The Best of Barrett's At DDW 2022

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June 4, 2022

NEW YORK SOCIETY FOR GASTROENTEROLOGY AND ENDOSCOPY
The Spring Course
BEST OF DDW 2022

Relevant Disclosures

- Castle Biosciences—Advisory Board
- Steris Endoscopy—Consultant

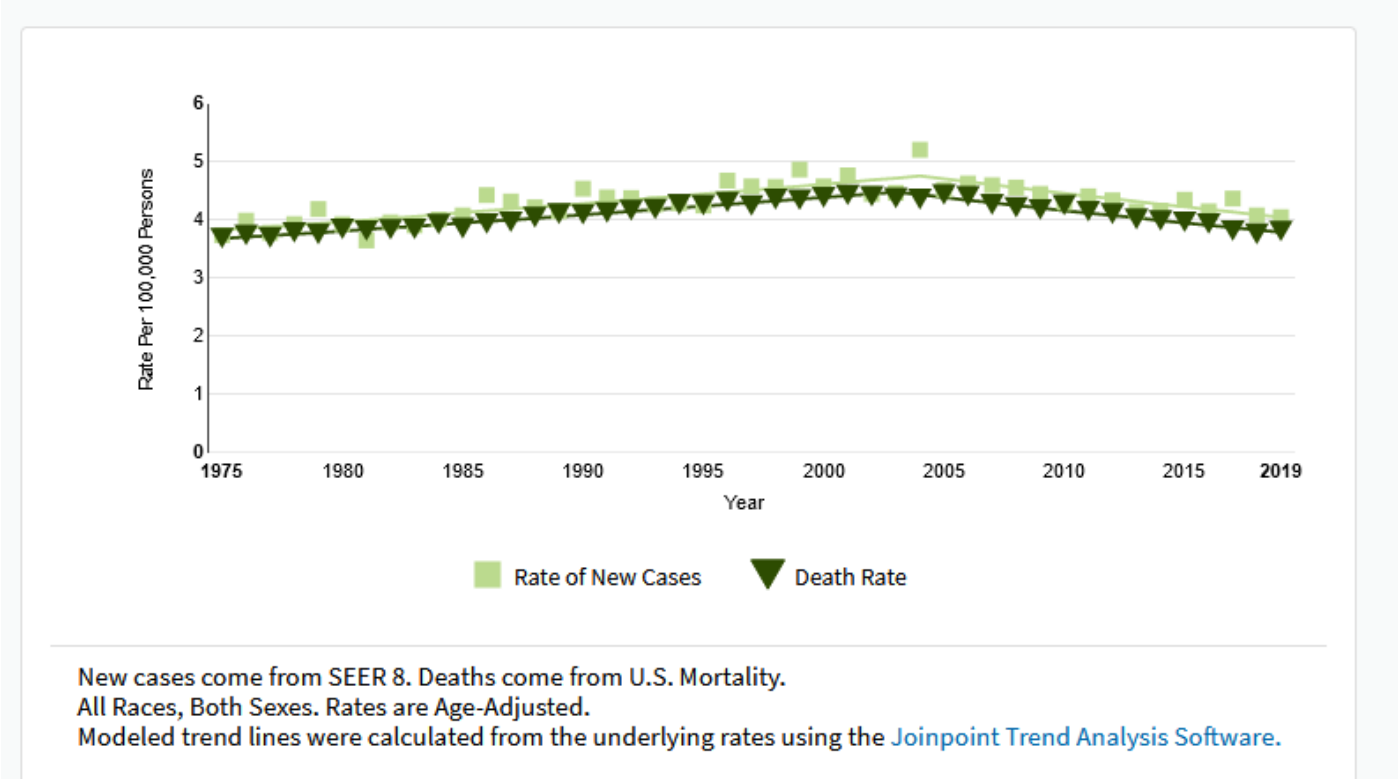
Abstract #671

Alarming Increase in Prevalence of Esophageal Cancer and Barrett's Esophagus in Middle-Aged patients: Findings from a Statewide Database of Over Five Million Patients

B. Qumseya, S. Yang, G. Yi

Background

- SEER 8 database shows plateauing incidence of new esophageal cancer
- Aim: assess prevalence of Barrett's esophagus (BE) and esophageal cancer (EC) based on age group in a large patient database



