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Comprehensive  
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**NCCN Clinical Practice Guidelines in Oncology™**

# **Colorectal Cancer Screening**

V.1.2010

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## NCCN Colorectal Cancer Screening Panel Members

\* Randall W. Burt, MD/Chair ☒ △  
Huntsman Cancer Institute at the University  
of Utah

James S. Barthel, MD ☒ ⊂  
H. Lee Moffitt Cancer Center and Research  
Institute

Kelli Bullard Dunn, MD ¶  
Roswell Park Cancer Institute

Donald S. David, MD ☒  
City of Hope Comprehensive Cancer Center

Ernesto Drelichman, MD ¶  
University of Alabama at Birmingham  
Comprehensive Cancer Center

James M. Ford, MD † ⊂ △  
Stanford Comprehensive Cancer Center

Francis M. Giardiello, MD, MBA ☒  
The Sidney Kimmel Comprehensive Cancer  
Center at Johns Hopkins

Stephen B. Gruber, MD, PhD, MPH † △  
University of Michigan Comprehensive  
Cancer Center

Amy L. Halverson, MD ¶  
Robert H. Lurie Comprehensive Cancer  
Center of Northwestern University

Stanley R. Hamilton, MD ≠  
The University of Texas M. D. Anderson  
Cancer Center

Mohammad K. Ismail, MD ☒  
St. Jude Children's Research  
Hospital/University of Tennessee Cancer  
Institute

Kory Jasperson, MS, CGC △  
Huntsman Cancer Institute at the University  
of Utah

Audrey J. Lazenby, MD ≠  
UNMC Eppley Cancer Center at  
The Nebraska Medical Center

Patrick M. Lynch, MD, JD ☒  
The University of Texas M. D. Anderson  
Cancer Center

Edward W. Martin, Jr, MD ¶  
The Ohio State University Comprehensive  
Cancer Center - James Cancer Hospital and  
Solove Research Institute

Robert J. Mayer, MD †  
Dana-Farber/Brigham and Women's  
Cancer Center

Reid M. Ness, MD, MPH ☒  
Vanderbilt-Ingram Cancer Center

Dawn Provenzale, MD, MS ☒ ⊂  
Duke Comprehensive Cancer Center

M. Sambasiva Rao, MD ≠ ☒  
Robert H. Lurie Comprehensive Cancer  
Center of Northwestern University

Moshe Shike, MD ☒ ⊂  
Memorial Sloan-Kettering Cancer Center

Gideon Steinbach, MD, PhD ☒ ⊂  
Fred Hutchinson Cancer Research  
Center/Seattle Cancer Care Alliance

Jonathan P. Terdiman, MD ☒  
UCSF Helen Diller Family Comprehensive  
Cancer Center

David Weinberg, MD, MSc ☒  
Fox Chase Cancer Center

☒ Gastroenterology  
△ Cancer Genetics  
⊂ Internal Medicine  
† Medical Oncology  
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\* Writing Committee Member

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## RISK ASSESSMENT FOR COLON CANCER

**Average risk:**

- Age  $\geq$  50 y
- No history of adenoma or colorectal cancer
- No history of inflammatory bowel disease
- Negative family history<sup>a</sup>

→ [See Average Risk Screening and Evaluation \(CSCR-2\)](#)

**Increased risk:**

## • Personal history

- ▶ Adenoma/sessile serrated polyp (SSP)<sup>b</sup>
- ▶ Colorectal cancer
- ▶ Inflammatory bowel disease  
(ulcerative colitis, Crohn's disease)

→ [See Follow-up of Clinical Findings:  
Adenoma/sessile serrated polyps \(CSCR-3\)](#)

→ [See Increased Risk Screening Based on Personal  
History of Colorectal Cancer \(CSCR-4\)](#)

→ [See Increased Risk Screening Based on Personal  
History of Inflammatory Bowel Disease \(CSCR-5\)](#)

## • Positive family history

→ [See Increased Risk Screening Based on Positive  
Family History \(CSCR-6\)](#)

**High risk syndromes:**

- Lynch Syndrome/Hereditary Nonpolyposis Colorectal Cancer (HNPCC) ([LS-1](#))
- Polyposis syndromes
  - ▶ Classical Familial Adenomatous Polyposis ([FAP-1](#))
  - ▶ Attenuated Familial Adenomatous Polyposis ([AFAP-1](#))
  - ▶ MYH-associated Polyposis ([MAP-1](#))
  - ▶ Peutz-Jeghers Syndrome ([PJS-1](#))
  - ▶ Juvenile Polyposis syndrome ([JPS-1](#))
  - ▶ Hyperplastic Polyposis Syndrome ([HPP-1](#)) (rarely inherited)

→ [See Criteria for Further Risk Evaluation for  
High Risk Syndromes \(HRS-1\)](#)

<sup>a</sup>Not having a first-degree relative or two second-degree relatives with colorectal cancer or multiple cases of Lynch syndrome/HNPCC -related cancers in the family.

<sup>b</sup>Sessile serrated polyp (SSP) is synonymous with sessile serrated adenoma but does not include classical hyperplastic polyp.

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

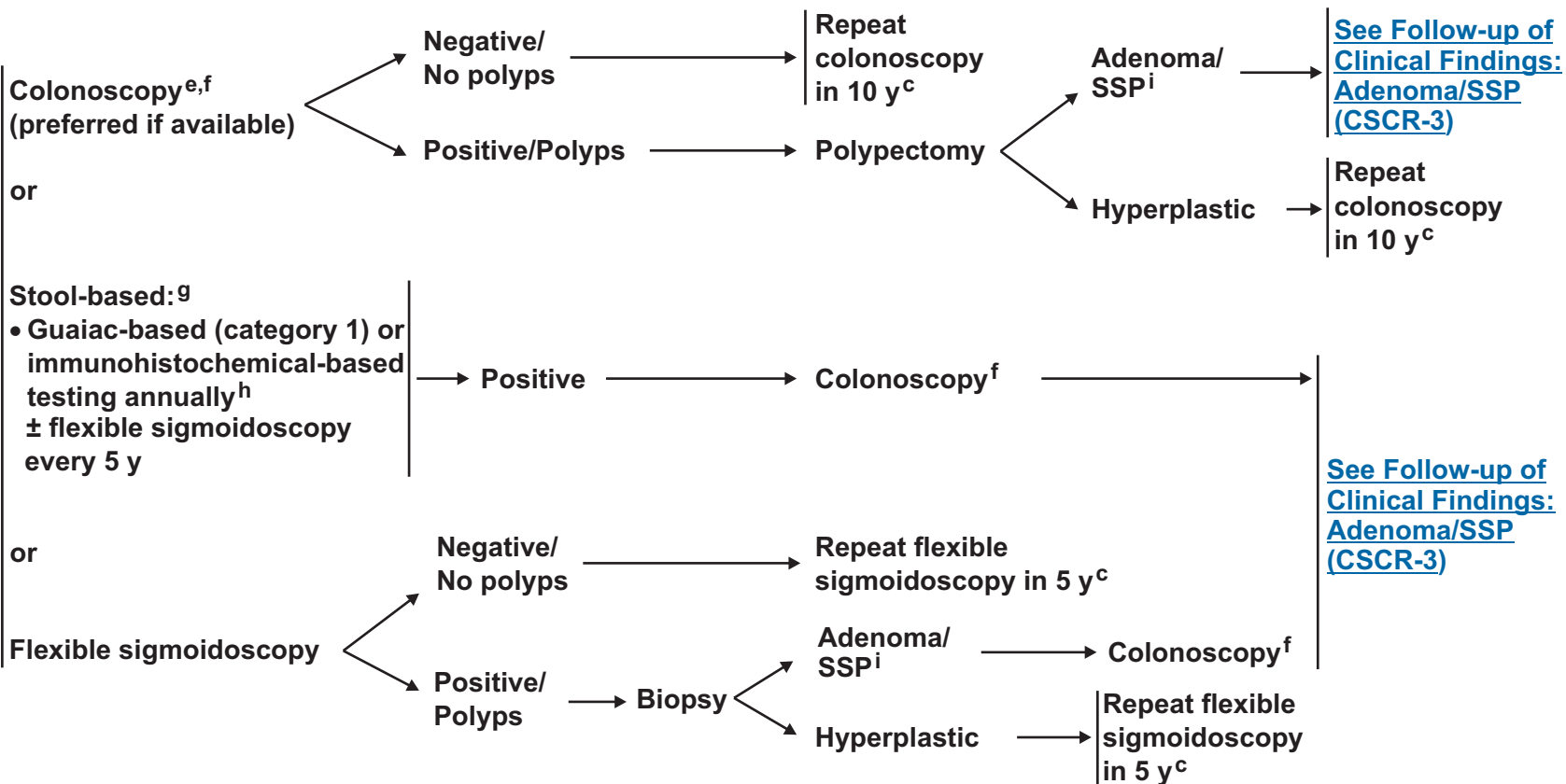
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RISK STATUS

SCREENING MODALITY AND SCHEDULE<sup>c,d</sup>

EVALUATION OF POSITIVE SCREENING FINDINGS

- Average risk:
- Age ≥ 50 y
  - No history of adenoma or colorectal cancer
  - No history of inflammatory bowel disease
  - Negative family history



<sup>c</sup>See Screening Modality and Schedule (CSCR-A).

<sup>d</sup>Currently there is not consensus on the use of CT colonography as a primary screening modality and it is evolving with regards to recommended/ programmatic frequency, polyp size leading to referral for colonoscopy, and protocol for evaluating extra-colonic lesions. However, the data available suggests, if CT colonography is negative/no polyps, then repeat CT colonography in 5 y and if positive/polyps lesions, colonoscopy should be performed.

<sup>e</sup>Other screening modalities such as double contrast barium enema should be reserved for those who are not able to undergo colonoscopy, or colonoscopy is technically incomplete.

<sup>f</sup>If colonoscopy incomplete, consider other screening modality or repeat colonoscopy at discretion of physician.

<sup>g</sup>Emerging technologies such as stool DNA have shown increasing evidence as a reasonably accurate screening test but there are limited data to determine an interval between screening. At present, stool DNA is not considered a first line screening test except in specific circumstances.

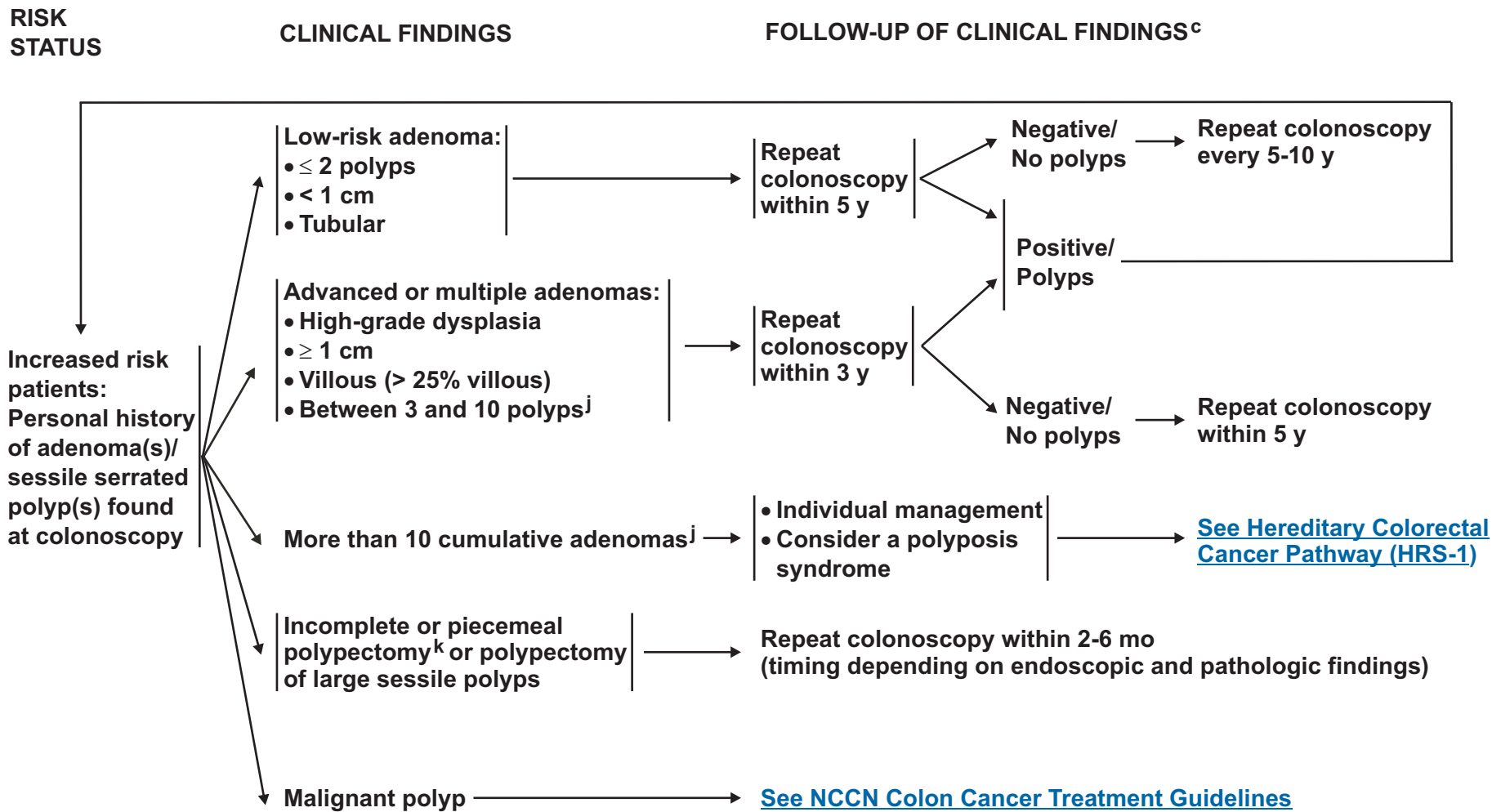
<sup>h</sup>Studies at the present time have demonstrated, fecal immunohistochemical testing (FIT) is as good, if not superior to guaiac- based testing.

