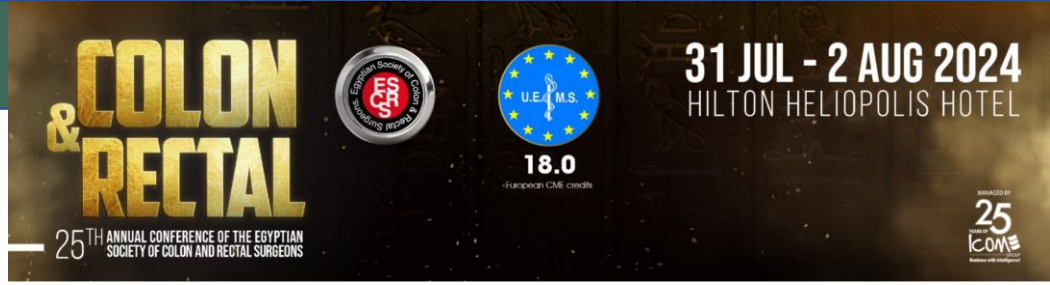

Hereditary Colorectal Cancer, what EVERY! Surgeon should know

Gabriela Moeslein

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@GabrielaMoslein


Adapting
Tech
Evolve
Shake Up
Change
Business
Challenge
Rethinking
Disrupt
Dramatic
Status Quo
Diverging
Technology
PARADIGM SHIFT
Significant
Opportunity
Scientific
Motivation
Marketing
Process
Unique
Computing
Concept
Idea
New
Traditional
Upheaval
Disrupt

"Biology is King; selection of cases is Queen, and the technical details of surgical procedures are princes and princesses of the realm who frequently try to overthrow the powerful forces of the King and Queen, usually to no long-term avail, although with some temporary apparent victories."

Blake Cady, MD (Surgeon) 1997

Impact of Genetics : 3 Scenarios

1. Tumor testing at cancer diagnosis
   - guiding therapy

2. Constitutional testing (blood, saliva etc.) at cancer diagnosis
   - guiding risk managment (surgical strategy)

3. Constitutional testing (blood, saliva etc.) for risk assessment
   - guiding risk managment (surgical strategy)

Scenario 1: Tumor testing at cancer diagnosis

1. Tumor testing at cancer diagnosis
   - guiding therapy

2. Constitutional testing (blood, saliva etc.) at cancer diagnosis
   - guiding risk managment (surgical strategy)

3. Constitutional testing (blood, saliva etc.) for risk assessment
   - guiding risk managment (surgical strategy)

mCRC: Pharmacologic milestones

- 1980: Best supportive care: 5 months median overall survival (OS)
- 1990: Mayo FU/FA: 11 – 14 months OS; ONE drug
- 1994: De Gramont FU/FA: 14 months OS; infusion less toxic
- 1999: Capecitabine: 13 months OS; ONE oral drug
- 2000: FOLFIRI: 17 – 18 months OS; TWO drugs
- 2004: Sequential FOLFIRI and FOLFOX: 20 – 24 months OS; THREE drugs

- 2006: Addition of Avastin and EGFRi: 30 - 36 months OS; FIVE drugs and addition of predictive biomarkers
- 2013: Extended use of Avastin, addition of Panitumumab, Aflibercept & Regorafenib: 36 months OS; EIGHT drugs
- 2016: Addition of Ramucirumab and Lonsurf: 36+ months OS; TEN drugs
- 2018: Addition of Pembrolizumab, Nivolumab and Ipilimumab in chemorefractory MSI-H mCRC THIRTEEN drugs (USA)
- 2019: Addition of Encorafenib + EGFRi for $BRAF^{V600E}$ mut mCRC FOURTEEN drugs
- 2020: Pembrolizumab as 1st line therapy for dMMR/MSI-High mCRC? 49++ months
- 2022+ Immunotherapy as (neo)adjuvant therapy for dMMR/MSI-High CRC? CURE??

ALL UNDERPINNED BY MULTIDISCIPLINARY TEAM CARE AND IMPROVEMENTS ACROSS THE WHOLE PATHWAY

KEYNOTE 177

The NEW ENGLAND JOURNAL of MEDICINE

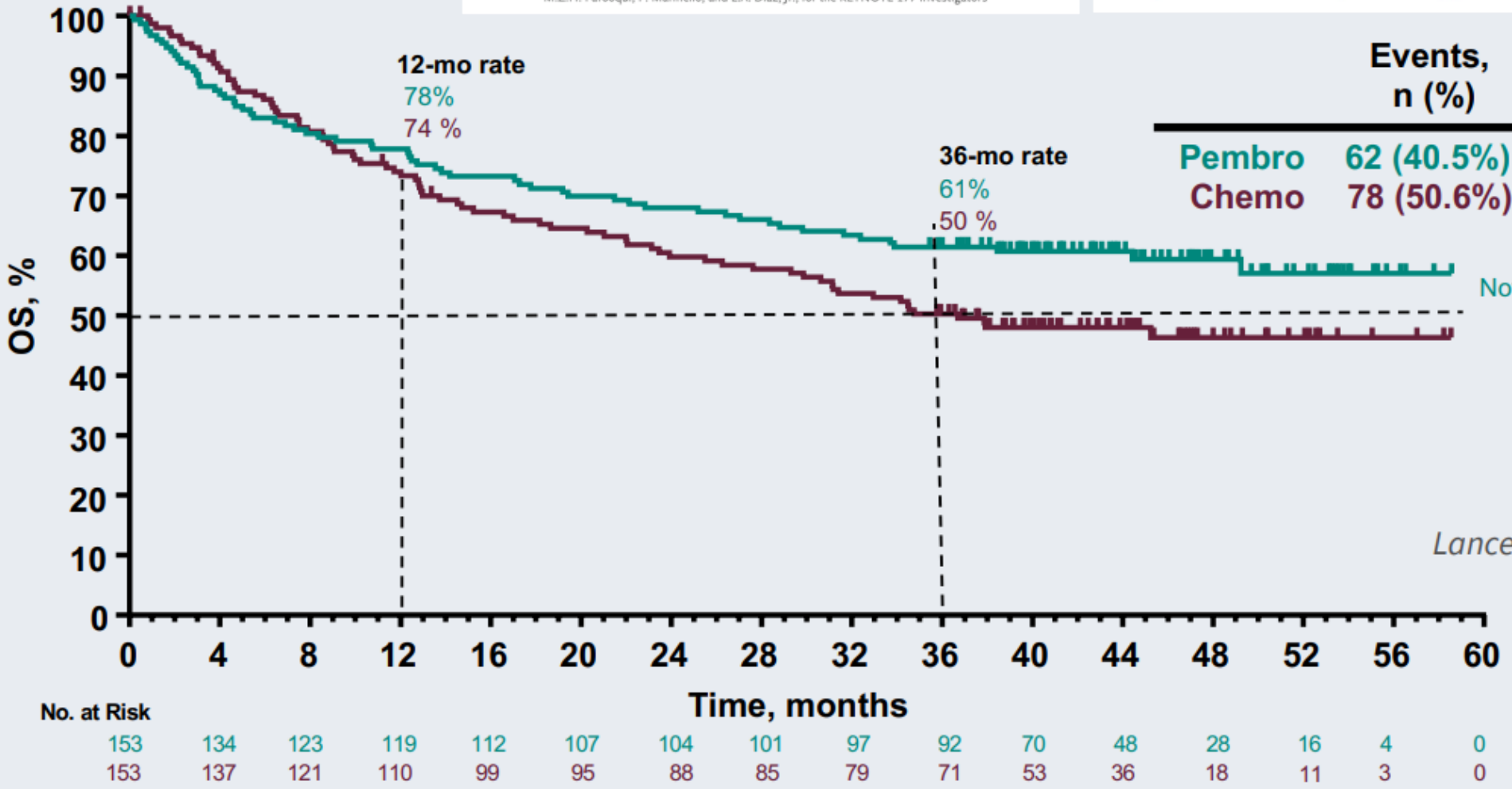
ESTABLISHED IN 1812 DECEMBER 3, 2020 VOL. 383 NO. 23

Pembrolizumab in Microsatellite-Instability–High Advanced Colorectal Cancer

T. André, K.-K. Shiu, T.W. Kim, B.V. Jensen, L.H. Jensen, C. Punt, D. Smith, R. Garcia-Carbonero, M. Benavides, P. Gibbs, C. de la Fouchardiere, F. Rivera, E. Elez, J. Bendell, D.T. Le, T. Yoshino, E. Van Cutsem, P. Yang, M.Z.H. Farooqui, P. Marinello, and L.A. Diaz, Jr., for the KEYNOTE-177 Investigators*

Pembrolizumab versus chemotherapy for microsatellite instability-high or mismatch repair-deficient metastatic colorectal cancer (KEYNOTE-177): final analysis of a randomised, open-label, phase 3 study

*Luis A Diaz Jr, Kai-Keen Shiu, Tae-Won Kim, Benny Vittrup Jensen, Lars Henrik Jensen, Cornelis Punt, Denis Smith, Rocio Garcia-Carbonero, Manuel Benavides, Peter Gibbs, Christelle de la Fourchardiere, Fernando Rivera, Elena Elez, Dung T Le, Takayuki Yoshino, Wen Yan Zhong, David Fogelman, Patricia Marinello, Thierry Andre, on behalf of the KEYNOTE-177 Investigators**



	Events, n (%)	HR (95% CI)	*P*
Pembro	62 (40.5%)	0.74 (0.53-1.03)	0.0359[a]
Chemo	78 (50.6%)		

Median (95% CI)

Not reached (49.2-NR)

36.7 mo (27.6-NR)

Lancet Oncol. 2021; **22**: 665-677

[a]**Pembrolizumab was not superior to chemotherapy for OS as one-sided α > 0.0246. Pre-specified sensitivity analyses to adjust for crossover effect by rank-preserving structure failure time model and inverse probability of censoring weighting showed OS HRs of 0.66 (95% CI 0.42-1.04) and 0.77 (95% CI 0.44-1.38).** Data cut-off: 19Feb2021.

ORIGINAL ARTICLE FREE PREVIEW

PD-1 Blockade in Mismatch Repair–Deficient, Locally Advanced Rectal Cancer

Andrea Cercek, M.D., Melissa Lumish, M.D., Jenna Sinopoli, N.P., Jill Weiss, B.A., Jinru Shia, M.D., Michelle Lamendola-Essel, D.H.Sc., Imane H. El Dika, M.D., Neil Segal, M.D., Marina Shcherba, M.D., Ryan Sugarman, M.D., Ph.D., Zsofia Stadler, M.D., Rona Yaeger, M.D., et al.

June 23, 2022
N Engl J Med 2022; 386:2363-2376
DOI: 10.1056/NEJMoa2201445

Every (!)CRC Must be tested for MSI

What is the intent of (neo)adjuvant (immuno)therapy?

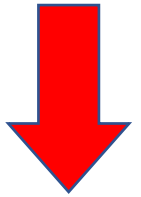
- Improve operability?
- Maximise local control?
- Organ preservation + deferral of surgery?
- Influence distant metastases?
- Improve overall survival (?vs?) quality of life?
- Allow assessment of disease biology
- Window of opportunity clinical trials?

What are our limits of knowledge, understanding and capabilities?

