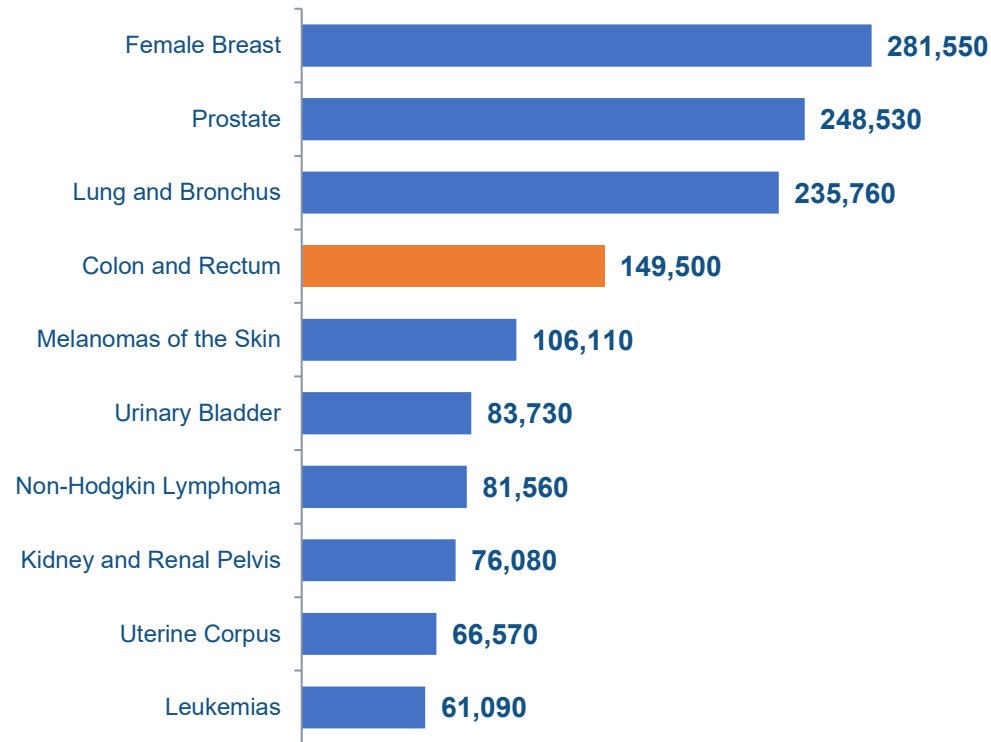


Colorectal Cancer (CRC) Screening Guidelines

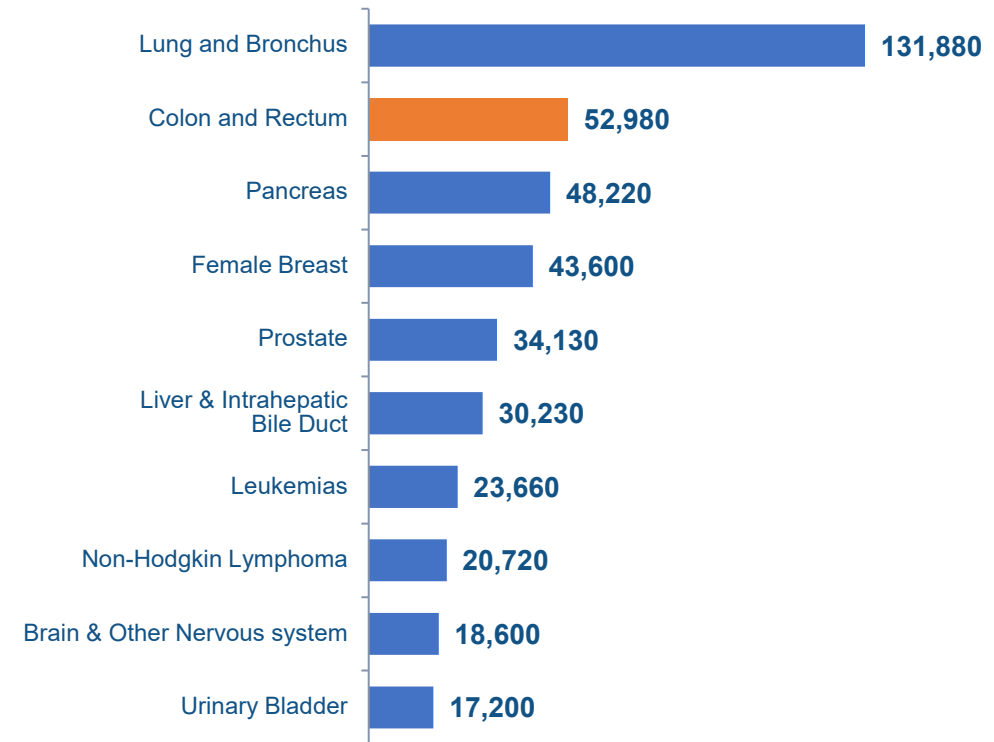
Burden of CRC in the United States & Overview of CRC Screening Guidelines

Estimated*† CRC Incidence and Mortality, US 2021

Top 10 Cancers by Number of New Cancer Cases (United States, 2021)¹



Top 10 Cancers by Number of Cancer Deaths (United States, 2021)¹



**Overall Lifetime
Risk of CRC:**



4.3% for men



4.0% for women

NOTE: These are model-based estimates that should be interpreted with caution and not compared with those for previous years.

*Estimates are rounded to the nearest 10; cases exclude basal cell and squamous cell skin cancers and in situ carcinoma except urinary bladder.

† The 2021 projections are based on currently available incidence and mortality and do not reflect the impact of COVID-19 on cancer cases and death.

CRC: colorectal cancer.

Estimated*† CRC Incidence and Mortality, US 2021

- An estimated 150,000 new cases of CRC will be diagnosed in the United States in 2021
- CRC remains the second leading cause of cancer mortality in the United States. The American Cancer Society estimates that ~53,000 patients will die from CRC in 2021
- The overall lifetime risk of developing CRC from birth to death for men is 4.3% (1 in 23) and for women is 4.0% (1 in 25)

*Estimates are rounded to the nearest 10; cases exclude basal cell and squamous cell skin cancers and in situ carcinoma except urinary bladder.

