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Biobehavioral examination of fatigue across populations: Report from a P30 Center of Excellence

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ABSTRACT

Objectives: This article reports the cross-studies analysis of projects from the P30 Center of Excellence for Biobehavioral Approaches to Symptom Management. Although the projects investigated diverse populations, a consistent theoretical and empirical approach guided each project.

Methods: Common data elements included the following measures of psychobehavioral variables: the PROMIS Short-Form Fatigue Scale, the Center of Epidemiologic Studies Depression Scale, and the Perceived Stress Scale. Plasma cytokines were measured as the shared biological data element.

Results: Data were analyzed from 295 participants with fibromyalgia (n = 72), second trimester pregnancy (n = 73), sickle cell anemia (n = 60), and cardiometabolic risk (n = 91). The mean age of participants was 35.4 years, and the most participants were female. Levels of symptoms were generally elevated across samples; the level of fatigue ranged from 18.9 to 24.7, depressive symptoms from 12.5 to 23.4, and perceived stress from 16.5 to 21.8. Intercorrelations among symptom measures and perceived stress were strong across the samples. However, correlations among psychobehavioral variables and cytokines were variable, indicating a separate relationship for the measures with cytokines.

Conclusions: Future work in symptom science could benefit from common data elements, including biomarkers, across populations to better develop the taxonomy of symptom profiles across conditions.

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Fatigue is a highly prevalent, complex, multidimensional symptom that adversely impacts quality of life (QOL) and health outcomes across the life span. In terms of economic burden, fatigue is associated with significant health-related lost productive time in U.S. workers, resulting in over \$136 billion dollars annually in lost productivity (Ricci, Chee, Lorandeau, & Berger, 2007). Fatigue is associated with decreased quality of life across the life span. Given such health-related costs, it is not surprising that publishing rates for

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studies of fatigue increased by about 90% over 2002 to 2011 (Friedberg, Caikauskaite, Adamowicz, Bivona, & Njoku, 2013). However, most studies of fatigue have focused on single populations, and relatively few investigators have concurrently measured biomarkers and associated symptoms. Furthermore, the use of multiple instruments to measure fatigue and the use of diverse sources of biological measures and measurement platforms for fatigue biomarkers have also contributed to the difficulty in comparing results across populations and from study to study. The Center of Excellence in Biobehavioral Symptom Management (P30 NR011403, Grap, principal investigator; 2009–2014) at Virginia Commonwealth University School of Nursing was designed to examine fatigue, associated symptoms (depressive symptoms and perceived stress), and biomarkers in different clinical populations using a consistent theoretical and empirical approach. In this article, we report the shared conceptualization, the selection of measures, and the results from the cross-studies analyses of studies that comprised the projects of the center. Although each study was designed to answer a population-specific research question with relevant population-specific measures, common data elements were selected a priori to guide the measurement of symptoms and biological variables across studies as part of the center's goals.

Background

Symptom science has been identified as a priority in nursing research (Grady, 2010). Although there have been advancements toward the goal of describing symptoms in health and illness, the symptom science field has been stymied by the lack of uniformity of measures and conceptualizations of concepts and measures. The symptom of fatigue may be a particularly vexing concept for research because it is pervasive and highly subjective; hence, there are multiple definitions of fatigue and many different measures. Some studies have used population-specific measures, and others have used general measures; typically one measure, either general or population specific, has been selected without considering the benefits of using a standardized measure of fatigue. Not surprisingly, given the backdrop of conceptual and operational heterogeneity in the measurement of fatigue, there have been conflicting results from studies focused on uncovering possible biological mechanisms or biomarker correlates of fatigue. Although data from animal models have generally supported a relationship of proinflammatory activation with fatigue (Kurzrock, 2001), studies in humans have been more variable across studies and disease conditions (Gibney & Drexhage, 2013). Even so, a number of studies have pointed to the importance of inflammation in the pathophysiology of fatigue (Dantzer, Heijnen, Kavelaars, Laye, & Capuron, 2014).

In accord with the big data era in science (Henly, 2013), the center was designed with elements of theoretical and operational "harmonization" so that we could examine variables of interest in the collective in addition to each individual project. Given the importance of fatigue in terms of clinical outcomes and the lack of clarity in the conceptualization and measurement of fatigue, it was important to ground the definition and operationalization of fatigue within a theoretical framework that accounted for both the psychobehavioral and the biological factors relevant to fatigue in diverse populations. It also was important to select a theoretical framework that was appropriate for all target populations of the center. The biobehavioral framework that we selected was a psychoneuroimmunology (PNI) framework that considers the relationships among commonly co-occurring symptoms and putative biological correlates (Figure 1). Given that PNI is useful for understanding the inter-relationships among mindbody interactions in health and illness (Zeller, McCain, Swanson, 1996), PNI provides a theoretical &

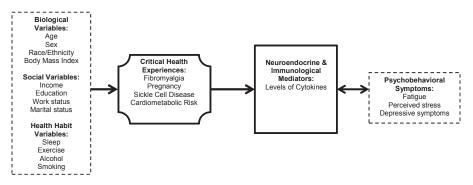


Figure 1 – PNI framework of the P30 Center of Excellence for Biobehavioral Approaches to Symptom Management. The PNI framework focuses on the interactions among biological, social, and behavioral factors and their effects on health outcomes. A critical health experience is a change in health or perception of change that places an individual at risk of experiencing distressing symptoms. Common biological, social, and behavioral variables as well as immunological mediators and psychobehavioral symptoms were used to examine the relationships between study variables across projects.

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