Scenario 1: Tumor testing at cancer diagnosis

1. Tumor testing at cancer diagnosis
   - guiding therapy

dMMR



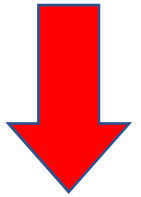
2. Constitutional testing (blood, saliva etc.) at cancer diagnosis
   - guiding risk managment (surgical strategy)

3. Constitutional testing (blood, saliva etc.) for risk assessment
   - guiding risk managment (surgical strategy)

Scenario 2: Constitutional Testing

1. Tumor testing at cancer diagnosis
   - guiding therapy

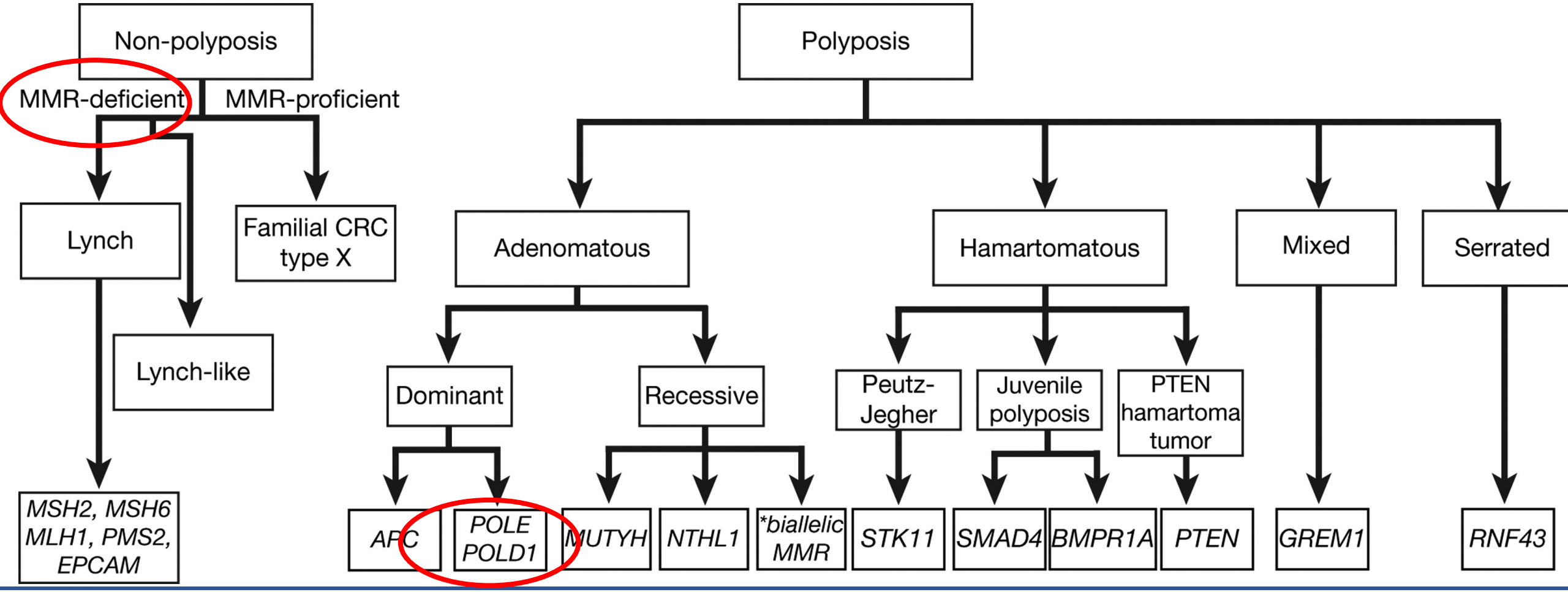
dMMR



2. Constitutional testing (blood, saliva etc.) at cancer diagnosis
   - **guiding risk managment (surgical strategy)**

3. Constitutional testing (blood, saliva etc.) for risk assessment
   - guiding risk managment (surgical strategy)

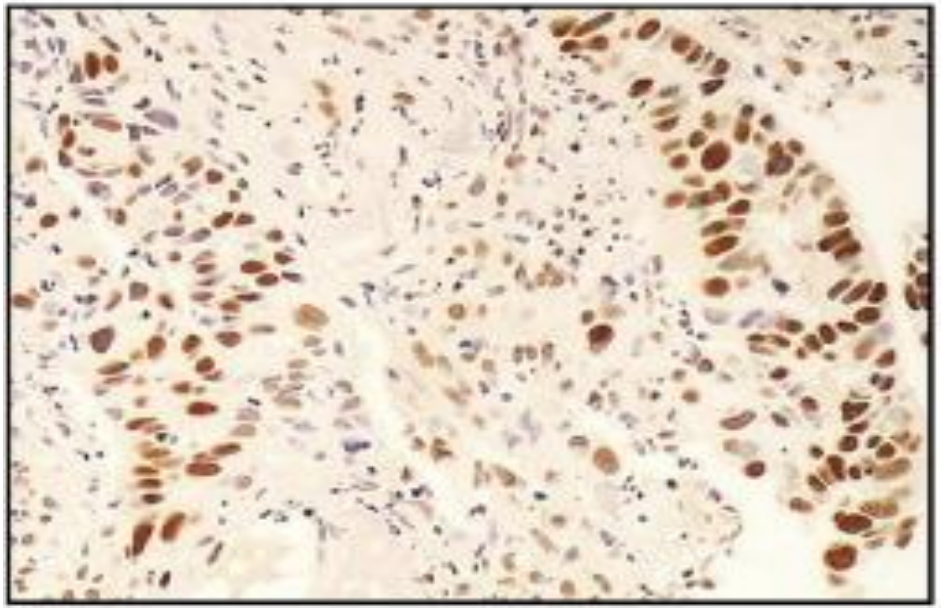
Valle L. Recent Discoveries in the Genetics of Familial Colorectal Cancer and Polyposis.
Clin Gastroenterol Hepatol 2016



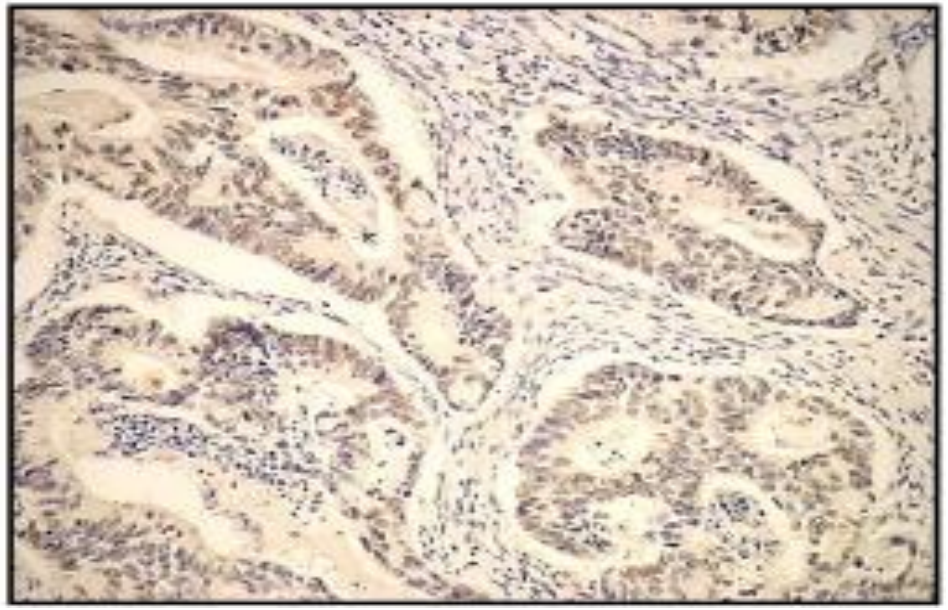
MSI testing in biopsies

Reflex testing via IH staining - biopsies

PMS2 Endoscopic biopsy



PMS2 Surgical material



Immunohistochemistry staining for PMS2 on endoscopic biopsies and surgical specimens from the same tumor

Lynch-Syndrom und HNPCC

Vilkin A et al. Human Pathology 2015: 1705-1711

SESSION IV – eoCRC PATHOLOGICAL AND ONCOLOGICAL PATH (O)

O.1)· Are· immunohistochemistry· analysis· for· mismatch· repair· proteins·or·molecular·microsatellite·analysis·necessary·in·eoCRC· endoscopic·biopsies?¶	LE·1B;·GR·A¶ Agreement:·100%·¶ (A+92.6%|A·7.4%)¶ Clarity:·100%¤
All· CRCs· should· undergo· evaluation· for· mismatch· repair· (MMR)· phenotype· (with· either· immunohistochemistry· or· microsatellite·instability)·regardless·of·the·age·at·diagnosis,· for· both· genetic· and· therapeutic· purposes.· It· is· not· mandatory·to·perform·both,·but·at·least·one.·The·analysis·of· immunohistochemistry·for·mismatch·repair·proteins·(IHC·for· MMR)·or·microsatellite·instability·(MSI)·can·be·performed·on· either·the·surgical·specimen·or·the·pre-operative·biopsies.¤	

Clinical Gastroenterology and Hepatology 2023;21:581–603

CLINICAL PRACTICE GUIDELINES

Delphi Initiative for Early-Onset Colorectal Cancer (DIRECt) International Management Guidelines

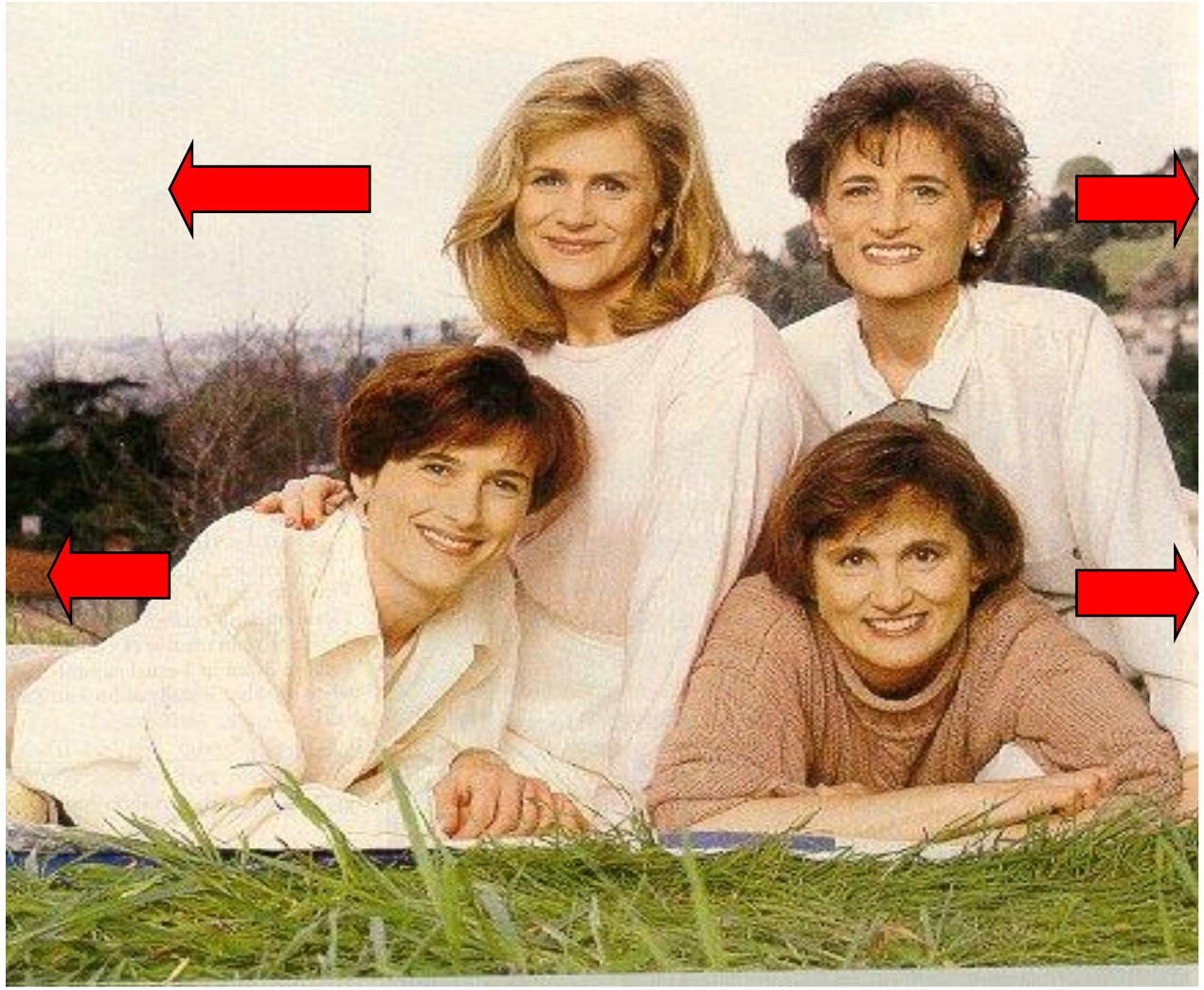
Giulia Martina Cavestro,[1,*] Alessandro Mannucci,[1,*] Francesc Balaguer,[2,3,‡] Heather Hampel,[4,‡] Sonia S. Kupfer,[5,‡] Alessandro Repici,[6,‡] Andrea Sartore-Bianchi,[7,‡] Toni T. Seppälä,[8,9,10,‡] Vincenzo Valentini,[11,‡] Clement Richard Boland,[12] Randall E. Brand,[13] Tineke E. Buffart,[14] Carol A. Burke,[15] Riccardo Caccialanza,[16] Renato Cannizzaro,[17] Stefano Cascinu,[18] Andrea Cercek,[19] Emma J. Crosbie,[20,21] Silvio Danese,[1] Evelien Dekker,[22] Maria Daca-Alvarez,[2] Francesco Deni,[23] Mev Dominguez-Valentin,[24] Cathy Eng,[25] Ajay Goel,[26] Josè G. Guillem,[27] Britt B. S. L. Houwen,[22] Charles Kahi,[28] Matthew F. Kalady,[29] Fay Kastrinos,[30] Florian Kühn,[31] Luigi Laghi,[32] Andrew Latchford,[33] David Liska,[34] Patrick Lynch,[35] Alberto Malesci,[1] Gianluca Mauri,[7,36] Elisa Meldolesi,[11] Pål Møller,[24] Kevin J. Monahan,[33,37] Gabriela Möslein,[38] Caitlin C. Murphy,[39] Karlijn Nass,[22] Kimmie Ng,[40] Cristina Oliani,[41] Enrico Papaleo,[42] Swati G. Patel,[43] Marta Puzzono,[1] Andrea Remo,[44] Luigi Ricciardiello,[45] Carla Ida Ripamonti,[46] Salvatore Siena,[7] Satish K. Singh,[47] Zsofia K. Stadler,[19] Peter P. Stanich,[48] Sapna Syngal,[49] Stefano Turi,[23] Emanuele Damiano Urso,[50] Laura Valle,[51,52] Valeria Stella Vanni,[42] Eduardo Vilar,[53] Marco Vitellaro,[54] Yi-Qian Nancy You,[55] Matthew B. Yurgelun,[49] Raffaella Alessia Zuppardo,[1] and Elena M. Stoffel,[56] on behalf of the Associazione Italiana Familiarità Ereditarietà Tumori, the Collaborative Group of the Americas on Inherited Gastrointestinal Cancer, the European Hereditary Tumour Group, and the International Society for Gastrointestinal Hereditary Tumours

