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Barrett's Esophagus Strategies to Avoid GEJ Cancers

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Disclosures

- Consultant: Boston Scientific, Pentax Medical, Exact Sciences, and Lucid Diagnostics.
- Research Support: Lucid Diagnostics
- Participate in clinical trials sponsored by ERBE, WATS-3D, Interscope Medical, Lucid Dx, Exact sciences.

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Location of Barrett's Adenocarcinoma

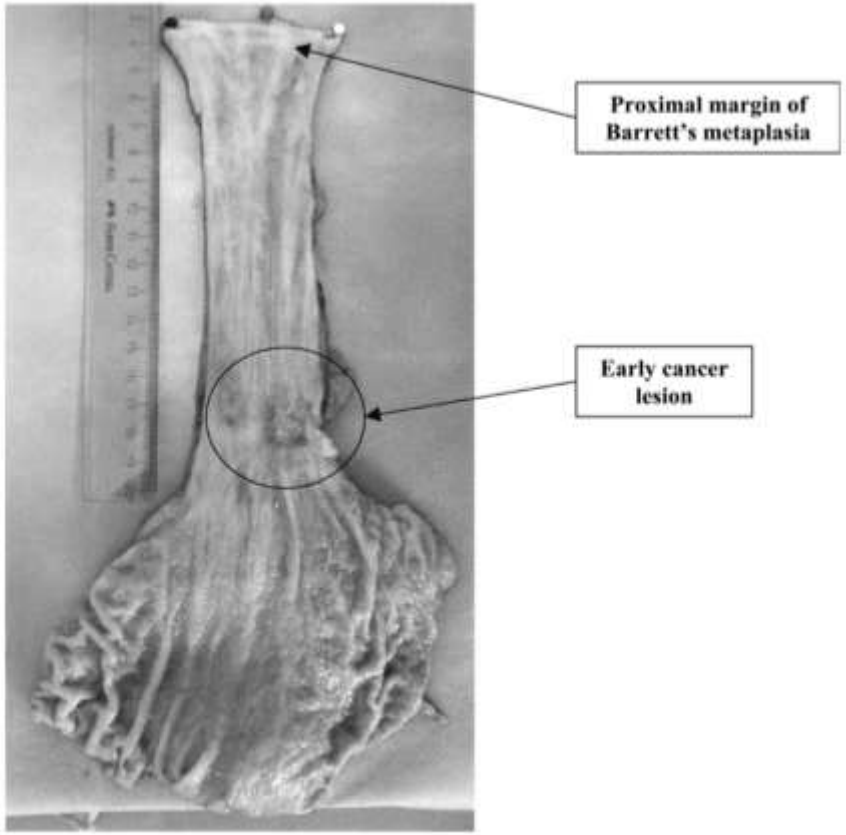

Table 1. Prevalence of the location and distribution of the cancer development

Barrett's mucosa	Early adenocarcinoma (n = 112)	Locally advanced adenocarcinoma (n = 77)
Distal third: n (%)	92/112 (82)	65/77 (84.4)
Proximal or middle third: n (%)	20/112 (18)	12/77 (15.6)
p Value	<0.05	<0.05

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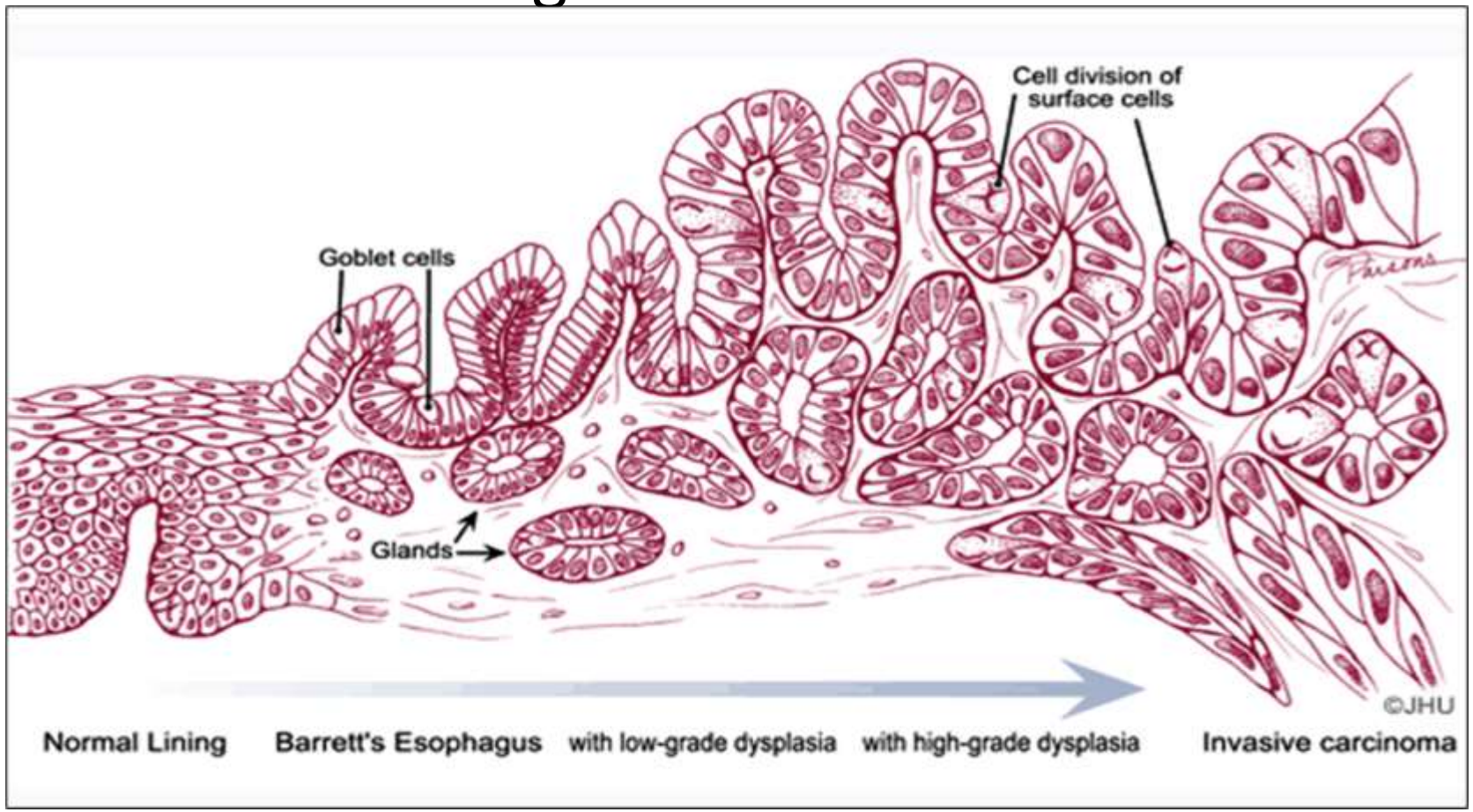
Surgical Endoscopy 2006; 20: 235-38

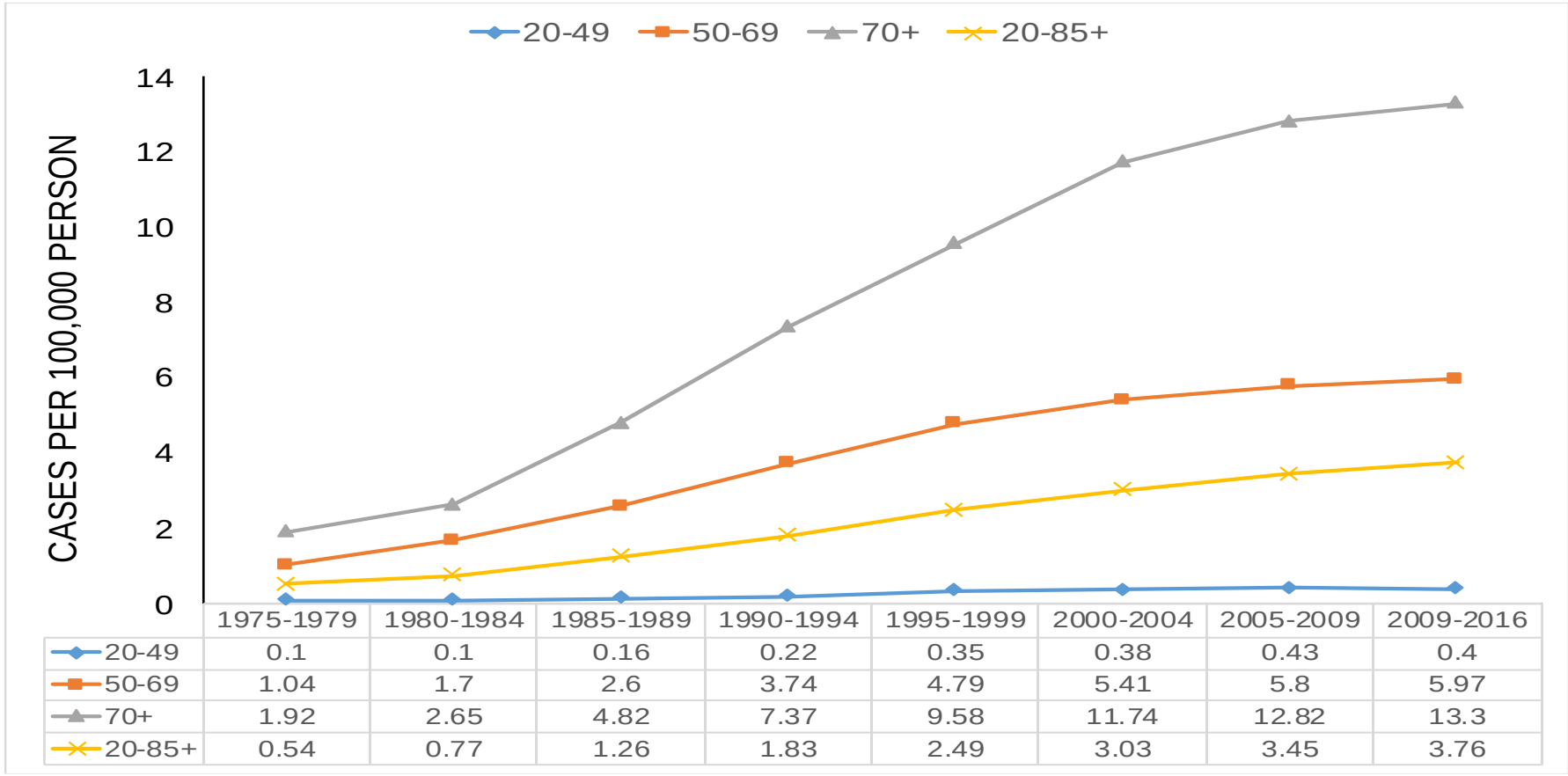
Progression to Cancer



0.3%-0.5% rate of progression from NDBE to dysplastic BE

Ong, World J Gastroenterol, 2010

RISING INCIDENCE OF ESOPHAGEAL ADENOCARCINOMA



	1975-1979	1980-1984	1985-1989	1990-1994	1995-1999	2000-2004	2005-2009	2009-2016
20-49	0.1	0.1	0.16	0.22	0.35	0.38	0.43	0.4
50-69	1.04	1.7	2.6	3.74	4.79	5.41	5.8	5.97
70+	1.92	2.65	4.82	7.37	9.58	11.74	12.82	13.3
20-85+	0.54	0.77	1.26	1.83	2.49	3.03	3.45	3.76