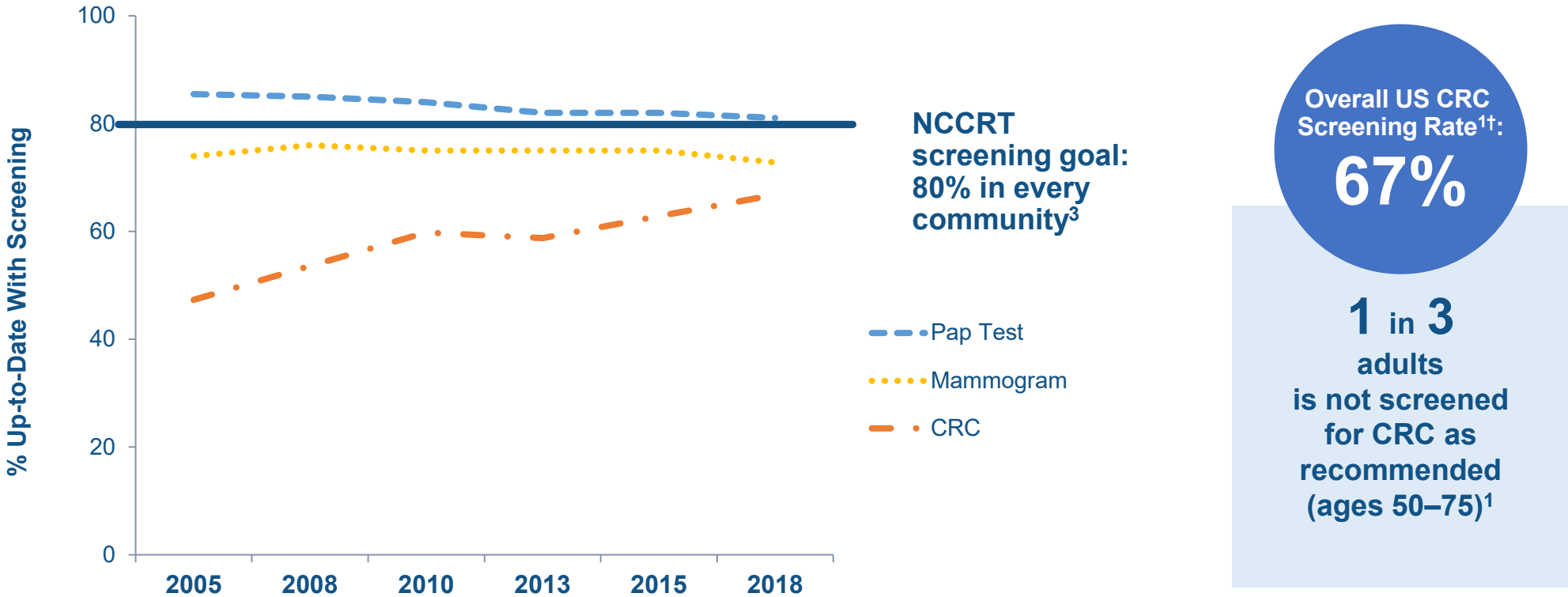
† The 2021 projections are based on currently available incidence and mortality and do not reflect the impact of COVID-19 on cancer cases and death.

CRC: colorectal cancer.

Siegel RL, Miller KD, Fuchs HE. Cancer Statistics, 2021. *CA A Cancer J Clin.* 2021;71(1):7-33. doi:10.3322/caac.21654.

CRC Screening Rates Remain Well Below National Goal

CRC Screening Rates Are Lower than for Breast and Cervical Cancers and Continue to Fall Short of the NCCRT National Goal (80%)^{1-3,*}



*The NCCRT has established the goal of 80% of adults ages ≥50 being regularly screened for CRC.³

†Source: National Health Interview Survey, 2018.

CRC: colorectal cancer, NCCRT: National Colorectal Cancer Roundtable.

1. ACS. Colorectal Cancer Facts & Figures 2020-2022. Atlanta: American Cancer Society; 2020. 2. ACS. Cancer prevention & early detection facts & figures tables and figures 2020. Atlanta: American Cancer Society; 2020. 3. NCCRT website. 80% in Every Community, talking points. Updated February 2019. Accessed April 2, 2021. <https://nccrt.org/80-in-every-community/>.

CRC Screening Rates Remain Well Below National Goal

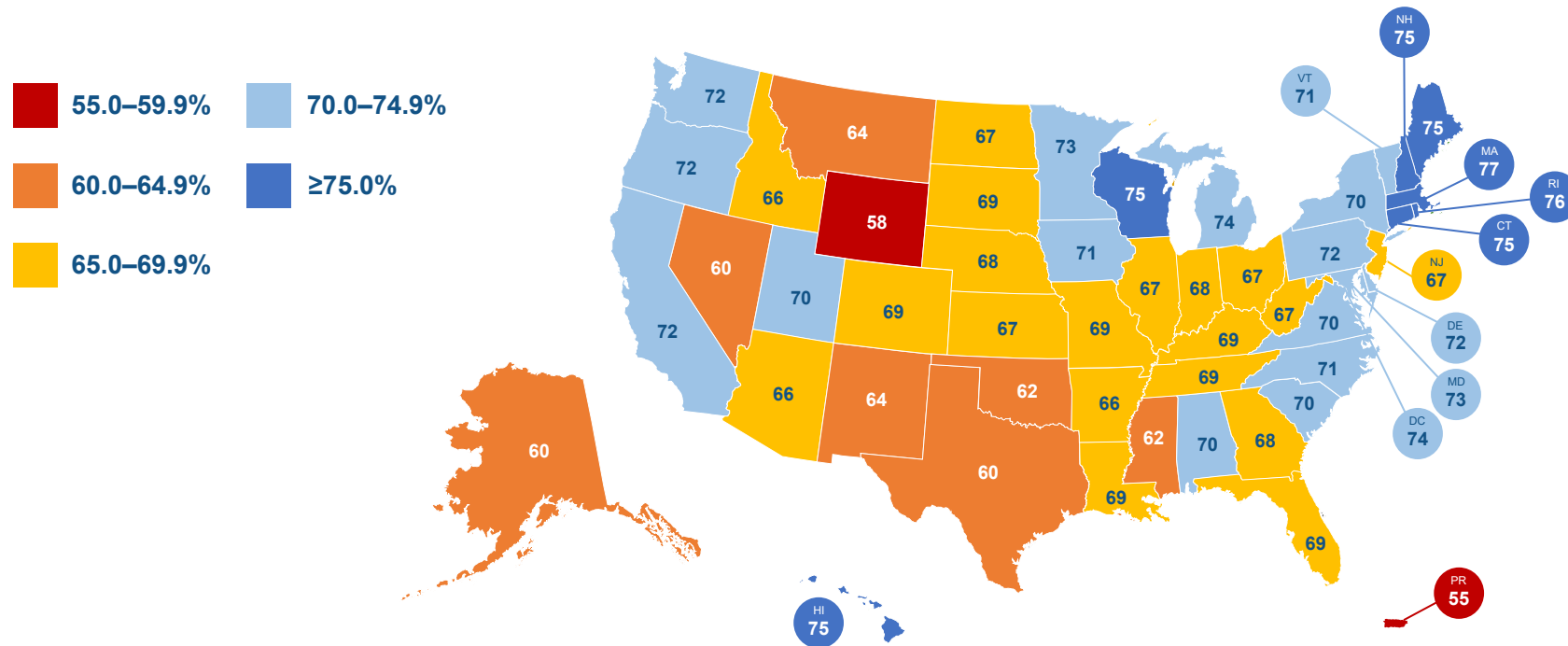
- According to the National Health Interview Survey (NHIS) conducted in 2018, screening rates for CRC (67%) continued to lag behind those for cervical cancer (81.1%) and breast cancer (72.8%)
- National screening rates for CRC also continue to fall short of the National Colorectal Cancer Roundtable's established national goal of 80% compliance with CRC screening in patients aged ≥50 years in every community
- Most recent NHIS data come from 2018 and does not reflect impact of COVID-19 pandemic

CRC: colorectal cancer, **NCCRT:** National Colorectal Cancer Roundtable.