Lynch Syndrom

Asc. Colon cancer 45 y

Ovarian cancer 38 y

Endometrial cancer 42 y



Endometrial cancer 42 y

No cancer

Metachronous cancer in Lynch syndrome

Systematic review

doi:10.1111/codi.13679

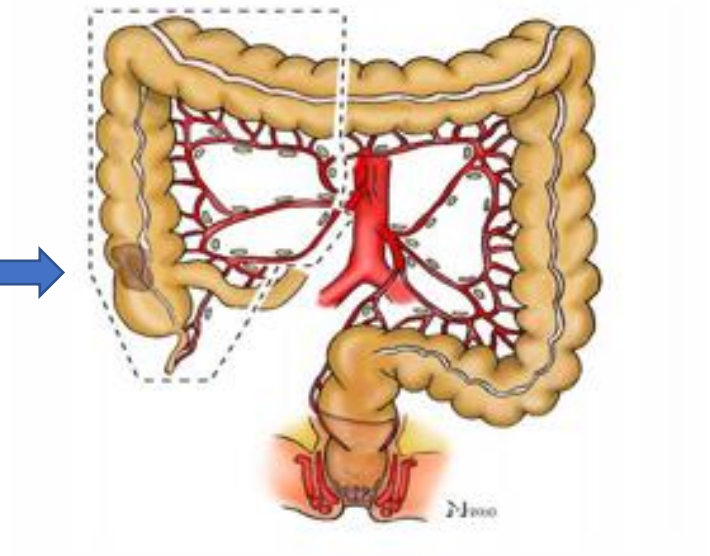
Risk of metachronous colorectal cancer following colectomy in Lynch syndrome: a systematic review and meta-analysis

C. C. Anele*† , S. O. Adegbola*†, A. Askari‡, A. Rajendran§, S. K. Clark*†, A. Latchford§ and O. D. Faiz*†

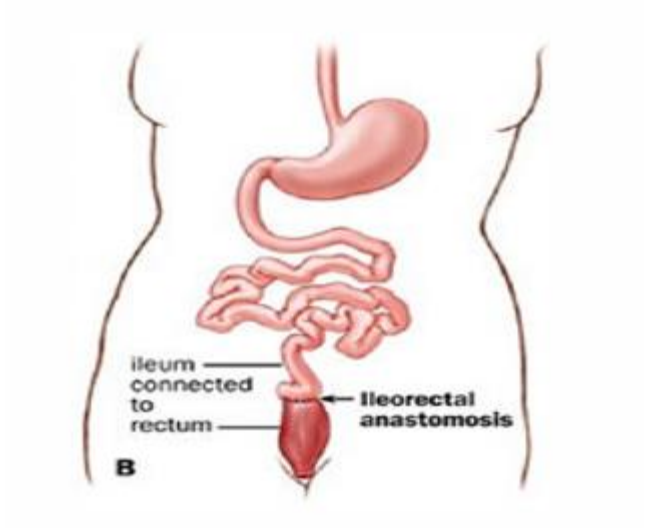
*Department of Surgery and Cancer, Imperial College London, London, UK, †St Mark's Hospital and Academic Institute, Middlesex, UK, ‡Surgical Epidemiology Trials and Outcomes Centre, St Mark's Hospital and Academic Institute, Middlesex, UK, and §Department of Gastroenterology, St Mark's Hospital and Academic Institute, Middlesex, UK

Conclusion: Prophylactically extended colectomy (IRA/ISA) at the time of the first CRC reduces the metachronous cancer risk by 4

„Routine“ or prophylactically extended resection



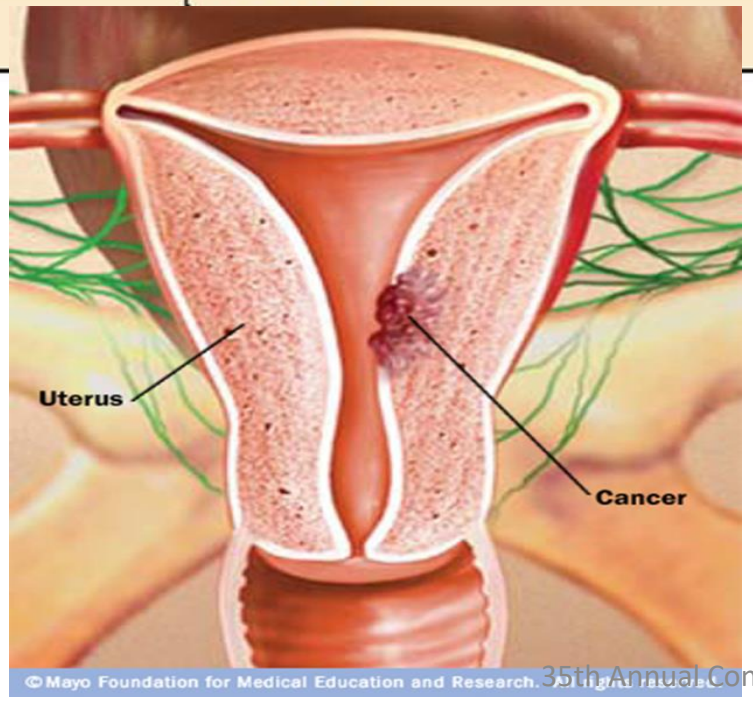
Right-sided colon cancer

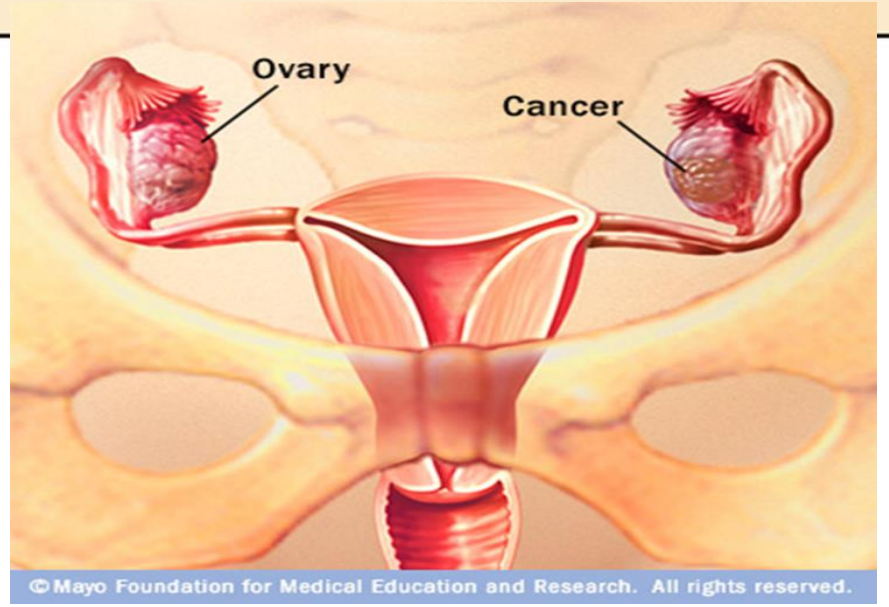


Extended (sub)total colectomy

Option: Simultaneous prophylactic hysterectomy, tbd prophylactic salpingectomy or salpingoophorectomy

3.3.28	Konsensbasierte Empfehlung
GCP	Mit Patientinnen mit Lynch- und HNPCC-Syndrom sollte mit 40 Jahren, bzw. fünf Jahre vor dem frühesten Erkrankungsalter in der Familie, eine prophylaktische Hysterektomie und ggf. eine Ovarektomie besprochen werden.

