Study Protocol Template

A study protocol is a requirement for any project requiring approval. This template is a suggested format that can be used if there has not been a protocol written for a study at this time.

Project Title

> *Example: Treatment of ductal carcinoma in situ of the breast in Queensland (Radiotherapy following breast conservation surgery)*

Investigators, contact details and participating institutions

> *Example: Dr John Brown, Cancer Services, 040219874, Princess Alexandra Hospital*

Background

Describe the significance and the objectives of the research/project.

> *Example:*
>
> *Ductal Carcinoma In-Situ (DCIS) is a non-invasive breast cancer with the potential to transform into an invasive cancer over time. DCIS diagnosis has become more common following the introduction of breast screening programs. 90% of DCIS patients are asymptomatic. Treatment of DCIS is recommended in order to prevent progression to invasive disease and typically consists of surgical excision (mastectomy or breast conservation surgery (BCS) with or without adjuvant radiotherapy. In some countries patients may also be treated with adjuvant hormone therapy to block or reduce oestrogen in the body.*
> *Adjuvant breast radiotherapy (RT) following BCS for DCIS has been shown in multiple phase 3 studies to reduce DCIS recurrence and invasive recurrence across all subgroups of patients. A Cochrane review showed ipsilateral recurrence at 5 years reduced from 15-20% to 5-9% and at 10 years was reduced from 24% to 12%. In those patients that recurred, 50% were recurrent DCIS and 50% were invasive disease.*
> *The natural history of DCIS is not well understood. There may be a subset of patients, for example low grade and ER positive DCIS, who have disease that is more indolent and may never progress to invasive disease. For these patients traditional treatment may be overtreatment. Previous studies have identified features that indicate a higher risk of local recurrence including age, size lesion, grade, presence of necrosis and pathological subtype, margin status and BCS without adjuvant radiation.*
> *Although there is evidence that all women benefit from adjuvant RT after BCS, radiation is associated with some risk of late effects including cardiac disease in left sided patients. If there is an identifiable population that can be managed with BCS alone and "watchful waiting" these patients may be spared potential late toxicity of RT. There is a need to identify the patients with low risk disease that may require less treatment and those with high risk who need adjuvant therapy. A better understanding of DCIS can only contribute to improving the future management of DCIS patients.*

Aims and or Hypothesis

Describe the specific aims, key research questions, and/or a clearly defined hypothesis (where appropriate).

> *Example:*
>
> *Aims:*
> - *To report characteristics of Queensland DCIS patients who received definitive BCS and the rate of adjuvant RT.*
> - *To report patterns of local recurrence in those patients treated with BCS and no RT.*
>
> *Secondary Aim:*
> - *To identify features associated with higher risk of local recurrence within this population.*

Research Methodology

Methods and techniques to be used – clearly identify the data sources and expected outcomes of the research. Describe the type of study (e.g. retrospective cohort study, case control study). The aims/objectives should reflect the datasets and variables requested. Please describe your cohort/study population, specifying any inclusion /exclusion criteria.

> *Example:*
> *This retrospective population based study of women who were diagnosed with DCIS was undertaken to examine the patterns of care of DCIS Queensland from the year 2003 to 2012. This part of the study is focusing specifically on DCIS patients who had definitive BCS with or without adjuvant radiotherapy. In addition, the study will examine the local recurrence patterns of patients in this cohort to see if omission of adjuvant therapy impacted on outcomes.*
> *Exclusions:*
> *Women treated with Mastectomy*
> *Prior diagnosis of invasive breast cancer in ipsilateral breast*
> *DCIS or invasive occurrence in opposite breast*
> *Definition of local recurrence:*
> *For the purpose of this project local recurrence has been defined as any subsequent in situ or invasive cancer of the same histological type in the ipsilateral breast more than six months after the initial diagnosis and treatment of DCIS.*
> *Limitations:*
> *RT utilisation in the earlier years may not have been recorded in electronic source systems. Due to this the observed differences in RT utilisation rates across demographic groups may be influenced by under recording. In addition, this may also result in the underestimation of the effects of radiotherapy of local recurrence.*

Example continued:

Data sources:
Data will be used from the Queensland Oncology Repository (QOR), a state wide cancer patient database that links cancer diagnosis data, deaths data and treatment data from public and private hospitals.
Radiotherapy treatment is imported electronically into QOR from most of the public and private radiotherapy centres in Queensland. Any gaps found in radiotherapy electronic data in QOR will be filled by manually reviewing individual patient records.
Sample Size:
3,039 women in total diagnosed with DCIS from 2003-2012. Women treated with mastectomy and who had an occurrence in opposite breast will be excluded from this study leaving 2,005 patients as the cohort for this study. The follow up period for this cohort is up to December 2013.

Statistical Analysis

Provide a statistical analysis plan outlining how the aims/objectives will be met, the statistical methods to be used, and who will be carrying out the analysis.

Example:

Univariate descriptive statistics will be examined to determine whether there are differences in the rates of radiotherapy and then the frequency of invasive recurrence by presence/absence of adjuvant RT, by age groups, clinical features of the DCIS diagnosis (size, grade, necrosis) and by surgical margins.

Multivariate Cox Regression (survival analysis) will be used to model association of RT treatment with cancer recurrence after adjusting for clinical and demographic features. This will allow inclusion of more recent DCIS diagnoses with censoring occurring for those who have limited follow up available.

Specific data elements required

List data elements required for the project

Example:
Data items required:
Age at diagnosis
SA2 of residence at diagnosis

References

References to support background, aims or hypothesis

Example:

1. AIHW 2010. Risk of invasive breast cancer in women diagnosed with ductal carcinoma in situ in Australia between 1995 and 2005. Cancer series 51. Cat. no. CAN 47. Canberra: AIHW. Viewed 23 October 2015
2. LA Habel, JR Daling, PA Newcomb, et al. Risk of recurrence after ductal carcinoma insitu of the breast. Cancer Epidemiol Biomarkers Prev 1998; 7:689-696.

Other Considerations

If there are any other important considerations that need to be captured

Example:

Return completed form to Cancer Alliance Queensland:	Need more information?
Email cancerdataQld@health.qld.gov.au	Contact the Cancer Control Information Manager
Or	P: 3176 4436
Submit on website	E: cancerdataQld@health.qld.gov.au
canceralllianceQld@health.qld.gov.au	W: canceralllianceQld@health.qld.gov.au