ISDE
19th ISDE World Congress for Esophageal Diseases
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A novel serum glycoprotein biomarker panel for screening of esophageal adenocarcinoma and surveillance of Barrett's esophagus

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Disclosures

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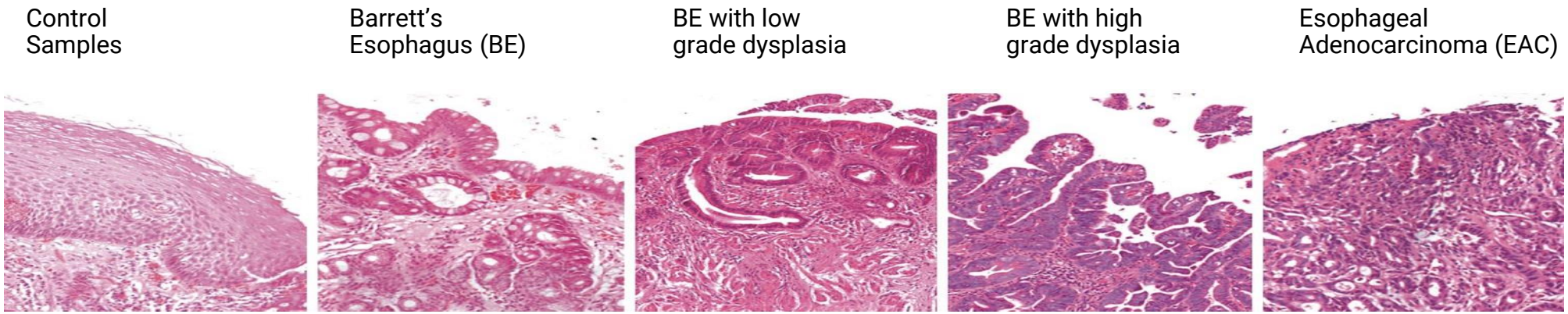
- The biomarker concentrations were measured by Proteomics International, and the risk scores were calculated using a proprietary algorithm
- This analysis used archived samples received via a collaboration with the QIMR Berghofer Medical Research Institute
- The study was funded by Proteomics International
- Presenter disclosures: Lipscombe is an employee and shareholder of Proteomics International Laboratories Ltd, which is the license owner of a patent covering the use of the biomarkers, consequently, Lipscombe may receive financial benefit from the commercial use of any test

Early detection enables simpler treatments

A precision diagnostics perspective

Introduction

- The overall five-year survival rate for esophageal cancer is approximately 20%
- An estimated 10-15% of patients with chronic acid reflux develop Barrett's Esophagus (BE), which has estimated prevalence of 1-2%.
- Currently patients with BE usually undergo endoscopy-biopsy surveillance with the degree of dysplasia assessed by histology



Aim

- **To develop a simple blood test for the diagnosis of esophageal adenocarcinoma (EAC) and Barrett's Esophagus (BE)**
- **To validate diagnostics models to screen EAC and BE based on a panel of glycoprotein biomarkers**

Study Design

- **Development cohort (N=249):** Participants from The Progression of Barrett's Esophagus to Cancer Network (PROBE-NET) study, Australia
- **Validation cohort (N=49):** Participants collected at Ochsner Healthy System, New Orleans, United States

Group 1 - Controls	Group 2	Group 3	Group 4
Samples with normal endoscopy	BE without/with low grade dysplasia	BE with high grade dysplasia	Esophageal Adenocarcinoma

Samples tested by endoscopy and biopsy

- Potential biomarkers analysed using a proteomics workflow, adapted for **glycoprotein** selection using a lectin magnetic bead array followed by targeted mass spectrometry (LC-MRM-MS)
- Multivariate regression performed

Serum | Bead-lectin capture | Analyse | Quantify

Robust
- Intraday CV is 9.3%
- Interday CV is 11.5%

Results - I

Development cohort (N=249)

- Five **glycoproteins** were found to show statistical correlation with disease state progression
- Three of these proteins remained significant after adjusting for patient age and sex

Validation cohort (N=49)

Controls versus EAC (Group 1 vs Group 4):

Model performance (N=24)	
Validation cohort:	
AUC (95% CI)	0.94 (0.85 – 1.00)
Sensitivity (%)	80%
Specificity (%)	93%
PPV(%)	89%
NPV(%)	87%

