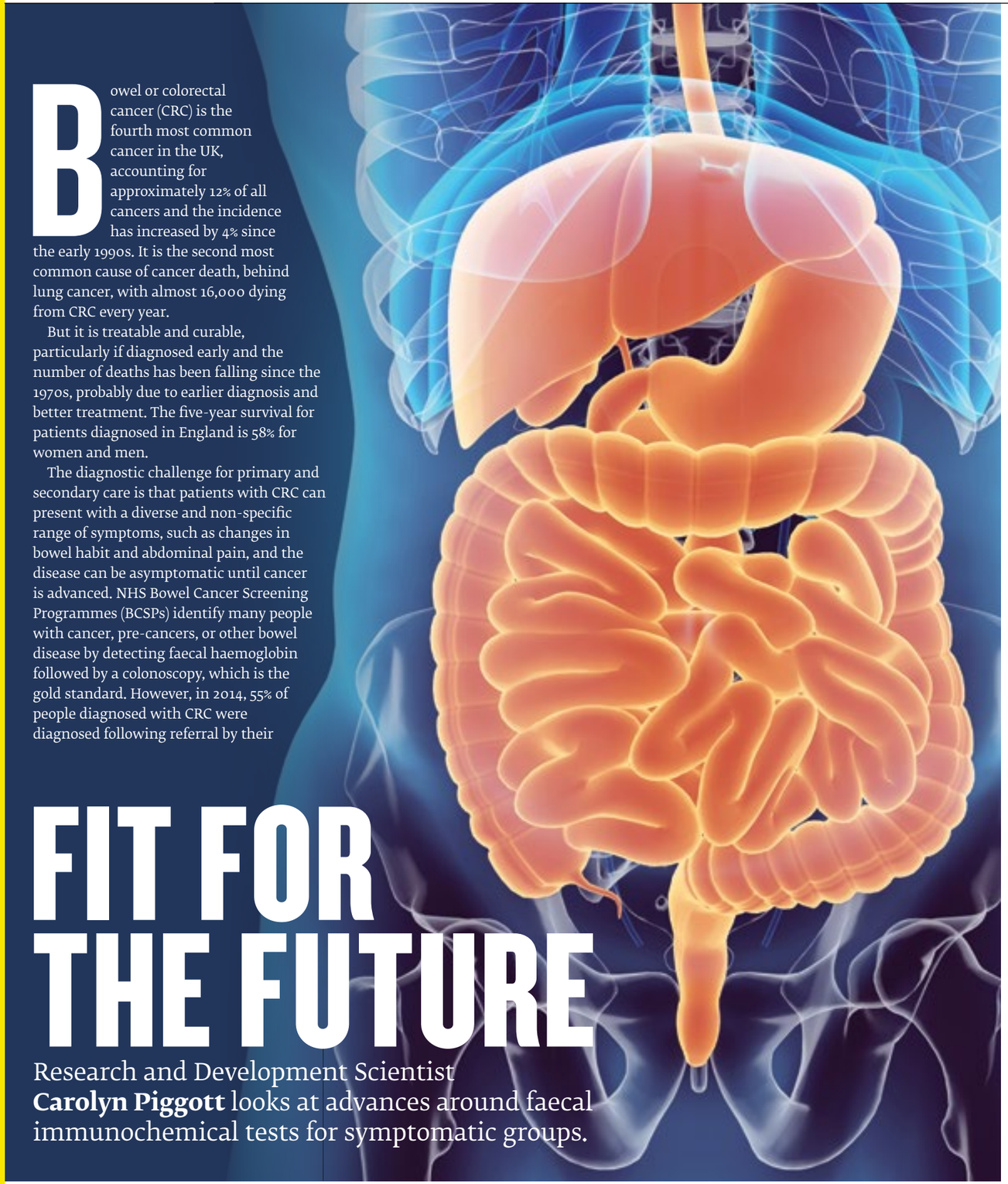

FIT FOR THE FUTURE

Research and Development Scientist **Carolyn Piggott** looks at advances around faecal immunochemical tests for symptomatic groups.

Bowel or colorectal cancer (CRC) is the fourth most common cancer in the UK, accounting for approximately 12% of all cancers and the incidence has increased by 4% since the early 1990s. It is the second most common cause of cancer death, behind lung cancer, with almost 16,000 dying from CRC every year.

But it is treatable and curable, particularly if diagnosed early and the number of deaths has been falling since the 1970s, probably due to earlier diagnosis and better treatment. The five-year survival for patients diagnosed in England is 58% for women and men.