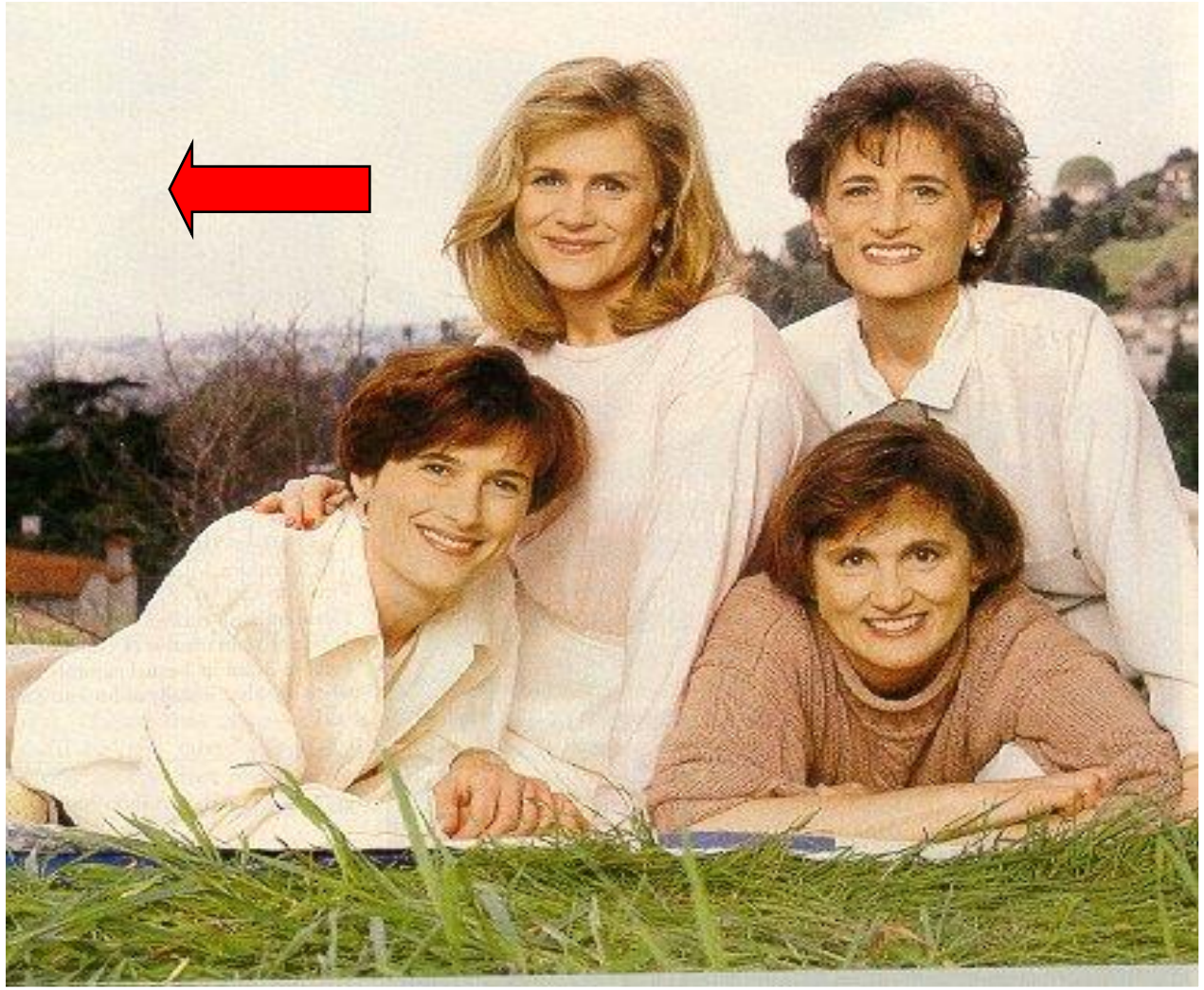




Lynch Syndrom

Right-sided colon cancer 45y

Subtotal colectomy
Simultaneous
(prophylactic) hysterectomy



SESSION·III·-·GENETICS·OF·eoCRC·(G)¶

G.1)· Who· should· receive· germline· genetic· testing· among· eoCRC· patients,·and·when·should·this·take·place?¶ All· eoCRC· patients· should· be· offered· genetic· counseling· and· multi-gene· panel· testing.· Testing· before· surgery,· although· difficult·to·achieve·in·clinical·practice,·maximizes·clinical·utility.¤	LE·1B;·GR·B·¶ Agreement:·96.3%·¶ (A+88.9%|A·7.4%|A·-·3.7%)¶ Clarity:·100%¤

Clinical Gastroenterology and Hepatology 2023;21:581–603

CLINICAL PRACTICE GUIDELINES

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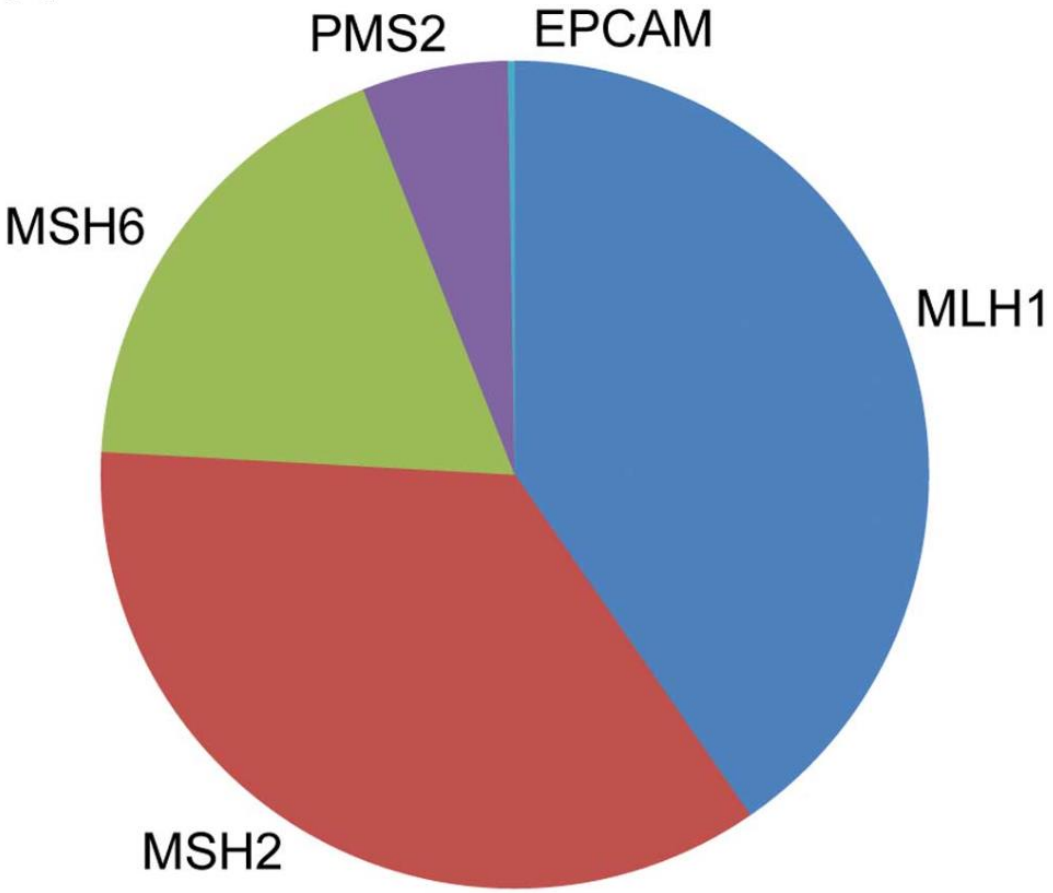
Lynch Syndrome

A



PLSD

The Prospective Lynch Syndrome Database

51,646 observation years

Gastroenterology 2018;155:1400–1409

Seppälä et al. Hereditary Cancer in Clinical Practice (2017) 15:18
DOI 10.1186/s13053-017-0078-5

Hereditary Cancer in Clinical Practice

RESEARCH Open Access

Colorectal cancer incidence in *path_MLH1* carriers subjected to different follow-up protocols: a Prospective Lynch Syndrome Database report

Seppälä et al. Hereditary Cancer in Clinical Practice (2019) 17:8
https://doi.org/10.1186/s13053-019-0106-8

Hereditary Cancer in Clinical Practice

Lynch Syndrome

Review

European guidelines from the EHTG and ESCP for Lynch syndrome: an updated third edition of the Mallorca guidelines based on gene and gender

T. T. Seppälä[1,2], A. Latchford[3,4], I. Negoi[11], A. Sampaio Soares[12], R. Jimenez-Rodriguez[13], L. Sánchez-Guillén[14], D. G. Evans[5], N. Ryan[6,7], E. J. Crosbie[6], M. Dominguez-Valentin[15], J. Burn[8], M. Kloor[16,17], M. von Knebel Doeberitz[16,17], F. J. B. van Duijnhoven[20], P. Quirke[9], J. R. Sampson[10], P. Møller[15,19] and G. Möslein[18,19], on behalf of the European Hereditary Tumour Group (EHTG) and European Society of Coloproctology (ESCP)

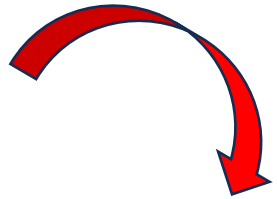
[1]Department of Surgery, Helsinki University Hospital, and University of Helsinki, Helsinki, Finland, [2]Department of Surgical Oncology, Johns Hopkins Hospital, Baltimore, Maryland, USA, [3]Department of Cancer and Surgery, Imperial College London, and [4]St Mark's Hospital, London North West Healthcare NHS Trust, London, [5]Manchester Centre for Genomic Medicine, Division of Evolution and Genomic Sciences, University of Manchester, Manchester University Hospitals NHS Foundation Trust, and [6]Division of Cancer Sciences, Faculty of Biology, Medicine and Health, University of Manchester, St Mary's Hospital, Manchester, [7]Centre for Academic Women's Health, University of Bristol, Bristol, [8]Faculty of Medical Sciences, Newcastle Upon Tyne Hospitals NHS Foundation Trust, Newcastle upon Tyne, [9]Pathology and Data Analytics, School of Medicine, University of Leeds, Leeds, and [10]Institute of Medical Genetics, Division of Cancer and Genetics, Cardiff University School of Medicine, Heath Park, Cardiff, UK, [11]Department of Surgery, Emergency Hospital of Bucharest, Carol Davila University of Medicine and Pharmacy, Bucharest, Romania, [12]Hospital Prof. Dr Fernando Fonseca, EPE, Lisbon, Portugal, [13]Department of Surgery, Hospital Universitario Virgen del Rocío, Seville, and [14]Colorectal Unit, Department of General Surgery, Elche University General Hospital, Elche, Alicante, Spain, [15]Department of Tumour Biology, Norwegian Radium Hospital, Oslo University Hospital, Oslo, Norway, [16]Department of Applied Tumour Biology, Institute of Pathology, University Hospital Heidelberg, and [17]Cooperation Unit Applied Tumour Biology, German Cancer Research Centre, Heidelberg, [18]Centre for Hereditary Tumours, Bethesda Hospital, Duisburg, and [19]University of Witten/Herdecke, Witten, Germany, and [20]Division of Human Nutrition and Health, Wageningen University and Research, Wageningen, the Netherlands

Correspondence to: Dr T. T. Seppälä, PO Box 340, 00029 HUS, Helsinki, Finland (e-mail: toni.seppala@fimnet.fi)

UPDATE ONGOING!!!

Impact of Genetics : 3 Scenarios

1. Tumor testing at cancer diagnosis
   - guiding therapy or „polyposis“



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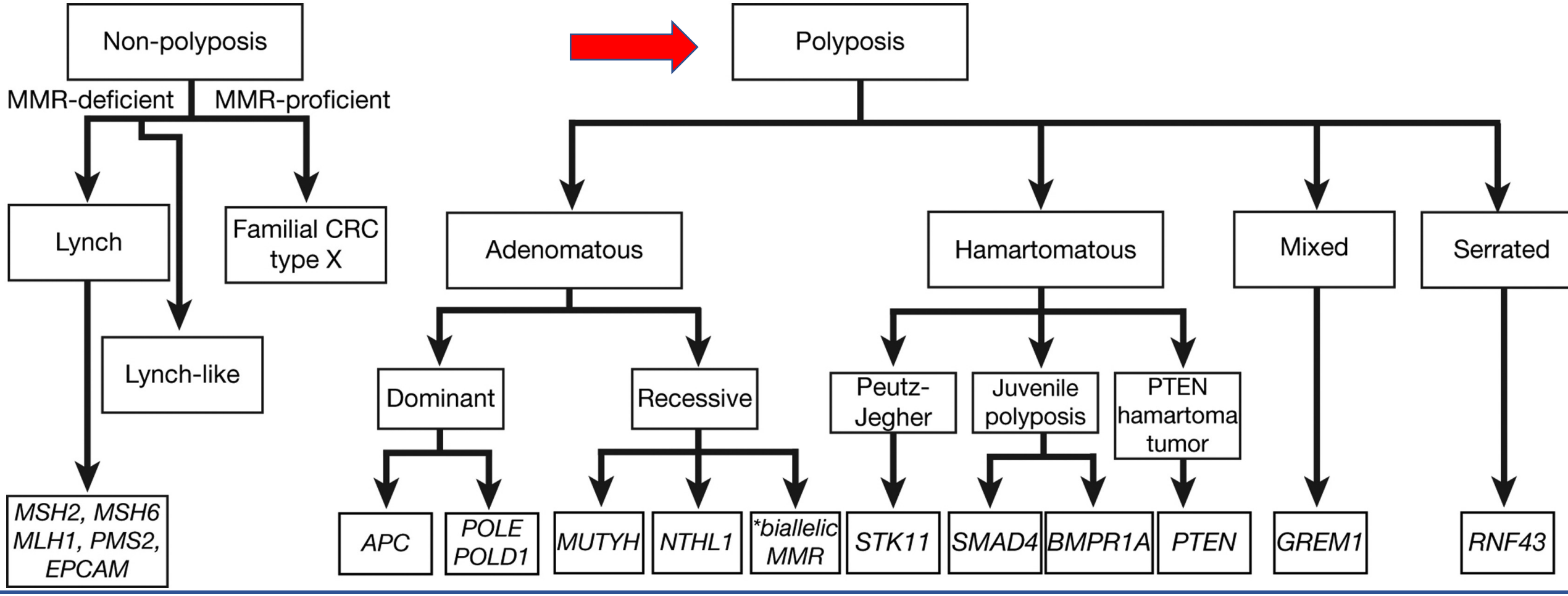
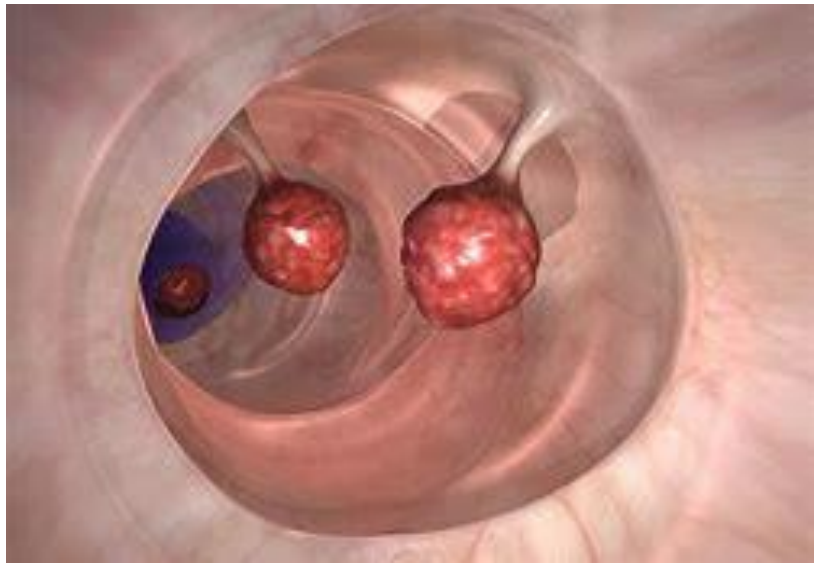
Valle L. Recent Discoveries in the Genetics of Familial Colorectal Cancer and Polyposis.
Clin Gastroenterol Hepatol 2016



