



Proteomics International

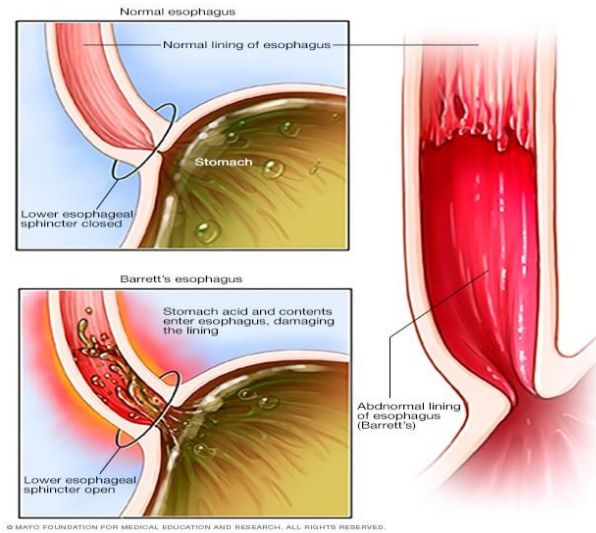
Development of a lectin bead-based diagnostic test for oesophageal cancer

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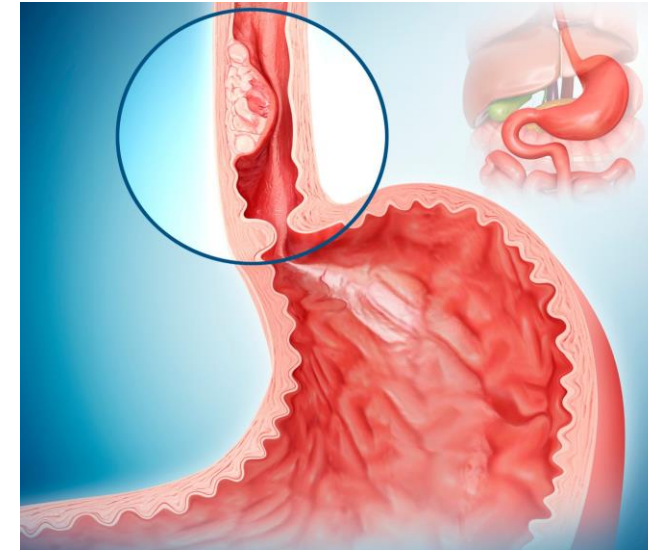
February 2023

Barrett's Oesophagus (BO)



Only known precursor

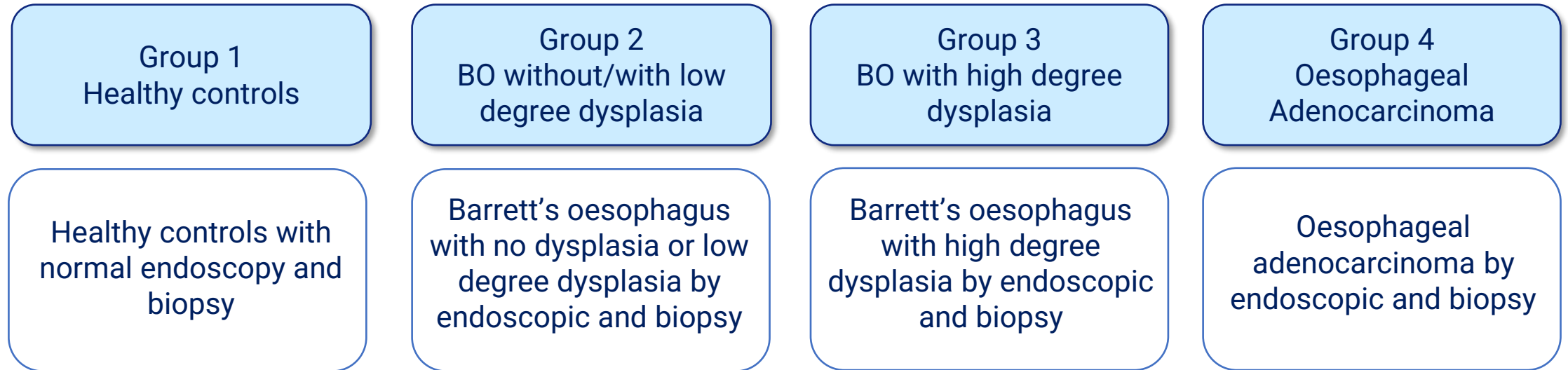
Oesophageal Adenocarcinoma (OAC)



