CHAPTER

6   Cumulative Stress and Health 🔓

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Abstract

Stressors have adverse effects on physical and mental health across the life span, and the accumulation of stressors is particularly damaging. Sociologists argue that the failure of prior research to account for a broad range of social stressors has underestimated the contributions of stress exposure to health behaviors and health status and to socioeconomic and racial/ethnic health inequities. The Midlife in the United States (MIDUS) study provides an unparalleled opportunity for studying the health consequences of stressor accumulation. The topic of cumulative stress is introduced, and challenges in operationalizing this construct are described. Examples of studies from MIDUS are highlighted that have considered multiple social stressors simultaneously, the interaction between daily and chronic stressors, genetic contributions to the effects of stressor on health, and accumulation of stressors at multiple points in the life course. Drawing on principles and models from life course epidemiology and developmental science, future research directions are discussed.

Keywords: MIDUS, cumulative stress, social stressors, health behaviors, preclinical health risk factors, health outcomes, health, life course epidemiology, developmental science

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Introduction

Decades of research show that psychosocial stressors—defined as social or contextual exposures that place a burden on adaptive capacities of an individual (Cohen, Janicki-Deverts, & Miller, 2007)—have significant adverse effects on physical and mental health across the life span, and that the accumulation of stressors is particularly damaging (Turner & Lloyd, 1995). Sociologists have argued that the failure of prior research to comprehensively account for a broad range of social stressors has traditionally underestimated the contributions of stress exposure to health behaviors and health status and to socioeconomic and racial/ethnic inequities in health (Sternthal, Slopen, & Williams, 2011; Turner & Lloyd, 1995; Turner, Wheaton, & Lloyd, 1995). Owing to its rich collection of social, behavioral, and biological information, combined with its unique longitudinal design with an embedded twin sample and daily diary study, the Midlife in the United States (MIDUS) study provides an unparalleled opportunity for studying the health consequences of stressor accumulation and tests of various life course models. The body of this chapter is organized into four sections. First, we introduce the topic of cumulative stress, including empirical approaches to measuring this construct, as well as challenges and limitations inherent to operationalizing this construct. Second, we highlight examples of studies from MIDUS that have jointly considered multiple social stressors in relation to health behaviors, biomarkers of future disease risk, and health outcomes, including studies of smoking behavior, allostatic load, body mass index (BMI), and cancer. Third, we highlight novel research advances using MIDUS data, including studies on the interaction between daily and chronic stressors; genetic contributions to the effects of stressors on health; and the accumulation of stressors at multiple points in the life course. In the final section, we draw on principles and models from life course epidemiology and developmental science research to ↳ describe some future research directions to advance understanding of the association between cumulative stress and health across the life span, including variability in stressor exposure over time, pathway models and moderators, and individual variation in sensitivity to context.

Approaches to the Study of Cumulative Stressors

Extensive research has shown that exposure to multiple stressors, or repeated exposure to the same stressors over time, far exceeds the detrimental health consequences of single exposures (Evans, Li, & Sepanski Whipple, 2013; Turner & Lloyd, 1995). Although substantial research has recognized the value of broad integration of stressors across domains and across time (Turner & Lloyd, 1995), it is relatively uncommon for research studies to aggregate a broad range of acute and chronic stressors. The MIDUS study is a valuable investigation within which to pursue the study of cumulative stressors, given that it queried respondents about multiple domains of stressors at repeated time points, including retrospective reports of childhood adversity, which allows for the aggregation of stressors across time and across stressor domains. A common strategy to evaluate the impact of cumulative stressors on health is to create a composite index by combining indicators for multiple risk factors, or recurrence of the same risk, into a summary score. There are several advantages to composite scores, including (a) robust prediction of a wide array of health outcomes; (b) parsimonious modeling with greater statistical power, given that the risk score is one independent predictor rather than multiple potentially collinear variables (i.e., individuals exposed to one form of risk often contend with other forms of adversity); and (c) ease of interpretation for laypersons and policymakers (Evans et al., 2013). Notably, composite scores typically weigh all risk factors the same and therefore avoid assumptions about the relative strength of different risk factors (a topic for which there is no empirical consensus). At present, there is insufficient empirical information to weigh the relative importance of multiple stressors within a composite score, particularly in a manner that is generalizable across developmental stage or health outcomes. Empirical investigations of this issue suggest that unitary weights are more robust predictors and are infrequently inferior in predictive ability relative to weighted scores (Evans et al., 2013; Wainer, 1976).