1. ACS. Colorectal Cancer Facts & Figures 2020-2022. Atlanta: American Cancer Society; 2020. 2. ACS. Cancer prevention & early detection facts & figures tables and figures 2020. Atlanta: American Cancer Society; 2020. 3. NCCRT website. 80% in Every Community, talking points. Updated February 2019. Accessed April 2, 2021. <https://nccrt.org/80-in-every-community/>.

CRC Screening Rates Have Not Reached National Goal of 80% in Any State

Adults Aged 50–75 Years Who Report Being Up-to-Date[†] With CRC Screening, by State (2018)



[†] Up-to-date: fecal occult blood test (FOBT) within 1 year, or sigmoidoscopy within 5 years, or colonoscopy within 10 years.

CRC: colorectal cancer

American Cancer Society. Colorectal Cancer Facts & Figures 2020–2022. Atlanta: American Cancer Society; 2020.

CRC Screening Rates Have Not Reached National Goal of 80% in Any State

- The percentage of adults aged 50 to 75 years who were up-to-date with colorectal cancer (CRC) screening increased by **1.4%** from 2016 to 2018.
 - 4.2 million more adults aged 50 to 75 years were screened for CRC
 - 21.7 million adults aged 50 to 75 years who have never been screened for CRC
 - 81% of adults who have never been screened are people aged 50 to 64 years
- **States with +/-3% difference vs 2016:**
- **States that had 3+% increases:** 1) MI (+4.4) 2) LA (+4.9) 3) OR (+3.2) 4) ID (+3.9) 5) AZ (+3.4) 6) NM (+5.5) 7) SD (+3.4) 8) OK (+3.2) 9) MO (+3.8) 10) IL (+3.2) 11) MS (+4.1) 12) IN (+3.4) 13) TN (+3.4) 14) GA (+4.8) 15) FL (+3.2) 16) MD (+3.5) 27) DC (+4.0)
- **States that -3% decreases:** 1) AK (-3.4) 2) WY (-2.9)

<https://www.cdc.gov/cancer/colorectal/statistics/pdf/colorectal-cancer-screening-tests-h.pdf>

CRC Screening Guidelines Updates

Organization	U.S. Preventive Services Task Force (USPSTF) ¹	American Cancer Society (ACS) ²	National Comprehensive Cancer Network [®] (NCCN [®]) ³	American College of Gastroenterology (ACG) ⁵	U.S. Multi-Society Task Force (MSTF) ^{7*}
Most Recent Update	2021 Published in <i>Journal of the American Medical Association</i> 18-May-21	2018 Published in <i>CA: A Cancer Journal for Clinicians</i> 30-May-18	2021 Published on <i>nccn.org</i> 13-Apr-21	2021 Published in <i>American Journal of Gastroenterology</i> 1-Mar-21	2021[†] Published in <i>Gastroenterology</i> 16-Nov-21
Next Update Expected	Not stated as recently updated	Not stated; previous update was 2008 ^{8†}	2021 Updated at least annually ⁴	Not stated; Previous update was 2009 ⁶	Not stated; previous update was 2017 ⁸

*MSTF includes the American College of Gastroenterology (ACG), the American Gastroenterological Association (AGA), and the American Society for Gastrointestinal Endoscopy (ASGE).

†2021 article reflects updates on age to start and stop colorectal cancer screening. See Rex DK, et al. *Am J Gastroenterol.* 2017;112(7):1016-1030 for additional MSTF recommendations.

CRC: colorectal cancer.

1. Davidson KW, et al. *JAMA.* 2021;325(19):1965-1977. 2. Wolf AMD, et al. *CA Cancer J Clin.* 2018;68(4):250-281. 3. National Comprehensive Cancer Network. Clinical practice guidelines in oncology - colorectal cancer screening. Version 2.2021. Updated April 13, 2021. Accessed April 19, 2021. https://www.nccn.org/professionals/physician_gls/pdf/colorectal_screening.pdf. 4. National Comprehensive Cancer Network. NCCN Guidelines & Clinical Resources. Updated July 21, 2020. Accessed April 2, 2021. <https://www.nccn.org/professionals/development.aspx>. 5. Shaukat A, et al. *Am J Gastroenterol.* 2021;116:458-479. 6. Rex DK, et al. *Am J Gastroenterol.* 2009;104(3):73.9-750. 7. Patel SG, et al. *Gastroenterol.* 2021; doi:10.1053/j.gastro.2021.10.007. 8. Rex DK, et al. *Am J Gastroenterol.* 2017;112(7):1016-1030.

CRC Screening Guidelines Updates

- NCCN, USPSTF, ACG, and MSTF recommendations were recently updated this year.

Note:

- NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) are generally updated on an annual basis
- Timelines for updates to the ACS and MSTF guidelines have not been publicized to date
- MSTF includes the American College of Gastroenterology (ACG), the American Gastroenterological Association (AGA), and the American Society for Gastrointestinal Endoscopy (ASGE). ACG has published an update in March 2021 (GI-specific recommendations)

Summary of Current Guideline Recommendations

Recommendations	USPSTF, 2021 ¹	ACS, 2018 ²	NCCN [®] , 2021 ^{3*}	ACG, 2021 ⁴	MSTF, 2021 ⁵
Age to Begin Screening	45 years (Grade B ^{**})	45 years (qualified [†])	45 years (category 2A [†])	45 years (conditional recommendation [suggested]; very low-quality evidence)	45 years (weak recommendation, low-quality evidence)
	50 years (Grade A ^{**})	50 years (strong)		50 years (strong recommendation; moderate-quality evidence)	50 years (strong recommendation; high-quality evidence)
Continue Screening Until Age	75 years (Grade A ^{**})	75 years (qualified [†])	75 years (category 2A)	75 years (strong recommendation; moderate-quality evidence)	75 years, up to date and prior negative screening, or life expectancy is <10 years (weak recommendation, low-quality evidence)
Screening After Age 75	Selectively screen adults aged 76-85, considering patient's overall health, prior screening and preferences (Grade C ^{**})	Individualized decision for screening at ages 76–85 years (qualified [†]) Discourage continuing screening of adults >85 years (qualified [†])	Individualized decision that should include a discussion of the risks and benefits based on comorbidity status and estimated life expectancy (category 2A)	Individualized decision for screening (conditional recommendation [suggested]; very low-quality evidence)	Consideration for screening up to age 85 in previously unscreened (recommendation based on patient age and comorbidities) (weak recommendation, low-quality evidence)

ACS: American Cancer Society; **CRC:** colorectal cancer; **MSTF:** United States Multi-Society Task Force on Colorectal Cancer, which includes the American College of Gastroenterology (ACG), the American Gastroenterological Association (AGA), and the American Society for Gastrointestinal Endoscopy (ASGE); **NCCN:** National Comprehensive Cancer Network; **USPSTF:** United States Preventive Services Task Force

^{**}The USPSTF concludes with moderate certainty that screening for CRC in adults aged 45 to 49 years has moderate net benefit (Grade B). The USPSTF concludes with high certainty that screening adults aged 50 to 75 years has substantial net benefit (Grade A). The USPSTF concludes with moderate certainty that there is a small net benefit of screening for colorectal cancer in adults aged 76 to 85 y who have been previously screened (Grade C).

