groups, and linking, where connections are across societal gradients.[16] In summary, cognitive social capital refers to how individuals *feel* about their social relationships while structural social capital refers to the connections people *have* within a social context.

Most reviews that have outlined how social capital is defined and measured in the context of CVD have done so in the broader context of chronic disease and mortality.[17,18]
To our knowledge, there is no contemporary review that focuses on cognitive and structural elements of social capital and their measurement, broadly, in the cardiovascular (CV) literature alone. The current review seeks to address this gap in the literature. To do so, definitions, characterizations, and measurements of social capital in the CV literature are first summarized. Then, bibliometric trends, themes, and research gaps regarding social capital and its association with CVD risk factors, incidence, and outcomes are identified to help inform future exploratory opportunities.

Methods

The multi-stage scoping review framework was used to achieve the aims of this paper, as outlined in a previously published protocol.[19] A summary of the approach and any deviations from the original protocol are outlined below.

Stage One: Identifying the Research Question

The primary research question, "How has social capital been characterized and measured in the literature related to CVD?", and sub-question, "What gaps exist in the evaluation of the relationship between social capital and CVD?", were guided by the PCC (Population, Concept, Context) framework (Table 1). There was a deviation from the original protocol, in that we opted to specify and expand the Population to, in alignment with the initial intent of the review, focus on adults with or without existing CVD which include evaluations of social capital and incident disease.

Stage Two: Identifying Relevant Studies

A thorough search was conducted in EMBASE, MEDLINE, Web of Science, and Google Scholar.[20] The keyword search strategy included a combination of subject headings, e.g. Emtree and MEdical Subject Headings (MESH), and Boolean terms, AND/OR, to identify relevant studies. Relevant article information found during the database searches, including authors, titles, and abstracts, were imported into the EndNote X9 reference management software, where duplicates were removed, and screening conducted. The full search strategy is outlined in the previously published protocol.[19]

Stage 3: Study Selection

Scoping reviews are typically iterative as authors become more familiar with the literature.[21] As such, modifications from the original protocol and the rationale for those modifications are provided below.[19]

Inclusion Criteria. In addition to the parameters outlined in the original protocol, studies that were published, peer-reviewed, and tested the association between social capital or one of its constructs and risk factors, incidence, or outcomes related to cardiovascular disease were included.[19] The breadth of outcomes was not defined in the original protocol; however, the decision was made to include clinical and humanistic measures, e.g., cardiovascular-specific mortality and quality of life measures, for reporting CV outcomes.

Exclusion Criteria. Records and/or articles that were unavailable, not original research, and where cardiovascular procedures, specifically, were the outcome of interest were excluded, as stated in the protocol.[19] In addition, studies that included cerebrovascular diseases, e.g. stroke, or congenital heart diseases or behaviors like self-care or medication adherence as the outcome of interest were added to the exclusion criteria stated in the original protocol. Studies that evaluated the impact of support-based interventions or the relationship between other social risks, e.g., education, income, neighborhood characteristics, and CVD were also excluded.

Relevant titles and abstracts were screened for inclusion by two reviewers (MP, YC). Full text articles that met the inclusion criteria were sourced and screened by the same reviewers (MP, YC). Differences between reviewers were resolved through consensus. Agreement between the primary reviewers on title/abstract and full text article inclusion was calculated using two methods: percent agreement and Cohen's kappa coefficient, (k). For the title/abstract screening stage, there was 90 percent agreement and $k = 0.71$, reflecting moderate agreement between the two reviewers.[22] For the full article screening stage, there was 83 percent agreement and $k = 0.67$, again, reflecting moderate agreement between the two reviewers.[22] Following the initial

reviews, consensus was reached between reviewers as to which title/abstract and articles to include; as such, escalation to another reviewer was not required.

A 10% sample of articles was screened by an independent reviewer (KR) to validate the final articles identified for inclusion, with 93 percent agreement on the final articles included in the review.

Stage 4: Charting Results

A table was developed in Microsoft Excel 2017 to chart data from the included full text articles. The headings used in the data extraction process were modified from the protocol and include primary author and year of publication, study design, CVD variable(s), CVD measure(s), social capital variable(s), social capital measure(s), and summary of related findings. The primary reviewer (MP) performed the data extraction process. First, a 10% sample of the full text articles was charted in the Excel tables to allow two reviewers (XF, SSB) to validate the consistency and accuracy of the data charting form, with discrepancies adjudicated by a third reviewer (AR). Once the final table headings and content were agreed upon by all reviewers (MP, XF, SSB, AR), the primary reviewer (MP) completed data extraction for the remaining full-text studies.

Stage 5: Collating, summarizing, and reporting the results

Methods described in the protocol were followed to collate existing knowledge on this broad topic.[19] The results are summarized and reported in the following manner:

- Bibliometric analyses to describe publication patterns, including publication and journal frequency as well as author and keyword co-occurrence network mapping. EndNote X9

was used to identify frequencies, which were tabulated and/or charted using Microsoft Excel. VOS Viewer1.6.17 was used to construct and visualize co-author and keyword co-occurrence networks using the EndNote X9 library; and

- Thematic analyses to describe patterns in social capital and CV terms and measurements using EndNote X9 library and Microsoft Word for Microsoft 365.

Results

Study Selection Process

Based on the database searches, we evaluated and screened 958 unique studies after duplicates were removed. We excluded 793 records because either the title or abstract did not include social capital or the CVD outcomes of interest. We read the full texts of 165 articles to assess eligibility for full review. From those 165 studies, 74 studies fit our criteria inclusion. A PRISMA diagram (Figure 1) details the results from the search, and study selection processes. The charted details of each study included in the review are presented in Appendix 1 in the supplementary material.

Summary of Study Designs

Of the 74 articles included in the scoping review, 37 (50%) used a cross-sectional study design to evaluate the relationship between social capital and CVD constructs, 21 (28%) were prospective in nature, and 13 (17.6%) employed longitudinal methods. The remaining study designs only accounted for 4 (5.4%) of the study designs used in the included articles.

Publication and Journal Analyses

Over the 10-year search window, there was an upward trend in the number of articles published (Figure 2). Most publications, 14, were in 2019, which was more than double any single year other than 2012 and 2020.

There were 68 journals represented by the included articles. Of these, 16 occurred in two or more instances. The most commonly occurring journals were Social Science and Medicine (5 occurrences), Heart (4 occurrences), and Journal of Behavioral Medicine and European Journal of Cardiovascular Nursing (each with 3 occurrences).

Network Analyses

Network and density visualizations were used to describe author and keyword relationships between the final articles. The network visualization displays the relationships in a traditional network analysis map, with nodes, edges, and clusters displayed in colors that represent relatedness to one another. The density visualization is another tool that describes relationship strength in a slightly different manner, whereby dense areas of color indicate where many nodes are located close to each other.

There were 425 authors across the 74 articles, with an average of 6.2 authors per publication. In a network analysis of co-authorship, author was the unit of analysis, using fractional counting with two minimum occurrences (Figure 3). There were 24 authors that co-occurred in two or more publications. Of the 22 clusters, two clusters contained the five authors that co-occurred in more than two publications: Moser, D.K and Lennie, T.A. (Cluster 1 with 4 links; includes Chung,

M.L., with three links within a separate, but overlapping, Cluster 3) and Lichtman, J.H. and Spertus, J.A. (Cluster 2 with 3 links). All remaining authors were in individual, albeit connected, clusters, except for Cene C.W. and Kivimaki, M. who were in unconnected clusters.

Three visualizations were created regarding the networks of co-occurrence of keywords frequently used in the 74 research articles – social capital-related keywords, CVD-related keywords, and their combination. Keywords related to study design were excluded from the visualizations. In each of the analyses, keyword co-occurrence was assessed based on fractional counting with three minimum occurrences. We observed 503 keywords and out of these, 77 total keywords meet the chosen threshold. In the combined network visualization, there were 38 key words and five clusters, with social support and risk factors the most frequently occurring keywords, 40 and 34 occurrences, respectively (Figure 4). In the CVD-related keyword analysis, there were 18 keywords and 3 clusters; risk factors (34 occurrences) and quality of life (8 occurrences) were the most commonly occurring keywords (Figure 5). There were 15 keywords and four clusters in the social capital-related keyword analysis; social support was the most frequently occurring keyword (40 total occurrences), followed by loneliness (10 total occurrences) and social isolation (9 total occurrences) (Figure 6).

Thematic Analyses

Over half of the included studies used validated surveys to assess social capital constructs (Figure 7). Studies that did not use validated studies included questions to assess specific aspects of social capital, e.g. loneliness, network size, interactions.

There were 16 unique social capital themes evaluated across the cognitive and structural constructs of social capital (Table 2). Both constructs were evaluated in more studies than either construct alone (38%). Social support, perceived or otherwise, was the most studied of the cognitive constructs (n = 33), while living arrangement measures, including marriage, cohabitation, and the converse, living alone, were the most examined structural constructs (n = 23). In eight studies, individual constructs of social support – emotional, instrumental, functional, and material support – were evaluated as independent measures of social capital.

There were four CVD themes and 44 CVD measures identified through the scoping review (Table 3). Mortality and myocardial infarction (MI) were the most studied CVD outcomes (26 and 15 studies, respectively). The next most common CVD outcome / risk factor measures were hypertension (HTN) and blood pressure (BP) in 13 and 12 studies, respectively. Relationships were observed between these outcomes: BP was used as an independent CVD outcome and as a determination criterion in seven of the studies where HTN was the CVD outcome variable of interest; in three of the studies where mortality was the CVD outcome variable, MI was the specific cause of death.

Discussion

The primary aim of this scoping review was to undertake a broad, rapid review of the CV literature to identify how social capital and its individual cognitive and structural constructs have been defined, measured, and evaluated in relation to CVD incidence, risk factors, and outcomes. Previous reviews have either included these elements as part of a larger review or focused solely

on specific social capital constructs or domains.[23-28] To our knowledge, this is the first review to gather and aggregate knowledge of social capital, broadly, as it relates solely to CVD.

After a thorough database search and assessment of eligibility, we identified 74 studies that examined the relationship between social capital constructs and CVD risk factors, incidence, and outcomes. The use of the term, social capital, in these studies was limited; rather, it was largely studied as other broad terms measured by specific indicators. The multitude of terms and indicators likely reflects the complex nature of social capital and the general lack of consensus in how it should be defined and measured. Social support, as the most studied indicator of social capital, may be the closest representation of a widely accepted measure of social capital.

Most studies used cross-sectional surveys to assess the relationship between specific social capital constructs and CVD measures. Individuals may take years to develop the primary mechanisms through which social capital is most beneficial – reciprocity, trust, and connections within and among groups. As such, measuring social capital as a single metric in time without regard to the life course or relation to life events may underrepresent the protection such relationships may provide.

There are some limitations to consider when interpreting the results of the present study. In alignment with scoping review methodologies, this review did not attempt to critically appraise the quality of included studies nor provide a comprehensive review of study results. Rather, a broad description of the bibliometrics and themes in the social capital and CV literature was provided and study results were included in the supplementary table. The intent of this review

was to identify how social capital is used in the CV literature; however, social capital was rarely identified as a keyword. While this limitation was addressed through expanded search terms, it is possible that relevant studies may have been omitted in this review. Moreover, the interest in the contributions of social risks, including social capital indicators, to health outcomes is a rapidly growing field, so there may be additional studies that were published prior to the dissemination of this research. Nonetheless, this review makes a substantive contribution to the existing literature in two ways: first, by describing how research about the association between social capital and CVD has been produced and organized, and second, in identifying themes and opportunities to expand this body of evidence.

Acknowledgements

The authors would like to thank Yu Chen for her assistance in reviewing abstracts and full texts and Katherine Reuben for her validation of the full text sample.

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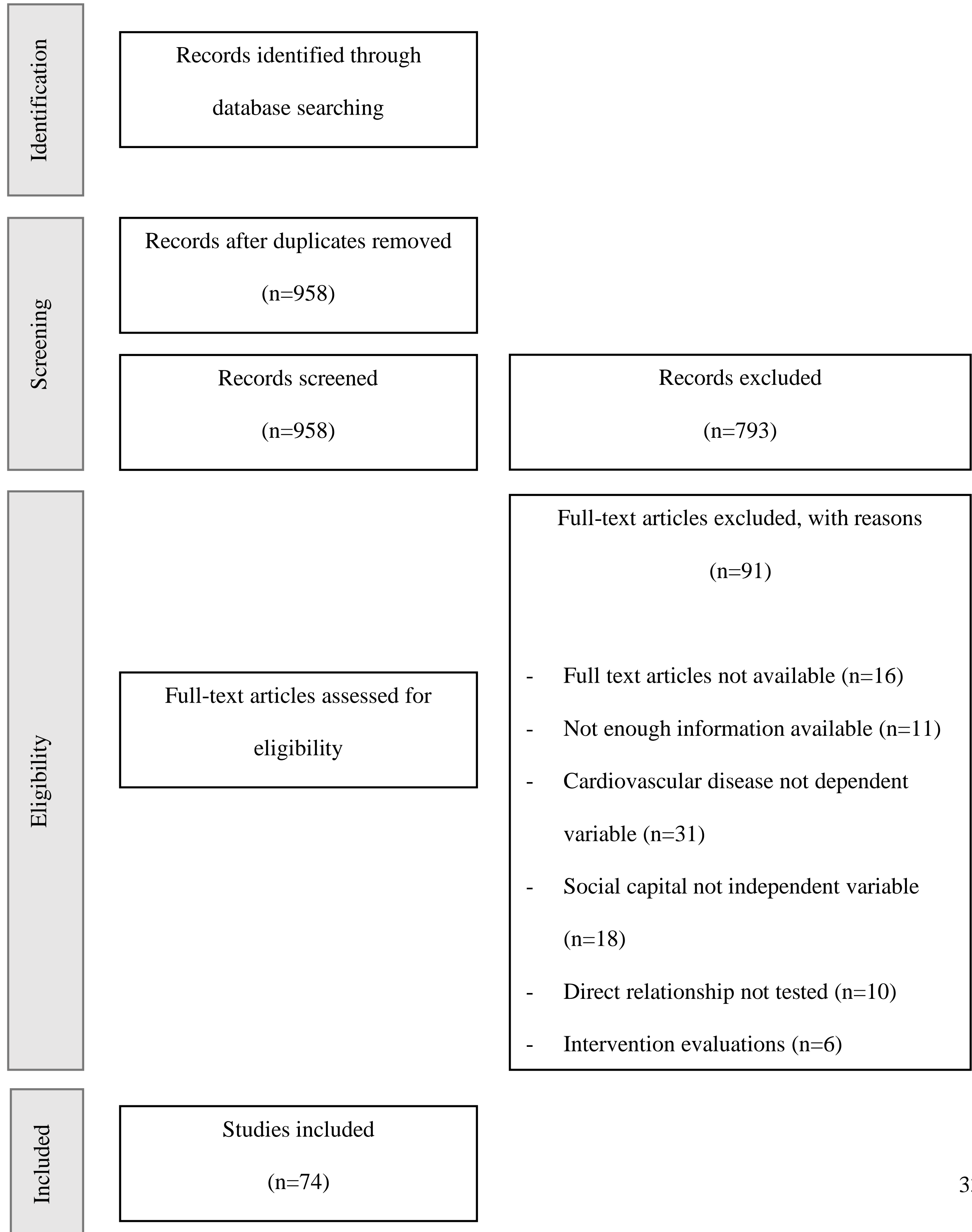
Figures and Tables

Figure 1. PRISMA diagram describing the study selection process.