In conducting cumulative stress research, researchers must make decisions about which risk factors should be included, how to combine cumulative risk variables from separate domains (i.e., those defined by "place," i.e., home, school, neighborhood; or those defined by type, i.e., structural and psychosocial environmental risks), and whether or not to establish risk "thresholds" for the individual components that must be combined (typically, in a standardized unweighted fashion) to create a composite score. In some circumstances, researchers will dichotomize the stressor measure to allow for the creation of an index or count (Farrington & Loeber, 2000; Sternthal et al., 2011). Our own research, and the research of others, suggests that results are not greatly influenced by the selected value for dichotomization split, providing they are generally similar (e.g., top tertile, quartile, or quintile) (Farrington & Loeber, 2000; Sternthal et al., 2011).

The operationalization of cumulative stress is often limited by the assumption of additivity (which precludes potential synergistic or interactive effects between factors), exclusion of information on intensity of each factor, nonspecific theoretical assumptions about how different types of adversity may have specific impacts on certain types of developmental outcomes, and failure to consider sequential timing of risk factors (Dohrenwend, 2006; Evans et al., 2013).

Alternatives to accumulation of risk models include factor analysis, structural equation modeling, cluster analysis, and recursive partitioning, which allow researchers to identify distinct dimensions or constellations of social and environmental experiences that may uniquely influence health. Focusing on child research, Evans and colleagues recently reviewed and summarized studies that compared cumulative risk indices to these alternative multiple risk metrics (Evans et al., 2013). From this review, it was unclear that any alternative method clearly exceeded the value of the cumulative risk indices, and there were conflicting findings regarding whether the specific constellation of risks was more important than the number of risk factors to which a child was exposed (Deater-Deckard, Dodge, Bates, & Pettit, 1998; Evans, 2003; Greenberg, Speltz, Deklyen, & Jones, 2001; Sanson, Oberklaid, Pedlow, & Prior, 1991). The rich data

collected in the MIDUS study provide an opportunity to study whether or when ↳ it is advantageous to use empirically derived constellations of risk (or protective) factors, or if cumulative indices are comparable or superior for explaining variances regardless of research question.

Cumulative stress research must also consider the timing of stress exposure across the life course. Sensitive periods reflect specific time points in development when physiological systems, or behavioral, emotional, or cognitive capacities, are maximally influenced by exposures (Ben-Shlomo & Kuh, 2002; Bornstein, 1989; Hertzman & Boyce, 2010; Knudsen, 2004; Zeanah, Gunnar, McCall, Kreppner, & Fox, 2011). Sensitive period models are used to evaluate the effects of social and environmental exposures during periods of development (e.g., prenatal, postnatal, adolescence) and have been most elegantly examined using experimental designs with animal models (Hertzman & Boyce, 2010). Human research has typically examined timing of stressors within childhood. In this work, researchers have considered both physical and mental health outcomes, for example, cortisol patterns (Bosch et al., 2012); adiposity (Jun et al., 2012; Ziol-Guest, Duncan, & Kalil, 2009); subcortical brain structures (Tottenham & Sheridan, 2010); somatic complaints (Flaherty et al., 2009); anxiety, depression, and externalizing disorders (Kaplow & Widom, 2007; Keiley, Howe, Dodge, Bates, & Pettit, 2001; Kotch et al., 2008); psychotic disorder (Fisher et al., 2010); and suicidal ideation (Thompson et al., 2012). By and large, this body of research suggests that timing matters; however, across existing observational studies, there are no consistent patterns to suggest that earlier or later exposure is more detrimental. More research is needed to identify the extent to which there may be sensitive periods in any stage of adulthood, including midlife and beyond.

