William Maclean*, Zahida Zahoor, Shane O'Driscoll, Carolyn Piggott, Martin B. Whyte, Timothy Rockall, Iain Jourdan and Sally C. Benton

Comparison of the QuikRead go® point-of-care faecal immunochemical test for haemoglobin with the FOB Gold Wide® laboratory analyser to diagnose colorectal cancer in symptomatic patients

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Abstract

Objectives: Faecal immunochemical testing for haemoglobin (FIT) is used to triage patients for colonic investigations. Point-of-care (POC) FIT devices on the market have limited data for their diagnostic accuracy for colorectal cancer (CRC). Here, a POC FIT device is compared with a laboratory-based FIT system using patient collected samples from the urgent referral pathway for suspected CRC.

Methods: A prospective, observational cohort study. Patients collected two samples from the same stool. These were measured by POC QuikRead go® (Aidian Oy, Espoo, Finland) and laboratory-based FOB Gold Wide® (Sentinel Diagnostics, Italy). Faecal haemoglobin <10 μg haemoglobin/g of faeces was considered as negative. At this threshold, comparisons between the two systems were made by calculating percentage agreement and Cohen's kappa coefficient. Proportion of negative results were compared with Chi squared testing. Sensitivities for CRC were calculated.

Results: A total of 629 included patients provided paired samples for FIT to compare the QuikRead go® and FOB Gold Wide®. The agreement around the negative threshold was 83.0% and Cohen's kappa coefficient was 0.54. The QuikRead go® reported 440/629 (70.0% of samples) as negative compared to 523/629 (83.1%) for the FOB Gold Wide®, this difference was significant (p-value<0.001). Sensitivities for CRC detection by the QuikRead go® and FOB Gold Wide® were 92.9% (95% confidence interval (CI): 68.5–98.7%) and 100% (CI: 78.5–100%) respectively.

Conclusions: Both systems were accurate in their ability to detect CRC. Whilst good agreement around the negative threshold was identified, more patients would be triaged to further colonic investigation if using the QuikRead go®.

Keywords: colorectal cancer; faecal immunochemical testing; point of care testing.

Introduction

Faecal immunochemical testing for haemoglobin (FIT) offers a non-invasive means to triage patients to colonic investigations for both the screening and symptomatic cohorts. There are a wide variety of point-of-care (POC) devices marketed for FIT [1–3]. Early diagnostic accuracy studies show that quantitative POC analysers can perform well [3–5]. A POC FIT analyser within a clinical setting provides the potential for faster decision-making and improved risk-stratification. This could be particularly beneficial when assessing for suspected colorectal cancer (CRC) on urgent referral pathways [6]. Awaiting a laboratory generated FIT result can delay referral from primary care or the initial secondary care appointment. Use of the POC FIT analyser could streamline the patient

***Corresponding author: William Maclean**, MB ChB, MRCS, Research Fellow in General Surgery at Royal Surrey NHS Foundation Trust, Guildford, UK, E-mail: William.maclean@doctors.org.uk. https://orcid.org/0000-0002-0336-6839
Zahida Zahoor and Shane O'Driscoll, Research Assistant at the Bowel Cancer Screening Hub at Royal Surrey NHS Foundation Trust, Guildford, UK. https://orcid.org/0000-0002-8693-3658 (S. O'Driscoll)
Carolyn Piggott, Research and Development Scientist at the Bowel Cancer Screening Hub at Royal Surrey NHS Foundation Trust, Guildford, UK. https://orcid.org/0000-0002-6343-6202
Martin B. Whyte, Clinical Reader in Metabolic Medicine at University of Surrey, Guildford, UK
Timothy Rockall and Iain Jourdan, Consultant Colorectal Surgeon at Royal Surrey NHS Foundation Trust, Guildford, UK
Sally C. Benton, Consultant Biochemist and Clinical Director at the Bowel Cancer Screening Hub at Royal Surrey NHS Foundation Trust, Guildford, UK. https://orcid.org/0000-0001-9230-9088

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pathway by facilitating a more rapid review of urgent referrals or support the implementation of "straight to test" strategies used in secondary care.

In England, samples for FIT are typically sent to laboratories for analysis. There are three laboratory FIT systems (FOB Gold Wide®, OC-Sensor™ and HM-JACKarc) that were recommended by NICE in 2017 [7]. A recent laboratory study carried out an analytical evaluation of three POC analysers and ascertained that the QuikRead go® (Aidian Oy, Espoo, Finland) was potentially suitable for quantitation of faecal haemoglobin (f-Hb) at POC [8]. It was also the most usable, as it was easily portable and could determine a result within 2 min [8]. To assess for clinical utility, it is necessary to compare the diagnostic accuracy and correlation of results to a laboratory-based system [6, 9].

