

# Report of AGA Consensus Workshop on Blood-Based CRC screening

WEO Meeting 5-17-24; Wash DC

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nce upon a time . . .





*HI THERE – I AM A ONE-WISH GENIE.  
WHAT WOULD YOU LIKE?*

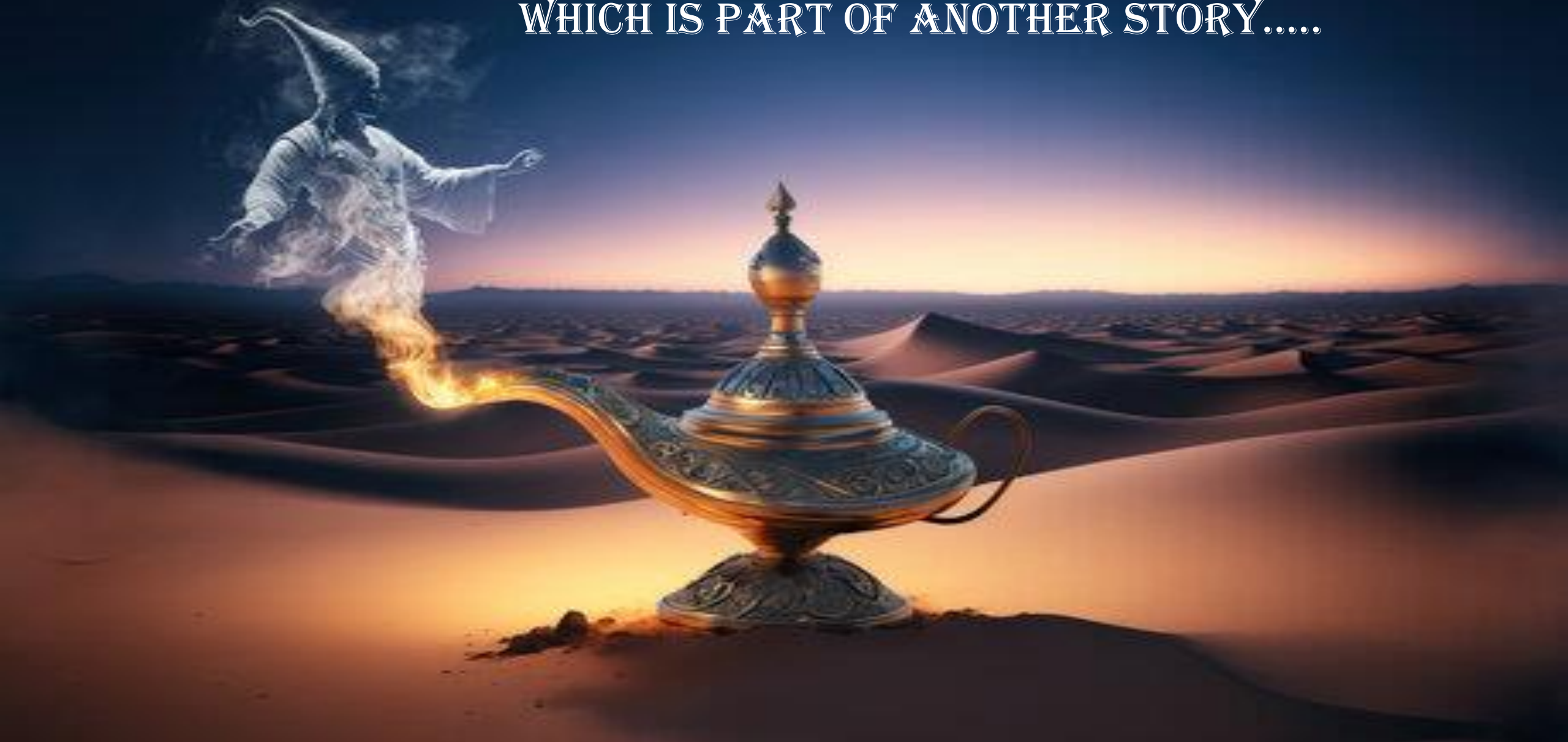
**How about a blood test to  
screen for colon cancer?  
Everyone would rush to get screened!  
Lives would be saved.**

