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## Considering the Role of Stress in Populations of High-Risk, Underserved Community Networks Program Centers

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### Abstract

**Background**—Cancer disparities are associated with a broad range of sociocultural determinants of health that operate in community contexts. High-risk populations may be more vulnerable to social and environmental factors that lead to chronic stress. Theoretical and empirical research indicates that exposure to contextual and sociocultural stress alters biological systems, thereby influencing cancer risk, progression, and, ultimately, mortality.

**Objective**—We sought to describe contextual pathways through which stress likely increases cancer risk in high-risk, underserved populations.

**Methods**—This review presents a description of the link between contextual stressors and disease risk disparities within underserved communities, with a focus on 1) stress as a proximal link between biological processes, such as cytokine responses, inflammation, and cancer and 2) stress as a distal link to cancer through biobehavioral risk factors such as poor diet, physical inactivity, circadian rhythm or sleep disruption, and substance abuse. These concepts are illustrated through application to populations served by three National Cancer Institute-funded Community Networks Program Centers (CNPCs): African Americans in the Deep South (the South Carolina Cancer Disparities Community Network [SCDCN]), Native Hawaiians (‘Imi Hale—Native Hawaiian Cancer Network), and Latinos in the Lower Yakima Valley of Washington State (The Center for Hispanic Health Promotion: Reducing Cancer Disparities).

**Conclusions**—Stress experienced by the underserved communities represented in the CNPCs is marked by social, biological, and behavioral pathways that increase cancer risk. A case is presented to increase research on sociocultural determinants of health, stress, and cancer risk among racial/ethnic minorities in underserved communities.

### Keywords

Psychological stress; vulnerable populations; cancer; community networks; racism; discrimination; African Americans; Hispanic Americans; Hawaii; Oceanic Ancestry Group

Cancer disparities are associated with a broad range of social determinants of health<sup>1</sup> that are related to exposure to stressors in high-risk, underserved populations.<sup>2–6</sup> In this article, concepts linking stress, biological sequelae, and putative effects on cancer risk profiles are related to examples drawn from populations served by three National Cancer Institute-funded CNPCs.

Existing conceptual models and frameworks describe the influence of social determinants on health, and many focus on the role of chronic stress in mediating biological processes that can cause disease.<sup>7,8</sup> An example of this as it relates to cancer is provided in Figure 1. Empirical research links social factors and stress to disparate health outcomes, including a variety of human cancers.<sup>9–11</sup> Low socioeconomic status, for example, is linked with a higher risk for many diseases and health practices.<sup>12–15</sup> Social position is a strong predictor of disease risk, even after accounting for factors that comprise socioeconomic status.<sup>16,17</sup> Lower social position is thought to contribute to increased stress and to observed differences in disease incidence<sup>18–20</sup> as well as to survival.<sup>21,22</sup> Psychosocial stressors can contribute to susceptibility to chronic diseases, including cancer.<sup>23–25</sup> Specifically, socially disadvantaged groups experience these impacts owing to their increased exposure to chronic unpredictable, uncontrollable stressors across the life span.<sup>15,26</sup> Marginalized groups may suffer from stressor overload, exhaustion of endogenous and exogenous coping mechanisms,<sup>27</sup> and contextual demands that exceed their adaptive capacity.<sup>15,28</sup>

Unhealthy behaviors, such as smoking, alcohol and drug abuse, poor diet/overeating, and sedentary behavior, are common high-risk coping responses to stressful situations<sup>29</sup> that can increase cancer risk.<sup>30–32</sup> Low-grade inflammation, caused by the release of inflammatory cytokines and adipokines from central adipose tissue, is another effect<sup>33,34</sup> and dysregulated cortisol responses are a primary product of stress reactivity in relation to adiposity.<sup>35–37</sup>

