
ACG INSTITUTE RESEARCH GRANTS AND AWARDS 2022
ACG INSTITUTE FOR CLINICAL RESEARCH AND EDUCATION
EIGHT different award types; INCREASED Junior Faculty FUNDING;
NEW Health Equity Research Award; Med Resident and Student Awards
www.gi.org/research-awards
Grant System Opens: September 7, 2021
Deadline: December 3, 2021
Read the Grant Flyer, FAQs, or visit the webpage for the full RFAs.

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NEW! ACG Institute
Health Equity Research Award
APPLY: gi.org/research-awards DEADLINE: December 3, 2021
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ACG INSTITUTE FOR CLINICAL RESEARCH AND EDUCATION

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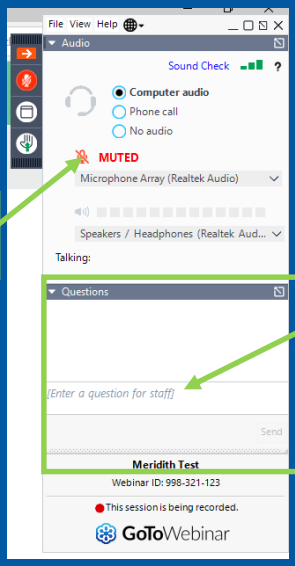
Virtual Grand Rounds

universe.gi.org

## Participating in the Webinar




All attendees will be muted and will remain in Listen Only Mode.

Type your questions here so that the moderator can see them. Not all questions will be answered but we will get to as many as possible.

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## How to Receive CME and MOC Points

**LIVE VIRTUAL GRAND ROUNDS WEBINAR**

ACG will send a link to a CME & MOC evaluation to all attendees on the live webinar.

**ABIM Board Certified physicians need to complete their MOC activities by December 31, 2021 in order for the MOC points to count toward any MOC requirements that are due by the end of the year. No MOC credit may be awarded after March 1, 2022 for this activity.**

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## MOC QUESTION

If you plan to claim MOC Points for this activity, you will be asked to: Please list specific changes you will make in your practice as a result of the information you received from this activity.

Include specific strategies or changes that you plan to implement.
THESE ANSWERS WILL BE REVIEWED.

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## ACG Virtual Grand Rounds

**Join us for upcoming Virtual Grand Rounds!**

**Week 32, 2021**
**Isolated GI Alpha-Gal Meat Allergy: What Clinicians Need to Know**
**Sarah K. McGill, MD, MSc**
**August 19, 2021 at Noon Eastern**

**Week 33, 2021**
**Hepatocellular Carcinoma: Epidemiology, Diagnosis and Treatment**
Patricia Jones, MD, MSCR
August 26, 2021 at Noon Eastern

Visit **gi.org/ACGVGR** to Register

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## Disclosures:

**Speaker:**
**Prasad G. Iyer, MD, MS, FACG**
***Research Funding: Exact Sciences, Pentax Medical. Consulting : Medtronic, Symple Surgical***

**Moderator:**
**Christina J. Tofani, MD**
***Dr. Tofani, faculty for this educational event, has no relevant financial relationship(s) with ineligible companies to disclose.***

*All of the relevant financial relationships listed for these individuals have been mitigated

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MAYO CLINIC

# Screening for Barrett's Esophagus : Beyond Upper Endoscopy

Prasad G. Iyer MD MSc
Professor of Medicine
Director, Esophageal Interest Group
Division of Gastroenterology and Hepatology
Mayo Clinic, Rochester, Minnesota

ACG Grand Rounds
2021

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# Objectives

- Understand rationale and challenges for BE/EAC screening
  - Context of current recommendations for BE screening
- Discuss progress in non-endoscopic BE screening
- Pitfalls and Next steps

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# Screening and (Surveillance) WHY ?

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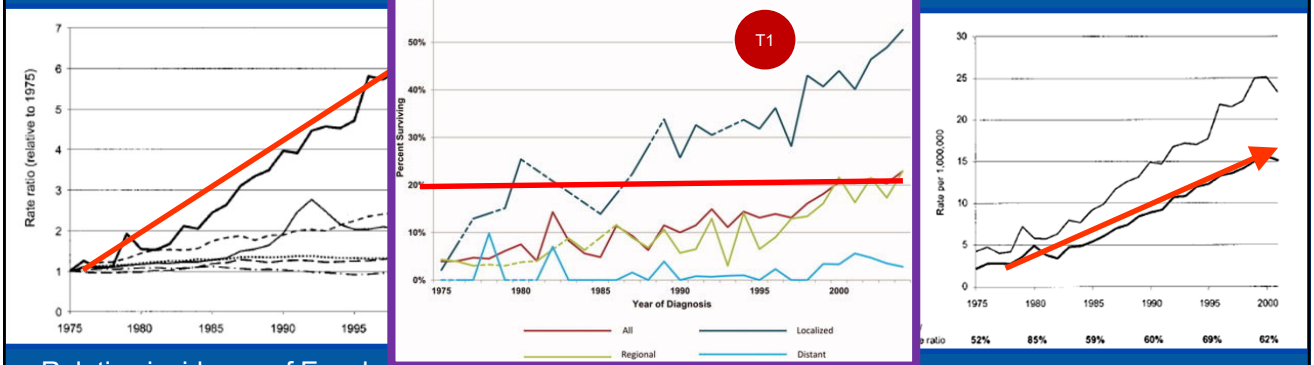
## EA Incidence, Mortality, Survival




