Early Diagnosis of Oesophageal Cancer and Cytosponge

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CANCER RESEARCH UK | CAMBRIDGE CENTRE

EARLY DETECTION PROGRAMME

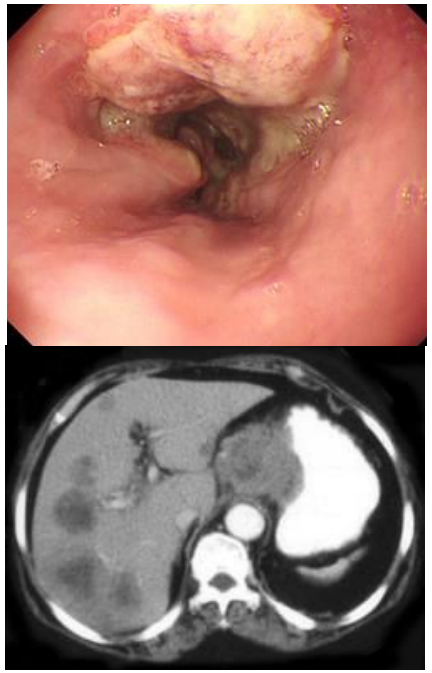
UNIVERSITY OF CAMBRIDGE

Disclosures

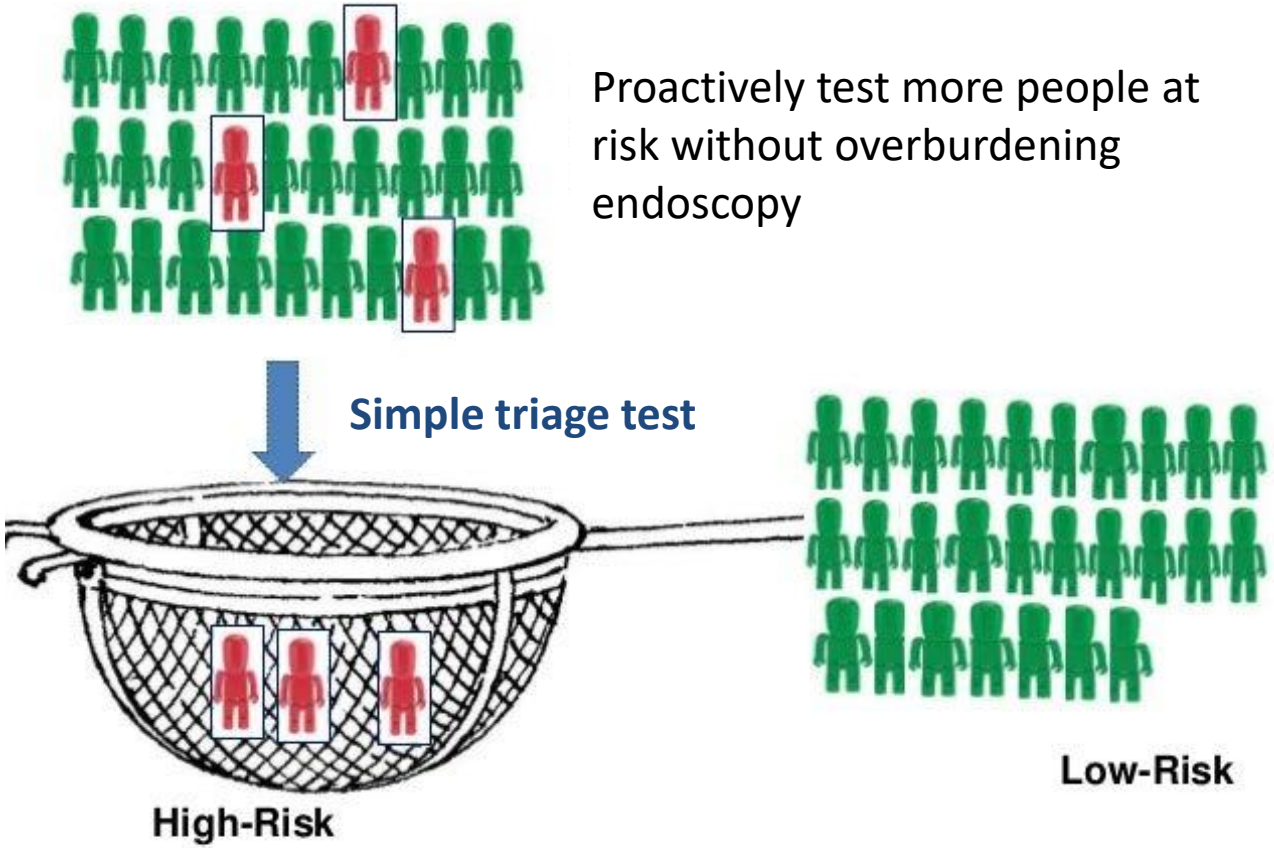
- Patent holder for Cytosponge and related technologies which have been licensed to Covidien (now Medtronic) by the Medical Research Council
- Co-founder, consultant and shareholder of Cyted Ltd, a company working on early detection technology

Vision for oesophageal adenocarcinoma: Select, Test, Treat *and transform outcomes*

