



2021 USPSTF Guideline Update

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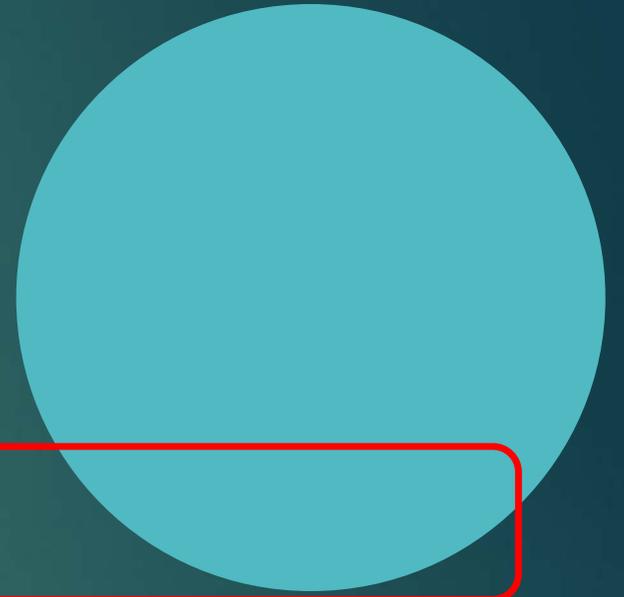
Aurora Health Care

Updated Guidelines for 2021



- ▶ Colorectal cancer screening
 - ▶ Start at age 45 (previously 50)
- ▶ Lung cancer screening
 - ▶ Start at age 50 (previously 55)
 - ▶ Minimum pack-year history reduced to 20 pack-years (previously 30)
- ▶ Diabetes screening
 - ▶ Start at age 35 (previously 40)

2021 USPSTF Colorectal Cancer Screening Guidelines



Recommendation Clarifications

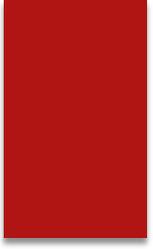
- ▶ This recommendation applies to adults 45+ years old who:
 - ▶ do not have signs or symptoms of colorectal cancer
 - ▶ are at average risk for colorectal cancer
 - ▶ No prior diagnosis of colorectal cancer
 - ▶ No adenomatous polyps
 - ▶ No inflammatory bowel disease
 - ▶ No personal diagnosis or family history of known genetic disorders that predispose them to a high lifetime risk of colorectal cancer, such as Lynch syndrome or familial adenomatous polyposis

Screening Strategies

- ▶ High-sensitivity guaiac fecal occult blood test (FOBT) or fecal immunochemical test (FIT) every year
- ▶ Stool DNA-FIT (Cologuard[®]) every 1 to 3 years
- ▶ Computed tomography colonography every 5 years
- ▶ Flexible sigmoidoscopy every 5 years
- ▶ Flexible sigmoidoscopy every 10 years + annual FIT
- ▶ Colonoscopy screening every 10 years

Evidence Basis

1. Systematic review to evaluate benefits and harms of screening for colorectal cancer in adults 40+ years old
2. Comparative modeling study to evaluate:
 - ▶ estimated life-years gained
 - ▶ colorectal cancer cases averted
 - ▶ colorectal cancer deaths averted
 - ▶ how the above vary by different starting and stopping ages for various screening strategies



Systematic Review

Analytical Framework



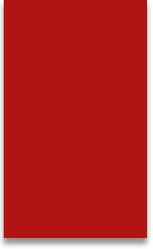
Key Question 1



Colonoscopy Cohort Studies



- ▶ This study included individuals younger than 50 years, although results for this age group were not reported separately



Modeling Study

Natural History of Colorectal Cancer



Simulation Models

1. Simulation Model of CRC (SimCRC)
 2. Microsimulation Screening Analysis (MISCAN)
 3. CRC Simulated Population Model for Incidence and Natural History (CRC-SPIN)
- ▶ All models assume that colorectal cancer arises from adenomatous polyps
 - ▶ Alternative ways in which colorectal cancer can arise (such as from serrated polyps) were not modeled
 - ▶ Outcomes were simulated for a hypothetical cohort of average-risk US adults who were unscreened and free of diagnosed colorectal cancer at age 40 years and were tallied through death

Simulation Model Differences

- ▶ SimCRC and MISCAN simulate categorical adenoma size
 - ▶ 1 to <6 mm; 6 to <10 mm; ≥ 10 mm
- ▶ CRC-SPIN simulates continuous adenoma size
- ▶ SimCRC and CRC-SPIN assume that all adenomas have the potential to progress to colorectal cancer
- ▶ MISCAN assumes that some adenomas do not grow or progress to cancer after reaching a certain size category and that the likelihood that an adenoma is progressive increases with age.