Chronic maladaptive coping, depressive symptomology, and “sickness behavior”<sup>38–41</sup> among populations exposed to chronic stress may alter neuropsychological, immune, and endocrine function along the hypothalamic–pituitary–adrenal axis that may, in turn, affect cancer prevention, incidence, and survival.<sup>11</sup> For instance, “sickness behavior” and, similarly, depression, which are associated with lethargy, inability to concentrate, and reduction in self-care behaviors, can be induced by stress-related increases in proinflammatory cytokines’ (e.g., interleukin-6, tumor necrosis factor- $\alpha$ ) effects on the brain.<sup>42</sup> Other stress-related behaviors, such as a preference for sweet<sup>43,44</sup> and/or high-fat<sup>45</sup> foods, are thought to be mediated by cortisol and may be associated with abdominal adiposity,<sup>46</sup> a risk factor for several cancers.<sup>47</sup>

Circadian disruption and chronobiological dysregulation often accompany stress.<sup>48</sup> Individuals in low-control, high-stress jobs<sup>49</sup> often work at odd hours of the day,<sup>50</sup> and those who are insecure about their employment may have disturbed sleep.<sup>51,52</sup> Symptoms of circadian disruption such as fatigue, sleep disruption, and depressive symptoms are associated with altered neuroendocrine and immune signaling and are accompanied by proinflammatory cytokine secretion.<sup>53,54</sup> Fatigue, poor sleep quality, and depression are associated with cancer and are often symptoms experienced by those with disrupted

circadian patterns.<sup>55</sup> These symptoms are reported to vary by race/ethnicity.<sup>56</sup> For example, African Americans differ in their endogenous circadian timing relative to European Americans,<sup>57</sup> and they are more likely than are European Americans to participate in shift work<sup>58,59</sup> (a risk factor for cancer and other chronic diseases<sup>48</sup>) and to experience poorly timed ambient light exposures<sup>60,61</sup> and poor sleep quality.<sup>58,62</sup>

Discrimination functions as both a chronic<sup>63,64</sup> and acute stressor,<sup>65</sup> producing mental and physical health effects.<sup>66</sup> Several studies show that discrimination is associated with increased levels of stress, risky health behaviors, and poor mental and physical health outcomes among racial and ethnic minorities.<sup>67</sup>

Allostatic load refers to the cumulative impact of health risks owing to repeated or prolonged stress over the course of a person's life that can lead to increased risk of disease.<sup>18,68,69</sup> This cumulative effect results in dramatically earlier onset of biological aging or "weathering" associated with increased cancer risk in minorities, with the strongest evidence in African Americans.<sup>70–72</sup>

Although the terms for describing the problem may vary from population to population, and between high-risk communities and academe, the role of stress in health is well appreciated across populations. Community-based participatory research (CBPR) provides a means for engaging with high-stress groups in designing research studies that would lead to practicable solutions to reduce stress. These could include interventions aimed directly at stress reduction, or at other lifestyle-related behaviors that are thought to reduce stress. There are many viable alternatives to randomized, controlled trials, which are probably inappropriate for such behavioral interventions in any event. These alternatives include randomizing before consent, single-arm, and selfselection study designs.

## Examples

To illustrate possible relationships between stress and cancer issues, we focus on three minority groups represented in the 23 CNPCs—African Americans, Latinos, and Native Hawaiians. All CNPCs use CBPR methods to engage communities to address cancer-related health disparities.<sup>73</sup>

### African Americans in South Carolina

The genotype of most African-American South Carolinians can be traced to purposeful selection of West African agrarian populations on the "Rice Coast" or the "Windward Coast," in the "Gambia" and "Sierra Leone."<sup>74–76</sup> Seventeenth-century South Carolina planters unfamiliar with rice cultivation used African slaves' rice cultivation skills to develop large plantations.<sup>77,78</sup> This led to creation of a lucrative market for "Rice Coast" slaves.<sup>74–77,79</sup> Besides there being a Black majority in South Carolina,<sup>80</sup> two other factors contributed to the retention of African culture and health behaviors<sup>81–83</sup>: 1) plantation hypersegregation between Whites and Blacks and 2) geographic, topographical, and climactic similarity to the African "Rice Coast."