Symptomatic cancer
Chemo/Radio/surgery
Or palliative therapy

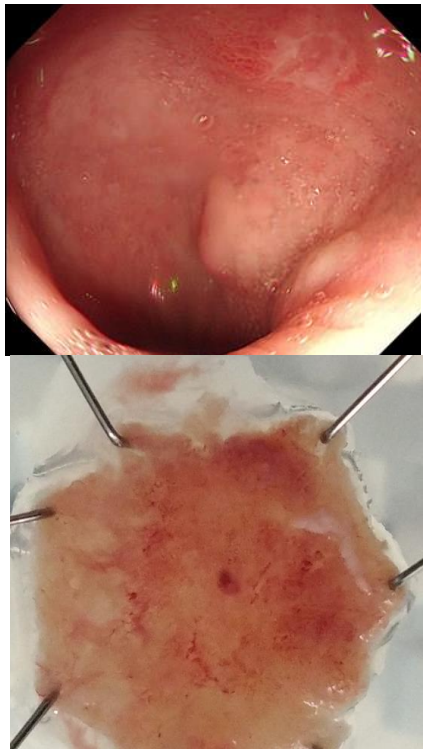


<20% 5 year survival



Proactively test more people at risk without overburdening endoscopy

Screening detected
Barrett's cancer
Endoscopically resected



>80% 5 year survival

The device

The tiny sponge that's saving lives

BBC Look East, Aug 2020

BBC NEWS

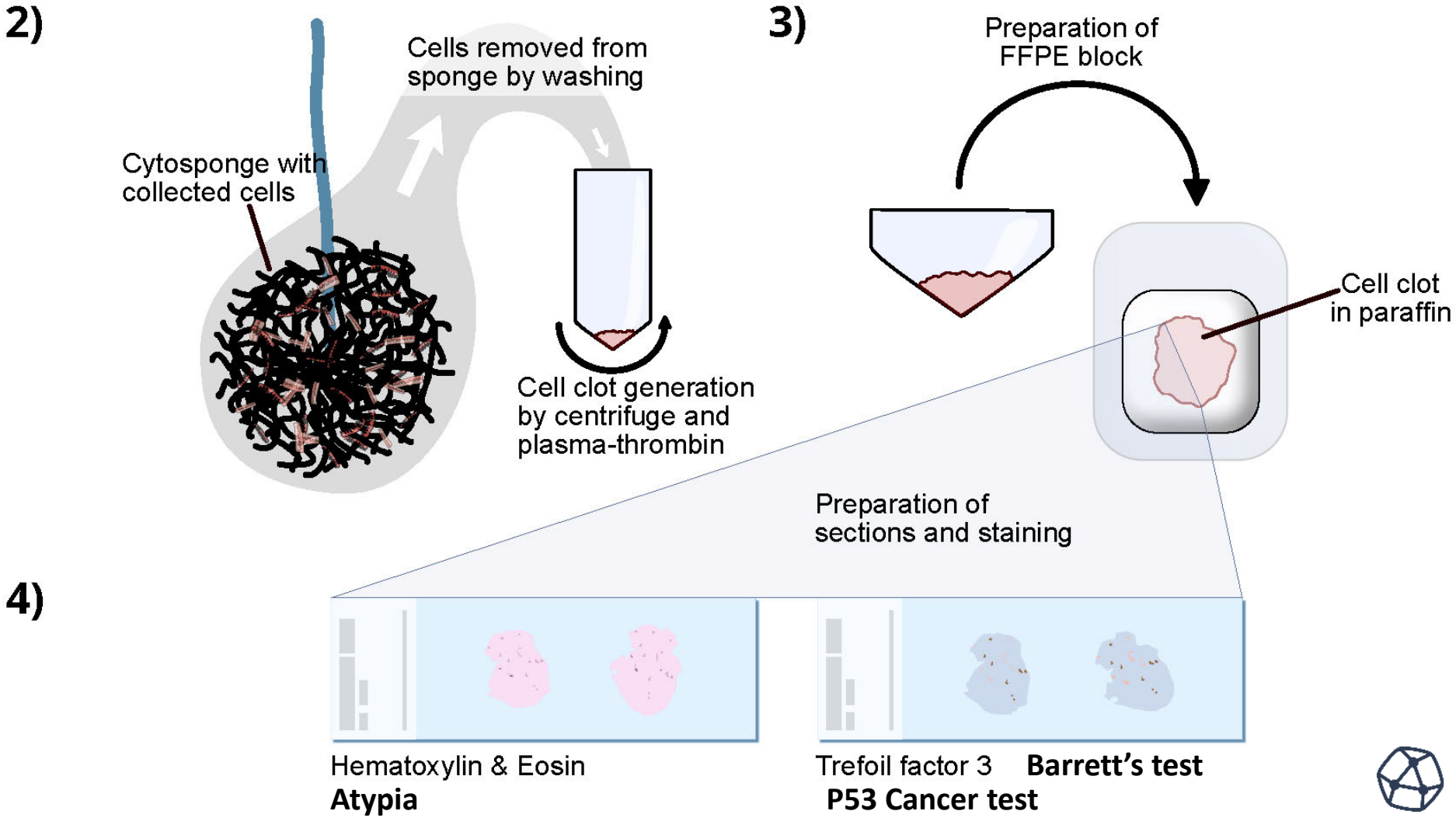
Scan me to watch the procedure on YouTube

Clinical procedure well suited to delivery in office setting including primary or community care

- Nurse-led clinic <30 min appointment
- Office-based procedure in <10 minutes
- Minimally invasive
- No sedation needed
- Minimal aerosol generation
- Excellent safety profile
- Excellent patient acceptability

