The Cardiometabolic Effects of Work and Family Stress

THE CARDIOMETABOLIC EFFECTS OF WORK AND FAMILY STRESS

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Abstract

Work and family stress is increasingly pervasive in today's workforce, and studies reveal that it may be related to worse employee cardiovascular health. However, it is unclear whether the combined stress from work and home relate to individual cardiometabolic risk factors over time and whether the workplace influences these risk factors. Further, no research has examined if these demands are associated with higher levels of inflammation in the body, which are meaningful indicators of cardiovascular disease (CVD). This dissertation seeks to address these gaps in the literature. We draw upon data from 1,524 predominantly female, ethnically and racially diverse extended-care employees who provide biological as well as self-reported data on a variety of sociodemographic, health and work and family variables at four study waves (baseline, 6 months, 12 months and 18 months). Specifically, Chapter 1 examines the observational effects of work and family conflict, conceptualized to represent perceived stress, on five cardiovascular risk factors (blood pressure, glycosylated hemoglobin, cholesterol, body mass index and cigarette consumption) used to establish a cardiometabolic risk score (CRS) over the 18 month study period. Chapter 2 investigates the effects of a workplace intervention designed to increase flexibility, schedule control and workplace support on employee markers of inflammation from baseline to 12 months as part of a prospective, randomized field experiment. Chapter 3 assesses manager- and worksite-level influences on the aforementioned CRS and

behavioral and biological variables representing CVD risk, all measured at the employee-level at baseline. We employ multilevel level modeling techniques to account for the nesting of employees within manager workgroups and worksites as well as multiple measures per employee where appropriate. Overall, we find that work and family conflict may relate to certain measures of cardiometabolic risk, such as BMI and cholesterol. Additionally, employees who work within the same worksite may have more similar cholesterol levels than employees working at different worksites. We do not find evidence that this particular workplace intervention lead to changes in employee levels of inflammation over time. Given the public health burden of CVD, we recommend that future research continue to examine the effects of work and family stressors on cardiovascular outcomes in a variety of settings.

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CHAPTER 1

Cardiometabolic Risks Associated with Work-to-Family Conflict: Findings from the Work Family Health Network

Abstract:

Introduction: Work and family conflict is increasingly pervasive in today's workforce and is associated with worse cardiovascular health. However, the extent to which this combined stress relates to individual risk factors of cardiovascular disease overtime is unclear. This study leverages a randomized field experiment and investigates the observational associations of work and family stressors with five cardiovascular risk factors (blood pressure, glycosylated hemoglobin (HbA1c), cholesterol, body mass index (BMI) and cigarette consumption) used to establish a recently developed cardiometabolic risk score (CRS) over an 18 month study period. We hypothesize that work-to-family conflict (WTFC) will be associated with worse markers of cardiometabolic risk at baseline and that high WTFC will be associated with a faster rate of increase in cardiometabolic risk over time, compared to low WTFC.

Methods: The current analyses utilized four waves of data (baseline, 6 months, 12 months and 18 months) among 1,524, predominantly female employees working in an extended care setting. Employees provided biological markers through dried blood spots as well as self-reported data on a variety of sociodemographic, health and work and family variables. We estimated multilevel linear models that accounted for multiple measures per employee as well as nesting of employees within worksites to test whether WTFC at baseline was associated with worse cardiometabolic outcomes (CRS and individual risk factors) over an 18 month study period. Secondarily, we tested the effects of family-to-work conflict (FTWC) at baseline on these outcomes as well.

Results: WTFC was positively associated with BMI at baseline (β=0.53, p=0.02, CI=(0.08, 0.98)) and in pooled outcome analyses across all four study waves (β=0.59, p=0.01, CI=(0.12, 1.04)). WTFC was associated with greater increases in BMI over time (β=0.08, p=0.0007, CI=(0.03, 0.15)) as well. Higher levels of WTFC were associated with lower HDL cholesterol averaged across waves (β=-0.32, p=0.01, CI=(-0.57, -0.08)) but not with the individual factors of HbA1c, total cholesterol, blood pressure or cigarette smoking at baseline or over the course of the study nor with CRS in pooled or longitudinal analyses.

Conclusion: Our data suggest that WTFC is consistently associated with BMI over the 18 month study period. We speculate that BMI, which is linked to potentially malleable behaviors, are more closely related to interrole conflict than biological markers. We recommend that future research continue to clarify the effects of work and family stressors on individual risk factors for CVD in a variety of occupational settings.

Introduction:

Employees report that dueling demands both at work and home are increasingly common [1], and research indicates that this interrole conflict is associated with poorer employee health, including worse cardiovascular outcomes [2-4]. However, the extent to which stress at home and at work relate to individual risk factors of cardiovascular disease over time warrants additional investigation. The current study examined associations between work and family conflict (WTFC), a measure intended to reflect perceived stress arising due to conflicting demands in these two realms of life, and a variety of behavioral and biological markers related to risk of cardiovascular disease (CVD). We test these relationships with an observational design based on a study assessing a randomized field experiment. This research largely draws on job strain theory

[5, 6], specifically the Demand-Control-Support model [7]. The model considers the combination of job demands and job control believed to produce a sense of strain and incorporates workplace social support hypothesized to combat these strains. The current study focuses on pressures both at work and in the home. A larger body of research has examined work strain and CVD outcomes specifically, and this literature focuses predominantly on Caucasian, male samples. We extended this work and investigated these relationships in a young, predominantly female and racially diverse occupational cohort of extended care employees. Because cardiovascular disease often develops gradually, biological markers of CVD risk serve as sensitive and meaningful pre-disease pathways for otherwise latent illness. They provide a useful assessment approach by which the effects of psychosocial stress on cardiovascular outcomes may be understood in a relatively healthy study population. In doing so, we built upon existing research that has examined the effects of work and family demands on "objective" cardiovascular measures [8, 9] and offer a longitudinal perspective on the link between WTFC and CVD in a unique study population.

Changes in labor dynamics and related transformations in the home have prompted an increasing number of Americans to experience work and family strains simultaneously. Female labor force participation has risen significantly in recent years (42% to 57% from 1950 to 2007), with the most pronounced increases among working mothers (47% to 71% from 1975 to 2007). National data also indicate that increases in self-reported work and life strains have been reported by all employed parents [1]. The incompatibility of home and professional life is often referred to as "work-family conflict," a term which Greenhaus and Beutell introduced thirty years ago to describe "a form of interrole conflict in which the role pressures from the work and family

domains are mutually incompatible in some respect" [10]. Frone and colleagues further posited that work-family conflict is a bidirectional phenomenon (operating work-to-family and family-to-work), presenting itself when efforts to fulfill responsibilities in one realm interfere with the ability to succeed in another [11, 12]. Though this study acknowledges the relevance of measures of family-to-work conflict and examines its effects, WTFC is the exposure of emphasis here given that an occupational cohort comprises the sample.

The current study focuses on work and family stress and its effects on risk of CVD, which currently contributes to one in four deaths in the U.S. [13]. Numerous studies suggest that a variety of work and family stressors are associated with overall CVD risk, proxies for and actual measures of cardiovascular disorders as well as individual risk factors of CVD, including blood pressure, cholesterol, smoking, diet, physical activity and obesity. Yet, much of this work is cross-sectional and among small samples. For example, research suggests that higher levels of support from managers for work and family issues was associated with lower CVD risk as measured by the presence of two or more of five modifiable risk factors among a cohort of 400 extended-care employees interviewed at one time point [2]. Prior work with our study sample also confirmed that higher demands related to work and family life may be associated with increased cardiometabolic risk as measured by a newly developed and validated cardiometabolic risk score (CRS) [14]. Berkman found that low family supportive supervisor behaviors at the level of the nursing home facility and high work-to-family conflict (WTFC) at the individual level were associated with increased cardiometabolic risk in a cross-sectional, baseline analysis [3]. In these studies, supervisor support is hypothesized to buffer the impact of work-family conflict on a number of outcomes.

Most other research considering risk of disease has been conducted in higher risk patient populations. For example, a longitudinal study of 80 female patients with atherosclerosis indicated that women with high self-reported stress from family or work experienced significant disease progression over a 3-year period, as measured by increased mean coronary luminal diameter. Women who did not report stress in one of these life realms experienced slower progression of atherosclerosis suggesting that satisfaction with work and home may be protective among female patients [4]. As part of the Stockholm Female Coronary Risk Study, Orth-Gomer and colleagues examined the effects of work stress and, separately, marital stress on risk of a recurrent cardiovascular event, such as death and myocardial infarction, among fewer than 300 women with existing coronary heart disease. They found that higher marital stress was associated with increased odds of recurrent event among partnered women but that work stress did not predict subsequent events over the course of nearly five years [15]. A follow-up study in the same sample found that higher exposure to work *and* marital stress resulted in the most heightened risk of recurrent coronary event, compared to no stress or one form of stress only [16].

Other work has considered work and family stress in relation to conditions and behaviors known to increase risk of cardiovascular disease. Twenty five years ago, Frankenhauser assessed blood pressure for 60 male and female Swedish white-collar employees. She noted that blood pressure increased during work hours and subsequently decreased after the workday in men only [9]. These results suggested that "total workload" (that is, the strain at work and home) affected biological functioning but that these processes are different for men and women. More recently, Frone and colleagues identified a significant, increased risk of developing hypertension with higher levels of WTFC (but not in the direction of family-to-work) among employed parents

(half men, half women, n=267) over a four year period [17]. Similarly, a cross sectional study of white-collar women found that reports of a high stress job coupled with caregiving responsibilities for children was associated with higher systolic and diastolic blood pressures (n=199) [18]. Among a predominantly female cohort of 398 health care employees with children at home, Thomas and Ganster conducted a series of path analyses and found that flexible scheduling and supportive supervisors positively impacted employee perceptions of control over work and family matters and reduced WTFC. WTFC was then significantly and associated with higher blood cholesterol but not blood pressure [19]. A similarly sized sample revealed that higher WTFC was associated with increased cigarette use indirectly through negative affect among a simple random sample of predominantly white, working mothers of adolescents [20]. Lallukka and colleagues utilized data from the British Whitehall II Study, the Finnish Helsinki Health Study, and the Japanese Civil Servants Study and tested the cross-sectional effects of WTFC on coronary risk related health behaviors in all three groups. They found that measures of WTFC were positively and significantly associated with current smoking among men but not women in the Finnish cohort; no associations with other behaviors in the Finnish cohort were evident. They also found no association with smoking, alcohol use, physical activity or diet or among the British or Japanese cohorts [21]. A longitudinal study of a workplace intervention to reduce WTFC among white-collar, retail employees (as part of pilot work for the current study, n=550), showed that the program increased the odds of quitting smoking and decreased smoking frequency [22]. This pilot study also found the intervention was associated with improvements in exercising behavior and promoting perceptions of adequate time for healthy meals [22, 23]. Multiple cross-sectional studies have also concluded that WTFC was associated with lower physical activity and poorer diet (i.e.: eating more high-fat foods and fewer healthy foods) [24-

28] though, again, most of these studies employed small sample sizes. Similarly, increased WTFC related to significantly increased odds of being obese in the cross-sectional MIDUS sample (n=1547) [29].

Despite evidence suggesting links between strain at home and work and a variety of outcomes related to cardiovascular disease risk, this scientific literature presents a number of shortcomings and challenges. Investigators have examined biological outcome measures such as blood pressure, cholesterol and progression or development of CVD events. However, studies on the same outcome are limited in number and, thus, the literature lacks consistency of evidence for a given risk factor. Further, some of this work focuses on patient populations [4, 16] for whom pathways between stress and disease might be different than those in healthy populations. With a few exceptions [21, 27, 29], most of the aforementioned analyses were conducted among small samples, which may result in chance findings or lack of power to detect significant effects. Participants within studies also tended to be racially homogeneous. Additionally, although we do reference a few longitudinal analyses [17, 22, 30] supporting these associations, many studies are cross-sectional. A recent review indicated that 89% of work-family research utilized only one exposure and outcome measure at a single point in time [31], a design which greatly constrains researcher's abilities to draw strong causal inferences about the relationship between work and family stressors and health. Cross-sectional designs are particularly troublesome because health limitations could very plausibly pose challenges to the successful management of work and family demands. Additionally, understanding the effects of work and family stressors on CVD is constrained by the fact that the outcome takes years, often decades, to emerge, and longitudinal research that anticipates the development of disease with long latency can be costly and logistically demanding.

We seek to address some of the limitations of this earlier work by conducting a longitudinal study among a predominantly female and racially and ethnically diverse sample and with a focus on behavioral as well as biological markers representing CVD risk. Biomarkers serve as a useful alternative in epidemiologic research to self-reported outcome measures. Typically collected by means of blood, saliva or urine, they serve as underlying risk factors for as well as potential intermediate variables along the pathway to disease, which is particularly useful for conditions that develop slowly over time. Biomarkers provide direct information on physiological processes in the body and are thus more reliable than subjective measures of health [32, 33], which reduces concerns of reverse causation in research. In addition, we examine behavioral outcomes associated with CVD risk such as smoking, which may be more susceptible to work and family stressors and more malleable over time compared to biological markers. Similarly, BMI is closely linked with behaviors that may also change more quickly than other biomarkers.

We hypothesize that WTFC will be associated with worse markers of cardiometabolic risk and that these associations will vary by level of WTFC over time. First, we pool outcome data over four study waves to increase the statistical power to identify these relationships, and then explicitly examine changes over the study period. Additionally, we control for treatment status in the randomized field experiment to disentangle the effects of the WFHN intervention on our outcomes of interest. Other analyses forthcoming assess the impact of the intervention directly on the cardiometabolic outcomes. To our knowledge, no longitudinal study of the effects of work and family stressors on a composite CVD risk score has been conducted, nor have a series of risk factors been examined over time. Specifically, we address the following aims and hypotheses:

Aim 1: Assess the effect of WTFC *on individual cardiovascular risk factors at baseline*.

Hypothesis 1: WTFC will be associated with less healthy markers of cardiometabolic risk at baseline.

Aim 2: Assess the effect of WTFC at baseline on *markers of cardiometabolic risk (CRS and individual risk factors) pooled across multiple study waves.*

Hypothesis 2: WTFC at baseline will be associated with less healthy markers of cardiometabolic risk averaged across baseline, 6 months, 12 months and 18 months.

Aim 3: Examine whether *the rate of change in markers of cardiometabolic risk (CRS and individual risk factors) from baseline to 18 months varies by levels of WTFC at baseline.*

Hypothesis 3: High WTFC at baseline will be associated with a faster rate of increase in cardiometabolic risk over time compared to low WTFC at baseline.

Methods:

Sample:

This study is part of Phase II of the Work Family Health Network (WFHN) project, a joint research endeavor sponsored by the National Institutes of Health and the Centers for Disease Control and Prevention, among others. This phase of the WFHN involved data collection from employees (as well as their managers, spouses and their children) over the course of 18 months as part of an employer-supported workplace intervention in a group randomized field experiment. The WFHN identified a New England company with numerous nursing home facilities, which we will refer to as "LEEF," and included thirty worksites that were distributed across Massachusetts, Maine, New Hampshire, Vermont, Connecticut, and Rhode Island.

Each of the 1,723 eligible employees within these worksites who worked more than 22 hours each week during the day or evening was invited to complete a computer-assisted personal interview (CAPI) [34]. A total of 1,524 LEEF employees participated at baseline, resulting in response rate of over 88%. Data were collected at four waves (baseline, 6 months, 12 months and 18 months) using the same procedures as baseline. The exposure, WTFC, was unrelated to dropout over the course of the study and, thus, we utilize all available employee data for subsequent waves and do not employ a complete case analysis (please see Sample Characteristics below for more details on missing data and dropout). We do not have data on non-participants. We also do not explicitly test intervention effects in this study but control for and examine the role of treatment status in a variety of ways (see Measures and Analysis below). Employees who provided all components for the larger WFHN study, including blood samples, received $60 for their participation.

Measures:

Trained field interviewers administered computer-assisted personal interviews and on-site health assessments at all waves as described elsewhere [35], which addressed employee demographics, socioeconomic status, family demographics, respondent's work environment, physical health, mental health, and family relationships. After obtaining written consent from all respondents, interviews and health assessments lasted approximately 50 and 20 minutes, respectively, and were on occasion collected on different days.

Exposure Variable

Work-to-family conflict is thought to reflect the extent to which responsibilities in the domains of work and family are incompatible [10]. The current study incorporated a widely-used measure of this inter-role conflict developed and validated by Netermeyer and colleagues among employed individuals in various industries [36]. The survey included five questions to address work-to-family conflict that asked whether the demands of work interfere with family or personal time, the employee's job produces strain that makes it difficult to fulfill family or personal duties and things employees want to do at home do not get done because of the demands work puts on them. Individual item responses were coded 1-5 (strongly disagree to strongly agree) and averaged to generate a continuous measure (internal consistency reliability of the scale was high; alpha=0.9). For the purposes of the current study, only baseline measures of WTFC were considered.

As mentioned, work-family conflict is thought to be bidirectional in nature and believed to operate from work-to-home as well as home-to-work. We explored inter-role conflict from home to work as well. Similar to the WTFC measure, employees were asked five questions to address family-to-work conflict (FTWC) (whether the demands of family interfere with work, employees have to put off doing things at work because of demands on time at home and family-related strain interfere with employee's ability to perform job-related duties). Individual item responses were coded 1-5 (strongly disagree to strongly agree) and averaged to generate a continuous measure (alpha=0.8). Again, only baseline measures of FTWC were examined in this analysis.

Outcome Variables:

Prior research established and validated a measure of cardiometabolic risk based on modifiable risk factors in the Framingham risk score [37], including blood pressure, cholesterol, HbA1c, BMI and cigarette smoking status. The score used here was calculated based on age- and sex-based means in our particular sample and was validated independently among Framingham offspring data to predict risk of a cardiovascular event [14]. We build upon a recent paper examining baseline, cross-sectional effects of WTFC on the CRS [3] and focused on the individual components of this score (at baseline and overtime), all of which were measured continuously.

Employees were asked to provide dried blood spots (DBS) by a finger stick. Interviewers wearing appropriate personal protective equipment disinfected the employee's middle or ring finger with an alcohol swab and proceeded to prick the finger with a sterile, disposable micro-lancet. As previously described [38], blood spots were collected, air-dried, and sealed in a plastic bag for room-temperature shipment with desiccant for storage at −86°C until assayed for cholesterol by means of a protocol specifically validated for this study from serum to DBS equivalents [39]. At the time of the blood draw, study staff also collected a 1 microliter blood droplet to measure HbA1c levels (DCA Vantage Analyzer, Siemens Healthcare Diagnostics, Frimley, Camberley, UK). Prior to blood sampling, three seated blood pressure readings were collected at least 5 minutes apart during the interview with wrist blood pressure monitors (HEM-637, Omron Healthcare, Bannockburn, IL). These three readings were averaged to create a continuous measure. Body mass index was calculated as height/weight^2 (height measured by Seca213/214 stadiometers, Seca North America, Hanover, MD; weight measured by Health-O-Meter 800KL, Jarden Corporation, Rye, NY). Height and weight measurements were taken at the

same time as other physical health assessments. Cigarette consumption was assessed by respondent self-report. Employees were asked if they smoke cigarettes every day, some days or not at all, how many days they smoke cigarettes on average in a week, and how many tobacco cigarettes they smoke on an average day. Responses were multiplied to produce a measure of cigarettes per week. Non-smokers received a score of zero cigarettes per week. Based on the aforementioned components, we calculated a cardiometabolic risk score for each subject (age- and sex-specific strata use different score calculations) [3, 14]. For additional information on specific measures, refer to Bray, 2013.

Covariates:

A number of sociodemographic variables and covariates relevant to the association between WTFC and cardiometabolic risk were also assessed: occupation (employee's official job title, coded nurse or other), marital status (currently married or do you have a permanent romantic partner that lives with you?), employee gender (male/female), income (assessed in $5,000 increments and categorized as greater than 300% of the national poverty threshold or less), age in years, total number of work hours (how many hours employees worked in a typical week at any job) and number of children less than or equal to 18 years old living in the household for 4 or more days/week (none/one or more). Race/ethnicity was coded as White, Black, Hispanic or other race. Dummy variables for each racial/ethnic group were generated, and the reference group was assigned to White race. Foreign-born status was coded yes/no depending on whether an employee was born in this country or not. Because this observational analysis is embedded within an existing randomized control trial in which a workplace program sought to reduce work-to-family conflict and improve health outcomes, we controlled for whether the

employee worked within a workgroup assigned to control or intervention status (blinded and labeled treatment 1 and treatment 2) in pooled and longitudinal analyses.

Similar to Berkman et al [3], we included a number of work environment measures (at the individual- and workgroup-levels) assessed at baseline as covariates to assess the independent effects of WTFC on cardiometabolic risk, above and beyond these factors. Job strain, a measure of employee stress that does not explicitly incorporate family context, was assessed through questions pertaining to psychological job demands and job control or decision authority. According to the work of Karasek and colleagues, high job demands paired with low control are hypothesized to be detrimental to physical and psychological wellbeing. In response to questions pertaining to physical activity, heavy lifting and awkward body positions (*job demands*) as well as degree of skill, task variability and autonomy (*job control*) at work, subjects strongly disagreed, disagreed, neither, agreed or strongly agreed (valued 1 - 5, respectively and measured continuously) that these elements were part of their jobs [5, 6, 40] (Cronbach's alpha=0.6 for job demands and Cronbach's alpha=0.6 for job control). A measure of managerial support, family supportive supervisory behavior (FSSB), tapped into employee appraisals of supervisor's behavior relating specifically to work and family. Research indicates that FSSB is negatively associated with employee reports of WTFC and turnover intentions and positively associated with positive work-to-family and family-to-work spillover as well as job satisfaction [41, 42]. The scale asked employees about four domains related to family-related supervisory support, including emotional support (supervisor makes you feel comfortable talking to him/her about conflicts between work and non-work), instrumental support (supervisor works effectively with employees to creatively solve conflicts between work and non-work), role modeling (supervisor demonstrates effective behaviors in how to juggle work and non-work issues) and

creative management (supervisor organizes departmental work to jointly benefit employees and the company). The current study used a short form of FSSB derived from employee responses to four items, categorized 1-5 (strongly agree to strongly disagree) and averaged to generate an overall score, with higher scores reflecting greater FSSB [43] (Cronbach's alpha=0.9). Similarly, we utilized a modified version of Thomas and Ganster's schedule control scale [44]. Employees were asked how much choice they had over when they took vacation, when they can take off a few hours, when workdays begin and end, working at another location, the number of personal phone calls they can make or receive during work, how much they take work home and about shifting to part time work if full time (and vice versa). Responses ranged from very little to very much (1-5) and an overall score of schedule control was obtained by calculating the average score of these 8 items (Cronbach's alpha=0.7).

