World Endoscopy Organization
Colorectal Cancer Screening Committee

Vienna 2014

6th Meeting of the Expert Working Group (EWG) – 'FIT for Screening'

Friday, 17 October 2014: 08:30–11:30

MEETING REPORT

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Expert Working Group (EWG) founding members:

- Jim Allison, University of California, San Francisco, USA (jallison@medsfgh.ucsf.edu)
- Callum Fraser, University of Dundee, Scotland (callum.fraser@nhs.net)
- Stephen Halloran, NHS Bowel Cancer Screening Programme & University of Surrey, UK (Chair) (s.halloran@nhs.net)
- Graeme Young, Flinders University of South Australia, Australia (graeme.young@flinders.edu.au)

Summary report prepared by Helen Seaman (helenseaman@nhs.net).

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More than 70 delegates attended the EWG meeting in Vienna on 17 October 2014.

Agenda items:

Slide set no. 1.	**1. Welcome & Introduction** – *Stephen Halloran*
	2. Programme design and implications for FIT – ***Ernst Kuipers (Chair)***
Slide set no. 2	Issues to consider – *Marie-Louise Heijnen and Iris Lansdorp-Vogelaar (the Netherlands)*
Slide set no. 3	Maximising uptake to the target population (including demographics, age, disabilities *etc*) – *Christian von Wagner (UK)*
Slide set no. 4	FIT & primary care involvement *Catherine Dubé (University of Ottawa, Canada)*
Slide set no. 5	FIT cut-off, screening intervals, resource implications – *Ernst Kuipers (the Netherlands)*
Slide set no. 6	Who should perform the FIT analysis? – *Callum Fraser (Scotland)*
Slide set no. 7	Lessons learnt: SCREESCO – *Rolf Hultcrantz (Sweden)*
Slide set no. 8	Lessons learnt: BowelScreen – *Alan Smith (Ireland)*
	3. Procurement – *Sally Benton (Chair)*
Slide set no. 9	Procuring the right FIT product for you – *Sally Benton (England)*
Slide set no. 10	Standardisation of FIT collection devices – *Stefano Rapi (Florence, Italy)*
Slide set no. 11	Piloting new FIT programmes – *Paula McDonald (Scotland)*
Slide set no. 12	Piloting new FIT programmes – *Stephen Halloran (England)*
Slide set no. 13	Lessons learnt: BowelScreen – *Alan Smith (Ireland)*
	4. Maintaining quality in FIT CRC screening programmes – *Callum Fraser (Chair)*
Slide set no. 14	How good should quantitative FIT analyses be? – *Callum Fraser (Scotland)*
Slide set no. 15	Quality in faecal immunochemical testing - what to monitor, what to control – *Paula McDonald (Scotland)*
Slide set no. 16	External Quality Assessment – *Jane French (UK)*
	5. Free papers
Slide set no. 17	The Basque Country colorectal screening programme – *Isabel Portillo Villares* (*Spain*)
Slide set no. 18	Diagnostic yield for advanced colorectal neoplasia using FIT with one or two samples – *Josep Mª Augé Fradera (Spain*)

Slide set no. 1: Stephen Halloran. 'Welcome'

Pending the retirement of some Founding Members of the EWG, Professor Ernst Kuipers (Erasmus MC, Rotterdam, The Netherlands) and Sally Benton (Bowel Cancer Screening Southern Programme Hub, Guildford, England) will continue to support the EWG in its efforts to promote the effective use of FIT for colorectal cancer (CRC) screening.

Since the last EWG meeting in Chicago (May 2014), the EWG has published four new papers and two more are pending (as of 27 October 2014) (13 publications in total, to date).

The topic for this, the 6th meeting of the EWG, was:

'*Developing a FIT-based CRC Screening Programme – challenges, opportunities and lessons learnt*'.

Slide set no. 2: Marie-Louise Heijnen and Iris Lansdorp-Vogelaar.