Screening Strategies

- ▶ The following screening modalities were evaluated:
 1. a fecal immunochemical test (FIT) representative of the OC-Sensor family of tests (Polymedco) with a cutoff of 20 μg of hemoglobin per gram of feces
 2. a stool DNA test with a FIT assay (sDNA-FIT), marketed as Cologuard (Exact Sciences)
 3. flexible sigmoidoscopy, alone or with FIT
 4. colonoscopy
 5. computed tomography colonography
- ▶ Multiple ages to begin screening (45, 50, 55 years) and end screening (70, 75, 80, 85 years) and screening intervals were evaluated for each modality, resulting in 163 unique strategies

Screening Strategies



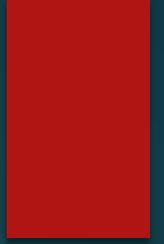
Life-Years Gained vs. Colonoscopies



Efficiency Analysis

- ▶ Within each class, estimated life-years gained (LYG) from screening increased when screening was initiated in the models at an earlier age, although the increase was smaller for MISCAN compared with SimCRC and CRC-SPIN.
- ▶ 49 unique screening strategies were efficient for all three models
 - ▶ The majority (41/49) were those with screening starting at age 45 years
 - ▶ None of the strategies highlighted in the 2016 recommendations, which specified screening from ages 50 to 75, were efficient in all 3 models

Efficiency Analysis for Colonoscopy



Efficiency Analysis

- ▶ No single age to end screening was predominant among efficient strategies
- ▶ For most modalities, the estimated increase in LYG from extending screening beyond age 75 years was small in comparison with the increase in colonoscopies
- ▶ Other than CT colonography (5-year interval), efficient strategies within each class included multiple screening intervals

Benefits



Benefits

- ▶ Models that lowered the age to begin screening showed:
 - ▶ 22 to 27 additional LYG (8%-9% increase)
 - ▶ 2 to 3 fewer colorectal cancer cases (4%-6% reduction)
 - ▶ 0.9 to 1 fewer colorectal cancer deaths (3%-5% reduction)
- ▶ They also showed:
 1. 0.1 to 2 additional complications (1%-14% increase)
 2. 161 to 784 additional colonoscopies (10%-23% increase)
 3. 0 (with colonoscopy) to 3553 additional noncolonoscopy tests (no change to a 24% increase) over the lifetimes of 1000 persons (numbers are mean estimates across models)

Conclusions

- ▶ In 2016, there was limited evidence to support screening before age 50 years. No trials have reported on the effect of screening among asymptomatic adults aged 45 to 49 and data on the findings at screening at these ages remain sparse
 - ▶ However, there is clearer evidence that colorectal cancer incidence in the US is increasing before age 50
- ▶ The SimCRC and CRC-SPIN models estimated that most efficient strategies begin at age 45 years
- ▶ MISCAN assumes some adenomas to be nonprogressive, and the probability that an adenoma is nonprogressive decreases with age at onset
 - ▶ Because of this age dependency, MISCAN estimates a smaller benefit from removing adenomas present at age 45



2021 USPSTF Lung Cancer Screening Guidelines

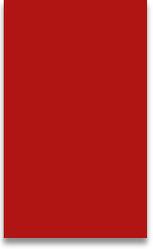


Screening Strategy

- ▶ Screen for lung cancer with low-dose computed tomography (CT) every year
- ▶ Stop screening once a person has not smoked for 15 years or has a health problem that limits life expectancy or the ability to have lung surgery

Evidence Basis

1. Systematic review to evaluate benefits and harms of screening for lung cancer and accuracy of low dose CT
2. Collaborative modeling study to provide information about:
 - ▶ optimum age at which to begin and end screening
 - ▶ optimal screening interval
 - ▶ relative benefits and harms of different screening strategies compared with modified versions of multivariate risk prediction models



Systematic Review

Evidence Basis

- ▶ Seven randomized clinical trials (n = 86,486) evaluated lung cancer screening with low dose CT. The two largest were:
 1. The National Lung Screening Trial (n= 53,454)
 2. Nederlands-Leuvens Longkanker Screenings Onderzoek (NELSON, N = 15,792)

NELSON Trial

- ▶ 13,195 men (primary analysis) and 2,594 women (subgroup analyses) between the ages of 50 and 74 were randomly assigned to:
 - ▶ undergo CT screening at T0 (baseline), year 1, year 3, and year 5.5
 - ▶ no screening
- ▶ Data on cancer diagnosis and date / cause of death were obtained through linkages with national registries in the Netherlands and Belgium
 - ▶ a review committee confirmed lung cancer as the cause of death when possible
- ▶ A minimum follow-up of 10 years was completed for all participants

