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**Point-of-care testing in the diagnosis of gastrointestinal cancers: Current technology and future directions**

Huddy JR *et al.* Point-of-care testing in gastrointestinal cancer

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**Abstract**

Point-of-care (POC) tests enable rapid results and are well established in medical practice. Recent advances in analytical techniques have led to a new generation of POC devices that will alter gastrointestinal diagnostic pathways. This review aims to identify current and new technologies for the POC diagnosis of gastrointestinal cancer. A structured search of the Embase and Medline databases was performed. Papers reporting diagnostic tests for gastrointestinal cancer available as a POC device or containing a description of feasibility for POC application were included. Studies recovered were heterogeneous and therefore results are presented as a narrative review. Six diagnostic methods were identified (fecal occult blood, fecal proteins, volatile organic compounds, pyruvate kinase isoenzyme type M2, tumour markers and DNA analysis). Fecal occult blood testing has a reported sensitivity of 66-85% and specificity greater than 95%. The others are at a range of development and clinical application. POC devices have a proven role in the diagnosis of gastrointestinal cancer. Barriers to their implementation exist and the transition from experimental to clinical medicine is currently slow. New technologies demonstrate potential to provide accurate POC tests and an ability to diagnose gastrointestinal cancer at an early stage with improved clinical outcome and survival.

**Key words:** Colorectal cancer; Gastric cancer; Esophageal cancer; Cancer-diagnosis; Diagnostic tests

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**Core tip:** Point-of-care tests are well established. They facilitate real time clinical decision-making and can be cost-effective, reduce in-patient hospital stay and increase patient satisfaction. Faecal Occult Blood has been used internationally since 1993 in screening for colorectal cancer. Six technologies for current or potential point-of-care diagnosis of gastro-intestinal cancer were identified from the literature (faecal occult blood, faecal proteins, volatile organic compounds, pyruvate kinase isoenzyme type M2, tumour markers and DNA analysis). Currently, three have commercially available point-of-care devices. New technologies demonstrate potential to provide accuracy and an ability to diagnose gastrointestinal cancer earlier leading to improved clinical outcome and survival.

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**INTRODUCTION**

Point-of-care (POC) testing enables near patient or bedside tests that provide instant or rapid results to facilitate real time clinical decision making within established patient care pathways. POC tests are well established in some areas of medical practice including monitoring of blood glucose levels, anti-coagulation and in pregnancy. They bring potential advantages by decreasing the time to diagnosis and institution of treatment, eliminating requirements for specialist clinical and laboratory staff to perform and analyse tests. This stream-lined approach to diagnostic medicine has further advantages including improved cost-effectiveness[1,2], reduced in-patient hospital stay and increased patient satisfaction[3]. Furthermore recent advances in analytical techniques such as microfluidics[4], metabolomics[5] and nanotechnology[6] has led to the development of POC testing with improved sensitivity and specificity for the diagnosis, monitoring and response to treatment in common disease processes including cancer.

The three most common sites for gastrointestinal cancer are colorectal, stomach and esophagus which together account for more than 56400 new cases of cancer each year in the United Kingdom[7] and early detection is paramount to improving outcomes. This is demonstrated by direct comparison between institutions in the East and the West that have shown a better long-term survival following surgical resection of gastric cancer in Eastern centres[8–11], where early detection and treatment of esophago-gastric cancers is achieved through the utilization of endoscopic screening programmes.

The current established diagnostic pathway for gastrointestinal cancers follows an index of clinical suspicion based upon presenting symptoms and clinical assessment in primary care leading to referral to secondary care, supported by two-week referral guidelines, and followed by specialist multidisciplinary investigation with endoscopy, histological diagnosis and radiology. This current diagnostic model may be subject to several points of potential failure, with the most important being the initial primary care assessment and index of suspicion which is highly assessor dependent and subject to bias. Therefore, these pathways often have a low sensitivity and result in large numbers of negative endoscopies representing significant financial waste along with patient discomfort and potentially harm.

