Besting Barrett's: Advances in the Diagnosis and Treatment of Barrett's Esophagus

Allon Kahn, M.D., FACG

Associate Professor of Medicine

Associate Program Director, GI&H Fellowship

Division of Gastroenterology and Hepatology

Mayo Clinic Arizona

MAYO CLINIC

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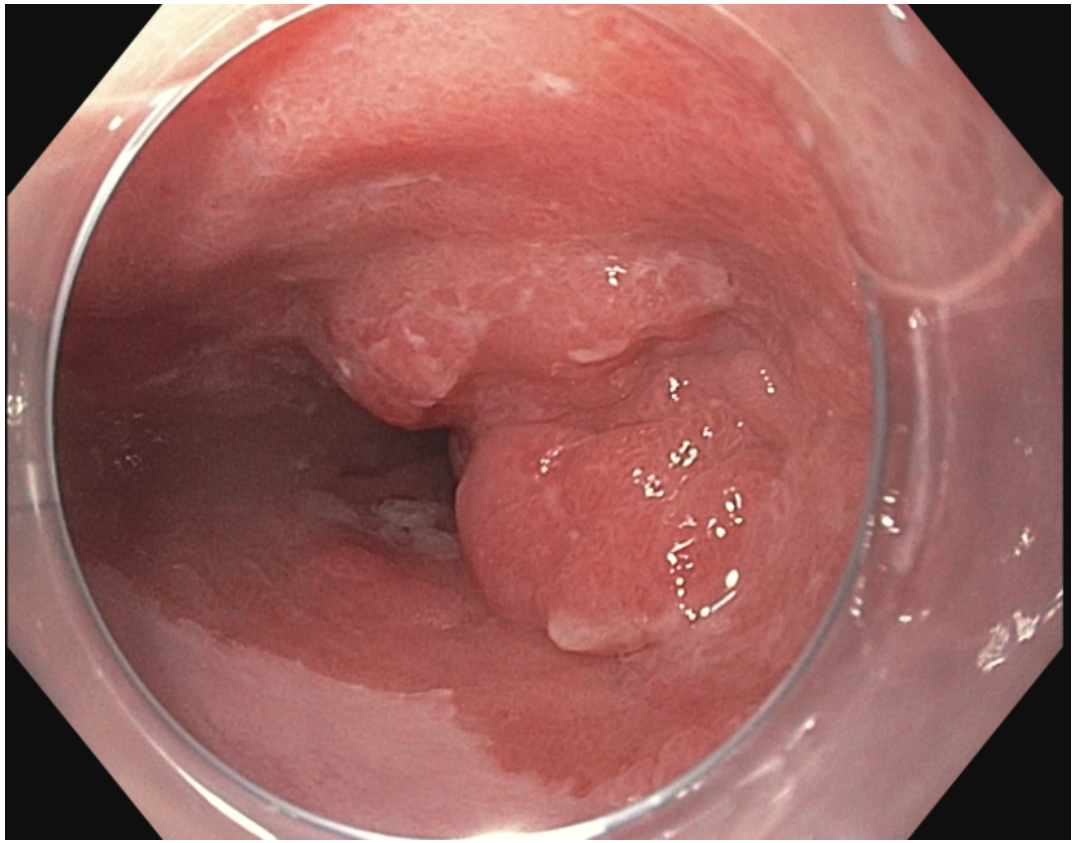
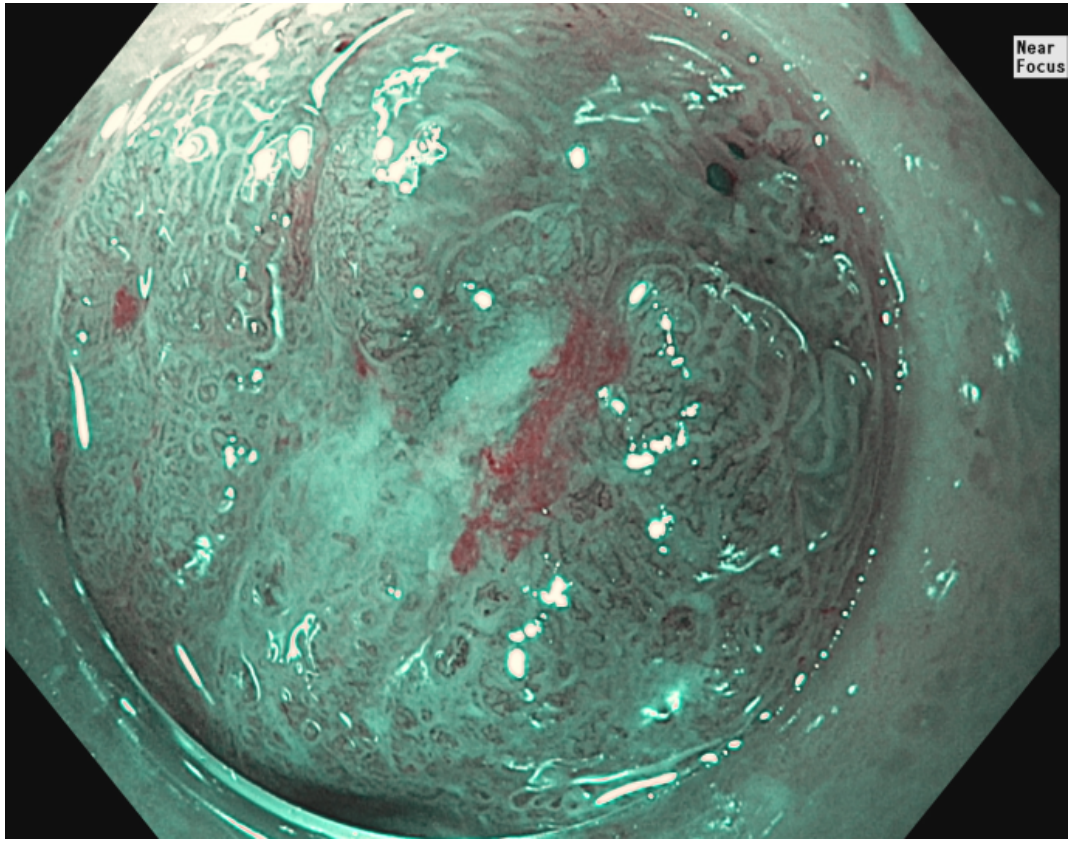
Case - Mr. H

- 72 year-old obese man referred for Barrett's esophagus
- No symptoms of GERD
- Former longstanding tobacco smoking
- Orthopedic surgery → GI bleeding → EGD
- EGD:
  - Erosive esophagitis
  - C5M6 BE changes
  - Nodularity – EMR shows focal HGD
- RFA "unsuccessful"
- Repeat biopsies LGD and HGD

Case (continued):

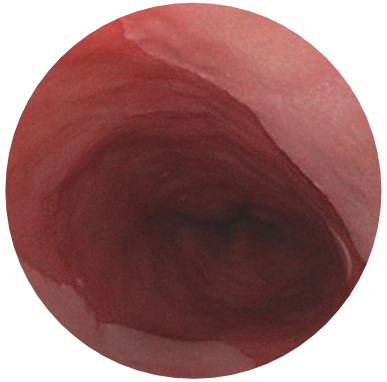




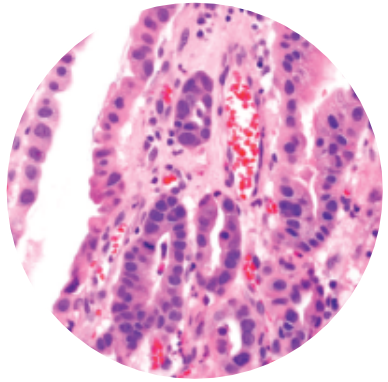
Biopsies: intramucosal adenocarcinoma, invading at least the muscularis mucosa

Patient at risk

- GERD
- Male sex
- White race
- Central obesity
- Tobacco use
- Family history



Barrett's Esophagus



Dysplasia (LGD/HGD)

Esophageal AdenoCA

Screening

Surveillance

Endoscopic Therapy

Patient at risk

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- Male sex
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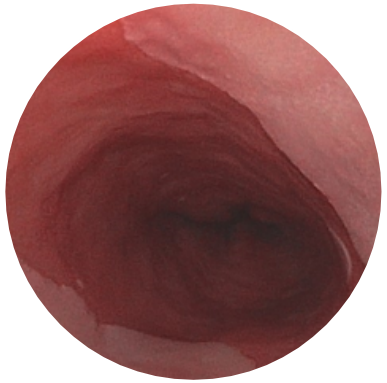
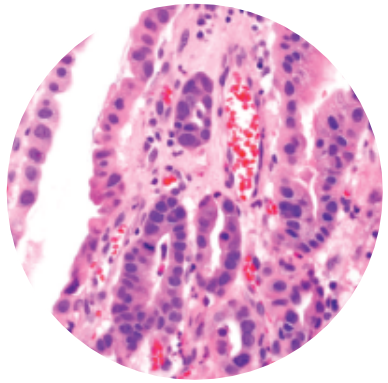


Barrett's Esophagus



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The Current State of BE Screening

- Large healthcare network study:
  - Only **38.7%** of screening-eligible patients underwent an EGD
- Current strategies only detect **~7%** of EAC

Eluri et al, *Am J Gastro*, 2022;117:1764-1771
Vaughan et al, *Nat Rev Gastroenterol,* 2015;12:243-248