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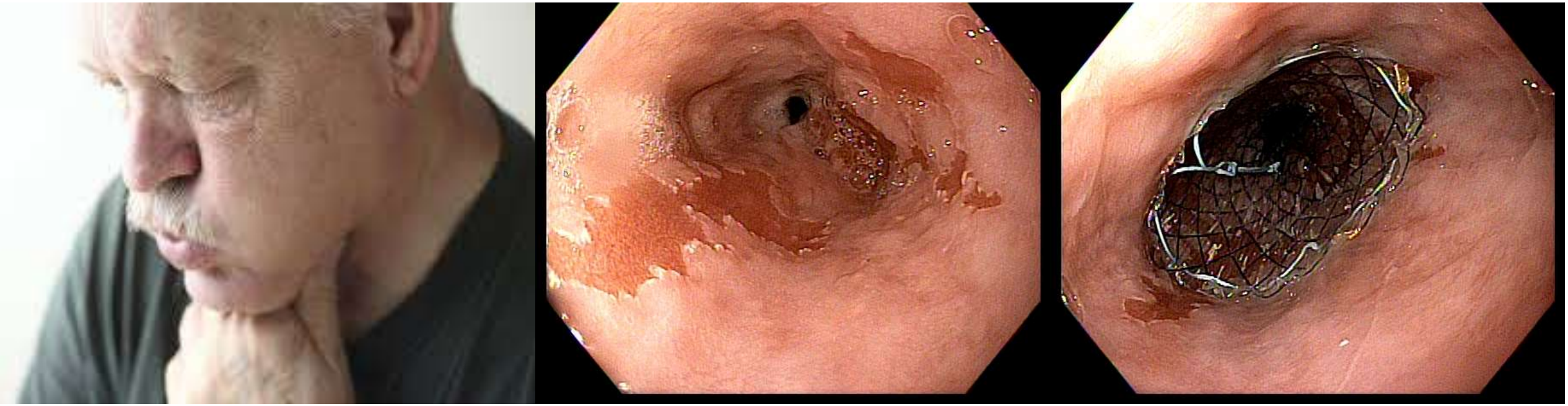
Figure Courtesy of Sachin Wani and adapted from : Kolb J, Han S, Wani S. Gastroenterology 2020

Strategies to avoid BE Cancers

- Identify patients to screen for BE
- High quality screening and surveillance exams
- Adequate endoscopic therapy and follow up

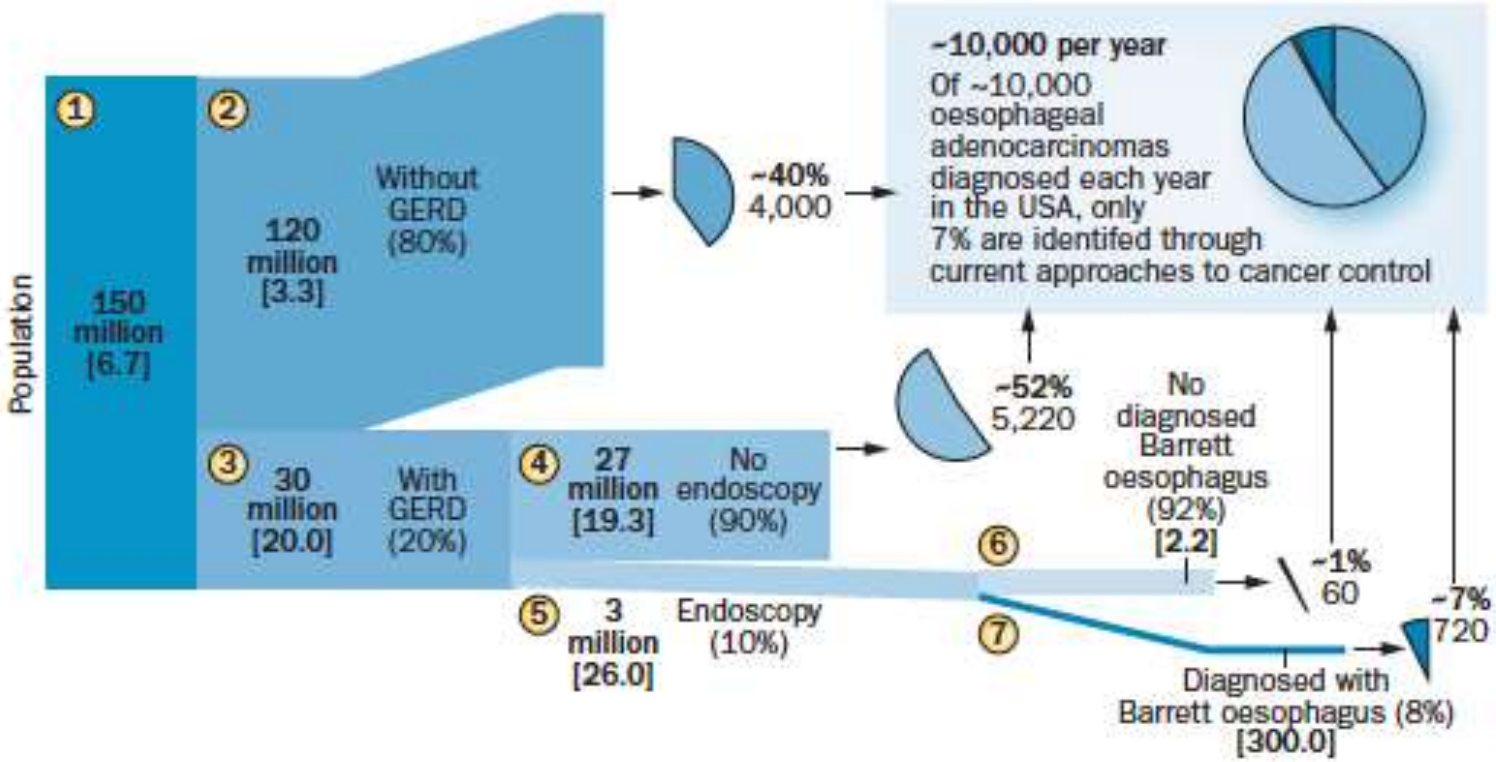
The all-too-common clinical occurrence



57% of new EAC also has a new diagnosis of BE

Tan et al. APT 2020; 52: 20-36

Problem with Current Screening



- Only 7% of EAC diagnosed via screening
- 40% of cases arise in pts w/out symptoms
- 52% of cases arise in pts with GERD symptoms

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Vaughn et al Nat Rev Gastro Hep 2015 12; 243-48

Prevalence of BE with risk factors

Risk Factor	Prevalence of BE	
Family history BE/EAC	23%	SCREEN
Age >50 y/o	6.1%	
Male sex	6.8%	
Smoking	3.2%	
Obesity	1.9%	
GERD	2.3%	
GERD + 1 risk factor	12.2%	SCREEN
GERD +2 risk factor	13.4%	SCREEN
GERD +3 risk factors	14.6%	SCREEN