'CRC Screening in The Netherlands; issues to consider'

Drs Heijnen and Lansdorp-Vogelaar outlined the background to the colorectal cancer screening programme in The Netherlands. Since January 2014, the Dutch programme has offered biennial screening using the FOB Gold FIT (Sentinel CH. SpA, Italy) on a BioMajesty analyser (contract partner: Sysmex Benelux; manufacturer: DiaSys Diagnostic Systems, GmbH) for men and women aged 55-75 years. The phased roll-out of the programme invited individuals aged 63, 65, 67, 75 and 76 years (in the period January 2014 to May 2014 mainly 75 and 76-year-olds) with an uptake of 65-68% and referral for colonoscopy (positivity) of 13% using at a cut-off of (75 ng Hb/mL buffer / 15 µg Hb/g faeces [*sic*]). (NOTE: conversion factor using FOB Gold = 0.17, so 75 ng/mL = 12.75 µg Hb/g faeces). Uptake and positivity were higher than expected (because mainly older people were invited) and the referral rate was unsustainable because of insufficient colonoscopy capacity and the PPV was lower than expected. To resolve the problem the rate of invitations was slowed temporarily and the cut-off for positivity was raised to 275 ng Hb/mL buffer (47 µg Hb/g faeces) in July 2014. Other possible adjustments that might be considered in the future include altering the screening interval, changing surveillance guidelines or age-/sex-specific faecal Hb concentration cut-offs.

Slide set no. 3: Christian von Wagner

'Maximising uptake to the target population: lessons from the NHS Bowel Cancer Screening Programme in England'

Dr von Wagner summarised the likely barriers to uptake of bowel cancer screening and the observed inverse relationship between gFOBt uptake and socioeconomic status - decreased uptake with increased social deprivation. The success of bowel cancer screening relies on repeat uptake of screening invitations and Dr Wagner presented data from the BCSP Southern Hub that indicated that over three episodes, 70.1% of the population invited participated in the gFOBt programme at least once, but only 44.4% participated three times. Once a subject has participated, repeat participation was high (87% at the second invitation and 94.5% at the third amongst consistent participants), but uptake of repeated invitations amongst previous non-participants was very low. Test-specific barriers to screening include disgust and complexity. In the BCSP, subjects who return a gFOBt card with 1-4 (out of 6) positive spots will be asked to complete a second (and possibly third) test kit to reach a definitive test result and some subjects drop-out of screening at this stage. Uptake of FIT is better than gFOBt for reasons that include the need for just one faecal sample and a simpler sampling technique.

Slide set no. 4: Catherine Dubé

'FIT and primary care involvement: insights for Canada'

Screening for CRC is provided by autonomous programmes in eight of the 10 Canadian provinces (the three territories in the north of the country do not have CRC screening programmes). Quebec and New Brunswick are planning a programme. The programmes in Manitoba (M) and Ontario (ON) use gFOBt and the other six (British Columbia (BC), Alberta (AB), Saskatchewan (S), Newfoundland and Labrador, Prince Edward Island and Nova Scotia) use a FIT. In ON there is good access to colonoscopy, although 24% of subjects with an abnormal screening test result wait more than six months for a follow-up colonoscopy. GPs are involved in Canadian programmes and a GP recommendation is a strong predictor of patient participation, although there is significant use of screening tests outside screening guidelines. In AB access to colonoscopy is limited. FIT (OC-SENSOR) replaced gFOBt in AB in November 2013 and the number of 'urgent priority' referrals for colonoscopy increased.

Slide set no. 5: Ernst Kuipers

'FIT cut-off, screening interval, resource implications'.

Professor Kuipers summarised Dutch screening studies exploring the various FIT screening strategies, including varying (a) the faecal Hb concentration used to define a positive result (cut-off) (b) screening intervals (one, two or three years) and (c) use of one-sample or two-sample FIT-based screening, and the estimated costs and effects using different FIT screening strategies.

Slide set no. 6: Callum Fraser

'Who should perform the FIT analysis? Pros and cons of FIT as a POCT v analysis in hospital laboratories'.

