Test interval and adherence have comparable impacts on colorectal cancer (CRC) incidence and mortality reduction: Results from a novel microsimulation model

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Background
- The clinical utility of a screening test depends not only on its performance characteristics but also on other factors, such as test interval and adherence.
- Despite national screening initiatives aiming to achieve 180% adherence for adults over age 50, only 67% are up-to-date on CRC screening.
- All current CRC screening strategies have implementation trade-offs: colonoscopy is recommended every 10 years but is invasive, whereas stool-based tests are more convenient but must be performed every 1-2 years, and they require handling of stool and substantial patient navigation.
- New blood tests can help overcome some of these barriers due to ease of sample collection and integration into routine blood work.

Objective
- To investigate the impact of screening interval and participation (i.e., initial uptake) on clinical outcomes for a hypothetical blood-based screening 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 existing 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.
- The simulation assumed that the hypothetical test had size-specific adenoma sensitivities (15mm: 89%; 6-9mm: 20%; 3-5mm: 30%); 100% CRC specificity, and 90% specificity.
- Participation and test interval scenarios are shown in Table 1.
- Outcomes were aggregated from age 40 to death, and individuals were screened from age 40 to 75.
- Outcomes were CRC incidence and mortality reduction compared to no screening.
- Test interval and screening participation were independent, varied from the base case to evaluate their impact on clinical outcomes.
- This model simulates CSC progression through the adenoma-carcinoma pathway and allows for evaluation of different screening strategies.

Results
- Assuming 100% participation, the base case (annual test) resulted in 11 CRC cases and 3 deaths from CRC as well as 243 life years gained per 1,000 individuals compared to no screening.
- The base case also showed a 83.4% and 87.9% reduction in CRC incidence and mortality, respectively, compared to no screening.
- CRC incidence and mortality reduction were sensitive to changes in test interval and screening participation. For example, changing from an annual test to a triennial test decreased CRC incidence and mortality reduction by 81.4% and 92.5%, respectively. Decreasing screening participation from 100% to 80% lowered CRC incidence and mortality reduction by 81.7% and 15%, respectively.

Conclusion
- This microsimulation study of a hypothetical blood-based CRC screening test using the CRC-MAPS model emphasizes the critical role of adherence in improving clinical outcomes.
- The impact of test interval, which can serve as a proxy for delayed screening, on CRC incidence and mortality reduction is comparable to that of patient participation.
- These results suggest that the availability of a blood test with improved adherence may significantly improve clinical outcomes from CRC screening.
- Future work will utilize the CRC-MAPS model to explore the impact of diagnostic colonoscopy and longitudinal testing rates on clinical outcomes.

References
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Presented at Digestive Disease Week 2021 | May 21–23, 2021 | Virtual Meeting