

Global colorectal cancer screening - appropriate or practical?

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FLINDERS CENTRE
for INNOVATION
in CANCER



Outline

- WHO criteria to justify screening
- Appropriateness:
 - Global variation in incidence
 - Who is screening?
 - What test is used and how is it implemented?
- Practicality:
 - Context.
 - Constraints and expectations.
 - Screening program elements
 - Program philosophy - matching the test



WHO criteria for screening

CRC itself:

- must be an important problem ? **appropriate**
- have a suitable natural history, be accurately diagnosable and effectively treated in the early stages 😊

The test should:

- Be shown in the absence of bias to reduce mortality (and incidence) 😊
- Be cost-effective 😊
- Be acceptable to the people being targeted ? 😊

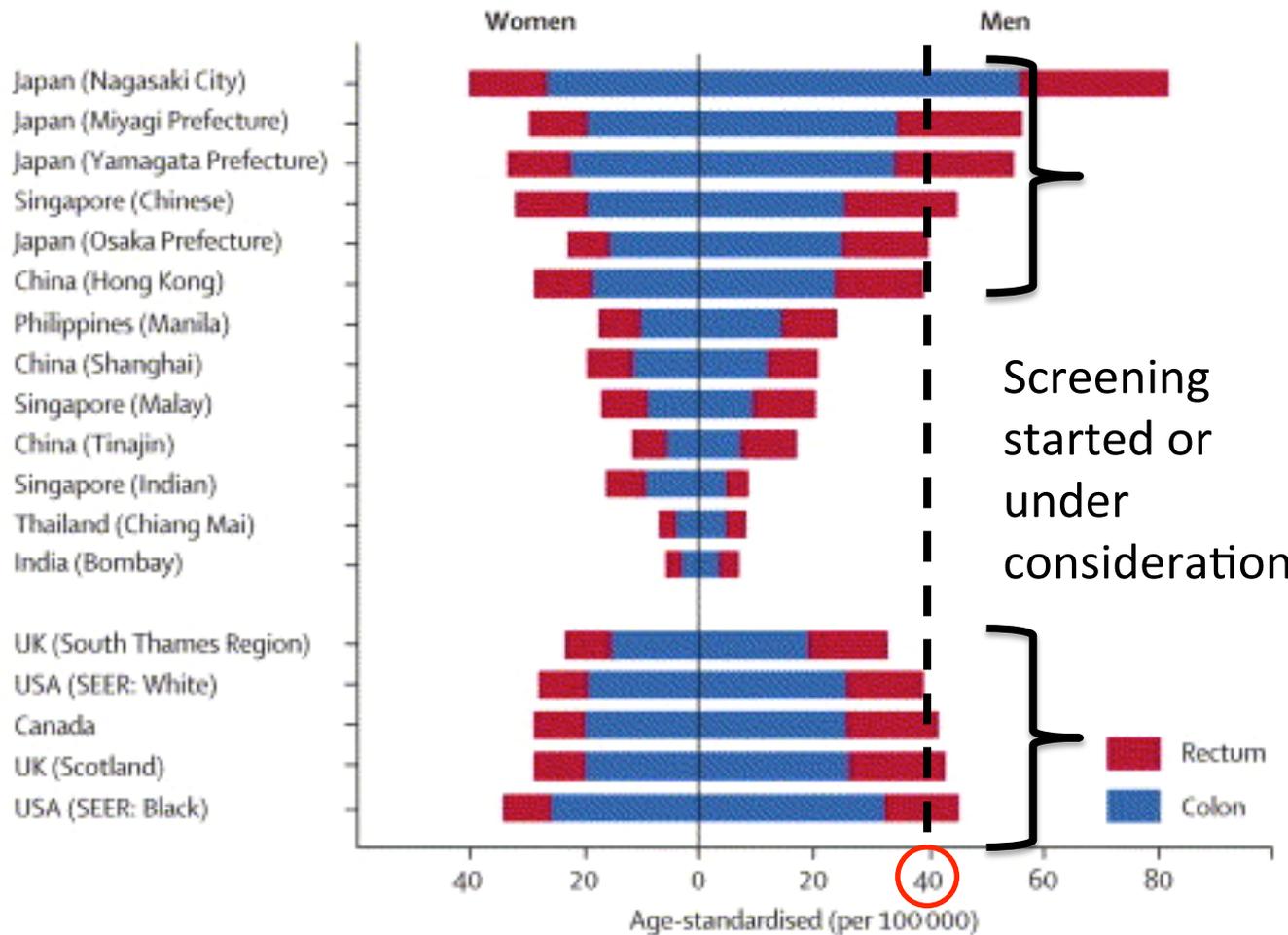
The program:

