RETHINKING GASTROSCOPY REFERRALS IN THE UK – IS IT TIME FOR TRIAGE?

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Introduction

Gastric cancer is a significant global health burden, with rising frequency and mortality rates. It ranks as the sixth most common cancer worldwide, with an age-standardised incidence rate of 11.1. In the UK, its prevalence is relatively low compared to other cancers – ranking 17th and accounting for 6,568 new cases annually – yet it remains one of the deadliest malignancies, with only 22 per cent of patients surviving beyond five years. Alarmingly, more than half of all gastric cancer cases are considered preventable, but late diagnosis continues to drive poor outcomes.[1–6]

The most prevalent form of the disease, gastric adenocarcinoma (GAC), accounts for 90 to 95 per cent of all cases,[7] and is strongly associated with atrophic gastritis (AG) – a common preneoplastic condition primarily caused by *Helicobacter pylori* (*H. pylori*) infection – and, less frequently, with autoimmune disease. Additional risk factors, including high salt intake, alcohol misuse and unhealthy diets, further contribute to disease progression.[8] Moderate to severe AG increases gastric cancer risk by up to 90-fold, making early detection strategies essential for improving patient outcomes.[9,10]

Chronic AG is often underestimated as a serious cancer risk factor, largely because it typically presents as dyspepsia – a broad set of symptoms including heartburn, indigestion, acid reflux and stomach pain. These common warning signs are frequently downplayed or attributed to a different cause, leading to missed opportunities for early intervention. While dyspeptic symptoms alone are not a reliable basis for identifying AG or assessing cancer risk, existing diagnostic pathways remain far from ideal. Confirming or excluding AG currently relies heavily on endoscopy, an invasive, resource-intensive procedure that is often constrained by delays and long waiting lists. Variability in clinical interpretation of endoscopy results further complicates consistent and early disease detection. These challenges underlines the need for an effective, non-invasive triage tool that can be used in primary care to rule out patients who are unlikely to benefit from further investigation and highlight those who may potentially have AG.

This white paper explores the potential of biomarker-based methods for identifying moderate to severe AG in dyspeptic patients before endoscopy – as recommended by the 2019 British Society of Gastroenterology (BSG) guidelines[11,12] – and how a rapid, point-of-care testing (POCT) approach could streamline diagnostic pathways and improve access to urgent endoscopy procedures for those most at risk of developing gastric cancer.

The standard treatment pathway for dyspeptic patients

Dyspepsia is a common gastrointestinal complaint that affects approximately 40 per cent of the UK population annually.[13] While most cases are self-managed, around five per cent of individuals will seek medical attention each year, contributing significantly to GP workloads. Of these patients, approximately one per cent are referred for upper endoscopy.[13]

Dyspeptic symptoms typically arise from an imbalance between acid production and the stomach's defence mechanisms, leading to inflammation of the lining of the stomach, oesophagus or duodenum. This imbalance is usually associated with common conditions such as peptic ulcers, gastro-oesophageal reflux disease (GORD), gastritis or hiatus hernia. Lifestyle factors such as poor diet, high intake of fatty or spicy foods, alcohol consumption, smoking and stress can exacerbate symptoms, and certain medications – including calcium antagonists, nitrates, theophylline, bisphosphonates, steroids, selective serotonin reuptake inhibitors (SSRIs) and nonsteroidal anti-inflammatory drugs (NSAIDs) – can disrupt this balance even further.[12] While many cases are benign, this common initial presentation can also signal serious underlying gastrointestinal conditions – including Barrett's oesophagus and gastric cancer – or may indicate causative factors for gastric cancer, such as *H. pylori* infection or AG.[14]