Medtronic

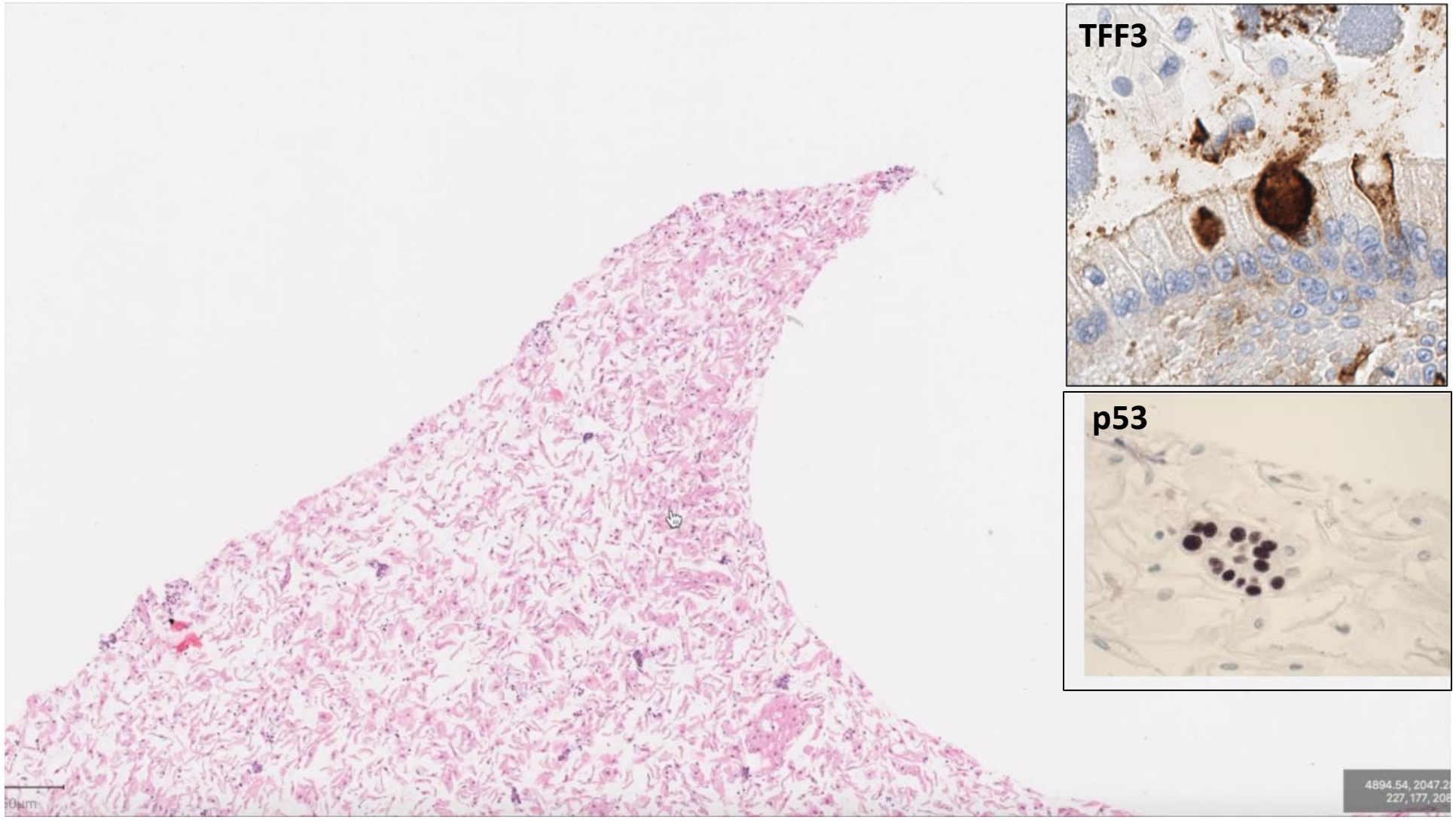
Centralised lab processing and reporting



