Author's response to reviews

Title: Comparison of breast cancer survival in two populations: Ardabil, Iran and British Columbia, Canada

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Author's response to reviews: see over
Reviewer # 1 (Dr. Terry Field)

Reviewer's report
Title: Comparison of breast cancer survival in two populations: Ardabil, Iran and British Columbia, Canada
Version: 1 Date: 28 October 2008
Reviewer: Terry Field

Reviewer's report:
Expanding the publication of information on breast cancer survival to include broader populations is of value both locally and internationally. This manuscript contributes to that information by comparing survival among women diagnosed with cancer in Ardabil, Iran to those in British Columbia, Canada. Several major issues in this paper lessen its value.

Major compulsory revisions:

1. No information is provided about breast cancer stage at diagnosis. This does not appear to be captured by the Ardabil registry. This missing information dramatically undermines the ability of the authors to both disentangle the potential causes of the low one-year survival rate in that area and present potential interventions for improvement. Stage at diagnosis is a very strong predictor of mortality, particularly over the short term. If women are diagnosed at stage IV, one year survival is low even in areas with available aggressive medical care. If diagnosis at late stage is responsible for the low survival rates in Ardabil, then recommendations for improvement may focus on screening. However, if few women diagnosed at earlier stages are surviving for one year, then improvements in treatment are a priority. Without information about stage, the discussion becomes moot. If staging is usually accomplished within the medical care facilities in the area but is not captured in the registry, additional work to locate and include that information would greatly improve the manuscript. Without this information, the conclusions and discussion section need major revisions to take into account this lack.

- We have addressed this comment on page 8. “Stage of the disease is an important determinant of survival in patients with breast cancer, but stage is unavailable in both the Ardabil and BC registries. Based on experience, we estimate that about 30% of Ardabil patients and 70% of BC patients are diagnosed at an early stage of the disease. We hypothesize that the improved survival observed in BC patients is partly because of this difference between Ardabil and BC regarding the distribution of disease stage.”

2. Insufficient information is provided about the two cancer registries. In order to interpret the results, the reader needs to understand how the cancer registries identify women with breast cancer, what information is collected on each case, and how it is collected. Have any validation studies been conducted to assess the extent to which the registries are complete and to identify any sub-groups of cancer patients who may be missed?
• Information regarding the Ardabil registry has been added in the Materials and Methods section on pages 5. “Ardabil province, located in the northwestern Iran, is a mountainous land with an area of nearly 18,000 square kilometres and a population of 1.1 million persons, 46% living in urban areas. The Ardabil Cancer Registry (ACR) was established in 2003 by the Digestive Diseases Research Center (DDRC) of Tehran University of Medical Sciences and Ardabil University of Medical Sciences (ARUMS), with collaboration of the International Agency for Research on Cancer (IARC). There are 4 kinds of information collected by the registry: patient demographics, tumor characteristics, treatment and patient outcome. Data are actively collected for newly-diagnosed cancer cases among permanent residents of Ardabil province. Patients who are diagnosed in other provinces are captured in the ACR through sharing of data among Iran's provinces. All rural residents are covered by a family physician network and have governmental medical insurance. Reporting cases of cancer to the ACR is obligatory for family physicians. Ardabil’s cancer patterns have been studied since the 1970s [8], its cancer registry is relatively complete, its population is largely homogeneous (98% being of Azeri ethnicity), and there is minimal immigration into this area [9].”

• A bit of additional information regarding data collection in Ardabil is given as part of the Discussion section on page 10. “In addition, the limitations of this study include the shortcomings of Ardabil cancer registry as it is newly established. However, the Ardabil cancer registry covers the entire province. Data are collected from hospitals, pathology laboratories, diagnostic radiology clinics, outpatient public and private clinics, death certificate files and an annual health census.”

• Information regarding the BC registry has been added on page 5-6. “In contrast, BC, the westernmost province in Canada, has a land area of nearly 945,000 square kilometres and a population of about 4 million persons with various ethnic backgrounds [10]. The provincial cancer registry was established in 1969, with cancer registration mandated by law. It has excellent standards of quality control, completeness of registration and follow-up. It contains personal and demographic information as well as information on diagnosis and death of all the cases of cancer diagnosed among BC residents (http://www.bccancer.bc.ca/HPI/CancerStatistics accessed May 8, 2009). For BC, there is universal health care and the majority of the population will have geographically accessible cancer treatment.”

3. There is also insufficient information provided in the manuscript about the two health care systems. How do patients access care? Are the major components of breast cancer care available locally? Are there out of pocket costs to patients for care? Are there wait lists for access?

