

**Appendix 3 (as supplied by the authors): Methodological quality evaluation: tool for studies of prognostic test (adapted from QUADAS-2 and REMARK)**

Domain	Patient Selection	Prognostic markers	Outcome	Flow	Timing	Confounding
Description	Describe methods of patient selection  Describe included patients (previous testing, presentation, intended use of index test, and setting)	Describe the prognostic marker and how it was conducted and interpreted	Describe the outcome measurement and how it was conducted and interpreted	Describe any patients who did not have the prognostic markers measured or for whom outcome was not measured or who were excluded from the 2 X 2 table (refer to flow diagram)	Describe the interval and any interventions between prognostic markers and the outcome measurement	Describe any method used to control for potential confounding
Signaling questions (yes, no, or unclear)	Was a consecutive or random sample of patients enrolled?  Was a case-control design avoided?  Did the study avoid inappropriate exclusions?	Were the prognostic marker results interpreted without knowledge of clinical data? (blinding)  If a threshold was used, was it prespecified?	Was the outcome measurement adequate?  Did all patients have their outcome evaluated the same way?  Were the outcome results interpreted without knowledge of the results of the prognostic markers? (blinding)	Did all patients have outcome measured?  Were all patients included in the analysis? (lost to follow-up? withdrawal? patients not tested? missing data? etc.)	Was there an appropriate interval between prognostic marker and outcome measurement? (sufficient time for outcome to occur?)	Did the study control for potential confounders?
Risk of bias (high, low, or unclear)	Could the selection of patients have introduced bias?	Could the conduct or interpretation of the prognostic marker have introduced bias?	Could the outcome measurement, its conduct, or its interpretation have introduced bias?	Could the patient flow have introduced bias?	Could the timing have introduced bias?	Confusion bias?
Concerns about applicability (high, low, or unclear)	Are there concerns that the included patients do not match the review question?	Are there concerns that the prognostic marker, its conduct, or its interpretation differ	Are there concerns that the outcome measure does not match the review			

Appendix to: Mercier E, Boutin A, Shemilt M, et al. Predictive value of neuron-specific enolase for prognosis in patients with moderate or severe traumatic brain injury: a systematic review and meta-analysis. *CMAJ Open* 2016. DOI:10.9778/cmajo.20150061. Copyright © 2016 The Author(s) or their employer(s).

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		from the review question?	question? (not clearly reported according to prognostic marker results or different dichotomisation of scales, etc.)			
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