POC techniques are already utilised in primary care for screening patients in gastrointestinal cancer for example fecal occult blood in colorectal carcinoma, and advances in technology and translational medicine suggest that POC tests may in the future be able to diagnose gastrointestinal cancers at the patient’s bedside, in the outpatient clinic or even by the patient self-testing at home. Ideally, new diagnostic tests should demonstrate diagnostic accuracy similar to or better than current reference tests, although it is conceivable that a poorer accuracy may be accepted as a tradeoff for the convenience of POC devices or a lower risk of associated complications. New tests must also be usable and cost-efficient in comparison to current standard tests.

POC technologies have the potential to dramatically alter established patient care pathways, as results can be immediately available in primary care or the home, resulting in a faster application of appropriate treatment or referral for further investigation. This needs evaluation to ascertain whether current treatment algorithms based on evidence generated from reference testing practices will still apply and how this will affect patient’s quality of life. For example patients self-diagnosing themselves with a new diagnosis of suspected cancer in their own home would leave them feeling unsupported, without access to information or counseling and may have a detrimental effect on their state of mind, compliance with further treatment and potential outcome from disease.

The aim of this present review is to identify and critically evaluate the current use of POC tests in the diagnosis and assessment of gastrointestinal cancer and consider the techniques and technology that demonstrate potential for the POC devices of the future.

**RESEARCH**

An initial review of the literature was performed. Electronic searches of Embase and Medline databases were searched from 1946 to October 2013. The search strategy consisted of keywords and MeSH headings designed to identify articles related to POC tests and gastrointestinal cancers and these were then combined with the Boolean operators AND and OR. The full search strategy used is described in Table 1.

Titles and abstracts were then reviewed to ensure relevance by meeting inclusion criteria. Papers describing a diagnostic test for gastrointestinal cancer that was achievable at the POC were included. Papers reporting diagnostic tests not yet commercially available as a POC device, but containing an explanation of feasibility for POC application were also included. Animal studies were included but papers not published in English were excluded during the initial review. Full texts of eligible papers were then reviewed.

This initial search was undertaken to identify POC devices and their underlying technologies. The studies recovered from the search were heterogeneous and therefore results are presented as a narrative review. Secondary literature searches were performed within Medline that were specific to identified technologies to ensure the full scope of current literature was evaluated and diagnostic tests that were recovered in these secondary searches were also included in the review.

**RESULTS**

The initial search highlighted 1014 articles after duplications were removed. 414 articles recovered in the initial search were related to POC testing for helicobacter pylori but these did not meet inclusion criteria and were excluded. From the review of titles and abstracts 20 were retrieved for further evaluation. Four further papers were excluded on review of the full manuscripts as they did not relate to POC technologies. Five POC methods were identified with a current or potential role in the diagnosis of gastrointestinal cancer and one further technology (volatile organic compounds) was also included as it was identified in the supplementary detailed technology-specific searches. These are summarized in Table 2.

The results are described individually with an overview of their development, role in patient care pathway and where possible validity.

***Fecal occult blood***

The most widely accepted POC test for gastrointestinal cancer is fecal occult blood (FOB) sampling. Whilst occult blood detection was first described in 1864, it was not until 1967 that the hypothesis was suggested for its role in the early detection of colorectal cancer with the first described guaiac based assays[12]. In 1993 the Minnesota Colon Cancer Control Study demonstrated that an annual screening programme of 50-80 year olds using guaiac based FOB kits and colonoscopy in patients testing positive decreased the 13 year cumulative mortality from colorectal cancer by 33%[13]. Since this landmark study national colorectal cancer screening programs have been widely adopted in countries across the world[14] including the United Kingdom[15].

