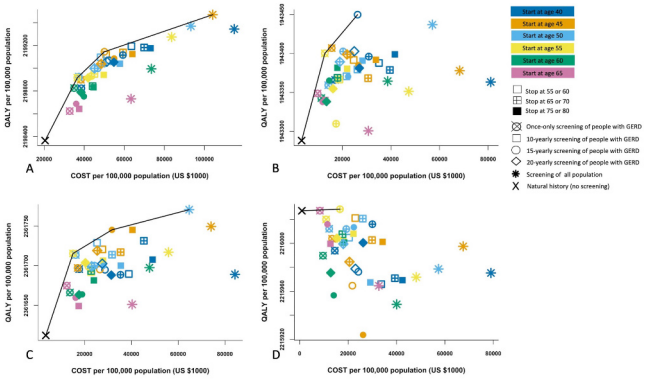

Figure. Cost-Effectiveness Plane of Screening. Panel A: white men, B: black men, C: white women, D: black women. Results are averaged across the three models. Starting age of screening is denoted by color. Frequency of repeated screening is denoted by shape. Stopping age of repeated screening is denoted by open, filled, or cross in the shape. For instance, one time screening of individuals with GERD at age 55 years (1GERD55) is denoted by a yellow open circle with a cross. Black lines connect the strategies that lie on the efficiency frontier. The slope of the line represents the inverse of the incremental cost-effectiveness ratio. GERD: gastroesophageal reflux disease, QALY: quality adjusted life years.

Table. Outcomes of Screening Strategies on Efficiency Frontier

	Clinical EAC	Screen Detected EAC	Total EAC	% EAC Prevented	EAC Deaths	% EAC Deaths Prevented	EGDs	Initial EET	Touch -up EET	Cost ($)	Life Years	QALYs	ICER ($/QALY)
White Men													
No Screening	654	0	654	0.0%	536	0.0%	0	0	0	20,457,639	2,198,517	2,198,365	Reference
GERD at Age 55	462	77	540	17.5%	409	23.6%	36,010	593	376	36,561,587	2,199,071	2,198,917	29,185
GERD at Ages 45 & 60	419	83	502	23.3%	374	30.1%	60,262	781	530	50,073,982	2,199,306	2,199,144	59,363
Entire Population at Age 45	267	191	459	29.9%	289	46.0%	136,427	922	586	104,143,978	2,199,686	2,199,470	166,017
Black Men													
No Screening	105	0	105	0.0%	84	0.0%	0	0	0	3,239,940	1,943,313	1,943,288	Reference
GERD at Age 55	75	11	86	17.4%	64	23.6%	19,867	109	72	12,816,031	1,943,433	1,943,400	85,418
GERD at Ages 40 & 55	72	12	83	20.3%	62	26.6%	37,456	120	91	26,280,546	1,943,496	1,943,450	270,556
White Women													
No Screening	125	0	125	0.0%	103	0.0%	0	0	0	3,406,619	2,361,638	2,361,612	Reference
GERD at Age 55	88	16	104	17.1%	78	24.3%	24,018	157	111	15,033,836	2,361,752	2,361,715	112,311
GERD at Ages 45 & 75	77	18	96	23.5%	70	31.8%	62,437	232	147	31,689,611	2,361,799	2,361,745	557,979
Entire Population at Age 50	37	44	81	35.0%	45	56.1%	108,820	296	193	64,712,882	2,361,859	2,361,771	1,296,411
Black Women													
No Screening	35	0	35	0.0%	29	0.0%	0	0	0	901,714	2,216,034	2,216,027	Reference
GERD at Age 65*	26	7	34	4.7%	23	20.8%	19,906	71	31	8,358,918	2,216,042	2,216,027	*
GERD at Ages 55 & 70	24	7	31	13.2%	21	27.4%	38,263	91	55	16,652,062	2,216,052	2,216,028	12,074,591

EAC: esophageal adenocarcinoma, EET: endoscopic eradication therapy, EGDs: esophagogastroduodenoscopies, GERD: gastroesophageal reflux disease, ICER: incremental cost-effectiveness ratio, QALYs: quality adjusted life-years. All results are per 100,000 individuals. Initial EET incudes 3.55 radiofrequency ablation sessions and 0.55 endoscopic resection sessions. Touch-up EET is one radiofrequency ablation session. Costs, Life Years, and QALYs are discounted. ICERs are compared to the next most effective strategy. Results are per 100,000 individuals. *Screening black women with GERD at age 65 is very close, but not on the efficiency frontier. It is displayed for comparison purposes.

