Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

was 750, with a median of 47·3 (IQR 35·7–57·5) across cancer vanguards (appendix p 5). The estimated number of undiagnosed oesophageal and gastric cancers that would have been treated curatively across England was 213, with a median of 11·0 (IQR 6·3–14·4) across cancer vanguards (appendix p 5).

Oesophageal and gastric cancers are particularly aggressive with a poor prognosis, primarily driven by a delayed presentation and advanced stage at diagnosis. The COVID-19 pandemic has led to huge reductions in diagnostic oesophagogastroduodenoscopies across England; as a result, a proportionally large number of patients with oesophageal and gastric cancer will remain undiagnosed. In England and Wales, approximately 30% of patients with oesophageal and gastric cancers are treated curatively; our data suggest that delays in diagnosis caused by the reduction in oesophagogastroduodenoscopy services will mean increasing numbers of patients presenting with advanced disease, who are less likely to be treated curatively.[5] Furthermore, time from diagnosis to initiation of treatment is often used as a quality metric for efficiency of the cancer treatment pathway.[6] Large increases in waiting lists for oncological and surgical treatment as a result of COVID-19 will substantially affect cancer waiting times, although the true effect of this delay on trust performance is not yet known, in part because oesophagogastroduodenoscopy screening pathways for oesophageal and gastric cancer in England are being reinstated at varied rates across hospital trusts. The necessary national endoscopy uptake and capacity for optimum diagnostic screening during the COVID-19 recovery compared with baseline is unclear. Regardless, clear oncological and surgical pathway planning is urgently needed so that upper gastrointestinal cancer services are able to adapt to the surge in new upper gastrointestinal cancer diagnoses that will inevitably be detected. One proposed strategy is the creation of cancer hubs that will provide capacity.[7] However, these hubs must be modelled to account for local patient factors, hospital capacity, and likely endoscopic detection rates.

JK reports grants from H2020 (ITN grant; GROWTH consortium), grants from the UK National Institute for Health Research (i4i grant; iEndoscope), grants from Cancer Research UK fellowship (PhD studentship), educational grants from Johnson and Johnson (PanSurg.org) and personal fees from Verb Robotics/Ethicon and Medtronic. JK is director (point-of-care testing) for Cerulean Health, has shares from OneWelbeck day surgery and SurgEase, and is on the advisory board for LNC Therapeutics. SRM and JC declare no competing interests.

*Sheraz R Markar, Jonathan Clarke, James Kinross, on behalf of PanSurg Collaborative group
s.markar@imperial.ac.uk

Department of Surgery and Cancer, Imperial College London, London W2 1NY, UK

1 Parasa S, Reddy N, Faigel DO, et al. Global impact of the COVID-19 pandemic on endoscopy: an international survey of 252 centers from 55 countries. *Gastroenterology* 2020; published online June 11. https://doi:10.1053/j.gastro.2020.06.009.

2 Lui RN, Tang RS, Chiu PW. Striving to protect patients and healthcare professionals in endoscopy units during pandemics: from SARS to COVID-19. *Gastroenterology* 2020; published online May 5. https://doi:10.1053/j.gastro.2020.05.002.

3 Penman I, Edwards S, Coleman M, McKinlay A. Endoscopy activity and COVID-19: BSG and JAG guidance. April 3, 2020. https://www.bsg.org.uk/covid-19-advice/endoscopy-activity-and-covid-19-bsg-and-jag-guidance/ (accessed June 27, 2020).

4 National Institute for Health and Care Excellence. Gastrointestinal tract (upper) cancers—recognition and referral. https://cks.nice.org.uk/gastrointestinal-tract-upper-cancers-recognition-and-referral#!scenario (accessed July 5, 2020).

5 Arhi CS, Markar S, Burns EM, et al. Delays in referral from primary care are associated with a worse survival in patients with esophagogastric cancer. *Dis Esophagus* 2019; **32:** 1–11.

6 National Oesophago-Gastric Cancer Audit. 2019 annual report. https://www.nogca.org.uk/reports/2019-annual-report/ (accessed June 27, 2020).