• This has been added as part of the registry information in the Materials and Methods section on pages 5-6.
4. The discussion section requires extensive edits. First, it should focus on the ramifications of the results. The summary of differences in survival across ethnic groups is drastically incomplete and not directly relevant. The recommendations provided for improving breast cancer diagnosis and treatment are very broad, including every aspect of care. However, there is no evidence in the study to support any one of these recommendations. This is a classic situation in which the primary recommendation should probably be a cry for more assessments of the situation to support setting priorities for improvement. This could include specific delineation of the data required to accomplish this.

- We have revised the primary recommendation to the need to obtain information on staging, treatment and screening within a given population in order to set priorities for improvement in survival in this population. We have addressed this comment on page 8. “Stage of the disease is an important determinant of survival in patients with breast cancer, but stage is unavailable in both the Ardabil and BC registries. Based on experience, we estimate that about 30% of Ardabil patients and 70% of BC patients are diagnosed at an early stage of the disease. We hypothesize that the improved survival observed in BC patients is partly because of this difference between Ardabil and BC regarding the distribution of disease stage.”

Minor required revisions

5. With all survival information apparently based on all-cause mortality rather than breast cancer-specific mortality, it is important to take this into account in discussing age differences in one-year survival.

- Some sentences that address this problem have been added to the Discussion section on page 11. “The relatively young population is particularly important in our comparison to BC because pre-menopausal breast cancer patients often have more aggressive disease than other women.”

6. Survival has often been found to be lower for women diagnosed pre-menopause. The discussion of the association of age and survival should take this into account.

- Some sentences that address this problem have been added to the Discussion section on page 10. “In any population, it is difficult to know whether a patient’s death is due to their breast cancer. This issue is particularly relevant in a comparison of populations with very different healthcare systems. Our analysis concerns the overall mortality of breast cancer patients, although the causes of death and the veracity of reported causes might be substantially different in Ardabil and BC.”

**Level of interest:** An article of limited interest  
**Quality of written English:** Acceptable
**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**
I declare that I have no competing interests.

**Reviewer # 2 (Dr. Ahmedin Jemal)**

**Reviewer's report**

**Title:** Comparison of breast cancer survival in two populations: Ardabil, Iran and British Columbia, Canada

**Version:** 1  **Date:** 6 October 2008  **Reviewer:** Ahmedin Jemal

**Reviewer's report:**

**Major comment:-**
The authors report that the one-year breast cancer survival rate in Ardabil (Iran) is 16%. This estimate is too low to be true. Even five-year survival rate for breast cancer in the least developed countries such as Africa is higher than 30%. For example, according to a recent paper by Coleman et al 2008 (Cancer Survival in five continents: a worldwide population-based study), the five-year relative survival rate for breast cancer in Algeria was 38.8%.

- Information on survival status and date of death was rechecked directly by contacting the registered cases or their families. We corrected the data and describe the data collection process at the Ardabil registry in the Materials and Methods section on page 5. “The Ardabil Cancer Registry (ACR) was established in 2003 by the Digestive Diseases Research Center (DDRC) of Tehran University of Medical Sciences and Ardabil University of Medical Sciences (ARUMS), with collaboration of the International Agency for Research on Cancer (IARC). There are 4 kinds of information collected by the registry: patient demographics, tumor characteristics, treatment and patient outcome. Data are actively collected for newly-diagnosed cancer cases among permanent residents of Ardabil province. Patients who are diagnosed in other provinces are captured in the ACR through sharing of data among Iran’s provinces. All rural residents are covered by a family physician network and have governmental medical insurance. Reporting cases of cancer to the ACR is obligatory for family physicians. Ardabil’s cancer patterns have been studied since the 1970s [8], its cancer registry is relatively complete, its population is largely homogeneous (98% being of Azeri ethnicity), and there is minimal immigration into this area [9].”

- Age specific one-year survival rates and the relative survival rate were recalculated for women by age groups. We modified table 1 and revised the Results section on page 7. "Breast cancer patients in BC had greater one-year survival rates than patients in Ardabil overall and for each age group under 60. The median age of breast cancer diagnosis was 61 years (range 24-104 years) in BC and 44 years (range 21-86 years) in Ardabil. About 23% of BC patients and 64% of Ardabil patients were younger than age 50 at the time of diagnosis. The age-standardized one-year relative survival rates in BC was 0.99 (SE = 0.004) for adult women younger than age 50 years and 0.97 (SE = 0.012) for women age 50 and older. The age-standardized 1-year relative survival rate in Ardabil was
0.92 (SE = 0.020) for adult women younger than age 50 and 0.95 (SE = 0.037) for women age 50 and older.”

**Level of interest:** An article of limited interest

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**
I declare that I have no competing interests.