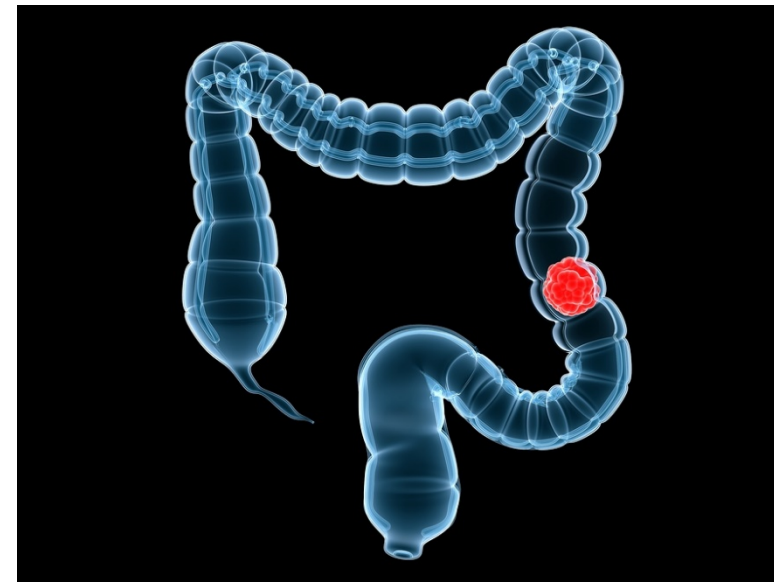




Background



- Despite an overall increase in the uptake of CRC screening, there remain a substantial disparity in the uptake and approximately 40% screening-eligible adult Americans not complying with the recommendations.

- Currently, CRC screening is recommended based only on age and family history. To the best of our knowledge, no prior study has directly examined whether the benefit of screening differs by risk profile.
- In 2020, the US Preventive Services Task Force (USPSTF) released the draft recommendation that average-risk adults may initiate routine screening at age 45 instead of 50.
- These data highlight the importance of tailored screening recommendations based on risk profile to optimize the benefit of screening and resource allocation at the population level.

Objectives

- We prospectively assessed the relative and absolute risk of CRC incidence and mortality associated with colonoscopy screening according to individuals' risk profiles within two large cohorts in the U.S., including the Nurses' Health Study (NHS) and Health Professionals Follow-up Study (HPFS).
- We also examined the age-specific CRC cumulative incidence and identified the ages when the threshold CRC risk at age 45 and 50, respectively, was attained among individuals with different CRC risk profiles.

Methods

- Study period: 1988-2014
- Study population: NHS, 75,873 women; HPFS, 42,875 men
- Main exposure: We defined a colonoscopy screening as those for routine, age-related CRC screening or because of a family history of CRC, but not for positive symptoms.
- Effect modifier: CRC risk score (range, 0-8) was defined as the number of the 8 CRC-high risk factors: having family history of CRC among the first-degree relatives, no regular use of aspirin, tall stature, overweight or obesity, current smoker or past smokers with pack-years ≥ 5 , low physical activity, heavy alcohol intake, and unhealthy diet (meeting less than 3 of the 6 dietary recommendations by the WCRF/AICR Report 2018, which included red meat <0.5 serving/d, processed meat <0.2 serving/d, dietary fiber ≥ 30 g/d, dairy products ≥ 3 servings/d, whole grains ≥ 48 g/d or account for at least half of total grains, and calcium supplement use).
- Outcomes: CRC incidence and mortality
- Statistical analysis: Cox regression models
- Measures: Absolute risk of CRC and colonoscopy screening – related absolute risk reduction

Key Findings

Table 1. Associations of individual risk factors and the risk score* with CRC incidence