- OAC is the most common form of oesophageal cancer in Australia. The overall five-year survival rate for oesophageal cancer is ~20%, but survival rates can range from 5% to 47%.
- An estimated 10-15% of patients with chronic acid reflux develop BO, which estimated prevalence is 2-5%.
- Currently, patients with Barrett's Oesophagus (BO) usually undergo endoscopy-biopsy surveillance with the degree of dysplasia assessed by histology to monitor risk of neoplastic progression.
- There is an unmet need to develop a costly and minimally invasive diagnostic procedure for cost-effectiveness screening and surveillance of at-risk populations.

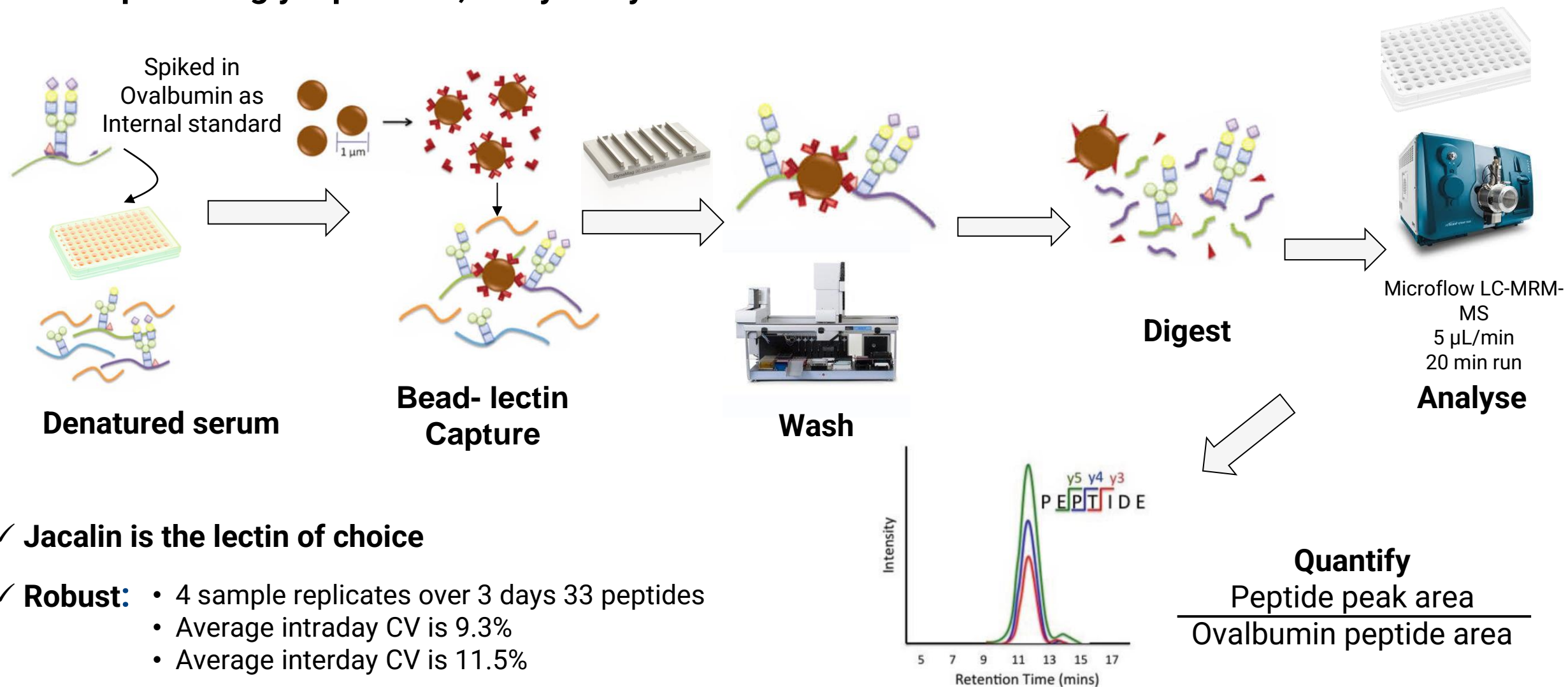
- This study aims to identify serum protein biomarkers associated with oesophageal adenocarcinoma by using the lectin magnetic bead array-coupled tandem mass spectrometry method.
- To develop a diagnostic model to differentiate samples from participants with oesophageal adenocarcinoma and Barrett's Oesophagus versus participants from healthy control group.