Relative incidence of Esophageal AdenoCa/other malignancies

Relative disease specific mortality of Esophageal AdenoCa/other malignancies

J Natl Cancer Inst 2005, Hur Cancer 2013

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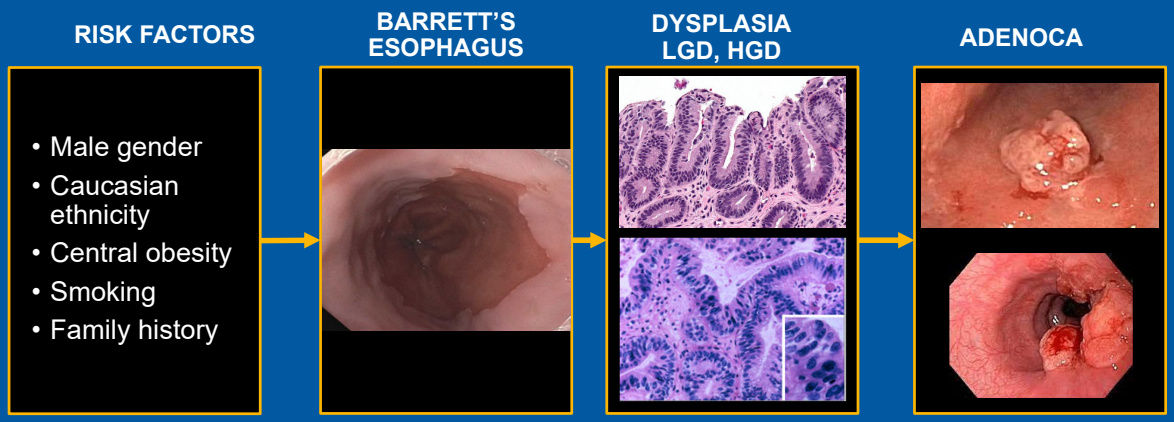
# Current BE-EAC Paradigm

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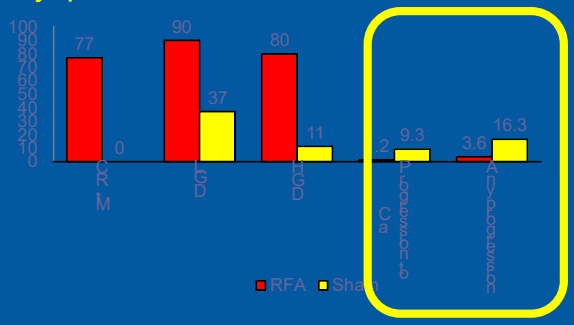
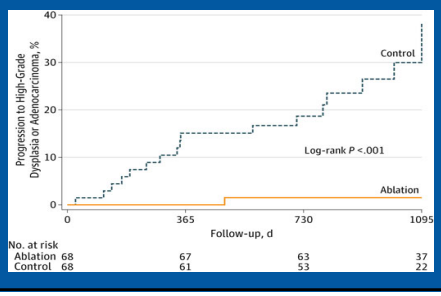
# Level 1 evidence

## Endoscopic Rx of Dysplasia : Reduced Cancer Incidence

Shaheen NEJM 2009 BE-HGD




Phoa JAMA 2014 BE-LGD




**Endoscopic Rx of Dysplasia**

↓

**Reduced EAC risk**

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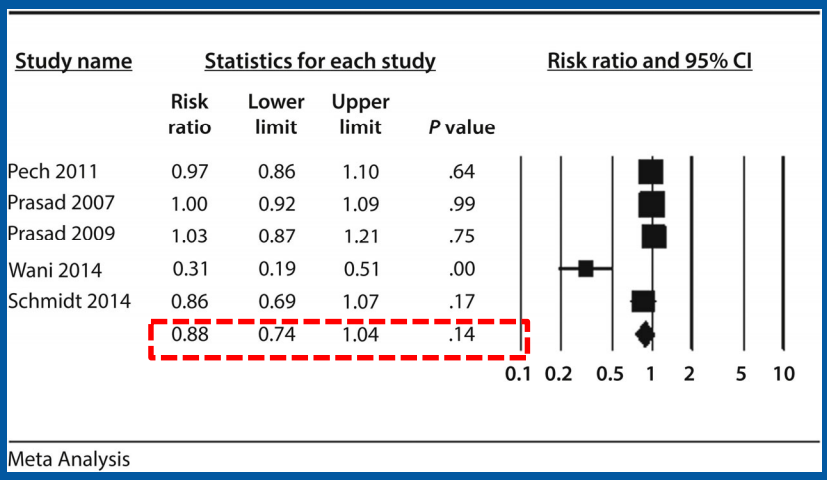
# Excellent Outcomes of EET for HGD/IMCa
## EET = Esophagectomy




*Overall 5-year survival*

ASGE SOP Guidelines for BE Endotherapy GIE 2018

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# Rationale for Early Detection of BE and BE related Dysplasia and Neoplasia

**Prevention : ↓ EA incidence**

**Treatment : ↑ EA free survival**

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# Challenges

BE screening : How ?

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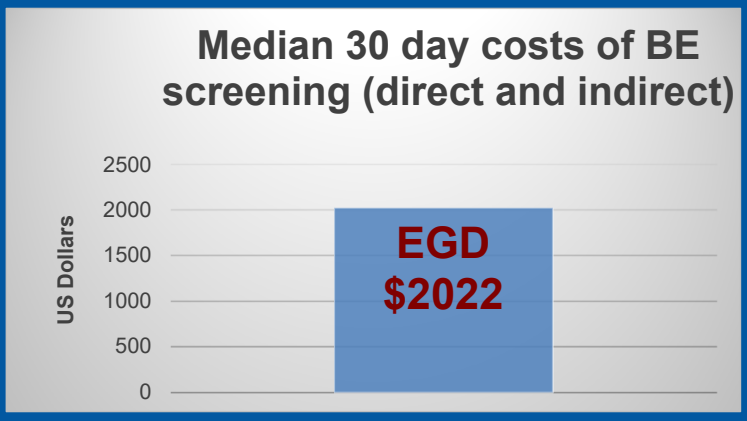
# Sedated EGD for BE screening

Costs associated with Barrett's esophagus screening in the community: an economic analysis of a prospective randomized controlled trial of sedated versus hospital unsedated versus mobile community unsedated endoscopy

James P. Moriarty,[1] Nilay D. Shah, PhD,[2] Joel H. Rubenstein, MD,[2] Christopher H. Blevins, MD,[3] Michele Johnson, CCRP,[3] David A. Katzka, MD,[3] Kenneth K. Wang, MD,[3] Louis Michel Wongkeesong, MD,[3] David A. Ahlquist, MD,[3] Prasad G. Iyer, MD, MS[3]