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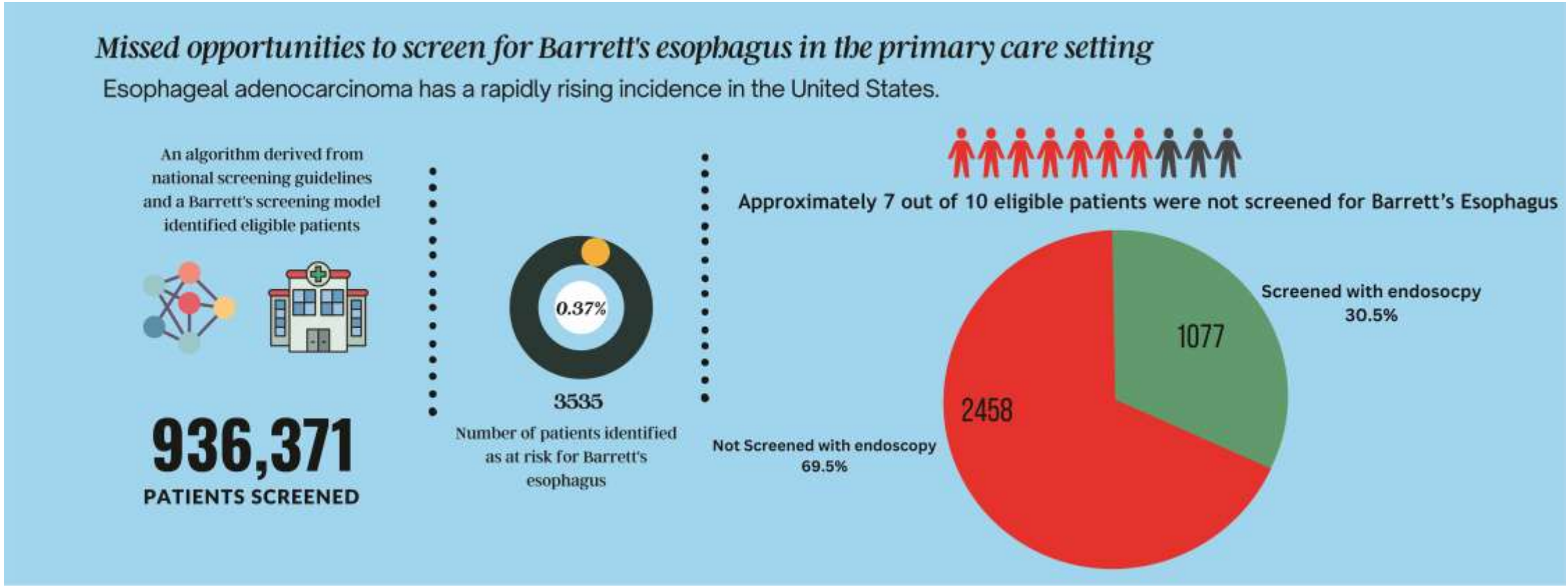
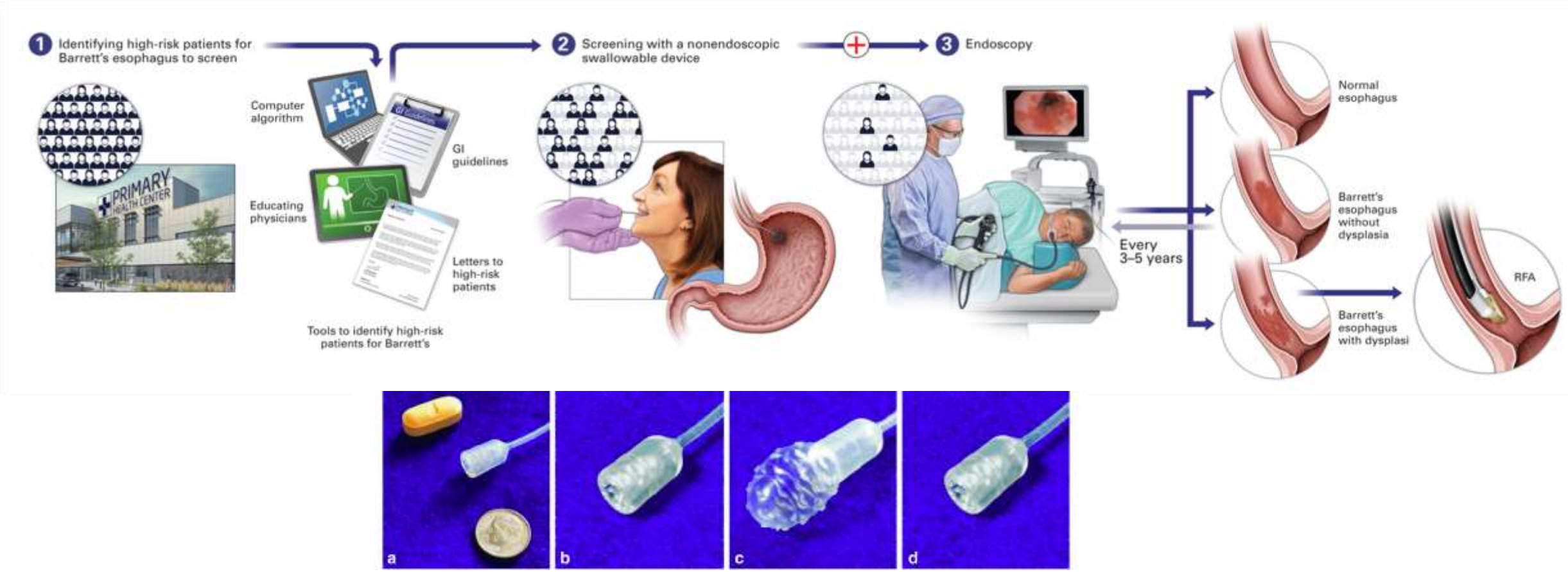
Qumseya et al GIE 2019; 90; 335-59
Shaheen et al. AJG 2022; 117: 559-587

Screening in primary care at Northwell Health

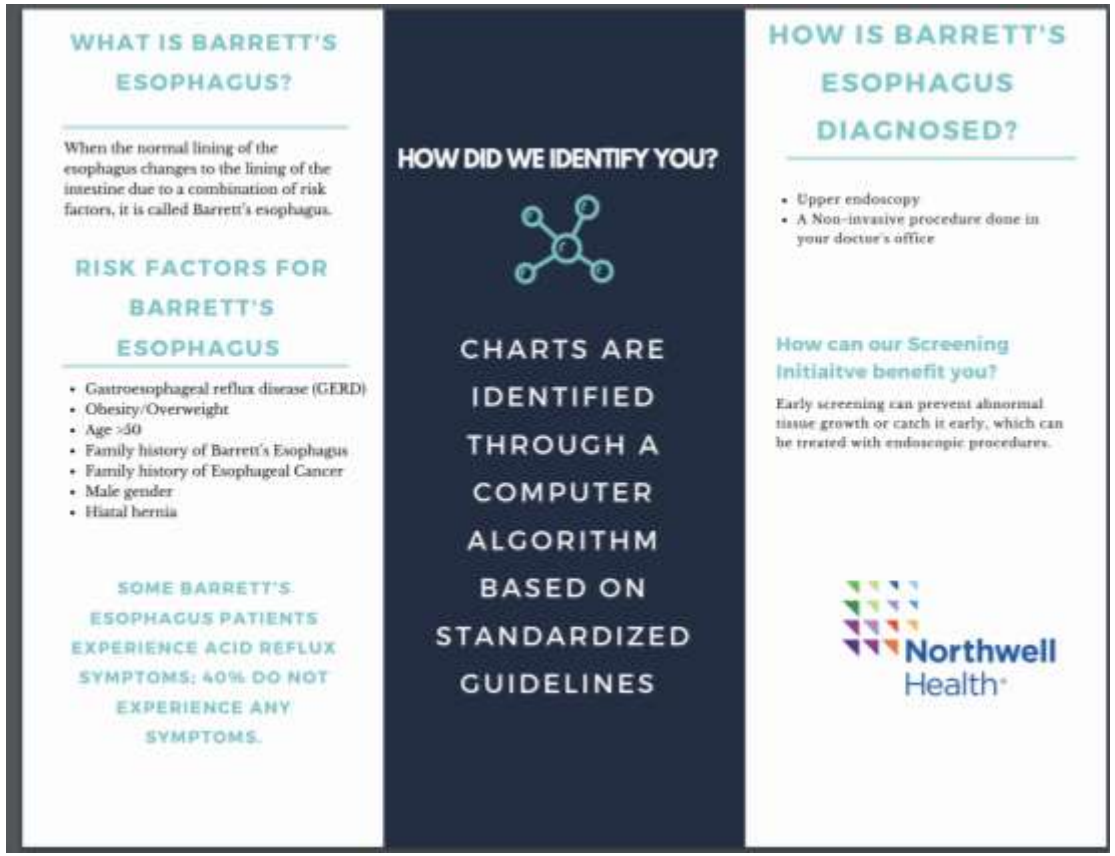


Trindade et al GIE 2023; 98: 162-69

How to Screen



Barrett’s screening brochures



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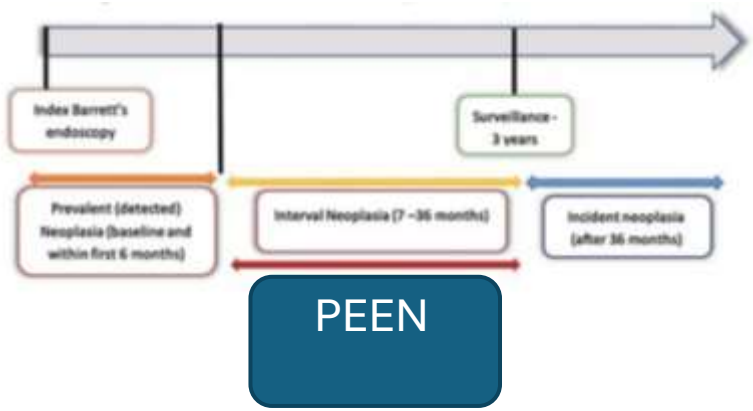
Importance of High-Quality Exam and PEEC

- PEEC-Post Endoscopy Esophageal Adenocarcinoma: EAC detected before the next surveillance endoscopy in a patient with NDBE
- PEEN-Post Endoscopy Esophageal Neoplasia: HGD/EAC detected before the next surveillance endoscopy in a patient with NDBE
- Time window of 6 months-3 years after screening or surveillance endoscopy



Wani et al. Gastroenterology 2022; 162: 366-372
Desai et al. Endoscopy 2022; 54:881-889

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Magnitude of PEEN/PEEC

Meta-analysis of 52 studies with 145,726 patients

- Proportion of PEEC was 21% (95%CI 13-31%)
- Proportion of PEEN was 26% (95% 19-34%)

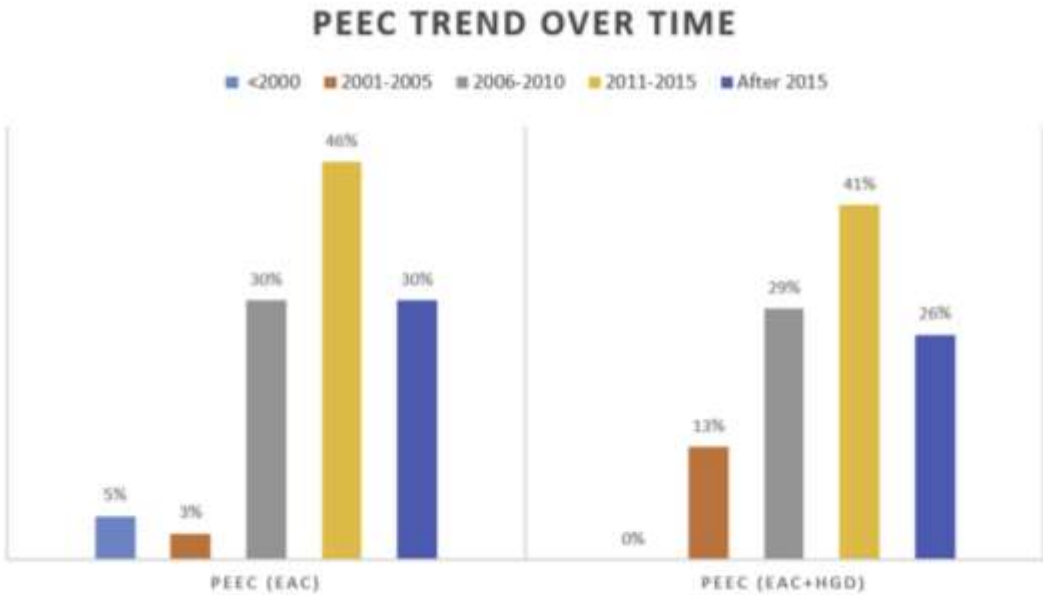

Figure 2. The trend of postendoscopy esophageal adenocarcinoma (PEEC) proportion over time. EAC, esophageal adenocarcinoma; HGD, high-grade dysplasia.