	Prevalence (%)	Age-adjusted HR (95% CI)	MV-adjusted HR (95% CI)
Family history of CRC			
No	84	1.00 (reference)	1.00 (reference)
Yes	16	1.31 (1.19-1.43)	1.40 (1.28-1.53)
Aspirin			
≥ 2 tablets/times per week	29	1.00 (reference)	1.00 (reference)
< 2 tablets/times per week	71	1.30 (1.19-1.42)	1.26 (1.15-1.37)
Height			
Lower 50% in each cohort	51	1.00 (reference)	1.00 (reference)
Upper 50% in each cohort	49	1.21 (1.12-1.30)	1.21 (1.12-1.31)
Body mass index			
18.5-24.9 kg/m ²	48	1.00 (reference)	1.00 (reference)
≥ 25 kg/m ²	52	1.24 (1.15-1.34)	1.21 (1.12-1.30)
Smoking			
No smoking or past smoking with pack-years < 5	56	1.00 (reference)	1.00 (reference)
Current smoking or past smoking with pack-years ≥ 5	44	1.32 (1.23-1.42)	1.25 (1.16-1.35)
Alcohol intake			
< 14 (women) or < 28 g/d (men)	88	1.00 (reference)	1.00 (reference)
≥ 14 (women) or ≥ 28 g/d (men)	12	1.37 (1.24-1.52)	1.34 (1.21-1.48)
Physical activity			
moderate-to-vigorous intensity activity for ≥ 30 min/d	26	1.00 (reference)	1.00 (reference)
moderate-to-vigorous intensity activity for < 30 min/d	74	1.16 (1.06-1.27)	1.07 (0.98-1.17)
Diet			
meeting ≥ 3 of the 6 WCRF dietary recommendations	25	1.00 (reference)	1.00 (reference)
meeting < 3 of the 6 WCRF dietary recommendations	75	1.29 (1.18-1.41)	1.13 (1.03-1.23)
CRC risk score			
0-2	14	1.00 (reference)	1.00 (reference)
3	22	1.21 (1.04-1.40)	1.19 (1.03-1.38)
4	30	1.55 (1.35-1.78)	1.51 (1.31-1.73)
5	23	1.84 (1.60-2.11)	1.77 (1.54-2.04)
6-8	11	2.56 (2.21-2.96)	2.45 (2.11-2.84)
P-trend		< 0.001	< 0.001