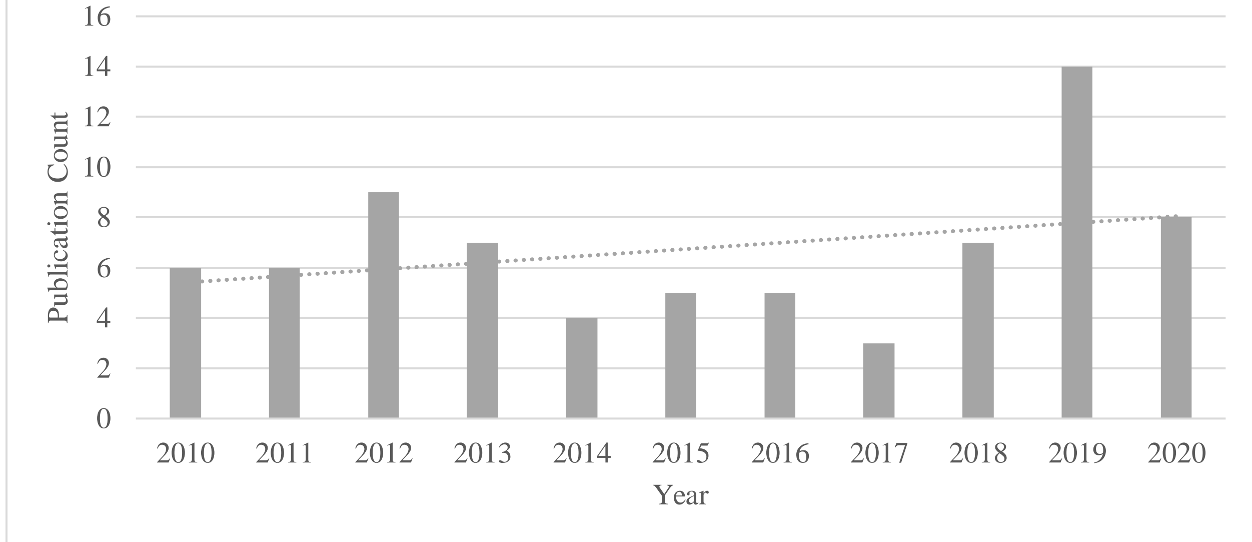


Figure 2. Publications per year between 2010 and 2020.
16
14
12
10
8
6
4
2
0
Publication Count
2010
2011
2012
2013
2014
2015
2016
2017
2018
2019
2020
Year

Figure 3. Clusters with authors that have 2 or more publications with a linkage between them.

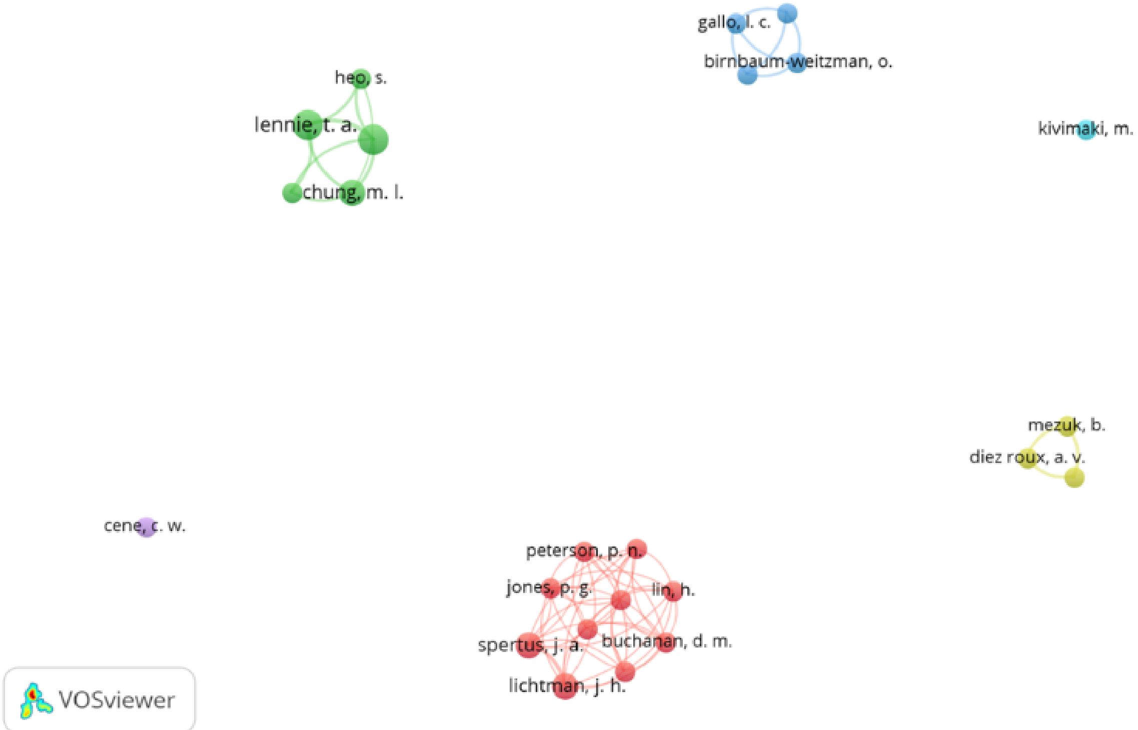


Figure 4. Clusters and associations of CVD- and social capital-related keywords.

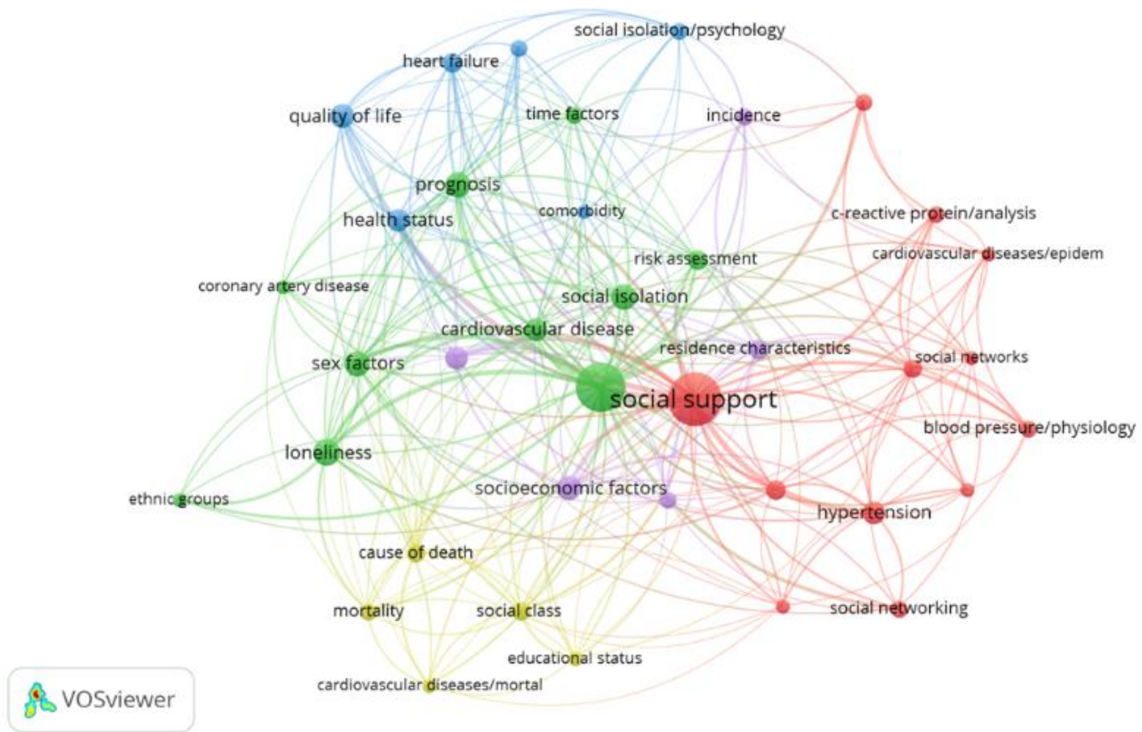


Figure 5. Clusters and associations of CVD-related keywords.

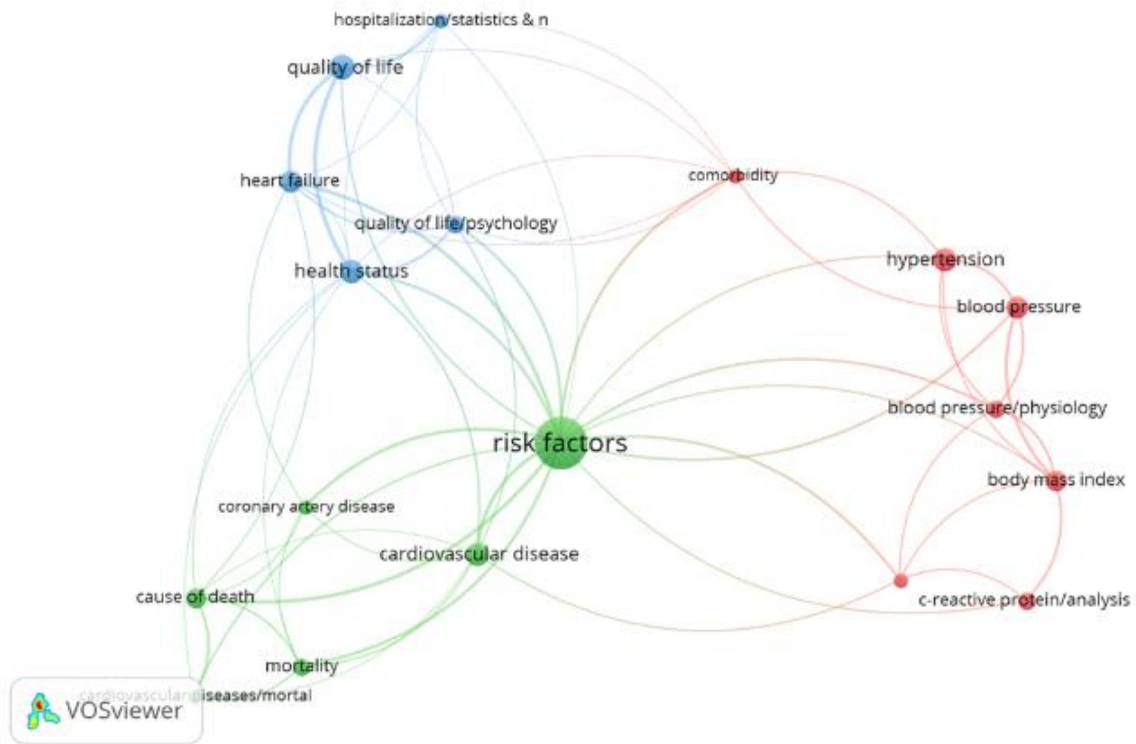
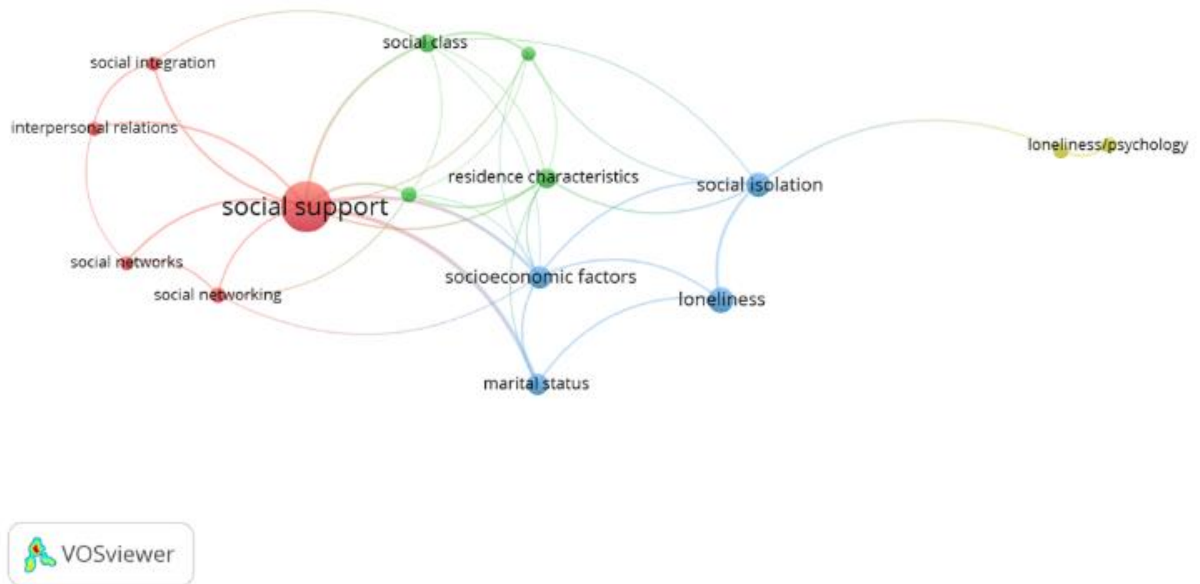


Figure 6. Clusters and associations of social capital-related keywords.



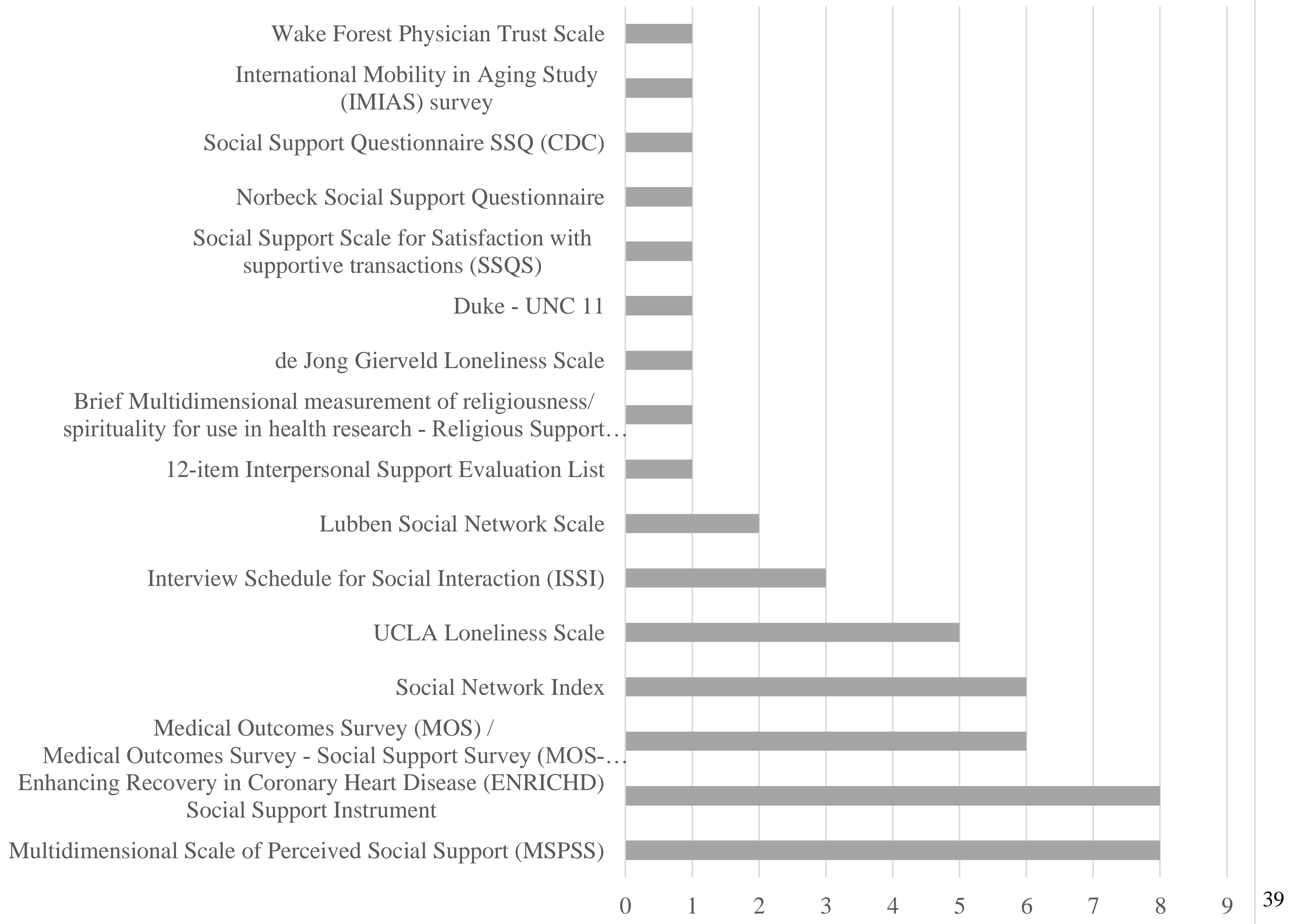


Figure 7. Validated social support scales and study occurrences.
Wake Forest Physician Trust Scale
International Mobility in Aging Study (IMIAS) survey
Social Support Questionnaire SSQ (CDC)
Norbeck Social Support Questionnaire
Social Support Scale for Satisfaction with supportive transactions (SSQS)
Duke - UNC 11
de Jong Gierveld Loneliness Scale
Brief Multidimensional measurement of religiousness/ spirituality for use in health research - Religious Support…
12-item Interpersonal Support Evaluation List
Lubben Social Network Scale
Interview Schedule for Social Interaction (ISSI)
UCLA Loneliness Scale
Social Network Index
Medical Outcomes Survey (MOS) / Medical Outcomes Survey - Social Support Survey (MOS-…
Enhancing Recovery in Coronary Heart Disease (ENRICHD) Social Support Instrument
Multidimensional Scale of Perceived Social Support (MSPSS)
0
1
2
3
4
5
6
7
8
9

Table 1. PCC Framework for Identifying the Main Concepts of the Scoping Review Study

PCC Element	Definition
<u>P</u>opulation	Adults with or without cardiovascular disease
<u>C</u>oncept	Social Capital, including cognitive and structural components Cardiovascular disease, including risk factors, incidence, and outcomes
<u>C</u>ontext	Research publications within the last 10 years (2010-2020) and published in English

Table 2. Social capital constructs and themes with study occurrence count, according to the scoping review.