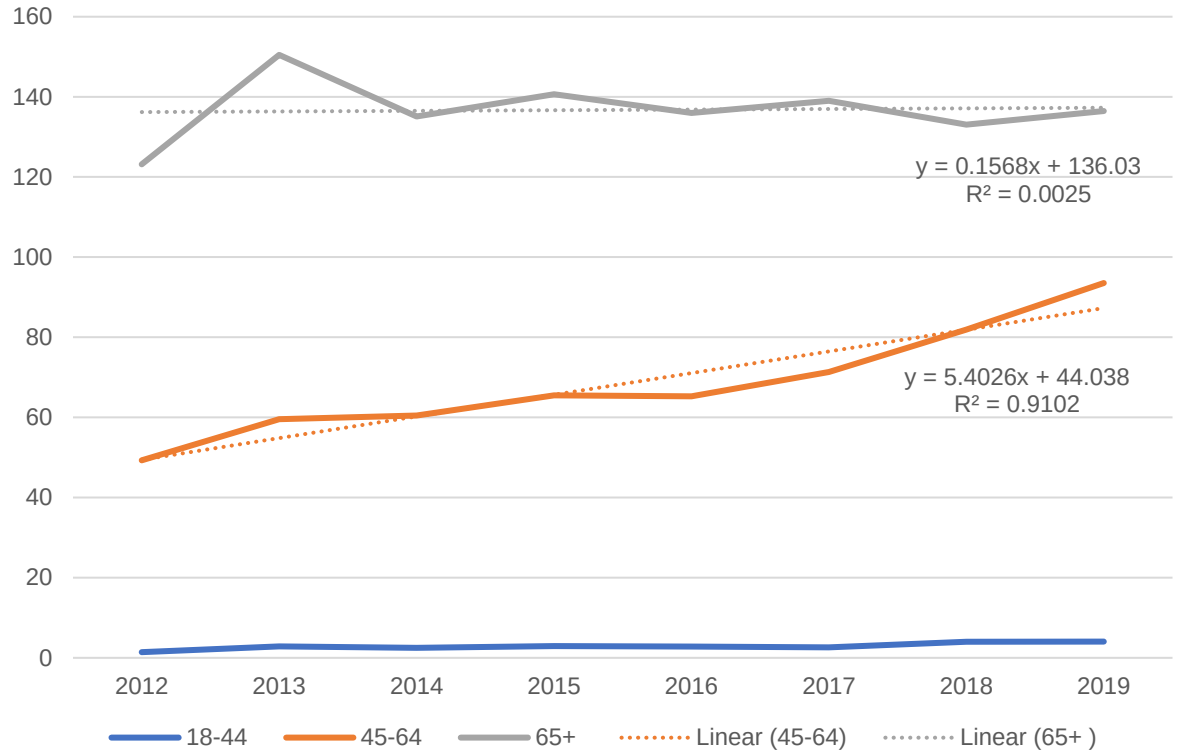
Slides for this abstract courtesy of Dr. Qumseya

Methods

- EHR data from the *OneFlorida* Clinical Data Research Network (covers >40% of Floridians, 4.2-5.4 million patients/year)
- ICD-9/10 codes used to identify patients with diagnoses of BE and EC in the overall population from 2012 to 2019
- Primary outcome: adjusted BE/EC prevalence in the population
  - ➢Adjusted per 100,000 patients
- 3 categories: young (**18-44**), middle-aged (**45-64**), elderly (**65+**)
- Regression analysis used to assess the link between number of risk factors and BE

Esophageal Cancer Prevalence by Age

- Prevalence varied significantly by age group: higher in elderly group ($p<0.0001$)
- EC Prevalence stable over time in elderly group
- Yet, increased from **49**/100K to **94**/100K in the middle-age group in 7 years



