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The voice of world endoscopy

The importance of a flexible positivity threshold – initial *interim* report on the global survey of FIT usage

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Acknowledgements and conflicts

- The ready willingness of 104 respondents to complete the survey.
- The initial colleagues who provided input into the survey design: Selby, Parry, Senore, Dekker, Benton, Symonds, Singh, Halloran, Fraser, Bresalier.
- The authors of the New Test Evaluation Recommendations paper (n=47)

Conflicts: Eiken Chem Co. (Institutional research support), Health-First Systems (consultancy)

Background & Aim

- In setting recommendations for evaluating non-invasive tests using new biomarkers, the WEO New Test EWG, emphasised the desirability of having flexibility to choose test accuracy that suits a screening program, rather than being locked into a fixed accuracy with a qualitative result.
- Flexibility comes from being able to adjust the positivity threshold.
- A range of positivity thresholds is in use.
- ***However, the range, the types of tests used in population-based organized screening (PBOS) programs, and the reasons behind their choice, are not well documented.***

- By documenting the importance of having this capability with FIT, we would strengthen the case to argue for such flexibility with new tests, no matter what the biomarker is.

<u>Survey Aim</u>

- To document:
  - how FIT are being used in the jurisdictions represented by SC members.
  - the type of FIT used (qualitative or quantitative),
  - the positivity thresholds (cut-off) in use, and how these vary between jurisdictions.
  - Why they are chosen, and
  - If they have changed

Survey design and uptake

- A survey comprising 8 main questions was drafted, and then critiqued by a panel of 11 members, before being finalized.
- All WEO SC members (1,500+) were then invited to complete the online survey.

- Responses received – 104
- Inclusion criteria met – 64
  - FIT-based PBOS program with specified test and threshold provided by non-industry individual.
- Sites:
  - 28 countries (geographic)
  - 50 specific sites/regions

Countries & sites

• Australia • Austria • Belgium • Brazil • Canada* • Czechia • Denmark • Egypt • Finland	• France • Germany* • Ireland – Republic • Italy • Japan* • Mexico • Netherlands • Norway • NZ	• Romania • Russia* • Slovenia • Spain • Sweden • Switzerland • Taiwan • UK* • USA

* Multiple sites with differing approaches

Brands of FIT

- Four countries used more than one brand of FIT, with discretion within regions to choose brand and/or threshold.
- The full range of brands used within 2 countries was not ascertainable.
- A number of companies provide a range of tests (varying in sampler, analyser and test read-out) based on their underlying test platform.

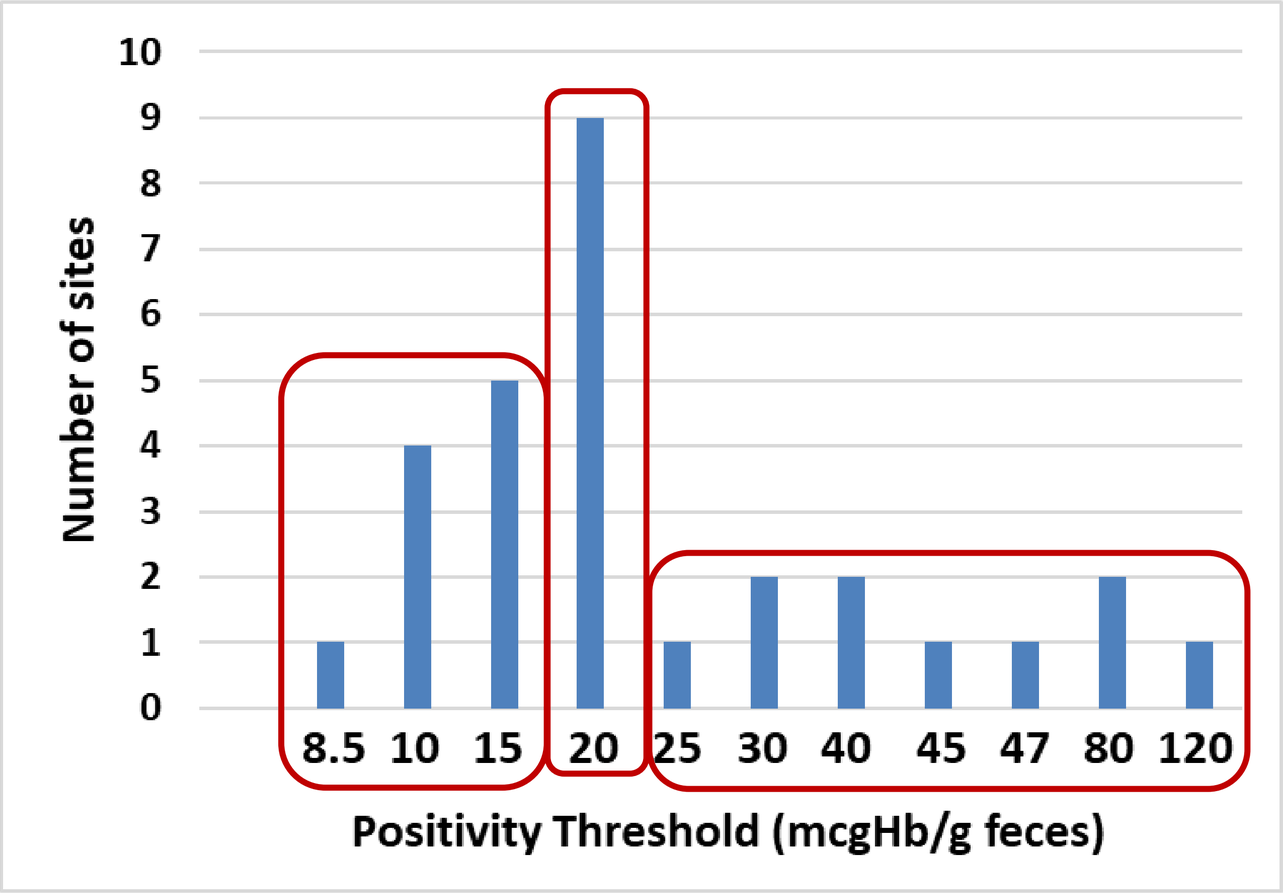
- Note: This is not the global frequency of use but that relating to information provided by the survey Length of time on the market influences frquency.