Whilst colorectal cancer screening programs have demonstrable benefit in reducing disease specific mortality[16–19], guaiac based tests do have inherent limitations that translate into a reduced sensitivity and specificity. These include a lack of specificity for human blood and therefore false positive results can be caused by meat, vegetable and fruit products containing peroxidase[20] as well as upper gastrointestinal sources of bleeding, especially when provoked by aspirin or non-steroidal anti-inflammatory drugs. Specificity can be improved to some extent by dietary and medication restrictions prior to test sampling and sensitivity by the rehydration of slides[13], although this is at the expense of specificity. A further disadvantage of guaiac based tests is the relatively low sensitivity (16%-31%)[21] for advanced adenomas.

To address the above limitations, newer immunochemical FOB tests have been developed that are specific for human FOB and exclude upper GI occult blood as globin is metabolised by gastric enzymes. Although more expensive, they achieve better sensitivity, with comparable specificity[22] and compliance is better due to the more amenable sampling procedure with fewer consecutive stool samples required for testing[23,24]. Accuracy of FOB test devices can be titrated accordingly to threshold levels, hydration state of slides and device or combination used, but pooled analysis suggests a sensitivity of approximately 79% and specificity of 94% with immunochemical tests[25]. Currently the FOB test represents the most widely applied POC test in the setting of gastrointestinal cancer. However, as described there are concerns regarding diagnostic accuracy associated with its application that have in more recent years suggested flexible sigmoidoscopy may represent an alternative screening investigation in asymptomatic individuals[26].

***Fecal proteins***

Several proteins including lactoferrin, lysozyme and albumin have been investigated as potential fecal markers of organic bowel pathology but with the exception of calprotectin they have shown little promise in view of their poor diagnostic accuracy[27].

Calprotectin is a protein derived predominantly from neutrophils and has been shown to be increased in inflammation and malignant processes within the large bowel[28]. It has been suggested that calprotectin can offer greater accuracy than FOB in the diagnosis of organic colorectal disease, as calprotectin is present continuously within the gut lumen as a result of leucocyte recruitment to tumour tissue and does not rely on intermittent bleeding[29]. However, calprotectin has a low specificity as it does not differentiate between inflammatory and cancer and therefore is unsuitable for screening in colorectal cancer[30–32]. A recent review reported a mean sensitivity of 83% and a specificity of 84%[33] for all organic bowel disease. POC test kits for calprotectin and FOB have been compared[34] and strategies for combination testing using FOB and calprotectin[35] have been proposed to increase accuracy but this has not been adopted into screening programmes at the present time.

Overall, it is diagnostic accuracy and specificity that prevents the widespread use of POC calprotectin testing in diagnosing gastrointestinal cancer. Although, its use as a combination approach with FOB to provide more accurate fecal screening or the ability to screen for all organic bowel disease including inflammatory conditions may permit continued commercial viability, further evidence is required to define the nature of this role.

***Volatile organic compounds***

Metabolomics is a fast growing area of medical research and represents an area of particular promising growth towards the development of POC diagnostic technology. Volatile organic compounds (VOC), resulting from the chemical output of metabolic processes within the body, can be measured in-vitro through exhaled air, sweat, urine and faeces with modern laboratory techniques. Selected ion flow tube mass spectrometry is one method that allows real time quantification of multiple VOCs in human breath without sample modification and therefore represents huge potential as a medium to allow non-invasive POC testing[36]. Preliminary work at our institution in VOC profiling for esophago-gastric cancer has led to the discovery of four VOCs (hexanoic acid, phenol, methyl phenol, and ethyl phenol) that are statistically different in the exhaled breath of patients with esophago-gastric cancer when compared to controls and gave an accuracy of 0.91 based on the integrated area under receiver operating characteristic curve[5]. Similar VOC profiling patterns in esophago-gastric cancer patients have been achieved for urine[37] and gastric contents[38].

Similar studies in colorectal cancer have demonstrated a different VOC pattern in the exhaled breath of colorectal cancer patients when compared to controls with a sensitivity of 86% and a specificity of 83%[39]. However technology utilised for this analysis was gas-chromatography mass spectrometry (GC-MS), which does not permit real-time on-line analysis.

