Purpose: The use of omics in patient assessment, diagnosis, and interventions will be discussed from the perspective of the family caregiver (FCG) as the client. While FCGs often assume essential roles for their aged or chronically ill family members, prolonged and intense caregiving effort exerts a devastating toll on their health. This is manifested as FCG burden, depression, reduced quality of life, increased risk for cardiovascular events and other chronic conditions. A better understanding of the other modifiable and non-modifiable correlates of depressive symptoms in FCGs is essential to direct FCG interventions. A better understanding of the biobehavioral characteristics of FCGs who experiences adverse outcomes to caregiving would inform more precise, personalized and efficient approaches to improving assessment of risk for poor FCG health outcomes and experiences as well as informing more precise approaches to improving FCG outcomes. Increased caregiver demands such as increased severity of illness of the chronically ill or HF patient as well as caregiver burden and strain are logically associated with greater depressive symptoms. One omic related factor to consider in association with depressive symptoms is the serotonin transporter-linked polymorphic region (5-HTTLPR) genotypes (XL/L, LL, L/S, S/S) which is a well-studied determinant of differential stress reactivity. The serotonin transporter gene (5HTT) promoter region (5HTTLPR) is located on chromosome 17. Short (S) versus long (L) variants are associated with emotional and stress hyperreactivity. Research posits that any S allele increases predisposition for affective disorders. Polymorphisms of 5HTTLPR have been linked to the immune response to acute stress and a variety of stress reactive phenotypes including PTSD, alcohol and substance abuse, and depression after medical illness, and in dementia FCGs. Additionally, a single nucleotide polymorphism (SNP) in the L allele of the HTTLPR locus (A/G), appears to have a functional effect, with L-G alleles behaving like S-alleles. The relationship between 5HTTLPR and depression may be moderated by stressful life events such as caregiving, and race and gender. Previous research in other populations suggests that any S allele genotype is associated with a predisposition towards depression especially in the context of life stressors.

Methods: While there are similarities in the demands of chronic caregiving, there are also important differences related to the population under study, thus the data from a study of FCGs of persons with HF will be used as an exemplar. The participants in this study were HF FCGs (n=127, mean age 55.3 ± 11.5 years, primarily women, majority African American (AA). Caregiver burden was moderately high, and around a third reported they provided care for others in addition to the person with HF. Variables and measures were demographic factors, FCG health status, depressive symptoms (CES-D), family functioning (FAD), social support, caregiving demands (Oberst Caregiving Demands, caregiver strain [CS], and behavioral factors of physical activity and sleep quality (PSQI). The 5-HTTLPR genotype was also measured in a subset of participants. Stepwise variable selection was used to identify the best predictors of CES-D scores and to inform construction of regression models for the total sample and the 5-HTTLPR genotypes of XL/L and any S (L/S, S/S) allele groups separately.

Results: At baseline prior to intervention, approximately 41.7% of the HF FCGs scored > 16 on the CES-D indicating significant depressive symptoms. Factors with significant relationships (p<.05) with CES-D scores included measures representing burden (caring for others, Oberst, mental and physical CS Caregiving Demands), health and health behavior (the FCG health rating and PSQI scores), the social context (family function, social support). Regression models accounted for a moderate amount (p<.001)
of the variability in CES-D scores with PSQI (p<.001), Oberst (p=.006), FAD (p=.005), caring for others (p=.003), and African American race (p=.016) significant as predictors. African Americans had lowered overall CES-D scores than White participants. In the 5-HTTLPR sub-analyses, family function and sleep were the only significantly associated factors with CES-D in the XL/L group. For the any S group, caring for others, and greater mental strain were significantly associated with CES-D scores.

**Conclusion:** Although in a smaller subset analysis of the sample, for HF FCGs in the XL/LL genotype group, caregiver demands/strain had less effect on depressive symptoms and more effect from their social context of family functioning and health behavior or poor sleep. On the other hand, burden/strain significantly affected the any S type group with higher depressive symptoms. These data support the likelihood that allele variants of the 5-HTTLPR may interact with caregiving burden to predict depressive symptoms differentially. While not modifiable, knowledge of a FCGs 5-HTTLPR allele combination could be used to highlight those likely to be at higher risk for depressive symptoms in the context of high caregiving demand. Greater depressive symptoms in HF FCGs overall were predicted by worse sleep quality, greater burden, and worse family functioning with AAs having lower depressive symptoms. The implications of the omic data in terms of ethics, and use in special populations defined by age, gender and race/ethnicity should be considered. Interactions between genotype and caregiving demand may help identify caregivers at greater risk for depressive symptoms such that earlier diagnosis of depressive symptoms in the context of intense caregiving and more focused interventions can be provided.

