2022 NCCRT Annual Meeting

CONCURRENT SESSION 4
EARLY-AGE ONSET

American Cancer Society | National Colorectal Cancer Roundtable | 80% In Every Community

Early-Age Onset Colorectal Cancer

Alison Rosen
MS
Director, Project ECHO
American Cancer Society

Kimmie Ng
MD, MPH
Associate Professor of Medicine
Harvard Medical School

Nancy You
MD, MHSc, FACS
Professor, University of Texas
MD Anderson Cancer Center

Andrea Cercek
MD
Section Head, Memorial Sloan
Kettering Cancer Center

Young-Onset Colorectal Cancer Center

Thursday, November 17, 3:30 PM

American Cancer Society | National Colorectal Cancer Roundtable | 80% In Every Community

Dana-Farber Cancer Institute | BWH BRIGHAM AND WOMEN'S HOSPITAL

DANA-FARBER/BRIGHAM AND WOMEN'S CANCER CENTER

Young-Onset Colorectal Cancer Center

Kimmie Ng, MD, MPH

Associate Chief, Division of Gastrointestinal Oncology
Associate Professor of Medicine, Harvard Medical School
Director, Young-Onset Colorectal Cancer Center
Co-Director, Colon and Rectal Cancer Center
Director of Translational Research in Gastrointestinal Cancer
Dana-Farber Cancer Institute, Boston, MA

November 17, 2022

Conflict of Interest Disclosure (2021-2022)

- Institutional Research Funding:
  - Pharmavite, LLC
  - Evergrande Group
  - Janssen
  - Revolution Medicines
- Advisory Board / Consulting:
  - Bicara Therapeutics
  - GlaxoSmithKline
  - Redesign Health
  - Bayer
  - Pfizer

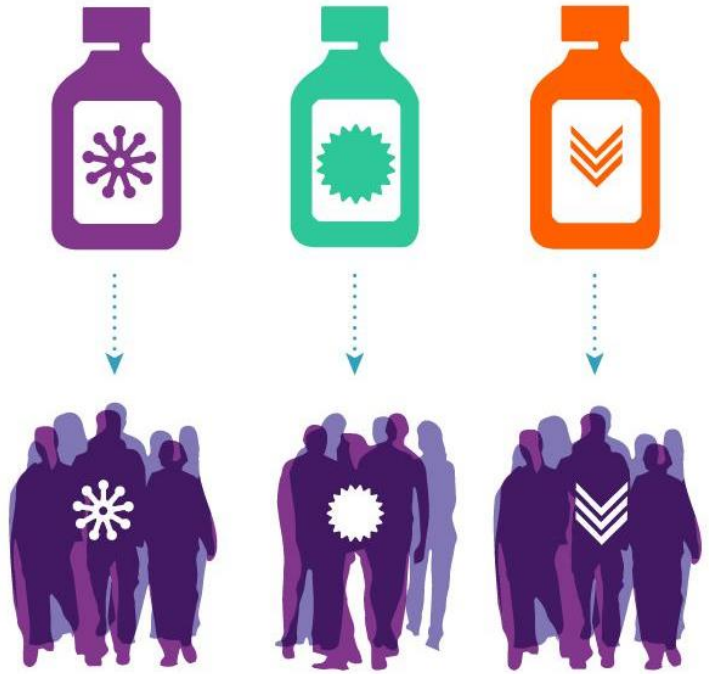
Young-Onset Colorectal Cancer Center: Mission statement

- **Clinical care**
  - Provide expert, compassionate, and multidisciplinary care to patients with young-onset colorectal cancer
- **Education and awareness**
  - Increase public education and awareness around the rising burden of colorectal cancer in young adults to improve prevention and early detection
- **Research**
  - Promote scientific discovery and innovation to elucidate underlying biological mechanisms, identify risk factors, and facilitate development of novel therapies

Clinical care: Unique clinical features and services

- **Multidisciplinary evaluation**
  - Upfront genetics appointment
  - Fertility, nutrition, sexual health, integrative oncology
- **Comprehensive psychosocial support**
  - Dedicated social worker with expertise in young patients
  - Customized programs tailored for young patients
- **Dedicated program coordinator**
  - Patient navigation
  - Liaison to clinical and research team

- **Personalized treatment**
  - GI TARGET program



Clinical care: Comprehensive care model for young-onset CRC

- Pioneered a new model of care for young patients
- Implemented psychosocial distress screen
  - ↑ social work referrals
- Robust psychosocial programming
  - First to use Zoom for support groups and events
  - Created new peer-to-peer mentor program

one to one | Connecting with someone who's been there.

Young-Onset Colorectal Cancer Center
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Education and Support Series:

Managing Cancer-Related Fatigue

Hanneke Poort, PhD will share information and strategies to manage cancer-related fatigue. Katelyn MacDougall, LICSW will facilitate time to connect with others treated for young-onset colorectal cancer (those diagnosed under 50) and their supporters.

Dana-Farber Cancer Institute
Young and Strong
Young-Onset Colorectal Cancer Center
Young Adult Program

Parenting Through Cancer and COVID

Join us for an interactive Q&A session focused on helping children and teens cope with a primary caregiver facing cancer and the pandemic. This will be co-led by Katelyn MacDougall, LICSW, a social worker with the Young-Onset Colorectal Cancer Center, Larissa Hewitt, LICSW, a pediatric social worker with the Jimmy Fund Clinic, and Kathleen Boyle, PA-C, a physician assistant with the Center for Gastrointestinal Oncology.

Young-Onset Colorectal Cancer Center
Dana-Farber Cancer Institute | Brigham and Women's Hospital
DANA-FARBER/BRIGHAM AND WOMEN'S CANCER CENTER

Lunch Break

Join us for a casual lunch to connect with others treated for young-onset colorectal cancer and their support people. This will be a space where you can chat about anything you would like, with other people who get it. Feel free to bring your lunch or not!

Education and awareness:
Creating community and educating healthcare professionals

Young-Onset
Colorectal Cancer Center

DANA-FARBER/BRIGHAM AND WOMEN'S CANCER CENTER

DR. NG'S LETTER

The **Young-Onset Colorectal Cancer Center** was launched at Dana-Farber Cancer Institute in March 2019 and is one of the first centers in the country dedicated to the care and research of young patients with colorectal cancer. The creation of this ground-breaking Center was spurred by the worrisome uptick in development of this cancer in young and otherwise healthy people. Even more concerning is the fact that no one knows why this is happening.

Increasingly perplexed and saddened by young patient after young patient walking through the doors of Dana-Farber, we decided to tackle this problem head on with the Center's three-fold mission:

1) Provide expert, multidisciplinary, and comprehensive care to address the unique needs and challenges of young-onset colorectal cancer patients

2) Promote scientific discovery and innovation to better understand the causes of young-onset colorectal cancer and develop new treatments

(continued on back page)

Patient Spotlight

JAIME COWELL

Mary-Brent Brown (Research & Program Coordinator): Tell us how you learned you had cancer.

Jaime Cowell: I had been sick for a year, going back and forth to the ER and various doctors with extreme intestinal pain. At one of my visits to the ER, an ultrasound discovered what was thought to be diverticulitis. I had it removed with surgery, and when it was biopsied, it came back positive for cancer. My surgeon broke the news to me when I went to have the staples removed from my surgery. It was a very surreal moment. I kind of stopped listening once I heard the word cancer - it was too difficult to comprehend. I definitely went into a state of shock. Thankfully, my mom - who has 30+ years of oncology nursing experience under her belt - was there with me and knew what to ask. She did my listening for me that day.

MBB: What was treatment like for you?

JC: My first 12 rounds of chemo were tough. Fatigue and neuropathy were my biggest hurdles. I tried to stay positive throughout it all - I used to look up jokes to tell all the nurses for when I had to get treatment. It was a regular thing for someone to walk by my chair and ask me what the joke of the day was. My dad usually came with me, and I'd make playlists for our commute and then dance and sing, because I knew that would cheer us both up a bit. I got diagnosed a second time - this time stage 4 - in January 2017. Treatment was a lot harder the second time around, both mentally and physically. I got really nauseous every time, and it was difficult to stay positive. I spent a lot of my time watching TV shows that cheered me up, like The Great British Baking Show. I went back to work before I initially planned to, when I was still going through treatment. That was huge for my mental health. Being able to get back to a semi-normal life made a great impact on my overall outlook of my situation.

MBB: In what ways are you different today than you were before you began your journey?

JC: I struggle with depression and anxiety, but I'm constantly trying to overcome it. There's always the fear that the cancer will come back, but I decided not to let that fear run my life. I adopted a puppy and bought a house. I got a tattoo I've been wanting for years. I travel whenever I can. I try to be happy. Some days are harder than others, but I've found that things are easier if you at least try to be happy.

MBB: What was the best and worst advice you got?

JC: So, admittedly, I did not take this advice but that's kind of how I know it's good advice - my oncologist told me to fight through the fatigue. To exercise if I could, or even just make myself get up and walk around the house if I had been sitting for too long. I found that my fatigue got

continued on page 2

We're now on Twitter! Follow us @DFarberYoungCRC

Young-Onset
Colorectal Cancer Center

Young-Onset Colorectal Cancer Center Patient and Family Forum

Beyond CRC: Better Understanding of Young-Onset Colorectal Cancer

Dana-Farber Cancer Institute | BRIGHAM AND WOMEN'S HOSPITAL

DANA-FARBER/BRIGHAM AND WOMEN'S CANCER CENTER

BEYOND CRC

Join the Young-Onset Colorectal Cancer Center for our second annual conference. This is a series of free educational events for individuals with young-onset colorectal cancer (diagnosed under 50 years old) and their supporters. Attendees will hear from experts, attend breakout sessions, and meet others within the community.

Registration required:

redcap.link/beyondcrc

Follow us on Twitter!
@DFarberYoungCRC

March 1st
6 - 7pm
Ibram X. Kendi: Hoping and Striving for an Antiracist Society While Living with Young-Onset Colon Cancer
Dr. Kendi is one of America's foremost historians and leading antiracist scholars. He is also a stage IV young-onset colon cancer survivor. Join us for a discussion about his cancer experience and how we can make cancer care and research equitable for all.

March 4th
6 - 7pm
Gut Instincts: Best Practices for Screening Young People
We're launching the first of our Gut Instincts Series, educational workshops focused on bringing you the latest in young onset colorectal cancer care. This event is a webinar for healthcare professionals and advocates that you are welcome to attend.
Separate registration required: bit.ly/bestpracticesyoung

March 8th
6 - 7pm
Meet and Greet Social
Get to know other patients and supporters beyond cancer in small, virtual break out groups.

March 11th
12 - 1pm
Lunch Break Social
Connect with others treated for young-onset colorectal cancer during our monthly informal support group.

March 15th
6 - 7pm
Living Well
Kalen Fletcher, MSW, LICSW, MPH

March 22nd
6 - 7:30pm
Let's Talk Diet and Exercise – What Should I Be Doing?
Jeffrey A. Meyerhardt, MD, MPH, FASCO
Hillary Wright, MEd, RD, LDN

March 29th
6 - 7:30pm
Expert Panel: Latest Updates in Young-Onset Colorectal Cancer Research
Introduction and Moderation: Kimmie Ng MD, MPH
Clinical Trial Overview: James Cleary MD, PhD
Microbiome Research: Wendy Garrett, MD, PhD
Immunotherapy Trials: Osama Rahma, MD

Hosted by the Young-Onset Colorectal Cancer Center

Dana-Farber Cancer Institute | BWH BRIGHAM AND WOMEN'S HOSPITAL

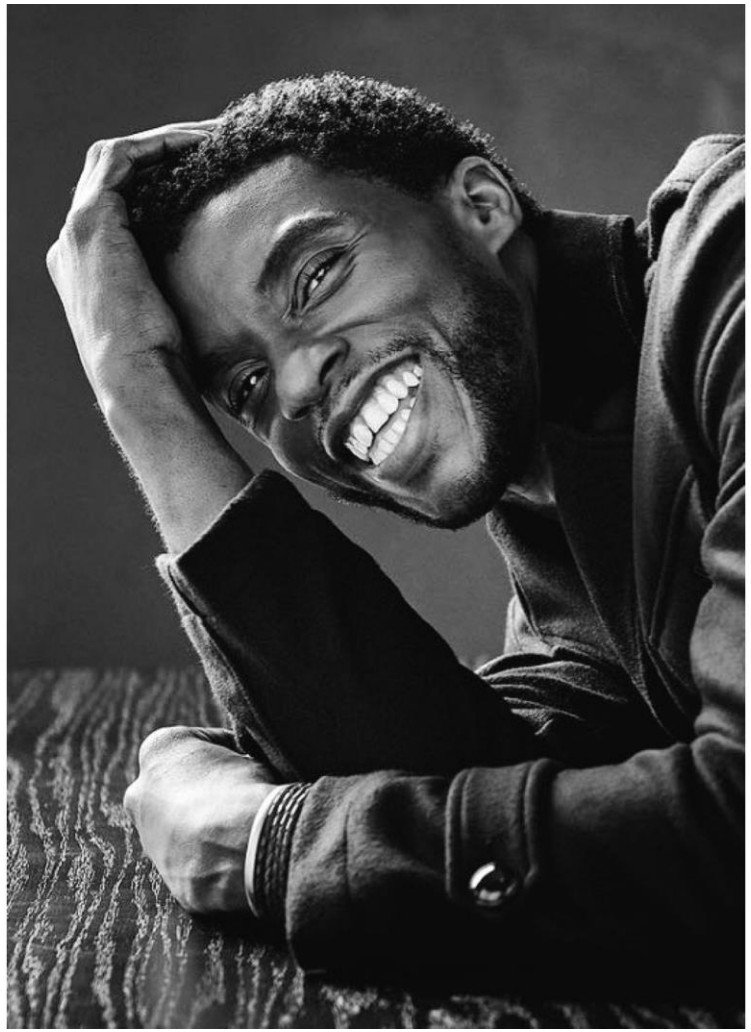
DANA-FARBER/BRIGHAM AND WOMEN'S CANCER CENTER

Gut Instincts:
A Series on Young-Onset Colorectal Cancer

Best Practices for Screening Young People

March 4, 2021 at 6 PM
Please register here:
bit.ly/bestpracticesyoung

Education and awareness:
National platform to raise general public awareness



TODAY

THE WALL STREET JOURNAL.

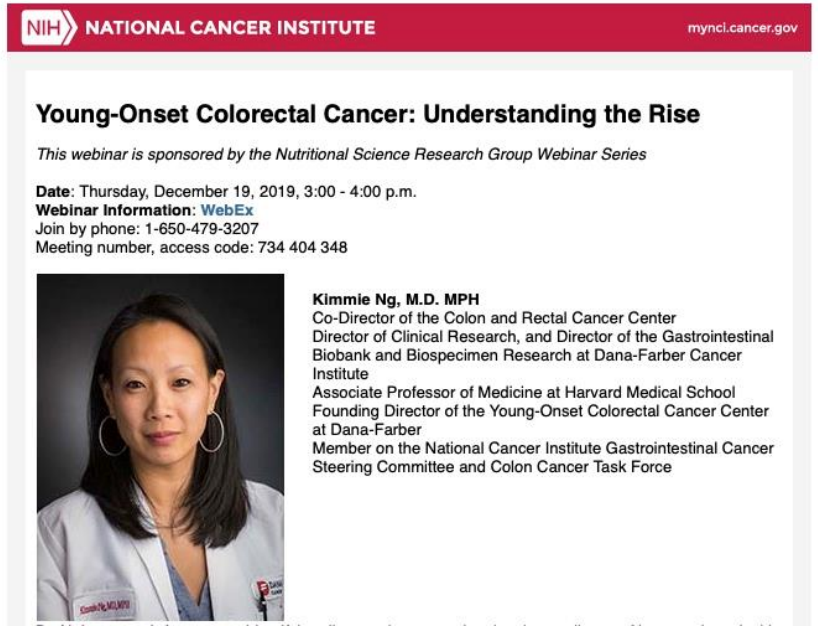
Adults as Young as 45 Should Be Screened for Colorectal Cancer, U.S. Panel Recommends

The final recommendation by the U.S. Preventive Services Task Force would lower the age for screening by five years and require many insurers to cover the testing

CNN

US task force proposes starting colorectal cancer screening at age 45

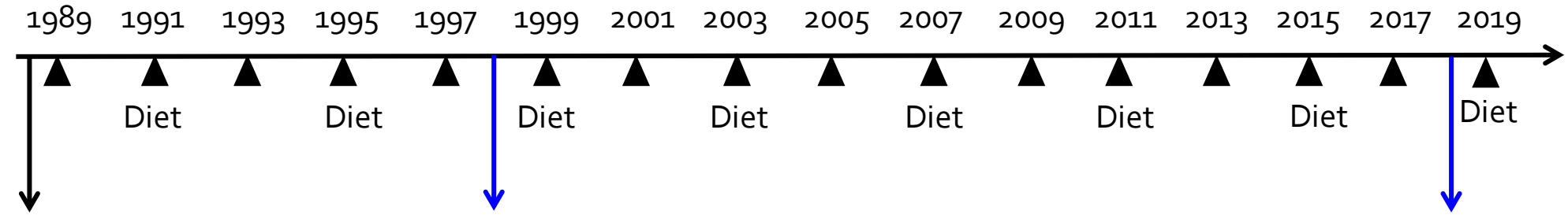
Education and awareness: Government advocacy and partnership



Young-Onset
Colorectal Cancer Center

Research:
Identification of Risk Factors in Nurses' Health Study 2

n = 116,430 female nurses aged 25-42



High school diet
Lifetime activity

Follow-up rates >90% in each 2-year cycle

Obesity is one leading hypothesis underlying young-onset CRC

JAMA Oncology | Original Investigation 2018; 5(1): 37-44

Association of Obesity With Risk of Early-Onset Colorectal Cancer Among Women

Po-Hong Liu, MD, MPH; Kana Wu, MD, MPH, PhD; Kimmie Ng, MD, MPH; Ann G. Zauber, PhD; Long H. Nguyen, MD, MS; Mingyang Song, MD, ScD; Xiaosheng He, MD; Charles S. Fuchs, MD, MPH; Shuji Ogino, MD, PhD, MS; Walter C. Willett, MD, DrPH; Andrew T. Chan, MD, MPH; Edward L. Giovannucci, MD, ScD; Yin Cao, MPH, ScD

Table 2. Current BMI and Risk of Early-Onset Colorectal Cancer

Variable	No. of Cases	No. of Person-Years	Age-Adjusted RR (95% CI)	Multivariable-Adjusted RR (95% CI)[a]
All Participants				
Current BMI				
18.5-22.9	29	455 250	1 [Reference]	1 [Reference]
23.0-24.9	20	217 271	1.27 (0.71-2.24)	1.33 (0.75-2.36)
25.0-29.9	30	296 763	1.32 (0.79-2.22)	1.37 (0.81-2.30)
≥30	35	230 169	1.86 (1.13-3.06)	1.93 (1.15-3.25)
Each 5-unit increase	NA	NA	1.18 (1.04-1.35)	1.20 (1.05-1.38)
P for trend[b]	NA	NA	.01	.01
Weight Change Since 18 Years of Age[d]				
Loss or gain <5.0 kg[e]	27	373 061	1 [Reference]	1 [Reference]	1 [Reference]
Gain of 5.0-19.9 kg	42	561 417	0.86 (0.53-1.41)	0.86 (0.52-1.42)	0.86 (0.52-1.43)
Gain of 20.0-39.9 kg	34	214 633	1.66 (0.99-2.77)	1.64 (0.96-2.81)	1.65 (0.96-2.81)
Gain ≥40.0 kg	11	47 342	2.25 (1.11-4.59)	2.15 (1.02-4.54)	2.15 (1.01-4.55)
Each 5-kg increase	NA	NA	1.09 (1.03-1.16)	1.09 (1.03-1.16)	1.09 (1.02-1.16)
P for trend[c]	NA	NA	.002	.006	.007

ARTICLE

JNCI Cancer Spectrum (2019) 2(4): pky073

Sedentary Behaviors, TV Viewing Time, and Risk of Young-Onset Colorectal Cancer

Long H. Nguyen, Po-Hong Liu, Xiaobin Zheng, NaNa Keum, Xiaoyu Zong, Xiao Li, Kana Wu, Charles S. Fuchs, Shuji Ogino, Kimmie Ng, Walter C. Willett, Andrew T. Chan*, Edward L. Giovannucci*, Yin Cao*

Table 2. Sedentary TV viewing time and risk of young-onset CRC diagnosed prior to age 50 years

	Sedentary TV viewing time, hours per week			
Young-onset CRC	≤7	7.1–14	>14	P_{trend}§
Cases	52	33	33	
Person-years	629 656	367 368	265 516	
Age-adjusted RR (95% CI)	1 (referent)	1.12 (0.72 to 1.74)	1.69 (1.09 to 2.63)	.02
Multivariable model 1 RR (95% CI)*	1 (referent)	1.15 (0.74 to 1.78)	1.75 (1.12 to 2.76)	.02
Multivariable model 2 RR (95% CI)†	1 (referent)	1.15 (0.74 to 1.79)	1.77 (1.12 to 2.78)	.02
Multivariable model 3 RR (95% CI)‡	1 (referent)	1.12 (0.72 to 1.75)	1.69 (1.07 to 2.67)	.03

Table 4. Sedentary TV viewing time and risk of young-onset CRC diagnosed prior to age 50 years by anatomic site

	Sedentary TV viewing time (hours per week)			
Young-onset CRC	≤7	7.1–14	>14	P_{trend}†
Colon cancer				
Cases	40	20	22	
Person-years	629 664	367 382	265 527	
Age-adjusted RR (95% CI)	1 (referent)	0.88 (0.51 to 1.51)	1.42 (0.84 to 2.40)	.25
Multivariable model 1 RR (95% CI)*	1 (referent)	0.90 (0.52 to 1.55)	1.47 (0.85 to 2.54)	.22
Rectal cancer				
Cases	12	13	11	
Person-years	629 696	367 385	265 534	
Age-adjusted RR (95% CI)	1 (referent)	1.92 (0.87 to 4.22)	2.62 (1.15 to 6.00)	.02
Multivariable model 1 RR (95% CI)*	1 (referent)	1.91 (0.86 to 4.25)	2.44 (1.03 to 5.78)	.04

Gut 2021

Sugar-sweetened beverage intake in adulthood and adolescence and risk of early-onset colorectal cancer among women

Jinhee Hur ,[1] Ebunoluwa Otegbeye ,[2,3] Hee-Kyung Joh,[1,4] Katharina Nimptsch,[1,5] Kimmie Ng,[6] Shuji Ogino ,[7,8,9] Jeffrey A Meyerhardt,[6] Andrew T Chan,[9,10,11,12,13] Walter C Willett,[1,8,12] Kana Wu,[1] Edward Giovannucci ,[1,8,12] Yin Cao [3,14,15]

Table 2 Sweetened beverage intake in adulthood and risk of early-onset colorectal cancer

Exposure	<1 serving/week	1 serving/week to <1 serving/day	1 serving/day to <2 servings/day	≥2 servings/day	P_{trend}*	Each serving/day increase
Sugar-sweetened beverages						
Person-years	536 446	504 341	178 886	138 469		
No. of cases	45	34	14	16		
Age- and energy-adjusted RR (95% CI)	1 (reference)	0.89 (0.56 to 1.41)	1.03 (0.55 to 1.92)	1.72 (0.93 to 3.20)	0.06	1.11 (0.96 to 1.29)
Multivariable RR (95% CI)†	1 (reference)	0.97 (0.61 to 1.55)	1.24 (0.65 to 2.39)	2.18 (1.10 to 4.35)	0.02	1.16 (1.00 to 1.36)
Artificially sweetened beverages						
Person-years	424 283	321 864	258 215	353 780		
No. of cases	32	33	19	25		
Age- and energy-adjusted RR (95% CI)	1 (reference)	1.25 (0.76 to 2.04)	0.95 (0.54 to 1.68)	0.86 (0.50 to 1.46)	0.32	0.96 (0.86 to 1.07)
Multivariable RR (95% CI)†	1 (reference)	1.20 (0.73 to 1.98)	0.86 (0.48 to 1.54)	0.73 (0.42 to 1.27)	0.11	0.93 (0.83 to 1.04)
Fruit juice						
Person-years	450 890	799 663	92 765	14 825		
No. of cases	44	59	5	1		
Age- and energy-adjusted RR (95% CI)	1 (reference)	0.81 (0.53 to 1.22)	0.66 (0.25 to 1.71)	0.90 (0.12 to 6.76)	0.41	1.04 (0.64 to 1.67)
Multivariable RR (95% CI)†	1 (reference)	0.86 (0.56 to 1.31)	0.77 (0.29 to 2.05)	1.20 (0.16 to 9.11)	0.69	1.20 (0.74 to 1.94)

One beverage serving is 8 oz.
*Calculated using the median of each category of beverage intake as a continuous variable.
†Additionally adjusted for race (white, non-white), height (continuous), body mass index (continuous), menopausal status and menopausal hormone use (premenopausal, postmenopausal never user, postmenopausal ever user, unknown menopausal status or hormone use), family history of colorectal cancer (yes, no), pack-years of smoking (continuous), physical activity (continuous), regular use of aspirin (yes, no), regular use of non-steroidal anti-inflammatory drugs (yes, no), current use of multivitamins (yes, no), intake of alcohol, red and processed meat, dietary fibre, total folate (from foods and supplements) and total calcium (all continuous), Alternative Healthy Eating Index-2010 score without sugar-sweetened beverages and alcohol (continuous) and lower endoscopy due to screening (yes, no) or for other indications within the past 10 years (yes, no).
RR, relative risk.