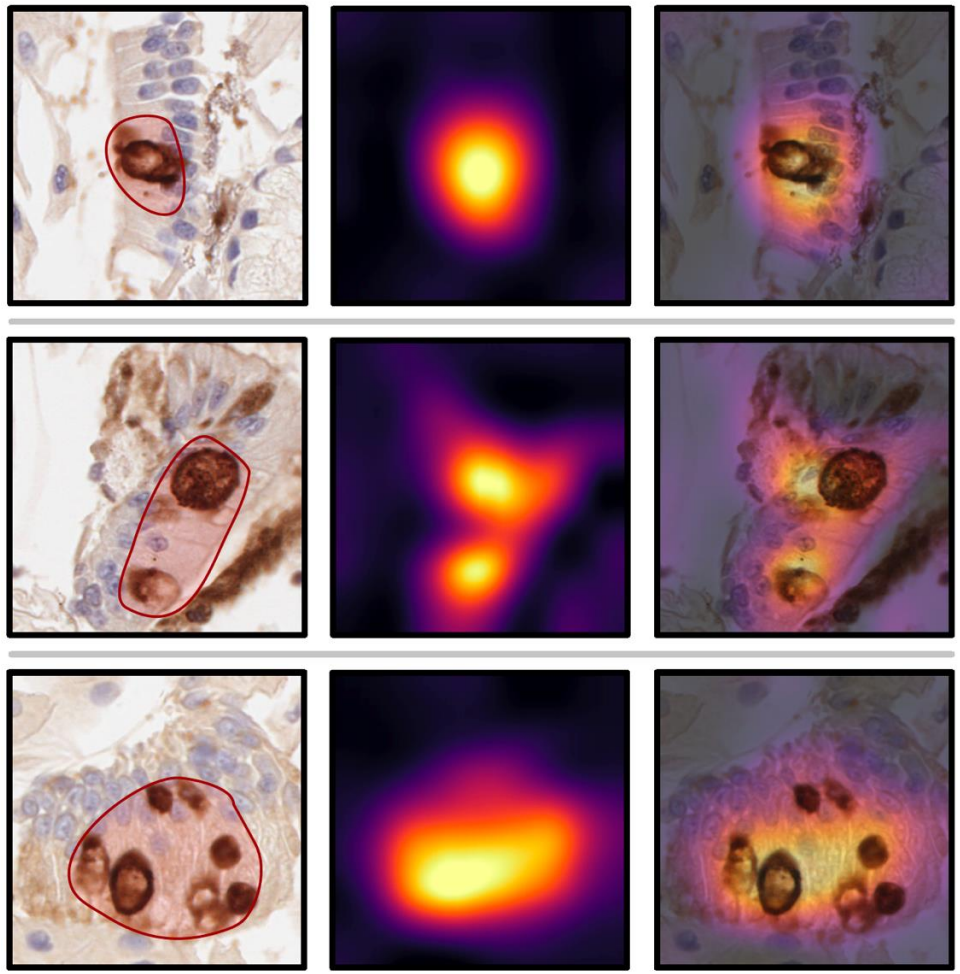
Cyted

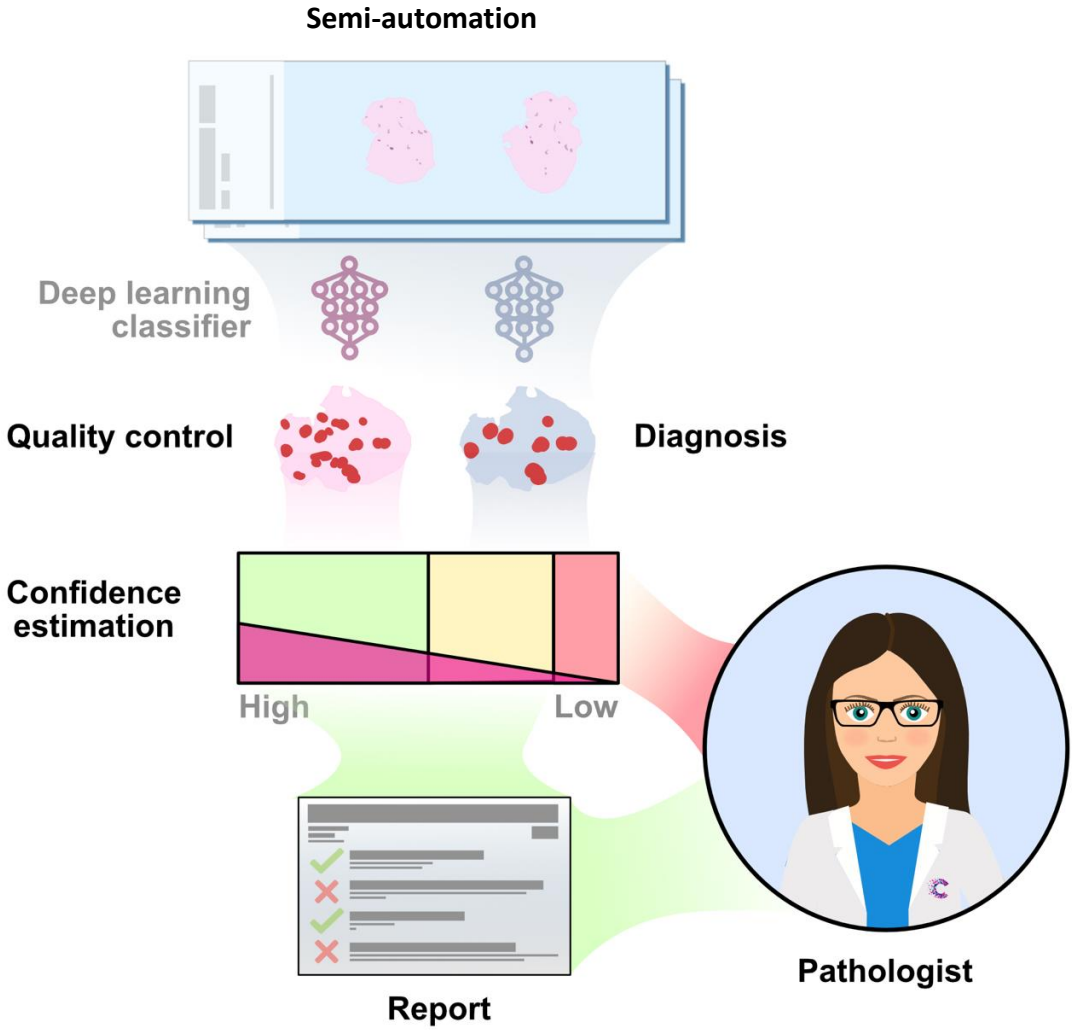
2022 Prix Galien award

Importance of precise molecular biomarkers



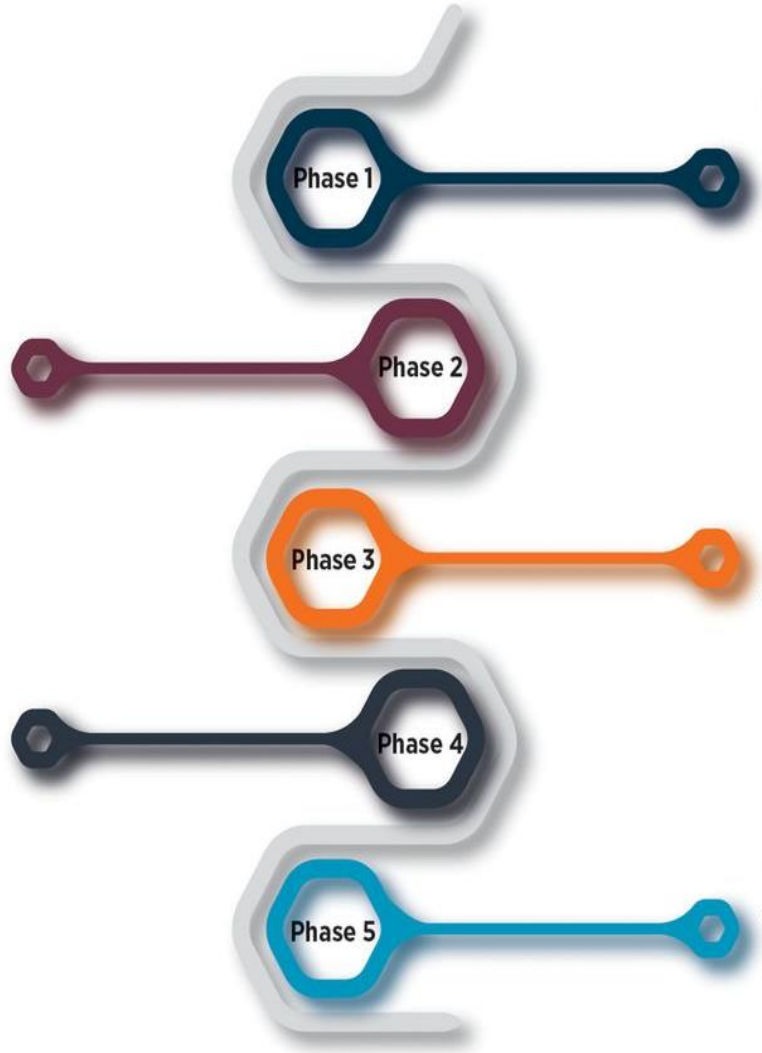
Scaling up for screening:
AI assisted triage





Gehrung et al. Nature Medicine 2021

Evidence based for Cytosponge-TFF3



Preclinical Exploratory
Promising biomarkers are identified.

