



Young Onset Colorectal Cancer

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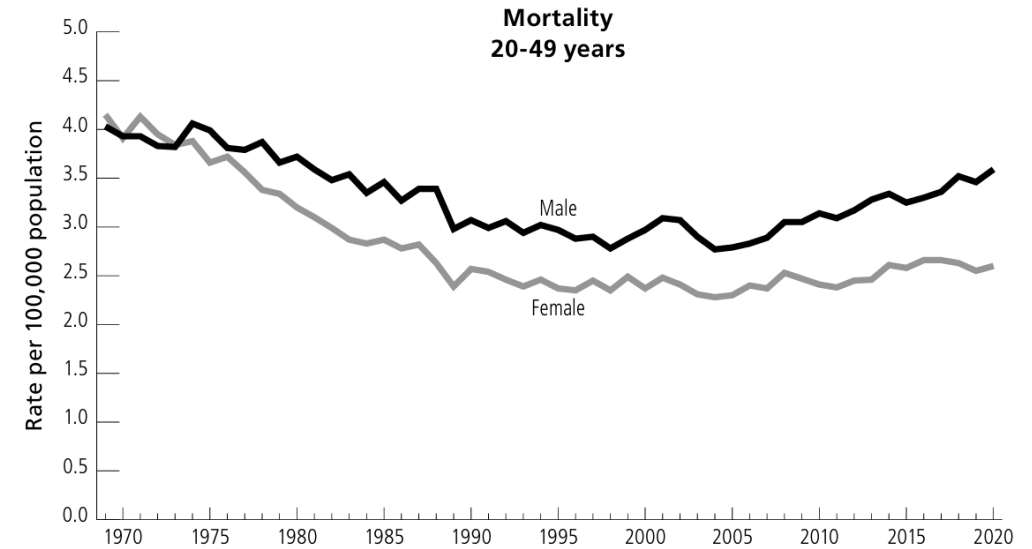
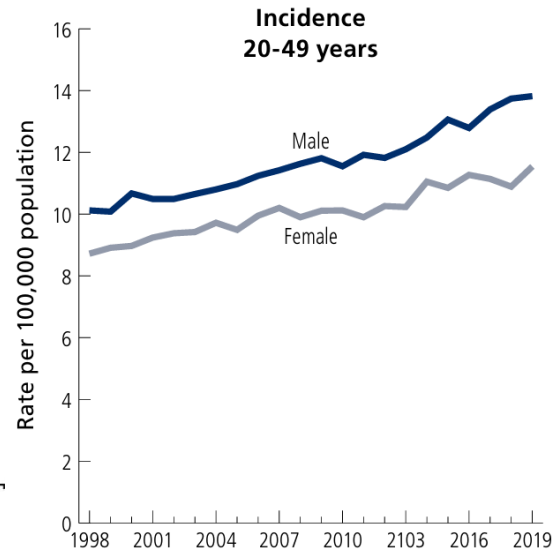
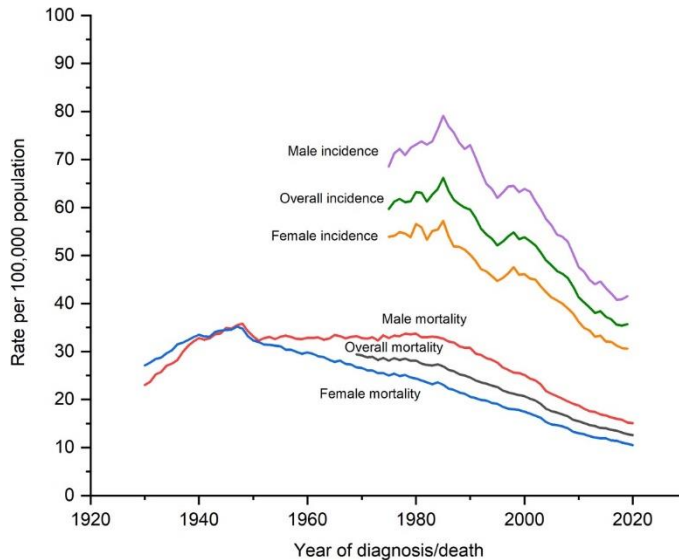
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Disclosures

- No relevant disclosures

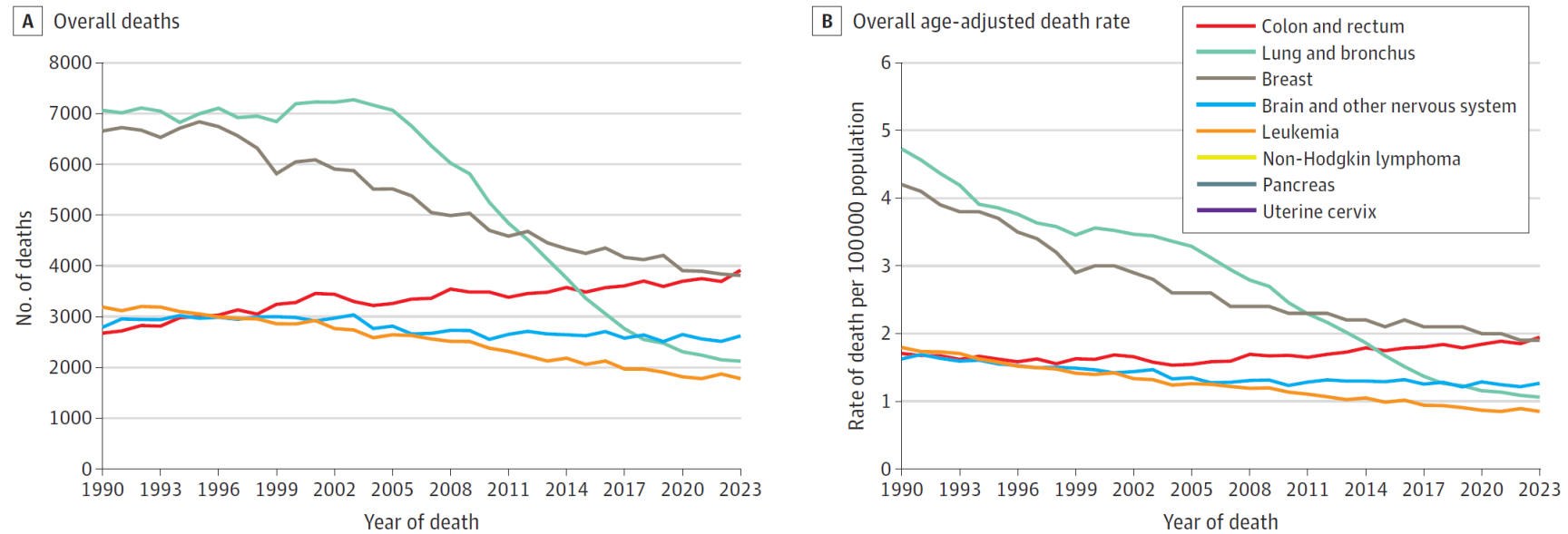


Decreasing CRC Overall But Alarming Rise in Early-Onset CRC



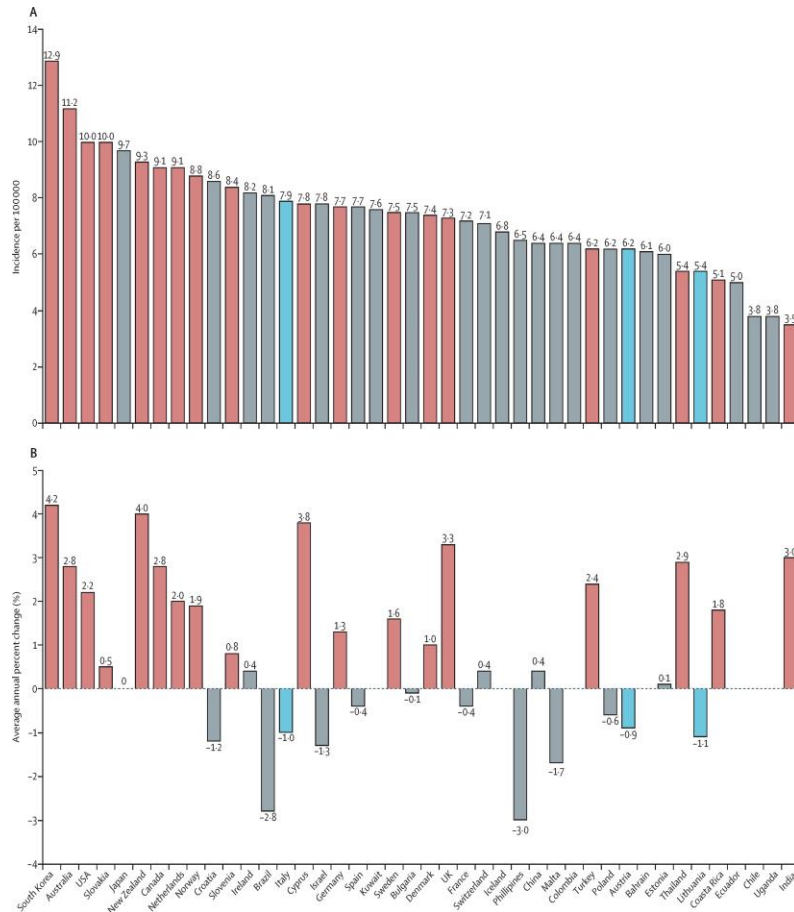
- EOCRC has increased by 51%, incidence $\uparrow$ 2% per year, mortality $\uparrow$ 1% per year
- 19,550 cases per year, 3,750 deaths per year