Sawas et al. Clin Gastroenterol Hep 2022; e31-e-50

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High Quality Screening and Surveillance Exams

Table 6. Ten-step approach to endoscopic examination of Barrett's esophagus

Approach	Rationale
Identify esophageal landmarks, including the location of the diaphragmatic hiatus, gastroesophageal junction, and squamocolumnar junction	Critical for future examinations
Consider use of a distal attachment cap (especially in patients with prior diagnosis of dysplasia)	Facilitate visualization
Clean mucosa well using water jet channel and carefully suction the fluid	Remove any distracting mucus or debris and minimize mucosal trauma
Use insufflation and desufflation	Fine adjustments to luminal insufflation can help with detection of subtle abnormalities
Spend adequate time inspecting the Barrett's segment and gastric cardia in retroflexion	Careful examination increases dysplasia detection
Examine the Barrett's segment using high-definition white light endoscopy	Standard of care
Examine the Barrett's segment using chromoendoscopy (including virtual chromoendoscopy)	Enhances mucosa pattern and surface vasculature
Use the Prague classification to describe the circumferential and maximal Barrett's segment length	Standardized reporting system
Use the Paris classification to describe superficial neoplasia	Standardized reporting system
Use the Seattle protocol (in conjunction with electronic chromoendoscopy) with a partially deflated esophagus to sample the Barrett's segment	Increases dysplasia detection

Adapted from Kolb and Wani (232).

Shaheen et al. AJG 2022; 117: 559-587

Prague Classification and ID of Landmarks

Fig. 4: Endoscopic diagnosis of Barrett oesophagus.

From: Barrett oesophagus

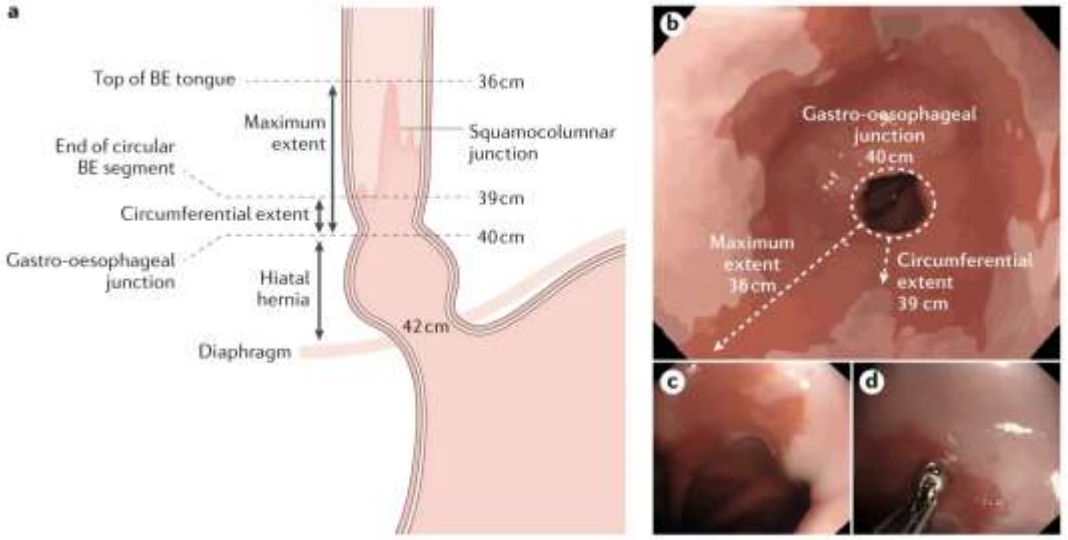


Table 1 American Gastroenterological Association Quality Indicators for the management of Barrett's esophagus.

Quality Indicator	Quality Statement
1	For patients in whom BE is being considered, the squamo-columnar junction, the gastroesophageal junction (GEJ), and the location of the diaphragmatic hiatus (if there is a hiatal hernia present) should be recorded on each upper endoscopy
2	If BE is suspected on an endoscopy, the endoscopist should document the extent of suspected BE using Prague criteria

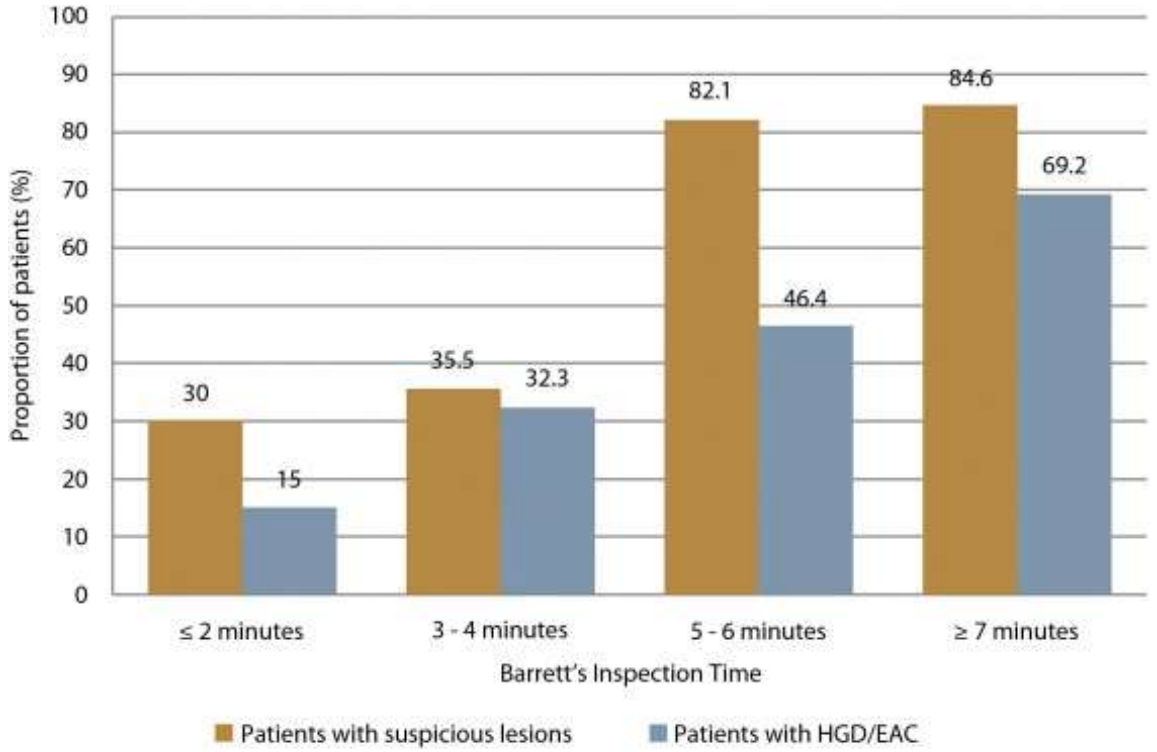
Table 3 Information regarding adherence to quality statements and correlation to dysplasia yield.

Statement (s)	Adherence vs. non-adherence	Dysplasia detection	*P*-Value
1	135 (78%) vs. 39 (22%)	48 (36%) vs. 5 (13%)	0.006
2	121 (70%) vs. 53 (31%)	43 (36%) vs. 10 (19%)	0.03
5	71 (41%) vs. 103 (59%)	25 (35%) vs. 28 (27%)	NS

Shaheen et al. AJG 2022; 117: 559-587

Antony et al. Clin Res Hepatol and Gastroenterol 2018; 42: 591-96

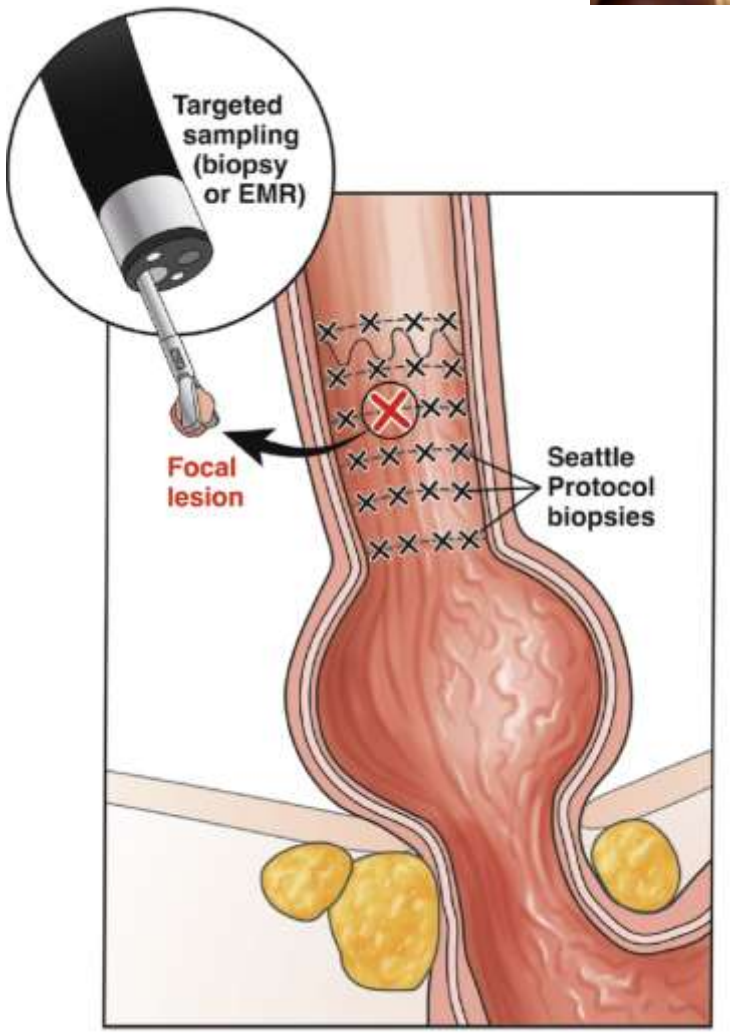
Inspection Time and Dysplasia Detection



Gupta et al GIE 2012; 76: 5131-8

Adherence to Seattle Protocol

- Dysplasia is focal despite molecular changes being a field defect.
- Adherence to SP only 20%
- Full compliance with SP samples only 5-10% of BE mucosa.
- Potential to miss a lesion if :
  - Not visible
  - Focal
  - Not captured by SP biopsy
  - Long segment of BE