The aim of the study was to compare the POC FIT method with a laboratory-based FIT method in the context of patients referred urgently for suspected CRC. This was achieved by determining the agreement between results and displaying paired f-Hb concentrations for the QuikRead go® (Aidian Oy, Espoo, Finland) and the FOB Gold Wide® (Sentinel Diagnostics, Italy). Diagnostic accuracies were also compared for CRC and serious bowel disease (SBD).

Materials and methods

Study design

The "POC FIT study" (REC: 19/LO/0889) was designed as a prospective observational cohort study. Paired sampling from the same faecal material was performed to allow testing on both the QuikRead go® POC analyser and the laboratory-based FOB Gold Wide® method used on the SENTiFIT® 270 analyser. This was to enable direct comparison between the f-Hb results and diagnostic accuracy of the two systems for patients on the colorectal urgent referral pathway for suspected CRC. The FOB Gold Wide® as a laboratory system, is established in symptomatic testing programmes and has been demonstrated to perform well analytically alongside other FIT systems [10]. Therefore, it was selected for comparison as an available system in the reference laboratory. This also provided the opportunity to expand the limited data for symptomatic patients for the FOB Gold Wide®.

Recruitment took place between July 2019 and March 2020 from symptomatic patients referred to the Royal Surrey NHS Foundation Trust (RSFT). These patients were invited by post and asked to provide two samples from the same bowel motion/faecal sample. The postage invitation supplied the patients with specialised collection devices suitable for both the QuikRead go® and FOB Gold Wide® (further details in Supplementary material, Appendix 1 – FITTER Checklist). They were asked to bring their samples to their clinic appointment, where written consent was obtained if they wished to enrol in the observational study.

Sample size calculation

Westwood et al. (2017) reported that the sensitivity for CRC of laboratory-based FIT in symptomatic patients was 92.1% (95% CI 86.9–95.3%) [11]. Under the assumption that POC QuikRead go® operated with the same sensitivity, a margin of error table (defined as the half-width of a 95% confidence interval) was computed. These computations assumed a CRC prevalence rate of 4% in the urgent referral pathway cohort [12]. The table showed that with a sample size of 600 subjects to undergo FIT, a sensitivity of 92.5% could be estimated within a margin of error of 10% to determine diagnostic accuracy.

Inclusion and exclusion criteria

Patients ≥18 years of age referred on the urgent referral pathway were included. This pathway consisted of patients referred from primary care to colorectal surgery at RSFT with "red flag" bowel symptoms or anaemia according to NG12 guidance [13]. Patients had to have capacity to consent and have provided their samples from fresh faeces and not a stoma bag. Patients who had collected their FIT samples more than 10 days prior to clinic appointment were excluded based upon sample stability recommendations by the manufacturer.

Patients were included in the diagnostic accuracy analysis only if a definitive colorectal investigation was subsequently made. This was either by colonoscopy or CT colonography as both are both highly sensitive for CRC [14]. Patients undergoing flexible sigmoidoscopy were only included if they had presented with perianal symptoms or anorectal bleeding (bright red blood seen separate to the stool in the pan or on the paper). All CRC diagnoses were confirmed by histology reports. High Risk adenomas (HRA) and inflammatory bowel disease (IBD) were also reported. HRAs were defined as either (i) any advanced adenoma (≥10 mm, any sessile serrated lesion or adenomas that contained high risk dysplasia), or (ii) if total number of polyps was ≥5, as per the British Society of Gastroenterology guidelines for surveillance [15]. SBD was defined as a diagnosis of CRC, IBD or HRA.

FIT sample analysis

Further details of specimen collection and handling, analysis, quality management and result recording can be found in Supplementary material, Appendix 1 where these headings are described according to the FITTER checklist [16]. Three colorectal doctors were trained to use the QuikRead go® and were involved in the recruitment from their clinics. They underwent guidance to use the analyser and followed an agreed standard operating procedure. All FOB Gold Wide® samples were analysed in the research laboratory based at the Bowel Cancer Screening Southern Hub in Guildford. All laboratory analysis was overseen by a state-registered biomedical scientist. The two assays used in this study are currently only used for research purposes and not routine clinical use, so are not accredited. However, FOB Gold Wide® has undergone thorough validation. All assays that are routinely used at RSFT bowel cancer screening hub and biochemistry department are UKAS accredited.

As this was an observational study, FIT results were not used to determine investigation outcomes. The POC processing was performed within the clinic appointment, but the results were blinded to

the patient and clinician to avoid potential bias and not influence investigation choice.

Data

A secure web-based clinical database, associated with RSFT and approved by the local information governance team, was developed to audit colorectal patients on the urgent referral pathway. Recruited participants for the study were assigned a unique trial number and their FIT results were entered into the database in a pseudonymised fashion. Access to this data was restricted to members of the research team.