Leading Cancer Deaths in People Younger Than 50 Years

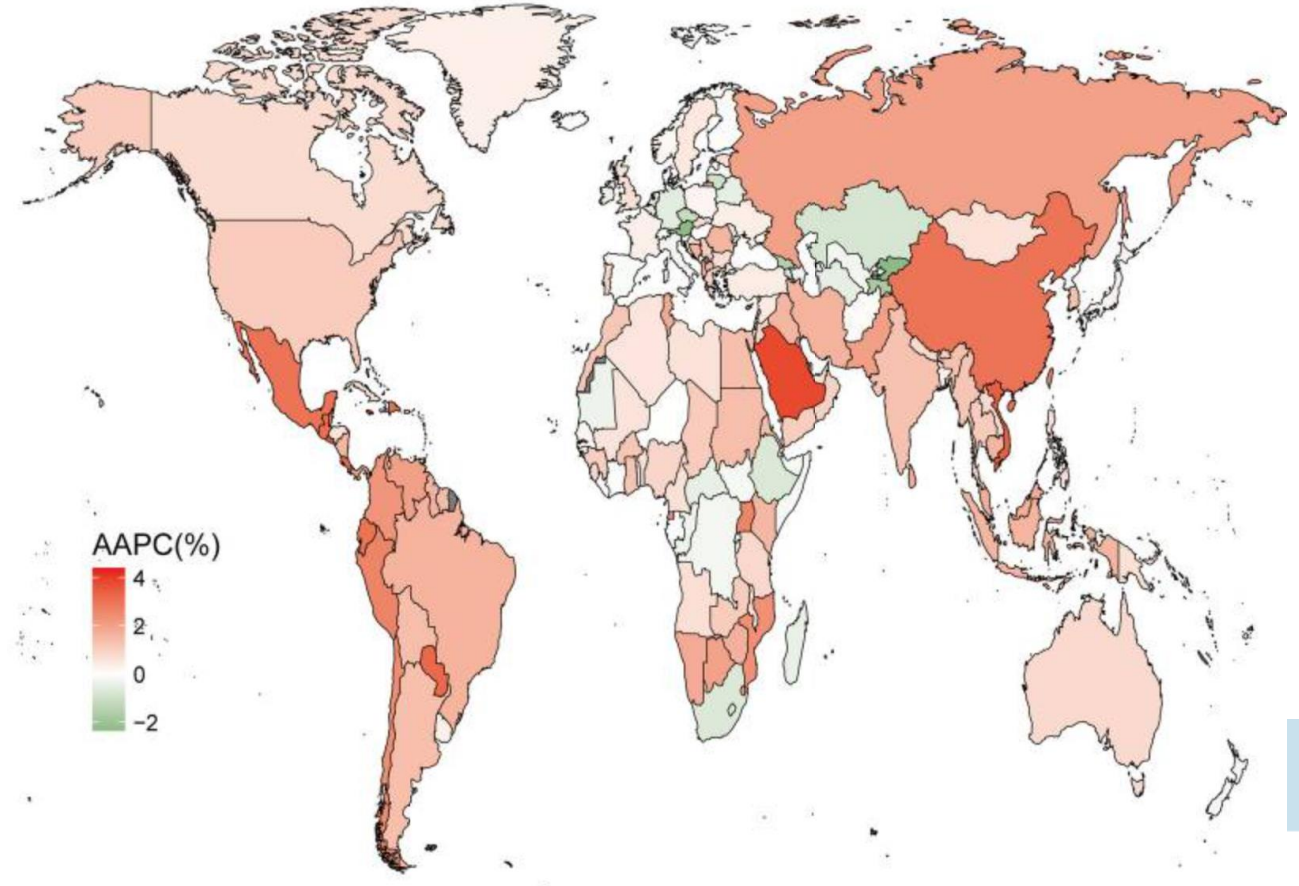


EOCRC is now #1 cause of cancer death for people under 50 years

Rise in EOCRC is Global



B



Worldwide incidence & average annual % change

EOCRC in Egypt



Egypt is one of the earliest and most striking examples worldwide of a high proportion of EOCRC

- 2024 study including 1,310 CRC patients from four Egyptian cancer centers
- 42.4% $\leq$ 45 years
- Rectal cancer higher in EOCRC; 54.7% vs. 40.6%
- No difference in stage, DFS, and OS
- Paradoxically, overall CRC incidence is low compared to US

Table 5 Age standardized incidence rates by gender in Gharbiah, Egypt and the United States Surveillance Epidemiology and End Results Program

	Gharbiah, Egypt 1999-2007			United States SEER 1999-2001			<i>P</i> value
	Total	Male	Female	Total	Male	Female	
Total cases	1364	737	627	55 480	27 892	27 588	
Total rate	5.5	6.1	4.9	32.0	37.7	27.4	< 0.0001 ¹
< 40 yr	1.3	1.4	1.2	1.2	1.3	1.2	
40-59 yr	12.0	12.8	11.2	37.9	43.3	32.8	
60-69 yr	19.4	22.5	15.8	154.0	185.4	126.4	
> 70 yr	21.2	24.4	18.6	311.3	369.8	270.8	

Young Father With Advanced Colorectal Cancer Urges Others to Act on Health Concerns

SEE ALL STORIES



Sisters Receive Young-Onset Colorectal Cancer Diagnosis Less Than One Year Apart

SEE ALL STORIES



Young Dad Recognizes Symptoms, Wins Battle with Colorectal Cancer

SEE ALL STORIES



Innovative Surgical Technique Treats Young Mom Diagnosed with Rectal Cancer

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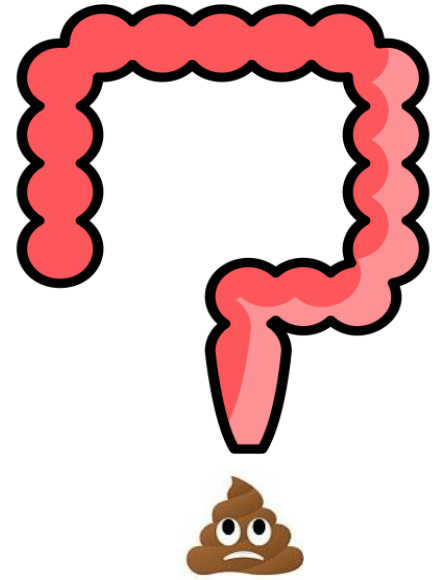
Young Father Overcomes Colorectal Cancer, Stresses the Importance of Knowing the Symptoms

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Important Considerations in EOCRC

- Why is the incidence increasing?
- Who is at highest risk?
- How can it be prevented?
- Different biology?
- **Special management considerations?**