Clinical Grade Assay Development and Verification
Demonstrate that the assay can accurately detect established cancers.

Retrospective Longitudinal Trial
These trials determine whether the assays can detect preclinical disease (before symptoms have developed) and a "screen positive" rule is defined.

Prospective Screening Trial
These trials determine the extent and characteristics of the disease detected by the test and the false referral rate is determined.

Cancer Control
The impact of screening on reducing cancer mortality in the population is quantified.

Preclinical: exploratory
Lao-Sirieix *et al* Gut 2009

Test Clinical Grade Assay
Lao-Sirieix *et al* Gut 2011

Pilot Study in Intended Screening Population BEST1
Kadri *et al* BMJ 2011

Case:Control study BEST2
92% specificity
80-90% sensitivity
Ross-Innes PLOS Medicine 2015

RCT screening vs usual care BEST3
10x Number Barrett's diagnosed
Fitzgerald *et al* The Lancet 2020

New American College Guidelines and NICE MedTech Briefing

We suggest that a swallowable, non-endoscopic capsule sponge device combined with a biomarker is an acceptable alternative to endoscopy for screening for BE in those with chronic reflux symptoms and other risk factors

Strength of recommendation: conditional

Diagnosis and Management of Barrett's Esophagus: An Updated ACG Guideline

Shaheen, Nicholas J; Falk, Gary W; Iyer, Prasad G. MD; Souza, Rhonda F; Yadlapati, Rena H. (GRADE Methodologist); Sauer, Bryan G. (GRADE Methodologist); Wani, Sachin

Coming up next: BEST4 Platform Trial

Definitive **RCT of targeted screening** using the Cytosponge-TFF3 test to determine whether it would have a clinically important **impact on OAC-associated mortality (n=140,000)**

Conduct a study to evaluate the use of Cytosponge and a **risk stratification biomarker panel for surveillance** of patients with newly diagnosed Barrett's

Establish a **biobank for patients with BO** including clinical data, Cytosponge samples, blood and saliva for use in other research studies

Establish a **cohort** willing to be contacted regarding **further research studies** e.g. behavioural studies, lifestyle interventions, chemopreventive medications