As appropriate, we also controlled for baseline medication use (i.e.; insulin for the outcome HbA1c, cholesterol medication for total cholesterol and HDL cholesterol and blood pressure medication for systolic and diastolic blood pressure). Because those individuals who were not diagnosed with a specific condition (i.e.: diabetes) were not asked about medication use, missing data for these questions were coded as non-use to provide a full sample of responses. Finally, for longitudinal analyses that sought to capitalize on multiple measures, wave of data collection (baseline, 6 months, 12 months and 18 months) was also included as a covariate and operationalized as a continuous measure.

Analysis:

To test whether WTFC was related to individual cardiometabolic risk factors at baseline only (Aim 1), we estimated multilevel linear regression models that accounted for the nesting of

employees within worksites by modeling random effects for the site level. To test whether WTFC was associated with the CRS and various cardiometabolic risk factors pooled across waves (Aim 2) and whether the rate of change in these outcomes varied over levels of WTFC (Aim 3), we estimated multilevel linear regression models that also accounted for multiple measures per employee by modeling random effects for the employee level. In these models, we used outcome data from four times points (baseline, six months, twelve months and eighteen months), a method which improves statistical power of cross-sectional analyses. We utilized baseline exposure and covariate data, which was not time updated with the goal of reducing reverse causality. A time*exposure interaction term was included separately in models to address Aim 3 specifically.[*]

Due to differences in our longitudinal CRS results compared to a previous baseline analysis [3], we conducted a post hoc analysis to verify the likelihood of reverse causation and tested the effects of the CRS at baseline on work and family stressors pooled across the fours study waves. Because this observational study is embedded within a randomized field

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[*]

Aim 1: $\text{Cardiomet}_{ij} = \beta_0 + \beta_1 (\text{WTFC}) + \beta_2 (\text{Covariates}) + e_{0ij} + u_{0j}$
Where: i= employee; and j = worksite
And:
$[e_{0ij}] \sim N(0, \sigma^2_{e0})$
$[u_{0j}] \sim N(0, \sigma^2_{u0})$

Aim 2: $\text{Cardiomet}_{tij} = \beta_0 + \beta_1 (\text{WTFC}) + \beta_2 (\text{Time}_{tij}) + \beta_3 (\text{Treatment}_j) + \beta_4 (\text{Covariates}) + t_{0tij} + e_{0ij} + u_{0j}$
Where: t= time; i= employee; and j = worksite
And:
$[t_{0tij}] \sim N(0, \sigma^2_{t0})$
$[e_{0ij}] \sim N(0, \sigma^2_{e0})$
$[u_{0j}] \sim N(0, \sigma^2_{u0})$

Aim 3: $\text{Cardiomet}_{tij} = \beta_0 + \beta_1 (\text{WTFC}) + \beta_2 (\text{Time}_{tij}) + \beta_3 (\text{WTFC}) (\text{Time}_{tij}) + \beta_4 (\text{Treatment}_j) + \beta_5 (\text{Covariates}) + e_{0ij} + u_{0j}$
Where: t= time; i= employee; and j = worksite
And:
$[t_{0tij}] \sim N(0, \sigma^2_{t0})$
$[e_{0ij}] \sim N(0, \sigma^2_{e0})$
$[u_{0j}] \sim N(0, \sigma^2_{u0})$

experiment, we conducted an additional post hoc analysis of pooled outcome models stratified by treatment status as well.

Models controlled for treatment status (in pooled and longitudinal analyses), sociodemographic variables (race, income, sex, occupation, age, foreign born status), possible antecedents of WTFC (marital status, number of children and work hours) and relevant work environment factors (FSSB, schedule control and job strain) at the individual- and group-levels, all measured at baseline. Model results do not differ with and without the inclusion of antecedents of WTFC nor work environment variables and, thus, we adjust for them in-line with the work of Berkman and colleagues. Where appropriate, we adjusted for baseline medication use as well (blood pressure and cholesterol medication as well as insulin use). We did not control for medication use in models with CRS as the outcome because multiple medication use measures would be warranted, and other model results did not change meaningfully with the inclusion of medication use. All outcomes were modeled continuously and analyses conducted using the mixed procedure in SAS.

Results:

Sample Characteristics:

At baseline, on a scale of 1 to 5, the mean work-to-family conflict score was 2.79 (sd = 0.91) (see Table 1.1 for descriptive statistics at baseline). The mean 10-year cardiometabolic risk score represents a 7.75% 10-year CVD risk (sd=8.15%), meaning that fewer than 8 out of 100 with the average level of risk will have a cardiovascular event in the next 10 years.[†] Mean BMI

[†] Over 20% is considered high global risk, according to some researchers [45]. Thus, the mean risk in our sample is fairly low.

Table 1.1: Descriptive Statistics

N=1524 baseline	N	Mean (sd) / %
Cardiometabolic Risk Score (% 10yr risk)	1412	7.75 (8.15)
BMI (height/weight^2)	1501	29.45 (7.03)
Total Cholesterol (mg/dL)	1464	190.79 (28.78)
HDL Cholesterol (mg/dL)	1473	63.56 (5.54)
Systolic Blood Pressure (mmHg)	1511	114.79 (13.09)
Diastolic Blood Pressure (mmHg)	1511	72.36 (9.40)
HbA1c (%)	1453	5.51 (0.61)
Cigarettes/week	1522	23.45 (45.87)
WTFC	1520	2.79 (0.91)
FTWC	1522	2.07 (0.58)
Work Hours	1520	39.95 (10.63)
FSSB	1510	3.69 (0.88)
Job Control	1511	3.45 (0.76)
Job Demands	1523	3.82 (0.75)
Schedule Control	1509	2.65 (0.73)
Age	1522	38.52 (12.48)
RN/LPN		
Yes	428	28.12
No	1094	71.88
Sex		
Male	118	7.74
Female	1406	92.26
Married/partnered		
Not married/partnered	566	37.14
Married/partnered	958	62.86
Race		
White	987	64.81
Black	200	13.13
Hispanic	204	13.39
Other race	132	8.67
Foreign Born		
Yes	405	26.57
No	1119	73.43
Income		
>300% poverty threshold	569	38.39
<300% poverty threshold	913	61.61
Children ≤ 18 years old		
None	710	46.59
One or more	814	53.41
Diabetes Medication (general)		
No	1510	99.08
Yes	14	0.92
Insulin Use		
No	1508	98.95
Yes	16	1.05
Blood Pressure Medication		
No	1308	85.83
Yes	216	14.17
Cholesterol Medication		
No	1510	99.08
Yes	14	0.92

in our sample was 29.45, nearly considered obese, and roughly 30% of employees smoked (an average of 23.45 cigarettes each week). Average total and HDL cholesterol, HbA1c and systolic and diastolic blood pressures were in-line with national levels [46]. We analyzed a total of 1,524 subjects enrolled at baseline, many of whom provided data at subsequent waves. Data were missing for roughly 16%, 29% and 34% of employees at 6 months, 12 months and 18 months, respectively. Related, roughly 40% of the sample dropped out of the study for at least one wave, whereas 27% and 13% dropped out of the study for two or three waves, respectively. General patterns for missing data (i.e.: non-participation in a survey) and dropout (i.e.: non-participation from one survey to the next) appear closely aligned. Older age and foreign-born status significantly predicted higher odds of missing survey data and dropout from the sample. We also find that higher job demands were associated with dropout for certain outcome variables, such as CRS and HDL cholesterol. WTFC at baseline was not associated with either missing data or dropout from the study. Accordingly, we do not employ a complete case analysis; we use all available data (thus, we can examine specific dropout patterns by outcome). Outcomes were highly correlated overtime; WTFC and related covariates were also highly correlated at baseline (see Appendices 1.1 and 1.2). Trends in outcome data over time are presented by treatment group in Appendix 1.3.

Results of statistical analyses:

While we did replicate baseline findings that suggest WTFC is associated with CRS at baseline, our primary exposure was not associated with CRS pooled across waves or longitudinally. Increased WTFC was associated with higher BMI at baseline and over the course of the study. Increased WTFC was also associated with lower HDL cholesterol in pooled

analyses but not in baseline or longitudinal analyses. WTFC was not associated with total cholesterol, blood pressure, HbA1c or cigarette smoking in any analysis. While not our primary research question of interest, we also conducted similar analyses with FTWC as the predictor variable and find that this exposure is also associated with higher BMI and lower HDL in pooled analyses but not any outcome in baseline or longitudinal analyses (see Table 1.2 and Appendix 1.4).

Baseline Associations:

At baseline, we found that one-point higher WTFC was associated with a half-point higher BMI (β=0.53, p=0.02, CI=(0.08, 0.98)). Baseline WTFC was not associated with baseline HDL cholesterol, total cholesterol, blood pressure, HbA1c or cigarette smoking. Baseline FTWC was not associated with any cardiometabolic risk factors at baseline.

Pooled Outcome Associations:

WTFC was not associated with CRS averaged across time. Pooled outcome analyses reflected a similar main effect between WTFC and BMI as baseline analyses (β=0.59, p=0.01, CI=(0.12, 1.04)). Higher WTFC at baseline was associated with lower HDL cholesterol averaged at all waves (β=-0.32, p=0.01, CI=(-0.57, -0.08)) but not other outcomes pooled over time. Higher FTWC at baseline was similarly associated with higher BMI in pooled analyses (β=0.62, p=0.05, CI=(-0.01, 1.25)) and lower HDL cholesterol (β=-0.41, p=0.02, CI=-0.76, -0.06)) but not other outcomes pooled across waves.

Table 1.2: Associations between baseline WTFC and markers of cardiometabolic risk

	Baseline			Pooled Outcome			Longitudinal		
				CRS					
	N=1334			**N= 1438 Obs=4281**			**N= 1438 Obs=4281**		
	Estimate	**Standard Error**	**p-value**	**Estimate**	**Standard Error**	**p-value**	**Estimate**	**Standard Error**	**p-value**
Intercept	3.81	0.97	0.001	3.14	0.94	0.003	3.14	0.94	0.00
WTFC	**0.37**	**0.16**	**0.02**	0.27	0.16	0.09	0.24	0.17	0.15
Time				0.04	0.03	0.14	0.04	0.03	0.14
WTFC*Time							0.01	0.03	0.73
				BMI					
	N=1417			**N=1438 Obs=4581**			**N=1438 Obs=4581**		
	Estimate	**Standard Error**	**p-value**	**Estimate**	**Standard Error**	**p-value**	**Estimate**	**Standard Error**	**p-value**
Intercept	27.48	1.34	<.0001	26.95	1.31	<.0001	26.94	1.31	<.0001
WTFC	**0.53**	**0.23**	**0.02**	**0.59**	**0.22**	**0.01**	0.42	0.23	0.07
Time				**0.06**	**0.02**	**0.004**	**0.06**	**0.02**	**0.002**
WTFC*Time							**0.08**	**0.02**	**0.0007**
				HDL Cholesterol					
	N=1397			**N= 1438 Obs= 4484**			**N= 1438 Obs= 4484**		
	Estimate	**Standard Error**	**p-value**	**Estimate**	**Standard Error**	**p-value**	**Estimate**	**Standard Error**	**p-value**
Intercept	58.35	1.79	<.0001	58.70	1.38	<.0001	58.70	1.38	<.0001
WTFC	-0.23	0.17	0.18	**-0.32**	**0.12**	**0.01**	-0.32	0.20	0.11
Time				**-0.29**	**0.06**	**<.0001**	**-0.29**	**0.06**	**<.0001**
WTFC*Time							-0.001	0.07	0.99
				Total Cholesterol					
	N=1388			**N=1438 Obs=4481**			**N=1438 Obs=4481**		
	Estimate	**Standard Error**	**p-value**	**Estimate**	**Standard Error**	**p-value**	**Estimate**	**Standard Error**	**p-value**
Intercept	148.25	8.70	<.0001	147.45	7.19	<.0001	147.44	7.19	<.0001
WTFC	0.23	0.81	0.78	-0.21	0.67	0.75	-0.31	1.03	0.77
Time				**2.89**	**0.32**	**<.0001**	**2.89**	**0.32**	**<.0001**
WTFC*Time							0.40	0.35	0.90

Table 1.2: Associations between baseline WTFC and markers of cardiometabolic risk (continued)

	Systolic Blood Pressure								
	N= 1425			N= 1438 Obs =4600			N= 1438 Obs =4600		
	Estimate	**Standard Error**	**p-value**	**Estimate**	**Standard Error**	**p-value**	**Estimate**	**Standard Error**	**p-value**
Intercept	119.83	2.45	<0.001	119.43	2.28	<.0001	119.41	2.28	<.0001
WTFC	-0.12	0.39	0.77	-0.05	0.35	0.89	-0.33	0.41	0.43
Time				**-0.93**	**0.09**	**<.0001**	**-0.93**	**0.09**	**<.0001**
WTFC*Time							0.13	0.10	0.20

	Diastolic Blood Pressure								
	N= 1425			N= 1438 Obs=4600			N= 1438 Obs=4600		
	Estimate	**Standard Error**	**p-value**	**Estimate**	**Standard Error**	**p-value**	**Estimate**	**Standard Error**	**p-value**
Intercept	77.18	1.87	<.0001	76.27	1.70	<0.001	76.27	1.70	<.0001
WTFC	-0.08	0.29	0.78	-0.21	0.26	0.40	-0.19	0.31	0.54
Time				**-0.60**	**0.07**	**<0.001**	**-0.60**	**0.08**	**<.0001**
WTFC*Time							-0.01	0.08	0.90

	HbA1c								
	N=1377			N= 1438 Obs=4402			N= 1438 Obs=4402		
	Estimate	**Standard Error**	**p-value**	**Estimate**	**Standard Error**	**p-value**	**Estimate**	**Standard Error**	**p-value**
Intercept	7.60	0.18	<.0001	8.46	0.18	<.0001	8.46	0.18	<.0001
WTFC	0.02	0.02	0.39	0.01	0.02	0.47	0.02	0.02	0.29
Time				**-0.04**	**0.00**	**<.0001**	**-0.04**	**0.00**	**<.0001**
WTFC*Time							-0.004	0.005	0.39

	Cigarettes/week								
	N=1437			N= 1438 Obs=4648			N= 1438 Obs=4648		
	Estimate	**Standard Error**	**p-value**	**Estimate**	**Standard Error**	**p-value**	**Estimate**	**Standard Error**	**p-value**
Intercept	-22.13	8.83	0.02	-23.88	8.34	0.01	-23.86	8.34	0.01
WTFC	1.84	1.45	0.21	0.78	1.33	0.56	1.43	1.45	0.32
Time				**-0.94**	**0.24**	**<.0001**	**-0.95**	**0.24**	**<.0001**
WTFC*Time							-0.30	0.26	0.25

All models control for treatment status, race, income, age, sex, marital status, foreign born status, occupation, work hours and number of children. Models also account for FSSB, job strain and schedule control at the individual- and group-levels and, where appropriate, medication

Longitudinal Associations:

We found that the average rate of change of BMI for each six-month wave when WTFC is zero was 0.06 units (p=0.002). The rate of change in BMI from baseline to 18 months also increased with higher levels of WTFC (β=0.08, p=0.01, CI=(0.03, 0.15)) (see Figure 1.1). No other longitudinal effects were observed in our data.

Post-hoc analysis to assess reverse causation:

We did not observe that WTFC was associated with the CRS in pooled or longitudinal analyses, however, previous findings from the same sample have suggested WTFC was associated with CRS in the baseline, cross-sectional setting [3]. To understand why we find a cross sectional association but not significant relationships in pooled or longitudinal analyses, we examined the effect of CRS at baseline on pooled WTFC as part of a post hoc analysis (β=-0.005, p=0.06, CI=(-0.001, 0.002)). These results suggest that CRS may marginally predict WTFC pooled across waves (see Appendix 1.5). We conducted the same analysis with FTWC at baseline and found that CRS did not predict this stressor in pooled analyses (β=-0.0005, p=0.79, CI=(-0.004, 0.003)).

Post-hoc analysis to examine treatment effects:

This observational study is embedded within a randomized field experiment. Thus, we examined pooled outcome models stratified by treatment status to verify residual effects of the intervention. In pooled outcome models stratified by treatment status, we observed that higher levels of WTFC at baseline are significantly associated with higher pooled CRS but only in the treatment group (β=0.47, p=0.03, CI=(0.05, 0.90); however, the effects of WTFC on CRS in the

control group were in the same direction (β=0.12, p=0.59, CI=(-0.32, 0.56)). Higher WTFC was associated with higher BMI but this was evident only in the control group (β=0.92, p=0.004, CI=(0.29, 1.55) and not the treatment group (β=0.23, p=0.46, CI=(-0.38, 0.84)). Associations of higher WTFC with lower HDL cholesterol observed in both the treatment (β=-0.31, p=0.08, CI=(-0.65, 0.04)) and control groups (β=-0.30, p=0.10, CI=(-0.65, 0.05)) were of borderline statistical significance. The effects of WTFC on other cardiometabolic outcomes were similar to non-stratified analysis. Further, there were no differences of WTFC on the rate of change in outcomes in models stratified and not stratified by treatment status (Data not presented).

Discussion:

The current study examined whether WTFC was associated with individual risk factors as well as a composite score for CVD in a longitudinal cohort of nursing home employees. Utilizing a range of behavioral and biological outcome measures, we found that WTFC was positively associated with BMI at baseline and in pooled analyses. The rate of change in BMI over time also increased with higher levels of WTFC at baseline. Higher WTFC was associated with lower HDL cholesterol in pooled analyses only. WTFC was not associated with CRS pooled across waves or longitudinally nor was this work and homelife stressor associated with total cholesterol, blood pressure, HbA1c or cigarette smoking in any analysis. Below we will first discuss our results for BMI, placing them in the context of theoretical perspectives and the scientific literature, before offering explanations for these findings in our sample. Then, we will proceed to discuss the findings on the association between WTFC and other outcomes in our study and review limitations and strengths of this research.

WTFC and BMI:

The most consistent and significant findings in this study pertain to the relationship between WTFC and BMI. Several theories help to explain why BMI, which has proximate behavioral risks for heart disease, might be associated with this form of stress. From a coping and mood-management perspective, individuals are believed to pursue activities and behaviors that result in a positive emotional and affective experience [47]. Thus scholars argue that inter-role conflict prompts individuals to seek comfort through food and inactivity, or other ultimately risk-related health behaviors, as a method for maximizing immediate and short term pleasure in the face of stress [48, 49]. In line with the role strain and conservation of resources perspectives, time and physical and mental energy are believed to be finite resources that impact health behaviors [50]. In terms of BMI, when faced with demands from work and home, competition for resources and priority setting in according with social roles (i.e.: being a "good" spouse, parent or employee) results in less time and energy for activities such as making a nutritious meal or exercising [51, 52].

The scientific literature offers evidence that work and/or family strains are positively associated with BMI and related outcomes, although this relationship may not be the same for men and women. Kivimaki and colleagues prospectively examined the effects of the work stress on BMI and found that job demands at baseline were associated with BMI in women after five years, adjusting for baseline BMI. Among men, job strain increased the likelihood of weight gain among those with the highest BMIs but predicted weight loss among individuals with the lowest BMIs, suggesting that some may eat more due to stress whereas others eat less [53]. In a nationally-representative study with the MIDUS sample, high job demands were associated with weight gain among men and women but more perceived constraints in life and strain in relations

with family were associated with weight gain only in women over the nine year study period [54]. While no studies to date have examined the combined effects of work and family stressors on BMI per se, higher WTFC has also been cross-sectionally linked with lower physical activity and poorer diet (i.e.: eating more high-fat foods and fewer healthy foods) and obesity [24-28]. In the information technology arm of our WFHN study, work-family strain, operationalized by spousal work hours, related to choices around exercise and diet, all measured at baseline. Specifically, among men, having an employed partner was associated with higher odds of infrequent exercise, and longer spousal work hours predicted fast food consumption among women [55]. Taken together, stressors related to work and home may be associated with increased weight and BMI, but the types of stressors that affect men and women could differ. The current study adds to this literature in examining the effects of combined work and family stressors on BMI over time in a predominantly female sample of lower and middle wage earners in health care. We encourage replication of this research question to confirm and clarify these relationships both in men and women as we were underpowered to examine gender differences here.

Our longitudinal findings may also reflect that BMI is more susceptible to changes in the social environment than biological markers representing CVD risk over the 18-month study period. Theoretical frameworks linking stress to health, such as the Integrated Model of Stress, suggest that behavioral pathways chronologically precede and subsequently relate to disease [56]. Both diet and physical activity may have a relatively quick impact on BMI. In a pilot workplace intervention related to the current WFHN study, a program to address work and family stress improved employee health-related behaviors but not general measures of health. Specifically, over a six month follow-up period, treatment workgroups exhibited improvements

in exercising behavior and perceptions of time to prepare healthy meals but no direct changes due to treatment in non-behavioral measures of well-being such as self-reported health and psychological distress were evident [22, 23]. The authors stated that they first focused on changing health-promoting behaviors, such as diet and physical activity, which are more likely to change over a relatively short period of time. In the current study, we similarly find that WTFC is associated with BMI but not many biological measures, perhaps because health behaviors are more easily and quickly changed than physiological indicators of disease. Our findings do not suggest any associations between WTFC and smoking behaviors measured by cigarette consumption.

WTFC and CRS and other risk factors:

WTFC was inversely associated with HDL cholesterol in pooled outcome analyses in our data. Unlike BMI, we did not detect any baseline or longitudinal associations between WTFC and this outcome, though effect estimates and confidence intervals for the effects of WTFC on BMI are not substantially different from analysis to analysis (Effect estimates for WTFC: B=-0.23, CI=(-0.56, 0.10); B=-0.32, CI=(-0.57, -0.08); B=0.32, CI=(-0.72, 0.07) in baseline, pooled and longitudinal analyses, respectively). Selection bias may explain why significant effects are observed for HDL cholesterol in pooled analyses only. Roughly 36% of the sample with any measure of HDL at baseline left the study by 18 months. Our data does not allow us to specifically examine whether those employees with the worst HDL cholesterol were the same ones dropping out of the study; only a small percentage (3.4%) of the sample had "risky" levels of HDL cholesterol (< 40 mg/dL), and none of these individuals left the study. Still, predictors of HDL attrition from baseline to 18 months do suggest that certain characteristics associated with

dropout may be resulting in a less healthy sample in which effects of WTFC on HDL cholesterol are detected across waves but not at baseline. For example, older age, higher job demands and foreign-born status are significantly associated with higher odds of dropout for this outcome over the course of the study. Data also suggests that older age and higher job demands are associated with significantly higher (i.e.: better) HDL at every time point. Thus, if older individuals and employees with the highest job demands are systematically leaving the study over time, those remaining in the sample will be less healthy, and we are more likely to detect the potentially deleterious effects of WTFC on HDL in the pooled analyses compared to baseline. There were no discernable differences in HDL levels by foreign-born status at any time point and, thus, differential dropout by this variable is unlikely to explain our findings.