---

**Title:**
Serotonin Transporter Gene Polymorphism and Family Caregiver Outcomes
Symposium

**Keywords:**
depressive symptoms, family caregiver and omics

**References:**


Sharpley CF, Palanisamy SK, Glyde NS, Dillingham PW, Agnew LL. An update on the interaction between the serotonin transporter promoter variant (5-HTTLPR), stress and depression, plus an exploration of non-confirming findings. *Behavioural brain research.* Oct 15 2014;273:89-105


**Abstract Summary:**
This abstract is part of a larger symposium on Omics and the Nursing Process. The serotonin transporter gene polymorphism and relationship with family caregivers of persons with chronic conditions will be presented with implications for research and family caregivers interventions.

**Content Outline:**

**Background**
Psychological and physical health impact of family caregiving for persons with chronic conditions

Prevalence of depression and depressive symptoms in family caregivers

Possible antecedent factors of demographic, social support and family context, caregiving demands, and overall health factors are associated with depressive symptoms in family caregivers of persons with heart failure.

An interesting genetic factor to explore is the serotonin transporter-linked polymorphic region (5-HTTLPR) genotypes (XL/L, LL, L/S, S/S). Previous research in other populations suggests that any S allele genotype is associated with a predisposition towards depression.

Historical evidence and review of predictive or family caregiving studies examining the 5-HTTLPR and depressive symptoms

Data from longitudinal study of family caregivers of persons with heart failure will be presented as an exemplar of relationship of 5-HTTLPR with caregiving relationships.

Issues in study of 5-HTTLPR in special populations defined by age, gender and race/ethnicity.

Conclusions and implications for practice and future research. Greater understanding of associated factors with depressive symptoms might inform more precise, personalized, and effective interventions.

First Primary Presenting Author
Primary Presenting Author

Sandra Dunbar, PhD
Emory University Nell Hodgson Woodruff School of Nursing
Associate Dean for Academic Affairs and Professor
Atlanta GA
USA

Professional Experience: Dr. Sandra Dunbar is a nurse scientist who has been conducting nursing research related to caregivers of patients with heart failure and/or diabetes for nearly 30 years. Author Summary: Dr. Sandra Dunbar is the Charles Howard Candler Professor of Cardiovascular Nursing and Associate Dean for Academic Advancement at Emory University School of Nursing. She is a cardiovascular nurse researcher whose program of research focuses on self-management and psychosocial responses to serious cardiac illness and co-morbidity including diabetes. Her NIH funded studies of CV patient and family responses have led to the development and testing of interventions to improve physical and psychosocial outcomes.

Second Author

Rebecca A. Gary, PhD, RN, FAAN, FAHA
Emory University
Nell Hodgson Woodruff School of Nursing
Associate Professor
Atlanta GA
USA

Professional Experience: broad research objectives are to improve symptom severity and quality of life in patients with chronic cardiovascular disease. Specifically, she is interested in understanding the link between the physiological and psychological responses associated with worsening symptom severity and disease progression in heart failure patients. Her funded research has included biobehavioral interventions using exercise and cognitive behavioral therapy as strategies to improve physical function, physiological biomarkers, symptom severity and depressive symptoms in heart failure patients. Author Summary: Has spoken at national and international meetings in a variety of cardiovascular research, nursing and care topics. She was a key co-investigator in the study which is used as an exemplar in this abstract.

Third Secondary Presenting Author

Corresponding Secondary Presenting Author

Elizabeth Corwin, PhD, RN, FNP
Emory University Nell Hodgson Woodruff School of Nursing
School of Nursing
Associate Dean for Research and Professor
Atlanta GA
USA

Professional Experience: I am a PhD prepared Physiologist, a bachelor-prepared nurse, and a masters-prepared nurse practitioner. I have been conducting research on maternal health and nursing science for nearly 20 years. Author Summary: Elizabeth Corwin, PhD, RN, FAAN, is the Associate Dean for Research and Professor at the Nell Hodgson Woodruff School of Nursing at Emory University. She is a PhD-prepared Physiologist
and a family nurse practitioner. Dr. Corwin is leading pioneering, interdisciplinary research aimed at uncovering the biological mechanisms responsible for adverse outcomes including symptoms, with a focus on the contributions of exaggerated inflammation, chronic stress, the microbiome, and metabolomic pathways on patient and family outcomes.