Table 3 Sugar-sweetened beverage intake at age 13–18 years and risk of early-onset colorectal cancer

	<1 serving/week	1 serving/week to <2 servings/day	≥2 servings/day	P_{trend}*	Each serving/day increase
Person-years	113 475	218 172	25 788		
No. of cases	12	17	6		
Age- and energy-adjusted RR (95% CI)	1 (reference)	0.73 (0.34 to 1.58)	2.43 (0.83 to 7.05)	0.05	1.19 (0.92 to 1.54)
Multivariable RR (95% CI)†	1 (reference)	0.78 (0.36 to 1.73)	3.41 (1.08 to 10.8)	0.01	1.32 (1.00 to 1.75)

One beverage serving is 8 oz.
*Calculated using the median of each category of beverage intake as a continuous variable.
†Additionally adjusted for race (white, non-white), height (continuous), body mass index at age 18 years (continuous), pack-years of smoking before age 20 years (continuous), intake of alcohol at age 15–17 years, red and processed meat, dietary fibre, total folate (from foods and supplements) and total calcium at age 13–18 years (all continuous), multivitamin use at age 13–18 years (yes, no) and physical activity at grade 9–12 (continuous).
RR, relative risk.

Total Vitamin D Intake and Risks of Early-Onset Colorectal Cancer and Precursors

Hanseul Kim,[1] Marla Lipsyc-Sharf,[2] Xiaoyu Zong,[3] Xiaoyan Wang,[3] Jinhee Hur,[4] Mingyang Song,[1,4,5,6] Molin Wang,[1,7,8] Stephanie A. Smith-Warner,[1,4] Charles Fuchs,[9] Shuji Ogino,[1,10,11,12] Kana Wu,[4] Andrew T. Chan,[5,8,12,13] Yin Cao,[3,14,15,§] Kimmie Ng,[16,§] and Edward L. Giovannucci[1,4,8,§]

Table 2. Total Vitamin D Intake and Risk of Early-Onset CRC in the NHS II, 1991-2015

		HR (95% CI)		
	Cases/person-years	Age-adjusted model	MV-adjusted model 1[a]	MV-adjusted model 2[b]
Total vitamin D intake, IU/day				
<300	64/528,107	1 [Ref]	1 [Ref]	1 [Ref]
300 to <450	20/316,264	0.52 (0.31–0.86)	0.51 (0.31–0.86)	0.51 (0.30–0.86)
≥450	27/406,189	0.57 (0.36–0.91)	0.56 (0.35–0.88)	0.49 (0.26–0.93)
P for trend[c]		.01	.01	.01
Per 400 IU/day increase		0.61 (0.41–0.91)	0.59 (0.39–0.89)	0.46 (0.26–0.83)

CI, confidence interval; HR, hazard ratio; MV, multivariable; other abbreviations as in Table 1.
[a]Additionally adjusted for nondietary factors: white (yes/no), height (continuous), BMI (continuous), smoking pack-years (continuous), physical activity (continuous), TV viewing time (continuous), alcohol intake (continuous), regular use of aspirin (yes/no), NSAID use (yes/no), family history of CRC (yes/no), and history of lower endoscopy within the previous 10 years (yes/no).
[b]Additionally adjusted for dietary intake (total energy, red/processed meat, dietary fiber, total folate, and Alternative Healthy Eating Index 2010, continuous).
[c]Calculated using the median of each total vitamin D intake category as a continuous variable.

Table 4. Total Vitamin D Intake and Risk of Early-Onset Conventional Adenoma and Serrated Polyp in the NHS II, 1991-2011

		OR (95% CI)		
	No. of cases	Age-adjusted model[a]	MV-adjusted model 1[b]	MV-adjusted model 2[c]
Any conventional adenoma				
Total vitamin D intake, IU/day				
<300	589	1 [Ref]	1 [Ref]	1 [Ref]
300 to <450	390	0.85 (0.75–0.97)	0.87 (0.76–0.99)	0.83 (0.71–0.96)
450 to <600	258	0.85 (0.73–0.99)	0.87 (0.75–1.02)	0.80 (0.66–0.97)
≥600	202	0.77 (0.65–0.91)	0.80 (0.68–0.94)	0.71 (0.56–0.89)
P for trend[d]		.001	.01	.002
Per 400 IU/day increase		0.82 (0.74–0.92)	0.85 (0.76–0.94)	0.76 (0.65–0.88)
Any serrated polyp				
Total vitamin D intake, IU/day				
<300	719	1[Ref]	1[Ref]	1[Ref]
300 to <450	518	0.94 (0.84–1.06)	0.96 (0.86–1.08)	0.91 (0.80–1.04)
450 to <600	360	0.98 (0.86–1.12)	1.02 (0.89–1.17)	0.93 (0.79–1.09)
≥600	281	0.88 (0.77–1.02)	0.94 (0.81–1.08)	0.85 (0.70–1.03)
P for trend[d]		.14	.54	.11
Per 400 IU/day increase		0.91 (0.84–1.00)	0.95 (0.87–1.03)	0.85 (0.75–0.97)

OR, odds ratio; other abbreviations as in Tables 1 and 2.
[a]Adjusted for age, time period of endoscopy, time since most recent endoscopy, number of reported endoscopies, and reason for current endoscopy.
[b]Additionally adjusted for nondietary factors: white (yes/no), height (continuous), BMI (in quintiles), alcohol intake (never, 0.1-4.9, 5-14.9, 15+ g/d), smoking (never, 0.1-4.9, 5-19.9, 20-39.9, 40+ pack-years), regular use of aspirin (yes/no), regular use of NSAIDs (yes/no), physical activity (METS in quintiles), TV viewing time (in quintiles), and family history of CRC (yes/no).
[c]Additionally adjusted for dietary intake (total energy intake, red and processed meat intake, dietary fiber intake, total folate intake, and Alternative Healthy Eating Index 2010, in quintiles).
[d]Calculated using the median of each total vitamin D intake category as a continuous variable.

ANNALS OF ONCOLOGY
driving innovation in oncology

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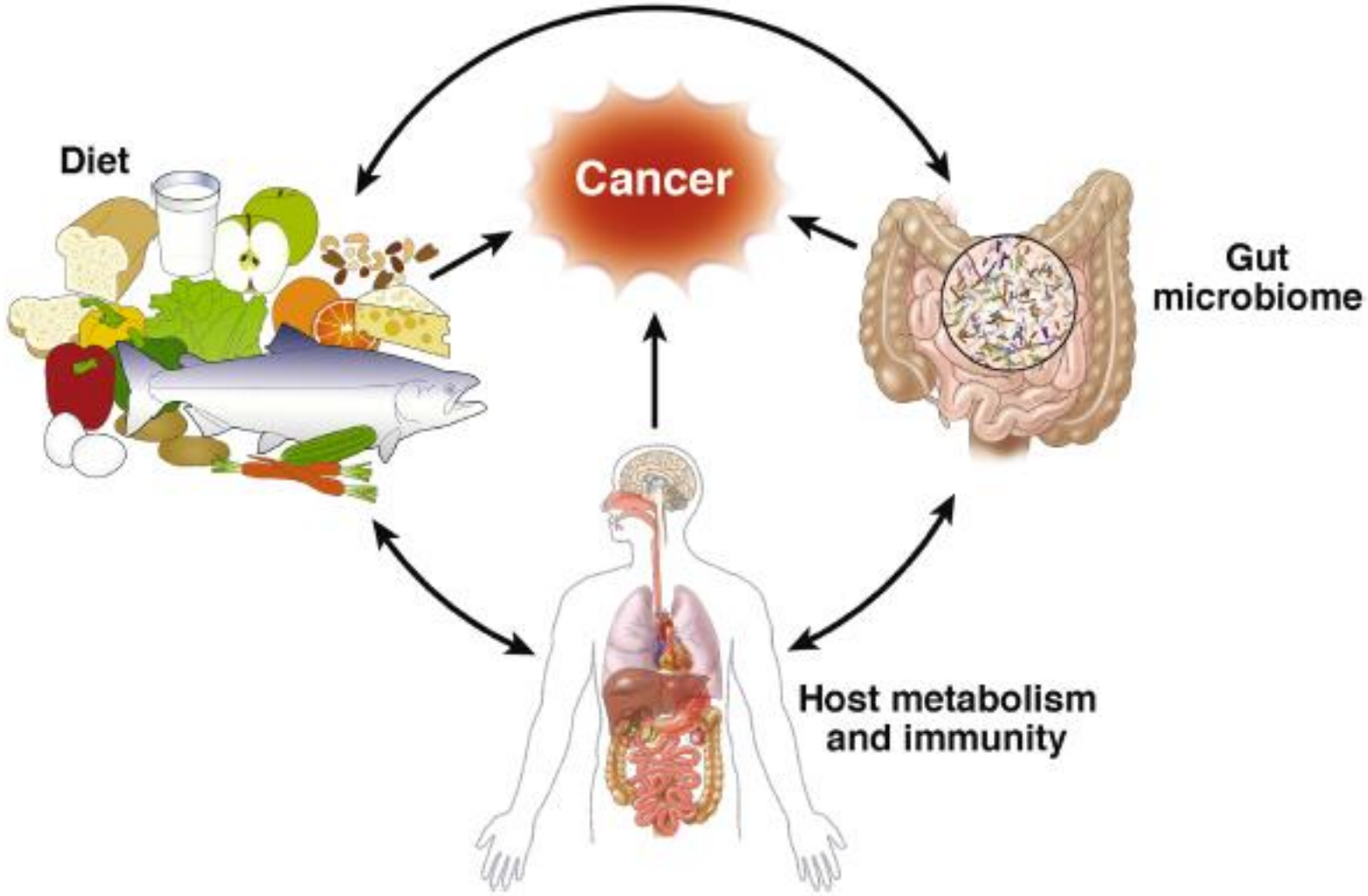
Prospective evaluation of dietary and lifestyle pattern indices with risk of colorectal cancer in a cohort of younger women

Y. Yue[1], J. Hur[1*], Y. Cao[2,3,4], F. K. Tabung[1,5,6], M. Wang[7,8,9], K. Wu[1], M. Song[1,7,9,10], X. Zhang[9], Y. Liu[9,11], J. A. Meyerhardt[12], K. Ng[12], S. A. Smith-Warner[1,7†], W. C. Willett[1,7,9†] & E. Giovannucci[1,7,9*†]

Table 3. Associations of cumulative average dietary and lifestyle indices with risk of colorectal cancer diagnosed before and after age 50 years in the Nurses' Health Study II, 1991-2015[a]

	Age at colorectal cancer diagnosis		*P*-heterogeneity[b]
	<50 years	≥50 years	
Number of events	111	221	
Prime diet quality score			
Age-adjusted HR (95% CI)[c]	0.90 (0.55-1.48)	0.84 (0.59-1.20)	0.82
Multivariable-adjusted HR (95% CI)[d]	0.90 (0.55-1.50)	0.91 (0.62-1.31)	>0.99
Overall plant-based diet index			
Age-adjusted HR (95% CI)[c]	1.13 (0.68-1.88)	1.03 (0.70-1.50)	0.75
Multivariable-adjusted HR (95% CI)[d]	1.24 (0.74-2.08)	1.10 (0.75-1.62)	0.70
Empirical dietary index for hyperinsulinemia			
Age-adjusted HR (95% CI)[c]	1.34 (0.80-2.27)	1.50 (1.02-2.19)	0.72
Multivariable-adjusted HR (95% CI)[d]	1.24 (0.72-2.16)	1.51 (1.00-2.29)	0.54
Empirical lifestyle index for hyperinsulinemia			
Age-adjusted HR (95% CI)[c]	1.71 (1.04-2.81)	1.17 (0.82-1.66)	0.21
Multivariable-adjusted HR (95% CI)[e]	1.86 (1.12-3.07)	1.20 (0.83-1.73)	0.16

Complex interplay of diet, host immunity, and microbiome



Song M and Chan AT. *Clin Gastroenterol Hepatol* 2019; 17: 275-289.

Putative early life and environmental exposures

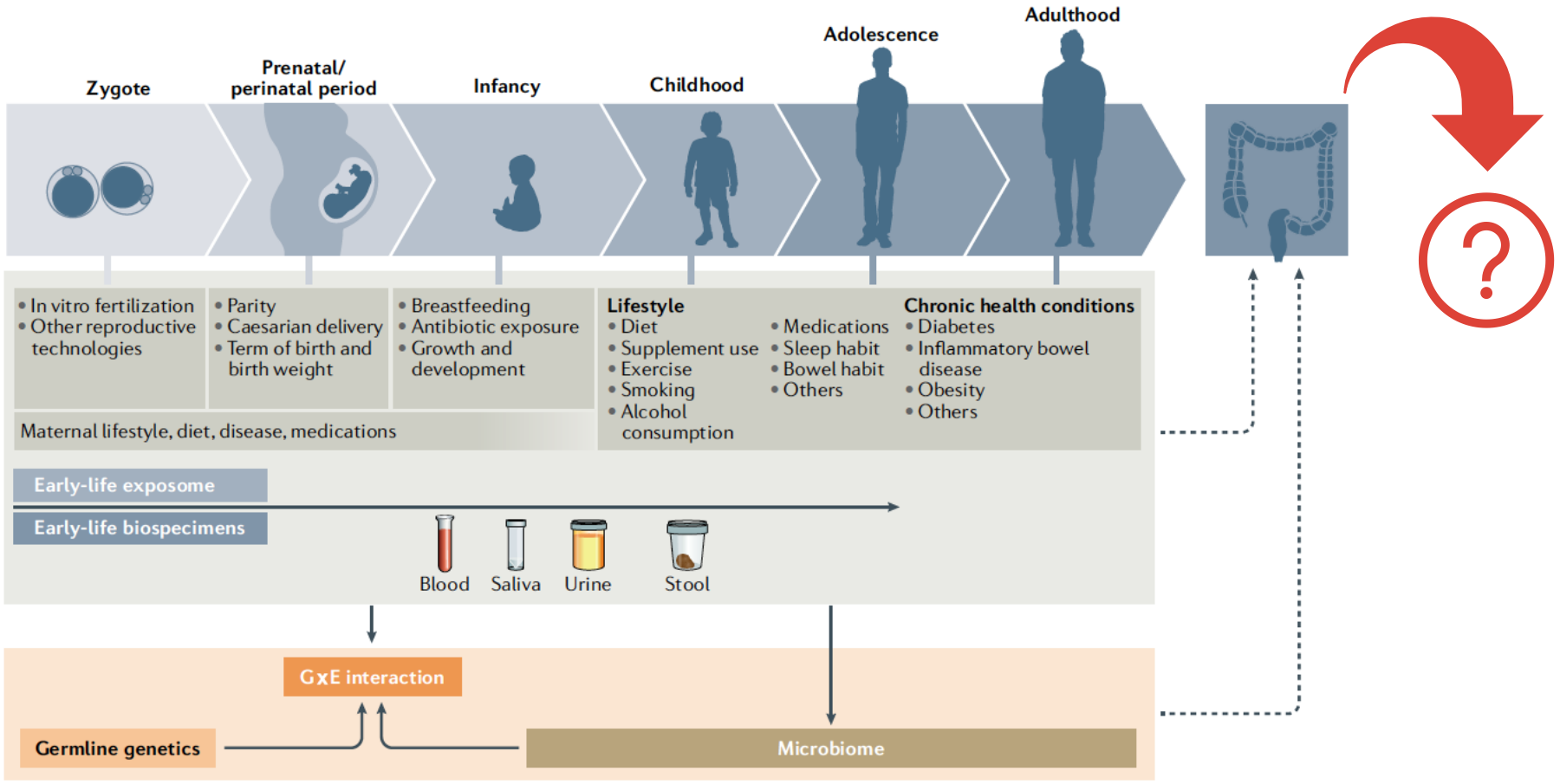


Fig. 1 | **Examples of life-course exposures with potential effects on CRC tumorigenesis.** The exposome describes the totality of exposures and interactions thereof. The exposome can influence disease processes at any time from early life (the prenatal to adolescent periods) to adulthood. Gene-by-environment (GxE) interactions during the life-course might have important roles in the aetiology of early-onset colorectal cancer (CRC). Early-life biospecimens, such as blood, stool, saliva, urine, cord blood and placental tissue collected from either mothers or their offspring (at various timepoints during childhood), or both, might provide information on the early-life exposome when analysed in future studies of the aetiological factors underlying early-onset CRC. Of note, the composition of the gut microbiota can be influenced by various life-course exposures and might, in turn, influence GxE interactions that affect the development of CRC.

Akimoto N, et al. *Nature Rev Clin Oncol* 2021; 18 (4): 230-43.