We anticipated that WTFC would be associated with the CRS over the course of the study's 18 months due to previous findings that suggested WTFC was positively and significantly associated with CRS at baseline in this same sample. For every 1 point increase in the WTFC scale, Berkman and colleagues found that cardiometabolic risk over a 10 year period increased almost 0.40 percentage points, CI= (0.04-0.74) [3]. While we do not find support that WTFC is associated with CRS in pooled or longitudinal analyses, we note that previous baseline findings are consistent with the baseline trends we detect between WTFC and individual risk factors in the current study. We speculate that, perhaps, BMI singlehandedly drove the baseline effects of WTFC on baseline CRS. We also find that 39% of the sample with CRS at baseline had left the study by 18 months and that older age predicted CRS values among employees that dropout over time. Like HDL cholesterol, older age is associated with significantly higher CRS at all time points. If older employees are leaving the study, the remaining sample is likely to be younger and healthier and, thus, it will be challenging to detect effects of WTFC on CRS over

time. Another explanation for failure to find effects on WTFC on CRS beyond baseline may reflect challenges in detecting changes in biological phenomena (vs. behaviors) over an 18 month study period. Reverse causation serves as another explanation for the discrepant results at baseline and across waves; worse cardiometabolic health could actually cause higher WTFC (and not the other way around). In fact, our post hoc analysis revealed that the effect of CRS at baseline on pooled WTFC across waves was of borderline statistical significance ($p=0.06$). These findings suggest that lower CRS could be associated with higher WTFC across waves. Therefore, the causal relationship between these variables may not be in the hypothesized direction because, for example, individuals with higher cardiovascular risk become more strained by work and family demands due to their poor health status. Finally, it is also possible that WTFC is not associated with CRS, and the baseline associations were found due to chance.

WTFC was not associated with HbA1c, total cholesterol, blood pressure or cigarette consumption at any point in time. Research on job strain and cardiovascular outcomes serves to support the plausibility of these relationships and motivates the current study. However, our null findings may be attributed to the unique composition of this sample as well as the fact that the combination of work and family stressors may not affect health the same way as job strain alone. As mentioned previously, the scientific literature suggests a strong link between work stress [6, 30, 57, 58], home life stress [15, 30, 59] and the combination of the two [2] with poorer cardiovascular outcomes. The most extensive work in this area concerns how workplace stress specifically is associated with incident heart disease. Kivimaki and colleagues report in a meta-analysis of prospective cohort studies that effect estimates vary from almost 40% increased risk to 2- or even 4-fold increases in risk of CVD (including incident coronary heart disease and ischemic heart disease as well as CVD death) due to some form of job strain (job demands and

decision authority, or job control). A recent systematic review also suggests that work stress may be related more consistently with the development of cardiovascular disease in men than in women [60]. Most of the samples referenced in job strain literature are predominantly male, Caucasian employees, whereas the WFHN occupational cohort is racially and ethnically diverse and overwhelmingly comprised of women. Further, multiple studies suggest that the dual demands of work and family affect men and women differently and, unlike the job strain literature, *women* may experience interrole strain and subsequent poor health more acutely [1, 61-64]. For example, a hallmark study examining blood pressure, heart rate and catecholamine excretion among Swedish white-collar workers indicated that biological markers were elevated among all employees during work hours but that differential stress responses were evident among men and women after work hours. After leaving work adrenaline, blood pressure and heart rate declined among men but not among women, suggesting perhaps that men are privileged to "unwind" at home while women's stress persists [9]. After noting the dearth of research on female-only samples, Orth-Gomer and colleagues studied the role of work and family stressors on recurrent cardiac event among women only and found that strain from both realms predicted worse health outcomes [15, 16]. Subsequently, these researchers examined the effects of behavioral interventions on stress attenuation among patients with acute coronary syndrome. Psychological assessments indicated that men and women exhibited unique discussion styles and preferences regarding group composition.

In light of these literatures, two plausible explanations for our predominantly null findings remain. It may be that work and family stress, like job strain, affects the CVD risk of men more than women, and we can attribute the lack of association between WTFC and most of our outcomes of interest to a predominantly female sample. Alternatively, if per the work and

family scholarship, these dual demands are indeed more pronounced in women, our results may indicate that work and family stress does not actually predict most individual CVD risk factors, at least not in a racially and ethnically diverse sample such as that used here. While disentangling these possibilities is beyond the scope of the current research, the linkage between work-family conflict and CVD risk factors warrants further scrutiny, and we encourage future research to focus on both male and female study populations.

Limitations and Strengths:

We acknowledge some limitations in the current study. WTFC is reported by employees, and this perception of work and family stress could be potentially misclassified. For example, sicker employees may report more conflict than their healthy counterparts, resulting in a possible overestimation of the effects of work-family stress on health. Similarly, employees consented to participate in the study and, though response rates were reasonably high, there is also a possibility that either healthier or sicker employees selected into the study, which could bias results in either direction. This observational study is embedded within a randomized field experiment in which an intervention was administered to employees in certain workgroups in an effort to improve health. Despite thoroughly examining the effects treatment status on our outcomes, it is plausible that the observed effects of WTFC on cardiometabolic risk factors such as BMI and HDL cholesterol across waves could be due to the intervention itself because randomization did not occur at the individual level. We found little evidence for this as part of a post hoc analysis, however. In models stratified by treatment status, the only outcome for which stronger, significant effects were observed in the intervention group was CRS, which was not significantly associated with WTFC in non-stratified pooled analyses, and it is worth noting that

the effects of WTFC on CRS were in the same direction in both treatment groups. We also note substantial attrition from baseline to 18 months. While we replicated our findings using outcome data at baseline, 6 months and 12 months only (thus, remedying some concern of attrition throughout the study period), failure of employees to continue in the study remains a limitation of our analysis. While the WTFC measure employed here is widely-used and validated among workers in many settings [36], the scale may not be appropriate for this particular study population. Additionally, the etiologic period for changing biological indicators of CVD risk (such as HbA1c, blood pressure and total cholesterol) due to WTFC is unclear, and the 18 month study may not be sufficient to detect these changes, assuming a causal relationship, particularly given that the few existing longitudinal studies using these variables have generally been of a longer duration. This may not be a large concern given that WTFC was measured at only one time point, however. Finally, although multiple worksites were involved in the study, the data also represents the experiences of a single industry that was willing to participate in a workplace intervention, which limits the generalizability of our findings to other industries. We suggest that the research pertaining to work and family demands and conditions continue to take place in a variety of settings.

This work also exhibits a number of substantive and methodological strengths. This is the first study to longitudinally examine work and family conflict and variety of biomarkers representing cardiovascular disease risk in an occupational cohort. Prior studies examining the effects of job strain and cardiovascular health are somewhat limited in scope, comprising of study populations that are predominantly male, Caucasian employees. Similarly, roughly three-quarters of the work-family literature utilizes predominantly Caucasian samples [31]. Our study represents racially and ethnically diverse, predominantly low wage cohort of healthcare workers,

offering a broader perspective on both the job strain and work-family literatures (though the heterogeneity of the sample could have resulted in a loss of statistical power and contributed to our null results as well).

Additionally, this study utilized predominantly objective outcome measures, including assessed measures of blood pressure, blood draws to ascertain HbA1c and cholesterol and validated methods for measuring BMI. The use of these biological markers and other objective measures offer meaningful improvement to the validity of work-family research. Cigarette consumption, work-to-family conflict and many covariates of interest were self-reported in our sample, however. Further, the majority of work-family scholarship is cross-sectional in nature [65], although a few exceptions do exist [66-70]. The use of multiple outcome measures strengthens our study's internal validity and helps to ensure that exposures precede outcomes. We also employ multilevel methods to appropriately account for the clustering of employees within worksites (and multiple time points per employee), a method which yields accurate standard errors and confidence intervals.

Conclusion:

A longitudinal study of nursing home employees indicates that WTFC is consistently associated with BMI but not many other biological and self-reported measures representing cardiovascular disease risk. We speculate that outcomes associated with behaviors are more closely linked to interrole conflict than biological markers, particularly with a relatively short study period of 18 months. We recommend that future research continue to clarify the effects of work and family stressors on individual risk factors for CVD in a variety of occupational settings.

Appendix 1.1: Correlations of individual outcomes across waves*

	Outcome at 6 months	Outcome at 12 months	Outcome at 18 months
CRS baseline (% 10yr risk)	0.96	0.95	0.92
HBA1c baseline (%)	0.83	0.75	0.73
Systolic Blood Pressure baseline (mmHg)	0.75	0.76	0.71
Diastolic Blood Pressure baseline (mmHg)	0.69	0.66	0.62
Total Cholesterol baseline (mg/dL)	0.38	0.40	0.34
HDL Cholesterol baseline (mg/dL)	0.35	0.42	0.30
BMI baseline (height/weight^2)	0.96	0.95	0.93
Cigarettes/week baseline	0.87	0.85	0.84

*All correlations $p<0.0001$

Appendix 1.2: Correlations between WTFC and related covariates

	FTWC	FSSB	Schedule Control	Job Demands	Job Control
Pearson Correlation Coefficients	0.41	-0.22	-0.20	0.32	-0.22
P-Value	<.0001	<.0001	<.0001	<.0001	<.0001
Sample Size	1519	1508	1505	1520	1508

Appendix 1.3 Outcomes across waves*

	Control					Treatment				
	Baseline		18 months			Baseline		18 months		
	N	Mean	N	Mean	p-value*	N	Mean	N	Mean	p-value*
WTFC	797	2.75	553	2.67	0.08	723	2.84	454	2.66	**0.01**
CRS	733	7.56	465	7.93	0.42	679	6.97	385	7.44	0.36
BMI	786	29.51	541	29.65	0.71	715	29.38	446	29.65	0.51
Total Chol	767	190.77	514	199.04	**<0.001**	697	190.82	417	201.36	**<0.001**
HDL	775	63.23	514	62.59	**0.03**	698	63.91	417	63.36	0.11
HbA1c	759	5.53	481	5.45	0.05	694	5.50	397	5.42	0.05
SBP	792	114.96	545	113.03	**0.01**	719	114.60	450	111.74	**0.0002**
DBP	792	72.64	545	71.27	**0.01**	719	72.06	450	70.25	**0.0009**
Cigarettes	799	24.05	553	21.34	0.26	723	22.78	454	18.24	0.09

* p-values tests whether values of a given variable are statistically different at baseline and at 18 months, within treatment arms

Appendix 1.4 Associations between baseline FTWC and markers of cardiometabolic risk

	Baseline			Pooled			Longitudinal		
	CRS								
	N=1339			**N=1439 Obs=4284**			**N=1439 Obs=4284**		
	Estimate	**Standard Error**	**p-value**	**Estimate**	**Standard Error**	**p-value**	**Estimate**	**Standard Error**	**p-value**
Intercept	3.49	0.94	0.001	3.13	0.94	0.003	3.13	0.94	0.003
FTWC	0.19	0.23	0.41	0.13	0.22	0.56	0.20	0.25	0.43
Time				0.04	0.03	0.14	0.04	0.03	0.15
FTWC*Time							-0.03	0.05	0.52
	BMI								
	N=1418			**N=1439 Obs=4584**			**N=1439 Obs=4584**		
	Estimate	**Standard Error**	**p-value**	**Estimate**	**Standard Error**	**p-value**	**Estimate**	**Standard Error**	**p-value**
Intercept	27.53	1.34	<.0001	26.99	1.32	<.0001	26.99	1.32	<.0001
FTWC	0.63	0.33	0.06	0.62	0.32	0.05	0.54	0.33	0.10
Time				**0.06**	**0.02**	**0.003**	**0.06**	**0.02**	**0.003**
FTWC*Time							0.04	0.03	0.26
	Total Cholesterol								
	N= 1389			**N= 1439 Obs=4484**			**N= 1439 Obs=4484**		
	Estimate	**Standard Error**	**p-value**	**Estimate**	**Standard Error**	**p-value**	**Estimate**	**Standard Error**	**p-value**
Intercept	148.36	8.67	<.0001	176.12	4.67	<.0001	176.09	4.67	<.0001
FTWC	-1.02	1.17	0.38	-0.85	0.97	0.38	-2.52	1.56	0.10
Time				**2.89**	**0.32**	**<.0001**	**2.91**	**0.32**	**<.0001**
FTWC*Time							0.76	0.55	0.17
	HDL Cholesterol								
	N=1398			**N=1439 Obs=4487**			**N=1439 Obs=4487**		
	Estimate	**Standard Error**	**p-value**	**Estimate**	**Standard Error**	**p-value**	**Estimate**	**Standard Error**	**p-value**
Intercept	58.57	1.79	<.0001	62.15	0.94	<.0001	62.15	0.94	<.0001
FTWC	-0.38	0.24	0.12	-0.41	0.18	0.02	-0.53	0.30	0.08
Time				**-0.28**	**0.06**	**<.0001**	**-0.28**	**0.06**	**<.0001**
FTWC*Time							0.05	0.11	0.62

Appendix 1.4 Associations between baseline FTWC and markers of cardiometabolic risk (continued)

Systolic Blood Pressure

	N= 1426			N=1439 Obs=4603			N=1439 Obs=4603		
	Estimate	**Standard Error**	**p-value**	**Estimate**	**Standard Error**	**p-value**	**Estimate**	**Standard Error**	**p-value**
Intercept	120.12	2.47	<.0001	113.95	2.20	<.0001	113.93	2.20	<.0001
FTWC	-1.01	0.56	0.07	-0.60	0.52	0.25	-1.29	0.62	0.04
Time				**-0.94**	**0.09**	**<.0001**	**-0.93**	**0.09**	**<.0001**
FTWC*Time							**0.32**	**0.16**	**0.04**

Diastolic Blood Pressure

	N=1426			N=1439 Obs=4603			N=1439 Obs=4603		
	Estimate	**Standard Error**	**p-value**	**Estimate**	**Standard Error**	**p-value**	**Estimate**	**Standard Error**	**p-value**
Intercept	77.27	1.88	<.0001	73.61	1.63	<.0001	73.60	1.63	<.0001
FTWC	-0.75	0.42	0.08	-0.53	0.37	0.15	-0.86	0.47	0.07
Time				**-0.60**	**0.08**	**<.0001**	**-0.60**	**0.08**	**<.0001**
FTWC*Time							0.15	0.13	0.25

HbA1c

	N=1378			N=1439 Obs=4405			N=1439 Obs=4405		
	Estimate	**Standard Error**	**p-value**	**Estimate**	**Standard Error**	**p-value**	**Estimate**	**Standard Error**	**p-value**
Intercept	7.60	0.18	<.0001	5.75	0.12	<.0001	5.75	0.12	<.0001
FTWC	0.01	0.03	0.68	0.00	0.03	0.95	0.02	0.03	0.63
Time				**-0.04**	**0.00**	**<.0001**	**-0.04**	**0.00**	**<.0001**
FTWC*Time							-0.01	0.01	0.27

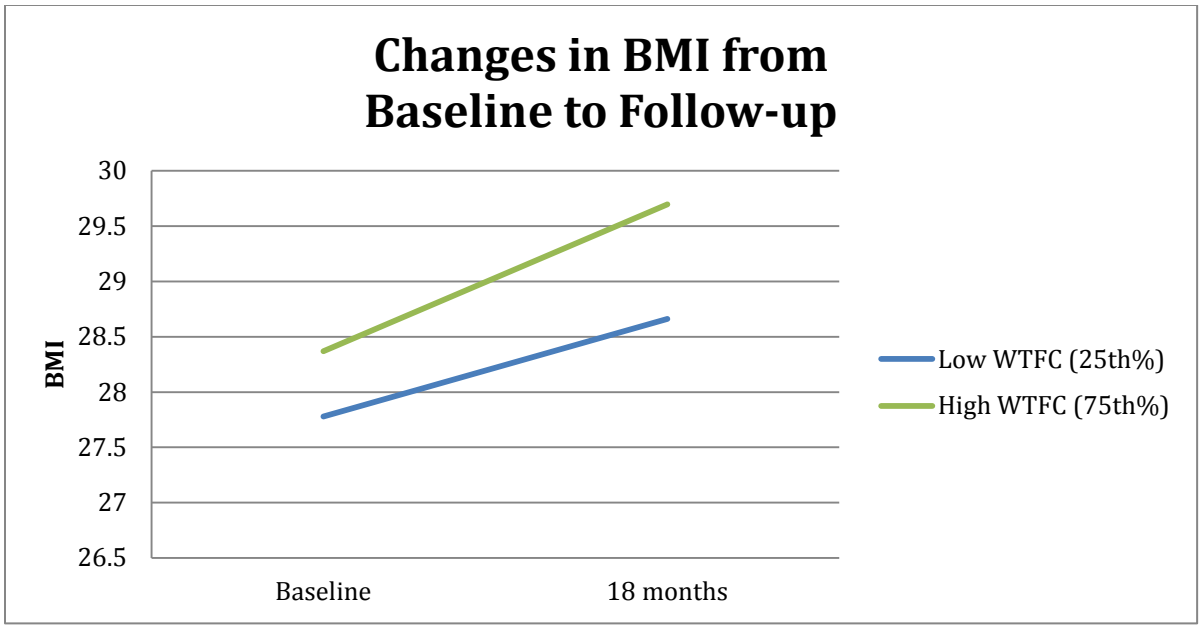
Cigarettes/week

	N=1438			N=1439 Obs=4651			N=1439 Obs=4651		
	Estimate	**Standard Error**	**p-value**	**Estimate**	**Standard Error**	**p-value**	**Estimate**	**Standard Error**	**p-value**
Intercept	-20.52	8.78	0.03	-21.96	8.30	0.01	-21.96	8.30	0.01
FTWC	-1.51	2.09	0.47	-1.81	1.92	0.34	-1.82	2.10	0.39
Time				**-0.94**	**0.24**	**<.0001**	**-0.94**	**0.24**	**<.0001**
FTWC*Time							0.004	0.41	0.99

All models control for treatment status, race, income, age, sex, marital status, foreign born status, occupation, work hours and number of children. Models also account for FSSB, job strain and schedule control at the individual- and group-levels and, where appropriate, medication

Appendix 1.5: Tests of reverse causation (Pooled)

	WTFC N=1338 obs=4333			FTWC N=1339 obs=4337		
	Estimate	**Standard Error**	**p-value**	**Estimate**	**Standard Error**	**p-value**
Intercept	2.94	0.09	<.0001	2.14	0.06	<.0001
CRS at baseline	*-0.005*	*0.00*	*0.06*	-0.0005	0.002	0.79
Time	-0.03	0.01	<.0001	0.00	0.01	0.48



* Figure generated using the following regression equation and inputting values for time and WTFC:
$BMI_{tij} = 26.94 + 0.42(WTFC) + 0.06(Time_{ij}) + 0.08(WTFC)(Time_{ij})$

Figure 1.1: Changes in BMI from Baseline to Follow-up by Level of WTFC*

CHAPTER 2

Effects of an Intervention to Improve Workplace Flexibility on Employee Biomarkers of Inflammation

Abstract:

Introduction: Studies suggest that inflammation may mediate the relationship between stress and cardiovascular disease. However, no research has examined whether the combined stress of work and family are associated with higher levels of inflammation in the body or if reducing this type of stress results in less inflammation. The current study aims to fill this gap in the literature and examines the effects of a workplace intervention designed to increase flexibility, schedule control and workplace support on employee markers of inflammation as part of a prospective, randomized field experiment.

Methods: Among 949 nursing home employees, treatment status and log transformed biomarkers of inflammation (CRP, IL-6 and IL-1β measured by dried blood spots) served as the primary exposure variable and outcomes, respectively. Data were collected at two time points (baseline and 12 months). We estimated multilevel linear regression models that account for multiple measures per employee as well as the nesting of employees within worksites. We also considered subgroup-specific effects in potential changes in employee markers of inflammation by parental status, foreign born status and age.

Results: The workplace intervention did not lead to significant changes in employee levels of inflammation from baseline to 12 months (β=0.10, p=0.28 for CRP, β=-0.02, p=0.70 for IL-6 and β=-0.11, p=0.36 for IL-1 β). We detected some differences in treatment effects from baseline to 12 months based on foreign-born status in both stratified analyses and models with three-way

interaction terms suggesting potentially worse CRP for foreign born employees, improvements in IL-1β for U.S. born employees and benefits in IL-6 for foreign born employees.

Conclusion: This study marks the first randomized field experiment to assess the effects of a workplace program to reduce work and family stressors on employee markers of inflammation over time. We speculate that failure to detect treatment effects may be a result of our healthy study population as well as a somewhat short study period of twelve months.

Introduction:

Demographic shifts in the U.S. prompt American workers to report rising levels of work and family stress [1, 16]. Research suggests that strain from both workplace and home life may contribute to the development of cardiovascular disease (CVD) [2, 16], which is the leading cause of death in our country. The current study seeks to assess the relationship between a novel workplace program designed to address work and family demands and a cardiovascular-related outcome in a racially and ethnically diverse prospective, occupational cohort. Given that CVD often develops over decades but does not manifest until middle or later adulthood, many studies of younger adults consider pre-disease markers to assess likely risk of developing CVD. Prior work has suggested that markers of inflammation serve as sensitive and meaningful indicators of cardiovascular disease risk [71, 72]. This study is the first randomized field experiment that can evaluate the effects of a workplace intervention to improve work and family strain on changes in employee levels of inflammation over time.

Work and Family Conflict and Related Policies:

The U.S. labor force has experienced incredible transformations over recent decades. Sixty years ago, less than half of American women participated in the workforce. Today, roughly 70% of women 18 to 64 years of age work outside the home, and a similar proportion of all women with children under the age of 18 years old are employed [73]. In 2008, eighty percent of the workforce lived in dual-earner households, with women contributing nearly half (44%) of the family income despite the persistence of a gender gap in earnings [1]. Roles attributed to men and women at home have evolved substantially as well, with fathers contributing more time today to childcare and household tasks than they did 30 years ago; men spent 2 hours per workday with children in 1977, compared with 3 hours per workday in 2008; women averaged 3.9 hours with children on workdays in both periods [1].

As a result, increasing numbers of women and men may experience competing work and family demands. The incompatibility of home and work life is often referred to as "work/family conflict," a term which Greenhaus and Beutell introduced thirty years ago to describe "interrole conflict in which the role pressures from the work and family domains are mutually incompatible in some respect" [10]. Numerous studies suggest a strong link between work/family conflict and worse mental health outcomes such as depression, anxiety, mood and substance disorders [11, 12, 67, 74-77] as well as poorer physical health outcomes as measured by worse ratings of global health, less sleep, obesity, musculoskeletal pain and harmful health behaviors like lower physical activity and unhealthy diet [2, 12, 78, 79].