Rochester, Minnesota; Ann Arbor, Michigan, USA

- Expensive
  - Not cost effective
- Invasive
- Endoscopist
- Sedation
- Unsuitable for widespread application
- 10% of those eligible screened




Gastrointestinal Endoscopy 2017

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# Inaccurate Targeting of EGD for BE screening

- VA study
- More EGDs :
  - Females, < 50 years
- GERD centric screening recommendations
  - 40-50% of BE/EAC patients do not have frequent GERD

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JAMA 2014, AJG 2014, Gastroenterology 2019

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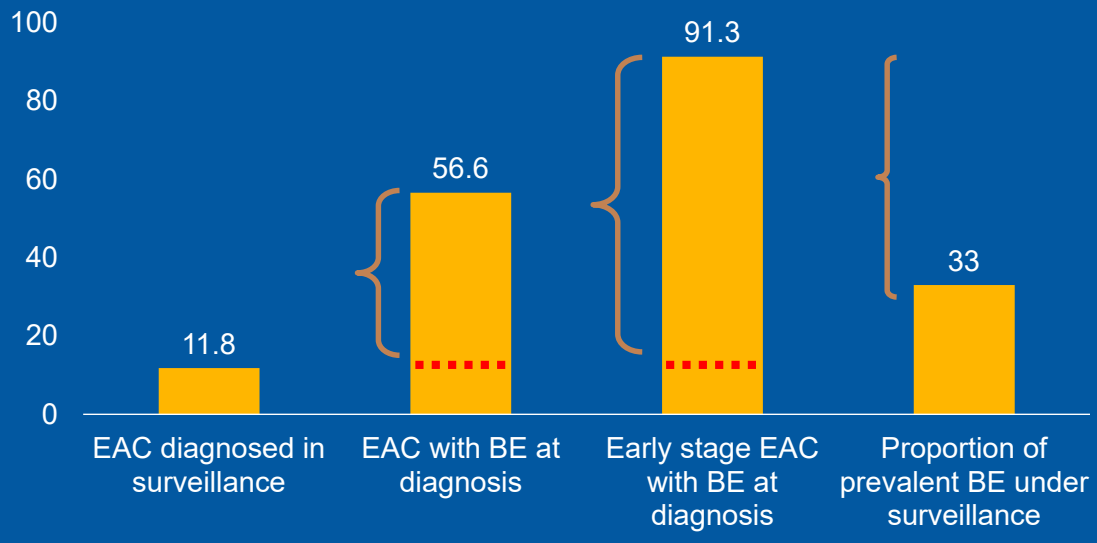
# Missed Opportunity for Early Detection ?




Tan, APT 2020, Jung Iyer AJG 2010

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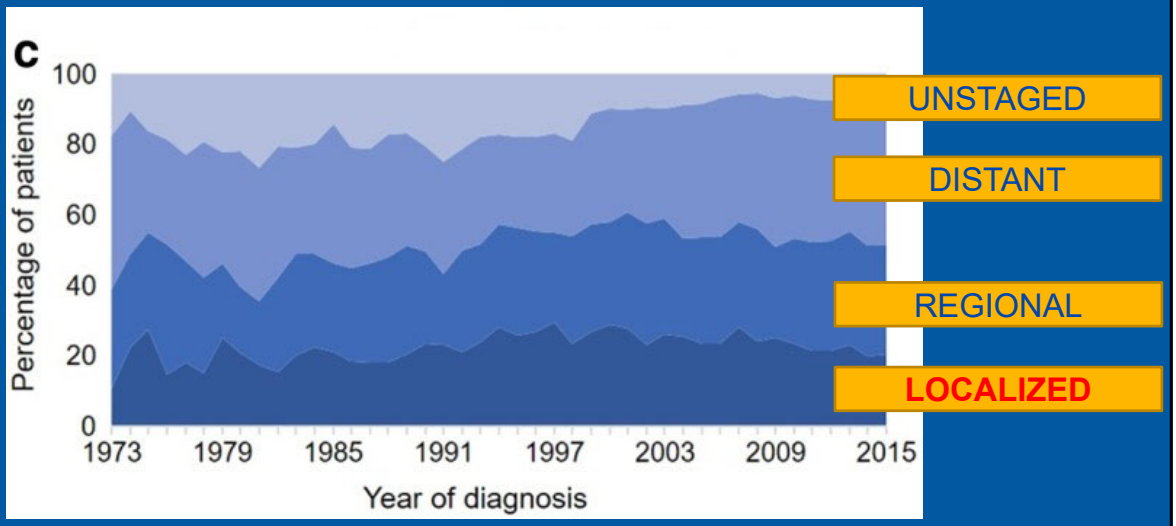
## Early Stage EAC : Small Proportion, No change




He H, Thorac Cancer. 2020

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## Solutions

## BE screening : How ?

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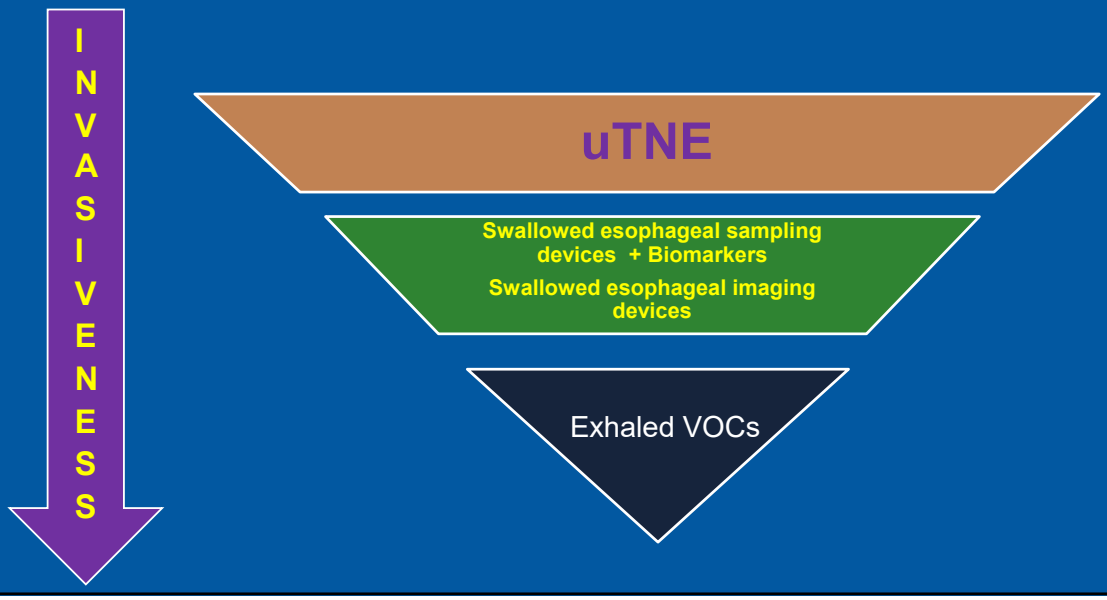
# Screening tests for BE

