

## Draft Key Questions 4/28/14

### Systematic Review of Long-Term Adverse Effects of Adjuvant Chemotherapy for Breast Cancer

**Scope:** What is the long-term adverse health and quality of life effects of the most commonly used breast cancer adjuvant chemotherapy regimens?

#### Key Questions to be Systematically Reviewed

In the target population of women with early stage breast cancer<sup>\*</sup>:

- 1) What is the effect of adjuvant therapy<sup>†</sup> on long-term, adverse health outcomes<sup>‡</sup> and how does it differ by age, race-ethnicity, and risk factors<sup>§</sup>?
- 2) What is the synergistic effect of the combination of multiple adjuvant therapy<sup>†</sup> treatment types on long-term adverse health outcomes<sup>‡</sup> and how does it differ by age and risk factors<sup>§</sup>?
- 3) What is the effect of adjuvant therapy<sup>†</sup> on patient quality of life and other patient-reported outcomes?

#### Contextual Question

1. Among women with left-sided breast cancer, what is the impact of radiation on long-term adverse health outcomes<sup>‡</sup>?

#### Research Approach

Category	Include	Exclude
Population	Women of all ages with early stage (I-III A) breast cancer with any receptor status	Men; women with advanced stage (IIIB-IV)
Intervention	Adjuvant chemotherapy regimens, used alone or in combination (anthracyclines [doxorubicin, epirubicin]; cyclophosphamide; taxanes; trastuzumab)	Outdated chemotherapy regimens (CMF)
Comparisons	Women with early stage breast cancer who did not receive adjuvant chemotherapy	<b>KQ 1-3:</b> Studies lacking comprehensively applied reference standard
Outcomes: Health	<b>KQ 1-2:</b> Chemotherapy-related long-term adverse health outcomes (cardiac toxicity; ovarian failure; secondary malignancies; neurotoxicity; cognitive dysfunction; depression?; lymphedema? osteoporosis) <b>KQ 3:</b> Quality of life; patient-reported outcomes	Outcomes not listed as included
Timing	Outcomes occurring or persisting beyond the first year of treatment	No follow-up; short-term follow-up (less than one year)
Setting	Developed Countries	Non-developed countries
Study Design	Randomized controlled trials (RCTs), cohort studies with concurrent control groups, other cohort studies, case series for novel toxicities,	Case reports

**Comment [n1]:** Typically a surgery-related outcome. It was brought up in discussion. I am inclined to exclude as we have so much on our plate.  
Others thoughts? -JM

<sup>\*</sup> Excludes men and women with advanced stage (IIIB-IV) breast cancer

<sup>†</sup> Adjuvant hormonal therapy regimens include anthracyclines (doxorubicin, epirubicin), cyclophosphamides, taxanes, and trastuzumab

<sup>‡</sup> Long term adverse health outcomes include cardiac toxicity, ovarian failure, secondary malignancies, neurotoxicity, cognitive dysfunction and osteoporosis

<sup>§</sup> Risk factors include: age, race/ethnicity, use of other medications especially Herceptin, hormone receptor status?, dose and side of radiation to chest, pre-existing chronic conditions: diabetes, depression, heart disease, dementia

<b>Language</b>	English-language abstracts (includes English-language abstracts of non-English papers) and papers	Non-English language papers
<b>Data Sources</b>	Pubmed, Embase, References of identified articles, B30 data, Early breast cancer clinical trialists group; Adjuvant breast cancer trial data registry (Cochrane)	Sources not listed as included
<b>Search Dates</b>	1990 - present	Pre-1990