Surveys of the American workforce indicated that employees report higher levels of work/family conflict in 2008, relative to the late 1970s [1]. Yet, unlike high income countries in Europe, the U.S. is notorious for its weak labor laws and limited family protection policies [80,

81], particularly legislation that protects women of childbearing age [82]. The U.S. remains 1 of 3 countries out of 173 worldwide that does not provide some level of paid parental leave. Aside from the Family and Medical Leave Act (FMLA), which offers up to 12 weeks of unpaid leave to parents who meet certain criteria, federal legislation for parental leave is non-existent. A handful of states expand upon FMLA to provide additional unpaid benefits, but only two states offer some paid entitlements following the birth of a child [83].

In the face of scarce national support, employers have started to acknowledge that effective policies and practices to reduce work and family stressors have the potential to benefit employees, families and organizations. Yet, these benefits remain limited and understudied. In 2000, eighty to ninety percent of employers offered full-time employees paid holiday and vacation leave, and between 20 and 25% of full-time employees receive paid personal leave. However, fewer than 10% receive any form of childcare support, and this proportion drops to l% among full-time employees in small firms [84]. Other forms of institutional support include flexible work arrangements, such as flextime, compressed work weeks, telecommuting and voluntary part-time work including job-sharing [85]. A recent national survey of employers indicates that at least some proportion of employees were allowed to change start and quit times within a range of hours (27%), compress the work week (7%), work from home occasionally (6%) or regularly (2%) and reduce work hours (6%) [86], but the Bureau of Labor Statistics reports that only about one-quarter (27.5%) of the American workforce actually works a so-called flexible schedule [87]. When alternate arrangements exist, they are often uneven, unpredictable and not formalized within organizations and remain largely at the discretion of individual managers, particularly in small and non-unionized organizations [85, 88]. Low-wage

workers in particular have less access to supportive work environments and policies and practices that promote employee and family health [89, 90].

Few scientific studies have examined the impacts of existing workplace policies and practices on work/family conflict and employee [88, 91] or employer [92] outcomes. Much of the work regarding policy adoption or implementation concerns what predicts adoption of these workplace programs [93-95], not the outcomes they intend to affect. Limited research has assessed the impact of workplace policies on employee well-being [19, 96-98], and few studies utilize longitudinal data to examine associations between work/family conflict and mental and physical health outcomes [19, 99]. Given their designs, these studies have not sufficiently answered the important question of whether changes to the work environment are *causally* linked to better employee health. We are not aware of any quasi-experimental or experimental studies examining these relationships prior to the research efforts associated with the current study [91].

Work/Family Strain and its Impact on CVD and Inflammatory Markers:

Work and family stressors may be particularly relevant for employee cardiovascular outcomes. One challenge to understanding the social and behavioral predictors of CVD is that the disease takes years, often decades, to emerge, and longitudinal research that anticipates the development of disease with long latency can be costly and logistically demanding. The collection of biomarkers, such as blood pressure, lipids, cortisol, and markers of inflammation, offers a useful alternative in epidemiologic research for a number of reasons. Biomarkers often serve as underlying risk factors for as well as intermediate variables along the pathway to disease, which is particularly useful for conditions that develop slowly over time. They also provide direct information about physiological processes in the body and are thus more reliable

than subjective, self-reported measures of health [32]. Research examining the effects of stress on cardiovascular health has started to utilize biomarkers as proxies for and intermediaries of disease [100] and indicates that markers of inflammation may be altered in response to a variety of stressors [101] and also indicate future CVD risk [72, 102, 103].

The current study focuses specifically on the following markers of inflammation as indicators of CVD risk: C-reactive protein (CRP), interleukin-6 (IL-6) and interleukin-1beta (IL-1β). The inflammatory response is typically initiated by injury, the entry of bacteria and/or infection in the body. Immune cells including cytokines IL-6 and IL-1β, which are part of the body's natural immune system (and, thus, are not pathogen-specific), are recruited into tissue and prompt the production of proteins in the liver, such as CRP, as well as lymphocytes and neutrophils involved in the immune response. Acute-phase inflammation is understood as adaptive and protective. It involves short-term elevations in inflammatory markers aimed at defending the host against infection and repairing injured tissue. Chronic, low-grade inflammation (characterized by levels of inflammation lower than those involved in acute-phase activity), however, may be maladaptive and implicated in longer-term health problems and disease processes like CVD as well as endocrine, mood and sleep disorders, disability and even mortality [71]. The recurring recruitment of pro-inflammatory cells is believed to result in endothelial injury, which research suggests can lead to the leakage of lipids into the subendothelial space and, ultimately, contribute to the atherosclerotic process. Unstable atherosclerotic plaques are particularly prone to rupture, leading to the formation of clots that may cause stroke, myocardial infarction or other negative cardiovascular outcomes [104]. CRP is also a response to cardiovascular events and thus the causal relationship between the two is controversial [105, 106].

Preliminary evidence suggests that a range of work-related stressors (which we conceptualize broadly to include measures of job strain, burnout, job dissatisfaction, etc.) may be associated with higher levels of inflammation, though most of this research is cross-sectional in nature and has been conducted with modestly sized samples. A small (n=74) study of working men evaluated the effects of effort–reward imbalance, conceptualized to represent chronic work stress, and found it was significantly associated with higher CRP after administering a laboratory mental stress test, but not at baseline prior to the stress test [107]. A German study of 272 men and 52 women working at an airplane manufacturing plant also indicated that low job control, high job demands and low social support at work were associated with higher circulating CRP [108]. Shirom and colleagues conducted a series of larger cross sectional studies with employed adults in Israel, one of which revealed that job-related burnout was associated with increased CRP among women (n=1563) and another indicated that lower job satisfaction was related to higher CRP among men (n=1539) [109, 110]. However, when they conducted a longitudinal analysis, they found that low perceived control, social support at work and high workload were not associated with changes in CRP levels over a 12 months period in a sample of 1,131 workers [111]. Among a simple random sample of the Whitehall II cohort, low job control and high job demands were not found to be significantly associated with CRP cross-sectionally among 283 men and women [112]. Research involving a variety of work stressors and cytokine outcomes appears more consistent. In samples ranging from 118 to 243 employees with data collected at a single time point (cross-sectional or case control designs), exposures such as low job satisfaction and high job demands were associated with increased levels of pro-inflammatory cytokines IL-4, IL-6 and IL-8 [113-116]. Longitudinal evidence from Italy among 101 nurses similarly suggests that low job satisfaction was associated with increased IL-1β over a 12 month follow-up [117];

however, a smaller study among 38 Korean nurses found that high work stress (objective and subjective) was not associated with this outcome 8 months later [118]. Despite this emerging work, we are unaware of research that examines both the effects of work and home stressors and related interrole conflict on employee markers of inflammation.

The current study examines whether **a workplace program designed to increase flexibility, schedule control and workplace support affects employee markers of inflammation** as an indicator of cardiovascular health**.** This work is based in the tradition of job strain theory [5, 6], specifically the Demand-Control-Support model which considers the combination of job demands and control that result in job strain and the role of workplace social support that protects against it [7]. Work and family conflict is conceptualized as a stressor or perceived form of stress, and we speculate that the intervention program will benefit all employees randomized to treatment, regardless of their levels of perceived stress at the time of randomization.

Specifically, we seek to address the following aims and hypotheses: **First**, we aim to assess whether a workplace intervention designed to decrease work-family conflict and improve employee well-being and effectiveness in work and family roles leads to reductions in levels of inflammation from baseline to 12 months. We hypothesize that employees randomized to the intervention group will demonstrate reduced levels of inflammation at 12 months post-intervention relative to baseline, compared to employees in the control group. **Second**, we aim to examine whether changes in levels of inflammation from baseline to 12 months are more substantial within certain subgroups. We hypothesize that beneficial effects of the intervention will be more pronounced in the following groups: employed parents who are more likely to

report work and family stressors [76]; foreign born employees that comprise a relatively substantial proportion of our sample and may experience more stress and worse health, relative to U.S. born employees [119-121]; and older employees for whom the effects of stress on immune function may be exacerbated [122].

Methods:

Sample:

This study is part of Phase II of the Work Family Health Network (WFHN) project, a joint research endeavor sponsored by the National Institutes of Health and the Centers for Disease Control and Prevention, among others. This phase involved data collection from employees (as well as their managers, spouses and their children) to assess an employer-supported workplace intervention in a group randomized field experiment. The WFHN identified a New England company with numerous nursing home facilities, which we will refer to as "LEEF" and included thirty worksites that were distributed across Massachusetts, Maine, New Hampshire, Vermont, Connecticut, and Rhode Island and able to support data collection and intervention delivery efforts. Sites were randomly assigned to intervention or control (usual practice) status using a biased coin adaptive randomization technique specifically tailored for group randomization, a flexible approach that offered strong internal validity and less opportunity for contamination across facilities [34], and matched based on number of employees, state and retention rate.

Trained WFHN site managers described the study to managers and employees at each work site and addressed any concerns during data collection. At baseline, each of the 1,723 eligible employees within these 30 worksites (n=15 intervention sites and n=15 control sites)

who worked more than 22 hours each week during the day or during the day and night combined (exclusively night workers were not eligible) were invited to complete a computer-assisted personal interview (CAPI) [34]. A total of 1,524 LEEF employees participated at baseline, resulting in a response rate of over 88%. A total of 1,470 employees provided biosamples at the start of the study, though employees who participated in the CAPI survey and those who provided biosamples were not entirely mutually exclusive. (See Figure 2.1 for study flowchart with details on baseline and 12 month data as well as employees excluded from our analytic sample. We excluded employees with biomarker data below predetermined lower levels of detection and truncated outcomes at the 99th percentile, as described in the Measures section. We also excluded employees who provided only CAPI or biosample data.). We do not have any information on employees who did not consent to participate in the study. The number of assays conducted on markers of inflammation at baseline varied due to laboratory processes (n=1366 for CRP, n=1344 for IL-6 and n=1190 for IL-1β before exclusions to our specific sample were made). The same data collection procedures were used and identical measures were collected at 12 months (n=1201 for CRP, n=949 for IL-6 and n=826 for IL-1β at 12 months before the aforementioned exclusions were made). As discussed further below, dropout from baseline to 12 months in this sample did not vary by treatment status. Employees who provided all data components for the larger WFHN study, including blood samples, received $60 for their participation.

Measures:

Trained field interviewers administered survey instruments and health assessments as described elsewhere [34] which addressed employee demographics, socioeconomic status,

family demographics, work environment, physical health, mental health, and family relationships. Identical data was collected at baseline and 12 months, although treatment status and covariates were not time updated, and only 12 month outcome measures were used in this analysis. After obtaining written consent from all employees, interviews and health assessments lasted approximately 50 and 20 minutes, respectively, and were on occasion collected on different days.

Exposure Variable:

The primary predictor of interest is exposure to the workplace program or intervention status. The workplace program focused on increasing work flexibility, control over how and when work is done as well as increasing the support of supervisors and co-workers for employees' work/family issues in an effort to promote employee health and organizational goals. The field experiment has been described more extensively elsewhere [34, 88, 123-125]. Briefly, over a four-month period, employees and managers in treatment workgroups participated in face-to-face sessions and corresponding exercises during work hours. These activities were geared toward work redesign and the identification of work practices and processes to increase employee control over work time while continuing to meet business needs. Employees and managers were encouraged to work individually and collectively toward the goal of achieving work and family balance for staff. Additionally, managers participated in separate face-to-face training sessions that covered ways to demonstrate support for employees' lives outside of work and performance on the job. Managers also received computer-based training which included tracking exercises to help managers put these lessons learned into practice and to monitor the fidelity of the intervention. Both employee and manager activities were scripted and structured

but encouraged participation and interaction. Workgroups randomized to control status continued with "business as usual" policies and practices [126]. The treatment variable, which was originally double blinded, was later coded yes/no to denote randomization to treatment as part of an intent-to-treat model.

Outcome Variables:

The primary outcomes of interest include three pro-inflammatory markers considered related to CVD risk: CRP and cytokines IL-6 and IL-1β. To obtain assays of these inflammatory biomarkers, employees were asked to provide dried blood spots (DBS) by a finger stick. Interviewers wearing appropriate personal protective equipment disinfected the employee's middle or ring finger with an alcohol swab and proceeded to prick the finger with a sterile, disposable micro-lancet. While venipuncture to draw blood plasma or serum is often employed to collect CRP and other proinflammatory cytokines like those measured here, DBS techniques for examining markers of inflammation are valid and particularly useful in field-based studies when venipuncture with a trained phlebotomist is not feasible or samples are desired from a more generalizable sample (participation rates with DBS are higher than with phlebotomy) [32, 127-130]. As previously described [38], up to five blood spots were collected at once, air-dried, and sealed in a plastic bag for room-temperature shipment by means of a protocol specifically validated for serum to DBS equivalents [39, 128]. For CRP, samples were assayed at the University of Washington laboratory of Dr. Mark Wener. A calibrated punch from the DBS was eluted in a buffer solution and transferred to a well on a microtiter plate coated with an antibody that recognizes a distinct antigenic determinant on the CRP molecule. CRP in the elution solution is bound by the anti-CRP mAb (solid phase immobilization). A conjugate solution

containing goat anti-CRP Ab coupled to peroxidase (enzyme-linked antibody) is then added to each well, resulting in CRP molecules being sandwiched between the solid phase and enzyme-linked antibodies. After incubation, the wells are washed to remove unbound material. A tetramethylbenzidine (TMB) and hydrogen peroxide (H_2O_2) solution is added; H_2O_2, cleaved by the peroxidase, reacts with TMB and causes the solution to develop color**.** The CRP concentration is directly proportional to the absorbance of the solution; absorbance is measured spectrophotometrically. Similarly, for IL-6 and IL-1β microtiter plate wells were also coated with capture antibodies against these cytokines at Northwestern University in the laboratory of Dr. Thomas McDade. Labeled detection antibody binds to the captured cytokine, and an electrochemiluminescent signal was used to quantify the concentration of each cytokine in each sample against a standard curve. The CRP assay lower limit of detection was 0.035mg/L, within-assay imprecision (CV) was 8.1% and between-assay imprecision was 11.0%. Lower levels of detection were 0.3 pg/mL for both IL-6 and IL-1β. For IL-6, within-assay CV ranged between 8.98 and 9.73% and between-assay CV ranged between 3.41 and 8.51%. For IL-1β the within-assay CV ranged between 8.32 and 9.34% and between-assay CV ranged between 6.89 and 15.78%. Because we utilized DBS measures (as opposed to the commonly used plasma concentration), we implemented the following DBS to plasma conversion for CRP: CRP_serum = (CRP_DBS*0.448) - 0.084. To avoid including individuals with acute inflammation due to extreme illness or infection, we excluded all outcomes above the 99th percentile. This criterion removed roughly an equal proportion of employees in the treatment and control groups from our sample (see Figure 2.1). All outcomes were measured continuously and transformed to the logarithmic scale to achieve a normal distribution.

Covariates:

Our final models (see explanation below) adjusted for: occupation (employee's official job title, coded nurse or other), marital status (currently married/permanent romantic partner living with you?), employee gender (male/female), education (high school or less vs. some college or higher) and age in years (measured continuously, as basic scatterplots depicted a fairly linear relationship with the outcomes). Race/ethnicity was coded as Non-Hispanic White, Non-Hispanic Black, Hispanic/Latino or other race. Indicator variables for each racial/ethnic group were generated, and the reference group was assigned to Non-Hispanic White race.

Stratification variables:

For stratified models, we also included foreign-born status (yes/no), number of children living in the household four or more days/week and under the age of 19 years (none vs. one or more) and dichotomized the aforementioned age variable (less than or equal to 45 years of age vs. over 45 years).

Analysis:

To examine whether the intervention affected changes in employee markers of inflammation (Aim 1), we used multiple outcomes per employee (with measures taken from employees at baseline and 12 months) and estimated multilevel linear regression models that account for multiple measures per employee and nesting of employees within worksites by modeling random effects for employee and site. Pro-inflammatory markers served as outcomes in separate models and treatment status as the exposure variable as part of an intent-to-treat analysis. We tested time*treatment interactions to examine changes in employee markers of

inflammation from baseline to 12 months. We then included a set of sociodemographic covariates hypothesized a priori to predict the outcomes of interest, an approach that improves the statistical power of our models. The primary treatment effect of interest (the regression coefficients for the time*treatment variable) was similar in models with or without covariates, and we present models with covariate adjustment.[‡] Finally, to test our secondary aim, we stratified this final model by parental status (no children vs. 1 or more), foreign born status (yes/no) and age (less than or equal to 45 years of age vs. over 45 years of age). We sought to confirm results from our stratified analyses with models using three-way interaction terms (i.e.: time*treatment*subgroup).

Results:

Sample Characteristics:

At baseline, we included a total of 949 LEEF employees with data available for the main variables of interest. Mean levels of CRP, IL-6 and IL-1β were 1.90 mg/L, 1.78 pg/mL and 53.02 pg/mL, respectively. Roughly half the sample was randomized to treatment (53.1%) and to control (46.9%) status (See Table 2.1 for complete descriptive statistics.). The majority of sociodemographic, health-related and work/family variables included in this study at baseline were not significantly different in the treatment group compared to the control group (including predictors of inflammation like smoking and obesity), although the proportion of females was

‡ $Inflamm_{tij} = \beta_0 + \beta_1 (Treatment_j) + \beta_2 (Time_{tij}) + \beta_3 (Treatment_j)(Time_{tij}) + \beta_4 (Confounders_{tij}) + t_{0tij} + e_{0ij} + u_{0j}$
Where: t= time; i= employee; and j = workgroup
And:
$[t_{0tij}] \sim N(0, \sigma^2_{t0})$
$[e_{0ij}] \sim N(0, \sigma^2_{e0})$
$[u_{0j}] \sim N(0, \sigma^2_{u0})$

Table 2.1: Descriptive Statistics (Baseline)

N= 949	N	Mean(sd) / %
CRP (mg/L)	949	1.90 (2.11)
IL-6 (pg/mL)	949	1.78 (1.71)
IL-1β (pg/mL)	949	53.02 (60.04)
Age	948	38.50 (12.33)
Treatment		
No	504	53.11
Yes	445	46.89
Occupation		
RN/LPN	264	27.88
Other	683	72.12
Sex		
Male	67	7.06
Female	882	92.94
Married/partnered		
Not married/partnered	337	35.51
Married/partnered	612	64.49
Race		
White	615	64.81
Black	116	12.22
Hispanic	138	14.54
Other race	80	8.43
Education		
Grades 1-8	7	0.74
Some High School	43	4.53
High School	326	34.35
Some College	467	49.21
College or more	106	11.17
Foreign Born		
No	711	74.92
Yes	238	25.08
Parent		
No	411	43.35
Yes	537	56.65

significantly higher and age significantly lower in the treatment group compared to the controls. No significant differences in mean outcome levels for CRP, IL-6 or IL-1β between treatment and control groups were present at baseline (see Table 2.2 for complete details).

There were no discernable differences in demographics between our final analytic sample and the overall study sample. However, employees who were excluded from our analytic sample had significantly lower CRP levels and were less obese than those analyzed in the current study (see Appendix 2.1 for descriptive statistics on original sample and Appendix 2.2 for comparisons between those excluded from versus included in the analytic sample). Data for 949 employees were analyzed at baseline and 621 employees at 12 months. Additionally, in predictive models of dropout from baseline to 12 months, we observed that baseline measures of CRP and IL-1β (but not other covariates) predicted subsequent dropout, although these relationships did not vary by treatment group.[§]

Effects of intervention on changes in employee inflammation:

In multilevel regression models, we found that the workplace intervention was not significantly associated with changes in employee inflammation from baseline to 12 months. Inclusive of aforementioned covariates, there was a 0.10-point greater change in CRP due to treatment from baseline to 12 months (p=0.28) (again, all outcomes log transformed).

[§] Predictors of dropout on log transformed markers of inflammation: $OR_{CRP\ at\ baseline} = 1.22$ (CI = (1.09 - 1.36)); $OR_{IL\text{-}1\beta\ at\ baseline} = 1.18$ (CI = 1.05 - 1.34) (there was no effect of baseline IL6 on subsequent dropout). Predictors of dropout did not appear to depend on treatment status, as there was no significant baseline inflammation*treatment interaction in these models. Though ORs for these interactions were small and NS, the effect of baseline CRP and IL-1β on subsequent dropout was lower for people in the treatment group than control. The association between baseline IL-6 and dropout was higher in the treatment group (although baseline IL6 did not predict dropout on its own).

Table 2.2: Descriptive Statistics by treatment status (Baseline)

	Treatment		Control		
N= 949	**N**	**Mean(sd) / %**	**N**	**Mean(sd) / %**	**p-value***
CRP (mg/L)	445	1.86 (1.96)	504	1.93 (2.23)	0.58
IL-6 (pg/mL)	445	1.77 (1.97)	504	1.79 (1.46)	0.91
IL-1β (pg/mL)	445	51.91 (58.90)	504	54.01 (61.06)	0.59
Age (years)	444	37.63 (12.34)	504	39.26 (12.30)	0.04
Occupation					0.56
RN/LPN	127	28.61	137	27.24	
Other	317	71.39	366	72.76	
Sex					0.001
Male	19	4.27	48	9.52	
Female	426	95.73	456	90.48	
Married/partnered					0.59
Not married/partnered	162	36.40	175	34.72	
Married/partnered	283	63.60	329	65.28	
Race					0.25
White	295	66.29	320	63.49	
Black	58	13.03	58	11.51	
Hispanic	54	12.13	84	16.67	
Other race	38	8.54	42	8.33	
Education					0.70
Grades 1-8	2	0.45	5	0.99	
Some High School	19	4.27	24	4.76	
High School	155	34.83	171	33.93	
Some College	224	50.34	243	48.21	
College or more	34	10.11	61	12.10	
Foreign Born					0.60
No	337	75.73	374	74.21	
Yes	108	24.27	130	25.79	
Parent					0.19
No	203	45.62	208	41.35	
Yes	242	54.38	295	58.65	

*p-values based on chi-square or F tests

The changes in IL-6 and IL-1β due to treatment from baseline to 12 months were also non-significant (IL-6: β=-0.02, p=0.70; IL-1β: β =-0.11, p=0.36) (see Table 2.3a).

Effects of intervention on changes in employee inflammation in subgroups:

Tests of subgroup differences in changes in employee inflammation from baseline to 12 months were conducted with stratified models and models with three-way interaction terms. In stratified models, there were no intervention effects for IL-6 in any strata of parental status, age or foreign born status (see Table 2.3b). For CRP, there was a marginal increase in inflammation due to treatment (a worse treatment effect) from baseline to 12 months for employees born outside the U.S. (β=0.28, p=0.09) but not those born in the U.S. (β=0.04, p=0.73). We also detected a marginal reduction in IL-1β due to treatment (a beneficial treatment effect) from baseline to 12 months for U.S. born employees (β=-0.27, p=0.03) but not those born outside the country (β=0.34, p=0.16).