A complex diagnostic pathway

Due to the severity of these potential underlying pathologies, dyspeptic patients presenting to their GP with red flag or alarm symptoms – including difficulty swallowing, unintentional weight loss, vomiting or gastrointestinal bleeding – are currently referred via the two-week urgent pathway for endoscopy to rule out serious illness.[15] For patients without alarm symptoms, clinicians will typically begin by assessing their symptom profile to guide initial management and treatment decisions. This approach sometimes involves lifestyle modifications, such as promoting healthy eating, weight reduction and stopping smoking. Proton pump inhibitors (PPIs) are also often prescribed to alleviate symptoms,[15] although they do not address underlying gastric pathologies and may even mask early warning signs of AG or GAC. Emerging evidence even suggests that the overuse of PPIs could potentially contribute to the development of cancer through the elevation of gastrin levels and the modification of gastric and intestinal microbiota, but further research is needed to confirm this association.[16] Patients with persistent symptoms may be referred for non-urgent upper endoscopy at this stage. Alternatively, they may instead undergo a blood test, or may be required to wait two weeks after their last dose of PPI before undergoing a carbon-13 urea breath test or stool antigen test, to test for *H. pylori* infection.[15]

The endoscopy dilemma

The absence of a clear management strategy for dyspeptic patients without alarm symptoms poses a significant challenge in clinical practice. Current guidelines do not recommend endoscopy as a first-line diagnostic tool for patients under 55 years of age without alarm symptoms. However, without a well-defined diagnostic pathway, many clinicians rely solely on symptomology to guide treatment decisions.

The current standard of care contributes to two critical issues: the overuse of endoscopy in low risk individuals and delayed diagnoses in high risk patients. While endoscopy can be valuable for diagnosing serious gastrointestinal conditions, its use at an advanced stage may be too late for patients with precursor lesions to gastric cancer. Delayed endoscopy in high risk patients can result in missed opportunities for early intervention – especially since some patients with precancerous gastric lesions may be asymptomatic – leading to poor clinical outcomes.

On the other hand, many endoscopies are performed unnecessarily, often revealing no serious pathology. In fact, audit data indicates that only 10 per cent of endoscopy referrals made under the two-week rule for suspected cancer actually result in a cancer diagnosis,[17] highlighting the limited diagnostic yield of this approach. In addition, up to 56 per cent of diagnostic upper GI endoscopy procedures are conducted in contradiction of clinical recommendations, demonstrating the widespread issues of inappropriate overuse.[18-22] Unfortunately, medical litigation may play a role in driving this current diagnostic trend. In the 2023/24 period, the NHS faced 13,784 new clinical negligence claims, with gastroenterology accounting for 3.1 per cent of these.[23] Faced with the potential legal repercussions, GPs and gastroenterologists are adopting an overcautious approach by referring patients directly for endoscopy to ensure thorough investigation and documentation. This defensive practice contributes to the overuse of the procedure, even when clinical guidelines do not support it.

Challenges in endoscopic diagnosis

On top of this, there are also diagnostic challenges associated with the technique itself; while it is very effective for detecting large, visible lesions, precancerous changes are often subtle and difficult to identify using standard techniques, and histopathological analysis of biopsy samples is essential. Advanced imaging techniques – such as virtual chromoendoscopy with magnification – offer much better visualisation of lesions,[24] but biopsies remain necessary for definitive diagnosis. However, the patchy distribution of gastric lesions introduces sampling errors even when biopsies are taken, as the selected tissue represents only a small fraction of the gastric mucosa, and the choice of biopsy sites can significantly impact results.
Efforts to improve diagnostic accuracy have led to

standardised biopsy protocols, such as the Updated Sydney System, which recommends sampling from multiple gastric regions, including the antrum, incisura, and lesser and greater curvatures.[25] However, this pattern is not always followed and it still only examines a very small cross section of the entire mucosa, leading to potentially undiagnosed cases. According to the European Society of Gastrointestinal Endoscopy, thorough endoscopic evaluations require at least seven minutes per procedure.[26] In practice, time constraints and patient discomfort often lead to shorter examinations, increasing the risk of incomplete assessments.

