One *vs* two FIT sampling?

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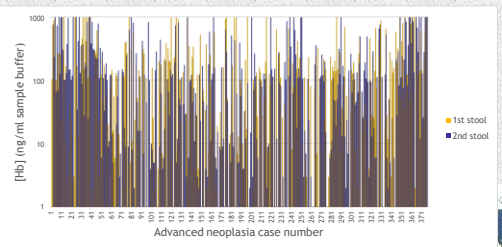
Outline

- Strategies to answer the question:
  - Logic (Key Considerations)
  - Modelling (accuracy)
  - Published Evidence (accuracy and participation)
- "DEW" analysis
  - Detection - Sensitivity
  - Effort – NNC (1/PPV)
  - Workload – test positivity
- Conclusions

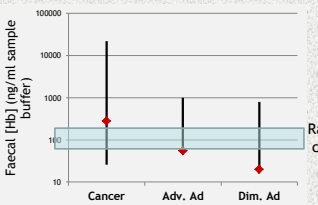
Key considerations - 1

1. If lesions bled into the same sized stool at the same rate each day we would only need one sample.



Key considerations - 2

2. Multiple stool sampling becomes more likely to be useful when the faecal [Hb] is close to the criterion value for positivity (the cut-off).
   - In other words, multiple sampling might not be needed for detection of cancers but is likely to be critical for detection of adenomas.



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The question

- How does a 1-sample compare to a 2-sample test in terms of accuracy and acceptance?
  - Can we use adjusted cut-off values with quantitative FIT, to advantage?

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Modelling - Informative data

- Characteristics of the data set (for performance)
  - Population: a screening population where colonoscopy has been done.
  - Intervention: a 2-sample quantitative FIT done on cases prior to colonoscopy.
- Data set used:
  - Personalised screening program (many at increased risk), n=17,331. OC-Sensor used.
  - Colonoscopy done regardless of FIT result in 2,078.
- Outcomes to be reported:
  - Sensitivity by lesion class
  - Specificity and resultant workloads at selected sensitivities
  - (Alternatives: ROC optimal point, selected FPR, selected colonoscopy workload)

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Modelling - Informative data

Details withheld as model development is still underway

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Principles emerging from modelling

- High Cancer sensitivity (near 90%)
  - 2-sample@20 is slightly more efficient than 1@10
- 80% sensitivity for cancer
  - 2-sample@40 is the most efficient
- Advanced lesion detection
  - 2-sample@20 is better than 1 or 2@10.
- Little use for 2-sample @10

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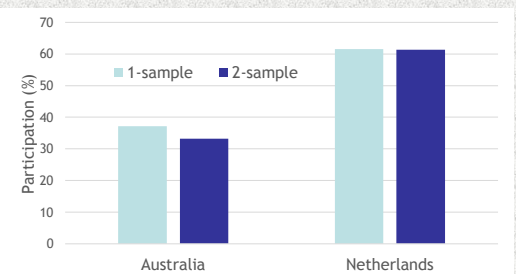
Participation



- Australia: Cole S et al, DDW 2006. n=1,200 (p=0.16)
- Netherlands: van Roon AH, CGH 2001. n=8,000+

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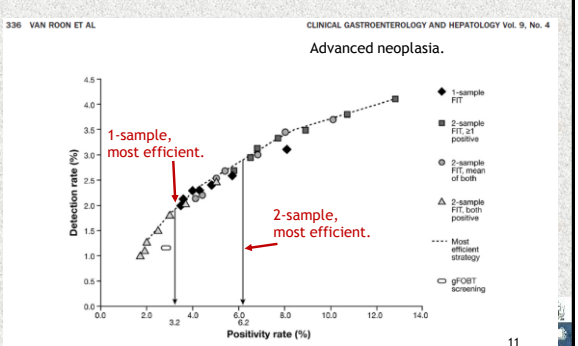
Evidence - France

Table 2. Comparison of Clinical Performances of Hemoccult II, Magstream, and OC Sensor Fecal Occult Blood Tests in Study Conditions, and According to Manufacturer Guidelines (Extrapolated)

		Study cut-off value[a]				Manufacturer cut-off value	
		Magstream FIT		OC Sensor FIT		Magstream FIT	OC Sensor FIT
	Guaiac test	1 sample	2 samples	1 sample	2 samples	1 sample	1 sample
Cut-off value (μg hemoglobin/g of stools)	NA	180	180	30	30	80	20
Cut-off value (ng hemoglobin/mL in the buffer)	NA	55	55	150	150	20	100
Positives	316	390	632	551	801	548	694
(positivity rate, %)	(1.60)	(1.97)	(3.19)	(2.78)	(4.05)	(2.77)	(3.51)
Colonoscopies	277	344	554	488	712	484	615
(colonoscopy rate, %)	(87.7)	(88.2)	(87.7)	(88.6)	(88.9)	(88.3)	(88.6)
Advanced neoplasias	83	146	210	225	290	209	275
(positive predictive value, %)	(30.0)	(42.4)	(37.9)	(46.1)	(40.7)	(43.2)	(44.7)
(true-positive rate, %)	(0.42)	(0.74)	(1.06)	(1.14)	(1.46)	(1.06)	(1.39)
Number needed to scope	3.3	2.4	2.6	2.2	2.5	2.3	2.2
Number needed to screen	238.5	135.6	94.3	88.5	68.3	94.7	72.0
Invasive cancers		146	210	225	290		44
(positive predictive value, %)		(42.4)	(37.9)	(46.1)	(40.7)		(7.2)
(true-positive rate, %)		(0.74)	(1.06)	(1.14)	(1.46)		(0.22)
Number needed to scope							14.0
Number needed to screen							449.9
False positives		2.4	2.6	2.2	2.5		340
(false-positive rate, %)		(0.98)	(1.66)	(1.74)	(2.13)		(1.72)

[a]Study cut-off value for Magstream is designed to equal the same number of false-positive results as Hemoccult II, as derived from prior studies. Study cut-off value for OC Sensor is designed to ensure comparability with other studies, while limiting the colonoscopy workload.

Finer adjustment – ROC analysis



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Conclusions

- There is no obvious participatory advantage.
- Decide:
  - if goal is detecting cancers or cancers and advanced adenomas. *If cancer*, 2-sample test is most efficient.
- *If it is advanced adenomas:* 3-dimensional DEW analysis shows that 2-samples@20 is best.
- Next steps:
  - make finer adjustments of the criterion value based on the ROC curve.
  - Full cost analysis including cost of test kits and small differences in participation.

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