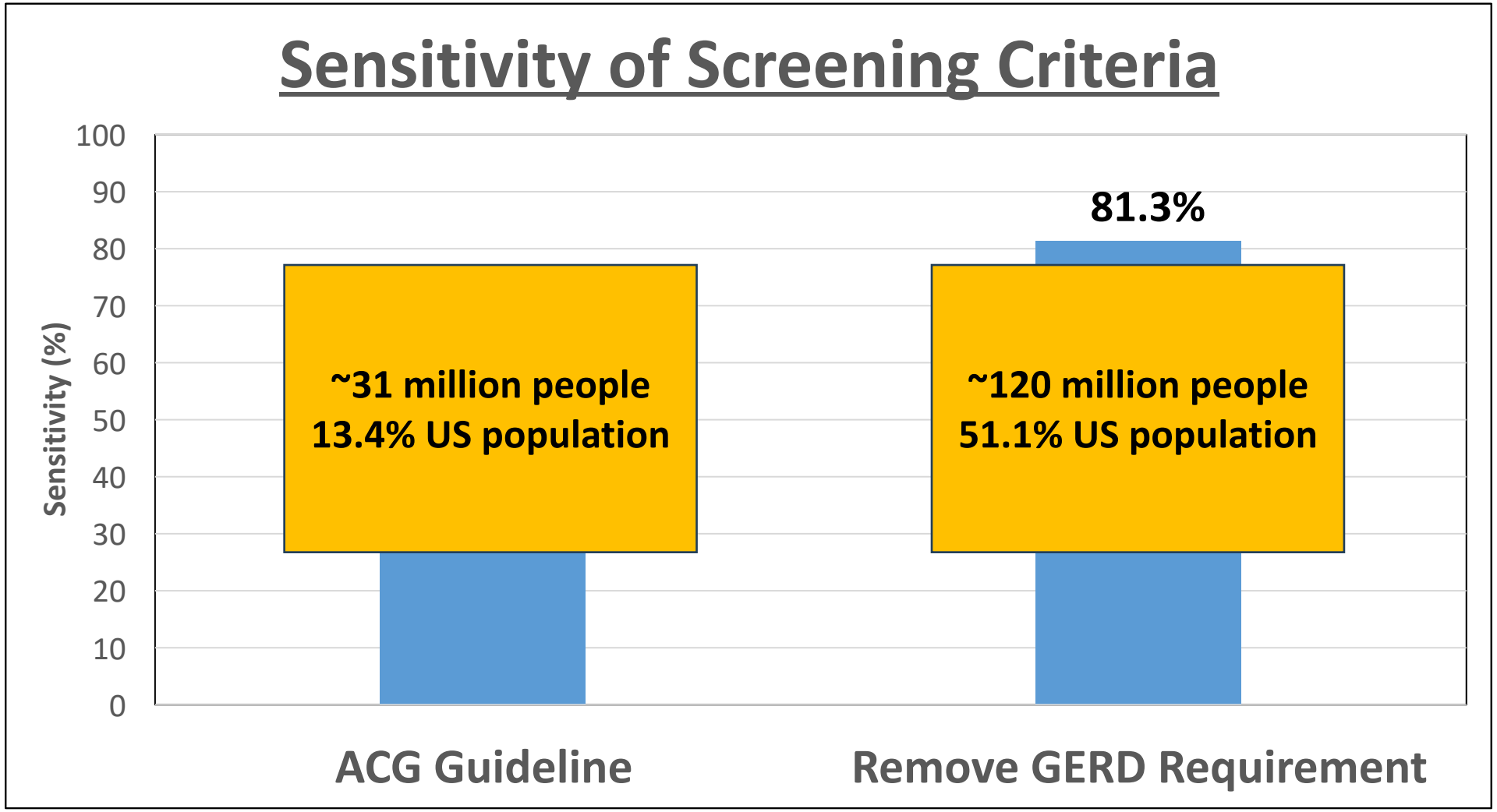
BE Screening Criteria

- ACG Guidelines 2022
  - Chronic GERD symptoms
    AND
  - 3 or more of:
    - Male sex
    - Age >50
    - White race
    - Tobacco smoking
    - Obesity
    - Family history BE/EAC

- AGA Clinical Practice Update 2022
  - 3 or more of:
    - **Chronic GERD**
    - Male sex
    - Age >50
    - White race
    - Tobacco smoking
    - Obesity
    - Family history of BE/EAC

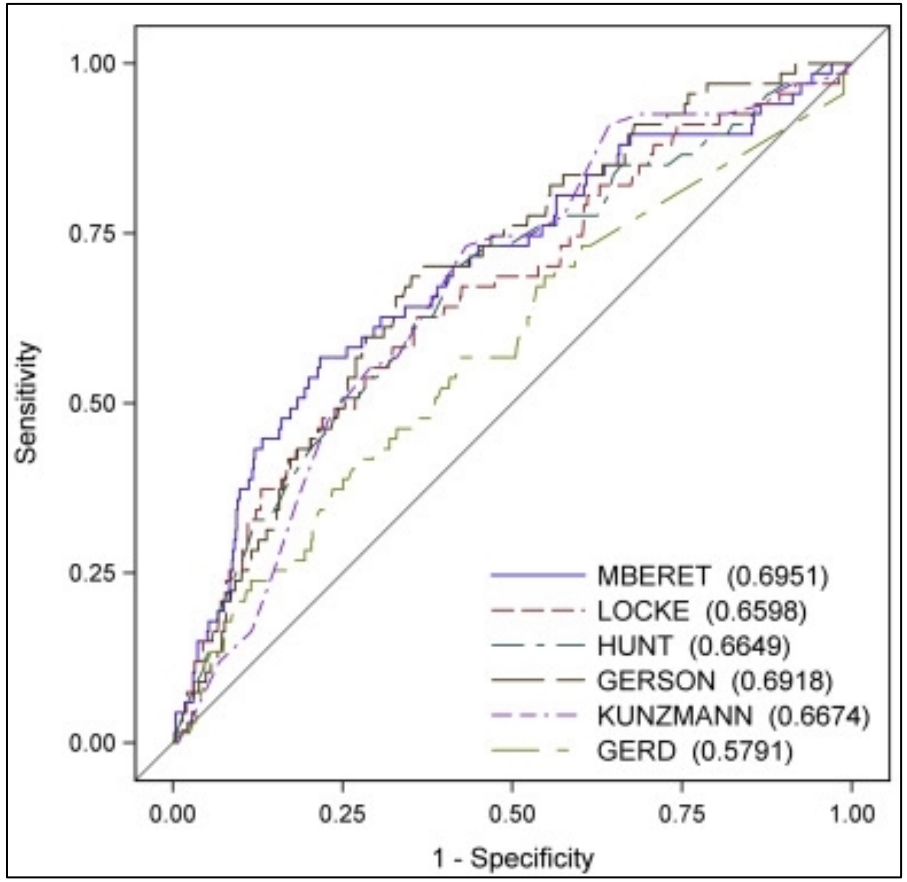
Shaheen et al, *Am J Gastro*, 2022;117:559-587
Muthasamy et al, *CGH,* 2022;20:2696-2706

Performance of Guideline Criteria



Sawas et al, *CGH*, 2022;20:1709-1718
Chandar et al, *Gastro*, 2023;165:283-285

Improve Patient Selection – Role of AI



AUC 0.58-0.69 → Machine Learning Model → AUC **0.84**

Rubenstein et al, *Gastro*, 2020;158:2082-2092
Iyer et al, *Clin Transl Gastroenterol*, 2023;14:e00637

Reduce Screening Burden – Negative Results

- Future BE occurrence after negative index EGD – **1.8-3.4%**
- GIQuIC study: normal/"irregular" z-line and **negative** biopsies
  - **20-24%** recommended surveillance

Take Home: Repeating EGD after negative one-time screening is **not recommended**

Dhaliwal et al, *CGH*, 2024;22:523-531
Rodriguez et al, *Am J Gastro,* 2008;103:1892-1897
Wani et al, *Am J Gastro,* 2020;115:1869-1878

Incorporate Non-Invasive Screening

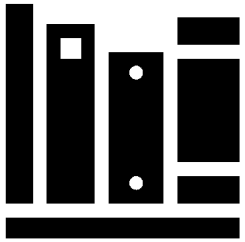
Innovation is **twofold**:

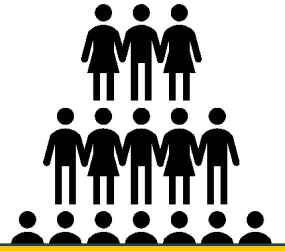
Non-Endoscopic Tissue Sampling

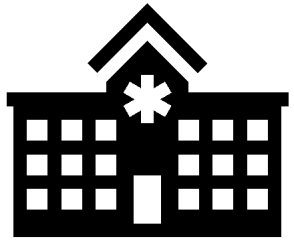
↓

Biomarker Assay
Immunohistochemistry
Methylated DNA Markers

Incorporate Non-Invasive Screening







2022 ACG Guideline: "Acceptable alternative to endoscopy for screening"

Effective

- New assays quantitative/ objective
- Sensitivity ~88%
- Specificity ~84%

- on 1st attempt
- Well tolerated – scores > EGD
- AE <0.05% (detachment, bleeding)

multiple populations
- Demonstrated in >100 PCP practices in UK

Cost-Effective

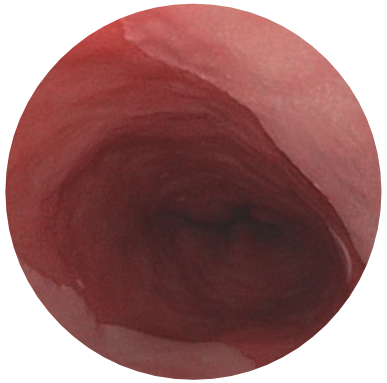
- Modeling study: most cost effective strategy for all scenarios

Iyer et al, *CGH*, 2024;22:1596-1604
Januszewicz et al, *CGH*, 2018;17:647-656

Fitzgerald et al, *Lancet*, 2020;396:333-344
Sami et al, *Am J Gastro,* 2021;116:1620-1631

Patient at risk

- GERD
- Male sex
- White race
- Central obesity
- Tobacco use
- Family history



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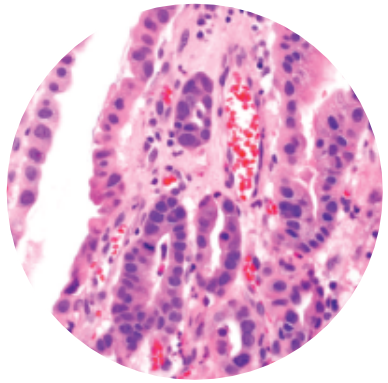