<sup>i</sup>Sessile serrate polyps are managed the same as adenomas.

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## INCREASED RISK BASED ON PERSONAL HISTORY OF ADENOMA/SESSILE SERRATED POLYP (SSP)<sup>i</sup>



<sup>c</sup>See [Screening Modality and Schedule \(CSCR-A\)](#).

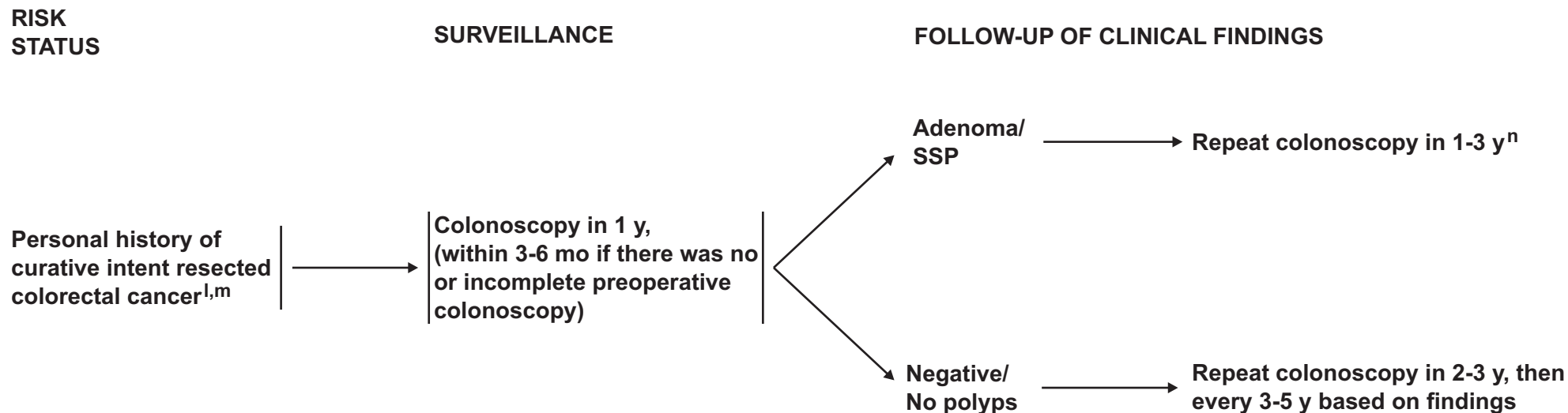
<sup>i</sup>Sessile serrate polyps are managed the same as adenomas.

<sup>j</sup>Fewer than 10 polyps in the setting of a strong family history or younger age (< 40 y) may sometimes be associated with an inherited polyposis syndrome.

<sup>k</sup>Ink lesion for later identification.

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## INCREASED RISK BASED ON PERSONAL HISTORY OF COLORECTAL CANCER



<sup>l</sup>Identify colorectal patients who meet Bethesda criteria. Those patients may require genetic counseling or individualized management. (See [High Risk Syndromes HRS-1](#) and [Lynch Syndrome LS-1](#)).

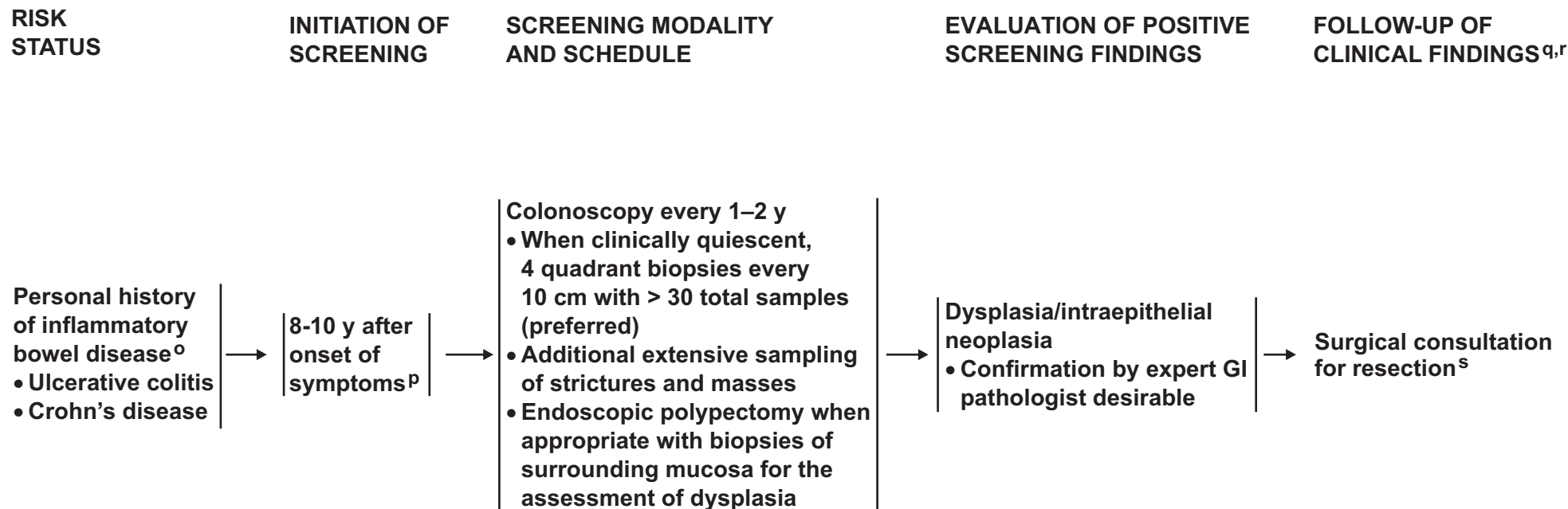
<sup>m</sup>In addition to the colonoscopy, patients with rectal cancer should also undergo periodic limited endoscopic evaluation of the rectal anastomosis to identify local recurrence. Optimal timing for surveillance is not known. Expert opinion supports repeat evaluation every 3-6 months for the first 2-3 years of surveillance. No specific data clearly support rigid versus flexible sigmoidoscopy. The utility of routine endoscopic ultrasound for early surveillance is not defined. See surveillance section of [NCCN Rectal Cancer Guidelines](#).

<sup>n</sup>The recommendation for intensive surveillance immediately following resection is based on studies that found a high rate of metachronous colorectal cancer and/or resectable recurrences in the 4-5 years following colorectal cancer resections, though the studies did not fully exclude patients with HNPCC.

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## INCREASED RISK BASED ON PERSONAL HISTORY OF INFLAMMATORY BOWEL DISEASE



<sup>o</sup>Information regarding the value of endoscopic surveillance of long-standing Crohn's disease is limited. Surveillance is at the discretion of the physician.

<sup>p</sup>Winawer S, Fletcher R, Rex D, et al. Colorectal cancer screening and surveillance: Clinical guidelines and rationale--update based on new evidence. *Gastroenterology* 2003;124:544-560.

<sup>q</sup>Optimal management of Crohn's-related dysplasia remains undefined. Patient and physician preference should be considered. Extent of resection for Crohn's-related dysplasia needs to be based upon the individual findings.

<sup>r</sup>Appropriate management of adenomatous polyps in the setting of ulcerative colitis is dependent on various factors and should be at the discretion of the treating physician.

<sup>s</sup>See [Definitions of Common Colorectal Resections \(CSCR-B\)](#).

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## INCREASED RISK BASED ON POSITIVE FAMILY HISTORY

### FAMILY HISTORY CRITERIA<sup>t</sup>

### SCREENING

First-degree relative with colorectal cancer age 50-60 y <sup>u</sup>	→	Colonoscopy beginning at age 40 y	→	Repeat every 5 y <sup>w</sup>
First-degree relative with colorectal cancer < age 50 y <sup>u,v</sup>	→	Colonoscopy beginning at age 40 y or 10 y before earliest diagnosis of colorectal cancer	→	Repeat every 3-5 y depending on other family history
First-degree relative with colorectal cancer at age ≥ 60 y <sup>u</sup>	→	Colonoscopy beginning at age 50 y	→	Repeat every 5 y
Two related first-degree relatives with colorectal cancer at any age <sup>v</sup>	→	Colonoscopy beginning at age 40 y or 10 y before earliest diagnosis of colorectal cancer	→	Repeat every 3-5 y depending on other family history
Two related second-degree relatives with colorectal at any age	→	Colonoscopy beginning at age 50 y	→	Repeat every 5 y
One second-degree relative or any third-degree relative(s) with colorectal cancer or First-degree relative with non-advanced adenoma(s)	→	<ul style="list-style-type: none"> <li>• Treat as average risk patients</li> <li>• Colonoscopy is preferred screening</li> </ul>		

<sup>t</sup>If a patient meets the criteria for an inherited colorectal syndrome, [see Criteria for Further Risk Evaluation for High Risk Syndromes \(HRS-1\)](#).

<sup>u</sup>First-degree relatives with advanced adenoma may confer the same risk as first-degree relatives with colorectal cancer, and any adenoma under age 40 y may confer a similar risk to colorectal cancer under age 50 y.

<sup>v</sup>In this circumstance or if any one of the revised Bethesda criteria ([see LS-B](#)) are met, IHC/MSI testing should be performed on the colon tumor of youngest family member with available colorectal cancer tissue. Also see Lynch Syndrome guidelines ([LS-1](#)).

<sup>w</sup>Shorter intervals may be needed depending upon the family history.

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## SCREENING MODALITY AND SCHEDULE (1 of 4)

- Colon cancer prevention should be the primary goal of colorectal cancer screening.
- Screening of average-risk individuals can reduce colorectal cancer mortality by detecting cancer at an early, curable stage and by detecting and removing clinically significant adenomas, and has been shown to be cost-effective compared to other screening programs.
- Although patient preferences and availability of resources play an important role in the selection of screening options, tests that are designed to detect both early cancer and adenomatous polyps should be encouraged.

**Screening Modalities that Detect Adenomatous Polyps and Cancer<sup>1</sup>**

- Colonoscopy every 10 years, or
- Flexible sigmoidoscopy every 5 years, or
- CT colonography every 5 years<sup>2</sup>

**Screening Modalities that Primarily Detect Cancer<sup>3</sup>**

- Stool based screening
  - Guaiac-based testing, annually or
  - Immunochemical-based testing, annually or
  - Stool DNA test with high sensitivity (interval for screening is uncertain)<sup>4</sup>

[Continued on next page](#)

<sup>1</sup>If other modalities are not available, double-contrast barium enema every 5 years may be useful.

<sup>2</sup>Currently there is not consensus on the use of CT colonography as a primary screening modality and it is evolving with regards to recommended/ programmatic frequency, polyp size leading to referral for colonoscopy, and protocol for evaluating extra-colonic lesions. However, the data available suggests, if CT colonography is negative/no polyps, then repeat CT colonography in 5 y and if positive/polyps lesions, colonoscopy should be performed.

<sup>3</sup>Annual stool based testing with every 5 year flexible sigmoidoscopy can be used in combination for screening.

<sup>4</sup>Emerging technologies such as stool DNA have shown increasing evidence as a reasonably accurate screening test but there are limited data to determine an interval between screening. At present, stool DNA is not considered a first line screening test except in specific circumstances.