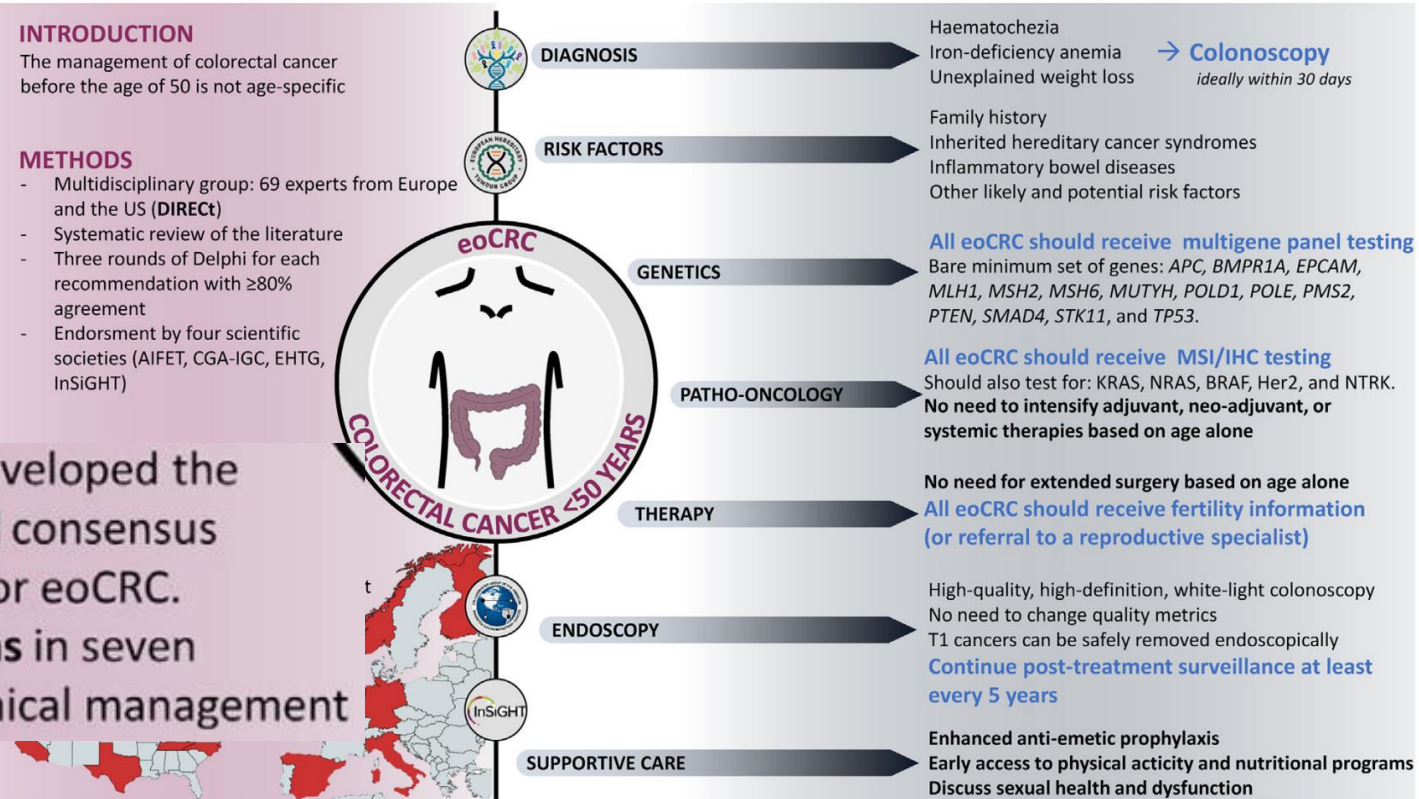
CLINICAL PRACTICE GUIDELINES

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



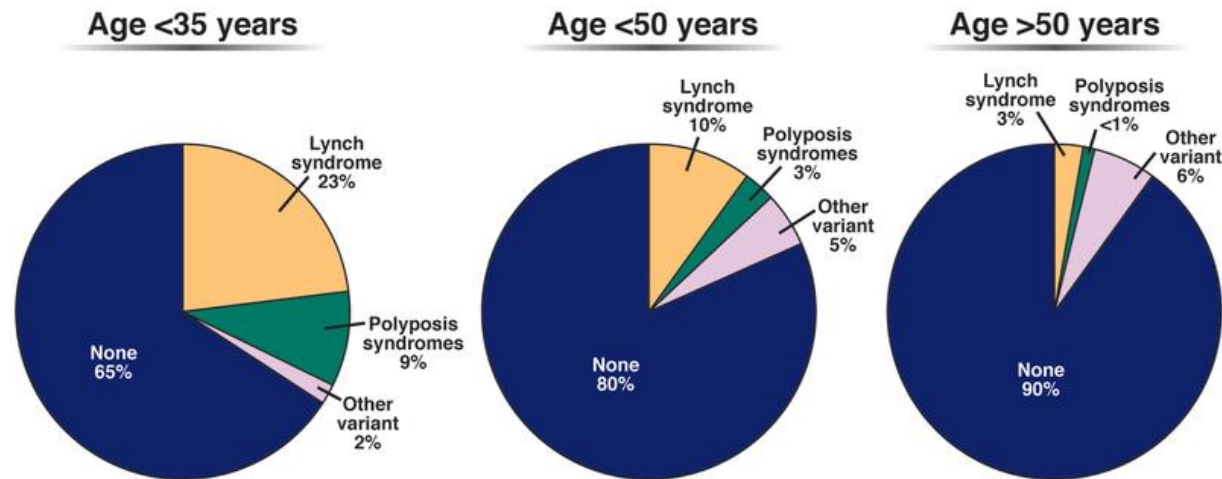
Giulia Martina Cavestro,^{1,*} Alessandro Mannucci,^{1,*} Francesc Balaguer,^{2,3,†} Heather Hampel,^{4,‡} Sonia S. Kupfer,^{5,‡} Alessandro Repici,^{6,‡} Andrea Sartore-Bianchi,^{7,‡} Toni T. Seppälä,^{8,9,10,‡} Vincenzo Valentini,^{11,‡} Clement Richard Boland,¹² Randall E. Brand,¹³ Tineke E. Buffart,¹⁴ 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 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,³ 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,³¹ Caitlin C. Murphy,³⁹ Karlijn Nass,²² Kimmie Ng,⁴⁰ Cristina Olini,⁴¹ Enrico Papaleo,⁴² Swati G. Patel,⁴³ Marta Puzzono,¹ Andrea Remo,⁴⁴ Luigi Ricciardiello,⁴⁵ Carla Ida Ripamonti,⁴ 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

The DIRECT group developed the first evidence-based consensus recommendations for eoCRC. 31 recommendations in seven areas relevant to clinical management



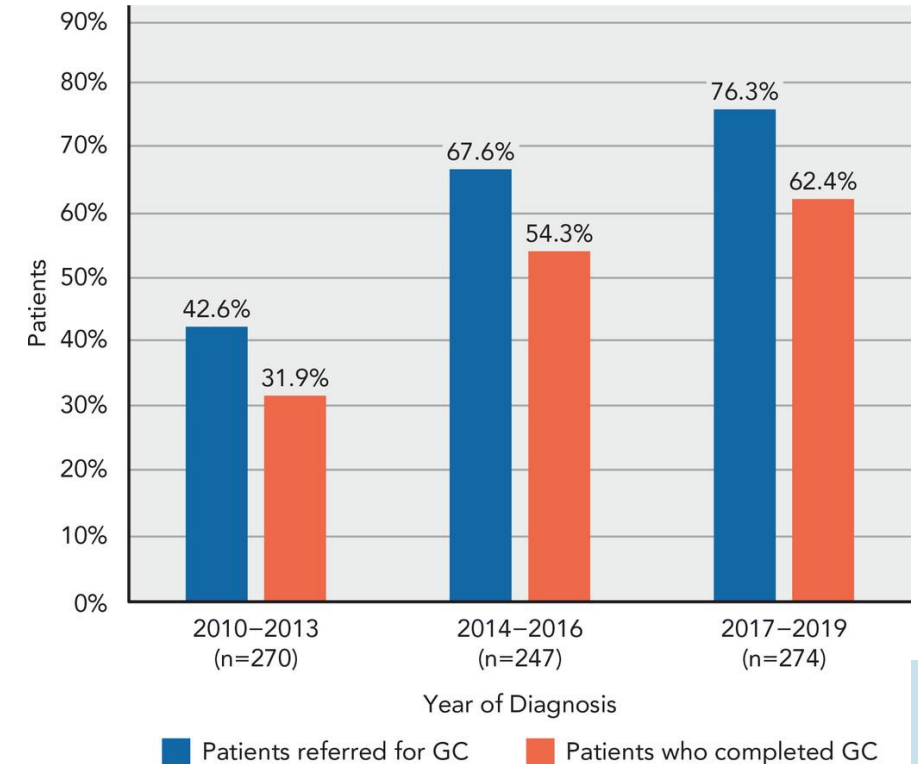
EOCRC—Optimizing Management Genetic Testing

