ASX Release
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PromarkerEndo advances toward clinical use with real-world validation data presented at World Congress on Endometriosis

- **Landmark results as PromarkerEndo blood test demonstrates high diagnostic accuracy across all stages of endometriosis using a single universal test**
- **The results consolidate earlier prototype models into a universal test with a simple 'traffic light' risk score - low, moderate, or high - indicating the likelihood of endometriosis for *any* patient**
- **PromarkerEndo test now offers a real-world solution for patients with symptoms or considering fertility treatments by diagnosing early-stage endometriosis**
- **Results from a study of 704 participants presented over the weekend at 16th World Congress on Endometriosis, Sydney, Australia**
- **Launch plans underway with commercial rollout of PromarkerEndo in Australia set for Q3 CY25**
- **PromarkerEndo targets a huge unmet need in diagnostics and fertility care - enormous market potential with 1 in 9 women affected - currently diagnosis typically takes an average of 7 years**

Proteomics International Laboratories Ltd (Proteomics International; ASX: PIQ), a pioneer in precision diagnostics, is pleased to announce another milestone in the development of its PromarkerEndo diagnostic test for endometriosis. New data presented at the prestigious World Congress on Endometriosis, held in Sydney, Australia, 21-24 May, confirms that PromarkerEndo is fast transitioning from prototype to a clinically viable, real-world solution for non-invasive diagnosis of endometriosis.

Endometriosis, a chronic condition affecting one in nine women and girls worldwide[1], often takes an average of seven years to diagnose due to the reliance on invasive laparoscopy. The latest results advance the breakthrough study published last December [ASX: 30 December 2024] by consolidating earlier prototype models into a single, universal diagnostic test. PromarkerEndo now provides a clear and simple 'traffic light' risk score - low, moderate, or high - indicating the likelihood of endometriosis for *any* patient, helping guide clinical decision-making.

The results, derived from the analysis of 704 plasma samples validate the performance of the PromarkerEndo test in detecting all stages of endometriosis with high accuracy. Proteomics International scientists, in collaboration with the Royal Women's Hospital and the University of Melbourne, compared cases of endometriosis, general population controls, and symptomatic controls. The test also delivered strong and improved diagnostic performance for early-stage disease (AUCs 0.89 - 0.94 for stages I–III), which is critical for real-world use.

PromarkerEndo is now positioned as a non-invasive, scalable tool for earlier diagnosis of endometriosis, potentially eliminating the current reliance on invasive surgical procedures such as laparoscopy.

[1] World Health Organisation (WHO.org); www.who.int/news-room/fact-sheets/detail/endometriosis

Proteomics International Managing Director Dr Richard Lipscombe said, *"this is a major step forward in making non-invasive endometriosis diagnosis a reality. PromarkerEndo has the potential to dramatically reduce diagnostic delays with its simplicity, accuracy, and broad applicability - including in fertility care. The advances support our commercialisation strategy and reinforce the potential for PromarkerEndo to become a standard part of the clinical diagnostic pathway."*

The findings were presented to leading clinicians and researchers at the 16th World Congress on Endometriosis on Saturday, highlighting strong global interest in the test's future adoption. The test is also being explored for its potential application in fertility settings, where undiagnosed endometriosis is known to affect treatment outcomes and is three times more common among women undergoing IVF treatment.

Professor Peter Rogers, endometriosis researcher and Research Director at the Royal Women's Hospital, commented, *"a simple, reliable blood test that can detect early-stage endometriosis could transform how we manage this condition. PromarkerEndo has the potential to reduce diagnostic delays and support timely intervention, especially in fertility cases where endometriosis often goes undiagnosed."*

Endometriosis is a common and painful disease that occurs when tissue similar to the lining of the uterus grows in other parts of the body where it does not belong. Endometriosis severity is classified by the American Society for Reproductive Medicine as stage I/minimal, stage II/mild, stage III/moderate and stage IV/severe.

Currently, there is no simple way to test for endometriosis, which can cause pain and infertility, and costs Australia $9.7 billion each year[2]. The current gold standard for detection is an invasive laparoscopy followed by histopathology, a surgical procedure where a camera is inserted into the pelvis through a small cut in the abdominal wall and then a biopsy is taken for analysis.