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## SCREENING MODALITY AND SCHEDULE (2 of 4)

**Colonoscopy**

- Colonoscopy is the primary method employed for colorectal cancer screening in average and high risk populations. However, screening with any of the available modalities is preferable to no screening.
- Caveats for every 10 years interval:
  - ▶ A 10 year interval is appropriate for average risk patients who had an optimal procedure.
  - ▶ Shorter intervals may be indicated based on the quality and completeness of the colonoscopy.
  - ▶ Individual risk factors and physician judgment should be included in the interval determination.
  - ▶ The number and characteristics of polyps as well as family history and medical assessment should influence judgment regarding the interval between colonoscopies.
  - ▶ Colonoscopy has limitations and may not detect all cancers and polyps.
- Accumulating data suggest that there is substantial variability in the quality, and by extension, the clinical effectiveness of colonoscopy. Improving the overall impact of screening colonoscopy requires a programmatic approach that addresses quality issues at several levels.
- These colonoscopy quality indicators include:
  - ▶ Cecal intubation rates
  - ▶ Withdrawal time
  - ▶ Adenoma detection rates
  - ▶ Appropriate intervals between endoscopic studies based on family and personal history, number and histological type of polyps on last colonoscopy
  - ▶ Minor and major complication rates
  - ▶ Pre-procedure medical evaluation
  - ▶ Appropriate prep instructions
- Standardized colonoscopy reports that contain, at a minimum:
  - ▶ Patient demographic and clinical factors
  - ▶ Procedure indications
  - ▶ Endoscopic findings
  - ▶ Photographic documentation of endoscopic landmarks
  - ▶ Estimate of quality of bowel preparation
  - ▶ Documentation of follow-up planning, including pathology results
  - ▶ Sedation administered

[Continued on next page](#)

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## SCREENING MODALITY AND SCHEDULE (3 of 4)

**Flexible sigmoidoscopy**

- May be performed alone or in combination with stool based screening
- Issues surrounding sigmoidoscopy are similar to colonoscopy except the colon is only examined distal to the splenic flexure
- Recommended every 5 years for average risk screening

**Stool based screening**

- Guaiac-based, nonrehydrated
  - ▶ Requires 3 successive stool specimens annually (not via digital rectal examination), prescribed diet, and coordination by health care provider
  - ▶ Any positive test requires further evaluation
  - ▶ Annual guaiac-based should not be performed if screening colonoscopy is used as a screening measure in an average-risk patient
- Fecal immunohistochemical testing (FIT)
  - ▶ Detects human globin
  - ▶ Prescribed diet is not required
  - ▶ Requires single stool annually
  - ▶ Any positive test requires further evaluation

[Continued on next page](#)

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## SCREENING MODALITY AND SCHEDULE (4 of 4)

**Radiographic****CT colonography (CTC)<sup>5,6,7</sup>****• Accuracy**

- ▶ > 10 mm lesions can be identified by CTC with an accuracy similar to colonoscopy
- ▶ Lesions 5-9 mm can be identified with an acceptable accuracy that is less than that identified for colonoscopy
- ▶ Lesions < 5 mm cannot be identified with acceptable accuracy

**• Follow-up of identified lesions**

- ▶ All identified lesions > 5 mm should be referred for colonoscopy
- ▶ When identified, lesions < 5 mm generally do not need to be referred for colonoscopy

**• The recommended performance interval of every 5 years is based solely on computer simulation models****• All visualized extracolonic findings should be described and recommendations provided as to appropriate follow-up****• The increased risk of cancer arising from the performance of a single CTC is estimated to be < 0.14%****• CTC interpretation should be accomplished only by those trained according to American Gastroenterological Association<sup>5</sup> or American College of Radiology (ACR)<sup>6</sup> guidelines****• Procedure quality should be tracked and assured using current ACR practice guidelines for patient preparation, image acquisition, study interpretation and reporting**

<sup>5</sup>See [American Gastroenterological Association CT Colonography Standards](#).

<sup>6</sup>See [American College of Radiology Practice Guideline for the Performance of Computed Tomography \(CT\) Colonography in Adults](#).

<sup>7</sup>Currently there is not consensus on the use of CT colonography as a primary screening modality and it is evolving with regards to recommended/ programmatic frequency, polyp size leading to referral for colonoscopy, and protocol for evaluating extra-colonic lesions. However, the data available suggests, if CT colonography is negative/no polyps, then repeat CT colonography in 5 y and if positive/polyps lesions, colonoscopy should be performed.

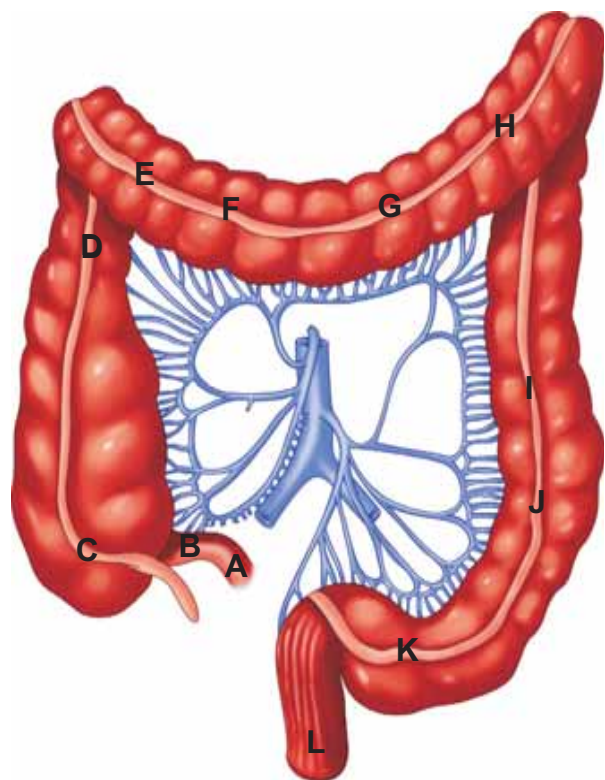
**Note:** All recommendations are category 2A unless otherwise indicated.

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## DEFINITIONS OF COMMON COLORECTAL RESECTIONS

The extent of colorectal resection depends upon the location of the tumor, any underlying condition (eg, inflammatory bowel disease, hereditary syndrome, etc.), and the vascular supply to the colorectum.

Definitions of common colorectal resections are as follows:<sup>1</sup>



A → C	Ileocectomy
A → D	Ascending colectomy
A → F	Right hemicolectomy
A → G	Extended right hemicolectomy
E → H	Transverse colectomy
G → I	Left hemicolectomy
F → I	Extended left hemicolectomy
J → K	Sigmoid colectomy
A → J	Subtotal colectomy
A → K	Total colectomy
K → L	Low Anterior Resection with sphincter preservation
K → L	Abdominoperineal resection without sphincter preservation

<sup>1</sup>Adapted and reprinted with permission from Bullard KM and Rothenberger DA. (2005). Colon, Rectum, and Anus. In Brunicaudi C (Ed.) Schwartz's Principles of Surgery, 8th Edition, page 1069. McGraw Hill: New York, NY.

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## CRITERIA FOR FURTHER RISK EVALUATION FOR HIGH RISK SYNDROMES

Individual meeting the Revised Bethesda Guidelines<sup>a</sup> ([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<sup>b,c</sup>

- 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<sup>b</sup>
- 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<sup>d</sup> ([See PJS-1](#))
- Juvenile Polyposis Syndrome<sup>d</sup> ([See JPS-1](#))
- Hyperplastic Polyposis Syndrome ([See HPP-1](#))
- No syndromes, but familial risk present → [See Positive Family History \(CSCR-6\)](#)

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

<sup>b</sup>[See Obtaining a Comprehensive Risk Assessment for Hereditary Colorectal Cancer \(HRS-A\)](#).

<sup>c</sup>A 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.

<sup>d</sup>Referral to a specialized team is recommended.

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OBTAINING A COMPREHENSIVE ASSESSMENT FOR HEREDITARY COLORECTAL CANCER

**Family History of Colorectal Cancer and Expanded Pedigree**

- It is essential to obtain a detailed family history, including:
    - ▶ Parents
    - ▶ Children
    - ▶ Siblings/half-siblings
    - ▶ Aunts and uncles
    - ▶ Grandparents
    - ▶ Great-grandparents
    - ▶ Cousins
    - ▶ Nieces and nephews
- [See Common Pedigree Symbols \(HRS-A 2 of 3\)](#)  
and  
[Pedigree: First-, Second-, and Third-degree Relatives of Proband \(HRS-A 3 of 3\)](#)
- Minimal data set on each relative:
    - ▶ Current age and age at diagnosis of cancer (medical record documentation of cancer strongly encouraged)
    - ▶ Age/availability of tumor sample and cause of death
    - ▶ Type of cancer (note multiple primaries)
    - ▶ Ethnicity/country of origin
    - ▶ Consanguinity
    - ▶ Suspected colon cancer syndromes and additional syndrome-specific features (eg, Muir-Torre, Turcot, Peutz-Jeghers, juvenile polyposis)<sup>1</sup>
    - ▶ All other inherited conditions and birth defects

**Detailed Medical and Surgical History**

- Polyps
- Inflammatory bowel disease
- Inherited syndromes:
  - ▶ Lynch syndrome
    - ◊ Muir-Torre syndrome
  - ▶ FAP and associated syndromes
    - ◊ Attenuated FAP
    - ◊ Gardner syndrome
    - ◊ Turcot syndrome
  - ▶ MYH-associated polyposis (MAP)
  - ▶ Peutz-Jeghers syndrome
  - ▶ Juvenile polyposis syndrome
  - ▶ PTEN-associated syndromes
    - ◊ Cowden syndrome
    - ◊ Bannayan-Riley-Ruvalcaba syndrome
  - ▶ Pathology verification strongly encouraged

**Directed examination for related manifestations**

- Colonoscopy
- Esophagogastroduodenoscopy
- Eye examination
- Skin, soft-tissue, and bone examination
- Oral examination

<sup>1</sup>Burt R and Neklason DW. Genetic testing for inherited colon cancer. Gastroenterology 2005;128:1696-1716.

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## OBTAINING A COMPREHENSIVE ASSESSMENT FOR HEREDITARY COLORECTAL CANCER

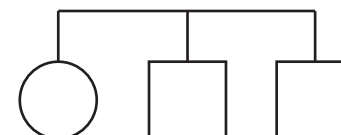
### COMMON PEDIGREE SYMBOLS<sup>2</sup>



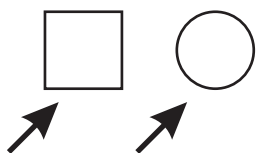
Male, Female



Mating



Sibship



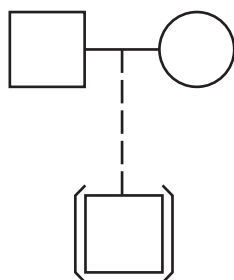
Proband  
(patient initiating  
genetic workup)



Affected  
with trait



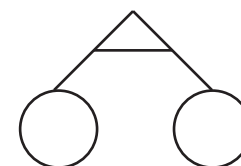
Deceased



Adopted into  
a family



Dizygotic  
twins



Monozygotic  
twins

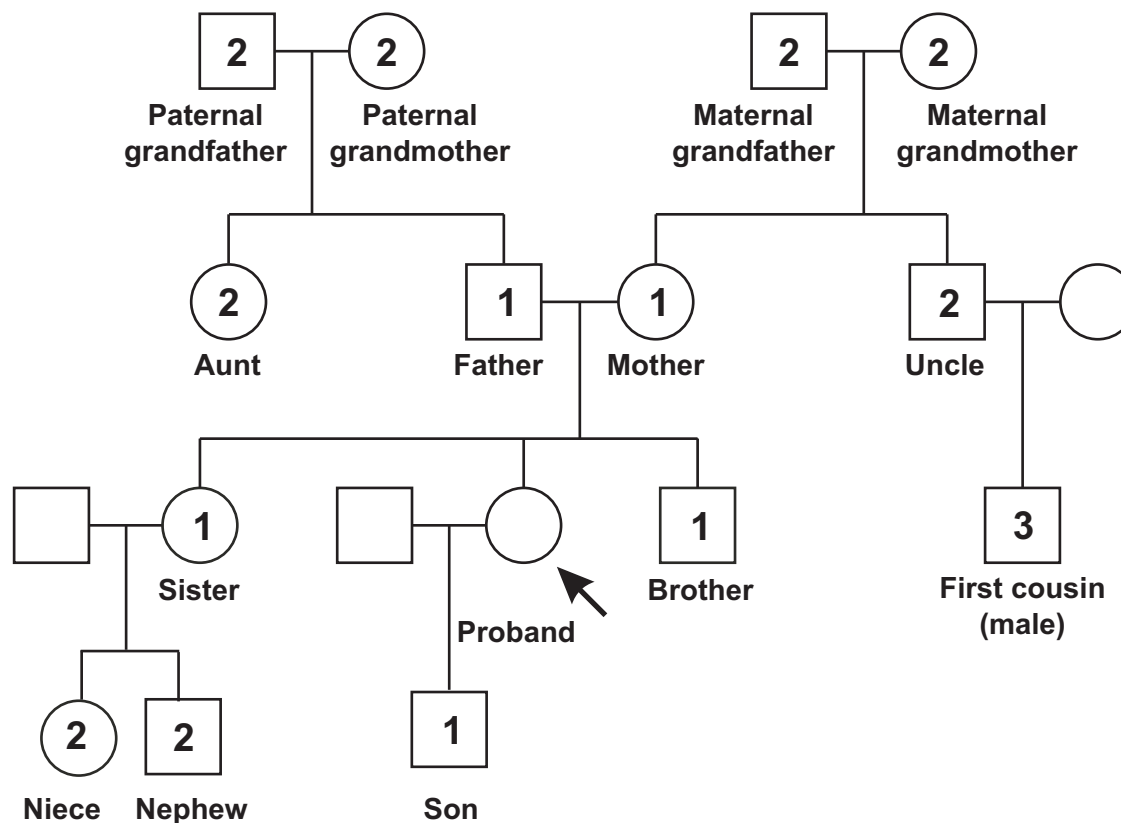
[See Pedigree: First-, Second- and Third-Degree Relatives of Proband \(HRS-A 3 of 3\)](#)

<sup>2</sup>Bennett RL, Steinhaus KA, Uhrich SB, et al. Recommendations for standardized human pedigree nomenclature. Am J Hum Genet 1995;56:745-752.

