Characteristics of a cost-effective blood test for colorectal cancer screening*

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- No conflicts of interest to report
- Views expressed are my own and not necessarily those of the RAND Corporation or the National Institutes of Health

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Agenda

- Research questions
- Methods overview
- Main results, equivalence thresholds
- Discussion

Can blood tests compete with FIT and colonoscopy?

- Under what conditions can blood tests be "as good as" colonoscopy or FIT in terms of:
  - Effectiveness:
    - Life-years gained (LYG)
    - Quality-adjusted LYG (QALYG)
  - Cost-effectiveness:
    - Not dominated by a combination of annual FIT or decennial COL
    - Net monetary benefit on par with COL or FIT

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Methods

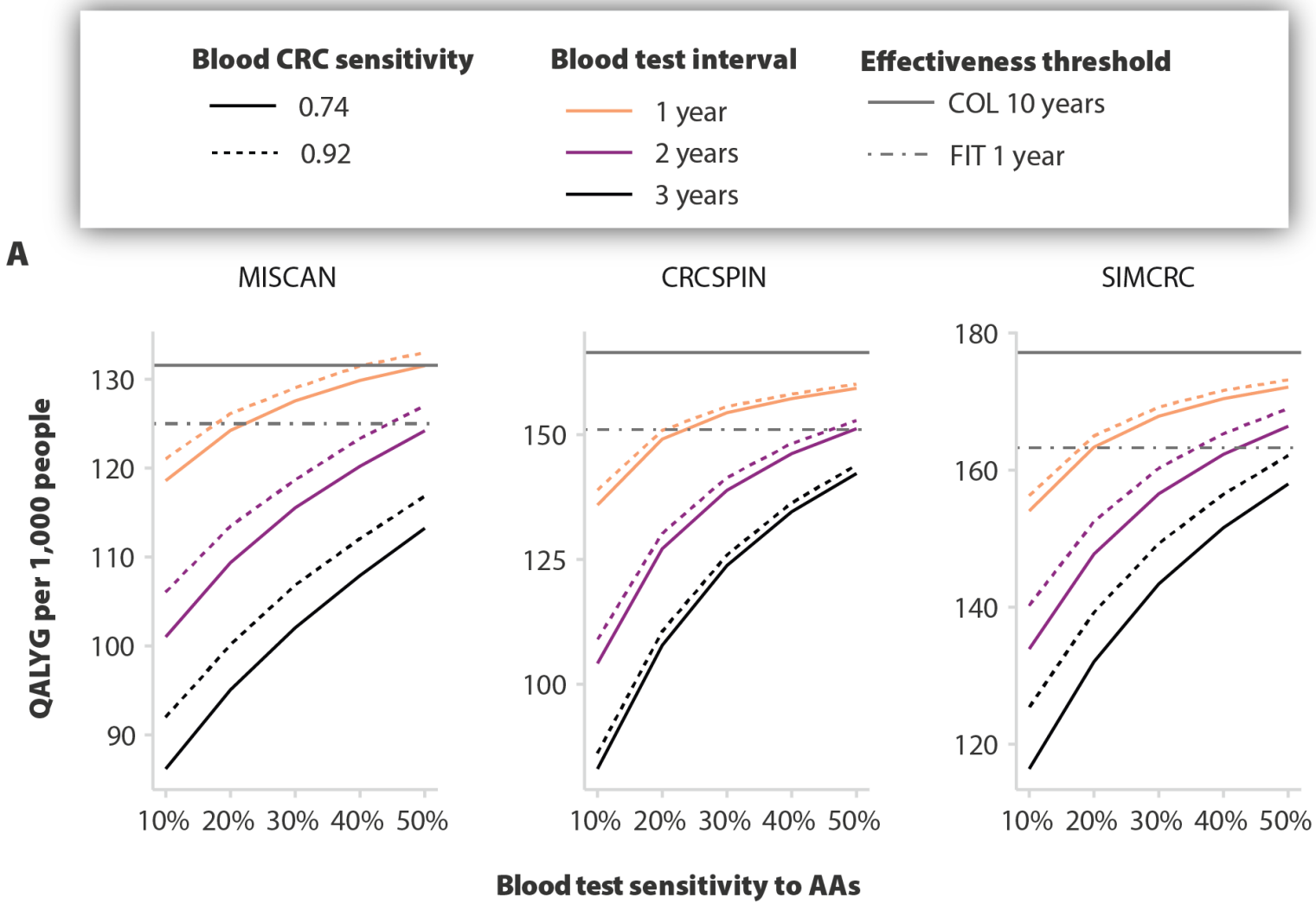
- Method:
  - Comparative threshold analysis using the three CISNET CRC models
- Assumptions:
  - Same population definition, CRC risk, baseline test characteristics and cost-effectiveness inputs as in van den Puttelaar et al. Gastroenterology, 2024.
- Outcomes:
  - **Benefits:** LYG and QALYG (LYG – disutility from disease, tests and treatments)
  - **Costs:** Net costs (screening, follow-up colonoscopy, surveillance, and treatment) relative to no screening
  - **Net monetary benefit** = wtp * QALYG – Net Costs