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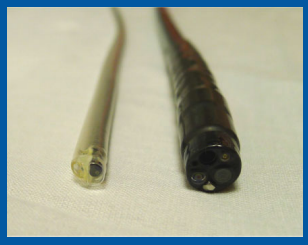
# U Transnasal Endoscopy




- Accurate (Sens and Spec > 90%)
- Well-tolerated, Safe,
- Comparable diagnostic yield, patient preference
- Can be done by non-physicians

Sami AJG 2015, Mortiarty GIE 2017, Blevins JCG 2017, Chak GIE 2015, Chak CGH 2015, Peery AJG 2014, Sami CGH 2018

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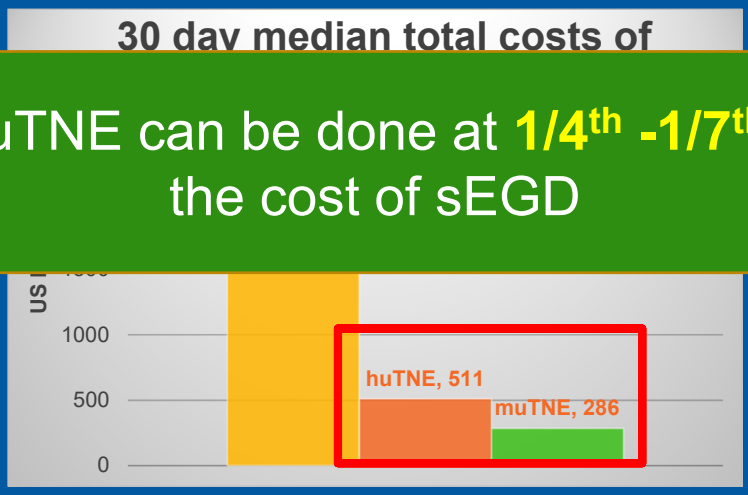
# uTNE : Lower costs

Costs associated with Barrett's esophagus screening in the community: an economic analysis of a prospective randomized controlled trial of sedated versus hospital unsedated versus mobile community unsedated endoscopy

James P. Moriarty,[1] Nilay D. Shah, PhD,[1] Joel H. Rubenstein, MD,[2] Christopher H. Blevins, MD,[3] Michele Johnson, CCRP,[3] David A. Katzka, MD,[3] Kenneth K. Wang, MD,[3] Louis Michel Wongkeesong, MD,[3] David A. Ahlquist, MD,[3] Prasad G. Iyer, MD, MS[3]

Rochester, Minnesota; Ann Arbor, Michigan, USA




Gastrointestinal Endoscopy 2017

Gastrointestinal Endoscopy 2017

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# Challenges to Widespread TNE use

## Provider

- Increasing utilization of deep sedation
  - Unsedated procedures performed less frequently
  - Lack of training in unsedated procedures
- Perception of patient discomfort and lack of patient preference
- Shorter scope : missing pathology ?
- $$$$

## Patient

- Lack of physician recommendation/buy-in
- Perception of discomfort ?
- Lower preference ?
  - Unsedated procedure (US)

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Faulx, GIE 2008, Atkinson Am J Gastroenterol 2008, Adler GIE 2012

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# Potential Advantages of Minimally Invasive Non-endoscopic Screening Tools

**DETECTION**
**=**
**SENSITIVITY *X***
**PARTICIPATION *X***
**ACCESS**

**RN administration : ↑ ACCESS**

**↑ PARTICIPATION**

**Lower Cost : Cost effective**

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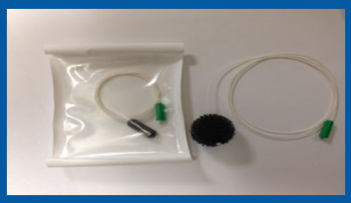
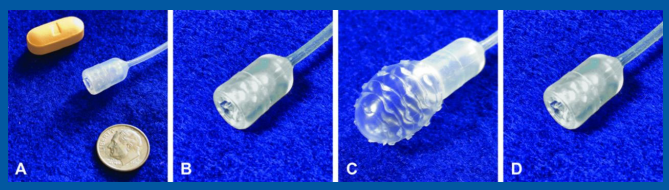
# Esophageal Cell Collection Devices + Biomarkers


CYTOSPONGE



ESOPHACAP




JASSS BALLOON/ESOCHEK

Non-endoscopic Esophageal sampling (cytology)

**Biomarkers**
Protein markers (TFF3)
IHC
Subjective interpretation
Methylated DNA markers
Quantitatively assessed
No subjective bias
Easily scalable
MicroRNAs

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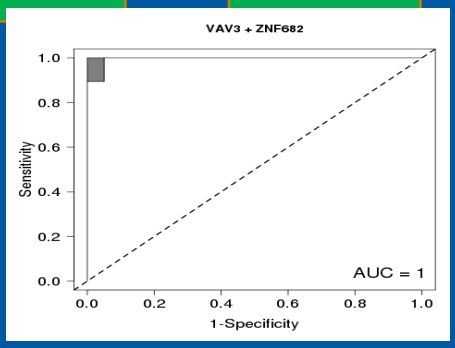
# BE MDM Discovery and Validation

Marker Discovery (RRBS) → Biological Marker validation (qMSP) → Whole Esophageal Brushings → **SOS 1 trial**
40 patients
20 BE cases 20 controls