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## OBTAINING A COMPREHENSIVE ASSESSMENT FOR HEREDITARY COLORECTAL CANCER

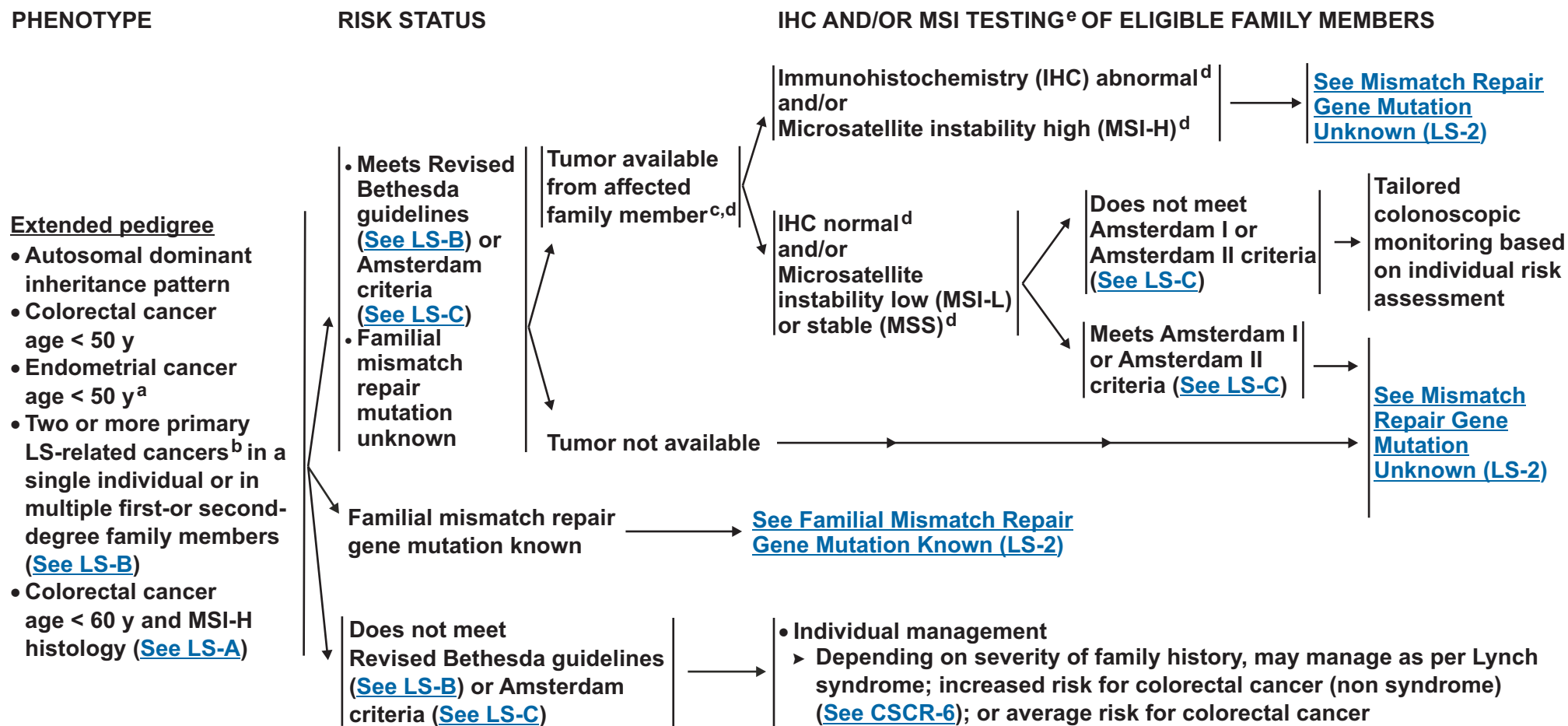
### PEDIGREE: FIRST-, SECOND-, AND THIRD-DEGREE RELATIVES OF PROBAND<sup>3</sup>



[See Common Pedigree Symbols \(HRS-A 2 of 3\)](#)

<sup>3</sup>First-degree relatives: parents, siblings, and children;  
Second-degree relatives: grandparents, aunts, uncles, nieces, nephews, and half-siblings;  
Third-degree relatives: great-grandparents and cousins.

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

<sup>b</sup>LS-related tumors 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 in Muir-Torre syndrome.

<sup>c</sup>With informed consent as designated by local practice and IRB standards.

<sup>d</sup>An alternative and efficient approach when a family meets the Amsterdam Criteria (See LS-C) is to proceed directly to genetic testing (whether or not tumor tissue is available) in the person most likely to carry the putative genetic mutation (usually the youngest living person in the family with colon or other Lynch syndrome cancer). If a mutation is not found by genetic testing, then one may consider IHC and/or MSI testing of colon cancer tissue due to the suboptimal detection rate of genetic testing.

<sup>e</sup>See Principles of IHC and MSI testing for Lynch Syndrome (LS-A).

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**GENETIC COUNSELING/TESTING OF ELIGIBLE FAMILY MEMBERS**

**Mismatch repair gene mutation unknown**

- Consider genetic testing of affected family member if possible to find a disease causing mutation
  - ▶ Genetic testing should begin with the gene most likely to harbor the mutation based on IHC results. If IHC testing cannot be performed or is uninformative, first test MSH2 or MLH1 and then MSH6 or PMS2 if a mutation is not found in the first two genes

**MUTATION STATUS**

Not tested

No familial mutation found

Mutation of unknown significant found

Positive familial mutation MLH1, MSH2, MSH6, or PMS2 found

Tailored surveillance based on individual and family risk assessment

- [See Lynch Syndrome Surveillance and Follow-up \(LS-3\)](#) and
- See pathway below to consider genetic testing for at-risk family members

- Familial mismatch repair gene mutation known**
- Consider genetic testing of at-risk family member<sup>f</sup> to find a disease causing mutation

Positive gene test (mutation present)

Not tested

Negative gene test (mutation not present)

[See Lynch Syndrome Surveillance and Follow-up \(LS-3\)](#)

Average risk screening ([See CSCR-2](#))

<sup>f</sup>At-risk family member can be defined as a first-degree relative of an affected individual and/or proband. If a first-degree relative is unavailable or unwilling to be tested, more distant relatives should be offered testing for the known mutation in the family.

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**SURVEILLANCE<sup>g,h</sup>**

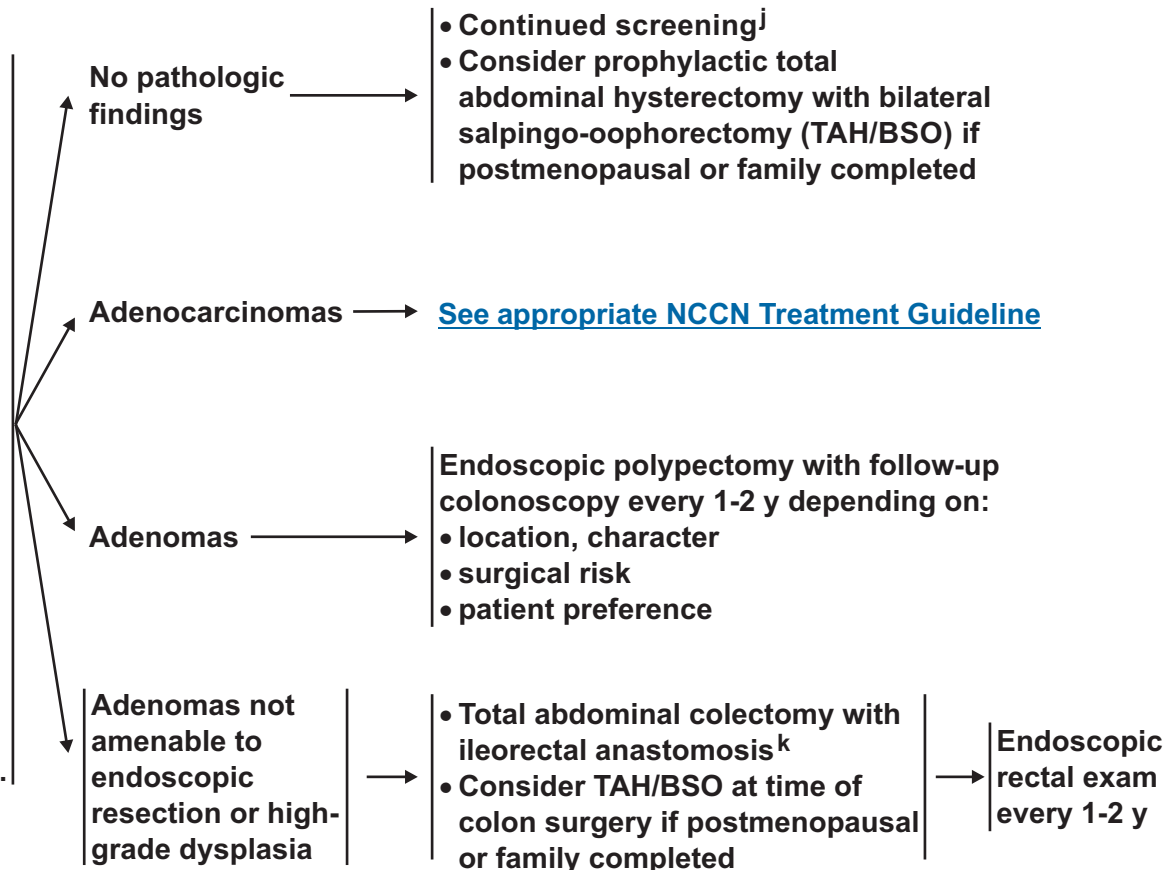
**Colon cancer:**

- Colonoscopy<sup>i</sup> at age 20-25 y or 10 y prior to the youngest age at diagnosis in the family, whichever comes first and repeat every 1-2 y.

**Extra-colonic:**

- Endometrial and ovarian cancer:
  - ▶ Consider referral to gynecologic oncologist for screening for gynecologic tumors
  - ▶ Encourage patient education and prompt response to endometrial cancer symptoms.
  - ▶ Prophylactic hysterectomy and bilateral salpingo-oophorectomy is a risk reducing option for women who have completed childbearing.
- Gastric and duodenal cancer: Consider upper GI endoscopy (including side-viewing examination) at age 25-30 y and repeat every 1-3 y depending on findings.
- Urothelial cancer: Consider annual urinalysis
- CNS cancer: Annual physical examination; no additional screening recommendations have been made.
- Pancreatic cancer: No recommendations have been made.

**FOLLOW-UP**



<sup>g</sup>See [Cancer Risk in Individuals with HNPCC up to Age 70 Years Compared to the General Population \(LS-D\)](#).

<sup>h</sup>Other than colon and endometrial cancer, screening recommendations are expert opinion rather than evidence based.

<sup>i</sup>Given the later average age of onset for MSH6 mutation carriers, consider starting colonoscopy at the age of 30-35 y or 10 y prior to the youngest age of diagnosis in the family, whichever comes first.

<sup>j</sup>May consider subtotal colectomy if patient is not a candidate for optimal screening.

<sup>k</sup>The type of surgical procedure chosen should be based on individual considerations and discussion of risk. Surgical management is evolving. [See Definitions of Common Colorectal Resections \(CSCR-B\)](#).

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## PRINCIPLES OF IHC AND MSI TESTING FOR LYNCH SYNDROME

Immunohistochemistry (IHC) and microsatellite instability (MSI) analyses are screening tests (either by themselves or in conjunction), typically done on colon cancer tissue to identify individuals at risk for Lynch syndrome (LS).

