Author’s response to reviews

Title: Diffusion of good practices of care and decline of the association with case volume: the example of breast conserving surgery

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Author’s response to reviews: see over
Answers to referees’ comments and changes in the revised manuscript

REFEREE 1

Comment 1. The authors should justify their cutpoints for volume groups, or emphasize that these were selected prior to data analyses. Numerous authors suggest it is more appropriate to analyze groups with equal numbers of patients.

Answer 1. When examining the effect of hospital caseload on process or outcome measures, some authors choose groups with equal number of patients, others with equal number of hospitals (e.g. those on mortality after coronary artery bypass grafting, with huge unbalances in patient numbers between the low-volume and the high-volume groups). We selected a-priori cut-points at 50 and 100 surgeries in order to better compare our results with recent studies carried out in Northern Italy: an analysis from the Piedmont Region found a lower BCS rate in hospitals under 50 surgeries/year [Rosato 2004]; an economic evaluation in the optimal workload for centres treating breast cancer demonstrated that an increase from 50 to 100 new cancer patients treated/year would reduce average cost by almost 50% [Pagano 2003]. The justification for volume cutpoints is now briefly reported in Methods of the revised paper.

Comment 2. The authors may wish to comment on potential ecological factors (e.g., hospital closures) that may explain the drop in percentage of cases in low-volume hospitals over time.

Answer 2. Out of 41 hospitals with less than 50 patients treated in 2000, in the last year of observation (2004) eight were no more active (hospital or ward closure), seven increased their activity above 50 surgeries, 26 remained with a low caseload (and overall decreased their activity); an additional low-volume hospital was active 2004. This has been added in the revised paper (fifth paragraph of Results); moreover, the new Table 3 shows the number of hospitals by case volume in the years 2000 and 2004 as well as availability of radiation therapy services.

Comment 3. The authors may wish to clarify in the results that the final number of 18644 records represents 18644 unique patients. If this is so, the authors may also wish to comment on the low number of repeated admissions (i.e., 1391).

Answer 3. The final 18644 records represent unique patients (as clarified in the revised paper). The number of repeated admissions is 1391: 1042 were within 90 days from the first surgery, a quite low percentage overall (6%), but above 9% when considering only BCS. Furthermore, since by means of discharge codes we could not differentiate diagnostic procedures from excisional biopsies with curative intent, we included surgical biopsies only when not followed by other breast surgery. The latter choice allowed a correct estimate of patients with breast cancer surgery, but could have led to an underestimation of repeat surgery (however this was not the main focus of our paper).

Comment 4. There are five sentences in the conclusion. It may be best to stop the paper after the first two sentences.

Answer 4. We’ve made the change suggested by the referee.
**Major compulsory revision.**
There are several unintelligible sections of the test that would benefit from an English speaking reviewer editing before re-submission.

**Answer**
The manuscript has been edited by an English speaking reviewer.

**Minor Essential Revisions**

**Comment 1.** If possible the authors should attempt to include data that dates back to the date of the first publications of randomized trials of breast conservation therapy (BCT) in Italy.

**Answer 1.** Unfortunately, hospital discharge records with personal identifiers are available for the Veneto Region since 1999, which was the baseline year used to remove prevalent cases; therefore all analyses were restricted to the 2000-2004 period.

**Comment 2.** The authors should reference their rates of breast conservation to published estimate of the appropriate rate of breast conservation, and to other institutions BCT outside of Veneto.

**Answer 2.** To estimate an appropriate rate of breast conservation we should have detailed data on tumour stage in order to precisely identify early-stage breast tumours; only a limited information on tumour stage was obtainable from discharge records. However, population-based data on rates of breast conservation published in other Italian studies are now reported in Discussion (second paragraph) of the revised manuscript. In particular, hospital discharge data from the Piedmont Region (2000-2002) indicate a BCS rate as high as 67%, which was that observed in Veneto at the end of the study period.

**Comment 3.** Why was age treated as a categorical variable rather than a continuous variable.

**Answer 3.** Recent studies examining determinants of breast surgery usually introduce age as a categorical rather than a continuous variable in the regression models. The reason is probably that the relationship between age and breast conservation is not linear: BCS rates tend to increase in the age range where screening programs are active (in Italy 50-69 years), and decline only among women in the oldest age classes. We therefore chose to examine four categories: before the breast screening age (<50); women invited to the screening (two classes, 50-59 and 60-69); and women older than the screening age. An other statistical approach is to maintain the categorical variable and to add a continuous variable with values 0 for women aged 70 or less, and [age-70] for older women. We conducted a parallel analysis according to this latter model, without substantial changes in the risk estimates: the effect of the oldest age class results “shared” with the new variable, and the effect of hospital volume is a bit more pronounced (see Table below).