**Selected best tolerated, safe sponge configuration with optimal DNA yield**




Top 2 markers
100% Sens
100% Spec
AUC=1

Iyer et al, Am J Gastro 2018

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# BE MDM Selection

Cases
≥ 1 cm BE
*Clinical endoscopy*

Controls
No known BE
*Clinical endoscopy*

SOS Test → Successful swallow and retrieval

Clinical EGD → Endoscopic evaluation
BE or no BE
Esophagitis

BE
Endoscopy + Histology

MC Rochester
MC Florida
MCHS Austin

Iyer et al, Am J Gastro 2020

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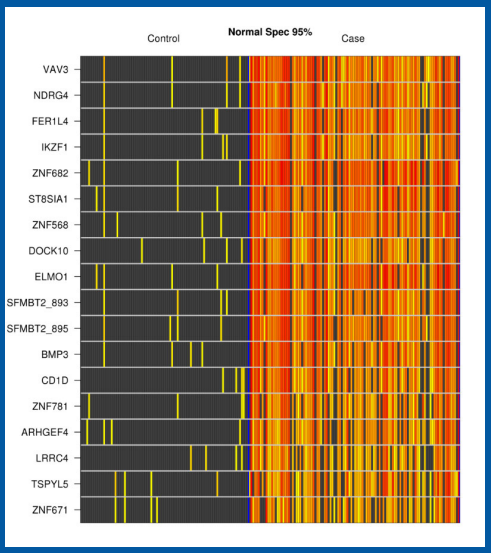
# High MDM levels in cases vs controls




Iyer et al, Am J Gastro 2020

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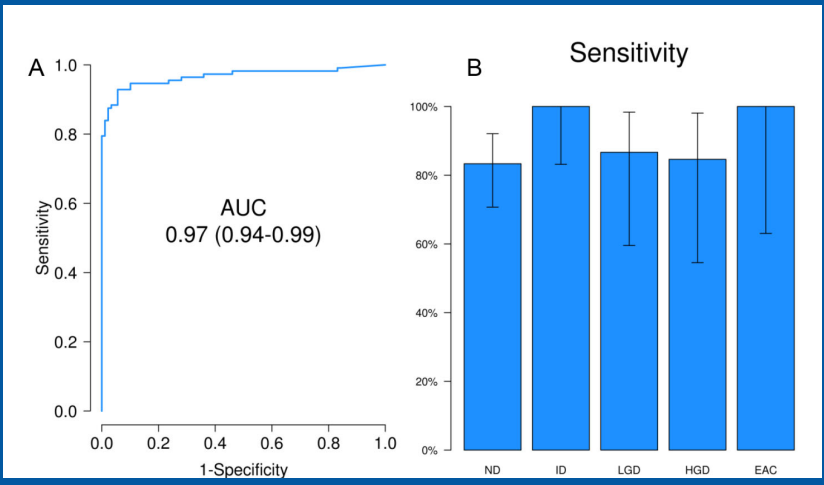
# 5 MDM Panel Performance

**ZNF682, VAV3, NDRG4, BMP3, ZNF568**




Iyer et al, Am J Gastro 2020

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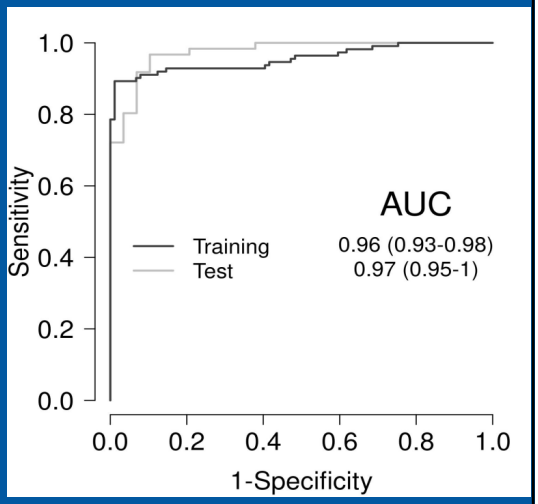
# Marker Selection : Independent Validation

**ZNF682, VAV3, NDRG4, BMP3, ZNF568**

| | Training Set N=201 BE=112, C= 89 | Test Set N=90 BE=61,C=29 |
|---|---|---|
| **Sensitivity** | **91%** | **92%** |
| **Specificity** | **90%** | **90%** |




Iyer Gastrointestinal Endoscopy 2021

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# Accuracy (other studies)

**Well-tolerated**
**Safe**
**Done by RNs, < 10 min**

| Device/Marker | Design | Sensitivity | Specificity |
|---|---|---|---|
| 30 mm Sponge TFF3 (UK) | Case Control N=1110 | **80%** | **92%** |
| 30 mm Sponge TFF3 (USA) | Case Control N= 191 | **76%** | **77%** |
| 18 mm Balloon MDMs | Case Control N=86 | **92%** | **88%** |
| 20 mm Sponge MDMs | Case Control N=95 | **94%** | **62%** |

Ross Innes PLoS Med 2014, Moinova Sci Trans Med 2018, DDW 2019, Wang CCR 2019

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# Several ongoing prospective studies in the US

| EsophaCap | EsoChek |
|---|---|
| • NCT04214119 | • NCT04295811 |
| • NCT03961945 | • NCT04293458 |
| • NCT03060642 | • NCT04880044 |