**Immunohistochemistry**

- IHC refers to staining tumor tissue for protein expression of the four mismatch genes known to be mutated in Lynch syndrome: MLH1, MSH2, MSH6, and PMS2. A normal IHC test implies all four mismatch repair proteins are normally expressed and thus no underlying mismatch repair gene mutation is present. An abnormal test means that one of the proteins is not expressed and an inherited mutation may be present in the related gene. Loss of protein expression by IHC in any one of the mismatch repair genes guides genetic testing (mutation detection) to the gene where protein expression is not observed.
- Ten to 15% of sporadic colon cancers exhibit abnormal IHC, often due to abnormal methylation of the MLH1 gene promoter, but occasionally due to an inherited mutation of one of the mismatch repair genes. Thus the presence of an abnormal IHC test increases the possibility of Lynch syndrome but does not make a definitive diagnosis. Genetic testing of peripheral blood DNA to find a disease causing mutation of one of the mismatch repair genes should then be done. Most patients will be found to have sporadic colon cancer and not a germline mutation. Those with a germline mutation are then identified as Lynch syndrome patients.
- There is a 5-10% false negative rate with IHC testing.

**Microsatellite instability**

- MSI-H (microsatellite instability-high) in tumors refers to changes in two or more of the five National Cancer Institute-recommended panels of microsatellite markers in tumor tissue. Its significance, use and implications are similar to that of IHC although the tests are slightly complementary.
- There is a 5-10% false negative rate with MSI testing.
- The Bethesda Criteria were developed in response to the emerging understanding of the pathologic spectrum and molecular characteristics of LS-related tumors. These criteria were intended to help identify colon cancer patients whose tumors should be tested for MSI, thereby identifying patients with a greater chance of having LS. The revised Bethesda Guidelines ([see LS-B](#)) are now widely used to identify tumors that should be tested for mismatch repair defects, either by MSI and/or IHC analysis. Although more sensitive than the Amsterdam criteria ([See LS-C](#)), up to 30% of patients with Lynch syndrome fail to meet even the revised Bethesda guidelines.
- Recently, IHC and/or MSI screening of all colorectal cancers and endometrial cancer regardless of age at diagnosis or family history, has been implemented at some centers to identify individuals at risk for Lynch syndrome.

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**THE REVISED BETHESDA GUIDELINES**  
**FOR TESTING COLORECTAL TUMORS FOR MICROSATELLITE INSTABILITY (MSI)<sup>1</sup>**

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

- Colorectal cancer<sup>2</sup> diagnosed in a patient who is less than 50 years of age.
- Presence of synchronous, or metachronous Lynch syndrome-associated tumors,<sup>3</sup> regardless of age.
- Colorectal cancer with the MSI-H histology<sup>4</sup> 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,<sup>3</sup> 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 cancers<sup>3</sup> regardless of age.

<sup>1</sup>Adapted 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(4):261-268.

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

<sup>3</sup>LS-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.

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

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**MINIMUM CRITERIA FOR CLINICAL DEFINITION OF HNPCC**  
**(AMSTERDAM CRITERIA I)**<sup>1,2</sup>

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)**<sup>1,2</sup>

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.

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

<sup>2</sup>Approximately 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.

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Cancer Risk in Individuals with HNPCC up to Age 70 Years Compared to the General Population<sup>1</sup>

Cancer	General Population Risk	HNPCC	
		Risks	Mean Age of Onset
Colon	5.5%	80%	44 years
Endometrium	2.7%	20%-60%	46 years
Stomach	<1%	11%-19%	56 years
Ovary	1.6%	9%-12%	42.5 years
Hepatobiliary tract	<1%	2%-7%	Not reported
Urinary tract	<1%	4%-5%	~55 years
Small bowel	<1%	1%-4%	49 years
Brain/central nervous system	<1%	1%-3%	~50 years

<sup>1</sup>Kohlmann W, Gruber SB (Updated November 29, 2006). Hereditary Non-Polyposis Colon Cancer. In: GeneReviews at GeneTests: Medical Genetics Information Resource (database online). Copyright, University of Washington, Seattle. 1997-2009. Available at <http://www.genetests.org>. Accessed October 21, 2009.

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**PHENOTYPE**

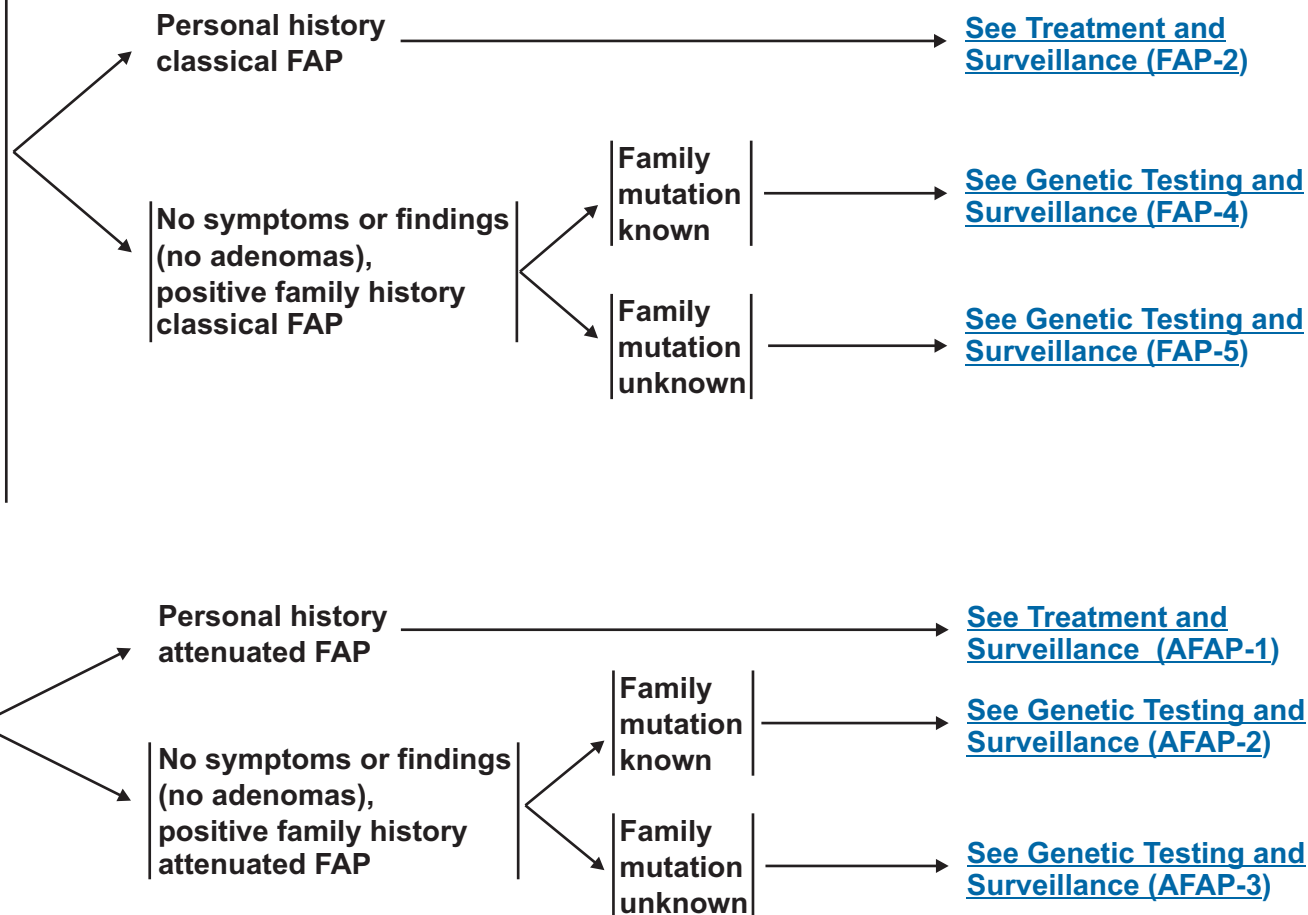
**Classical familial adenomatous polyposis (FAP):**

- Presence of  $\geq 100$  polyps<sup>a</sup> (sufficient for clinical diagnosis) or fewer polyps at younger ages, especially in a family known to have FAP
- Autosomal dominant inheritance<sup>b</sup> (except with de novo mutation)
- Possible associated additional findings
  - Congenital hypertrophy of retinal pigment epithelium (CHRPE)
  - Osteomas, supernumerary teeth, odontomas
  - Desmoids, epidermoid cysts
  - Duodenal and other small bowel adenomas
  - Gastric fundic gland polyps
- Increased risk of medulloblastoma, papillary carcinoma of the thyroid (<2%), hepatoblastoma (usually  $\leq$  age 5 y)
- Pancreatic cancers (<2%)
- Gastric cancers (<1%)

**Attenuated FAP**

- Presence of < 100 adenomas<sup>a</sup> (average of 30 polyps)
- Frequent right-sided distribution of polyps
- Adenomas and cancers at age older than classic FAP (mean age > 50)
- Upper GI findings and thyroid cancer risk is similar to classic FAP
- Other extraintestinal manifestations, including CHRPE and desmoids are rare

**RISK ASSESSMENT**



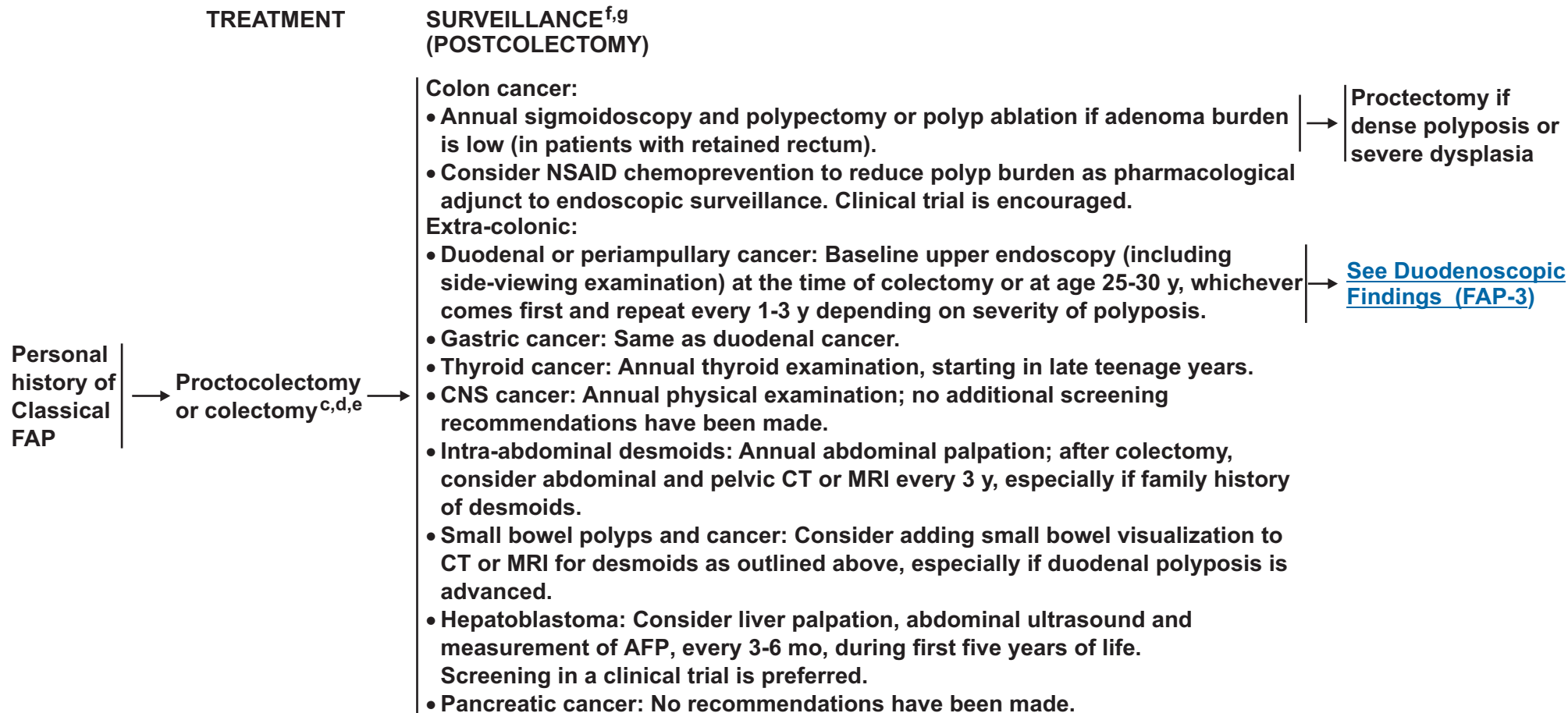
<sup>a</sup>Individuals with 100 or more polyps occurring at older ages (35 to 40 years or older) may be found to have attenuated FAP.