Rebecca Fitzgerald, Uni of Cambridge

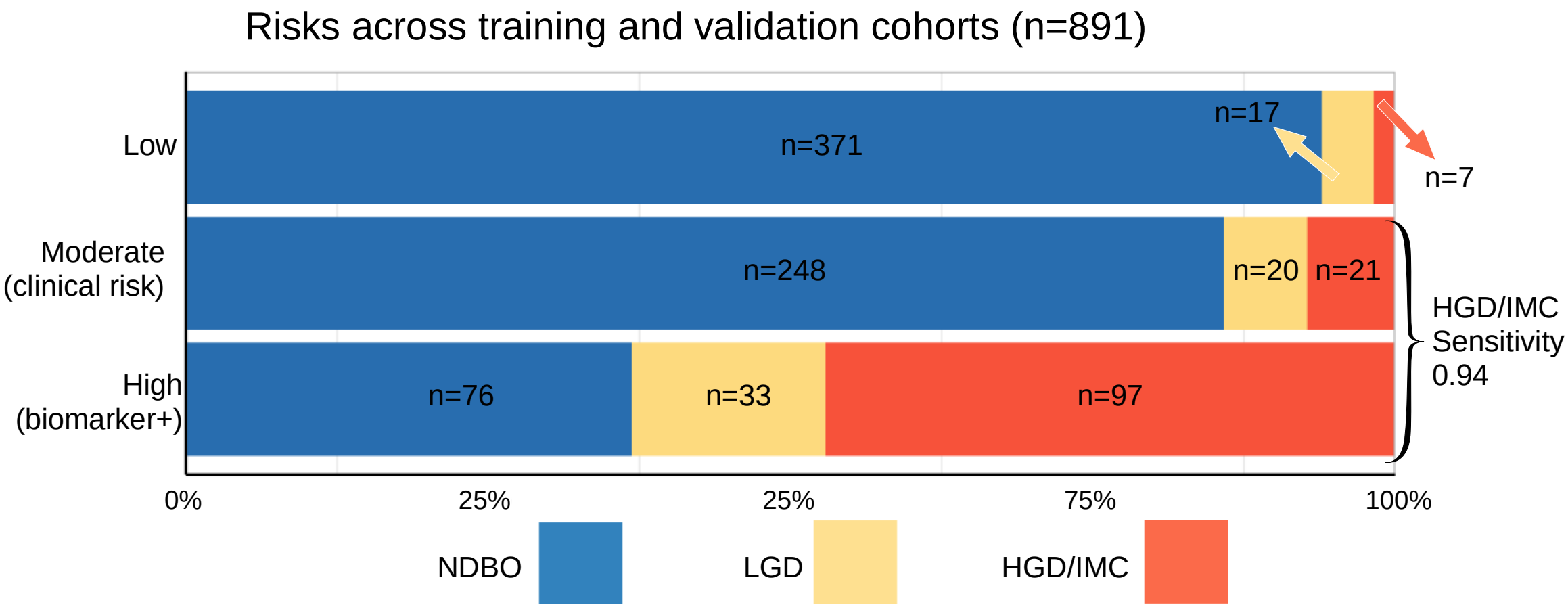
Peter Sasieni, Kings College London

Cytosponge as a diagnostic test: Implementation pilots during Covid-19

Cyted

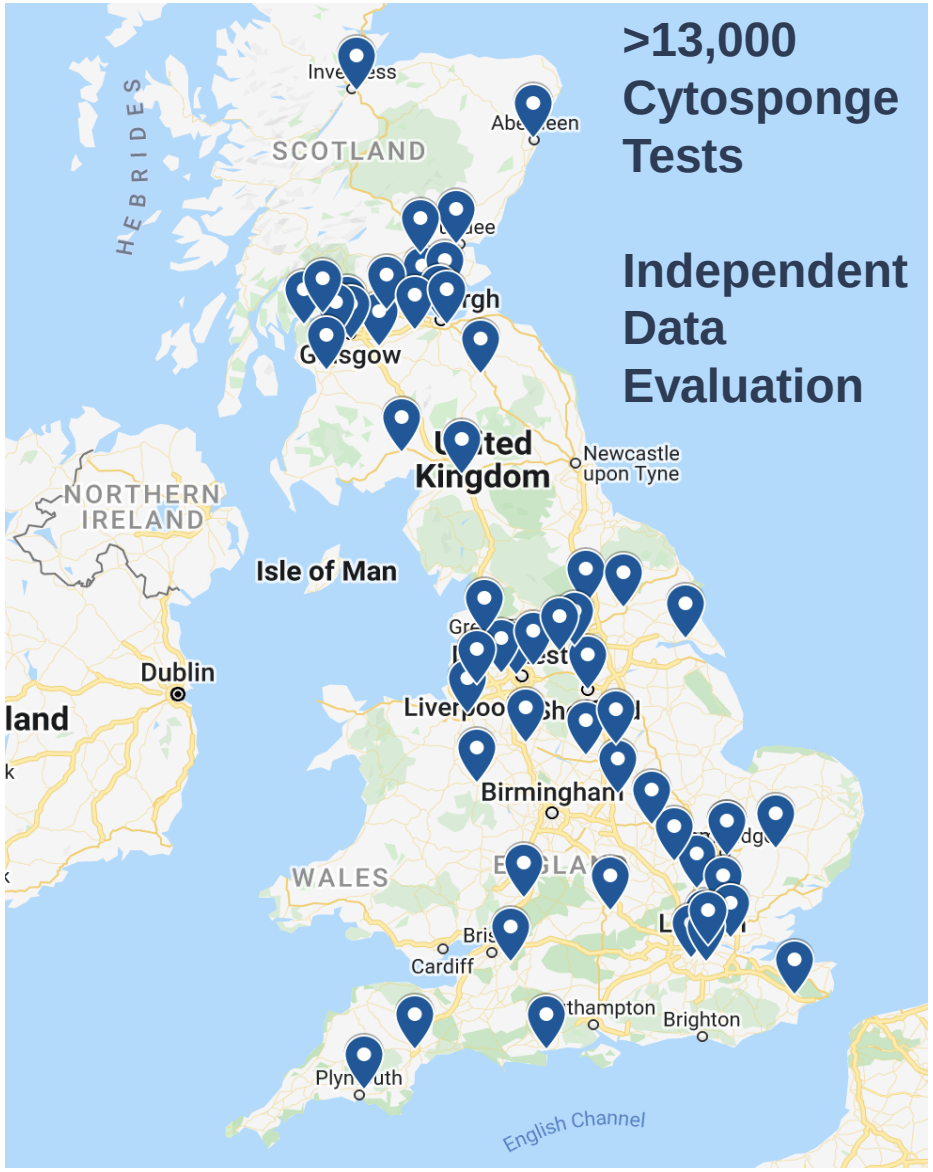
Targeted Screening	Symptomatic Referrals	Barrett's Surveillance
For people identified by GP with risk factors for Barrett's[1]	For individuals who present with reflux symptoms without alarm symptoms of cancer	For patients with known Barrett's Oesophagus
As a proactive test to detect Barrett's Oesophagus	As a test to guide the management of patients and triage for endoscopy	As a test to detect early oesophageal cancer and triage for endoscopy
One biomarker used to assess for intestinal metaplasia (TFF3)	Biomarkers assessed for intestinal metaplasia (TFF3) and dysplasia (p53, atypia)	Biomarkers assessed for intestinal metaplasia (TFF3) and dysplasia (p53, atypia)
Available via primary or community care[2] including Project DELTA	Available via primary care and selected secondary care centers[2] including NHS England	Available via selected secondary care centers[2] including NHS Scotland and Project DELTA

Evidence base for Cytosponge in surveillance: Biomarkers p53 and atypia



Pilonis, Killcoyne *et al* Lancet Oncology 2022

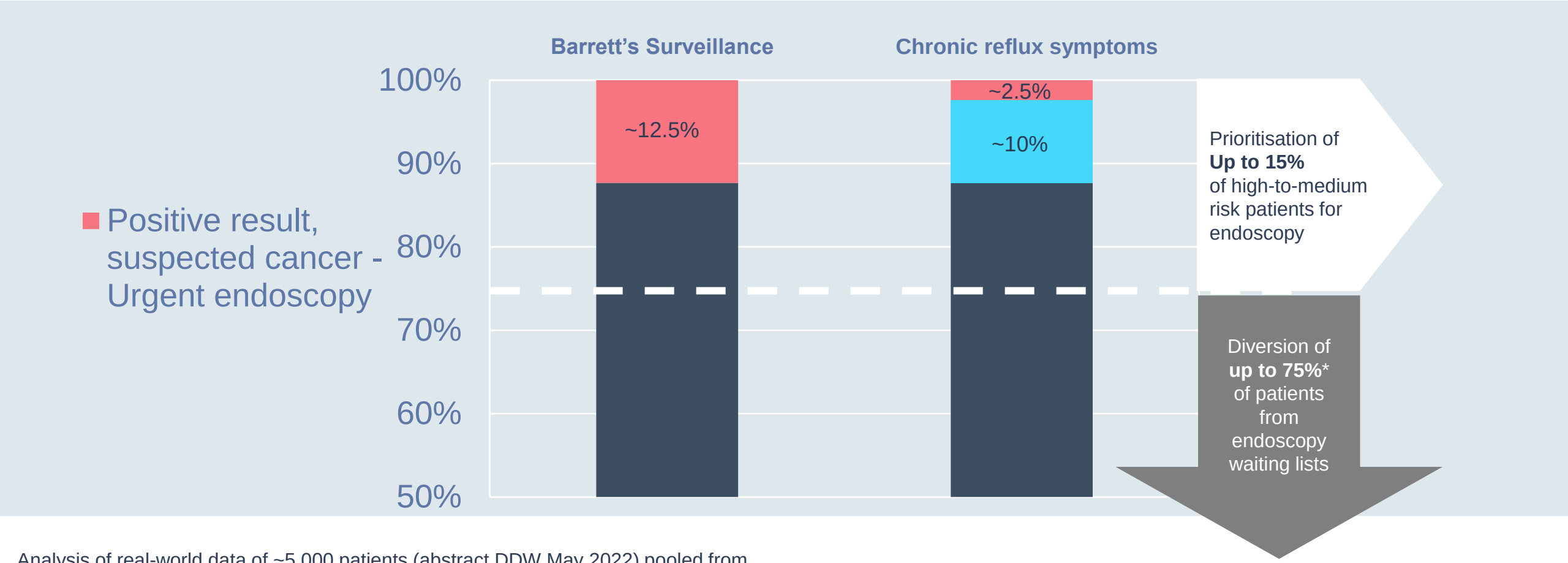
Real world NHS implementation in Covid-19 era