Statistical analysis

Whilst the samples were taken from the same bowel motion/faecal sample, the heterogenic blood distribution within faeces means that the f-Hb are not identical for each paired sample [17]. The two systems have different limits of detection (<10 µg/g for QuikRead and <3 µg/g for FOB Gold Wide®) and quantification (>200 µg/g for QuikRead go® and >1700 µg/g for FOB Gold Wide®). For comparison of paired samples, results outside these ranges were excluded and subsequent non-paired data points were also excluded. To exclude bias, results outside <10 µg/g and >200 µg/g for FOB Gold Wide® were also excluded. The relationship of these pairs were demonstrated by a Bland–Altman plot.

Results where f-Hb <10 µg/g was considered a negative result. The proportion of results that showed f-Hb <10 µg/g was compared between the two systems using Chi squared testing. Inter-assay percentage agreement at this same threshold was calculated and assessed with Cohen's Kappa coefficient [18]. Diagnostic accuracy for CRC and serious bowel disease (SBD) was calculated using the EP12-A2 protocol [19]. Receiver operator characteristic (ROC) curves were created using Analyse-it (Software version: Method Validation edition Ltd, Leeds, UK) on a Windows 10 platform. Area under the curves (AUC) were estimated using the DeLong test [20] and was considered significant if p-value<0.05.

Results

Figure 1 displays the pathway for results to be analysed. 832 patients were invited to the study and 199 patients were not consented. The reasons for not consenting were: not attending appointment or appointment cancelled (n=16), reporting to have not received the pack (n=5) or not sampling at home to bring to clinic (n=178). All remaining 633 patients provided the two FIT samples and were consented. Two pairs of samples were later excluded as days between sampling and analysis were >10 days and two other pairs were excluded as the samples were taken from a stoma. 629 samples were suitable for analysis. The demographics for these patients are shown in Table 1.

Agreement

After excluding results outside the limits of detection and quantification (<10 µg/g or >200 µg/g for the QuikRead go®) and subsequent non-paired data, there were 58 paired data points. Figure 2 shows a Bland–Altman plot showing six points outside the 95% confidence interval. In this graph,

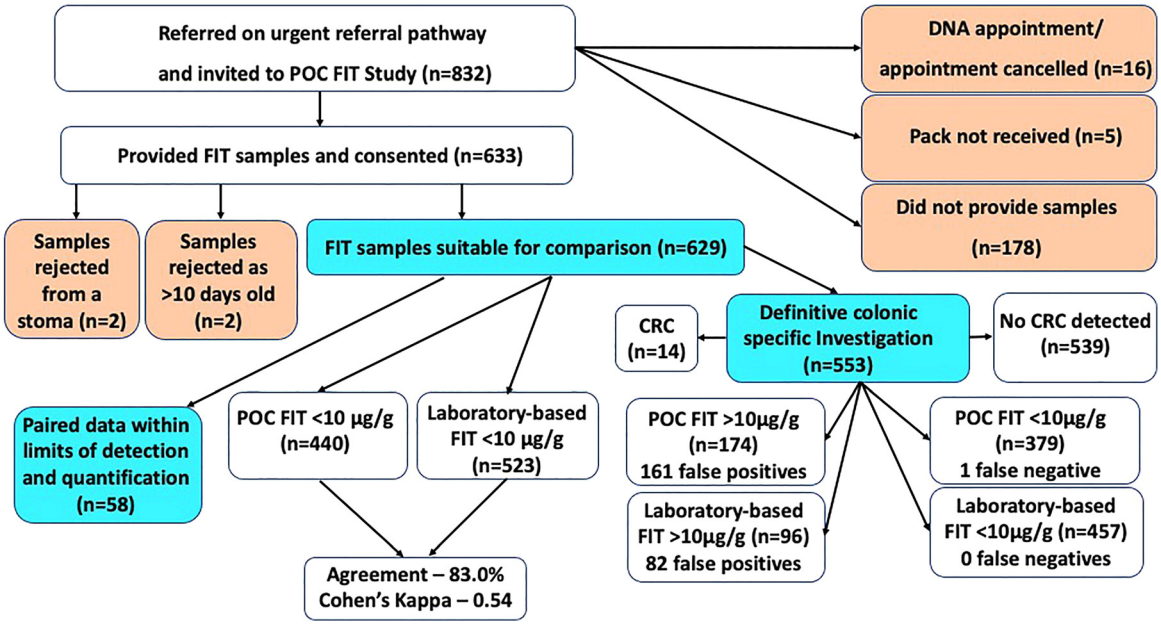

Figure 1: Pathway for results to be analysed.
POC, point-of-care; FIT, faecal immunochemical testing; DNA, did not attend; CRC, colorectal cancer.

Table 1: Age and sex of 629 patients that provided samples and included in comparison.

Variable	Number (% of total)
Sex	
Male	307 (48.8%)
Female	322 (51.2%)
Age, years	
18–39	18 (2.9%)
40–49	40 (6.4%)
50–59	128 (20.3%)
60–69	158 (25.1%)
70–79	183 (29.1%)
80–89	95 (15.1%)
≥90	7 (1.1%)

the bias was -3 µg/g and positive difference was when the f-Hb for QuikRead go® was higher than f-Hb for FOB Gold Wide®. The median values of the 58 paired results were 32 µg/g for both the QuikRead go® and FOB Gold Wide®.