Construct	Theme
Cognitive (n = 6)	Emotional support (n = 1)
	Fairness (n = 1)
	Loneliness (n = 9)
	Perceived social support / social support (n = 13)
	Religious support (n = 1)
Structural (n = 8)	Isolation (n = 6)
	Interaction (n = 1)
	Living arrangements / marital status / cohabitation / living alone (n = 7)
	Network (n = 9)
	Participation (n = 2)
Cognitive and Structural (n = 18)	Attachment (n = 2)
	Emotional support (n = 4)
	Functional support (n = 1)
	Interaction (n = 7)
	Instrumental support (n = 1)
	Isolation (n = 1)
	Living arrangements / marital status / cohabitation / living alone (n = 16)
	Loneliness (n= 3)

	Material support (n= 1)
	Network (n = 9)
	Participation (n = 3)
	Perceived social support / social support (n = 20)
	Relationships (n = 1)
	Trust (n = 1)

Table 3. Cardiovascular themes and measures with study occurrence count, according to the scoping review.

Theme	Measure
Condition (n = 7)	Heart failure (n = 7)
	Heart murmur (n = 1)
	Hypertension, including awareness and control (n = 13)
	Left ventricular mass (n = 1)
	Other heart condition (n = 1)
	Peripheral artery disease (n = 1)
	Rheumatic heart disease (n = 1)
Event (n = 13)	Abnormal heart rhythm / atrial fibrillation / cardiac arrythmia / ventricular tachycardia / ventricular fibrillation (n = 5)
	Angina (n = 5)
	Cardiac arrest (n = 1)
	Cardiac event (self-reported) (n = 1)
	Cardiac procedure (self-reported) (n = 1)
	Cerebrovascular accident / stroke (fatal and non-fatal) (n = 6)
	Coronary heart disease (fatal) (n = 1)
	Death / mortality (n = 26)
	Emergency department visit (n = 2)
	Heart infarct / myocardial infarction (fatal and non-fatal) (n = 15)
	Hospitalization / rehospitalization / readmission (n = 6)

	Stent implants / target vessel revascularization (n= 2)
	Transient ischemic attack (n = 1)
Quality of Life (n = 5)	HeartQoL (n = 1)
	Kansas City Cardiomyopathy Questionnaire (KCCQ) (n = 1)
	Left Ventricular Dysfunction Scale (LVD-36) (n = 1)
	Minnesota Living with Heart Failure Questionnaire (MHLFQ) (n = 6)
	Seattle Angina Questionnaire (SAQ) (n = 4)
Risk Factor (n = 19)	Atrial natriuretic peptide (n = 1)
	Body mass index (n = 1)
	Blood pressure / Blood pressure control / SBP (n = 12)
	Blood urea nitrogen (n = 1)
	Coronary artery calcium (n = 2)
	Creatinine (n = 1)
	C-reactive protein (n = 8)
	Fibrinogen (n = 3)
	Hemoglobin A1c (n = 1)
	Homocysteine (n = 1)
	Hypercholesterolemia / high cholesterol (self-reported) / lipid profile (n = 3)
	Interleukin-6 (n = 2)
	Left ventricular mass (n = 1)
	Metabolic syndrome (n = 1)

	Obese / obesity (n = 3)
	Obstructed arteries (n = 1)
	Smoking (n = 1)
	TNF-alpha (n = 1)
	White blood cells (n = 1)

S1 Table. Summary of peer-reviewed publications included in scoping review of social capital and cardiovascular disease (CVD).						
Primary Author and Year	**Study Design**	**CVD Variable(s)**	**CVD Measure(s)**	**Social Capital Variable(s)**	**Social Capital Measure(s)**	**Related Findings**
Alcaraz, K. I. 2019	Prospective	Mortality	International Statistical Classification of Disease and Related Health Problems (ICD) -9 codes 390–459 and 798; (ICD) -10 codes I00–I99 and R96	Social isolation	- Simplified Berkman–Syme Social Network Index (SNI)	Social isolation was associated with CVD mortality across race-sex subgroups (P for trend < 0.03).

Aragão, E. I. S. 2017	Cross-sectional	Hypertension (HTN)	Self-reported	Support network Perceived social support	- Number of close friends and relatives - Participation in religious, social, or political group activities, in non-governmental organizations - Engagement in sports and artistic activities	HTN was not associated with close relatives, network size, or engaging in sports or artistic activities. There was a statistically significant positive association with attending religious services regularly (OR = 1.56; 95% CI: 1.14-2.14).

					Medical Outcomes Study (MOS)	There were positive associations between HTN and the four realms (material, emotional, information and positive social interaction).
Årestedt, K. 2012	Cross-sectional	Health-related quality of life (HRQoL)	Minnesota Living with Heart Failure Questionnaire (MLHFQ)	Social support	Interview Schedule for Social Interaction (ISSI)	There was a significant association between social support and HRQoL when controlling for gender, age, and disease severity: the higher

						level of social support, the higher HRQoL.
Barutcu, C. D. 2013	Cross-sectional	HRQoL	Left Ventricular Dysfunction Scale (LVD-36)	Perceived social support	Multidimensional Scale of Perceived Social Support (MSPSS)	There was a moderately negative relationship between perceived social support and quality of life (r= -0.356, p=0.001).
Bell, C. N. 2010	Retrospective	HTN	Average blood pressure (BP), excluding the first measurement, where HTN was defined as systolic BP ≥140 mm Hg and/or diastolic BP ≥90 mm	Social support	- Marital status - Can you count on anyone to provide you with emotional support such	Neither emotional and financial support nor marital status affected the race/ethnicity ORs of HTN. Among those with either emotional or

			Hg, or currently taking antihypertensive medication		as talking over problems or helping you make a difficult decision? - If you need some extra help financially, could you count on anyone to help you; for example, by	financial support, blacks had more than two times the odds of being hypertensive compared to whites (OR = 2.28, 95% CI = 1.23–4.22). Blacks with both emotional and financial support had almost two times the odds of being hypertensive than their white counterparts (OR = 1.82, 95% CI = 1.58–2.10).

					paying any bills, housing costs, hospital visits, or providing you with food of clothes?	Mexican Americans with both emotional and financial support were less likely to be hypertensive than their white counterparts (OR = 0.66, 95% CI = 0.48–0.91).
Berard, D. M. 2012	Prospective	HRQoL	Kansas City Cardiomyopathy Questionnaire - Physical limitation subscale (KCCQ-PL)	Social support	Medical Outcomes Survey - Social Support Survey (MOS-SSS)	Increasing levels of informational support, social, and overall support were weakly and significantly associated with less

						decline in KCCQ-PL changes.
Bu, F. 2020	Longitudinal	CVD events	Self-reported doctor-diagnosed or administrative records, using ICD-10 codes from I00 to I99, and death registry	Loneliness Social isolation	Three-item subscale of the UCLA Loneliness Scale - Living alone - Having less than monthly contact with children - Relatives and friends - Not belonging	Loneliness but not social isolation, is independently associated with higher risk of onset CVD and CVD- related hospital admissions

					to any social organization or club - Not working and not volunteering	
Bucholz, E. M. 2014	Prospective	Mortality HRQoL	Mortality 1- and 12-month post discharge after acute myocardial infarction (AMI) Seattle Angina Questionnaire (SAQ) 1- and 12-month after AMI	Perceived social support	Enhancing Recovery in Coronary Heart Disease (ENRICHD) Social Support Instrument	Crude mortality at 1 and 12 months was very low in this cohort of young patients (~2% overall) and did not differ by social support status. After multivariable adjustment, including

						baseline health status, low social support was associated with lower quality of life at 12 months (all P<0.001).
Cene, C. W. 2012	Prospective	Incident heart failure (HF)	ICD-9 discharge code of 428 or death certificate with ICD-9 code of 428/ICD-10 code of 150	Social isolation	10-item Lubben Social Network Scale	The unadjusted hazard of developing incident HF is greater for those in the higher compared with the low social isolation groups (HR 1.29, 95% CI 1.15–1.24). Those in the moderate/high/isolated

						group had significantly greater risk of developing HF in age-, gender-, race/study community-, and educational level-adjusted analyses (HR 1.18, 95% CI 1.06–1.32). This association remained significant after additional adjustment for current smoking and alcohol use (HR 1.13, 95% CI 1.01–1.26), and for HTN, diabetes, CHD,

						and BMI (HR 1.21, 95% CI 1.08–1.35).
Chang, S. C. 2017	Prospective	Incident cases of first non-fatal myocardial infarction (MI) and fatal coronary heart disease (CHD)	Self-report of nonfatal MI, verified by medical records and/or interview, letter confirming hospitalization Hospital records or autopsy, where CHD was listed as cause of death on the death certificate with	Social integration	SNI	When compared with the least socially integrated women (referent), the age-adjusted HR of total CHD in most socially integrated women was 0.73 (95% CI, 0.65–0.82); when adjusting for health-related lifestyle behaviors, the association for total CHD incidence was

			evidence of prior CHD			substantially attenuated (most versus least socially integrated group: HR, 0.92; 95% CI, 0.82–1.03). In the age-adjusted models, women in the highest level of social integration, respectively, had HR (95% CI) of 0.80 (0.71–0.92) and 0.47 (0.35–0.63) for nonfatal MI and fatal CHD, compared with

						the referent; in models that further adjusted for lifestyle-related behaviors, the highest level of social integration remained significantly associated with fatal CHD (HR, 0.68; 95% CI, 0.51–0.92) but not nonfatal MI (HR, 0.97; 95% CI, 0.85–1.10).
Charlemagne-Badal, S. J. 2016	Cross-sectional Prospective	Self-reported HTN	Self-reported diagnosis of HTN	Religious support	Brief Multidimensional measurement of religiousness/	Anticipated support significantly predicted HTN both cross-sectionally and

					spirituality for use in health research - Religious Support (Long Form)	prospectively but that this relationship appeared to be mediated by BMI.
Christensen, A. V., et al. 2020	Cross-sectional	HRQoL Registry-documented cardiac events (MI, stroke, cardiac arrest, ventricular tachycardia/fibrillation)	HeartQoL ICD-10 codes I21 (MI); I60-I64, I67 (stroke); I46 (cardiac arrest), I49 (ventricular tachycardia / fibrillation)	Cohabitation Loneliness	Living alone, married couple, other couple, and household consisting of several people from more than one family (e.g. nursing home or collective)	Women and men feeling lonely reported a significantly lower quality of life score compared with those not feeling lonely. After adjustment for potential confounders, men living alone had an increased risk of

					Does it ever happen that you are alone even though you would prefer to be with other people?	cardiac events (HR 1.39 (95% CI 1.05 to 1.85).
Chung, M. L. 2013	Cross-sectional	HRQoL	MLHFQ	Perceived social support	MSPSS	When age, gender, NYHA class, and self-reported functional status were controlled, decreased social support (sβ = −. 132; P < .001) was independently associated with poorer quality of life.

Cornwell, E. Y. 2012	Cross-sectional	HTN	Self-report whether medical doctors had ever told respondent that they had high blood pressure (HBP) or HTN Mean BP (on the basis of all readings taken) exceeded either 140 mm Hg systolic or 90 mm Hg diastolic were considered hypertensive, with lower cutoffs of	Social connectedness and support	- Spouse or coresident partner - Number of people listed in network roster - How often talk with each network member - How likely to discuss a health problem or medical	Network characteristics and emotional support are associated with HTN diagnosis and control. The risks of undiagnosed and uncontrolled HTN are lower among those with larger social networks—if they discuss health issues with their network members. When these lines of communication

			either 130 mm Hg systolic or 90 mm Hg diastolic for respondents who reported that they had been diagnosed with diabetes		treatment with each network member - Can "sometimes" or "often" rely on Family members; Friends - Can "sometimes" or "often" open up to Family members; Friends	are closed, network size is associated with greater risk for undiagnosed and uncontrolled HTN.

Coulon, S. M. 2015	Cross-sectional	BP	Average of the second and third BP readings	Perceived social support	MSPSS	Perceived social support demonstrated an inverse relation with diastolic BP (B = −1.76, p = .014), with lower support related to higher diastolic BP, and higher support related to lower diastolic BP.
Das, A. 2019	Longitudinal	BP	Wave-specific mean of repeated readings for SBP and DBP	Loneliness	UCLA Loneliness Scale	Loneliness had no linkages with either of the two BP outcomes, SBP or DBP.

Djekic, D. 2020	Cross-sectional	Coronary Artery Calcium (CAC)	CAC score from cardiac computed tomography (CT)	Social Support	ISSI (condensed)	In a logistic regression model, after adjustment for 12 cardiovascular risk factors, the odds ratio (95% confidence intervals) for CACS > 0 in women with the lowest social integration, emotional attachment, and social support groups (reference: highest corresponding group) were 2.47 (1.23–5.12), 1.87 (0.93–3.59), and 4.28 (1.52–12.28),

						respectively. There was no association found in men.
Foti, S. A. 2020	Cross-sectional	CVD prevalence	Self-report of one or more of the following conditions: MI, congestive HF, rheumatic heart disease, atrial fibrillation, stroke, transient ischemic attack, aortic aneurysm, or peripheral arterial	Loneliness	revised UCLA Loneliness Scale	Adjusting for age, sex, income, BMI, depression, smoking status, study site, ethnic background, marital status, and years in the U.S., loneliness was significantly associated with CVD: OR =1.10, (95 % Cl = 1.01 – 1.20), p <.05).

			disease, excluding angina			
Fuller, K. C. 2018	Cross-sectional	BP	Average of the last two of three resting BP readings, with systolic BP (SBP) corrected by 10mmHg and diastolic BP (DBP) by 5mmHg for medication use	Network structure	Name 30 people that you know by sight or by name that you could contact today if you needed to, with characteristics and nature of relationships;	For SBP and DBP, two different network characteristics improved each model, although only one was significantly associated after Bonferroni correction, i.e. percent of central positions

				Network composition	How likely is it that Alter A and Alter B talk to each other when you are not around? - Mean betweenness centrality (average number of shortest paths in network) - Mean distance (average of	occupied by family was significantly associated with SBP (p-value = 0.01) and percent of alters who are family was significantly associated with DBP (p-value = 0.004).

					shortest paths between alters)	
Gallagher, R. 2016	Cross-sectional	HRQoL	MLHFQ	Perceived social support HF-specific social support	MOS-SSS HF-specific social support questionnaire, specific to person who provides the most support - Perception of the adequacy of their carer's HF knowledge and	Social support independently predicted the emotional domain and overall HRQL so that patients with a high level of social support reported less negative effect of HF on HRQL.

					attention to their HF symptoms - Provision of practical and emotional support - Quality of their relationship	
Gandhi, S. 2019	Longitudinal	Major Adverse Cardiovascular Events (MACE)	CV death, nonfatal or fatal MI, and nonfatal or fatal stroke	Living arrangement status	Living alone or Not living alone	After adjustment, there were no differences in MACE among patients living alone compared to those living with others; however, men living alone were at higher risk for MACE (HR 1.17, 95% CI

						1.002–1.36, p=0.047) as opposed to women living alone (HR 0.82, 95% CI 0.65–1.04, p=0.099).
Gettler, L. T. 2019	Cross-sectional	CVD risk factors	White blood cells (WBC) and C-reaactive protein (CRP), measured via blood sample Average of three of three BP measurements	Social support	- Can you count on anyone to provide you with emotional support such as talking over problems or helping you make a	Men with greater reported social support had higher SBP and DBP

					difficult decision? - In the last 12 months, who was most helpful in providing you with emotional support? - In the last 12 months, could you have used more emotional support than you received?	