Next Steps:

- PromarkerEndo commercialisation planning underway with target launch date Q3 CY25 in Australia.
- The launch will leverage the Direct to Consumer (DTC) framework built for other Promarker tests, and in parallel target primary care (GP's) and clinicians focused on women's health and fertility.
- Analytical methodology is being adapted for use in a clinical environment under the ISO 15189 (clinical testing) pathway.
- Regulatory pathway applications, ongoing clinical studies and partner engagement continue in parallel.
- Patents pending in all major jurisdictions.
- Proteomics International will provide further updates as it moves toward bringing PromarkerEndo to market.

PromarkerEndo is one of multiple assets in Proteomics International's pipeline of precision diagnostics and represents a substantial commercial opportunity in the global women's health market.

Summary of Study

Presented at the 16th World Congress on Endometriosis, Sydney, Australia, May 21-24 [presentation attached]

Titled: *"Validation of a novel plasma protein biomarker test for diagnosing endometriosis"*

Authors: K Peters[1], E Schoeman[1], S Bringans[1], M Duong[1], J Girling[2], M Healey[2], B Boughton[2], H Lim[1], M Mead[1], R Lipscombe[1], S Holdsworth-Carson[2,3], P Rogers[2].

[1] Proteomics International, Perth, Australia; [2]University of Melbourne & Royal Women's Hospital, Melbourne, Australia; [3] Julia Argyrou Endometriosis Centre, Melbourne, Australia

[2] endometriosisaustralia.org/

Aim: To advance the prototype version of the Promarker®Endo diagnostic test into a real-world clinical solution by integrating the individual models of the prototype into a single, universal test, PromarkerEndo, applicable to all individuals regardless of disease stage.

Method: A panel of protein biomarkers[3] were analysed by targeted mass spectrometry, combined with age and BMI values, and used to compare plasma samples from 436 endometriosis cases, 142 general population controls, and 126 symptomatic controls. Previously developed statistical models were integrated in a step-wise manner, and further refined using a 'traffic light' risk scoring system - low, moderate, or high - indicating the likelihood of endometriosis.

The new algorithm was trained on disease extremes (stage IV vs controls) and then validated by testing across all stages of disease (I-IV) to ensure broad clinical applicability.

Results: The integrated PromarkerEndo test demonstrated excellent discrimination in diagnosing all stages of disease when compared against symptomatic controls and general population controls, and improved upon the performance of the previously published results:

Promarker®Endo performance:Endometriosis stage (number of patients, N) vs All controls (n=268)	AUC	Sensitivity (Sn)(%)	Specificity (Sp) (%)
All Stages (N=436)	0.92	83	95
Stage I Endometriosis (N=228)	0.89	75	95
Stage II Endometriosis (N=64)	0.93	86	95
Stage III Endometriosis (N=57)	0.94	89	95
Stage IV Endometriosis (N=87)	0.98	98	95

Conclusions:

- The PromarkerEndo blood test now accurately distinguishes endometriosis from both symptomatic and general population controls using a single universal test
- The unified diagnostic platform demonstrated improved performance over the prototype test, with strong performance across all endometriosis stages, including early-stage disease (stage I / minimal)
- Real-world applications in women's health and fertility care
- Further clinical validation of these biomarkers in independent populations will fortify the robustness and reliability of this diagnostic tool and facilitate its integration into clinical practice

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 disease, 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 without disease, a test correctly identifies 75 as not having the condition.
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

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[4]:

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

[3] Human Reproduction: doi.org/10.1093/humrep/deae278

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

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

ENDS

About Promarker®Endo

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 blood test. It is a powerful alternative to genetic testing. PromarkerEndo is a diagnostic blood test for endometriosis, which could provide early screening to rule in or out the need for invasive surgery for women and girls presenting with symptoms of endometriosis. Endometriosis is a common and painful condition that affects one in nine women and girls, occurring when tissue similar to the lining of the uterus grows in other parts of the body where is does not belong. The current way to test for the condition is a surgical laparoscopy, with diagnosis taking an average of 7 years.