The need for a more efficient diagnostic approach

The overreliance on endoscopy for persistently dyspeptic patients without alarm symptoms presents significant challenges and has a substantial detrimental effect on systemic inefficiencies. While it is a critical technique for identifying serious gastric pathologies, it is often used either too late or unnecessarily, and its invasive nature, resource intensity and inefficiencies add considerable pressure to medical services, making it unsustainable as a long-term solution. Instead, a more targeted, non-invasive diagnostic strategy is needed to reduce unnecessary procedures, optimise use of healthcare resources, and enhance early detection of gastric cancer in high risk individuals, ensuring that those who need endoscopy most receive it promptly. An improved triage system that prioritises non-invasive diagnostic tools to more effectively differentiate between functional dyspepsia and precancerous gastric conditions at the primary care level is essential. An early screening programme and effective risk stratification could also help healthcare providers to reduce unnecessary endoscopies, ease the burden on healthcare resources, and ensure that high risk patients are identified and monitored appropriately to prevent the progression of AG to cancer.

Learning from global screening models

Countries with existing national gastric cancer screening programmes, such as Japan and South Korea, have significantly improved early detection of AG, subsequently leading to better prognoses for patients with this precancerous condition. In fact, South Korea's endoscopy-based screening for individuals over 40 has reduced mortality by 41 per cent.[27] However, the adoption of similar screening programmes in other regions, including the UK, US and much of Europe, has largely been limited. Fortunately, awareness of the rising cases of gastric cancer in younger populations – and the high mortality rates associated with the disease – has sparked discussions at the European Council on the need for more effective disease detection and prevention strategies.

One promising outcome of these discussions is the TOGAS project (*Towards Gastric Cancer Screening Implementation in the European Union*), the first pan-European effort dedicated to evaluating strategies for reducing gastric cancer mortality.[28] The project aims to equip national health ministries with the latest evidence-based insights through a series of targeted pilot studies, each focusing on key aspects of stomach cancer screening and early detection. With a strong emphasis on cost-effectiveness and medical ethics, TOGAS will provide crucial data to help each EU member state design and implement effective stomach cancer prevention programmes. Although the UK is no longer part of the EU, it frequently aligns with European healthcare trends, making the TOGAS findings potentially relevant beyond the EU's borders. If TOGAS successfully influences gastric cancer screening policy within the EU, the UK may then also consider implementing similar approaches to enhance early detection and improve patient outcomes.

The case against screening: is it justified?

Despite the potential benefits of early detection, there are several reasons why mass gastric cancer screening in the UK has not yet been widely implemented. One of the main concerns is that screening may not be cost-effective due to the relatively low incidence rate of gastric

❝ Dyspepsia is extremely common, but only a small percentage of cases have serious underlying pathology, making diagnosis difficult. Gastric cancer is often detected too late, leading to low survival rates, whereas countries with screening programmes, like Japan and South Korea, see much better outcomes. We urgently need a strategy to identify high risk individuals early and prevent late-stage diagnoses. ❞

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cancer compared to other malignancies – such as bowel, breast or cervical cancer – all of which have established national screening programmes. This lower prevalence makes it difficult to justify a dedicated screening initiative, especially in the face of limited NHS resources and competing healthcare priorities.

The practical challenges of current diagnostic methods also present a significant barrier. The high cost, invasiveness and resource-intensive nature of existing diagnostic protocols – such as endoscopy – render them impractical for large-scale screening purposes. Endoscopy teams in the UK are already struggling to meet demand for urgent referrals,[29] and expanding the use of endoscopy for screening too would place further strain on already overstretched services and lead to even longer waiting lists. The ideal solution would be a structured triage system – preferably based on a non-invasive, easy to sample biomarker – to determine which patients require endoscopy but, without this, implementing a screening programme could exacerbate service bottlenecks rather than resolving them.

Another stumbling block standing in the way of gastric cancer screening is funding. If a patient is referred for endoscopy from primary care, the cost of that procedure is typically covered through block

or activity-based contracts between Integrated Care Boards (ICBs) and secondary care providers.[30,31] These contracts are commissioned centrally, and paid for through broader NHS budgets that flow from primary to secondary care settings, meaning that GPs don't directly bear the cost of referring a patient for an endoscopy.