- Must be feasible within the health care system ? **practical**
 - Diagnosable, follow-up testing, reparticipation in screening
 - Benefit outweighs the down-side

(Watson and Junger WHO Public health Paper no 34, 1968)



An important problem? Incidence *cf* Screening Action

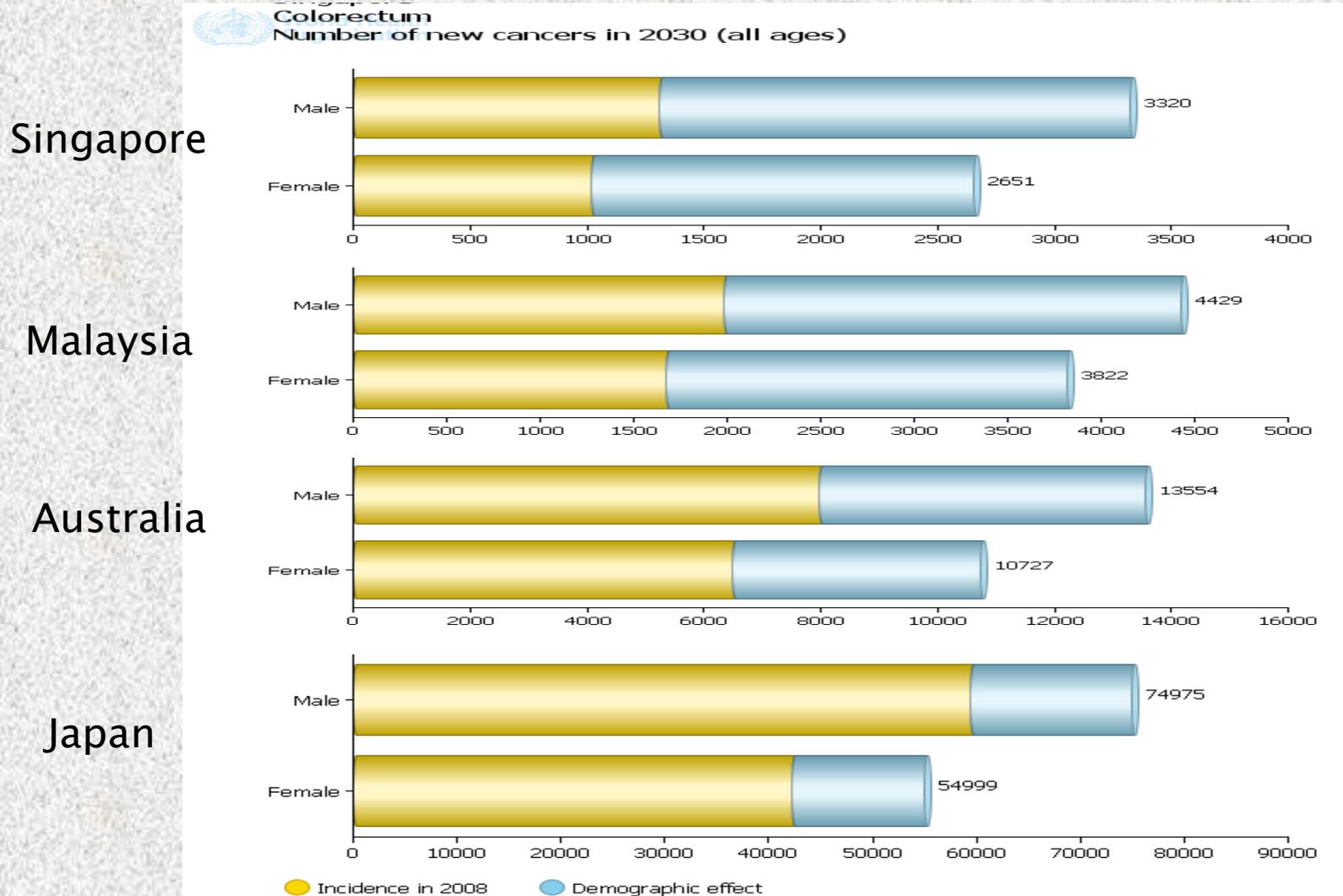


- Incidence of cancer in the colon and rectum in Asian populations compared with US and UK populations (1993-97)
- Data extracted from *Cancer Incidence in Five Continents* volumes I-VIII, IARC CancerBase number 7, Lyon, 2005.
- Sung JJY et al



But incidence is not static!

