



The ideal number of samples for FOBT screening.

Graeme P Young




Background

- Bleeding from colorectal cancer has been considered to be intermittent, based on the early crude tests for faecal occult blood.
- For decades now, use of FOBT of any technology has often utilised more than one sample to reduce the chance of missing lesions because of variations in faecal blood levels that fall below the detection limit.
- Traditionally, FOBT have used two and usually three stool samples to reduce the risk of false negative results due to intermittent or variable bleeding.



Survey results

No. of samples collected	Test used	
	GFOBT	FIT
One	5 (13%)	22 (54%)
Two	3 (8%)	16 (39%)
Three	31 (79%)	3 (7%)



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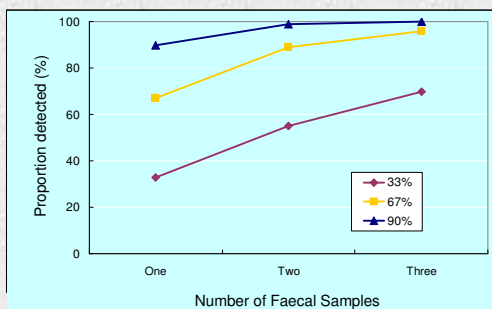
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Chance of detection by sample number

Once-off sensitivity of test	Detection Rate		
	One sample	Two samples	Three samples
33%	33%	55%	70%
67%	67%	89%	96%
90%	90%	99%	99+%



Chance of detection by sample number



Main variables affecting detection

- Criterion (cut-off) chosen for positivity
 - Dictates the positivity rate
 - Represents the colonoscopy rate
 - Is the sum of the true- and false-positives
- Number of samples collected and tested



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Detection is not the only issue.

Several simple questions will ultimately drive our choice:

- At what point does doing extra colonoscopies not justify the effort?
- How many colonoscopies do we believe we can do in a target population?
- Does increasing sample number reduce participation?
- Does increasing sample number substantially influence cost of the FOBT?



Practical application

- Are those cases detected by a two-sample method, also detected by a one-sample method set at a lower threshold?
- FIT-tested screening/surveillance population comprised of 4325 people, where a cut-off of 100ng/ml haemoglobin (in the sampling device) was used to trigger colonoscopy.
 - OC-Sensor Dianna (Eiken)



Detection and effort

Haemoglobin Cut-off Sample Number	Cancers or significant adenomas detected	Positivity Rate	Number needed to colonoscope to detect one lesion
200ng/ml; 2 samples (n=166)	55 (69%)	4.2%	3.3
150ng/ml; 2 samples (n=204)	62 (78%)	5.2%	3.6
100ng/ml; 2 samples (n=272)	80 (100%)	6.9%	3.7
100ng/ml; 1st sample (n=175)	53 (66%)	4.5%	3.7

*Provided either was positive at 100ng/ml



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Detection and effort

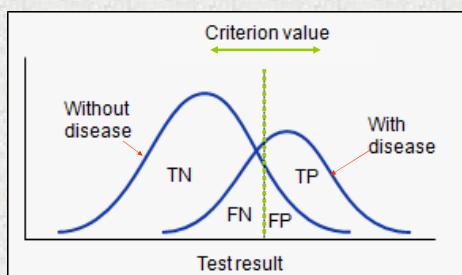
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100ng/ml; 1st sample (n=175)	53 (66%)	4.5%	3.7
50ng/ml; 1st sample* (n=196)	62 (78%)*	6.9%	(4.8)

* Difference 0.42%, 95%CI 0.22 to 0.61%

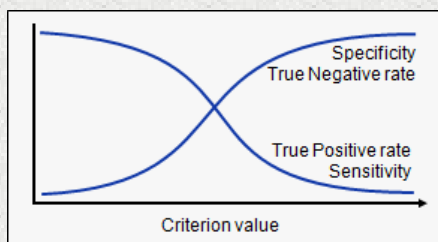
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Background Theory



