

# Apolipoprotein E Genotype and Cognitive Function in Postmenopausal Women With Early-Stage Breast Cancer

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**B**reast cancer is the most prevalent form of cancer, excluding skin cancer, among women in the United States, with an estimated 232,340 new cases of invasive breast cancer and 64,640 new cases of carcinoma in situ diagnosed in 2013 (American Cancer Society, 2013). Fortunately, in the United States, the overall five-year relative survival rate for women with breast cancer, inclusive of all stages, is 89% (Howlader et al., 2011), making women with breast cancer the largest group of cancer survivors in the United States at 2.9 million women (American Cancer Society, 2013). However, survivorship comes with long-term and late effects related to cancer and/or cancer treatment for a large number of breast cancer survivors.

One of the most common and problematic phenomenon experienced by breast cancer survivors is adjuvant therapy-related cognitive decline (Bender et al., 2006; Downie, Mar Fan, Houédé-Tchen, Yi, & Tannock, 2006; Hurria et al., 2006; Jenkins et al., 2006; Mehnert et al., 2007; Schagen et al., 1999; Schilder et al., 2009; Shilling & Jenkins, 2007). A large body of evidence exists to objectively support these reported deficits (Falletti, Sanfilippo, Maruff, Weih, & Phillips, 2005). In addition, growing evidence suggests that women with breast cancer have poorer cognitive function compared to healthy women prior to the initiation of adjuvant therapy (Hermelink et al., 2007; Schilder et al., 2010; Wefel et al., 2004; Wefel, Saleeba, Buzdar, & Meyers, 2010). Even small changes in cognitive function can have a major impact on a survivor's quality of life, affecting relationships with family and friends, educational and career decisions, job performance, emotional state, the ability to make informed treatment decisions, and adherence to cancer therapy (Boykoff, Moieni, & Subramanian, 2009; Munir, Burrows, Yarker, Kalawsky, & Bains, 2010; Myers, 2012; Stille, Bender, Dunbar-Jacob, Sereika, & Ryan, 2011; Tchen et al., 2003; Von Ah, Habermann, Carpenter, & Schneider, 2013).

**Purpose/Objectives:** To examine the role of apolipoprotein E (APOE) genotype in the cognitive function of postmenopausal women with early-stage breast cancer prior to initiation of adjuvant therapy and over time with treatment.

**Design:** Longitudinal, genetic association study.

**Setting:** Urban university cancer center.

**Sample:** Three cohorts of postmenopausal women: 37 women with breast cancer receiving chemotherapy and anastrozole, 41 women with breast cancer receiving anastrozole alone, and 50 healthy women.

**Methods:** Cognitive function was evaluated three times during a 12-month period using a comprehensive neuropsychological test battery. Participants were genotyped and classified based on the presence or absence of at least one APOE  $\epsilon$ 4 allele. Multiple linear regression was used to determine if APOE genotype accounted for observed variability in cognitive function data.

**Main Research Variables:** APOE genotype, breast cancer treatment, and cognitive function.

**Findings:** Performance or changes in performance on tasks of executive function, attention, verbal learning and memory, and visual learning and memory were found to be influenced by APOE genotype and/or interactions between APOE genotype and study cohort.

**Conclusions:** The results indicate that cognitive function in postmenopausal women with breast cancer is modified by APOE genotype and the combination of APOE genotype and treatment.

**Implications for Nursing:** APOE genotype, along with other biomarkers, may be used in the future to assist nurses in identifying women with breast cancer most at risk for cognitive decline.

**Key Words:** breast neoplasms; cognition; genes; biologic markers

*ONF*, 41(6), E313–E325. doi: 10.1188/14.ONFE313-E325

However, discrepancies remain in the percentage of women with breast cancer exhibiting cognitive changes, the severity of the change, and the specific cognitive