[†]The “qualified” designation indicates that there is clear evidence of benefit (or harm) but some uncertainty on the balance of benefits/harms or patient values/preferences, which can influence individual decisions.

*All recommendations are category 2A unless otherwise indicated. The National Comprehensive Cancer Network (NCCN[®]) makes no representations or warranties of any kind regarding their content, use or application and disclaims any responsibility for their application or use in any way.

[‡]Recommend a discussion of potential harms/risks and benefits and consideration of all recommended CRC screening options.

1. Davidson KW, et al. *JAMA*. 2021;325(19):1965-1977. 2. Wolf AMD, et al. *CA Cancer J Clin*. 2018;68(4):250-281. 3. NCCN Clinical practice Guidelines in Oncology (NCCN Guidelines) - Colorectal Cancer Screening. Version 2.2021. Updated April 13, 2021. Accessed September 21, 2021. https://www.nccn.org/professionals/physician_gls/pdf/colorectal_screening.pdf 4. Shaikat A, et al. *Am J Gastroenterol*. 2021;116:458-479 5. Patel SG, et al. *Gastroenterol*. 2021; doi:10.1053/j.gastro.2021.10.007

Summary of Current Guideline Recommendations

- National guidelines have updated their recommendations to lower the starting screening age to 45 in individuals at average risk
- Guidelines suggest that whether to screen patients older than 75 should be an individualized decision based on such factors as patient health, comorbidities, life expectancy, previous CRC screening history, and patient preferences
- Guidelines are also in agreement that among patients at average risk who are older than 75, those with no screening history are most likely to benefit from CRC screening

Summary of Current Guideline Recommendations & Choice of Test

Recommendations	USPSTF 2021 ¹	ACS 2018 ²	NCCN [®] 2021 ^{3*}	ACG ⁴	MSTF 2021 ^{5‡}	
Choice of Test	Clinicians and patients may consider a variety of factors in deciding which test may be best for each person	High-sensitivity stool-based test or a structural (visual) exam, depending on patient preference and test availability	Discussion of potential harms/risks and benefits and consideration of all recommended CRC screening options	Colonoscopy and FIT as primary screening modalities, with flex sig, mt-sDNA, CTC, or colon capsule for those unable or unwilling to undergo colonoscopy or FIT	Screening with colonoscopy every 10 years or annual FIT as first-tier options	
Direct Visual Examination	Colonoscopy	Every 10 years	Every 10 years	Every 10 years	Every 10 years (Tier 1)	
	CT colonography	Every 5 years	Every 5 years	Every 5 years	Every 5 years (Tier 2)	
	FS	Every 5 years	Every 5 years	Every 5-10 years	Every 5 or 10 years (Tier 2)	
	FS with FIT	FS every 10 years with annual FIT	--	--	--	--
	Capsule colonoscopy	--	--	--	Every 5 years	Every 5 years (Tier 3)
Stool-based Tests	hs-gFOBT	Annual	Annual	Annual	--	
	FIT	Annual	Annual	Annual	Annual (Tier 1)	
	mt-sDNA[†]	Every 1 to 3 years	Every 3 years	Every 3 years	Every 3 years (Tier 2)	

All Positive Results On Non-colonoscopy Screening Tests Should Be Followed Up with a Timely Colonoscopy¹⁻⁵

ACG: American College of Gastroenterology, **ACS:** American Cancer Society, **CRC:** colorectal cancer, **CTC:** computed tomography colonography, **FIT:** fecal immunochemical test, **FS:** flexible sigmoidoscopy, **hs-gFOBT:** high sensitivity guaiac-based fecal occult blood test, **MSTF:** United States Multi-Society Task Force on Colorectal Cancer, which includes the American College of Gastroenterology (ACG), the American Gastroenterological Association (AGA), and the American Society for Gastrointestinal Endoscopy (ASGE), **mt-sDNA:** multi-target stool DNA test, **NCCN:** National Comprehensive Cancer Network, **USPSTF:** United States Preventive Services Task Force.

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[†]Nomenclature based on different guidelines: mt-sDNA, sDNA-FIT or FIT-FECAL DNA.

[‡]See Rex DK, et al. *Am J Gastroenterol.* 2017;112(7):1016-1030 for additional MSTF recommendations.

1. Davidson KW, et al. *JAMA.* 2021;325(19):1965-1977. 2. Wolf AMD, et al. *CA Cancer J Clin.* 2018;68(4):250-281. 3. National Comprehensive Cancer Network. Clinical practice guidelines in oncology. Colorectal cancer screening. Version 2.2021. Updated April 13, 2021. Accessed September 20, 2021. https://www.nccn.org/professionals/physician_gls/pdf/colorectal_screening.pdf 4. Shaukat A, et al. *Am J Gastroenterol.* 2021;116:458-479. 5. Patel SG, et al. *Gastroenterol.* 2021; doi:10.1053/j.gastro.2021.10.007

Summary of Current Guideline Recommendations & Choice of Test

- The “--” in the table means there were no recommendations given
- Following negative CRC screening in average-risk patients, guidelines have varying intervals for recommended rescreening dependent on the screening modality¹⁻⁴
- The US Preventive Services Task Force (USPSTF), American Cancer Society (ACS), National Comprehensive Cancer Network (NCCN), and US Multi-Society Task Force (MSTF) include mt-sDNA as a CRC screening test to be performed every 3 years in patients at average risk^{1-3, 5}
 - MSTF includes the American College of Gastroenterology, the American Gastroenterological Association, and the American Society for Gastrointestinal Endoscopy
 - In 2017 and 2018, the ACS, NCCN, MSTF, and other national organizations have converged on recommendations for a 3-year interval for mt-sDNA following a negative result
 - Exact Sciences and the Cologuard label do not specify an interval for mt-sDNA use
- **It is important to note that single digital FOBT is not recommended as a screening method for CRC^{3,5}**
 - When digital FOBT is performed as part of a primary care physical examination, negative results do not decrease the odds of advanced neoplasia (exceptionally low sensitivity)

1. Davidson KW, et al. *JAMA*. 2021;325(19):1965-1977. 2. Wolf AMD, et al. *CA Cancer J Clin*. 2018;68(4):250-281. 3. National Comprehensive Cancer Network. Clinical practice guidelines in oncology. Colorectal cancer screening. Version 2.2021. Updated April 13, 2021. Accessed September 20, 2021.

https://www.nccn.org/professionals/physician_gls/pdf/colorectal_screening.pdf 4. Shaukat A, et al. *Am J Gastroenterol*. 2021;116:458-479. 5. Patel SG, et al. *Gastroenterol*. 2021; doi:10.1053/j.gastro.2021.10.007

2021 USPSTF Final Recommendation Statement

Recommendation Summary¹

Population	Recommendation	Grade
Adults ages 50 to 75 years	Screen all adults aged 50 to 75 years for colorectal cancer	A
Adults ages 45 to 49 years	Screen adults aged 45 to 49 years for colorectal cancer	B
Adults ages 76 to 85 years	Selectively screen adults aged 76 to 85 years for colorectal cancer, considering the patient's overall health, prior screening history, and patient's preferences	C

USPSTF Grade Definitions²

Grade	Definition	Suggestions for Practice
A	The USPSTF recommends the service. There is high certainty that the net benefit is substantial	Offer or provide this service
B	The USPSTF recommends the service. There is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial	Offer or provide this service
C	The USPSTF recommends selectively offering or providing this service to individual patients based on professional judgment and patient preferences. There is at least moderate certainty that the net benefit is small	Offer or provide this service for selected patients depending on individual circumstances

USPSTF: United States Preventive Services Task Force.