Projections: 2008-2030



Can we target subgroups?

- There are a range of options including simple case-finding strategies.
- It would be possible to undertake centrally organised screening if ASI <40/100,000, by inserting an additional risk profiling step.
 1. Various risk-algorithms are available.
 - *Gut. 2011;60:1236-41.* The Asia-Pacific Colorectal Screening score: a validated tool that stratifies risk for colorectal advanced neoplasia in asymptomatic Asian subjects. Yeoh KG et al.
 2. Why not pilot the use of an FOBT (FIT) and ascertain the PPV for colorectal neoplasia?



Global CRC screening programs (2008)

- 43 programs identified worldwide
 - 8 could not provide the requested data
- 35 programs from 24 countries

	Europe (n=20)				Americas (n=11)			Western Pacific (n=4)	
Program type	FOBT	FS	TC	FOBT+FS	FOBT	TC	FOBT+TC	FOBT	TC
Full program	13	1	2	0	4	2	1	3	0
Pilot program	3	0	0	1	2	2	0	1	0

- Expectations are uncommonly explicitly stated in terms of outcomes or approach.

Practicality - Provider Contexts

1. Personal application of screening:

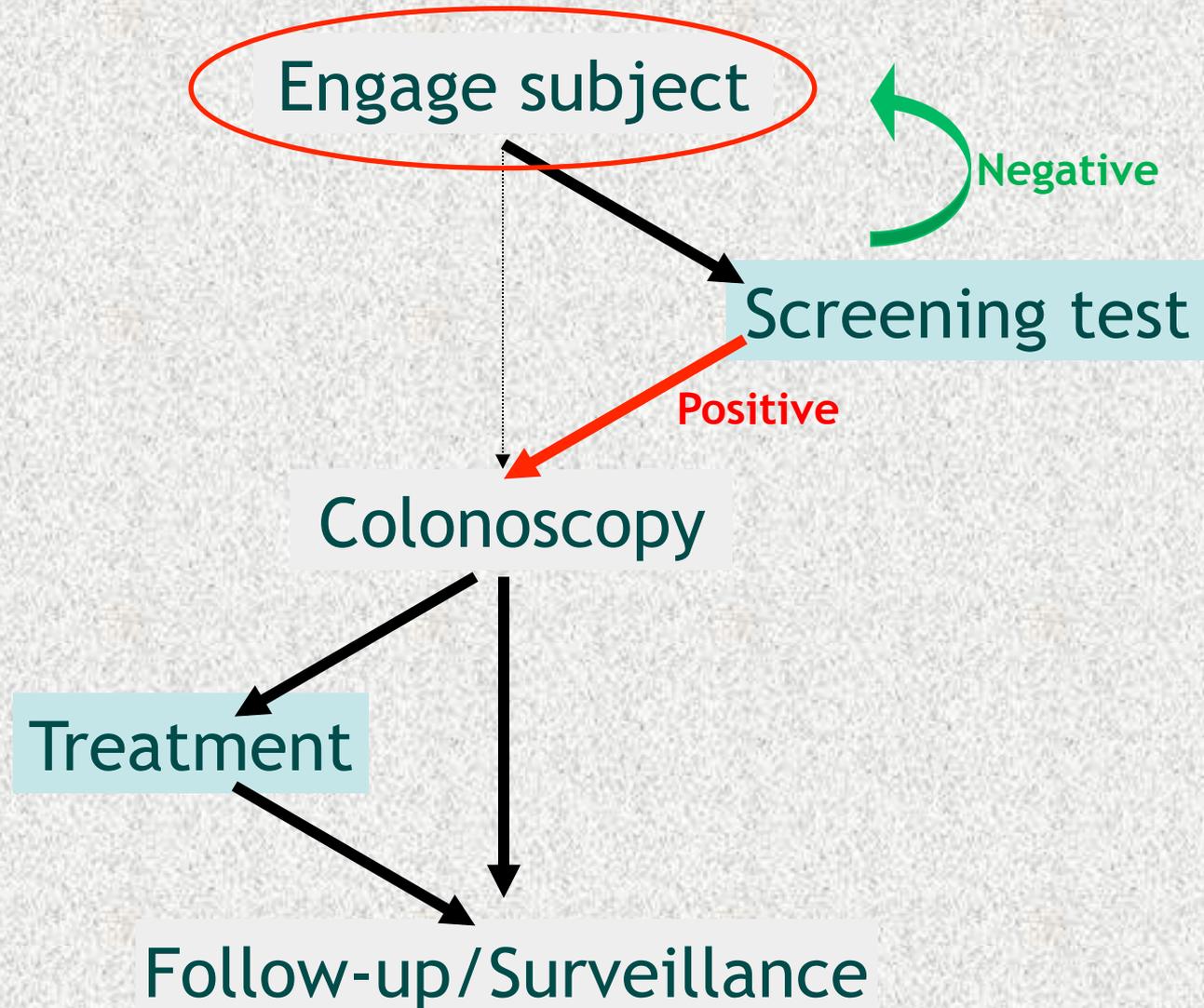
- Goal: Minimise morbidity and/or avoid death
 - Issues: duty of care, individual choice, do what is best (cost is less important)
 - Colonoscopy is predominant test