- On germline multi-gene panel testing (MGPT) up to 30% of EOCRC carry a germline pathogenic variant regardless of family history
- The diagnosis of a hereditary cancer syndrome has important treatment and surveillance implications for patients and their families
- → NCCN guidelines 2022 recommend germline MGPT in all CRC patients < 50 y/o

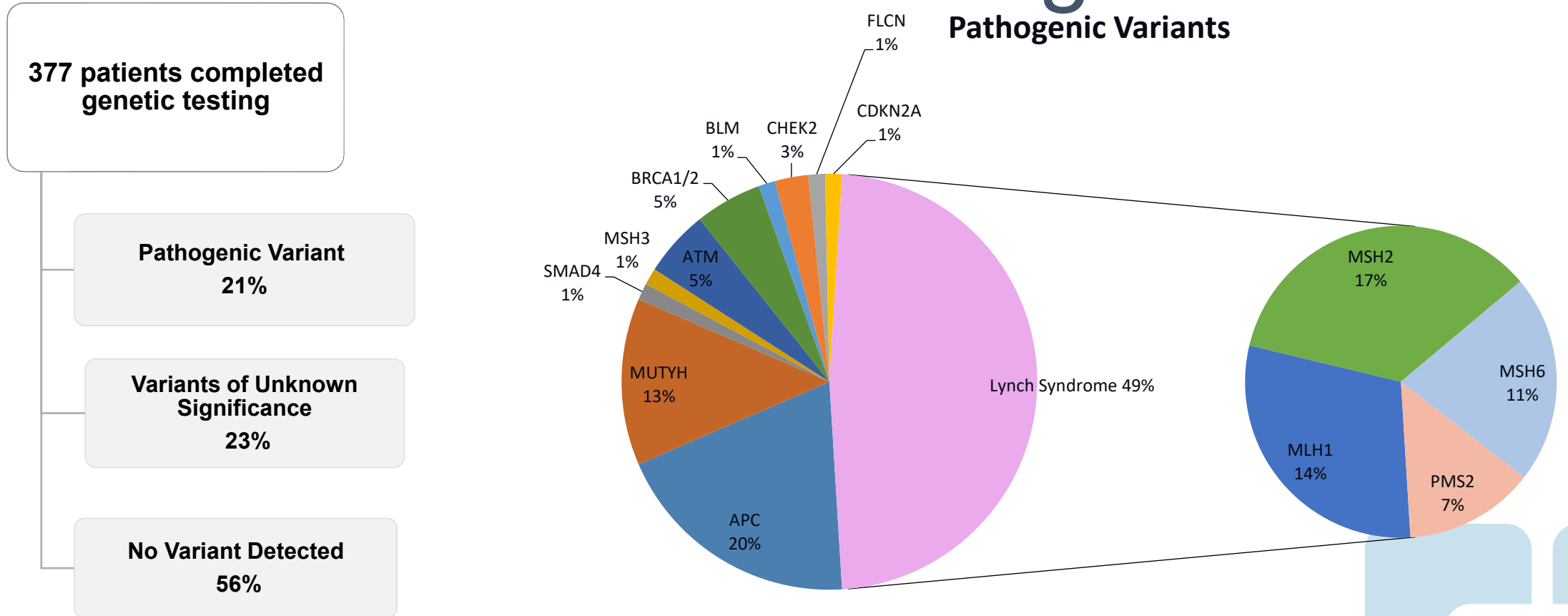


EOCRC—Optimizing Management Genetic Testing

- N = 791 EOCRC patients seen at CCF 2010-2019, mean age 44
- Genetic counseling (GC) referral increasing over time, yet even recently ~25% not referred
- Younger age and family history of CRC associated with referral to GC



EOCRC—Optimizing Management Genetic Testing



EOCRC—Optimizing Management Genetic Testing

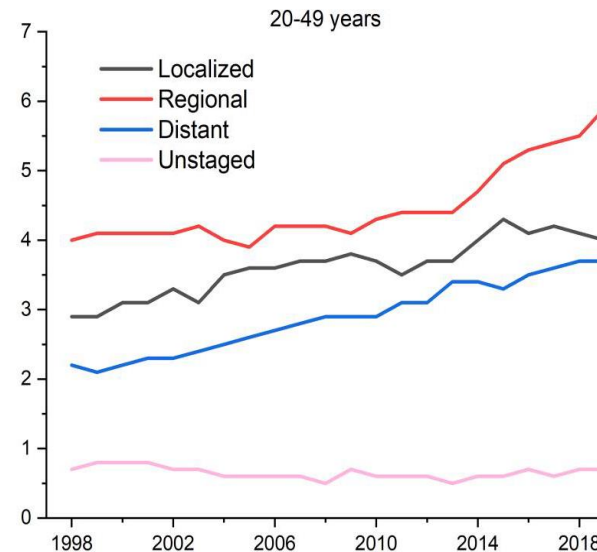
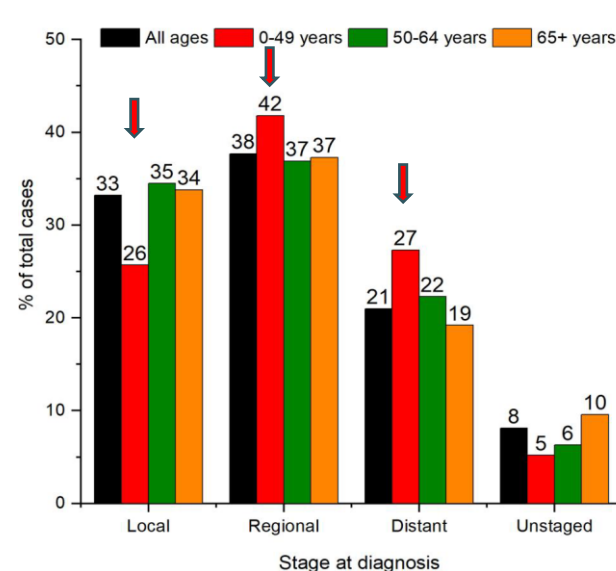
1 in 5 EOCRC patients have germline pathogenic variants

Lynch syndrome and adenomatous polyposis being most common

- Important treatment considerations
 - Neoadjuvant immunotherapy for dMMR patients
 - Consider extended resections (TAC/IRA vs. TPC/IPAA) for *MLH1*, *MSH2*, *APC*, *MUTYH*, *POLE/POLD1*, ...
- Surveillance Considerations
- Cascade testing of family members
- ~25% of EOCRC patients not referred for genetic counseling
- **→ Need to implement care pathways to optimize genetic counseling referral and testing in all EOCRC patients**

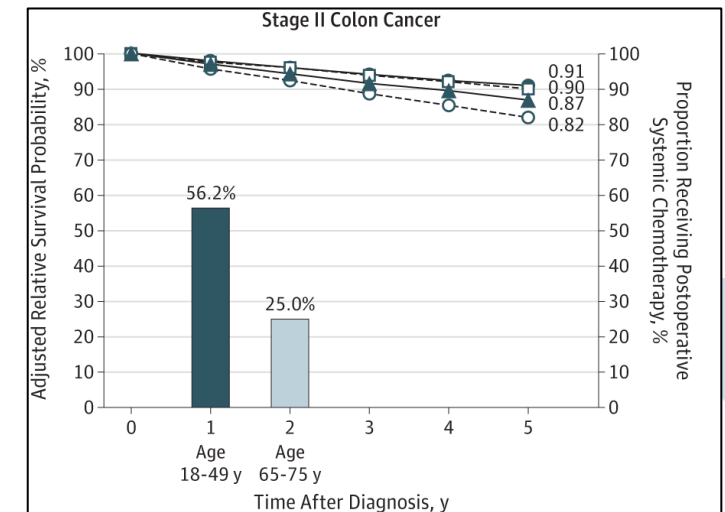
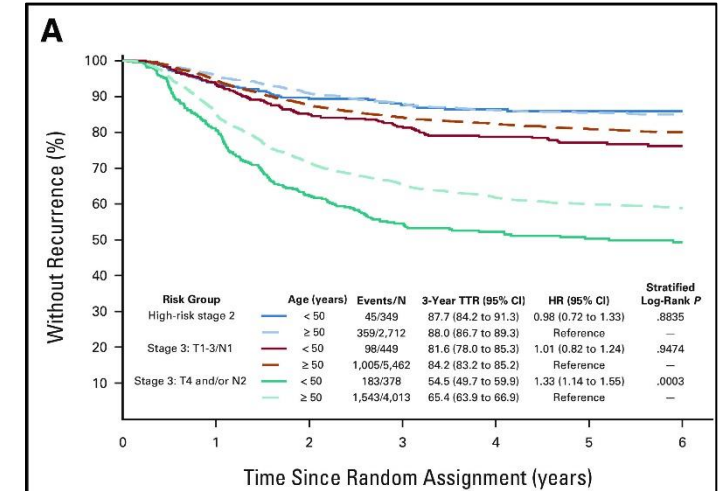
EOCRC—Optimizing Management Advanced Disease