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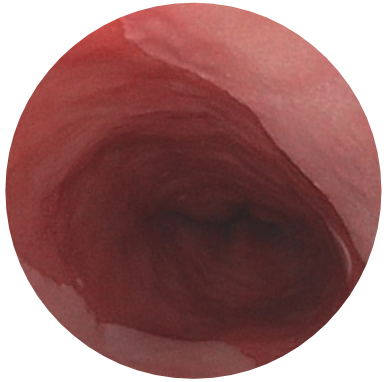

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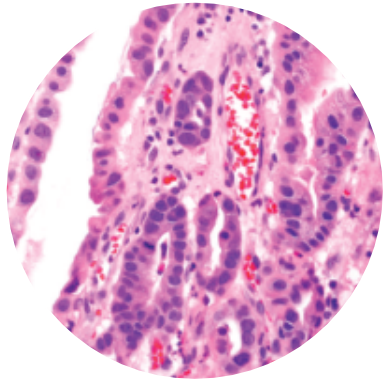

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Post-Endoscopy EAC

EAC ≤ 1 year after negative EGD

Gastroenterology 2016;150:599–607

Magnitude of Missed Esophageal Adenocarcinoma After Barrett's Esophagus Diagnosis: A Systematic Review and Meta-analysis

Kavel Visrodia,[1,*] **Siddharth Singh**,[1,2,3,*] Rajesh Krishnamoorthi,[1] David A. Ahlquist,[1] Kenneth K. Wang,[1] Prasad G. Iyer,[1] and David A. Katzka[1]

27 studies
>60,000 BE pts → 25.3%

Gastroenterology 2023;165:909–919

Magnitude and Time-Trends of Post-Endoscopy Esophageal Adenocarcinoma and Post-Endoscopy Esophageal Neoplasia in a Population-Based Cohort Study: The Nordic Barrett's Esophagus Study

Sachin Wani,[1] Dag Holmberg,[2] Giola Santoni,[2] Joonas H. Kauppila,[2,3] Martti Farkkila,[4] My von Euler-Chelpin,[5] Nicholas J. Shaheen,[6] and Jesper Lagergren[2,7]

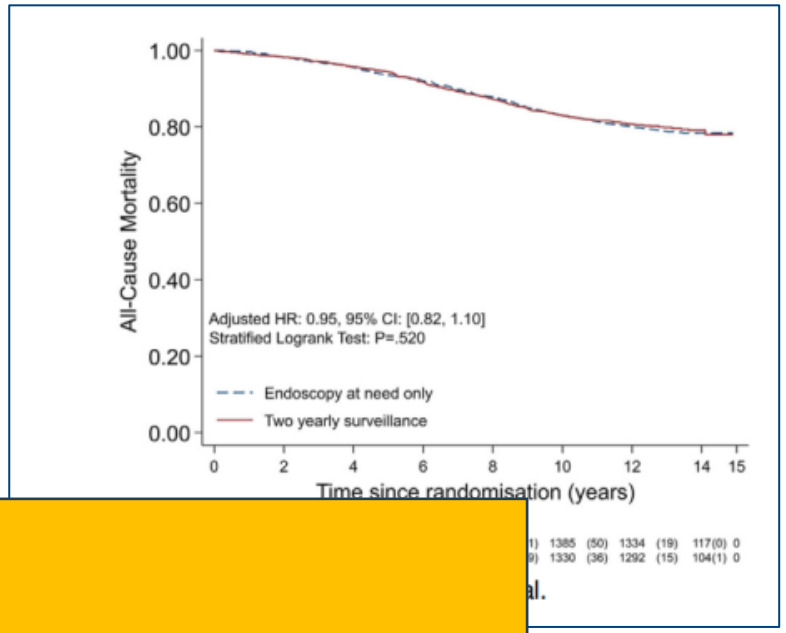
20,588 BE pts → 23.5%

The BOSS trial

- Randomized clinical trial in the UK over 10y
- 3453 pts w/ NDBE randomized to 2 groups:
  - EG
  - EG
- No dif
- **Limita**
  - Underpowered (assumed much larger effect)
  - 59% of “at need” had EGD, similar interval
    - Essentially “more vs. less”

Take Home:

- Use updated length-stratified intervals (3-5y)
- High-quality EGD is **essential**



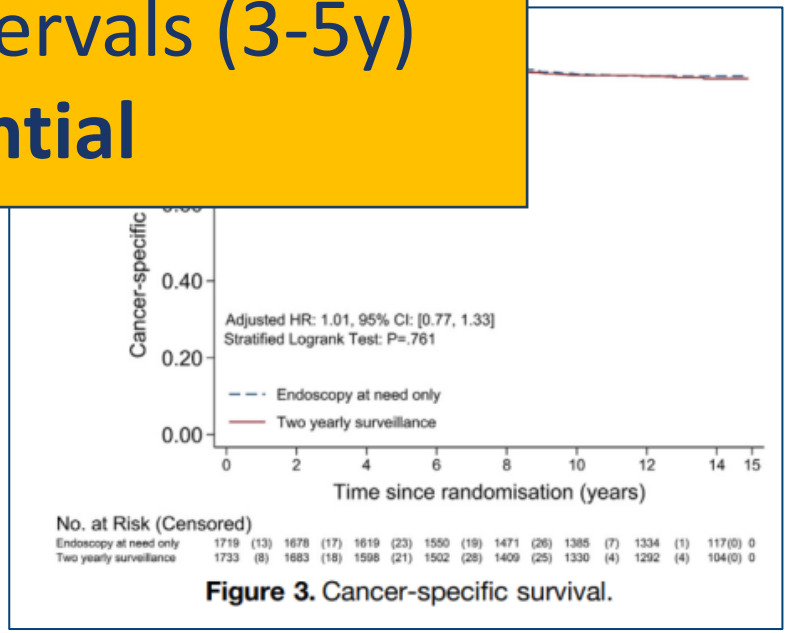
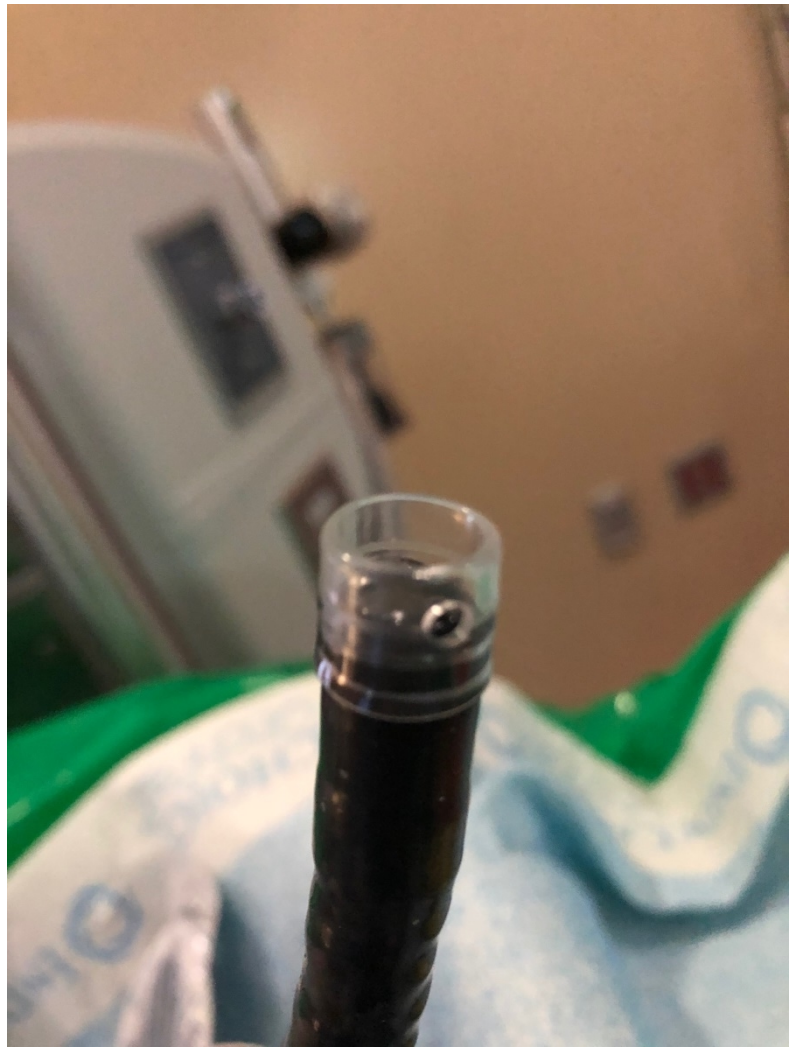


Figure 3. Cancer-specific survival.