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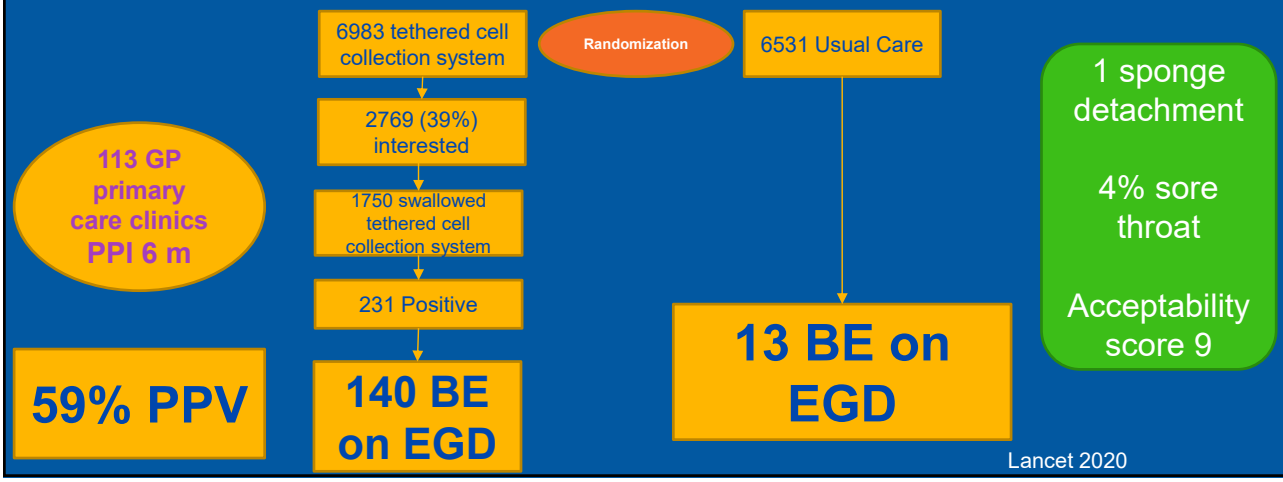
**Cytosponge-trefoil factor 3 versus usual care to identify Barrett's oesophagus in a primary care setting: a multicentre, pragmatic, randomised controlled trial**

*Rebecca C Fitzgerald, Massimiliano di Pietro, Maria O'Donovan, Roberta Maroni, Beth Muldrew, Irene Debiram-Beecham, Marcel Gehrung, Judith Offman, Monika Tripathi, Samuel G Smith, Benoit Aigret, Fiona M Walter, Greg Rubin, on behalf of the BEST3 Trial team*, Peter Sasieni*




Lancet 2020

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# Tethered Cell Collection System arm : BE dysplasia + Stage 1 EAC

| | Usual care group (n=6388) | Intervention group | | |
|---|---|---|---|---|
| | | Underwent the Cytosponge procedure (n=1750) | Did not undergo the Cytosponge procedure (n=5084) | Overall (n=6834) |
| Grade of dysplastic Barrett's oesophagus | | | | |
| No dysplasia | 13 | 116 | 13 | 129 |
| Indefinite | 0 | 7 | 0 | 7 |
| Low-grade | 0 | 1 | 0 | 1 |
| High-grade | 0 | 3 | 0 | 3 |
| Total | 13 | 127 | 13 | 140 |
| Oesophago-gastric cancer stage | | | | |
| I | 0 | 4 | 1 | 5 |
| II | 1 | 0 | 0 | 0 |
| III | 1 | 0 | 0 | 0 |
| IV | 1 | 0 | 2 | 2 |
| Total number of participants with Barrett's oesophagus, cancer, or both | 16 | 131 | 16 | 147 |

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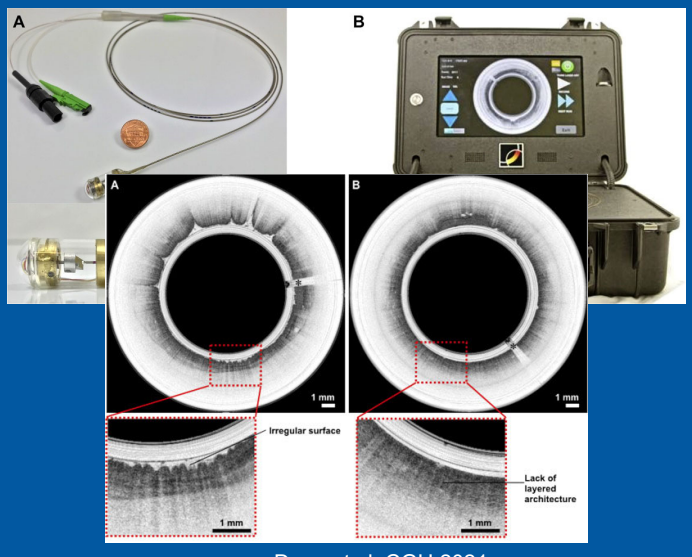
# Optical Capsule Endomicroscopy

- Tethered capsule (reusable)
  - 25 by 13mm
- OFDI and Near-infrared wavelength imaging (≈VLE)
- Cross sectional images of esophagus
- Squamous Versus BE
- Multicenter Study
  - 116/149 (79%) BE patients swallowed
  - BE detected on TCE
  - High correlation with endoscopy




Dong et al, CGH 2021

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# Exhaled Volatile Organic Compounds

- Three metal oxide sensors interact with exhaled VOCs
- Digital breath print specific to BE
- High patient uptake

| USA<br>BE : N=101, Control : N= 89 | | |
|---|---|---|
| **Sensitivity** | **Specificity** | **AUC** |
| 90% | **69%** | 0.84<br>*(High PPI)* |
| 90% | **53%** | 0.76<br>*(Low PPI)* |

| Netherlands<br>BE : N=129, GERD : N=141, Control : N=132 | | |
|---|---|---|
| **Sensitivity** | **Specificity** | **AUC** |
| 91% | 74% | 0.91<br>*(All comers)* |
| *64%* | *74%* | *0.73*<br>*(GERD)* |

DDW 2019. Peters. Gut 2020

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ACG Clinical Guideline: Diagnosis and Management of Barrett's Esophagus

Nicholas J. Shaheen, MD, MPH, FACG[1], Gary W. Falk, MD, MS, FACG[2], Prasad G. Iyer, MD, MSc, FACG[3] and Lauren B. Gerson, MD, MSc, FACG[4]

- Screening : **males with chronic and/or frequent reflux and 2 or more risk factors**
  - Caucasian race
  - Central obesity
  - Ever smoking
  - Confirmed family history in a first degree relative

Strong recommendation
Moderate level of evidence

- Screening is **NOT** recommended in females
  - Low risk of EA
- **Unsedated TNE** is an alternative
- Consider **life expectancy of patient**