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 precision 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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Validation of a Novel Plasma Protein Biomarker Test for Diagnosing Endometriosis

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May 24th 2025

Presented at the 16th World Congress on Endometriosis (WCE) 2025 in Sydney, Australia

Overview & Aims

The Challenge

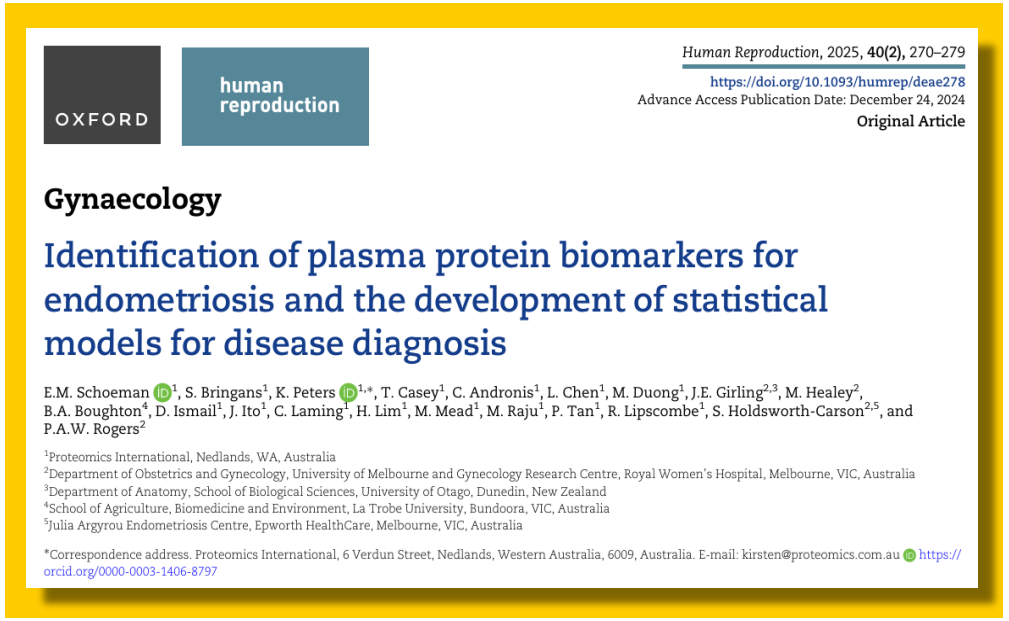
- Endometriosis diagnosis is often delayed (avg 7 years) due to symptom variability and reliance on invasive methods[1].

The Solution

- **Promarker®Endo** - a non-invasive blood test to reduce diagnostic delays.

Prototype Test (Schoeman et al., 2025)

- Identified and analytically validated 10 diagnostic biomarkers.
- Developed 3 statistical models for endometriosis diagnosis.



OXFORD human reproduction

Human Reproduction, 2025, **40(2)**, 270–279
https://doi.org/10.1093/humrep/deae278
Advance Access Publication Date: December 24, 2024
Original Article

Gynaecology

Identification of plasma protein biomarkers for endometriosis and the development of statistical models for disease diagnosis

E.M. Schoeman[1], S. Bringans[1], K. Peters[1,*], T. Casey[1], C. Andronis[1], L. Chen[1], M. Duong[1], J.E. Girling[2,3], M. Healey[2], B.A. Boughton[4], D. Ismail[1], J. Ito[1], C. Laming[1], H. Lim[1], M. Mead[1], M. Raju[1], P. Tan[1], R. Lipscombe[1], S. Holdsworth-Carson[2,5], and P.A.W. Rogers[2]

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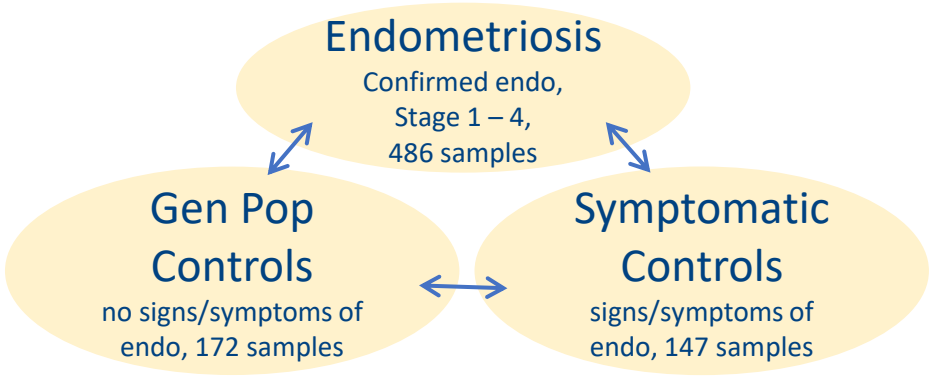
Current Focus

- Advance the prototype into a real-world clinical solution by integrating the individual models into a single, universal test, **Promarker®Endo**, applicable to all individuals regardless of disease stage.