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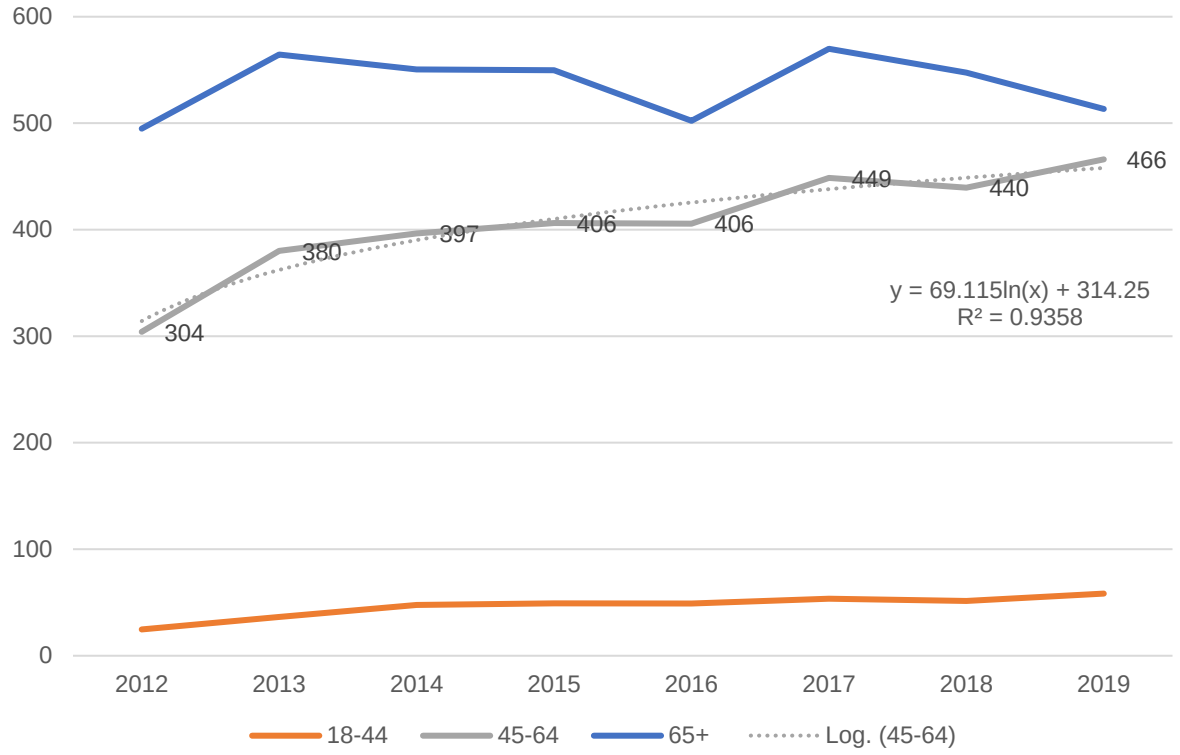
Barrett's Esophagus Prevalence by Age

- Prevalence of BE also increased in the middle-age group
- Rates rose from **304**/100K in 2012 to **466**/100K in 2019



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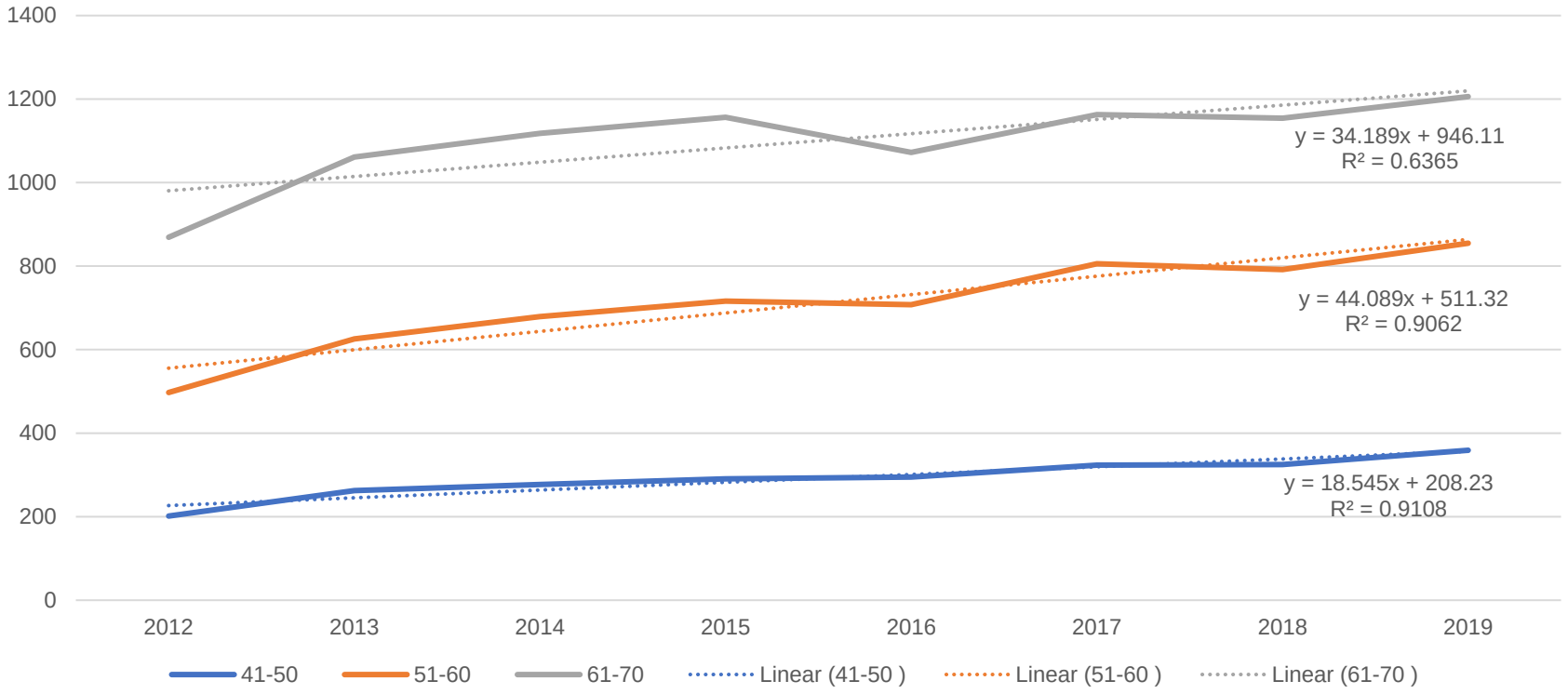
Subgroup Analysis: BE in 41-70 Year Olds