Cumulative stress research can be valuable for understanding the etiology of health outcomes, as well as health disparities by race/ethnicity and socioeconomic position, given that multiple or enduring exposure may function as underlying mechanisms that can partially account for racial/ethnic or socioeconomic disparities (Sternthal et al., 2011). Researchers have posited that stress has a central role in racial/ethnic and socioeconomic patterns of physical and mental health outcomes (Dohrenwend, 2006; Paradies, 2006)—suggesting that disparities may be due to excess exposure to stressors among disadvantaged groups—although a limited body of research has explicitly evaluated this hypothesis. Given the heterogeneity of socioeconomic status (SES) and oversample of African Americans in the Milwaukee, Wisconsin, substudy, this is a hypothesis that can be carefully examined in future MIDUS research.

Cumulative Stress and Health Research in MIDUS

MIDUS provides an opportunity to study cumulative stress in relation to a wide range of physical and mental health outcomes and behaviors. Both MIDUS 1 and 2 surveys included an extensive set of stressor measures that reflect demands people experience in key roles and contexts of daily life, with the majority of stressors assessed in both surveys. Accordingly, researchers are able to consider accumulation of multiple forms at a single time point, as well as accumulation of singular and multiple types of stressors over a 9- to 10-year period. For example, MIDUS 1 and 2 collected information about psychological work stress (e.g., job security, skill discretion, decision authority, demands, control, coworker and supervisor support; Karasek, 1985); physical work stress (e.g., physical work strain, risk of accident or injury on the job); work–family conflict (e.g. work-to-family spillover and family-to-work spillover; Grzywacz, 2000); perceptions of inequality (related to the family, housing and neighborhood conditions, and work; Ryff, Magee, Kling, & Wing, 1999); relationship stress (e.g., family strain, friendship strain, marital risk and strain; Walen & Lachman, 2000); financial stress, neighborhood stress (i.e., safety and trust in residential context; Keyes, 1998); discrimination (e.g., major discrimination events, discrimination on the job, everyday discrimination; Williams, Yan Yu, Jackson, & Anderson, 1997); inventories of problems in immediate family during the past year (e.g., for spouse, parents, and children); stressful life events (with information about perceived stressfulness). MIDUS has also included a set of retrospective questions about childhood experiences, which allows researchers to study cumulative stress during the childhood period as well (e.g., SES in childhood, residential moves, childhood relationship with parents, abuse experiences; Straus, 1979). The breadth of stressor domains included in the MIDUS is far more extensive than is typical in large US population-based surveys with health measures, and the majority of the stressor measures originated from validated scales with excellent ↳ psychometric properties. Below, we highlight a selection of MIDUS studies that examine cumulative stressors, or simultaneous consideration of multiple stressors, in relation to health-related outcomes. Notably, we have summarized only a select set of relevant MIDUS studies, giving primary emphasis to studies we conducted.

p. 78

Cumulative Stress Research in MIDUS by Our Group

Our team has conducted several studies of cumulative stressors and health, using data from the MIDUS study and elsewhere (Slopen et al., 2012, 2013; Slopen & Williams, 2014; Sternthal et al., 2011). In this work, we have attempted to capture stressor exposure as comprehensively as possible by incorporating a broad set of measures. Specifically, our approach involves creating composite scores separately for multiple stressor domains (based on conceptually grouped categories of stressors) in three steps: First, the component measures for a given domain are individually standardized into z-score distributions; second, the z-score values are summed; and third, the resulting values are standardized into a z-score (to allow for comparison of effect sizes across the domains). Finally, we create a cumulative stress score (to combine across multiple types of stressors) in two ways: first by summing the stressor domain z-scores and standardizing this value into a z-score and second by creating a count score for the number of domains for which the individual scored above a certain threshold based on the distribution of scores in the sample (e.g., top quartile). Our approach was informed by empirical research that suggests that the overall quantity of exposure, rather than specific constellations of stressors, may be the most important characteristic for health outcomes, and also the pattern of findings are typically robust to the selected threshold, and the rank order of effect size across multiple stressors is unlikely to be affected (Evans et al., 2013; Farrington & Loeber, 2000; Sternthal et al., 2011).