[1] Ellis K, et al., 2022 *Front Glob Womens Health*, 3:902371

Published Prototype Test

- Protein biomarkers measured using a targeted mass spectrometry assay
- Assessed 805 samples across 3 clinical groups:
  - Confirmed endometriosis – confirmed by laparoscopy
  - Symptomatic controls – confirmed by laparoscopy
  - Non-symptomatic general population controls
- Statistical models (logistic regression and random forest) to distinguish endometriosis cases from controls
- 10 biomarkers (plus age and BMI) with biological functions relevant to disease pathophysiology
- AUC (area under the receiver operating characteristic curve) with sensitivity (Sn), specificity (Sp), positive and negative predictive values (PPV/NPV)



Protein Biomarker Name	Accession #
Vitamin K-dependent protein S	P07225
Haemoglobin subunit beta	P68871
Serum paraoxonase/arylesterase 1	P27169
Afamin	P43652
Coagulation factor XII	P00748
Complement component C9	P02748
Neuropilin-1	O14786
Inter-alpha-trypsin inhibitor light chain	P02760
Selenoprotein P	P49908
Proteoglycan 4	Q92954

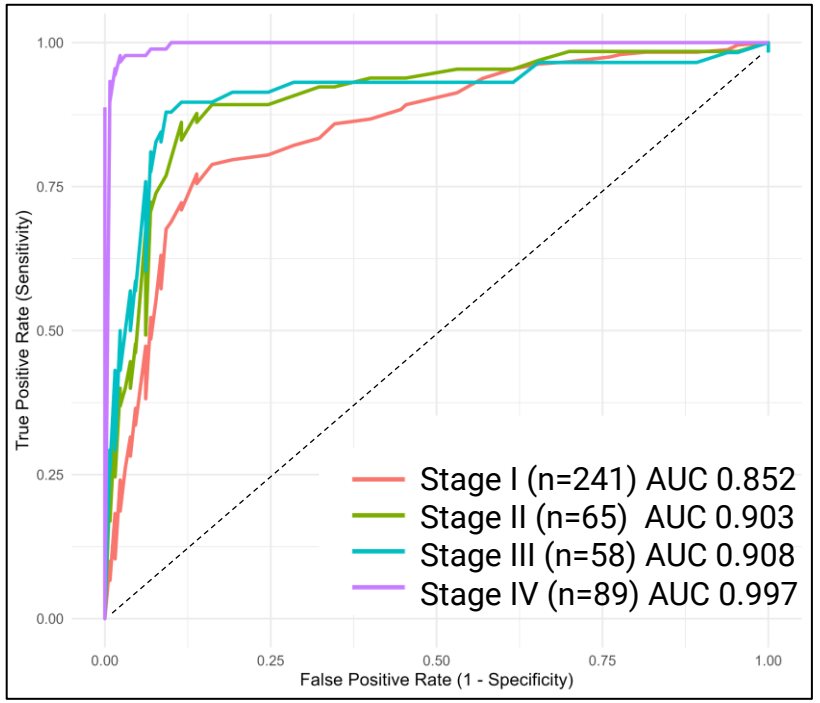
Protein names in orange previously linked with endometriosis.

Schoeman et al., 2025 *Human Reproduction*, 40(2), 270–279.