- Subgroup analysis: rate of increase in prevalence was highest in the **51-60** year old age group



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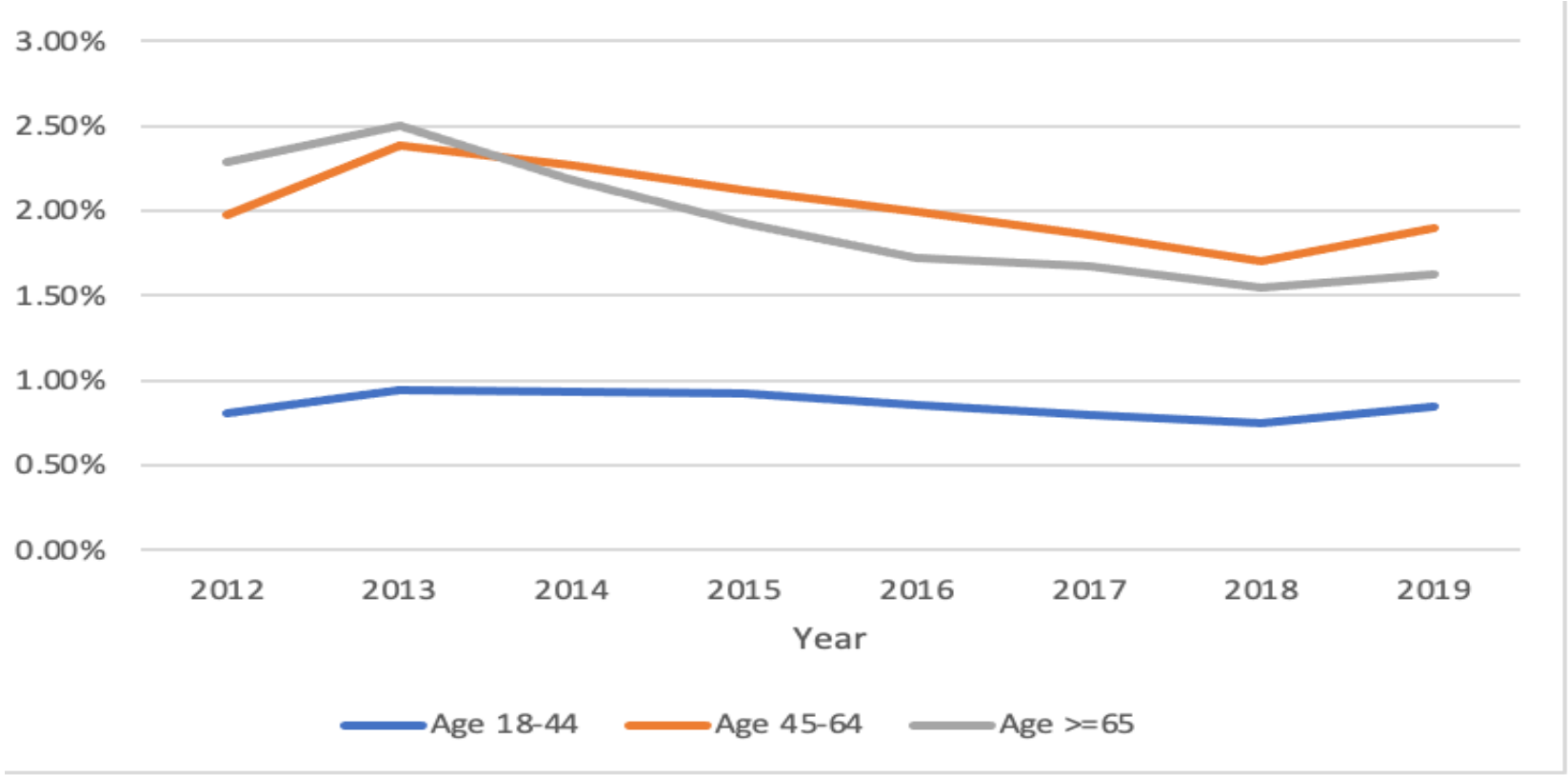
Prevalence Changes Not Due to Endoscopy Utilization

- In the same time period, utilization of EGD in the population was stable



How Does This Affect My Practice?

