Feasibility of the implementation of Cytosponge™ as a triage test for reflux symptoms in primary care: Barrett's oEsophagus Screening Trial 3 (BEST3)

Irene Debiram-Beecham[3], Anne-Marie Lydon[3], Beth Muldrew[1], Benoit Aigret[1], Maria O'Donovan[2], Monika Tripathi[2], Zohrah Khan[1], Ashley Wilson[1], Laura Baseley[1], Judith Offman[1], Sam Smith[4], Francesca Pesola[1], Roberta Maroni[1], Nicholas Swart[5], Fiona Scheibl[3], Fiona Walter[3], Greg Rubin[6], Stephen Morris[5], Peter Sasieni[1], Rebecca C. Fitzgerald[3]

1. Cancer Research UK & King's College London Cancer Prevention Trials Unit, 2. Cambridge University Hospitals NHS Foundation Trust, 3. University of Cambridge, 4. Leeds Institute of Health Sciences, 5. University College London, 6. Newcastle University

1. Objective

To determine the operational requirements of implementing the Cytosponge™-TFF3 test in primary care. This includes the ease of deployment of a novel clinical technique, laboratory processing of samples to Good Clinical Laboratory Practice (GCLP) with result feedback to the patient and primary care physician in real time and trigger of a confirmatory endoscopy if required.

2. Background

- Oesophageal adenocarcinoma (OAC) has increased 6-fold in the West since the 1990s, with a 5-year survival of <20%[1]. Barrett's oEsophagus (BE), the precursor lesion to OAC, can be detected and treated endoscopically.
- The Cytosponge™, a non-commercial non-endoscopic device, combined with biomarker Trefoil Factor 3 (TFF3) has been tested in 4 clinical studies numbering >4,000 procedures. It has been found to be safe, accurate and acceptable to patients.

Figure 1: Diagram of the Cytosponge™ withdrawal procedure (**A**), Cytosponge™ capsule compared to two paracetamol tablets (**B**), expanded Cytosponge™ (left) and capsule (right) (**C**)

- The device capsule will dissolve 5 minutes after swallowing. The sponge is withdrawn by the attached string, collecting cells from the length of the oesophagus. Sensitivity for BE is 79.5–87% and improves with increasing length of Barrett's segments, and has a specificity of 92.4% for diagnosing BE.[2,3]

3. Methods

- A randomised controlled trial of 110 primary care sites is near completion (BEST3). Randomisation is 1:1 to the usual care or intervention arm (including both cluster and patient-level), where the Cytosponge™ test is offered to participants at their local General Practice (GP) surgery.[4]
- Either a primary care Clinical Research Network (CRN) nurse or practice-employed nurse model is used to deliver the intervention.

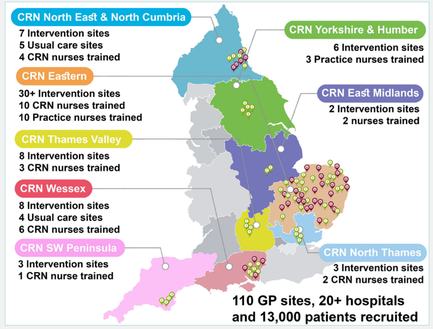

Figure 2: Geographical distribution of BEST3 primary care sites, CRN nurses and Practice-employed nurses

- A centralised nursing training programme was conducted using a combination of video demonstrations, slide presentations and a live Cytosponge™ clinical procedure.
- Nurses were observed post-training in a primary care clinical setting. A competency review was performed on all nurses prior to independently administering the device to participants.

4. Results

- The novel procedure has been carried out in over 70 UK sites, with >1700 patients receiving the test administered by 35 newly-trained CRN nurses and 10 practice nurses.
- Device administration was successful in one attempt in 86% of patients and a further 10% successfully swallowed after a second attempt. Nurses were deemed competent to administer the test after undertaking 5-10 procedures under supervision.

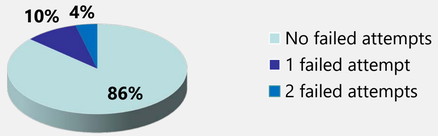

Figure 3: Percentage of Cytosponge™ procedures performed without an unsuccessful attempt, with 1 unsuccessful attempt and 2 unsuccessful attempts.

- All Cytosponge™ samples have been processed by a laboratory following GCLP guidelines. A full clinical report is sent to the GP on average 18 days following the test (median: 17 days, range 6 - 63 days) using a standard pathology reporting template.

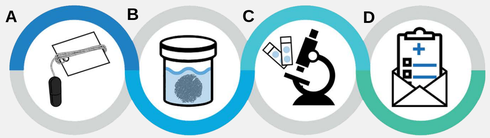

Figure 4: Eligible patients are invited to swallow the Cytosponge™ by their GP (**A**), Cytosponge™ samples are processed into a formalin-fixed, paraffin-embedded (FFPE) tissue block and stained for TFF3 (**B**), Pathologist reviews the sample for TFF3 and benign conditions with a pathology report sent to the GP (**C**) GP informs patient of the result, with an endoscopy arranged for TFF3 positive participants (**D**)

4. Results (Continued)

- A TFF3 result suggestive of BE and other abnormal findings (e.g. dysplasia, ulceration) is communicated to the GP via an immediate electronic notification, the first real-time reporting in a Cytosponge™ trial.

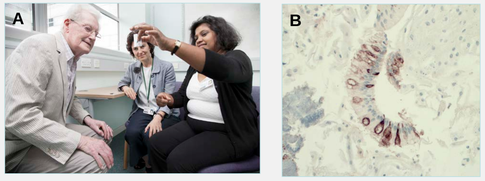

Figure 5: The Cytosponge™ can be easily administered by nurse in primary care setting. Image courtesy of Cambridge University Hospitals (**A**), Representative picture of positive TFF3 staining (**B**)

5. Conclusion

This pragmatic clinical trial explores current data regarding the feasibility of deploying a nurse-led novel procedure in primary care. Our findings suggest the Cytosponge™-TFF3 test can be easily administered in primary care by newly-trained nurse cohorts as part of routine clinical care and the results processed to GCLP standards in a clinically-meaningful timeframe.

6. References

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2. Kadri S et al. BMJ 2010; **341**: c4372.
3. Ross-Innes C et al. PLoS Med 2015; **12**: e1001780.
4. Offman J et al. BMC Cancer 2018; **18(1):** 784.