BEYOND CRC

Better understanding of
YOUNG ONSET colorectal cancer

Dana-Farber Cancer Institute

Young-Onset
Colorectal Cancer Center

Limitations of current cohorts

- Limited number of cases in existing contemporary cohorts
- Minimal racial, ethnic, and geographic diversity
- Lack of stool specimens for microbiome analyses
- Non-uniform, non-validated collection of dietary and lifestyle data
- No genomic correlates
- Single time point of collection of biospecimens and data
- Suboptimal clinical annotation

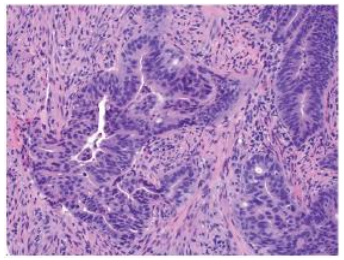
BEYOND CRC Better understanding of YOUNG ONSET colorectal cancer

Study objectives

1) Improve our understanding of risk factors and biology of young-onset colorectal cancer

2) Discover novel means of prevention, early detection, and treatment for young-onset colorectal cancer

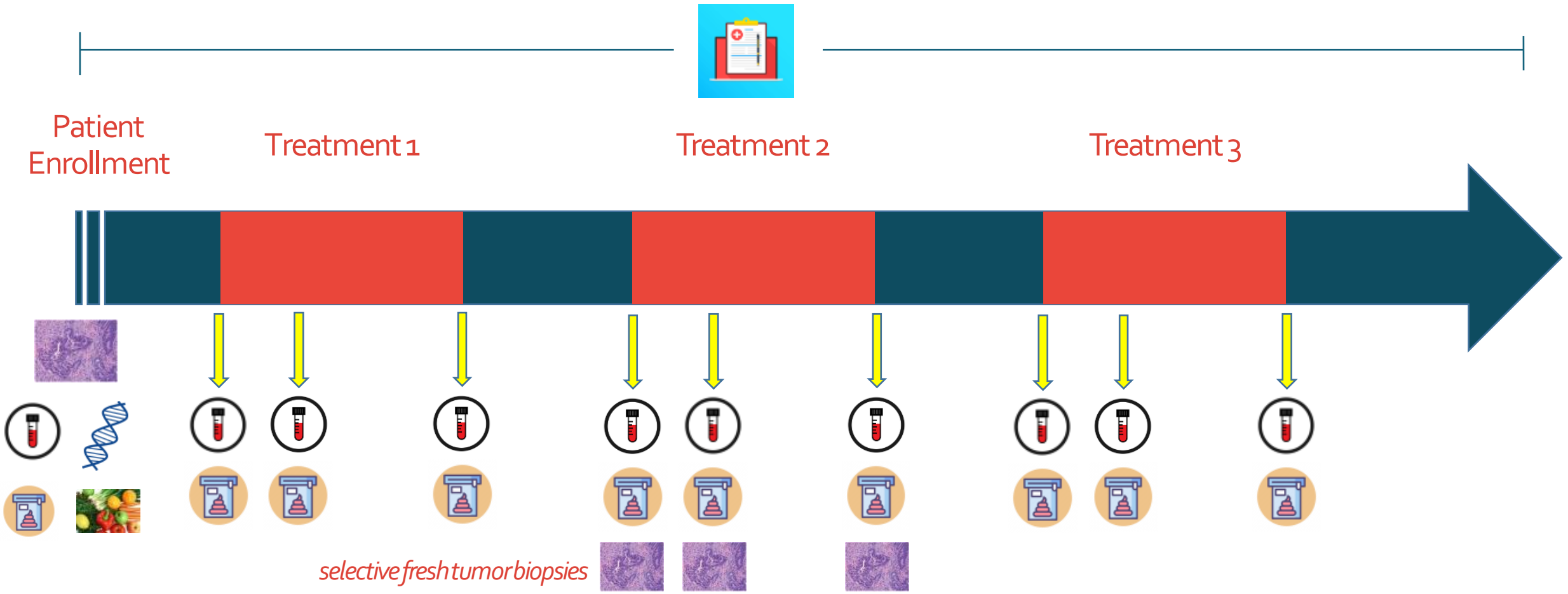
Prospective longitudinal cohort study



Patients diagnosed with CRC <50 years old

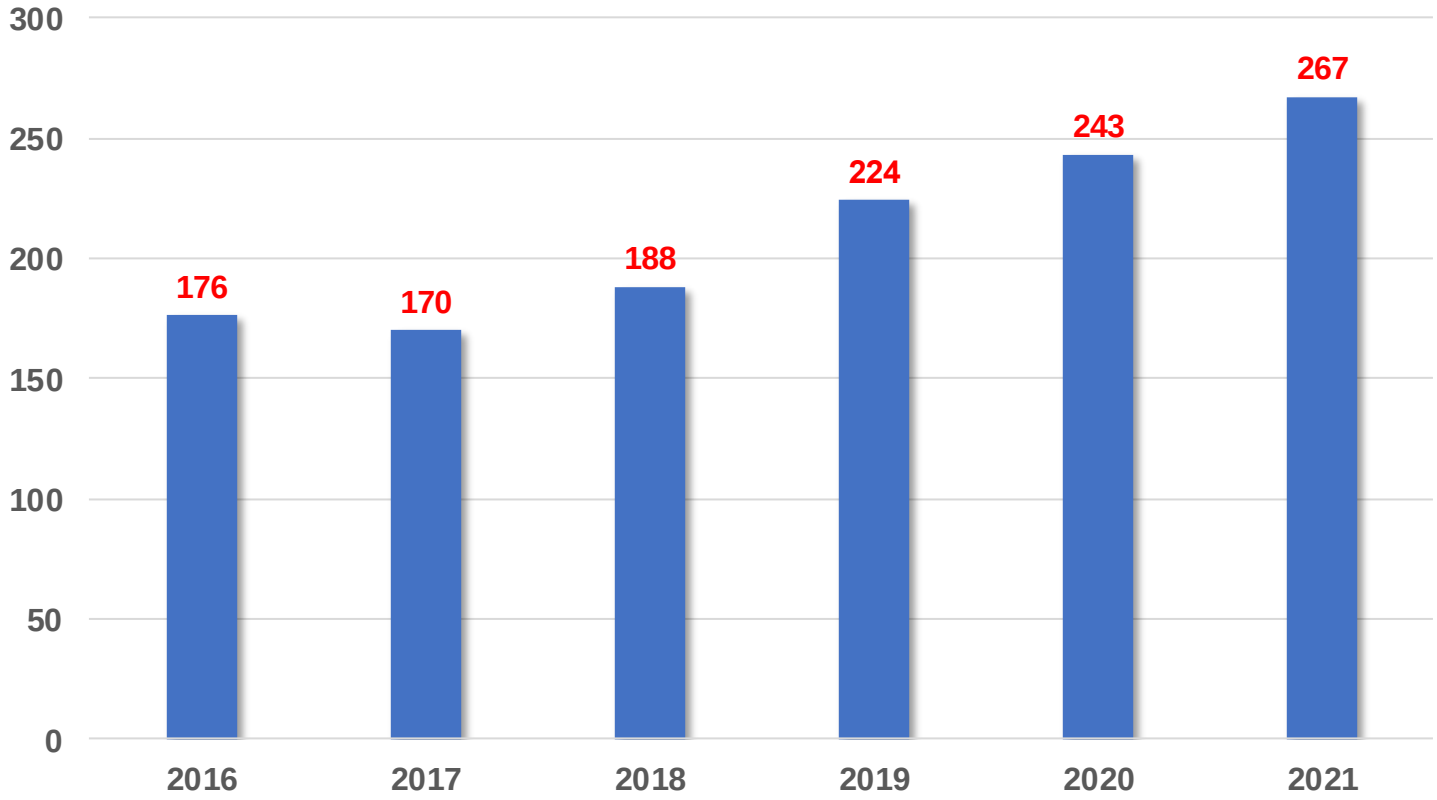
Healthy control patients <50 years old

Data and biospecimen collection



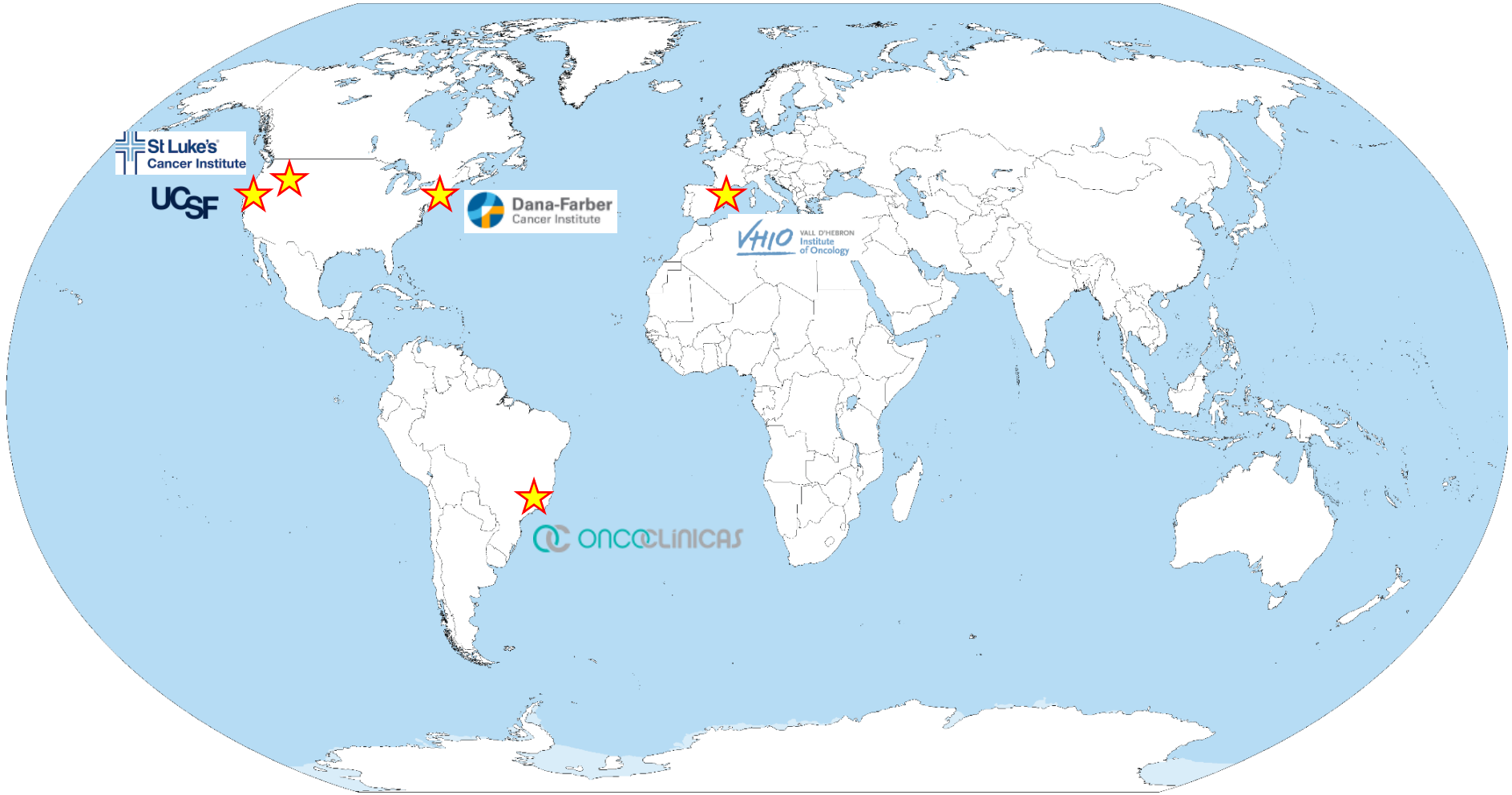
Dana-Farber Cancer Institute

Number of New Patients Seen at the Young-Onset Colorectal Cancer Center



Young-Onset
Colorectal Cancer Center

Beyond CRC: National and international expansion



Count Me In: Patient-partnered research is the future

- Digital social media platform to directly engage and partner with patients to accelerate colorectal cancer research
- Allows for much more rapid accrual and collection of biospecimens and data
- Enhances diversity and inclusion in research
  - Racial/ethnic
  - Socioeconomic
  - Geographic
- Enables research to continue during pandemic times

Count Me In

Dana-Farber Cancer Institute

Emerson Collective

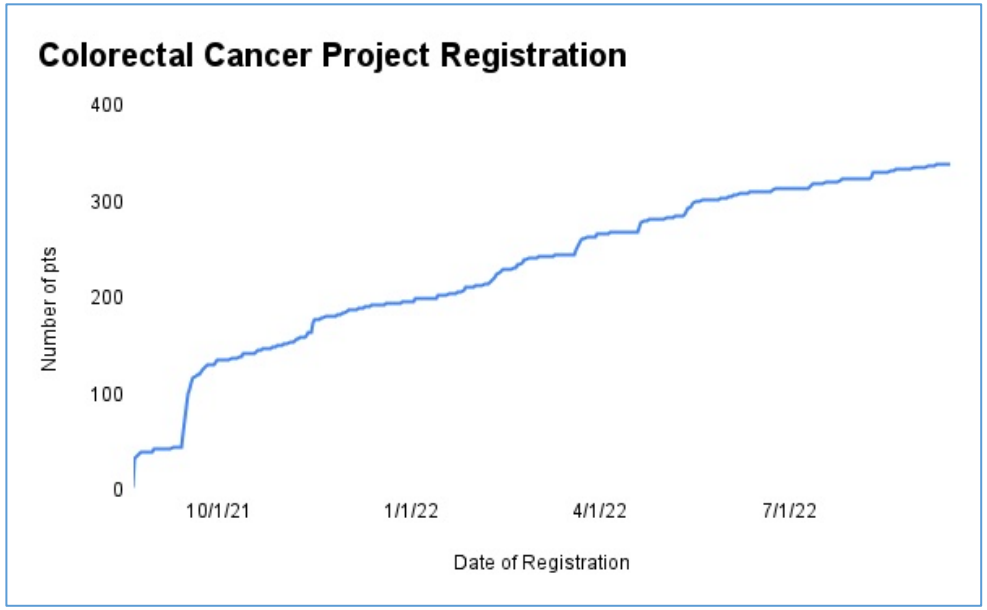
BIDEN CANCER INITIATIVE

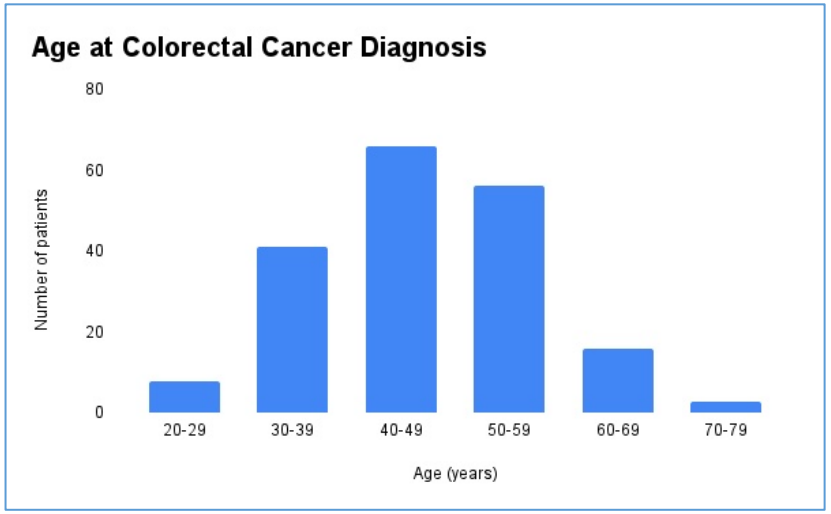
BROAD INSTITUTE

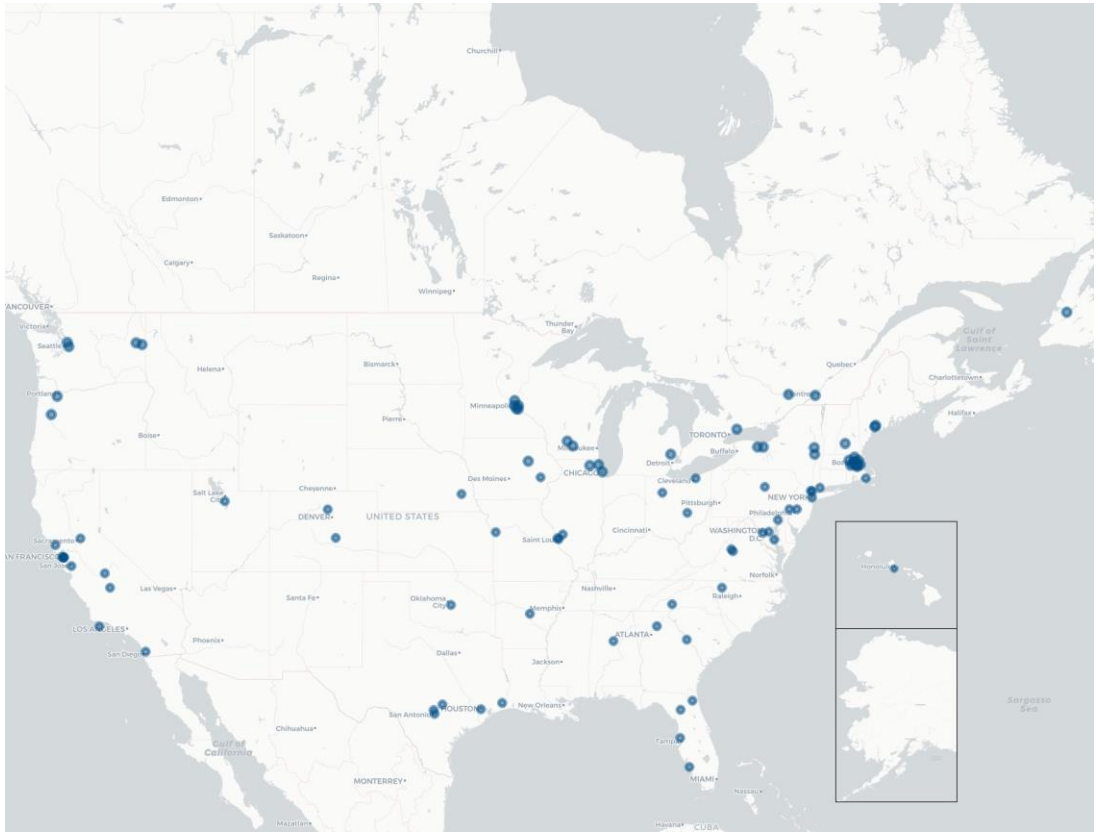
Colorectal Cancer Project

https://colorectalcancerproject.org/

Count Me In: Current enrollment







As of May 2022

Young-Onset
Colorectal Cancer Center

Co-Scientific Leads:
Kimmie Ng, MD, MPH
Andrea Cercek, MD

BEYOND CRC

Acknowledgments

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- Lauren Brais, MPH
- William Tan, MSW, LCSW
- Mary-Brent Brown
- Brigette Arsenault
- GCC research data specialists

VALL D'HEBRON INSTITUTE OF ONCOLOGY

- Josep Tabernero, MD, PhD
- Paolo Nuciforo, MD, PhD
- Elena Elez, MD, PhD
- Iosune Baraibar, MD
- Alejandro Piris, PhD
- Neus Bayo, PhD
- Mireia Sanchis

BROAD INSTITUTE / COUNT ME IN TEAM

HARVARD T. H. CHAN SCHOOL OF PUBLIC HEALTH

- Curtis Huttenhower, PhD
- Edward Giovannucci, MD, ScD
- Mingyang Song, ScD

UNIVERSITY OF CALIFORNIA, SAN FRANCISCO

- Alan Venook, MD
- Chloe Atreya, MD, PhD
- Erin Van Blarigan, ScD
- Sorbarikor Piawah, MD, MPH

ST. LUKE'S CANCER INSTITUTE

- Dan Zuckerman, MD

PATIENT ADVOCATES

- Patrick Beauregard
- David Thau
- Laura Porter
- Candace Henley

Dana-Farber Cancer Institute

CANCER RESEARCH UK

Congressionally Directed Medical Research Programs CDMRP Department of Defense

colorectal cancer alliance

NIH NATIONAL CANCER INSTITUTE

Thank You!

American Cancer Society | National Colorectal Cancer Roundtable | 80% In Every Community

Young-Onset Colorectal Cancer Program

Thursday, November 17, 3:30 PM

American Cancer Society | National Colorectal Cancer Roundtable | 80% In Every Community

THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center
Making Cancer History®

Young-Onset Colorectal Cancer Program

Y. Nancy You, MD, MHSc
Devon Harrison
Benny Johnson, DO
Grace Li Smith, MD PhD MPH

We are the place for you. We are with you every step of the way.

Young-onset Colorectal Cancer (CRC)

Opportunity for Interception

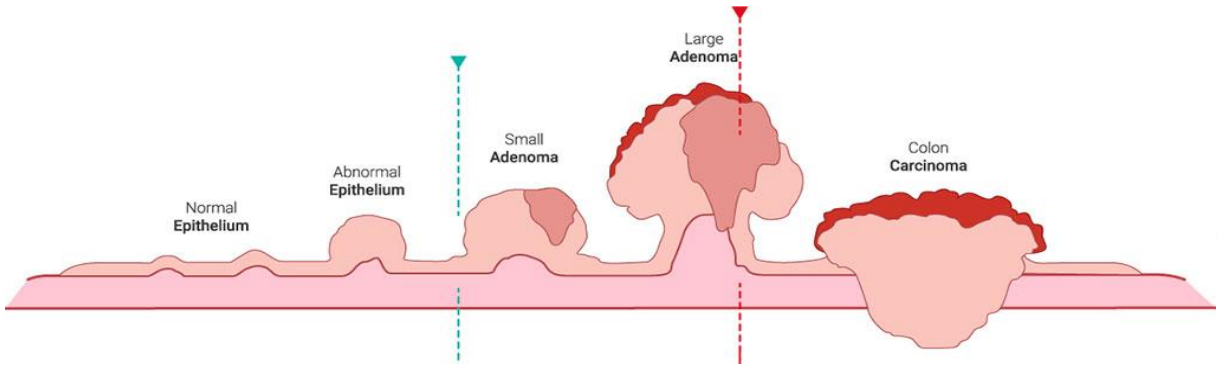
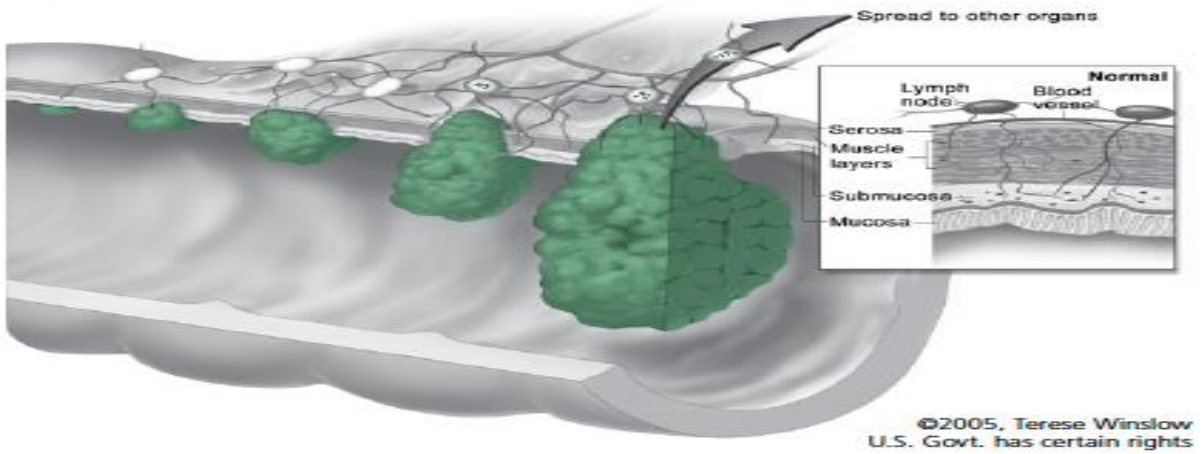


Figure 2. Stages of Colorectal Cancer Growth

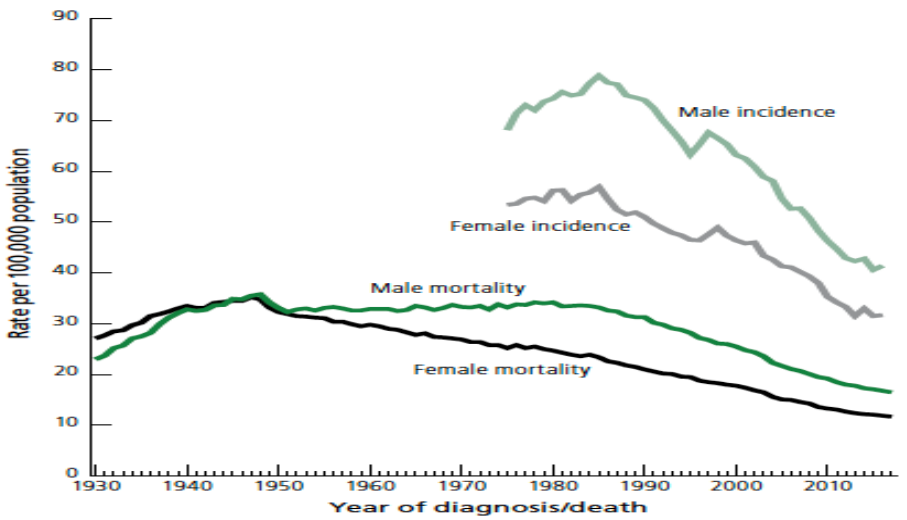


2009 Report on the Status of Cancer/Edwards et al

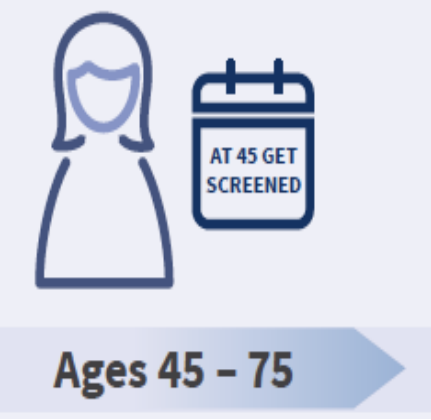
Colorectal Cancer Facts & Figures 2020-2022