Manufacturer	Usage
Alfresa Pharma – NS-Prime and NESCAUTO	2 countries (regional in one)
Eiken Chem. Co. – OC-Sensor test family	19 countries (not sole test in 3)
Alpha Laboratories – HM-JACKarc	2 countries (not sole test in 1)
Polymedco Somagen Diagnostics – test family	2 countries – 9 regions therein
Sentinel Diagnostics – FOB Gold, SENTiFIT	4 countries (not sole test in 1)
Discretionary use of a range of tests	4 countries (tests used not available for 2)

Thresholds in use (mcg Hb/g faeces

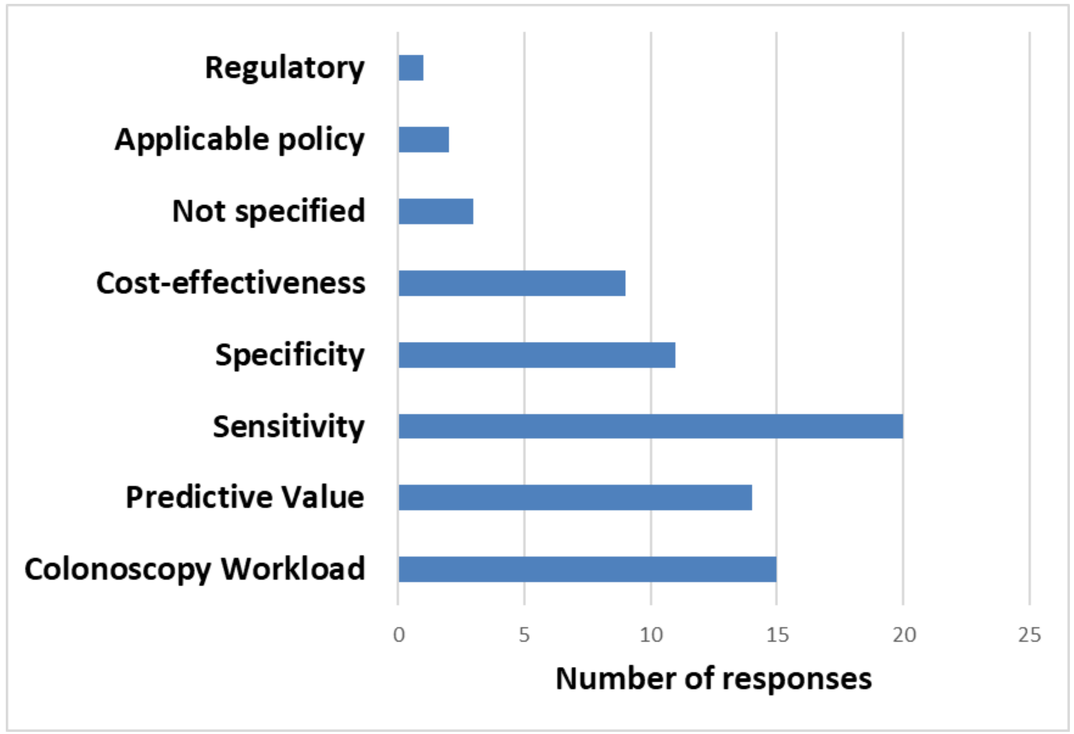
- Qualitative only 16/28 countries
- All recorded the quantified result.
- One country used a different threshold for each gender
- One country used 2 different tests where the thresholds were not unified.