Screening Test Results



- ▶ An indeterminate screening test required a repeat CT scan to calculate volume-doubling time before the final screening-test outcome could be defined
- ▶ 264 of 22,600 screened participants over all rounds (1.2%) had a false positive test

Lung Cancer Incidence and Mortality



Lung Cancer Stages

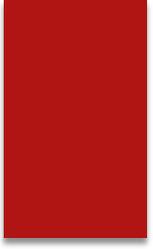


Causes of Death



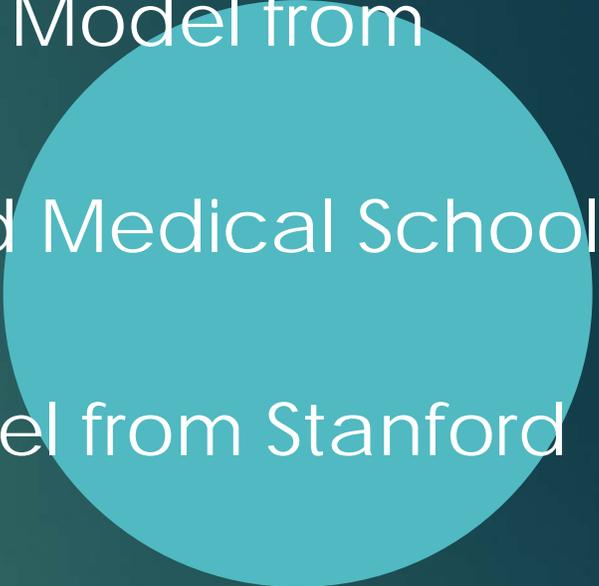
Overdiagnosis

- ▶ An excess of 40 cases (344 vs. 304) was found among the male participants in the screening group 10 years after randomization
 - ▶ This suggests an excess-incidence overdiagnosis rate of 19.7%
- ▶ Extending the follow-up to 11 years after randomization reduced the number of excess cases to 18
 - ▶ This yields an excess-incidence overdiagnosis rate of 8.9%
 - ▶ This number is in line with modeling analyses suggesting that the lead time of CT screening can be as long as 9 to 12 years for some cancers
- ▶ The clinical management strategy in the NELSON trial was highly restrictive with respect to invasive diagnosis and treatment of persistent subsolid nodules



Modeling Study

Simulation Models



1. Microsimulation Screening Analysis-Lung Model from Erasmus University Medical Center
2. Massachusetts General Hospital–Harvard Medical School model
3. Lung Cancer Outcomes Simulation model from Stanford University
4. University of Michigan model

Simulation Models

- ▶ The central component of each model is a dose-response module that predicts age- and sex-specific lung cancer incidence risk as a function of individual smoking history
- ▶ A key component to all models is the shared Smoking History Generator, a validated microsimulator that simulates individual smoking histories for the US population
- ▶ The models were calibrated to both the NLST and the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial.

