ASX release
27 September 2022

ASX code: PIQ

New Promarker test for Oesophageal Cancer demonstrates strong diagnostic performance

- **Prototype version of potential ground-breaking test for oesophageal cancer correctly identified up to 90 in 100 people with the disease**
- **Milestone a significant step in the development of a simple blood test for oesophageal cancer following the study of 300 patients across two independent clinical cohorts**
- **Results presented at the International Society for Diseases of the Esophagus 18th World Congress (ISDE 2022) held virtually and in Tokyo, Japan 26-28 September 2022**
- **Test targets both oesophageal adenocarcinoma and patients with pre-malignant condition Barrett's oesophagus which affects 1-2% of adults and can arise from chronic acid reflux**
- **Current screening requires a specialist endoscopy procedure and the annual expenditure on treating oesophageal cancer in the US is $2.9 billion with a five-year survival rate <20%**

Proteomics International Laboratories Ltd (Proteomics International; ASX: PIQ) is pleased to announce its prototype diagnostic test for oesophageal adenocarcinoma has shown strong diagnostic performance detecting up to 90% of people with the frequently fatal condition. The results were presented overnight at the 18th World Congress for Esophageal Diseases being held virtually, and in Tokyo, Japan 26-28 September 2022.

Oesophageal adenocarcinoma is the most common form of oesophageal cancer and is an area of significant unmet medical need, with current screening requiring a specialist endoscopy procedure that costs US$2,750 per patient in the United States[1], where the total expenditure on treating oesophageal cancer was $2.9 billion in 2018[2]. The overall five-year survival rate for this cancer is less than 20%, and 1 in 20 cancer deaths worldwide in 2018 were attributed to oesophageal cancer[3].

Proteomics International Managing Director Dr Richard Lipscombe said the results were an exciting milestone in the development of a new accurate, easy to use test for oesophageal adenocarcinoma using biomarkers—protein 'fingerprints' in the blood—to diagnose the disease.

The test is targeted at both oesophageal adenocarcinoma and patients with Barrett's oesophagus, a pre-malignant condition associated with an increased risk of oesophageal adenocarcinoma. An estimated 10-15% of patients with chronic acid reflux develop Barrett's oesophagus, a condition which is asymptomatic and affects 1-2% of Western populations[4]. People with Barrett's oesophagus are much more likely to get oesophageal adenocarcinoma, and are advised to get regular endoscopies to screen for oesophageal cancer [PIQ Annual Report 2022].

Dr Lipscombe said, "*These results form the basis for a simple blood test for the disease. It's a*

[1] www.newchoicehealth.com/endoscopy
[2] *JAMA Netw Open,* 2021;. doi:10.1001/jamanetworkopen.2021.27784
[3] Nature Reviews Gastroenterology & Hepatology, 2021, doi.org/10.1038/s41575-021-00419-3
[4] American Society for Gastrointestinal Endoscopy, www.asge.org

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significant step towards diagnosing this cancer earlier without the need for an endoscopy."

The Oesophageal Cancer Diagnostic is Proteomics International's latest test from the Company's Promarker™ pipeline. The results build on a successful collaboration with the QIMR Berghofer Medical Research Institute [ASX: 4 February 2022] which validated a select panel of biomarkers in a study of more than 300 patients across two independent clinical cohorts. Proteomics International owns the exclusive worldwide rights to commercialise the biomarkers, which are patented in multiple jurisdictions [ASX: 21 June 2022].

In the current study a series of statistical models were developed to assess the accuracy of the biomarker panel in diagnosing different levels of disease severity, from oesophageal adenocarcinoma to a comparison with the pre-malignant condition of Barrett's oesophagus as well as a comparison to healthy controls.

These novel diagnostic tools demonstrated that the biomarkers added statistically significant (P<0.05) performance to the clinical models, with the validated performance for sensitivity (Sn) of 76-90% across the key categories, with specificity (Sp) of 64-89%, and Area Under the Curve (AUC) scores of 0.71-0.87.