As well as mass spectrometry techniques, nanosensors based on gold nanoparticles have also been shown to be effective at differentiating between VOC profiles in colorectal[40] and gastric[41] cancer. VOCs in colorectal cancer from breath and fecal samples have even been distinguished from controls with impressive sensitivity and specificity by canine scent detection without confounders for benign disease or inflammation[42].

Advances in metabolomics has allowed identification of individual VOC profiling of diseases such as tuberculosis and cancer, giving each in effect a recognizable and quantifiable signature[43,44]. This is an area for future investigation before VOC profiling becomes widely applied in cancer diagnostics, however the results of these preliminary studies do suggest that VOC analysis has tremendous potential as a non-invasive POC test for a wide variety of important diseases including cancer. Whilst VOC profiles can be quantified in association with certain disease states, the mechanism of VOC production in these disease states is poorly understood. This is clearly an area for further investigation before the widespread application of this technology in POC testing.

***Pyruvate kinase isoenzyme type M2***

Pyruvate kinase isoenzyme type M2 (M2-PK) has been proposed as a biomarker of many cancers, including gastric, esophageal and colorectal. Different isoenzymes of pyruvate kinase are expressed depending on the metabolic functions of tissues and during rapidly dividing cells such as seen in tumour formation tissue specific isoenzymes are replaced with M2-PK in the dimeric form[45]. Therefore, M2-PK has been investigated as a potential diagnostic marker for various cancers particularly colorectal[46,47]. POC test devices are now commercially viable for stool analysis of fecal M2-PK with sampling requiring only one stool sample. Like calprotectin, these assays do not rely on tumours bleeding and have improved specificity by excluding other bowel sources of bleeding such as haemorrhoids and fissures. A recent pooled analysis demonstrated M2-PK detection by either ELISA or the POC lateral flow rapid test as having a sensitivity of about 80% for colorectal cancer and 44% for an adenoma greater than 1 cm[48]. This concluded that M2-PK should be used routinely for colorectal cancer screening, however this assertion has two limitations. Firstly, this justification of this was based on a combined analysis of the laboratory ELISA methods as well as the POC device and secondly as noted in regards calprotectin assay devices, the studies included are small in size and underpowered, and even when combined with pooled analysis the 12 studies together included just 704 cancer samples between them. Therefore larger studies with significant power are required to give weight to these proposals before this technology can be implemented on a wider scale.

***Tumour markers***

Modern techniques such as dielectrophoresis[49], microfluidics and nanotechnology have allowed multiple complex laboratory processes to be scaled down and automated leading to the development of so-called ‘lab on a chip’ devices. Circulating tumour cells are cells released by certain tumour types into the bloodstream but occur in small quantities making detection technically difficult[50], Dielectrophoresis has been demonstrated in the laboratory to be able to quantify these cells using an electrical field to separate circulating tumour cells from blood cells by way of their different charge characteristics. Experimental dielectrophoresis within a microfluidic chip has been studied for stool sample analysis of circulating tumour cells in a laboratory setting. HTC 116 cells were isolated from a mixture of human embryonic kidney 293 (HEK 293) and E. coli cells demonstrating its feasibility[51] but so far this has not been translated into a test appropriate for clinical use. Whilst, these advances have definite potential for POC devices to assay circulating tumour cells in vitro and therefore provide diagnostic tools, current methodologies still require the pre-treatment of samples and the technology is not yet fulfilled for POC testing.

Further down the design pathway and therefore closer to implementation are POC devices for common tumour markers. Gold nanoparticle microfluidic chips for tumour markers such as carcinogenic embryonic antigen (CEA) where feasibility studies for POC have been reported[52]. Whilst this test has been demonstrated, CEA does not currently serve a role in the screening or diagnosis of colorectal cancer[53] and this could therefore impact on its role in POC as the test is unlikely to be utilized or affect the patient diagnostic pathway. CEA is used for follow up of patients and to prompt further investigation, in most cases in an outpatient setting and therefore the benefit of rapid assay is negated unless justification can be demonstrated by improved cost-effectiveness, accuracy or patient experience.