In our first study to use this approach (Slopen et al., 2012), we examined cumulative stressors and smoking behaviors in 592 middle-aged African Americans from Milwaukee, a subset of MIDUS 2 (2004–2006; ages 34–85 years). We chose to conduct this analysis among the MIDUS Milwaukee participants exclusively, in

light of the need for research on factors associated with smoking among urban racial/ethnic minorities (Dell, Whitman, Shah, Silva, & Ansell, 2005; Delva et al., 2005). Although prior studies had documented that cigarette use is more common among those reporting higher levels of discrimination (Williams & Mohammed, 2009); stressful life events (McKee, Maciejewski, Falba, & Mazure, 2003); work strain (Ayyagari & Sindelar, 2010); financial strain (Siahpush, Spittal, & Singh, 2007); relationship stress (Stein et al., 2008); and generalized measures of perceived stress or counts of stressful life events (Berg et al., 2010; Webb & Carey, 2008), the majority of studies that examine stressors in relation to smoking have examined these domains of stressors individually. Accordingly, there was limited information about the relative impact of different types of stressors on smoking or quitting, which could provide useful information for the design of prevention and cessation programs.

We examined psychological and physical work stress, work–family conflict, perceived inequality, relationship stress, neighborhood stress, discrimination, financial stress, recent problems, stressful events, and childhood adversity in relation to smoking status (current, previous, and never). Using multinomial models adjusted for age, gender, education, and income, we found that 7 of the 11 stressors and the cumulative score were associated with higher odds of current smoking compared with never smoking (i.e., neighborhood, financial, relationship, and psychological work stress; perceived inequality; stressful events; childhood adversity; p values < .05; odds ratios [OR] ranged from 1.28 to 1.77). Compared to participants with no stressor scores in the top quartile of the distribution, participants with stressor scores in the top quartile for five or more stressors were nearly four times as likely to be current smokers (OR = 3.74, 95% CI = 2.09–6.71) and roughly twice as likely to be previous smokers. Overall, this study documented a cross-sectional association between a broad range of psychosocial stressors and smoking among middle-aged African Americans in Milwaukee and was consistent with other prospective research among African Americans (Berg et al., 2010). The results of our study, in combination with other research (Ayyagari & Sindelar, 2010; McKee et al., 2003), suggest that it may useful for public health practitioners to incorporate stress reduction techniques within cessation intervention programs and for individuals and communities to address root causes of psychosocial stress.

In another MIDUS study on cumulative stressors and smoking that used a similar approach to operationalizing cumulative stress (Slopen et al., 2013), we investigated the association between ↳ multiple psychosocial stressors and smoking persistence, cessation, and relapse among the 4,938 individuals participating in the MIDUS 1 and 2 waves (Slopen et al., 2013). For this study, we took advantage of MIDUS's repeated assessments of a broad range of stressors over a 9- to 10-year period, which provided an opportunity to examine chronic exposure to a high level of stress across numerous domains. For both time points of assessment, we created composite measures of stressors pertaining to relationships, finances, work–family conflict, perceived inequality, neighborhood, discrimination, and past year family problems and then created dichotomous indicators of "high stressor exposure" to reflect whether the participant's score was in the top quartile of the distribution. Participants were categorized into four possible groups based on smoking status at baseline and follow-up: nonsmokers (baseline and follow-up), persistent smokers (regular smokers at baseline and follow-up), ex-smokers (smoker at baseline but not at follow-up), and relapsed smoker (ex-smoker at baseline, smoker at follow-up). Individuals with persistently high stressor exposure were associated with increased odds of persistent smoking for stressors pertaining to relationships, finances, work, perceived inequality past-year family problems, and the overall summary score, even after adjusting for both income and education. When looking at respondents who already smoked at baseline, high stressor exposure at both time points for relationship stress, perceived inequality, and past year family problems was associated with nearly double the odds of quitting failure. This study is consistent with and extends existing cross-sectional studies (Berg et al., 2010; Slopen et al., 2012; Stein et al., 2008) and prospective studies (Ayyagari & Sindelar, 2010; McKee et al., 2003) of psychosocial stress and smoking by examining a broad set of stressors at multiple time points in a large population-based cohort.