For comparison, the statistical performance of the Prostate-Specific Antigen (PSA) diagnostic test (blood test measuring the concentration of the PSA protein) for the diagnosis of prostate cancer is[5]:

- Prostate cancer versus no cancer: AUC 0.68, P = <0.001
- PSA cut-off threshold 3ng/ml: Sensitivity 32%, Specificity 87%

Dr Lipscombe said the next steps in commercialising the prototype test are to:

- further develop the statistical modelling to improve the test's sensitivity and specificity. This will use the 'traffic light' system developed for the Company's PromarkerD predictive test for diabetic kidney disease;
- refine the reproducibility of the biomarker measurements to produce a test suitable for the US Laboratory Developed Test (LDT) pathway via CLIA certified clinical laboratories;
- confirm the clinical performance of the test in an additional independent patient cohort;
- conduct formal Economic Health Benefit Modelling and Clinical Utility Studies to demonstrate how the new test could significantly change doctors' treatment decisions and improve outcomes for patients and healthcare systems.

The Company anticipates that these additional analyses will be completed in stages over the next 12 months. If successful, the outcome would be a clinically validated blood test able to offer simpler and earlier diagnosis of oesophageal adenocarcinoma and the pre-malignant sub-categories of the disease. Proteomics International believes a validated test will garner significant interest, both commercially and in the clinic.

International Society for Diseases of the Esophagus 18th World Congress 2022, Oral presentation OA03.06; [copy attached; summary below]

Titled: *Establishing a Mass Spectrometry based diagnostic Test for Oesophageal Cancer*

Marisa Duong[1], Scott Bringans[1], Katherine Chen[1], Gareth Fernadez[1], Tammy Casey[1], Connor Laming[1], Patsy Di Prinzio[1], Michelle Hill[2], Richard Lipscombe[1]

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Summary of the Diagnostic Model Development Study

Method: To generate the diagnostic test Proteomics International's scientists analysed clinical

[5] pubmed.ncbi.nlm.nih.gov/15998892/

samples from a “development cohort” of 253 people collected by the Progression of Barrett’s Esophagus to Cancer Network (PROBE-NET, Australia). Patients were classified as having oesophageal adenocarcinoma [OAC]; positive for Barrett’s esophagus [BE+]; Barrett’s esophagus with High Grade Dysplasia (severely abnormal cells) [BE-HGD]; healthy controls. A series of statistical models were then built using clinical variables and protein biomarkers to attain optimal diagnostic performance in the development cohort. The performance of the statistical models was then tested in an independent “validation cohort” of 49 patient samples from the Ochsner Health System in New Orleans, United States.

Results: Selected diagnostic models for discriminating disease severity performed strongly in both the development and validation cohorts:

- For Healthy controls vs oesophageal adenocarcinoma: (Validation cohort) AUC 0.80, Sn 90%, Sp 64%. Comment: offers the potential to provide an early screening tool to minimise the requirements for an endoscopy.
- For Barrett’s oesophagus (pre-malignant) vs oesophageal adenocarcinoma positive by endoscopy: (Validation cohort) AUC 0.87, Sn 80%, Sp 89%. Comment: an important 'real world' comparison indicates the test is discriminating between cancer and pre-malignant states.

In interpreting these initial results, it is important to recognise that the total cohort size is 300 patients and the validation cohort is relatively small. Consequently, further work in additional patient samples is required to confirm the statistical significance of these results.

Conclusions: 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 Barrett’s oesophagus, a common pre-malignant condition. Further refinement of the diagnostic models would be beneficial to optimise rule-in/rule-out criteria.