- The incidence of Barrett's and esophageal cancer in 45-64 year old Floridians rose by **53%** and **92%**, respectively, in just 7 years!
- The greatest rate of increase appears to be in the 51-60 year olds
- Do we need to start thinking earlier about BE-related cancers, just as we have shifted our thoughts on colorectal cancer screening to age 45+?
- Limitations of this study: retrospective study of a less typical BE cohort (more females, less white), no incidence rates yet

Abstract #695

An Objective, Fully Automated Barrett's Risk Prediction Assay Outperforms Pathology in Risk Stratifying Barrett's Esophagus with Low-Grade Dysplasia

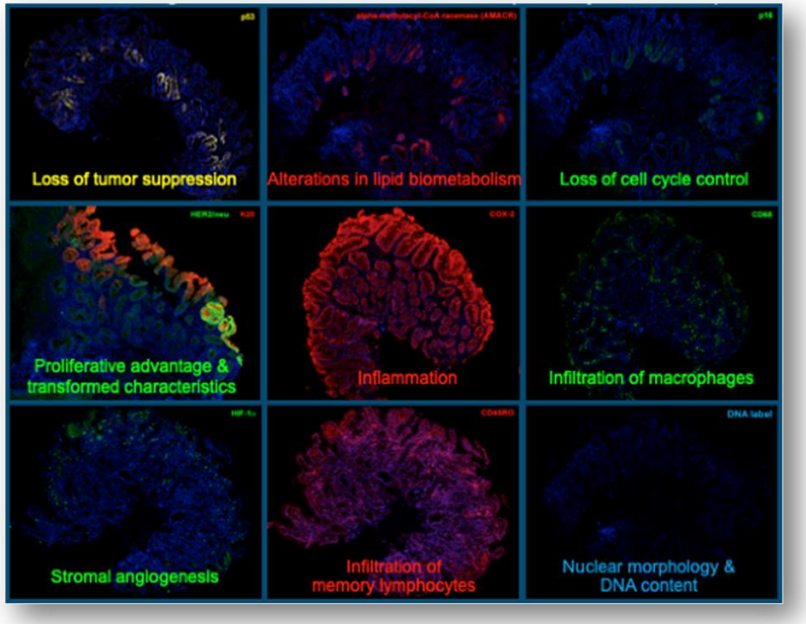
A.M. Khosiwal, N.F. Frei, L.C. Duits, R.E. Pouw, Barrett's SURF LGD Study Pathologist Consortium, E. Bossart, M. Wilhelm, R. Chritchley-Thorne, J.J. Bergman

Background

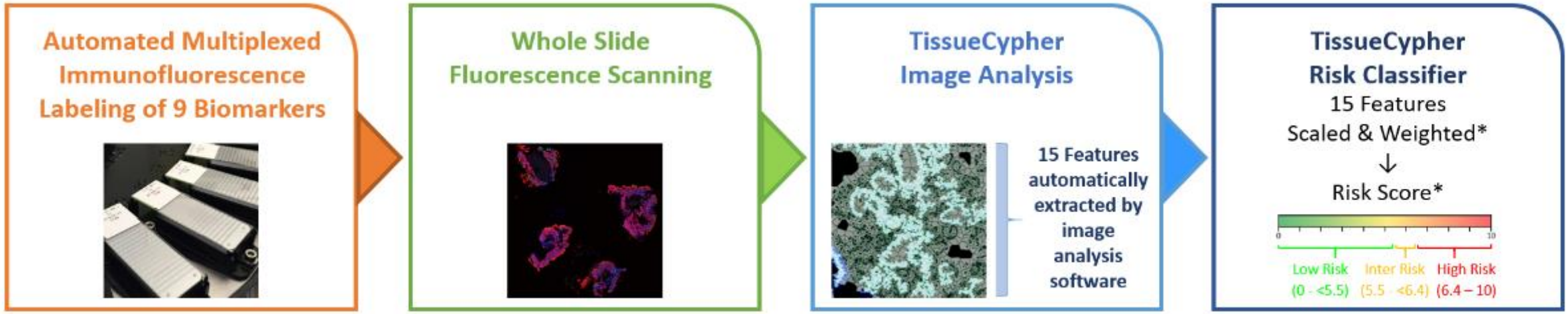
- Low-Grade Dysplasia (LGD) is the strongest predictor of BE progression to High-Grade Dysplasia (HGD) or cancer
- Distinguishing reactive “atypia” from early neoplastic changes can be challenging
- Confirmed LGD progression rates are 10-13% per year, but ~3/4 of cases are downstaged to non-dysplastic disease (NDBE) and carry the standard 0.3% per year progression risk
- But there are issues with “expert review” too—accessibility, logistical challenges and variability to name a few