7 Swanton C, Scowcroft H. Protecting "Covid protected" cancer hubs. *BMJ* 2020; **369:** m2062.

Use of Cytosponge as a triaging tool to upper gastrointestinal endoscopy during the COVID-19 pandemic

Published **Online**
July 30, 2020
https://doi.org/10.1016/S2468-1253(20)30242-9

During the COVID-19 pandemic, endoscopy services have been severely curtailed—eg, in England, UK, a 30% reduction of diagnostic endoscopies has been reported for the period between January and April, 2020, compared with the same period in 2019, with an estimated 750 oesophagogastric cancers going undiagnosed.[1] A delay in oesophageal cancer diagnosis could adversely affect outcomes, such as has previously been seen with low endoscopy referral rates being linked with poor outcomes from oesophageal cancer.[2]

The Cytosponge is a non-endoscopic diagnostic tool that was developed to detect Barrett's oesophagus in patients with reflux symptoms. Cytosponge consists of a tethered capsule that is swallowed in a primary or secondary care office setting and collects oesophageal cells, which can be assessed for morphology and immunohistochemical biomarkers of intestinal metaplasia (TFF3) and dysplasia (atypia and p53).[3,4] The safety, acceptability, and diagnostic accuracy of this approach has been assessed in three clinical trials, including the recent BEST3 trial.[5–7] In light of COVID-19 restrictions, we assessed whether Cytosponge could triage patients referred for urgent investigation of alarm oesophageal symptoms.

Between April 8 and May 26, 2020, 123 patients were referred to our department at Cambridge University Hospital (Cambridge, UK) for urgent endoscopy, of whom 14 with dysphagia Mellow score of 3 or more received fast-track endoscopy, while 72 with mild symptoms and no dysphagia were managed via telephone. The remaining 37 patients

See Online for appendix

were deemed eligible for Cytosponge, 21 of whom denied COVID-19 symptoms and accepted the test. Mean patient age was 59·9 years (SD 11·4; range 41–80). Most had dysphagia, with a median Mellow score of 1 (range 0–2; appendix pp 1–2). The nurse administering the Cytosponge reported an incomplete swallow on the basis of string tension on withdrawal (which was considered a high-risk feature) in four patients. Two of these four patients were found to have glandular atypia and p53 positive cells suggestive of dysplasia or cancer (appendix p 3). In the other two patients, an absence of glandular cells confirmed incomplete passage of the Cytosponge. Another four patients had evidence of cellular atypia suggesting a possible neoplastic process. All eight patients were referred for an urgent endoscopy and cancer was diagnosed in four of them. In the other four patients, endoscopy did not identify any concerning findings. Three patients had TFF3 positive cells suggestive of intestinal metaplasia (appendix p 3) and had evidence of peptic disease on endoscopy, with intestinal metaplasia on biopsies in two patients. The remaining ten patients had a normal Cytosponge result (appendix p 3) and were managed via telephone follow-up. Five of these ten patients received an endoscopy subsequently during the study period, which showed reassuring findings.

One patient had particularly interesting findings. A man, aged 54 years, with moderate dysphagia and weight loss had evidence of glandular atypia and aberrant p53 on the Cytosponge specimen. Endoscopy revealed a malignant stricture with tongues of dysplastic Barrett's oesophagus above it (appendix p 3). Thus, although the Cytosponge did not traverse the tumour, it was able to sample sufficiently to provide a diagnosis.

The Cytosponge is an example of an innovation that has undergone rigorous evaluation for diagnosing Barrett's oesophagus. The COVID-19 pandemic has offered the opportunity for more rapid adoption of this tool but the different patient group than originally intended merits careful audit. Although dysphagia was an exclusion criterion in previous trials for Cytosponge, it is safe in patients with eosinophilic oesophagitis.[8] Our data suggest that Cytosponge is a potentially useful test to triage patients with mild-to-moderate dysphagia and other oesophageal symptoms, among whom the conversion rate to cancer at endoscopy is less than 4%.[9] Atypical cells, aberrant p53 expression, and evidence of incomplete swallow were high-risk criteria for cancer. In our small series, all patients with cancers showed at least one high-risk feature.