Old et al, *Gastro*, 2025

Improving Surveillance – High Quality EGD



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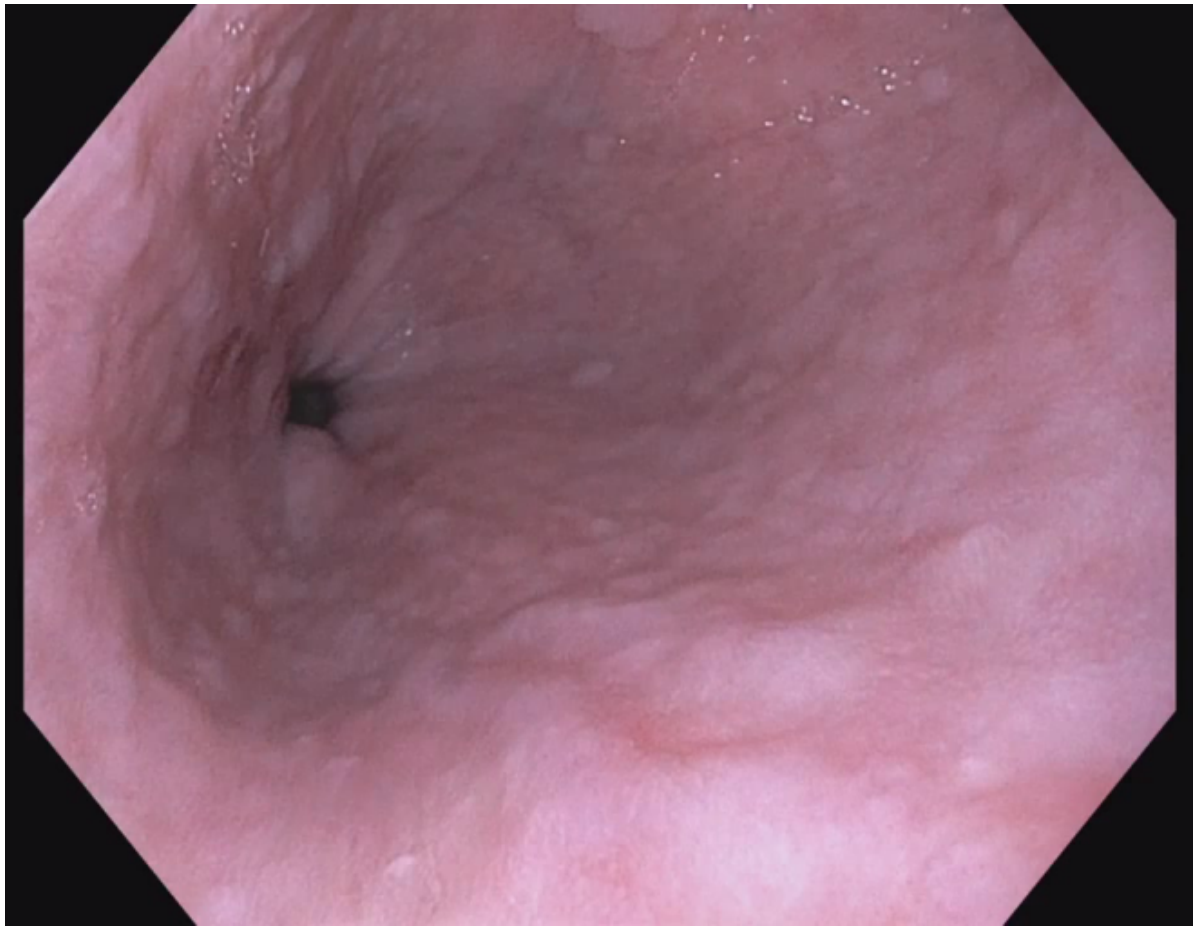

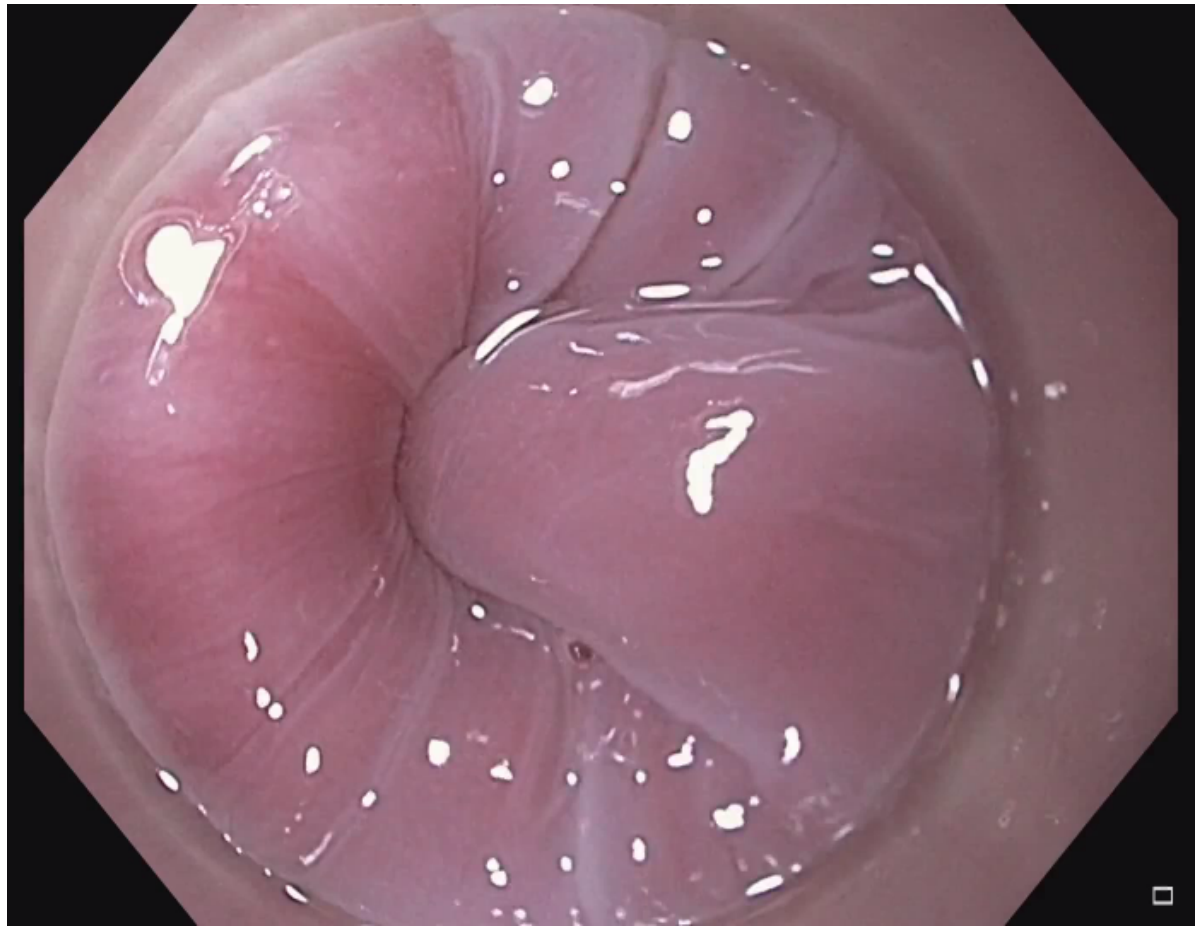

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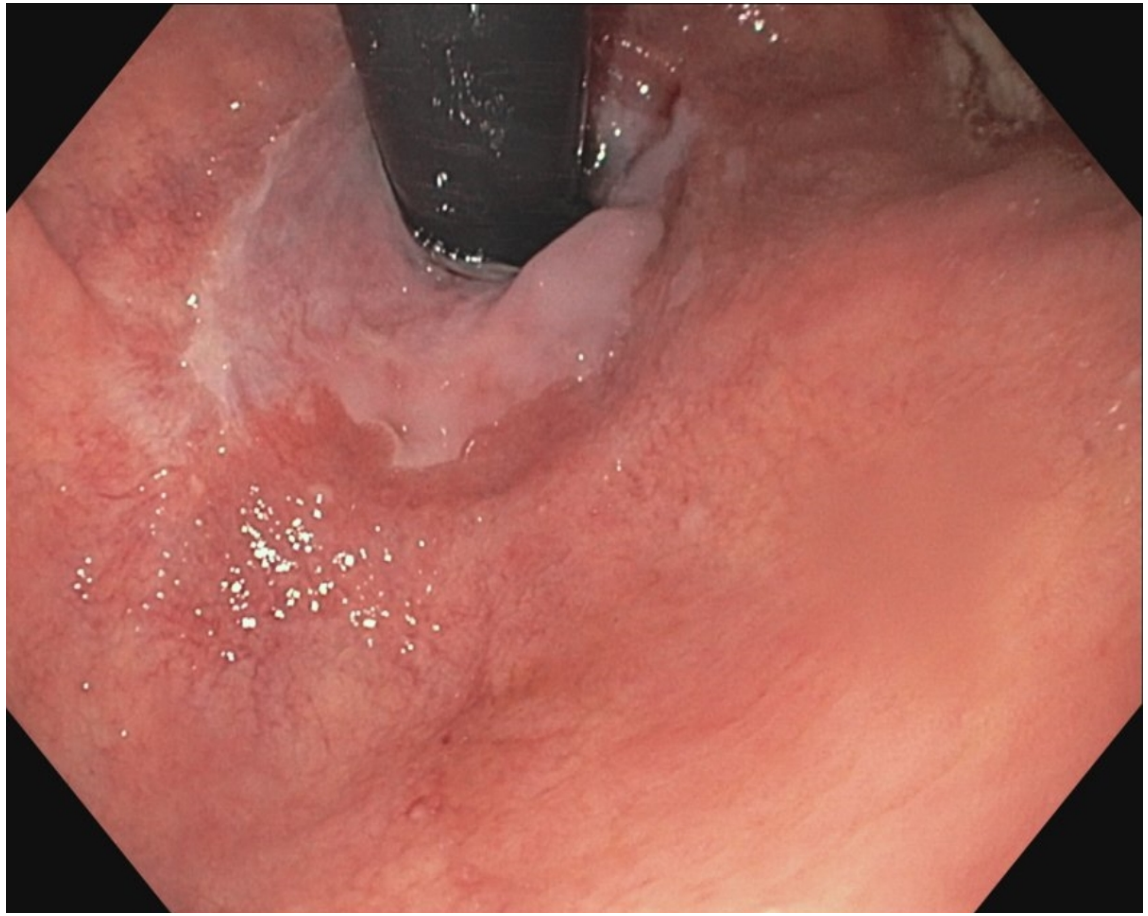