Glossary

Sensitivity (Sn) (true positive rate)	The ability of a test to correctly identify those with the disease. E.g. sensitivity of 80% means that for every 100 people with oesophageal cancer, the test correctly diagnosed 80 with the condition.
Specificity (Sp) (true negative rate)	The ability of the test to correctly identify those without the disease. E.g. specificity of 75% means that for every 100 people with symptoms but no oesophageal cancer, a test correctly identifies 75 as not having the condition.
Negative Predictive Value (NPV)	The probability that people who get a negative test result truly do not have the disease. In other words, it is the probability that a negative test result is accurate.
Positive Predictive Value (PPV)	The probability that a patient with a positive (abnormal) test result actually has the disease.
Probability (P)	The *P* value, or calculated *probability*, that an observation is true. Most authors refer to statistically significant as $P < 0.05$ and statistically highly significant as $P < 0.001$ (less than one in a thousand chance of being wrong).
AUC	"Area Under the ROC Curve". A receiver operating characteristic curve, or ROC curve, is a graphical plot that illustrates the performance of a classifier system.
Interpreting AUC values	Conventionally the clinical significance of AUC is: > 0.7 acceptable discrimination > 0.8 excellent discrimination > 0.9 outstanding discrimination

Proteomics International is currently rolling-out PromarkerD, the world's first predictive diagnostic test for diabetic kidney disease. The Company also has advanced research programs targeting novel diagnostics for endometriosis, oxidative stress, asthma and COPD.

Authorised by the Board of Proteomics International Laboratories Ltd (ASX.PIQ).

ENDS

About the Promarker™ Platform

Proteomics International's diagnostics development is made possible by the Company's proprietary biomarker discovery platform called Promarker, which searches for protein 'fingerprints' in a sample. This disruptive technology can identify proteins that distinguish between people who have a disease and people who do not, using only a simple blood test. It is a powerful alternative to genetic testing. The technology is so versatile it can be used to identify fingerprints from any biological source, from wheat seeds to human serum. The Promarker platform was previously used to develop PromarkerD, a world-first predictive test for diabetic kidney disease, that is currently being commercialised. Other tests in development include for endometriosis, asthma & COPD, oesophageal cancer, diabetic retinopathy and oxidative stress.

About Proteomics International Laboratories (PILL) (www.proteomicsinternational.com)

Proteomics International (Perth, Western Australia) is a wholly owned subsidiary and trading name of PILL (ASX: PIQ), a medical technology company at the forefront of predictive diagnostics and bio-analytical services. The Company specialises in the area of proteomics – the industrial scale study of the structure and function of proteins. Proteomics International's mission is to improve the quality of lives by the creation and application of innovative tools that enable the improved treatment of disease.

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18th World Congress for Esophageal Diseases (ISDE 2022)

Proteomics International

Oral Presentation | September 26-28th, 2022

| Virtual & Tokyo, Japan

Establishing a Mass Spectrometry Based Diagnostic Test for Oesophageal Cancer

Marisa Duong [1], Scott D. Bringans [1], Katherine Chen [1], Gareth Fernandez [1], Tammy Casey [1], Connor Laming [1], Patsy Di Prinzio [1], Michelle Hill [2], Richard Lipscombe [1]

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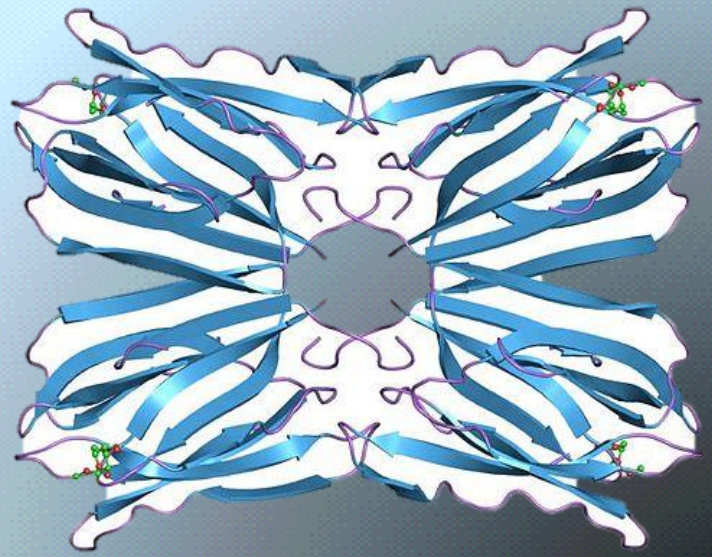