Impact of Screening

Figure 6. Trends in Colorectal Cancer Incidence (1975-2016) and Mortality (1930-2017) Rates by Sex, US



American Cancer Society®



U.S. Preventive Services TASK FORCE

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center

Young-onset Colorectal Cancer

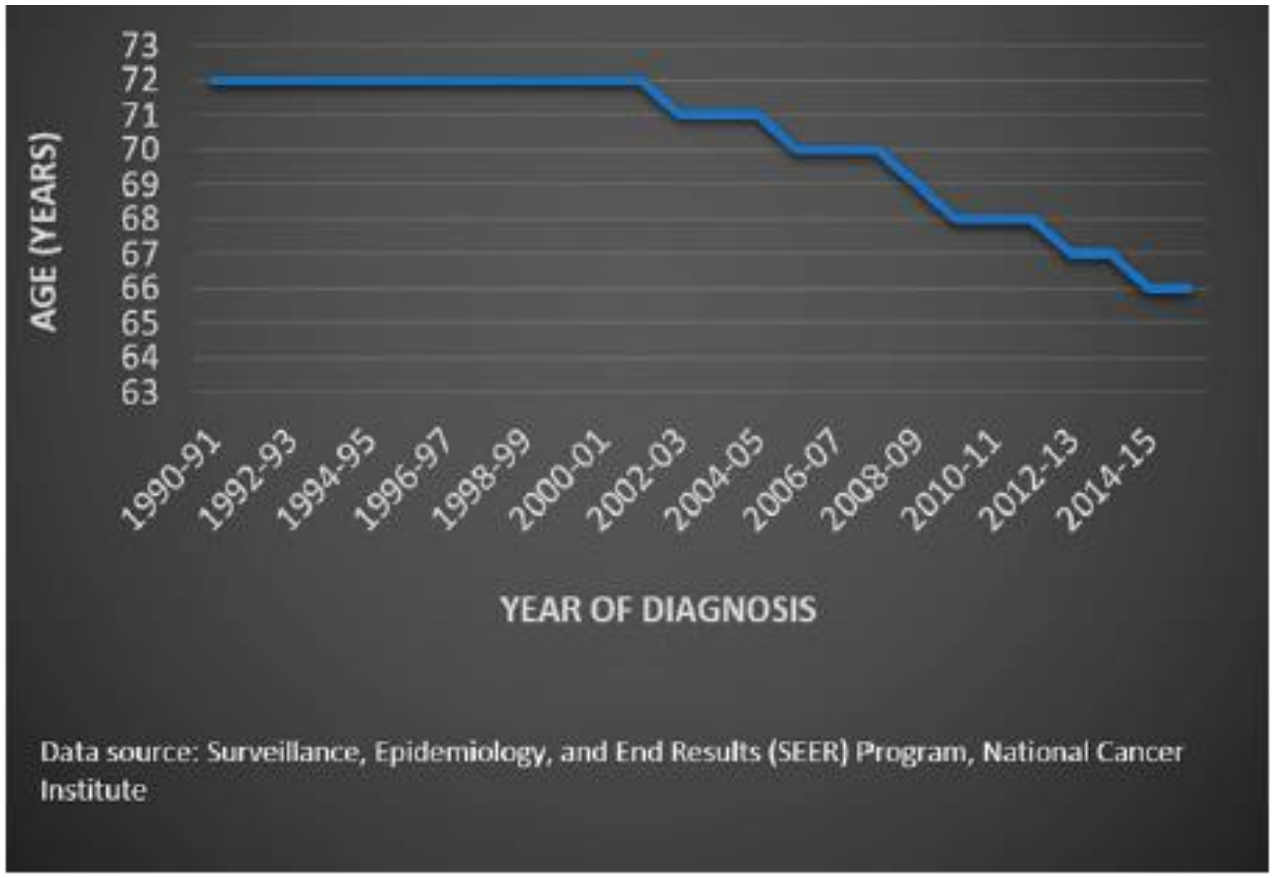
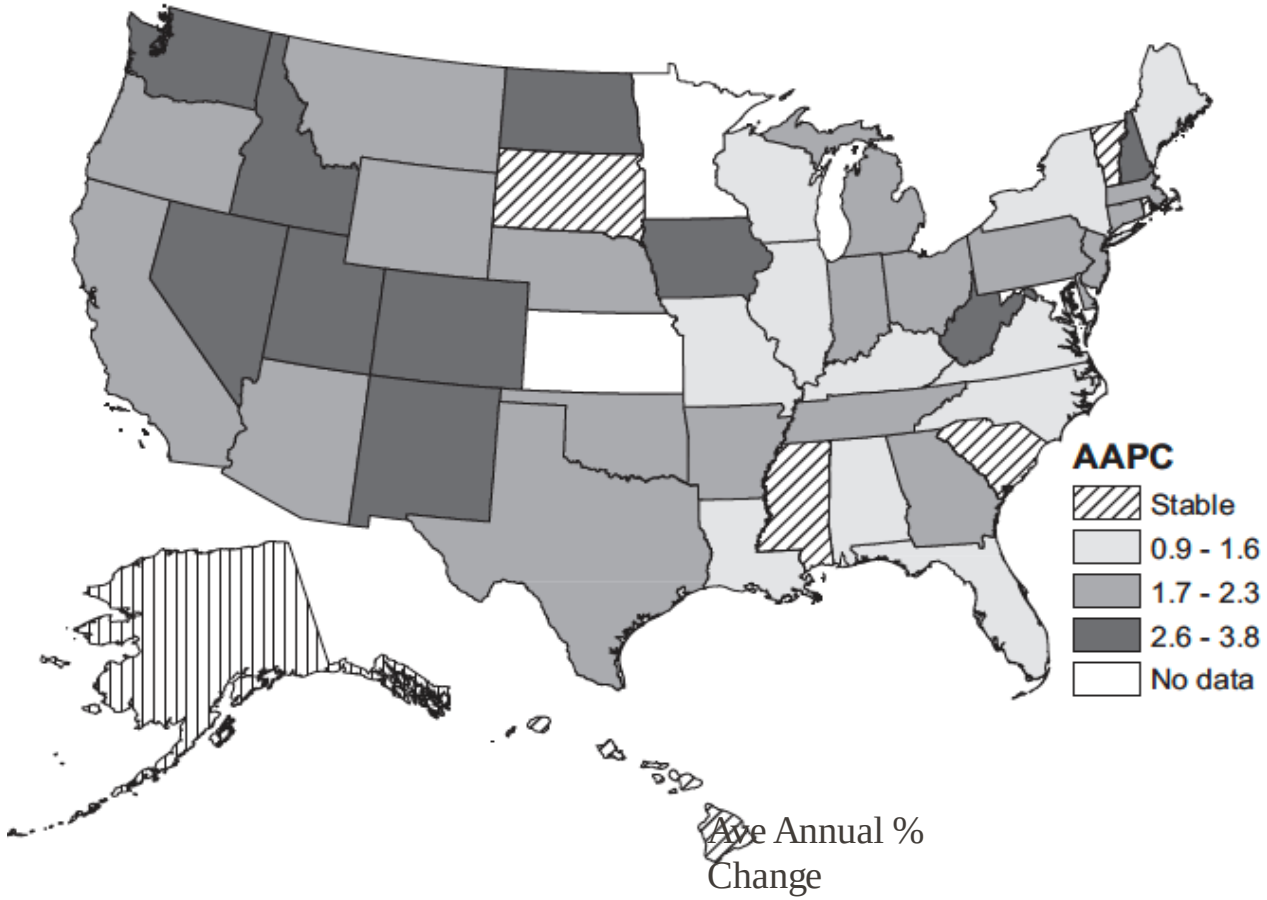


FIGURE 1. Median Age at Colorectal Cancer Diagnosis in the United States, 1990–2016

Siegel et al,ASCO Ed Bk 2020



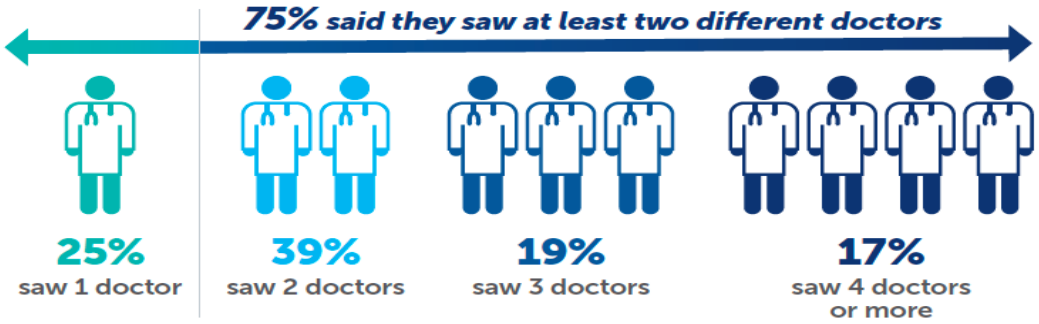
Among 47 states reporting data, increased incidence is reported in 42 (89.4%)

- Highest rates in Southern/Western states

Siegel et al, JNCI 2019

Young-onset Colorectal Cancer

Risk Factors Unknown; Diagnosis Difficult



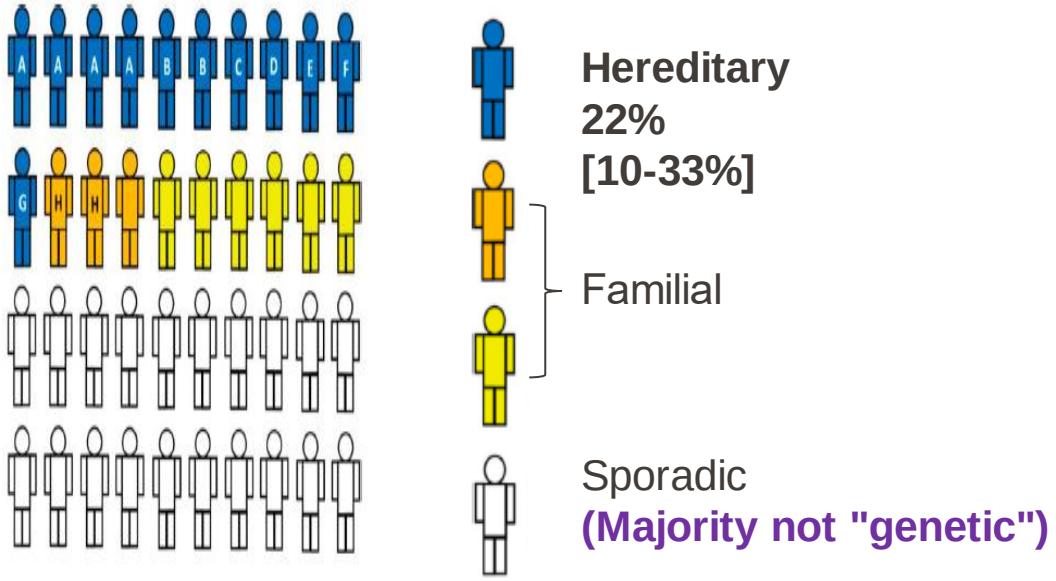
NEVER TOO YOUNG SURVEY REPORT 2020 — Colorectal Cancer Alliance

"When young colorectal cancer patients come to see us, they are completely lost and feel out of control."

Table 1 | **Exposomal elements driving EOCRC**

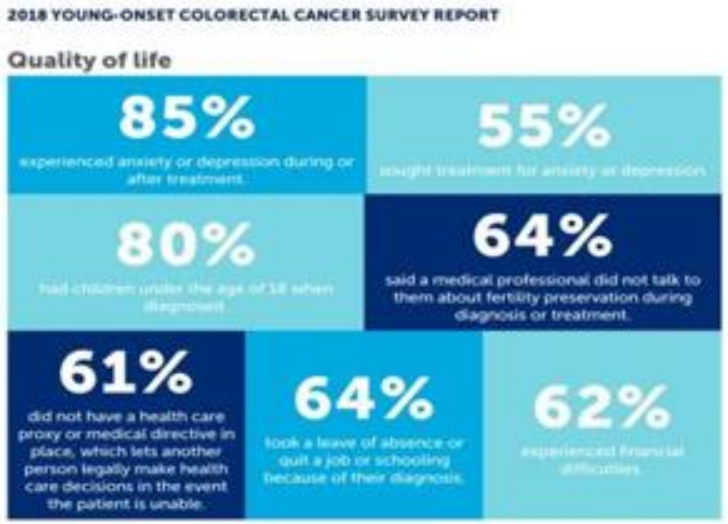
Exposomal element	Temporal trend	Global trend	Effect on inflammation/ microbiome or known effect on distal colon or rectum	Exposure during development (conception to adulthood)
Westernized diets	Yes[140]	Yes[140]	Yes[138,148]	Yes[129,130]
Red and processed meat	Yes[20,140,157,158]	Yes[20,140,157,158]	Yes[160,161,253,254]	Yes[20,157,158]
Obesity	Yes[101,103,140]	Yes[101,103,140]	Yes[108,109]	Yes[105–107]
Stress	Yes[118]	Yes[117]	Yes[255,256]	Yes[118,119,257]
Antibiotics	Yes[258]	Yes[168]	Yes[169–171]	Yes[162]
Synthetic dyes	Yes[186,200]	Yes[186,200]	Yes[192,193,259,260]	Yes[200]
Monosodium glutamate	Yes[261,262]	Yes[261,262]	Yes[201,202,263–265]	Yes[261]
Titanium dioxide	Yes[266]	Yes[266]	Yes[206,208,209,267]	Yes[206,207,266]
High-fructose corn syrup	Yes[210,215,268]	Yes[210,215,268]	Yes[216,269]	Yes[217]

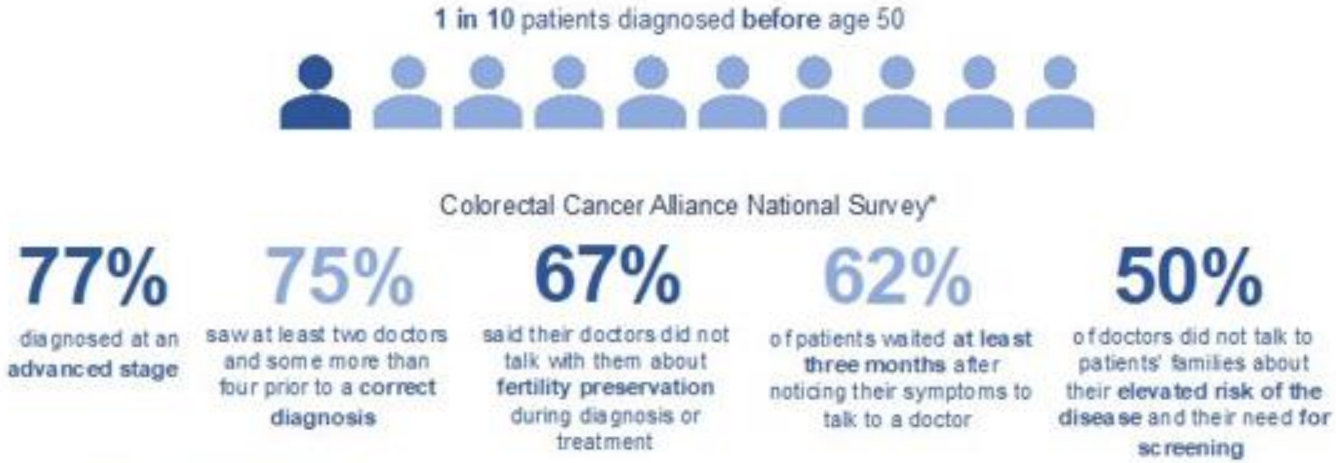
Key exposomal suspects driving early-onset colorectal cancer (EOCRC) emerge when four metrics are fulfilled: first, a temporal relationship exists, similar to EOCRC; second, exposure is global, as is EOCRC; third, molecular evidence exists of inflammatory or microbiome-modifying properties or evidence of an effect on the distal colon or rectum; and four, exposure occurs at any time during development from conception until adulthood.



Hofseth et al. Nat Rev Clin Onc 2020;
Mauri et all, *Molecular Oncology* 2019

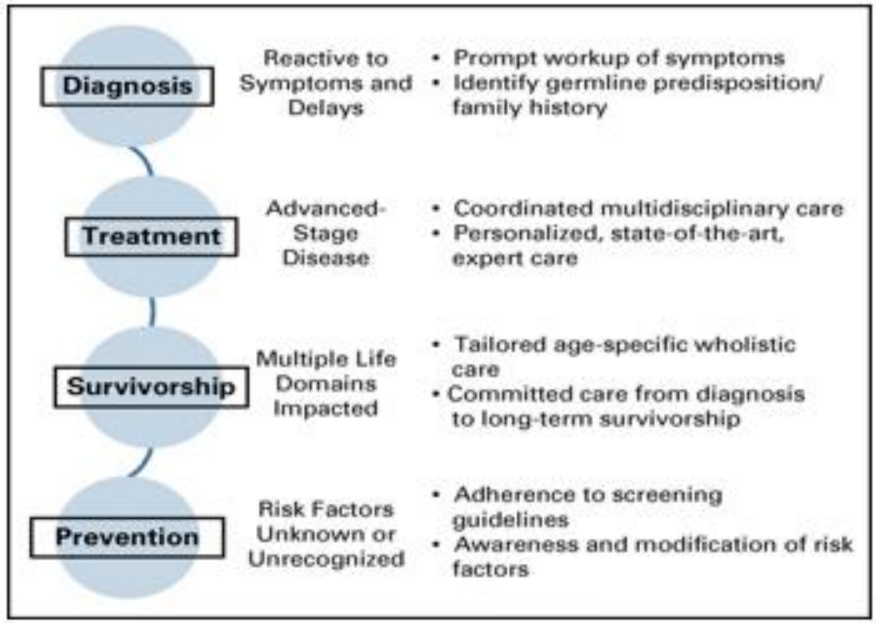
Young-onset CRC
Scope & Urgency





The Increasing Incidence of Young-Onset Colorectal Cancer: A Call to Action

Ahnen et al. *Mayo Clinic Proceedings* 2015;
You et al. *J Onc Pract 2020*

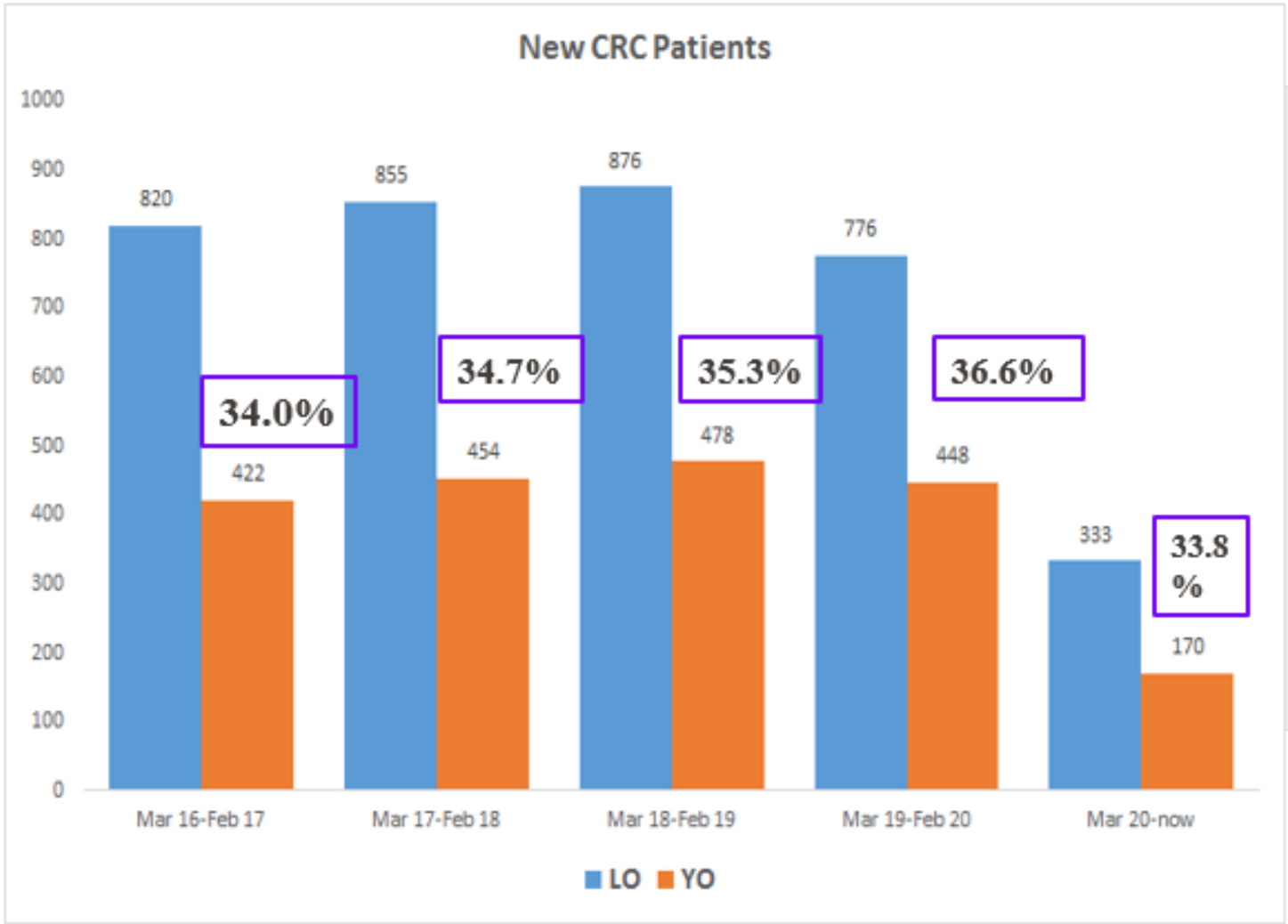


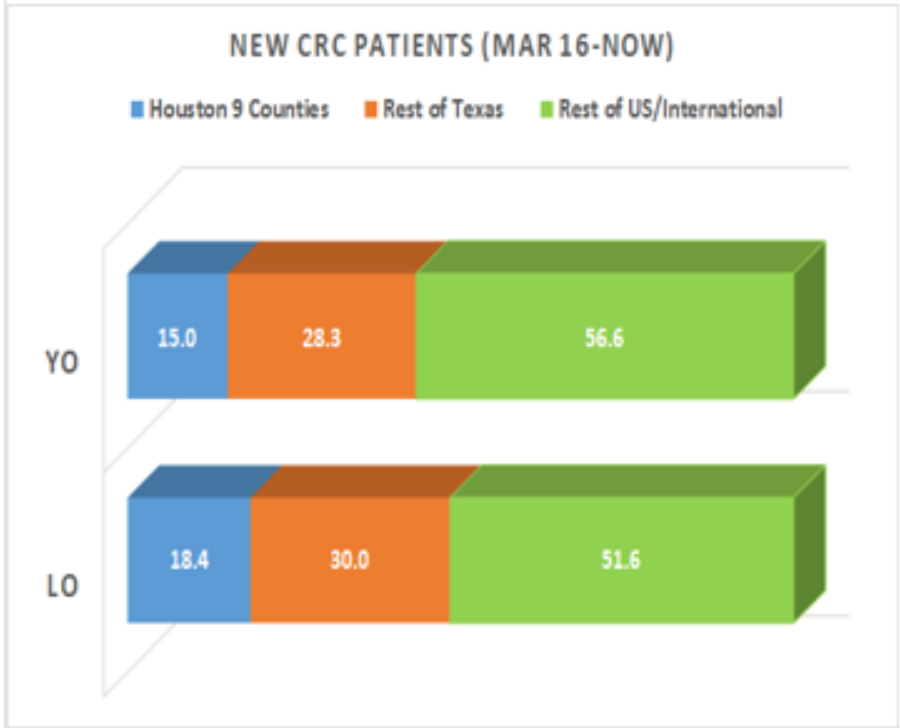
Young-Onset Colorectal Cancer Program

Y. Nancy You, MD, MHSc
Devon Harrison
Benny Johnson, DO
Grace Li Smith, MD PhD MPH

We are the place for you. We are with you every step of the way.

