**Background**
- Blood tests for colorectal cancer (CRC) with high sensitivity and specificity can facilitate early detection and help reduce mortality from CRC.
- The detection and subsequent removal of adenomas reduces CRC incidence and mortality.
- A recent national coverage determination from the Centers for Medicare & Medicaid Services offered clinical performance guidelines for a blood test's specificity and CRC sensitivity, but not for adenoma sensitivity.

**Objective**
- To investigate the impact of CRC test performance characteristics on clinical outcomes for a hypothetical blood test using a novel, validated microsimulation model: CRC-MAPS (CRC - Microsimulation of Adenoma Progression and Screening).

**Methods**
- A semi-Markov microsimulation model of the adenoma-carcinoma pathway was developed and calibrated to autopsy, SEER, and CT colonography data (Figure 1).
- Model validation was assessed through cross-model comparisons against validated CISNET models (Figures 2, 3).
- This study simulated perfect adherence to a hypothetical annual, blood-based CRC screening test among previously unscreened individuals who have not yet been clinically diagnosed with CRC.
- Outcomes were aggregated from age 50 to death, and individuals were screened from age 50 to 75.
- The base case assumed size-specific adenoma sensitivities (15mm: 16%; 4-9mm: 20%; 10-13mm: 30%); 50% CRC sensitivity, and 95% specificity.
- Primary outcome included CRC cases and deaths, life years gained, and CRC incidence and mortality reduction compared to no screening.
- Each performance characteristic was independently varied ±5% from the base case to evaluate its impact on clinical outcomes.

**Results**
- The base case resulted in 11 CRC cases and 3 CRC deaths, as well as 243 life years gained per 1,000 individuals compared to no screening.
- The base case also showed an 83.4% and 87.9% reduction in CRC incidence and mortality, respectively, compared to no screening.
- CRC incidence and mortality reduction was 79.8–85.5% and 85.5–89.3%, respectively, when all adenoma sensitivity (pooled small, medium, and large) was varied from the base case.

**CONCLUSIONS**
- This microsimulation study of a hypothetical blood-based CRC screening test using the CRC-MAPS model provides insights into the relative impact of test performance characteristics on clinical outcomes.
- The analysis revealed that changes in adenoma sensitivity had a greater impact on CRC incidence and mortality reduction than changes in either specificity or CRC sensitivity.
- This study suggests that earlier detection of colorectal neoplasia improves clinical outcomes and highlights the benefits of preventing CRC through adenoma detection and lifelong colonoscopy surveillance.
- Future work will utilize the CRC-MAPS model to explore additional benefits and harms of different CRC screening strategies.

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Adenoma sensitivity has a greater impact on colorectal cancer (CRC) incidence and mortality reduction than CRC sensitivity or specificity: Results from a novel microsimulation model

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