We evaluate blood tests in 900 scenarios

- Three CISNET models: CRCSPIN, MISCAN and SIMCRC
- Five screening regimens (all from 45-75 years)
  - Existing alternatives: No screening, FIT every year, Colonoscopy every 10 years
  - Three blood test strategies: blood test every 1,2 or 3 years
- Fifteen blood tests sensitivity assumption sets:
  - Five adenoma sensitivity scenarios, varying sensitivity to advanced adenomas (AAs) from 0.1 to 0.5.
  - Three CRC sensitivity scenarios: 0.74, 0.82 and 0.92.
  - Specificity constant at 90% (CMS coverage decision as a constraint).
- Twenty blood test cost assumptions
  - $25-$500 in increments of $25

Under which conditions would blood-based screening be as **effective** as annual FIT or decennial colonoscopy?

AA sensitivity is crucial for effectiveness non-inferiority



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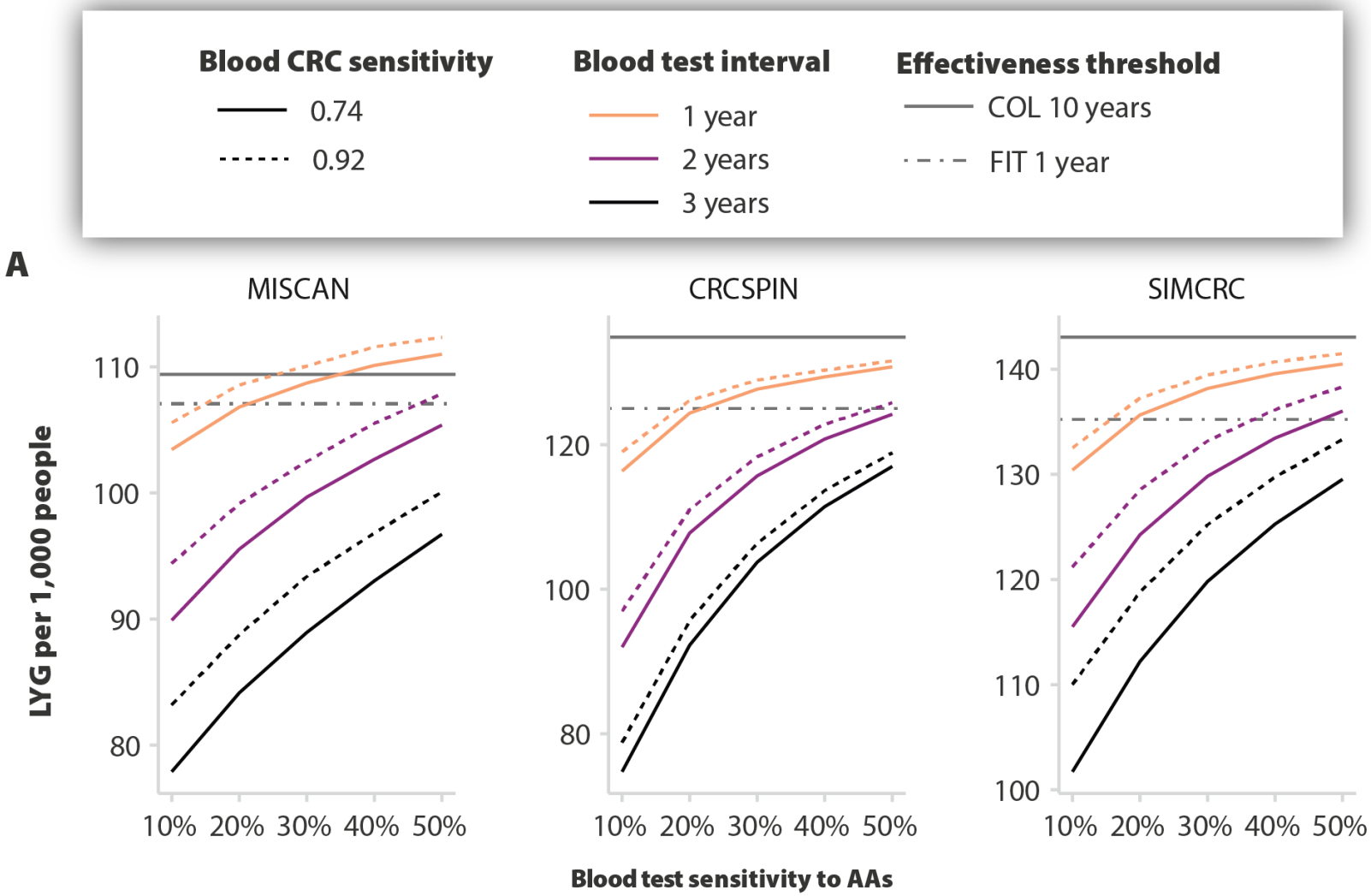
LYG results are similar