Prototype Test Performance

- All models had strong diagnostic performance (AUCs 0.72 – 0.997)
  - Model 1: Endometriosis vs. general population controls
  - Model 2: Stage II-IV endometriosis vs. symptomatic controls
  - **Model 3:** Stage IV endometriosis vs. symptomatic controls

- Model 3 **developed** on stage IV vs. symptomatic controls
  - AUC 0.997
  - Sn 98%; Sp 96%; NPV 98%; PPV 95%
- Model 3 **validated** by testing across stages I - III endometriosis:
  - AUCs 0.852 – 0.908
  - Sn 82% - 91%; Sp 72% - 84%; NPVs 75% - 96%; PPVs 72% - 85%



Prototype test performance by ASRM stage.
Endometriosis (n=453) vs. Symptomatic Controls (n=130)

- **Prototype Test → Toward a Validated Clinical Test**
  - Develop a universal test with improved performance particularly for early-stage disease

Schoeman et al., 2025 *Human Reproduction*, 40(2), 270–279.

AUC, area under the curve; Sn, sensitivity; Sp, specificity; PPV/NPV, positive and negative predictive value

From Prototype to Validated Test:

- Refine the algorithm by integrating prototype models using a sequential two-step approach to calculate individual risk
- The algorithm combines the concentration of a panel of protein biomarkers with age and BMI to generate a risk score for endometriosis (0-100%)
- Introduce a ‘traffic-light’ risk classification system:

LOW RISK	MODERATE RISK	HIGH RISK
Low probability of endometriosis	Moderate probability of endometriosis	High probability of endometriosis

- Select test cut-offs to maximise Sn/NPV (lower), Sp/PPV (upper)
- Develop the algorithm on disease extremes (Stage IV vs. controls)
- Validate by testing across all stages (I-IV) to ensure broad clinical applicability
- Assess diagnostic performance using AUC, Sn, Sp, PPV and NPV

Use of this test is subject to country-specific regulatory approval

Study Participants

- Clinical validation cohort (n=704) across three clinical groups:
  - **Endometriosis cases (n=436)**: laparoscopy and histopathology confirmed
  - **Symptomatic controls (n=126)**: laparoscopy confirmed absence of endo
  - **General population controls (n=142)**: Healthy volunteers from Perth, no endo-like symptoms

Controls

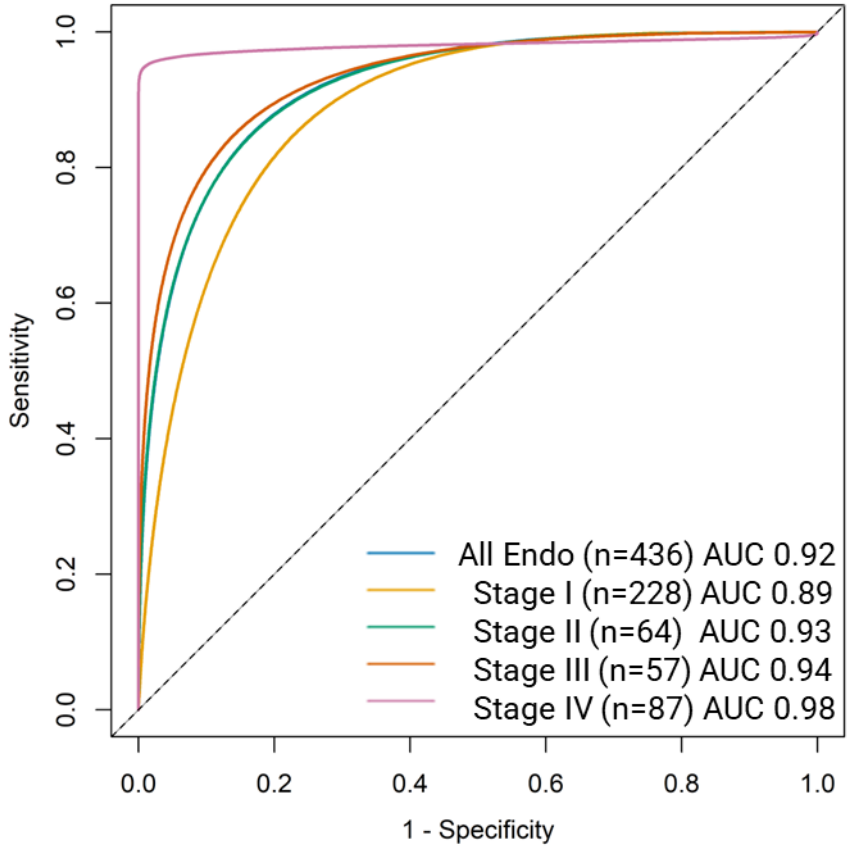
Endo and Pelvic Pain Clinic
Royal Women's Hospital,
Melbourne, Australia
2012-2022