Using the Cytosponge for this indication has several advantages when endoscopy provision is restricted. Cytosponge is an office-based procedure, which can be administered by a single non-medically qualified operator. Additionally, a low rate of aerosol generation is likely given that device removal only takes 3–5 s. Finally, if results are normal and subsequent symptom resolution occurs, testing can offer reassurance and enable prioritisation of endoscopy for those with a more urgent need. However, our findings have limitations. For instance, half the patients with negative Cytosponge results did not receive an endoscopy; therefore, we cannot exclude missed cancers. The device is not designed to detect gastric pathology, so attention is required on screening to elucidate the nature of the symptoms. Nonetheless, this study allowed us to develop an alternative clinical pathway to triage patients referred for urgent endoscopy (appendix p 4).

RCF and MO are named on patents for Cytosponge and related assays that have been licensed by the Medical Research Council to Covidien GI Solutions (now Medtronic). They are shareholders and consultants for Cyted Ltd, which aims to provide solutions for early diagnosis. All other authors declared no competing interests.

*Massimiliano di Pietro, Ines Modolell, Maria O'Donovan, Catherine Price, Nastazja D Pilonis, Irene Debiram-Beecham, *Rebecca C Fitzgerald*
RCF29@MRC-CU.cam.ac.uk

MRC Cancer Unit, Hutchison-MRC Research Centre, University of Cambridge, CB2 0XZ, UK (MdP, IM, MO, NDP, ID-B, RCF); Department of Gastroenterology, Cambridge University Hospitals NHS Foundation Trust, UK (MdP, IM, CP, RCF); and Department of Gastroenterology, Cambridge University Hospitals NHS Foundation Trust, UK (MO)

1 Markar SR Clarke J, Kinross J. Practice patterns of diagnostic upper gastrointestinal endoscopy during the initial COVID-19 outbreak in England *Lancet Gastroenterol Hepatol* 2020; published online July 16. https://doi.org/10.1016/ S2468-1253(20)30236-3.

2 Shawihdi M, Thompson E, Kapoor N, et al. Variation in gastroscopy rate in English general practice and outcome for oesophagogastric cancer: retrospective analysis of Hospital Episode Statistics. *Gut* 2014; **63:** 250–61.

3 Paterson AL, Gehrung M, Fitzgerald RC, O'Donovan M. Role of TFF3 as an adjunct in the diagnosis of Barrett's esophagus using a minimally invasive esophageal sampling device-The Cytosponge™. *Diagn Cytopathol* 2020; **48:** 253–64.

4 Ross-Innes CS, Chettouh H, Achilleos A, et al. Risk stratification of Barrett's oesophagus using a non-endoscopic sampling method coupled with a biomarker panel: a cohort study. *Lancet Gastroenterol Hepatol* 2017; **2:** 23–31.

5 Kadri SR, Lao-Sirieix P, O'Donovan M, et al. Acceptability and accuracy of a non-endoscopic screening test for Barrett's oesophagus in primary care: cohort study. *BMJ* 2010; **341:** c4372.

6 Ross-Innes CS, Debiram-Beecham I, O'Donovan M, et al. Evaluation of a minimally invasive cell sampling device coupled with assessment of trefoil factor 3 expression for diagnosing Barrett's esophagus: a multi-center case-control study. *PLoS Med* 2015; **12:** e1001780.

7 Fitzgerald RC, Di Pietro M, O'Donovan M, et al. Cytosponge-trefoil factor 3 versus usual care to identify Barrett's oesophagus in a primary care setting: a multicentre, pragmatic, randomised controlled trial. *Lancet* 2020; **396:** 333–43.

8 Katzka DA, Smyrk TC, Alexander JA, et al. Accuracy and safety of the Cytosponge for assessing histologic activity in eosinophilic esophagitis: a two-center study. *Am J Gastroenterol* 2017; **112:** 1538–44.

9 Kapoor N, Bassi A, Sturgess R, Bodger K. Predictive value of alarm features in a rapid access upper gastrointestinal cancer service. *Gut* 2005; **54:** 40–45.