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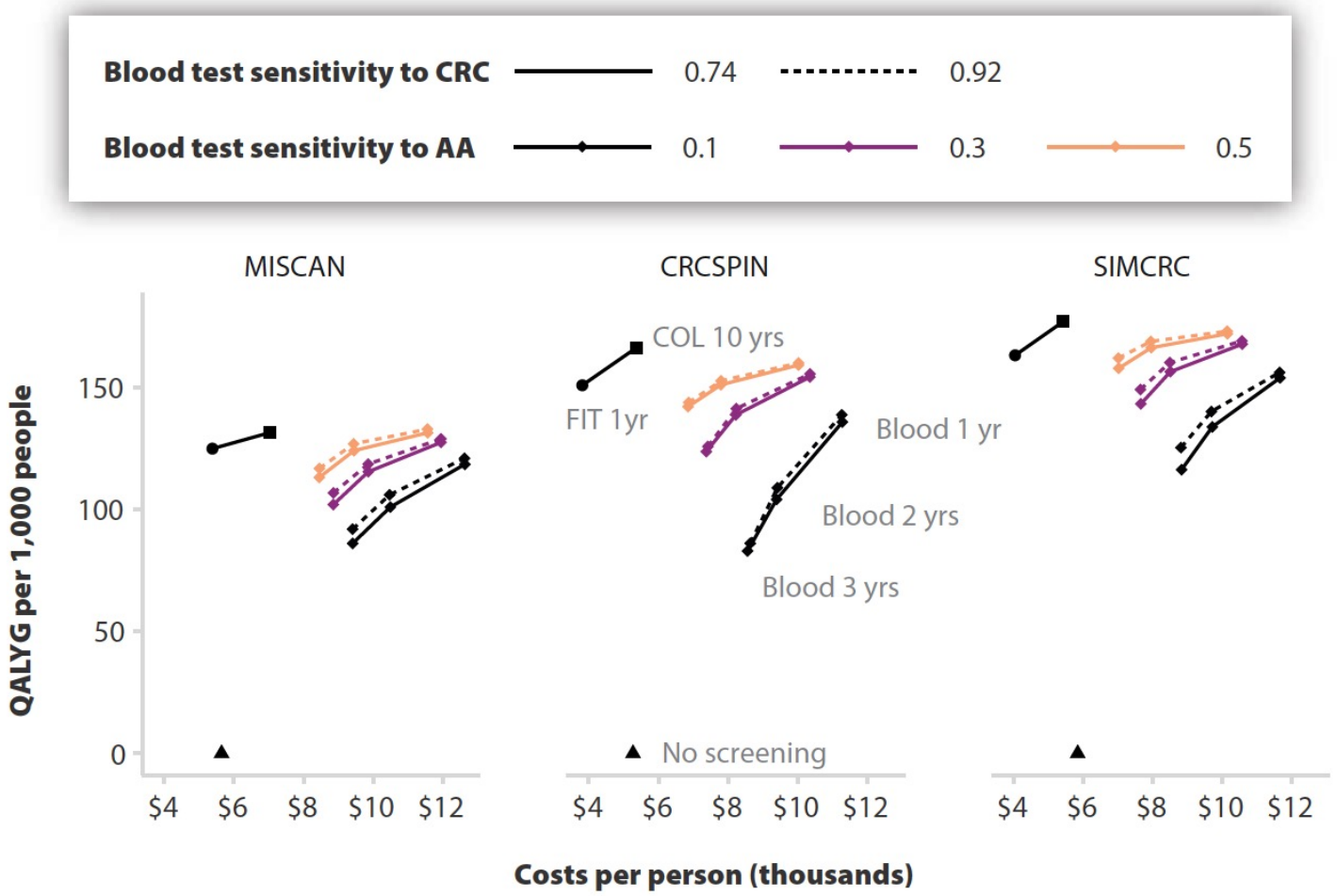
Can a $500 blood test be cost-effective in any of those scenarios?

No.

A $500 blood test would not be cost-effective even with 50% AA sensitivity and 92% CRC sensitivity