**HMMM – I CAN DO IT....  
BUT IT MIGHT NOT BE PERFECT**

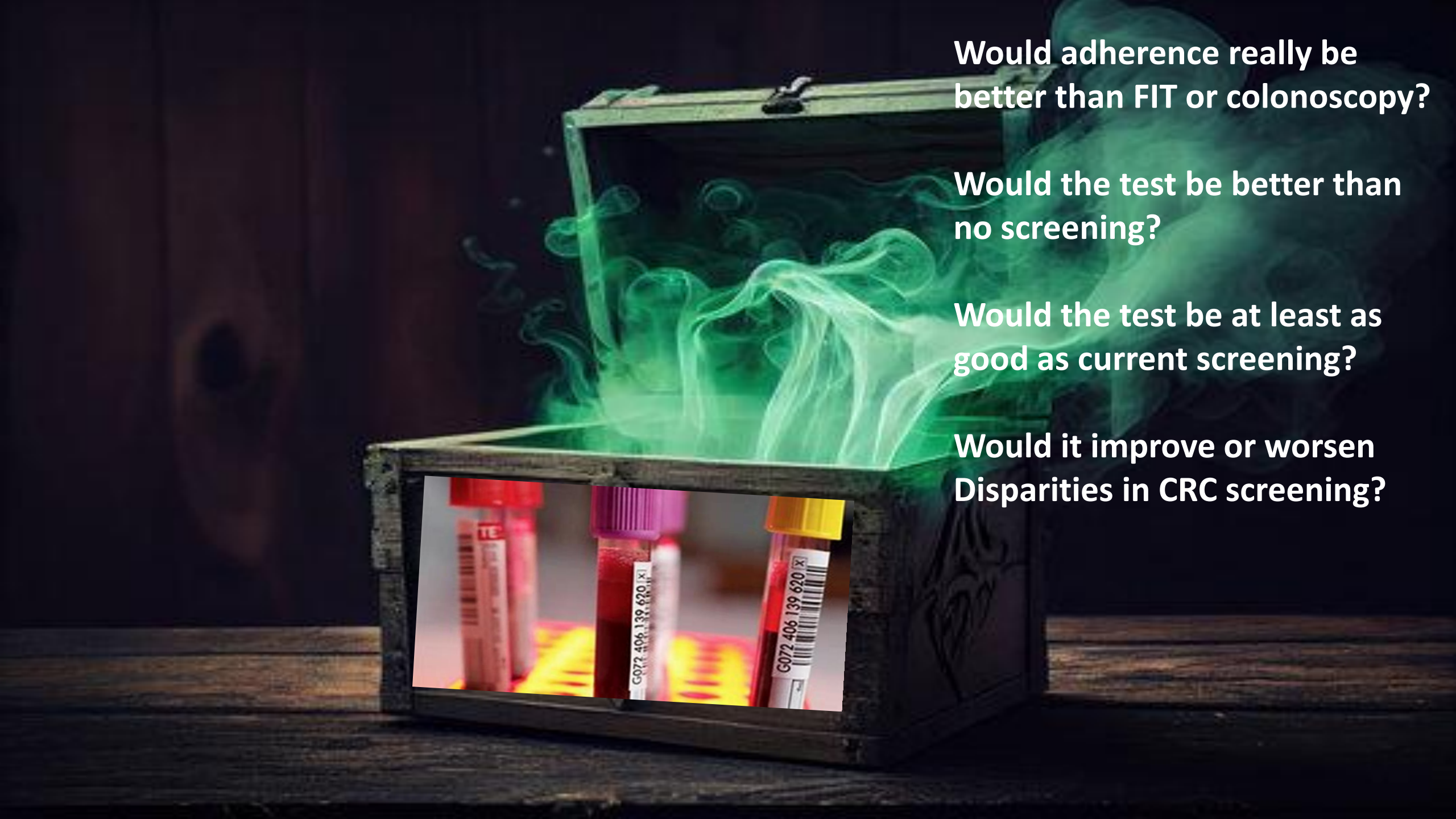
**That's ok. We can let  
Decision modelers figure it out**



OK – BUT IT MIGHT OPEN UP PANDORA’S BOX,  
WHICH IS PART OF ANOTHER STORY.....





A wooden box is shown with a glowing green smoke effect rising from it. In the foreground, there is a close-up of several blood test tubes with labels. The labels on the tubes include the text "G072 406 139 620 X".

**Would adherence really be better than FIT or colonoscopy?**

**Would the test be better than no screening?**

**Would the test be at least as good as current screening?**

**Would it improve or worsen Disparities in CRC screening?**

# AGA Workshop: Blood-Based CRC Screening

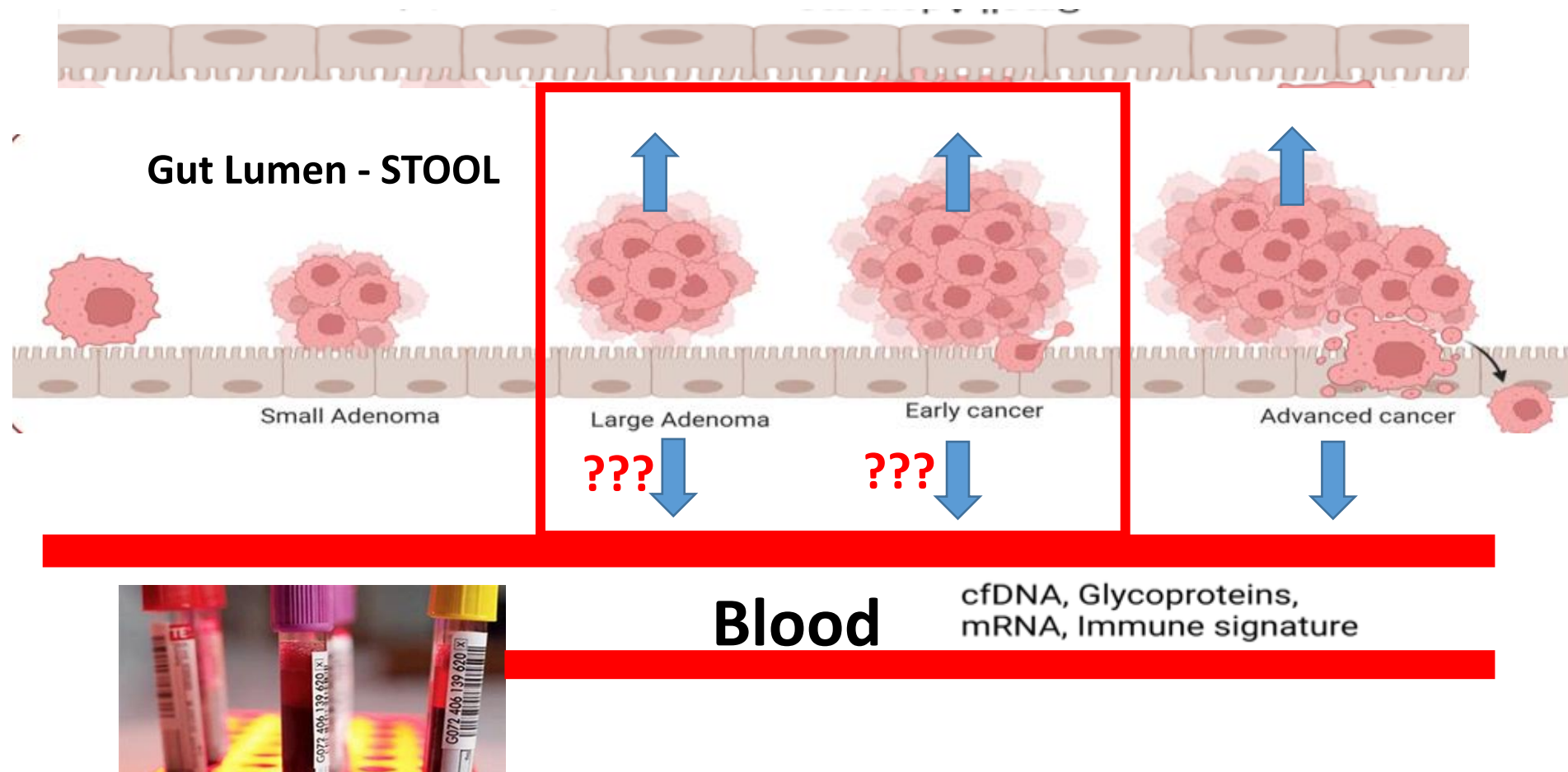
- Expert, multi-discipline panel
- Modeling groups:
  - CISNET – 3 models
  - Laudabaum model
- Charge to modeling groups:  
Using CMS minimum criteria (CRC Sens 74%; Spec 90%):
  - Compare with no screening
  - Compare to currently recommended tests: FIT, mt-sDNA, Colonoscopy
  - Endpoints of note:
    - CRC mortality
    - CRC incidence
    - QALYG
    - Cost effectiveness