- ~25% higher risk for advanced stage (III-IV) disease in EOCRC
- Rising incidence of EOCRC primarily due to increased diagnosis of advanced stage
- 40% longer time to diagnosis for symptomatic EOCRC patients
 - ?delayed diagnosis vs. disease biology



EOCRC—Optimizing Management Advanced Disease

- EOCRC patients have better performance status
 - More likely to receive multiagent chemotherapy
 - Higher dose intensity and adherence
 - Higher incidence of GI toxicity
- No significant improvement in outcomes
 - Concern for overtreatment of EOCRC



EOCRC—Optimizing Management Advanced Disease

- In well selected patients, surgery for metastatic disease can prolong survival and offers a chance for cure
- Young patients are better candidates for high-risk surgery

Liver

Series Author, Year	Patients (n)	Median DFS (mo)	DFS (%)	Median OS (mo)	OS (%)	Operative Mortality Rate (%)	Major Complication Rate (%)
Fong et al, ⁶ 1999	1001	—	—	69	5-y: 37 10-y: 22	2.8	31
Pawlik et al, ⁴⁵ 2005	557	—	—	74	5-y: 58	0.9	—
Nordlinger et al, ¹⁷ 2008; Nordlinger et al, ¹⁸ 2013 (RCT)	364	11–18	3-y: 28.1–36.2	54.3–61.3	5-y: 47.8–51.2	1.3	16–25
Rees et al, ⁴⁴ 2008	929	—	—	42.5	5-y: 36 10-y: 23	1.5	25.9
de Jong et al, ⁴⁶ 2009	1669	23	5-y: 30	36	5-y: 47.3	—	—
House et al, ⁴⁷ 2010	1600	—	5-y: 33	64	5-y: 43	1	44

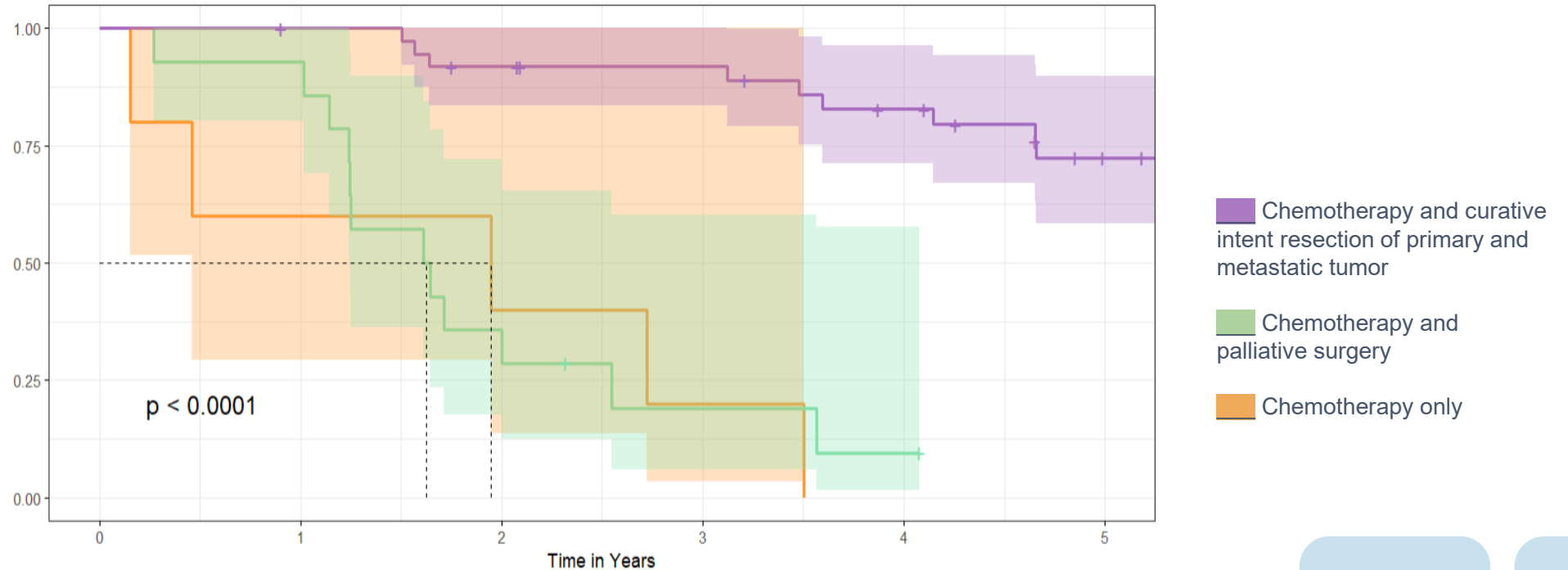
Peritoneum

Series Author, Year	Patients (n)	Perfusion Technique	Median OS (mo)	5-y Survival (%)	Operative Mortality Rate (%)	Major Morbidity Rate (%)
Glehen et al, ¹⁰⁵ 2004	506 (28 institutions)	HIPEC and EPIC, multiple drugs	32.4	31	4	22.9
Verwaal et al, ¹⁰⁶ 2008 (only RCT)	105	Open, MMC	48	45	8	19
Elias et al, ¹⁰⁷ 2010	523 (23 institutions)	HIPEC and EPIC, multiple drugs	30.1	27	3.3	31
Ung et al, ¹⁰⁸ 2013	211	HIPEC (MMC) or EPIC (IP 5-FU)	46.8	42	1	44.3
Kuipers et al, ¹⁰⁹ 2013	660	Open, MMC and oxaliplatin	33	31	3	34
Esquivel et al, ¹⁰⁰ 2014	705	Oxaliplatin or MMC	41	58	—	—
Levine et al, ¹⁰³ 2014	248	MMC	—	15	3.8	42

Lung

Case Series Author, Year	Patients (n)	Median RFS (mo)	RFS (%)	Median OS (mo)	OS (%)	Operative Mortality Rate (%)	Major Complication Rate (%)
Kanemitsu et al, ¹¹⁷ 2004	313	—	—	38.4	5-y: 38.3	1.3	—
Onaitis et al, ¹¹⁸ 2009	378	24	3-y: 28	—	3-y: 78	1	10
Borasio et al, ¹¹⁹ 2011	137	35.6	3 y: 51.1	36.2	5-y: 55.4	0	13.1
Blackmon et al, ¹²⁰ 2012	229	19.4	—	70.1	5-y: 55.4	0	1.7
Zampino et al, ¹²¹ 2014	199	35	—	50.4	5-y: 43	0	—
Hernandez et al, ¹²² 2016	522	28.3	—	54.9	5-y: 46.1	0.38	15.7

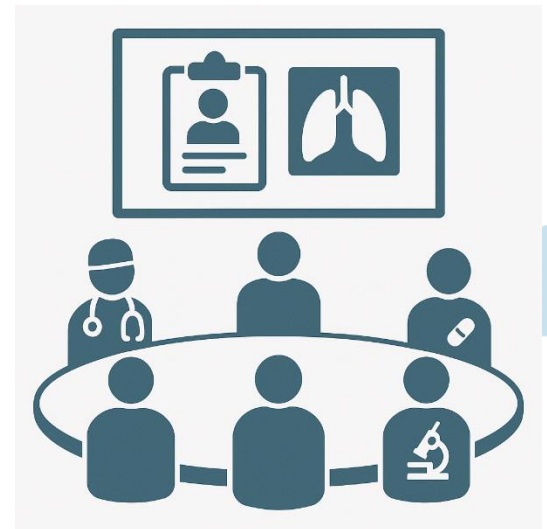
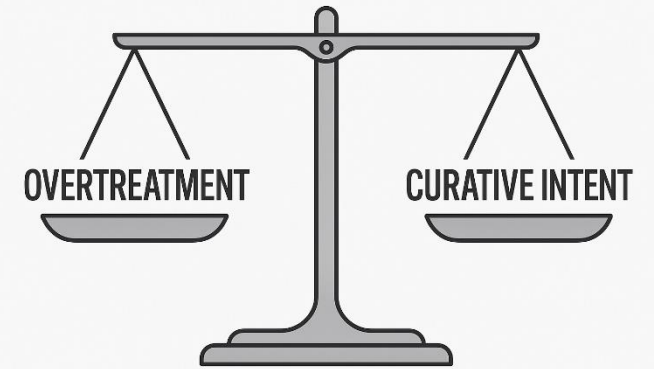
EOCRC—Optimizing Management Advanced Disease