- Serum samples from approximately 300 participants across four clinical groups were used to validate potential biomarkers using a proteomics (targeted mass spectrometry) workflow.



- **Development cohort (N=249):** Participants from The Progression of Barrett's Oesophagus to Cancer Network (PROBE-NET) study
- **Validation cohort (N=49):** Participants collected at Ochsner Healthy System, New Orleans, United States were analysed as validation cohort.
- Panels of biomarkers statistically associated with Barrett's Oesophagus with high degree dysplasia and oesophageal adenocarcinoma will be selected as candidate biomarker for further model development.

Lectin capture of glycoproteins, analysis by LC-MS/MS

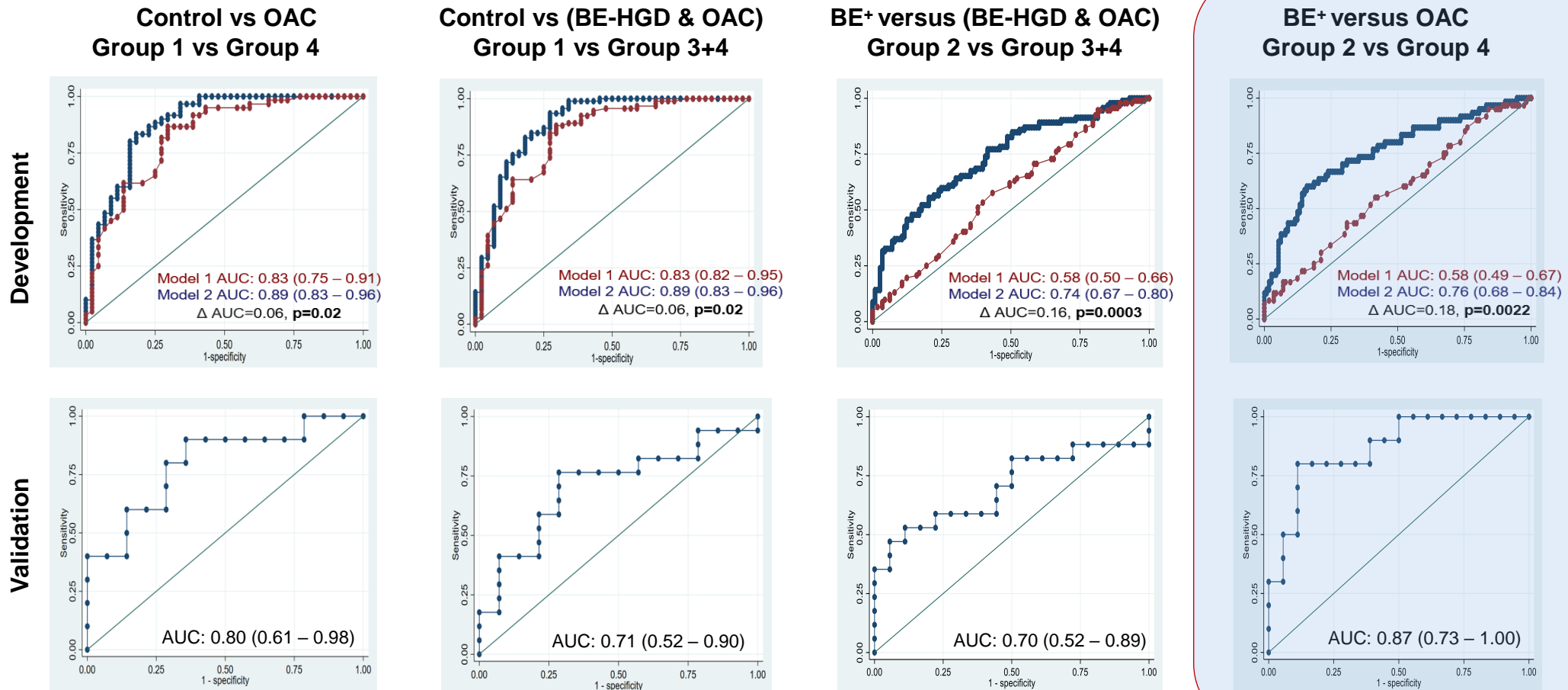


✓ **Jacalin is the lectin of choice**

- ✓ **Robust:**
- 4 sample replicates over 3 days 33 peptides
 - Average intraday CV is 9.3%
 - Average interday CV is 11.5%

Results

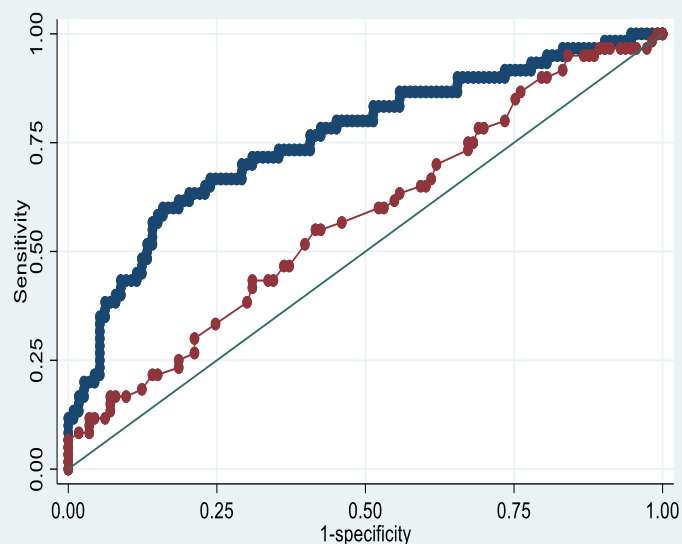
Receiving Operative Curve (ROC) generated by selected biomarkers with demographic factors (age and sex) and ROC generated by demographic factors only showed as followed:



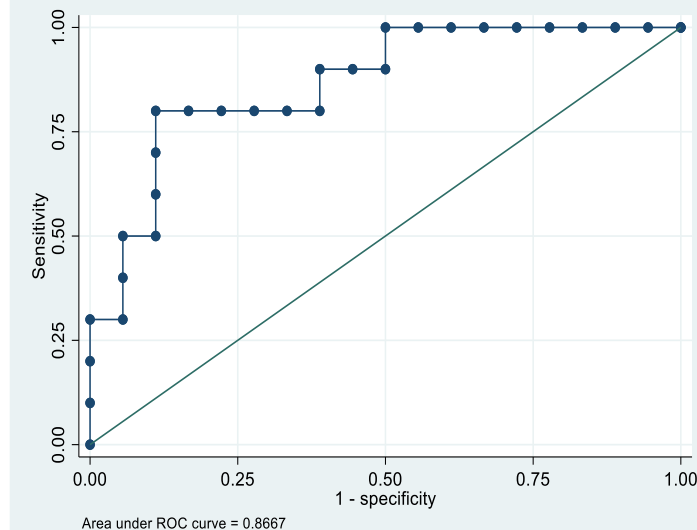
BE+ versus OAC (Group 2 vs Group 4):