2. Population application of screening:

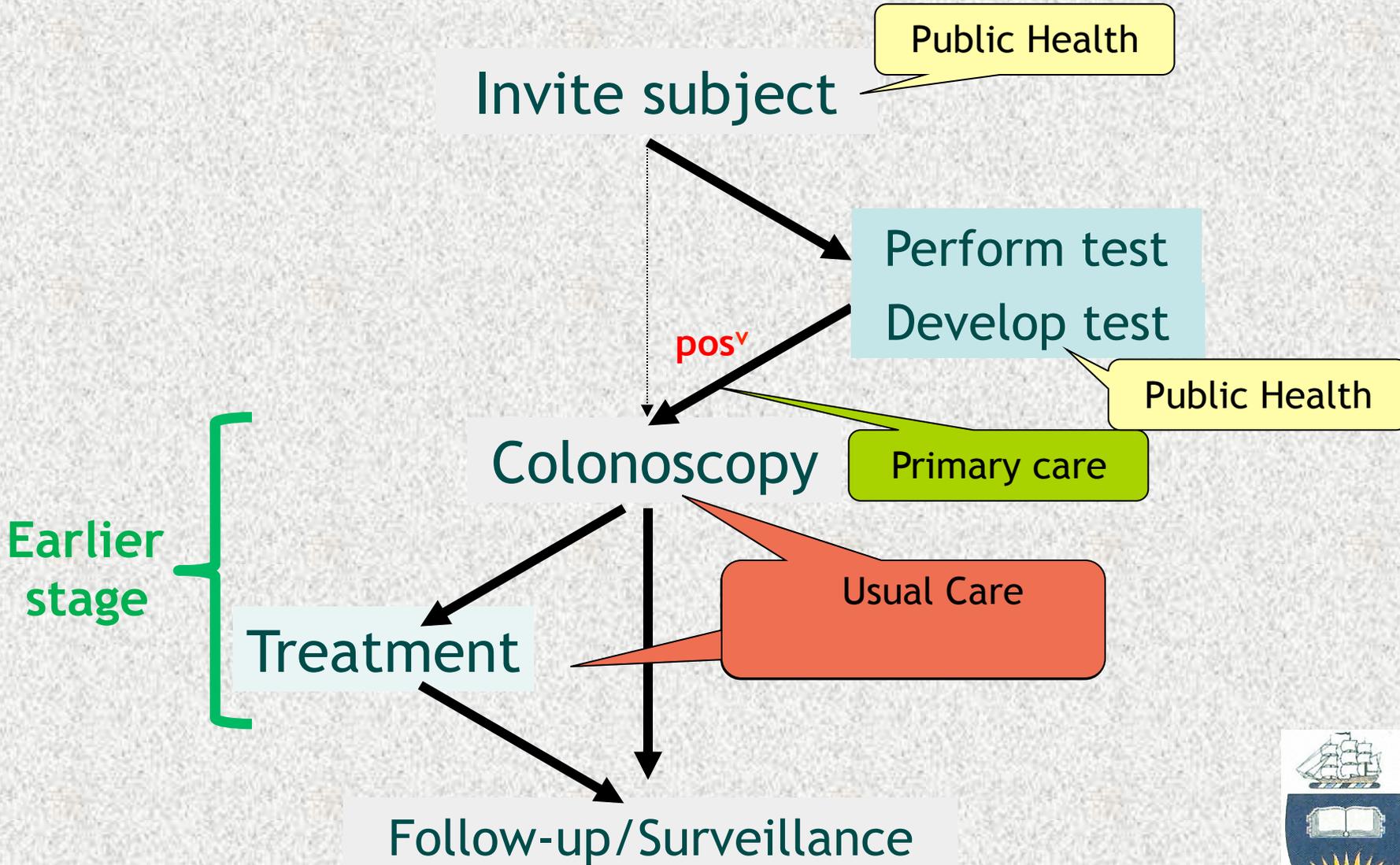
- Goal: Implement a program that reduces the burden to the community
 - Issues: cost, acceptability to majority, risks.
 - FIT is the predominant test



An accurate test must get done!