1. Davidson KW, et al. Screening for colorectal cancer: US Preventive Services Task Force recommendation statement. JAMA. 2021;325(19):1965-1977. doi: 10.1001/jama.2021.6238. 2. US Preventive Services Task Force. Grade definitions. Updated June 2018. Accessed May 18, 2021.

<https://www.uspreventiveservicestaskforce.org/uspstf/about-uspstf/methods-and-processes/grade-definitions>.

2021 USPSTF Final Recommendation Statement

USPSTF Assessment for A, B, C recommendations for this recommendation:

- Grade B = The USPSTF concludes with moderate certainty that there is a moderate net benefit of starting screening for colorectal cancer in adults aged 45 to 49 y
- Grade A = The USPSTF concludes with high certainty that there is a substantial net benefit of screening for colorectal cancer in adults aged 50 to 75 y
- Grade C = The USPSTF concludes with moderate certainty that there is a small net benefit of screening for colorectal cancer in adults aged 76 to 85 y who have been previously screened
- **OBJECTIVE and Brief Background** To update its 2016 recommendation, the US Preventive Services Task Force (USPSTF) commissioned a systematic review to evaluate the benefits and harms of screening for colorectal cancer in adults 40 years or older. The review also examined whether these findings varied by age, sex, or race/ethnicity. In addition, as in 2016, the USPSTF commissioned a report from the Cancer Intervention and Surveillance Modeling Network Colorectal Cancer Working Group to provide information from comparative modeling on how estimated life-years gained, colorectal cancer cases averted, and colorectal cancer deaths averted vary by different starting and stopping ages for various screening strategies.
- **IMPORTANCE:**
 - Colorectal cancer is the third leading cause of cancer death for both men and women, with an estimated 52 980 persons in the US projected to die of colorectal cancer in 2021.
 - Colorectal cancer is most frequently diagnosed among persons aged 65 to 74 years.
 - It is estimated that 10.5% of new colorectal cancer cases occur in persons younger than 50 years.
 - Incidence of colorectal cancer (specifically adenocarcinoma) in adults aged 40 to 49 years has increased by almost 15% from 2000-2002 to 2014-2016. In 2016, 26% of eligible adults in the US had never been screened for colorectal cancer and in 2018, 31% were not up to date with screening.

USPSTF: United States Preventive Services Task Force.

1. Davidson KW, et al. Screening for colorectal cancer: US Preventive Services Task Force recommendation statement. JAMA. 2021;325(19):1965-1977. doi: 10.1001/jama.2021.6238. 2. US Preventive Services Task Force. Grade definitions. Updated June 2018. Accessed May 18, 2021. <https://www.uspreventiveservicestaskforce.org/uspstf/about-uspstf/methods-and-processes/grade-definitions>.

CRC Screening Recommendations Starting at Age 45

Guideline Recommendations on Earlier Screening Age

Most major professional organizations recommended screening for colorectal cancer in average-risk adults starting at age 45

Guideline	Recommendation to Begin Screening at Age	Considerations
USPSTF 2021 ¹	≥45 yo average-risk individuals	<ul style="list-style-type: none"> Screen adults aged 45-49 years for colorectal cancer. Grade B*
NCCN [®] 2021 ²⁺	≥45 yo average-risk individuals	<ul style="list-style-type: none"> The choice of a particular screening modality should include a conversation with the patient concerning their preference and availability
ACS 2018 ³	≥45 yo average-risk individuals	<ul style="list-style-type: none"> <i>Qualified</i>** recommendation based on disease burden, modeling data and expectation that screening performs similarly in 45-49 yo group as in 50+ group
MSTF 2021 ⁴	≥45 yo average-risk individuals	<ul style="list-style-type: none"> Weak recommendation; low-quality evidence Average-risk individuals not screened before age 50 should be offered CRC screening beginning at age 50 (strong recommendation, high-quality evidence)
ACG 2021 ⁵	Average-risk individuals 45-49 yo	<ul style="list-style-type: none"> Conditional recommendation strength based on very low quality of evidence

USPSTF: United States Preventive Services Task Force, **NCCN:** National Comprehensive Cancer Network, **ACG:** American College of Gastroenterology, **YO:** year old, **ACS:** American Cancer Society, **MSTF:** United States Multi-Society Task Force on Colorectal Cancer, which includes the American College of Gastroenterology (ACG), the American Gastroenterological Association (AGA), and the American Society for Gastrointestinal Endoscopy (ASGE)

*The USPSTF concludes with moderate certainty that screening for CRC in adults aged 45 to 49 years has moderate net benefit (Grade B).

***Qualified* recommendation: clear evidence of benefit (or harm) but less certainty either about the balance of benefits and harms or about patients' values and preferences, which could lead to different individual decisions.

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1. Davidson KW, et al. *JAMA*. 2021;325(19):1965-1977. 2. National Comprehensive Cancer Network. Clinical practice guidelines in oncology - colorectal cancer screening. Version 2.2021. Updated April 13, 2021. Accessed April 19, 2021. https://www.nccn.org/professionals/physician_gls/pdf/colorectal_screening.pdf 3. Wolf AMD, et al. *CA Cancer J Clin*. 2018;68(4):250-281. 4. Patel SG, et al. *Gastroenterol*. 2021; doi:10.1053/j.gastro.2021.10.007 5. Shaukat AK, et al. *Am J Gastroenterol*. 2021;116(3):458-479.

Guideline Recommendations on Earlier Screening Age

Most major professional organizations recommended screening for colorectal cancer in average-risk adults starting at age 45 in addition to recommendation to screen eligible adults >50yo (strong recommendations). Their recommendations come with additional considerations as there's lack of empirical data to support screening at an earlier age. Most of the recommendations base earlier age of screening on modeling estimations and recent SEER data observations of increased incidence in younger populations.

USPSTF:

- Screen adults aged 45 to 49 years for colorectal cancer. Grade B - The USPSTF concludes with moderate certainty that there is a moderate net benefit of starting screening for colorectal cancer in adults aged 45 to 49 y

NCCN Guidelines® :

- The data on starting screening at age 45 is based largely on modeling studies
- A relative increase of 30% in the incidence of CRC observed in 40+
- Consideration for the starting age may be dependent on race/ethnicity, patient preference and resources available. Shared decision making is emphasized

ACG:

- Very low quality of evidence - any estimate of effect is very uncertain

Guideline Recommendations on Earlier Screening Age (continued)

ACS:

- A *strong recommendation* conveys the consensus that the benefits of adherence to the intervention outweigh the undesirable effects and that most patients would choose the intervention.
- A *qualified recommendation* indicates there is clear evidence of benefit (or harm) but less certainty either about the balance of benefits and harms or about patients' values and preferences, which could lead to different individual decisions.

