Could fecal immunochemical tests (FIT) be used to identify individuals who do not have colorectal neoplasia?

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How best to use colonoscopy resources?

Current approach:

- Use qFIT to find cases with a high-risk of colorectal cancer (CRC)

- Follow-up those cases with colonoscopy if FIT-positive

However:

- Current qFIT positivity thresholds in use can miss at least 20% of CRCs (even >50%)

- Recent evidence*: very low f-Hb suggests a low chance of having CRC or advanced precursors (AP).

QUESTIONS: *Would a low f-Hb rule out (or delay) the need for colonoscopy* in those who are symptomatic, undergoing CRC high-risk surveillance or average-risk screening?

* Wassie et al. *Clin Gastro Hepatol* 2023; 21:2389-2398

AIMS & POPULATION

Aims

- Can FIT be used to identify subjects in a CRC surveillance population with a very low risk for CRC or advanced precursors?
- What f-Hb level is needed for this?
- Are existing FIT sufficiently sensitive for this purpose?

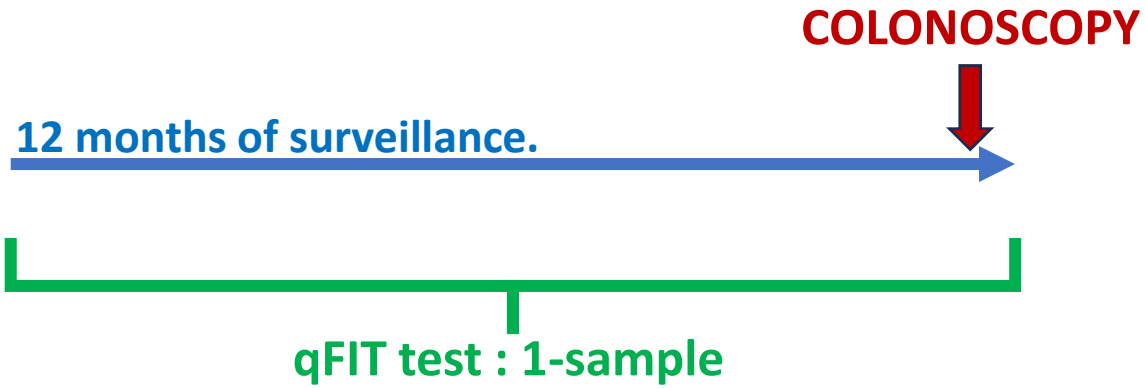
Population

- An observational study
- Subjects undergoing surveillance colonoscopy in the SCOOP program* for individuals at elevated risk for CRC (due to family history of CRC or personal history of neoplasia),
- who had completed a 1-sample FIT in the interval between colonoscopies (n = 32,485 tests).

* Symonds EL et al. *Med J Aust* 2018; 208:492-6

METHODS

- Fecal hemoglobin levels (f-Hb) were determined using the qFIT OC-Sensor (Eiken Chemical Co., Tokyo, Japan;
  - limit of detection (LoD) previously 3.8, now 1.8 μg Hb/g feces).
- FIT accuracy for CRC and advanced neoplasia (AN; inclusive of CRC or AP), was estimated across a wide range of f-Hb positivity thresholds in the subgroup who had undergone colonoscopy in the 12 months following a FIT (n = 4,110).