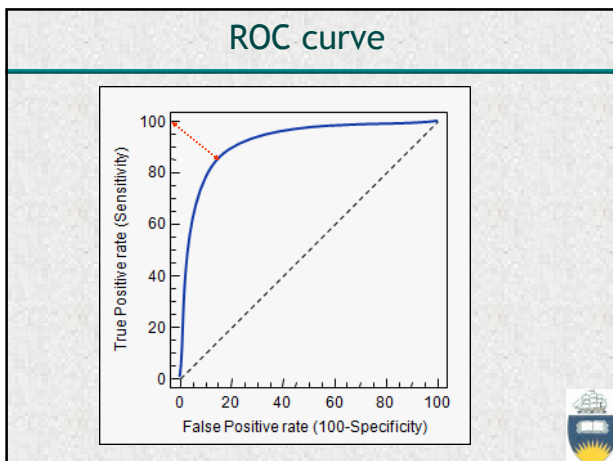
Criterion for cut-off and true-positives

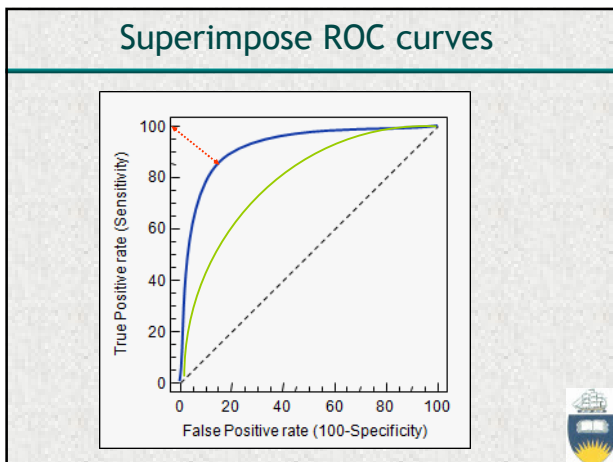


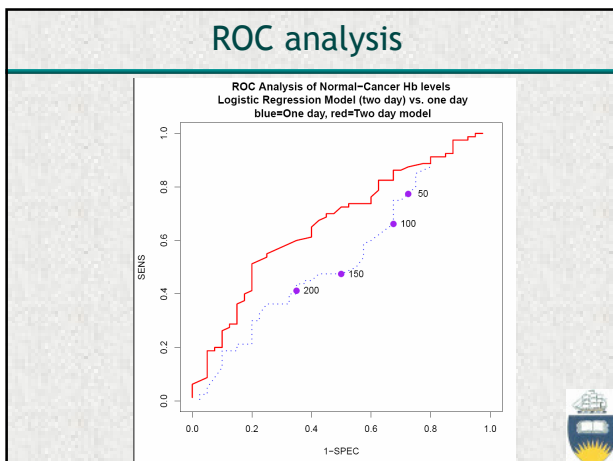
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Conclusions

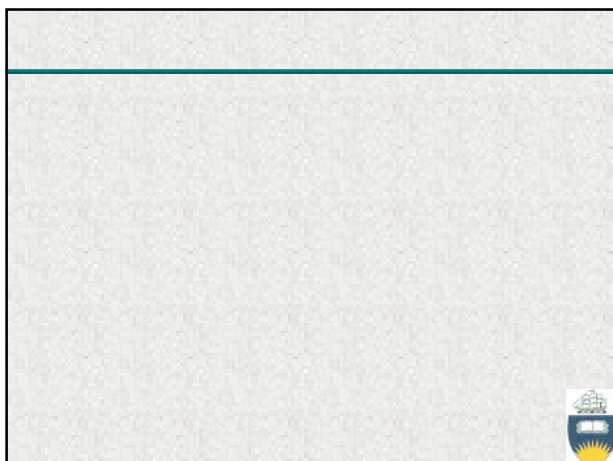
- We remain uncertain still as to the best approach in terms of sample-number/threshold trade-off
 - 2-sample approach seems better
- For sure, some lesions detected by a two-sample approach are not detected by a more sensitive one-sample approach.
- Detection alone cannot be the only criterion:
 - Participation, extra colonoscopic effort to achieve detection need consideration



Participation

- 1200 invitees aged 50-75 years were selected at random from the Australian electoral roll and allocated to either two-stool or single-stool mode.
- Identical invitations-to-screen for CRC were sent by mail and included test kits with instructions for either two-stool or single-stool mode.
- End point: participation in screening at 12 weeks from invitation.
- Results: Two-stool mode: 199/600, 33.2%; One-stool mode: 223/600, 37.2% (p=0.16).





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