New Technique for Tissue Analysis

- Measuring key tissue systems processes (epithelial, stromal, including immune, and morphology) in the context of tissue architecture can generate clinically actionable information.
- Quantitative Features/Measures:
  - Biomarker intensities
  - Co-expression of up to 3 biomarkers
  - Ratios of biomarkers
  - Nuclear morphology within tissue compartments and within populations of cells defined by expression of up to 3 biomarkers
  - Microenvironment-based biomarker measurements



How the Technique Works



- 5 independent clinical validation studies in the US and Europe have demonstrated this approach predicts malignant progression in BE patients with clinically impactful sensitivity

Slides for this abstract courtesy of Dr. Bergman

Methods

- 154 patients from the SURF Trial with a community-based diagnosis of LGD followed for a median of 7 years (122 males, mean age 62 yrs, median Prague C3M4)—24 were progressors to HGD or EAC
- All slides reviewed by 15 expert BE pathologists and 15 community-based pathologists, plus tested with the assay
- Primary outcome: 5 year risk of progression to HGD/EAC by the pathologists vs. the assay (high + intermediate risk vs. low risk)

Pathologist Review of Baseline Biopsies

- On average, over 2/3 of samples were downstaged to NDBE (but range of doing so was 12-88%!)
- ~1/8 samples were called as indefinite for dysplasia (another big range 0-75!)
- Progression rates increased as BE stage worsened

	All pathologists
Downstaged to NDBE, (%)	68 [12-88]
IND, (%)	13 [0 – 75]
Confirmed ≥LGD, (%)	19 [8 - 41]
Progression to HGD or cancer during follow-up	
Progression of NDBE, (%)	1.7 [1 - 3.2]
Progression of IND, (%)	3.0 [0 – 6.7]
Progression of ≥LGD, (%)	9.2 [3.9 – 13.3]