MDACC: YOCRC significantly over-represented (35% vs. ~12% nationally)





https://www.mdanderson.org/patients-family/diagnosis-treatment/care-centers-clinics/gastrointestinal-cancer-center/young-onset-colorectal-cancer-program.html

Mission

To offer the best integrated care for young-onset colorectal cancer patients across the cancer spectrum, including diagnosis, treatment, survivorship and prevention

Vision

To be a worldwide leader dedicated to ending the burden of young-onset colorectal cancer

Values

PATIENT CENTRICITY

We focus on coordinated and whole-person care to provide a personalized, holistic and caring experience.

INNOVATION

We strive for modern, innovative approaches and utilize technology to advance the mission.

EXCELLENCE

We deliver state-of-the-art, expert clinical care integrated with research.

YOUNG-ONSET COLORECTAL CANCER PROGRAM

Goals

- Expedite and coordinate access to cancer and multidimensional consults
- Create a technology platform for patient care navigation and communication
- Offer universal genetic testing with novel care delivery (telegenetics)
- Provide research-driven care with molecular profiling (solid and liquid)
- Build a multidisciplinary clinical trials pipeline (neoadjuvant, adjuvant, metastatic)
- Launch a longitudinal research repository
- Standardize care pathways throughout MD Anderson and MD Anderson Cancer Network®

Clinical Operations

Research

Administration

Education

Advancement

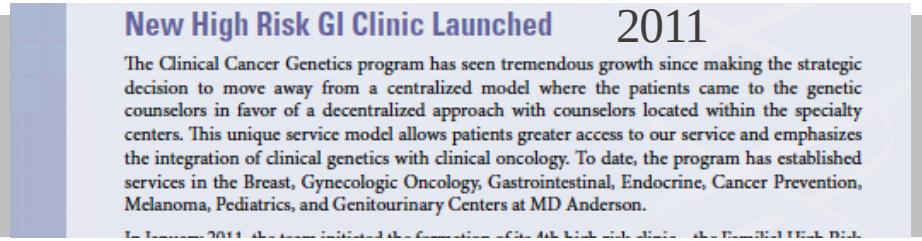
Young-onset CRC
Universal germline testing

- 2009 Universal tumor screening for DNA mismatch repair deficiency (dMMR)
  - **11 % dMMR**

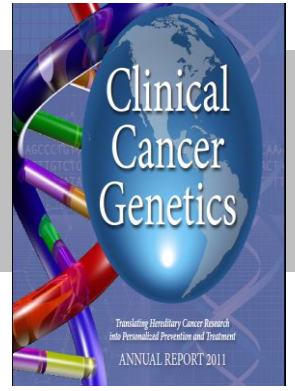
Dineen et al, JNCCN 2015

- 2019 Universal germline multiplex testing
  - **25 (19.2%): Pathogenic mutations**
  - 23 (17.7%): Variant of uncertain significance

You et al, *DCR* in press


New High Risk GI Clinic Launched 2011

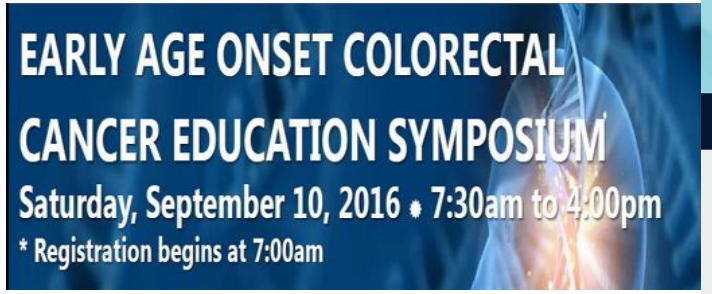
The Clinical Cancer Genetics program has seen tremendous growth since making the strategic decision to move away from a centralized model where the patients came to the genetic counselors in favor of a decentralized approach with counselors located within the specialty centers. This unique service model allows patients greater access to our service and emphasizes the integration of clinical genetics with clinical oncology. To date, the program has established services in the Breast, Gynecologic Oncology, Gastrointestinal, Endocrine, Cancer Prevention, Melanoma, Pediatrics, and Genitourinary Centers at MD Anderson.



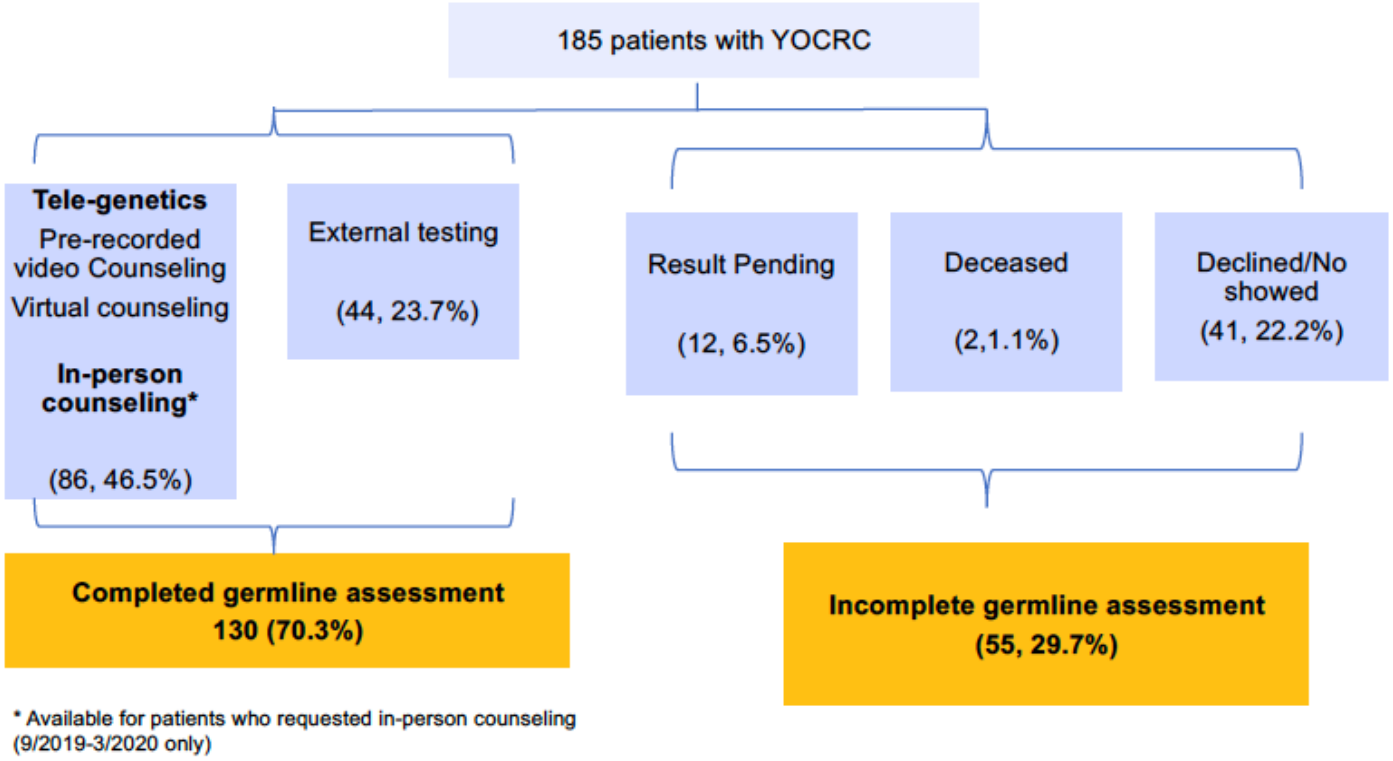
Tele-Genetics

Patients & Families with germline inherited predisposition to CRC

Diagnosis | Treatment | Surveillance | Survivorship

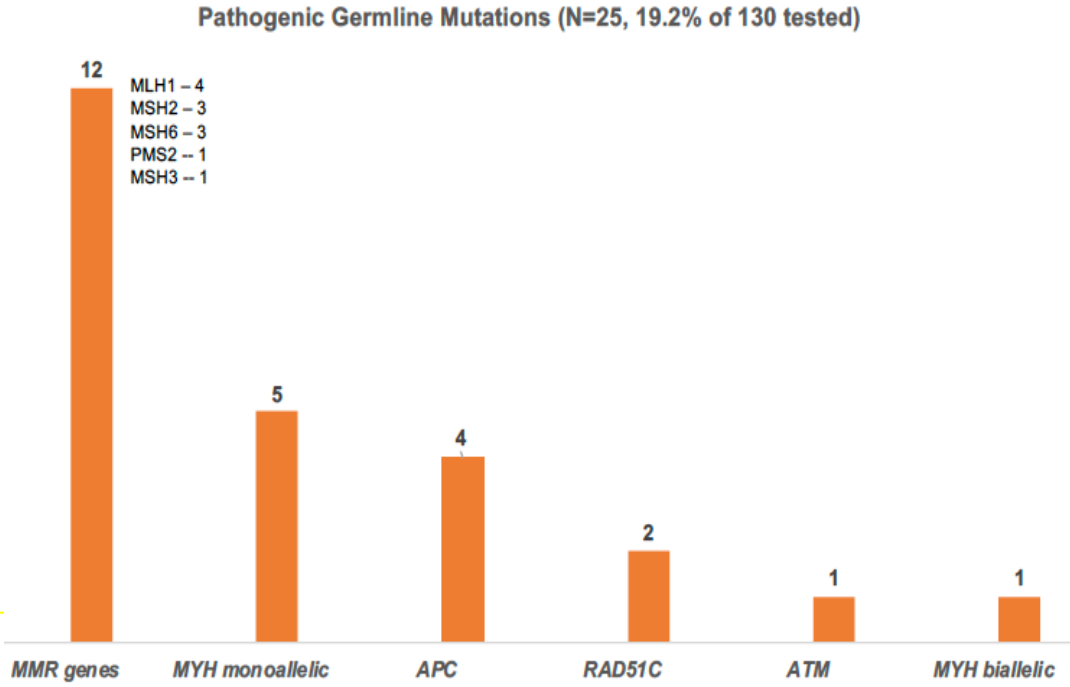


GOAL 3. Offer Universal Genetic Testing With Novel Care Delivery (Tele-genetics)



Among 130 patients with test results:

- **25 (19.2%): Pathogenic mutations**
- 23 (17.7%): Variant of uncertain significance



Pathogenic germline mutation was found in:
71% dMMR vs. 13% pMMR tumors [p<0.001]
32% positive family history vs. 12% no family history [p=0.015]

You et al, *DCR* in press

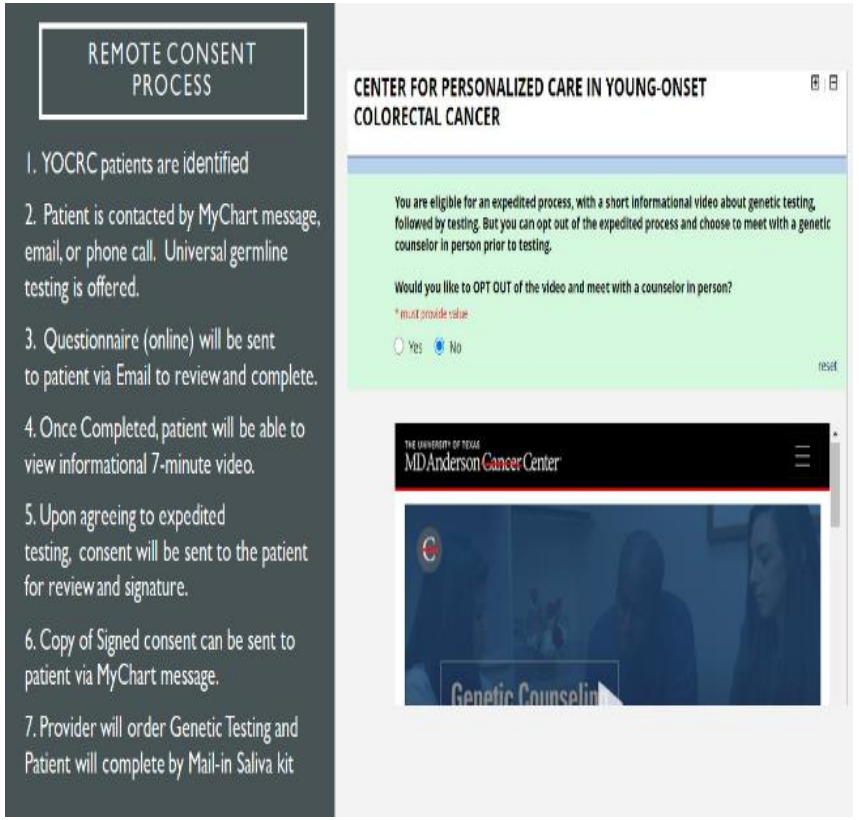
GOAL 3. Offer Universal Genetic Testing With Novel Care Delivery (Tele-genetics)

Pre-test Genetic counseling:

- Self-view a pre-taped session (7 min),
- or Attend a live session (in person or virtual).

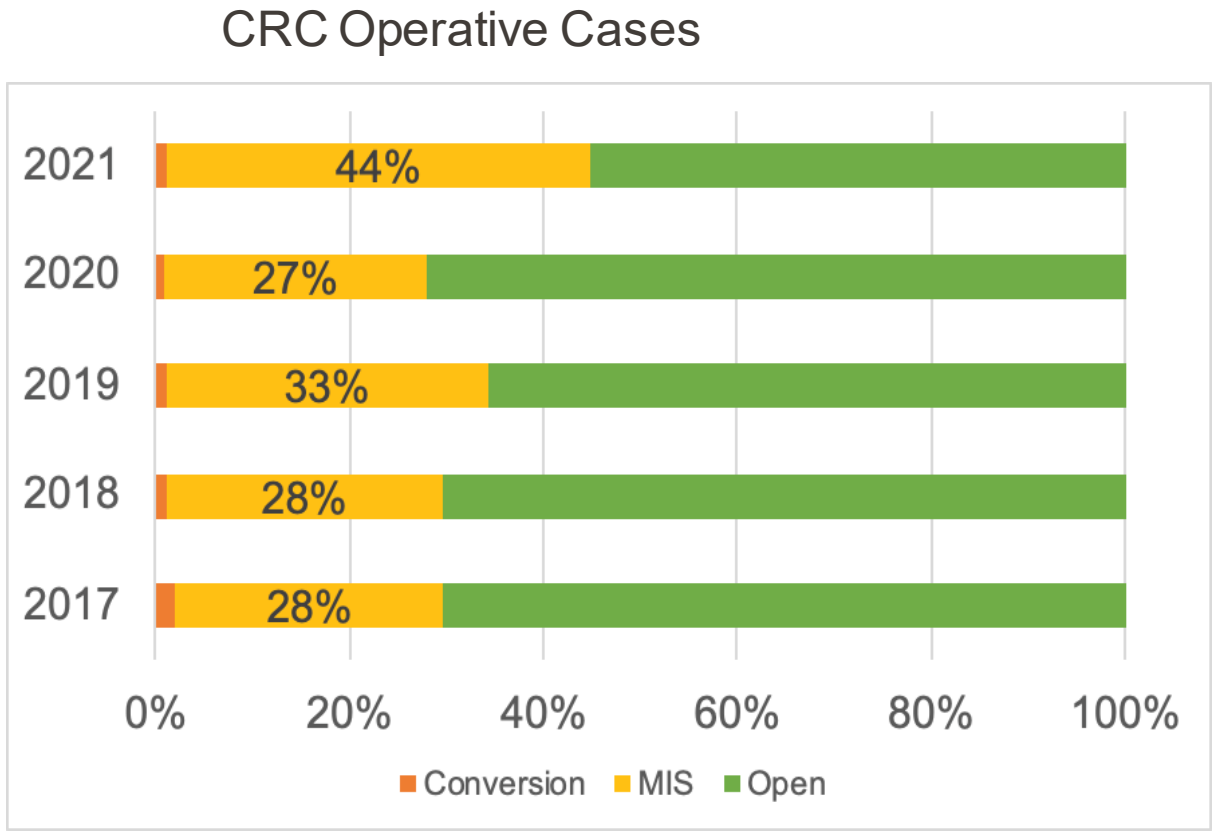
Test: 47-gene Common Hereditary Cancer Panel

Post-test: Counseling & High-risk clinic

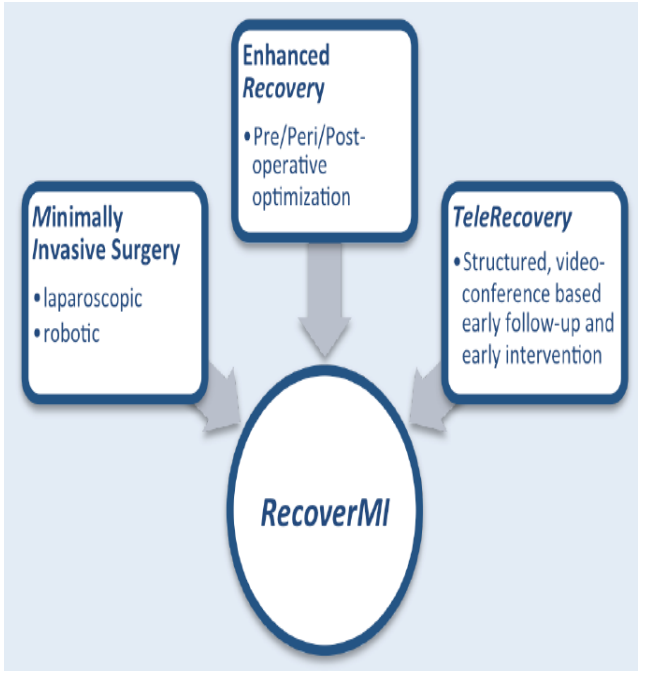


** Will not replicate testing if pre-referral testing available; extremely low insurance denial rate; video-consent successful in pilot*

Young-onset CRC
Patient-centric Care Experience



Enhance Patient Surgical Experience



Price, et al. BMJ Open 2017;
Bednarski et al, BJS 2019

Patient-centric Treatments

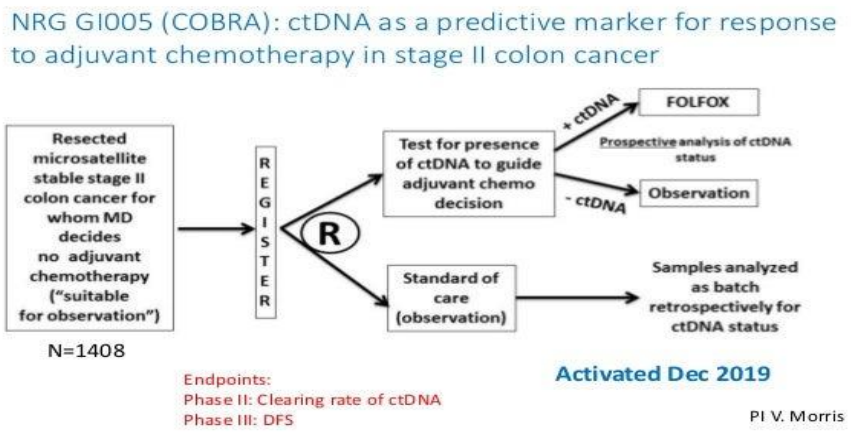
Intense multi-modality therapy

Neoadjuvant Regimen: Response adaptive & individualized

Precision Adjuvant Therapy

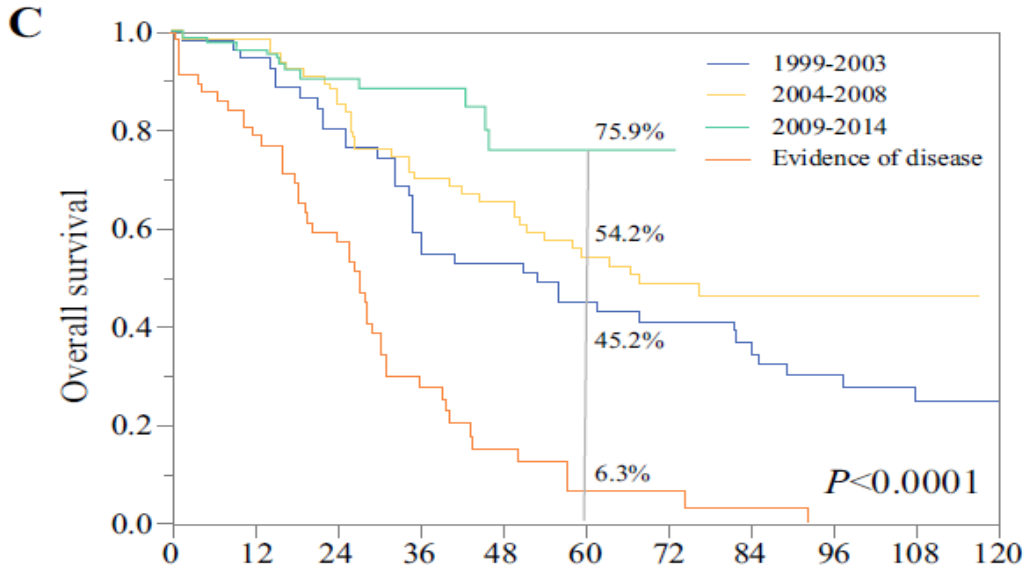
Benchmarking Outcomes for Definitive Treatment of Young-Onset, Locally Advanced Rectal Cancer

- Median: 6cm from anal verge; 75% locally advanced90% tri-modality therapy



Individualized Treatment Sequencing Selection Contributes to Optimized Survival in Patients with Rectal Cancer and Synchronous Liver Metastases

- 1999-2014, rectal primary and synchronous resectable liver mets: N=268



Taku et al, Clin CRC 2022; Conrad et al, Ann Surg Onc 2017

Patient-centric Treatments

Biomarker-directed: Metastatic, adjuvant, neoadjuvant, pre-emptive settings

PHASE III ATOMIC TRIAL

N = 700

Eligibility Criteria

- Stage III colon adenocarcinoma with any tumor (Tx-T4, N1-2M0; including N1C) originating or entirely located in colon
- Completely resected tumor
- dMMR
- No residual involved lymph node or metastatic disease at time of registration
- No prior chemotherapy, immunotherapy, biologic, targeted therapy, or radiation therapy; 1 previous cycle of mFOLFOX6 permitted.
- ECOG performance status ≤2
- No known active autoimmune disease or hepatitis B or C

Experimental arm: mFOLFOX6 with atezolizumab (12 cycles) followed by atezolizumab (6 months)

Control arm: mFOLFOX6 (12 cycles)

Endpoints:

Primary DFS

Secondary OS, AEs

AE indicates adverse event; DFS, disease-free survival; dMMR, DNA mismatch repair; mFOLFOX6, modified leucovorin calcium, fluorouracil, and oxaliplatin; OS, overall survival.