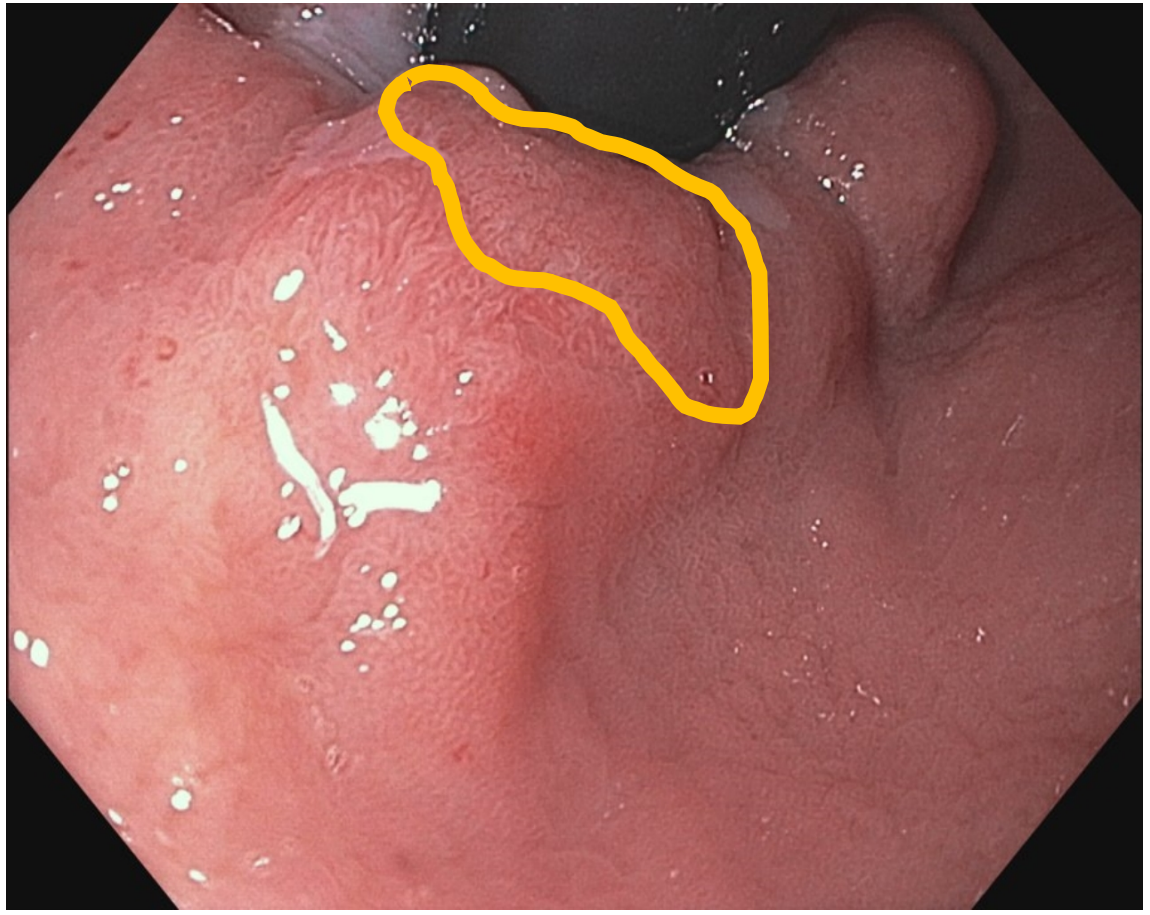

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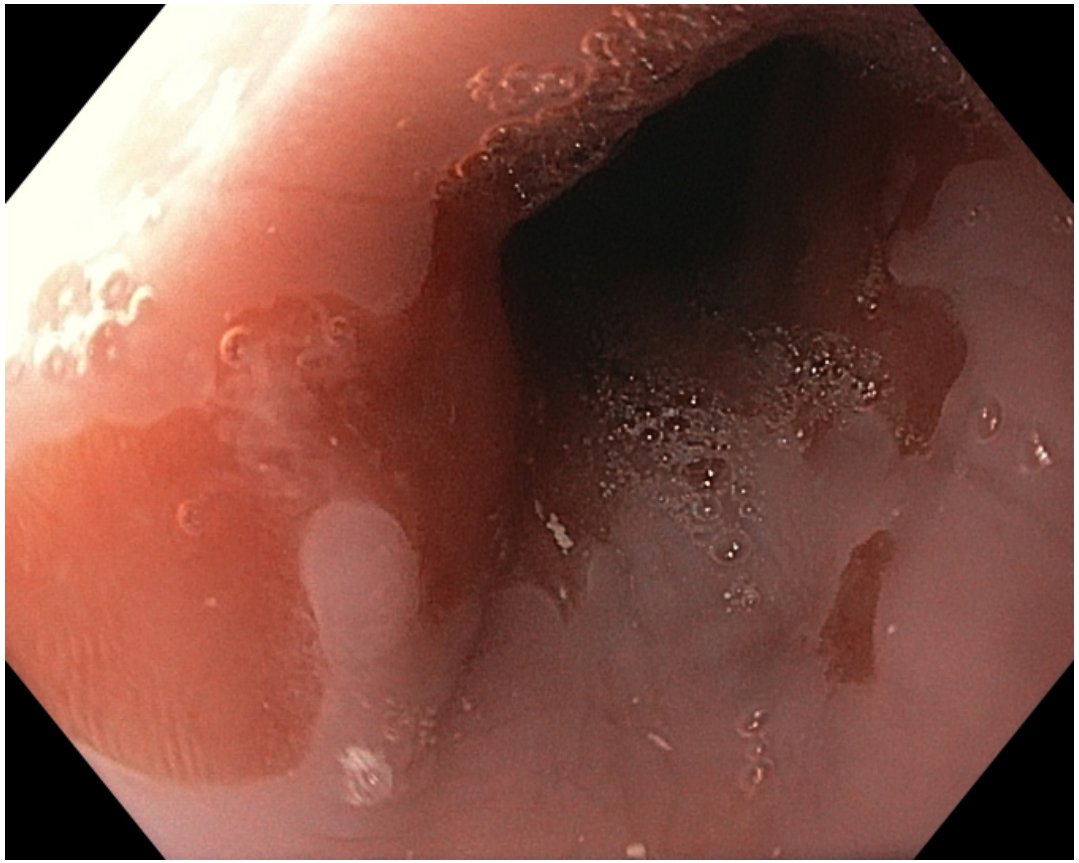
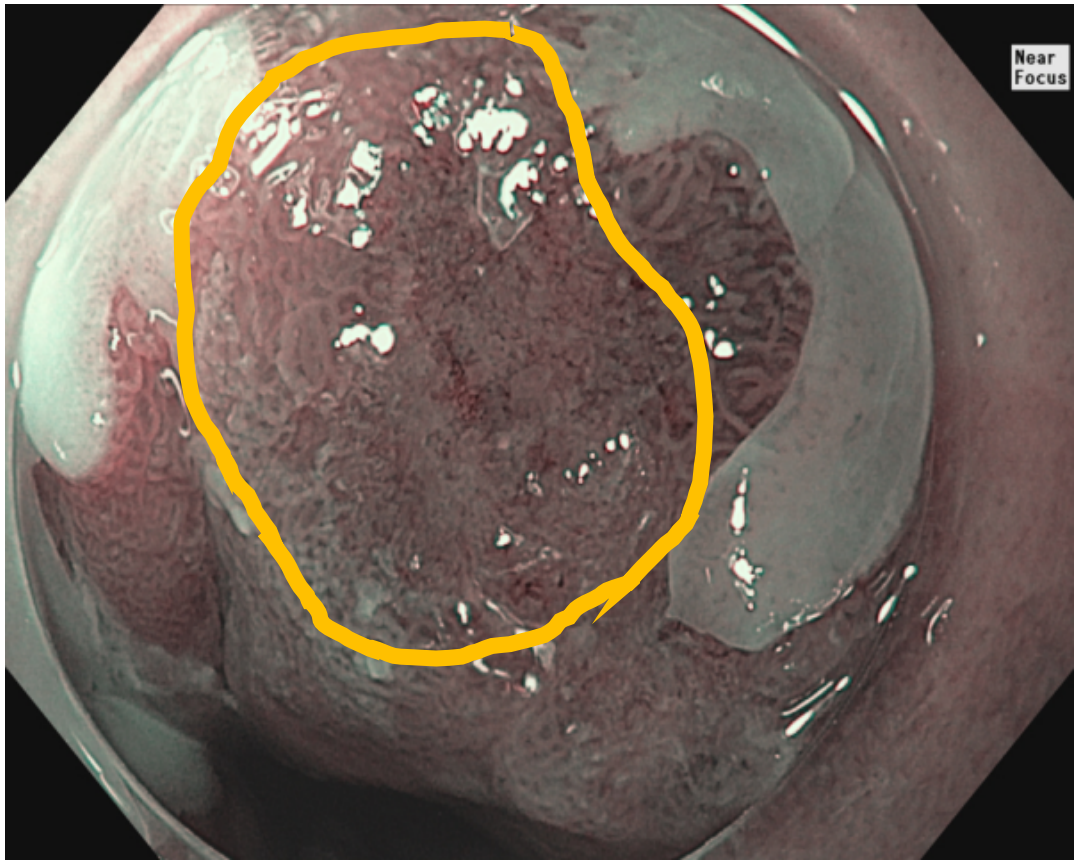
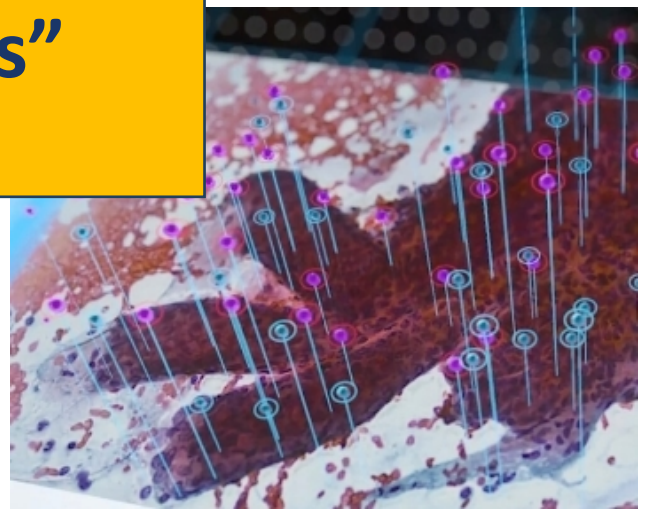




Improving Surveillance – Adjunctive Sampling

- **<u>Premise:</u>** Reduce forceps sampling error, improve dysplasia detection
- Brushing →
- Independent
- **<u>Incremental</u>** HGD/EAC
- **62.5% negat** dysplasia
- Management of discordant result?