Polyposis syndrome(s)



Few polyps,
many polyps,
cancer,
multiple cancers

- Familial adenomatous polyposis (FAP)
- **MUTYH-associated polyposis (MAP)**
- **NTHL-1 associated polyposis (NAP)**
- Juvenile polyposis (JP)
- Hyperplastistic (serrated) polyposis (HP)
- Oligopolyposis (Multiple Adenoma) MA
- Polymerase Proofreading-associated polyposis (PPAP)

Lynch Syndrome

10-30% EOCRC have a pathogenic consitutional mutation

JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

Cancer Susceptibility Gene Mutations in Individuals With Colorectal Cancer

Matthew B. Yurgelun, Matthew H. Kulke, Charles S. Fuchs, Brian A. Allen, Hajime Uno, Jason L. Hornick, Chinedu I. Ukaegbu, Lauren K. Brais, Philip G. McNamara, Robert J. Mayer, Deborah Schrag, Jeffrey A. Meyerhardt, Kimmie Ng, John Kidd, Nanda Singh, Anne-Renee Hartman, Richard J. Wenstrup, and Sapna Syngal

Conclusion

Germline cancer susceptibility gene mutations are carried by 9.9% of patients with CRC. MSI/MMR testing reliably identifies LS probands, although 7.0% of patients with CRC carry non-LS mutations, including 1.0% with *BRCA1/2* mutations.

Published at ascopubs.org/journal/jco on January 30, 2017.

Prophylactic surgery:

When, why and how?

MEN-2 (path gene alterations in RET Proto-oncogene) Hereditary (medullary) Thyroid cancer

- Clinical diagnosis and genetic testing
- Predictive testing
- Pathological variant:
- Prophylactic thyroidectomy
  - preschool…..

MEN-2 (path gene alterations in RET Proto-oncogene) Hereditary (medullary) Thyroid cancer

Penetrance ⇑

Age of manifestation ⇓

Heterogeneity ⇓

Loss of organ = „uneventful“

MEN-2	FAP
Penetrance ⇑	Penetrance ⇑
Age of manifestation ⇓	Age of manifestation ⇓⇑
Heterogeneity ⇓	Heterogeneity ⇓⇑
Loss of organ = „uneventful“	Loss of organ = „complex but tolerable“

FAP	Lynch Syndrom
Penetrance ⇑	Penetrance ⇓⇑
Age of manifestation ⇓⇑	Age of manifestation ⇑
Heterogeneity ⇓⇑	Heterogeneity ⇓⇑
Loss of organ = „ complex but tolerable“	Loss of organ = depends…„complex but tolerable“

EHTG-ESCP Joint dynamic Guidance for FAP and rare adenomatous polyposis syndromes

BJS

UPDATED EUROPEAN GUIDELINES FOR CLINICAL MANAGEMENT OF FAMILIAL ADENOMATOUS POLYPOSIS (FAP), MUTYH-ASSOCIATED POLYPOSIS (MAP), GASTRIC ADENOCARCINOMA, PROXIMAL POLYPOSIS OF THE STOMACH (GAPPS) AND OTHER RARE ADENOMATOUS POLYPOSIS SYNDROMES: A JOINT EHTG-ESCP REVISION

Journal:	*British Journal of Surgery*
Manuscript ID	BJS-2145-Nov-23.R1
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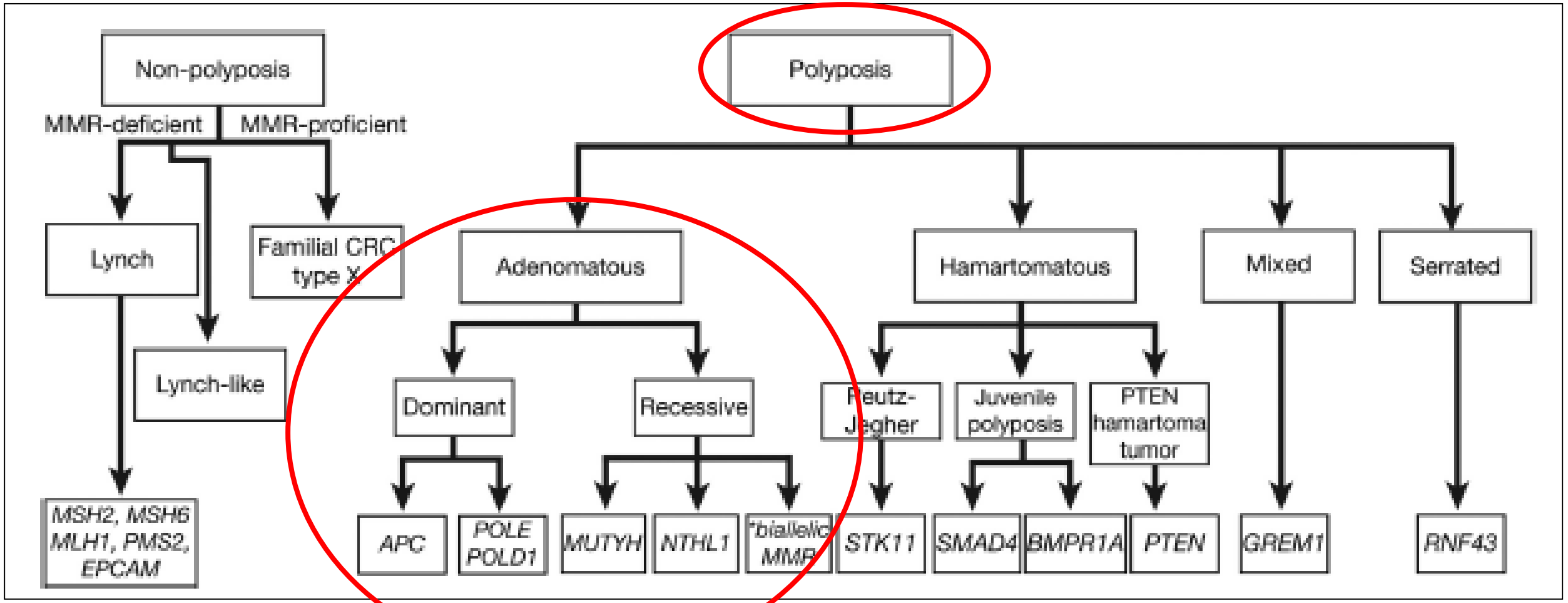
Date Submitted by the Author:	12-Feb-2024
Complete List of Authors:	Zaffaroni, Gloria; Bethesda Hospital, Center for Hereditary Tumors; University of Milan Faculty of Medicine and Surgery Mannucci , Alessandro; Vita -Salute San Raffaele University, IRCCS San Raffaele Scientific Institute, Gastroenterology and Gastrointestinal Endoscopy Unit

Valle L. Recent Discoveries in the Genetics of Familial Colorectal Cancer and Polyposis. Clin Gastroenterol Hepatol 2016 (Epub ahead of print)



Scenario 3: Constitutional testing for risk assessment

1. Tumor testing at cancer diagnosis
   - guiding therapy

2. Constitutional testing (blood, saliva etc.) at cancer diagnosis
   - guiding risk managment (surgical strategy)

3. Constitutional testing (blood, saliva etc.) for risk assessment
   - **guiding risk managment (surgical strategy)**

Risk-adapted (individual decision-making)

Scenario 4: Genetic Health testing

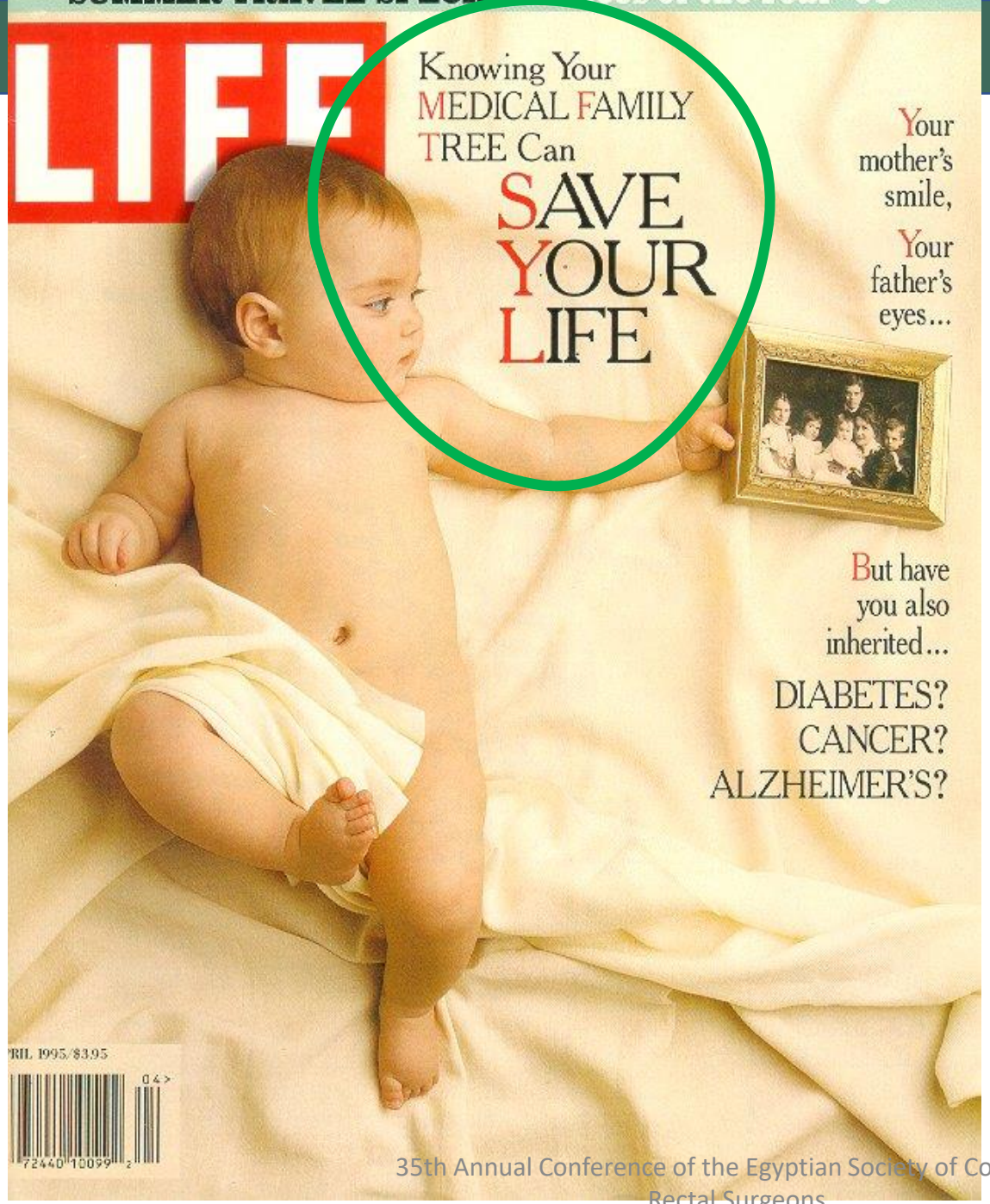
1. Tumor testing at cancer diagnosis
   - guiding therapy