Dimensions of care; Australia NBCSP



Scenarios: Constraints and expectations

1. *Limited colonoscopy resource* with a need to constrain test positivity rate;
2. A priority for *maximum colorectal neoplasia detection* with little need to constrain colonoscopy workload;
3. An ‘adequate’ endoscopy resource that allows *balancing the benefits of detection with the burden of service provision*;
4. A need to *maximize participation* in screening.

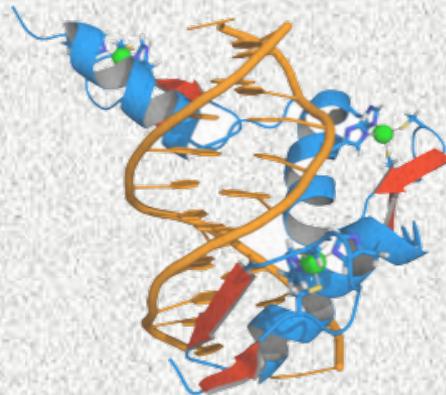
Young et al. Advances in fecal occult blood tests - the FIT revolution.

Dig Dis Sci 2015, in press.

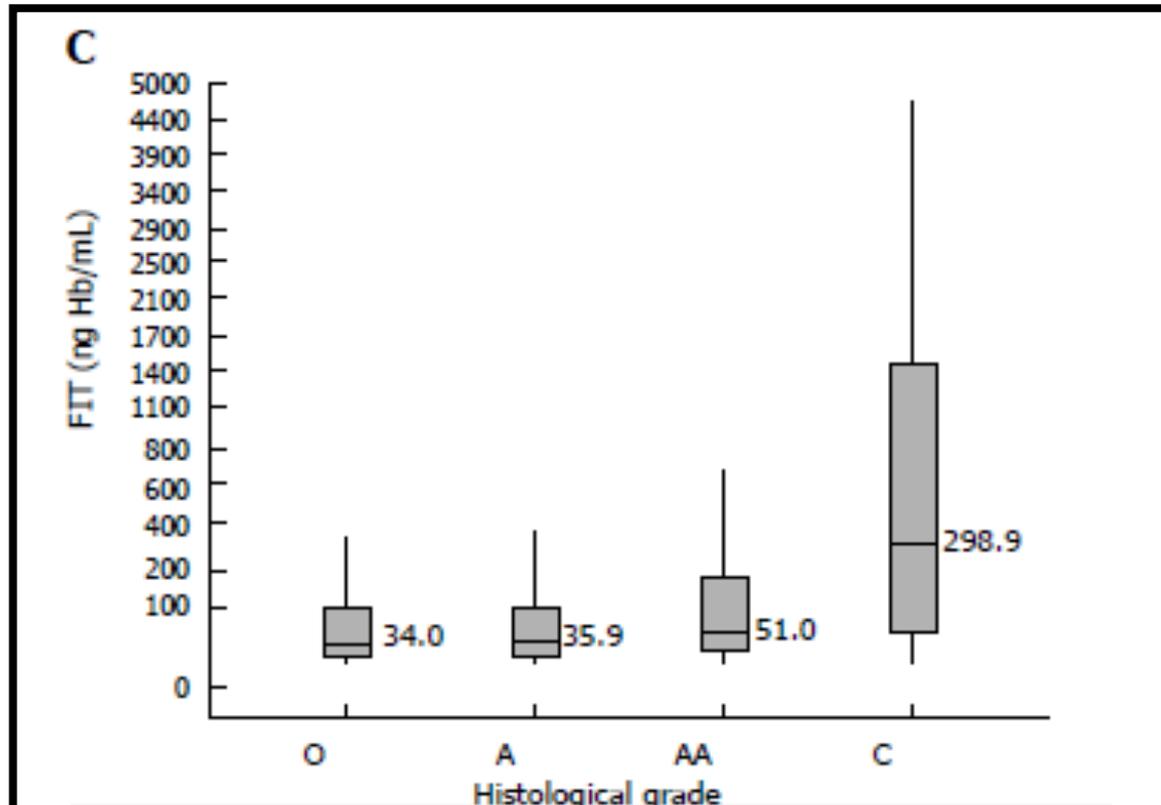


Test options need matching to these scenarios

- Faecal occult blood test
 - guaiac-FOBT (gFOBT)
 - faecal immunochemical test (FIT) for haemoglobin
- Flexible sigmoidoscopy
- Colonoscopy
- Molecular tests of blood or faeces



A quantitative FIT is ideal.