Models with three-way interaction terms indicated that changes in IL-6 from baseline to 12 months significantly varied by foreign born status (β=-0.26, p=0.009); the effects of treatment did not vary by foreign born status for other markers of inflammation (p-value was 0.34 for CRP and 0.09 for IL-1β). P-values for three-way interaction terms testing variations in treatment effects by parental status were 0.87 for CRP, 0.34 for IL-6 and 0.38 for IL-1β; p-values for three-way interaction terms testing variations in treatment effects by age were 0.41 for CRP, 0.43 for IL-6 and 0.94 IL-1β (results not presented).

Table 2.3a – Main effects of a workplace intervention on employee inflammatory markers from baseline to 12 months

	CRP (log) N= 944 Obs = 1383			IL-6 (log) N= 944 Obs = 1383			IL-1 β (log) N= 944 Obs = 1383		
	Estimate	**Standard Error**	**p-value**	**Estimate**	**Standard Error**	**p-value**	**Estimate**	**Standard Error**	**p-value |**
Intercept	-0.69	0.30	0.03	0.16	0.14	0.26	3.38	0.25	<.0001
Treatment vs. Control	0.01	0.11	0.91	-0.05	0.04	0.27	-0.02	0.09	0.84
12 months vs. Baseline	-0.07	0.06	0.24	-0.04	0.03	0.17	0.03	0.08	0.69
Treatment*12 months	0.10	0.09	0.28	-0.02	0.05	0.70	-0.11	0.12	0.36

All models control for race, education, age, sex, occupation and marital status

Table 2.3b – Stratified models indicating subgroup effects of a workplace intervention on employee inflammatory markers from baseline to 12 months

	CRP (log)					
	Estimate	**Standard Error**	**p-value**	**Estimate**	**Standard Error**	**p-value**
	Without children N= 408 Obs =585			**With children N= 535 Obs =797**		
Intercept	-0.59	0.42	0.17	-0.70	0.45	0.13
Treatment vs. Control	-0.04	0.14	0.78	0.02	0.13	0.91
12 months vs. Baseline	-0.12	0.09	0.20	-0.04	0.08	0.62
Treatment*12 months	0.12	0.14	0.37	0.09	0.13	0.47
	Less than or equal to 45 years N= 652 Obs =956			**Older than 45 years N= 292 Obs =497**		
Intercept	-0.25	0.30	0.43	-0.83	0.58	0.16
Treatment vs. Control	0.03	0.13	0.79	0.09	0.17	0.59
12 months vs. Baseline	0.01	0.09	0.94	-0.13	0.10	0.18
Treatment*12 months	0.05	0.12	0.68	0.22	0.16	0.16
	Not Foreign Born N= 706 Obs =1036			**Foreign Born N= 238 Obs =347**		
Intercept	-0.21	0.39	0.60	-0.67	0.54	0.23
Treatment vs. Control	0.09	0.12	0.44	-0.26	0.17	0.14
12 months vs. Baseline	-0.07	0.07	0.31	-0.06	0.11	0.55
Treatment*12 months	0.04	0.11	0.73	0.28	0.17	0.09

All models control for race, education, age, sex, occupation and marital status

Table 2.3b – Stratified models indicating subgroup effects of a workplace intervention on employee inflammatory markers from baseline to 12 months (continued)

	IL-6 (log)					
	Estimate	**Standard Error**	**p-value**	**Estimate**	**Standard Error**	**p-value**
		Without children N= 408 Obs =585			**With children N= 535 Obs = 737**	
Intercept	0.28	0.20	0.18	0.19	0.21	0.39
Treatment vs. Control	-0.04	0.06	0.54	-0.06	0.05	0.26
12 months vs. Baseline	-0.03	0.05	0.56	-0.05	0.04	0.17
Treatment*12 months	-0.002	0.08	0.98	-0.03	0.06	0.62
	Less than or equal to 45 years N= 652 Obs =956			**Older than 45 years N= 292 Obs = 427**		
Intercept	0.13	0.15	0.40	0.09	0.30	0.77
Treatment vs. Control	-0.01	0.05	0.84	-0.16	0.08	0.07
12 months vs. Baseline	-0.04	0.04	0.37	-0.06	0.05	0.26
Treatment*12 months	-0.07	0.06	0.26	0.10	0.09	0.25
	Not Foreign Born N= 706 Obs =1036			**Foreign Born N= 238 Obs =347**		
Intercept	0.65	0.19	0.002	0.49	0.26	0.07
Treatment vs. Control	-0.05	0.05	0.34	-0.02	0.08	0.83
12 months vs. Baseline	-0.06	0.04	0.14	-0.02	0.06	0.72
Treatment*12 months	-0.0005	0.06	0.94	-0.07	0.10	0.49

All models control for race, education, age, sex, occupation and marital status

Table 2.3b – Stratified models indicating subgroup effects of a workplace intervention on employee inflammatory markers from baseline to 12 months (continued)

	IL-1β (log)					
	Estimate	**Standard Error**	**p-value**	**Estimate**	**Standard Error**	**p-value**
		Without children N= 408 Obs =585			**With children N= 535 Obs = 797**	
Intercept	3.59	0.36	<.0001	3.14	0.35	<.0001
Treatment vs. Control	0.02	0.14	0.86	-0.03	0.11	0.77
12 months vs. Baseline	0.06	0.12	0.64	0.02	0.10	0.85
Treatment*12 months	-0.05	0.19	0.79	-0.17	0.16	0.28
	Less than or equal to 45 years N= 652 Obs =956			**Older than 45 years N= 292 Obs = 497**		
Intercept	2.99	0.24	<.0001	3.17	0.49	<.0001
Treatment vs. Control	0.03	0.11	0.78	0.05	0.16	0.76
12 months vs. Baseline	-0.12	0.11	0.25	0.19	0.14	0.18
Treatment*12 months	-0.08	0.14	0.55	-0.16	0.23	0.49
	Not Foreign Born N= 706 Obs =1036			**Foreign Born N= 238 Obs =347**		
Intercept	3.66	0.32	<.0001	3.15	0.41	<.0001
Treatment vs. Control	0.01	0.09	0.91	-0.12	0.19	0.54
12 months vs. Baseline	0.05	0.09	0.58	-0.04	0.15	0.80
Treatment*12 months	-0.24	0.14	0.09	0.34	0.24	0.16

All models control for race, education, age, sex, occupation and marital status

Discussion:

This study marks the first randomized field experiment to assess the effects of a workplace program to address work and family stressors on change in employee levels of inflammation over time. Below we will summarize findings and offer possible explanations for the null main effects. Finally, we discuss limitations, strengths and overall conclusions from the study.

Summary of findings and explanations for subgroup differences:

Analyses indicated there was no effect of the WFHN's intervention on three markers of inflammation among employees assessed one year after randomization. Models with three-way interaction terms indicated that changes in IL-6 from baseline to 12 months varied by foreign born status such that the intervention was more beneficial for foreign born employees than those born in the U.S. Stratified models, however, indicated that there was a borderline, deleterious effect on CRP due to treatment from baseline to 12 months for employees born outside the U.S. and a marginal improvement in IL-1β due to treatment from baseline to 12 months for U.S. born employees. Generally, it does not appear that particularly higher risk groups gained greater benefit from the intervention with regard to improving inflammatory status. Understanding the mechanisms at play in these particular relationships is beyond the scope of this study, and it is also possible that these treatment effects are simply due to chance. We caution the interpretation of our stratified analyses in particular as sample sizes were reduced in these models, and we conducted six subgroup analyses (parents, non-parents, U.S. born, foreign born, older employees and younger employees).

Explanations for null findings:

The translation of observational epidemiological evidence into experimental findings remains one of the fundamental struggles in the social sciences [131]. The epidemiologic literature offers examples of compelling, longitudinal studies reflecting strong links between psychosocial and behavioral exposures and health outcomes, but the randomized control trials (RCTs) aiming to change these conditions have often generated null results. Notably, numerous observational studies have suggested that depression and social support are associated with mortality following a myocardial infarction. Yet, a large RCT, Enhancing Recovery for Coronary Heart Disease Patients (ENRICHD), found no differences in post-MI survival in the treatment and control groups. Similarly, although vast observational evidence suggests that depression is associated with secondary cardiac events following a myocardial infarction, very few psychological interventions have successfully reduced total deaths, risk of revascularization, or non-fatal infarction [132].

Despite predominantly cross-sectional, observational evidence suggesting there may be a link between work strain and employee markers of inflammation (evidence in longitudinal research is less consistent), we did not find support for this hypothesis in the current randomized field experiment. We offer two broad explanations to explain the overall null main effects of the WFHN intervention on changes in employee inflammation: **1)** the WFHN intervention is not causally related to changes in employee markers of inflammation and the pathways by which we assumed the intervention to affect inflammation are not correct; and **2)** the WFHN intervention is causally related to changes in inflammation but did not produce results in the current study context due to incorrect etiologic period and/or issues of selection in our sample. We discuss these possibilities below in more depth.

The intervention does not affect markers of inflammation:

Evidence from other WFHN research suggests that this workplace intervention changed certain health (psychological distress and smoking) and organizational outcomes (organizational citizenship behavior and safety compliance). Still, the WFHN workplace intervention may not influence employee health as measured by changes in levels of inflammation. A lack of effect may be due to the fact that: a**)** the intervention did not change the mediators that it sought to affect along the causal pathway to employee markers of inflammation, namely work-to-family conflict, schedule control and supervisory support; and/or b) changes in these mediators are not causally related to CRP, IL-6 and IL-1 β.

Preliminary evidence from WFHN researchers investigating the effects of an identical intervention at an information technology (IT) company suggests that the workplace program offered statistically significant, albeit modest, improvements in levels of reported work-to-family conflict and other proposed mediators. This study also found that the intervention was most effective among IT employees with high family demands and those with less supportive work environments [126]. A similar study conducted among our sample of extended care workers, however, revealed that the effects of the intervention on organizational outcomes, such as safety compliance and organizational citizenship behavior, did not operate through alterations in work-to-family conflict, schedule control and supervisory support [133]. Thus, it is possible that workplace programs seeking to reduce work and family strain may operate through these pathways in some populations but not in our particular sample, making it challenging to detect overall intervention effects on employee levels of inflammation in this study.

The notion that changes in the proposed mediators relate causally to changes in employee levels of inflammation also warrants further scrutiny. The literature indicates that certain forms

of perceived stress, including interpersonal stress and caregiving responsibilities, correlate with higher levels of pro-inflammatory markers [134]. Research on work stressors and employee markers of inflammation has also started to emerge. While many cross-sectional, observational studies suggest higher work stress is associated with elevated levels of inflammation [107, 108, 113, 117], the limited longitudinal studies in this area have shown mixed results [111, 117, 118]. Like our analysis, these studies have been conducted among relatively healthy employee populations, not individuals presumed to have higher than average levels of stress or inflammation. Thus, it is difficult to know if work stress is simply not associated with employee levels of inflammation or if these effects are diluted by the healthy nature of the individuals in the study. We are also not aware of existing experimental data to support the association between work stress and inflammation nor studies, neither observational nor experimental, to support a link between work and family conflict and levels of employee inflammatory markers specifically.

Given the possibility that this intervention program may not affect the intended mediators and/or that these mediators may not relate to employee markers of inflammation, it is also useful to keep in mind that the overall treatment effect on employee inflammation (c) is equal to the product of the effect of the intervention on the hypothesized mediators (a) and the effect of these mediators on employee markers of inflammation (b) (a*b = c), assuming linear relationships. We can determine rough and comparable estimates for (a), (b) and (c) by consulting the literature and making use of z-transformations. Preliminary WFHN findings from the IT industry suggest significant intervention effects on WTFC from baseline to follow-up [126]. Based on the regression coefficients provided for the treatment*time interaction, we can calculate a predicted effect of treatment on WTFC at follow-up (-0.116). We can also standardize this estimate by the

mean and standard deviation of WTFC in our sample, as the authors did not report this statistic in their publication ((-0.116)/.92= -0.126) for a rough estimate of (a). While there is no research on the effects of work and family stressors on markers of inflammation per se, one study indicates that job burnout is significantly associated with CRP (β=0.30) [110]. When we standardize this estimate by the standard deviation of the exposure in that study, we generate a rough estimate for (b) (0.30/0.78=0.385). These rough estimates suggest that the overall effect of the intervention on CRP may plausibly be -0.049 (a*b= -0.126*0.385).

We are likely underpowered to detect treatment effects of this size given our sample size of 949 employees. In fact, in regression models for CRP, confidence intervals for the effects of treatment from baseline to 12 months (time*treatment) include this estimated effect (-0.049). Of course it is also possible that workplace programs operate through alternate mechanisms. For example, it may be easier to change employee health behaviors relating to markers of inflammation, like BMI, than perceptions of their work environment. We suggest that future research rigorously examine both pathways (that is, a and b referenced above) and explore alternate mechanisms by which workplace interventions may succeed in promoting healthy levels of inflammation.

The intervention does affect markers of inflammation, but these effects were not present in our study:

Assuming that a workplace program designed to improve work-to-family conflict, schedule control and the support of supervisors for work and family issues causally influences markers of inflammation, it may be that the intervention operates through more latent mechanisms than those proposed by the WFHN and this study. To our knowledge, no

psychosocial workplace intervention has attempted to change inflammation levels directly over time. In animal lab studies, experimental surgery, introduction of a virus or wound infliction has resulted in elevated CRP as quickly as 24 hours [135-137]. In humans, laboratory-induced stress has resulted elevated levels of CRP and cytokines such as IL-6 in a little as 10-30 minutes [107, 138-140]. These studies suggest that it is physiologically plausible for our outcomes of interest to change in short periods of time; however, it is not clear whether one year is a sufficient etiologic period for a workplace program to effectively alter work and family stressors and subsequently change markers of inflammation. Interestingly, two related cross sectional studies in Israel suggested that work-related stressors were associated with CRP [109, 110]. However, a subsequent longitudinal study by the same researchers found no association between work stressors and changes in circulating CRP levels over a 12 months period [111], suggesting that even when evidence on work-related exposures and markers of inflammation does exist, the etiologic period to change these outcomes may be longer than one year. We urge future research to investigate the plausibility of these relationships and the time required for psychosocial exposures to effectively change markers of inflammation in a non-laboratory setting.

Last, a causal relationship between the workplace intervention and markers of inflammation may not be detectable given issues of selection in our sample. While plausible, we do not feel that selection sufficiently explains the absence of main effects of our study. Employees who were excluded from the analytic sample had significantly lower levels of CRP and obesity at baseline than those who were analyzed, but no other notable differences were present. We also found that baseline levels of employee inflammation may predict dropout of our sample from baseline to 12 months for CRP and IL-1β but that these associations did not vary by treatment status. Thus, “healthier” employees may have been excluded from our original sample,

which would potentially exaggerate results, but we also see that "sicker" individuals left our study over time, which would drive our overall results toward the null. Most importantly, no overwhelming selection trends were detected and, thus, any biases due to exclusion criteria or dropout are likely to be minimal.

Limitations and strengths:

We note some limitations of this research. Our study includes workers only and, in general, employed individuals exhibit better health than those who do not participate in the labor force [141-143], which may make it challenging to detect improvements in markers of health over the course of the study. It is also important to keep in mind that the levels of biomarkers of inflammation studied here do not represent cardiovascular disease risk per se. They serve as correlates of disease [72], though whether they also represent an intermediary along the causal pathway to disease remains debated [100, 144]. Thus, it is difficult to make claims about the intervention effects on overall cardiovascular health from these data. Employees consented to participate and there is also a possibility that either healthier or sicker employees selected into the study, which could bias results in either direction. Finally, the results of this study are only generalizable to employees (predominantly women) in the healthcare industry, and it is not certain whether findings can be extrapolated to other settings.

This research exhibits a number of strengths as well. Most notably, this study represents the first experimental examination of the effects of a workplace program to address work and family strain on changes in employee markers of inflammation over time. Alongside the WFHN, we were able to capitalize on funded research efforts to conduct a randomized field experiment, interview, follow employees longitudinally and collect biomarkers of health, all of which are

extremely time- and financially-intensive endeavors. Cardiovascular disease takes decades to develop, particularly among a relatively young cohort such as the one analyzed here, and markers of inflammation serve as meaningful indicators of cardiovascular disease risk in a short time frame. We were fortunate to access this unique data to rigorously and causally test an unanswered and relevant scientific question. We also make important methodologic contributions to the work/family literature by utilizing data at multiple time points and multilevel modeling techniques to appropriately account for the clustering of multiple measures for each employee as well as the nesting of employees within worksites. This method produces accurate standard errors and confidence intervals. Last, our sample includes racially and ethnically diverse employees, which the job strain (and to some extent work/family) literature greatly lacks.

Conclusion:

In light of major labor force changes in recent decades, the current study examined the effects of a nursing-home based intervention to improve employee work/family conflict, schedule control and support from supervisors on employee markers of inflammation. While we did not detect any significant effects of this particular intervention on the outcomes of interest, we believe this research question warrants continued examination given the prevalence of work-to-family conflict and the burden of heart disease in the U.S. We are optimistic that the WFHN workplace program offers an opportunity to improve employee health, as related research has revealed it does benefit employee mental health and behaviors such as smoking. We recommend future research attempt to replicate or refute this study's findings in a variety of study populations, examine the etiologic period necessary for workplace programs to change markers

of inflammation and investigate pathways by which workplace policies and practices may benefit employee well-being more generally.

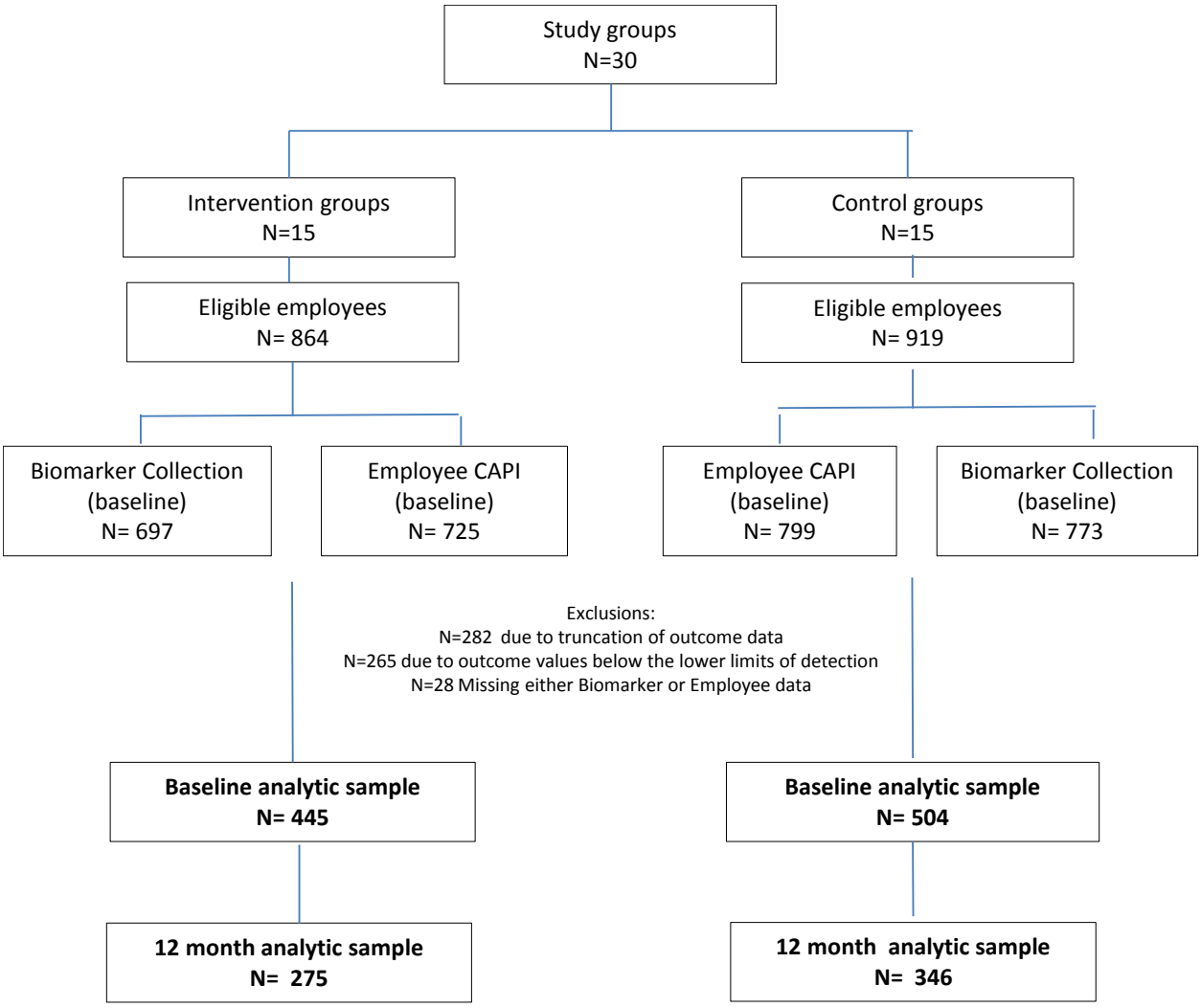
Appendix 2.1: Descriptive Statistics – Original Sample

N= 1524	N	Mean (SD) /
CRP	1366	2.09 (2.95)
IL-6	1344	1.70 (1.40)
IL1-β	1190	55.42 (67.02)
Age		
Treatment		
No	799	52.43
Yes	725	47.57
Obese		
No	934	61.29
Yes	590	38.71
Occupation		
RN/LPN	430	28.25
Other	1092	71.75
Sex		
Male	118	7.74
Female	1406	92.26
Married/partnered		
Not married/partnered	566	37.14
Married/partnered	958	62.86
Race		
White	985	64.63
Black	199	13.06
Hispanic	204	13.39
Other race	136	8.92
Education		
Grades 1-8	11	0.72
Some High School	77	5.06
High School	495	32.5
Some College	756	49.64
College or more	184	12.08
Foreign Born		
No	1119	73.43
Yes	405	26.57
Parent		
No	675	44.32
Yes	848	55.68

Appendix 2.2: Descriptive Statistics – Excluded from vs. Included in Analytic Sample

	Excluded*		Included (in analytic sample)		
	N=656		N=949		
	N	Mean(sd) / %	N	Mean(sd) / %	p-value*
CRP	488	1.57 (2.02)	949	1.90 (2.11)	**0.004**
IL-6	132	1.75 (1.79)	949	1.78 (1.71)	0.82
IL-1β	132	53.84 (55.41)	949	53.02 (60.04)	0.88
WTFC	574	2.76 (0.90)	946	2.82 (0.91)	0.21
Age	574	38.56 (12.71)	948	38.50 (12.33)	0.93
Treatment					0.49
No	280	48.70	504	53.11	
Yes	295	51.30	445	46.89	
Occupation					0.17
RN/LPN	166	28.87	264	27.88	
Other	409	71.13	683	72.12	
Sex					0.20
Male	51	8.87	67	7.06	
Female	524	91.13	882	92.94	
Married/partnered					0.09
Not married/partnered	229	39.83	337	35.31	
Married/partnered	346	60.17	612	64.49	
Race					0.21
White	370	64.35	615	64.81	
Black	83	14.43	116	12.22	
Hispanic	66	11.48	138	14.54	
Other race	56	9.74	80	8.43	
Education					0.21
Grades 1-8	4	0.70	7	0.74	
Some High School	34	5.92	43	4.53	
High School	169	29.44	326	34.35	
Some College	289	50.35	467	49.21	
College or more	78	13.59	106	11.17	
Foreign Born					0.09
No	408	70.96	711	74.92	
Yes	167	29.04	238	25.08	
Parent					0.33
No	264	45.91	411	43.35	
Yes	311	54.09	537	56.65	
Smoke					0.81
No	402	70.16	659	69.44	
Yes	171	29.84	290	30.56	
Obese					**<0.001**
No	396	68.67	538	56.59	
Yes	179	37.73	411	43.31	

*Note: Excluded employees may have data from any dataset (employee or any of two datasets that comprise the biosample (DBS and Cytokine)). Because these datasets are not mutually exclusive, the sum of the excluded and included referenced here (n=1605) surpasses that of the previously described employee baseline sample (n=1524).