The QuikRead go® reported 440/629 (70.0% of samples) with an f-Hb <10 µg/g compared to 523/629 (83.1%) for FOB Gold Wide®. The proportion of samples testing negative on each analyser, using f-Hb <10 µg/g as a cut-off, was statistically different (p-value<0.001). With the same f-Hb threshold for both tests, an agreement of 83.0% was found and Cohen's Kappa coefficient was 0.54.

Diagnostic accuracy

Of the 629 patients with paired FIT results, 553 underwent colonic investigations that were suitable to give definitive diagnostic outcomes for comparison. There were 14 patients diagnosed with CRC. Results where the f-Hb was <10 µg/g were considered negative, there was one false negative out of 379 negative samples from the QuikRead go® and no false negatives out of 457 negative samples from the FOB Gold Wide®. This breakdown is displayed in Figure 1. In the case of the false negative for the QuikRead go®, the f-Hb reading for the FOB Gold Wide® was 120 µg/g.

The sensitivities to CRC for the QuikRead go® and FOB Gold Wide® were 92.9% (95% confidence interval (CI): 68.5–98.7%) and 100% (CI: 78.5–100%) respectively. The specificities for the QuikRead go® and FOB Gold Wide® were 70.1% (CI: 66.1–73.8%) and 84.8% (81.5–87.6%) respectively. There were 29 diagnoses of HRA and 9 diagnoses of IBD making a total of 52 SBD diagnoses (including CRC). The sensitivities of the QuikRead go® and FOB Gold Wide® for SBD were 76.9% (CI: 63.9–86.3%) and 65.4% (CI: 51.8–76.9%) respectively. Further sensitivities and specificities at other cut-offs are displayed in Table 2 for CRC and Table 3 for SBD.

CRC diagnostic accuracy is displayed with ROC curves in Figure 3. There was an AUC for the QuikRead go® of 0.92 (CI: 0.83–1.00) and an AUC for the FOB Gold Wide® of 0.97 (CI: 0.95–0.99). Both results were significantly different from 0.50 with a p-value<0.001. The difference noted between the two values (0.92 and 0.97) using the DeLong method was not significant (p-value=0.97). SBD diagnostic accuracy is displayed with ROC curves in Figure 4. There was an AUC for the QuikRead go® of 0.81 (CI: 0.74–0.88) and an AUC for the FOB Gold Wide® of 0.80 (CI: 0.73–87). Both results were significantly different from 0.50 with a p-value<0.001.

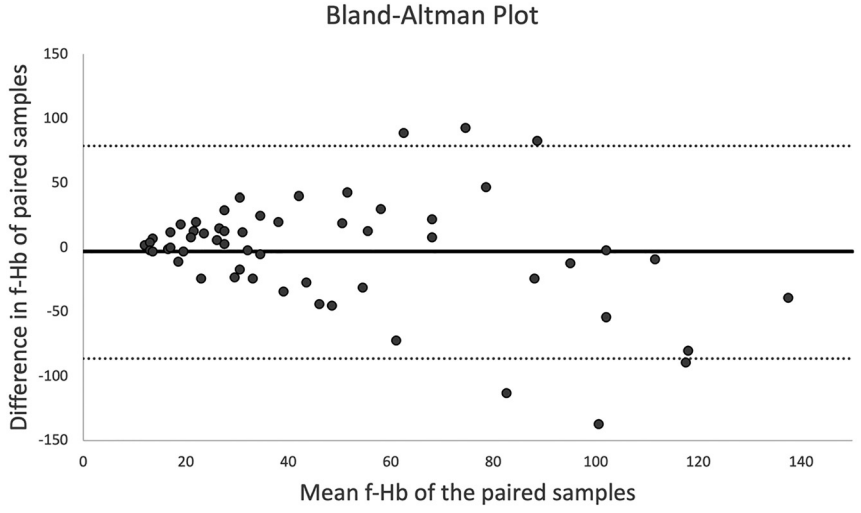

Figure 2: Bland–Altman plot to show the relationship of the 58 paired f-Hb results between the QuikRead go® and FOB Gold Wide® when results were between the limits of detection and quantification.

Table 2: Colorectal cancer diagnostic accuracy according to faecal haemoglobin cut-off.

