Breast cancer survival in Canada and the USA: meta-analytic evidence of a Canadian advantage in low-income areas

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Background This study tested the hypothesis that relatively poor Canadian women with breast cancer have a survival advantage over their counterparts in the USA.

Methods Seventy-eight independent retrospective cohort (incidence between 1984 and 2000, followed until 2006) outcomes were synthesized. Fixed effects meta-regression models compared women with breast cancer in low-income areas of Canada and the USA.

Results Low-income Canadian women were advantaged on survival [rate ratio (RR) = 1.14; 95% confidence interval (CI) 1.13–1.15] and their advantage was even larger among women <65 years of age who are not yet eligible for Medicare coverage in the USA (RR = 1.21, 95% CI 1.18–1.24). Canadian advantages were also larger for node positive breast cancer, which may present with greater clinical and managerial discretion (RR = 1.40, 95% CI 1.30–1.50), and smaller when Hawaii, the state providing the most Canadian-like access, was the US comparator (RR = 1.12, 95% CI 1.01–1.20).

Conclusions More inclusive health care insurance coverage in Canada vs the USA, particularly among each country’s relatively poor people, seems the most plausible explanation for such Canadian advantages. Provision of health care for all Americans would likely prevent countless early deaths, particularly among the relatively poor.

Keywords Breast cancer, socio-economic factors, place, survival, node positive breast cancer, meta-analysis, health insurance, single payer, Canada, USA

The CONCORD study’s worldwide population-based analysis estimated that the USA and Canada, respectively, rank number one and two at the top of the world’s breast cancer survival distribution, and that the overall difference between them may be fairly characterized as miniscule [5-year relative survival rate ratio (RR) = 1.02; 95% confidence interval (CI) 1.00–1.04]. The first observational study to specifically compare Canada with the USA on this sentinel health outcome also observed an extremely small breast cancer survival advantage among US women. However, neither of these studies accounted for socio-economic factors in any way. The first study to do so hypothesized and found an income-by-country interaction. Based on a health insurance theory, it observed a relatively large survival advantage among low-income women with breast cancer in a large Canadian metropolitan area (Toronto, Ontario) as compared with their US counterparts in Detroit.
Michigan (RR = 1.30, 95% CI 1.23–1.38). Its null findings were equally interesting. No between-country survival differences were observed among its middle- or high-income groups. It suggested that more equitable access to Canada’s single payer health care system was the most plausible explanation for its pattern of findings.

This field’s health insurance theory developed over time through key sub-cohort comparisons. For example, it was hypothesized that the observed Canadian survival advantage ought to be even larger among low-income women, <65 years of age, who are not yet eligible to participate in the USA’s Medicare program. This age-stratified hypothesis was affirmed yet eligible to participate in the USA’s Medicare program. It will also exhaustively explore clinical, contextual and methodological study variability.

Methods
Selection of studies
MEDLINE was searched in September of 2008 on the following key word scheme: breast cancer and survival and Canada and the USA. This search for published research literature was augmented with conceptually similar searches for unpublished research reports: Digital Dissertations, world wide web searches and personal contact with key informants within this field’s scholarly network. Additionally, studies had to meet these inclusion criteria: (i) their within- and between-country comparisons integrated socio-economic factors and (ii) their analytic models minimally adjusted for within- and between-country age differences. Eight studies were so selected.3–5,8–12 Socio-economic status (SES)–breast cancer survival associations that were observed among different age cohorts in different places were treated as independent hypotheses. A total of 78 such independent study outcomes (within- or between-country comparisons) were included in this meta-analysis and summarized within seven hypothetical domains, each tested among all adult and younger adult (<65 years of age) samples. These included breast cancer survival in middle-income areas compared with high-income areas within-Canada and within the USA, low-income areas compared with high-income areas within-Canada and within the USA, and the survival of Canadian women with breast cancer compared with their US counterparts, each within relatively high- middle- or low-income areas.