*Note: Number of employees providing biomarker and employee data are not mutually exclusive. Additionally, as mentioned in Appendix 2.2, the total number of employees who provided biosample data (n=1470) originate from two unique datasets (DBS and Cytokine).

Figure 2.1: Randomization Flowchart*

CHAPTER 3

Workplace-Level Factors and Employee Cardiometabolic Risk

Abstract:

Introduction: Research has investigated the impact of workplaces on a variety of employee health outcomes and reveals potential benefits of supportive occupational environments on employees' overall risk of cardiovascular disease (CVD). However, the impact of the job setting on individual risk factors for CVD, which offer unique clues to an individual's overall cardiometabolic risk, warrants further examination. The current study of employees in an extended care setting assesses manager- and worksite-level influences on a cardiometabolic risk score (CRS) and components of the CRS including blood pressure, glycosylated hemoglobin (HbA1c), cholesterol, body mass index (BMI) and cigarette consumption, all measured at the employee-level. Primarily, we examine whether employees who work for the same manager or within the same worksite exhibit CVD risks that are more similar than employees in different manager workgroups or worksites. We also investigate specific aspects of the occupational setting that may predict employee CVD risk. We hypothesize that managers and worksite-level environments influence the cardiometabolic health of employees and that more supportive workplaces will predict lower CVD risk.

Methods: Data are from the Work Family Health Network study which aimed to examine the effects of workplace supports and stressors on employee wellbeing. Hypotheses were tested using baseline data among 1,524, predominantly female employees working in an extended care setting. Employees provided biological markers through dried blood spots, measured blood pressure, height and weight as well as self-reported data on a variety of sociodemographic, health behavior and work and family variables. We estimated multilevel linear models that accounted

for multiple employees per manager as well as nesting of manager workgroups within worksites. As a preliminary step toward understanding aspects of the work environment that may improve employee cardiometabolic risk, we examined the proportion of total variance of our CVD risk outcomes explained at the manager- and site- levels, relative to the individual-level. Next, we examined whether variables aggregated at the manager group-level and conceptualized to represent work and family supports (family supportive supervisory behaviors and schedule control) and stressors (work-to-family and family-to-work conflict) predicted employee cardiometabolic risk. As part of post hoc analyses, we also examine worksite-level influences on employee outcomes.

Results: In three-level models, the proportion of variance explained by the manager-level was generally small and not significantly different from zero. A greater and significant proportion of variance was explained by the site-level for some outcomes, including 26% for total cholesterol (CI=15-33%), 18% for HDL cholesterol (CI=9-24%) and 3% for cigarette consumption (CI=0.2-5%). We identified smaller proportions of site-level variability for other outcomes that were not significantly different from zero (0.4% for BMI (CI=(-1-2%)), 1% for diastolic blood pressure (CI=-0.4-3%), 1% for systolic blood pressure (CI=-1-2%), 1% for CRS (CI=-0.5-3%), and 0.1% for HbA1c (CI=-1-1%)). The majority of the variance of all outcomes could be attributed to the employee level. When examined in separate models, we found that variables such as family supportive supervisory behaviors, schedule control, work-to-family conflict and family-to-work conflict aggregated at the manager group-level did not predict employee CVD risk.

Conclusion: We find that work environments, specifically worksites, may be relevant to employee cholesterol but appear less influential for other measures of CVD risk. Our data suggest managers in this setting may not have as strong an effect on employee wellbeing as

originally hypothesized, however, we note limitations in this research including possible selection issues and lack of data pertaining to important workplace attributes. We speculate that our results may reflect unique aspects of the extended care facilities comprising this sample and recommend that research continue to assess the possible role of the workplace on employee health, particularly CVD risk, in a variety of occupational venues.

Introduction:

Research reveals the potential benefits of supportive workplaces on employee wellbeing [19, 77], including lower overall risk of cardiovascular disease (CVD) [2]. However, the role of the occupational environment on a variety of individual risk factors of CVD, such as blood pressure, glycosylated hemoglobin (HbA1c), cholesterol, body mass index (BMI) and cigarette consumption has not been examined in a single study. One method for quantifying the potential importance of workplace settings on employee health is to examine whether there is clustering of individual CVD risk by *manager workgroup* or the *worksite*. In other words, do employees who work for the same manager or within the same worksite exhibit CVD risks that are more similar than employees in different manager workgroups or worksites? Conceptually, this approach is based in the tradition of multilevel epidemiologic theories such as ecosocial theory, which posits that individual health arises in a social context [145, 146], as well as individual-level workplace theories including the Demand-Control-Support model [7], which considers the combination of job demands and job control believed to produce a sense of strain and incorporates workplace social support hypothesized to combat these strains. The extent to which workplace factors contribute to the variability of cardiometabolic risk can be estimated with multilevel modeling techniques that partition workplace- from individual-level variance with respect to a variety of

behavioral and biological markers representing CVD risk. Because cardiovascular disease often develops gradually over time, biological markers serve as sensitive and meaningful pre-disease indicators for otherwise latent illness. These measures offer a useful assessment approach by which the effects of workplace-level factors, such as the role of managers and worksites, on cardiovascular outcomes may be understood in a relatively healthy study population.

Labor force changes have swept our country in recent decades. Most notably, the female workforce has increased substantially. The majority of employed women work full time, and increasing proportions of them are mothers. In 1975, 47% of women with children under 18 participated in the labor force; just thirty years later, this percentage rose to 71% [1]. These dramatic demographic shifts prompt increasing numbers of women and men to experience the demands of both work and home life simultaneously. Greenhaus and Beutell introduced the term 'work-family conflict' thirty years ago, referring to "a form of interrole conflict in which the role pressures from the work and family domains are mutually incompatible in some respect" [10]. Numerous studies suggest a link between these dual demands and worse mental and physical health outcomes ranging from depression, substance abuse, musculoskeletal disorders, poor sleep and overall risk of CVD [11, 12, 67, 74-77].

The link between work and family stress and cardiometabolic risk has been of particular interest to investigators given that CVD is the cause of one in four deaths in the U.S. today [13] Prior work with our study sample found that higher demands related to work and family life may be associated with increased cardiometabolic risk operationalized by a newly developed and validated cardiometabolic risk score (CRS) [3, 14]. The literature also indicates that strains from work and home may be related to individual cardiometabolic risk factors. In a four year

longitudinal study, Frone and colleagues identified a significant, increased risk of developing hypertension with higher levels of work and family stress among employed parents [17]. Among white-collar, retail employees, a workplace intervention to reduce work and family strains increased the odds of quitting smoking and decreased smoking frequency over a six month period [22], and multiple cross-sectional studies have concluded that these dual demands were associated with lower physical activity and poorer diet [24-28] as well as increased odds of obesity [29].

The aforementioned literature suggests a link between work and family demands and CVD risk but focuses on factors conceptualized to occur and/or that are measured at the *individual-level.* However, a variety of theoretical models look beyond the individual actor to consider a wide range of variables, often nested in a social hierarchy, that influence health. Krieger's ecosocial theory encourages the consideration of multiple levels of disease causation, assumes their interaction and suggests that individuals embody numerous experiences that ultimately accumulate and influence wellbeing [145, 146]. Thus, organizational policies related to work and family balance are hypothesized to interact with individual disease risk factors as well as societal influences such as federal leave legislation and access to health care to ultimately inform employee health. Related, social informational processing theory posits that beliefs and perceptions of employees are shaped by values and expectations present in the work environment, above and beyond individual worker characteristics [148, 149]. This theory suggests that employees may be more likely to seek support for work and family balance if the organizational culture values and is accommodating of non-work demands and if one's peers are also pursuing pro-family work arrangements.

Research increasingly incorporates *"higher" level predictors* of health in their design and

measures, especially studies that examine social networks [150] and specific social environments such as schools [151], neighborhoods [147, 152] and workplaces [153]. For example, work and family research suggests that supervisors play a role in employee health. Berkman demonstrated that managers' family-friendly attitudes and practices were associated with lower overall risk of cardiovascular disease, considered by the presence of two or more out of five modifiable risk factors, and higher sleep duration in the extended care setting [2]. In this same cohort of nursing homes, Ertel similarly highlighted the beneficial effect of support from supervisors on depressive symptoms [77], though both these studies were cross-sectional in nature. A quasi-experimental, longitudinal study of grocery store workers similarly revealed that a program to improve managers' family-supportive supervisory behaviors resulted in a significant improvement in a composite score representing self-reported physical health (but no change in job satisfaction or turnover intentions) [154].Similarly, Thomas and Ganster examined mechanisms linking family supportive organizational policies and practices to a variety of psychological, physiological and behavioral outcomes. This work revealed that flexible scheduling and supportive supervisors, reported by individuals and confirmed at the institutional-level, reduced work-to-family conflict (WTFC) and that WTFC was associated with higher blood cholesterol but not blood pressure measured at one time point only [19].

Other work-family research has explicitly examined how group-level factors impact employee outcomes, though these studies are predominantly cross-sectional and observational in design. Among 2,229 Dutch public service employees in 85 workgroups, higher workgroup-level burnout and lower team-level work engagement was associated with a variety of individual-level outcomes (increased exhaustion and cynicism and reduced professional efficacy) and work engagement variables (worse vigor, dedication, and absorption), after adjusting for individual

members' job demands and resources [155]. Similarly, Bhave and colleagues found that higher WFTC at the work group-level resulted in increased employee WTFC adjusting for individual-level factors like sex, number of dependents, marital status, age, tenure, work hours, job strain and size of the work group [148]. In a sample of 1,346 employees from 56 firms in the Norwegian food and beverage industry, workplace norms (measured individually and aggregated at the group level) explained 12.7% of the variance of individual-level job stress and 6.2% of the variance of subjective health symptoms [156]. Likewise, among 784 information technology employees working on 120 teams, Moen and colleagues investigated whether measures of job stress were patterned at the workgroup-level, such that some workgroups experienced more stress than others. Results indicated that nearly 18% of the total variance of WTFC could be attributed to the team-level and, similarly, that a substantial portion of job satisfaction (17%), emotional exhaustion (13%), schedule control (14%), job demands (14%) and work hours (15%) could be explained by this level [153].

The work-family literature offers persuasive evidence for the role of "higher" level predictors, particularly the role of managers, on employee work and health outcomes. However, gaps remain in our understanding of the organizational influences of employee CVD risk. For example, the role of supportive workplaces on a variety of individual CVD risk factors, such as blood pressure, glycosylated hemoglobin (HbA1c), cholesterol, body mass index (BMI) and smoking, has not been examined in a single study. (We note that Thomas and Ganster examined the role of organizational policies on a variety of employee health outcomes, including cholesterol and blood pressure; however, their analyses do not focus solely on higher-level predictors of employee wellbeing nor do they exclusively emphasize employee CVD risk [19].)

Additionally, with the exception of a few studies [156], most of the aforementioned "multilevel" occupational health research fails to quantify statistically the extent to which workplace-level factors account for employee outcomes, relative to the employee-level, using variance partitioning coefficients or intra-class correlations. Thus, it is unclear the degree to which employees who work for the same manager or within the same worksite possess *similar* cardiometabolic risk. Last, although there is evidence that group-level traits affect individuals, it is not evident what, if any, manager-level factors predict CVD risk.

The current study seeks to address these shortcomings in the existing literature. We embrace multilevel perspectives and view them as complements to individual-level job strain theories, such as the Demand-Control-Support model [7], which posits that job demands and job control relate to stress and that workplace social support serves to ameliorate these strains. An example of how employee-level *and* workplace-level conditions relate to worker wellbeing is highlighted in the work of Moen and colleagues [153]. They hypothesize that there is a dynamic interplay between individual- and workplace-level job conditions which separately and collectively contribute to employee work and family stress and mental health. We extend this model to include physical health outcomes, such as CVD risk (see Figure 3.1).

Specifically, we seek to **investigate the cross-sectional associations of workplace-level factors on employee CVD risk, as measured by a number of behavioral and biological measures** among a predominantly female and racially and ethnically diverse sample. We aim to quantify the extent to which the workplace (versus the individual employee) accounts for variability in a cardiometabolic risk score (CRS) [14], representing overall CVD risk, as well as individual CVD risk factors such as blood pressure, HbA1c, cholesterol, BMI and cigarette consumption. As mentioned, biomarkers serve as underlying risk factors for as well as potential

intermediate variables along the pathway to disease, which is particularly useful for conditions that develop slowly over time. They provide direct information on physiological processes in the body and are thus more reliable than subjective measures of health [32, 33]. We also examine outcomes largely shaped by behaviors and associated with CVD risk such as BMI and smoking, which may be more susceptible to work and family demands. While we don't consider individual characteristics of managers, we account for the clustering of employees within manager groups (which we refer to interchangeably with "workgroups") and worksites. In this setting, workgroups are organized by type of service or floor of the nursing home facility. Last, we examine whether specific manager-level factors predict employee CVD risk. For example, supportive supervisory policies and practices, including flexibility and control over scheduling, at the manager-level (which we refer to interchangeably with "manager group-level" and "workgroup-level) may be particularly important in offering employees opportunities to improve their cardiometabolic well-being (more time for physical activity or less stress, both of which have been linked with better cardiovascular health). Specifically, this study seeks to address the following aims and hypotheses:

Aim 1: Determine the extent to which variability of cardiometabolic risk, measured by CRS, blood pressure, HbA1c, cholesterol, BMI and smoking, can be explained at the manager-level relative to the employee-level.

Hypothesis 1: A proportion of the overall variability of cardiometabolic risk, measured by CRS, blood pressure, HbA1c, cholesterol, BMI and smoking, will be explained at the manager level.

Aim 2: Examine whether variables aggregated at the manager group-level, including family supportive supervisory behaviors (FSSB) and schedule control, conceptualized to represent support for work and family balance, as well as well as WTFC and family-to-work conflict (FTWC), conceptualized to represent work and family stress, predict individual-level cardiometabolic risk.

Hypothesis 2: Higher FSSB and schedule control aggregated at the manager-level will predict lower individual cardiometabolic risk. Higher WTFC and FTWC aggregated at the manager-level will predict higher individual cardiometabolic risk.

Methods:

Sample:

This study is part of Phase II of the Work Family Health Network (WFHN) project, a joint research endeavor sponsored by the National Institutes of Health and the Centers for Disease Control and Prevention, among others. This phase of the WFHN involved data collection from employees (as well as their managers, spouses and their children) over the course of 18 months as part of an employer-supported workplace intervention in a group randomized field experiment. The WFHN identified a New England company with numerous nursing home facilities, which we will refer to as "LEEF" and included thirty worksites that were distributed across Massachusetts, Maine, New Hampshire, Vermont, Connecticut, and Rhode Island.

Each of the 1,723 eligible employees within these worksites who worked more than 22 hours each week during the day or evening was invited to complete a computer-assisted personal interview [34]. A total of 1,524 LEEF employees participated at baseline, resulting in response

rate of over 88%. We do not have data on non-participants. Employees who provided all components for the larger WFHN study, including blood samples, received $60 for their participation.

Measures:

Trained field interviewers administered computer-assisted personal interviews and on-site health assessments as described elsewhere [35], both of which were conducted by trained field staff and addressed employee demographics, socioeconomic status, family demographics, respondent's work environment, physical health, mental health, and family relationships. After obtaining written consent from all respondents, interviews and health assessments lasted approximately 50 and 20 minutes, respectively, and were on occasion collected on different days.

Manager-Level Variability:

We analyzed a total of 1,524 subjects enrolled at baseline nested within 30 worksites and 139 managers. Most worksites had four managers supervising employees, though some sites had as few as 2 or as many as 8 managers. Managers in our sample supervised an average of roughly 11 employees, with workgroups ranging from 1 to 33 employees (see Figure 3.2). We do not have data on employees or managers who did not participate in the survey. Each worksite averaged roughly 50 employees (range 24-89). Multilevel conceptual frameworks that motivate the current study suggest that employees who share the same manager or work in the same site will have correlated data and do not provide as much unique information as employees who do not share work environments. Thus, we model the embeddedness of employees within manager groups and worksites in our statistical approaches. The survey data utilized in the current study

was collected at the employee level. Employees were asked to specify their primary manager. These responses were used to link employees to managers in worksites, and we explicitly consider this nesting structure in our analyses. We do not have data on the length of time that employees belong to a particular workgroup, however.

Outcome Variables:

All CVD risk outcome measures were assessed as continuous variables at one point in time. Prior research established and validated a measure of cardiometabolic risk based on modifiable risk factors in the Framingham risk score [37], including blood pressure, cholesterol, HbA1c, BMI and cigarette smoking status. The score used here was calculated based on age- and sex-based means in our particular sample and was validated independently among Framingham offspring data to predict risk of a cardiovascular event [14].

We also examined the individual components of this score. Employees were asked to provide dried blood spots (DBS) by a finger stick. Interviewers wearing appropriate personal protective equipment disinfected the employee's middle or ring finger with an alcohol swab and proceeded to prick the finger with a sterile, disposable micro-lancet. As previously described [38], blood spots were collected, air-dried, and sealed in a plastic bag for room-temperature shipment with desiccant for storage at −86°C until assayed for cholesterol by means of a protocol specifically validated for this study from serum to DBS equivalents [39]. At the time of the blood draw, study staff also collected a 1 microliter blood droplet to measure HbA1c levels (DCA Vantage Analyzer, Siemens Healthcare Diagnostics, Frimley, Camberley, UK). Prior to blood sampling, three seated blood pressure readings were collected at least 5 minutes apart during the interview with wrist blood pressure monitors (HEM-637, Omron Healthcare, Bannockburn, IL).

These three readings were averaged to create a continuous measure. Body mass index was calculated as height/weight^2 (height measured by Seca213/214 stadiometers, Seca North America, Hanover, MD; weight measured by Health-O-Meter 800KL, Jarden Corporation, Rye, NY). Height and weight measurements were taken at the same time as other physical health assessments. Cigarette consumption was assessed by respondent self-report. Employees were asked if they smoke cigarettes every day, some days or not at all, how many days they smoke cigarettes on average in a week and how many tobacco cigarettes they smoke on an average day. Responses were multiplied to produce a measure of cigarettes per week. Non-smokers received a score of zero cigarettes per week. Based on the aforementioned components, we calculated a cardiometabolic risk score for each subject (age- and sex-specific strata use different score calculations), representing 10-year CVD risk [3, 14]. We note that dichotomous smoking status (yes/no) was used to calculate the CRS, and our analyses utilize cigarette consumption as a continuous variable. For additional information on specific measures, refer to Bray, 2013.

Workgroup-level Predictors

To address our secondary hypothesis, manager group aggregated variables conceptualized to represent support and stress around work and family balance were averaged within employees sharing a manager and included in separate regression models predicting individual CVD risk factors. For these variables, individual employee scores were excluded from the average manager-level scores.

As mentioned, we posited that supportive supervisory policies and practices, including flexibility and control over scheduling, may result in better employee cardiometabolic health. Specifically, supportive managers could offer concrete opportunities for employees to pursue

healthy activities outside of the workplace (visit the doctor or engage in physical activity) that may reduce CVD risk. We utilize a measure of managerial support, *family supportive supervisory behavior,* that taps into employee appraisals of supervisor's behavior relating specifically to work and family. Using a scale developed and validated by Hammer and colleagues, employees were asked about four domains related to family-related supervisory support, including emotional support (supervisor makes you feel comfortable talking to him/her about conflicts between work and non-work), instrumental support (supervisor works effectively with employees to creatively solve conflicts between work and non-work), role modeling (supervisor demonstrates effective behaviors in how to juggle work and non-work issues) and creative management (supervisor organizes departmental work to jointly benefit employees and the company) [41, 42].. The current study used a short form of FSSB derived from employee responses to four items, categorized 1-5 (strongly agree to strongly disagree) and averaged to generate an overall score, with higher scores reflecting greater FSSB [43] (Cronbach's alpha=0.9).

We also utilized a modified version of Thomas and Ganster's *schedule control* scale [44]. Employees were asked how much choice they had over when they took vacation, when they can take off a few hours, when workdays begin and end, working at another location, the number of personal phone calls they can make or receive during work, how much they take work home and about shifting to part time work if full time (and vice versa). Responses ranged from very little to very much (1-5) and an overall score of schedule control was obtained by calculating the average score of these 8 items (Cronbach's alpha=0.7).

Perhaps less influential than FSSB and schedule control, stress pathways are another plausible mechanism by which managers could influence employee cardiometabolic health.

Work-to-family conflict (WTFC) is thought to reflect the extent to which responsibilities in the domains of work and family are incompatible [10]. The current study incorporated a widely-used measure of this inter-role conflict developed and validated by Netermeyer and colleagues among employed individuals in various industries [36]. The survey included five questions to address work-to-family conflict that asked whether the demands of work interfere with family or personal time, the employee's job produces strain that makes it difficult to fulfill family or personal duties and things employees want to do at home do not get done because of the demands work puts on them. Individual item responses were coded 1-5 (strongly disagree to strongly agree) and averaged to generate a continuous measure (internal consistency reliability of the scale was high; Cronbach's alpha=0.9). For the purposes of the current study, only baseline measures of WTFC were considered

Similar to the WTFC measure, employees were asked five questions to address *family-to-work conflict* (FTWC) (whether the demands of family interfere with work, employees have to put off doing things at work because of demands on time at home and family-related strain interfere with employee's ability to perform job-related duties). Individual item responses were coded 1-5 (strongly disagree to strongly agree) and averaged to generate a continuous measure (Cronbach's alpha=0.8). Again, only baseline measures of FTWC were examined in this analysis.