					- Would you say that you could have used a lot more, some, or a little more emotional support? - If you need some extra help financially, could you count on anyone to help you; for example, by	

					paying any bills, housing costs, hospital visits, or providing you with food or clothes? - In general, how many close friends do you have?	
Goldman, A. W. 2016	Cross-sectional	CRP	CRP, measured via blood sample	Social network	Respondent named up to five individuals with whom they had discussed	The full model demonstrates that the relationship between bridging kin and the probability of

					‘important matters’ in the prior year, describing the nature, closeness of relationship and frequency of contact Bridging was measured by respondent report that at least one pair of network members of a given type (kin or	presenting elevated CRP remains statistically significant ($p < .001$). Greater average closeness with alters remains predictive of a lower probability of presenting elevated CRP ($p < .05$) (OR = .59, SE = .14), while more frequent contact with network alters predicts a higher likelihood of this

					non-kin) were totally unconnected or only poorly connected to each other (i.e., they interact once a year or less often)	outcome ($p < .05$) (OR = 1.26, SE = .15).
Grewal, K. 2011	Longitudinal	Recurrent cardiac event or procedure, or hospital admission	Self-reported recurrent cardiac event or procedure, or hospital or emergency room admission in the intervening 9 months	Social support	ENRICHD Social Support Instrument (ESSI)	Social support was not significantly related to recurrent events.

			on the follow-up survey			
Hakulinen, C. 2018	Retrospective	AMI Death	Recorded from the death register and hospital admission using (ICD)-10 codes: I21.X, I22.X, I23.X, I24.1 and I25.2	Social isolation	- Including yourself, how many people are living together in your household? - How often do you visit friends or family or have them visit you? - Which of the following	In analyses adjusted for age, sex and ethnicity, social isolation was associated with higher risk of AMI (HR 1.43, 95% CI 1.32 to 1.55, P<0.001). However, when adjusted for all risk factors, the association was attenuated by 84% to 1.07 (95% CI 0.99 to 1.16) and did not

				Loneliness	(leisure/social activities) do you engage in once a week or more often? - Do you often feel lonely? - How often are you able to confide in someone close to you?	remain statistically significant (P=0.109). Social isolation was associated with higher risk of mortality after AMI (HR 1.50, 95% CI 1.25 to 1.79, P<0.001) in the analyses adjusted for age, sex and ethnicity; after adjusting for all risk factors, the association was attenuated by 50% to 1.25 (95% CI 1.03 to 1.51) but remained

						statistically significant (P=0.023). Loneliness, in turn, was not associated with mortality among participants who had incident AMI.
Hamano, T. 2011	Cross-sectional	SBP	2nd SBP measurement	Social capital	Fairness – Do you think most people would try to take advantage of you if they got a chance, or would they try to be fair?	Systolic blood pressure increased with a difference of one unit in the proportion of lack of fairness (P < 0.05), after adjustment for individual confounders.

					Trust – Would you say that people in your neighborhood can be trusted or that you need to be very careful in dealing with people in your neighborhood? Helpfulness – Would you say that most of the time people try to	

					be helpful, or are they mostly looking out for themselves?	
Han, H. R. 2013	Cross-sectional	BP Control	Average of the second and third of three BP readings; BP control was defined as BP <140/90 mm Hg	Living arrangements	- Living alone - Living with spouse - Living with child(ren), with or without spouse	Those who were living alone were at last two times more likely to have BP control than were those living with a spouse, after controlling for other variables.
Heffner, K. L. 2011	Case-Control	CRP CHD death	CRP, measured via blood sample	Social integration	- Current marital status	In the unadjusted model, those at the lowest level of social

			ICD 9 codes (410e414.9) or ICD 10 codes (21.9e69.4)		- How many close friends and relatives do you usually talk with or see once per week? - List churches, clubs, associations, societies, or unions of which they were a member	integration had more than twice the odds of CHD death compared to those at the highest level of social integration (OR = 2.63; 95% CI = 1.14-6.10). This association was not changed by adjustment for age, gender, or Framingham risk score (OR = 2.52; 95% CI = 1.02-6.17). Those at the lowest level of social

					- How many times in the past three months have you attended a meeting (or worship service) or participated in a group project in any of these?	integration continued to have greater odds of dying from CHD-related causes (OR = 2.40; 95% CI = 1.03-5.64) compared to those at the highest level of social integration. After adjustment for age, gender, and Framingham risk category, the association between low social integration and greater risk for

						CHD death remained (OR = 2.66; 95% CI = 1.03-6.85).
Hegeman, A. 2018	Cross-sectional	CVD	Self-reported angina, heart infarct, cardiac arrhythmia, HF, any other heart condition	Loneliness	11-item de Jong Gierveld Loneliness Scale	No significant association between loneliness and cardiovascular disease was found after adjustment for confounders. However, a significant association between loneliness and CVD was found in women but not in men.

Heo, S. 2012	Prospective	HRQoL Event-free survival Cardiac mortality	- MLHFQ - Time to the first event (hospitalization or death) from the enrollment date - Death from any cardiac cause	Social Support	Quality of perceived social support - How would you rate the quality of the support you receive? Emotional support - MSPSS Marital status - currently married or currently unmarried (divorced,	Only better quality of perceived support was related to better HRQoL.

					separated, widowed, or single)	
Heo, S. 2014	Cross-sectional	HRQoL	MLHFQ	Social Support	- Marital status - Social networks (number of significant others who were contacted regularly)	When all types of social support were entered into the model at the same time, only marital status was significantly related to HRQOL (R2 = .062, p = .036).

					- Relationships with healthcare providers (Wake Forest Physician Trust Scale) - Emotional support (MSPSS) - Instrumental support (Social Support Scale- Instrumental - Heart Failure)	

					- Family relationships (subscales of the FES- Family Relationship Index)	
Hernandez, D. C. 2014	Cross-sectional	Self-reported high blood pressure (HBP) and high cholesterol	Please indicate if you have had any of the following medical problems...” (yes versus no)	Social support	12-item Interpersonal Support Evaluation List (ISEL)	Results from the multivariate logistic regression models indicated that none of the three types of functional social support – appraisal, belonging, tangible – were significantly

						related to CVD risk factors. However, adults with high levels of cumulative social support were at 2% lower odds of experiencing high blood pressure (aOR = 0.98, 95% CI = 0.95, 0.99). High levels of cumulative social support were not related to high cholesterol.

Hernandez, R. 2018	Cross-sectional	CV risk factors	- HTN, defined as systolic blood pressure 140 mmHg, diastolic blood pressure 90 mmHg, or use of antihypertensive medication - Hypercholesterolemia if they were currently taking lipid-lowering medication or if any of their recorded	Social network	SNI (subset) - Total number of living children, parents, and inlaws - Extent of regular contact with children, parents, and in-laws (interaction at least once every 2 weeks) - Number of perceived close	There were no significant cross-sectional associations of structural support indices with abdominal obesity, HTN, hypercholesterolemia, or smoking status. There was a marginally significant (OR: 1.05; 95%CI 0.99–1.11) trend toward higher odds of obesity in participants reporting a larger family unit (including children,

			cholesterol levels were elevated - Participants with a BMI of 30.0 or greater were categorized as obese - Elevated abdominal obesity, defined as a waist-to-hip ratio 0.85 cm for women and 0.95 cm for men - Smokers were defined as those		ties with extended family relatives (e.g., aunt, uncle, grandparents) - How many other relatives (other than your spouse, parents & children) do you feel close to?	parents, and in-laws) and those with closer ties with extended family relatives (OR: 1.04; 95%CI 0.99–1.09).

			self-reporting currently smoking cigarettes			
Joo, W. T. 2018	Cross-sectional	CAC	CAC score (CACS), measured by computed tomography	Social network betweenness	- Network size, defined as the total number of social network members - Only family network, considered when a participant did not enumerate any non-family members in his	The association between CACS and network size (odds ratio [OR], 0.95; 95% confidence interval [CI], 0.83–1.08; p=0.412) or OF networks (OR, 1.50; 95% CI, 0.95–2.35; p=0.080) was not statistically significant at the 0.05 level; however, NC networks

					or her network list - No cutpoint network, considered when a respondent did not serve as a cutpoint (a person whose deletion breaks up the remaining group into two or more disconnected	had significant association with CACS >400 when separately considered.

					groups) for his or her networks	
Kamiya, Y. 2010	Longitudinal	CV risk markers	- HTN defined as SBP and DBP ≥ 140/90 mmHg [49] or SBP ≥ 140 (isolated systolic hypertension) or using hypertensive medication	Social participation	- Current membership or participation in any of a list of groups and associations divided into: (1) political, trade union or environmental group; (2) tenants' groups,	Social participation was inversely associated with all four of the CV risk markers ($p < 0.05$). In those who had a pre-existing CVD, social ties had a protective effect by lowering the hsCRP level (OR = 0.84, 95% CI: 0.7160.995) and

			- Obesity measured by BMI - CRP, fibrinogen measured via blood samples	Social ties	residents' groups or neighborhood watch; (3) church or other religious organization; (4) charitable associations; (5) an education, arts or music group or evening class; (6) social club (e.g. Rotary Club,	emotional support increased the odds of being obese (OR = 1.58; 95% CI: 0.998-2.50). Being married was inversely associated with hypertension and fibrinogen.

				Emotional support	elderly lunch group, women's group); and (7) any other organizations, clubs or societies - How many of your children/relatives/friends would you say you have a close	

				Marital status	relationship with? - How much respondents feel their spouse/partner (children/relatives/friends) understand(s) their feelings - How much respondents can rely on their spouse/ partner	

					(children/relatives/friends) if they have a serious problem - How much respondents can open up to their spouse/partner (children/relatives/friends) if they need to talk	

					- Married (or cohabiting) - Not married (never married, separated or divorced, and widowed)	
Kilpi, F. 2015	Prospective	MI incidence and mortality	Hospital discharge records and the cause of death register (ICD-10 codes I21-I22)	Living arrangements	- Living with marital partner - Cohabiting (living with non-marital partner)	After full adjustment, living arrangements no longer displayed any statistically significant effect on MI incidence risk in women. In men, living alone remained

					- Living with someone other (or others) than a partner and living alone	associated with 18% higher risk, and cohabitation with 16% higher risk of MI incidence compared to being married. After full adjustments, odds ratios remained statistically significant for all groups not living with a marital partner, except for women living alone. The highest odds in men were for the group

						living with others, which were nearly twice of those of married men, and for women in the cohabiting group. When all covariates were incorporated to the model, the higher risks of long-term fatality remained statistically significant for men living with others or living alone,

						and for cohabiting women.
Kitamura, T. 2013	Longitudinal	MACE Total deaths	HF, recurrent MI, unstable angina, and stroke Death	Living arrangements	Whether or not participant lived with their family or others	Living alone was found to be independently associated with a higher risk of composite endpoint consisting of MACEs and total deaths (adjusted HR 1.32; 95% CI: 1.11–1.58). In each cardiovascular event, living alone was significantly associated with a higher risk of

						recurrent MI among male patients (adjusted HR 1.71; 95% CI: 1.11–2.64).
Leifheit-Limson, E. C. 2010	Prospective	HRQoL	SAQ – Angina Frequency and Quality of Life subscale	Perceived social support	5 emotional items from ESSI	In models accounting for site, repeated outcome measures over time, and baseline level of outcome, patients with low SS had a significantly greater risk of SAQ AF (RR, 1.43; 95% confidence interval [CI], 1.25, 1.64) and lower mean SAQ QoL (mean

						difference β = -6.21; 95% CI, -8.09, -4.33) than their high SS counterparts. After further risk adjustment, SS remained significantly associated with all outcomes. No significant differences were observed when comparing moderate SS patients with high SS patients.
Leifheit-Limson, E. C.	Prospective	HRQoL	SAQ – Angina Frequency and	Perceived social support	5 emotional items from ESSI at baseline and 1-	In risk-adjusted models comparing the 4 categories of social

2012			Quality of Life subscale		month post-discharge	support changes, patients with worsened support had a greater risk of having angina (defined by SAQ AF) and lower mean SAQ QoL scores than their persistently high support counterparts. Patients with improved support had higher mean SAQ QoL and a marginally reduced risk of having angina ($p = 0.086$) than patients

						with persistently low support.
Leung Yinko, S. S. 2014	Prospective	HRQoL	SAQ	Social support	ESSI	Social support appeared to be particularly important, being statistically significant for physical limitation, and disease perception outcomes.
Liu, L. 2011	Prospective	Mortality	Heart disease as cause of death, ICD-10: I00-I51	Social connections	- Talk on phone with friend/neighbors - Talk on phone with relatives	Among African American and White American adults, an increased lack of social connections score had significantly higher

					- Get together with friends/neighbors - Get together with relative - Go to church or temple services - Go to sports, movies events, etc.	hazard ratios of death from heart disease.
Lu, X. 2019	Cross-sectional	HTN	Mean of the latter two of three measurements; SBP of 140 mmHg or	Social support	Duke-UNC Functional Social Support	Social support had a direct impact on HTN: participants with high social support were

			higher or DBP of 90 mmHg or higher; or use of antihypertensive drugs	Social network	Questionnaire SNI	48% less likely to have HTN compared with those with low social support (OR: 0.52, 95% CI: 0.33, 0.81). SNI score was not significantly associated with HTN.
Menéndez-Villalva, C. 2015	Longitudinal	Cardiovascular mortality Cardiovascular events	Mortality from deaths registry HF, angina pectoris, MI, cerebrovascular accident	Social support Social network	Duke-UNC 11 (modified) Number of social contacts using the Black-McKay Method	Patients with low social networks presented with more CVEs (HR 2.1 (95% CI: 1.1; 4.1)) than those with an adequate social network.

						Low functional social support (HR 2.6 (95% CI: 1.1; 6.1)) was observed to be independently associated with CVE-related mortality.
Meza, B. P. L. 2020	Cross-sectional	BP	Mean SBP and DBP from three measurements	Social network composition Social network density	Proportion of network who were family, friends, older children (age 8–17), female, neighbors, perceived as having HBP,	In the multivariable models, having a high proportion of older children (age 8–17 years) in one's network was associated with a 4.0% (95%CI 0.07, 8.01; $p = 0.05$) higher mean SBP (equal to a

					provided material support Ratio of participant-reported social ties between network members divided by all possible ties between network members	4.9 mmHg (95%CI −0.28, 10.10) difference in non-log transformed analyses) and a 3.7% (95%CI −0.73, 8.34; p = 0.10) higher mean DBP (equal to 3.4 mmHg (95%CI −0.11, 6.91) difference in non-log transformed analyses). Having a high proportion of friends in one's network was associated with a

						−3.6% lower DBP (95%CI −7.64, 0.70; p = 0.10) (equal to −3.1 mmHg in non-log transformed analyses (95%CI −6.55, 0.40)).
Mezuk, B. 2010	Cross-sectional	CV risk markers	Interleukin-6 (IL-6), CRP and fibrinogen, measured via blood sample	Perceived emotional social support	ESSI	In bivariate analyses, low social support was associated with higher levels of all three markers. In adjusted models, low support was associated with higher lnCRP among men but not women.