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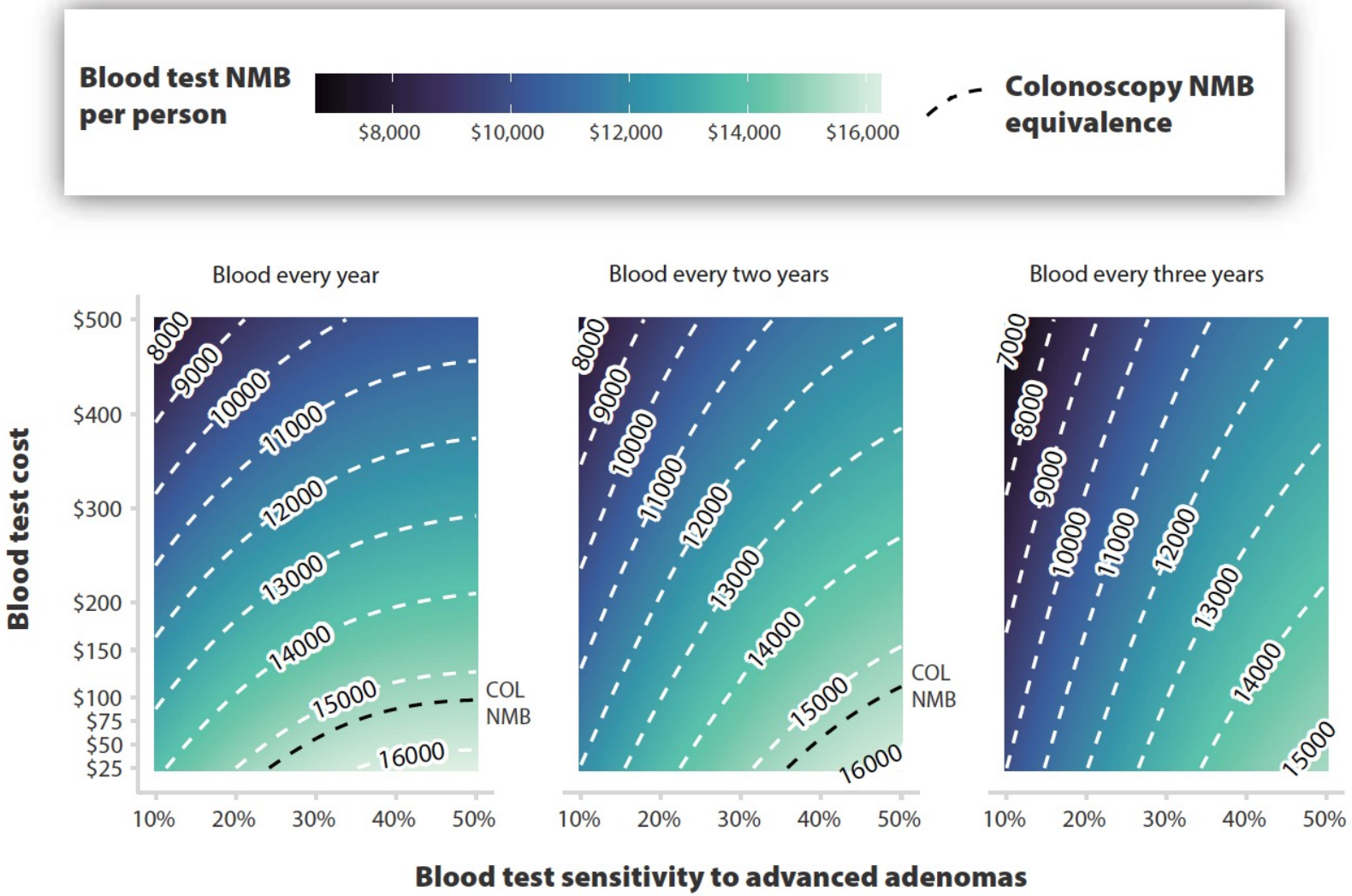
Under which conditions can blood tests provide NMB on par with colonoscopy?

An ~ $100 blood test with 40% AA sensitivity would provide comparable value relative to COL or FIT



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Conclusions

1. If blood tests cost $500, only meet minimum CMS accuracy criteria, and are used every three years, their **adoption could eliminate 52% to 70% of the NMB afforded by colonoscopy** for individuals who would otherwise follow colonoscopy screening.
2. Blood tests that only meet CMS coverage requirements **should not be recommended to patients who would otherwise undergo screening by colonoscopy or FIT** due to lower benefit.
3. Blood tests **need higher AA sensitivity (above 40%) and lower costs (below $125) to be cost-effective**.

Slides, paper coming soon:

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What about adherence?

Napkin math can help you think about it

- Simple way to think about this: Assume that a fraction of people simply choose to never screen *and* that this choice is random (no selection bias):
- With that assumption, it is easy to find the adherence needed for the same benefit (or NMB).
  - $NMB'_{col} = a_{col} NMB_{col}$ and $NMB'_{blood} = a_{blood} NMB_{blood}$
  - If $NMB'_{blood} \geq NMB'_{col}$, then

$$a_{blood} \geq \frac{a_{col} NMB_{col}}{NMB_{blood}}$$

- Example: if adherence of the comparator is ~45%, and blood tests have a 50% NMB gap then:

$$a_{blood} \geq \frac{0.45}{0.5} > 90\%$$

- Several weaknesses in this argument: It hinges on poor adherence of the comparator, it does not account for adherence to follow up colonoscopy, it can't compensate major NMB gaps, and it does nothing to the effectiveness for those who are adherent to the comparator.