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AN OBJECTIVE, FULLY AUTOMATED BARRETT'S RISK PREDICTION ASSAY OUTPERFORMS MOST PATHOLOGISTS IN RISK STRATIFYING BARRETT'S ESOPHAGUS WITH LOW GRADE DYSPLASIA

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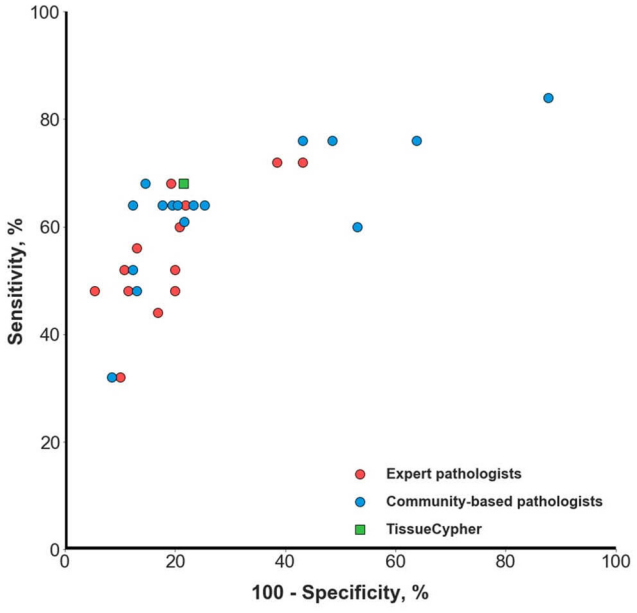
Introduction: Low-grade dysplasia (LGD) is the best predictor of malignant progression in Barrett's Esophagus (BE). LGD is over-diagnosed in up to 75% of community-based cases. Guidelines therefore recommend expert histological revision of LGD. However, it is unclear what defines an expert pathologist and such review is not widely available. TissueCypher is an objective, fully automated BE risk prediction assay which has been previously validated. It analyzes 15 features of 9 biomarkers associated with malignant progression, using multiplexed fluorescence. **Aim:** To evaluate the predictive value of TissueCypher in BE patients with a community-based diagnosis of LGD and to benchmark its performance against an international panel of expert and non-expert pathologists. **Methods:** A cohort of BE patients with community-based LGD was derived from the screening cohort of the randomized SURF trial comparing Surveillance vs. RFA for confirmed LGD. Ten 5-micron slides from all biopsies of the baseline LGD-endoscopy were assessed by TissueCypher, which classifies patients as low-, intermediate- or high-risk for progression to high-grade dysplasia (HGD) or esophageal adenocarcinoma (EAC). Two H&E and 1 p53 immunohistochemistry slides were digitized for histology revision. All digital slides were independently reviewed by 29 pathologists, including 2-3 BE experts and 3-4 community-based pathologists from each of the following countries USA, UK, Germany, Netherlands and Belgium. **Results:** 155 patients (79% male), with a median age of 62±10 years, median BE length of C3M4, median follow-up of 7 years (IQR 4.4-9.7), and a mean number of 3±2 endoscopies, were studied. 25 patients developed HGD/EAC within 5 years (progressors) and 130 did not (non-progressors). The panel of pathologists downstaged a mean of 69% (range 13–88%) LGD cases to NDBE and confirmed LGD in 18% (7–41%) of the cases. Pathologists classified 13% (0–74%) of cases as indefinite for dysplasia (IND). TissueCypher downstaged 71% of the cases to low-risk and scored 29% of the cases intermediate/high risk for progression. Sensitivity and specificity of TissueCypher and pathologists for predicting progression is shown in Table 1 and Figure 1. Pathologists showed significant variability in sensitivity (range 32-84%) and specificity (12-95%). TissueCypher had a sensitivity for identifying progressors that outperformed 79% of pathologists (85% of experts and 75% of non-experts) , while having a specificity in line with most pathologists. The 6 pathologists (21%) with a higher sensitivity than TissueCypher had unacceptable low specificity rates (Fig 1) **Conclusion**: Histological review of community-based LGD showed a high inter-observer variability with a significant number of cases classified as non-informative. TissueCypher provides an objective reassessment of LGD, outperforming the vast majority of pathologists.