Am J Gastroenterology 2016

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# BE Screening Guidelines

| AGA (2011) | ASGE (2019) | ACP (2012) | BSG (2013) |
|---|---|---|---|
| In patients with multiple risk factors for esophageal adenocarcinoma, screening is recommended[1] (weak recommendation, moderate quality evidence)<br><br>Screening the general population not recommended.[1] (strong recommendation, moderate quality evidence) | Consider in at-risk population<br><br>family history of EAC or BE (high risk) [3] | EGD may be considered<br><br>use, and intra-abdominal distribution of fat) | Screening can be considered in patients with chronic reflux symptoms ultiple risk factors (at three of age 50 years er, white race, male besity). Decrease by presence of at least rst-degree relative Barrett's or EAC<br><br>ening with endoscopy feasible or justified unselected population with gastro-oesophageal reflux symptoms[5] |

**Common themes**

1. Chronic GERD (symptoms)
2. Multiple risk factors
3. No population screening

Gastroenterology 2011
Gastrointestinal Endoscopy 2019,
Ann Int Medicine 2012. Gut 2013

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# Unresolved Questions

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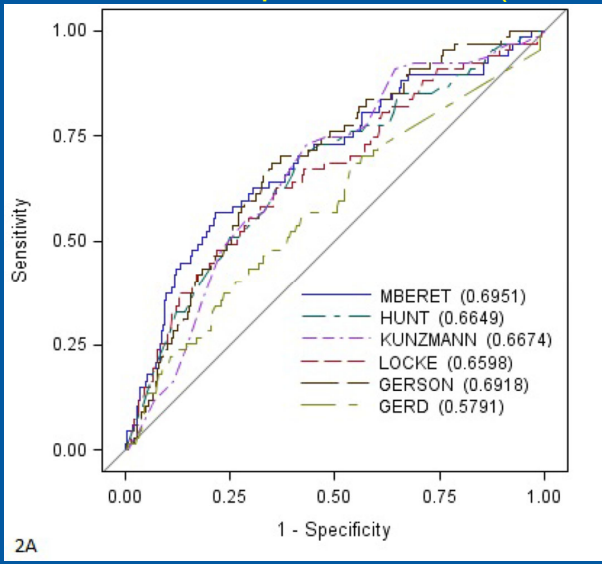
# Who to Screen ?

## GERD alone inadequate, GERD+ (other risk factors) risk scores




**AUC (BE)**

**GERD = 0.58**

**GERD+ = 0.67- 0.69**

Rubenstein, Gastroenterology 2021

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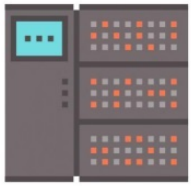
# EAC and GEJAC Prediction Tool

Validation of Tools for Predicting Incident Adenocarcinoma of the Esophagus (EAC) or Esophagogastric Junction (EGJAC)

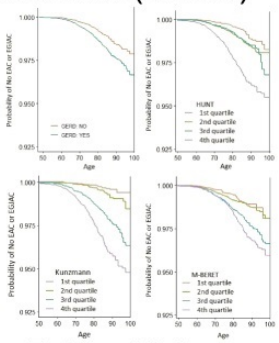
206,974 people examined 1964-1973

319 cancer cases mean 32 years later

Questionnaires & body measurements



Cancer Registry



Tools predicted cancer better than GERD alone

Rubenstein, JH, et al. *Am J Gastroenterol.* 2021.doi:10.14309/ajg.0000000000001255

OFFICIAL JOURNAL OF THE AMERICAN COLLEGE OF GASTROENTEROLOGY | ACG

AJG The American Journal of GASTROENTEROLOGY

Rubenstein, AJG 2021

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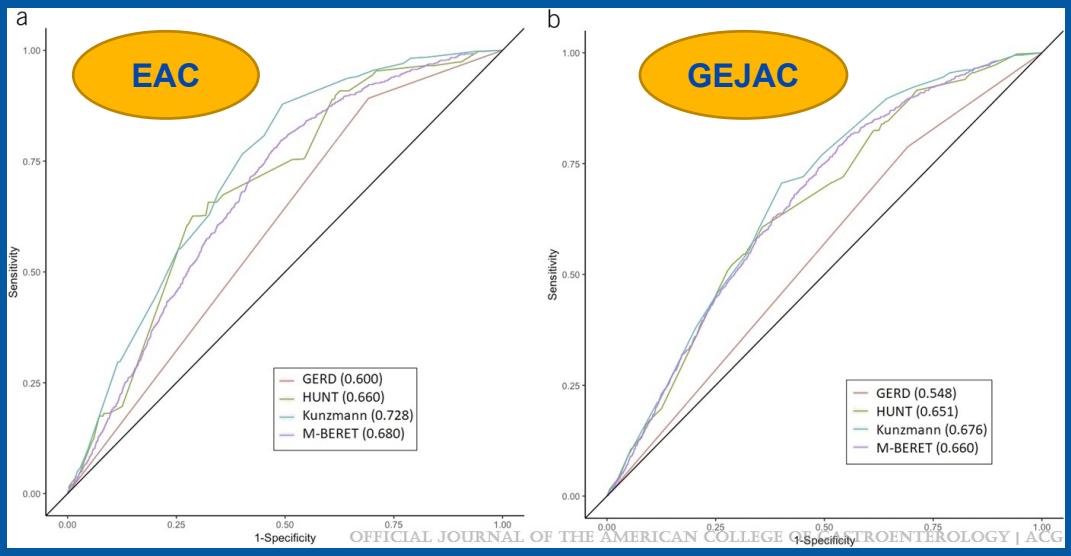
# GERD + Tools predicted EAC/GEJAC better than GERD alone