Liao C-S et al. *World J Gastroenterol.* 2013; 19: 8366-8372

Figure 3 Age, gender, and fecal immunochemical test concentration in association with histological grade of colorectal tumor. A: Age; B: gender; C: FIT. The differences in age, gender, and FIT concentrations (Y-axis) in the different histological groups (X-axis). (Kruskal-Wallis test, all $P < 0.001$). FIT: fecal immunochemical test; O: Other; A: Adenoma; AA: Advanced adenoma; C: Cancer.

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Conclusions

- Appropriateness
 - 40/100,000 ASI is the precedent set
 - But major subpopulations at such risk exist in countries with a lower overall incidence - they require some form of risk-profiling.
- Practicality
 - Contexts and approaches vary considerably.
 - The expectation needs to be set and the tool matched to that expectation.
 - Quantitative FIT provide the greatest adaptability





The test must be acceptable

- Without participation, detection is impossible!
- ***Detection*** of cancer in a *population* is not only related to accuracy

Detection =

sensitivity X *participation*



Simple tests refine likelihood

- Likelihood Ratio (LR) expresses the chance that neoplasia is present when the test is positive relative to negative.

$$\text{LR} = \text{Sensitivity} / 1 - \text{specificity}$$

- For Danish RCT of Hemocult (GFOBT) screening
 - $0.5 / 0.02 = \underline{25\text{-fold}}$ more likely to have neoplasia
- For Minnesota RCT (rehydrated Hemocult)
 - $0.92 / 0.08 = \underline{12\text{-fold}}$ more likely to have neoplasia

Note: These sensitivities apply to programmatic (repeated) application



What is screening?

- Screening is the testing for presence of disease in apparently healthy people, where they have no recognised increase in risk for that disease.
- Screening concept proposed in 1968.
 - Colorectal cancer (CRC) screening was not proven to be effective until 1993.
- Key goal: To reduce the *community* burden of “dis-ease”
 - Targets the suffering caused by disease!



Outline

- Screening; definition and process
- WHO criteria justifying screening
 - Incidence
 - Screening process
 - Natural history of colorectal cancer (CRC)
 - Screening test options
 - The evidence for efficacy and effectiveness
 - Engaging the population (participation)
 - (Cost-effectiveness)
- Future perspectives



What is screening?

- “Screening” is testing for the presence of disease in apparently healthy people, where they have no recognised increase in risk for that disease.
 - “Surveillance” is applied to those at increased risk.
- Screening concept proposed in 1968.
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- Key goal: To reduce the *community* burden of “dis-ease”
 - Targets the suffering caused by disease!



Screening Provider Contexts Vary

- By Health care system
 - Is there a public health process?
- By doctors
- By whoever pays for screening. Models:
 1. User pays all costs (Singapore)
 2. Reimbursement by insurer (USA)
 3. Government takes responsibility for some program elements (Australia)
 4. Government takes responsibility for all program elements (UK)



FOBT Technologies

Faeces



Guaiac; peroxidase.

Interference by
Meat, vegies, vitamin C, NSAIDs.

Detects bleeding from
Stomach, small & large intestine.

gFOBT

Immunochemical.

NO Interference.

Detects bleeding from
large intestine.