Model performance in Development cohort and Validation cohort

Development cohort



Validation cohort



Model performance

Development cohort:

Base clinical model	
AUC (95% CI)	0.58 (0.49 – 0.67)
Biomarker model	
AUC (95% CI)	0.76 (0.68 – 0.84)
Sensitivity (%)	60%
Specificity (%)	84%
Δ AUC, p	0.18, $p=0.0022$

Validation cohort:

AUC (95% CI)	0.87 (0.73 – 1.00)
Sensitivity (%)	80%
Specificity (%)	89%

- A panel of serum biomarkers associated with oesophageal adenocarcinoma and Barrett's oesophagus with high grade dysplasia.
- A series of diagnostic models were developed where novel plasma biomarkers added significant independent value to clinical variables for diagnosing oesophageal adenocarcinoma, including:
 - comparison to participants from healthy control group;
 - identifying patients who requires further treatment intervention;
- *Proteomics International seeks clinical cohorts for the validation of a simple blood test to detect the early stages of oesophageal adenocarcinoma. .*
- ***For seeking collaboration: info@proteomics.com.au***

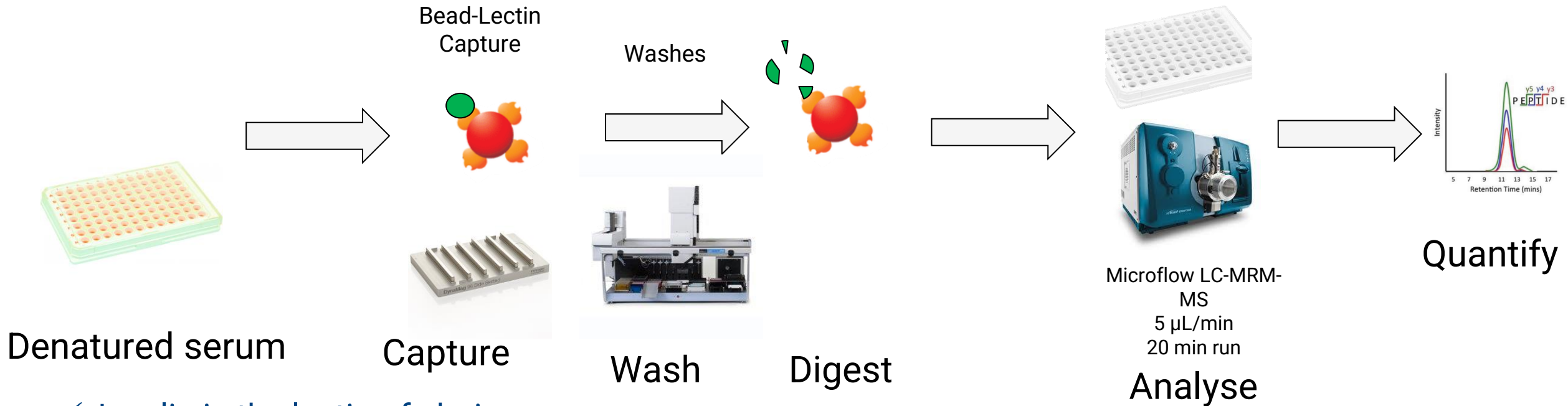
Appendices (unlikely to have time for these slides)

Summary of model performance

	Control versus OAC Group 1 vs 4	Control versus (BE-HGD & OAC) Group 1 vs (3+4)	BE ⁺ versus (BE-HGD & OAC) Group 2 vs (3+4)	BE ⁺ versus OAC Group 2 vs 4
Development cohort:				
Sample size	44 vs 60	44 vs 92	117 vs 92	117 vs 60
Clinical model (age, sex) AUC (95% CI)	0.83 (0.75 – 0.91)	0.83 (0.82 – 0.95)	0.58 (0.50 – 0.66)	0.58 (0.49 – 0.67)
Clinical + Biomarkers AUC (95% CI)	0.89 (0.83 – 0.96)	0.89 (0.83 – 0.96)	0.74 (0.67 – 0.80)	0.76 (0.68 – 0.84)
Δ AUC	0.06	0.06	0.16	0.18
p values	0.02	0.02	0.0003	0.0022
Sensitivity (%)	83%	93%	77%	60%
Specificity (%)	82%	73%	58%	84%
Validation cohort:				
Sample size	14 vs 10	14 vs 17	18 vs 17	18 vs 10
AUC (95% CI)	0.80 (0.61 – 0.98)	0.71 (0.52 – 0.90)	0.70 (0.52 – 0.89)	0.87 (0.73 – 1.00)
Sensitivity (%)	90%	76%	53%	80%
Specificity (%)	64%	71%	89%	89%