Neoadjuvant Pembrolizumab for Patients with Mismatch Repair Deficient Localized and Locally Advanced Solid Cancers
ESMO 2021

Pathological Tumor Response Following Immune Checkpoint Blockade for Deficient Mismatch Repair Advanced Colorectal Cancer

JNCI J Natl Cancer Inst (2021) 113(2): djaa052

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

A. Cercek, M. Lumish, J. Sinopoli, J. Weiss, J. Shia, M. Lamendola-Essel, I.H. El Dika, N. Segal, M. Shcherba, R. Sugarman, Z. Stadler, R. Yaeger, J.J. Smith, B. Rousseau, G. Argiles, M. Patel, A. Desai, L.B. Saltz, M. Widmar, K. Iyer, J. Zhang, N. Gianino, C. Crane, P.B. Romesser, E.P. Pappou, P. Paty, J. Garcia-Aguilar, M. Gonen, [illegible] eiser, K.A. Schalper, and L.A. Diaz, Jr.

N ENGL J MED 386;25

EA2201: An ECOG-ACRIN phase II study of neoadjuvant nivolumab plus ipilimumab and short course radiation in MSI-H/dMMR rectal tumors.
ASCO *2022*

We are the place for you. We are with you every step of the way.

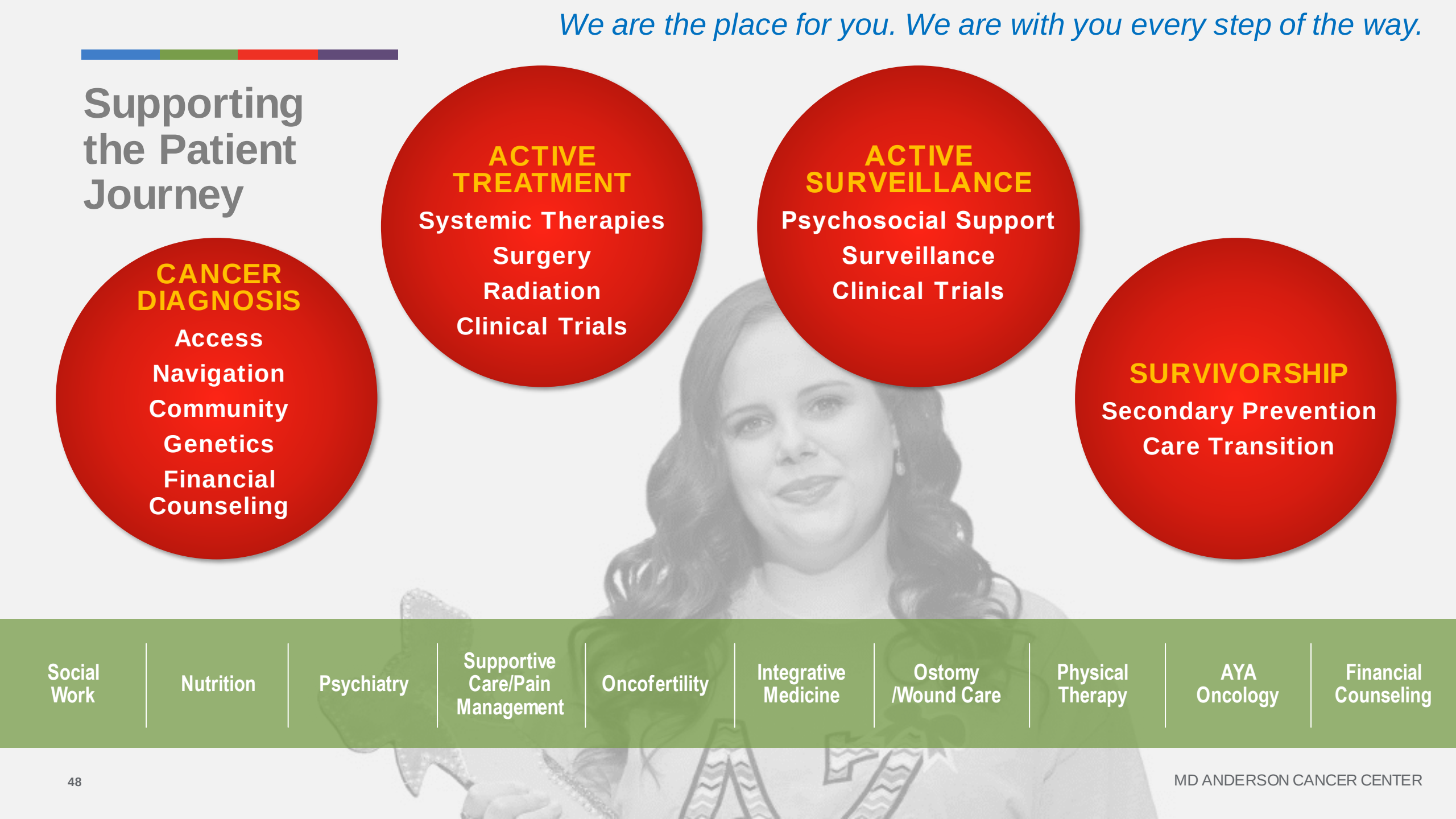
Supporting the Patient Journey

CANCER DIAGNOSIS
- Access
- Navigation
- Community
- Genetics
- Financial Counseling

ACTIVE TREATMENT
- Systemic Therapies
- Surgery
- Radiation
- Clinical Trials

ACTIVE SURVEILLANCE
- Psychosocial Support
- Surveillance
- Clinical Trials

SURVIVORSHIP
- Secondary Prevention
- Care Transition

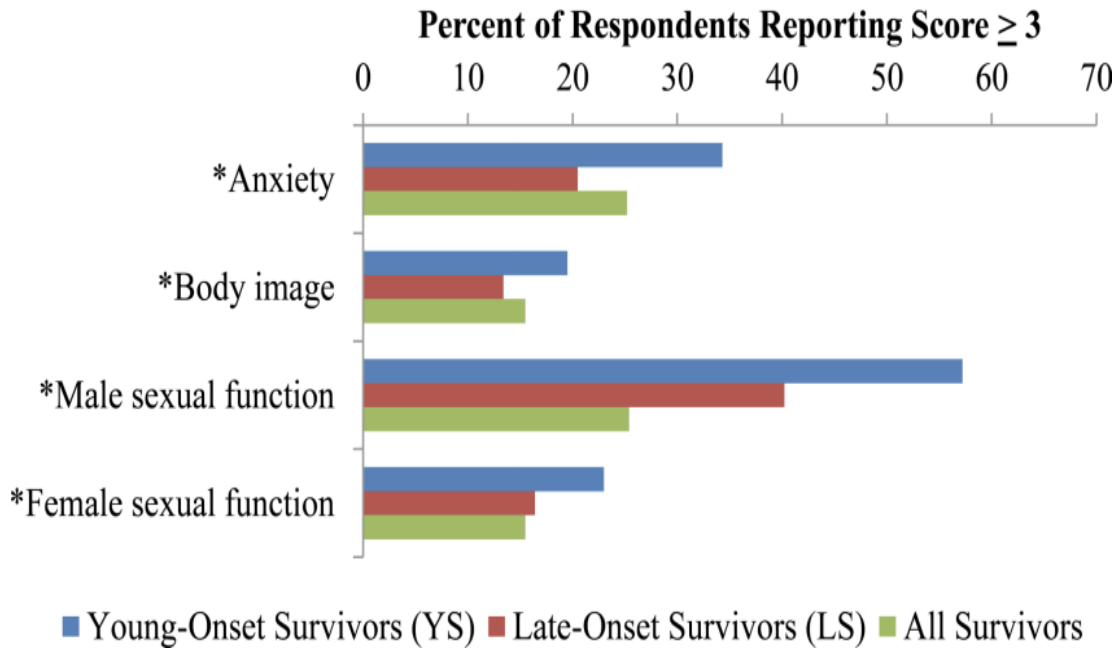


Social Work | Nutrition | Psychiatry | Supportive Care/Pain Management | Oncofertility | Integrative Medicine | Ostomy /Wound Care | Physical Therapy | AYA Oncology | Financial Counseling

Goal 1: Expedited & Coordinated Access to Multi-Dimensional Care

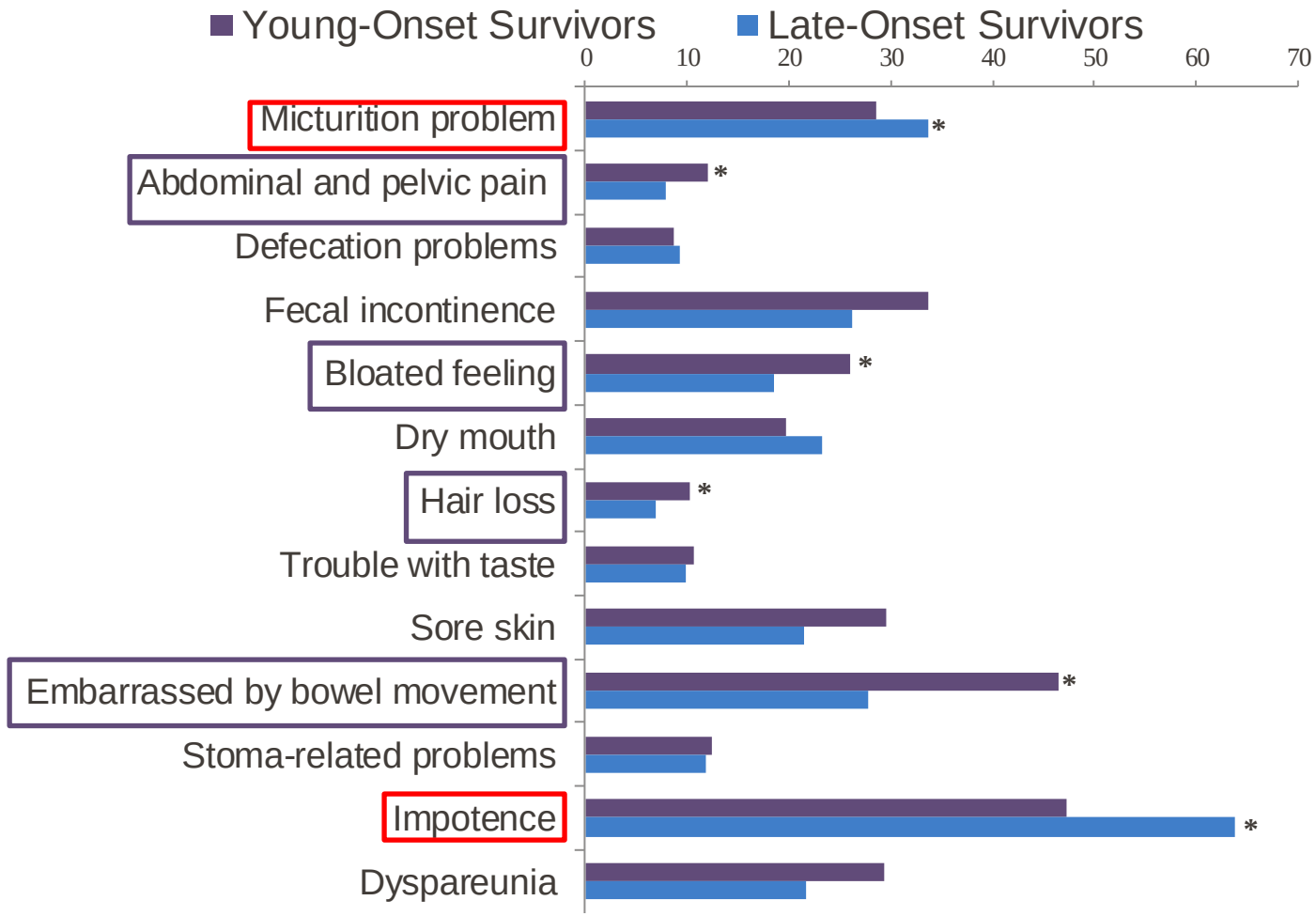
Survivorship: How does cancer impact life?

Functional Deficits and Symptoms of Long-Term Survivors of Colorectal Cancer Treated by Multimodality Therapy Differ by Age at Diagnosis



Bailey/You et al. *J GI Surg 2015*

EORTC Symptoms Scales



Bailey/You et al. *J GI Surg 2015*

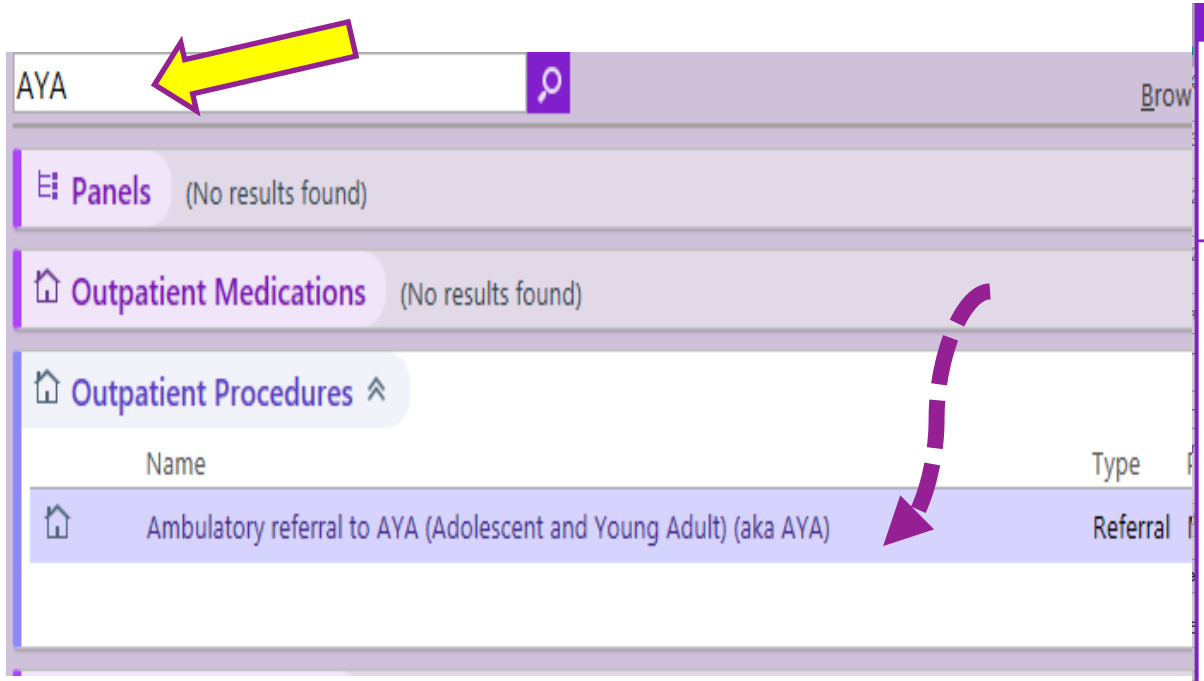
Age 31-50 : SUPPORT Consult Bundle SmartSet

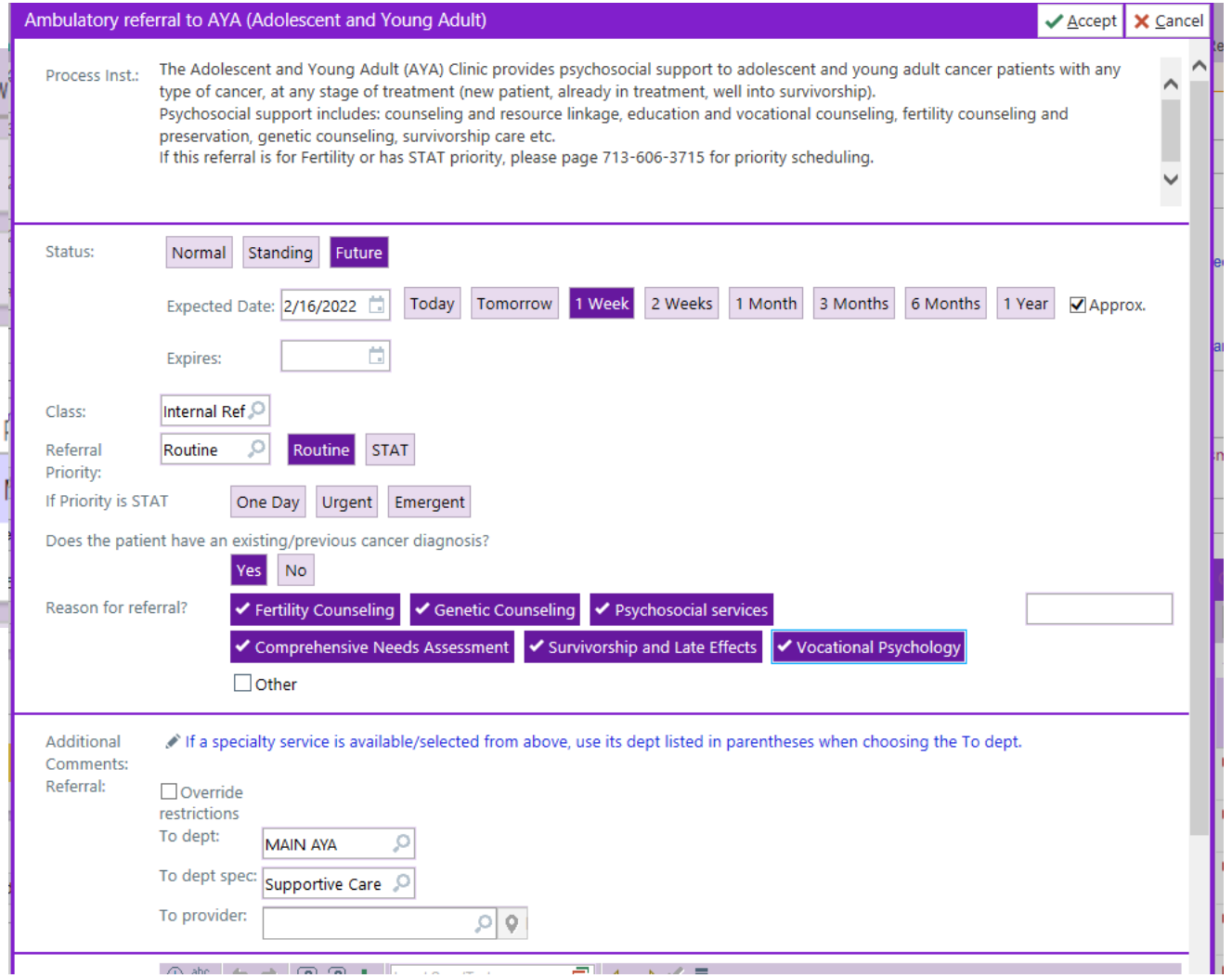
- Select any or all that are applicable for the patient

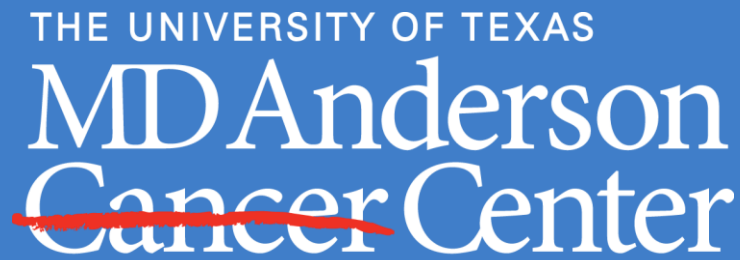
SUPPORT

GI High Risk & Genetics
Social work
Nutrition
Psychiatry
Supportive care
Oncofertility
Integrative medicine
Ostomy/wound
Physical Therapy

Age 18-30 : AYA Oncology Consult Bundle







ynyou@mdanderson.org

Making Cancer History®

Thank You!