<sup>b</sup>Thirty percent spontaneous new mutation rate, thus family history may be negative. Especially noteworthy if onset < age 50 y.

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**CLASSICAL FAP TREATMENT AND SURVEILLANCE: PERSONAL HISTORY**



<sup>c</sup>APC genetic testing is recommended in a proband to confirm a diagnosis of FAP and allow for mutation specific testing in other family members. Additionally, knowing the location of the mutation in the APC gene can be helpful for predicting severity of polyposis, rectal involvement, and desmoid tumors.

<sup>d</sup>[See Surgical Options for Treating the Colon And Rectum in Patients with FAP \(FAP-A\)](#).

<sup>e</sup>Timing of colectomy in patients under age 18 y is not established. In patients under 18 y with mild polyposis and without family history of early cancer or severe genotype, the timing of colectomy can be individualized. Annual colonoscopy if surgery is delayed.

<sup>f</sup>It is recommended that patients be managed by physicians or centers with expertise in FAP and that management be individualized to account for genotype, phenotype, and personal considerations.

<sup>9</sup>Other than colon cancer, screening recommendations are expert opinion rather than evidence based.

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

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## DUODENOSCOPIC FINDINGS

SURVEILLANCE<sup>h</sup>

Stage 0,  
No polyposis

Repeat endoscopy every 4 y

Stage I,  
Minimal polyposis (1-4 tubular adenomas, size 1-4 mm)

Repeat endoscopy every 2-3 y

Stage II,  
Mild polyposis (5-19 tubular adenomas, size 5-9 mm)

Repeat endoscopy every 1-3 y

Stage III,  
Moderate polyposis ( $\geq 20$  lesions, or size  $\geq 1$  cm)

Repeat endoscopy every 6-12 mo

Stage IV,  
Dense polyposis or high grade dysplasia

- Surgical evaluation
- Expert surveillance every 6-12 mo
- Complete mucosectomy or duodenectomy, or Whipple procedure if duodenal papilla is involved

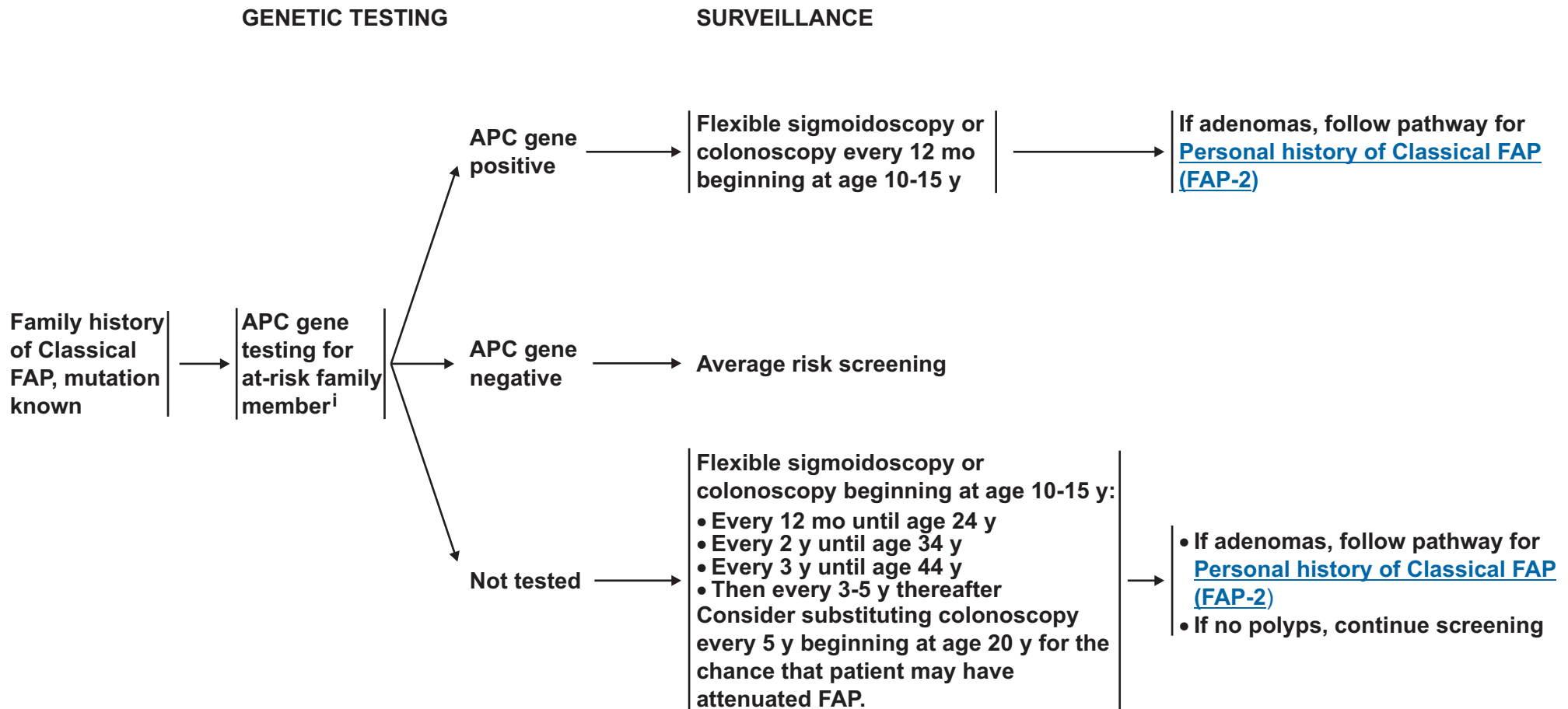
<sup>h</sup>Duodenal Surveillance:

- It is recommended that patients be managed by physicians or centers with expertise in FAP and that management be individualized to account for genotype, phenotype, and personal considerations, including potential risks and benefits. Management that includes endoscopic treatment may require shorter intervals.
- Recommend examination with side-viewing endoscope, use of Spigelman's or other standardized staging, and extensive biopsy of dense lesions to evaluate for advanced histology. More intensive surveillance and/or treatment is required in patients with large or villous adenomas, and with advancing age  $> 50$  y. Surgical counseling is advisable for patients with stage IV polyposis. (Spigelman AD, Williams CB, Talbot IC et al. Upper gastrointestinal cancer in patients with familial adenomatous polyposis. *Lancet* 1989;2(8666): 783-785).
- Endoscopic treatment options include endoscopic papillectomy in addition to excision or ablation of resectable large ( $> 1$  cm) or villous adenomas, as well as mucosectomy of resectable advanced lesions, including contained high grade dysplasia, to potentially avert surgery while observing pathology guidelines for adequate resection.
- Surgery is recommended for invasive carcinoma as well as dense polyposis or high grade dysplasia that cannot be managed endoscopically.

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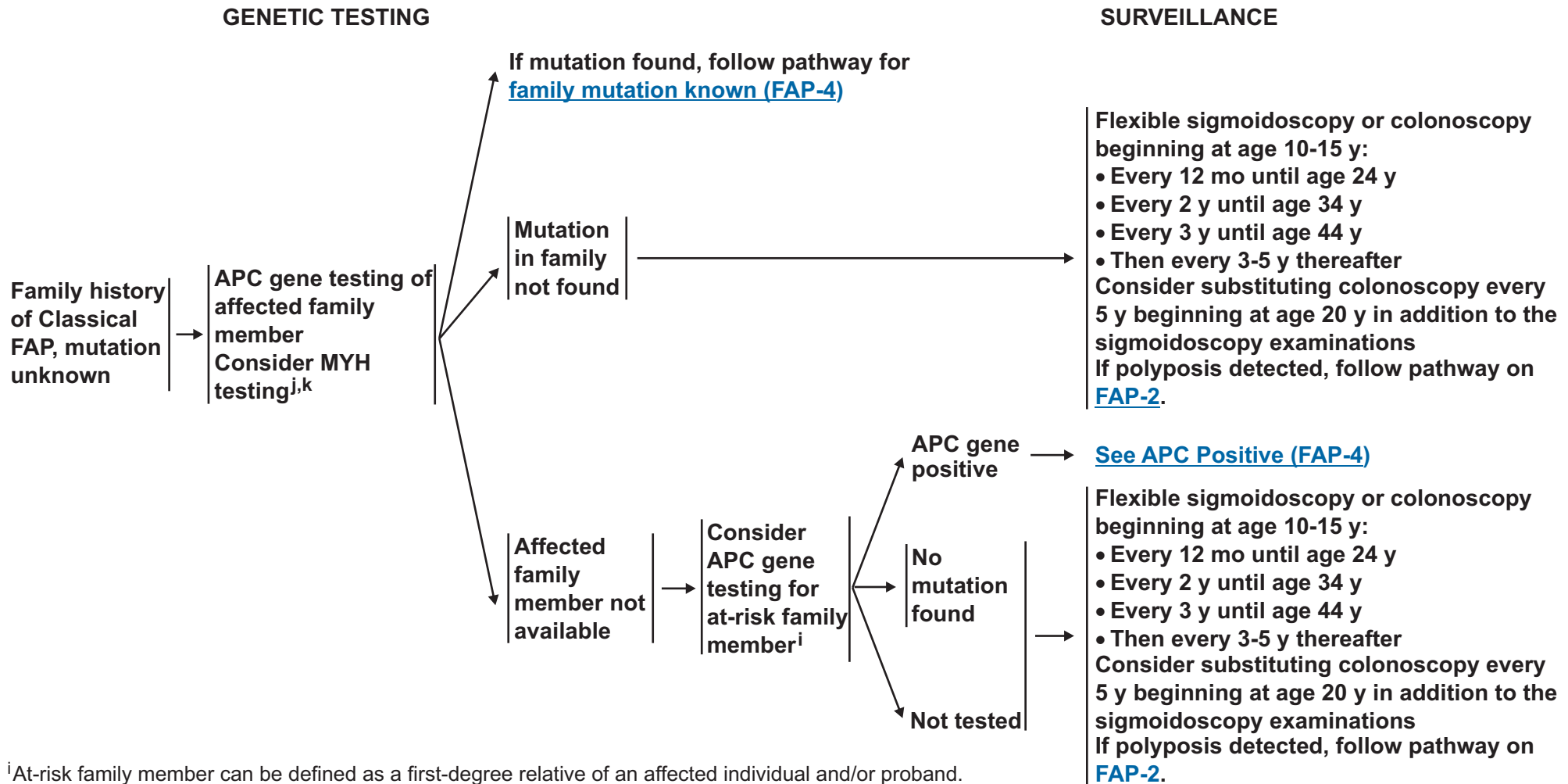
CLASSICAL FAP GENETIC TESTING AND SURVEILLANCE: FAMILY HISTORY OF CLASSICAL FAP MUTATION KNOWN



<sup>i</sup>At-risk family member can be defined as a first-degree relative of an affected individual and/or proband. If a first-degree relative is unavailable or unwilling to be tested, more distant relatives should be offered testing for the known mutation in the family.

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CLASSICAL FAP GENETIC TESTING AND SURVEILLANCE: FAMILY HISTORY OF CLASSICAL FAP  
MUTATION UNKNOWN



<sup>i</sup>At-risk family member can be defined as a first-degree relative of an affected individual and/or proband.

<sup>j</sup>See [MYH-Associated Polyposis \(MAP-1\)](#).

<sup>k</sup>When polyposis is present in a single person with negative family history, consider testing for a *de novo* APC mutation; if negative, follow with testing for MYH. When family history is positive only for a sibling, consider recessive inheritance and test for MYH first. In a polyposis family with clear autosomal dominant inheritance, and absence of APC mutation, MYH testing is unlikely to be informative. Such families are treated according to the polyposis phenotype, including classical or attenuated FAP.