Meta-analysis
This meta-analysis adhered closely to the analytic plan seminally outlined by Greenland.13 Age-adjusted survival rate ratios (RRs) estimated primary study relative risks. Fixed and random effects meta-analytic models were initially explored for pooling RRs, and their pooled estimates typically differed by only a few hundredths of a decimal place. Heterogeneity of RR distributions within the 14 domains of meta-analytic interest was also explored. Most of them (11 of 14) were not significantly heterogeneous. Therefore, this meta-analysis used fixed effects models that assume substantial homogeneity of effects within specific categories of interest. Natural logarithms of study RRs were weighted by their inverse variances, computed from standard errors (1/SE²) so that larger, more precise studies weighed more. Standard errors were estimated from study statistics, generally from reported 95% CIs. Such precision-weighted effects were then pooled within the 14 domains of interest using weighted regression models. Pooled RRs within 95% CIs were calculated from regression statistics, as were tests of heterogeneity within pooled groups (χ²) and comparisons between groups (z).13,15 If significant heterogeneity was observed (P < 0.05), its possible sources—contextual, clinical and methodological—were examined through subgroup analyses. Certain subgroups were determined a priori. That is, at least one of the primary studies suggested their significance and direction. For example, SES–survival associations may be larger in province-wide analyses than in more specific places, and Canadian–US survival differences in low-income areas may be larger for node positive breast cancer, but smaller when the US context is Hawaiian or when area median annual household income is used, rather than low-income or poverty measures of SES. The potential moderating affects of other study characteristics were explored: incident cohort dates, urban or rural, racial/ethnic sample composition, city size, survival measurement (observed all-cause or cancer-specific), SES quantiles (tertiles, quintiles or deciles) and length of follow-up. Study characteristics were abstracted independently from full primary study manuscripts by two coders. After discussion and resolution of non-systematic discrepancies, their agreement was 100%. 
Results

Sample description

All of the eight included studies were large, cancer registry-based, retrospective cohorts (ranging from 1789 to 74,949 participants, median = 7888; Table 1). The aggregate population-based meta-analytic sample was 130,083 women with invasive breast cancer that was diagnosed, for the most part, in the mid-1980s to the early 1990s and followed until the mid- to late-1990s. One cohort of women with breast cancer was diagnosed between 1998 and 2000 and followed until 2006. All of the cohorts were followed for 5 years, except for one that was variably followed it seems for 2–5 years. Five of the studies restricted their samples to large metropolitan areas. In each of these, Toronto, Ontario was compared with various US cities: Detroit (three studies), Honolulu, Hawaii and an aggregation of San Francisco, California–Seattle, Washington–Hartford, Connecticut in another. One study focused on smaller urban areas (Winnipeg, Manitoba and Des Moines, Iowa) and two studies compared the province of Ontario with the state of California or the USA as a whole. The provincial state study purposively sampled diverse places (large to small urban and rural places) while the provincial national study included the population of women with breast cancer in Ontario and a Surveillance, Epidemiology and End Results (SEER) program-based US sample. Such contextual variability represents meta-analytic opportunities to better understand Canadian–US differences in breast cancer care.

All of the eight studies were ecological with respect to SES measurement. Most of the income measures were based on census tracts (CTs). One used enumeration areas (somewhat smaller urban populations than CTs) and two used census subdivisions (somewhat larger rural populations than CTs). Seven studies used measures of low-income (Canada) and poverty (USA) prevalence and two used measures of median household income (one study used both). All of the studies accounted for age distribution differences within- and between-countries, but only one accounted for case-mix differences on the stage of disease at the time of diagnosis. Finally, all of the studies’ outcomes were of observed survival (four all-cause and four cancer-specific). Again, such methodological variability presents meta-analytic opportunities to better understand Canadian–US differences in breast cancer care and outcomes.