The diagnostic challenge for primary and secondary care is that patients with CRC can present with a diverse and non-specific range of symptoms, such as changes in bowel habit and abdominal pain, and the disease can be asymptomatic until cancer is advanced. NHS Bowel Cancer Screening Programmes (BCSPs) identify many people with cancer, pre-cancers, or other bowel disease by detecting faecal haemoglobin followed by a colonoscopy, which is the gold standard. However, in 2014, 55% of people diagnosed with CRC were diagnosed following referral by their GP, and 20% by emergency hospital presentation, either because they are outside of the BCSP invitation age, they decline to take part in screening, or the cancer/pre-cancer if present is not bleeding when the sample is collected.

Referring

GPs and gastroenterologists are unable to refer all patients with symptoms for colonoscopy because the procedure is expensive and the system is struggling to keep up with demand, which is predicted to increase in the foreseeable future.

Also, importantly, the procedure carries an uncommon but occasionally significant risk to the patient, including bowel perforation. Furthermore, many colonoscopies do not find either cancer or significant bowel disease, so a test to select patients with low-risk symptoms for colonoscopy is beneficial.

Historically the guaiac faecal occult blood test (gFOBt) has been performed in pathology labs to help clinicians to decide which patients should be referred for colonoscopy. gFOBt detects small amounts of blood in faeces by the peroxidase activity of haem; the test is very simple and gives a straightforward quantitative positive or negative result, but it also has a number of limitations.

False positives can be caused by animal blood in food, some vegetables have peroxidase activity and vitamin C inhibits peroxidase activity. Haem also remains intact during transit through the gut, so there can be interference from bleeding in the upper GI tract. For the hema-screen gFOBt the minimum concentration of f-Hb detected is 600µg Hb/g faeces. The test is also far from ideal because it is manual, the result is usually read by eye and interpretation is subjective. Inevitably, the gFOBt test has been phased out from most labs.

FIT advantages

The faecal immunochemical test (FIT) for haemoglobin (f-Hb) measurement is an enhanced FOBt that can be quantitative or qualitative and uses antibodies specific to human globin, typically in an immunoturbidimetric or lateral flow palette method. FITs have a number of advantages over gFOBts. The tests are many times more sensitive than gFOBt because of the use of polyclonal antibodies in the reagent. There is no interference from non-human blood or vegetables, and there is less interference from bleeding in the upper GI tract. The test can be automated and if quantitative gives a numerical result. Due to the increased sensitivity and specificity of FIT compared with gFOBt, fewer samples are required, so the test is more convenient for the patient. Samples can also be taken from faeces collected into traditional stool collection pots but globin is less stable than haem so any samples collected this way are not recommended for FIT.

FIT f-Hb measurement is now being introduced into the pathology repertoire following publication of the NICE guidance in July 2017, which recommends FIT "for adoption in primary care to guide the referral for suspected cancer in people without rectal bleeding who have unexplained symptoms but do not meet the criteria for a suspected cancer pathway referral".

Three quantitative FITs are recommended by the NICE Diagnostics Guidance: FOB Gold, HM-JACKarc and OC-Sensor. Faecal sample collection devices can be used by the patient to collect a small amount of stool onto a probe which is inserted into a bottle containing a preservative buffer. Samples collected this way typically have a stability of seven to 14 days at room temperature, so using these devices has an advantage over collecting samples into the traditional stool pots, where f-Hb degrades more quickly. Samples can easily be collected at home and sent to the laboratory via the GP or by post and the collection devices are designed to load straight onto the analyser.

> *Faecal immunochemical tests look set to become part of the pathology repertoire*

Analytical challenges

FIT methods have been used in bowel cancer screening programmes worldwide for a number of years, and are ideal for this use because a "cut-off" f-Hb concentration can be chosen to match screening colonoscopy capacity. FITs have only recently been introduced for symptomatic populations and research studies published. A recent systematic review of FIT studies including symptomatic patients concluded: "There is evidence to suggest that triage using FIT at a cut-off around 10µg Hb/g faeces has the potential to correctly rule out CRC and avoid colonoscopy in 75% to 80% of symptomatic patients."

The FIT method presents several analytical challenges. Currently, there is no international standardisation of FIT methods. Manufacturers have been working with an International Federation of Clinical Chemistry working group to address this. External quality assessment schemes are in their infancy and being refined to serve FIT. There are pre-analytical factors to take into account: distribution of blood in stools may not be heterogeneous, not all tumours bleed, and sample collection is reliant on the patient.

FIT looks set to become another part of the pathology repertoire, so that precious colonoscopy resources can be used for the patients most likely to need them. BMS

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IMAGE: ISTOCK