Table 1. Sensitivity and specificity of TissueCypher, expert pathologists, community-based pathologists

Progression to HGD/EAC within 5 years	TissueCypher	Expert pathologists (n=13)	Community-based pathologists (n=16)
	High/Intermediate *vs.* Low Risk Score	LGD+IND *vs.* NDBE	LGD+IND *vs.* NDBE
Sensitivity, %	68	55 (32-72)	64 (32-84)
Specificity, %	79	81 (57-95)	70 (12-92)

For pathologists, sensitivity and specificity is shown as percentage and (range)

Figure 1: Visualization of the predictive accuracy of TissueCypher and individual pathologists.



Perfect score is in the left upper corner. Pathologist diagnoses were assessed as LGD+IND vs. NDBE.

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EVALUATING A NOVEL ELECTRONIC PATIENT-REPORTED OUTCOME TOOL FOR ASSESSING PAIN PHENOTYPES IN ADULTS WITH CHRONIC PANCREATITIS

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BACKGROUND AND AIMS. Chronic pancreatitis (CP) is a fibro-inflammatory disease affecting over 80% of patients with abdominal pain, and associated with high rates of anxiety, depression, and pain catastrophizing tendencies. Pancreatic quantitative sensory testing (P-QST) is a neurosensory testing technique designed to evaluate nociception and identify patterns of hyperalgesia and has done so independent of psychiatric comorbidity. The unique features of visceral CP pain make existing patient-reported outcome (PRO) tools used for testing somatic pain hard to interpret. Advances in technology allow for the creation of more sophisticated, patient-centered, digital PRO tools that can meet the unique needs of CP patients. Aims of this study were to determine if a new electronic animation-based PRO tool can 1) differentiate CP pain from chronic somatic pain, and 2) determine whether the characteristics of pain described using the electronic PRO tool associate with P-QST phenotypes or catastrophizing. METHODS. Participants with painful CP and control patients with history of chronic, non-abdominal somatic pain were enrolled. All participants completed *Painimation* - an electronic, animation-based PRO tool to assess pain location, quality, and intensity among adults with chronic pain - on a mobile tablet, as well as a paper version of the Pain Catastrophizing Scale (PCS). All participants underwent P-QST testing for nociceptive phenotyping. *Painimation* data was compared between patients with CP and controls. P-QST phenotypes were compared between CP and controls. T-tests, Chi square and Fisher's exact test were used to test the association between *Painimation* responses, P-QST phenotypes, and PCS scores. RESULTS. A total of 34 CP patients (mean age 51.9, 35% male) and 22 control patients (mean age 50.5, 64% male) were enrolled. Patients with CP were significantly more likely than controls to choose the "stabbing" graphic (or painimation) (50% vs 18.1%, p=0.02). No significant differences were seen between CP patients and controls for choice of other painimations (Table 1). Hyperalgesia was seen more frequently in patients with CP than in controls (61.8% vs 22.7%) (p=0.004), though its presence was not associated with significantly higher PCS score. Among selections of painimations by all patients, the choice of "burning" graphic was associated with a significantly higher PCS score (Table 2). CONCLUSION. In CP patients, choice of the stabbing painimation appears to differentiate CP patients