Mezuk, B. 2016	Cross-sectional	CV risk markers	CRP and fibrinogen, measured via blood sample	Loneliness	UCLA Loneliness Scale	There was no association between feelings of loneliness, measured as either a continuous score or a categorical variable, and CRP, either in unadjusted models or after accounting for demographic characteristics and risk factors. Higher levels of loneliness were associated with lower

						levels of fibrinogen, although associations were of small magnitude.
Miao Jonasson, J. 2020	Longitudinal	CHD	First occurrence of MI, definite silent MI, or death due to definite CHD or possible CHD	Social support Social network size	MOS-SSS - Marital status (married/ in an intimate relationship vs. not) - Club ties (attended clubs/ lodges/groups last	Being married or in an intimate relationship was related to decreased risk of CHD compared with not being married or in an intimate relationship across three models (HRs [95% CI] were 0.80 [0.67–0.95], 0.81 [0.68–0.96], and 0.82

					month; yes vs. no) - Religious ties (yes vs. no)	[0.69–0.97], respectively).
Momtaz, Y. A. 2012	Cross-sectional	HTN	Have you ever been told by a doctor that you have the following chronic medical conditions?	Loneliness	How much do you feel lonely?	HTN is significantly associated with loneliness ($\chi2 = 13.12$, $p \leq .001$). Adjusting for sociodemographic factors and chronic medical conditions, older persons who reported a lot of loneliness (OR = 1.31,

						95% CI = 1.04-1.66) had a significantly higher prevalence of HTN as compared with older person with low level of loneliness.
Nichols, G. A. 2020	Cross-sectional	HF hospitalization	HF hospitalization	Social support	MOS-SSS	Patients with a recent HF hospitalization had significantly lower scores on the KCCQ-12 Quality of Life (52.6 vs. 59.6, p = 0.016) and Social Limitations (48.4 vs. 55.5, p = 0.009) scales as well as the Clinical Summary

						Scale (50.8 vs. 55.3, p = 0.048) and Total KCCQ-12 score (49.6 vs. 56.8, p = 0.003).
Novak, M. 2020	Longitudinal	CV mortality	ICD-10 codes I.00-I.99	Perceived loneliness	Do you feel lonely?	There was no significant increased risk of mortality was observed for men with loneliness compared to men with no loneliness for cardiovascular mortality (HR 1.52 95% CI 0.78–2.96). However, women with loneliness had

						significantly higher risks of cardiovascular mortality compared to women with no loneliness (HR 2.25 95% CI 1.14–4.45).
Nyaaba, G. N. 2019	Cross-sectional	HTN control	A participant on antihypertensive medication with BP < 140/90 mmHg	Social support	- Number of cohabitants - Relationship status - Religious attendance frequency - Satisfaction with social support	Among all males, cohabiting with two persons or less or with 3–4 persons was associated with lower odds of having controlled HTN compared to those cohabiting with five or more persons after

					received (Social Support Scale for Satisfaction with supportive transactions (SSQS))	adjustment for age and SES [odds ratio (OR) 0.30; 95% CI 0.16–0.57; 0.60; 0.34–1.04, respectively].
O'Luanaigh, C. 2012	Cross-sectional	CRP, homocysteine, HbA1c, and lipid profile	CRP, homocysteine, HbA1c, and lipid profile measured via blood samples	Loneliness	Do you feel lonely?	The comparison of means between loneliness and the various vascular biomarkers showed loneliness to be significantly associated with HbA1c ($p<0.005$)

						but not with the other biomarkers.
Otani, A. 2019	Retrospective	MACE	Composite of all cause death, acute MI (AMI), and target vessel revascularization (TVR)	Living status	Living alone or living together	Living alone was significantly associated with the MACE (Odds ratio: 1.770, 95% confidence interval 1.018–3.077, P = 0.043) after known clinical risk factors.
Patterson, A. C. 2010	Longitudinal	Mortality	ICD-9 codes listed on death certificates, categorized as all-cause, from ischemic heart disease, and	Loneliness	How often respondent felt 'very lonely or remote from other people'?	Loneliness did not display a statistically significant effect on mortality from ischemic heart disease. The effect of loneliness

			other cardiovascular disease		Changes in loneliness between current or most recent wave and the preceding wave.	on mortality from other cardiovascular diseases lost significance after controlling for other factors.
Pirkle, C. M. 2018	Longitudinal	HTN awareness HTN control	Self-reported by answer to Has a doctor or nurse ever told you that you have HBP or HTN? Average of the second and third of three BP measurements,	Social network ties and community integration	International Mobility in Aging Study (IMIAS) survey If participant engaged in religious activities, attended	High level of support from friends was significantly negatively associated with uncontrolled (OR: 0.43; 95% CI: 0.21– 0.86) and undiagnosed (OR: 0.23; 95% CI: 0.09–0.60) HTN compared to controlled HTN.

			defined as clinical HTN if ≥140/ 90		community or recreational centre(s) and/or was a member of a professional association.	High support from children was positively associated with uncontrolled (OR: 2.17; 95% CI: 1.09–4.33) and undiagnosed (OR: 3.55; 95% CI: 1.32–9.56) HTN compared to no HTN.
Pushkarev, G. 2019	Prospective	CVD mortality	Death from CV causes within 1 year after surgery	Social Support	MSPSS	Adjusted HR for death from cardiovascular causes on social support score was 0.97 (with 95% CI, 0.94–1.00, p=0.048).

Rodriguez, C. J. 2011	Cross-sectional	Left ventricular mass	Calculated left ventricular mass	Social isolation	How many people do you know well enough to visit with in their homes?	In fully adjusted models, social isolation showed a non-significant trend for predicting increased left ventricular mass in the total cohort. Among Hispanics, left ventricular mass averaged 3.9 gm/m2.7 higher among the more socially isolated Hispanics versus those not socially isolated (p=0.002).

Roohafza, H. 2012	Case-Control	ACS	AMI or unstable angina pectoris based on consensus guidelines	Functional support Network support	Norbeck Social Support Questionnaire	After adjusting for age, sex, and traditional coronary artery disease risk factors, total functional support and network support were significantly associated with ACS.
Saito, H. 2019	Prospective	Rehospitalization due to HF	HF rehospitalization within 90 days after discharge	Social isolation	Lubben Social Network Scale (LSNS-6)	HF rehospitalization within 90 days was significantly higher in the social isolation group (p=0.036). Social isolation was one of the strongest predictors of HF rehospitalization,

						showing larger effects than other established risk factors.
Sanchez-Martínez, M. 2016	Prospective	BP	Mean BP of the last two of three readings Ambulatory systolic blood monitoring over 24 hours, measured at 20 min intervals during the day and 30 min intervals at night	Social support	- Marital status - Cohabitation - Frequency of contact with relatives living apart - Frequency of contact with friends or neighbors - Emotional support, defined as	Being married was significantly associated with lower daytime and nighttime SBP and lower night/day ratio. Not living alone was significantly associated with lower daytime and nighttime SBP. Being accompanied when going out was significantly associated with lower nighttime

					having someone to share confidences, feelings, and problems with, or someone to trust in - Instrumental support, defined as having someone to help at home - Outdoor companionship	SBP and night/day ratio. After full adjustment, 1 additional point in the social support score was associated with a decrease of 0.928 mmHg in nighttime SBP (p=0.039), totaling 2.8 mmHg decrease for a score of 3 versus 0.

					, defined as usually being accompanied when going out	
Smith, P. 2013	Cross-sectional	Atrial natriuretic peptide (ANP)	ANP, measured via blood samples	Social support	ISSI	High social support levels were associated with lower levels of ANP in unadjusted analyses (β= -0.23 [95 % CI 0.05, 0.41], P=0.012, R^2=0.052) and remained significantly associated after

						adjustment (β=-0.23 [95 % CI 0.05, 0.41], P=0.014, Δ R^2=0.048).
Tan, J. 2019	Prospective	Mortality	CVD (I00-I78) and heart disease (I00-I09, I11, I13, I20-I51)	Social support Social integration	- How often do you get the social and emotional support you need? - Past two weeks contacts with relatives or friends, either in person or	In the fully-adjusted model, social support was not associated with CVD mortality: HR = 0.99, 95% CI = 0.93–1.06. For CVD mortality, compared to those in the lowest social integration group, those in the highest social integration group had a

					over the telephone - Past two weeks attending a religious service, a group social activity, or going out to eat - Marital status	33% reduced risk of CVD mortality (HR = 0.67, 95% CI = 0.53–0.86). In the fully adjusted models, the results were similar in magnitude for heart disease mortality (HR = 0.65, 95% CI = 0.49–0.85).
Tillmann, T. 2017	Prospective	Mortality	ICD-10 codes I00-I99	Social support	- Marital status - Are you a member of a club / organization?	Following full adjustment, infrequent contact with relatives, infrequent contact with friends (for female participants only), and

					- How often are you in contact with relatives outside of your household? - How often do you visit friends outside of your household?	single marital status remained associated with the outcome.
Tomfohr, L. M. 2015	Cross-sectional	Inflammatory markers	IL-6, CRP, and TNF-alpha measured via blood samples	Perceived social support	MOS-SSS (modified)	After controlling for covariates, social support was not directly associated with IL-6 or CRP but was

						associated with TNF-alpha in women.
Valtorta, N. K. 2018	Longitudinal	Incident CVD	Fatal events derived from the UK National Health Service Central Register, using ICD-9 codes 390–459 and ICD-10 codes I00–I99; Self-reported non-fatal events including angina, heart attack, CHF, a heart murmur, an abnormal heart	Loneliness Social isolation	Much of the time during the past week, you felt lonely. UCLA Loneliness Scale - Living alone - Less than monthly face-to-face, telephone or written/e-mail	There was no evidence of a cumulative association for loneliness over time: those who reported loneliness twice were not at greater risk of disease compared with those who reported loneliness once only (OR 0.81, 95% CI 0.50–1.32). In the multivariable model adjusting for age,

			rhythm or any other heart trouble		contact with children outside the household - Less than monthly contact with other relatives outside the household - Less than monthly contact with friends not participating in	gender, wealth and social isolation, the association between loneliness and CVD persisted (OR comparing one or more to no report of loneliness 1.28, 95% CI 1.02–1.60). Social isolation was not identified as an independent predictor of CVD risk.

					any organizations, religious groups, or committees - Not currently employed	
Volz, A. 2011	Prospective	Cardiac-related Readmission HRQoL	First cardiac-related unplanned readmission after study entry MLHFQ	Social support	ESSI	Social support was not significantly related to readmission, but was associated with HRQoL
Walter, N. 2019	Cross-sectional	HTN	Average of three BP readings, coded into HTN (defined as	Health-related social network	List up to five people with whom	An increase in health-related social ties was not significantly

			SBP 140 mmHg and/or DBP 80 mm Hg) and non-HTN categories		respondents discuss issues related to health, with relationship role and gender	associated with a reduced likelihood for HTN (OR = .98, p = .748, 95% CI [.81, 1.31]).
Wen, W. 2019	Prospective	Mortality	National Death Index files containing (ICD-10) codes I00–I69	Religious involvement	- How often did you attend religious or faith services during the year? - How spiritual or religious do you consider yourself to be?	Religious involvement was not associated with CV-specific mortality

					- How much is religion, faith, or God a source of strength and comfort to you?	
Whittaker, K. S. 2012	Prospective	CVD event CVD risk factors	CVD event was defined as a composite of non-fatal stroke, nonfatal myocardial infarction (MI), CHF, or death related to CVD	Social Network	SNI	Controlling for disease covariates (age, smoking, history of diabetes, history of obstructive coronary artery disease) attenuated the relationship and Social

			BP, BMI, and presence of metabolic syndrome			Networks (0.74 [0.58–0.95]).
Wiesmaierova, S. 2019	Cross-sectional	ACS disease severity and prognostic indicators	Troponin, ST-elevated myocardial infarction (STEMI), stent implants, obstructed arteries, blood urea nitrogen (BUN), creatinine	Perceived social support	ESSI - items 1-6	There were no significant correlations between social support and STEMI, troponin-I, the number of obstructed arteries, or the number of stents; however, there were significant correlations between social support

						and indicators of renal function (BUN and creatinine).
Wu, C. Y. 2010	Cross-sectional	BP	An average of three seated blood pressure BP readings	Social support	MSPSS	No statistically significant correlations were found between BP and social support scores, except for the “significant others subscale” ($r = -.18$, $p \leq .05$) which was negatively correlated with SBP. No statistically significant associations

						were found between SBP or DBP and social support or subscale of social support after adjusting for age, BMI, education, and income. In the logistic regression analyses, social support was not found to be related to HTN.
Wu, J. R. 2013	Prospective	Cardiac Event-free Survival	Composite endpoint of time to the first occurrence of one of the following events:	Perceived social support	MPSSS	Patients who had lower perceived social support had 1.89 times the risk of experiencing

			cardiac emergency department visits, cardiac hospitalizations, and cardiac mortality			a cardiac event than those patients who had higher support.
Yang, Y. C. 2015	Longitudinal	SBP HTN	Mean readings from each wave BP above the clinical cut points (systolic 140 mmHg or diastolic 90 mmHg) or ever diagnosed with high BP by a medical doctor	Social integration	- Marital status - Religious attendance - Frequency of socializing with family or friends - Frequency of volunteering	Respondents with low and moderate levels of support had greater increases in log SBP than those with the highest level of support, with the increases being the largest for those at the lowest level of support ($\beta = 0.034$, $p = 0.027$).

				Social support	- Frequency of socializing with neighbors - Attendance at organized meetings - How often a respondent can open up to their spouse, family and friends - How often a respondent can rely on their	Compared to the most socially integrated, respondents with the lowest level of integration at Wave 1 had a 75.3% increase (95% CI = [1.04, 2.95], p = 0.036) in risk of HTN across waves.

					spouse, family, and friends	
Zhu, T. 2019	Cross-sectional	HTN	Mean BP, categorized as controlled and uncontrolled (SBP ≥ 130 or DBP ≥ 80 for patients with diabetes mellitus, coronary heart disease or renal disease, and SBP ≥ 140 or DBP ≥ 90 for all others)	Social support	MOS-SSS	Uncontrolled HTN was associated with lower social support ($t[d.f=2349] = 5.37$, $p<0.001$).

Chapter III. An Examination of the Longitudinal Relationship between Social Isolation and Hypertension

Introduction

Hypertension (HTN) is an important and prevalent modifiable risk factor that contributes to cardiovascular disease (CVD) morbidity and mortality.[1] There is substantial risk of adverse cardiovascular outcomes associated with HTN, with increasing odds of CVD-related death as the age of HTN onset decreases.[2] In adults less than 40 years of age, adverse CVD events in later life stages are significantly higher for those with elevated blood pressure (BP) and HTN compared with those with normal BP before the age of 40, and independent of current and later risk factors.[3,4]

Despite billions of dollars spent on medical care associated with HTN, the estimated proportion of adults with controlled BP decreased in recent years to the extent that there was no meaningful difference between the proportion of adults with controlled BP between 2005-2006 and 2017-2018.[5,6] The lack of return on financial investments in medical care is likely attributable to the finding that social determinants, non-medical factors that exist outside of the healthcare ecosystem in the places where people are born, live, work, and age, account for 80-90% of health outcomes.[7] The influence of determinants like socioeconomic status, racism and discrimination, and neighborhood characteristics, on BP has been well-established.[8]

Relationships are a social determinant manifested through two primary constructs: social networks, which describe structural aspects of the relationship, and social support, which reflects

the perceived or actual resources an individual receives through the relationship.[9] The association between social isolation, or the absence or weakness of network ties, and BP or HTN has been studied with mixed results: some studies have shown that more social ties are detrimental to BP while others have found positive effects of ties based on number or and type (marriage).[10-12] Beyond the variability in results, additional limitations of these evaluations include largely cross-sectional datasets, limited follow-up periods, or are conducted in older populations where HTN is more common simply as a function of age. As a result, these studies provide neither direct evidence regarding the long-term impacts of social isolation nor allow exploration of stages across the life-course when individuals may be particularly susceptible to exposure (social isolation) or outcome (HTN).