Other covariates

A number of sociodemographic variables were also assessed and modeled as potential confounders: occupation (employee's official job title, coded nurse or other), marital status (currently married or do you have a permanent romantic partner that lives with you?), employee

gender (male/female), education (high school or less vs. some college or higher) and age in years. Race/ethnicity was coded as White, Black, Hispanic or other race. Indicator variables for each racial/ethnic group were generated, and the reference group was assigned to White race. Because of its effects on CVD risk, we also considered medication use as a potential covariate. Only data on blood pressure medications was available with enough respondents to warrant its inclusion. We found that blood measure medication use did not predict systolic or diastolic blood pressure nor did it alter the proportion of workplace-level variability for these outcomes in two-level models.

Analysis:

Analysis of Manager-Level Effects

To test our first hypothesis that a proportion of the overall variability of cardiometabolic risk will be present at the manager-level, we estimated multilevel linear regression models that accounted for the nesting of employees within manager as well as managers within worksites by modeling random effects for the workgroup- and worksite-levels. Statistical models were as such: $\text{CVDRisk}_{ijk} = \beta_0 + \beta_1 (\text{Covariates}_{ijk}) + e_{0ijk} + u_{0jk} + v_{0k}$ where: i= employee, j = manager workgroup and k= worksite and $[e_{0ijk}] \sim N(0, \sigma^2_{e0})$,$[u_{0jk}] \sim N(0, \sigma^2_{u0})$ and $[v_{0k}] \sim N(0, \sigma^2_{v0})$. To test our second hypothesis examining whether certain workgroup-level variables contributed to manager-level variability of cardiometabolic risk, we included FSSB, schedule control, WTFC and FTWC aggregated at the manager-level in separate statistical models.

For the first hypothesis, we were interested in the variance partitioning coefficient (VPC) which revealed the extent to which the manager-level comprises the overall variance of the outcome in three-level models, operationalized as $\sigma^2_{u0}/(\sigma^2_{e0}+ \sigma^2_{u0}+ \sigma^2_{v0})$. Confidence intervals

for these VPCs were also derived. For the second hypothesis, we were interested in the regression coefficients and confidence intervals associated with each manager group aggregated variable. Models controlled for employee-level sociodemographic variables (race, age, sex, occupation, and marital status) all measured at baseline. Analyses were conducted in MLwiN 2.11.

Post-Hoc Analyses

Our initial results prompted us to conduct a number of post hoc analyses. We conducted two-level models for all outcomes, with the employee as level one and manager or worksite as level two (in separate models). In these two-level models, we examined manager-level VPCs ($\sigma^2_{u0}/(\sigma^2_{e0}+\sigma^2_{u0})$) as well as worksite-level VPCs ($\sigma^2_{v0}/(\sigma^2_{e0}+\sigma^2_{v0})$). We investigated cholesterol measures thoroughly to rule out data error. Last, we examined whether particular sites were contributing a substantial portion of the higher-level variability for these outcomes by removing sites step-wise from the sample a re-running the aforementioned models.

Results:

Sample Characteristics:

We analyzed a total of 1,524 subjects enrolled at baseline nested within 30 worksites and 139 managers. Managers supervised an average of roughly 11 employees, with workgroups ranging from 1 to 33 employees (see Figure 3.2). The mean 10-year cardiometabolic risk score represents a 7.75% 10-year CVD risk (sd=8.15%), meaning that fewer than 8 out of 100 with the

average level of risk will have a cardiovascular event in the next 10 years.[**] Mean BMI in our sample was 29.45, almost considered obese, and roughly 30% of employees smoked (an average of 23.45 cigarettes each week). Average total and HDL cholesterol, HbA1c and systolic and diastolic blood pressures were in-line with national levels [46]. On scales of 1-5, workgroup-level averages of FSSB, schedule control, WTFC, FTWC and were 2.79, 2.55, 2.07 and 3.69, respectively (see Table 3.1 for descriptive statistics). To understand how different these manager group aggregated variables were from their corresponding employee-level values, we examined the correlation of the two: r= 0.39, p=<0.001 for mean manager group aggregated FSSB and mean employee FSSB, r=0.37, p<0.001 for mean manager group aggregated schedule control and mean employee schedule control, r=0.36, p<0.001 for mean manager group aggregated WTFC and mean employee WTFC, and r=0.33, p<0.001 mean manager group aggregated FTWC and mean employee FTWC.

Results of statistical analyses

Three-level models to examine manager-level variability of cardiometabolic risk:

In three-level models, the proportion of variance explained by the manager-level was generally small and not significantly different from zero: 1% for total cholesterol (CI=-2-4%), 1% for HDL cholesterol (CI=-2-3%), 1% for BMI (CI=-2-3%) and 0.1% for cigarettes consumed each week (CI=-2-2%). The manager-level variance parameters and the respective standard errors generated

[**] Over 20% is considered high global risk, according to some researchers [45]. Thus, the mean risk in our sample is fairly low.

Table 3.1: Descriptive Statistics (Baseline)

N=1524	N	Mean (sd) / %
Cardiometabolic Risk Score (%	1412	7.75 (8.15)
BMI (height/weight^2)	1501	29.45 (7.03)
Total Cholesterol (mg/dL)	1464	190.79 (28.78)
HDL Cholesterol (mg/dL)	1473	63.56 (5.54)
Systolic Blood Pressure (mmHg)	1511	114.79 (13.09)
Diastolic Blood Pressure (mmHg)	1511	72.36 (9.40)
HbA1c (%)	1453	5.51 (0.61)
Cigarettes/**week**	1522	23.45 (45.87)
WTFC (group level)	1524	2.79 (0.20)
FTWC (group level)	1524	2.07 (0.11)
FSSB (group level)	1524	3.69 (0.18)
Schedule Control (group level)	1524	2.55 (0.44)
Age	1522	38.52 (12.48)
Treatment		
Yes	725	47.57
No	799	52.43
RN/LPN		
Yes	428	28.12
No	1094	71.88
Sex		
Male	118	7.74
Female	1406	92.26
Married/partnered		
Not married/partnered	566	37.14
Married/partnered	958	62.86
Race		
White	985	64.63
Black	199	13.06
Hispanic	204	13.39
Other race	136	8.92
Education		
High school or less	583	38.28
Some college or more	940	61.72

for diastolic and systolic blood pressures, CRS and HbA1c were zero and, thus, no confidence intervals could be derived. A greater and significant proportion of variance was explained by the worksite-level for some outcomes, including 26% for total cholesterol (CI=15-33%), 18% for HDL cholesterol (CI=9-24%) and 3% for cigarette consumption (CI=0.2-5%). Smaller proportions of worksite-level variability were present for other outcomes but were not significantly different from zero (0.4% for BMI (CI=(-1-2%)), 1% for diastolic blood pressure (CI=-0.4-0.3%), 1% for systolic blood pressure (CI=-1-2%), 1% for CRS (CI=-0.5-3%), and 0.1% for HbA1c (CI=-1-1%)). The proportion of variance explained by the employee-level was more substantial and significant for all variables: 82% for HDL cholesterol (CI=76-91%), 73% for total cholesterol (67-85%) and above 97% for all other outcomes (see Table 3.2). We included manager group-level factors such as FSSB, schedule control, WTFC and FTWC in separate models and found that most did not predict employee CVD risk, with the exception of one somewhat counterintuitive result suggesting that higher manager-level schedule control predicts higher individual-level BMI ($\beta = 0.88$, CI=(0.03, 1.73)) (see Table 3.3).

Two-level models to examine manager-level variability of cardiometabolic risk:

We found that three-level models for some outcomes produced questionable manager-level variance parameters (and associated standard errors) that were exactly zero and proceeded to run two sets of two-level models. In the first set, we allowed level one to be employee and level two to be manager. Results indicated that 27% (CI=21-31%) of the total variance for total cholesterol

Table 3.2: Three-Level Models Reflecting Influence of Cardiometabolic Risk

		Total Cholesterol	**HDL Cholesterol**	**BMI**	**Diastolic Blood Pressure***	**Cigarettes/ Week**	**Systolic Blood Pressure****	**CRS**	**HBA1c**
		n=1458	n=1467	n=1495	n=1505	n=1516	n=1505	n=1408	n=1447
Worksite VPC	VPC	**0.26**	**0.18**	0.004	0.01	**0.03**	0.01	0.01	0.001
	95% CI	**(0.15, 0.33)**	**(0.09, 0.24)**	(-0.01, 0.02)	(-0.004, 0.03)	**(0.002, 0.05)**	(-0.01, 0.02)	(-0.005, 0.03)	(-0.01, 0.01)
Manager VPC	VPC	0.01	0.01	0.01	0	0.001	0	0	0
	95% CI	(-0.02, 0.04)	(-0.02, 0.03)	(-0.02, 0.03)	N/A	(-0.02, 0.02)	N/A	N/A	N/A
Employee VPC	VPC	**0.73**	**0.82**	**0.99**	**0.99**	**0.97**	**0.99**	**0.99**	**0.99**
	95% CI	**(0.67, 0.85)**	**(0.76, 0.91)**	**(0.98, 1.01)**	**(0.97, 1.00)**	**(0.95, 1.00)**	**(0.98, 1.01)**	**(0.97, 1.00)**	**(0.98, 1.01)**

All models control for, race, age, sex, marital status, and occupation.

Table 3.3: Three-Level Models Reflecting Influence of Cardiometabolic Risk with Manager Group Aggregated Variables

		Total Cholesterol	HDL Cholesterol	BMI	Diastolic Blood Pressure	Cigarettes/Week	Systolic Blood Pressure	CRS	HBA1c
		n=1458	n=1467	n=1495	n=1505	n=1516	n=1505	n=1408	n=1447
Models with FSSB Group Mean	β	1.33	0.17	-0.52	0.005	3.23	0.38	0.20	0.03
	95% CI	(-2.32, 4.97)	(-0.56, 0.91)	(-1.41, 0.37)	(-1.15, 1.16)	(-2.56, 9.01)	(-1.14, 1.91)	(-0.42, 0.82)	(-0.04, 0.10)
Models with WTFC Group Mean	β	1.26	0.18	0.15	0.48	2.20	-0.03	0.19	-0.03
	95% CI	(-3.26, 5.79)	(-0.73, 1.10)	(-0.93, 1.23)	(-0.92, 1.88)	(-4.90, 9.30)	(-0.12, 0.05)	(-0.57, 0.95)	(-0.12, 0.05)
Models with FTWC Group Mean	β	-1.19	-0.25	-0.07	0.08	-7.57	-1.15	-0.04	-0.13
	95% CI	(-8.35, 5.97)	(-1.69, 1.19)	(-1.83, 1.69)	(-2.17, 2.34)	(-18.93, 3.79)	(-4.11, 1.81)	(-1.25, 1.17)	(-0.26, 0.01)
Models with Schedule Control Group Mean	β	-3.38	-0.66	**0.88**	-0.06	2.57	-0.05	0.05	0.03
	95% CI	(-6.89, 0.14)	(-1.37, 0.04)	**(0.03, 1.73)**	(-1.15 1.03)	(-2. 96, 8.10)	(-1.49, 1.38)	(-0.54, 0.64)	(-0.04, 0.10)

All models control for race, age, sex, marital status, and occupation.

and 18% (CI=13-22%) of the total variance for HDL cholesterol could be attributed to the higher-level and that these proportions were significantly different than zero. We found that smaller and non-significant proportions of the variance were attributed to level-two for other outcomes (3% for cigarette consumption (CI=-0.02-5%), 1% for BMI (CI=-1-3%), 1% for DBP (CI=-1-3%) and 0.1% for systolic blood pressure (CI=-2-2%). Again, manager-level variance parameters and the respective standard errors generated for CRS and HbA1c were zero and, thus, no confidence intervals could be derived. Similar to three-level models, the proportion of variance explained by the employee-level in these models was more substantial and significant for all variables (note: we could not derive confidence intervals for employee-level variance parameters for CRS and HbA1c because the manager-level variance parameters for these variables was zero) (Table 3.4).

In the second set of models, we allowed level one to be employee and level two to be worksite (see Table 3.5). Results indicated that 26%, 18% and 3% of the overall variance for total cholesterol (CI=15-34%), HDL cholesterol (CI=9-24%) and cigarette consumption (CI=0.3-5%), respectively, could be attributed to the higher-level and that these proportions were significantly different than zero. Smaller and non-significant proportions of the variance appeared to be attributed to level-two for other outcomes: 1% for BMI (CI=-1-2%), 1% for diastolic blood pressure (CI=-0.4-3%), 1% for systolic blood pressure (CI=-1-2%), 1% for CRS (CI=-0.5-3%) and 0.2% for HbA1c (CI=-1-1%). Again, we find that overwhelmingly the proportion of variance for all outcomes could be attributed to the employee-level in these models (see Table 3.5).

Table 3.4 Two Level Models Reflecting Influence of Cardiometabolic Risk (Level 2 is Manager)*

		Total Cholesterol	**HDL Cholesterol**	**BMI**	**Diastolic Blood Pressure**	**Cigarettes/ Week**	**Systolic Blood Pressure**	**CRS**	**HBA1c**
		n=1458	n=1467	n=1495	n=1505	n=1516	n=1505	n=1408	n=1447
Manager VPC	VPC	**0.27**	**0.18**	0.01	0.01	0.03	0.001	0	0
	95% CI	**(0.21, 0.31)**	**(0.13, 0.22)**	(-0.01, 0.03)	(-0.01, 0.03)	(-0.0002, 0.05)	(-0.02, 0.02)	N/A	N/A
Employee VPC	VPC	**0.73**	**0.82**	**0.99**	**0.99**	**0.97**	**0.999**	1.0	1.0
	95% CI	**(0.69, 0.79)**	**(0.78, 0.87)**	**(0.97, 1.01)**	**(0.97, 1.01)**	**(0.95, 1.00)**	**(0.98, 1.02)**	N/A	N/A

All models control for race, age, sex, marital status, and occupation.
*With Group-level hypertension medication included, VPC = 0.01, CI=(-0.01, 0.03)
** With Group-level hypertension medication included, VPC = 0.001, CI=(-0.02, 0.02)

Table 3.5: Two Level Models Reflecting Influence of Cardiometabolic Risk (Level 2 is Site)*

		Total Cholesterol	**HDL Cholesterol**	**BMI**	**Diastolic Blood Pressure***	**Cigarettes/ Week**	**Systolic Blood Pressure****	**CRS**	**HBA1c**
		n=1458	n=1467	n=1495	n=1505	n=1516	n=1505	n=1408	n=1447
Worksite VPC	VPC	**0.26**	**0.18**	0.01	0.01	**0.03**	0.01	0.01	0.002
	95% CI	**(0.15, 0.34)**	**(0.09, 0.24)**	(-0.01, 0.02)	(-0.004, 0.03)	**(0.003, 0.05)**	(-0.01, 0.02)	(-0.005, 0.03)	(-0.01, 0.01)
Employee VPC	VPC	**0.74**	**0.82**	**0.99**	**0.99**	**0.97**	**0.999**	**0.99**	**0.99**
	95% CI	**(0.66, 0.85)**	**(0.76, 0.91)**	**(0.98, 1.01)**	**(0.97, 1.00)**	**(0.95, 1.00)**	**(0.98, 1.01)**	**(0.97, 1.00)**	**(0.99, 1.01)**

All models control for race, age, sex, marital status, and occupation.

*With Group-level hypertension medication included, VPC = 0.01, CI=(-0.004, 0.03)

** With Group-level hypertension medication included, VPC = 0.01, CI=(-0.01, 0.02)

Examination of cholesterol outcomes

The aforementioned results reflect high VPCs for cholesterol measures in both two-level and three-level models. To rule out data error, we extensively examined data for these outcomes. Manager-level and worksite-level means for both HDL and total cholesterol were reflective of the overall means for these variables (See Appendices 3.1a and 3.2a). Scatterplots and histograms for these outcomes did not reveal any obvious outliers. Data appeared normally distributed, even at the worksite-level (See Appendices 3.1b and 3.2b). The aforementioned two-level models produced nearly identical level-two variance parameters, regardless of whether level two was manager or worksite. These findings suggest that the higher-level variability in our outcomes was likely attributed to the worksite-, not the manager-, level, as was the case in our three-level models. In other words, managers may not provide unique information beyond the worksite in this sample.

Because no glaring data errors were revealed, we examined the extent to which certain sites contributed to the high-level variance for these outcomes. We speculated that worksite cultures could be particularly strong at certain facilities. Approximately 18% of the variance of HDL cholesterol could be attributed to the non-employee level. Our data suggest that three sites in particular (sites 4, 15 and 23) are responsible for about 8 percentage points of this variance. When these three sites are removed from the sample sites (n=201 employees), 10% (CI=4-14%) of the variance of HDL cholesterol can be explained at the site level, regardless of what sites remain in the sample. Similarly, roughly 26% of the variance of total cholesterol can be attributed to higher-levels, and four sites (sites 2, 14, 18 and 26) appear to carry about 11 percentage points of this variance. With the omission of these four sites (n=220 employees), the variance of total cholesterol explained at the site-level is closer to 15% (CI=7-22%). Removing

other sites does not reduce the site-level variance parameter further (results not presented). Further, exclusion of the smallest or largest worksites does not appear to meaningfully change the clustering of employee cholesterol values.

Discussion:

The current study examined the workplace-level influences of employee CVD risk, as measured by a number of behavioral and biological measures, among a predominantly female and racially and ethnically diverse sample. Prior work and family research has investigated the impact of supervisors and other higher-level organizational factors on employee-level outcomes; however, the impact of the occupational setting on individual risk factors for CVD has not been sufficiently explored. In this examination of 30 extended care facilities, our findings suggest that worksites may contribute to employee cardiovascular health, above and beyond the manager- or individual-level. The workplace may also be particularly relevant for employee cholesterol outcomes but, as we explain below, we caution the interpretation of these results. Counter to our hypothesis that manager-level factors would predict employee health, we generally did not find that FSSB, schedule control, WTFC or FTWC aggregated at the workgroup-level was associated with individual CVD risk.

In this study, we expand upon prior work and family research that has previously investigated the role of managers and workgroups, operationalized both as independent variables in regression models and as explicitly higher levels in a social hierarchy, on employee outcomes. Both approaches suggest that context matters for employee wellbeing. While we are unaware of workplace studies that have examined "higher-level" predictors of CVD risk factors, the

neighborhood literature offers evidence that the social environment is relevant to behavioral and biological measures of cardiovascular health at the individual level. Diez Roux found that, across four counties, neighborhood factors (such as income, home values and education) were consistently associated higher odds of smoking (self-reported) and increased serum cholesterol and blood pressure (assessed through blood draws and seated readings, respectively) above and beyond individual factors [152]. Davey Smith similarly found that area-based measures representing poverty (including male unemployment, overcrowding, car ownership, and proportion in the lowest social classes) predicted higher levels of individual-level blood pressure, BMI and smoking in a prospective Scottish study [157].

Our results support the notion that the social milieu, in this case the worksite, may be relevant to some individual-level measures of cardiovascular health. However, counter to our original hypotheses that managers would influence employee outcomes, three-level models suggest that they do not provide unique information beyond the worksite in our sample. We speculate that within-site culture at the surveyed extended care facilities may be strong and that managers may not have the opportunity to differ much from one another. For example, within-site policies and practices may preclude managers from offering exclusive benefits that could improve the cardiometabolic health of their employees, such as flexible scheduling to attend a doctor's appointment or to engage in physical activity outside of work (Due to the available data, we note that we were not able to explicitly test these possibilities.). We encourage researchers to replicate these analyses in other occupational settings in which managerial autonomy can be quantified to assess whether our results reflect a true lack of manager-level influence on employee CVD risk or if supervisors in our sample simply were limited in their ability to diverge from their peers in order to provide cardiometabolic benefits to their employees.

We find that the worksite may be especially relevant to employee cholesterol levels. In fact, roughly one-fifth and one-quarter of the variability of HDL and total cholesterol, respectively, was attributed to the worksite-level. Because we did not find any data error to explain results for cholesterol outcomes, we conducted a number of post hoc analyses to understand our findings. Sets of two-level models in which level two was assigned to both manager and worksite produced nearly identical level two variance parameters that were also very similar to worksite-level variance parameters in three-level models. These results suggest that the higher-level variability detected may be occurring at the site-, not the manager-, level and that omission of the worksite as a hierarchical level moves this variability to the manager. Further investigation revealed that certain site-level traits may be swaying the proportion of variance explained at this level. For both HDL and total cholesterol, a handful of worksites appear to contribute a substantial proportion of the total variability for these outcomes. Without these sites in our analyses, worksite-level VPCs for HDL and total cholesterol fall to roughly 10% and 15%, respectively. Further, these sites share characteristics that may make them different from other sites and more influential than others. For example, sites 4, 15 and 23 have lower (worse) HDL cholesterol than other sites. These sites tend to be younger, and younger employees have lower HDL cholesterol in this particular sample. Additionally these sites have more Hispanics and more low income employees, who also appear to have lower (worse) HDL in our sample. In the case of total cholesterol, sites 2, 14, 18 and 26 may share characteristics that make them healthier. These sites tend to have more black employees and employees with lower job demands, both of which correlate with lower total cholesterol in this study population. Though our models adjusted for these covariates at the individual-level, we speculate that there may be unmeasured, shared, worksite-level properties that heavily influence the proportion of

variance explained for cholesterol outcomes. For example, there may be an unmeasured contextual effect of geography leading to a patterning of CVD risk at the worksite-level. It is also possible there is residual confounding with respect to the aforementioned individual-level traits.

We argue that a variety of mechanisms exist by which extended care facilities could impact the cholesterol of individual workers. Worksite-specific culture and policy could promote healthy behaviors that ultimately affect employee cholesterol levels. More specifically, the promotion of flexible scheduling at the worksite-level may offer employees the opportunity to prepare healthy meals at home with family or time outside of work to engage in physical activity. Geographic patterning of nursing home facilities is also plausible. Some worksites may be located in neighborhoods with an abundance of either healthy or unhealthy food outlets or access to a built environment that facilitates physical activity, which can influence cholesterol levels. (We note that this mechanism may conflate area- and worksite-level effects, however.)

Despite these potential pathways, we interpret VPCs for cholesterol with caution. We are not aware of any studies that have reported similar parameters for cholesterol or other individual CVD risk factors. An occupational health study examining workgroups in Norway revealed that 12.7% and 6.2% of individual-level job stress and physical health measured as self-reported somatic and psychological complaints in past 30 days, respectively, were explained by the workgroup-level [156]. These results suggest that the worksite-level VPCs for cholesterol reported here *may be* theoretically plausible, particularly once the aforementioned sites are removed from our sample. Still, our results remain challenging to place in context. We urge future research to confirm or deny our cholesterol findings, particularly because the aforementioned mechanisms would presumably impact worksite-level clustering of other

behavior-linked outcomes, such as BMI and blood pressure, for which we found no evidence in the current sample.