# Blood-Based CRC screening results

Study	n	CRC Sens	AA Sens	Specificity	Invalid
CMS Minimum		74%	Not Included	90%	

# Stool and Blood-Based CRC Screening Tests



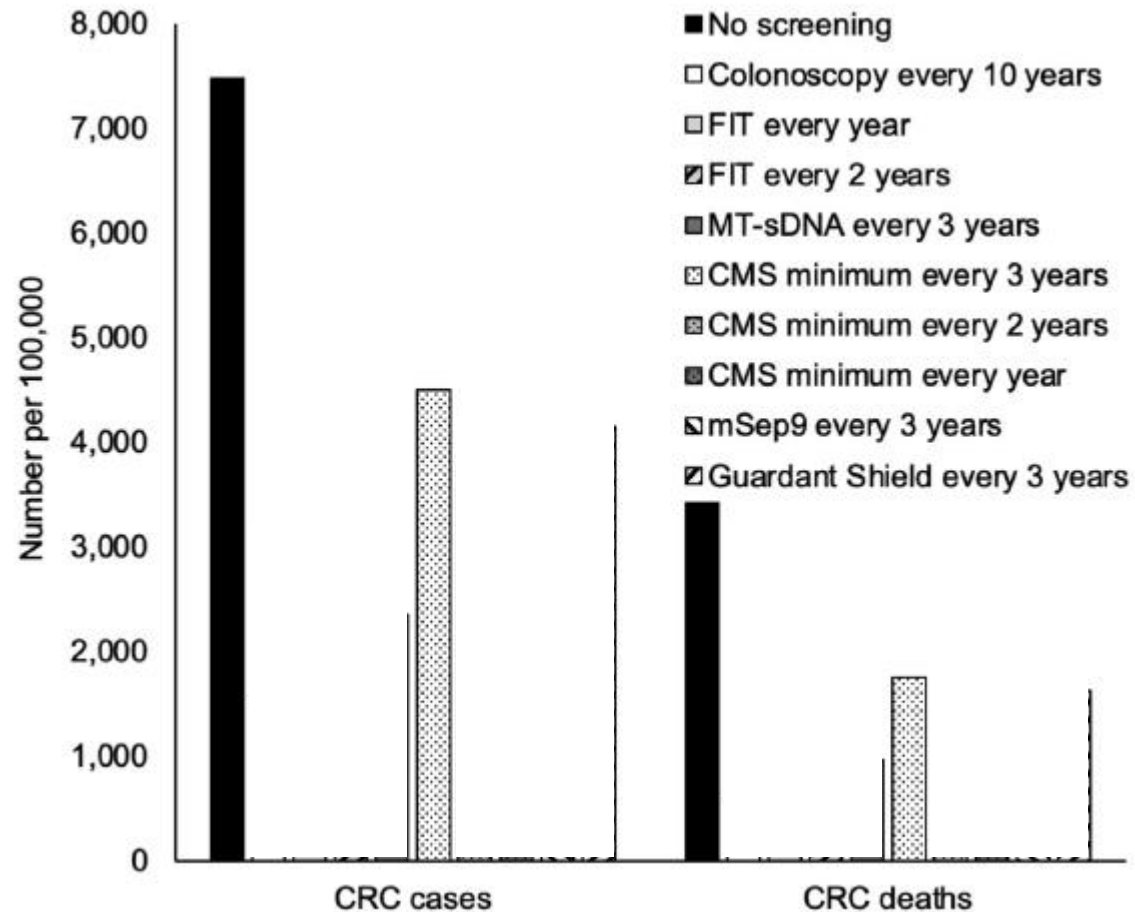


# Consensus Statements: New test vs No Screening

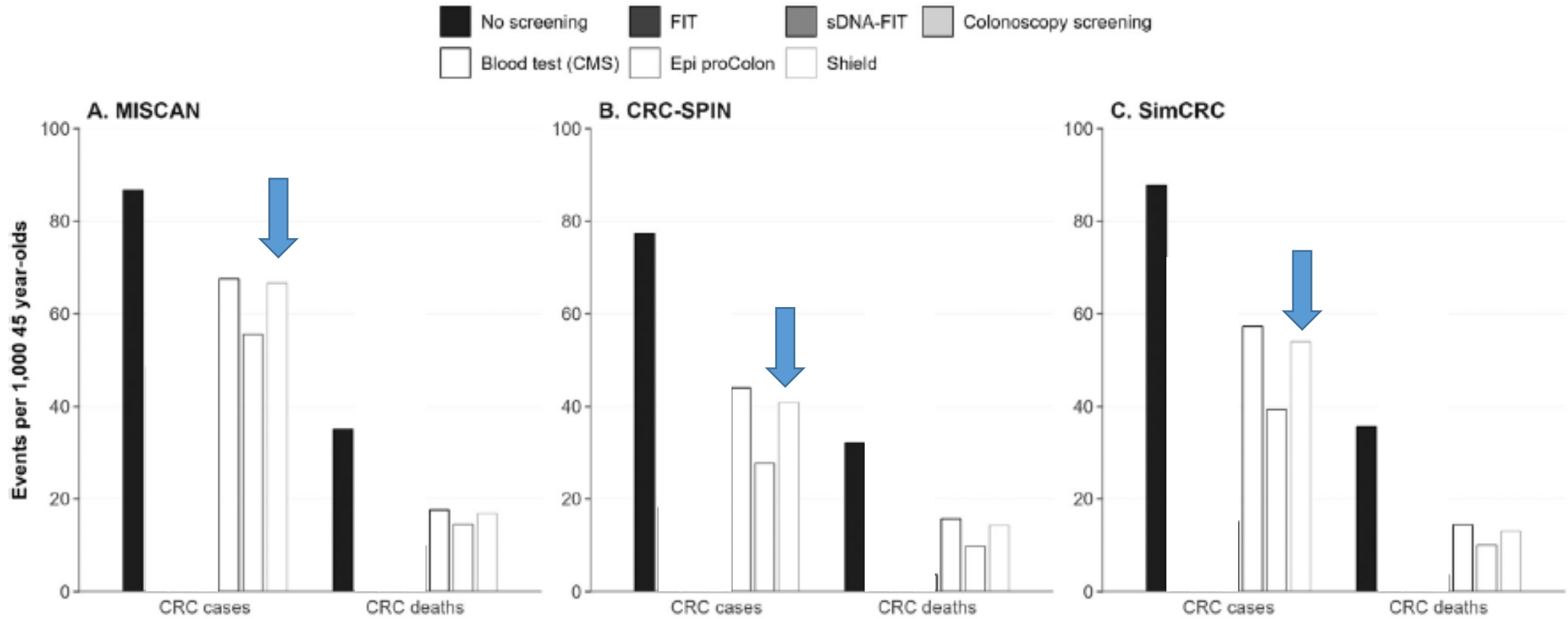
Statement	Comment
<p><b>New blood test compared to no screening:</b></p> <ol style="list-style-type: none"><li>1. A new test which improves outcomes compared to no screening can be recommended to