In this study, the overall stress score was not a better predictor of smoking behavior relative to certain individual stressor domains, reflecting the fact that chronically elevated levels of some of the stressor domains (e.g., neighborhood stress, work–family conflict) were not even marginally associated with smoking behavior. In future research, it will be important to build on these findings in order to inform intervention development. For example, future studies on the association between psychosocial stressors and smoking would benefit from careful consideration of buffering factors, as it is plausible that individual characteristics (e.g., personality, coping styles, social support) and contextual factors (e.g., local smoking laws, availability of cigarettes) could moderate associations between stressors and smoking behavior. From a clinical perspective, this study suggests that patients chronically exposed to high levels of stress may require more intensive interventions to quit successfully.

Cumulative Stress Research in MIDUS by Other Investigators

Using the same approach to the operationalizing cumulative stressor exposure, Reading and colleagues (2016) examined cumulative stressors assessed in MIDUS 2 in relation to allostatic load, measured based on 24 biomarkers from seven physiological regulatory systems among the Biomarker substudy participants (n = 1,182, ages 34–84). Specifically, the authors used a cumulative measure of psychosocial stressor burden that combined information about 11 domains of stressors: psychological and physical work stress, work–family spillover stress, perceived inequality, discrimination, past year problems in the immediate family, stressful life events, relationship, neighborhood, current financial and early life stressors. Using linear mixed-effect regression models, the cumulative psychosocial stressor score was positively associated with elevated allostatic load, and smaller associations were also observed for 4 of the 11 individual stressor domains (i.e., perceived inequality, discrimination, current financial stress, and stressful life events).

Other researchers have used different approaches to assess multiple forms of stressors in relation to health outcomes in MIDUS. For example, Block and colleagues (Block, He, Zaslavsky, Ding, & Ayanian, 2009) examined the association between psychosocial stress and weight gain in 1,355 males and females over the 9- to 10-year period between MIDUS 1 and 2. In sex-stratified analyses weighted to reflect the national US population, the authors examined an assortment of psychosocial stressors related to relationships, work, finances, and life constraints in relation to change in BMI. All stressors were considered separately in this analysis. This study revealed that men with high BMI at baseline had weight gain associated with increasing levels of stress related to job demands, lack of skill discretion, and lack of decision authority and had trouble paying bills. Women with high BMI at baseline had weight gain associated with job demands, perceived life constraints, strain in family relations, and difficulty paying the bills.

p. 80 As a final example, Morton and colleagues (Morton, Schafer, & Ferraro, 2012) examined cumulative stressors during childhood in relation to cancer risk among 3,032 respondents in MIDUS 1 and 2,101 participants in MIDUS 2. These authors used 16 indicators to reflect childhood misfortune, including items such as family receipt of welfare for longer than 6 months, lack of male figure in a household, parental divorce, and abuse. The 16 indicators were conceptually divided to create five categories of misfortune: household SES, household composition, health at 16 years, physical abuse, and emotional abuse. These five categories were then added to create count variables that ranged from 0 to 5. Analysis revealed that for men, additive childhood misfortune, abuse from their fathers, and frequent abuse from either parent were associated with an increased risk of cancer. For women, physical abuse by their mothers and frequent abuse from either parent were associated with increased cancer risk.

