**Proposal for Approach to Systematic Review of the Effects of Breast Cancer**

**Chemotherapy on Long-term Cognitive Function**

A large portion of the current literature on cognitive impairment evaluations of chemotherapy for breast cancer consists of cross-sectional studies. In these studies chemotherapy has a small to moderate impact on cognition in the short run, when women who are undergoing or have just completed chemotherapy are compared at one point in time to women who have not had chemotherapy. This effect is not significant in some studies; its magnitude depends on study design; and domains affected varies by study: Jim - verbal ability and visuospatial ability; Ono – attention, executive function, motor function, processing speed and short-term memory.

Short-term prospective studies (mostly few weeks – 6 months) show improvement over time in chemotherapy group compared with baseline measures. Studies vary in selection of the comparison group and include women with breast cancer not treated with chemotherapy, women treated with hormonal therapy, and a healthy comparison group (without breast cancer).

Given the current state of published articles and meta-analyses investigating cognitive function following adjuvant chemotherapy in early stage breast cancer setting, we propose the following criteria for our systematic review:

1. Limit inclusion to longitudinal studies with >= 1 year follow-up that either:
   1. Investigate change from baseline chemo group alone, or
   2. Investigate change from baseline and compare the change to a control group: with may be either women with breast cancer but no chemo or women without breast cancer
2. Examine the moderating effects of these variables: type of comparison group ( no breast cancer vs breast cancer without chemotherapy vs endocrine tx), age, IQ, education, and measures of mood/anxiety/depression/fatigue
3. Consider outcomes by domain to allow comparisons of effect sizes by study and to report summary mean effect size.
4. Examine the within and across study effect sizes of individual tests and identify commonly used individual measures with larger effect sizes
5. Examine whether common individual measures based on neuropsychological tests might represent cognitive domains, which may enable the recommended use of specific tests in future studies to reduce the redundant testing?

**Questions to Ben:**

Wefel, Fan, Tager and Ahles have reported standardized scores. Tager, Jenkins and Ahles have not reported individual test scores for each time point. Tager reported the standardized baseline (T0) scores and F test (DF, F value and p values) results for time and domain scores – but no actual scores for T1 and T2.

Jenkins reported regression (R^2, R^2\_adj, F, p, factors, beta, t, p) on baseline (Table 3) and percentage of each group showing reliable change for each test at T2 and T3 (Table 4) - but no baseline scores.

Ahles reported domain scores adjusted for age, education and baseline score (Table 3) – no individual (single) test scores.

1. We are writing to Tager, Jenkins, and Ahles to request the unadjusted mean scores from each time point with the hope getting additional data. In the event of we do not receive the requested data, is it possible to use any of these studies’ reported data obtain comparable effect sizes for changes over time in either domains or individual tests?

The Fan study (largest study) only included only a comparison group of women without breast cancer; all the other (smaller) included studies used either a comparison group with breast cancer not receiving chemotherapy, or the no-chemo group with an additional, no-breast cancer comparison group.

1. Can we consider pooling the difference of differences of studies using differently defined comparison groups?

1. With whatever studies we are ultimately able to include(based on questions 1 and 2), will we have sufficient sample size to investigate the moderating effects ofthese variables: type of comparison group (healthy vs women with breast cancer not receiving chemotherapy), presence or absence of additional endocrine treatment, age, IQ, education, mood/anxiety/depression/fatigue