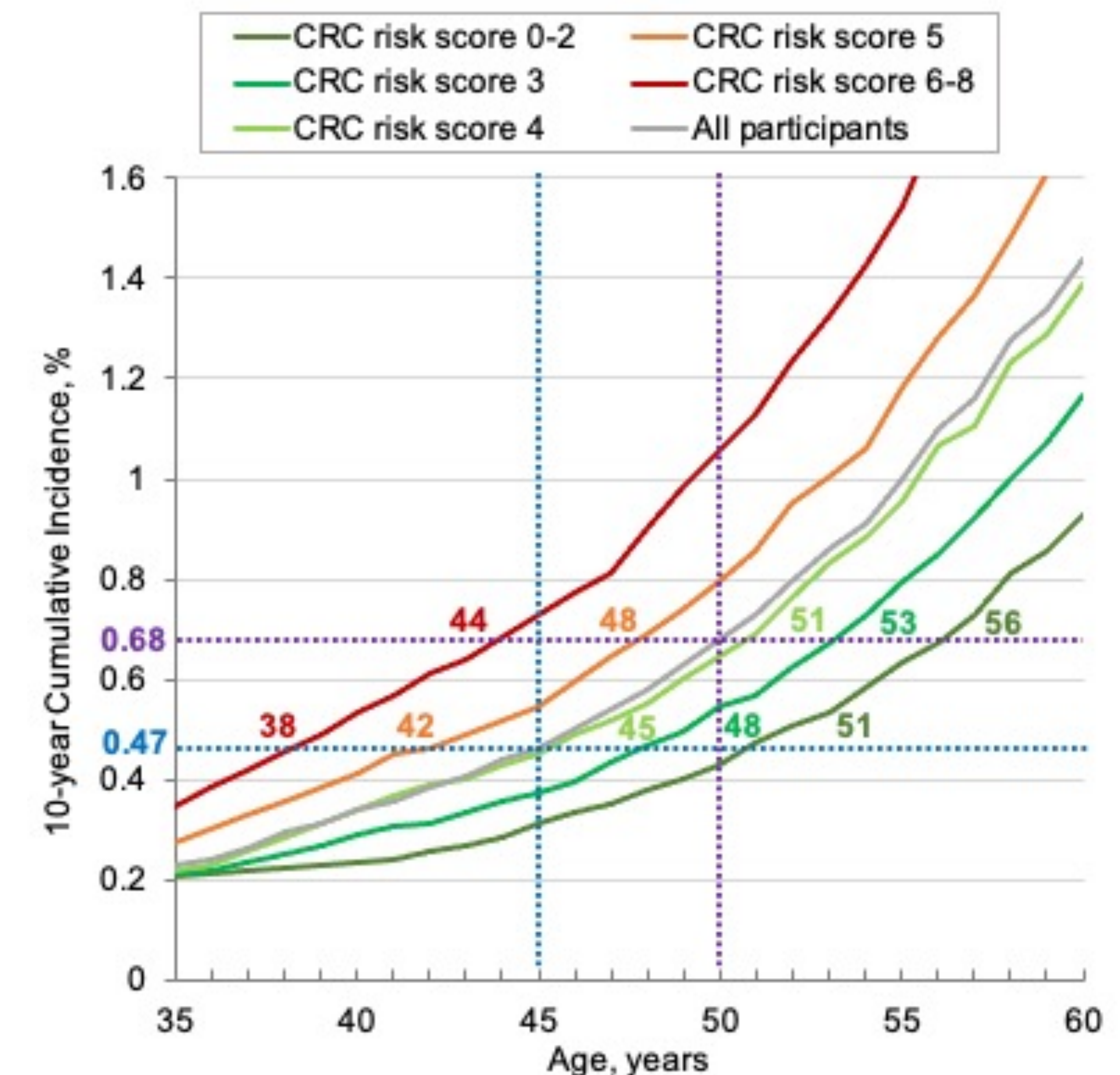
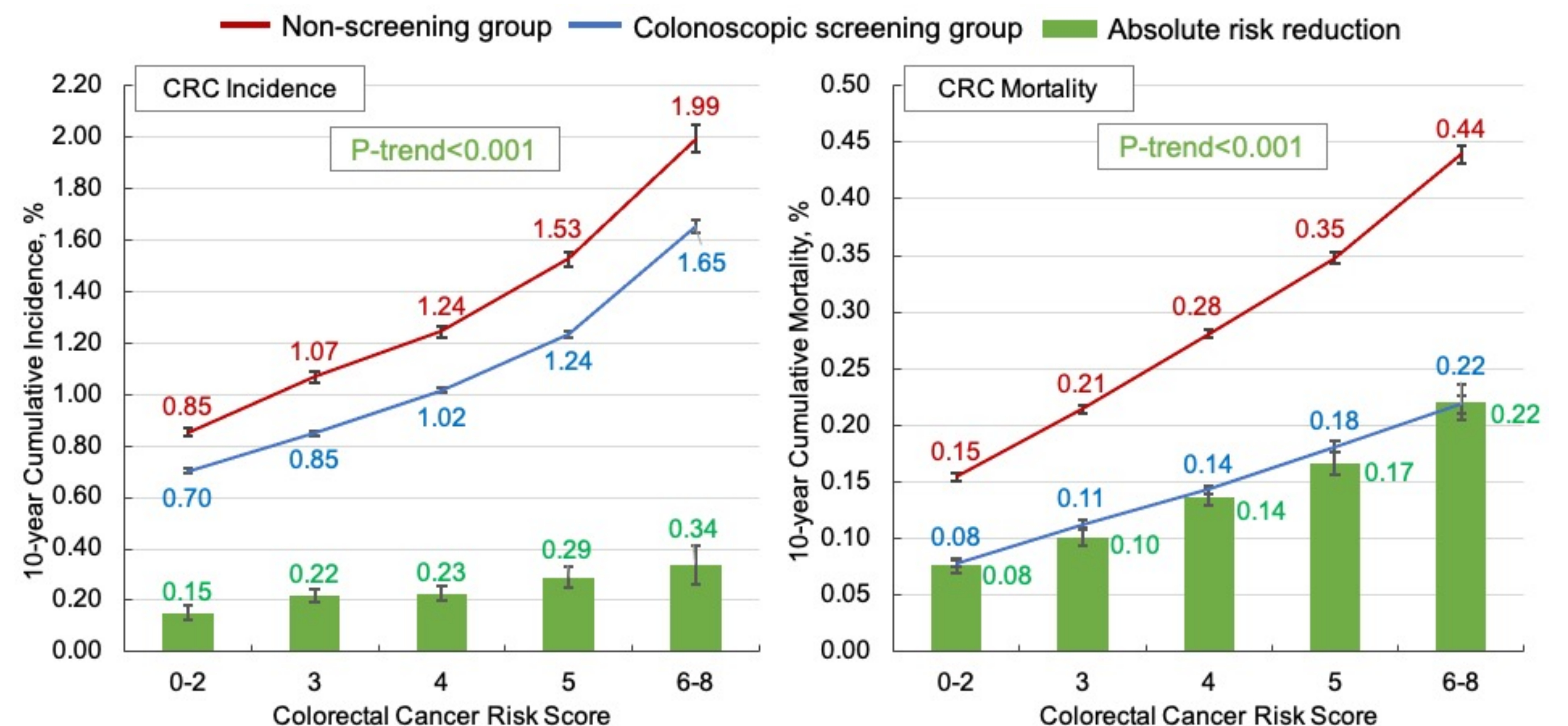


Figure 2. Multivariable-adjusted 10-year cumulative incidence of CRC by age in all participants and according to CRC risk score.

Figure 1. Multivariable-adjusted 10-year cumulative incidence (left panel) and mortality (right panel) of CRC and the corresponding absolute risk reduction according to CRC risk score.



Summary Points

- The absolute benefits of colonoscopy screening for the prevention of CRC and related death are more than twice higher for individuals with the highest than lowest CRC risk profile.
- Individuals with a high and low CRC risk profile may start CRC screening up to 6-7 years earlier and later, respectively, than the recommended age of 45 or 50 years.
- These findings provide evidence for the development of tailored colonoscopy screening recommendations based on individuals' risk profiles.

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