American Cancer Society | National Colorectal Cancer Roundtable | 80% In Every Community

Center for Young Onset Colorectal Cancer: A Clinical and Research Center

Thursday, November 17, 3:30 PM

American Cancer Society | National Colorectal Cancer Roundtable | 80% In Every Community

Center for Young Onset Colorectal Cancer: A clinical and research center

Andrea Cercek, MD
Section Head, Colorectal Cancer
Co-Director, Center for Young Onset Colorectal & Gastrointestinal Cancers
Memorial Sloan Kettering Cancer Center

Early Onset Colorectal Cancer: The incidence is rising

Currently

- Incidence of CRC is declining among people over 50
- But the incidence is increasing among people under 50

By 2030:

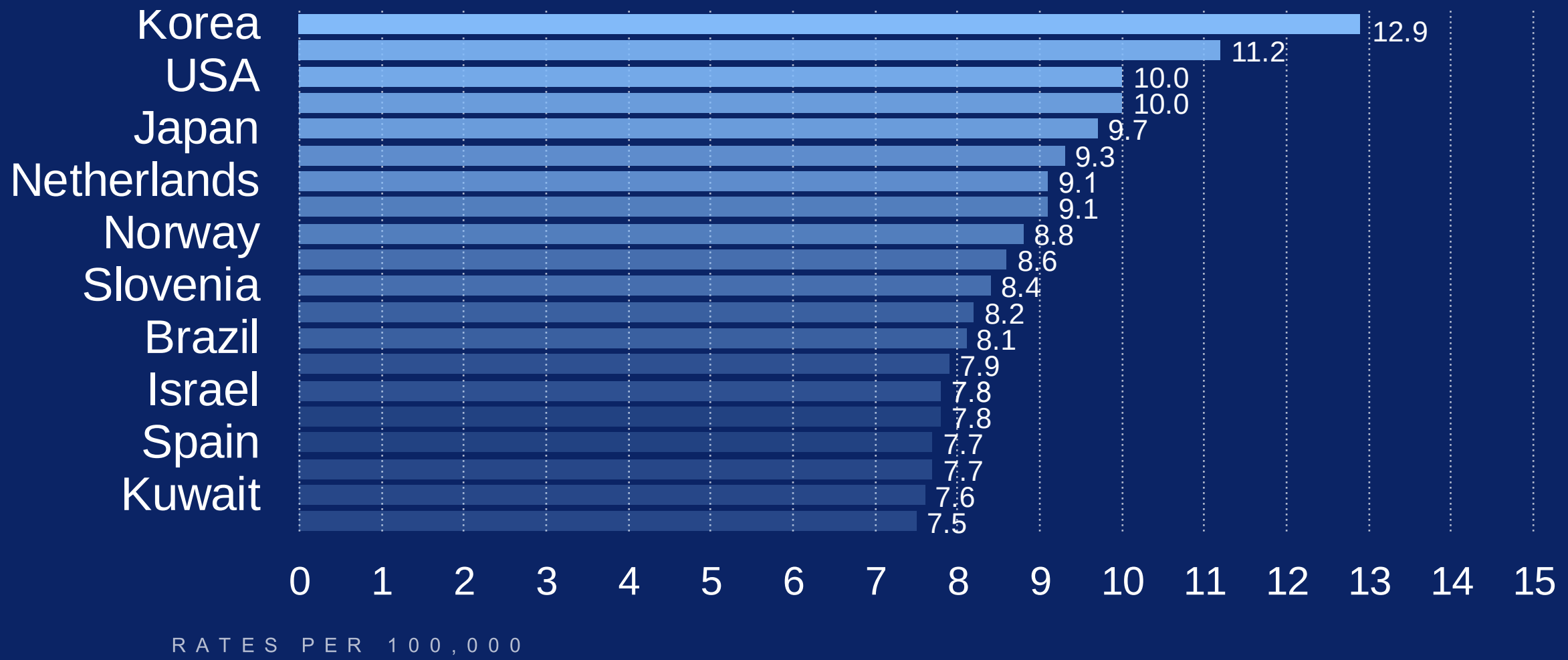
- Incidence of CRC in young adults will nearly **DOUBLE**
- **1 in 10 colon** and **1 in 4 rectal** cancers will be diagnosed in those younger than 50

Early Onset Colorectal Cancer: The cause is unknown




GLOBAL PHENOMENON

Early Onset Colorectal Cancer: Top 20



Center for Young Onset Colorectal Cancer

Established March 2018
First in the World

Main Objectives:

- Coordinated clinical program
- Clinical database, biospecimen repository, research

	2018	2022
Patients Enrolled	**201**	**2101**

Center for Young Onset Colorectal Cancer

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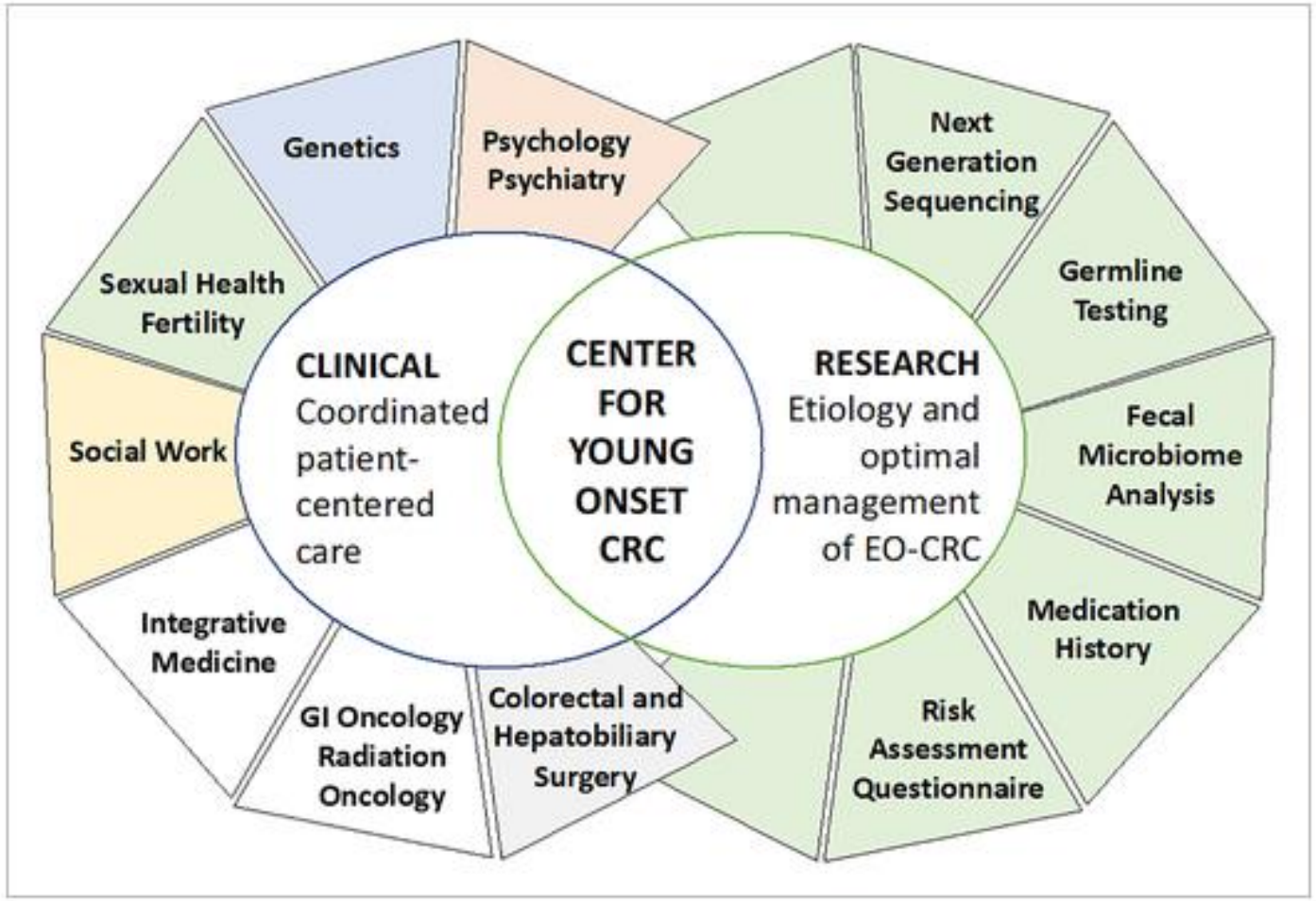
First in the World

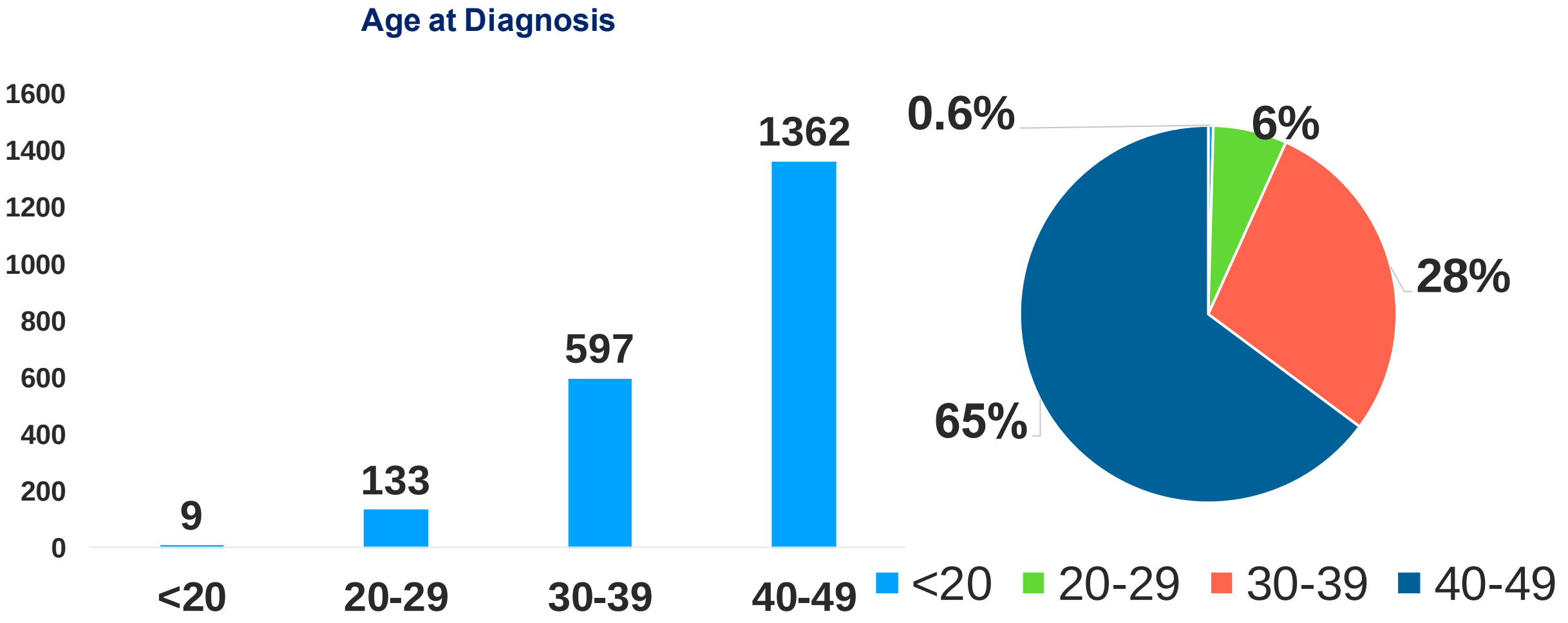


https://www.mskcc.org/cancer-care/types/colorectal/colorectal-cancer-young-adults

Mendelsohn, Palmaira, Cercek The Oncologist 2021

Center for Young Onset Colorectal Cancer

A Coordinated Clinical and Research Center



Center for Young Onset Colorectal Cancer

Established March 2018
First in the World

Optimize introduction of ancillary services

Optimize patient communication/engagement

Research in tumor biology, microbiome and epigenetics

Outreach programs to raise awareness of young onset CRC

Clinical Trials designed to improve outcomes

https://www.mskcc.org/cancer-care/types/colorectal/colorectal-cancer-young-adults

Mendelsohn, Palmaira, Cercek The Oncologist 2021

Center for Young Onset Colorectal Cancer

Established March 2018
First in the World

Evaluation of Patient Utilization of Ancillary Services

Initial 2 year experience

Ancillary Service	Patient Usage (%)
Social Work	86%
Integrative Medicine	28%
Nutrition	69%
Psychology and Psychiatry	27%
Fertility	22%
Online Portal Use	97%
12-245 Part A (tumor genomics)	83%
12-245 Part C (germline)	79%

https://www.mskcc.org/cancer-care/types/colorectal/colorectal-cancer-young-adults

Mendelsohn, Palmaira, Cercek The Oncologist 2021

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First in the World

Patient Satisfaction Survey Results

Patient Reported Service Utility and Timing (n=91)		
Support Service Used	**Positive Service Utility[1]**	**Appropriate Timing**
Social Work (n=51)	70.59%	83.70%
Nutrition (n=54)	88.89%	88.50%
Fertility (n=18)	77.78%	100.00%
Sexual Health (n=16)	87.50%	68.80%
Integrative Medicine (n=31)	70.97%	80.00%
Psychology/Psychiatry (n=16)	87.50%	75.00%

1: Patient rating 4 or 5 (somewhat helpful or very helpful)
n = patients who used and remembered using the service

https://www.mskcc.org/cancer-care/types/colorectal/colorectal-cancer-young-adults
Mendelsohn, Palmaira, Cercek The Oncologist 2021

Colorectal Cancer Under Age 50

What we know about early onset colorectal cancer

70% have late disease - stage 3/4

67% saw at least 2 physicians before diagnosis

60% of cases under 50 years of age are random — not genetic

Is Early Onset Colorectal Cancer Biologically Different?

- Genetic analysis of tumors: 1,446 MSK patients
- More rectal tumors in younger onset
- Same cancer biology in both younger and older patients

Cercek et al, JNCI 2021

Is Early Onset Colorectal Cancer What is the Etiology?

Ongoing research effort to identify etiology

- Risk factor questionnaire and stool collection for analysis of microbiome
- Further investigation of disease biology

Troubling New Trend:
Other young onset GI cancers are also rising

621

New Patients
Center expansion in 2021

Pancreas
Appendix
Gastric and others

Ongoing Research:

What's Causing the Rise in Cases and how to improve treatment?

- Optimizing clinical care
- Collaboration with other academic centers
- Research in etiology
- Clinical Trials

--early treatment

--changes in reproductive and sexual health in people with early onset colorectal cancer (NCT041812912)

Ongoing and Future Research:

What's Causing the Rise in Cases and how to improve treatment?

- Optimizing clinical care
- Collaboration with other academic centers
- Research in etiology
- Clinical Trials

--early treatment

--changes in reproductive and sexual health in people with early onset colorectal cancer (NCT041812912)

Clinical Trials

Locally advanced rectal cancer

Goal is to move therapy into early stage to improve outcomes AND decrease treatment related toxicity

Phase II Study of Induction PD-1 Blockade in Patients with Locally Advanced Mismatch Repair Deficient Rectal Adenocarcinoma

NCT04165772

EARLY STAGE RECTAL CANCER

Standard Of Care

Chemo

Radiation

Surgery

RECTAL CANCER INITIAL TREATMENT

Cure is frequently achieved, but radiation and surgery can have life-altering consequences

GOAL: OPTIONS TO STANDARD OF CARE

Reduce, Eliminate Radiation Side Effects

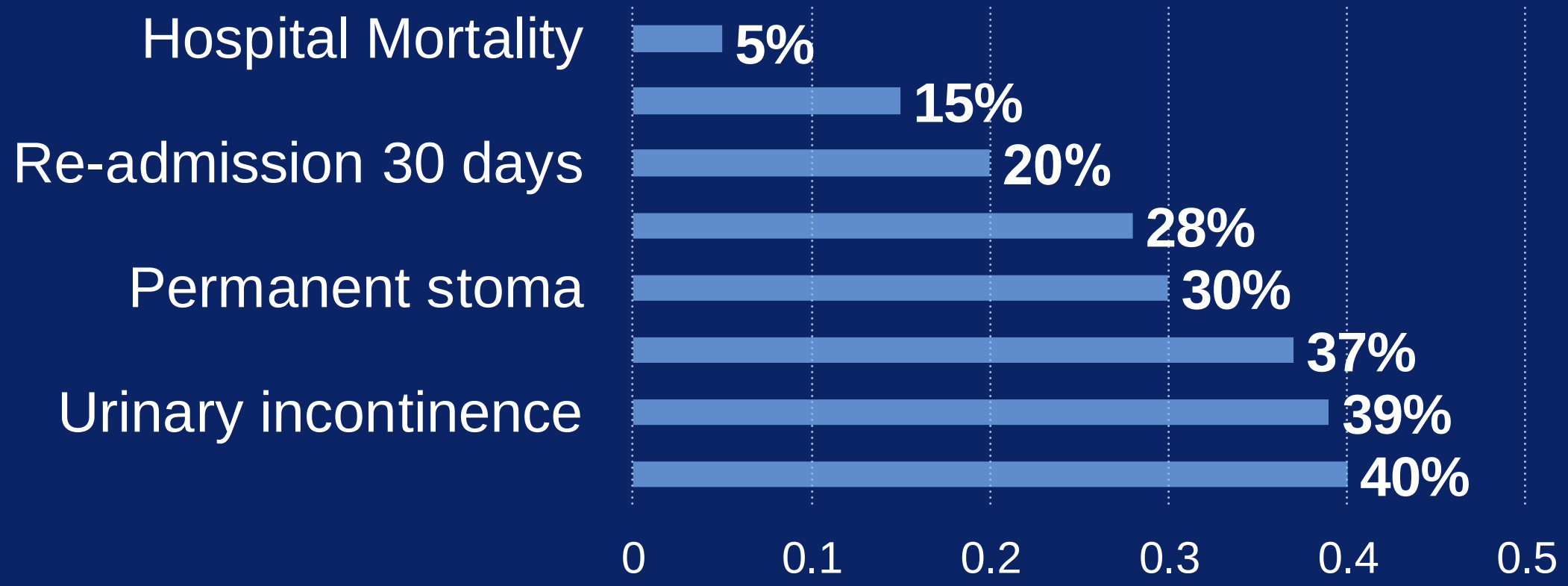
Short- and long-term toxicity, negatively impacting the function of:

- Bowels
- Bladder
- Sexual functioning
- Reproductive organs

GOAL: OPTIONS TO STANDARD OF CARE

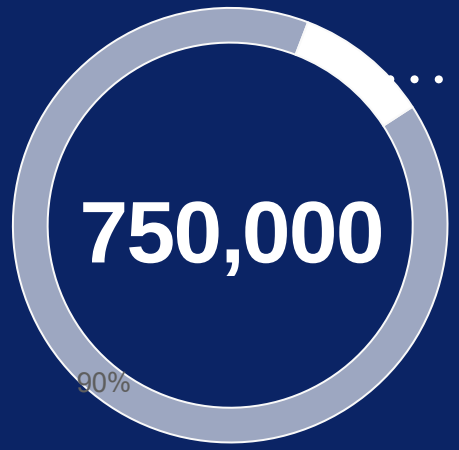
Reduce, Eliminate Radical Surgery Side Effects

Significant Bowel Removal Surgery* Can Result in One or More Complications



*Total Mesorectal Excision

Biomarker: Mismatch Repair Deficient Rectal Cancer



Global annual incidence rectal cancer

5-10%

Mismatch Repair-Deficient rectal cancer cases (40,000 to 75,000 patients annually)

EARLY STAGE RECTAL CANCER

Standard Of Care Prior To Study

Chemo

Radiation

Surgery

RECTAL CANCER INITIAL TREATMENT

Cure is frequently achieved, but radiation and surgery can have life-altering consequences

Checkpoint Blockade

TREATMENT OF METASTATES

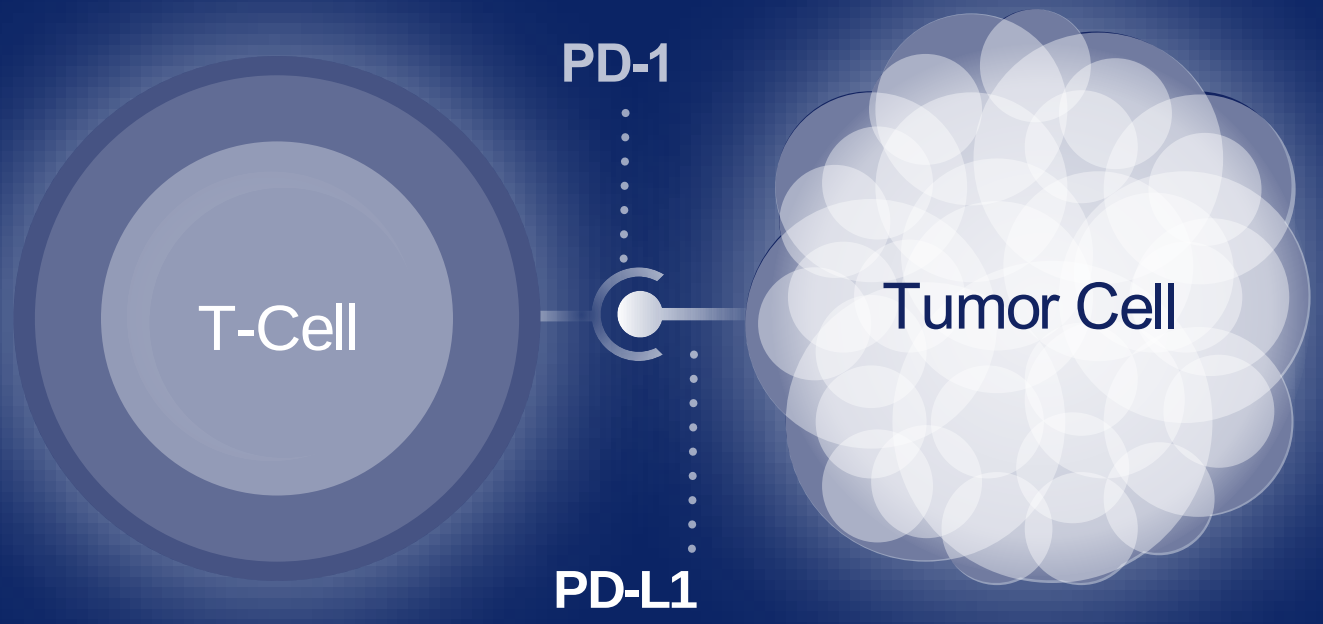
Successful treatment of Mismatch Repair Deficient of MSI that has spread or metastasized

MONOCLONAL ANTIBODIES

Treatment Uses a Highly Specific Drug to Target Cancer Cells

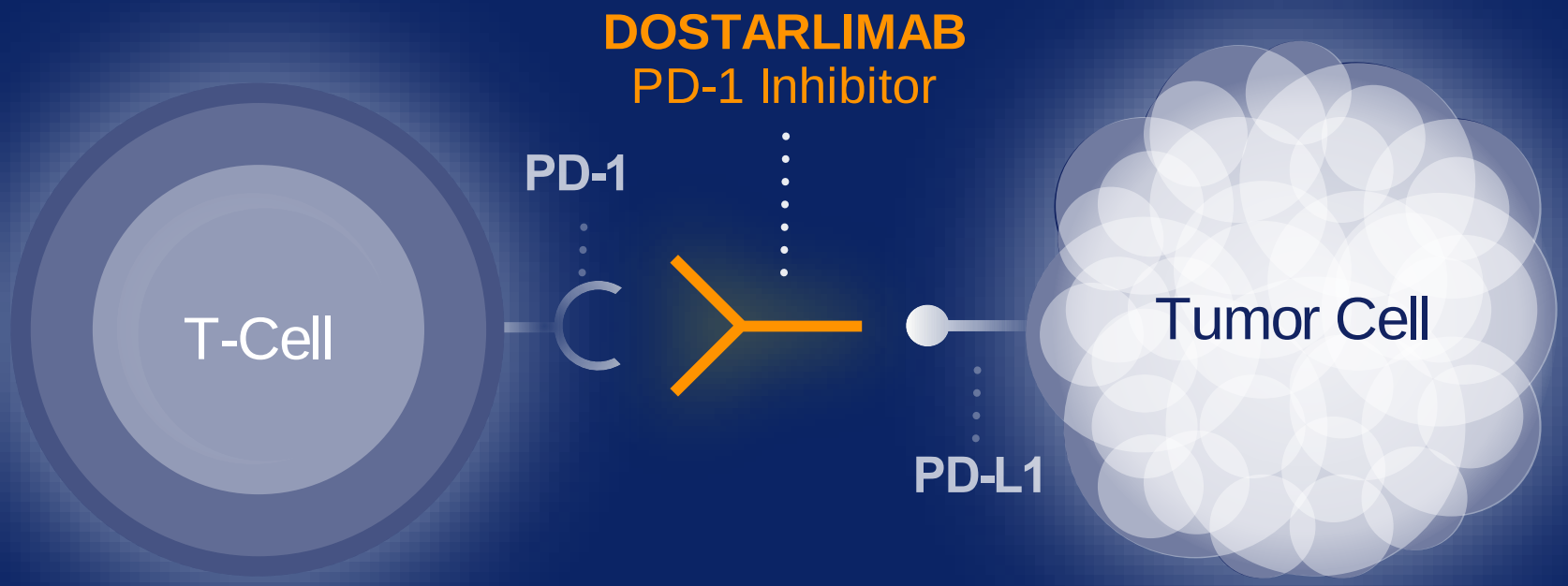
Treatment

Restarts the natural T-cell physiological process (that had been “turned off” by tumor) that plays a key role in the elimination of damaged, unwanted, and diseased cells.