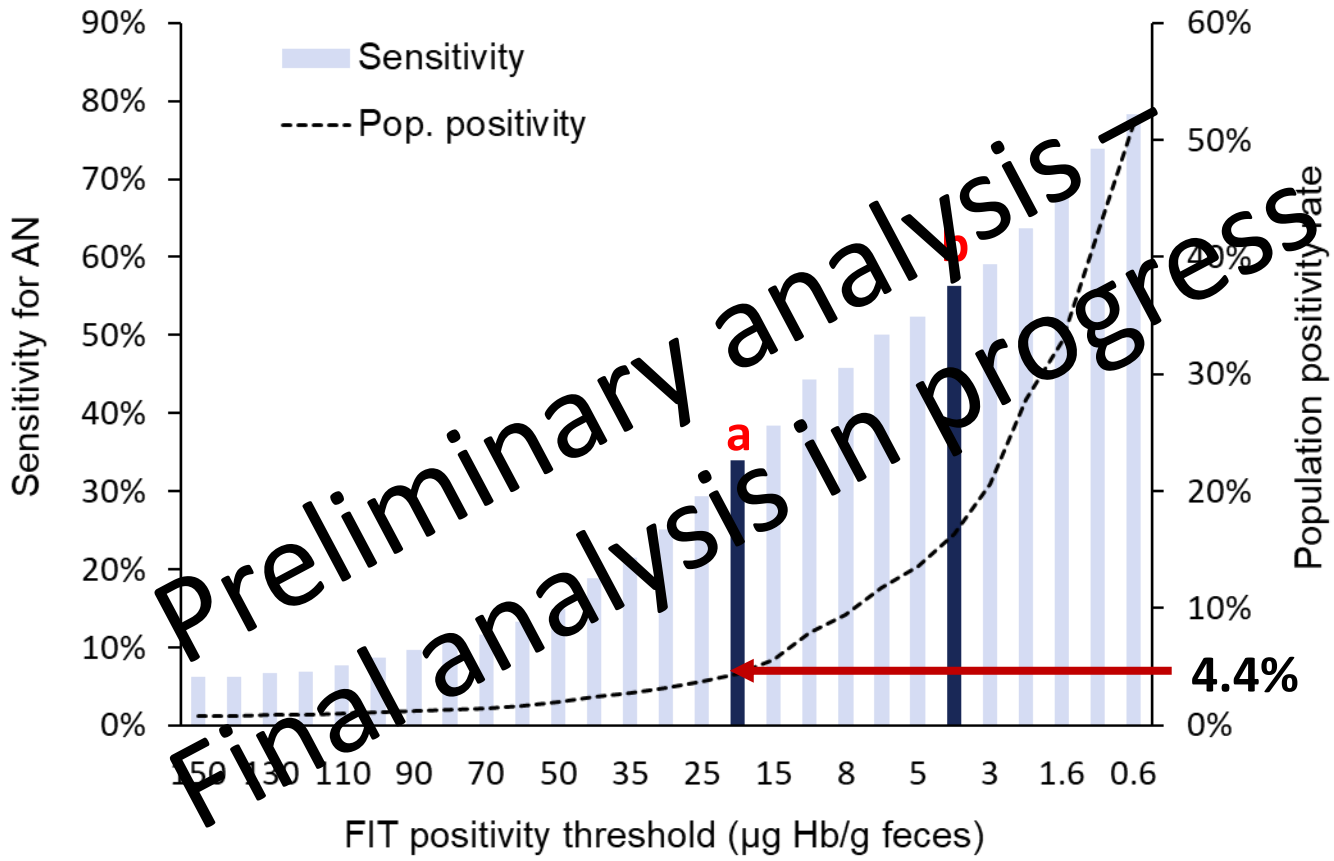


- Predictive values for CRC or AP at different f-Hb thresholds were estimated using the entire population.

*AP includes: adenomas with features of size ≥ 10 mm, high grade dysplasia, or villous change, or ≥ 3 small tubular adenomas; sessile serrated lesions with dysplasia, or traditional serrated adenomas.