Method (old slide)

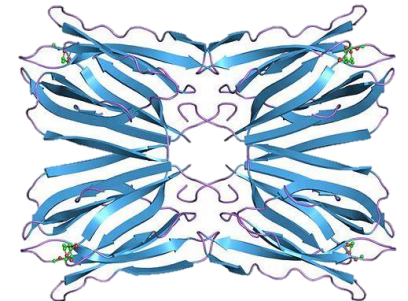
Lectin capture of glycoproteins, analysis by LC-MS/MS



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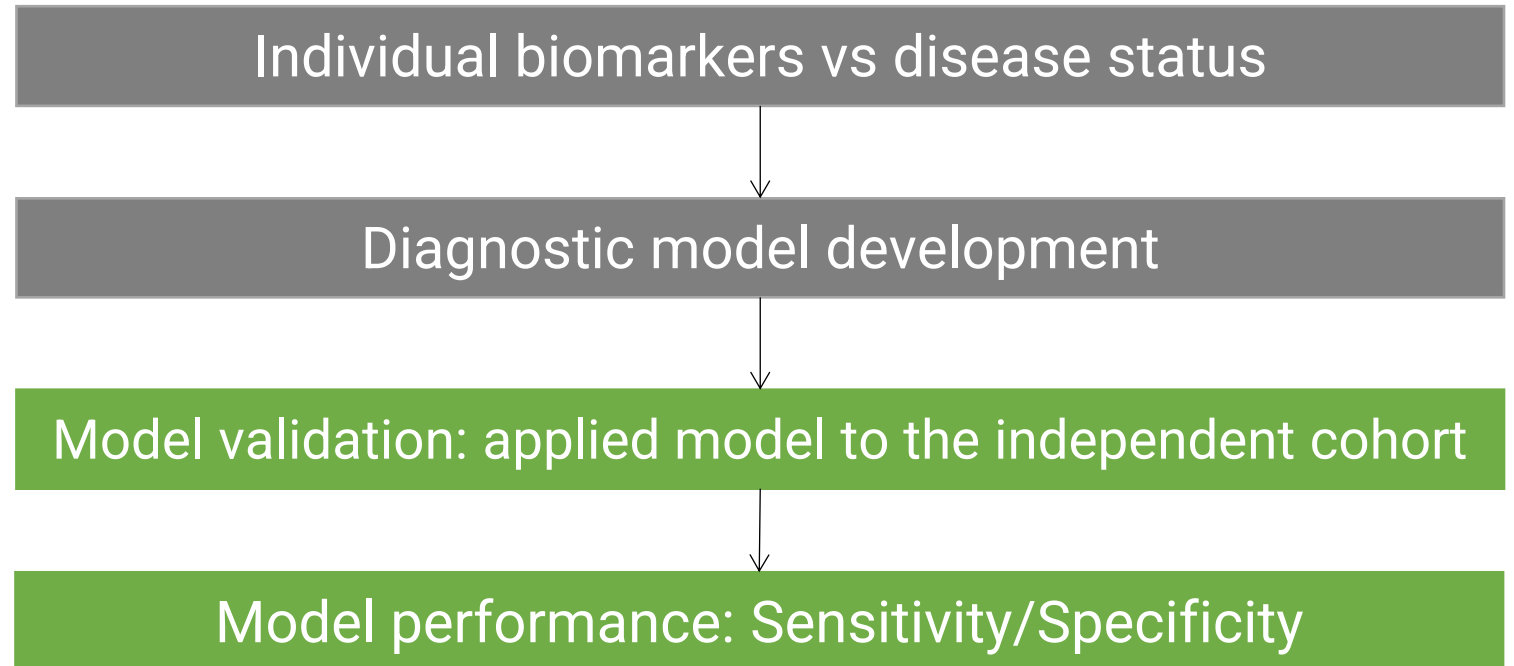
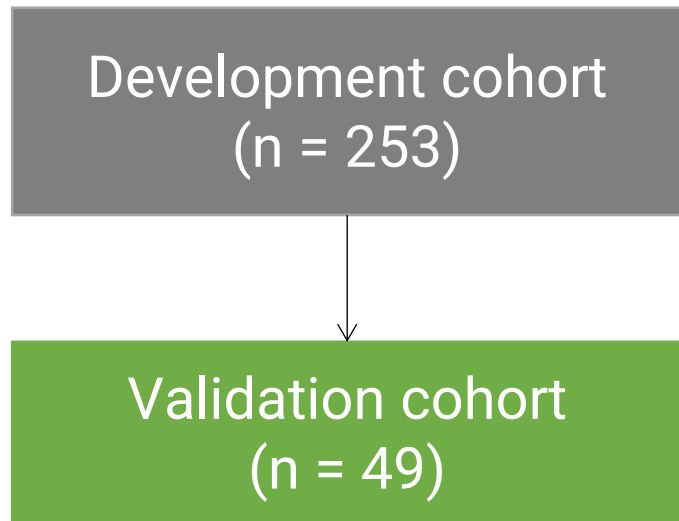