EOCRC patients with isolated liver metastases have improved survival when selected for curative intent surgery/liver directed tx

EOCRC—Optimizing Management Advanced Disease

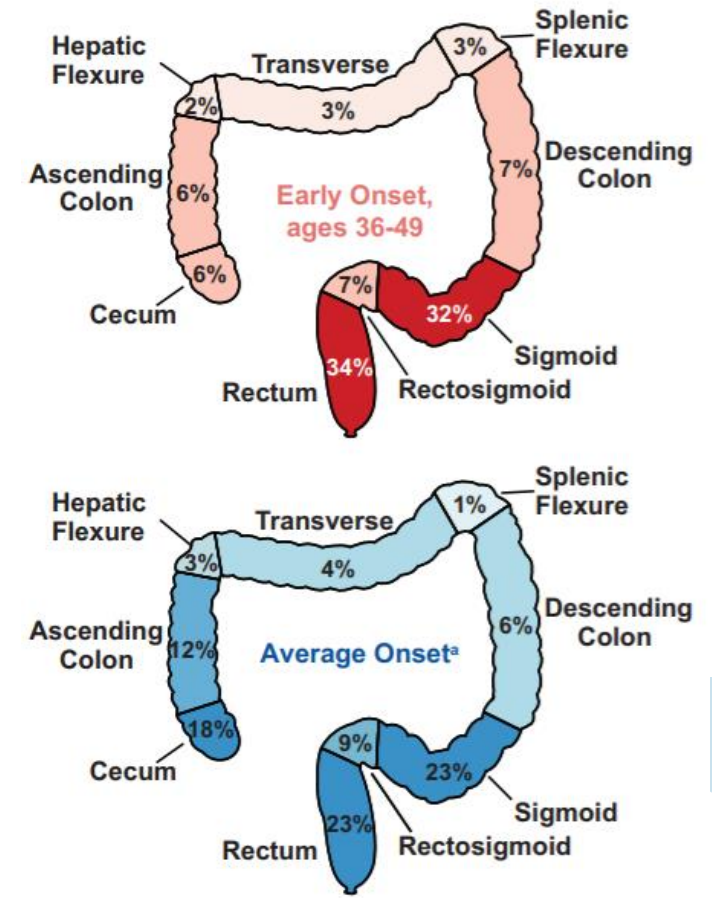
- Good PS, less frail → candidates for surgery for oligometastatic disease combined with multiagent chemotherapeutic regimens
- →MDT decision making to judiciously select Stage IV patients for curative-intent surgery
- → Shared decision making



EOCRC—Optimizing Management

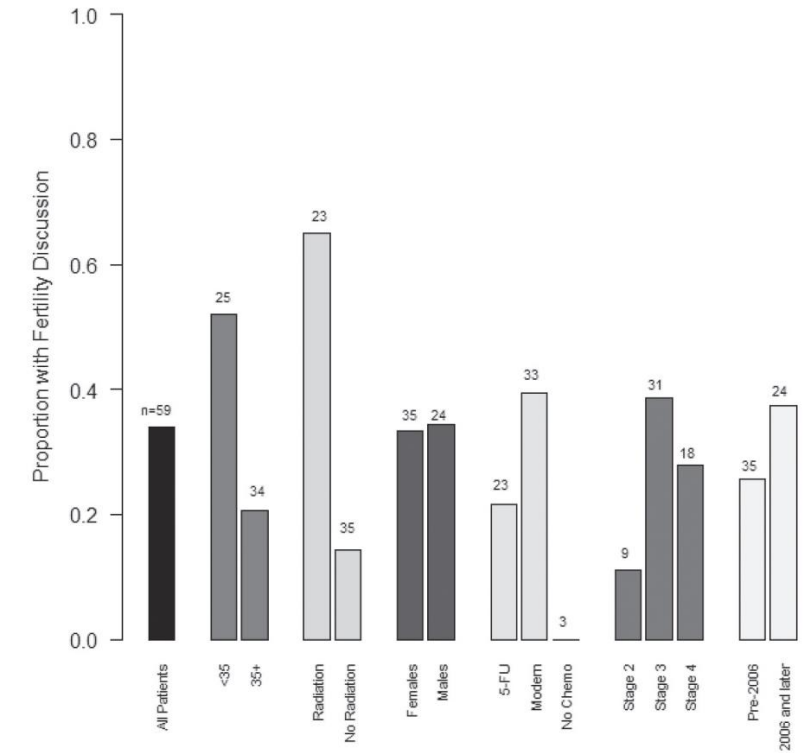
Higher incidence of Rectal Cancer

- 41% of all EOCRC are in the rectum/rectosigmoid
 - 30% higher than AOCRC
- Need for multimodal treatment
 - XRT, Chemotherapy, Surgery
- Significant long-term sequelae and survivorship concerns
 - Infertility
 - Sexual dysfunction
 - Premature menopause, ED
 - Bowel dysfunction
 - LARS
 - Body image
 - Ostomy

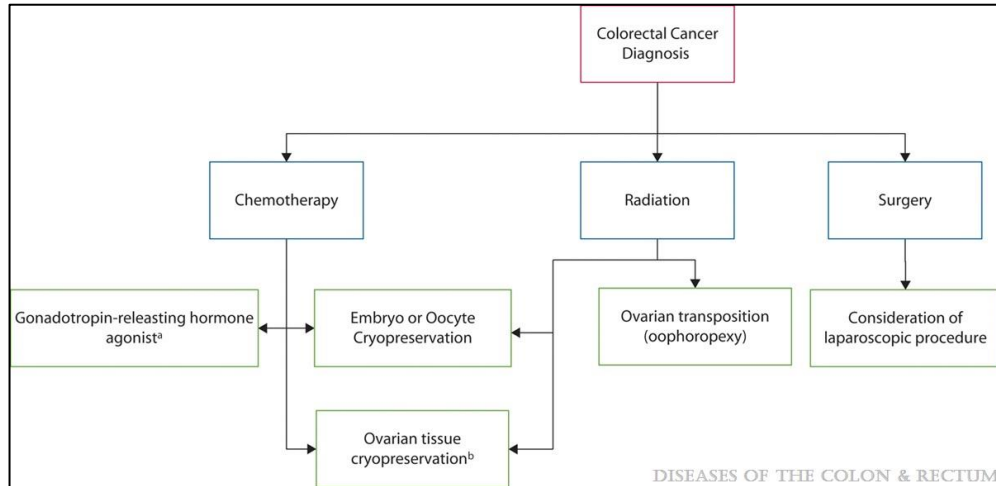


EOCRC—Optimizing Management Fertility Preservation

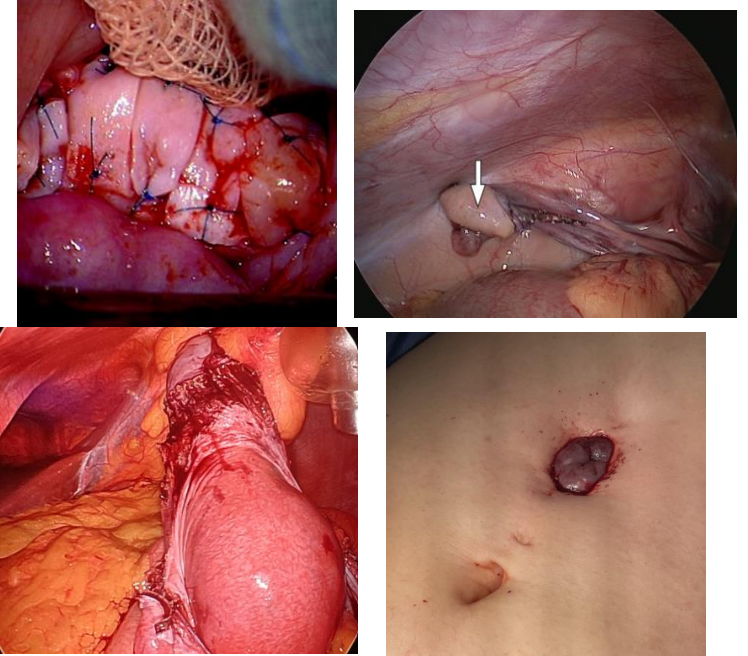
- Cytotoxic drugs, pelvic surgery and radiotherapy have a significant impact on male and female fertility
 - Majority of female patients undergoing pelvic XRT will experience ovarian failure
- Guidelines recommend discussion of fertility preservation with all reproductive-age patients
 - Poor adherence with guidelines