<table>
<thead>
<tr>
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<th>RR</th>
<th>CI</th>
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<tbody>
<tr>
<td>50-59 years</td>
<td>1.05</td>
<td>1.02-1.08</td>
</tr>
<tr>
<td>60-69 years</td>
<td>1.00</td>
<td>0.97-1.04</td>
</tr>
<tr>
<td>70+ years</td>
<td>0.78</td>
<td>0.74-0.83</td>
</tr>
<tr>
<td>Each additional year over 70</td>
<td>0.98</td>
<td>0.98-0.99</td>
</tr>
<tr>
<td>Non-localized disease</td>
<td>0.76</td>
<td>0.71-0.80</td>
</tr>
<tr>
<td>Charlson &gt;0</td>
<td>0.89</td>
<td>0.83-0.94</td>
</tr>
<tr>
<td>Medium volume hospitals</td>
<td>1.13</td>
<td>1.08-1.19</td>
</tr>
<tr>
<td>High volume hospitals</td>
<td>1.17</td>
<td>1.11-1.23</td>
</tr>
<tr>
<td>2001</td>
<td>1.06</td>
<td>1.02-1.11</td>
</tr>
<tr>
<td>2002</td>
<td>1.09</td>
<td>1.05-1.14</td>
</tr>
<tr>
<td>2003</td>
<td>1.14</td>
<td>1.09-1.19</td>
</tr>
<tr>
<td>2004</td>
<td>1.16</td>
<td>1.11-1.21</td>
</tr>
</tbody>
</table>
Comment 4. The authors should reference some of the literature on who patient preferences for BCT have been shown to vary by age, regions, distance of travel etc.

Answer 4. In Discussion (third paragraph) of the revised paper we added findings from other studies on determinants of breast conservation (socioeconomic status, detection of the malignancy through screening programs, travel distance from radiation treatment facilities); to this purpose we also included some additional references (23, 24, 25).

Comment 5. The authors should address whether there were any changes in hospital amalgamations, or affiliations over the years of study.

Answer 5. Through the study period we observed that some low-volume hospitals stopped or transferred activity; see also Answer 2 to referee 1. This now has been added in Results (fifth paragraph) of the revised paper, and is shown by the new Table 3.

Comment 6. A map, or table of the geographic distribution of the hospitals would be useful, particularly in their relationship to centres with radiotherapy capability. Or at least a statement, or grouping of hospitals with attachments to radiotherapy facilities.

Answer 6. A map with the distribution of hospitals performing breast cancer surgery with indication of radiotherapy facilities has been added in the revised paper (Figure 2). The Veneto Region is divided in seven Provinces, and each provincial capital has a radiotherapy capability: the rationale is to assure an adequate geographical distribution of such services. Overall, there were 9 radiotherapies: 5 were placed in high-volume and 4 in medium-volume hospitals. It was not feasible to concurrently analyze by regression models the effect of hospital volume and presence of radiotherapy due to collinearity (large hospitals tended to be those with a radiotherapy capability). Anyway, crude BCS rates (among high and medium volume hospitals combined) were only slightly higher in those with (65%) than in those without radiotherapy (62%). See also answer to referee 3.

Comment 7. More data on the case mix (age, disease severity and patient comorbidity) according to the hospital volumes.

Answer 7. Case mix unbalances (in particular with respect to age) in relation to hospital volumes are reported in Results (second paragraph) of the revised paper. Low-volume hospitals tend to treat older women (40% aged ≥70) with respect to medium (33%) and high volume hospitals (25%); notwithstanding, low-volume hospitals showed a marked increase in BCS rates through the study period.

Comment 8. Figure 1: it would be nice to know why some hospitals dropped to zero women treated in 2004.

Answer 8. See Answer 5.
REFEREE 3

**General comment.**
Could it be that the larger centers offered adjuvant radiation therapy or were close to centers that did, whereas the smaller centers which were perhaps more rural did not? As well, were larger hospitals teaching hospitals? *(see also Discretionary revisions)*
What about the use of immediate reconstruction?
What about the surgeons in these hospitals -- were they different in terms of specialization or fellowship training?

**Answer**
Nine centres offered radiation therapy (no low-volume, four medium-volume and five high-volume hospitals); this has been added in Results (and in the new Table 3) of the revised paper. A map showing the geographical distribution of centres with and without radiotherapy has been added (Figure 2), see also Answer 6 to referee 2.
Two of the high-volume hospitals were both teaching hospitals and offered radiation therapy (this is now cited in Results of the revised paper); overall among high-volume hospitals we observed only a slightly higher BCS rate in teaching (67%) with respect to non-teaching hospitals (64%).
In our database it is difficult to disentangle by means of regression models the effect of hospital-level variables such as case-volume, presence of a radiotherapy capability, and being an academic hospital (see sentence added in last paragraph of Discussion). Below is a Table showing crude BCS rates according to a classification which tries to combine the above characteristics; a large independent effect of case-volume seems to persist.

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>% BCS</th>
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<tbody>
<tr>
<td>Low volume</td>
<td>3249</td>
<td>51.6</td>
</tr>
<tr>
<td>Medium/high volume, no radiotherapy</td>
<td>6435</td>
<td>61.6</td>
</tr>
<tr>
<td>Medium/high volume, radiotherapy</td>
<td>3520</td>
<td>62.4</td>
</tr>
<tr>
<td>Two academic large-volume hospitals with radiotherapy</td>
<td>5440</td>
<td>66.7</td>
</tr>
</tbody>
</table>

Immediate reconstruction was rarely performed in the same hospitalization of breast cancer surgery: intervention codes 85.7 and 85.8x were mentioned only in 205 discharges (1.1%), with minor differences according to hospital volume.
There is no difference in terms of specialization or formal training among surgeons performing breast surgery, although there could be substantial variation in the individual percentage of breast-related practice [Cancer 2006;106:1462-6]; information on activity of individual surgeons is not available from discharge records. A deeper discussion of possible determinants of breast cancer therapy at the patient and at the hospital level has been introduced in the revised paper (with some added references).