Disease background

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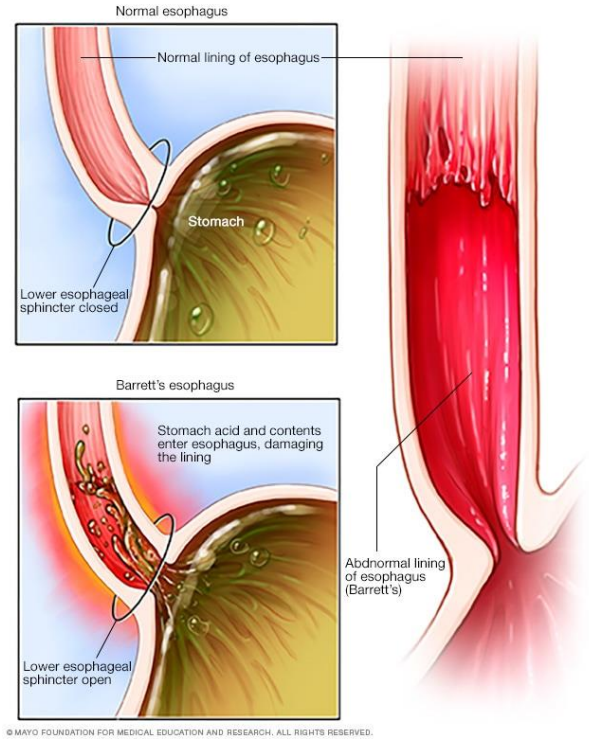
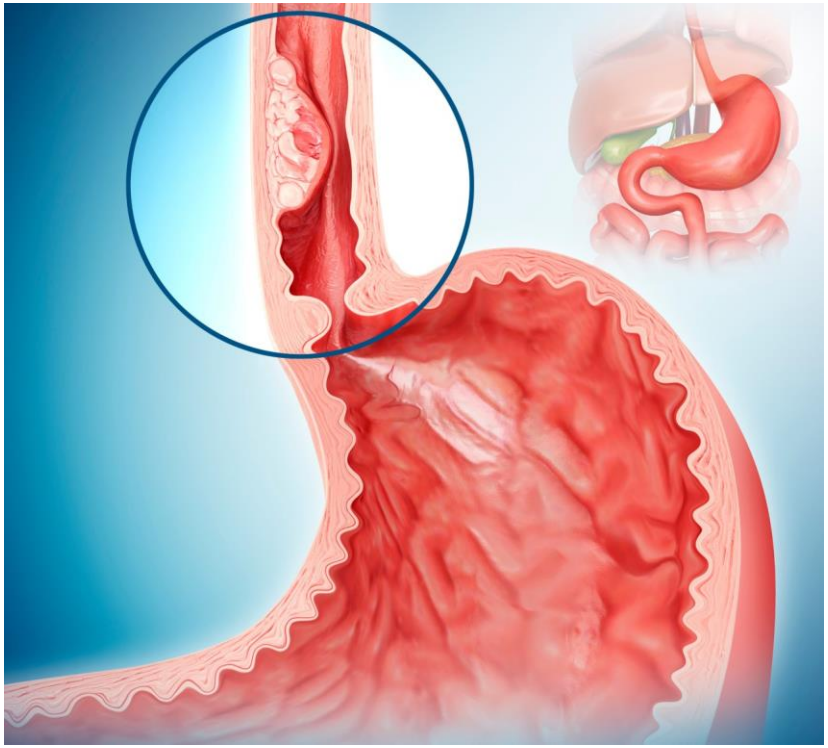
Barrett's Esophagus (BE)



Increase risk

Oesophageal adenocarcinoma (OAC)