individuals who decline any current screening test</li><li>2. Based on modeling, a blood test meeting CMS criteria* is <b>better than no screening</b></li></ol>	<p>Blood test could expand screening pool to include more unscreened individuals</p>

\* CMS criteria: CRC sensitivity 74%; Specificity 90%:  
No criteria for advanced adenoma detection

# Laudabaum model



# CISNET



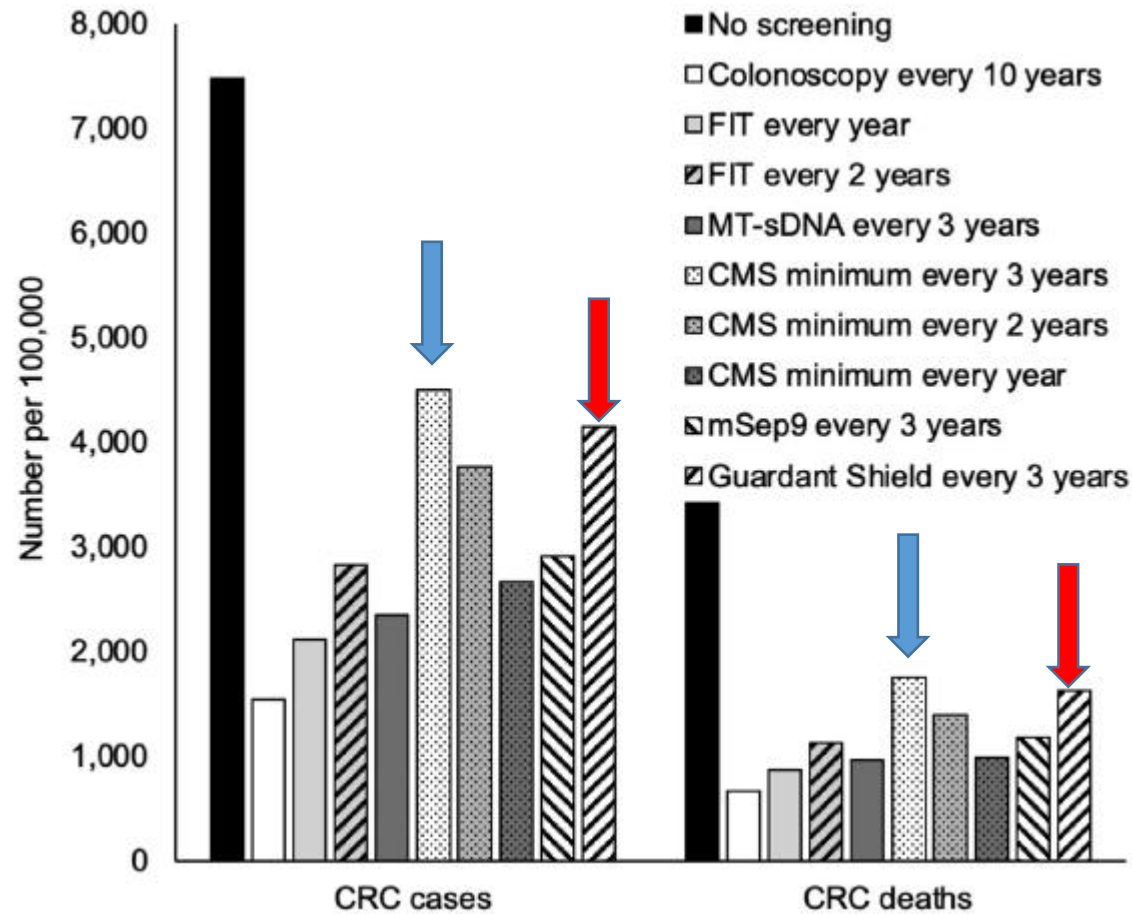
van den Puttelaar et al;  
<https://doi.org/10.1053/j.gastro.2024.02.012>