2. Constitutional testing (blood, saliva etc.) at cancer diagnosis
   - guiding risk managment (surgical strategy)

3. Constitutional testing (blood, saliva etc.) for risk assessment
   - guiding risk managment (surgical strategy)

4. Genetic Health Testing – Huge preventative potential!

Oncology, pharmacogentics, cardiology, neurology, endocrinology, rheumatology…



Knowing Your Genes can

Save

Your

Life

Take Home Messages

- MSI testing for all (unselected) Cancers (Biopsy)
- Constitutional testing for all dMMR patients (driver mutations and hereditary disposition)
- Constitutional, **preoperative** NGS panel testing for all EaO-CRC
- Risk-adapted surgery (Counselling!!)
- Preventive potential for index patient and family
- Huge preventative potential knowing your genes!

PLSD
Prospective Lynch Syndrome Database

Prospective Lynch Syndrome Database (PLSD) - cumulative risk for cancer by age, genetic variant, and gender in carriers subject to colonoscopy

Any cancer | Carrier without previous cancer | Carrier with previous cancer | About

Calculation of cumulative risk for first cancer

Cancer type

Colorectal cancer

Current age

25 45 70

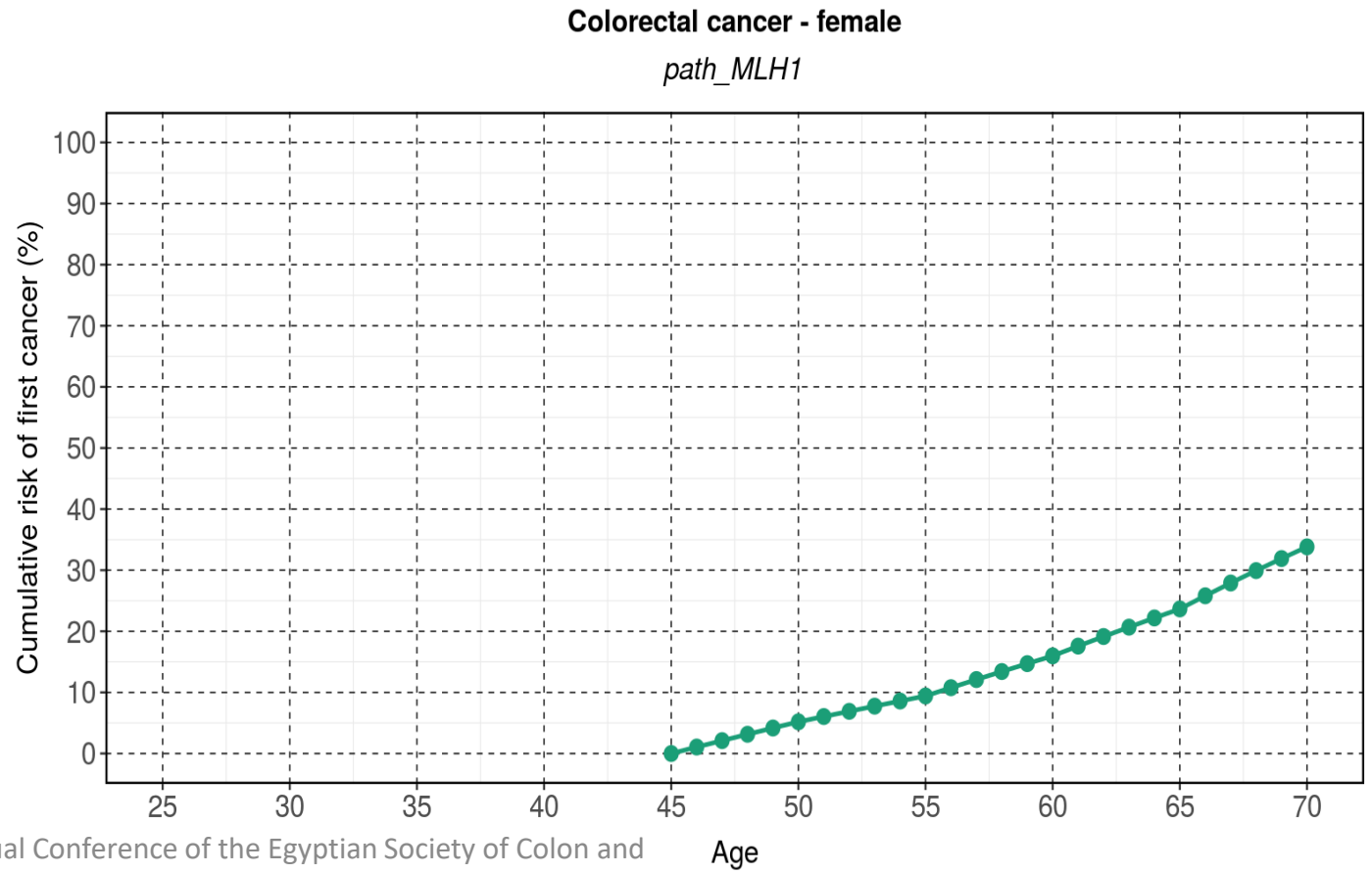
25 30 35 40 45 50 55 60 65 70

Gender

Female

Genetic variant

path_MLH1



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Cancer type

Colorectal cancer

Current age

25 45 70

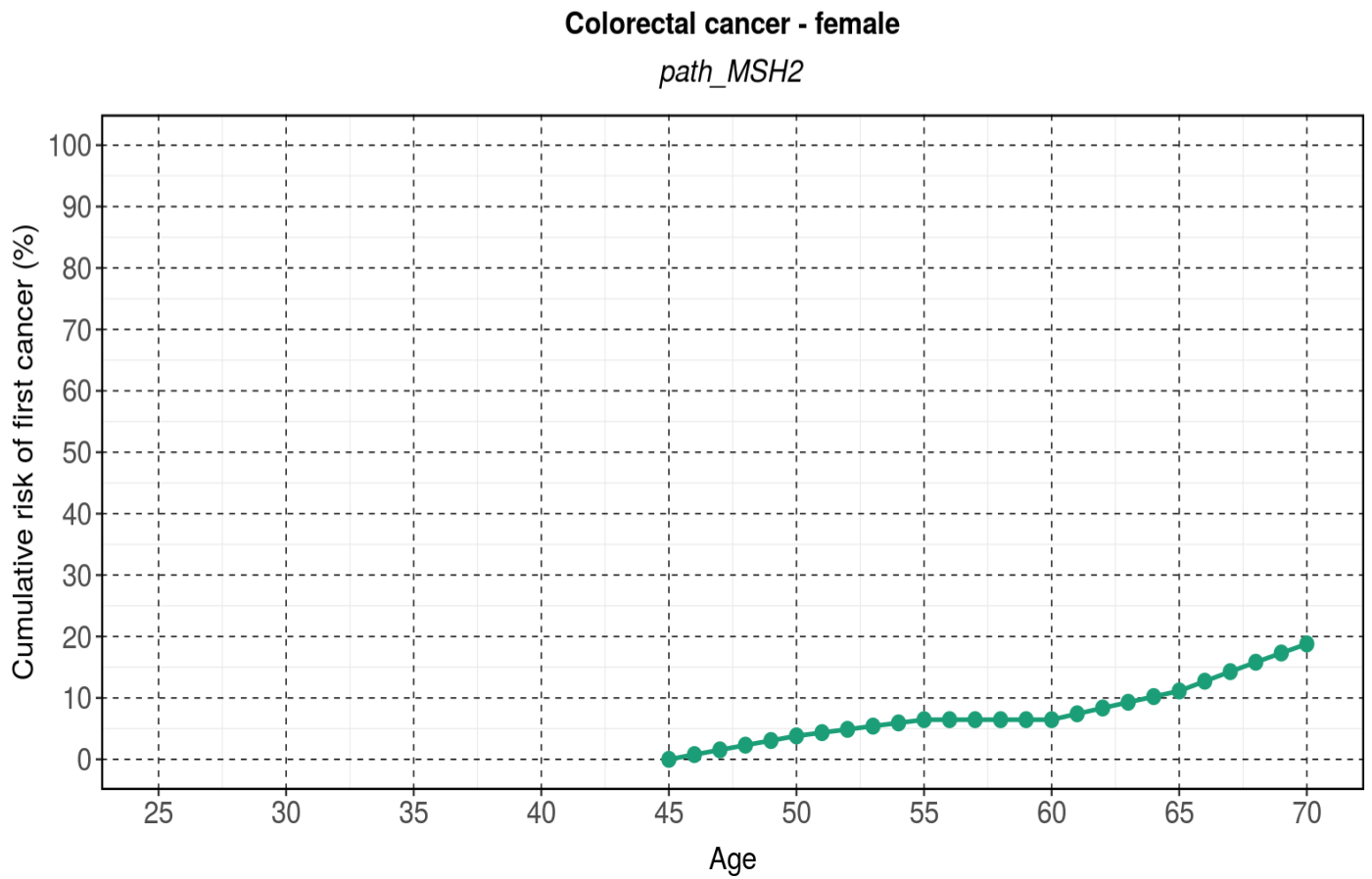
25 30 35 40 45 50 55 60 65 70

Gender

Female

Genetic variant

path_MSH2



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Cancer type

Colorectal cancer

Current age

25 45 70

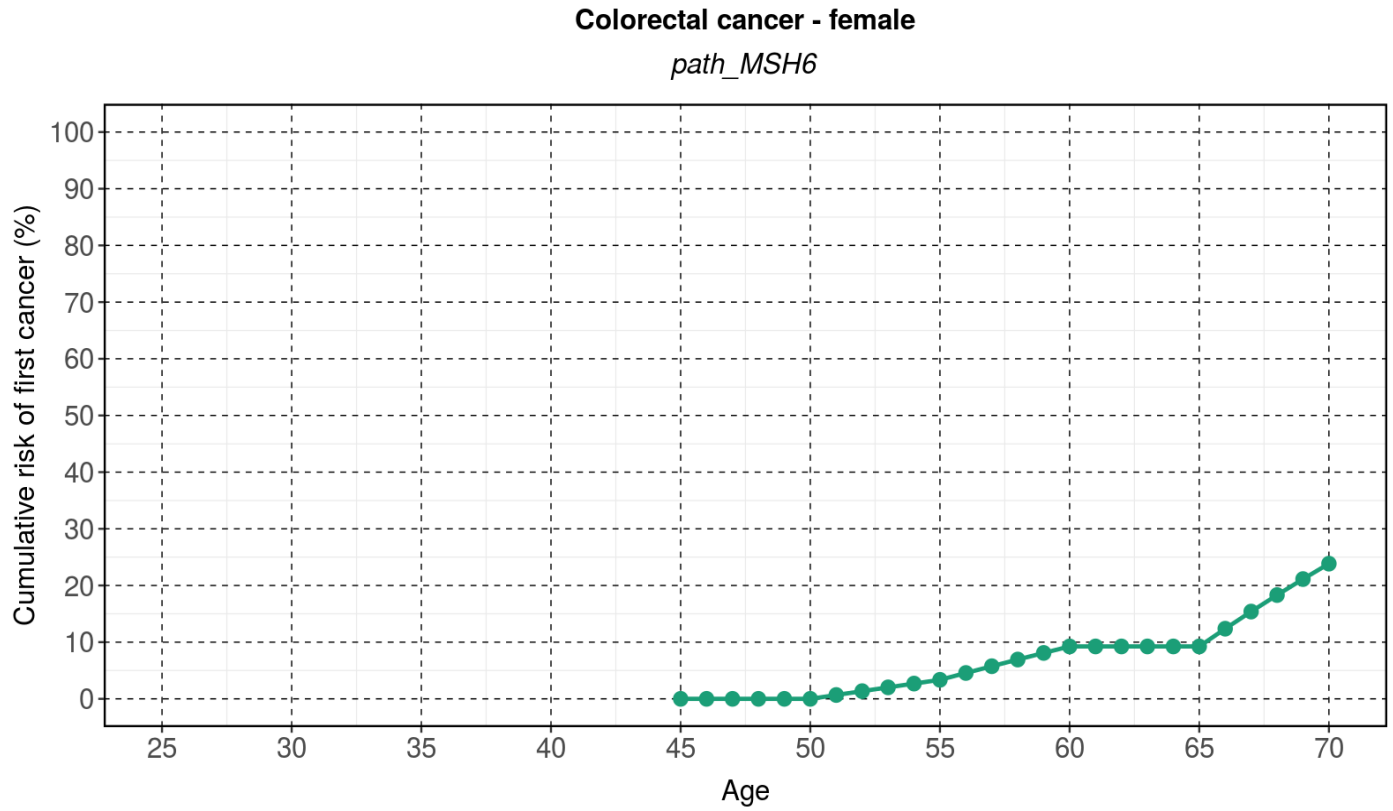
25 30 35 40 45 50 55 60 65 70

Gender

Female

Genetic variant

path_MSH6



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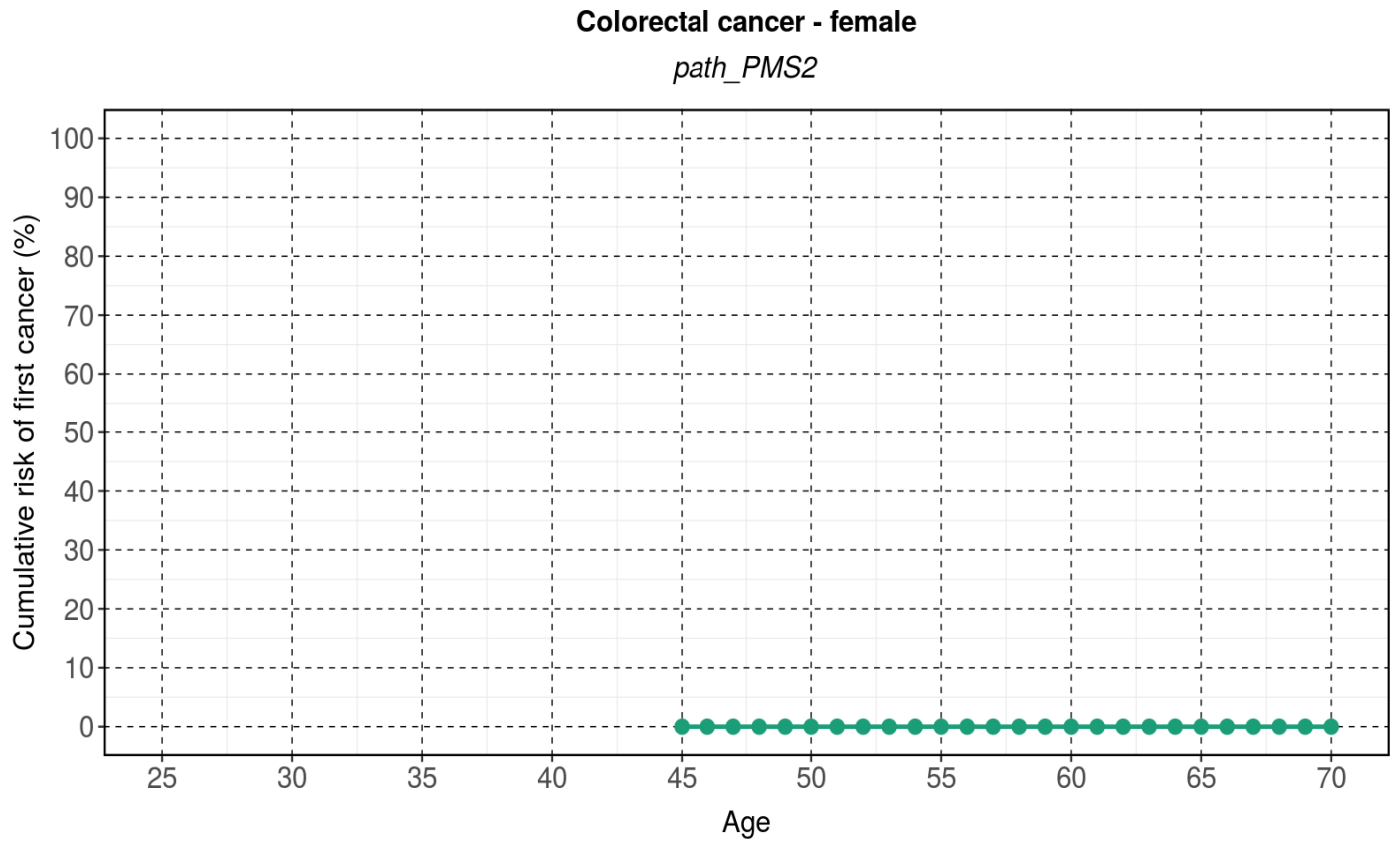
25 30 35 40 45 50 55 60 65 70

Gender

Female

Genetic variant

path_PMS2

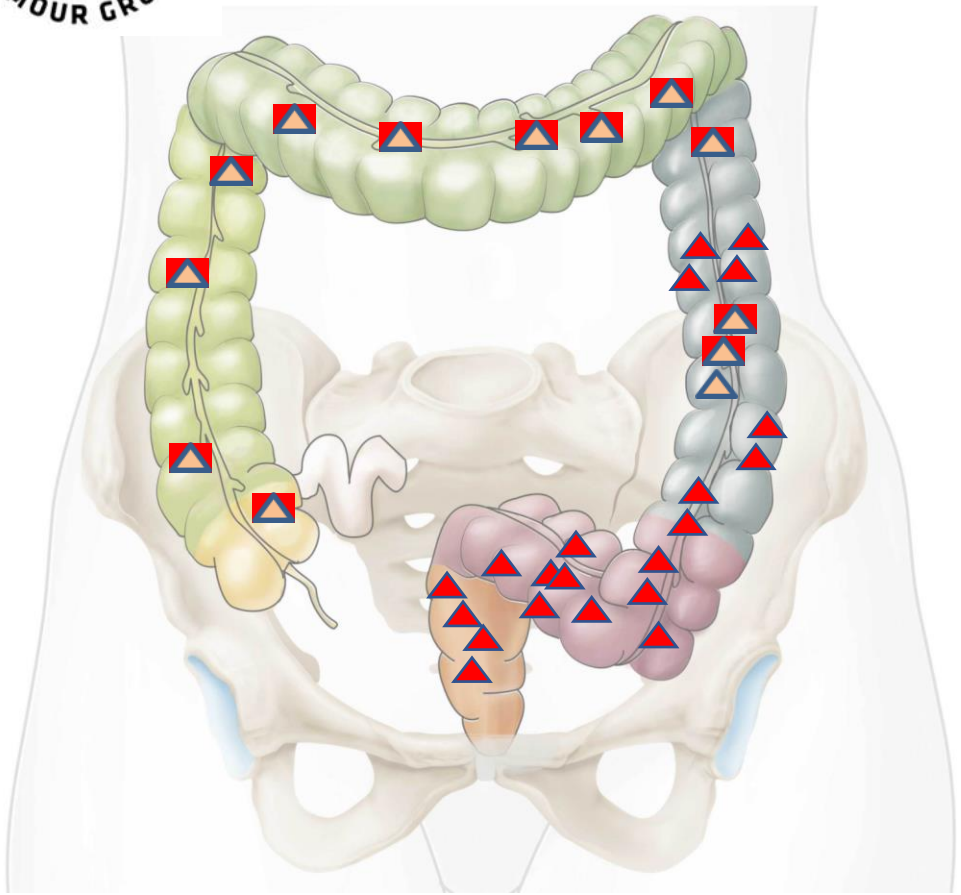


Familial adenomatous polyposis (FAP)

- Incidence 1:8.300 – 1:14.025
- left untreated: CRC ~ 39 yoa
- Penetrance 100%
- ~ 30% sporadic

- Prophylactic surgery

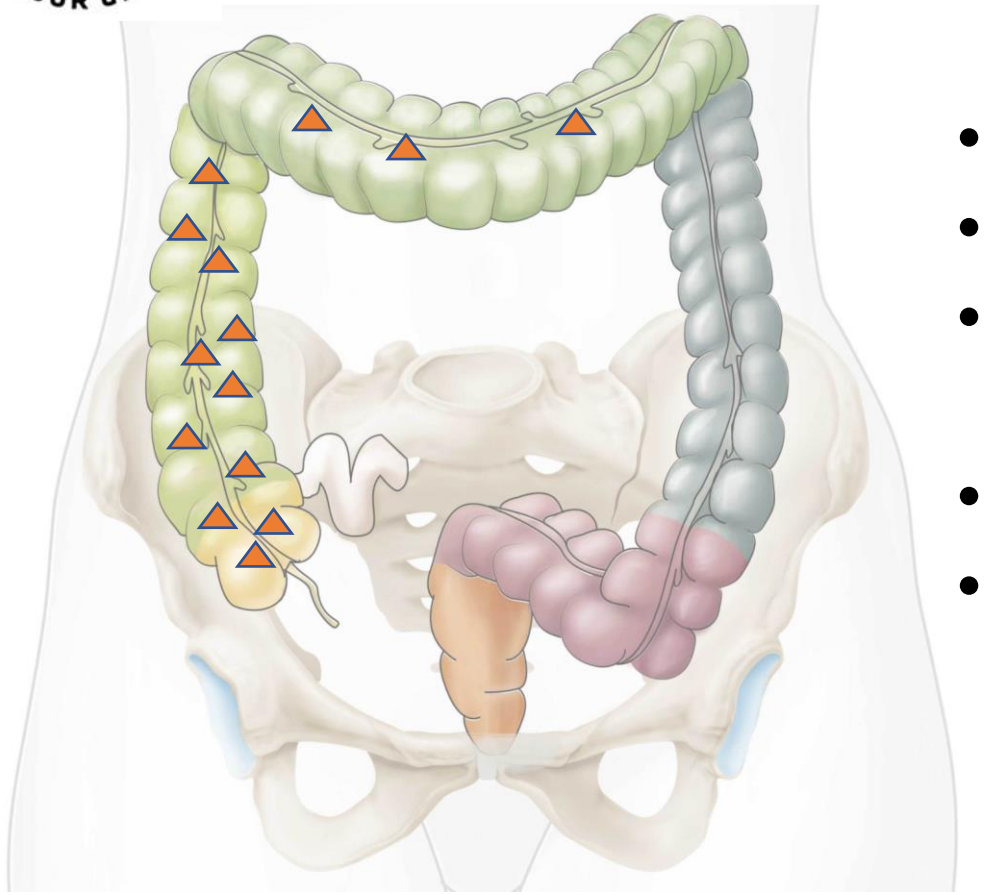
(individual timing)