Pooled SES–breast cancer survival associations

Within-country SES–survival gradients

SES was not strongly related to breast cancer survival in most of the Canadian contexts studied. Three of the four pooled within-Canada RRs displayed in Table 2 were null. Even studies that compared women with breast cancer in the lowest-income quantiles, observed very little overall survival disadvantage among them compared with those in the highest-income areas (RR = 0.94, 95% CI 0.93–0.95). This distribution was significantly heterogeneous though. As expected, income–survival associations were larger in province-wide analyses (two outcomes) than in specific urban or rural places (seven outcomes), respectively (RR = 0.80, 95% CI 0.78–0.82) and (RR = 0.99, 95% CI 0.98–1.00). The specific places were largely represented by greater metropolitan Toronto, but one small city (Windsor, Ontario) and a rural Ontario sample were also represented. The affect of income on breast cancer survival seems not to be homogeneously experienced across Ontario’s diverse places. Clearly in some places such as Toronto during the mid-1980s to the mid-1990s, there seems to have been no such relationship, but in other places, not specifically identified yet, a modest relationship must have existed.

On the other hand, SES did seem to be consistently and strongly related to breast cancer survival across all of the US contexts studied. All of the four pooled within-US RRs displayed in Table 2 were notable. Moreover, among all adult and younger adult US samples, meta-analytic trends, suggestive of a causal income–survival relationship, were observed. That is, survival among women with breast cancer in middle-income areas was lower than that observed among their counterparts in the highest-income areas, and survival among such women in the lowest-income areas was incrementally lower than that observed in middle-income areas. In terms of practical policy or public health importance, studies that compared women with breast cancer in the USA’s lowest-income areas with those in its highest-income areas, observed a very large survival disadvantage among relatively low-income women (RR = 0.73, 95% CI 0.72–0.74). Overall, their risk of dying, most typically within 5 years of being diagnosed, was nearly 30% greater than the risk experienced by relatively high-income women. Given the prevalence of breast cancer over the life course of women in the USA, this could represent a huge additional population-level risk among poor women.

Between-country hypothesis tests

Respective, null and trivial Canadian–US breast cancer survival differences were observed in the highest- and middle-income areas. But as hypothesized, in the lowest-income areas studies, Canadian women were advantaged (RR = 1.14, 95% CI 1.13–1.15), and this advantage was even larger among younger women, not yet eligible for Medicare in the USA (RR = 1.21, 95% CI 1.18–1.24). Both of these effect distributions were more heterogeneous than would be expected due to sampling variability alone and both of their pooled effects were moderated as expected by stage of disease and place (Table 3). Canadian–US survival differences in low-income
<table>
<thead>
<tr>
<th>Reference</th>
<th>Sampling frame</th>
<th>Cohort incidence years</th>
<th>Followed until</th>
<th>Aggregate sample</th>
<th>Socio-economic measure</th>
<th>Groups compared</th>
<th>Survival Measure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gorey et al. 2000</td>
<td>Toronto vs Hololulu</td>
<td>1986–1990</td>
<td>1996</td>
<td>7590</td>
<td>CT</td>
<td>Deciles</td>
<td>5-year All-cause</td>
</tr>
<tr>
<td>Gorey et al. 2003</td>
<td>Winnipeg vs Des Moines</td>
<td>1984–1992</td>
<td>1998</td>
<td>3928</td>
<td>CT</td>
<td>Quintiles</td>
<td>5-year All-cause</td>
</tr>
<tr>
<td>Boyd et al. 1999</td>
<td>Ontario vs USA&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1987–1992</td>
<td>1995</td>
<td>74,949&lt;sup&gt;c&lt;/sup&gt;</td>
<td>CT, EA and CSD</td>
<td>Mdn Income</td>
<td>2- to 5-year Cancer-specific</td>
</tr>
<tr>
<td>Gorey et al. 1998</td>
<td>Toronto vs Detroit</td>
<td>1986–1988</td>
<td>1994</td>
<td>1789</td>
<td>CT</td>
<td>Quintiles</td>
<td>5-year Cancer-specific</td>
</tr>
<tr>
<td>Gorey et al. 2009</td>
<td>Ontario&lt;sup&gt;b&lt;/sup&gt; vs California&lt;sup&gt;b&lt;/sup&gt;</td>
<td>1998–2000</td>
<td>2006</td>
<td>1923</td>
<td>CT and CSD</td>
<td>Mdn Income</td>
<td>5-year All-cause</td>
</tr>
<tr>
<td>Zhang-Salomons et al., 2006</td>
<td>Toronto vs Detroit</td>
<td>1988–1993</td>
<td>1999</td>
<td>21,970</td>
<td>CT</td>
<td>Quintiles</td>
<td>5-year Cancer-specific</td>
</tr>
</tbody>
</table>