Analyser	≥Cut off value (µg Hb/g faeces)	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value, %	Negative predictive value, %	Likelihood ratio (+ve)	Likelihood ratio (–ve)
QuikRead go®	10	92.9% (68.5–98.7)	70.1% (66.1–73.8)	7.5	99.7	3.1	0.1
	100	71.4% (45.4–88.3)	94.6% (92.4–96.2)	25.6	99.2	13.3	0.3
	150	57.1% (32.6–78.6)	95.9% (93.9–97.3)	26.7	98.9	14.0	0.5
FOB Gold Wide®	3	100% (78.5–100)	77.0% (74.8–81.7)	10.1	100	4.35	0
	10	100% (78.5–100)	84.8% (81.5–87.6)	14.6	100	6.57	0
	100	92.9% (68.5–98.7)	93.9% (91.5–95.6)	28.3	99.8	15.17	0.1
	150	78.6% (52.4–92.4)	94.8% (92.6–96.4)	28.2	99.4	15.13	0.2

Table 3: Serious bowel disease diagnostic accuracy according to faecal haemoglobin cut-off.

Analyser	≥Cut off value (µg Hb/g faeces)	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value, %	Negative predictive value, %	Likelihood ratio (+ve)	Likelihood ratio (–ve)
QuikRead go®	10	76.9% (63.9–86.3)	74.7% (70.7–78.3)	24.0	96.9	3.03	0.31
	100	38.5 (26.5–52.0)	96.2 (94.2–97.6)	51.3	93.8	10.14	0.64
	150	28.8 (18.3–42.3)	97.0 (95.1–98.2)	50.0	92.9	9.63	0.73
FOB Gold Wide®	3	71.2% (57.7–81.7)	81.4 (77.8–84.6)	28.5	96.5	3.83	0.35
	10	65.4 (51.8–76.9)	87.6 (84.5–90.2)	35.4	96.1	5.28	0.40
	100	44.2 (31.6–57.7)	95.4 (93.2–96.9)	50.0	94.3	9.63	0.58
	150	38.5 (26.5–52.0)	96.2 (94.2–97.6)	51.3	93.8	10.14	0.64

Discussion

In this study, we report on the agreement around an f-Hb threshold of <10 µg/g and the diagnostic accuracies between a POC analyser and a laboratory-based system for FIT. Both systems are highly sensitive for CRC. The heterogeneity of faeces means that two paired faecal samples collected this way will not give identical results [17]. However, the Bland–Altman plot demonstrates a good relationship between the two systems and there is no clear overall bias from one analyser to the other. It is reassuring that the results did demonstrate a high percentage agreement, and the diagnostic accuracies for both CRC and SBD were not significantly different.

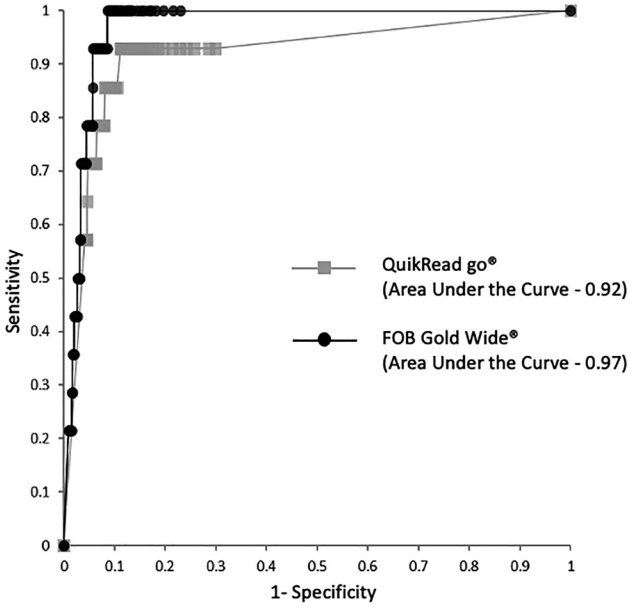

Figure 3: Receiver operator characteristic curves for QuikRead go® and FOB Gold Wide® for colorectal cancer.

Regarding f-Hb <10 µg/g as a negative result, there was a significant difference in the proportion of patients that tested negative using the QuikRead go® compared to the FOB Gold Wide® (70.0 vs. 83.1%). Therefore, if using the QuikRead go®, more patients would potentially be referred for colonoscopy. This is also demonstrated in the positive predictive value of the FOB Gold Wide® being nearly double than that of the QuikRead go® (14.6 vs. 7.5%), which could have an impact on the number needed to scope for CRC. The higher number of false positives may also induce unnecessary and avoidable stress for patients, who would have otherwise avoided a colonoscopy. Cohen's kappa coefficient demonstrated moderate agreement. However, this is lower than the agreement found by Chapman et al. who used this to comparing two

