April 9, 2026

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Center for Clinical Standards and Quality
Centers for Medicare & Medicaid Services
7500 Security Boulevard
Baltimore, MD 21244

Re: Proposed Decision Memo: Screening for Colorectal Cancer – Non-Invasive Biomarker Tests (CAF-00440R)

Dear Acting Director Baldwin:

The American Cancer Society (ACS) and the American Cancer Society Cancer Action Network (ACS CAN) appreciate the opportunity to comment on the proposed decision memo for changes to the existing National Coverage Decision (NCD) 210.3 related to screening for colorectal cancer (CRC) using non-invasive biomarker tests. The ACS mission is to improve the lives of people with cancer and their families through advocacy, research, and patient support, to ensure everyone has an opportunity to prevent, detect, treat, and survive cancer. ACS, operating throughout the United States (US), is the largest voluntary health organization in the country. ACS CAN is making cancer a top priority for public officials and candidates at the federal, state, and local levels. ACS CAN is the nonprofit, nonpartisan advocacy affiliate of ACS, advocating for evidence-based public policies to reduce the cancer burden for everyone. ACS CAN empowers advocates across the country to make their voices heard and influence evidence-based public policy change, as well as legislative and regulatory solutions that will reduce the cancer burden.

ACS has estimated that in 2026, 108,860 cases of colon cancer would be diagnosed in the United States and an estimated 55,230 people would die from the disease.[1] Colorectal cancer remains one of the deadliest forms of cancer.[2] Colorectal cancer is the third most commonly diagnosed cancer and the third most common cause of cancer-related death in both men and women in the United States.[3] Almost half (45%) of new diagnosis are in individuals under age 65, up from 27% in 1995.[4]

Regular screening is the most effective way of detecting precancerous growths and early colorectal cancer. Removal of precancerous lesions can prevent colorectal cancer, and cancers found at an early stage can be treated more easily, and lead to greater survival.[5] For colorectal

[1] American Cancer Society. *Cancer Facts & Figures 2026.* Atlanta: American Cancer Society; 2026.
[2] Siegal RL, Miller KD, Fuchs HE, Jemal A. Cancer statistics, 2021. *Cancer.* 2021; 71:7-33. doi 10.3322/caac.21654.
[3] American Cancer Society. *Colorectal Cancer Facts & Figures 2023-2025*. Atlanta: American Cancer Society; 2024.
[4] Siegel RL, Wagle NS, Star J, Kratzer, Smith RA, Jemal A. Colorectal cancer statistics, 2026. *CA Cancer J Clin.* 2026; 76(2)(e70067). doi:10.322/caac.70067.
[5] American Cancer Society. *Cancer Prevention & Early Detection Facts & Figures 2023-2024*. Atlanta: American Cancer Society; 2024.

cancer, the five-year survival rate is 91% when the cancer is discovered and treated early.[6] In contrast, individuals aged 65 and older whose colorectal cancer is found at a later stage, after the cancer has metastasized, have a 10% five-year survival rate.[7]

We are pleased to see the reconsideration given the updated scientific evidence and clinical recommendations available. We have the following comments:

II. CLINICAL REVIEW

A. Background

The proposed decision memo states that colorectal cancer is the fourth most common cancer and the second leading cause of cancer deaths in the U.S., citing Siegel, et al. 2024. We recommend that the decision memo qualify this statistic as follows: Colorectal cancer is the third most common cancer in both women and men, and the second leading cause of cancer death in the United States.

We would also like to bring to the attention of the Centers for Medicare & Medicaid Services (CMS) that estimates of new cancer cases are derived by the ACS each year – not, as noted in the proposed decision memo, by the National Cancer Institute (NCI). In fact, the NCI cites the ACS estimates on the SEER website. We ask that when the decision memo is finalized that CMS properly attribute the source of these yearly annual estimates of expected new cases and deaths to ACS. The methodology for deriving the estimates can be found in ACS' annual publication of our Cancer Facts and Figures.[8] We also urge CMS to use the most current data, 2026, in its final decision memo. These can be found in the *ACS Facts and Figures 2026*,[9] or preferably the annual cancer statistics in the CA: A Cancer Journal for Clinicians.[10]

At the end of paragraph two in this section, the proposed decision memo states: "Colonoscopy is the gold standard for CRC screening." Most organizations, and especially those that issue clinical guidelines and recommendations, have stopped claiming that colonoscopy is a gold standard. Instead, collectively these organizations all say the best test is the one that individuals will undertake. All colorectal cancer tests produce lifetime benefits similar to colonoscopy when colorectal cancer screening with any recommended test is done regularly over the period that screening is recommended. Since many individuals do not wish to undergo an invasive screening test but are willing to be screened with beneficial noninvasive tests, we urge CMS to not diminish the value of other recommended tests by placing colonoscopy in an exalted position.

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[6] *Colorectal Cancer Facts & Figures 2023-2025.*
[7] Id.
[8] See *Cancer Facts & Figures 2026* at page 41.
[9] Id.
[10] Colorectal cancer statistics, 2026.

E. Assessment of the Evidence

4. Limitations

Bullet 8 cites the lack of long-term follow-up to measure morbidity and mortality. Given that the natural history of colorectal cancer is well established, as is the efficacy of screening based on multiple randomized clinical trials utilizing different colorectal cancer screening tests, there is broad consensus that new screening technology only needs to demonstrate the detection of surrogate indicators (advanced neoplasia in the form of precursor lesions and cancer) with an established comparison test, with both followed up with colonoscopy as the reference test. New tests would remain in limbo for a decade or more if a mortality endpoint were required. It is unreasonable to expect these studies to follow up to mortality because it is unnecessary. As for morbidity, there is next to no morbidity associated with a noninvasive screening test. Any morbidity that occurs associated with the volume of follow-up colonoscopy can be estimated based on established data, but the morbidity occurs with the follow-up test, not from collecting stool or a blood draw. We therefore recommend that this bullet also be deleted from the final decision memo.