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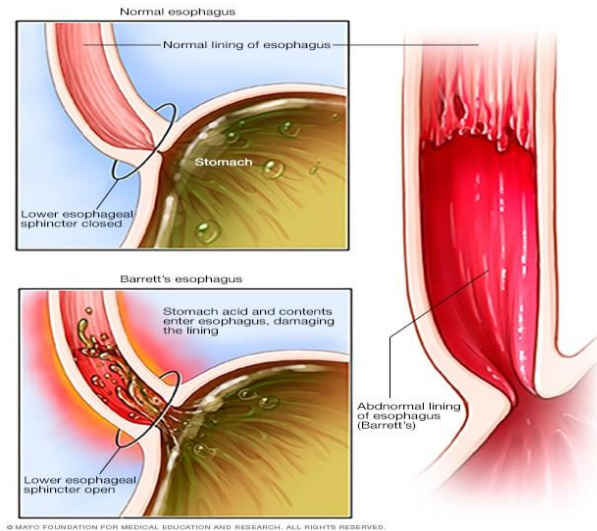
Group comparison:



Data analysis:

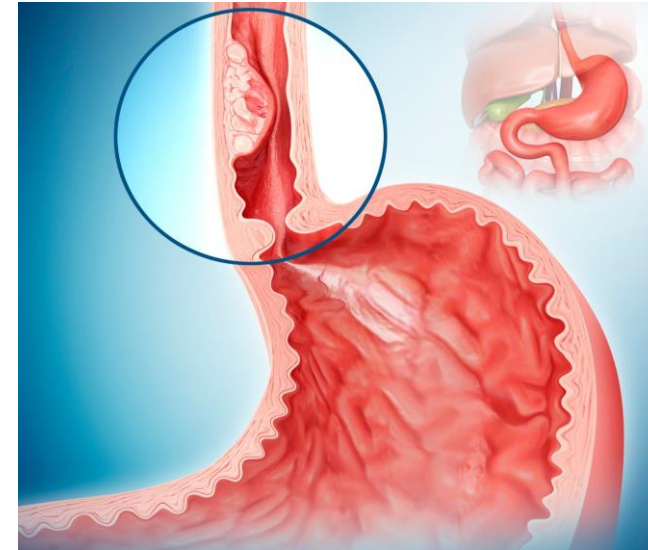


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