As such, the purpose of this study is to examine the longitudinal relationship between social isolation and HTN prevalence in early middle adulthood. Using data from a nationally representative study of adolescents followed into adulthood, the following hypotheses are tested:

(1) the association between social isolation in early middle adulthood and hypertension is stronger than the relationship in adolescence;
(2) those who experience persistent social isolation through early middle adulthood are more likely to have HTN than those who are socially connected through the same period; and
(3) those who move into social isolation are more likely to have HTN than those who have no, or limited, exposure to social isolation over time.

Methods

Study Sample

The present study used restricted-use data from the National Longitudinal Study of Adolescent to Adult Health (Add Health), a longitudinal cohort study using a multistage stratified cluster design to recruit a nationally representative sample of more than 20,000 adolescents in grades 7th–12th (aged 12-19) in the United States in 1994–1995. The cohort has been followed through adolescence and into adulthood with in-home interviews across five waves: (Wave I), 1996 (Wave II), 2001–02 (Wave III), 2008–09 (Wave IV) and 2016–18 (Wave V). Additional details of the Add Health design can be found in previous publications.[13]

The analytic sample of this study includes respondents who participated in each in-home interview across Waves I, IV, and V, and provided biomarker data of interest in Wave V. The sample was restricted to those with biomarker sample weights in Wave V to adjust for the different proportion of subjects who have biomarker data as well as non-response and missing data to estimate population-average models.[14,15] Previous studies have found that non-responses are negligible after incorporating post-stratification sampling weights.[16,17] There was one respondent with missing data on the outcome measure. After adjusting for missing sampling design information and accounting for the loss of one respondent, the final analytic sample contained 5,049 observations.

Independent Variable - Social isolation

The measures of social isolation were adapted from the Berkman-Syme Social Network Index (SNI) and consistent with previous research using ADD Health data.[18,19] The SNI, developed by

Berkman and Syme, measures adult social integration as a composite across four domains: marital status, connection with others, religious involvement, and civic participation. Marital status is not a valid measure for adolescents (Wave 1) and may under-represent meaningful adult relationships reflected by cohabitation; therefore, a variable was created to describe similar relationships in each life stage. Adolescents participating in the Add Health study were not asked directly about their number of close friends, however, numerous studies have used friend nominations to document the number and quality of friendships.[20] Religious attendance was documented using identical questions in each wave. Group participation, much like close friendships, differed between adolescent and adult waves due to differing questions. The definitions and cut points for these variables are displayed in Table 1.

For adolescence (grades 7 – 12), young adulthood (ages 24 – 32), and early middle adulthood (ages 33-42) waves, independent 'life stage' measures of social isolation were constructed. Each SNI item was assigned one point if the respondent met the threshold and summed to create a wave-specific index variable with 0 or 1 being the most socially isolated scores and 2, 3, and 4 representing increasing social connectedness. The wave-specific SNI was then used to create a dichotomous measure of social isolation (SI) where individuals were considered socially isolated if the SNI score was 0 or 1 and, if the SNI score was 2, 3, or 4, not socially isolated. To examine whether social isolation patterns are associated with hypertension, eight trajectories were constructed to represent all possible permutations of social isolation from adolescence to early middle adulthood: persistent social isolation or connectedness, social isolation in one wave but not the other two waves, and social isolation in two waves but not the other one wave.

Dependent variable – Hypertension

Data on CVD risk factors were collected for respondents who, at the end of the Wave V survey, agreed to participate in the home exam, between 2016 and 2018, when respondents were between 31 and 42 years of age. Hypertension, the outcome of interest for this analysis, was constructed from four data points collected during the home exam. Respondents were flagged as having HTN if the respondent had EITHER a BP measure classified as HTN stage 1 or 2 based on the Seventh Report of the National Committee on the Detection, Evaluation, and Treatment of High Blood Pressure (JNC7) guidelines OR took an antihypertensive medication in the past 4 weeks OR had ever been diagnosed with HBP or HTN. To construct average BP measures and classify them into stages of HTN, systolic and diastolic blood pressure (SBP and DBP, respectively) were measured once respondents had rested with both feet on the floor and legs uncrossed for five minutes. Three measurements were taken at 30-second intervals, with the last two measures used to calculate average BPs. If either of the last two measures were missing, the single available measure; in the event both were missing, the first BP measure was used. Based on the average measures, respondents were classified as having stage 1 HTN if SBP 140-159 millimeter of mercury (mmHg) or DBP 90-99 mmHg or stage 2 HTN if SBP $\geq$ 160 mmHg or DBP $\geq$ 100 mmHg. Respondents were asked 'Has a doctor, nurse, or health care provider ever told you that have any of the following? A. High blood pressure or hypertension' and 'Have you taken any prescription medications the last four weeks?' to determine HTN diagnosis status and use of antihypertensive medications.[21,22]

Confounders

Respondent-level demographic and health variables, along with parent-level socioeconomic status indicators, were included as potential confounders. Age (at Wave V) was constructed based on complete interview dates and date of birth month/year and 15 as the universal assigned day of birth. Sex was documented by the interviewer during the Wave I in-home interview (male = 1; female = 0). Race/ethnicity categories were created using two Wave I self-report questions about respondents' Hispanic or Latino origin and race (non-Hispanic White = 0; non-Hispanic Black = 1; Hispanic = 2; non-Hispanic Asian = 3; non-Hispanic American Indian/other = 4).[23] The variable, US nativity (yes = 1; no = 0), is based on the Wave I question, 'Were you born in the US?'. Self-reported health in adolescence was categorized by the respondent's response to 'In general, how is your health? Would you say…' (excellent, very good, good = 1; fair or poor = 0). Lack of health insurance was assessed in Wave V by asking respondents to describe their current health insurance situation (any health insurance = 1; no health insurance = 0). Parent-level socioeconomic status was used to describe socioeconomic status in adolescence using the highest level of school completed (less than bachelor's degree = 0; bachelor's degree or higher = 1) of the mother or other female head of household and family income (at or below federal poverty level (FPL) for a family of four in 1995 = 1; above the FPL = 0),

Statistical Analysis

Descriptive characteristics of the analytic sample are presented as means (standard error, SE) for continuous variables and count (%) for categorical variables. The association of timing, duration, and transitional patterns of social isolation with HTN in early middle adulthood were examined using simple and multiple binary logistic regression models. Multiple binary logistic regression

models were adjusted for demographic variables, adolescent socioeconomic, and health-related confounders. Analyses were performed with SAS 9.4 (SAS Institute, Cary, NC), incorporating survey design and unequal probability of selection per Add Health user guidance.[24] Statistical significance is defined as a *p*-value < 0.05.

Results

The characteristics of the analytic sample are presented in Table 2. There was a higher proportion of males (60.45% vs 43.62%), non-Hispanic Blacks (22.54% vs 13.21%), and families living at or below the federal poverty level during the respondent's adolescent years (30.72% vs 25.58%) in the HTN group. Although most respondents in both groups reported excellent, very good, or good health in adolescence, fewer with HTN did so (90.15% vs 94.61%). Social isolation was higher in all life stages among individuals with HTN (adolescence: 37.91% vs 35.35%, young adulthood: 51.48% vs 44.03%, and early middle adulthood: 61.42% vs 51.75%). Similarly, the HTN group had lower mean SNI scores in adolescence (0.94 vs 1.03), young adulthood (0.70 vs 0.84), and early middle adulthood (0.55 vs 0.71).

Wave-specific Social Isolation

The results for wave-specific social isolation and HTN are presented in Table 3. Neither social isolation measure in adolescence (Wave I) was significant (SNI OR = 0.961, 95% CI = [0.879–1.052]; SI OR = 0.976, 95% CI = [0.803 – 1.185]). After controlling for potential confounders, increased social connectedness in young adulthood (Wave IV) and early middle adulthood (Wave V) was protective against HTN in early middle adulthood (SNI OR = 0.861, 95% CI = [0.774 – 0.958]; SNI OR = 0.812, 95% CI = [0.714 – 0.924], respectively). Similarly, those who

were socially isolated in young adulthood or early middle adulthood had greater odds of having HTN in early middle adulthood than those who were not socially isolated (SI OR = 1.294, 95% CI [1.072 – 1.561]; SI OR 1.424 [1.153 – 1.758], respectively).

Social Isolation Patterns

Results for SI patterns and HTN in early middle adulthood are presented in Table 4. After controlling for demographic, adolescent socioeconomic, and general health variables, HTN in early middle adulthood was significantly associated with persistent SI across all life stages – adolescence, young adulthood, and early middle adulthood SI OR = 1.399, 95% CI = [1.016 – 1.927]). Similarly, individuals who moved into persistent SI after adolescence were significantly more likely to have HTN in early middle adulthood (SI OR = 1.607, 95% CI = [1.179 – 2.190]). The relationship between HTN and movement into SI in early middle adulthood was of marginal significance across all models (SI OR = 1.358, 95% CI = [0.991 – 1.861]).

Discussion

Using a longitudinal design, the present study identifies social isolation trends over time and establishes temporal relationships between social isolation and HTN in early middle adulthood. The findings broadly support the three relational hypotheses of social isolation and HTN in early middle adulthood: the life stage hypothesis where the effect of social isolation would be strongest in early middle adulthood, the duration hypothesis in which those with persistent social isolation would be more likely to have HTN than those without, and the transitional pattern hypothesis by which movement into social isolation would be associated with greater odds of HTN than limited, or no, social isolation throughout the life course.

An increase in the prevalence and degree of social isolation over each life stage is observed, for which there are plausible life course explanations. On the one hand, individuals tend to self-select into smaller networks as they age, preferring fewer, more meaningful relationships over more contacts.[25] On the other hand, life events associated with specific life stages may necessitate smaller networks, e.g. family and career investments occurring during the early and middle adulthood life stages may lead to decreased involvement in activities like volunteering to maintain or expand their social networks.[26]

There is no evidence for an association between HTN in early middle adulthood and adolescent social isolation; however, social isolation and the degree to which individuals are socially isolated in each stage of adulthood is strongly associated with HTN in early middle adulthood. The lack of association between social isolation in adolescence and HTN in early adulthood has been found in other studies using the Add Health dataset.[27,28] However, these studies did not find a significant relationship between social isolation in later life stages and HTN; perhaps because the outcome of interest, HTN, was measured in wave IV, when Add Health respondents were younger and had lower rates of HTN, or the variation in social isolation measures may have diluted the strength of the relationship.

From a life course perspective, two duration and transition patterns of social isolation are significantly associated with the likelihood of HTN in early middle adulthood: those who were persistently socially isolated throughout adulthood and those who moved from social connectedness in adolescence into social isolation across both life stages of adulthood. (The

relationship between social isolation in early middle adulthood and HTN reached moderate statistical significance, noted in the results but not warranting substantive explanations). To our knowledge, these results are the first to describe the longitudinal relationship of social isolation patterns and HTN in a younger population, as most studies are of limited follow-up or in older populations.[29-31]

There are several limitations to consider when reviewing the findings of this study. First, there was insufficient data available in wave III to create repeated social isolation measures across the life course; as such, the formative years between the ages of 18-26 were not accounted for in this analysis. Second, social isolation was assessed using a validated measure used commonly in social capital research. However, the SNI is largely a measure of structural components and does not measure the quality of existing relationships. It is possible that, even with large networks, individuals may feel lonely and experience adverse health consequences as result. Lastly, social isolation was evaluated as a composite variable, without considering the independent contributions of each observed variable to the individual social isolation status.

Despite any limitations, the findings of this study contribute substantively to understanding when and how social isolation matters to the development of HTN in early middle adulthood. The time horizon for social isolation and HTN are important considerations, both of which can only be truly understood using a life course approach. Social relationships take time to develop and confer health benefits; likewise, HTN develops after longstanding elevated BP and exerts negative effects in later life stages. As such, the life course approach of this analysis provides

insights regarding appropriate timing for effective interventions that reduce the incidence of HTN earlier and, possibly, other adverse CV-related health outcomes later in life.

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Tables and Figures

Table 1. Definitions and Cut Points for Social Network Index Variables				
Life Stage (Wave)	**Living Arrangements**	**Close Friends**	**Religious Attendance**	**Group Participation**
Adolescence (Wave I)	Living with two parents[32]	6 or more friend nominations	Religious attendance at least once a month (=12 or more times each year)	Participated in any clubs, organizations, or teams at school
Early adulthood (Wave IV)	Married or living with romantic or sexual partner	6 or more close friends	Religious attendance at least once a month (=12 or more times each year)	Volunteered at least one hour in the past 12 months
Early middle adulthood (Wave V)	Married or living with romantic or sexual partner	6 or more close friends	Religious attendance at least once a month (=12 or more times each year)	Volunteered at least one hour in the past 12 months

Table 2. Descriptive Characteristics of Adolescents enrolled in Grade 7-11 during 1994-1995 interviewed in 1995 (Wave I), 2008 (Wave IV), & 2018 (Wave V), National Longitudinal Study of Adolescent to Adult Health (Add Health), n (%) or mean (SE)			
	Total sample (N = 5,050)	**Respondents without evidence of hypertension (n = 3,523)**	**Respondents with evidence of hypertension (n = 1,526)**
Demographic Variables			
Age	37.20 (0.12)	37.04 (0.13)	37.50 (0.13)
Male	2006 (49.14%)	1227 (43.62%)	778 (60.45%)
Race / Ethnicity			
Non-Hispanic White	3143 (68.43%)	2233 (70.55%)	909 (63.98%)
Non-Hispanic Black	964 (16.24%)	579 (13.21%)	385 (22.54%)
Hispanic	572 (10.40%)	435 (11.03%)	137 (9.11%)
Non-Hispanic Asian	293 (3.38%)	223 (3.79%)	70 (2.53%)
Non-Hispanic Native American / Other	70 (1.55%)	48 (1.41%)	22 (1.84%)
US nativity	4754 (95.04%)	3298 (94.74%)	1455 (95.67%)
Adolescent Socioeconomic Variables			
Parent education - bachelor's degree or higher	3889 (76.68%)	2746 (77.54%)	1142 (74.85%)

Family income - At or below federal poverty level, 1995 (family of four; ≤ $15,000)	1227 (27.32%)	798 (25.58%)	428 (30.72%)
Health-related Variables			
Self-reported health in adolescence (good, very good, and excellent)	4710 (93.16%)	3325 (94.61%)	1384 (90.15%)
Health insurance coverage	4670 (91.88%)	3282 (92.04%)	1387 (91.52%)
Social Isolation Variables			
Wave I			
Social Network Index	1.00 (0.04)	1.03 (0.04)	0.94 (0.04)
Social Isolation	1636 (36.10%)	1105 (35.25%)	531 (37.91%)
Wave IV			
Social Network Index	0.80 (0.02)	0.84 (0.03)	0.70 (0.03)
Social Isolation	2181 (46.43%)	1454 (44.03%)	727 (51.48%)
Wave V			
Social Network Index	0.66 (0.02)	0.71 (0.03)	0.55 (0.04)
Social Isolation	2564 (54.85%)	1698 (51.75%)	866 (61.42%)
Hypertension Variables			

Systolic blood pressure	123.66 (0.35)	117.75 (0.27)	135.82 (0.58)
Diastolic blood pressure	80.18 (0.26)	75.70 (0.18)	89.41 (0.43)
Took antihypertensive medication within last 4 weeks	608 (12.84%)	-	608 (39.60%)
Has ever been diagnosed with high blood pressure or hypertension	937 (19.89%)	-	937 (61.40%)

Table 3. Associations Between Wave-Specific Social Isolation Measures and Evidence of Hypertension, Odds Ratios (95% CI)

	Model 1	**Model 2**	**Model 3**	**Model 4**
Social Isolation Measure				
Wave 1				
Social Network Index	0.890 (0.813 – 0.974)*	0.930 (0.853 – 1.014)	0.936 (0.856 – 1.023)	0.961 (0.879 – 1.052)
Social Isolation	1.122 (0.927 – 1.358)	1.028 (0.850 – 1.242)	1.026 (0.846 – 1.244)	0.976 (0.803 – 1.185)
Wave IV				
Social Network Index	0.833 (0.758 - 0.915)**	0.838 (0.759 - 0.925)**	0.848 (0.764 - 0.940)**	0.861 (0.774 - 0.958)**
Social Isolation	1.348 (1.134 - 1.602)**	1.322 (1.106 - 1.580)**	1.330 (1.111 - 1.592)**	1.294 (1.072 - 1.561)**
Wave V				
Social Network Index	0.786 (0.694 - 0.890)**	0.787 (0.693 - 0.894)**	0.799 (0.704 - 0.907)**	0.812 (0.714 - 0.924)**
Social Isolation	1.484 (1.217 - 1.811)**	1.484 (1.210 - 1.820)**	1.461 (1.187 - 1.800)**	1.424 (1.153 - 1.758)**

*p<0.05, ** p<0.01
Note: Associations between wave-specific social isolation and hypertension were estimated using binary logistic regression. Model 1 is unadjusted. Model 2 adjusts for demographic variables (age, sex, race / ethnicity, and US nativity). Model 3 adjusts for variables in Wave 2 and adolescent socioeconomic status (parental education and family income). Model 4 adjusts for variables in both Model 2 and 3 along with general health variables (adolescent health status and health insurance coverage).