EOCRC—Optimizing Management Fertility Preservation



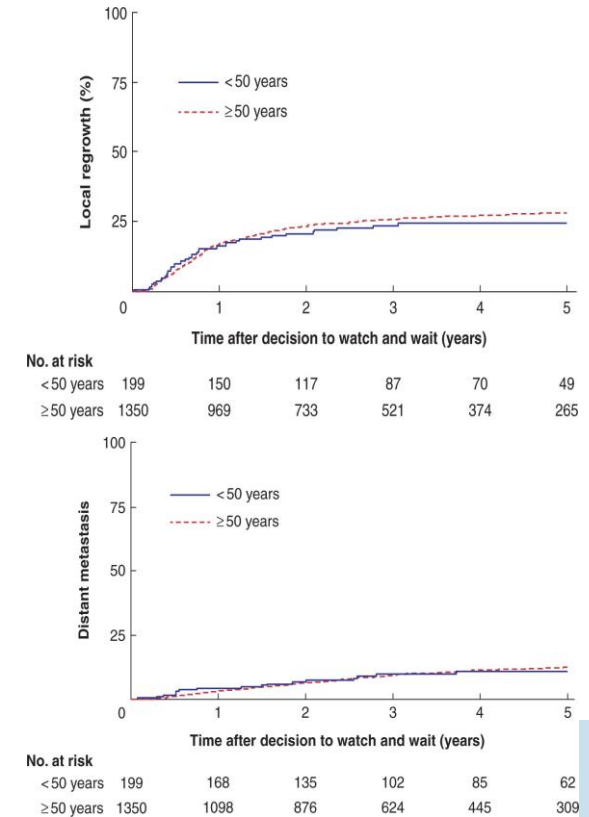
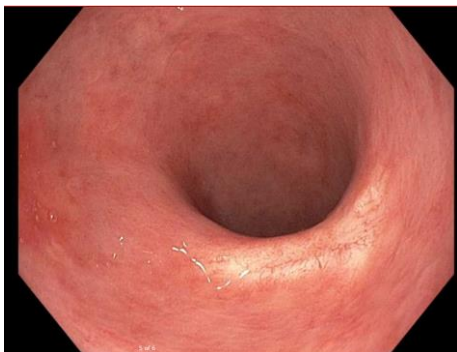
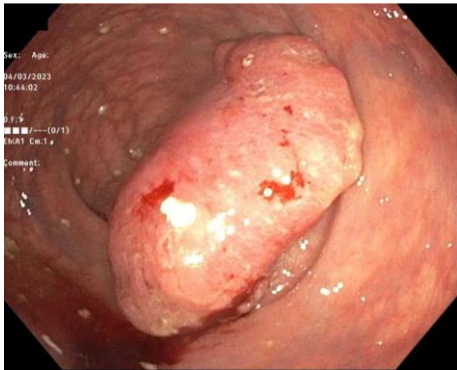
- Sperm cryopreservation
- Embryo cryopreservation
- Oocyte cryopreservation
- Ovarian tissue cryopreservation
- Ovarian transposition
- Uterine transposition/fixation



- Fertility counseling has been shown to reduce long-term regret and dissatisfaction among survivors
- **Fertility counseling for all EOCRC patients of childbearing age**

EOCRC—Optimizing Management Organ Preservation / W&W

- IWWD 199 patients < 50 with cCR and managed with W&W
- MSKCC 98 patients < 50 managed with W&W
- 3-year local regrowth, metastasis rate, and DFS similar to > 50
- “There is no difference in oncological risk between young patients and older ones, so there should not be a reason to dissuade young patients from an organ-preserving treatment”



EOCRC—Optimizing Management Financial Toxicity

- EOCRC at higher risk for financial toxicity:
 - Increased out-of-pocket cost
 - Employment disruption
 - Loss of income

TABLE 1 Financial toxicity indicators in the study cohort

	<i>n</i> = 157 <i>n</i> (%)
<i>Payment issues</i>	
Two or more bills sent to collections	34 (21.7)
Application or granting of a payment plan for medical bills	22 (14.0)
One or more bills reaching settlement	39 (24.8)
Declaration of bankruptcy	1 (0.6)
<i>Utilization of financial assistance programs</i>	
Utilization of a financial assistance program for medical costs	45 (28.7)
Utilization of a copay assistance program for drug costs	11 (7.0)
Enrollment in a social work philanthropy fund	46 (29.3)

Of the 157 patients, 31 had two indicators and 5 had three indicators

TABLE 3 Multivariable regression analysis for association with financial toxicity (*n* = 758)

Characteristic	OR	95 % CI	p-value
<i>Age (10-year decrease)</i>	1.30	1.14–1.48	< 0.001
<i>Median income (\$50,000 decrease)</i>	1.35	1.05–1.74	0.020
<i>Sex</i>			
Male	–	–	
Female	1.44	0.99–2.10	0.060
<i>Marital status</i>			
Partnered	–	–	
Nonpartnered	1.37	0.93–2.03	0.11

EOCRC—Optimizing Management Financial Toxicity

- EOCRC at higher risk for financial toxicity:
 - Increased out-of-pocket cost
 - Employment disruption
 - Loss of income
 - Career stagnation
 - > Material hardship, psychological distress, ↓QoL
 - > Cost-related care nonadherence
- **Need for:**
 - **Financial Screening**
 - **SW navigation**
 - **Psychosocial support**

You're talking about a really catastrophic hit to your career. I mean I was [in my 30s] when I was diagnosed. I was supposed to be tenure track. And now I'm not.

Once you realize "I'm going to survive this," you need to worry about how you're going to pay for everything.

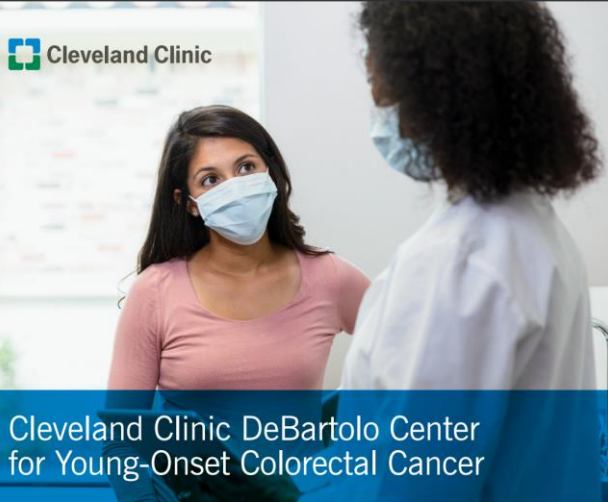
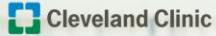
I didn't sign up for the max so the amount that I was getting only covered my rent, so my family still had to pay the rest of my bills, but at least I still had somewhere to live, because I really would have been **homeless.**

EOCRC—Optimizing Management Summary

- Specific diagnostic and treatment consideration that require specialized multidisciplinary care including:
 - Genetic counseling and testing
 - Multidisciplinary treatment of advanced/metastatic disease
 - Fertility Preservation
 - Psychosocial support
 - Surveillance and Survivorship
 - Sexual/Hormonal Health (male and female)
 - GI dysfunction: Nutrition, LARS, Ostomy care/support
 - Consideration for Organ Preservation
 - Wellness and Prevention



EOCRC—Optimizing Management Summary



Cleveland Clinic DeBartolo Center for Young-Onset Colorectal Cancer



David Linka, MD, FACS, FASCRS
Director, Center for Young-Onset
Colorectal Cancer

The Cleveland Clinic Center for Young-Onset Colorectal Cancer is dedicated to the care of patients diagnosed with colorectal cancer before the age of 50. While a cancer diagnosis at any age requires specialized care, young people with colorectal cancer face unique challenges and concerns. Our center is composed of a multidisciplinary team of experts who provide young colorectal cancer patients coordinated, comprehensive, and individualized care with the goal of optimizing oncologic outcomes, quality of life, and psycho-social wellbeing.