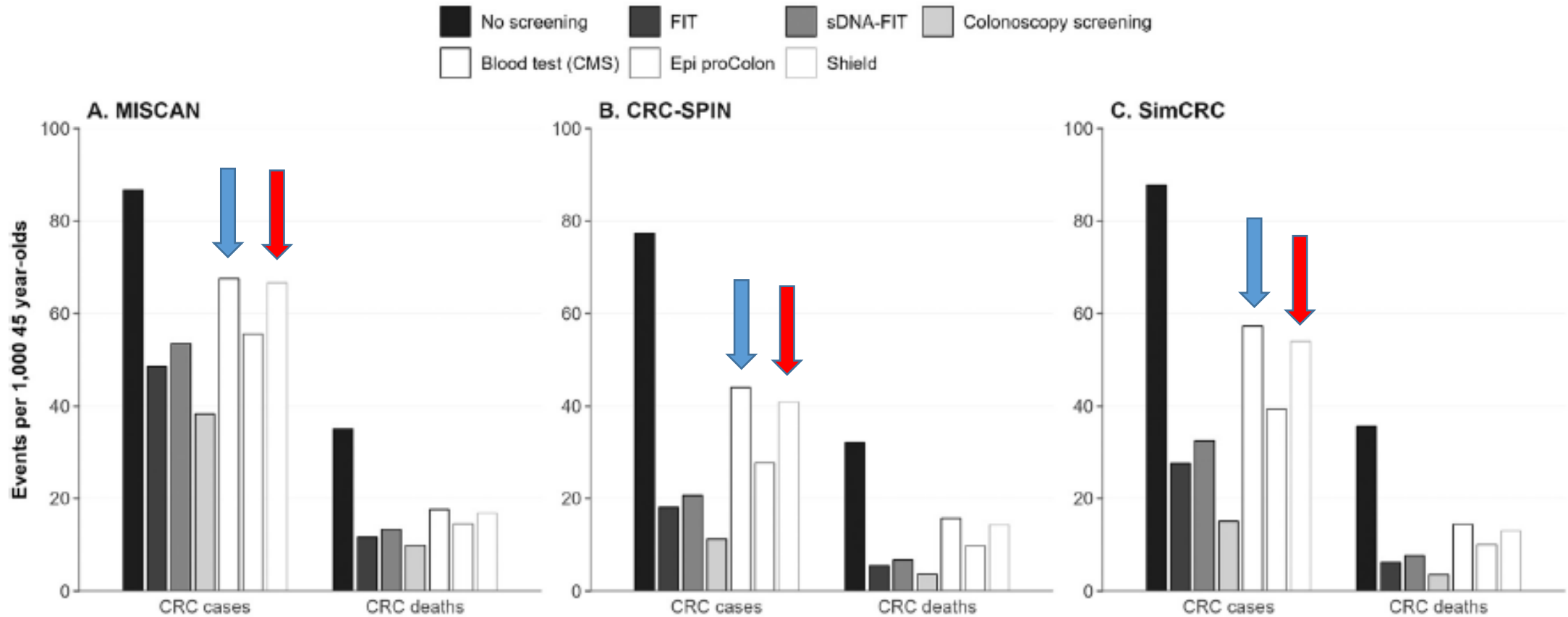
# Consensus Statements: New Test to Replace current test

Statement	Comment
<p><b>New blood test to replace current screening:</b></p> <ol style="list-style-type: none"><li>1. <u>Should be as effective or better</u> than current screening</li><li>2. A new test which is not equivalent, should <b><u>not</u></b> be recommended to replace current screening</li><li>3. Modeling demonstrates that a test meeting CMS criteria is <u>less effective</u> than current screening, with wide range of assumptions about adherence</li></ol>	<ol style="list-style-type: none"><li>1. Tests not meeting these criteria, may cannibalize effective tests and harm patient outcomes</li><li>2. Models indicate that detection of advanced adenomas is a key driver of effectiveness</li></ol>

# Laudabaum model



# CISNET



van den Puttelaar et al;  
<https://doi.org/10.1053/j.gastro.2024.02.012>



What would it take for Blood test to be as effective as current screening?

1. ? High adherence



# Laudabaum Model - Adherence

**Table 2.** Overall All-or-None<sup>a</sup> Participation Rates Required for Screening Every 3 Years With a Blood-Based Test That Meets Centers for Medicare & Medicaid Services' Minimum Performance Thresholds in Order for That Strategy to Match the Clinical Outcomes of Annual Fecal Immunochemical Testing at Varying Levels of All-or-None Participation Rates With Fecal Immunochemical Testing

Variable	Participation rate (%) with blood-based test every 3 y that yields outcomes equivalent to annual FIT (all-or-none over time)						
	Overall FIT participation rate of 10%	Overall FIT participation rate of 20%	Overall FIT participation rate of 30%	Overall FIT participation rate of 40%	Overall FIT participation rate of 50%	Overall FIT participation rate of 60%	Overall FIT participation rate of 70%
CRC cases prevented	18	36	54	72	90	Blood test cannot match FIT	Blood test cannot match FIT
CRC deaths prevented	15	29	44	59	74	88	Blood test cannot match FIT
QALYs gained vs no screening	14	28	43	57	71	85	Blood test cannot match FIT

QALYs, quality-adjusted life-years (discounted).

<sup>a</sup>For illustrative purposes, scenarios reflect perfect participation with every screening round over time in a given fraction of the population with a given test (defined as "participation rate"), and no screening at all in the remainder.