1) Wani S et al. GIE 2019; 90: 732-741
2) Iyer & Chak. Gastroenterology 2023; 164:707-18

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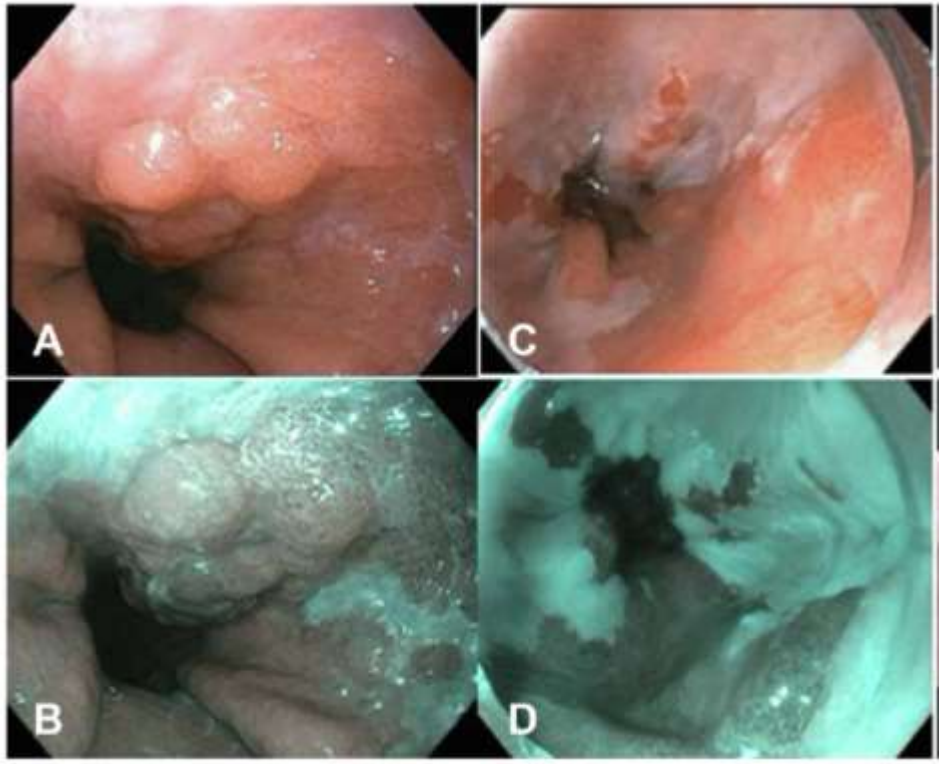
Importance of Recognition of Lesions

- Essential to recognize VL:
  - VLs harbor dysplasia
  - EMR for complete removal and staging.
- A recent video-based survey study of 22 academic and 22 community physicians
  - 28% of HD-WLE VLs missed
  - 31% of NBI VLs missed
  - Volume of 5 surveillance EGDs a month associated with improved VL detection with NBI.



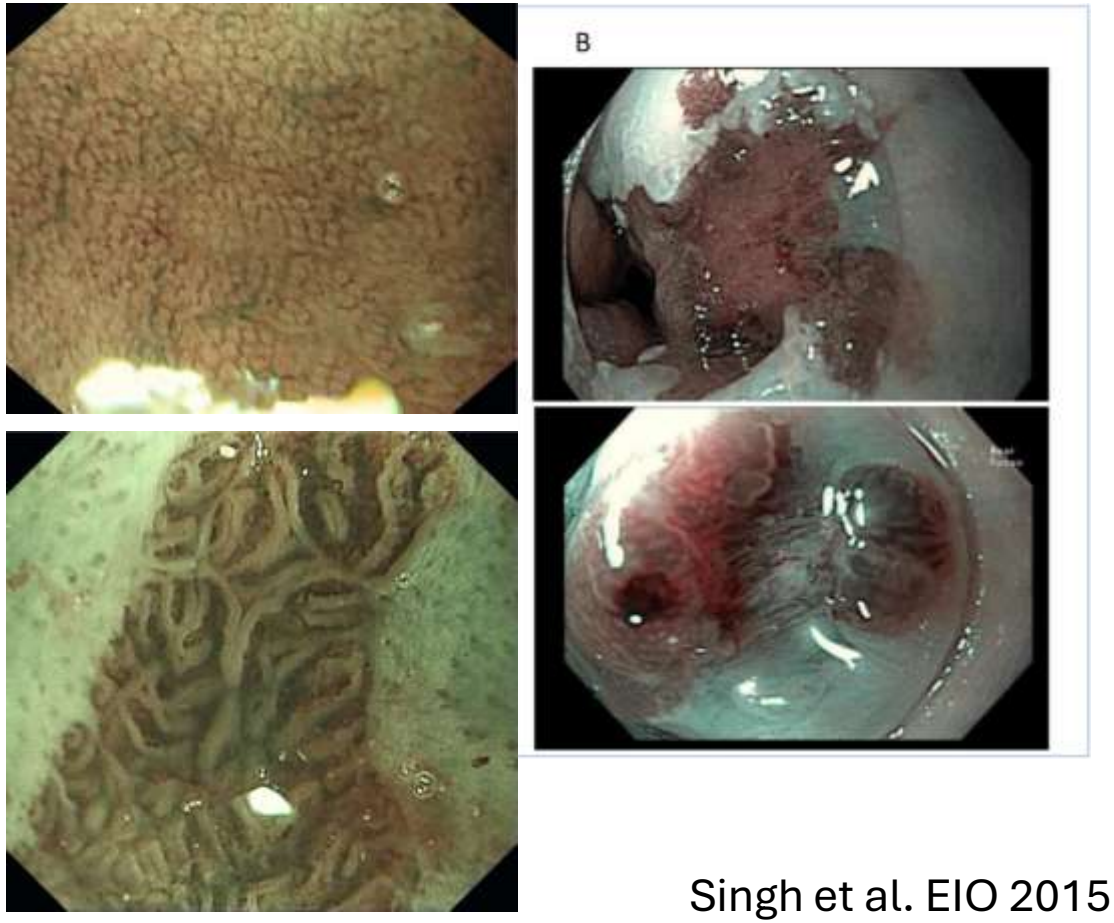
Beveridge CA et al. GIE 2023; 97: 241-7

NBI/Virtual Chromoendoscopy

Table 3. Barrett's Esophagus International Group NBI Classification of Mucosal Appearance Suggestive of Barrett's Esophagus-related Dysplasia[29]

Mucosal pattern	Classification
Circular, ridged, villous, or tubular	Regular
Absent or irregular	Irregular

Vascular patterns	
Regular blood vessel appearance along or between mucosal ridges with normal, long-branching patterns	Regular
Focally or diffusely distributed vessels not following normal mucosal architecture	Irregular



