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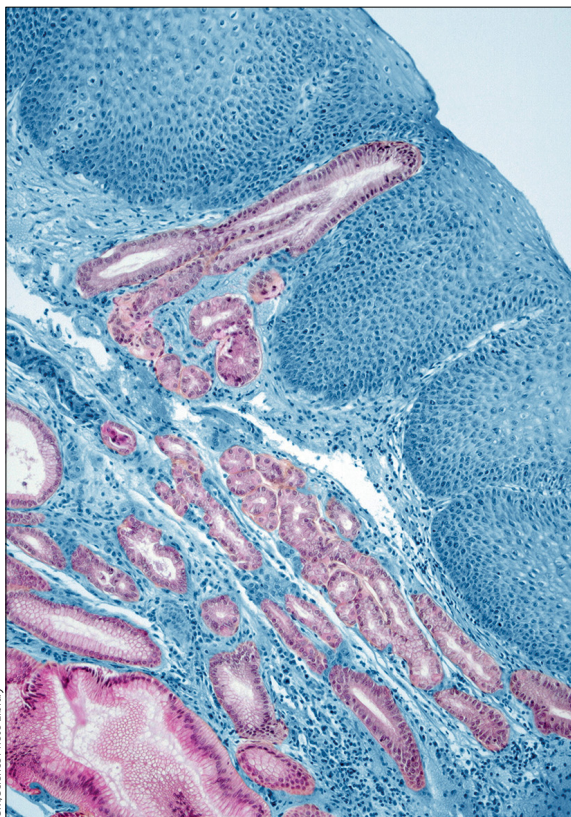
Screening for Barrett's oesophagus: is now the time?

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Screening for cancer is an important aspect of medical practice in this new millennium. It is well accepted that to decrease mortality due to oesophageal carcinoma, it is necessary to identify the malignancy at earlier, curable stages. In *The Lancet*, Rebecca Fitzgerald and colleagues¹ report the results of a prospective, multicentre, pragmatic, randomised controlled trial, done at 109 sociodemographically diverse general practice clinics in England, which investigated whether offering the Cytosponge-trefoil factor 3 (TFF3) procedure to patients on medication for gastro-oesophageal reflux would increase the detection of Barrett's oesophagus compared with standard management. In this study,¹ 13 657 eligible patients were randomly assigned to either the usual care group (n=6531) or the intervention group (n=6983). Participants in the usual care group received standard management of gastro-oesophageal reflux, and participants in the intervention group were offered the Cytosponge-TFF3 procedure to collect cytological specimens,

which were stained with an antibody against TFF3 to detect Barrett's oesophagus, and a subsequent endoscopy if TFF3-positive cells were identified. 1750 participants met all of the eligibility criteria on a telephone screening interview and underwent the procedure. Most of these participants (1654 [95%]; median age 69 years; 858 [52%] female) swallowed the Cytosponge successfully. The Cytosponge¹⁻³ is an orally administered, single-use, gelatine-encapsulated sponge device. Approximately 5 min after swallowing the Cytosponge, the capsule dissolves in the stomach to release the sponge, which is then manually drawn through the oesophagus by an attached string to collect oesophageal cytological specimens.

The primary endpoint of the study was the diagnosis of Barrett's oesophagus at 12 months after enrolment, expressed as a rate per 1000 person-years, in all participants in the intervention group (regardless of whether they had accepted the offer of the Cytosponge-TFF3 procedure) compared with all participants in the usual care group. The aim was to establish whether the offer of the Cytosponge-TFF3 test in general practice results in an increase in Barrett's oesophagus diagnoses. Overall, 140 (2%) of 6834 participants in the intervention group and 13 (<1%) of 6388 participants in the usual care group were diagnosed with Barrett's oesophagus (absolute difference 18.3 per 1000 person-years [95% CI 14.8–21.8]; overall rate ratio [RR] 10.2 [5.8–18.1]; RR adjusted for cluster randomisation 10.6 [6.0–18.8], $p < 0.0001$). The results showed that 131 (59%) of 221 participants who underwent endoscopy after testing positive for TFF3 had Barrett's oesophagus or early-stage oesophago-gastric cancer. Of those participants who underwent the Cytosponge-TFF3 procedure, only one serious adverse event associated with the device was reported (detachment of the sponge from the string, requiring endoscopic retrieval). 142 (9%) of 1654 participants who swallowed the Cytosponge successfully reported an adverse event, with a sore throat being the most commonly reported. The investigators are to be congratulated on completing a difficult prospective randomised trial in the primary care setting; a context that resembles one in which the device is anticipated to be clinically applied. These encouraging results



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prompt us to consider whether the Cytosponge-TFF3 procedure should now be accepted as a screening tool for oesophago-gastric cancer.

National Health Service (NHS) screening recommendations for certain cancers are largely based on the age-specific prevalence of the disease.^{4,5} Notably, in this study by Fitzgerald and colleagues,¹ the screening population was restricted to patients who had been taking acid-suppressant medication for at least 6 months, which was used as a surrogate marker for gastro-oesophageal reflux disease (GORD). This strategy avoided the need to use GORD screening questionnaires, which might have been difficult to implement in the primary care setting. However, being male, which is one of the strongest risk factors for the development of oesophago-gastric cancer, was not incorporated in the screening criteria.⁶

The Cytosponge-TFF3 procedure is a promising non-endoscopic screening tool and will represent a component in the screening for Barrett's oesophagus and oesophago-gastric cancer. As with colorectal cancer, this procedure is unlikely to be the sole screening tool, as multiple tests will be needed to enhance participation in a screening programme. For instance, although intended for routine use in primary care, in the current environment of an infectious disease (COVID-19) pandemic, the Cytosponge-TFF3 procedure might be difficult to implement, given its

potential to generate aerosolised particles during sponge withdrawal. It might also be necessary to enrich disease prevalence in the screened population by limiting this population to males and people with other risk factors, in order to make this test more cost-effective than previously shown. As the study¹ authors comment, determining the ideal enrichment criteria will be crucial to ensuring the success of a Barrett's oesophagus screening method.

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US withdrawal from WHO is unlawful and threatens global and US health and security



On May 29, 2020, President Donald Trump announced the USA would sever its relationship with WHO and redirect funds to US global health priorities.¹ On July 6, 2020, the US administration officially notified UN Secretary-General António Guterres of its intention to withdraw from WHO membership.² This notification coincides with record daily increases in COVID-19 cases worldwide and rising infections in more than three-quarters of the US states.^{3,4} In response, 750 leaders from academia, science, and law have urged the US Congress to block the president's action.⁵

The US Congress, the courts, and the public all have the power to block this reckless decision. The USA

entered WHO membership through a 1948 joint resolution passed by both houses of Congress and this resolution has been supported by successive administrations. Former President Harry Truman explicitly referenced that resolution as his legal basis for joining WHO.⁶ The current US administration's unilateral action notifying the UN that the USA is withdrawing violates US law because it does not have express approval of Congress to leave WHO. A Supreme Court precedent has made clear that "When the President takes measures incompatible with the expressed or implied will of Congress, his power is at its lowest ebb."⁷

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