Endo severity rASRM
- Stage 1/minimal (n=228)
- Stage 2/mild (n=64)
- Stage 3/ moderate (n=57)
- Stage 4/ severe (n=87)

	Endometriosis (N=436)	Symptomatic Controls (N=126)	P-value (a)	General Population Controls (N=142)	P-value (b)
Age (years) (mean +/- SD)	30±7	29±8	0.051	28±8	<0.001
BMI (kg/m^2) (mean +/- SD)	25±5	26±6	0.026	25±6	0.64
Smoking status (% current or past/ never/ unknown)	41/59/0	37/62/1	0.56	30/70/0	0.019
Age at menarche (years) (mean +/- SD)	13±2	13±2	0.58	13±2	0.69
Family history of endometriosis (% yes/ no/ unknown)	28/68/4	24/67/9	0.62	3/93/4	<0.001
Pain (% menstrual/ pelvic/ interc/ comb/ none/ unknown)*	5/1/1/89/1/3	2/0/1/94/2/1	0.20	NA	NA
Cycle length (% 14-20/ 21-27/ 28/ 29+ days/ other**)	33/8/30/21/8	45/11/21/14/9	0.024	0/16/52/32/0	<0.001
Cycle stage (% menses/ prolif/ secret/ other)¥	4/25/24/47	1/22/25/52	0.54	9/43/39/9†	<0.001
Exogenous hormone medication (% yes/ no/ unknown)	38/61/1	50/50/0	0.029	36/64/0	0.64
Hormone medication type (% oral/ IUD/ depo/ comb)	75/20/4/1	69/26/3/2	0.68	67/18/4/0§	<0.001
Gravidity (% 0/ 1/ 2/ 3+)	67/15/11/7	63/9/9/19	0.056	74/9/8/9	<0.001
Live births (% 0/ 1/ 2/ 3+)	80/10/8/2	71/11/9/9	0.008	82/5/10/3	<0.001
Problems conceiving (% yes/ no/ not tried/ unknown)	17/22/50/11	12/24/51/13	0.51	NA	NA
Ethnicity (% AS/ AMR/ AFR/ EUR/ other/ unknown)	10/1/1/76/5/7	5/1/0/84/8/2	0.40	18/5/1/61/6/9	<0.001

P-value (a)=endometriosis vs symptomatic controls; P-value (b)=endometriosis vs general population controls. Statistical tests for P-values: Mann-Whitney U test, Chi-square test or Fisher's exact test, as appropriate. *Pain: inter=intercourse, comb=combination of pain symptoms (menstrual, pelvic and intercourse). **Cycle length: other=unknown, unsure or not cycling. ¥ Cycle stage: menses=menstruation; prolif=proliferative phase; secret=secretory phase; other=progestin, inactive, unknown or abnormal. IUD=intrauterine device; depo=depot injection; comb=combination of hormone types (oral, iud and depo). AS=Asian; AMR=Central or South America; AFR=African; EUR=European; other=admixture. †Self-reported data. § Other hormone type in 11%. NA, data on pregnancy problems and pain was not available.