Taken together, the described MIDUS studies by our group and by others suggest robust associations between a broad range of stressors and cumulative stress with smoking and quitting (Slopen et al., 2012, 2013), allostatic load (Reading et al., 2016), weight change (Block et al., 2009), and cancer (Morton et al., 2012). The study by Morton et al. (2012) is distinct in that it focused on the accumulation of stressors

specific to the childhood period, whereas some of the other studies included both early childhood and adult stressors (Reading et al., 2016; Slopen et al., 2012, 2013). Notably, it is possible to detect patterns of similarity, whereby stressful life events, financial strain, perceived inequality, family problems, work stress, and relationship stress displayed associations across multiple studies included in our review. Two of the included studies (Morton et al., 2012; Slopen et al., 2013) had results whereby the cumulative score was not a stronger predictor compared to specific types of stressors, thereby highlighting the value of simultaneous consideration of cumulative scores alongside individual stressor domains. Finally, the studies by Block et al. (2009) and Morton et al. (2012) demonstrate that it is important to test for interactions by sex in research on cumulative stress and health outcomes, as the associations between certain stressors and specific types of outcomes may vary based on sex.

Novel Research Advances on Stress and Health in MIDUS

In the following section, we highlight three research advances made possible by the unique sampling design, in-depth substudies, and comprehensive psychosocial and physiological assessments of MIDUS participants. In particular, we describe a selection of studies to showcase MIDUS research on the interaction between daily stressors and chronic strain, the genetic contributions to the effects of stressors on health, and the accumulation of stressors at multiple points in life course.

Interaction Between Day-to-Day and Chronic Strains

The MIDUS 1 National Study of Daily Experiences (NSDE) and MIDUS 2 Daily Stress Project compliment the MIDUS questionnaire-based assessments of stressor exposure by collecting daily reports of both exposure to day-to-day life stressors and reactivity to these stressors for a representative subsample of MIDUS participants. Grzywacz and colleagues used daily diary data over eight consecutive nights from 802 MIDUS 1 participants in the NSDE (Grzywacz & Almeida, 2008) to examine if associations between daily stressors and "stress pileup" were associated with increased risk of binge drinking (i.e., consumption of five or more drinks for males and four or more drinks for females in a 24-hour period). A further question was whether this association was modified by SES (indicated by educational attainment). Daily stress and stress pileup were evaluated using the Daily Inventory of Stressful Experiences (DISE), which has seven stem questions that are used to identify whether stressful events occurred in various areas of life. After every daily interview, participants who responded yes to any of the stem questions were given a value of 1 on an indicator variable of "any stress" and were coded 0 otherwise. A minor or trivial annoyance was given a score of 1, while a score of 4 signified a severely disruptive event. Next, any stress was combined with the coder's rating of how unpleasant the stressor was, which formed a four-category daily stressor variable (none, low stressor, medium stressor, high stressor). Results showed that odds of binge drinking were higher on the days that an individual faced more severe stressors compared to days with no reported stressors. In addition, odds of binge drinking were also higher as stressors accumulated (i.e., "piled up") after consecutive days. Notably, this study found that these associations were modified by SES, whereby binge drinking in response to daily stress was less likely among individuals with low education relative to those with college degrees, and binge drinking in response to stress accumulation (i.e., ↳ pileup) was more likely among individuals with low education in comparison to those with college degrees. By combining daily stress with contextual information about SES, this study reinforced the importance of assessing multiple timescales of stress and of situating day-to-day stressors within the social context in which they occur.