Program Coordinators

Navigating through multidisciplinary cancer care can often be confusing and overwhelming. Our center includes coordinators to the care of patients with young-onset colorectal cancer. Their primary goal is to facilitate and coordinate the scheduling of appointments and personalized referrals based on a specific patient's needs. Our coordinators are here to make this process as easy as possible for our patients.

Colorectal Surgery

As part of the multidisciplinary team, our surgeons, specialized in oncologic colorectal surgery, utilize advanced techniques and risk for cancer recurrence while maintaining optimal quality of life and allowing for accelerated recovery and return to work/family life.

- Laparoscopic/robotic surgery and endoluminal surgery (ESD, TAMIS)
- Surgery for recurrent and/or metastatic colorectal cancer
- Cytoproductive surgery and HIPEC
- Enhanced Recovery after Surgery (ERAS)

Oncology

Patients with young-onset colorectal cancer are provided with a comprehensive and personalized treatment plan by our oncologists specialized in gastrointestinal malignancies. Oncologic treatment during all phases of care, including

the neoadjuvant (pre-surgical), adjuvant (post-surgical) periods is individualized based on a patient's tumor characteristics and genetic makeup, medical history, and goals of care.

Radiation Oncology

Our team of radiation oncologists provide comprehensive care individualized for each patient at all phases of their treatment journey prior to initiation of radiation treatment, during radiation treatment, and after radiation treatment/survivorship. Especially in young patients, it is important to minimize the long-term side effects that can be associated with radiotherapy. We have cutting edge technology coupled with compassionate physicians, nurses, and staff with significant expertise that allow us to optimize treatment plans for each patient.

Genetics

Colorectal cancer in young people is more commonly associated with an inherited genetic syndrome than in older people. These inherited conditions can be detected by a simple blood draw. Genetic testing results can guide treatment and future screening for the patient and their family. We therefore recommend that all patients with young-onset colorectal cancer have a consultation with a genetic counselor to discuss genetic testing options. Genetic testing is typically covered by insurance and billing is discussed during your appointment. If testing reveals a hereditary colorectal cancer predisposition, patients will be referred to our hereditary colorectal cancer registry (Weiss Center) for further specialized care.

Liver & Thoracic Surgery

Young patients are more frequently diagnosed with colorectal cancer at an advanced stage, with cancer spread to other organs, such as the liver or lungs. To maximize survival and cure, our patients are seen by liver and thoracic surgeons who are specialized in treating colorectal metastases, utilizing state-of-the-art surgical procedures, including:

- Minimally invasive liver resection and microwave ablation
- ALPPS procedure
- Liver transplantation
- Minimally invasive lung resection (VATS)

Gastroenterology

Young patients with a history of colorectal cancer have a higher first-degree relative and advanced risk of developing colorectal polyps and cancers. Our team of gastroenterologists with expertise in high-risk colorectal



cancer screening and surveillance, help guide a risk-based colonoscopic surveillance protocols for patients and their family members.

Male Fertility and Sexual Health

Cancer and its treatment can sometimes impact fertility and sexual health in men. Our center includes specialized physicians that can assist with:

- Fertility preservation, such as sperm banking before initiation of treatment
- Fertility services after treatment
- Evaluation and treatment of sexual function concerns, such as erectile dysfunction and ejaculatory abnormalities

Female Fertility Preservation

Many young women undergoing cancer treatment have concerns about their ability to conceive children in the future. Our Fertility Preservation Program provides comprehensive reproductive care to facilitate family planning by providing:

- Fertility preservation services, including egg, embryo, and ovarian tissue freezing
- Fertility preserving surgery
- Suppressing ovarian activity during chemotherapy
- Consultations on the impact of cancer treatments on fertility
- Fertility services after treatment

Female Hormonal and Sexual Health

Women with a history of colorectal cancer can have complex women's health needs. Our Subspecialty Women's Health Program addresses issues related to hormonal changes and sexual health. We utilize a comprehensive team-based approach for evidence-based treatment options addressing:

- Menopausal health, including hormonal and non-hormonal treatment options
- A comprehensive sexual health program for any woman, with special emphasis on the most appropriate treatments after cancer treatment
- Hormonal and non-hormonal treatments for osteoporosis

Maternal Fetal Medicine

Patients who receive a cancer diagnosis during pregnancy or who have undergone cancer treatment prior to pregnancy face unique challenges. As part of an interdisciplinary team of experts, our Maternal Fetal Medicine specialists (high-risk pregnancy experts) provide:

- Individualized care from preconception through pregnancy, delivery, and the postpartum period
- Guidance on the provision of the most effective cancer treatment that can be administered safely during pregnancy and lactation
- Monitoring of the condition of the mother/baby during pregnancy and guide delivery timing
- Postpartum contraceptive planning and guide transition from pregnancy to ongoing care with the interdisciplinary oncology team

Psychology

Young adults confronted with a cancer diagnosis face challenges outside of everyday experience that may include disruption of life plans, education/volunteering/relationship/family, decisions about treatment, parenting while ill, reshuffling family roles, communication and social support, managing symptoms (fatigue, pain, sleep, moods) and coping with uncertainty. Our team includes licensed clinical psychologists with expertise in providing psychological support to young people with cancer, including:

- Brief psychotherapy for coping skills and problem-solving
- Ongoing psychotherapy for anxiety, depression and stress-related symptoms
- Consultation for specific issues (e.g., how to talk to children about illness and treatment)

Social Work

A cancer diagnosis can be frightening and stressful. Social Workers at Taussig Cancer Center offer support to help patients and families cope with challenges related to cancer.

Social workers offer:

- Counseling support for patients and care partners
- Assistance with financial, insurance, disability and employment concerns
- Support and assistance with Advance Care Planning (Health Care Power of Attorney and Living Will)
- Advocacy to help you navigate the health care system and access support services
- Assistance with mental health referrals

To contact a Taussig Cancer Institute social worker, please call the toll free line at 833.291.3438

Wellness, Preventative & Integrative Medicine

We also encourage young patients with colorectal cancer to see one of our experts at the Department of Wellness and Preventive Medicine for Integrative and Lifestyle Medicine Consults. Utilizing a holistic approach, our providers cover a variety of concerns including cancer prevention, lifestyle modification, and cancer treatment-induced symptom palliation.

- Nutrition counseling, dietary intervention, weight management, vitamin/supplement counseling
- Stress management practices
- Natural treatment of symptoms associated with cancer and its treatments including: Acupuncture, chiropractic care, massage therapy, yoga, personal training, mind-body psychotherapy

For questions and appointments, please call 216.444.4325

Palliative Medicine

Palliative medicine is a form of specialized medical care for people living with serious illness (including stage IV cancer), designed to provide relief from both the symptoms and stress of this illness. Palliative care integrated alongside cancer-directed treatment has been shown in some patients with metastatic cancer to improve quality of life, and even survival. The palliative medicine team can assist young-onset colorectal cancer patients and their families with:

- Management of physical symptoms (pain, nausea)
- Assistance with medical decision making, ensuring treatments pursued are consistent with big-picture goals
- Assistance with advanced care planning and planning for all future possible outcome scenarios (best case/worst case)

For more information

To schedule an appointment or learn more about our services, please call us at 216.444.5731 or email us at yoCRC@ccf.org

The young-onset colorectal cancer caregivers offer appointments at many Cleveland Clinic locations, and some may be able to schedule an appointment virtually. Please call our office or visit our website to see what scheduling options may be available to you.

Edward J. DeBartolo, Jr. Family Center for Young-Onset Colorectal Cancer
9500 Euclid Avenue
Cleveland, OH 44195



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EOCRC—Optimizing Management Conclusion

EOCRC has multiple specific treatment considerations that require a comprehensive, coordinated, and compassionate approach provided by a multidisciplinary team of experts





Center for YOCRC—Team





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Every life deserves world class care.