Professor Fraser outlined the advantages and disadvantages of qualitative and quantitative FIT devices.

Hospital laboratories are ideal for large sophisticated programmatic screening efforts, especially when health services are well-organised nationally or regionally and financed properly.

When only smaller screening initiatives are possible, point-of-care testing (POCT) may be appropriate. The MHRA document 'Management and use of IVD point of care test devices' was highly recommended (http://www.mhra.gov.uk/Publications/Safetyguidance/DeviceBulletins/CON071082).

Slide set no. 7: Rolf Hultcrantz

'SCREESCO: SCREEning of Swedish COlons'.

Eighteen of the 21 counties in Sweden participate in the SCREESCO trial to explore various screening methods and compliance with screening, the experience, the health economics and CRC mortality and incidence during 15 years of follow-up. Invitees aged 59-62 years are offered a once-only colonoscopy or a FIT (two-sample FIT [OC-SENSOR] in years 1 and 3). A control group is not offered screening. Preliminary data from the FIT arm of the study demonstrate 49% compliance and 10% positivity (cut-off $\geq$ 48 µg Hb/g faeces).

Slide set no. 8: Alan Smith

'BowelScreen: the National Bowel Screening Programme' (FIT experience).

BowelScreen – The National Bowel Screening Programme in Ireland – uses OC-SENSOR. The initial cut-off for positivity of 100 ng Hb/mL buffer (20 µg Hb/g faeces) yielded an unsustainable positivity of 8.06% and in February 2014 the cut-off was increased to 225 ng Hb/mL buffer (45 µg Hb/g faeces). Positivity data for October 2014 showed a fall in positivity to 5.2%. Advice from Ireland is, if there is uncertainty around endoscopy capacity, to consider weighting initial invitations towards younger people amongst the eligible population and not to hesitate to adjust the faecal Hb cut-off if necessary to control referral to colonoscopy.

Slide set no. 9: Sally Benton

'Procuring the right FIT product for you'.

The EWG had drafted a short discussion document outlining considerations when procuring a FIT system (http://www.worldendo.org/assets/downloads/pdf/activities/weo_expert_working_group_fit_discussion_doc_no6_pr.pdf). The presentation developed the issues and highlighted the practicalities of providing information for the target population; kit design, packaging and distribution, laboratory processes and communication of results, and the contribution needed from the diagnostics industry before going out to tender. Feedback on the EWG document is welcome.

Slide set no. 10: Stefano Rapi

'Standardisation of collection devices for faecal material for the detection of haemoglobin with immunochemical tests'.

This presentation outlined a project designed to identify, design and develop a standard and appropriate FIT sample collection device to reduce variation in the amount of material collected. A European collaboration is planned to develop new guidelines.

Slide set no. 11: Paula McDonald

'Piloting new FIT programmes' (Scotland).

The Bowel Screening Programme in Scotland uses a gFOBt as the first line screening test. Between July 2010 and January 2011, a study was performed to assess quantitative FIT as a first line test (FFLT) in two NHS Health Boards in Scotland. 70,000 individuals were asked to complete a FIT (one-sample OC-SENSOR at 80 µg Hb/g faeces cut-off). The study found that faecal haemoglobin concentrations are lower in women than men, increase with age in both sexes and are directly related to disease severity. There is also an association between faecal Hb concentrations and deprivation. These important observations inform not only feasibility and clinical outcome, but also other important considerations for implementing FIT screening.

Slide set no. 12: Stephen Halloran

'Piloting new FIT programmes' (England).

The Bowel Cancer Screening Programme in England invites 69-74-year-olds for biennial gFOBt screening and 55-year-olds for a once-only flexible sigmoidoscopy. For six months in 2014 (April to September) the BCSP ran a FIT Pilot study to gauge the potential merits of FIT as a replacement for gFOBt, to assess the practicalities of adopting FIT and to collect clinical, economic and organisational data for a business case. 40,000 FIT were distributed (one in every 28 invitations) and subjects were asked to complete one FIT (OC-SENSOR). The faecal Hb cut-off for positivity was 20 µg Hb/g faeces (100 ng Hb/mL buffer). Two of the five Hubs in the BCSP ran the Pilot, each using two OC-SENSOR DIANA analysers.