MONOCLONAL ANTIBODIES

Treatment Uses a Highly Specific Drug to Target Cancer Cells



STUDY PROPOSAL

Change Treatment for 'Mismatch Repair-Deficient' Rectal Cancer Patients

Checkpoint Blockade

Hypothesis based on success of treating advanced **metastatic mismatch repair-deficient** (complete response rate of about 10%)

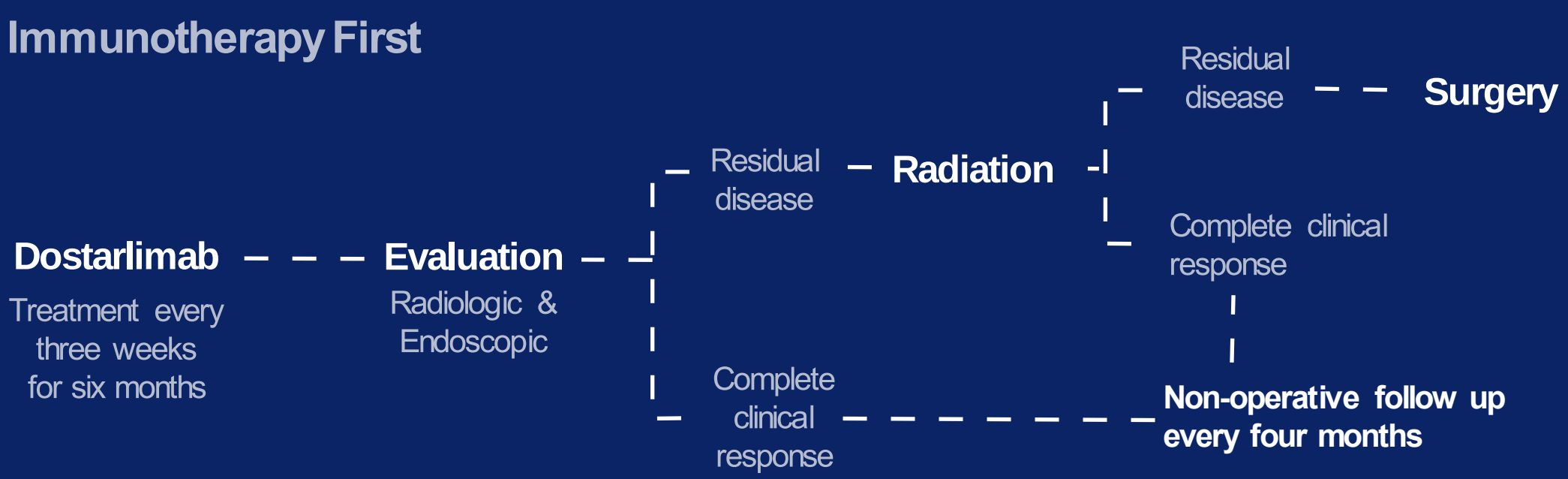
Chemo

Radiation

Surgery

GOAL TO REPLACE ANY / ALL PREVIOUS TREATMENTS

Study Design



FIRST TIME USE OF IMMUNOTHERAPY AS INITIAL TREATMENT

Clinical Trial Approach

14 Patients

Ages 26 to 78

Stage II or III (Mismatch Repair Deficient Rectal cancer)

Consultations

Patients met with oncologists, surgeons, radiological oncologists

Dostarlimab

Single dose, every three weeks, for six months

Patient on study: planned treatment for 6 months

ENDOSCOPY IMAGES: PATIENT #2

Months

Baseline

1.5

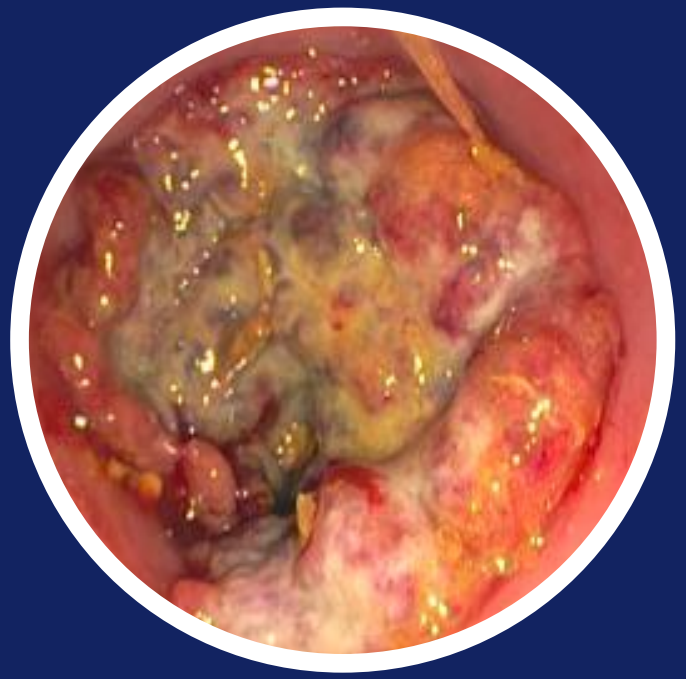
3.0

6.0

FU2 14

FU3 18

FU4 22



Cercek A, et al. *N Engl J Med*. 2022;386 MONTHS (25):2363-2376.

After 3 Treatments

ENDOSCOPY IMAGES: PATIENT #2

Months

Baseline

1.5

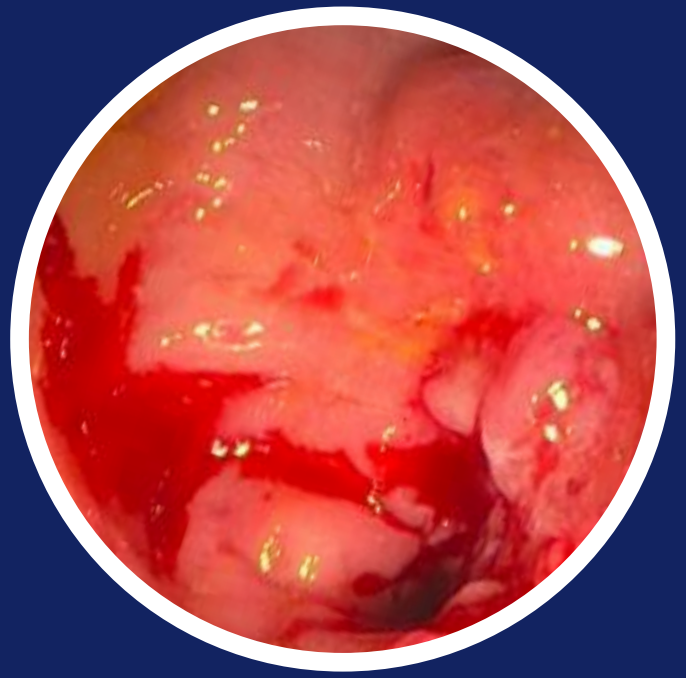
3.0

6.0

FU2 14

FU3 18

FU4 22



3 month assessment

ENDOSCOPY IMAGES: PATIENT #2

Months

Baseline

1.5

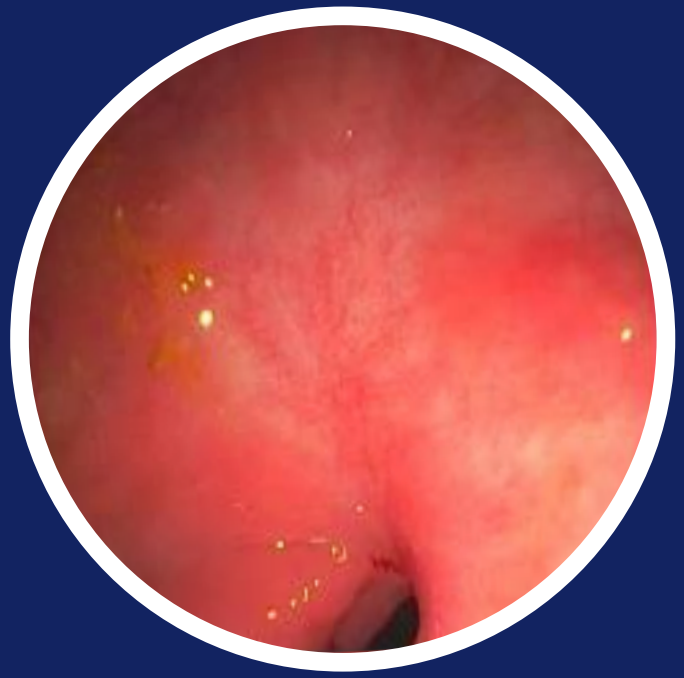
3.0

6.0

FU2 14

FU3 18

FU4 22



6 month assessment; end of treatment

ENDOSCOPY IMAGES: PATIENT #2

Months

Baseline

1.5

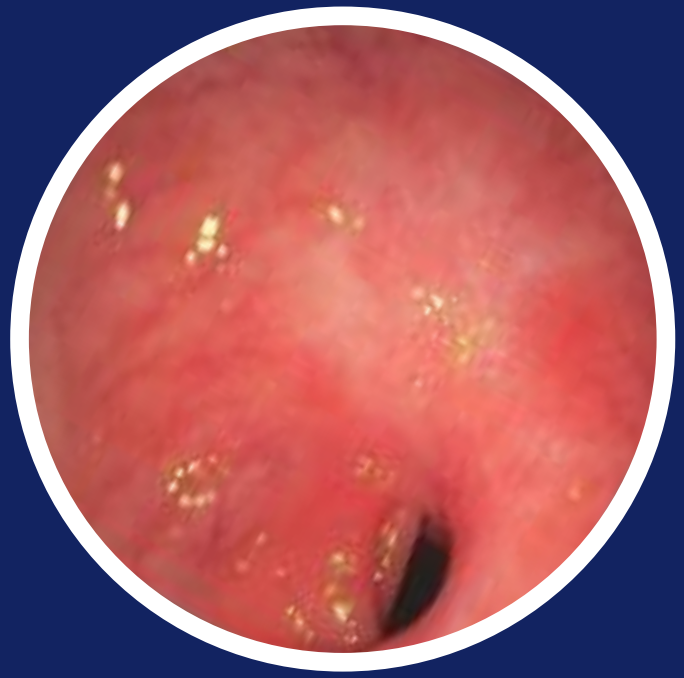
3.0

6.0

FU2 14

FU3 18

FU4 22



Non-operative Follow up 14 months

ENDOSCOPY IMAGES: PATIENT #2

Months

Baseline

1.5

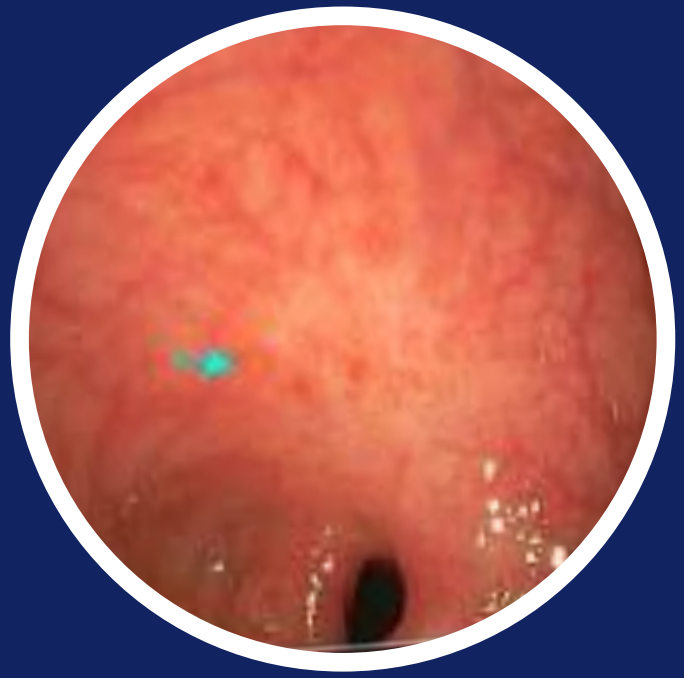
3.0

6.0

FU2 14

FU3 18

FU4 22



Non-operative Follow up 18 months

ENDOSCOPY IMAGES: PATIENT #2

Months

Baseline

1.5

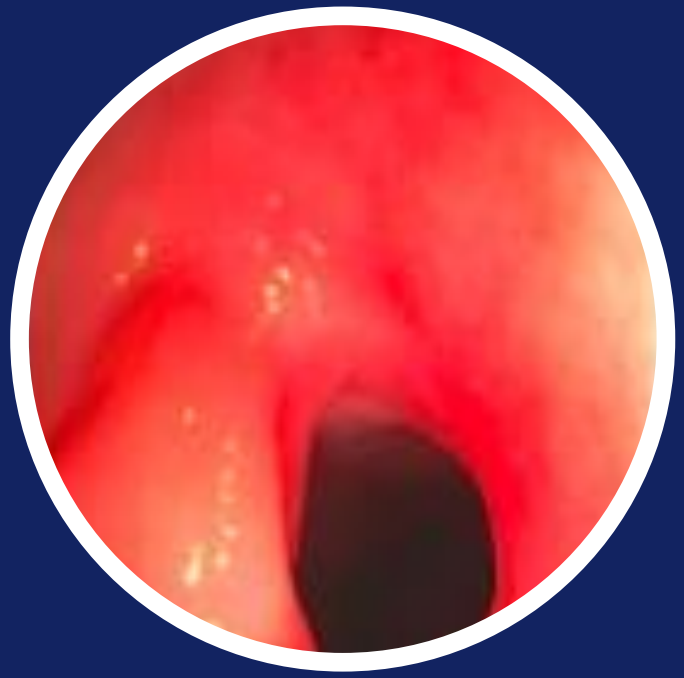
3.0

6.0

FU2 14

FU3 18

FU4 22



Non-operative Follow up 22 months; patient remains disease free

ENDOSCOPY IMAGES: PATIENT #2

Months

Baseline

1.5

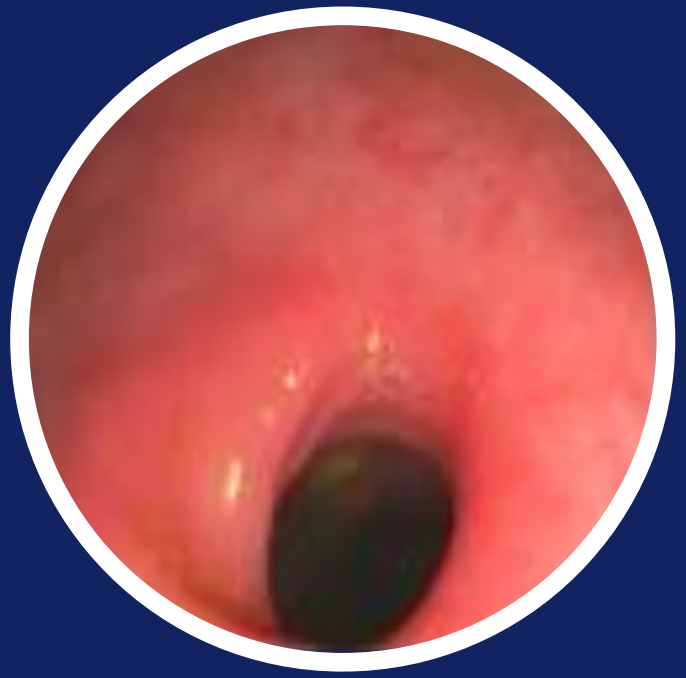
3.0

6.0

FU2 14

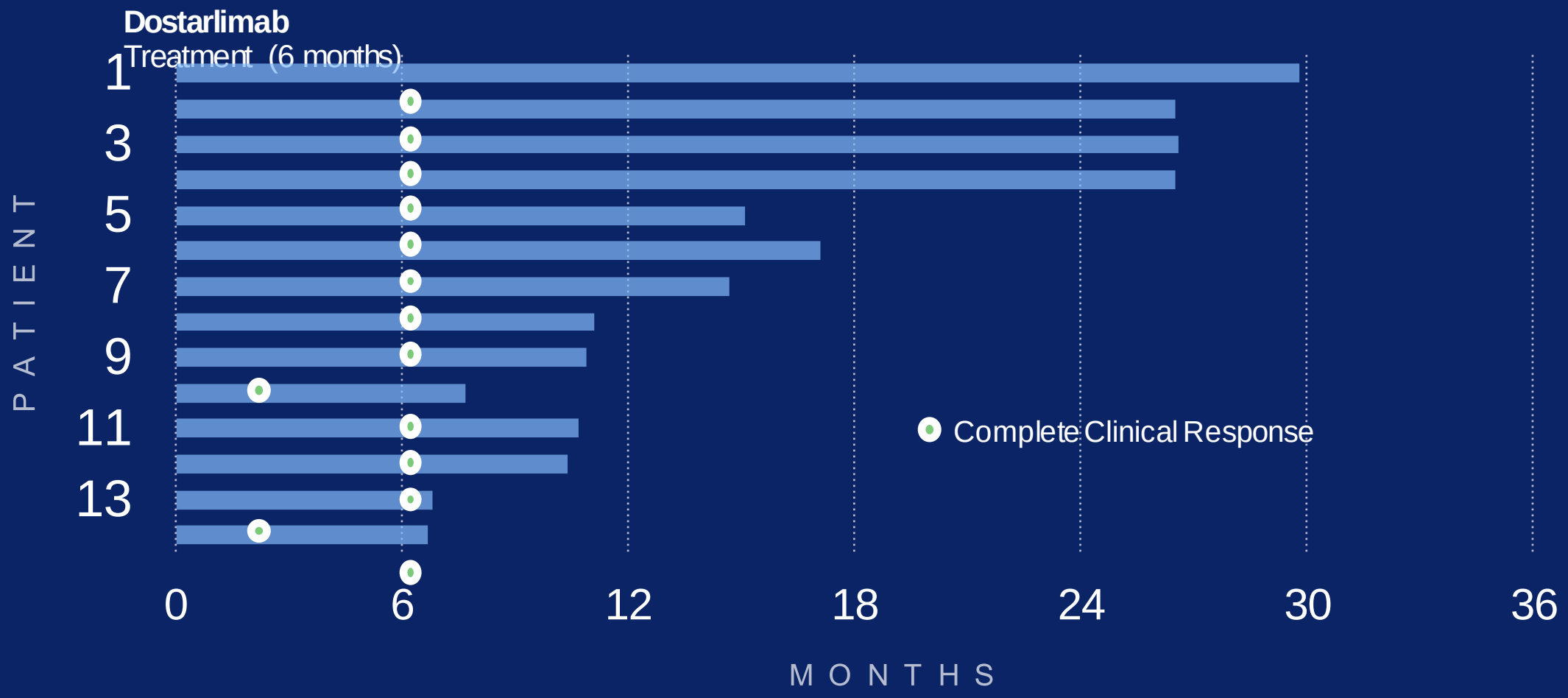
FU3 18

FU4 22



OUTCOMES (JUNE 2022)

Duration of Response



Future Research in Early Onset Colorectal Cancer :

- Genetics
- Dedicated Clinical Research Fellow
- Collaboration with basic science
- Evaluation of microbiome
- US and International Partnerships Colorectal Cancer

  --Project: DFCI and Broad Institute of MIT and Harvard
- Clinical Trials

Q U E S T I O N S

Thank You!

American Cancer Society | National Colorectal Cancer Roundtable | 80% In Every Community

Thank You!

nccrt.org #NCCRT2022 @NCCRTnews #80inEveryCommunity