Patients advised to get regular endoscopies to screen for OAC

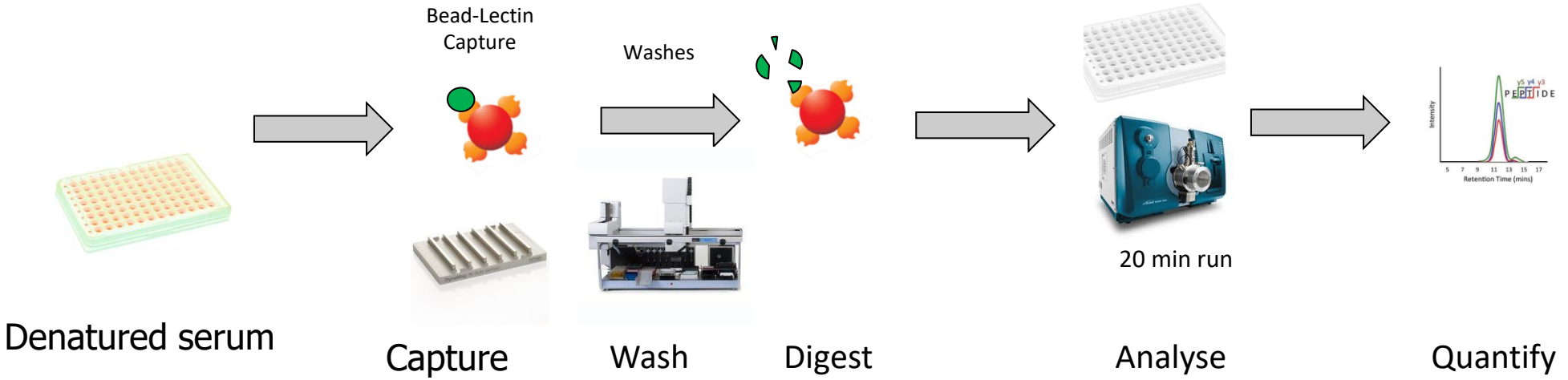
Aim: To develop a simple blood test to improve disease diagnosis

Method

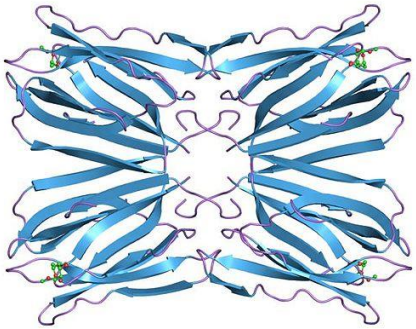
QIMR Berghofer Medical Research Institute