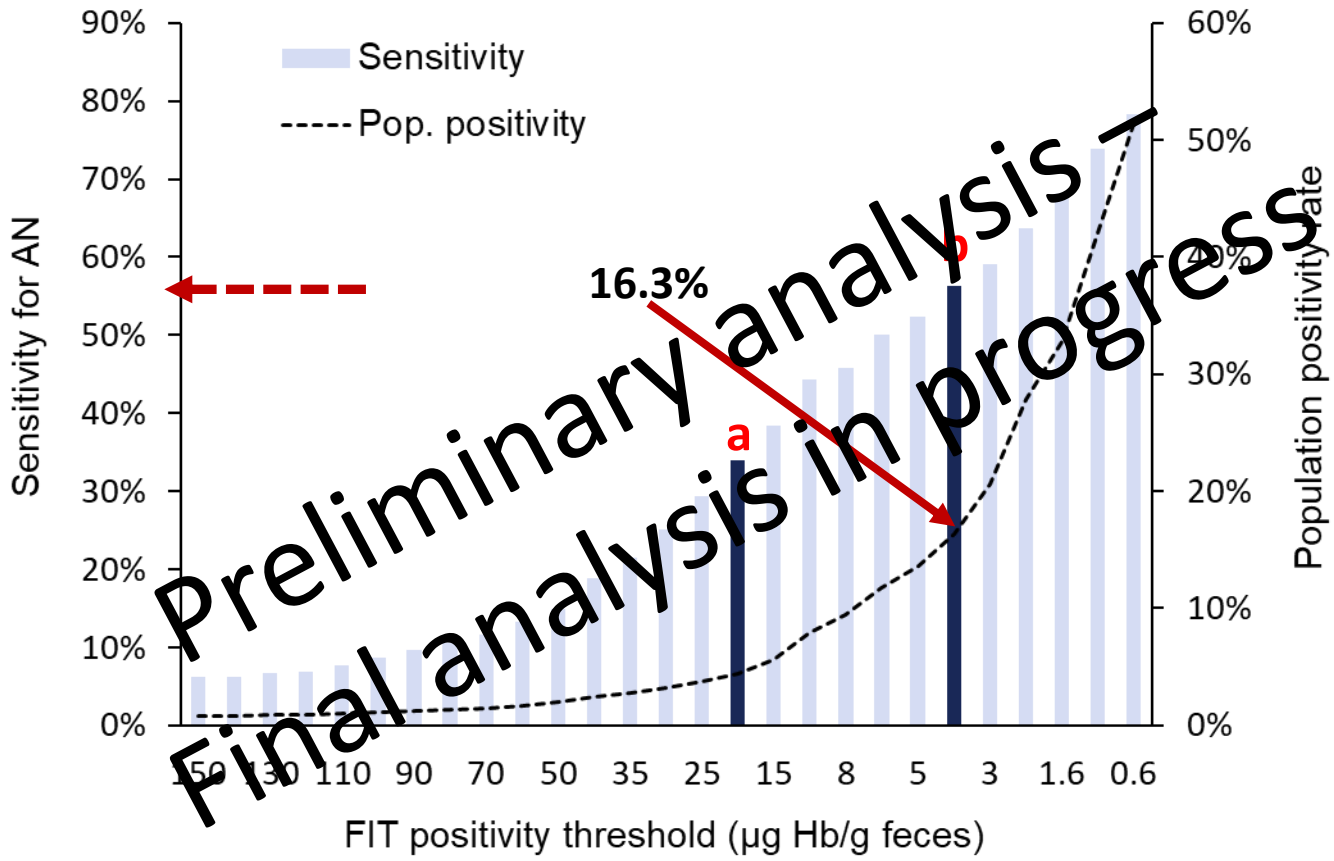
RESULTS – population and threshold implication

- The colonoscoped population included 94 with CRC (2.3%) and 603 with AP (14.7%), the rest had non-significant or no pathology.
- As thresholds were lowered from 20 µg/g (a threshold commonly used in CRC screening; see **a**), the population positivity rate (the colonoscopy workload) rose very quickly from 4.4%, compared to the rate of rise in sensitivity for CRC or advanced precursors (AN).