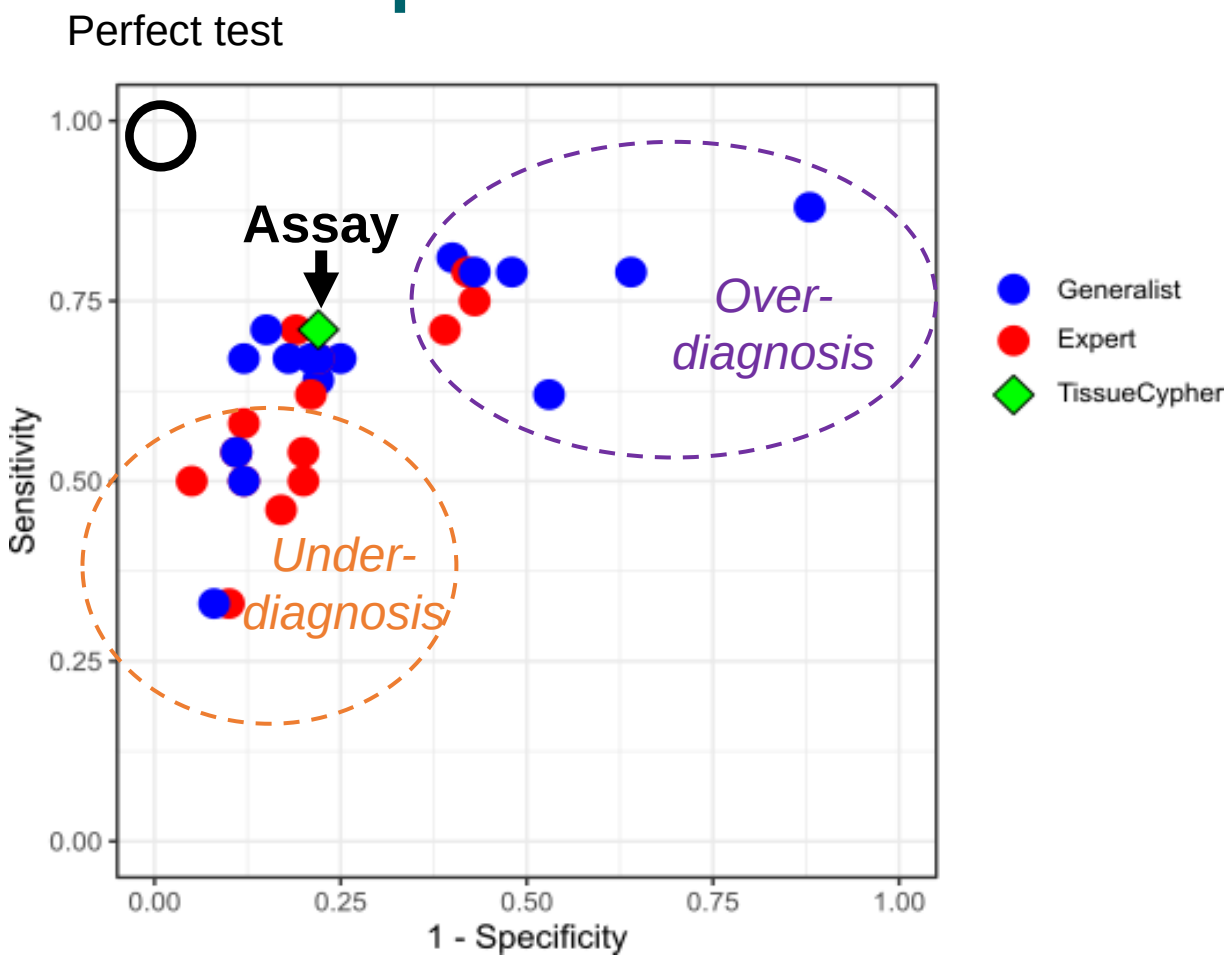
Performance of the Assay

Assay Results	154 Samples With Community-Based LGD	Progressed to HGD/EAC Within 5-Year Follow-Up
Down-staged (Low-risk score (<5.5))	109 (71.0%)	7
Confirmed (Intermediate/high-risk (>5.5))	45 (29.0%)	17

- The assay identified 17/24 progressors (sensitivity **71%**)
- The assay correctly downstaged 109/130 non-progressors (specificity **78%**)

Slides for this abstract courtesy of Dr. Bergman

Comparison of the Assay and Pathologists



	Pathologist Alone	Assay Alone
% Progressors Detected	63.2 [33-88]	**71.4**
Progression Rate in "Positives" (%/yr)	7.1 [3.2-12.6]	**7.6**
Progression Rate in "Negatives" (%/yr)	1.7 [1-3.2]	**1.2**

Assay detects more early progressors

Progression rate with high/intermediate assay result is clinically actionable

Low risk assay results have a lower progression rate

Pathology results extremely variable!

Slides for this abstract courtesy of Dr. Bergman

How Does This Affect My Practice?

- Given the rates of downgrading (and some upgrading) of community-based LGD diagnoses, adding this assay can provide greater confidence in assessment of risk progression
- Even when we have access to “expert” pathologists, the results are highly variable and less consistent than a standardized assay
- The assay evaluated here is easily accessible, highly reproducible, performs as well as the best expert pathologists, outperforms most pathologists, and reduces the chance of underdiagnosing a progressor to HGD or cancer by 43%; should this become a part of our algorithm for assessing LGD pre-ablation?

Abstract #618

Liquid Nitrogen Spray Cryotherapy in the Esophagus is Performed with Minimal Bleeding Risk Regardless of Concurrent Antithrombotic Therapy

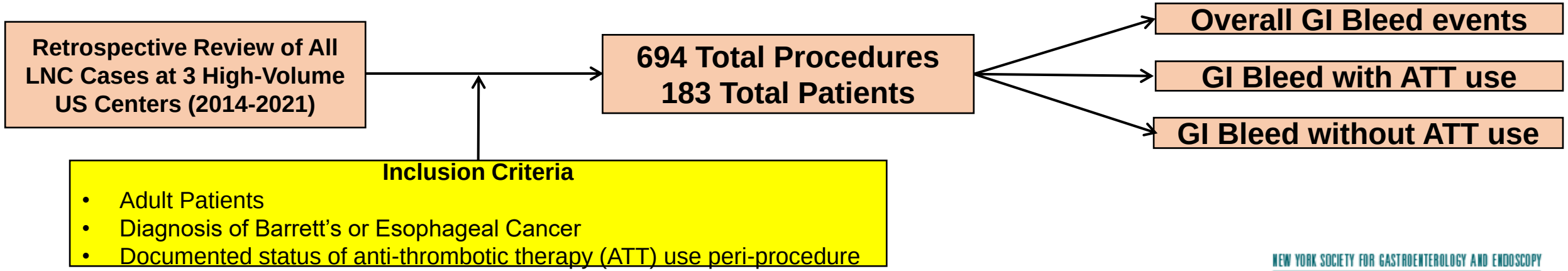
N.R. Sharma, A. Perisetti, R.M. Leibowitz, M. Sehmbhi, E. Park, Z.A. Malik, K.R. Mushtaq, C.M. Zelt, N.J. Talabiska, J. Klein, C.T. Hogan, M.S. Smith