Slide set no. 13: Alan Smith

'Bowel Screen: the National Bowel Screening Programme (Procurement)'.

The programme in Ireland completed a FIT procurement exercise that allocated marks according to weighted parameters: costs (45 marks), test performance characteristics (30 marks), contract management/ quality procedures (15 marks) and availability and delivery (10 marks).

Slide set no. 14: Callum Fraser

'How good should quantitative FIT analyses be?'

The EWG has prepared a short discussion document on *Internal Quality Control & External Quality Assessment*: (http://www.worldendo.org/assets/downloads/pdf/activities/weo_expert_working_group_fit_discussion_doc_no4_iq.pdf). The document provides recommendations that will ensure acceptable international analytical performance in CRC screening, enable screening programmes to provide evidence that analysis is of adequate quality and enable and encourage publications that describe the use of FIT to include standardised information about analytical performance and quality. To date, however, the analytical quality needed for FIT has received little attention. There is a need to establish traceable calibrators for FIT analysis, criteria for acceptable imprecision; bias should be eliminated. It was proposed that a sub-group of the EWG could be set up to prepare a discussion document on the effect of FIT performance on outcomes and advise on objective analytical quality specifications.

Slide set no. 15: Paula McDonald

'Quality in faecal immunochemical testing – what to monitor, what to control'.

Within an analytical system, results will be influenced pre-analytically by biology, sampling and handling variables, and then by reagents and instrument calibration and control. Awareness of pre-analytical variation and including these in setting analytical performance goals is required. Analytical variation can be measured, reviewed and manipulated to reduce bias within the system. Overall control of the system requires a multifaceted approach to ensure that each component operates within pre-set analytical quality specifications, as evidenced by satisfactory performance in a External Quality Assessment Scheme.

Slide set no. 16: Jane French

'External Quality Assessment'

The preparation of EQA specimens for the BCSP gFOBt uses All Bran breakfast cereal and tinned pumpkin mixed with sterile water containing a known amount of Hb. It was not known if the current EQA material was suitable for use with FIT. Non-BCSP laboratories performing FOB or FIT analyses were asked to assess the bran and pumpkin-based material, which was probably satisfactory for a qualitative card-based FOB testing EQA but was too particulate for quantitative FIT EQA. The challenge is to produce a material that is homogenous and suitable for sampling using the current variety of faecal specimen collection devices. A synthetic medium has so far not proved useable.

Slide set no. 17: Isabel Portillo Villares

'The Basque Country Colorectal Screening Programme'

Population-based CRC screening in the Basque Country of 2.2 million inhabitants commenced in 2009 with biennial FIT for 50-69-year-olds. Coverage, participation and disease detection are good, with input from GPs, a robust information system and affordable cost. There is scope to improve participation and reduce inequities, however, as well as to achieve improved sensitivity, a reduction in the number of false positives and implementation of quality assurance processes.

Slide set no. 18: Josep Maria Augé Fradera

'Diagnostic yield for advanced colorectal neoplasia using FIT with one or two samples'.

This presentation described a study to assess the diagnostic yield of one-sample FIT (HM-JACKarc, Kyowa Medex Co. Ltd., Tokyo) versus the higher faecal Hb concentration from two FIT samples in 209 symptomatic individuals (mean age: 60.7 years) scheduled for colonoscopy. Using two FIT samples increased the sensitivity and detection of advanced colorectal neoplasia (ACRN; cancer or high-risk adenoma) but increased positivity and the number of subjects needed to scope to detect one ACRN. The findings were consistent with other studies in that one-sample FIT with a lower faecal Hb cut-off for positivity equals or improves upon the performance of two-sample FIT.

The slide sets are available on the EWG web pages:

http://www.worldendo.org/fit-for-screening-meeting-reports.html