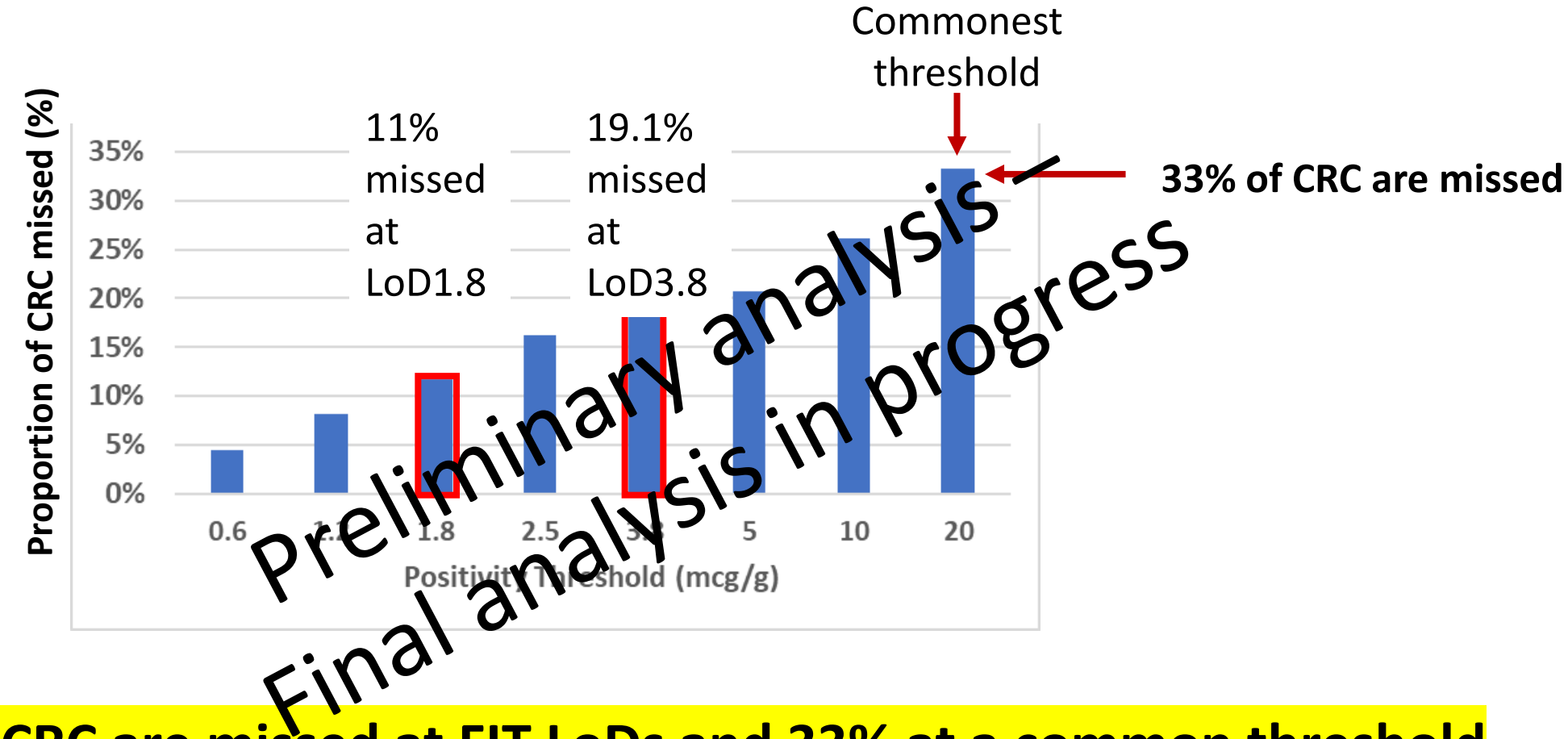


RESULTS – fewer neoplasms are missed at lower threshold

- At a test LoD of 3.8 µg Hb/g (see **b**):
  - sensitivity for advanced neoplasia (AN) was 56.3%.
  - But 16.3% of the population would need colonoscopy.
  - However, *19.1% of CRC would still have been missed* (next slide).