In fact, endoscopy is not only funded, but actively incentivised under the 2025/26 NHS Payment Scheme, as it is included as an elective Best Practice Tariff (BPT).[31] This means that hospitals are paid according to nationally defined unit prices for each procedure, provided they meet criteria that ensure clinical effectiveness and efficiency – for example, delivering procedures in outpatient settings where appropriate.

In contrast, if a GP surgery uses POCT tools to help decide whether an endoscopy referral is necessary, the costs fall on the practice itself. This includes purchasing test kits, maintaining equipment, and providing and training staff to perform the test. POCT approaches are not currently included in national tariffs or the BPT system, nor are they commonly reimbursed through local commissioning arrangements.

This creates a clear misalignment in funding: endoscopy is routinely commissioned and reimbursed, while more proactive POCT methods are not. This may discourage primary care providers from adopting screening methods, despite their potential to generate significant cost savings for the NHS as a whole, in this case by reducing unnecessary endoscopies and preventing the need for aggressive and expensive treatments further down the line.[32,33]

A systematic shift – redirecting the outdated care pathway toward structured triage – is required to overcome these challenges, and experts have called for clearer commissioning pathways to enable the wider use of POCT across primary care.[34] However, implementing such a change would demand substantial effort and a realignment of budgets. The NHS Change Model Guide advocates for embracing change to improve health outcomes and system performance,[35] but concerns remain over the reliability of alternative screening methods – such as biomarker-based approaches – in the UK population. While these methods have proven effective in Asian populations, the lack of robust UK-specific data and the associated costs of implementing new screening pathways remain significant obstacles to their widespread adoption.

The case for triage: a step toward earlier detection

Overcoming cost and political barriers requires greater awareness of benefits at the national and commissioning care network level. Instead of focusing on individual budgets, the NHS should take a holistic view, considering the broader savings and efficiencies a structured biomarker triage pathway could deliver. Evidence from South Korea's national cancer screening programme shows that total medical expenses over five years were 5.1 per cent lower for individuals who underwent screening compared to those who were not screened.[36] This demonstrates the potential for early diagnosis to generate long-term NHS savings by reducing overall treatment costs, particularly by lowering the financial burden associated with late-stage cancer care.

Beyond economic considerations, the most compelling argument for gastric cancer diagnosis is its potential to improve survival rates. In the UK, gastric cancer is often diagnosed too late, leading to poor five- and 10-year survival rates. Earlier detection could significantly improve these outcomes. Research has shown that eliminating *H. pylori* infection may reduce gastric cancer mortality by up to 48 per cent, underscoring the importance of identifying and monitoring high risk individuals before cancer develops.[37]

There is substantial evidence from successful screening programmes in other countries that deserves serious consideration by gastroenterologists and policy makers in the UK, and may well encourage the adoption of similar strategies. By showcasing international successes, healthcare providers may feel more confident in implementing structured screening protocols, knowing they are backed by robust data and have the potential to improve patient outcomes.

> A targeted triage pathway could also help to ease pressures on existing diagnostic services. The overuse of endoscopy in low risk patients contributes to long waiting times and inefficiencies in the system. A structured 'screen-and-treat' model – where individuals are first assessed using non-invasive biomarker tests – could help triage patients more effectively, ensuring that only those at highest risk undergo endoscopy. This approach aligns with broader cancer prevention efforts and is already being explored in other European nations.[38]

Can biomarker-based testing improve the UK diagnostic pathway?