- Only 9 countries applied the commonest threshold.
  - 10 were below this
  - 8 were above it

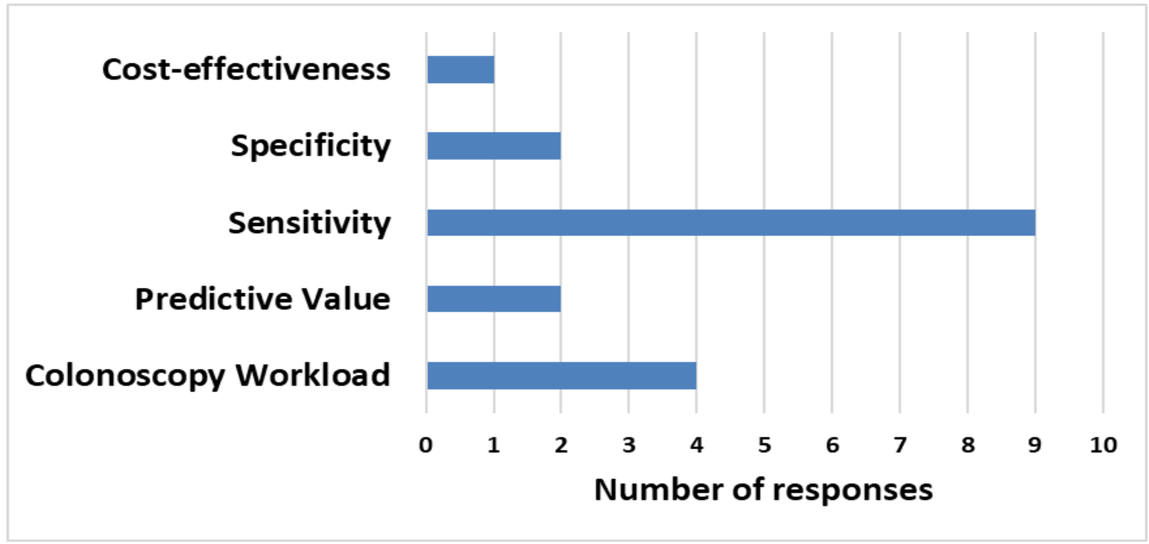


Reasons for the thresholds

Respondents were asked to identify any reasons that applied (multiple allowed).



Respondents to a supplementary survey were asked to identify the main reason.



Threshold Changes; follow-up survey

- 8 of 27 countries had made changes to the threshold since commencement
  - In one country this was done in 4 regions during the *SARS-CoV-2* pandemic

In a follow-up survey (limited numbers):

10 of the 18 respondents had conducted a **pilot study**, and in 6 this led to a change in the preliminary threshold or brand of test.

4 of the 18 respondents used **2-sample testing** (1-sample in the remainder)

15 of the respondents tested **biennially** while 3 tested **annually**

Conclusions

- Five main brands are used:
  - 4 are quantitative
  - The fifth is a version of one of the four but constrained to qualitative use by regulatory conditions
- Only 9/28 use the commonest threshold.
  - That threshold is generally used for regulatory and initial clinicla studies
- 8/28 needed to make a change in the threshold from the original selection.
- Thus most sites wish to use a test where the threshold is flexible.

- The main reasons for choosing the threshold were:
  - sensitivity for Cancer and Precursor lesions and
  - colonoscopy workload considerations.

- New non-invasive screening tests will ideally allow for a flexible threshold
  - In some jurisdictions, this will require studies reporting test accuracy against a set of several thresholds that might be applicable.

Range of thresholds

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