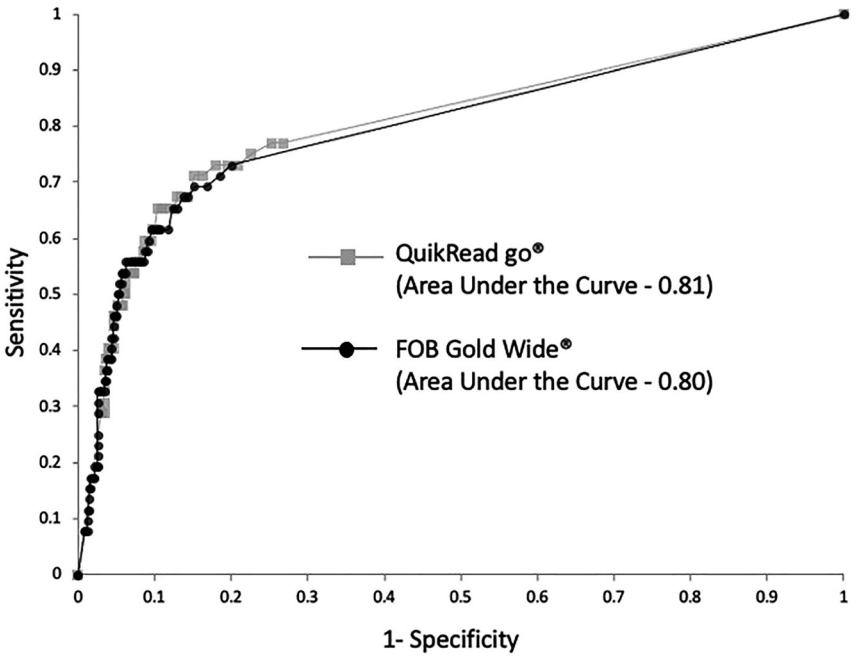

Figure 4: Receiver operator characteristic curves for QuikRead go® and FOB Gold Wide® for serious bowel disease.

laboratory-based systems (OC-Sensor™ and HM-JACKarc) and found kappa to be 0.79 [21].

The emergence of COVID-19 has prompted a greater need to rationalise endoscopic resources, which has broadened the application of FIT within the symptomatic population [22]. This use of triage has enabled significant reduction in the overall need for colonoscopy [23, 24]. However, if different FIT systems are used, the lack of standardisation creates variation between the quantitative results [10, 25]. There is currently no standardisation of FIT methods [26]. Using different systems, whilst maintaining the same cut-off concentration for positivity, has been shown to alter referral rates [21, 27]. This has implications for both risk stratification for patients as well as resource and cost implications.

The high sensitivity for CRC of the QuikRead go® was similar to that of the FOB Gold Wide® implying that the POC analyser is safe for clinical use. The 92.9% CRC sensitivity and 76.4% SBD sensitivity of the QuikRead go® is in line with the recent multi-centre NICE FIT study that reported laboratory-based FIT in the suspected cancer cohort with high-risk symptoms to be 90.9% for CRC and 62.6% for SBD using <10 μg/g as a cut-off [28]. Use of higher thresholds such as 100 or 150 μg/g, as shown in Table 2, was poorer for the QuikRead go® as CRC sensitivity dropped to 71.4 and 57.1% respectively for CRC. However, the FOB Gold Wide® did maintain a high sensitivity at the 100 μg/g cut-off and would have missed only one CRC. Use of higher thresholds can be beneficial in grading risk for patients, particularly in resource limited situations, such as the COVID-19 pandemic [24]. The difference in sensitivity using <10 μg/g as a cut-off between the QuikRead go® and FOB Gold Wide® was made by noting one false negative reading by the QuikRead go® analyser. In this case, there was a wide difference in the two f-Hb readings. Whilst the QuikRead go® reported <10 μg/g, the FOB Gold Wide® gave a reading of 120 μg/g. Such a wide difference could highlight a sampling error exacerbated by the request to perform the two samples from the same faeces. A possible reason for a false negative is no stool being placed into the sampling grooves. We cannot exclude the possibility that this discrepant result was due to no faecal material being present in the QuikRead go® collection device.

The POC system, used within an outpatient setting for the symptomatic patient, removes the need for laboratory sample delivery and processing time. Having a device that is comparable in its diagnostic accuracy to laboratory-based testing can provide reassurance to patients and clinicians for its utility. Usability for a POC device is also a key consideration for application [6], the results from the QuikRead go® would have all been available within the timeframe of each consultation within the study. The analyser is easily portable and can return a result within 2 min [8].

Whilst FIT collection devices were sent to patients in the post for this study, the collection devices could instead be provided to patients as part of an initial GP appointment for them to bring to their secondary care appointment. Use of a standard operating procedure, documentation as per study protocols and use of a database allowed for accurate

recording of results. For better entry into electronic patient records, the QuikRead go® has the potential to be integrated into hospital results systems and for a barcode reader to scan a barcode on the device. This would better facilitate audit and service evaluation to meet the governance responsibilities [9].

Ideally, the POC system could be used in primary care, however, further evidence generation centred around this as a clinical pathway is needed to evaluate its potential impact [9]. Using the device within a single consultation would be the most efficient, but faecal sampling would need to be performed at home and brought back for a further appointment, if samples are collected by the patient. Alternatively, a clinician may be able to collect a sample at clinical examination via a digital rectal examination, two studies have described this technique [29, 30]. If this method is to be deemed accurate, then potential for POC FIT within a single consultation would be more viable.