Table 4. Associations Between Social Isolation Patterns and Evidence of Hypertension, Odds Ratios (95% CI)						
Life Stage			**Model 1**	**Model 2**	**Model 3**	**Model 4**
Adolescence	**Young Adulthood**	**Early Middle Adulthood**				
0	0	0	1.00	1.00	1.00	1.00
I	0	0	1.049 (0.751 - 1.465)	0.957 (0.673 - 1.362)	1.032 (0.710 - 1.498)	1.040 (0.714 - 1.515)
0	I	0	1.092 (0.760 - 1.568)	1.044 (0.714 - 1.525)	1.050 (0.722 – 1.527)	1.063 (0.728 – 1.551)
0	0	I	1.313 (0.969 - 1.780)*	1.342 (0.984 - 1.830)*	1.349 (0.984 - 1.849)*	1.358 (0.991 - 1.861)*
I	I	0	1.049 (0.709 – 1.553)	1.035 (0.707 – 1.514)	1.061 (0.728 - 1.546)	1.026 (0.685 - 1.537)
I	0	I	1.230 (0.833 - 1.816)	1.180 (0.782 - 1.783)	1.110 (0.730 - 1.688)	1.058 (0.704 - 1.592)

0	I	I	1.533 (1.145 - 2.054)***	1.580 (1.165 - 2.141)***	1.599 (1.072 - 2.009)***	1.607 (1.179 - 2.190)***
I	I	I	1.637 (1.203 - 2.229)***	1.480 (1.078 – 2.030)**	1.468 (1.072 – 2.009)**	1.399 (1.016 – 1.927)**
0 = not isolated, I = isolated						
*p<0.10, **p<0.05, ***p<0.01						
Note: Associations between wave-specific social isolation and hypertension were estimated using binary logistic regression. Model 1 is unadjusted. Model 2 adjusts for demographic variables (age, sex, race / ethnicity, and US nativity). Model 3 adjusts for variables in Wave 2 and adolescent socioeconomic status (parental education and family income). Model 4 adjusts for variables in both Model 2 and 3 along with general health variables (adolescent health status and health insurance coverage).						

Chapter IV. Race/Ethnicity, Hypertension, and Social Connections: A Mediation Analysis

Introduction

Cardiovascular disease (CVD) is the leading cause of morbidity and mortality across the globe, with nearly three-fourths of CVD cases and deaths attributed to modifiable risk factors.[1,2] In the United States, hypertension (HTN) is a predominant and costly CVD risk factor: almost half of all adults have HTN, defined as systolic blood pressure (SBP) $\geq$ 130 mmHg, a diastolic blood pressure (DBP) $\geq$ 80 mmHg, or taking anti-hypertensive medications, and costs, on average, $131 billion each year.[3,4]

The burden of HTN and occurrence of CVD-related adverse health outcomes is heavier on minority populations living in the United States. When compared to Whites, African Americans / Blacks have significantly higher mean DBP and nearly double the prevalence of hypertension (HTN).[5] Hypertension control leads to a lower incidence of CVD and death; however, HTN control rates are 7-8% lower for non-Hispanic Black adults than non-Hispanic White adults.[6] Moreover, excess Black mortalities have been directly attributed to racial disparities in blood pressure (BP) control.[7]

Because significant investments across the US healthcare ecosystem have failed to address racial disparities in CVD-related health outcomes, non-medical factors have been identified as potential explanatory factors as to why these disparities persist. Social relationships are one of those factors, described as the social networks which provide the structure through which social support, the provision of perceived or actual resources, is received and delivered.[8] Studies that

have sought to understand the role of social relationships and connection in HTN differences between Blacks and Whites have been inconsistent: some have been shown to significantly and positively modify the effect of race on HTN prevalence while others have not found such an association.[9-11] Regardless, the cross-sectional design of these and other studies fail to account for various forms of social connections and the importance of timing and/or duration of social relationships in the realization of the protective health-related benefits they confer.

To that end, the purpose of this study is to determine whether the association between race/ethnicity and HTN in early middle adulthood differs by social connection measures. Using data from a nationally representative study of adolescents followed into adulthood, we test the hypotheses that non-Hispanic Black/White differences in HTN are attenuated when social connections are considered, and the effect is greater when social connectedness is persistent across adulthood.

Methods

Study Sample

Restricted-use data from the National Longitudinal Study of Adolescent to Adult Health (Add Health), a longitudinal cohort study of a nationally representative sample of more than 20,000 adolescents in grades 7th–12th (aged 12-19) in the United States in 1994–1995, was used for this analysis. The cohort has been followed from adolescence into adulthood with a series of in-home interviews across five waves: 1995 (Wave I), 1996 (Wave II), 2001–02 (Wave III), 2008–09 (Wave IV) and 2016–18 (Wave V). Additional details of the Add Health design can be found in previous publications.[12]

The analytic sample of this study included Black and White respondents who participated in the in-home interviews across Waves I, IV, and V and agreed to participate in the home exam where outcome-related data were collected. The sample was restricted to those with complete sampling weights in Wave V to account for the different proportion of respondents with biomarker data and adjust non-response and missing data to estimate population-average models.[13,14] Previous studies have found that non-responses are negligible after incorporating post-stratification sampling weights.[15,16] There were approximately 604 respondents excluded due to item non-response on the outcome variable (6.1% non-Hispanic Black, 13.9% non-Hispanic White), resulting in a final analytic sample of 4,107 respondents.

Independent Variable – Race/Ethnicity

Race/ethnicity was identified using two Wave I self-report questions about respondents' Hispanic or Latino origin and race. Respondents were first asked about Hispanic or Latino origin and, for affirmative responses, were marked as Hispanic and eliminated from other race categories. When identifying race, respondents were able to select more than one answer; however, they were placed in only one category based on the following prioritization: (1) Black or African American, (2) Asian or Pacific Islander, (3) American Indian or Native American, and (4) White.[17] For the purposes of this analysis, race was coded as a dichotomous variable: race as non-Hispanic Black or African American = 1 and non-Hispanic White = 0.

Dependent variable – Hypertension

CVD risk factors were collected when ADD Health respondents were between 31 and 42 years of age (Wave 5), through anthropometric measurements and biospecimen collection. For the purposes of this analysis, HTN is used to estimate CVD risk on the basis that, of all modifiable risk factors, it is associated with the strongest evidence of causation.[18,19] Respondents were flagged as having hypertension if the respondent had EITHER a blood pressure measure classified as hypertension stage 1 or 2 based on JNC7 OR took an antihypertensive medication in the past 4 weeks OR had ever been diagnosed with high blood pressure or hypertension.[20,21]

Mediating Variables - Social Connections

The measures of social connection were adapted from the Berkman-Syme Social Network Index (SNI) and informed by previous research using Add Health data.[22-24] The SNI is a composite measure of social connectedness: marital status, sociability, church group membership, and membership in other community organizations. While other studies have looked at the relationship of the composite measure and CVD measures, the current analysis decomposes the index to evaluate the individual contribution of each measure on the association of race/ethnicity and HTN in early middle adulthood.

Because marital status may under-represent meaningful adult relationships reflected by cohabitation, a variable was created to include living with a romantic or sexual partner in the affirmative marital status group. Sociability was measured using the response to ‘How many

close friends do you have?', where less than six friends were coded as '0' and six or more friends as '1'. Religious attendance was coded as '1' if respondents attended religious services once or more each month. Similarly, group participation was coded as '1' if respondents volunteered at least once in the last year.

Confounding Variables

Demographic and adolescent socioeconomic variables were included as potential confounders. Age was assessed in Wave V using complete interview dates and birth months/years with a universal birth day of 15 and reported as a continuous variable. Sex was documented in Wave I via interviewer assessment or inquiry; male =1, female = 0). Health insurance status was assessed in Wave V by asking respondents to describe their current health insurance situation; any health insurance = 1, no health insurance = 0. Lower socioeconomic status in childhood and adolescence is associated with increased risk and prevalence in HTN among African Americans and may account for Black/White differences in HTN rates.[25,26] Maternal education (Bachelor's degree or higher = 1) and family income (at or below federal poverty level = 1) were used to account for socioeconomic status in adolescence.

Statistical Analysis

Descriptive statistics are reported as means and standard error (SE) and percentages by race/ethnicity. The association of race/ethnicity (non-Hispanic Blacks compared to non-Hispanic

Whites) with the outcome of interest, HTN, and each social support measure was calculated using binary logistic regression models. Because both mediator and outcome were binary, causal mediation analysis was conducted using PROC CAUSALMED to quantify the total, direct, and indirect effects of social support on the relationship between race/ethnicity and HTN.[27,28] The directed acyclic graph of relationships among these variables is depicted in Figure 1. Standard errors for the regression coefficients were computed using percentile bootstrapping. Potential confounders used in the main effects models were used in the mediation analysis. The proportion of the total effect attributed to mediation was also calculated. Sensitivity analyses were conducted to determine the effect of persistent social support across young and early middle adulthood. All statistical procedures were performed using SAS 9.4 (SAS Institute, Cary, NC), incorporating survey design and unequal probability of selection per Add Health user guidance.[29]

Results

The characteristics of respondents included in the analysis are in Table 1. Compared to non-Hispanic Whites, non-Hispanic Blacks had lower rates of health insurance coverage (87.19% vs 93.56%) and lower adolescent socioeconomic status, measured by lower maternal education status (68.96% vs 82.09%) and higher rates of poverty-level family income (45.96% vs 20.77%). Social connection was lower for non-Hispanic Blacks across three of the four measures; religious attendance was the only measure where non-Hispanic Whites had significantly lower rates (30.46% vs 39.71%). There was a higher prevalence of HTN among non-Hispanic Blacks (45.20% vs 30.48%), with each defining factor higher than that of non-Hispanic Whites.

Race/Ethnicity Associations

Table 2 shows the association of race/ethnicity with HTN and social connection measures. After adjusting for demographics and adolescent socioeconomic status, non-Hispanic Blacks were more likely to have HTN than non-Hispanic Whites (OR = 1.827; 95% CI = [1.415 – 2.360]). Non-Hispanic Blacks were more likely than non-Hispanic Whites to have attended religious services more than once each month over the past year (OR = 1.513; 95% CI = [1.117 – 1.952]); however, they were less likely to be married or living with a romantic or sexual partner or have six or more close friends (OR = 0.383; 95% CI = [0.294 – 0.500] and OR = 0.625; 95% CI = [0.393 - 0.995], respectively). Similarly, non-Hispanic Blacks were less likely to have volunteered more than once over the last 12 months than non-Hispanic Whites; however, that relationship was attenuated after accounting for demographics and adolescent socioeconomic status (OR = 0.870; 95% CI = [0.674 – 1.123]).

Mediation Analyses

Given the association between race/ethnicity and both HTN and social connection measures, mediation analyses were conducted to better understand the mechanisms by which social connection in early middle adulthood intervenes in the relationship between race/ethnicity and HTN (Table 3). The indirect effects of two early middle adulthood social support measures – married or living with a romantic or sexual partner and volunteering more than once within the past year – were statistically significant, indicating that each of these measures partially mediated the relationship between race/ethnicity and HTN (β = 0.1112, bootstrap SE = 0.0332 β = 0.0277, bootstrap SE = 0.0126, respectively). Being married or living with a romantic or sexual partner

in early middle adulthood was the largest mediating factor, accounting for 17.58% of the higher risk of HTN among non-Hispanic Blacks in the fully adjusted model.

Sensitivity Analyses

All measures of persistent social connection across young and early middle adulthood partially explained racial differences in HTN (Table 4). Being married or living with a romantic or sexual partner remained in young and early middle adulthood remained the largest mediating factor (proportion mediated = 9.09%); however, this indirect effect was attenuated in the full model ($\beta = 0.0575$; bootstrap SE = 0.0317; $p = 0.0563$). Having six or more close friends in both adult life stages, as compared to early middle adulthood, explained a significant and larger proportion of the racial differences in HTN (3.03% vs 2.13%). Similarly, attending religious services more than once a month in young and early middle adulthood had a stronger, inconsistent mediating effect on observed non-Hispanic Black/White differences in HTN (-5.74% vs -2.45%). The proportion mediated by volunteering across adult life stages was similar to that in early middle adulthood alone (4.29% and 3.57%, respectively).

Discussion

There is a substantial amount of research documenting racial/ethnic disparities in the prevalence of HTN among adults in the US.[30,31] The current study provides additional evidence of Black-White disparities in HTN prevalence: HTN rates in early middle adulthood were nearly 15% higher in non-Hispanic Blacks, conferring an 82.7% increase in the likelihood of HTN when compared to non-Hispanic Whites. Similarly, differences found in this study regarding social connection measures between non-Hispanic Blacks and non-Hispanic Whites support the

findings of previous studies, where non-Hispanic Blacks report lower rates of marriage and volunteering, fewer friends, and higher rates of religious involvement.[32,33] Moreover, these studies and others have found similar effects of social connections on racial disparities in HTN.[9,32,33] Few studies, however, have examined the timing and/or duration of social connection may have on the relationship between race/ethnicity and HTN. In that regard, this study expands the current literature.