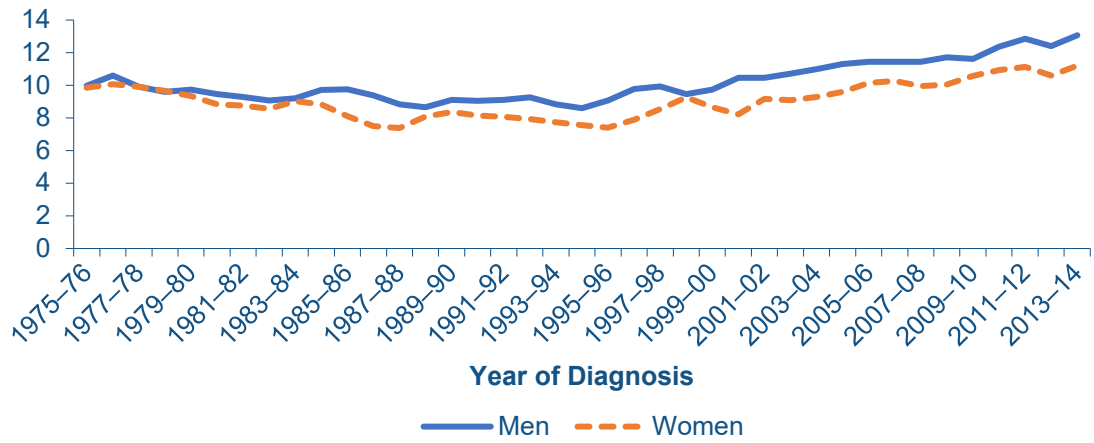
MSTF:

- Suggests that clinicians offer CRC screening to all average-risk individuals age 45-49 (weak recommendation; low-quality evidence). For average-risk individuals who have not initiated screening before age 50, MSTF recommends that clinicians offer CRC screening to all average-risk individuals beginning at age 50 (strong recommendation, high-quality evidence).”

1. Davidson KW, et al. *JAMA*. 2021;325(19):1965-1977. 2. National Comprehensive Cancer Network. Clinical practice guidelines in oncology - colorectal cancer screening. Version 2.2021. Updated April 13, 2021. Accessed April 19, 2021. https://www.nccn.org/professionals/physician_gls/pdf/colorectal_screening.pdf 3. Wolf AMD, et al. *CA Cancer J Clin*. 2018;68(4):250-281. 4. Patel SG, et al. *Gastroenterol*. 2021; doi:10.1053/j.gastro.2021.10.007 5. Shaukat AK, et al. *Am J Gastroenterol*. 2021;116(3):458-479.

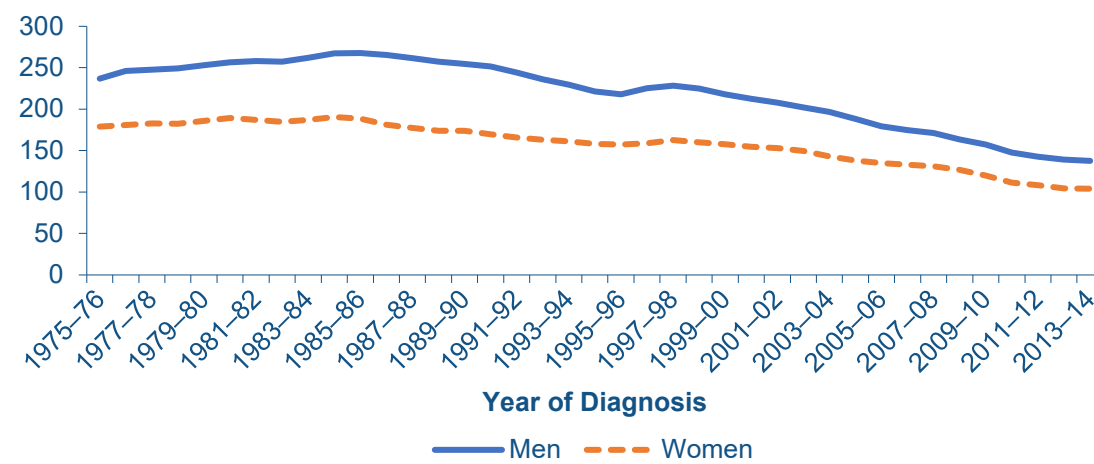
Trends in Colorectal Cancer Incidence Rates by Age (Ages 20–49 and Ages 50+) and Sex, 1975 to 2014¹

Colorectal Cancer Cases per 100,000 Persons Aged 20–49 Years



- There has been a 51% increase in CRC incidence among adults < 50 years since 1994¹
- CRC incidence among adults < 50 years increased 2.2% annually from 2012 to 2016²

Colorectal Cancer Cases per 100,000 Persons Aged 50+ Years



- CRC incidence has gradually declined over the past 20 years in the population ≥ 50 years due to influence of screening and changes in exposure to risk factors¹

CRC: colorectal cancer.

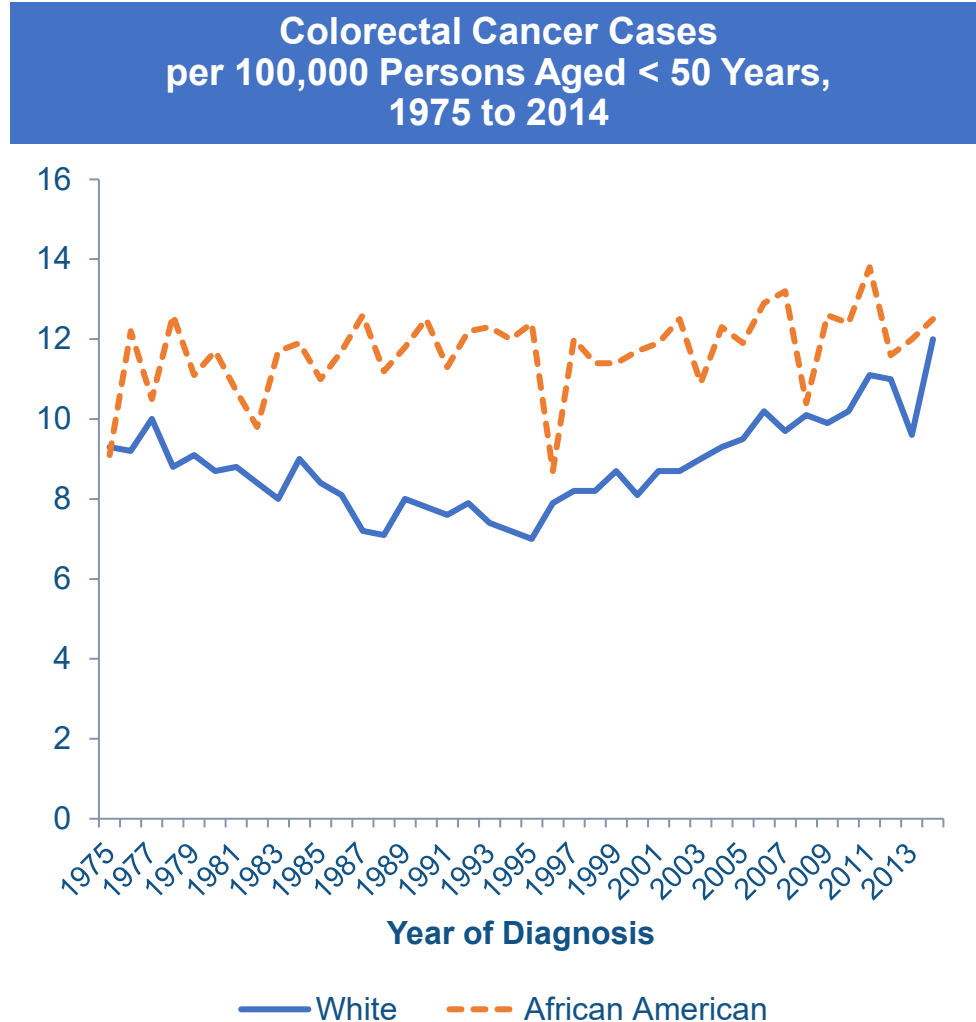
Trends in Colorectal Cancer Incidence Rates by Age (Ages 20–49 and Ages 50+) and Sex, 1975 to 2014¹

