Similar responsiveness of health-related quality of life outcomes in patients with breast cancer undergoing systemic therapy

Using network meta-analysis to develop hierarchies for data-extraction in systematic reviews

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Extracting and combining data from different outcome measures is important in any meta-analysis.

Ideally, the most responsive outcome measure is the best choice considering it is a valid outcome measure.

Large impact on effect size of the choice of outcome for data-extraction.

In clinical trials including patients with breast cancer, multiple patients reported outcome measures (PROMs) has been used to assess health-related quality of life (HRQoL)
Aims

to compare the responsiveness of cancer specific, breast cancer specific and generic health related quality of life (HRQoL) used in randomised controlled trials (RCTs), evaluating exercise interventions in patients with breast cancer undergoing systemic therapy.
MEDLINE, EMBASE, CINAHL and CENTRAL were searched for RCTs evaluating exercise interventions in patients with breast cancer undergoing systemic therapy reporting at least two different HRQoL outcomes.

Network meta-analysis using a random effects model (REML) was performed on the standardised mean difference (SMD).

Inconsistency was evaluated based on the difference between direct and overall estimates of the three comparisons between the PROMs, breast cancer-specific, cancer-specific and generic outcomes of HRQoL.

Probability values were reported as the surface under the cumulative ranking (SUCRA). SUCRA = 1 if an outcome consistently ranks first (most responsive)
Twelve studies measured HRQoL with both a breast cancer-specific and cancer-specific outcome; two had both a cancer-specific outcome and a generic HRQoL outcome, and two reported HRQoL outcome in all three outcome groups.
Results

Network meta-analysis plot (size of bubble showed the number of studies)

Low inconsistency – difference between direct comparison (green) and all study (direct and indirect) comparison (red)
Results

The generic PROMs were the most responsive, with 53.9% confidence, followed by the breast cancer-specific with 36.4% confidence.

<table>
<thead>
<tr>
<th>Comparison</th>
<th>SMD (95% CI)</th>
<th>trials in direct comparison</th>
<th>SMD favours</th>
<th>Confidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast Cancer specific vs Generic</td>
<td>0.024 (-0.235 to 0.283)</td>
<td>2</td>
<td>Breast Cancer specific HRQoL</td>
<td>Very lowabc</td>
</tr>
<tr>
<td>Breast Cancer specific vs Cancer specific</td>
<td>-0.035 (-0.158 to 0.088)</td>
<td>14</td>
<td>Generic HRQoL</td>
<td>Lowac</td>
</tr>
<tr>
<td>Cancer specific vs Generic</td>
<td>0.059 (-0.168 to 0.286)</td>
<td>4</td>
<td>Generic HRQoL</td>
<td>Lowac</td>
</tr>
</tbody>
</table>

Confidence is based on the GRADE approach evaluating study limitation, inconsistency, indirectness, imprecision and publication bias (i.e., small study bias).

Low to very low confidence for no difference in responsiveness between breast cancer-specific, cancer specific and generic HRQoL

<table>
<thead>
<tr>
<th>Health related quality of life outcome</th>
<th>Breast Cancer specific</th>
<th>Cancer specific</th>
<th>Generic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Most responsive</td>
<td>36.4</td>
<td>9.7</td>
<td>53.9</td>
</tr>
<tr>
<td>Second responsive</td>
<td>41.4</td>
<td>39.7</td>
<td>18.9</td>
</tr>
<tr>
<td>Least responsive</td>
<td>22.2</td>
<td>50.6</td>
<td>27.2</td>
</tr>
</tbody>
</table>
Low number of included studies with two and more HRQoL measures. Therefore, the PROMs were grouped as breast cancer-specific, cancer-specific and generic instead of performing the analysis on the individual PROMs.

Some variations of the exercise prescription components (frequency, intensity, and duration) and delivery mode (supervised, partly- or unsupervised).

However, due to the low number of included studies addressing these differences was not possible.
Conclusions

No clinically or statistically significant difference in responsiveness between the disease-specific and generic HRQoL PROMs in breast cancer patients undergoing systemic therapy.

The choice of PROMs may not impact the heterogeneity in the meta-analysis of HRQoL in patients with breast cancer undergoing systemic therapy.

Hierarchy of patient reported outcomes can be developed based on network meta-analysis.
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