FIT



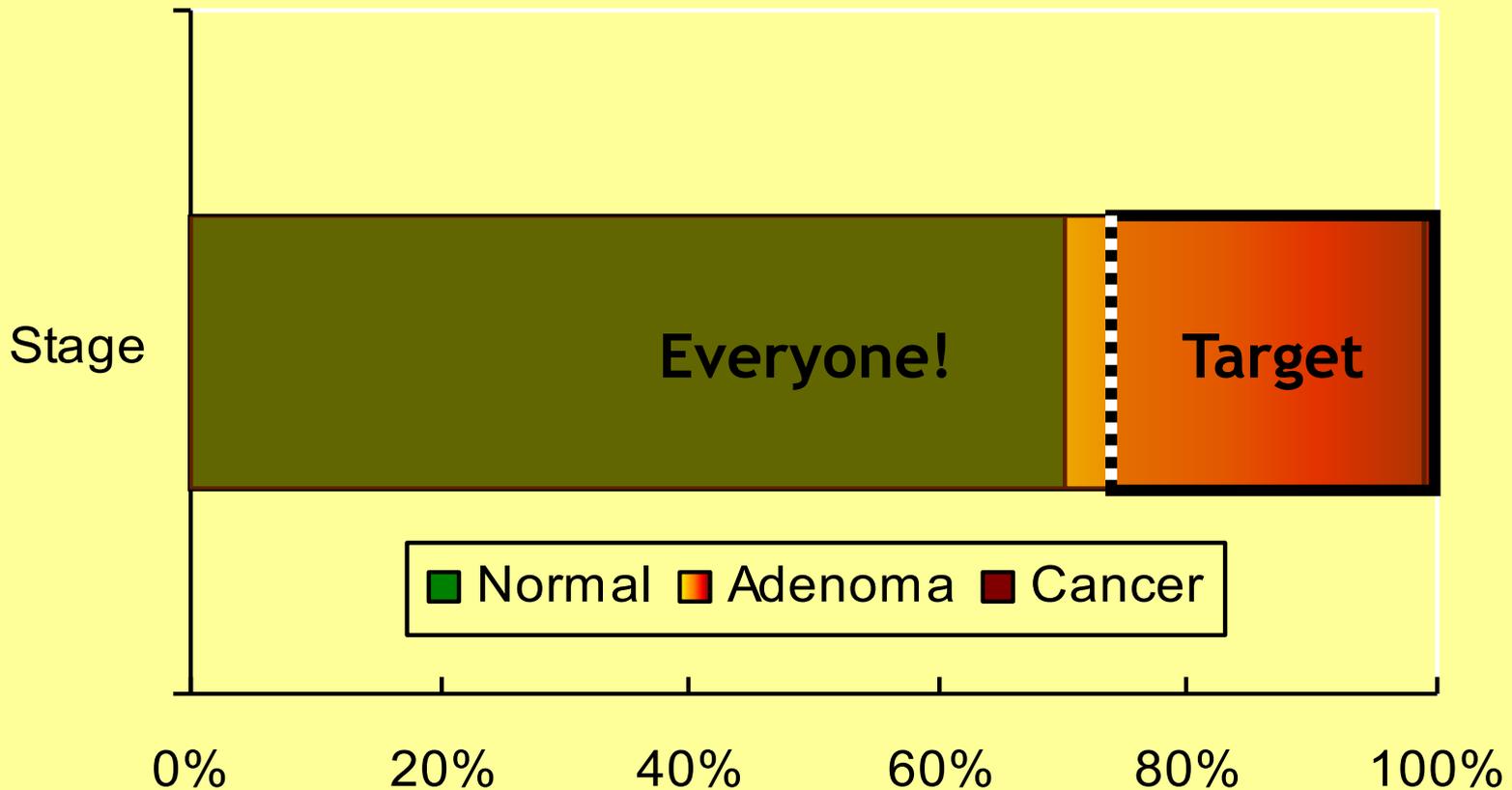
Test simplicity varies

- Colonoscopy
 - Requires bowel wash-out and *sedation*
- FS
 - Requires enema and per-anal examination



Why not straight to colonoscopy?

Status of colon in lifetime once reached age of 50 years



AVERSION - Novel stool sampling

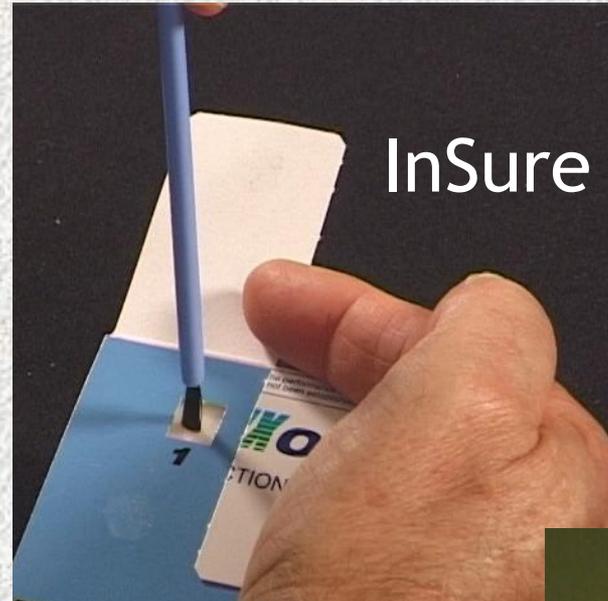
guaiac-FOBT



Three FlexSure[®] OBt collection cards are shown. Each card is white with a purple header and footer. The header contains the Beckman Coulter logo and the product name 'FLEXSURE[®] OBt IMMUNOCHEMICAL FECAL OCCULT BLOOD TEST'. The footer contains instructions: 'Open tab only when ready to use'. The middle card is partially filled out with patient information.