The focus of the study was in obtaining f-Hb concentrations for the two systems and determining diagnostic accuracies. Therefore, we have not carried out a cost benefit analysis of POC FIT compared to laboratory-based FIT as part of the study. Such an analysis would need to assess the potential benefits against more than just reagent costs, but also equipment procurement, maintenance costs and extra staffing requirements as part of a new service evaluation.

Study limitations

The number of CRCs detected in our cohort of suspected cancer patients was low. This created a wider confidence interval around the sensitivity than anticipated for our sample size. However, the confidence interval for SBD is more precise. The authors also recognise that the gold standard comparison of colonoscopy, CT colonography or flexible sigmoidoscopy provides potential error as none of these tests are themselves 100% sensitive for CRC [14]. Verification by correlating the results with the FOB Gold Wide®, that is a registered laboratory-based method, contributes to validating the results we have found for the POC device. All CRCs detected by the original gold standard colonic investigation were subsequently confirmed by histological diagnoses.

Conclusions

The QuikRead go® POC analyser showed a good percentage agreement to the FOB Gold Wide® method and both systems were highly sensitive for CRC. This offers potential to faster decision-making, cost saving opportunities and patient experience in the suspected cancer pathway. However, using f-Hb <10 μg/g as a cut-off means that significantly more patients would test positive if using the QuikRead go®. This has implications on the proportion of patients that would be triaged to further colonic investigation.

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Author contributions: All authors have accepted responsibility for the entire content of this manuscript and approved its submission.

Competing interests: Authors state no conflict of interest.

Informed consent: Informed and written consent was obtained from all individuals included in this study.

Ethical approval: Ethics for the project was approved by the London - South East Research Ethics Committee on 28th May 2019 (REC reference: 19/LO/0889, IRAS ID: 260384).

Clinical trial registration: The study was registered on clinicaltrials.gov (Identifier: NCT04402424). The study was adopted onto the NIHR portfolio.

References

1. Nicholson B, Thompson M, Price CP, Heneghan C, Pluddemann A. Point-of-Care faecal occult blood testing. Horiz Scan Rep 0035 [Internet] 2014:85–94. Available from: https://www.community.healthcare.mic.nihr.ac.uk/reports-and-resources/horizon-scanning-reports/point-of-care-faecal-occult-blood-testing.
2. Nicholson BD, Price CP, Heneghan C, Plüddemann A, Thompson M. Home-use faecal immunochemical testing: primary care diagnostic technology update. Br J Gen Pract 2015;65:156–8.
3. Gies A, Cuk K, Schrotz-King P, Brenner H. Direct comparison of ten quantitative fecal immunochemical tests for hemoglobin stability in colorectal cancer screening. Clin Transl Gastroenterol 2018;9:168.

