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Current clinical selection strategies for identification of hereditary non-polyposis colorectal cancer families are inadequate: a meta-analysis.

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Present guidelines to identify hereditary non-polyposis colorectal cancer (HNPCC) families are criticized for limitations in accuracy. The Amsterdam criteria I and II (AC I and AC II) are used to predict a germline mutation in one of the mismatch repair genes. In families not fulfilling the AC I and AC II criteria, individual indications to test cancer specimens for microsatellite instability (MSI) are guided by the Bethesda Guidelines (BG). Germline mutation testing is then performed in patients who conform to the BG and show MSI. We investigated the sensitivity and specificity of AC I, AC II, and BG. A meta-analysis of studies on the value of the AC I and AC II criteria for predicting germline mutation, as well as a meta analysis of BG for the detection of MSI was performed. For the AC I, sensitivity varied from 54 to 91% and specificity varied from 62 to 84%. For the AC II, the pooled sensitivity was 78% and specificity ranged between 46 and 68%. Post-test probabilities of a positive test result were 0.61 and 0.46 for the AC I and AC II, respectively. Post-test probabilities of a negative test result were 0.17 and 0.21 for the AC I and AC II, respectively. For the BG, the pooled sensitivity was 89% and pooled specificity was 53%. Post-test probability of a positive test result was 41%, and post-test probability of a negative test result was 9%. The sensitivity and specificity of the Amsterdam criteria for predicting a germline mutation that causes HNPCC is not sufficient. The BG are useful for the detection of MSI in a group of patients suspected of having familial colorectal cancer (CRC), but sensitivity is very low in the total group of newly diagnosed CRC patients. Therefore, a new strategy is needed for the identification of HNPCC.