



## Effects of adjuvant treatment on cognitive function in women with early breast cancer

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### A B S T R A C T

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**Purpose:** Whether adjuvant therapy impairs cognitive function in women with breast cancer (BC) is unclear. We determined the effects of adjuvant therapy on cognitive function in women with early BC. **Methods:** We consecutively and prospectively enrolled women aged 40–69 years who had a positive radiographic finding from the mammography screening program at Stockholm South General Hospital. All women completed the Headminder Web-based neuropsychological battery Cognitive Stability Index (CSI) for response speed, processing speed, memory, and attention before diagnosis (T1), after surgery and before adjuvant treatment (T2), 6 months after start of adjuvant treatment (T3), and after another 3 months of follow-up (T4). Women with BC were divided into those receiving chemotherapy, hormone therapy, or no adjuvant medical therapy. Women without a diagnosis of BC served as healthy controls. **Results:** Of the 146 women enrolled, 77 had BC of whom 18 received chemotherapy; 45, hormone therapy, and 14, no adjuvant medical therapy; 69 were healthy controls. Memory scores for women with BC were significantly lower than those for controls over time, even after controlling for age and education. Memory and response speed scores were lower after chemotherapy than before ( $P < 0.01$  for both). Processing speed and attention improved significantly over time in all groups, a result consistent with a practice effect. **Conclusion:** Our results indicate subtle changes related to time course and treatment. Especially, that chemotherapy may impair memory and response speed in women with BC, consistent with those reported by BC survivors after adjuvant medical treatment.

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### Introduction

Systemic therapy has reportedly impaired cognition in women treated for early breast cancer (BC) (Anderson-Hanley et al., 2003; Vardy et al., 2007; Vardy et al., 2008). In addition, women with early BC receiving adjuvant chemotherapy often report difficulties with cognitive function, including memory, attention, and executive function (Shilling and Jenkins, 2007; Berglund et al., 1991). Cognitive function commonly includes a variety of skills, such as the ability to process information automatically (processing speed), the ability to react and decide automatically (response speed), attention, calculation, imagination, learning, memory and visuo-spatial abilities. Magnetic resonance imaging and positron

emission tomography have detected alterations mostly in the frontal-subcortical circuitry, which affects memory, attention, processing, and response speed (Vardy et al., 2008).

In a previous study, we reported that the diagnosis and subsequent surgery for BC may not impair cognitive function (Hedayati et al., 2011). Other have reported that 20% of BC patients have lower cognitive function than expected before adjuvant treatment (Correa and Ahles, 2008; Cimprich et al., 2009), after controlling for age and education level (Wefel et al., 2004a,b; Ahles et al., 2008). Early cross-sectional studies found that the prevalence of impaired cognitive function was 28–75% among women with BC treated with chemotherapy (Ahles et al., 2002; Wieneke and Dienst, 1995; Schagen et al., 1999; Downie et al., 2006). Prospective studies have also reported that about 30% of women experience some cognitive decline after chemotherapy (Collins et al., 2009a; Hermelink et al., 2007; Hurria et al., 2006).

Lately, the effect of adjuvant hormone therapy on cognition has been studied. Hormone therapy for BC consists of selective estrogen

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receptor modulators (SERMs) and aromatase inhibitors (AIs). The neuroprotective mechanisms of SERMs on brain function have been assessed in two studies, one using magnetic resonance imaging and the other positron emission tomography, and the results have been conflicting (Eberling et al., 2004; Ernst et al., 2002). The primary and most cited cross-sectional study found no cognitive differences between former and non-users of SERMs, but current users had lower mean scores on narrative writing tasks (Paganini-Hill and Clark, 2000). Further cross-sectional studies comparing SERMs users to AI users or to healthy controls found that both hormone therapies impaired verbal memory and processing speed (Jenkins et al., 2004; Schilder et al., 2009; Bender et al., 2007).

Prospective studies on the effect of hormone therapy on cognition have been few and contradictory (Jenkins et al., 2008; Hermelink et al., 2008; Collins et al., 2009b). For example, neuropsychological performance was worse in women receiving both chemotherapy and hormone therapy than in women treated with chemotherapy alone (Collins et al., 2009a; Bender et al., 2006;

Castellon and Pa Ganz, 2004). The literature emphasizes the need for well-designed, prospective studies that control for age, education, depression, anxiety, anemia, pain, and fatigue (Minisini et al., 2004; Anderson-Hanley et al., 2003; Vodermaier, 2009).