With the exception that 3% of the variability in cigarette consumption can be attributed to worksite, less than 1% of the total variance of other CVD risk outcomes can be explained by the manager- or worksite-levels, and these VPCs were not significantly different from zero. As mentioned, we acknowledge there is no prior precedent in occupational health research for reporting the proportion of variance of CVD risk explained by the workplace-level, and it is somewhat challenging to compare our results to other research examining the effects of the job environment on employee cardiometabolic outcomes. These null findings do align with results testing our second hypothesis that suggest manager group-level predictors conceptualized to represent work and family supports (FSSB and schedule control) and stressors (WTFC and FTWC) are not associated with employee CVD risk. We believe that we were sufficiently powered to detect significant effects of these manager group aggregated variables on our outcomes of interest.[††] Yet, our data reveals only one statistically significant but counterintuitive result: that higher manager-level schedule control predicts higher individual-level BMI ($\beta = 0.88$, CI=(0.03, 1.73)). However, given the small amount of variance explained at the manager-level, the unexpected direction of this finding and the fact that we examined four manager-level predictors across 8 outcomes (32 models total), we speculate that this result may be due to chance.

[††] Power calculations suggest that roughly 276 and 565 employees are required to detect significant effects of FSSB and WTFC, respectively, on our outcomes of interest (Given $n_{eachgroup} = [(Z_{\alpha/a} + Z_{\beta})^2 x2V]/\delta^2$ where $Z_{\alpha/a} = 1.96$, $Z_{\beta} = 0.80$, $V_{FSSB}= 0.50$, $V_{WTFC}= 0.77$, $\delta_{FSSB}=0.25$ and $\delta_{WTFC} =0.18$, as per the current sample and Hammer, 2011) [154]. However, the nested structure of our data requires that we consider two separate design effects (DE) as part of these calculations (one to capture the correlation of employee and manager data as well as manager and worksite data). Given DE=1+ rho(m-1) where rho=0.06 and $m_{emp/manager}= 11$ and $m_{manaer/site}= 4$, as per Hammer, 2004 [156] and this sample, we calculate that DE $m_{emp/manager}= 1.24$ and DE $_{manaer/site}= 1.66$. After taking the product of these design effects and the aforementioned sample sizes, we conclude that our cohort of 1524 should be sufficient to detect significant effects of manager-aggregated variables on our outcomes.

Our null findings are a bit counter to prior research in the extended care setting indicating that managers' family-friendly attitudes and practices were associated with lower overall risk of cardiovascular disease [2] and research in this same cohort suggesting that that low FSSB and high WTFC at the individual level was associated with increased employee CRS [3]. However, we do note that other analyses with this sample have found individual-level measures of WTFC and FTWC were not associated with most of the CVD risk factors examined here, with the exception that individual-level WTFC predicted employee BMI [158]. Taken together, we speculate that work and family support and stress variables are generally not closely tied to individual CVD risk factors in this occupational cohort and that, in the case of the CRS representing overall CVD risk, the employee represents the primary level of influence – not the manager or worksite.

Limitations and Strengths

This study exhibits some shortcomings. While we did employ models with multiple hierarchical levels, selection and endogeneity may be particularly problematic in multilevel analyses. Individuals may choose to work, live and study in certain contexts because they offer benefits (i.e.: cleaner air, better leave policies, and safer parks). Selection into worksites is plausible in the current study and could result in biases toward or away from the null. Employees may not have much authority over who is assigned their direct supervisors within an occupational setting, however. Additionally, confounding may be an issue, as there could be unobserved common prior causes of group-level exposures and health outcomes (for example, low socioeconomic status may conflate the association between workplace conditions and employee well-being) [159]. Much of our covariate (and some of our outcome) data was

reported by employees and could potentially be misclassified. In the case of one of our manager group aggregated variables, schedule control, one could argue that sicker employees may report less workplace support for flexible scheduling than their healthy counterparts, resulting in a possible overestimation of the workplace effects on employee health. Our study is a preliminary assessment of the role of the workplace on employee CVD risk, but we do not examine the quality of managers or worksites; we simply investigate whether variability in outcomes can be attributed to these organizational levels. Last, we do not know how long employees worked within their manager groups or facilities. Presumably, employees would need to have worked within these hierarchical levels for a sufficient amount of time in order for them to influence their cardiometabolic health. Though it does not capture time within a manager group or worksite, we did replicate the aforementioned models with a company tenure covariate, and it did not alter our findings (results not presented).

Our study also exhibits numerous strengths. First, we add to the work/family scholarship by investigating the role of "higher-level" predictors of employee health. In doing so, we employ multilevel methods to appropriately account for the clustering of employees within workgroups, a method which yields accurate standard errors and confidence intervals. These methods are preferred to the alternatives: 1) a purely individual-level or traditional risk factor analysis, which ignores the embeddedness of individuals in the social world around them and commits a so-called psychologistic fallacy [160]; and 2) an entirely group-level analysis which suffers from ecological fallacy that occurs when one takes results from higher-level data (typically group means) and attempts to draw inferences about individuals [161]. Methodologically, multilevel analyses embrace this notion that individuals exist in a social context and often utilize group-level measures, which may be more objective than individual-level measures as they attempt to

reflect a collective perception of the individual's environment. With proper statistical tools, multilevel analyses such as those presented here account for the lack of unique information nested structures provide (that is, the measurement of employees and workgroups results in clustered or non-independent data). This study also utilized predominantly objective outcome measures, including assessed measures of blood pressure, blood draws to ascertain HbA1c and cholesterol and validated methods for measuring BMI. The use of these biological markers and other objective measures offer meaningful improvement to the validity of work-family research.

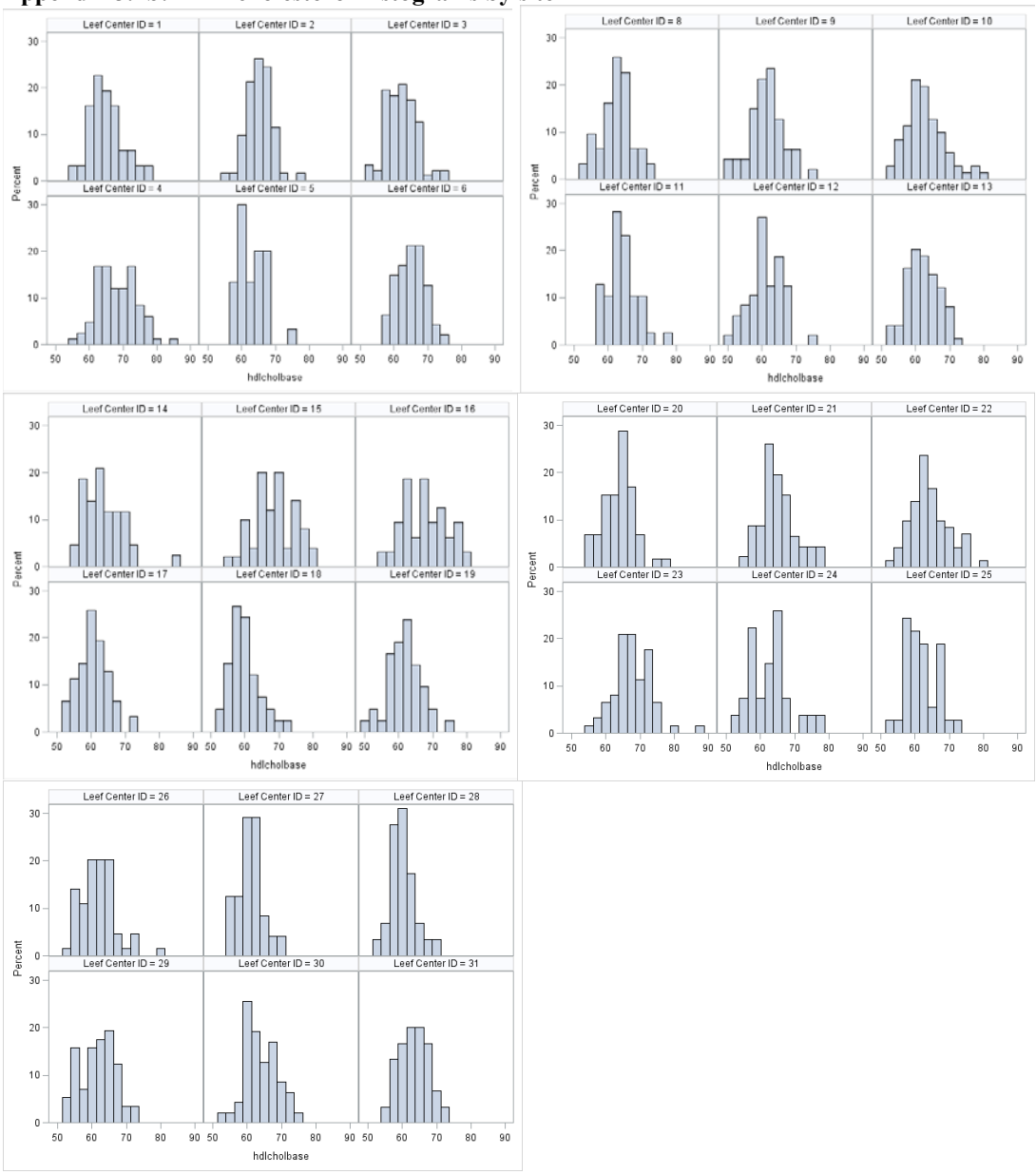
Conclusion:

The current study seeks to illuminate the role of the workplace on a variety of behavioral and biological markers representing individual cardiovascular disease risk. We utilize multilevel modeling techniques that explicitly partition worksite- and manager- from employee-level variance. We find that work environments, specifically worksites, may be relevant to employee cholesterol but appear less meaningful for other measures of CVD risk in our sample of predominantly female, racially and ethnically diverse extended care workers. The proportion of manager-level variance was negligible for all outcomes, and most of the manager group aggregated stress and support variables examined did not predict individual CVD risk in this cohort. Taken together, we conclude that supervisors may not have as strong an effect on employee wellbeing in this sample as originally hypothesized but that the worksite may be an especially important level of influence for employee wellbeing. We recommend that research continue to confirm the possible role of the occupational setting on worker health, particularly CVD risk, in a variety of settings.

Appendix 3.1a: HDL cholesterol descriptive statistics by site

Site	Average # employees/site	Mean (mg/dL)	Standard Deviation	Variance
18	46	59.44	4.47	19.96
28	29	60.02	3.77	14.23
17	63	60.67	4.55	20.66
27	24	61.29	3.79	14.38
12	49	61.30	5.05	25.47
9	50	61.43	5.09	25.94
19	43	61.72	4.92	24.20
29	59	61.76	5.15	26.50
25	39	61.76	4.69	21.97
26	66	61.80	5.21	27.10
3	89	62.18	4.40	19.35
13	76	62.19	4.75	22.55
8	33	62.27	4.72	22.28
24	27	62.66	5.84	34.08
5	30	62.81	4.04	16.31
10	73	62.87	5.90	34.81
31	30	63.30	4.08	16.63
14	46	63.64	5.76	33.14
20	60	63.80	4.50	20.22
30	48	63.94	4.77	22.73
11	40	64.17	4.54	20.62
22	75	64.32	5.72	32.73
1	31	64.80	5.25	27.57
21	50	65.01	5.40	29.17
6	52	65.19	4.37	19.13
2	62	65.20	3.92	15.33
16	33	67.64	6.20	38.46
23	62	67.91	5.60	31.40
4	87	68.14	5.73	32.81
15	52	68.69	6.14	37.66
Average within site		63.40	4.94	24.91
Overall		63.56	5.54	30.71

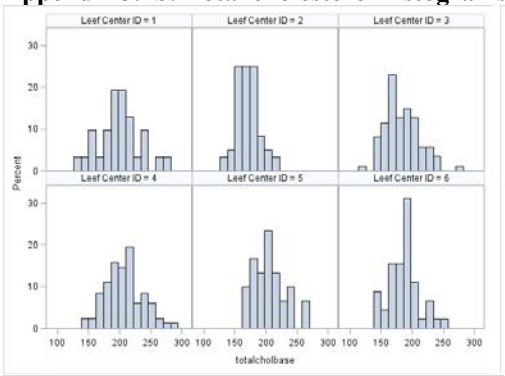
Appendix 3.1b: HDL cholesterol histograms by site

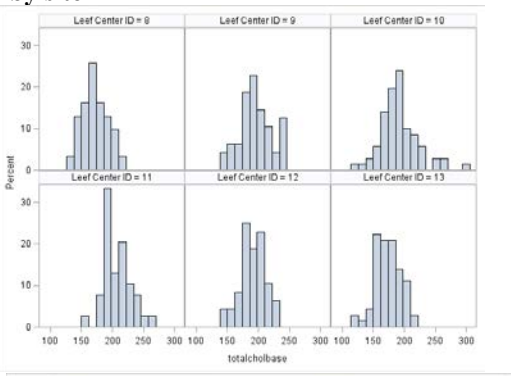


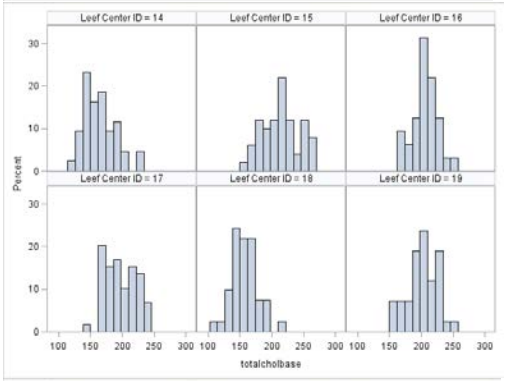
Appendix 3.2a: Total cholesterol descriptive statistics by site

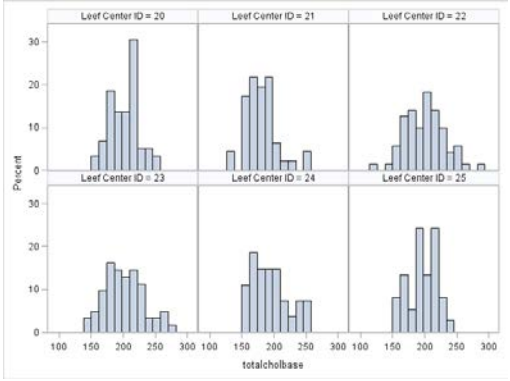
Site	Average # employees/site	Mean (mg/dL)	Standard Deviation	Variance
18	46	157.53	22.18	491.89
14	46	165.12	24.65	607.76
26	66	165.44	19.43	377.39
2	62	171.15	18.02	324.62
8	33	171.65	20.23	409.22
13	76	173.15	20.56	422.89
21	50	179.38	24.56	603.02
3	89	184.11	27.88	777.11
6	52	186.96	24.64	606.93
31	30	187.92	24.13	582.21
28	29	188.49	22.37	500.28
29	59	190.52	23.55	554.44
10	73	190.64	30.33	919.63
12	49	192.00	20.70	428.30
30	48	192.38	21.40	458.04
24	27	194.71	29.93	895.68
9	50	196.18	25.15	632.57
17	63	196.48	24.18	584.74
25	39	196.49	23.03	530.33
1	31	199.39	32.56	1059.90
22	75	200.41	29.98	899.05
23	62	201.99	31.00	961.07
19	43	202.19	21.81	475.55
20	60	203.34	22.72	516.23
5	30	205.83	25.26	637.90
16	33	206.00	19.22	369.55
11	40	206.64	22.44	503.54
4	87	207.44	29.51	870.71
15	52	214.33	28.31	801.69
27	24	215.18	27.62	762.59
Average within site		191.43	24.58	618.83
Overall		190.79	28.78	828.25

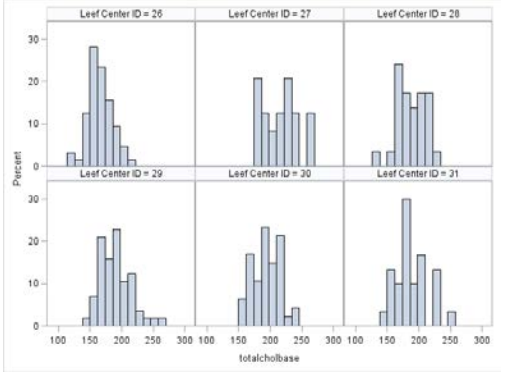
Appendix 3.2b: Total cholesterol histograms by site

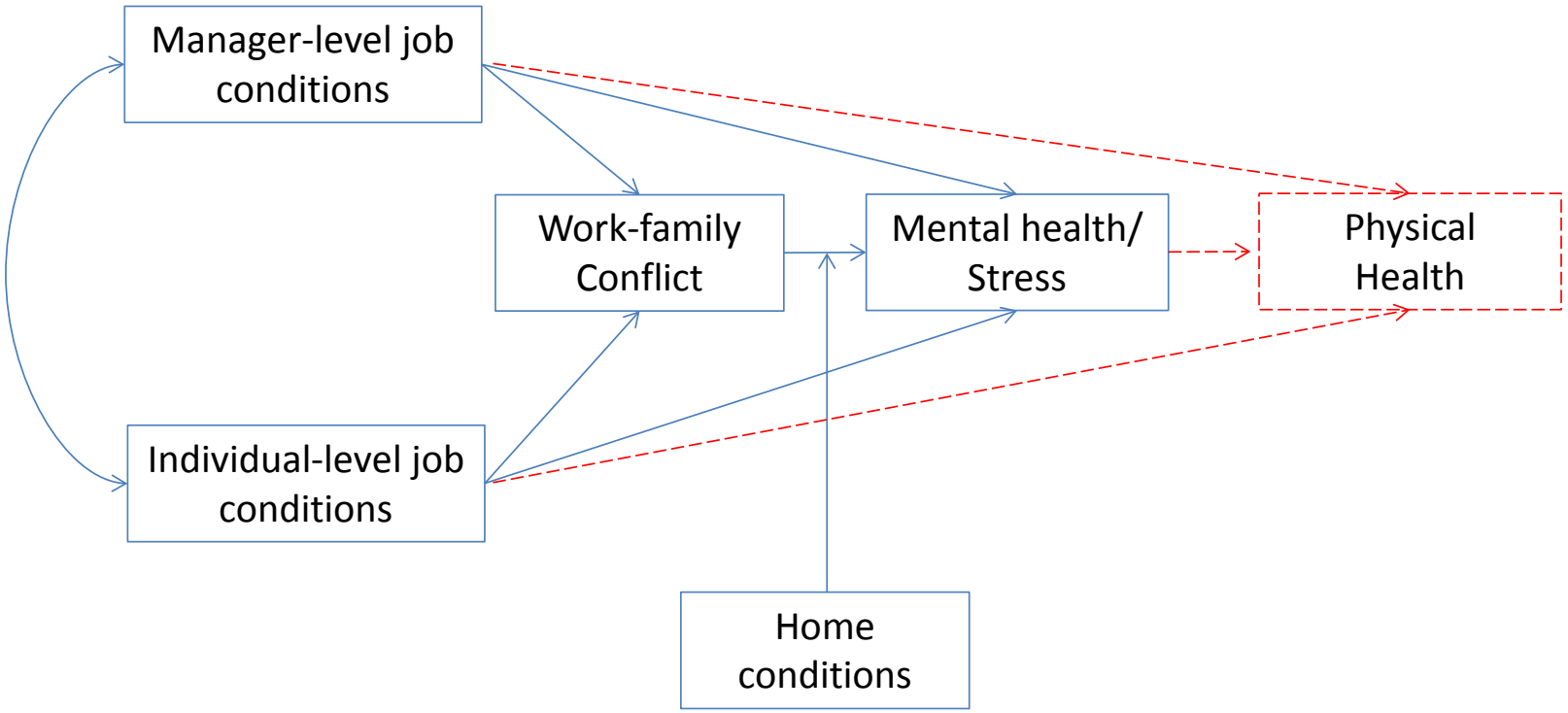






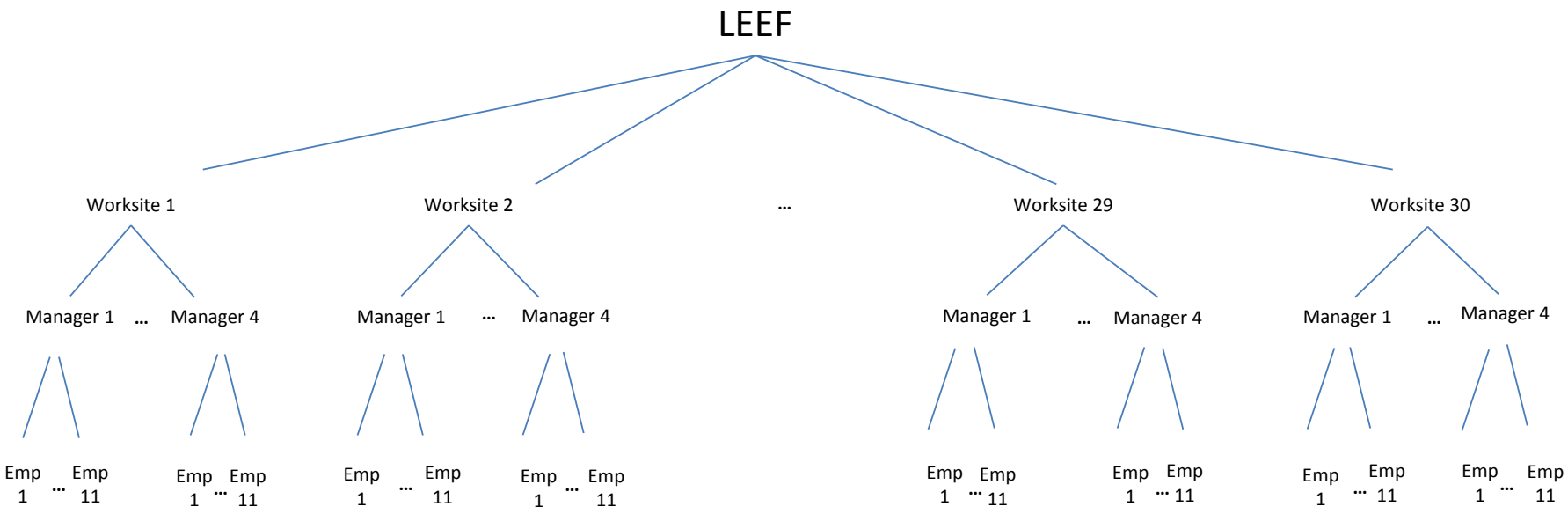






*As referenced in Moen, 2015, with updated pathways in red dashes

Figure 3.1: Multilevel Pathways to Employee Health*



* Note: the current study analyzed a total of 1,524 subjects enrolled at baseline nested within 30 worksites and 139 managers. Most sites had 4 managers supervising employees, though some sites had as few as 2 or as many as 8 managers, Managers supervised an average of roughly 11 employee, with workgroups ranging from 1 to 33 employees. Each worksite averaged roughly 50 employees, ranging from 24 to 89 employees. The average number of managers within sites and employees within managers is reflected in the figure above.

Figure 3.2: LEEF Organizational Structure*

References

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