Singh et al. EIO 2015; 3; E14-18
Holzwanger et al. TIGE 2023; 2: 257-66

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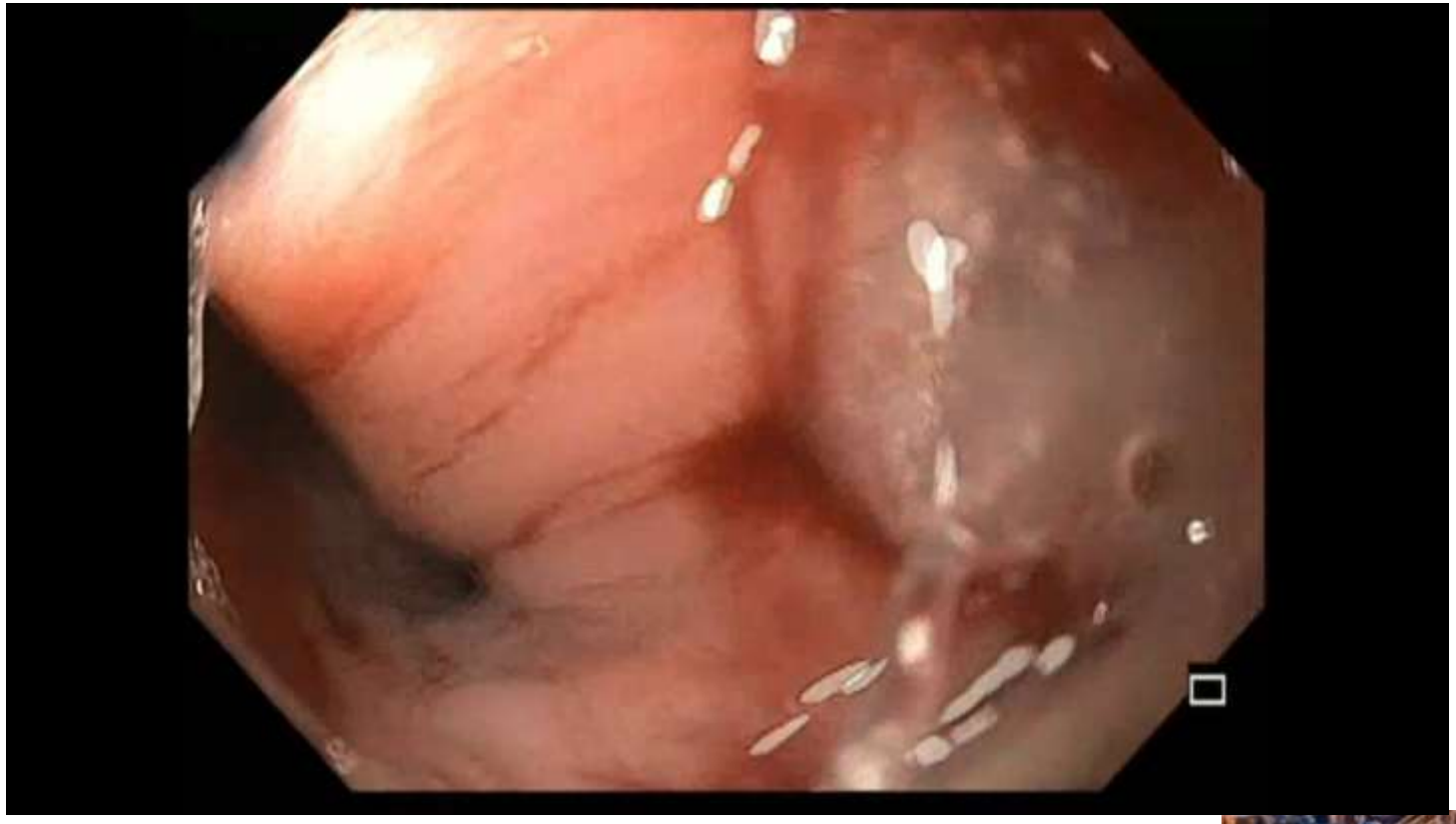
NBI Example

- 62-year-old male with abdominal pain.
- Initial EGD 4 weeks prior negative.
- imaging+ CBD stone.
- Referred for ERCP.



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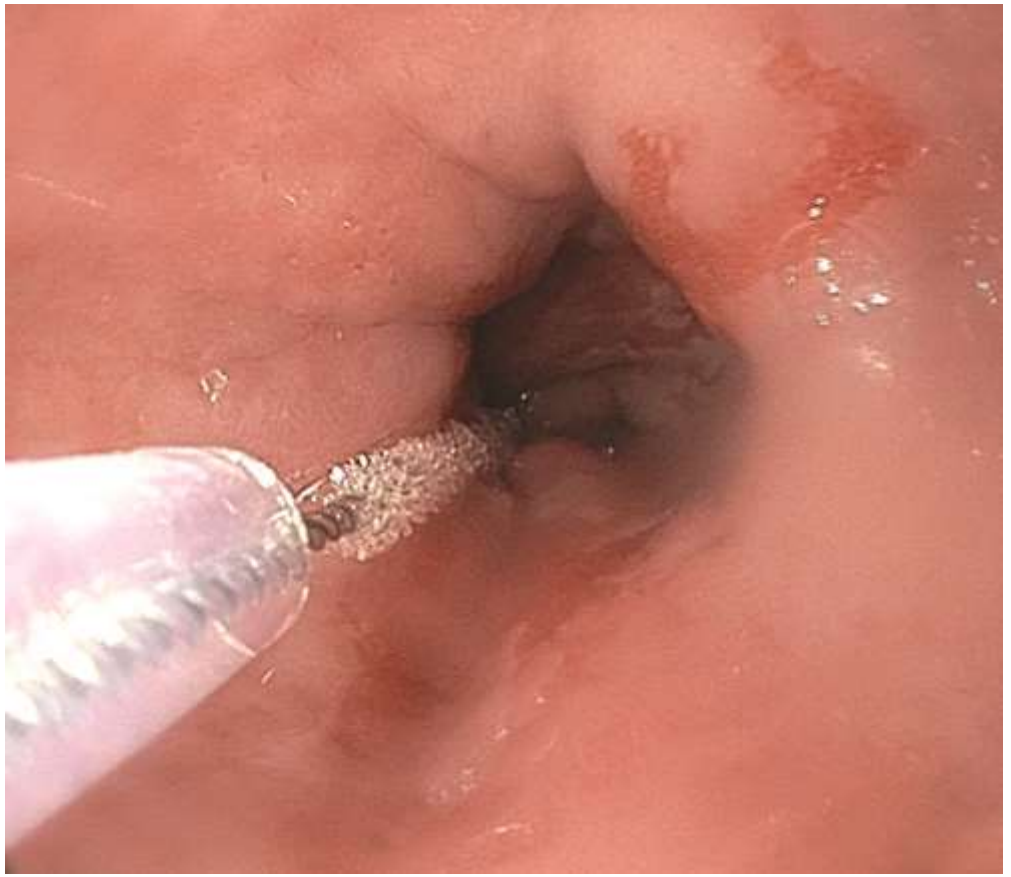
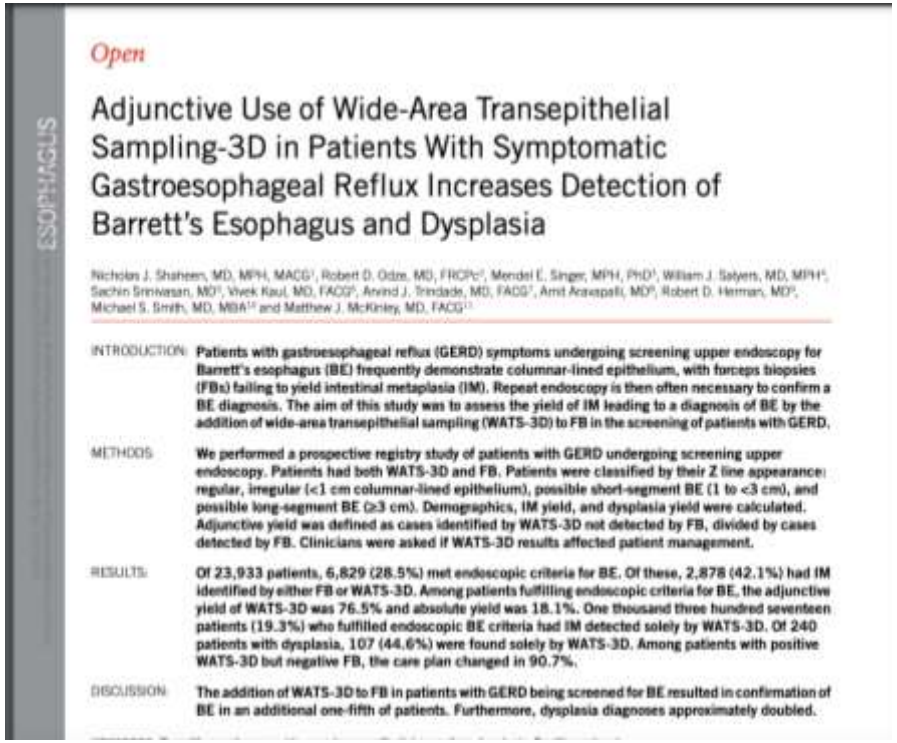
Adjunctive Use of WATS-3D



Recent WATS-3D Studies



ESOPHAGUS

Open

Adjunctive Use of Wide-Area Transepithelial Sampling-3D in Patients With Symptomatic Gastroesophageal Reflux Increases Detection of Barrett's Esophagus and Dysplasia

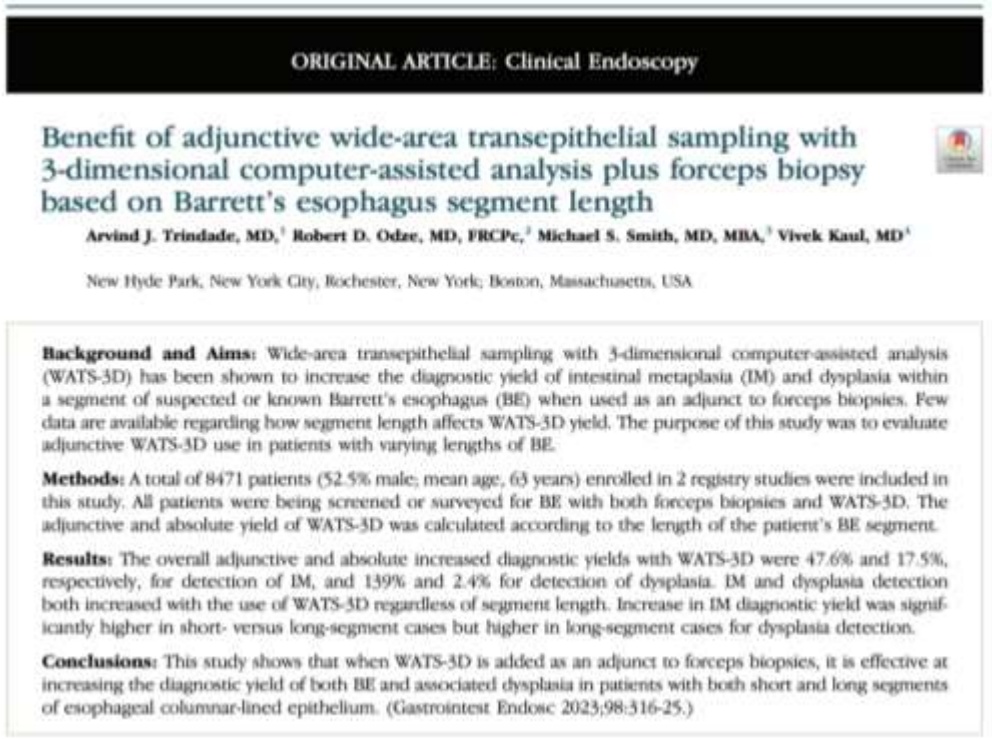
Nicholas J. Shaheen, MD, MPH, MACG[1], Robert D. Odze, MD, FRCPc[2], Mendel E. Singer, MPH, PhD[3], William J. Salyers, MD, MPH[4], Sachin Srinivasan, MD[5], Vivek Kaul, MD, FACG[6], Arvind J. Trindade, MD, FACG[7], Amit Aravapalli, MD[8], Robert D. Herman, MD[9], Michael S. Smith, MD, MBA[10] and Matthew J. McKinley, MD, FACG[11]