2022 ACG Guideline:
"Could not make a recommendation on the use of WATS-3D analysis"



Codipilly et al, *GIE*, 2022;95:51-59

Improving Surveillance – Risk Stratification

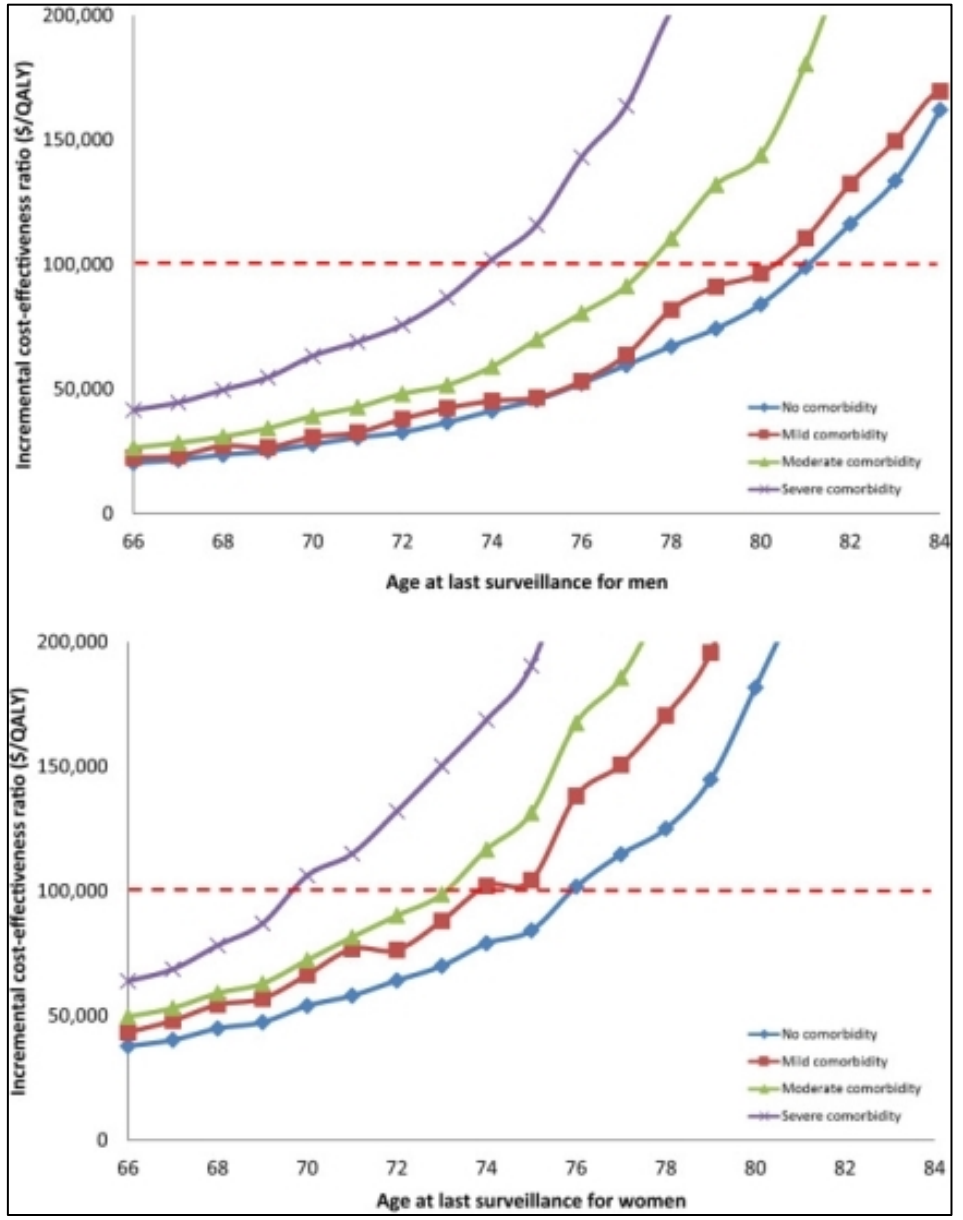
- Tissue Systems Pathology Test
  - Quantitative molecular testing
  - Poole… …ity **94%**
- Epigene…
  - Quan…
  - One study – **AUC 0.73**
    - High-risk score 6.4X more likely to progress than low risk

2022 ACG Guideline:
"Could not make a recommendation on the use of predictive tools in addition to standard histopathology"

Iyer PG et al., *CGH,* 2022;20:2772-2779
Laun SE et al. *Am J Gastro*, 2025;120:1296-1306

Improving Surveillance - Knowing when to stop

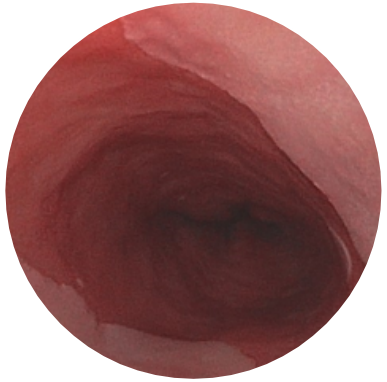
- Mean age at diagnosis = 63.6
- Most will die of non-EAC causes
- Modeling study – optimal cessation age:
  - **No comorbidities:**
    - Men – 81
    - Women – 75
  - **Severe comorbidities:**
    - Men – 73
    - Women - 69



Gatenby et al, *World J Gastro*, 2014;20:9611-9617
Solaymani-Dodaran et al, *Gastro*, 2013;144:1375-1383
Omidvari et al, *Gastro*, 2021;161:487-494

Patient at risk

- GERD
- Male sex
- White race
- Central obesity
- Tobacco use
- Family history



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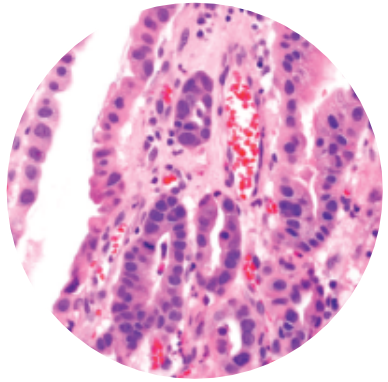

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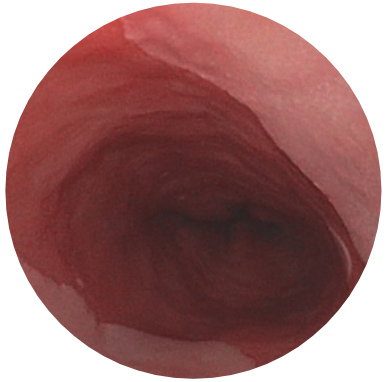

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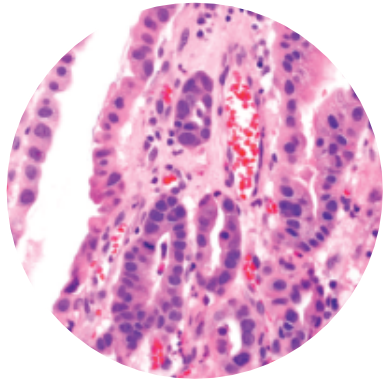

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Endoscopic therapy – Treatment Selection

Ablation is used in <u>NON-NODULAR</u> dysplastic Barrett's esophagus

Endoscopic therapy – Treatment Selection

- Endoscopic resection (EMR/ESD) both **diagnostic** and **therapeutic**
- Change in diagnosis for **28-34%**
- "Upstaged" in **10-53%**
- Better than EUS for T-staging cancer
- Provides EAC prognostic data (depth, grade, LVI, etc)

Leggett et al, *CGH,* 2015;13:658-664
Wani et al, *Dig Dis Sci*, 2013;58:1703-1709
Clermont et al, *Gastrointest Interv*, 2013;2:90-93

Endoscopic therapy – Treatment Selection

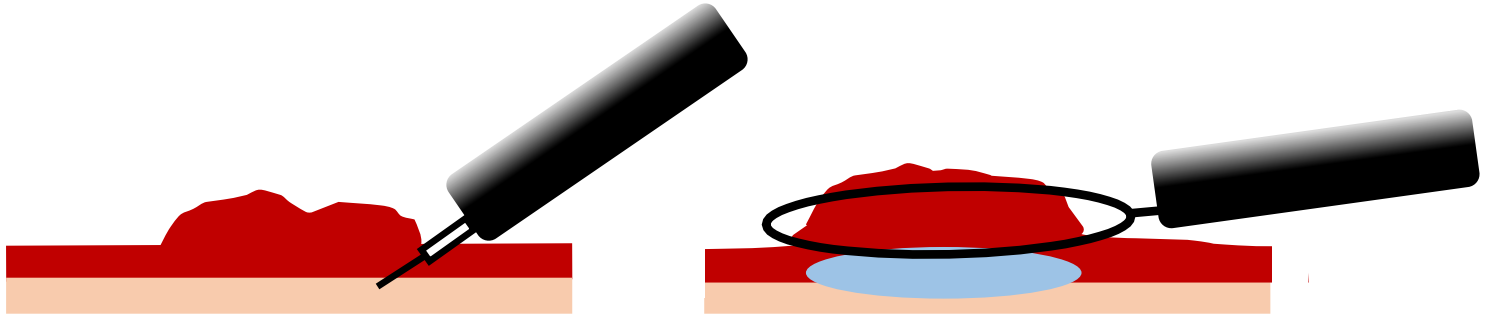
2022 ACG Guideline:
"We suggest initial endoscopic resection of any visible lesions before the application of ablative therapy"

