



NCCN Guidelines™ Version 2.2011

High Risk Syndromes

CRITERIA FOR FURTHER RISK EVALUATION FOR HIGH RISK SYNDROMES

Individual meeting the Revised Bethesda Guidelines^a (See [LS-B](#))
or
Individual from a family meeting Amsterdam criteria (See [LS-C](#))
or
> 10 adenomas in same individual (See [FAP-1](#) and [MAP-1](#))
or
Individual with multiple gastrointestinal hamartomatous polyps (See [PJS-1](#) and [JPS-1](#)) or hyperplastic polyps (See [HPP-1](#))
or
Individual from a family with a known hereditary syndrome associated with colorectal cancer, with or without known mutation (See appropriate hereditary syndrome)

RISK ASSESSMENT/ GENETIC COUNSELING^{b,c}

- Obtain detailed family history
- Obtain detailed medical and surgical history
- Directed examination for related manifestations
- Psychosocial assessment and support
- Risk counseling
- Education support
- Discussion of genetic testing^b
- Obtain informed consent

HEREDITARY SYNDROME

- Lynch syndrome (See [LS-1](#))
- Classical FAP (See [FAP-1](#))
- Attenuated FAP (See [AFAP-1](#))
- MYH-associated polyposis (See [MAP-1](#))
- Peutz-Jeghers Syndrome^d (See [PJS-1](#))
- Juvenile Polyposis Syndrome^d (See [JPS-1](#))
- Hyperplastic Polyposis Syndrome (See [HPP-1](#))
- No syndromes, but familial risk present → See [Positive Family History \(CSCR-6\)](#)

^aEndometrial cancer < 50 y is not included in the revised Bethesda guidelines, however recent evidence suggests that these individuals should be evaluated for Lynch syndrome.

^bSee [Obtaining a Comprehensive Risk Assessment for Hereditary Colorectal Cancer \(HRS-A\)](#).

^cA genetic counselor and/or medical geneticist should be involved early in counseling patients who (potentially) meet criteria for an inherited syndrome. Genetic counseling is advised when genetic testing is offered.

^dReferral to a specialized team is recommended.

Note: All recommendations are category 2A unless otherwise indicated.

Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.



THE REVISED BETHESDA GUIDELINES FOR TESTING COLORECTAL TUMORS FOR MICROSATELLITE INSTABILITY (MSI)¹

Tumors from individuals should be tested for MSI in the following situations:

- Colorectal cancer² diagnosed in a patient who is less than 50 years of age.
- Presence of synchronous, or metachronous Lynch syndrome-associated tumors,³ regardless of age.
- Colorectal cancer with the MSI-H histology⁴ diagnosed in a patient who is less than 60 years of age.
- Colorectal cancer diagnosed in a patient with one or more first-degree relatives with an LS-related cancer,³ with one of the cancers being diagnosed under age 50 years.
- Colorectal cancer diagnosed in a patient with two or more first- or second-degree relatives with LS-related cancers³ regardless of age.

¹Adapted with permission from Umar A, Boland CR, Terdiman JP, et al. Revised Bethesda Guidelines for hereditary nonpolyposis colorectal cancer (Lynch syndrome) and microsatellite instability. *J Natl Cancer Inst* 2004;96:261-268.

²Endometrial cancer < 50 y is not included in the revised Bethesda guidelines, however recent evidence suggests that these individuals should be evaluated for Lynch syndrome.

³LS-related cancers include colorectal, endometrial, gastric, ovarian, pancreas, ureter and renal pelvis, biliary tract, brain (usually glioblastoma as seen in Turcot syndrome), and small intestinal cancers, as well as sebaceous gland adenomas and keratoacanthomas as seen in Muir-Torre syndrome.

⁴Presence of tumor infiltrating lymphocytes, Crohn's-like lymphocytic reaction, mucinous/signet-ring differentiation, or medullary growth pattern.

Note: All recommendations are category 2A unless otherwise indicated.

Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.



MINIMUM CRITERIA FOR CLINICAL DEFINITION OF HNPCC (AMSTERDAM CRITERIA I)^{1,2}

At least three relatives with colorectal cancer (CRC); all of the following criteria should be present:

- One should be a first-degree relative of the other two;
- At least two successive generations must be affected;
- At least one of the relatives with colorectal cancer must have received the diagnosis before the age of 50 years;
- Familial adenomatous polyposis (FAP) should be excluded;
- Tumors should be verified by pathologic examination.

REVISED MINIMUM CRITERIA FOR CLINICAL DEFINITION OF HNPCC (AMSTERDAM CRITERIA II)^{1,2}

At least three relatives must have a cancer associated with hereditary nonpolyposis colorectal cancer (colorectal, cancer of endometrium, small bowel, ureter or renal-pelvis); all of the following criteria should be present:

- One must be a first-degree relative of the other two;
- At least two successive generations must be affected;
- At least one of the relatives with cancer associated with hereditary non-polyposis colorectal cancer should be diagnosed before the age 50 years;
- Familial adenomatous polyposis (FAP) should be excluded in the colorectal cancer case(s) (if any);
- Tumors should be verified whenever possible.

¹From Vasen HFA. Clinical diagnosis and management of hereditary colorectal cancer syndromes. J Clin Onc 2000;18(suppl 1):81s-92s.

²Approximately 50% of patients with HNPCC will be missed by these criteria and approximately 50% of patients will meet the criteria and not have HNPCC but a high familial risk of uncertain etiology.

Note: All recommendations are category 2A unless otherwise indicated.

Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.