The proposed decision memo states in the first bullet of the list of limitations, "All studies of commercially available CRC tests (Cologuard®, ColoSense®, Shield™) were supported by the companies that developed the tests." Although this limitation is commonly listed in systematic reviews when including industry sponsored research, it is a risk of bias without substantiation, and it signals to readers that the reviewers carried this sense of anticipated bias when reviewing the literature. Scientific research must be entirely judged on the basis of the quality of the research, without a cloud of suspicion based on who sponsored the research. We note, compared with the following limitations, there is no citation to support that an industry sponsored study is inherently biased. We also note that industry commonly recruits academic leaders to run their studies, knowing that scientists with unimpeachable reputations will add credibility to the investigation. These studies tend to be published in leading high impact journals and always have undergone peer review. It is for these reasons that we recommend deleting this bullet from the final decision memo.

5. Relevance and Generalizability to Medicare Beneficiaries

Most guidelines/recommendations have an allowance for screening past age 75, based on estimated longevity and shared decision making. All recommendations and guidelines also stress as a condition of undergoing screening, regardless of age, that individuals should be in good health and not suffer from life-limiting co-morbid conditions. In the final version of the decision memo, we urge CMS to make note that guidelines organizations do not adhere to a strict maximum age for screening before the age of 80 or 85.

IV. CMS COVERAGE ANALYSIS

B. CMS Analysis for Coverage of CRC screening

2. Test Criteria

In previous comments to CMS, we have expressed concerns about test criteria thresholds, specifically the combination of sensitivity/specificity performance characteristics for the detection of invasive colorectal cancer that must be met for coverage. We question why these thresholds are only set for cancer, without also including criteria for advanced precursor lesions (APLs). It has recently been estimated that we are reducing more colorectal cancer mortality by interrupting the natural history of disease when we detect and remove APLs. All recommended CRC tests have better sensitivity for cancer compared with APLs, but we want to see that these tests have at least respectable performance for detecting APLs. Given the variability of definitions of APLs in the literature, CMS might just focus on high grade dysplasia. Specificity should be defined as the absence of advanced colorectal neoplasia. Second, most of the sensitivity and specificity statistics are based on the performance of a single test. Tests with shorter screening intervals are expected to have better performance over comparable time periods (3 yrs., 5 yrs., 10 yrs.). We recommend that CMS consider adding test criteria for the detection of cancer and APLs adjusted for comparable periods of regular screening.

With respect to sensitivity and specificity criteria, the proposed NCD claims that there is an inverse relationship between sensitivity and specificity. At the upper limits this is true, but with quality improvement, screening tests, particularly those that involve some degree of operator dependence, can see simultaneous improvements in both sensitivity and specificity. The assumption that there is an "iron law" of the inverse relationship between sensitivity and specificity further complicates the statement that: "If the test manufacturer decided to increase screening test sensitivity, then it is likely that specificity would decrease for the screening test. If the test manufacturer decided to increase screening test specificity, then it is likely that sensitivity would decrease." We see the following problems with these thresholds:

- All thresholds are expressed as "equal to or greater than."
- Criteria 1 and 2 have uneven differences between sensitivity and specificity: 3 percentage points for Criteria 1, and 11% points for Criteria 2
- For Criteria 1, an improvement in sensitivity from 90% to 94% that led to a half point decline in specificity 86.5% would disqualify the test compared with only met minimum criteria.
- We wonder why CMS is prepared to accept a screening test that is only done every 3 years, but with a sensitivity of 79% would miss 21% of invasive cancers.

In general, missing the thresholds by small numbers could mean that new tests that outperform the point sensitivity and specificity of many tests in the recommended categories, specifically gFOBT and FIT that are cleared by the Food and Drug Administration (FDA) and widely used today, would be disqualified.[11]

c. Implementation of Threshold Test Performance Criteria

We concur with the ordering requirements including physician assistants, nurse practitioners, or clinical nurse specialists who will use the results in the management of the patient.

We are surprised that there is no mention of the comparatively poor performance of blood-based tests in the detection of precursor lesions. The one blood-based test that is currently available for CRC screening includes cautionary language that their test has low sensitivity to detect precursor lesions compared with other colorectal cancer screening tests. Given that modeling data show that a substantial fraction of reduced incidence and mortality derives from detecting and removing precursor lesions, patients should know the limitations of these tests compared with other recommended tests that have better performance for detecting precursor lesions. On the other hand, attention should be given to the possibility that these tests may be acceptable to individuals who are repeatedly non-adherent to recommendations for colorectal cancer screening, or who state that they are not willing to undergo any of the currently recommended tests.

3. Evidence Questions -- Answered

With respect to the answers to evidence questions 1 and 2, we concur with CMS' decision to include these tests in coverage for Medicare beneficiaries.

CONCLUSION

Thank you for the opportunity to comment on the proposed decision memo related to screening for colorectal cancer – non-invasive biomarker tests. If you have any questions, please feel free to have your staff contact Anna Schwamlein Howard, Interim Managing Director, Public Policy at Anna.Howard@cancer.org.

Sincerely,

William Dahut, MD
Chief Scientific Officer
American Cancer Society

Lisa A. Lacasse, MBA
President
American Cancer Society Cancer Action Network

[11] See, Levy BT, Xu Y, Daly JM, Hoffman RM, et al. Comparative Performance of Common Fecal Immunochemical Tests : A Cross-Sectional Study. *Ann Intern Med*. Oct 2024;177(10):1350–1360. doi:10.7326/M24-0080.