Biopsies: High-grade dysplasia

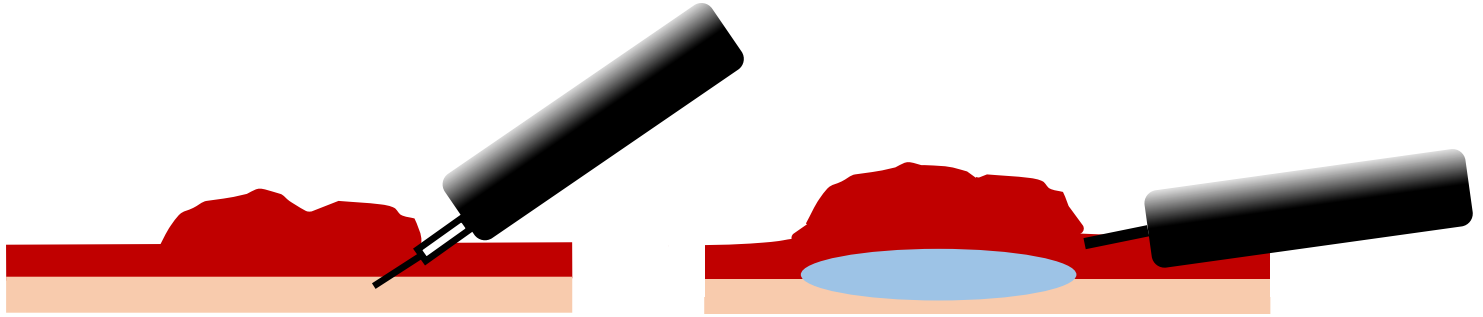
EMR: Intramucosal adenoCA

Endoscopic therapy – EMR vs. ESD

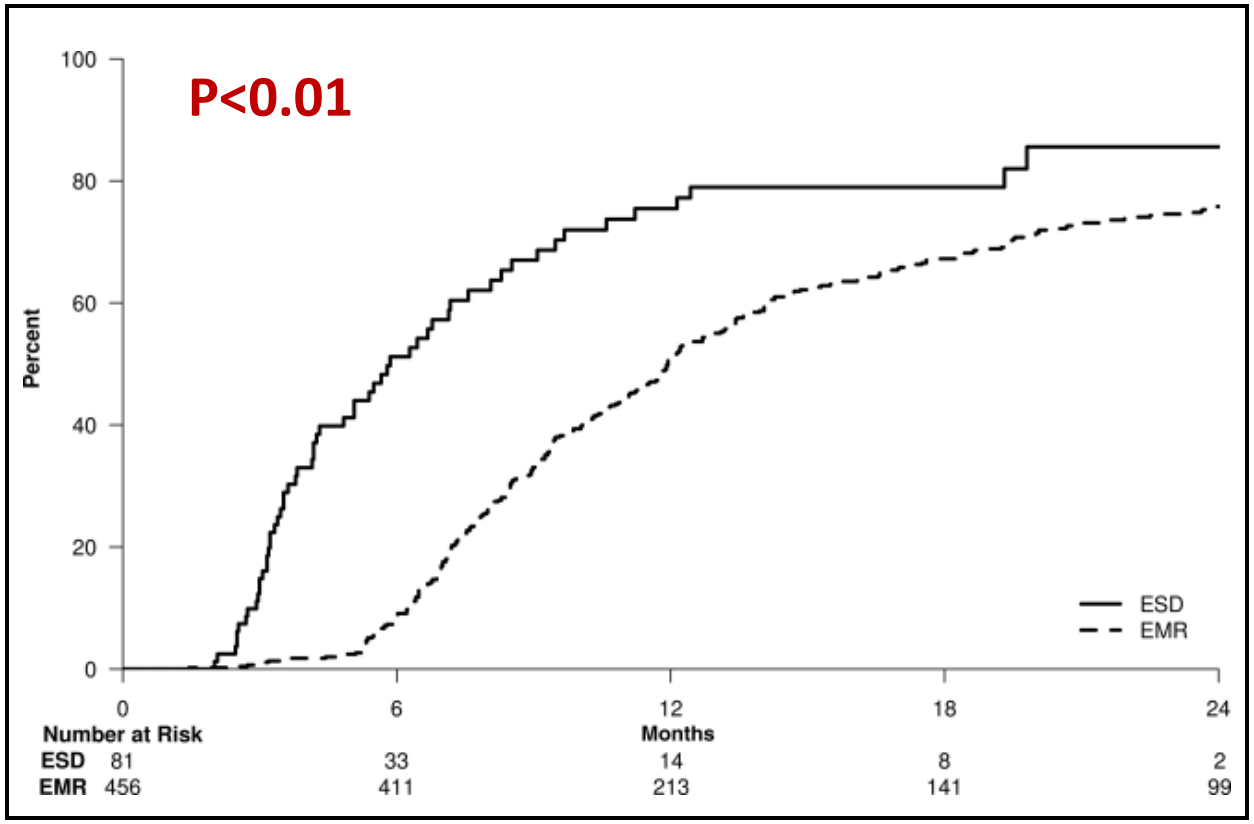
Endoscopic Mucosal Resection (EMR)



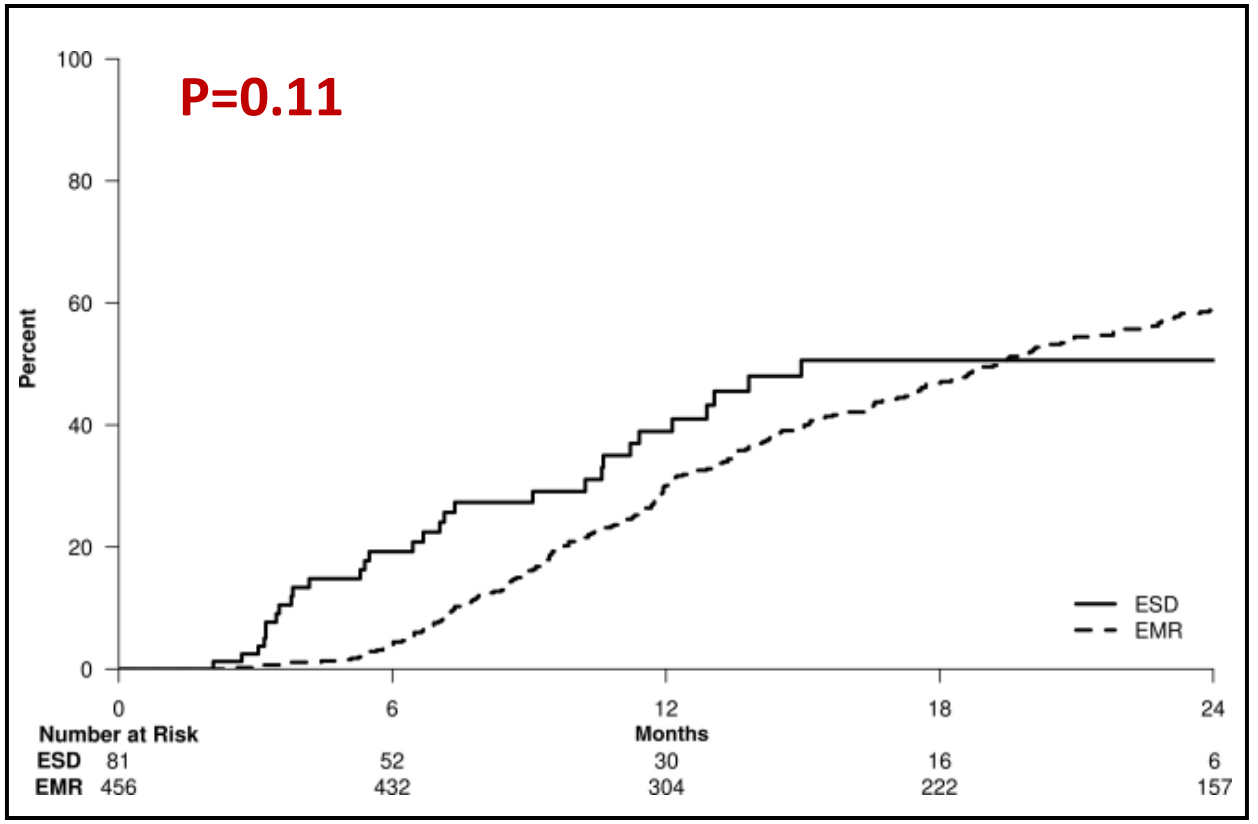
Endoscopic Submucosal Dissection (ESD)



Endoscopic therapy – EMR vs. ESD



Eradication of Dysplasia



Eradication of Intestinal Metaplasia

Codipilly et al, *CGH*, 2022;20:65-73

Endoscopic therapy – EMR vs. ESD

- 2024 Meta-analysis:
  - ESD higher **en-bloc resection** and **R0 resection**
  - "Curative resection" ↑, local recurrence ↓ in ESD,
    - Not statistically significant
  - No difference in eradication of dysplasia
  - No difference in adverse events