As the South Carolina Slave Codes were instigated and cotton replaced rice as the dominant crop, slaves' diets became more controlled by plantation owners.<sup>84</sup> Preservative salt added to the diet of a highly sodium-responsive population could add to the stressors of slavery by inducing exaggerated neural responses to stress.<sup>85–87</sup> Unpredictable, uncontrollable violence, lack of control over personal health decisions, physical exhaustion, and environmental stressors also accompanied this shift in Deep South slave-holding practices,<sup>88</sup> which resulted in the loss of stress-buffering cultural traditions.<sup>89,90</sup>

The lingering effects of racism include psychosocial stress<sup>91–93</sup> and “downstream” effects on factors that have implications for cancer, such as inflammation<sup>94</sup> and sleep disturbances.<sup>95</sup> Indeed, we found that, in a population of overweight and obese African-American churchgoers experiencing racism, there were very high levels of C-reactive protein, a marker of systemic inflammation, that decreased with an intervention that included stress reduction.<sup>96</sup> In another study we found that African-American Medicaid recipients with type II diabetes (a condition known to be related to inflammation and stress) had an elevated risk of colorectal cancer, beyond that of diabetic European Americans.<sup>97</sup>

Historical factors provide the backdrop to current stressors, which may produce epigenetic effects<sup>98</sup> for the descendants of African Slaves.<sup>26</sup> Epigenetic effects among African Americans in South Carolina occur not only through diet, allostatic overload, and destruction of adaptive social ties,<sup>99</sup> but also through chronic poverty and chronic unpredictable, uncontrollable exposure to contextual stressors.<sup>98</sup> In other work, we demonstrated that skin color is related to stress, blood pressure, and body mass index,<sup>63</sup> risk factors associated with numerous health outcomes, including cancer. Cultural adaptations, in particular strengthening gender roles in positive modifiable health behaviors<sup>100</sup> and a prominent focus on religion and spirituality,<sup>96,101</sup> provide both ameliorating effects and opportunities for effective intervention. Indeed, other work conducted through the SCCDCN shows the influence of African-American pastors' food identity<sup>101</sup> on church-level factors related to food/diet and physical activity messaging.<sup>102</sup> In addition to obesity,<sup>63</sup> SCCDCN researchers also have found that racism-related stress is associated with psychosocial<sup>103</sup> and cognitive cancer risk factors,<sup>104</sup> as well as higher resting blood pressure.<sup>105,106</sup>

Today, African Americans in our target communities often are employed in low-status,<sup>107</sup> low-control,<sup>108</sup> insecure, service sector jobs that typically entail little physical activity and frequently require working odd and/or long hours.<sup>109</sup> Disproportionately, they reside in rural and impoverished urban communities that are unsafe, offer limited access to healthy foods, and provide little opportunity for physical activity.<sup>110,111</sup> Calorie-dense/nutrient sparse diets,<sup>112,113</sup> physical inactivity (worse in the rural South than anywhere else in the United States),<sup>114</sup> and high rates of obesity and diabetes,<sup>113,115,116</sup> are all known cancer risk factors.<sup>97,117,118</sup>

The SCCDCN recognizes that economic development undergirds social, environmental, and health-related justice. Our work with churches, as cited, and other community partners is predicated on making connections with social and economic structures in which the community operates to promote health and sustain change. The SCCDCN has developed programs that engage women, who are disproportionately represented as community leaders

and heads of households, as a means to address the range of “upstream” factors, from examining institutional racism to increasing economic opportunity and enabling healthy lifestyle choices (e.g., building on plant-based dietary traditions of the African Diaspora, promoting social ties among community members,<sup>99,108</sup> and engaging in culturally salient physical activities).

### Latinos in the Lower Yakima Valley

As with African Americans, Hispanics in the United States have experienced historical trauma. From initial Spanish domination to *Bracero* (guest worker) programs,<sup>119,120</sup> the Hispanic population has been subjected to domination by populations of European ancestry.<sup>119</sup> The population that has emerged is characterized by poverty and stigma.<sup>120–122</sup> The literature suggests that this ethnic group is associated with worse mental and physical health as compared with the non-Hispanic White (NHW) population.<sup>123–128</sup> As a group, Hispanics have limited access to health care, with 38.3% having no health insurance compared with 12.0% for NHWs. Overweight prevalence is higher in Hispanics (67.0%) than NHWs (59.2%).<sup>129</sup> Additionally, Hispanics are, on average, much less likely than others to utilize mental health services.<sup>130</sup>