Note: CT, census tract; EA, enumeration area; CSD, census subdivision; Mdn, median. All adult samples were ≥20–25 years of age. Three studies additionally analysed younger/older groups (<65/65+).<sup>4,5,11</sup> One study analysed staged groups (node negative/positive breast cancer).<sup>11</sup> <sup>a</sup>SEER program based.<sup>b</sup>Respectively, sampled large metropolitan areas (greater metropolitan Toronto and the San Francisco Bay area), smaller cities (Windsor and Modesto) and rural places in both Ontario and California.<sup>c</sup>Sample not reported. Estimated by secondary analysis.<sup>d</sup>Most extreme comparison used in each study.
areas were larger for node positive breast cancer, and they were smaller when the state studied was Hawaii. The observed relative US disadvantage seemed particularly large among younger women, not yet eligible for Medicare, with node positive breast cancer (RR = 1.40, 95% CI 1.30–1.50). Low-income patients in the USA may be much more disadvantaged than their Canadian counterparts at the hands of the greater clinical and managerial discretion (surgical and adjuvant innovations of varying costs and evidentiary supports) that has attended the contemporary treatment of node positive breast cancer. After age, disease stage and place were accounted for, no other contextual or study methodological characteristic could further explain study outcome variability.

**Discussion**

This study found that women with breast cancer who live in low-income areas of the USA were
disadvantaged on 5-year survival compared with their Canadian counterparts. Moreover, US women <65 years of age who are not yet Medicare eligible were even more disadvantaged. US breast cancer survival disadvantages were also larger for node positive breast cancer and in states where the prevalence of the uninsured was relatively higher. Along with the consistent and relatively large direct income–survival gradients observed among US samples, all of the between-country meta-analytic findings were consistent with the health insurance theory that is at the center of this field’s inquiry. Moreover, its between-country ecological findings have been convergently validated by recent within-USA studies that have consistently observed very strong relationships between various under- and uninsured statuses, measured at the individual level, and relatively later stage at breast cancer diagnosis, lack of treatment access and early death.13–16 This study’s findings were also consistent with a recent, but as of yet unpublished, California–Ontario study that found that low-income Canadian women with breast cancer gained greater access to adjuvant radiation therapy, and contrary to common wisdom, experienced treatment delays that were no different than those of their US counterparts. Canada’s single payer health care system seems to provide much more equitable breast cancer care than does the USA’s multiple payer system. The Canadian system’s most pronounced evidence-based advantage is clearly among the relatively poor who typically experience much better breast cancer outcomes in Canada than in the USA.