Integrating biomarker-based tests into primary care could provide GPs with a cost-effective, non-invasive alternative to endoscopy to streamline the suspected gastric cancer diagnostic pathway, allowing earlier intervention without burdening endoscopy services. For instance, GastroPanel® is a non-invasive POCT device that detects three stomach-specific AG biomarkers – pepsinogen I (PGI), pepsinogen II (PGII) and gastrin-17 (G-17) – and *H. pylori* IgG. These biomarkers provide a comprehensive view of stomach mucosal function, with PGI and PGII reflecting corpus integrity, and G-17 indicating antral mucosal health and acid production.[39-41] A lower PGI/PGII ratio and elevated gastrin levels, particularly in the absence of *H. pylori* antibodies, are indicative of advanced atrophic changes.[42,43] GastroPanel can be used in combination with *H. pylori* serology to quickly and accurately detect stomach pathologies such as moderate to severe AG.[44] The integration of biomarker-driven tools like GastroPanel into clinical practice therefore offers the potential to improve early detection of cancer risk and reduce reliance on time-consuming and invasive endoscopies.

Assessing highly accurate biomarker testing for AG

A recently published single-centre prospective diagnostic accuracy study used the GastroPanel ELISA to analyse the blood samples of 324 dyspeptic patients without alarm symptoms at the Gastroenterology Department of Homerton University Hospital.[45] These individuals had been referred for non-urgent gastroscopy in line with BSG guidelines.[11,12] Results were classified into diagnostic categories by GastroSoft™ software, a software application specifically designed to assist clinicians in interpreting GastroPanel test results. Gastroscopy and biopsies were also performed, with samples processed and analysed for pathology. Histopathologists, blinded to GastroPanel results, assessed the biopsies for *H. pylori* infection, AG, gastric intestinal metaplasia and dysplasia. In addition, key metrics like sensitivity, specificity and predictive values were calculated for the GastroPanel biomarkers.

The study demonstrated strong agreement (90 per cent, Kw: 0.828) between GastroPanel and histology for detecting moderate to severe AG. Biomarker analysis showed that the PGI/PGII ratio (cut-off 3.0 µg/l) had an area under the curve (AUC) of 0.960, demonstrating excellent diagnostic ability, with 75 per cent sensitivity and 98 per cent specificity. The PGI (cut-off 25 µg/l) achieved an AUC of 0.840, demonstrating good diagnostic ability, with 75 per cent sensitivity and 99 per cent specificity. Positive GastroPanel results indicated an 86 per cent probability of moderate to severe AG, while negative results had a 1 per cent post-test probability. These findings highlight GastroPanel's precision in identifying moderate to severe AG, and its potential to improve diagnostic pathways for gastric cancer by reducing unnecessary endoscopies and guiding targeted patient care.

Enhancing early detection and optimising healthcare resources

The findings of this study provide further evidence supporting the potential advantages of biomarker-based approaches – including GastroPanel – in the detection and management of precancerous conditions in dyspeptic individuals. Such methods align with current BSG guidelines,[11,12] which advocate for early detection strategies to improve patient outcomes. By combining biomarker data with clinical risk scores, these tests may contribute to enhanced risk stratification and improve the accuracy of predictive assessments. This enables better prioritisation of patients who require further investigation, such as targeted endoscopy and advanced imaging techniques. The high sensitivity and specificity of GastroPanel, in particular, may also help address challenges related to variability in histological evaluations, aiding in the distinction between functional dyspepsia and high risk AG cases.