- CRC incidence has declined steadily over the past 20 years in the population ≥ 50 years due to influence of screening and changes in exposure to risk factors
- There has been a 51% increase in CRC incidence among adults < 50 years since 1994
- CRC incidence among adults < 50 years increased 2.2% **annually** from 2012 to 2016

CRC: colorectal cancer.

1. Wolf AMD, et al. *Ca Cancer J Clin*. 2018;68(4):250-281. 2. American Cancer Society. Cancer Facts & Figures 2020. Atlanta: American Cancer Society; 2020.

Trends in Colorectal Cancer Incidence and Mortality Rates in Younger Adults by Race

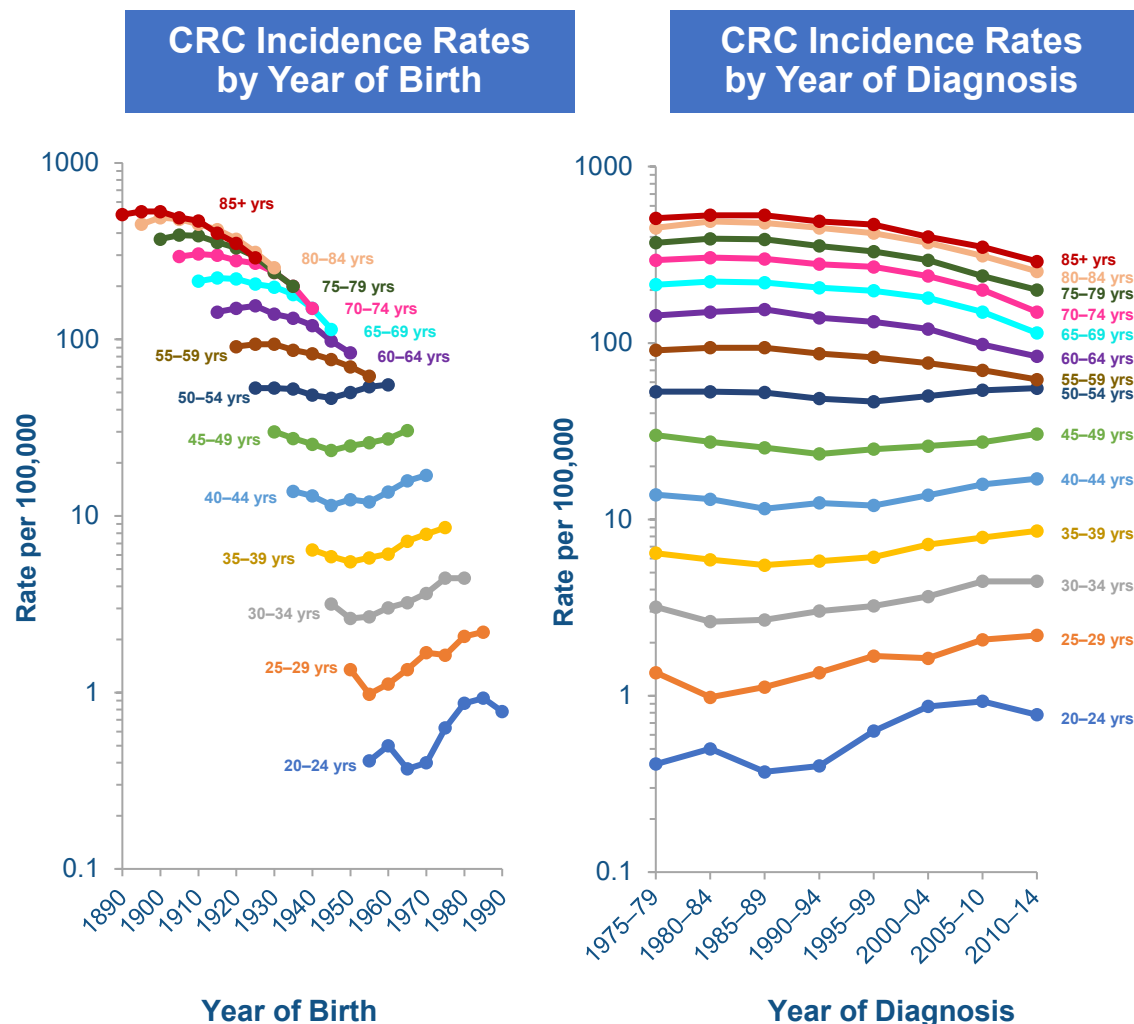


- While **incidence rates** in White adults < 50 years have risen, incidence rates for African American adults < 50 years have remained mostly stable, resulting in current comparable incidence between both groups
- **CRC mortality rates** have been increasing in White adults aged 40-54 since 2005
- **CRC mortality rates** have been decreasing in African American adults aged 20-54, however, the rates remain ~50% higher in comparison with White adults in 2014 (age group 20-54: 6.1 vs 4.1 per 100,000)

Trends in Colorectal Cancer Incidence and Mortality Rates in Younger Adults by Race

- CRC incidence rates in the United States have historically varied by sex, race and ethnicity
- Until age 35, CRC incidence is similar in women and men (all races), and later, is higher for men, and the gap widens with age
- **CRC incidence** in African Americans, including <50 years, has historically been higher than that among White adults, Hispanic adults, and Asian Americans
- While **incidence** rates in whites <50 years have risen, incidence rates for African American adults <50 years have remained mostly stable, resulting in current comparable incidence between both groups
- **CRC mortality rates** have been increasing in White adults aged 40-54 since 2005
- **CRC mortality rates** have been decreasing in African American adults aged 20-54, however the rates remain ~50% higher in comparison with White adults in 2014 (age group 20-54: 6.1 vs 4.1 per 100,000)

Trends in Colorectal Cancer Incidence Rates by Age and Year of Birth, and by Age and Year of Diagnosis, US, 1975 to 2014



- Younger-birth cohorts carry an elevated risk of developing CRC with age¹
- Incidence rate for *colon* cancer began increasing in the mid-1990s for adults aged 40–49 (1.3%/year), and is > 2x for adults aged 50–54 years (0.5%/year)¹
- A 2.3%/year increase in *rectal* cancer incidence rates began in the 1990s in adults 40–54 years²
- A retrospective cohort analysis of SEER data from 1974-2013 found that adults born ~1990 have **2x** the risk of *colon* cancer and **4x** the risk of *rectal* cancer compared with adults born ~1950, who have the lowest risk²

CRC: colorectal cancer, SEER: Surveillance, Epidemiology, and End Results.