***DNA analysis***

It is well established that mutations in the DNA of oncogenes and tumor suppressor genes are involved in the process of carcinogenesis. Specific genetic mutations have been attributed to several cancers and identification of these with DNA sequencing can play a role in stratifying risk, predicting response to treatment and in early diagnosis. Feasibility reports of POC devices for DNA mutation analysis are now present in the literature[54] and stool DNA testing has shown promising results[31,55,56]. DNA mutations associated with colorectal cancer include Kirsten-ras (K-ras) (seen in 40% of colorectal cancer patients and 60% of adenomas greater than 1cm)[57,58], adenomatous polyposis coli (APC) , deleted in colorectal cancer (DCC) and tumor protein 53 (p53) and associated mutations can predict carcinogenesis or be indicative of specific events such as the activation of adenoma to carcinoma.

More recently, DNA methylation biomarkers including *SEPT9* (ColoVantage®) and *vimentin* (ColoSureTM) have been investigated for their potential in colorectal cancer diagnosis[59]. DNA methylation occurs early in carcinogenesis and therefore biomarkers for these epigenetic events may permit the diagnosis of cancer earlier.

Combining biomarker assays for DNA mutation and DNA methylation can improve accuracy and has been the focus of novel test development. The United States Food and Drug Administration has recently approved Cologuard (Exact Sciences Corporation, Madison, WI, United States), a multitarget stool DNA test in screening for colorectal cancer. Cologuard combines molecular assays for aberrantly methylated *BMP3* and *NDRG4* promoter regions, mutant *KRAS* and *β-actin* (a reference gene for human DNA quantity) with an immunochemical assay for human hemoglobin (as used in immunochemical FOB testing)[60]. A large study of asymptomatic patients[61] using this multitarget approach demonstrated a significantly better sensitivity for cancer than immunochemical FOB testing alone (92.3% *vs* 73.8% *P* = 0.002) but this was at the expense of specificity. Whilst non-invasive the test is not currently available as a POC device with amplification and detection undertaken in a laboratory using Quantitative Allele-specific Real-time Target and Signal Amplification (QuARTSTM) technology.

Technology for DNA based biomarkers is progressing. Microfluidics have led to lab on a chip technology that has the potential for DNA sequencing in a POC device. Kitano at al describe a point of care device able to perform extraction, purification, DNA amplification, mutation detection and interpretation in an automated analyser taking 70 min. Furthermore, Toumazou *et al*[62] have since used pH-sensing complementary metal-oxide semiconductor technology to develop their platform that has reduced genotyping to 30 min on a chip the size of a finger-nail.

Whilst at present the cost of these technologies is high[63], the scaling and portability of DNA sequencing devices with multitarget approaches to detect the genetic and epigenetic events that arise from cancer presents exciting promise for highly sophisticated and accurate POC tests for the future. However, this technology remains in its infancy and will require significant investment in research development before translation into viable clinical POC tests for cancer.

**DISCUSSION**

POC devices have a proven role in the diagnosis and assessment of gastrointestinal cancer. There are also exciting new technologies at various stages of development showing significant promise for the future. FOB testing is well established and validated in multiple commercially available POC devices. Along with helicobacter pylori testing these devices have consistently demonstrated that POC devices are acceptable to patients and clinicians, economically viable and can play a role in the clinical care pathway of gastrointestinal disease. However, the gold standard for diagnosis of gastrointestinal disease and specifically cancer remains endoscopy with histological diagnosis, despite being invasive, expensive and carrying the associated risks of bleeding and perforation.