**Lack of health insurance vs alternative explanations**

A number of possible alternative explanations have been advanced by opposing theorists: (i) there is a wider economic divide between the relatively rich and poor in the USA; (ii) there are greater disadvantages associated with being a member of a racial/ethnic minority group in the USA; (iii) Canadians are advantaged in lifestyle and life expectancy; and (iv) Canadian women may merely be diagnosed earlier, any observed breast cancer care and outcome advantages only being apparent, the result of lead time bias, rather than of any systemic Canadian health care advantage.3 This meta-analysis’ systematic replications across diverse contexts and methods provided robust rejoinders to essentially rule out such alternative explanations. Canadian breast cancer survival advantages were observed across diverse Canada–USA comparisons, including those in which the income divide was demonstrably wider in the Canadian sample (Winnipeg, Manitoba vs Des Moines, Iowa). The Canadian advantage was consistently observed across racially/ethnically diverse US samples, including comparisons with samples prevalently represented by African American (Detroit), Asian American (San Francisco) and Hispanic (Modesto, California) women. This meta-analysis could not adjust for this factor as Canadian cancer registries do not code race/ethnicity. A number of the reviewed studies, however, did replicate key findings with the following conservative low-income area comparison: non-Hispanic white women in the USA vs the entire diverse sample of Canadian women.3,4 The age-adjusted, all-cause Canadian survival advantage was validated with cancer-specific survival analyses that accounted for competing causes of death. Finally, stage-adjusted analyses effectively ruled out lead time bias as a potent alternative explanation. In fact, the even larger Canadian survival advantage observed among low-income women with node positive breast cancer, a presentation that tends to maximize clinical and managerial discretion, only served to further indict the US health care system.

This meta-analysis could conceivably be limited by its combining all-cause and breast cancer-specific

### Table 3

<table>
<thead>
<tr>
<th>Stage at diagnosis</th>
<th>Unstaged</th>
<th>Node positive US places</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Hawaii</td>
<td>Other</td>
</tr>
<tr>
<td>Adult samples: ≥25 years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study outcomes</td>
<td>1</td>
<td>9</td>
</tr>
<tr>
<td>Total participants</td>
<td>193</td>
<td>30,014</td>
</tr>
<tr>
<td>RR (95% CI)</td>
<td>1.22 (1.02,1.46)</td>
<td>1.13 (1.12,1.14)</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>7</td>
</tr>
<tr>
<td>Younger adult samples: &lt;65 years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study outcomes</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Total participants</td>
<td>183</td>
<td>2,525</td>
</tr>
<tr>
<td>RR (95% CI)</td>
<td>1.40 (1.30,1.50)</td>
<td>1.18 (1.15,1.22)</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>1,470</td>
<td>10,555</td>
</tr>
<tr>
<td></td>
<td>1.12 (1.01,1.20)</td>
<td>1.24 (1.20,1.29)</td>
</tr>
</tbody>
</table>

Notes. Each paired comparison within age categories—node positive vs unstaged or Canada–USA comparisons that used Hawaiian vs other US samples—was significantly different (z), P < 0.05. Each paired comparison between age categories (e.g. node positive breast cancer among women ≥25 years of age vs node positive breast cancer among women <65 years of age) was significantly different (z), P < 0.05.
study outcomes. For the following reasons it probably was not. First, all-cause vs cancer-specific survival outcomes did not moderate this review’s within- or between-country main effects. Secondly, though length of survival is highly accurate in US cancer registries, the underlying cause of death is not. Therefore, this review’s systematic replication of cancer-specific with all-cause findings served to bolster confidence in review inferences related to overall population cancer burdens. Next, cancer is the underlying cause of death among the vast majority of women with cancer, and the underlying cause of death among the vast majority of overall population cancer burdens. Next, cancer is the underlying cause of death among the vast majority of women with cancer, and the underlying cause of death among the vast majority of overall population cancer burdens. Therefore, this review’s systematic replication of cancer-specific with all-cause findings served to bolster confidence in review inferences related to overall population cancer burdens. Next, cancer is the underlying cause of death among the vast majority of women with cancer, and the underlying cause of death among the vast majority of overall population cancer burdens. Therefore, this review’s systematic replication of cancer-specific with all-cause findings served to bolster confidence in review inferences related to overall population cancer burdens.

