Program sensitivity of FIT over time

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Disclosure

DFR was, from 1998-2002, a paid consultant to Exact Sciences.

Since 2002, he has had no paid consulting role, equity, speaking fees, or any other income from any maker of a CRC-related product.

Program sensitivity of FIT over time

Definition
Importance
Research
  How to learn what program sensitivity is
Future
  Challenges, Suggestions

Definitions

Sensitivity:

$$\frac{\text{\#with positive test}}{\text{\#with disease (true state)}}$$

•standard definition: ***Application*** **Sensitivity**
If CRC is present, what proportion is detected by 1 application of a test?
-Design: cross-sectional; do true state exam (CS)

Definitions

Sensitivity

$$\frac{\text{\#with positive test}}{\text{\#with disease (true state)}}$$

•***Program*** **Sensitivity** (no clear definition)
asks: *If CRC is present, what proportion is detected by* ***program*** *of repeat testing* ***over time****?*
-Design: longitudinal; learning true state: complicated

Importance: Screening is done in program of repeated testing over time.

Can program sensitivity be estimated by knowing application sensitivity?

Example: If FIT application sensitivity is 70%, what is program sensitivity?

If subsequent result is ***independent,*** then program sensitivity rises over time.

If applied to 1000 ppl c CRC	If sens is 70%, then # detected	# undetected
round 1	700	300
round 2	300x.70= 210	90
round 3	90x.70= 63	27

Program sensitivity = (700+210+63) 973/1000= **97%**

Example: If FIT application sensitivity is 70%, what is program sensitivity?

If subsequent result is ***dependent,*** then program sensitivity does not rise.

If applied to 1000 ppl c CRC	If sens is 70%, then # detected	# undetected
round 1	700	300
round 2	0	300
round 3	0	300

Program sensitivity = 700/1000= **70%**

Is independence vs dependence important?

Answer: Yes, for example policy-making

- In USPSTF modeling, FIT testing results are assumed to be independent. So 70% sensitivity at one application would lead to higher program sensitivity.

How might these issues affect comparisons of programs of FIT vs FIT-DNA?

Test Characteristic		Test
	FIT	**FIT-DNA**
Application Sensitivity		
CRC	73.8%	92.3%
large adenoma	23.8%	42.4%
Application Specificity		
negative colonoscopy	96.4%	89.8%

Imperiale, NEJM 2014;370:1287

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Question: How high is FIT sensitivity, in **program** over time?

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Question: How high is FIT sensitivity, in **program** over time?

The point here is not 'which is better'; that's complicated.

The point: It's important to know 'sensitivity' in a program over time, or to be clear about limitations and assumptions.

So are test results in a program independent or dependent?

Answer: determined by *biology*.

- If some lesions never bleed or only at very late stage (e.g, R-sided), a FIT may be less useful.
- If some lesions do not have DNA mutation/methylation, a DNA test will be less useful.

If we don't know biology, how do we determine independent vs dependent?

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Annals of Internal Medicine ORIGINAL RESEARCH

Fecal Immunochemical Test Program Performance Over 4 Rounds of Annual Screening

A Retrospective Cohort Study

Purpose: To assess FIT sensitivity at each application over ~4 yrs of screening.

Method: 323,349 persons; CRC was dx'd after pos. FIT *or* because of symptoms and w/u within a year ('look-back').

Result: Screening detected 80.4% of persons with CRC within 1 yr of testing (84.5% in round 1, 73-78% in each of subsequent rounds.)

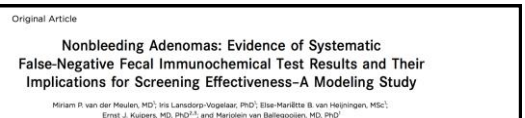
Comment/Questions:

a. FIT is not 100% dependent.

b. But do we know True State in all? Would longer follow-up show different results?

c. Is stage distribution of CRCs different, important?

Ann Intern Med 2016; XXX


Original Article

Nonbleeding Adenomas: Evidence of Systematic False-Negative Fecal Immunochemical Test Results and Their Implications for Screening Effectiveness–A Modeling Study

Purpose: To estimate what % of adenomas do not bleed and may be missed by FIT.

Method: MISCAN models were used to fit findings of Dutch CORERO FIT screening trial, using different estimates of test-dependence.

Results:

- FIT systematically missed ~28% of adv. adenomas.

Comments/Questions

- CRC not directly studied. Could some CRCs (R-sided?) never bleed?

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Challenges, Suggestions in 2016

Challenges

- Knowing program sensitivity is important in modeling and has implications for policy.
- It's hard to estimate or to measure!

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Challenges, Suggestions in 2016

Suggestions

- In empirical studies:
  - -follow people longer
  - -consider stage distribution in comparisons
  - -discuss limitations, implications
- In modeling:
  - -do sensitivity analyses
  - -discuss limitations, implications

We need to put the issue - program sensitivity and test independence/dependence - on our radar.