Although Hispanics have a lower incidence of many cancers, they tend to have higher mortality.<sup>131</sup> Part of the reason may be biological, but much is related to low access to care and late diagnoses and treatment of disease.<sup>131</sup> For example, Latinas have a significantly lower breast cancer incidence compared with NHWs; however, their mortality rates are comparable.<sup>131</sup> Further, when asked about stress in their lives, more than 50% of Hispanics reported having high mental and physical stress owing to jobs that entail physical labor and low wages.<sup>130</sup> For example, Latinos hold 48.9% of the jobs in agriculture,<sup>132</sup> an occupation that involves hard work and low pay. Another large proportion of Latinos hold jobs in the service industry and in housekeeping, also physically demanding, low-paying occupations.<sup>132</sup>

The Hispanic Community Network to Reduce Cancer Disparities began working in Yakima Valley in Eastern Washington in 2005. The lower Yakima Valley is a “majority minority” area, with Hispanics’ comprising approximately 67% of the population. Many Hispanics work in agriculture as well as in the service industry. It is the mission of the CNPC to improve the lives of Hispanics who live in the valley by providing education and research to enhance accessibility to cancer screening, treatment, and survivorship. To learn more about Latino experiences with perceived racism and other forms of discrimination, the CNPC conducted qualitative, in-depth interviews among Latino residents of the lower Yakima Valley (unpublished data provided by B. Thompson). Respondents reported exposure to several types of perceived racism, including discrimination based on race/ethnicity, language, and legal status. The most common settings in which discrimination occurred were at work and in local businesses. Coping responses to perceived racism included ignoring it, avoiding it, talking with someone about it, and praying. Respondents reported health effects of perceived racism and other stressors, including problems sleeping, changes in diet and physical activity, and increased alcohol use.

In a study examining 70 Hispanics and 87 NHWs in the area, all of whom had type II diabetes, we found that Hispanics were much less likely than NHWs to engage in activities such as diet and physical activity to control their diabetes.<sup>133</sup> This difference may have been due to having few resources to purchase appropriate foods and/or living in neighborhoods where physical activity was unsafe or impractical. Further, the more acculturated the Hispanics, the more likely they were to engage in lifestyle behaviors to address their diabetes. Thus, acculturative stress may have an impact on chronic disease management.

In a study examining Hispanic agricultural workers and Hispanic nonagricultural workers, differences in perceived stress were examined (unpublished data provided by B. Thompson). Agricultural workers were more likely to experience stress in all five stress categories (work, community, family, psychological, and acculturation) that influenced their well-being compared with nonagricultural workers. Specifically, as stress increased, well-being, as measured by the World Health Organization Well-Being Index, decreased. The Well-Being Index includes mental well-being, physical well-being, sleep disturbances, and interest in daily life.

The data indicate that the underserved Hispanic population is subject to chronic stressors that have an impact on health, including chronic diseases. More work is needed to understand this phenomenon in the population, and ways to alleviate the stress should be identified and tested using rigorous methods.

### **Native Hawaiians in Hawai'i**

Native Hawaiians are descendants of the original inhabitants of the Pacific archipelago now called Hawai'i. European explorers to Hawai'i in 1778 found a robust and vibrant native population, numbering about 800,000, with a sophisticated socioreligious order that ensured equitable distribution of life-sustaining resources. U.S. influence and aspirations led to the overthrow of the Hawaiian Kingdom in 1883, followed by its annexation in 1898 and statehood in 1959, all of which were strongly opposed by Native Hawaiians.<sup>134</sup>

Many scholars postulate that the health and well-being of Native Hawaiians were adversely affected by the U.S. occupation of Hawai'i and its compulsory acculturation process.<sup>135–139</sup> Today, Native Hawaiians have a much greater prevalence of obesity (44%), diabetes (20%), depression (13%), cigarette smoking (27%), and alcohol and drug abuse (26%) than do NHWs and other ethnic groups in the state.<sup>140</sup> Native Hawaiians are more likely to work in low-paying jobs and to be undereducated, incarcerated, and living in poorer conditions than are other ethnic groups in Hawai'i.<sup>141</sup> These conditions manifest in a much shorter life expectancy for Native Hawaiians, as compared with Chinese, Japanese, Korean, Filipino, and NHW residents.<sup>142</sup>