Another key advantage of biomarker-driven diagnostic tools is their non-invasive nature, which may reduce reliance on repeated endoscopic examinations while improving the patient experience. Minimising unnecessary endoscopies allows healthcare systems to allocate resources more effectively, ensuring that invasive procedures are reserved for those at higher risk. Optimising diagnostic pathways in this manner could yield significant cost savings for healthcare providers by reducing unnecessary endoscopies.
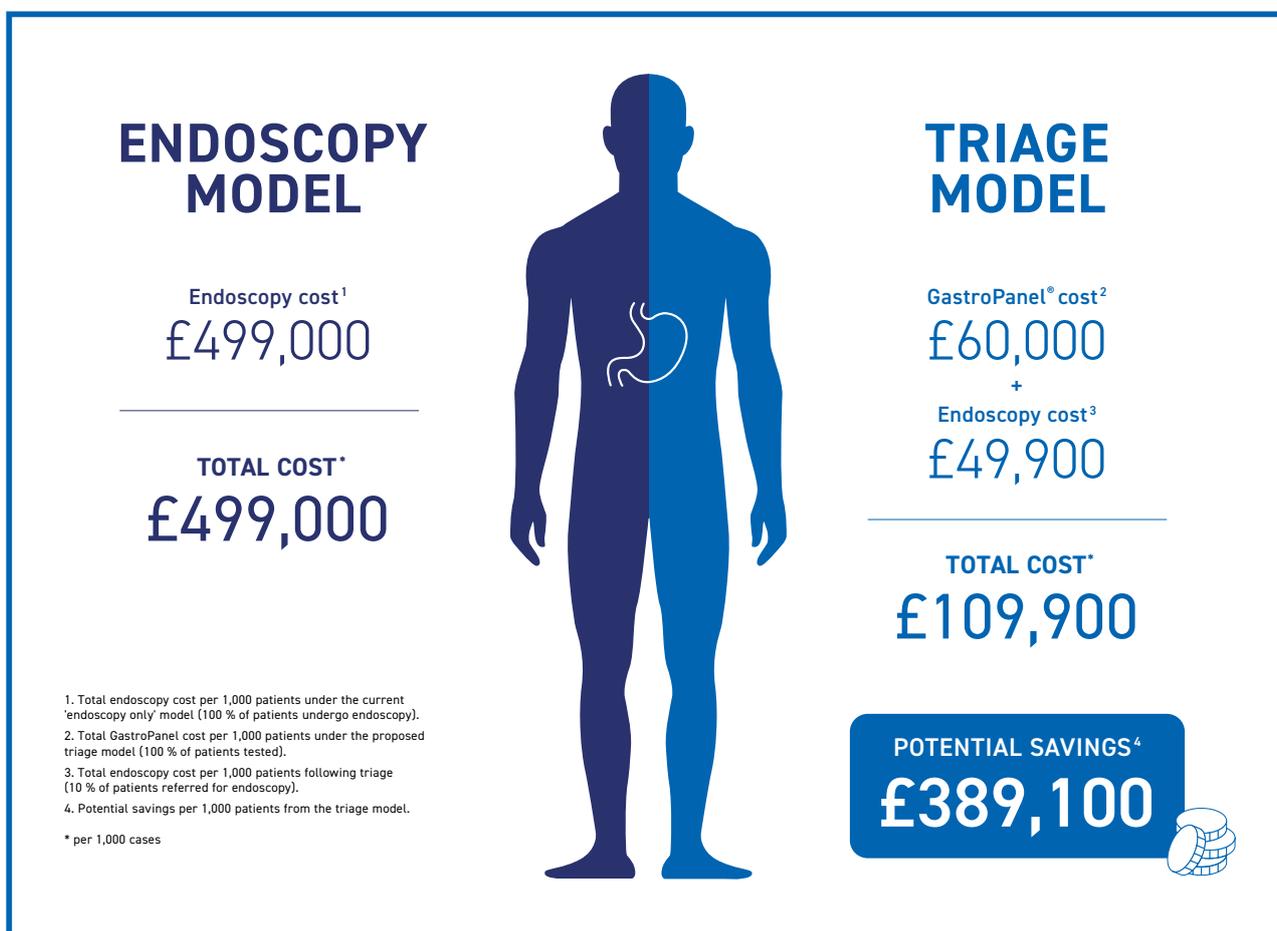

ENDOSCOPY MODEL

Endoscopy cost[1]
£499,000

TOTAL COST*
£499,000

1. Total endoscopy cost per 1,000 patients under the current 'endoscopy only' model (100 % of patients undergo endoscopy).
2. Total GastroPanel cost per 1,000 patients under the proposed triage model (100 % of patients tested).
3. Total endoscopy cost per 1,000 patients following triage (10 % of patients referred for endoscopy).
4. Potential savings per 1,000 patients from the triage model.