4. Gies A, Cuk K, Schrotz-King P, Brenner H. Combination of different fecal immunochemical tests in colorectal cancer screening: any gain in diagnostic performance? Cancers 2019;11:16–8.
5. Tsapournas G, Hellström PM, Cao Y, Olsson LI. Diagnostic accuracy of a quantitative faecal immunochemical test vs. symptoms suspected for colorectal cancer in patients referred for colonoscopy. Scand J Gastroenterol 2020;55:184–92.
6. Huddy JR, Ni MZ, Markar SR, Hanna GB. Point-of-care testing in the diagnosis of gastrointestinal cancers: current technology and future directions. World J Gastroenterol 2015;21:4111–20.
7. National Institute for Health and Care Excellence. Quantitative faecal immunochemical tests to guide referral for colorectal cancer in primary care Diagnostics guidance [Internet]. Diagnostics Guidance DG30; 2017. Available from: https://www.nice.org.uk/guidance/dg30/resources/quantitative-faecal-immunochemical-tests-to-guide-referral-for-colorectal-cancer-in-primary-care-pdf-1053744003781 [Accessed 15 Aug 2021].
8. O'Driscoll S, Carroll M, Maclean W, Piggott C, Jourdan I, Benton SC. Assessment of the analytical performance of point-of-care faecal immunochemical tests for haemoglobin. Ann Clin Biochem 2021; 58:181–9.
9. Huddy JR, Ni M, Misra S, Mavroveli S, Barlow J, Hanna GB. Development of the point-of-care key evidence tool (POCKET): a checklist for multi-dimensional evidence generation in point-of-care tests. Clin Chem Lab Med 2019;57:845–55.
10. Piggott C, Carroll MRR, John C, O'Driscoll S, Benton SC. Analytical evaluation of four faecal immunochemistry tests for haemoglobin. Clin Chem Lab Med 2021;59:173–8.
11. Westwood M, Ramos IC, Lang S, Luyendijk M, Zaim R, Stirk L, et al. Faecal immunochemical tests to triage patients with lower abdominal symptoms for suspected colorectal cancer referrals in primary care: A systematic review and cost-effectiveness analysis. Health Technol Assess 2017;21:1–234.
12. D'Souza N, Hicks G, Benton SC, Abulafi M. The diagnostic accuracy of the faecal immunochemical test for colorectal cancer in risk-stratified symptomatic patients. Ann R Coll Surg Engl 2019; 102:174–9.
13. National Institute for Health and Care Excellence. Suspected cancer: recognition and referral NICE guideline [Internet]. Available from: https://www.nice.org.uk/guidance/ng12https://www.nice.org.uk/guidance/ng12/resources/suspected-cancer-recognition-and-referral-pdf-1837268071621 [Accessed 15 Aug 2021].
14. Martín-López JE, Beltrán-Calvo C, Rodríguez-López R, Molina-López T. Comparison of the accuracy of CT colonography and colonoscopy in the diagnosis of colorectal cancer. Colorectal Dis 2014;16:82–90.
15. Rutter MD, East J, Rees CJ, Cripps N, Docherty J, Dolwani S, et al. British society of gastroenterology/association of coloproctology of great Britain and Ireland/public health England post-polypectomy and post-colorectal cancer resection surveillance guidelines. Gut 2020;69:201–23.
16. Fraser CG, Allison JE, Young GP, Halloran SP, Seaman H. A standard for faecal immunochemical TesTs for haemoglobin evaluation reporting (FITTER). Ann Clin Biochem 2014;51:301–2.
17. Auge JM, Rodriguez C, Espanyol O, Rivero L, Sandalinas S, Grau J, et al. An evaluation of the SENTiFIT 270 analyser for quantitation of faecal haemoglobin in the investigation of patients with suspected colorectal cancer. Clin Chem Lab Med 2018;56: 625–33.
18. Gisev N, Hons BP, Bell JS, Chen TF. Interrater agreement and interrater reliability: key concepts, approaches, and applications. Res Soc Adm Pharm 2013;9:330–8.
19. Garrett PE. User protocol for evaluation of qualitative test performance; Approved Guideline – Second Edition. CLSI/NCCLS Doc EP12-A2, Approv Guidel, 2nd Ed. Wayne, PA: Clinical and Laboratory Standards Institute; 2008:28 p.
20. DeLong ER, DeLong DM, Clarke-Pearson DL. Comparing the areas under two or more correlated receiver operating characteristic curves: a nonparametric approach. Biometrics 1988;44:837–45.
21. Chapman CJ, Banerjea A, Humes DJ, Allen J, Oliver S, Ford A, et al. Choice of faecal immunochemical test matters: comparison of OC-Sensor and HM-JACKarc, in the assessment of patients at high risk of colorectal cancer. Clin Chem Lab Med 2021;59:721–8.
22. Arasaradnam RP, Bhala N, Evans C, Greenaway J, Logan R, Penman I, et al. Faecal immunochemical testing in the COVID-19 era: balancing risk and costs. Lancet Gastroenterol Hepatol 2020;5:717–9.
23. Tolley T, Whewell H, Davies DR, Codd RJ, Swarnkar KJ, Williams GL. Colorectal cancer referrals during the COVID-19 pandemic: the utility of CT and faecal immunochemical testing. Br J Surg 2021;108:E119–20.
24. Maclean W, Limb C, Mackenzie P, Whyte MB, Benton SC, Rockall T, et al. Adoption of faecal immunochemical testing for 2-week-wait colorectal patients during the COVID-19 pandemic: an observational cohort study reporting a new service at a regional centre. Colorectal Dis 2020;23:1622–9.
25. O'Driscoll S, Piggott C, Bruce H, Benton SC. An evaluation of ten external quality assurance scheme (EQAS) materials for the faecal immunochemical test (FIT) for haemoglobin. Clin Chem Lab Med 2021;59:307–13.
26. Benton SC, Symonds E, Djedovic N, Jones S, Deprez L, Kocna P, et al. Faecal immunochemical tests for haemoglobin: analytical challenges and potential solutions. Clin Chim Acta 2021;517: 60–5.
27. Chiang TH, Chuang SL, Chen SLS, Chiu HM, Yen AMF, Chiu SYH, et al. Difference in performance of fecal immunochemical tests with the same hemoglobin cutoff concentration in a nationwide colorectal cancer screening program. Gastroenterology 2014; 147:1317–26.
28. D'Souza N, Delisle TG, Chen M, Benton S, Abulafi M. Faecal immunochemical test is superior to symptoms in predicting pathology in patients with suspected colorectal cancer symptoms referred on a 2WW pathway: a diagnostic accuracy study. Gut 2021;70:1130–8.
29. Khan AA, Klimovskij M, Harshen R. Accuracy of faecal immunochemical testing in patients with symptomatic colorectal cancer. BJS Open 2020;4:1180–8.
30. Grainger J, Skaife P. PWE-338 Digital rectal examination: a discriminatory test in the diagnosis of colo rectal cancer: abstract PWE-338 Table 1. Gut 2015;64:A358.

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