PILL Proteomics International

Lectin capture of glycoproteins, analysis by Mass Spectrometry



10 proteins were analysed in the assay



Statistical method

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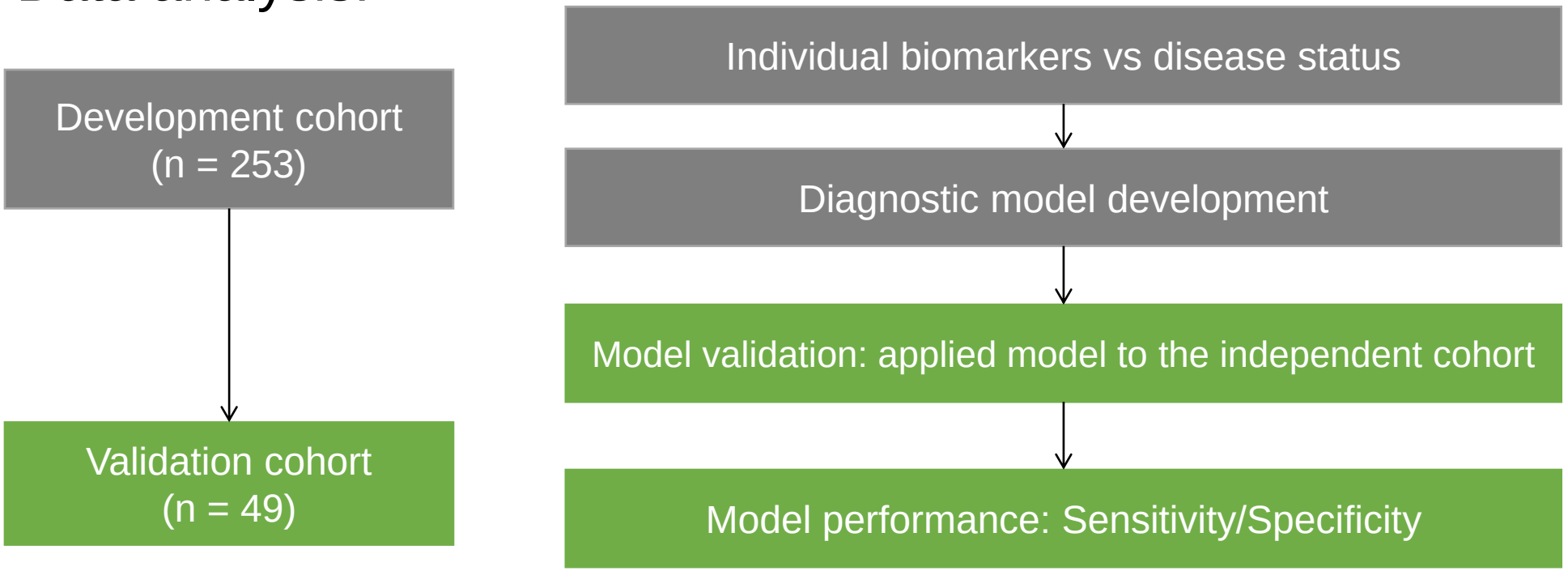
Group comparison:

Group 1 Control	Group 2 BE+	Group 3 BE-HGD	Group 4 OAC

Data analysis:



OAC: oesophageal adenocarcinoma; BE+: positive for Barrett's esophagus; BE-HGD: Barrett's esophagus with High Grade Dysplasia