Researchers affiliated with 'Imi Hale Native Hawaiian Cancer Network have found evidence that acculturative stress and ethnic discrimination could be increasing Native Hawaiians' risk for stress-related diseases. In a study of 496 adult Native Hawaiians, the prevalence of type 2 diabetes was examined across four modes of acculturation: integrated (high ethnic and high mainstream identity), traditional (exclusively high ethnic identity), assimilated (exclusively high mainstream identity), and marginalized (low ethnic and mainstream

identity).<sup>143</sup> After accounting for differences in sociodemographics, degree of Hawaiian ancestry, and biological correlates, researchers found that the prevalence of type 2 diabetes was nearly two times greater among Native Hawaiians categorized as having a traditional mode of acculturation, as compared with those with an integrated mode of acculturation (28% vs. 15%, respectively). This suggests that the differences are owing to the experience of greater acculturative stress and unique psychosocial factors, such as perceived racism.<sup>143</sup>

A study of 94 adult Native Hawaiians examined the effects of perceived racism and other acculturation factors on the prevalence of hypertension.<sup>144</sup> Native Hawaiians who had a stronger Hawaiian ethnic identity were more likely to report that other social groups discriminated against them. Further, perceptions of discrimination were associated significantly with self-reported hypertension, after adjusting for sociodemographics and degree of Hawaiian ethnic and American cultural identity. Perceptions of discrimination seemed to have mediated the relationship between Hawaiian cultural identity and hypertension status, which supports the possibility that Native Hawaiians in a traditional mode of acculturation are experiencing more acculturative stressors.

A third study examined effects of perceived racism on cortisol levels and blood pressure as two indices of physiological health.<sup>93</sup> Among 143 adult Native Hawaiians, those who reported a stronger Hawaiian ethnic identity also perceived more racism in their environment, and perception of racism was associated significantly with lower diurnal cortisol levels and higher systolic blood pressure. However, after adjusting for different sociodemographic, biological, and psychosocial characteristics, the researchers noted that only the significant correlation between cortisol level and perceived racism persisted. Contrary to the normal response of increased cortisol in situations of acute stress, a low level of cortisol output is believed to be indicative of chronic stress and has been observed in victims of domestic violence,<sup>145</sup> caregivers for ill family members,<sup>146</sup> and people diagnosed with posttraumatic stress disorder.<sup>147</sup> Hypocortisolism is associated with a risk for stress-related disorders, such as atherosclerosis, hypertension, obesity, and diabetes.<sup>148,149</sup>

Collectively, these studies support the notion that racial/ethnic discrimination may be a chronic psychosocial stressor for Native Hawaiians. Strong perceptions of discrimination seem to be associated with stress-related chronic diseases, such as hypertension and diabetes. Associations between perceived discrimination and cancer have not been reported for Native Hawaiians, and further research in this area is recommended.

## Discussion

Psychological stress experienced by the underserved populations discussed here manifests in both biological and behavioral outcomes<sup>150,151</sup> that can result in increased cancer risk. However, research on social determinants of health, stress, and cancer risk among racial/ethnic minorities must overcome serious barriers: 1) a history of distrust in minority communities contributing to their underrepresentation in clinical, psychosocial, and biomedical studies including, but not limited to, randomized trials, 2) researchers not actively seeking methods to improve communication and trust with racial/ethnic minority

populations, and 3) linguistic and sociocultural differences that limit effectiveness of psychosocial intervention research.

The CNPCs are committed to using CBPR approaches to define and identify solutions to problems that increase risk of disease and disability.<sup>152</sup> This has the effect of markedly reducing the probability of type III error (incorrect inference resulting from a faulty conception of how things work or selection of a study design that produces an answer [even if correct] to the wrong question [because it is fundamentally biased]).<sup>153,154</sup> Rather than researchers' requiring changes that are culturally inappropriate, untimely, or unwise, the underserved community works with researchers to develop solutions and strategies to attain solutions. In South Carolina, for example, the partnership with the Baptist Church, which ensures that education and health activities correspond with the prevailing culture and attitudes, taps into the roles of resilience<sup>155</sup> and spirituality<sup>156,157</sup> that are important stress buffers in the face of adversity. In the Yakima Valley of Washington State, the CNPC conducts activities with the Hispanic community during Mexican activities, such as *Cinco de Mayo*. They also conduct activities with extended families, because this is important in the Mexican-American culture. In the Hawaiian CNPC, well-received interventions have incorporated traditional cultural values, been based in Hawaiian churches and civic clubs, and featured traditional activities, such as hula dancing and canoe paddling. Further, Hawaiian community members have been empowered to lead, deliver, and test these interventions.