1. Wolf AMD, et al. *Ca Cancer J Clin.* 2018;68(4):250-281. 2. Siegel RL, et al. *J Natl Cancer Inst.* 2017;109(8).

Trends in Colorectal Cancer Incidence Rates by Age and Year of Birth, and by Age and Year of Diagnosis, US, 1975 to 2014

- The younger birth-cohorts are carrying an elevated risk of developing CRC as they age¹
- An increase in **colon** cancer incidence rate was observed in the mid-1990s for adults aged 40-49 years (1.3% per year), and is more than twice that of adults aged 50-54 years (0.5% per year)¹
- 2.3% per year increase in **rectal** cancer incidence rates began in early to mid-1990s in adults aged 40-54 years
- A new convergence of CRC incidence rates was observed in the groups aged 50-54 years and 55-59 years²:
 - In 1990s, CRC incidence rates in 50–54 year group were one-half of those in 55-59 year group
 - In 2012–2013, the difference in colon cancer rates was 12.4%, and rectal cancer rates were the same for the 2 age groups
- A retrospective cohort analysis of SEER data from 1974 to 2013 found that adults born around 1990 have twice the risk of colon cancer and 4 times the risk of rectal cancer compared with adults born around 1950, who have the lowest risk

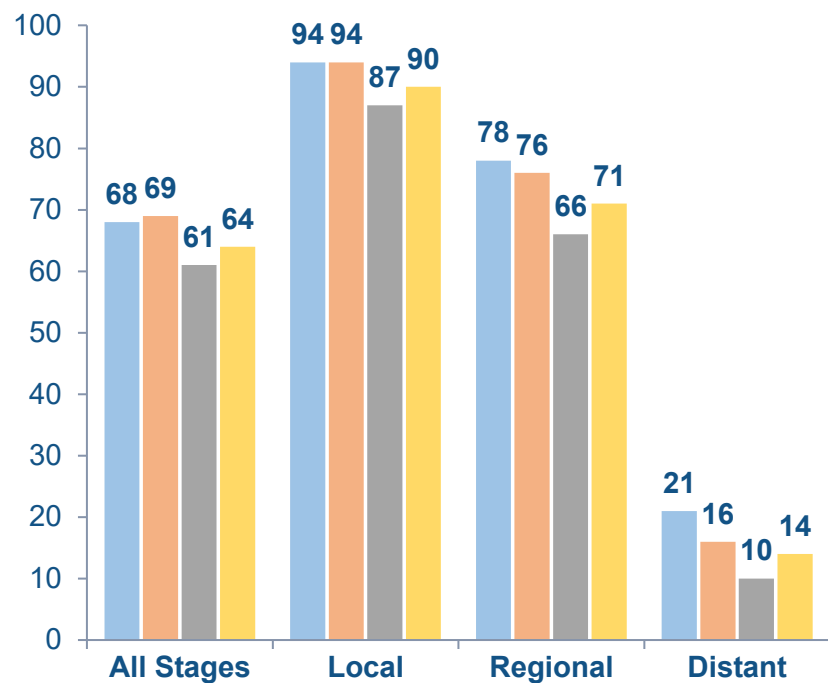
CRC: colorectal cancer, SEER: Surveillance, Epidemiology, and End Results.

1. Wolf AMD, et al. *Ca Cancer J Clin.* 2018;68(4):250-281. 2. Siegel RL, et al. *J Natl Cancer Inst.* 2017;109(8).

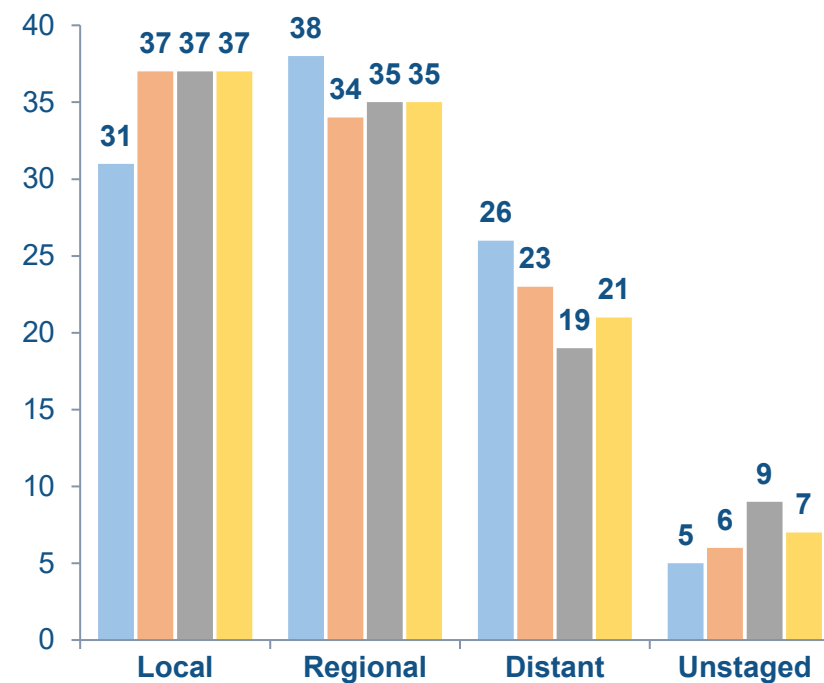
CRC 5-year Survival and Stage Distribution in Younger Adults

- 0-49 age group has 5-year survival rate of 68% for all CRC stages
- However, 0-49 age group has the highest proportion diagnosed with Regional (38%) and Distant (26%) CRC stages
- Distant stage CRC has the lowest 5-year survival rate (21%)

Colorectal Cancer 5-year Survival (%) by Age



Colorectal Cancer Stage Distribution (%) by Age



■ 0-49 years ■ 50-64 years ■ 65+ years ■ All Ages

Local: confined to primary site, Regional: spread to regional lymph nodes, Distant: cancer has metastasized.

CRC: colorectal cancer.

CRC 5-year Survival and Stage Distribution in Younger Adults

Background info (AJCC staging):

- **Localized:** There is no sign that the cancer has spread outside of the colon or rectum. This includes AJCC stage I, IIa, and IIb cancers.
- **Regional:** The cancer has spread outside the colon or rectum to nearby structures or lymph nodes. This includes stage IIc and stage III cancers in the AJCC system.
- **Distant:** The cancer has spread to distant parts of the body such as the liver, lungs, or distant lymph nodes. This includes stage IV cancers.