Methodological quality assessment of study investigating the Breast Cancer Index

Study feature	Qualities sought	Jerevall *et al.* (2011)[122]
Sample of patients	Inclusion criteria defined	Y
	Sample selection explained	Y
	Adequate description of diagnostic criteria	Y
	Clinical and demographic characteristics fully described	Y
	Representative (random or consecutive)	Y (random)
	Assembled at a common (usually early) point in the course of their disease	Y
	Complete (all eligible patients included)	N
Follow-up of patients	Sufficiently long	Y
Outcome	Objective	Y
	Unbiased (e.g. assessment blinded to prognostic information)	U
	Fully defined	Y
	Appropriate	Y
	Known for all or a high proportion of patients	Y
Prognostic variable	Fully defined, including details of method of measurement if relevant	Y
	Precisely measured	Y (detail provided)
	Available for all or a high proportion of patients	Y
	If relevant, cut-point(s) defined and justified	Y (detail provided)
Analysis	Continuous predictor variable analysed appropriately	Y
	Statistical adjustment for all important prognostic factors	Y
Intervention subsequent to inclusion in cohort	Fully described	Y
	Intervention standardised or randomised	Y

N, no; U, unclear/not reported; Y, yes.

Summary of results: Breast Cancer Index

<table>
<tr><th>Study</th><th>Outcomes/end points</th><th>Results</th><th>Authors' conclusions</th><th>Comments</th></tr>
<tr><td>Jerevall et al. (2011)[122]</td><td>Time to distant metastasis
DMFS
BCSD</td><td>
Development and testing of HOXB13:IL17BR (H:I) + MGI as a continuous index (BCI)
Developed a continuous algorithm using G1 (training set) and tested on G2 (test set)
G1: BCI classified 59% as low risk (rate of distant recurrence: 1.7%, 95% CI 0% to 3.5%; rate of death: 1.1%, 95% CI 0% to 2.6%); 22% as intermediate risk (rate of distant recurrence: 17.8%, 95% CI 7.6% to 26.8%; rate of death: 14.5%, 95% CI 5.2% to 22.9%); and 18.4% as high risk (rate of distant recurrence: 20.0%, 95% CI 8.7% to 30.0%; rate of death: 14.7%, 95% CI 4.7% to 23.6%)
G2: BCI classified 53% as low risk (rate of distant recurrence: 8.3%, 95% CI 4.7% to 14.4%; rate of death: 5.1%, 95% CI 1.3% to 8.7%); 27% as intermediate risk (rate of distant recurrence: 22.9%, 95% CI 14.5% to 35.2%; rate of death: 19.8%, 95% CI 10.0% to 28.6%); and 20% as high risk (rate of distant recurrence: 28.5%, 95% CI 17.9% to 43.6%; rate of death: 28.8%, 95% CI 15.3% to 40.2%)
BCI is a strong prognostic factor for distant recurrence and BCSD independent of tumour size, grade, HER2 status and PR status (although tumour size did contribute prognostic value to distant recurrence)
<table>
<tr><th></th><th>St Gallen</th><th>BCI</th></tr>
<tr><td>G1</td><td></td><td></td></tr>
<tr><td>Low risk (rate of recurrence, 95% CI) (%)</td><td>22 (5.2, –0.5 to 10.9)</td><td>59 (7.1, 0 to 3.5)</td></tr>
<tr><td>Intermediate risk (rate of recurrence, 95% CI) (%)</td><td>78 (8.5, 4.9 to 12.1)</td><td>22 (17.8, 7.6 to 26.8)</td></tr>
<tr><td>High risk (rate of recurrence, 95% CI) (%)</td><td>NA</td><td>18.4 (20.0, 8.7 to 30.0)</td></tr>
<tr><td>G2</td><td></td><td></td></tr>
<tr><td>Low risk (rate of recurrence, 95% CI) (%)</td><td>19 (8.8, 1.4 to 16.2)</td><td>5.3 (8.3, 4.7 to 14.4)</td></tr>
<tr><td>Intermediate risk (rate of recurrence, 95% CI) (%)</td><td>81 (17.0, 11.7 to 22.3)</td><td>27 (22.9, 14.5 to 35.2)</td></tr>
<tr><td>High risk (rate of recurrence, 95% CI) (%)</td><td>NA</td><td>20 (28.5, 17.9 to 43.6)</td></tr>
</table>
NA, not available.

Prognostic utility of BCI also assessed in comparison to Adjuvant! Online for G2. Both BCI and Adjuvant! Online were significant predictors of BCSD (BCI: HR 2.3, 95% CI 1.5 to 3.7, $p<0.001$; Adjuvant Online: HR 1.4, 95% CI 1.0 to 1.8, $p<0.04$) and distant recurrence (BCI: HR 2.0, 95% CI 1.3 to 3.1, $p<0.001$; Adjuvant! Online: HR 1.4, 95% CI 1.0 to 1.8, $p<0.003$) (calculated HRs are relative to an increment of their interquartile ranges: 2.484 for BCI, 6 for Adjuvant Online!)
</td><td>Retrospective analysis of this randomised, prospective trial cohort validated the prognostic utility of H:I+MGI and was used to develop and test a continuous risk model that enables prediction of distant recurrence risk at the patient level</td><td>Only data related to the BCI have been extracted (rather than data on H:I+MGI)</td></tr>
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