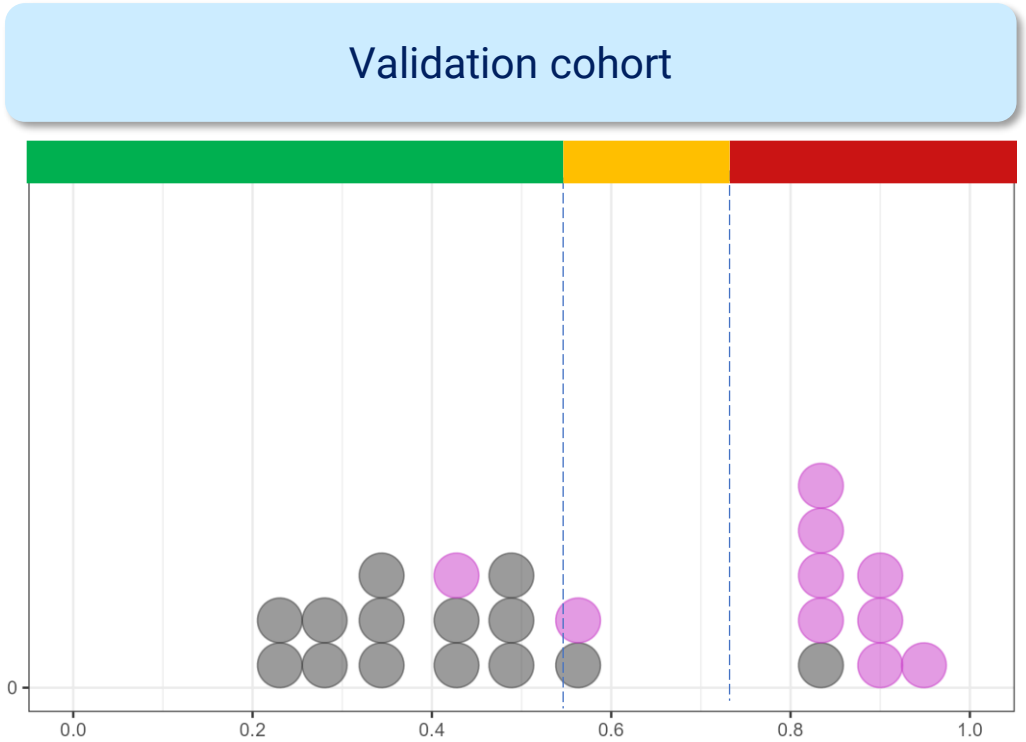
Controls versus BE-HGD & EAC (Group 1 vs Group 3+4):

Model performance (N=31)	
Validation cohort:	
AUC (95% CI)	0.79 (0.70 – 0.88)
Sensitivity (%)	59%
Specificity (%)	93%
PPV(%)	91%
NPV(%)	65%

Results - II

Controls versus EAC (Group 1 vs Group 4):

Frequency dot plot of Control and EAC



n = 14 controls

n = 10 EAC

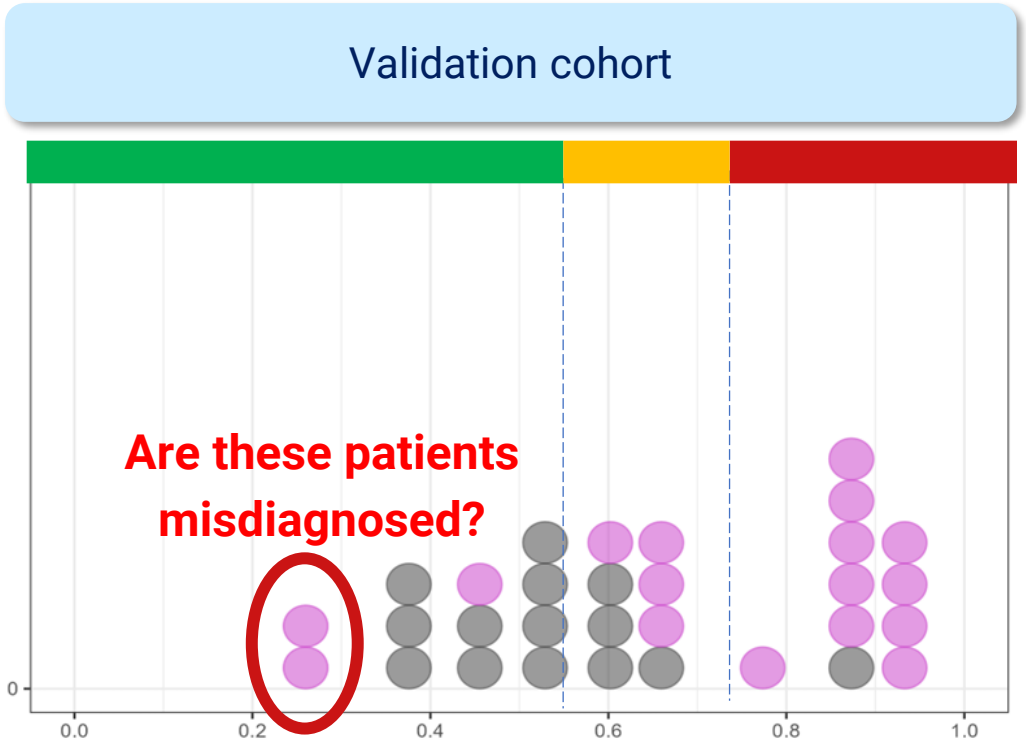
Classification	EAC	Controls	Accuracy
Red High probability	8	1	89%
Amber Moderate	1	1	
Green Low probability	1	12	92%

Traffic light system indicates if a patient is at risk of having EAC

Results - III

Controls versus BE-HGD & EAC (Group 1 vs Group 3+4):

Frequency dot plot of Control and BE-HGD & EAC



n = 14 controls

n = 17 BE-HGD & EAC

Classification	BE-HGD & EAC	Controls	Accuracy
Red High probability	10	1	91%
Amber Moderate	4	4	
Green Low probability	3	9	75%

Traffic light system indicates if a patient is at risk of having BE-HGD & EAC

Conclusions

- Panel of novel serum biomarkers (glycoproteins) were validated as showing significant correlation with esophageal adenocarcinoma and Barrett's esophagus with *high* grade dysplasia
- Diagnostic model developed as a potential simple screening tool for differentiating patients:
  - with EAC from negative controls
  - who required endoscopic surveillance (BE-HGD & EAC) from negative controls

- Further work required on larger cohorts to:
  - confirm diagnostic accuracy of test
  - establish a potential diagnostic tool to differentiate patients who require endoscopic surveillance (BE-HGD & EAC) from patients having BE with *low* grade/no dysplasia

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Thank you!

PILL Proteomics International

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Endometriosis — PromarkerEndo

Diabetic Kidney Disease — PromarkerD