INTRODUCTION: **Patients with gastroesophageal reflux (GERD) symptoms undergoing screening upper endoscopy for Barrett's esophagus (BE) frequently demonstrate columnar-lined epithelium, with forceps biopsies (FBs) failing to yield intestinal metaplasia (IM). Repeat endoscopy is then often necessary to confirm a BE diagnosis. The aim of this study was to assess the yield of IM leading to a diagnosis of BE by the addition of wide-area transepithelial sampling (WATS-3D) to FB in the screening of patients with GERD.**

METHODS: **We performed a prospective registry study of patients with GERD undergoing screening upper endoscopy. Patients had both WATS-3D and FB. Patients were classified by their Z line appearance: regular, irregular (<1 cm columnar-lined epithelium), possible short-segment BE (1 to <3 cm), and possible long-segment BE (≥3 cm). Demographics, IM yield, and dysplasia yield were calculated. Adjunctive yield was defined as cases identified by WATS-3D not detected by FB, divided by cases detected by FB. Clinicians were asked if WATS-3D results affected patient management.**

RESULTS: **Of 23,933 patients, 6,829 (28.5%) met endoscopic criteria for BE. Of these, 2,878 (42.1%) had IM identified by either FB or WATS-3D. Among patients fulfilling endoscopic criteria for BE, the adjunctive yield of WATS-3D was 76.5% and absolute yield was 18.1%. One thousand three hundred seventeen patients (19.3%) who fulfilled endoscopic BE criteria had IM detected solely by WATS-3D. Of 240 patients with dysplasia, 107 (44.6%) were found solely by WATS-3D. Among patients with positive WATS-3D but negative FB, the care plan changed in 90.7%.**

DISCUSSION: **The addition of WATS-3D to FB in patients with GERD being screened for BE resulted in confirmation of BE in an additional one-fifth of patients. Furthermore, dysplasia diagnoses approximately doubled.**



ORIGINAL ARTICLE: Clinical Endoscopy

Benefit of adjunctive wide-area transepithelial sampling with 3-dimensional computer-assisted analysis plus forceps biopsy based on Barrett's esophagus segment length

Arvind J. Trindade, MD,[1] Robert D. Odze, MD, FRCPc,[2] Michael S. Smith, MD, MBA,[3] Vivek Kaul, MD[4]

New Hyde Park, New York City, Rochester, New York; Boston, Massachusetts, USA

Background and Aims: Wide-area transepithelial sampling with 3-dimensional computer-assisted analysis (WATS-3D) has been shown to increase the diagnostic yield of intestinal metaplasia (IM) and dysplasia within a segment of suspected or known Barrett's esophagus (BE) when used as an adjunct to forceps biopsies. Few data are available regarding how segment length affects WATS-3D yield. The purpose of this study was to evaluate adjunctive WATS-3D use in patients with varying lengths of BE.

Methods: A total of 8471 patients (52.5% male; mean age, 63 years) enrolled in 2 registry studies were included in this study. All patients were being screened or surveyed for BE with both forceps biopsies and WATS-3D. The adjunctive and absolute yield of WATS-3D was calculated according to the length of the patient's BE segment.

Results: The overall adjunctive and absolute increased diagnostic yields with WATS-3D were 47.6% and 17.5%, respectively, for detection of IM, and 139% and 2.4% for detection of dysplasia. IM and dysplasia detection both increased with the use of WATS-3D regardless of segment length. Increase in IM diagnostic yield was significantly higher in short- versus long-segment cases but higher in long-segment cases for dysplasia detection.

Conclusions: This study shows that when WATS-3D is added as an adjunct to forceps biopsies, it is effective at increasing the diagnostic yield of both BE and associated dysplasia in patients with both short and long segments of esophageal columnar-lined epithelium. (Gastrointest Endosc 2023;98:316-25.)

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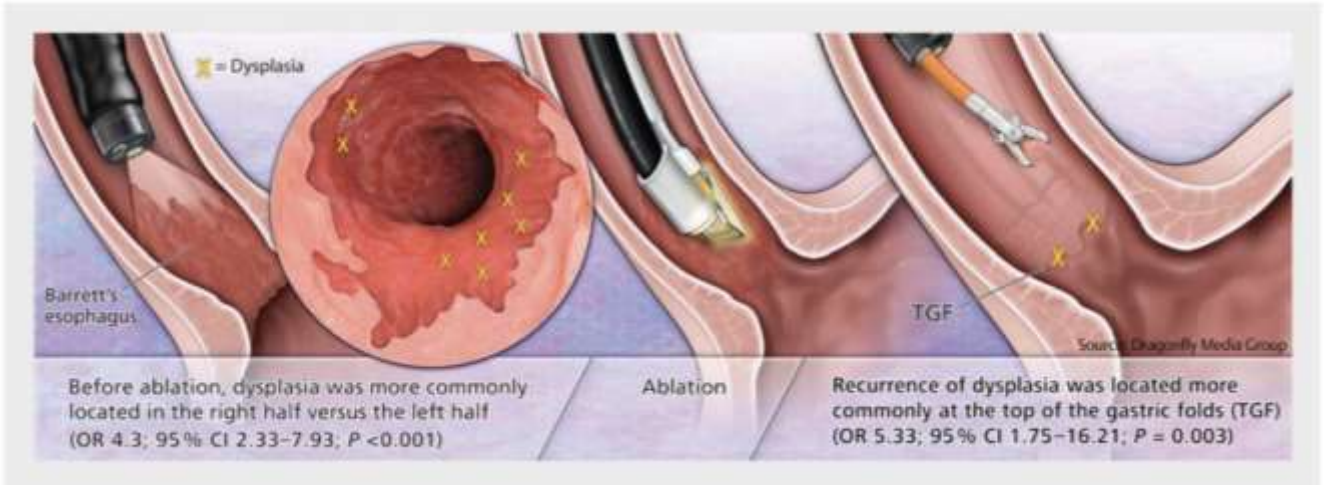
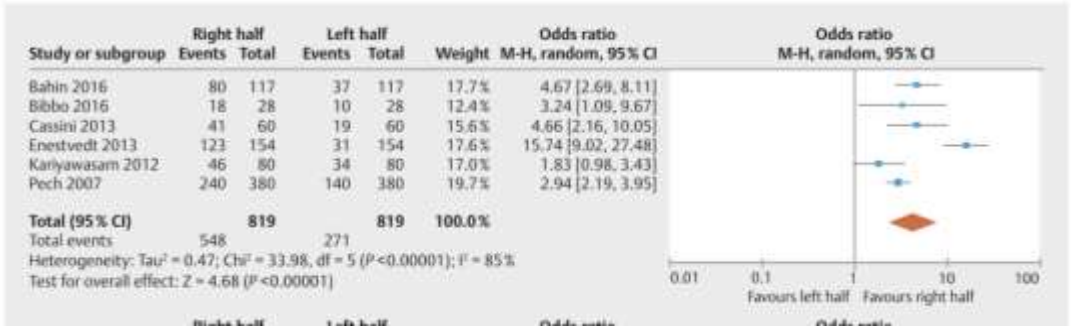
Risk Stratification of Nondysplastic BE

- Tissue Cypher
  - Biomarkers (p53, p16, AMCAR, HER-2, CD68, COX2, HIF1 alpha, CD45R0)
  - Spatial biology via AI algorithm
  - 5-year progression risk score (score 0-10)
- Previse EsoPredict
  - 4 DNA methylation markers
  - 5-year progression risk level, score, and progression rate
    - Low
    - Low-moderate
    - High-moderate
    - High

High risk scores may allow for closer inspection in tertiary centers and decreased surveillance intervals

Location of Dysplasia

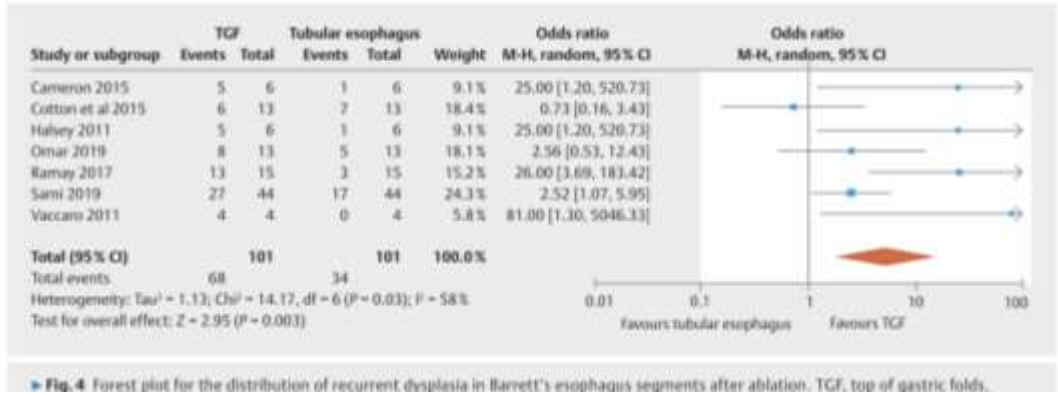




Study or subgroup	Right half Events	Total	Left half Events	Total	Weight	Odds ratio M-H, random, 95% CI
Bahin 2016	80	117	37	117	17.7%	4.67 [2.69, 8.11]
Bibbo 2016	18	28	10	28	12.4%	3.24 [1.09, 9.67]
Cassini 2013	41	60	19	60	15.6%	4.66 [2.16, 10.05]
Enestvedt 2013	123	154	31	154	17.6%	15.74 [9.02, 27.48]
Kariyawasam 2012	46	80	34	80	17.0%	1.83 [0.98, 3.43]
Pech 2007	240	380	140	380	19.7%	2.94 [2.19, 3.95]
Total (95% CI)		**819**		**819**	**100.0%**	
Total events	548		271			