Future research needs

Not surprisingly, as no US cancer registry routinely collects socio-economic data, all of the studies included in this meta-analytic review were ecological with respect to the measurement of SES. The construct and predictive validities of the most prevalent low-income, typically CT-based measures have been well established in US contexts. However, even the most extremely low-income areas represented among the US samples included in this review were only in the range of 20–25% poor. Such neighbourhoods were substantially less impoverished than the extremely vulnerable, concentrated poverty neighbourhoods where >40% of the households were poor and were the focus of Jargowsky’s validation. Such extremely poor neighbourhoods have not been specifically studied in this field. Future study in these most vulnerable of USA neighbourhoods would be of great human and scientific interest and policy importance. This field has used two conceptual measures of SES, both ecological that principally describe CTs: the prevalence of low-income households in each CT and CT median household income. In Canadian contexts, however, the relative predictive validity of these two SES measures has been debated. It is important to note that such measurement variability did not confound this review’s central hypothesis related to advantaged Canadian survival in low-income areas. It relates though to the interpretation of this review’s within-Canada descriptive findings. Consistent with a recent study of median neighborhood income and endometrial cancer survival in Ontario, this review found that SES did not seem to be related to breast cancer survival in most of the Canadian contexts studied. The few included province-wide analyses suggested that income–survival gradients probably do exist somewhere in the province. These reviewed studies did not identify where such gradients might exist, but another recent median income-based analysis of breast cancer survival in Ontario suggested that they may, in fact, be restricted to certain small cities with less than adequate health care service endowments. This study, however, did not have sufficient meta-analytic power to adequately resolve these issues. Notwithstanding the typical worldwide robustness of the SES–cancer survival relationship to various definitions of SES, studies that advance our Canada-specific understandings of their construct and predictive validities are needed. They would further enable our ability to practically interpret this field’s equivocal SES–breast cancer survival gradients, from null to modest across Canada’s diverse places.

Conclusion

This study found consistent evidence that women with breast cancer who live in low-income areas of the USA are considerably less likely to survive for
5 years than are their Canadian counterparts, whereas, such women who, respectively, reside in the middle- and high-income areas of each country do not practically differ. It robustly affirmed a health insurance theory to explain this pattern. More inclusive health care insurance coverage in Canada vs the USA, particularly among each country’s relatively poor people, seems the most plausible explanation for such a Canadian advantage. Provision of health care for all Americans would likely prevent countless early deaths from breast cancer and other common diseases, particularly among the poor. As it sentinel’s caution against policies that would further privatize and thus add payer tiers to the Canadian health care system, this study suggests that US policy makers probably have much to learn from their counterparts to the north.

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Conflict of interest: None declared.

KEY MESSAGES
- The association of neighbourhood-level SES with breast cancer survival is much stronger in the USA than it is in Canada.
- Low-income Canadian women with breast cancer are more likely to survive for 5 years after their diagnosis than are similarly poor women with breast cancer in the USA.
- Younger low-income Canadian women with breast cancer are even more advantaged as compared with their US counterparts who are not yet eligible for Medicare.
- More inclusive health care insurance coverage in Canada seems the most plausible explanation for such consistently observed Canadian advantages.

References
Commentary: How does ‘insurance’ improve equity in health?

Barbara Starfield

In a meta-analysis of eight studies on overall mortality in women with breast cancer, Kevin Gorey makes a powerful case that better equity in survival in Canada than in the USA is a direct result of universal financial coverage for health services in the former country. The combined studies made it possible to examine age-adjusted survival rates in different age groups (under and over the age of 65 years), with different geographic units of analysis, in different types of place of residence, and with different specifications for socio-economic characteristics. All in all, 78 different comparisons were made in seven domains [two socio-economic status (SES) group comparisons in each of the two countries and one comparison in each of three socio-economic strata of the two countries]. The main findings were as follows.

1. SES is not strongly related to overall survival in almost all of the Canadian contexts.
2. SES is strongly and consistently related to poorer survival in all US contexts.
3. There is an SES gradient (‘dose response’) in the US contexts.
4. Survival is shorter in women of lower SES in the USA, suggesting either later diagnosis (more serious disease) or less adequate treatment.
5. The cross-country difference in survival is present in low-income areas, but not in high- or middle-income areas.

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