Whilst screening programmes have been designed and investigated worldwide, the accuracy of POC devices remains its drawback. To some extent this can be seen as a tradeoff for its non-invasive nature but current vogues in colorectal cancer screening are shifting away from POC tests towards flexible sigmoidoscopy[26,64]. Furthermore esophago-gastro-duodenoscopy remains the choice of test for surveillance of pre-malignant conditions including Barrett’s esophagus and diagnosis of upper gastro-intestinal cancers. This is understandable given that in the current care pathway histological confirmation is critical in the appropriate diagnosis, staging and allocation of treatment for gastrointestinal cancers. However, POC can still have a hugely valuable role if developed with robust methodology and validation to assign risk of gastrointestinal cancer. This will allow more appropriate allocation of diagnostic endoscopy, which may in turn lead to a reduction in negative endoscopies and a more cost-effective diagnostic pathway.

With more modern techniques such as VOC biomarkers, circulating tumour cells and DNA analysis which have the potential of providing the clinician with accurate POC tests the landscape for the diagnosis of gastrointestinal cancer has the potential to change rapidly, completely re-defining the patient care pathways as they currently exist. Changes in patient diagnostic and treatment algorithms resulting from the institution of POC tests must be carefully introduced with particular attention paid to the psychological and economic effects of these changes.

Even tests that are well established take a great deal of time to make the transition from the laboratory to clinical usage. Hold ups occur at multiple levels as seen in FOB sampling that was first described over a century before its role in colorectal cancer was discovered and a further 26 years passed before there was sufficient evidence to justify its use in screening programmes. With the potential advantages of POC devices barriers to their implementation need to be identified and overcome. Hold-ups in implementation can occur at multiple levels and industry, clinicians, researchers, policy makers and patients all have a role.

The POC diagnostic industry is expanding rapidly with an estimated 35% share of the in vitro diagnostic market within the USA and was valued at $15.1 billion in 2011[65]. This is forecast to grow and similar trends can be seen across the developed and developing world. The potential for commercial gain by novel POC diagnostic tests especially in prevalent diseases such as gastrointestinal cancer is apparent and therefore there should exist a clear motive to industry to pursue evidence generation in evaluating these products further but when assessing the literature this is not seen.

One reason for this apparent void of evidence generation maybe that further studies are in fact being performed but results are not being published in the literature as there exists a publication bias against negative results, particularly with diagnostic test studies, compounded by the restricted access to intellectual property regarding design process and evaluation within industry. The prevalence of unknown reporting in this respect is difficult to determine and it is understandable that industry may want to protect their investment potential with emerging commercial devices.

Whilst a detailed description of design methodology is outside the scope of this review it is worth considering the route a new technology takes from proof of concept to a commercially available device, as this will highlight various barriers to their implementation. A design process is undertaken, usually within industry, which incorporates the validity of the testing methods into a device that is usable by the appropriate population, meets safety and regulatory standards and demonstrates a sustainable business model to justify this initial financial outlay. Usability is particularly important with POC devices as the user may have minimal or no training and all involved steps including sample collection, analysis and interpretation of result interface must be tested with the appropriate population as each may be the subject of heterogeneity that can adversely affect the overall quality and accuracy of results gained.

Effective design is a time consuming and expensive process that increases exponentially with complexity, this is especially true of medical devices with the inherent hazards of poor design. Device evaluation has the potential to benefit greatly if a culture of coordinated and complimentary evidence generation from both industry and clinical academia can be achieved, with a shared aim to drive concepts along this pathway so that the benefits of new technologies can be realised.

Once launched, POC tests challenge established patient diagnostic pathways. Current pathways are based on best evidence, almost universally developed with reference testing methods and it is vital that evidence based clinical practice remains valid with the introduction of new POC test devices. This will depend both on the accuracy of new tests but also their impact on patient care pathways.