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## SURGICAL OPTIONS FOR TREATING THE COLON AND RECTUM IN PATIENTS WITH FAP

**TOTAL ABDOMINAL COLECTOMY WITH ILEORECTAL ANASTOMOSIS (TAC/IRA)**

- **Indications:**
  - ▶ Asymptomatic patient with few (<20) rectal polyps and mild colonic disease (<100) polyps
  - ▶ Attenuated FAP with rectal sparing
- **Contraindications:**
  - ▶ Curable cancer in colon or rectum
  - ▶ Severe rectal or colon disease (size or number of polyps)
  - ▶ Patient not reliable for follow-up surveillance of retained rectum
- **Advantages:**
  - ▶ Technically straightforward
  - ▶ Relatively low complication rate
  - ▶ Good function outcome
  - ▶ No permanent or temporary stoma
  - ▶ Avoids risk of proctectomy (sexual or bladder dysfunction)

**TOTAL PROCTOCOLECTOMY WITH END ILEOSTOMY (TPC/EI)**

- **Indications:**
  - ▶ Very low, advanced rectal cancer
  - ▶ Inability to perform IPAA
  - ▶ Patient with IPAA with unacceptable function
  - ▶ Patient with contraindication to IPAA
- **Advantages:**
  - ▶ Removes risk of colorectal cancer
  - ▶ One operation
- **Disadvantages:**
  - ▶ Risks of proctectomy
  - ▶ Permanent stoma
  - ▶ May discourage family members from seeking evaluation for fear of permanent stoma

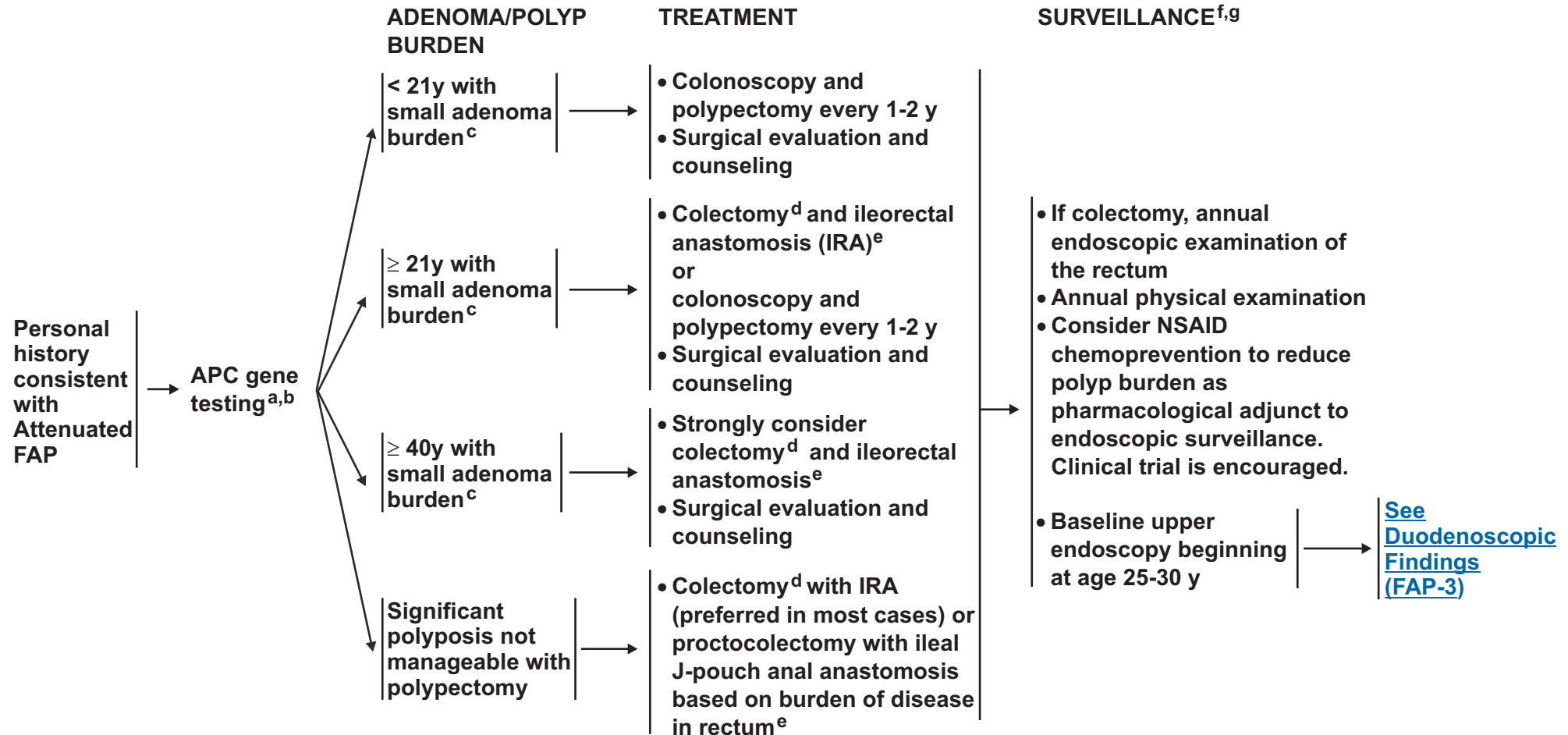
**TOTAL PROCTOCOLECTOMY WITH ILEAL POUCH ANAL ANASTOMOSIS (TPC/IPAA)**

- **Indications:**
  - ▶ After TAC/IRA with unstable rectum
  - ▶ Patient unreliable for follow-up after TAC/IRA
  - ▶ Severe disease in colon and/or rectum
  - ▶ Curable colon or rectal cancer
- **Contraindications:**
  - ▶ Incurable cancer
  - ▶ Intra-abdominal desmoid
  - ▶ Advanced low rectal cancer
  - ▶ Patient not a candidate for IPAA (ie, concomitant Crohn's disease, anal sphincter dysfunction, etc)
- **Advantages:**
  - ▶ Negligible risk of rectal cancer
  - ▶ No permanent stoma
  - ▶ Reasonable bowel function
- **Disadvantages:**
  - ▶ Complex operation
  - ▶ Usually involves temporary stoma
  - ▶ Risks of proctectomy (sexual or bladder dysfunction)
  - ▶ Functional results can be unpredictable

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ATTENUATED FAP TREATMENT AND SURVEILLANCE: PERSONAL HISTORY



<sup>a</sup>APC gene testing is recommended in a proband to confirm a diagnosis of AFAP and allow for mutation specific testing in other family members. Additionally, knowing the location of the APC mutation can be helpful in determining extra-colonic cancer risks in affected individuals.

<sup>b</sup>MYH testing if APC mutation not found ([See MAP-1](#)).

<sup>c</sup>Small adenoma burden is defined (somewhat arbitrarily) as fewer than 20 adenomas, all < 1 cm in diameter and none with advanced histology, so that colonoscopy with polypectomy can be used to effectively eliminate the polyps. Colectomy may be indicated before this level of polyp profusion, especially if colonoscopy is difficult. Surgery is strongly advised when polyp burden is

greater than 20, some polyps have reached a size > 1 cm, or advanced histology is encountered in any polyp.

<sup>d</sup>[See Surgical Options for Treating the Colon And Rectum in Patients with FAP \(FAP-A\)](#).

<sup>e</sup>Earlier surgical intervention should be considered in patients with family history of cancer under age 40 or noncompliant patients.

<sup>f</sup>It is recommended that patients be managed by physicians or centers with expertise in FAP and that management would be individualized to account for genotype, phenotype, and personal considerations.

<sup>9</sup>Surveillance for upper GI findings for attenuated FAP is similar to classical FAP.

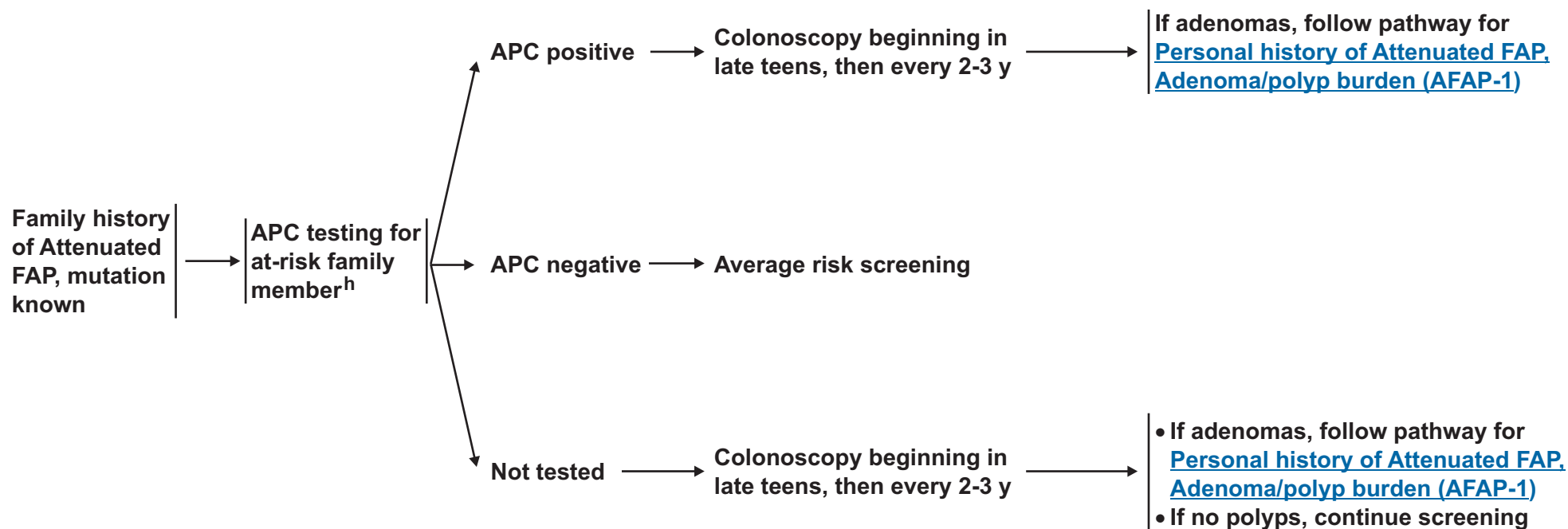
Note: All recommendations are category 2A unless otherwise indicated.

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ATTENUATED FAP GENETIC TESTING AND SURVEILLANCE: FAMILY HISTORY OF ATTENUATED FAP MUTATION KNOWN

GENETIC TESTING

SURVEILLANCE



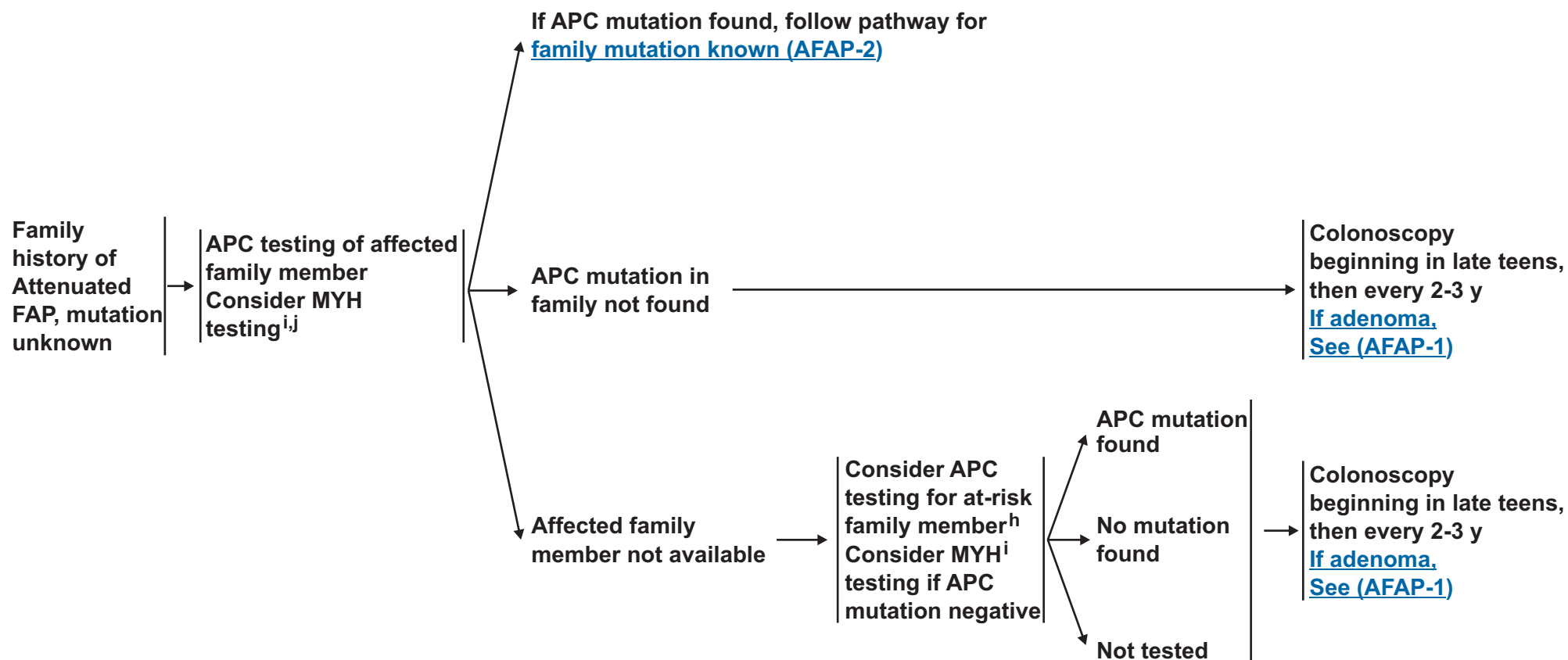
<sup>h</sup>At-risk family member can be defined as a first-degree relative of an affected individual and/or proband. If a first-degree relative is unavailable or unwilling to be tested, more distant relatives should be offered testing for the known mutation in the family.