# CISNET - Adherence

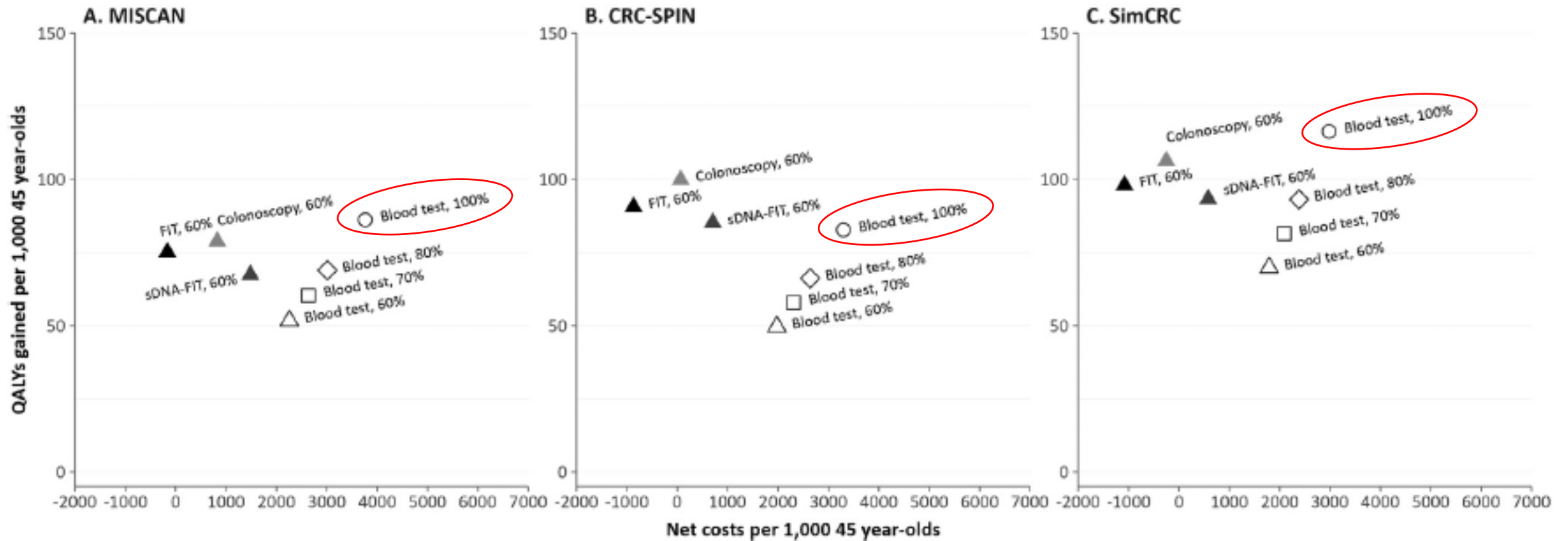


Figure 3. QALYs gained and net costs for a cohort of 45-year-olds with different uptake scenarios for FIT, sDNA-FIT, colonoscopy, and blood-based screening. Test characteristics of the blood test were based on the CMS coverage criteria. Costs are expressed in thousands (eg, 5000 is 5,000,000).

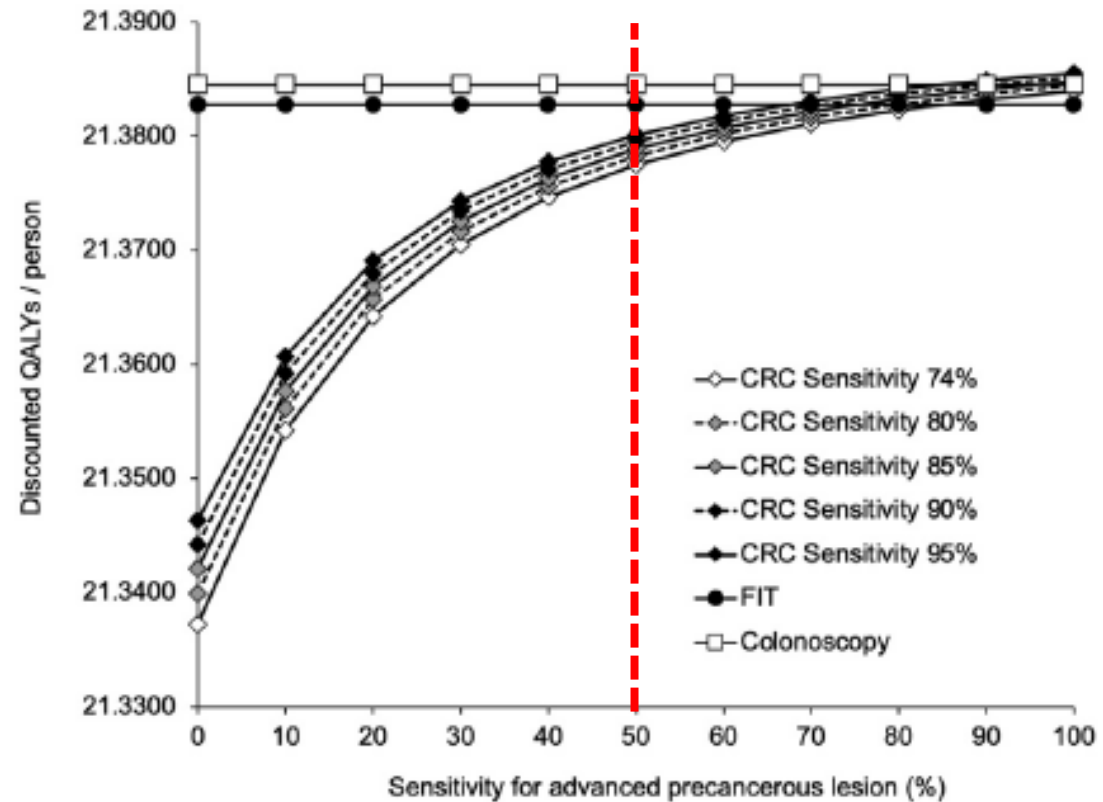


What would it take for Blood test to be as effective as current screening?