We conducted a prospective study to determine whether measures of cognitive function declined over time in women with early BC treated with surgery and adjuvant chemotherapy, adjuvant hormone therapy, or no adjuvant medical therapy and whether these measures differed from those of healthy women. We assessed cognitive function before a diagnosis of cancer was made and therefore before the start of adjuvant treatment. Our design is also unique in that our control group consisted of healthy women without BC but who had undergone the same stresses of diagnostic reassessment.

## Materials and methods

The ethics committee of the Karolinska Institute, in compliance with the 1964 World Medical Association's Declaration of Helsinki

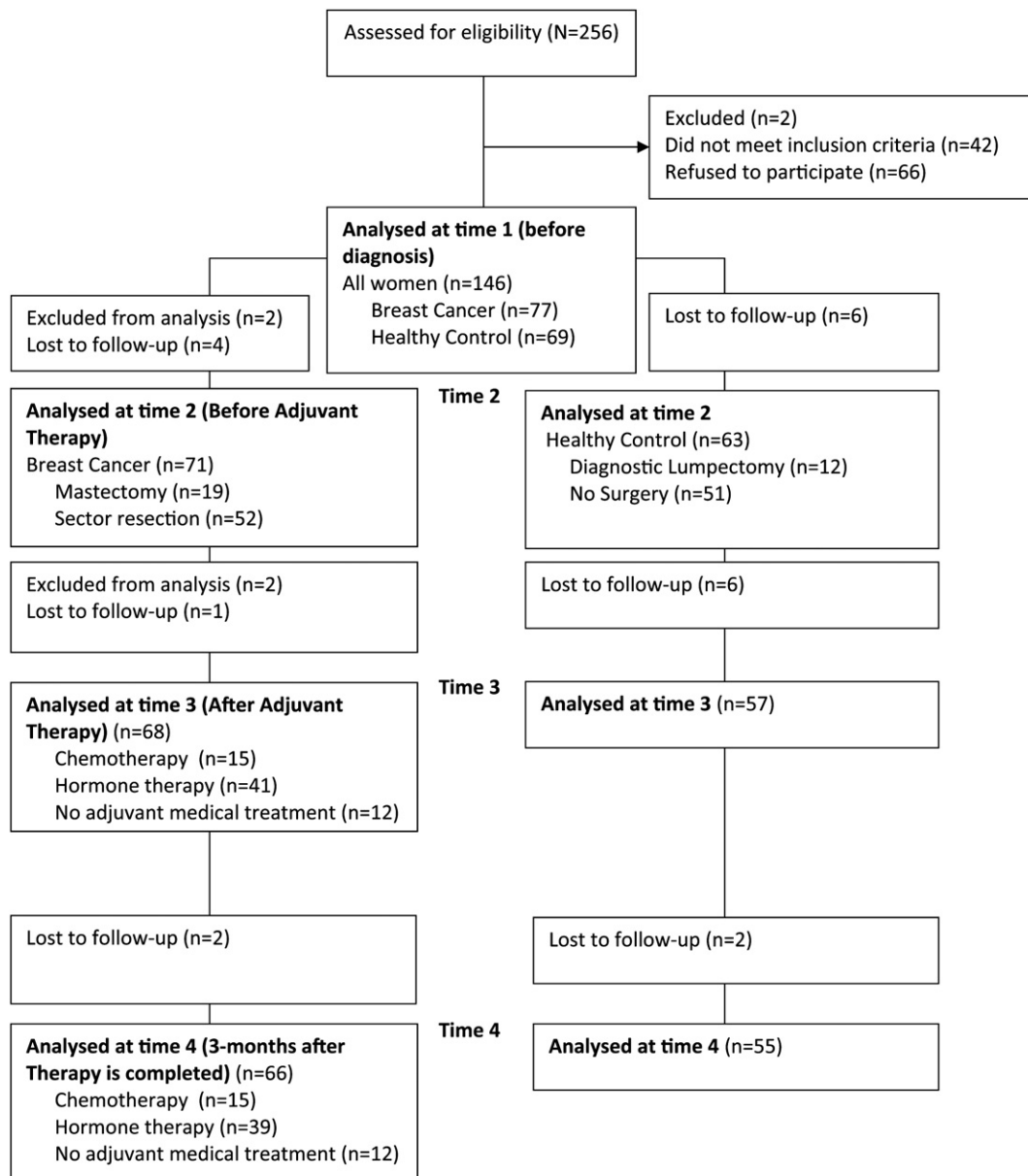


Fig. 1. Disposition of 146 women in a test of cognitive function after notification of a positive mammographic screening test, after the diagnosis was ruled out or after sector resection or mastectomy, after 6 months or after adjuvant treatment and again after additional 3 months follow-up.

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