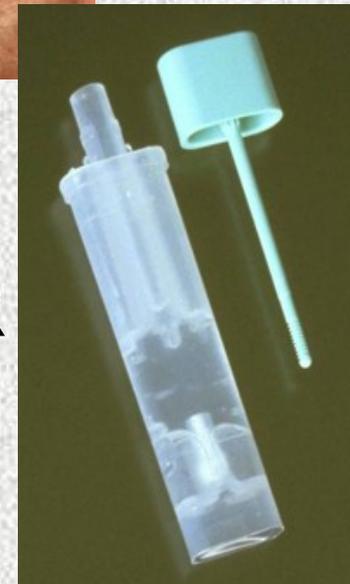
Collection Card	Collection Card	Collection Card
	PATIENT NAME _____ AGE _____	
	PATIENT IDENTIFICATION _____	
SAMPLE COLLECTION DATE _____	SAMPLE COLLECTION DATE _____	SAMPLE COLLECTION DATE _____
	PHYSICIAN NAME _____	
	STORE AT CONTROLLED ROOM TEMPERATURE	

Faecal immunochemical test - FIT



Hemoccult;
Needs diet for accuracy

OC-SENSOR



[Hb] rises with progression

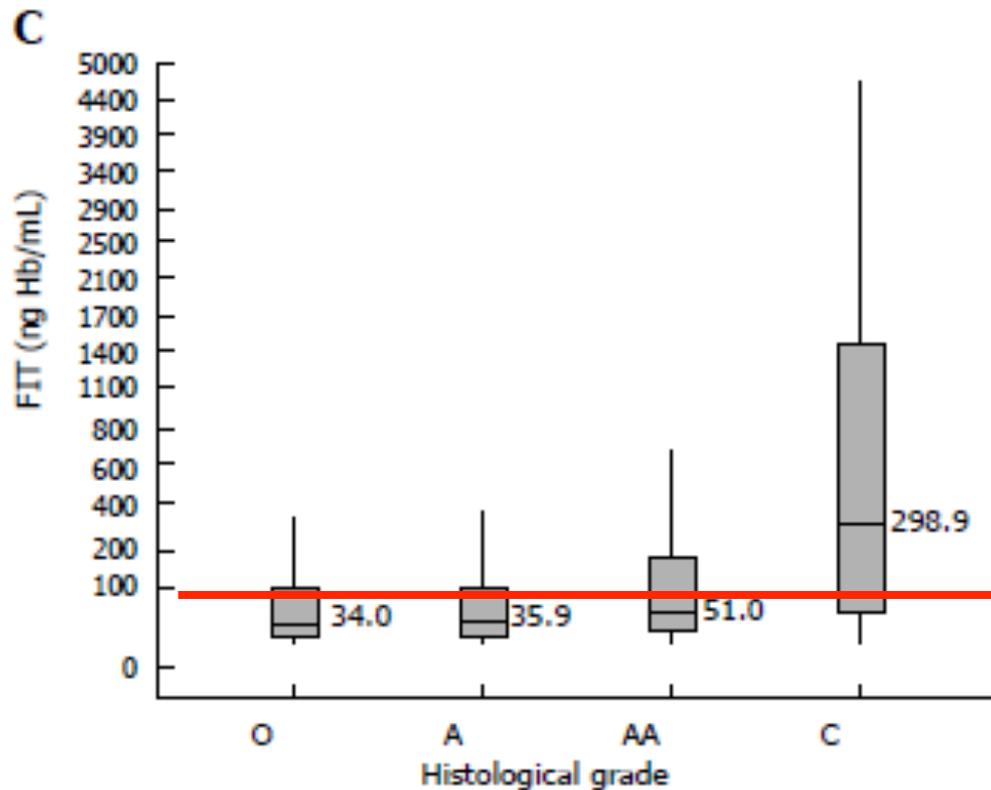


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