Genetic Contributions to the Effects of Stressors on Health

Genetically informative study designs, such as twin samples, allow researchers to test for confounding of associations by genetic factors (Felson, 2014). MIDUS 1 included a national sample of twin pairs (n = 1,914), which has enabled researchers using MIDUS to parse out genetic and environmental contributions to health outcomes. Drawing on MIDUS 1 data from the twin substudy, Schnittker (2010) examined the genetic influences on the relationship between multiple types of stressors and depression symptoms and disorder. The stressors considered included health and disability stressors (i.e., chronic conditions, trouble with activities of daily living); family (i.e., marital disagreement life events for spouse or children); unemployment and financial strain; discrimination (i.e., lifetime and everyday); and perceived neighborhood status. Schnittker found that although many measures of stress have moderate heritability— meaning that genes influence exposure to environment—the associations between stressors and depression typically persist even after accounting for gene–environment correlations (with some exceptions, including marital conflict). Overall, the results indicated that the association between stressors and depression is robust, even after accounting for genetic predispositions. This type of genetically informed design made possible by the MIDUS twin sample is valuable in advancing traditional observational research, as it can provide evidence for a causal relationship for the association between cumulative stress and health.

Accumulation of Stressors at Multiple Points in the Life Course

Using data from the MIDUS 2 Biomarker Project (n = 1,180, mean age 57.3 years), Hostinar and colleagues (Hostinar, Lachman, Mroczek, Seeman, & Miller, 2015) examined the joint contributions of cumulative adversities in childhood and recent life events in adulthood for inflammation at midlife, operationalized as a composite of five biomarkers from serum samples (i.e., C-reactive protein, interleukin 6, fibrinogen, E-selectin, and ICAM-1 [intercellular adhesion molecule 1]). In this study authors tested three competing models put forth by life course theory: stress generation, stress accumulation, and early life stress sensitization (i.e., that would lead to "synergistic effects"). The results indicated that childhood adversities and recent life event were independently associated with high levels of inflammation (i.e., in the same model), thus supporting an accumulation model whereby stressors at distinct time points in the life course have unique additive effects (i.e., that is, the effect of childhood adversity is not "explained by" greater exposure to stressors in adulthood). The interaction between childhood adversity and recent life events was not significant and thus did not provide evidence for the stress sensitization hypothesis. This study also identified higher urinary norepinephrine output, greater waist circumference, smoking, and lower levels of exercise as mediators of the association between childhood adversity and inflammation in midlife, thereby advancing our knowledge about how cumulative stress is biologically incorporated across the life course to influence risk of chronic disease.

In sum, by utilizing various data features of the MIDUS study, researchers have employed sophisticated strategies (a) to improve causal inferences, (b) to study interaction between day-to-day and chronic experiences of stressors, and (c) to explore the potential importance of stressors at distinct temporal periods in the life course. The valuable study features that facilitated these unique studies are infrequently available or incorporated into cumulative stress and health research and point to important future directions for research.

Future Directions

In the final section of this chapter, we draw on principles and models from life course epidemiology and developmental science research (traditionally conducted with younger samples) to describe some future research directions in MIDUS to advance our understanding of the association between cumulative stress and health at all stages of the life course. Specifically, we propose that research on the relationship between cumulative stress and health will be enhanced by additional investigation of (a) variability in stressor exposure over time, (b) pathway models and moderators, and (c) individual variation in sensitivity to context.

Variability over time.

Beyond issues of accumulation of risk and timing of exposure, there is a small but important body of research that suggests that variability in certain health-related constructs that fluctuate over time, such as SES (McDonough, Duncan, Williams, & House, 1997), may have implications for health. For example, prior research has shown that income instability is associated with mortality in a manner similar to persistent low income (McDonough et al., 1997). Given the repeated assessment of a broad range of stressors, MIDUS is well designed for researchers to characterize the variability in accumulation of stressors that individuals experience from midlife into older age (Slopen et al., 2013) and how this variability is associated with health outcomes. We view stressor variability as an important direction for future research on cumulative stress and health, and MIDUS is an excellent resource for this research given its comprehensive battery of stressor measures.

Pathway models and moderators.