Health economics:
CISNET Clin Gastro Hepatol 2017
Swart et al EClinicalMedicine 2021

Acceptability:
Januszewicz *et al* Clin Gastro Hepatol 2019
Offman et al BMJ Open 2022

Cytosponge and endoscopy recovery



Analysis of real-world data of ~5,000 patients (abstract DDW May 2022) pooled from implementation of the Cytosponge test across NHS England and NHS Scotland

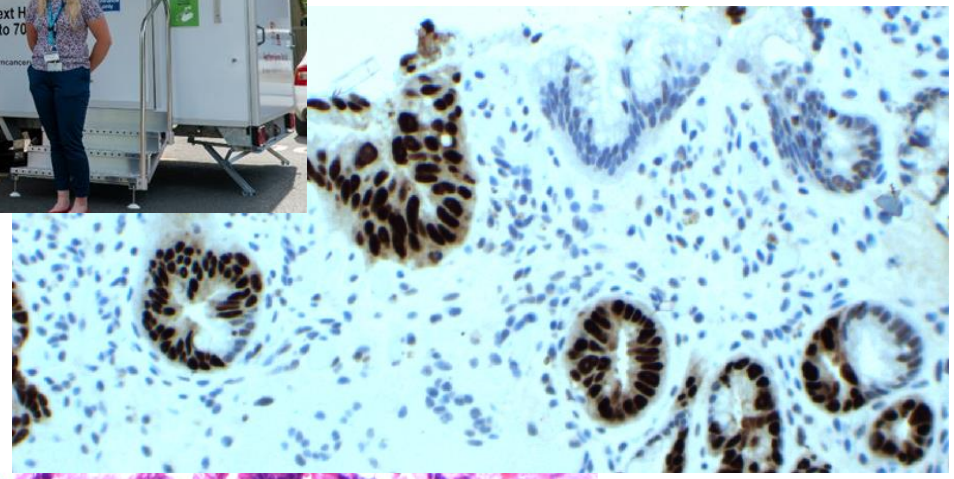
Now >13,000 patients tested

*Preliminary results from national NHS England pilot in evaluation by IQVIA, and NHS Scotland academic report both expected 2023

Case Study 1: New self-referral for reflux via Mobile Unit

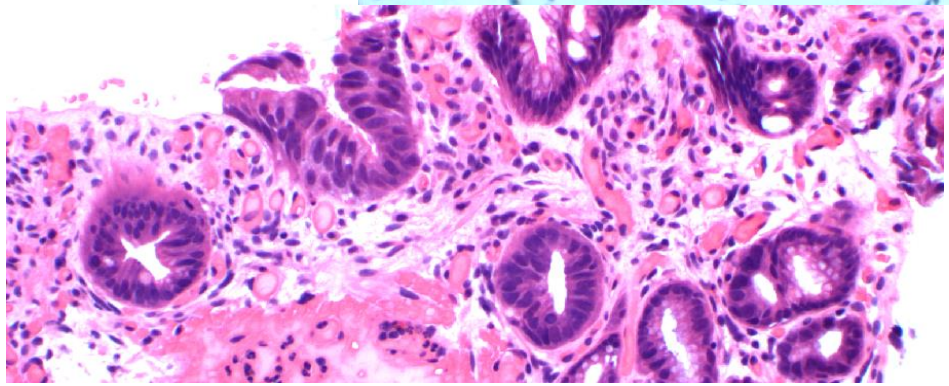
73 yr old female
Reflux induced cough
Ex-smoker
On PPI 10 yrs, no OGD

Multiple TFF3+ groups (8 and 10)
P53 equivocal and Atypia present



Very nervous about having endoscopy

After much persuasion attended for OGD
13 cm segment Barrett's
low and high grade dysplasia, p53 aberrant