Modeling techniques can be used to evaluate these changes in more detail and demonstrate cost-effectiveness. This ensures that the analysis is based not just on a test-by-test comparison basis but a full evaluation of pathways and outcomes associated with implementing new devices. This evidence is vital for large healthcare organisations such as the National Health Service.

Finally, patient and public involvement is required to implement POC testing strategies and the benefits offered should be enough to achieve this, providing safety is not compromised. POC technologies tend to be non-or minimally-invasive and provide rapid results and therefore studies repeatedly demonstrate better adherence to treatment, patient satisfaction and quality of life, especially at home where new devices can be integrated with wireless or mobile technology to completely alter the way healthcare is delivered.

In conclusion, there exists a wide range of technologies described as POC relating to gastrointestinal cancer. Whilst some are in routine clinical use, others remain described only in theory and ex-vitro experiments. There is a broad scope of exciting promise for the future and the potential benefits that they can bring but we can see from experience that barriers to their implementation exist and their transition from experimental to clinical medicine is slow. Further work needs to address these obstacles to provide better efficiency in evidence generation so that current POC proposals do not follow the example of FOB in taking over a century to translate from discovery to clinical use. With the creation of the National Institute for Health Research Diagnostic Evaluation Cooperatives this paucity of evidence aims to be addressed and this standardized pathway of stream-lined, efficient development and validation of POC devices will be the focus of future investigation.

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**Table 1 Full search strategy used is described**

|  |
| --- |
| **Medline search strategy**  |
| 1. [(point of care or near patient or poc or rapid or bedside) adj3 (test\* or analys\* or immunoassay\* or technique\* or assay\* or diagnos\* or technology\* or system?)].mp |
| 2. Point-of-Care Systems/ |
| 3. 1 or 2 |
| 4. exp Gastrointestinal Neoplasms/ |
| 5. [(oesohag\* or esophag\* or gast\* or stomach\* or duoden\* or ile\* or jeun\* or caec\* or append\* or cec\* or colo\* or rect\* or anal or anus or intestin\*) adj2 (cancer? or carcinoma? or malignancy or malignant or neoplasm?)].mp |
| 6. 4 or 5 |
| 7. 3 and 6 |
| **Embase search strategy** |
| 1. [(point of care or point-of-care or near patient or poc or rapid or bedside) adj3 (test\* or analys\* or immunoassay\* or technique\* or assay\* or diagnos\* or technology\* or system?)].mp |
| 2. "point of care testing"/ |
| 3. 1 or 2 |
| 4. [(oesohag\* or esophag\* or gast\* or stomach\* or duoden\* or ile\* or jeun\* or caec\* or append\* or cec\* or colo\* or rect\* or anal or anus or intestin\*) adj2 (cancer? or carcinoma? or malignancy or malignant or neoplasm?)].mp |
| 5. digestive system cancer/ or exp esophagus cancer/ or exp intestine cancer/ or exp stomach cancer/ |
| 6. 4 or 5 |
| 7. 3 and 6 |

**Table 2 Described methods of testing for gastrointestinal cancer and accuracy of commercially available tests based on recent evidence (point-of-care)**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Technology** | **Commercial available POC device**  | **POC Sensitivity** | **POC Specificity**  | **Level of evidence** | **Papers retrieved in primary search (*n*)** |
| Occult Blood | Yes | 79%[25] | 94%[25] | 1 | 10[20,22,34,66–72] |
| Fecal Proteins | Yes | 83%[33] (calprotectin) | 84%[33] (calprotectin) | 2 | 3[34,73,74] |
| Volatile Organic Compounds | No |  |  |  | 0 |
| Pyruvate kinase isoenzyme type M2 | Yes | 80.3%[48] | 95.2%[48] | 1 | 1[72] |
| Tumour Markers | No |  |  |  | 6[47,49,68,75-77] |
| DNA mutation analysis | No |  |  |  | 4[56,76,78,79] |
| Multitarget stool DNA test | No |  |  |  | 0 |

POC: Point-of-care.