**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[[1]](#footnote-1):

1. What is the effect of adjuvant therapy[[2]](#footnote-2) on long-term, adverse health outcomes[[3]](#footnote-3) and how does it differ by age, race-ethnicity, and risk factor[[4]](#footnote-4)?
2. What is the synergistic effect of the combination of multiple adjuvant therapy† treatment types on long-term adverse health outcomes‡ and how does it differ by age and risk factors§?
3. What is the effect of adjuvant therapy† 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‡?

**Research Approach**

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| **Category** | **Include** | **Exclude** |
| **Population** | Women of all ages with early stage (I-IIIA) 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used alone or in combination(anthracyclines [doxorubicin, epirubicin]; cyclophosphamide; taxanes; trastuzumab) | Outdated chemotherapy regimens (CMF) |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 | **KQ 1-3:** Studies lacking comprehensively applied reference standard |
| **Outcomes:**  **Health** | **KQ 1-2:** Chemotherapy-related long-term adverse health outcomes (cardiac toxicity; ovarian failure; secondary malignancies; neurotoxicity; cognitive dysfunction; depression?; lymphedema? osteoporosis)  **KQ 3**: 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 |
| **Language** | English-language abstracts (includes English-language abstracts of non-English papers) and papers | Non-English language papers |
| **Data Sources** | 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 |
| **Search Dates** | 1990 - present | Pre-1990 |

1. Excludes men and women with advanced stage (IIIB-IV) breast cancer [↑](#footnote-ref-1)
2. Adjuvant hormonal therapy regimens include anthracyclines (doxorubicin, epirubicin), cyclophosphamides, taxanes, and trastuzumab [↑](#footnote-ref-2)
3. Long term adverse health outcomes include cardiac toxicity, ovarian failure, secondary malignancies, neurotoxicity, cognitive dysfunction and osteoporosis [↑](#footnote-ref-3)
4. Risk factors include: age, race/ethnicity, use of other medications especially Herceptin, hormone receptor status?, dose and side of radiation to chest, pre-existing g chronic conditions: diabetes, depression, heart disease, dementia [↑](#footnote-ref-4)