1. High adherence
2. **Adenoma Detection**



# Laudabaum Model – Advanced Adenoma Detection



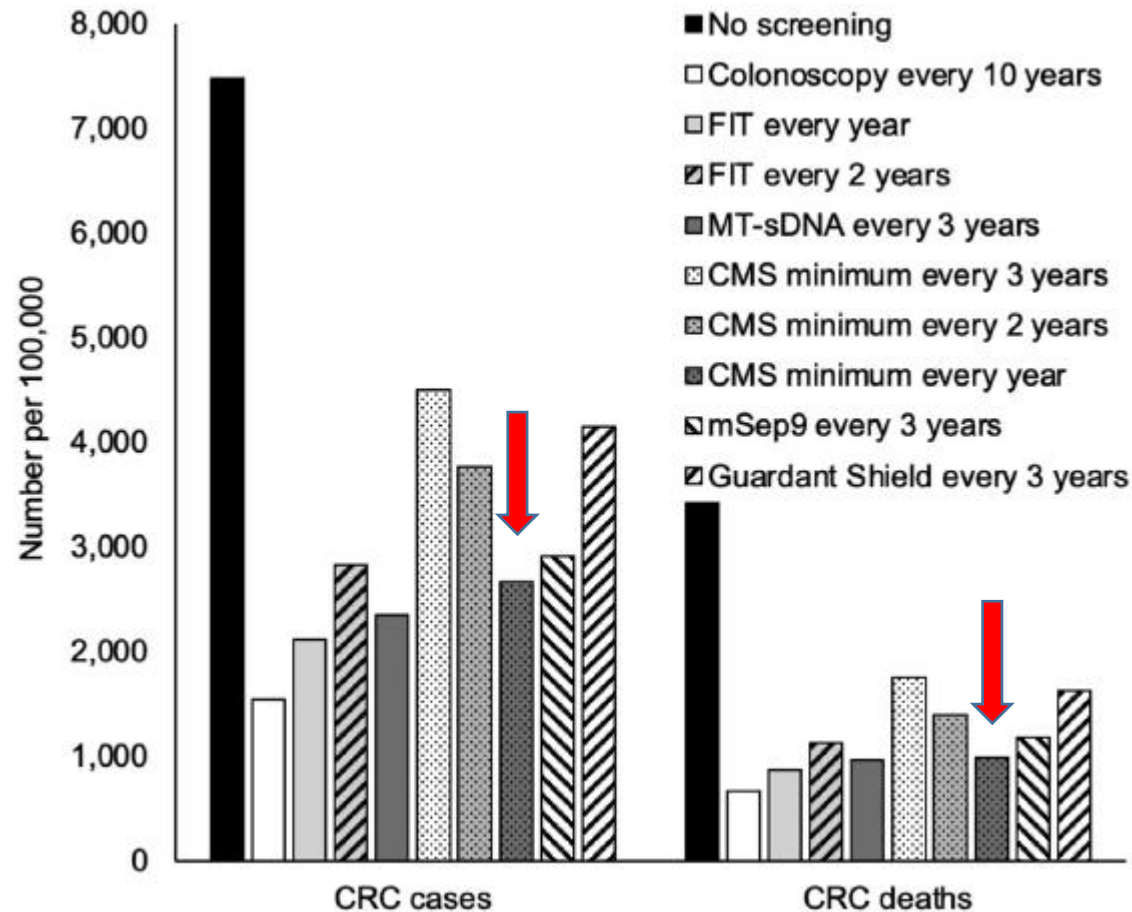
**Figure 3.** Impact of sensitivity for APL on the effectiveness of a blood-based test performed every 3 years. Improving APL sensitivity had a much greater impact than improving CRC sensitivity. FIT screening is annual. Colonoscopy screening is every 10 years.

What would it take for Blood test to be as effective as current screening?