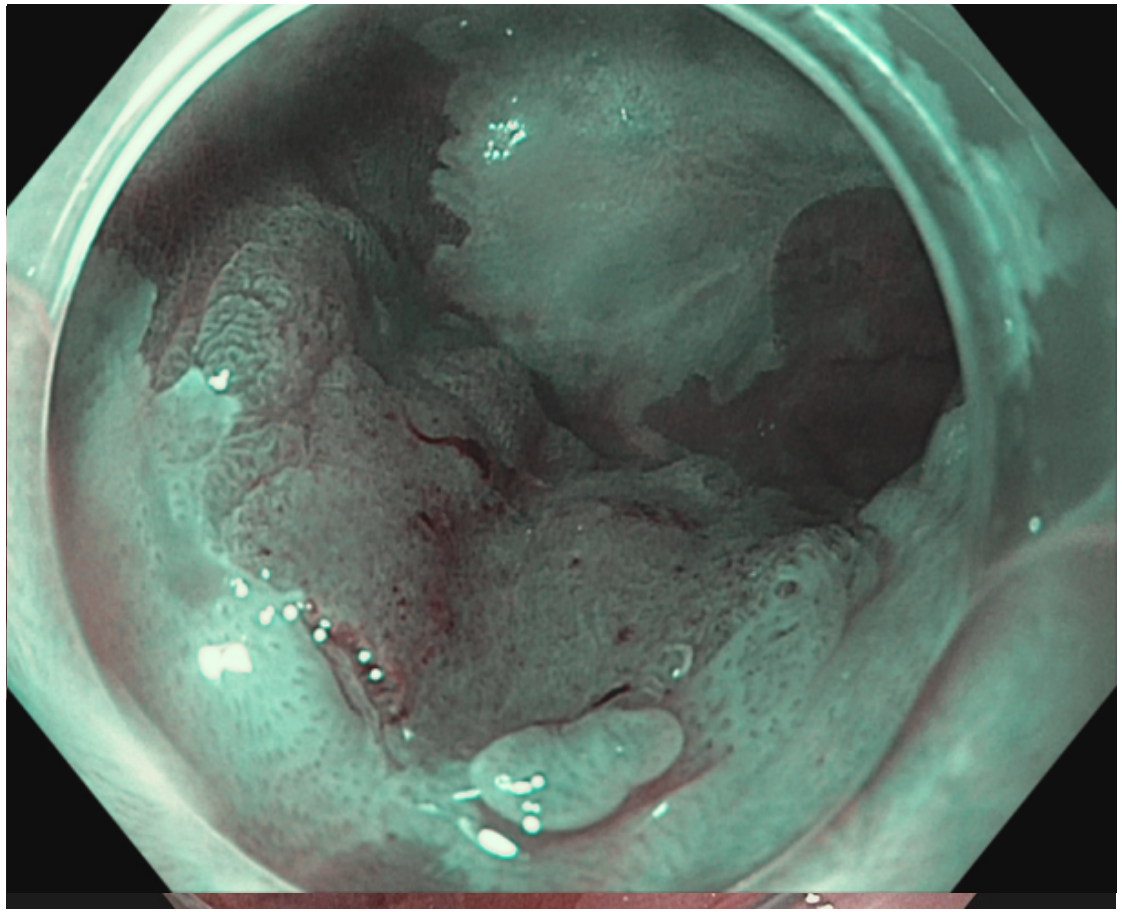
Fujiyoshi et al, *GIE*, 2024;100:817-828

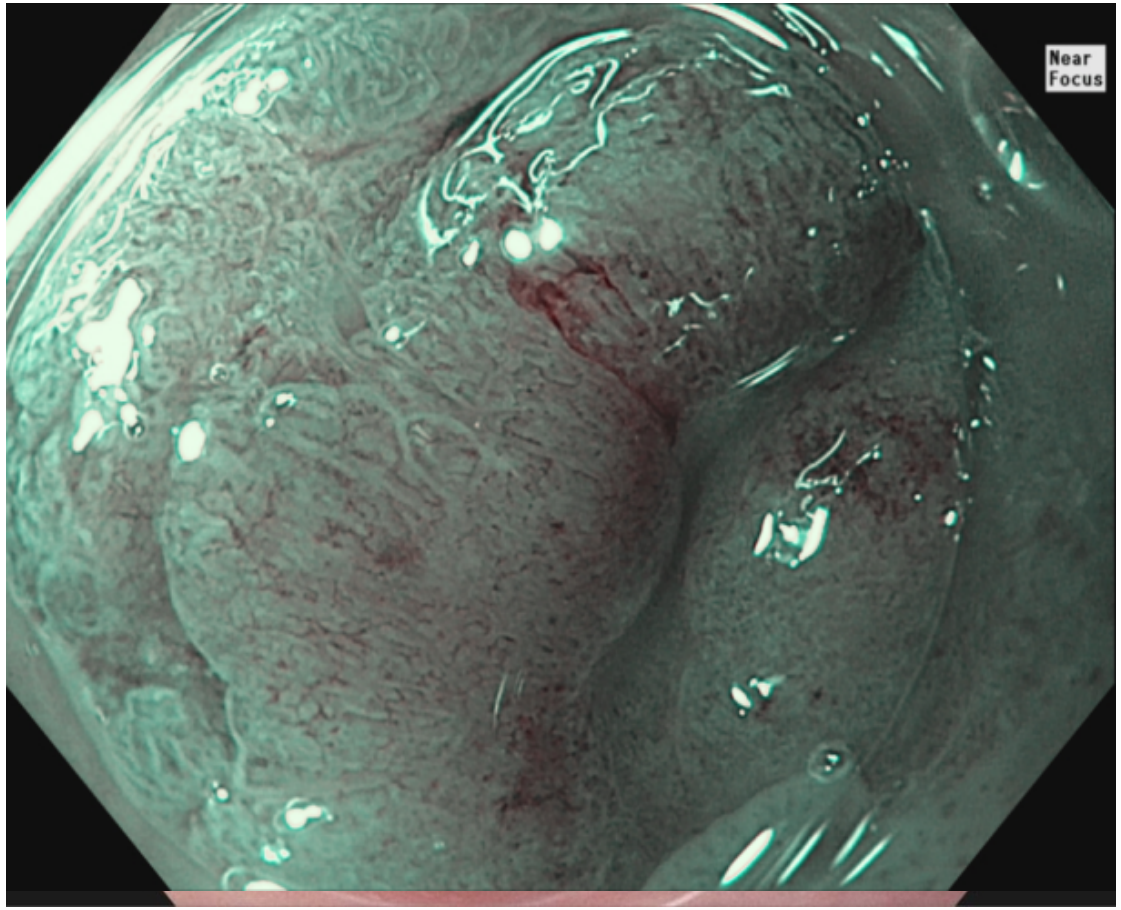
EMR vs. ESD – Which One to Use?

1. Are there any concerns for submucosal invasion based on endoscopic appearance?
   - Large/bulky lesion
   - Failure to lift
   - Surface pattern
   - Wall tension

Yang et al, *CGH*, 2019;17:1019-1028

EMR vs. ESD – Which One to Use?





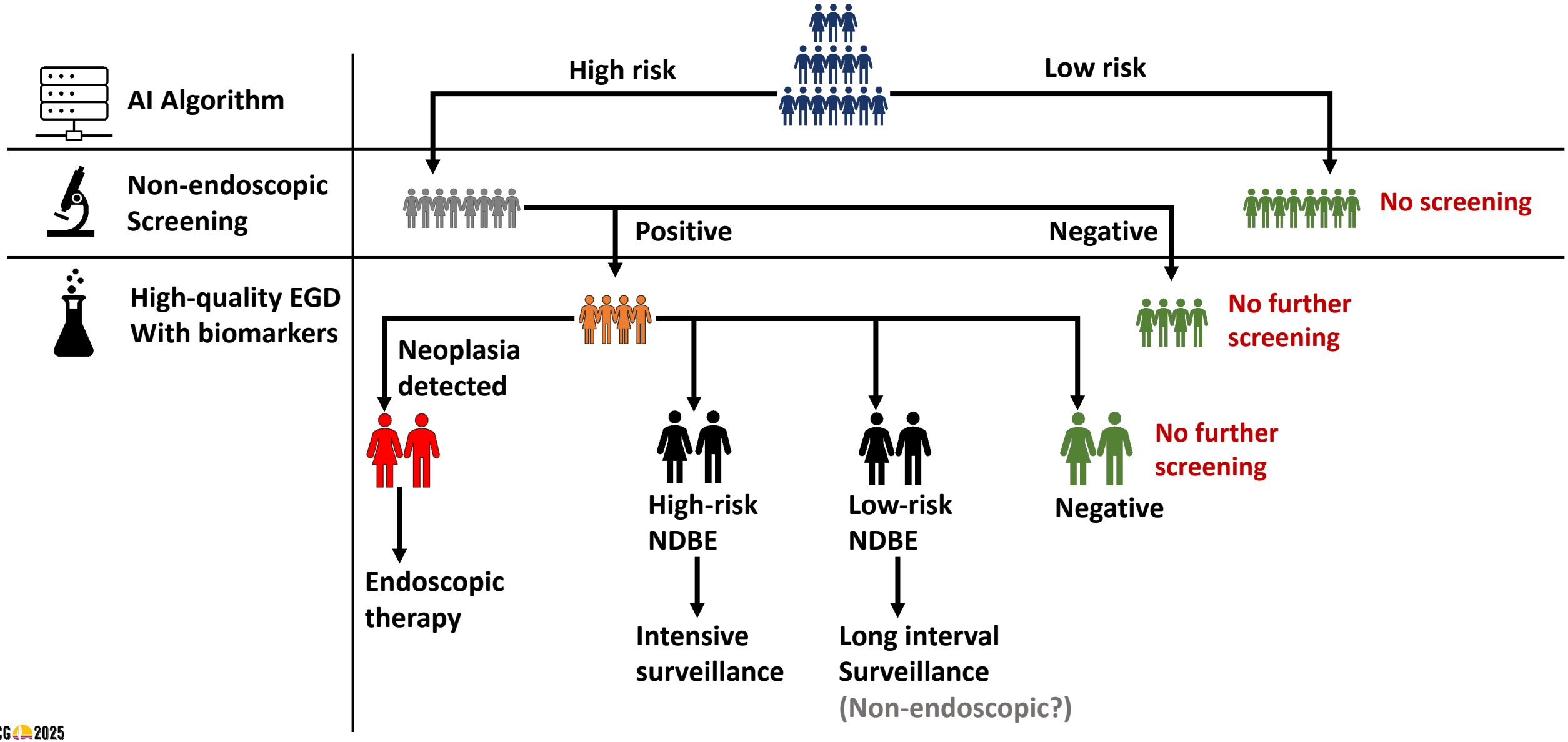
EMR vs. ESD – Which One to Use?

1. Are there any concerns for submucosal invasion based on endoscopic appearance?
2. What is

2024 AGA Guideline:
"Suggests the use of either EMR or ESD based on lesion characteristics…the vast majority of neoplastic lesions may be managed with EMR rather than ESD"

Rubenstein et al, *Gastro,* 2024;166:1020-1055

How do we “best” Barrett’s Esophagus?



Thank You

kahn.allon@mayo.edu

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