Within life course epidemiology and developmental science research, pathway or "chain-of-risk" models refer to sequentially linked social, biological, or psychological factors (or exposures) whereby one factor influences the likelihood another will occur, ultimately leading to a final exposure that is causally related to disease onset (Ben-Shlomo, Mishra, & Kuh, 2014; Power, Kuh, & Morton, 2013). In this model, all social, biological, or psychological factors can act as *mediating* (i.e., pathway) or *modifying* (i.e., a third variable that alters the association between an exposure and an outcome) factors. For example, within our research on cumulative stress and smoking behavior, a future direction is to understand the mechanisms that link cumulative stress to smoking as well as to identify those factors that could amplify or attenuate the association.

In future MIDUS research to examine the association between cumulative stress and health, it will be important for researchers to take advantage of the multiple time points of data collection to empirically evaluate pathway models that delineate the mechanisms driving observed associations. MIDUS is an ideal cohort for investigations of underlying mechanisms given the host of social and biological data over nearly two decades, and this research direction has the potential to contribute to improved etiological models as well as intervention efforts.

Currently, there is an emphasis on understanding the individual- and family-level mechanisms and moderators linking socioeconomic position to health (Corna, 2013), and there is limited research on institutional and structural factors as mediators or moderators of health inequities over the life course (Jones-Rounds, Evans, & Braubach, 2014; Slopen, Non, Williams, Roberts, & Albert, 2014). There is an independent body of research that links structural factors to individual-level exposures, but this represents only part of the pathway. It is now possible to link the home address of each MIDUS respondent to tract-

level data from the 2000 US Census (Fuller-Rowell et al., 2016), which provides the opportunity to consider area-level structural characteristics as modifiers of the association between cumulative stress and health.

Individual variation in sensitivity to context.

There is increasing interest in individual variability in the effects of social and physical contexts on human health and development (e.g., why some individuals are able to thrive despite environments characterized by profound adversity) (Allen, Kelly, & Committee on the Science of Children Birth to Age 8: Deepening and Broadening the Foundation for Success, 2015; Masten, 2014; Rutter, 2012). Emerging research indicates that some individuals are more sensitive to *both* positive and negative factors across development (Boyce et al., 1995; Ellis, Boyce, Belsky, Bakermans-Kranenburg, & van Ijzendoorn, 2011; Obradovic, Bush, Stamperdahl, Adler, & Boyce, 2010). Identifying behavioral or biological mechanisms that underlie individual variation in health outcomes is a topic of growing interest because understanding sources of variation could provide insight on the etiology of stress-related pathologies and sources of individual vulnerability and resilience to illness (Boyce & Kobor, 2015). The MIDUS data are an ideal resource to study individual variation in sensitivity to context in an aging population, as the study has information on a host of individual-level traits (e.g., personality, psychological dispositions, and health characteristics) spanning over two decades, which may serve as important modifiers of the association between cumulative stressors and health outcomes.

Conclusion

The study of cumulative stressors has led to important insights about the progression of well-being and disease development across the life course. Taken together, studies from MIDUS and elsewhere generally show that the accumulation of stressors is a critical dimension for consideration in research on how the social environment influences health. In addition, the findings highlighted in this chapter also illustrate the

value of simultaneously ↳ examining a variety of types of stressors separately, as certain stressors may be more or less relevant for a given health outcome. In summary, by studying—both separately and cumulatively—a broad range of stressors, investigators can gain a more comprehensive understanding of how stressors shape the health of populations and influence health disparities by race/ethnicity and SES. Moving forward, it will be valuable for cumulative stress research—using MIDUS and other data sources— to rigorously incorporate principles and models from life course epidemiology and developmental science. These will allow for development of alternatives to traditional additive risk models; exploration of sensitive periods for exposure to stressors at different stages of the life course; careful consideration of variability in stressor exposure over time; delineation of underlying psychological and physiologic mechanisms linking cumulative stressor exposure to health; and discovery of factors that influence individual variation in sensitivity to stressors. These advances are important for research on cumulative stress and health research, which as a field has the potential to inform the development of policies and interventions that can reduce health disparities and promote well-being across the population.

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