Results

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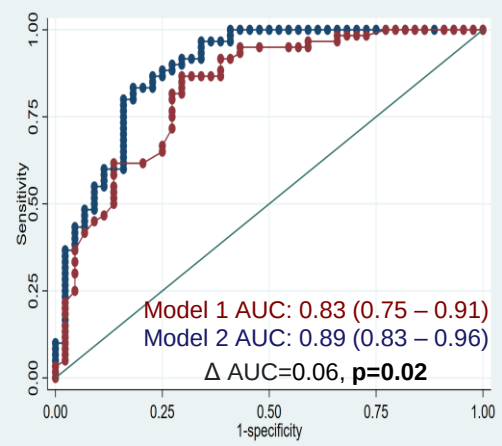
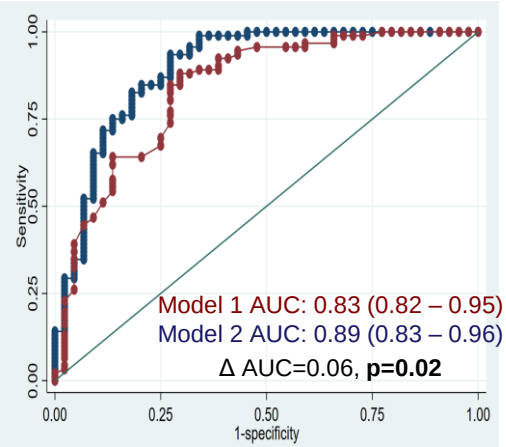
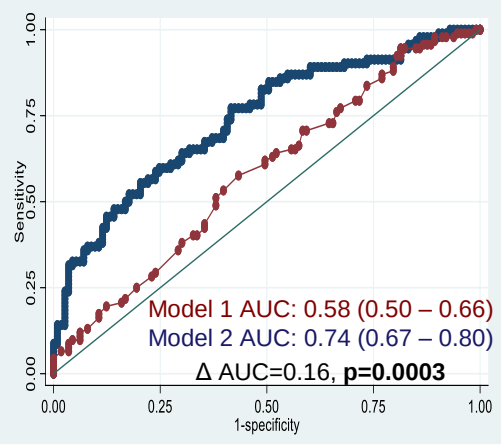
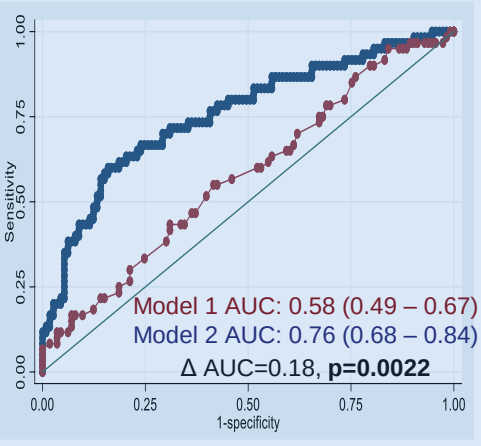
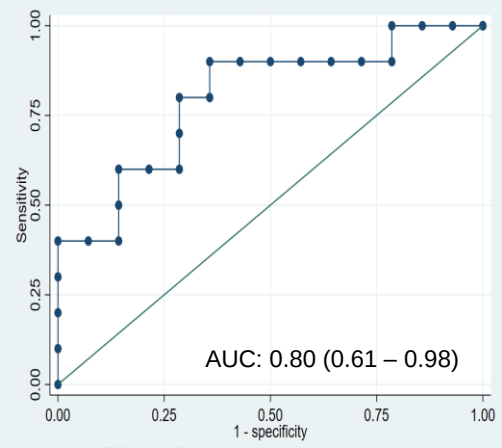
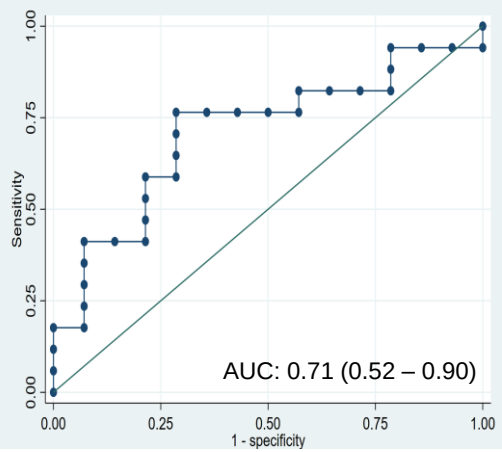
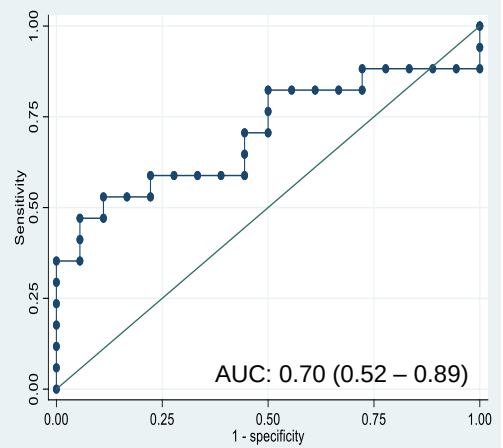
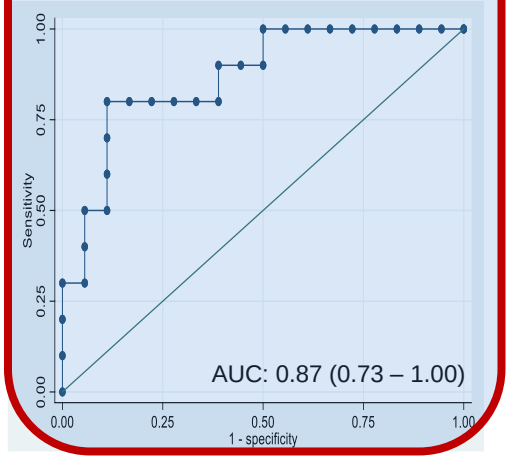
	Control vs OAC Group 1 vs Group 4	Control vs (BE-HGD & OAC) Group 1 vs Group 3+4	BE+ versus (BE-HGD & OAC) Group 2 vs Group 3+4	BE+ versus OAC Group 2 vs Group 4
Development				
Validation				