Background

- Liquid nitrogen (-196ºC) delivered via a catheter advanced through the endoscope contacts tissue prior to phase shift, generating ice crystal formation, cell membrane damage, protein denaturation and apoptosis while preserving tissue architecture and extracellular matrix
- Low pressure spray (< 3 psi at site) of non-toxic cryogen
- Treats *en face* or in retroflexion, through stents and over uneven surfaces
- Used in multiple foregut disorders including Barrett's, cancer and GAVE
- Reports of any adverse events are rare (12.2% in recent meta-analysis), with minimal published data on associated GI bleeding

Aims/Study Flow Diagram

- To assess the overall risk of GI bleed in patients undergoing LNC
- To identify frequency of LNC-related bleeds requiring transfusions
- To quantify the risk of LNC-associated GI bleeding with concomitant antithrombotic therapy (ATT) use



Patient Demographics

Patients (n=183)	
Patient Characteristic	*Result*
Age (mean [SD])	67.9 years (10.8)
Gender, Male (%)	142 (77.6%)
Barrett's Esophagus grade (%)	
Non-Dysplastic	34 (18.6%)
Indefinite for Dysplasia	11 (6.0%)
Low Grade Dysplasia (LGD)	41 (22.4%)
High Grade Dysplasia (HGD)	68 (37.2%)
Esophageal cancer (%)	65 (35.5%)
Other Indication (%)	1 (0.55%)
Procedures (n=694)	
Antithrombotic Therapy (ATT) Status (%)	
Continued During LNC	315 (45.4%)
Held For LNC	104 (15.0%)
No Recent/Current ATT	270 (38.9%)
Unknown	5 (0.7%)
ATT Medications (%)	426 (61.4%)
Aspirin (Any Dose)	258 (37.2%)
Clopidogrel	75 (10.8%)
Warfarin	75 (10.8%)
Direct Acting Oral Anticoagulants	59 (8.5%)

- Older heavily male cohort consistent with demographics of Barrett's/esophageal cancer
- ~2/3 of patients treated for BE, ~1/3 for esophageal CA
- **>60%** of patients were on some form of ATT, with at least **74%** (315/426) continuing treatment during LNC

Results

Bleeding Outcomes Requiring Inpatient Treatment			
	No bleeding event	**Bleeding events requiring transfusion**	**Bleeding events requiring fluid resuscitation**
LNC Procedures	689	3 (0.4%)	2 (0.3%)

Bleeding Outcomes by ATT Status				
	No bleeding event	**Bleeding events requiring transfusion**	**Bleeding events requiring fluid resuscitation**	**p***
ATT Held For LNC	104	1 (0.94%)	1 (0.94%)	Ref
ATT Continued During LNC	314	0	1 (0.32%)	n.s.
Unknown	5	0	0	n.s.
No ATT	267	2 (0.75%)	0	n.s.

- 5/694 (0.72%) LNC procedures had associated GI bleeding events
- No mortality noted
- No significant difference noted in bleeding events with or without ATT use

Bleeding Case Details

Subject	ATT use	Comments
1	Aspirin use	• Symptomatic anemia (melena). • Managed conservatively with PPI, IVF for 3 days
2	Aspirin and Clopidogrel use	• Upper GI bleeding (hematemesis) • Upper endoscopy showed esophageal bleeding vessel at prior cryotherapy site requiring clip therapy • Discharged safely post treatment
3	Warfarin	• Symptomatic anemia (hematemesis) • Treated conservatively
4	None	• Upper GI bleeding (coffee ground emesis) • Treated conservatively with packed cells and PPI therapy
5	None	• Symptomatic anemia requiring packed cells. Treatment conservatively

Note: PPI- Proton pump infusion, IVF- Intravenous fluids, GIB- Gastrointestinal Bleeding

- 4 cases required blood transfusion, only 2 of which involved peri-procedure ATT

How Does This Affect My Practice?

- Bleeding events are extremely rare with esophageal LNC
- Peri-procedure ATT use is not associated with an increased risk of hospitalization or transfusion for GI bleeding
- These data strongly support the current practice of administering ATT without interruption while ablating in the esophagus with LNC
- As ATT use increases, LNC allows patients to avoid risking cardiovascular complications by choosing to proceed with ablation
- Safe LNC use on ATT may offer additional advantages, including an enhanced patient experience and cost reduction by avoiding bridging therapies

Please email me with any questions!

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