Heterogeneity: Tau² = 0.47; Chi² = 33.98, df = 5 (P<0.00001); I² = 85%
Test for overall effect: Z = 4.68 (P<0.00001)

Odds ratio M-H, random, 95% CI
0.01 0.1 1 10 100
Favours left half Favours right half



Study or subgroup	TGF Events	Total	Tubular esophagus Events	Total	Weight	Odds ratio M-H, random, 95% CI
Cameron 2015	5	6	1	6	9.1%	25.00 [1.20, 520.73]
Cotton et al 2015	6	13	7	13	18.4%	0.73 [0.16, 3.43]
Halvey 2011	5	6	1	6	9.1%	25.00 [1.20, 520.73]
Omar 2019	8	13	5	13	18.1%	2.56 [0.53, 12.43]
Ramay 2017	13	15	3	15	15.2%	26.00 [3.69, 183.42]
Sami 2019	27	44	17	44	24.3%	2.52 [1.07, 5.95]
Vaccaro 2011	4	4	0	4	5.8%	81.00 [1.30, 5046.33]
Total (95% CI)		**101**		**101**	**100.0%**	
Total events	68		34			

Heterogeneity: Tau² = 1.13; Chi² = 14.17, df = 6 (P = 0.03); I² = 58%
Test for overall effect: Z = 2.95 (P = 0.003)

Odds ratio M-H, random, 95% CI
0.01 0.1 1 10 100
Favours tubular esophagus Favours TGF

▸ **Fig. 4** Forest plot for the distribution of recurrent dysplasia in Barrett's esophagus segments after ablation. TGF, top of gastric folds.

Trindade et al. Endoscopy 2021; 53: 6-14

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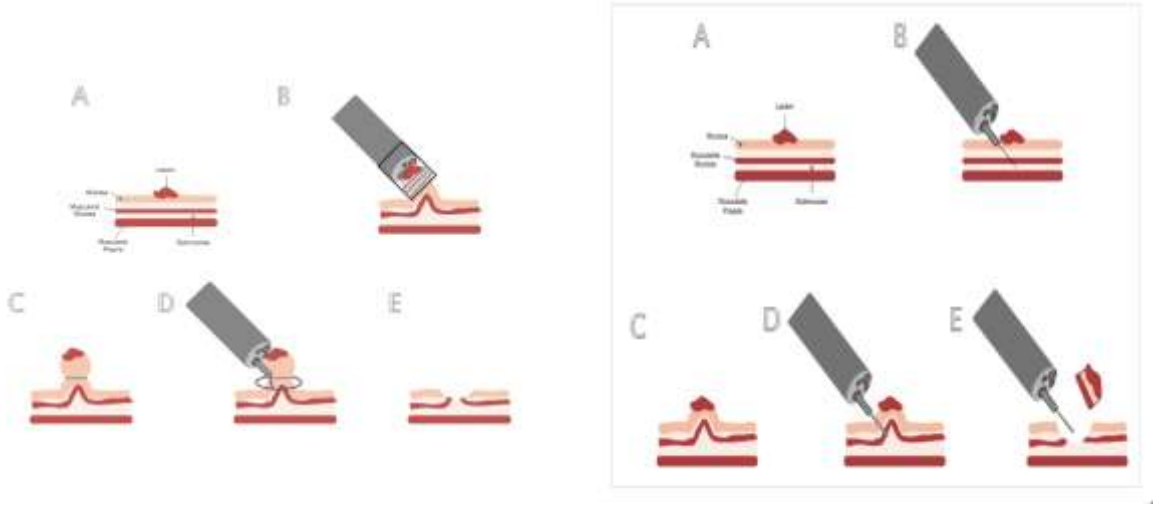
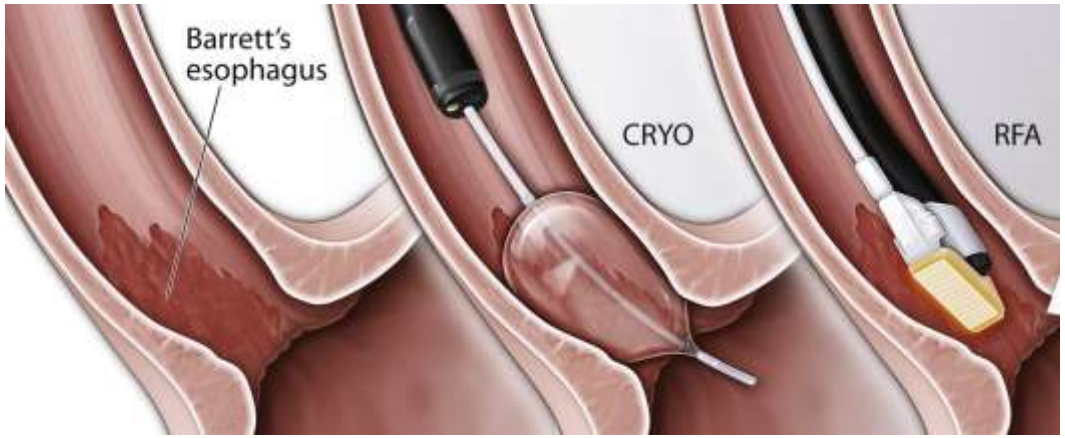
Adequate Eradication of BE with Dysplasia

Raised BE



Flat BE



GOAL of Endoscopic Therapy is Eradication of ALL BE

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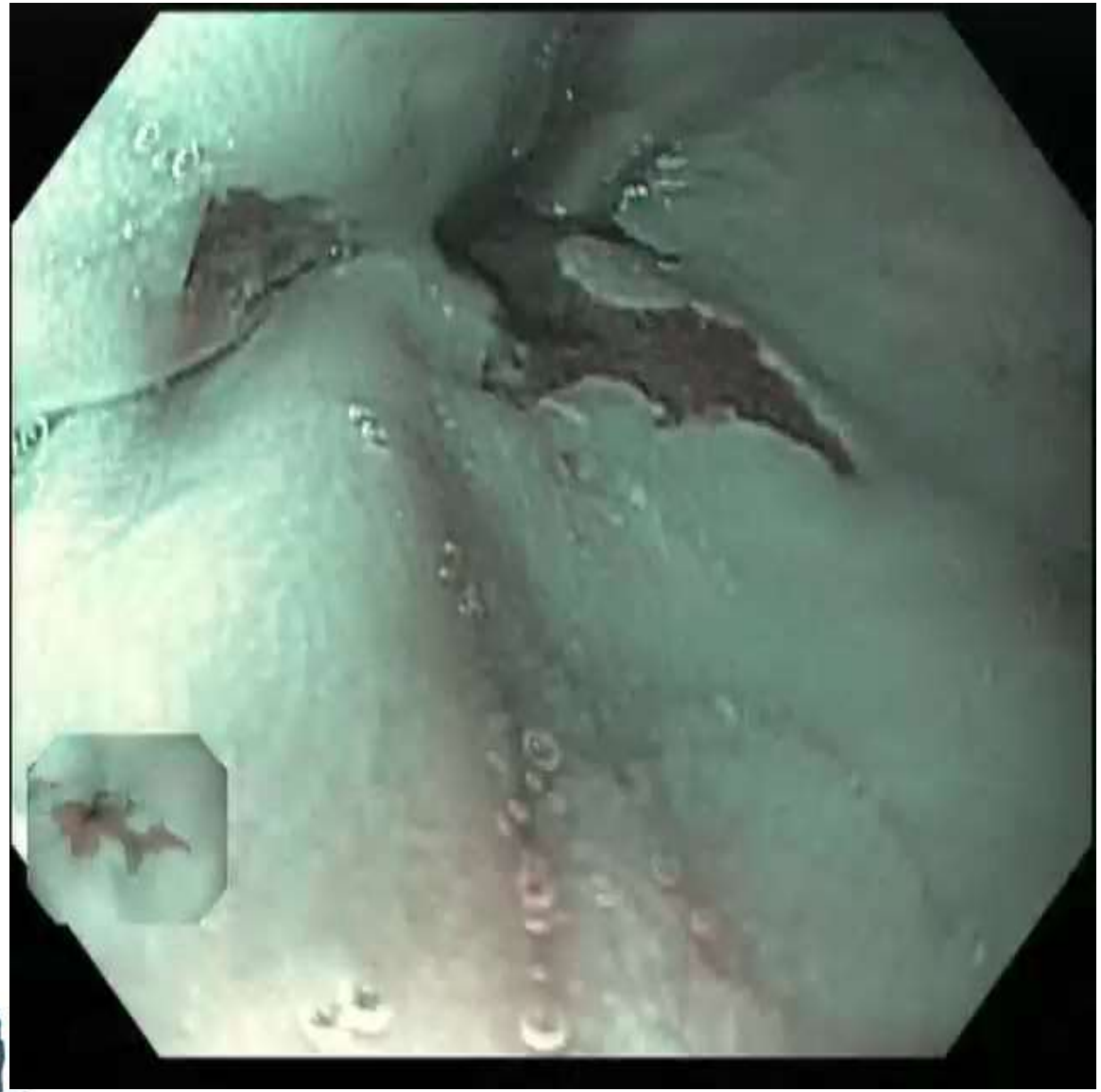
Ablate the GEJ/TOGF to Prevent Recurrence



Adequate Post Treatment Surveillance

Table 7. Recommended endoscopic surveillance intervals following CEIM based on worst pretreatment histology

Worst pretreatment histology	Suggested endoscopic surveillance
Low-grade dysplasia	1 yr following CEIM 3 yr following CEIM Every 2 yr thereafter
High-grade dysplasia	3 mo following CEIM 6 mo following CEIM 12 mo following CEIM Annually thereafter
Intramucosal carcinoma	3 mo following CEIM 6 mo following CEIM 12 mo following CEIM Annually thereafter

CEIM, complete eradication of intestinal metaplasia.

Shaheen et al. AJG 2022; 117: 559-587

Conclusion: Strategies to avoid BE Cancers

- Identify patients to screen for BE
- High quality screening and surveillance exams
- Adequate endoscopic therapy and follow up

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Thank You

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