OAC: oesophageal adenocarcinoma; BE+: positive for Barrett's esophagus; BE-HGD: Barrett's esophagus with High Grade Dysplasia

Results

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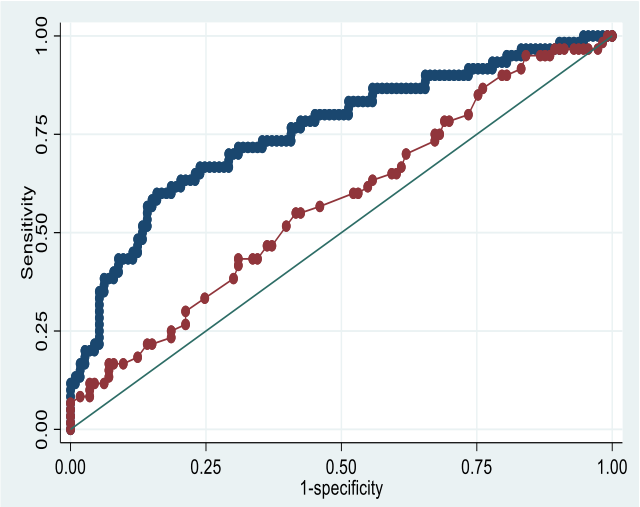
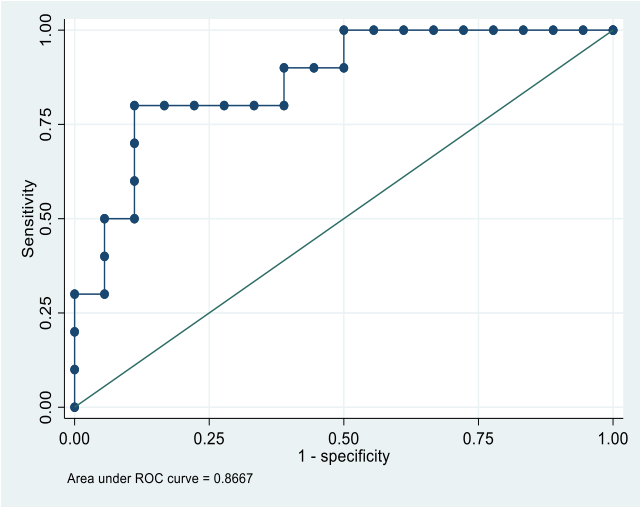
BE+ versus OAC (Group 2 vs Group 4):

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%
PPV (%)	65%
NPV (%)	80%
Δ AUC	0.18
p values	**0.0022**
Validation cohort:	
AUC (95% CI)	0.87 (0.73 – 1.00)
Sensitivity (%)	80%
Specificity (%)	89%
PPV (%)	80%
NPV (%)	89%

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%

OAC: oesophageal adenocarcinoma; BE+: positive for Barrett's esophagus; BE-HGD: Barrett's esophagus with High Grade Dysplasia

Conclusion

Proteomics International

- Protein biomarkers added significant performance to clinical variables across all diagnostic models
- Simple blood test using mass spectrometry platform shows strong diagnostic potential to discriminate Barrett's esophagus (BE) from oesophageal adenocarcinoma (OAC)
- Models developed with 253-patient cohort and validated with independent 47-patient cohort
- AUC of 0.76-0.89 for Development cohort and 0.70-0.87 for Validation cohort
- Seeking collaborations for assessing further cohorts: *info@proteomics.com.au*