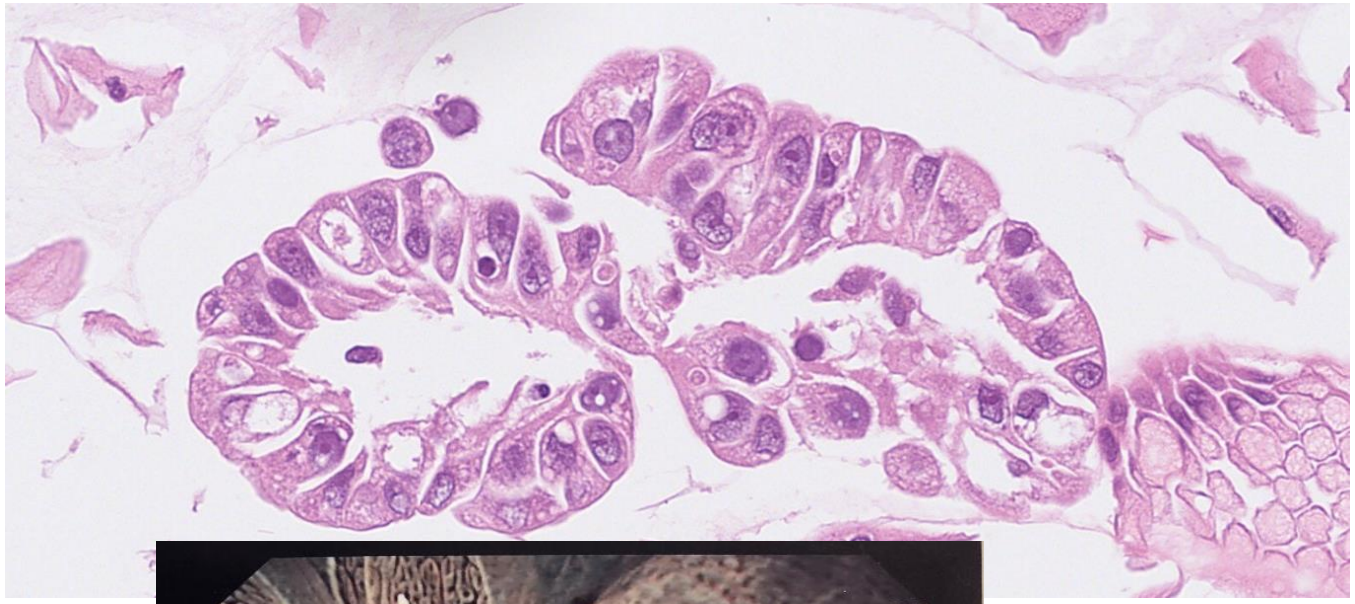
Undergoing endoscopic treatment

Case Study 2: Endoscopy surveillance backlog

- 67 yr old Female
- Retired ITU consultant, Leicester
- Diagnosed C1,M3 Barrett's 2012
- Surveillance 2015 and due 2020

- Surveillance delayed Covid
- Cytosponge April 2022:
- Dysplastic cells

- Early cancer resected



Coming up next: CYTOPRIME2

Why: To find patients with oesophageal cancer earlier

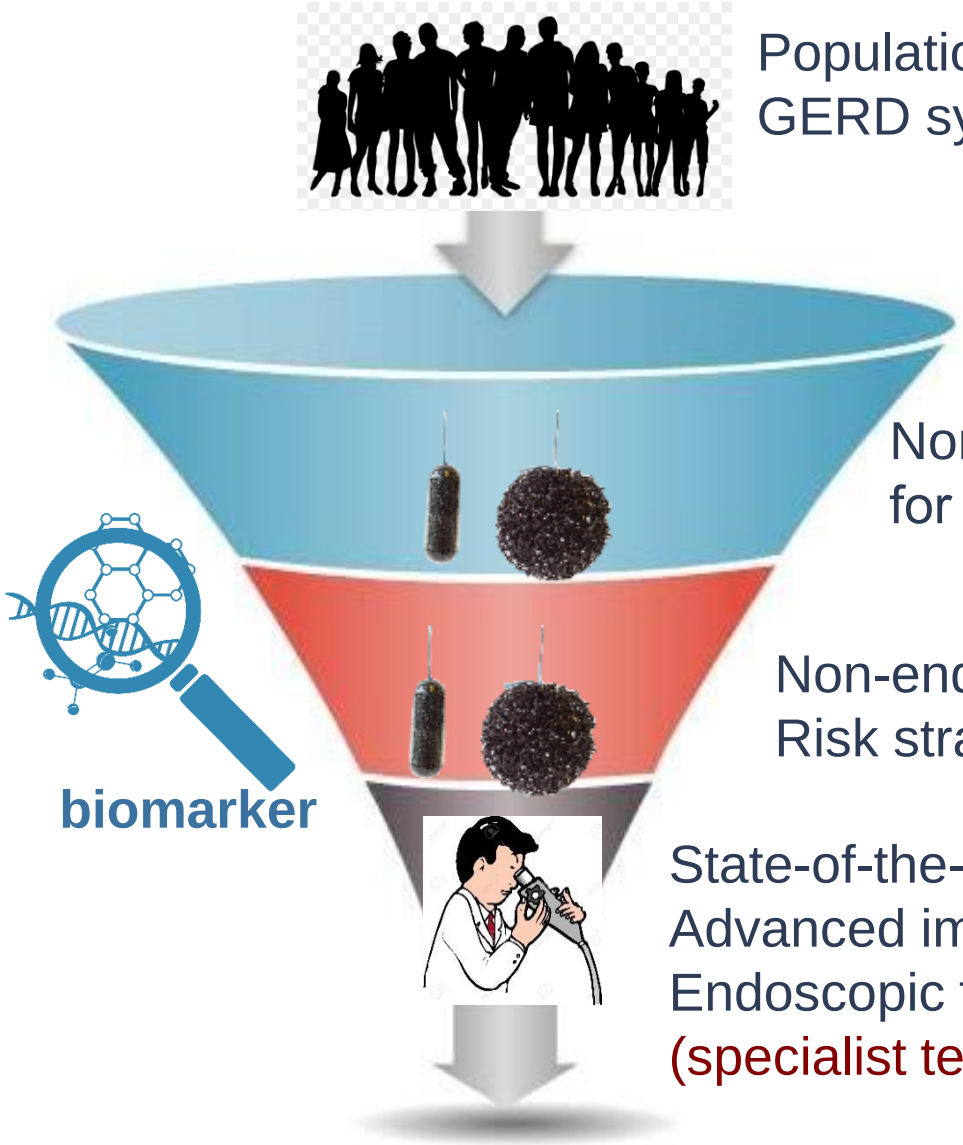
What: A £4 million, 18-month project

- Part of the 2022 NHS Cancer Programme
- Funded by SBRI Healthcare and NHSE&I
- In partnership with 4 Cancer Alliances

How:

- To test 2400 people with chronic reflux
- In community-based clinics for Cytosponge tests
- By enabling GPs to identify & refer patients at risk (over 50 years old and on long-term proton-pump inhibitor medication)

Precision screening and surveillance for oesophageal adenocarcinoma: a new era



Population at risk:
GERD symptoms + age, sex, ethnicity, BMI, smoking

Non-endoscopic triage test
for Barrett's oesophagus (primary care/ community hub)

Non-endoscopic surveillance
Risk stratification (secondary care or community hub)

State-of-the-art endoscopy
Advanced imaging and molecular analysis
Endoscopic therapy for early cancer/high-risk
(specialist tertiary centre)

Thank you!

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UKRI Innovate UK

Rosetrees Trust
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NHS National Institute for Health Research

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