Classical FAP

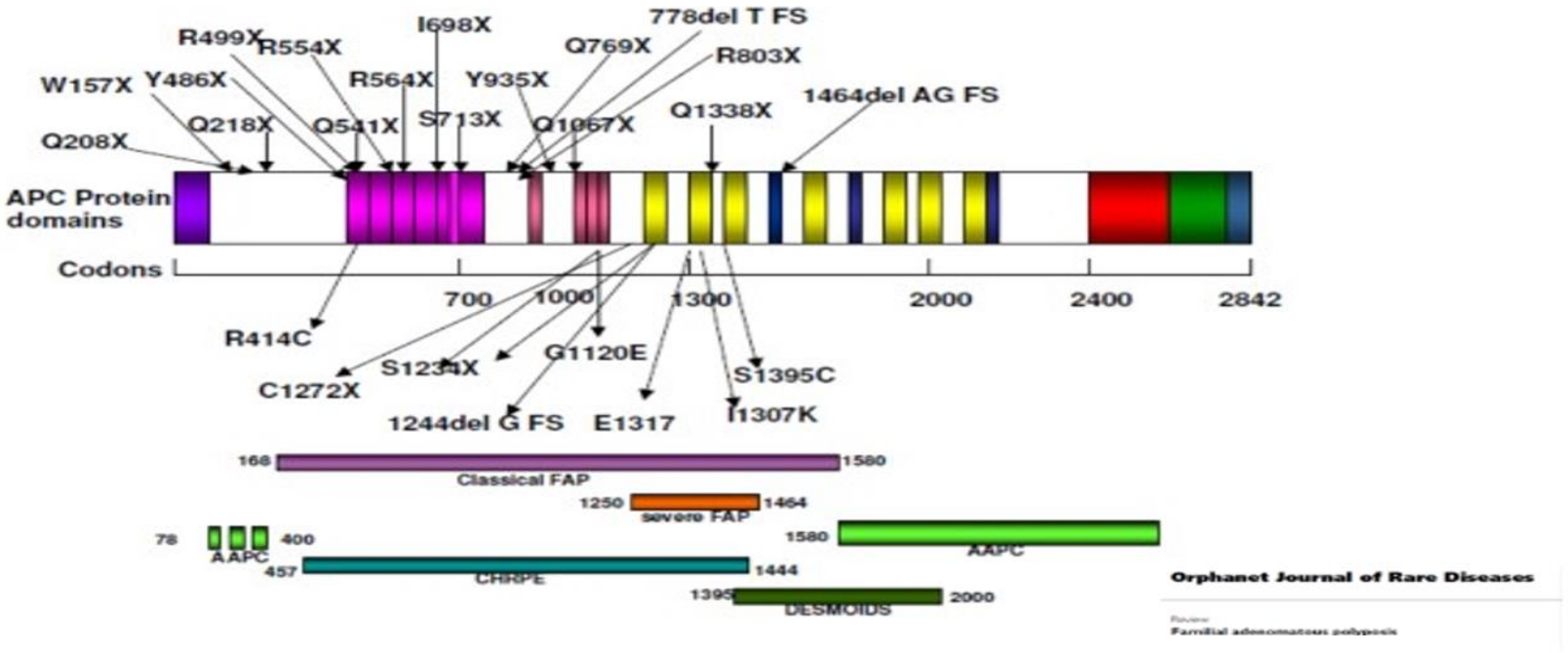
- Leftsided predominance of polyps/cancers
- High penetrance of mutation (APC Gene)
- Endoscopic management **not** an option
- Total proctocolectomy with ileoanal pouch
- Laparoscopic, without diverting ileostomy
- One stage procedure

Attenuated FAP (aFAP)



- Rightsided predominance of polyps/cancer
- High penetrance of mutation (APC gene)
- Endoscopic management an option depending on phenotype (age!)
- Prophylactic (sub)total colectomy
- Laparoscopic

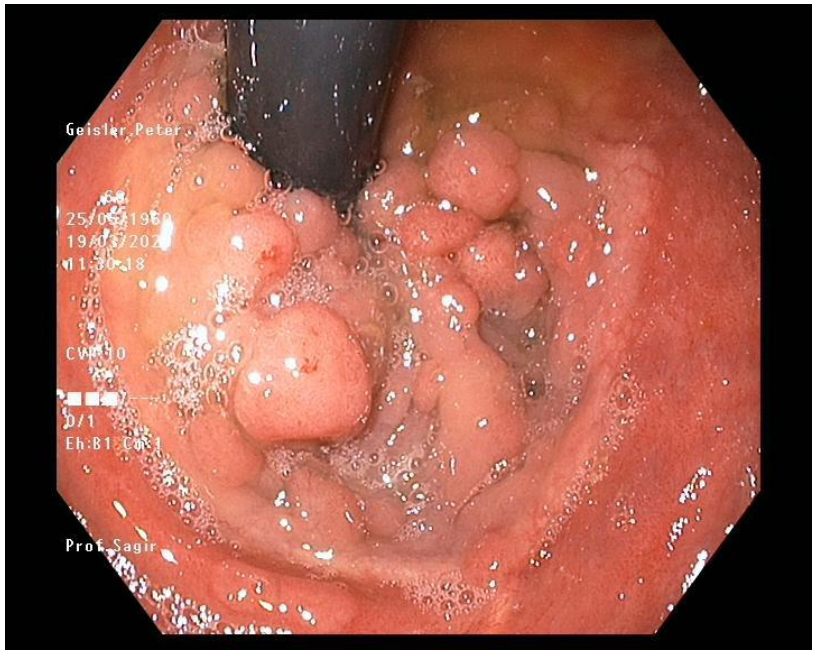
Adenomatous Polyposis Syndrome
APC Gene



The problem of the rectal remnant in double-stapled anastomosis

Previous guideline 2008

Double-stapled anastomosis



Guideline 2021

- Try to avoid the rectal remnant
- Patients >50 years of age and patients with >1000 colonic adenomas at the time of colectomy were more prone to ileal pouch adenomas and cancers**
- IMPORTANCE OF SURVEILLANCE REMAINS IN THE UPDATE

°Lee CHA, Kalady MF, Burke CA, et al. Incidence and Management of Rectal Cuff and Anal Transitional Zone Neoplasia in Patients With Familial Adenomatous Polyposis. *Dis Colon Rectum*. 2021;64(8):977-985. doi:10.1097**Tonelli F, Ficari F, Bargellini T, Valanzano R. Ileal pouch adenomas and carcinomas after restorative proctocolectomy for familial adenomatous polyposis. Dis Colon Rectum. 2012;55(3):322-329. doi:10.1097/DCR.0b013e318241e6f2

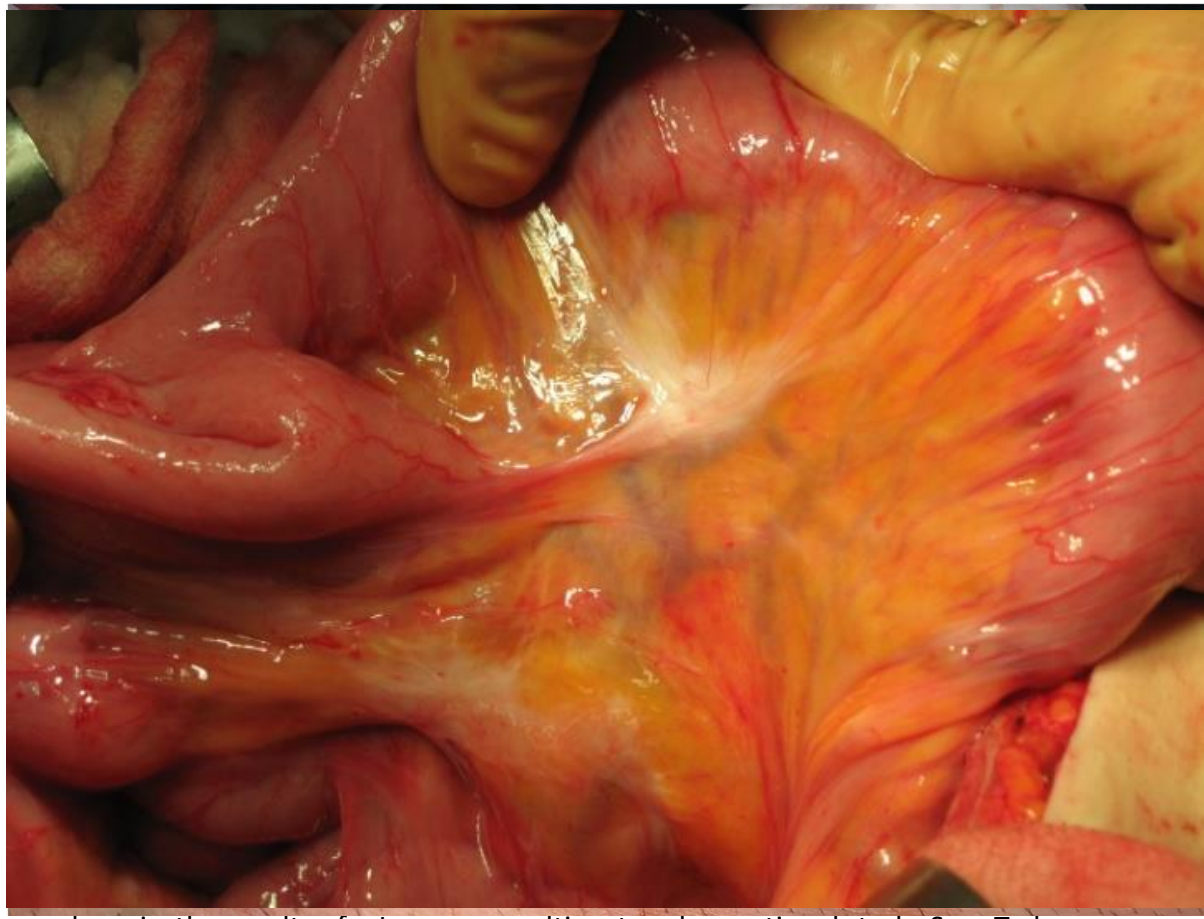
Desmoid tumors

Previous guideline 2008

Previous guidelines: reference to management: that sulindac in combination with tamoxifen is effective…Also small non-controlled studies indicate that chemotherapy or radiotherapy may be of benefit

Guideline 2023

- New studies with good result of regression with cytotoxic chemotherapy for intra-abdominal DT* °
- Assessment of a correct screening protocol**



*Inoue Y, Ishida H, Ueno H, et al. The treatment of desmoid tumors associated with familial adenomatous polyposis: the results of a Japanese multicenter observational study. Surg Today. 2017;47(10):1259-1267. doi:10.1007/s00595-017-1500-3

°Vincenzi, Bruno, et al. "FAP-related desmoid tumours treated with low dose chemotherapy: Results from a multicentre retrospective analysis." (2018): 11556-11556.

**Mete, L. Sanchez, et al. "OC. 04.9 surveillance protocol for abdominal desmoid tumours in familial adenomatous polyposis (fap): experience of a regional referral centre." Digestive and Liver Disease 2.48 (2016): e86.

Gut 2008;**57**:704–713. doi:10.1136/gut.2007.136127

Guidelines

Guidelines for the clinical management of familial adenomatous polyposis (FAP)

H F A Vasen,[1] G Möslein,[2] A Alonso,[3] S Aretz,[4] I Bernstein,[5] L Bertario,[6] I Blanco,[7] S Bülow,[8] J Burn,[9] G Capella,[10] C Colas,[11] C Engel,[12] I Frayling,[13] W Friedl,[4] F J Hes,[14] S Hodgson,[15] H Järvinen,[16] J-P Mecklin,[17] P Møller,[18] T Myrhøi,[5] F M Nagengast,[19] Y Parc,[20] R Phillips,[21] S K Clark,[21] M Ponz de Leon,[22] L Renkonen-Sinisalo,[16] J R Sampson,[13] A Stormorken,[23] S Tejpar,[24] H J W Thomas,[25] J Wijnen[14]

UPDATE 2023:

ESCP-EHTG Evidence based dynamic guidance

EHTG-ESCP Joint dynamic Guidance for FAP and rare adenomatous polyposis syndromes

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