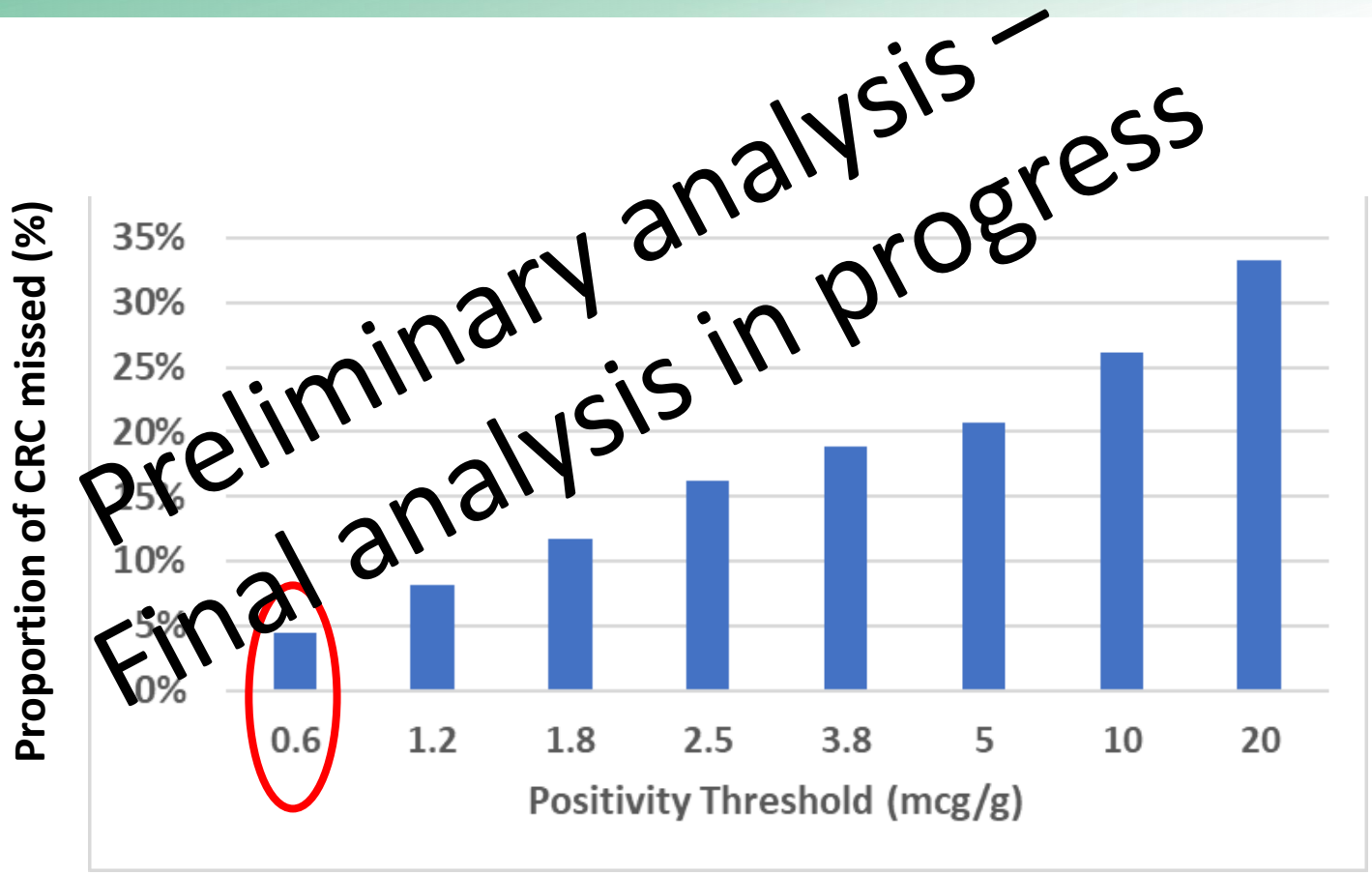
Proportion of CRC missed at FIT LoDs



11-19% CRC are missed at FIT LoDs and 33% at a common threshold

To detect 95% of CRC, a lower threshold is needed

- If a threshold of ***0.6 µg/g*** (below any FIT's Limit-of-Detection) were feasible,
  - 5% of CRC would have been missed,
  - 78% of all CRC and advanced precursors would have been detected,
  - And colonoscopy could have been delayed or avoided **in 48.6%** of the surveillance population.



Comments and Conclusions

- Contexts where rule-out or delay of colonoscopy might be applicable
  - Symptomatic cases,
  - Colonoscopic surveillance in above-average-risk people (this study)
  - FIT-based screening (colonoscopic screening is also practiced)
- A low f-Hb could be used to rule out or delay the need for colonoscopy, but what risk is acceptable in each and would different thresholds apply?
- At the best currently available LoD, 11% CRC would have been missed.
- 15-20% are missed below LoQ.
- A threshold of 0.6 mcg/g (well below the LoQ and LoD) is required to achieve a miss rate of ≈5%.
- Existing qFIT do not have the required analytic sensitivity and it is speculative to set the threshold based on this modelling.
- **FITs with high analytic accuracy at low f-Hb levels need to be developed for widespread application of a FIT-based rule-out or delay strategy for colonoscopy.**