In short, by working with communities, rather than imposing the will of culturally different groups, we have an opportunity to prevent and control cancer in a way that is meaningful for the populations we are trying to reach. When cancer prevention and control interventions are part of a group's culture, they are more likely to engage the group. Such efforts may contribute to the reduction of cancer disparities among the underserved.

The World Health Organization Commission on Social Determinants of Health provides several strategies for taking action on social determinants of health.<sup>17,158</sup> Approaches include creating policies that reduce oppressed groups' vulnerability to the health effects of social inequality and prevent the unequal health consequences of social inequality. Strategies that use this approach involve increasing racial/ethnic minorities' resources to deal with stressors, such as efforts to increase community empowerment or encourage positive coping strategies, which may reduce the negative health effects of stress. What we have shown is that race/ethnicity-related stress operates through two, related pathways: 1) through direct proinflammatory, epigenetic, or other biological processes that can exert toxic effects and 2) through unhealthy coping lifestyles and behaviors that are themselves risk factors for cancer. The history of public health has shown that improving the economic circumstances of individuals can have a ripple effect through a variety of processes such as stress reduction, increased opportunities to improve diet and physical activity, and better access to health care.<sup>159,160</sup>



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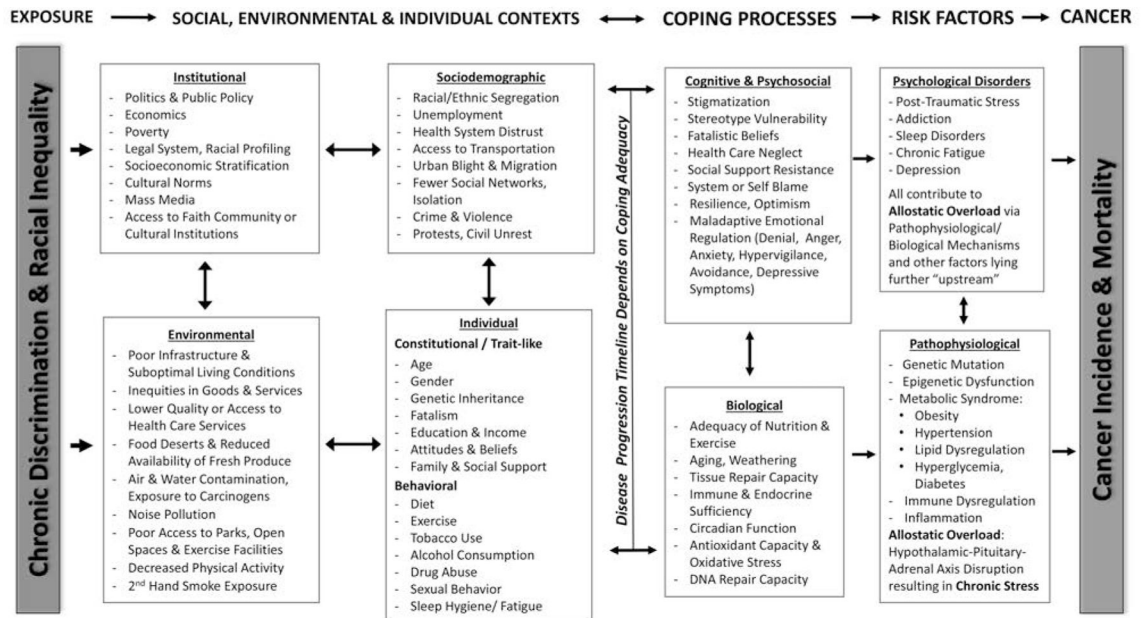
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**Figure 1. Pathways from Stress to Cancer**

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