

Methodological quality assessment of the study investigating the IHC4 test

Study feature	Qualities sought	Cuzick <i>et al.</i> (2011) ⁸⁴
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 sample)	Y
	Assembled at a common (usually early) point in the course of their disease	Y
	Complete (all eligible patients were included)	Y
Follow-up of patients	Sufficiently long	Y
Outcome	Objective	Y
	Unbiased (e.g. assessment blinded to prognostic information)	U
	Fully defined	U
	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 (reference provided)
	Precisely measured	Y
	Available for all or a high proportion of patients	Y
	If relevant, cut-point(s) defined and justified	Y
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

U, unclear/not reported; Y, yes.

Summary of results: IHC4

Study	Outcomes/ end points	Results	Authors' conclusions	Comments
Cuzick <i>et al.</i> (2011) ⁸⁴	Distant recurrence (within 10 years) TTDR	G1: 195 recurrences of which 145 were distant recurrences; in LN- women there were 101 recurrences of which 67 were distant recurrences The median IHC4 score for all patients was -4.2 (IQR -29.9 to 29.9). The HR for a change from the 25th to the 75th percentile of the IHC4 score for all patient was 5.7 (95% CI 3.4 to 9.7) in univariate analysis and 3.9 (95% CI 2.4 to 6.7) when added to clinical score G2: IHC4 score was highly significantly predictive of outcome for a change from the 25th to 75th percentile in a univariate analysis (HR 4.8, 95% CI 2.2 to 10.2), and gave similar results when added to clinical score (HR 4.4, 95% CI 2.0 to 9.3, $\Delta\chi^2 = 26.61$, $p < 0.0001$)	Additional studies are needed to determine the general applicability of the IHC4 score	