1. High adherence
2. Adenoma Detection
3. **Test Interval: 1 year**

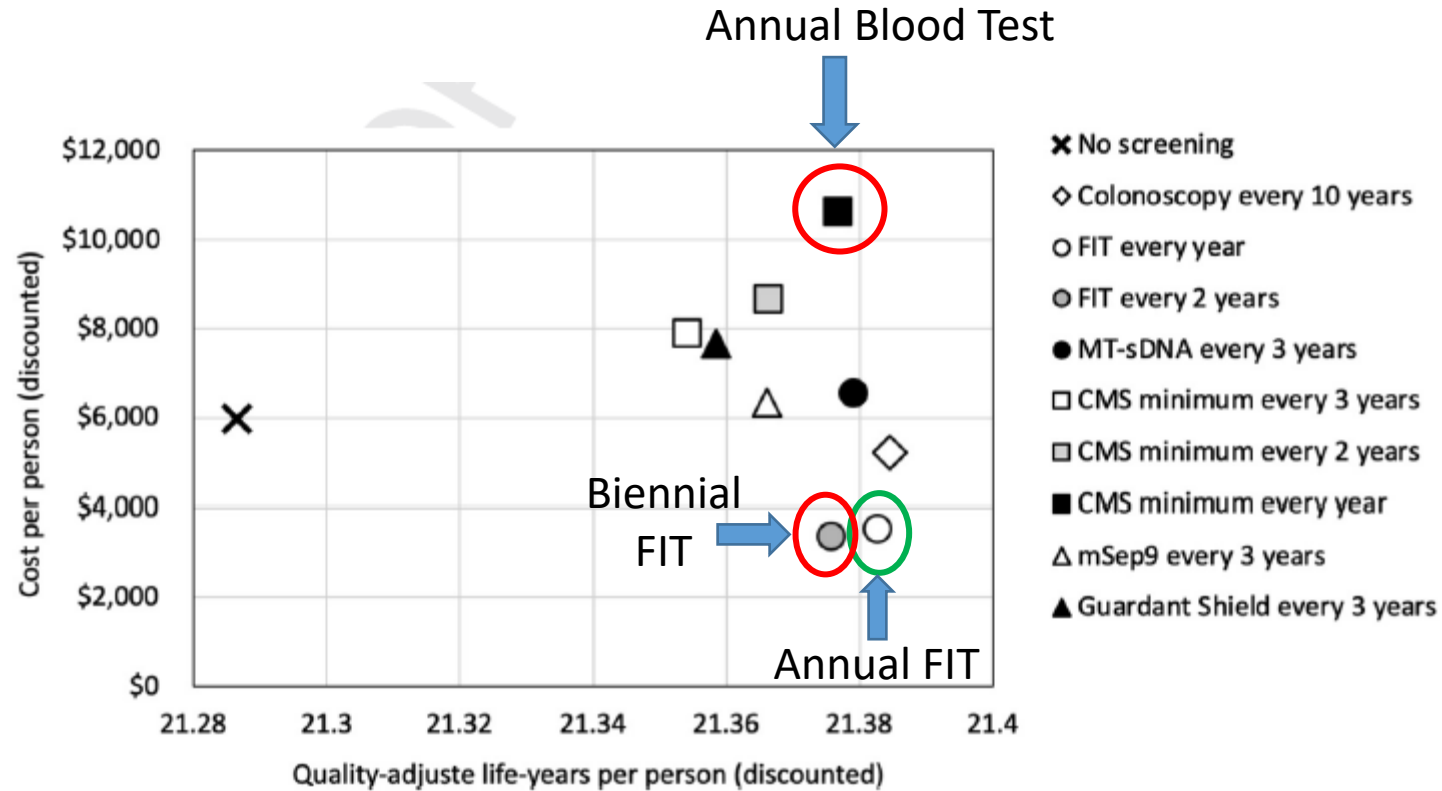


# Laudabaum model



**Annual test can achieve results similar to biennial FIT**

# Laudabaum Model



Cost assumption: \$500/test



# Consensus Statements: Disparities

Statement	Comment
Key outcomes of screening: improve CRC outcomes	Reduce CRC mortality, incidence Increase QALYG
New blood test improves outcomes compared with no screening based on modeling	Could expand screening pool
New blood test should NOT be recommended to replace current tests	Modeling shows that outcomes would worsen if a new test meeting CMS criteria replaced current tests
<b>Any new test should NOT worsen disparities</b>	<b>New blood test could worsen existing disparities due to</b> <ol style="list-style-type: none"><li><b>1. Access, cost, insufficient navigation</b></li><li><b>2. Lack of trust in health care system due to concerns about genetic information</b></li></ol>

# High Level Consensus Blood-Based CRC Screening

- Evidence suggests that **adherence would be higher** than stool test or colonoscopy
- Compared to **no** screening:  
*CMS minimum has **better outcomes***  
**Can be recommended to those who decline other tests**
- Compared to **current tests**:  
*CMS minimum has **inferior outcomes** and is more costly across a wide range of different assumptions*  
**Cannot be recommended to replace other tests**
- To achieve comparable clinical outcomes to current tests:
  - Adherence needs to be **very high** – 80-90%
  - Advanced adenoma detection needs to be >30-50%
  - Frequency of testing may need to be annual



What will the next story be?

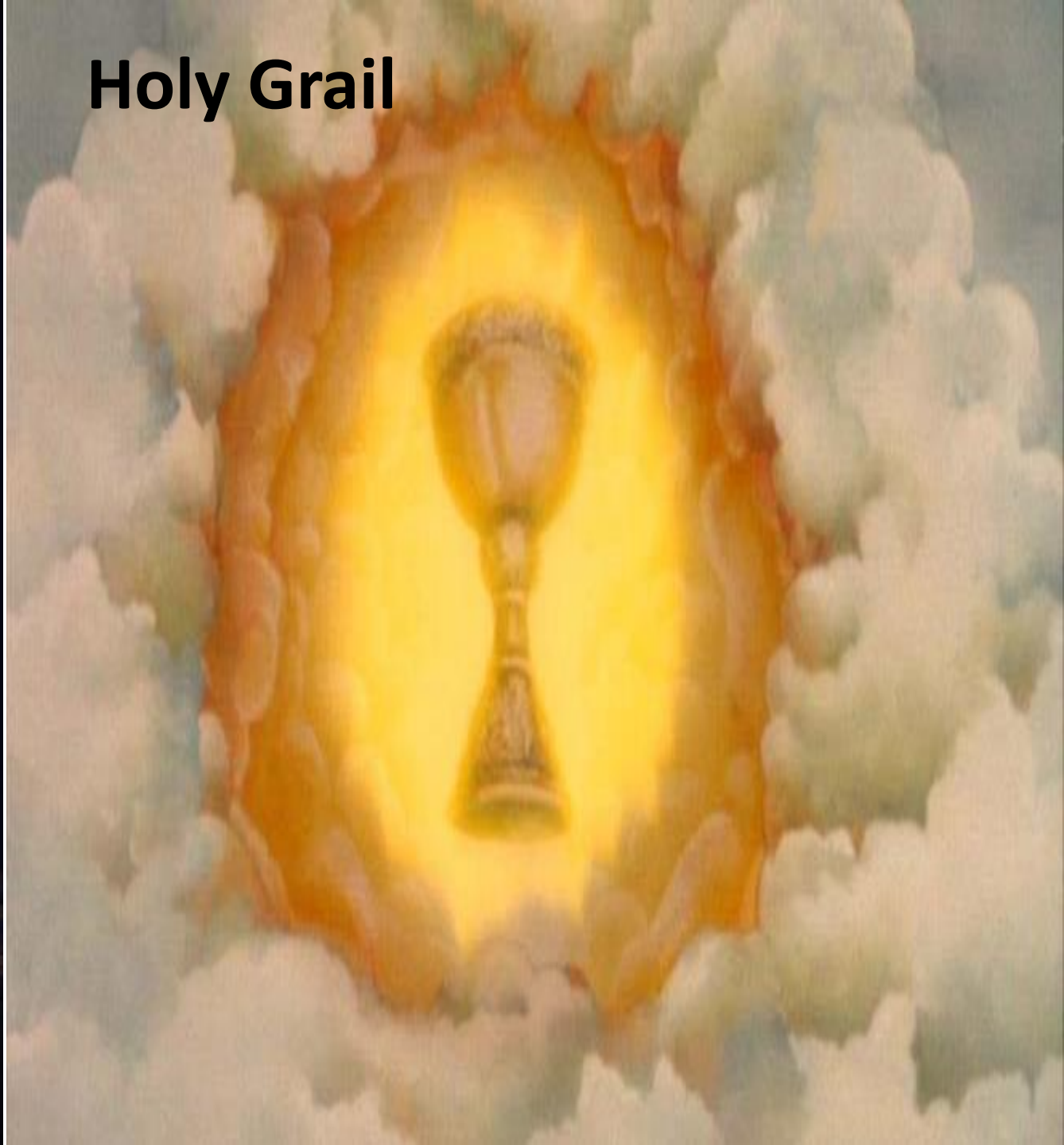




**Pandora's Box**



**Holy Grail**



*Stay*  
TUNED