The most robust effect was being married or living with a romantic or sexual partner in early middle adulthood, to which nearly 20% of the relationship between race/ethnicity and HTN in this life stage could be attributed. The strength of this relationship contributes new data in support of prior studies' results documenting racial differences in marriage/cohabitation and CV-related health outcomes.[9,34] The observed magnitude of this relationship warrants deeper investigation in the context of Black-White differences in marriage trends, where non-Hispanic Blacks are less likely to be married prior to age 40 and more likely to be divorced at any given age, and potential explanations rooted in structural disadvantage.[35]

While not significant in early middle adulthood alone, having six or more friends and attending religious services at least once a month over the past year on the relationship between race/ethnicity and HTN in early middle adulthood demonstrated significant mediation effects across both adult life stages. Regarding regular religious attendance, there was an inconsistent mediation effect which occurs when at least one mediated effect has a different sign than other or direct effects.[36] To explain, non-Hispanic Blacks were more likely to have HTN than non-Hispanic Whites (i.e. positive direct effect). In a similar manner, non-Hispanic Blacks were more

likely to regularly attend church services (positive effect a); however, based on previous evidence, regular attendance of religious services decreases the likelihood of HTN (negative effect b). Because religious engagement has been linked to improved health care practices, e.g. annual BP screenings, and lower ambulatory BP among African Americans, interventions that encourage integrated preventive activities in religious settings may be successful in reducing Black-White differences in HTN rates.[37,38]

There are some limitations that deserve mention. First, a critical assumption of causal mediation analysis is that there are no unmeasured confounders and, when this assumption is violated, causal mediation effects may be under- or overestimated.[39] It is unlikely that every possible confounder has been measure and adjusted in the present study. Second, the current study assessed social integration measures which reflect the quantity of social connections rather than the quality of social interactions that would have been captured using social support measures. Research has shown that as individuals age, the size of their networks decrease in size towards a preference for fewer, more meaningful relationships.[40] Furthermore, the quality of close relationships like marriage have been linked directly to BP control and other related health outcomes.[41,42] Third, and lastly, the social connection measures examined in this study did not fully explain the observed racial/ethnic differences in early middle adulthood HTN. While this study was focused on social connection-related mechanism, there is evidence to suggest that other behavioral and clinical mediators that may explain a larger portion of the relationship.[43,44]

Conclusions

The results of this study confirm existing knowledge and extend the evidence regarding the importance of social relationships in CVD and racial disparities. In this study, non-Hispanic Blacks had significantly higher odds of HTN than non-Hispanic Whites in early middle adulthood. Being married or living with a partner significantly mediated this relationship, accounting for more of the association between race/ethnicity and HTN in early middle adulthood than other social connection measures. The accumulation of social connectedness by way of close friendships and regular religious attendance, across young and early middle adulthood, mediated a larger portion of racial differences in HTN than that of those connections in early middle adulthood alone. Further investigation into upstream causes for lower social connection in non-Hispanic Blacks and interventions that promote increased social integration.

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Figures and Tables

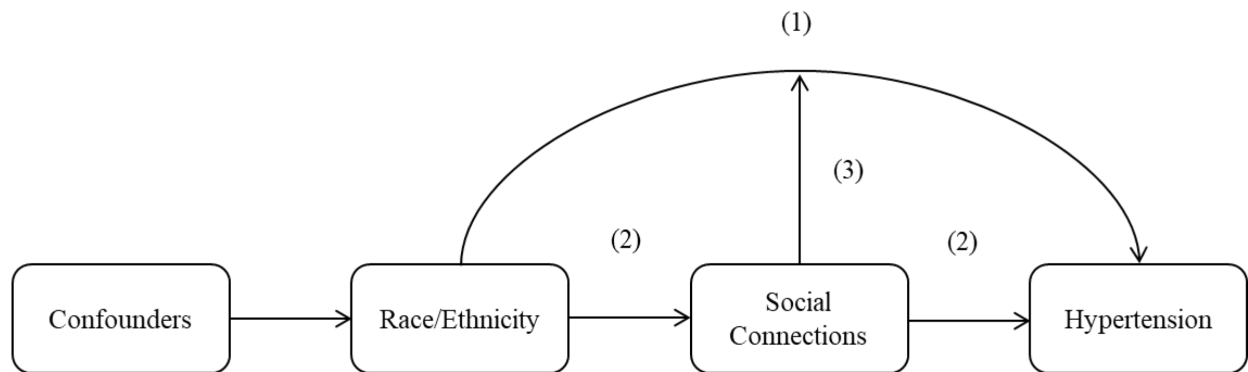

Figure 1. Conceptual framework of the mediation analysis. (1) Direct effect of race/ethnicity on hypertension; (2) Indirect effect via social connections; (3) Total effect, whereby social connections modify the association between race/ethnicity and hypertension. Confounders: age, sex, health insurance status, parental education, family poverty in adolescence.

Table 1. Descriptive Characteristics of non-Hispanic White and Black Respondents in the Analytic Sample, Wave V of the National Longitudinal Study of Adolescent to Adult Health (Add Health), n (%) or mean (SE)

	non-Hispanic White (n = 3143)	**non-Hispanic Black (n = 964)**
Demographics		
Age	37.10 (0.14)	37.58 (0.23)
Male	1299 (48.90%)	305 (46.90%)
Health insurance coverage	2961 (93.56%)	842 (87.19%)
Adolescent socioeconomic status		
Parent education - bachelor's degree or higher	2655 (82.09%)	680 (68.96%)
Family income - at or below federal poverty level, 1995 (family of four; ≤ $15,000)	538 (20.77%)	364 (45.96%)
Social connection		
Married or living with a romantic or sexual partner	536 (16.37%)	88 (10.10%)
Six or more close friends	1898 (58.32%)	453 (46.77%)
Attends religious services ≥ 1 time each month	981 (30.46%)	430 (39.71%)
Volunteered ≥ 1 time over the past 12 months	1464 (42.04%)	390 (36.89%)
Hypertension	909 (30.48%)	385 (45.20%)

Systolic blood pressure	122.95 (0.38)	129.07 (0.93)
Diastolic blood pressure	79.70 (0.27)	83.71 (0.65)
Took antihypertensive medication within last 4 weeks	335 (11.01%)	184 (21.29%)
Has ever been diagnosed with high blood pressure or hypertension	517 (17.21%)	269 (31.72%)

Table 2. Non-Hispanic Black/White Associations with Hypertension and Social Support in Early Middle Adulthood, Odds Ratios (95% CI)

	Model 1	**Model 2**	**Model 3**
Outcome			
Hypertension	1.881 (1.547 - 2.288)****	1.810 (1.457 - 2.250)****	1.827 (1.415 - 2.360)****
Mediators			
Married or living with a romantic or sexual partner	0.359 (0.280 - 0.460)****	0.373 (0.290 - 0.480)****	0.383 (0.294 - 0.500)****
Six or more close friends	0.574 (0.376 - 0.875)**	0.576 (0.374 - 0.885)**	0.625 (0.393 - 0.995)*
Attends religious services ≥ one time each month	1.504 (1.166 - 1.940)***	1.527 (1.186 - 1.966)***	1.513 (1.117 - 1.952)***
Volunteered ≥ one time over the past 12 months	0.806 (0.643 - 1.009)*	0.804 (0.637 - 1.014)*	0.870 (0.674 - 1.123)

*p<0.1, **p<0.05, ***p<0.01, ****p<0.0001

Note: Associations between predictor (race) and outcome (hypertension) and predictor (race) and mediators (social support measures) were estimated using binary logistic regression. Model 1 is unadjusted. Model 2 adjusts for demographic variables (age, sex, and health insurance status). Model 3 adjusts for the variables in Model 2 along with adolescent socioeconomic variables (parent education and family income).

Table 3. Mediation Analysis of Middle Adulthood Social Support Measures and the Association between Race/Ethnicity and Hypertension, Excess Relative Risk (β (Bootstrap SE)) and Proportion Mediated (%)

	Model 1				Model 2				Model 3			
	B	**SE**	***p*-value**	**%**	**β**	**SE**	***p*-value**	**%**	**β**	**SE**	***p*-value**	**%**
Married or living with a romantic or sexual partner (Wave V, n = 2359)												
Total Effect	0.6265	0.1310	<0.0001		0.7008	0.1454	<0.0001		0.6327	0.1424	<0.0001	
Direct Effect	0.5045	0.1245	<0.0001		0.5784	0.1409	<0.0001		0.5215	0.1361	<0.0001	
Indirect Effect	0.1220	0.0003	0.0003		0.1224	0.0346	0.0006		0.1112	0.0332	0.0008	
Proportion Mediated				19.47				17.47				17.58
Six or More Close Friends (Wave V, n = 579)												
Total Effect	0.6305	0.1313	<0.0001		0.7047	0.1391	<0.0001		0.6371	0.1399	<0.0001	
Direct Effect	0.6192	0.1303	<0.0001		0.6886	0.1384	<0.0001		0.6235	0.1388	<0.0001	

Indirect Effect	0.0113	0.0127	0.3570		0.0161	0.0118	0.1719		0.0136	0.0108	0.1977	
Proportion Mediated				1.79				2.29				2.13
Attended Religious Services At Least One per Month for the Past Year (Wave V, n = 1310)												
Total Effect	0.6251	0.1299	<0.0001		0.6948	0.1452	<0.0001		0.6283	0.1421	<0.0001	
Direct Effect	0.6466	0.1326	<0.0001		0.7110	0.1482	<0.0001		0.6437	0.1442	<0.0001	
Indirect Effect	-0.0215	0.0149	0.1623		-0.0162	0.0160	0.3122		-0.0154	0.0176	0.3630	
Proportion Mediated				-3.44				-2.33				-2.45
Volunteered More than Once within Past Year (Wave V, n = 1743)												
Total Effect	0.6431	0.1295	<0.0001		0.7144	0.1434	<0.0001		0.6451	0.1440	<0.0001	

Direct Effect	0.6038	0.1260	<0.0001		0.6757	0.1388	<0.0001		0.6174	0.1413	<0.0001	
Indirect Effect	0.0393	0.0140	0.0047		0.0387	0.0142	0.0049		0.0277	0.0126	0.0232	
Proportion Mediated				6.11				5.42				4.29
Note: Model 1 is unadjusted. Model 2 adjusts for demographic variables (age, sex, and health insurance status). Model 3 adjusts for variables in Model 2 and adolescent socioeconomic variables (parent education and family income).												

Table 4. Sensitivity Analysis of Persistent Social Support in Adulthood and the Association between Race/Ethnicity and Hypertension, Excess Relative Risk (β (Bootstrap SE)) and Proportion Mediated (%)												
	Model 1				Model 2				Model 3			
	B	SE	*p*-value	%	β	SE	*p*-value	%	β	SE	*p*-value	%
Married or living with a romantic or sexual partner (Waves IV and V, n = 1837)												
Total Effect	0.6239	0.1296	<0.0001		0.7028	0.1400	<0.0001		0.6321	0.1433	<0.0001	
Direct Effect	0.5645	0.1299	<0.0001		0.6391	0.1451	<0.0001		0.5746	0.1420	<0.0001	
Indirect Effect	0.0594	0.1299	0.0440		0.0638	0.0332	0.0477		0.0575	0.0317	0.0563	
Proportion Mediated				9.51				9.08				9.09
Six or More Close Friends												

(Waves IV and V, n = 376)												
Total Effect	0.6232	0.1321	<0.0001		0.7019	0.1403	<0.0001		0.6313	0.1434	<0.0001	
Direct Effect	0.6056	0.1311	<0.0001		0.6805	0.1394	<0.0001		0.6121	0.1413	<0.0001	
Indirect Effect	0.0176	0.0107	0.1022		0.0215	0.0106	0.0404		0.0192	0.0102	0.0481	
Proportion Mediated				2.82				3.05				3.03
Attended Religious Services At Least One per Month for the Past Year (Waves IV and V, n = 948)												
Total Effect	0.6267	0.1353	<0.0001		0.7024	0.1338	<0.0001		0.6310	0.1417	<0.0001	
Direct Effect	0.6674	0.1392	<0.0001		0.7389	0.1383	<0.0001		0.6672	0.1461	<0.0001	

Indirect Effect	-0.0407	0.0164	0.0145		-0.0365	0.0173	0.0346		-0.0363	0.0187	0.0421	
Proportion Mediated				-6.50				-5.19				-5.74
Volunteered More than Once within Past Year (Waves IV and V, n = 1046)												
Total Effect	0.6256	0.1285	<0.0001		0.7038	0.1387	<0.0001		0.6328	0.1408	<0.0001	
Direct Effect	0.5935	0.1259	<0.0001		0.6730	0.1364	<0.0001		0.6102	0.1382	<0.0001	
Indirect Effect	0.0320	0.0113	0.0039		0.0308	0.0115	0.0060		0.0226	0.0099	0.0205	
Proportion Mediated				5.12				4.37				3.57

Note: Model 1 is unadjusted. Model 2 adjusts for demographic variables (age, sex, and health insurance status). Model 3 adjusts for variables in Model 2 and adolescent socioeconomic variables (parent education and family income).

Chapter V. Dissertation Summary and Future Directions in Research

There is a wealth of evidence that social capital, a broad construct that describes human relationships and the nature of those relationships, is directly related to health and health outcomes.[1] Moreover, several studies have described health-related effects of the interplay between social capital and the timing or duration of its presence of absence across the life course.[2-4] As cardiovascular disease (CVD) is the leading cause of death and driver of health expenditures in the US, it should be no surprise that there have been numerous studies documenting the negative shocks to cardiovascular (CV) health associated with social capital and life course trajectories.[5-10] However, few studies have examined the relationship between life course social capital, directly or indirectly, and cardiovascular disease (CVD); those that have are limited to cross-sectional or limited follow-up periods and use older populations.[11-13]

To address these gaps and limitations, three studies were conducted to answer the following research questions:

1. *How has social capital been defined, classified, and measured in the existing CVD literature?*
2. *What is the association between life course social isolation and HTN in early middle adulthood?*
3. *Do racial differences in the prevalence of HTN in early middle adulthood change when social connections are considered?*

A scoping review was conducted to address the first research question. After a comprehensive database search, 74 studies were included in the review. The review provided several insights

regarding the examination of social capital and its relationship to CV risk, incidence, and outcomes:

1. The term 'social capital' is not widely used in the CV literature. Instead, the construct has been studied by the individual dimensions it represents.
2. There are several validation instruments that measure social capital dimensions. However, it is not uncommon that these instruments are modified to accommodate data availability within existing datasets.
3. Most studies are cross-sectional or over limited follow-up periods.
4. Social support is commonly studied within the CV literature. The measures of social support largely describe the quality of a variety of relationships.
5. The status of one's living arrangements, e.g., alone, married, or cohabitating, is a common structural measure of social capital.
6. Cardiac events, e.g., myocardial infarction and death, were the most frequently studied CV measures. Blood pressure measures and HTN were the most common risk factors studied, although usually in older populations.

The insights of this broad review of the CV literature to understand the way social capital is defined, classified, and measured helped to identify research gaps upon which the additional research questions and studies within this dissertation were constructed. Furthermore, these insights may provide direction for future research to explore less-studied social capital dimensions and CV measures.

Based on the findings of the scoping review, the second research question sought to understand the relationship of social capital, from a life course perspective, and HTN in earlier in the life

cycle, early middle adulthood. Data from the National Longitudinal Study of Adolescent to Adult Health (Add Health) study, a nationally representative sample followed from adolescence over five waves, was used to answer this question. The study found that social isolation, particularly in and across adult life stages, significantly increases the likelihood of HTN in early middle adulthood. These results suggest that a life course perspective is critical when considering the type, timing, and duration of interventions reduce the incidence of HTN earlier in life.

The third research question sought to build upon the existing literature and the findings of the previous study. Racial and ethnic disparities in HTN prevalence are well documented, yet there is little evidence that describes the role of social capital, specifically social connections, in explaining the disparity. From the previous study, specific social connections and their timing in adulthood were evaluated to determine if they explained the observed race/ethnicity differences in early middle adulthood HTN. In this study, non-Hispanic Blacks had higher rates of HTN in early middle adulthood and fewer social connections in early middle adulthood. Marriage or cohabitation in early middle adulthood explained a significant portion of the racial differences in HTN prevalence during the same life stage, while close friendships and participation in religious services significantly explained a small portion only when maintained over young and early middle adulthood. The findings provide direction into which social relationships are most impactful and warrant further exploration as well as the life stages during which interventions may be the most successful in reducing the disproportionate incidence and prevalence of HTN among non-Hispanic Blacks in early middle adulthood.

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