* per 1,000 cases

TRIAGE MODEL

GastroPanel® cost[2]
£60,000
+
Endoscopy cost[3]
£49,900

TOTAL COST*
£109,900

POTENTIAL SAVINGS[4]
£389,100

Figure 1: llustration of the potential cost savings per 1,000 non-urgent referrals if GastroPanel were used as a gastroscopy triage test.

According to a study carried out by Beg *et al.*, 3,000 oesophagogastroduodenoscopies (OGDs) are performed for every 250,000 people annually.[46] Using 2025 UK population figures (approximately 69.5 million), BIOHIT conservatively estimated that, of the 834,000 non-urgent diagnostic OGDs performed each year, a quarter of them are for stomach-related symptoms, totalling around 208,500 procedures each year. With this in mind, at a cost of £499 per gastroscopy (best practice tariff),[31] the NHS may be spending over £104 million on this case load in gastroscopies per year. By replacing 90 per cent of this case load with GastroPanel – at a cost of £60 per test – while reserving endoscopy for 10 per cent of cases, the NHS could save a staggering £81.13 million annually.

Is it time to overhaul OGD referral pathways in the UK?

The current UK diagnostic model for the detection and diagnosis of gastric disease relies heavily on endoscopy, particularly for patients with alarm symptoms such as unexplained weight loss or difficulty swallowing. Those without red flag symptoms are often given empirical treatment with PPIs or placed on long-wait non-urgent referral pathways. However, the endoscopy-first approach is neither efficient nor effective; far too few referrals lead to a cancer diagnosis, while long waiting times and inconsistent risk stratification contribute to missed high risk cases and delayed diagnosis.

Biomarker-based triage offers a promising alternative. Assays such as GastroPanel have the potential to serve as accurate first-line detection tools in primary care settings, streamlining the triage of dyspeptic patients and contributing to more efficient diagnostic pathways. GastroPanel offers precision in identifying atrophic and autoimmune gastritis through biomarkers like PGI, PGII and G-17 and, in doing so, it addresses critical gaps in the current dyspepsia pathway. Its quick test format further streamlines diagnostics in primary care and bedside settings, reducing laboratory delays and improving testing accessibility for high risk patients. Despite these clear benefits, shifting clinical practice away from an endoscopy-first approach may be challenging. Many clinicians are accustomed to using endoscopy as the gold standard, and the

> ❝ *Endoscopy is overused in low risk patients, overwhelming healthcare systems and delaying care for those with serious conditions like advanced AG. GastroPanel offers a non-invasive way to triage dyspepsia patients in primary care, ensuring only high risk cases are referred for endoscopy. This approach could reduce unnecessary procedures, conserve resources and support early detection of gastric cancer.* ❞
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transition to non-invasive alternatives requires both education and confidence in the accuracy of these methods. Additionally, integrating biomarker-driven diagnostics into routine practice might require structural changes in healthcare pathways, as well as sufficient training to ensure correct interpretation and implementation.

What is certain though is that the status quo is no longer sustainable. The increasing burden on NHS endoscopy services, coupled with long waiting times and inefficiencies in patient triage, calls for a more effective, evidence-based approach to gastric disease detection. Countries like South Korea and Japan have successfully demonstrated that structured screening leads to earlier detection, improved survival rates and reduced healthcare costs. The UK must now reconsider its approach to gastric cancer prevention, drawing on international success stories while tailoring strategies to its own healthcare landscape.

The growing body of evidence supporting biomarker-driven diagnostics provides a compelling case for change. Innovative tools like GastroPanel have already demonstrated their potential to improve patient outcomes, reduce reliance on invasive procedures and alleviate strain on NHS resources. By embracing a risk-stratified triage model, the UK has an opportunity to improve early detection rates and ultimately reduce gastric cancer mortality. The question is no longer whether this is necessary, but rather, how soon it can be implemented.

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