Lung Cancer Deaths Averted



Life-Years Gained



Efficiency Analysis



Efficient Strategies

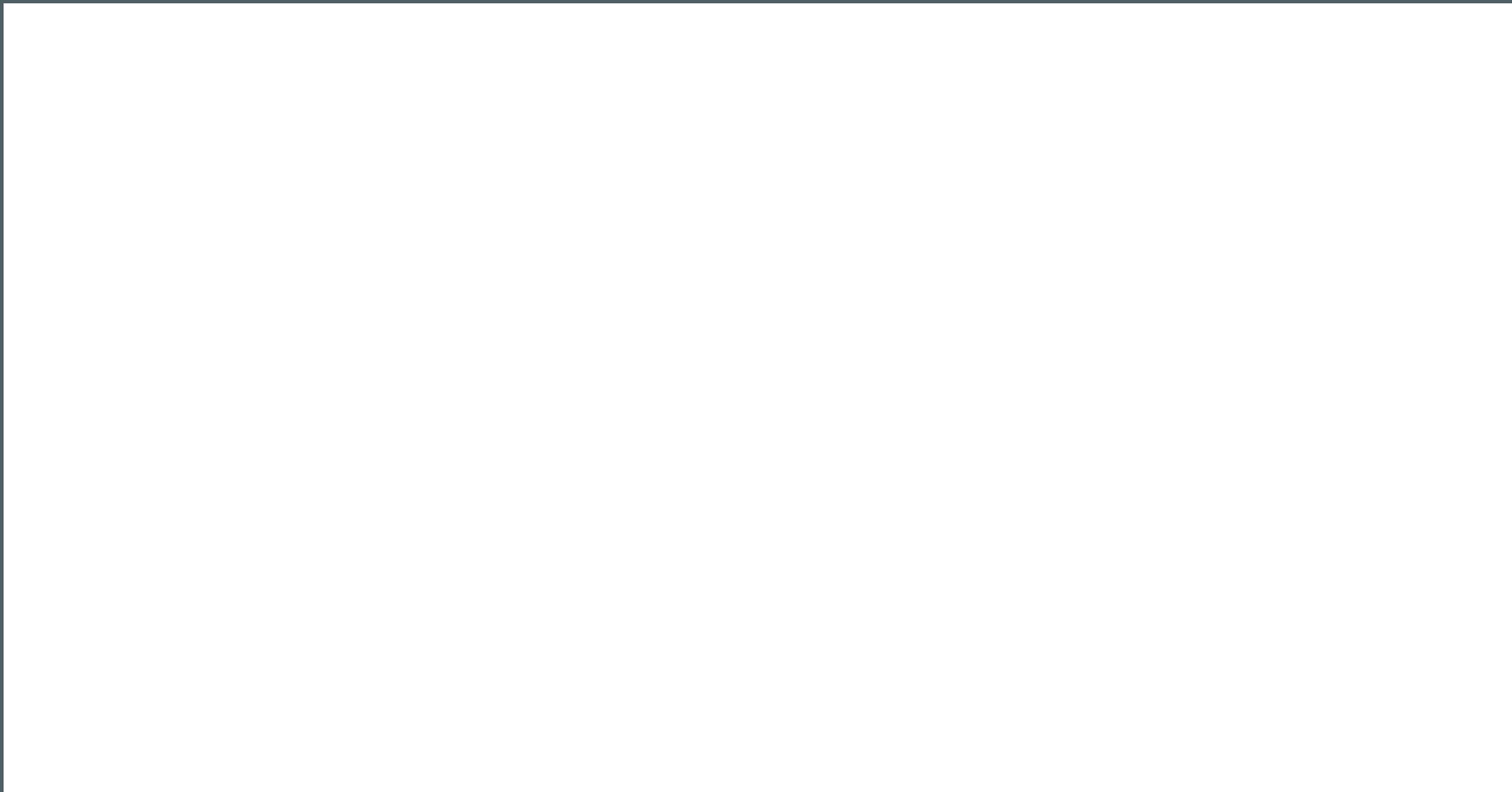


Harms of Efficient Strategies



Conclusions

- ▶ While the analysis could not identify a single optimal strategy, it identified a set of screening programs estimated to yield most benefits for a given level of screening
- ▶ Screening strategies for individuals 50 or 55 years through age 80 with 20 or more pack-years of smoking exposure are efficient
 - ▶ These strategies would result in more benefits than the 2013 USPSTF guidelines but also more harms
- ▶ The comparisons made by sex and race/ethnicity suggest that the relative increase in eligibility for screening from reducing the pack-year criterion to 20 pack-years would be larger for women than for men
 - ▶ They would also be larger for non-Hispanic Black, Hispanic, and American Indian/Alaska Native individuals than for non-Hispanic White and Asian individuals



2021 USPSTF Diabetes Screening Guidelines



Screening Strategies

- ▶ Overweight is defined as a BMI ≥ 25
- ▶ Obese is defined as a BMI ≥ 30
- ▶ Consider screening at an earlier age if the patient is from a population with a disproportionately high prevalence of diabetes (American Indian/Alaska Native, Black, Hispanic/Latino, Native Hawaiian/Pacific Islander)
 - ▶ Consider screening at a lower BMI (≥ 23) if the patient is Asian American
- ▶ Screening tests include HbA1c, fasting glucose, or oral glucose tolerance test

Evidence Basis

1. Systematic review to evaluate screening for prediabetes and type 2 diabetes in asymptomatic, nonpregnant adults
 - ▶ Also evaluated preventive interventions for those with prediabetes
2. Data suggesting that the incidence of diabetes increases at age 35 years compared with younger ages



Interventions in Recently Dx Diabetes



Interventions in Prediabetes



Conclusions

- ▶ Based on:
 1. Data suggesting that the incidence of diabetes increases at age 35 years compared with younger ages
 2. The evidence for the benefits of interventions for newly diagnosed diabetes
- ▶ The USPSTF decreased the age at which to begin screening to 35 years.

Summary



- ▶ Colorectal cancer screening
 - ▶ Start at age 45 (previously 50)
- ▶ Lung cancer screening
 - ▶ Start at age 50 (previously 55)
 - ▶ Minimum pack-year history reduced to 20 pack-years (previously 30)
- ▶ Diabetes screening
 - ▶ Start at age 35 (previously 40)
- ▶ Modeling studies are playing an increasingly important role in the development of national screening recommendations

Questions?

- ▶ Acknowledgments: David Hamel, MD



Analytical Framework



Analytic Framework

