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**Can the performance of a quantitative FIT-based colorectal cancer screening programme be enhanced by lowering the threshold and increasing the interval?**

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We read with interest the work by Haug et al. published in Gut.<sup>1</sup> Longitudinal data from 4,523 participants in the first round of a faecal immunochemical test for haemoglobin (FIT) based screening programme, of whom 3,427 also participated in the second round, were studied. In both first and second rounds, a threshold of 10 µg Hb/g faeces was used. The cohort was followed up for two years. The cumulative positivity and the number of participants diagnosed with neoplasia over the two rounds of screening were determined and compared with a hypothetical strategy involving single round screening with use of lower faecal haemoglobin concentration (f-Hb) thresholds and omission of the second round. It was suggested that lowering the f-Hb threshold and extending the screening interval could possibly enhance population-based screening programmes.

In our pilot evaluation of FIT-based screening in Scotland, a much higher f-Hb threshold ( $\geq 80$  µg Hb/g faeces) was employed.<sup>2</sup> Moreover, a much larger cohort of screened individuals (30,893) was available for study. 753 participants with f-Hb  $\geq 80$  µg Hb/g were referred for colonoscopy. Of 30,140 with a negative screening test result, 27,890 that had participated were eligible to be invited for the next screening round (January 2011 to January 2013). Of 24,669 responders, 450 had a positive screening test result and were referred for colonoscopy. In the two rounds of screening studied, the first with quantitative FIT using a threshold of  $\geq 80$  µg Hb/g faeces and the second using the standard gFOBT/FIT two-tier reflex algorithm used in Scotland,<sup>3</sup> the positivity in the first round was 2.5%: there were 30 screen-detected cancers (SDC) and 31 interval cancers (IC).<sup>4</sup> In the first round, 753 colonoscopies were performed. At the second round, there were 25 SDC, making a total of 55 SDC over two rounds.

Assuming that IC and CRC detected at the subsequent screening round would have been present in some form during the initial screening round, the scenarios that would have eventuated by omitting the second screening round and using lower f-Hb thresholds are listed in Table 1. The f-Hb threshold that would have given double the positivity rate of that found using  $\geq 80 \mu\text{g Hb/g}$  faeces was identified as  $\geq 28 \mu\text{g Hb/g}$  faeces.

This f-Hb threshold would have generated the same number of colonoscopies in a single four year screening round as a threshold of  $\geq 80 \mu\text{g Hb/g}$  faeces would have in two rounds of biennial screening. In this situation, which is colonoscopy resource neutral, three IC and nine second round CRC would have been detected during the first round of screening. It follows that the remaining 16 SDC found in the second round would have become IC, or at least have been more advanced when detected at the next screening episode. This would have resulted in 42 SDC diagnosed in a four year screening round, considerably fewer than the total of 55 SDC with biennial screening, and the number of IC could have potentially increased from 31 to 44.

Therefore, the concept of lowering f-Hb cut-off and lengthening screening interval to improve test sensitivity without an increase in colonoscopy requirement is not supported by our data since a modest decrease in IC would be offset by the majority of second round SDC being missed. Other strategies such as the use of f-Hb concentration to

determine the length of the subsequent screening interval for individual participants may be a better option when evolving to more intelligent use of FIT.

**Table 1. Alternative scenarios using lower faecal haemoglobin concentration (f-Hb) threshold for the 1st round and omitting 2nd round**

<b>f-Hb cut-off (<math>\geq</math> <math>\mu\text{g Hb/g}</math> faeces)</b>	<b>Positivity in 1st round</b>	<b>Screen-detected cancer in 1st round</b>	<b>Interval cancers now detected</b>	<b>2nd round cancer now detected in 1st round</b>	<b>Colonoscopies required in 1st round*</b>
<b>60</b>	3.1%	36	2/31	4/25	946
<b>40</b>	3.9%	38	3/31	5/25	1194
<b>30</b>	4.7%	41	3/31	8/25	1422
<b>28</b>	5.0%	42	3/31	9/25	1500
<b>20</b>	6.3%	47	5/31	12/25	1935
<b>15</b>	7.4%	52	8/31	14/25	2288
<b>10</b>	9.4%	54	8/31	16/25	2900

**\*Numbers of colonoscopies derived from positivity**

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## **Competing interests**

CGF undertook consultancy with Immunostics Inc., Ocean, NJ, USA, and Kyowa-Medex, Tokyo, Japan. All other authors had no competing interests.

## **Ethics approval**

Ethical approval was not required for this study as it involved analysis of routinely collected screening data. The FIT pilot was approved by the Programme Board, Scottish Bowel Screening Programme as an evaluation of an established screening modality.



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