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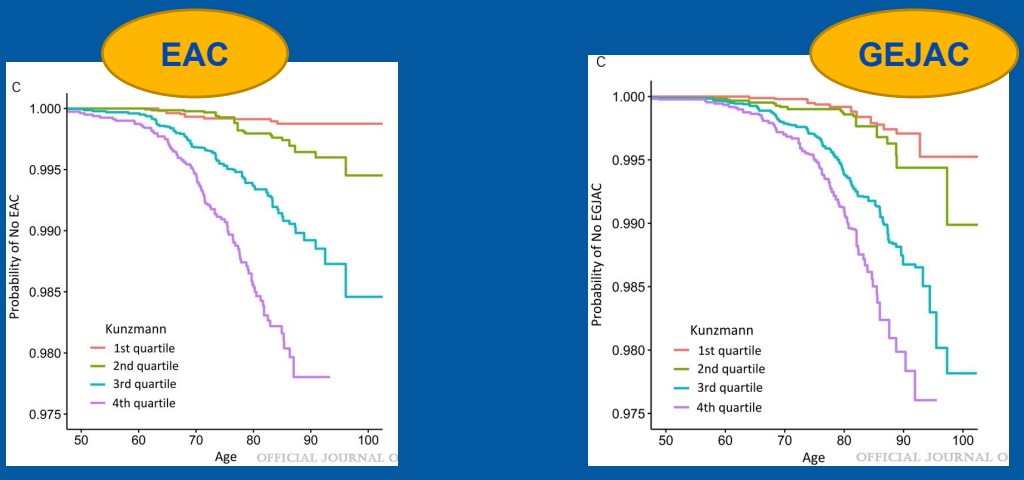
# EAC and GEJAC : Absolute Risk




Lifetime EAC + GEJAC risk : 4th Quartile of Kunzman Score ≈ 5% (Lifetime risk of CRC)

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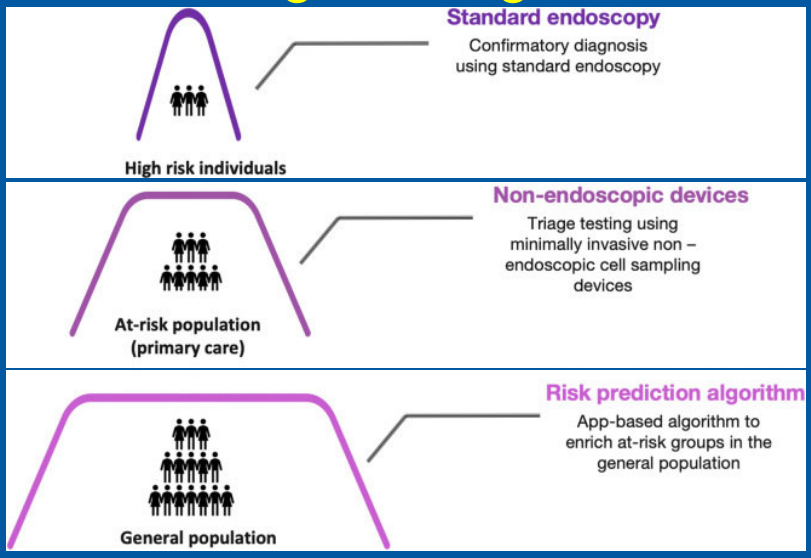
# BE Screening Paradigm ?




Yusuf CTOG 2021

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## Comparative Cost-Effectiveness of Reflux Based and Reflux Independent Strategies of Barrett's Esophagus Screening

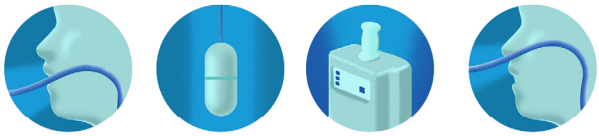
**Population**

**3 scenarios with 50 year old individuals:**

- **GERD-based** (white men) with BE prevalence **8.0%**
- **GERD-independent** (all races, men & women) with BE prevalence **5.0%**
- **GERD-independent** (all races, men & women) with BE prevalence **1.6%**

**Interventions**

sEGD | Swallowable Devices w/ Biomarkers | E-Nose | hTNE/mTNE



vs

**No Screening**

**Results**

Screening individuals aged 50 years old in a GERD-independent manner with minimally invasive non-endoscopic tests **is cost effective compared to no screening**.

**Non-endoscopic swallowed capsule sponge based strategies were the favorable strategies** in all three screening scenarios compared to other endoscopic BE screening modalities.

Author name, et al. *Am J Gastroenterol*, 2021
Image source info

Logo here

Sami, Iyer et al. AJG. 2021

AJG The American Journal of GASTROENTEROLOGY

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# Is detection of more BE alone sufficient to improve EAC outcomes ?


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**PERSPECTIVES IN CLINICAL GASTROENTEROLOGY AND HEPATOLOGY**

**Screening for Barrett's Esophagus and Esophageal Adenocarcinoma: Rationale, Recent Progress, Challenges, and Future Directions**

Sarmed S. Sami,* Krish Ragunath,* and Prasad G. Iyer‡

*University of Nottingham, Digestive Diseases Centre, National Institute for Health Research, Biomedical Research Unit, Nottingham, United Kingdom; and ‡Barrett's Esophagus Unit, Division of Gastroenterology and Hepatology, Mayo Clinic, Rochester, Minnesota

**Screening tool** (simple, acceptable, accurate, and cost-effective):

- TNE
- Cytology sponge
- Capsule endomicroscopy
- Future blood biomarkers

VOCs

**Target population** (Caucasian male, age ≥50 years, chronic GERD, positive family history, centrally obese):

- Validation of M-BERET and other BE risk prediction models.
- Future blood biomarkers.

**Screen for BE**

**Detect and treat** prevalent HGD/EAC

**surveillance**

**Risk stratify** remaining patients with BE:

- Clinical: LSBE.
- Histological: LGD, p53.
- Future blood biomarkers.
- Combination of the above.

Low risk = **observe or discharge**

High risk = **endotherapy or chemoprevention**

CGH 2014

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# Summary

- BE screening has the potential to improve EAC outcomes
  - Increasing detection of those at EAC risk
- Minimally invasive non-endoscopic BE detection tools substantial progress
  - Safe and accurate
  - Increase access and ? participation
  - May enter clinical realm in near future
- Identifying target population, improved dysplasia detection and risk stratification critical next steps

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# Questions?

**Speaker:**
**Prasad G. Iyer, MD, MS, FACG**

**Moderator:**
**Christina Tofani J. Tofani, MD**

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