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ATTENUATED FAP GENETIC TESTING AND SURVEILLANCE: FAMILY HISTORY OF ATTENUATED FAP MUTATION UNKNOWN

GENETIC TESTING

SURVEILLANCE



<sup>h</sup>At-risk family member can be defined as a first-degree relative of an affected individual and/or proband.

<sup>i</sup>See [MYH-Associated Polyposis \(MAP-1\)](#).

<sup>j</sup>When polyposis is present in a single person with negative family history, consider testing for a *de novo* APC mutation; if negative, follow with testing for MYH. When family history is positive only for a sibling, consider recessive inheritance and test for MYH first. In a polyposis family with clear autosomal dominant inheritance, and absence of APC mutation, MYH testing is unlikely to be informative. Such families are treated according to the polyposis phenotype, including classical or attenuated FAP.

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## PHENOTYPE

## RISK ASSESSMENT

**MYH -associated polyposis (MAP)**

- Polyposis or colon cancers consistent with autosomal recessive inheritance (ie, parents unaffected, siblings affected)
- Fewer than 100 adenomas (range 0-100's and uncommonly > 1000)
- Adenomas and colorectal cancer at age older than classical FAP (median CRC age > 50 y)
- Duodenal adenomas are uncommon
- Attenuated polyposis with negative APC gene mutation

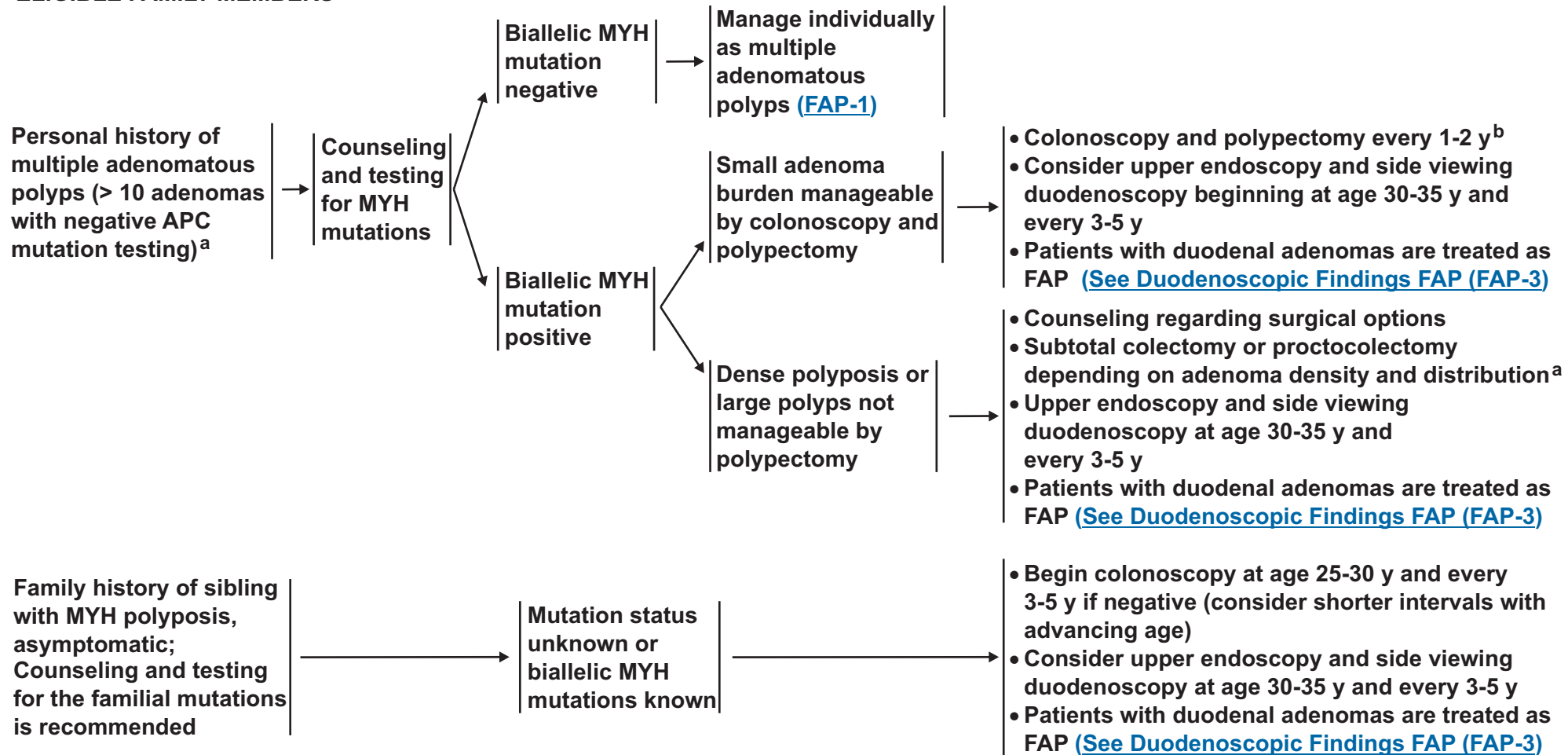
Personal history  
or  
Family history  
(ie, known mutation in patient or sibling)

[See MYH-Associated Polyposis \(MAP-2\)](#)

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GENETIC COUNSELING/TESTING OF ELIGIBLE FAMILY MEMBERS



<sup>a</sup>When polyposis is present in a single person with negative family history, consider testing for a *de novo* APC mutation; if negative, follow with testing for MYH. When family history is positive only for a sibling, consider recessive inheritance and test for MYH first. In a polyposis family with clear autosomal dominant inheritance, and absence of APC mutation, MYH testing is unlikely to be informative. Such families are treated according to the polyposis phenotype, including classical or attenuated FAP.

<sup>b</sup>In patients with MYH, the absolute risk of colorectal cancer and the role of surgery and endoscopically manageable adenomas is not known. The lifetime colon cancer risk may be very high.

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**Peutz-Jeghers syndrome (PJS) Definition:**<sup>1,2</sup>

- A clinical diagnosis of PJS can be made when an individual has two or more of the following features:
  - ▶ Two or more Peutz-Jeghers-type hamartomatous polyps of the small intestine
  - ▶ Mucocutaneous hyperpigmentation of the mouth, lips, nose, eyes, genitalia, or fingers
  - ▶ Family history of PJS

**Surveillance considerations:**

- The majority of cases occur due to mutations in the STK11(LKB1) gene and clinical genetic testing is available.
- Referral to a specialized team is recommended and participation in clinical trials is especially encouraged.
- Surveillance should begin at the approximate ages on [PJS-2](#), if symptoms have not already occurred and any early symptoms should be evaluated thoroughly.
- The surveillance guidelines ([See PJS-2](#)) for the multiple organs at risk for cancer are provisional, but may be considered in view of the cancer risks in PJS and the known utility of the tests. There is limited data regarding the efficacy of various screening modalities in PJS.

[See Cancer Risk and Surveillance Guidelines \(PJS-2\)](#)

<sup>1</sup>Tomlinson IP, Houlston RS: Peutz-Jeghers syndrome. J Med Genet 1997; 34(12):1007-1011.

<sup>2</sup>Due to the rarity of the syndrome and complexities of diagnosing and managing individuals with Peutz-Jeghers syndrome, referral to a specialized team is recommended.

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

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Peutz-Jeghers Syndrome: Cancer Risk and Surveillance Guidelines

<u>Site (% risk)</u>	<u>Screening procedure and interval</u>	<u>Initiation age (y)</u>
Breast (45-50%)	<ul style="list-style-type: none"> <li>• Mammogram and breast MRI annually</li> <li>• Clinical breast exam every 6 mo</li> </ul>	~ 25 y
Colon (39%)	Colonoscopy every 2-3 y	~ Late teens
Pancreas (11-36%)	<ul style="list-style-type: none"> <li>• Magnetic resonance cholangiopancreatography and/or endoscopic ultrasound every 1-2 years</li> <li>• CA 19-9 at similar intervals</li> </ul>	~ 30 y
Stomach (29%) and small intestine (13%)	Upper endoscopy every 2 to 3 years and small bowel visualization (CT enterography, small bowel enteroclysis) every 2-3 years, or with symptoms	~ 10 y
Ovary (18-21%), cervix 10%, uterus (9%)	<ul style="list-style-type: none"> <li>• Pelvic examination and PAP smear annually</li> <li>• Consider transvaginal ultrasound</li> </ul>	~ 18-20 y
Testes	Annual testicular exam and observation for feminizing changes	~ 10 y
Lung (15-17%)	No specific recommendations have been made. Provide education about symptoms and smoking cessation.	

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

**Juvenile Polyposis Syndrome (JPS) Definition:**<sup>1</sup>

- A clinical diagnosis of JPS is considered in an individual who meets at least one of the following criteria:
  - ▶ At least three to five juvenile polyps of the colon
  - ▶ Multiple juvenile polyps found throughout the gastrointestinal tract
  - ▶ Any number of juvenile polyps in an individual with a family history of JPS

**Surveillance considerations:**

- Some JPS cases occur due to mutations in the BMPR1A and SMAD4 genes and clinical genetic testing is available.
- Referral to a specialized team is recommended and participation in clinical trials is especially encouraged.
- Surveillance should begin at these approximate ages listed below, if symptoms have not already occurred and any early symptoms should be evaluated thoroughly.
- The following surveillance guidelines for the multiple organs at risk for cancer may be considered. Limited data exist regarding the efficacy of various screening modalities in juvenile polyposis syndrome.

**Juvenile Polyposis Syndrome: Cancer Risk and Surveillance Guidelines**

<u>Site (% risk)</u>	<u>Screening Procedure and Interval</u>	<u>Initiation age (y)</u>
Colon (40-50%)	Colonoscopy: repeat annually if polyps are found and if no polyps, repeat every 2-3 years	~ 15 y
Stomach (21% if multiple polyps)	Upper endoscopy: repeat annually if polyps are found and if no polyps, repeat every 2-3 years	~ 15 y
Small intestine (rare, undefined)	No recommendations have been made	
Pancreas (rare, undefined)	No recommendations have been made	

<sup>1</sup>Due to the rarity of the syndrome and complexities of diagnosing and managing individuals with juvenile polyposis syndrome, referral 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.

**Hyperplastic Polyposis Syndrome Definition:**<sup>1</sup>

- A clinical diagnosis of hyperplastic polyposis is considered in an individual who meets at least one of the following criteria:
  - ▶ > 20-30<sup>2</sup> cumulative hyperplastic polyps distributed throughout the colon<sup>3</sup>
  - ▶ > 5 hyperplastic polyps proximal to the sigmoid colon with 2 > 1 cm
  - ▶ > 1 hyperplastic polyp proximal to the sigmoid colon and a first degree relative with hyperplastic polyposis
- HPS is rarely inherited

**Surveillance recommendations for individuals with hyperplastic polyposis:**

- Colonoscopy with polypectomy until all polyps  $\geq 5$  mm are removed, then colonoscopy every 1 to 3 years depending on number and size of polyps. Clearing of all polyps is preferable but not always possible.
- Consider surgical referral if colonoscopic treatment and/or surveillance inadequate or if high grade dysplasia occurs.

**Surveillance recommendations for individuals with a family history of hyperplastic polyposis:**

- The risk of colorectal cancer in relatives of individuals with hyperplastic polyposis is still unclear.
- First-degree relatives should be encouraged to undergo average risk screening colonoscopy. Increased screening may be warranted for individuals with a family history of multiple adenomas and/or colorectal cancer.

<sup>1</sup>Sessile serrated polyps, traditional serrated polyps and/or mixed adenomas can be substituted for hyperplastic polyps in all parts of the definition.

<sup>2</sup>The total number of polyps necessary to make a diagnosis of hyperplastic polyposis is unclear. A lower threshold of polyps (> 20) has also been used to make a diagnosis of hyperplastic polyposis.

<sup>3</sup>Multiple hyperplastic polyps localized to the rectal sigmoid is unlikely to be hyperplastic polyposis syndrome.

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**Discussion** To view the most up-to-date discussion, [click here](#).

#### **NCCN Categories of Consensus**

**Category 1:** The recommendation is based on high-level evidence (e.g. randomized controlled trials) and there is uniform NCCN consensus.

**Category 2A:** The recommendation is based on lower-level evidence and there is uniform NCCN consensus.

**Category 2B:** The recommendation is based on lower-level evidence and there is nonuniform NCCN consensus (but no major disagreement).

**Category 3:** The recommendation is based on any level of evidence but reflects major disagreement.

**All recommendations are category 2A unless otherwise noted.**