PromarkerEndo Test Performance

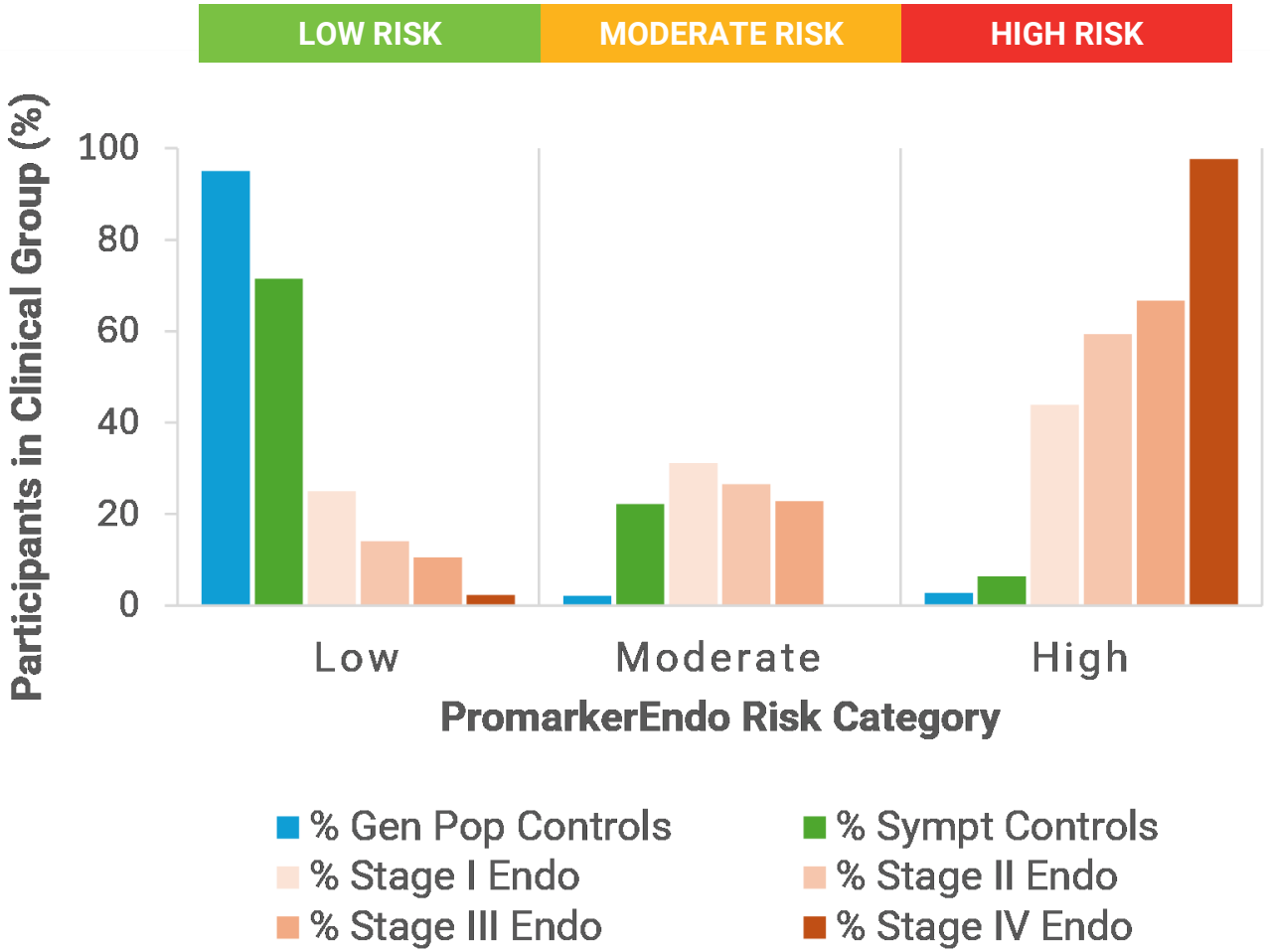


PromarkerEndo test performance by ASRM stage.
Endometriosis Cases (n=436) vs. Controls (n=268; including 126 Symptomatic Controls plus 142 General Population Controls).

- PromarkerEndo had excellent diagnostic performance to distinguish endometriosis from both symptomatic and general population controls
  - AUC 0.92 (95% CI 0.90-0.94)
    - Low/Moderate cut-off: Sn 83%; NPV 75%
    - Moderate/High cut-off: Sp 95%; PPV 96%
  - **83% of endometriosis cases correctly classified as moderate/high-risk**
  - **84% of controls correctly classified as low-risk**
  - **96% of people reported by the test as high-risk had endometriosis**
  - **75% of people reported by the test as low-risk did not have endometriosis**
- By endometriosis stage:
  - AUCs 0.89 – 0.98
  - 75% (stage I), 86% (stage II), 89% (stage III), 98% (stage IV) of endometriosis cases correctly classified as moderate/high-risk

AUC, area under the curve; Sn, sensitivity; Sp, specificity; PPV/NPV, positive and negative predictive value

PromarkerEndo Risk Classification



Endometriosis:

- 98% of stage IV → high-risk
- 90% of stage III → 23% moderate, 67% high-risk
- 86% of stage II → 27% moderate, 59% high-risk
- 75% of stage I → 31% moderate, 44% high-risk

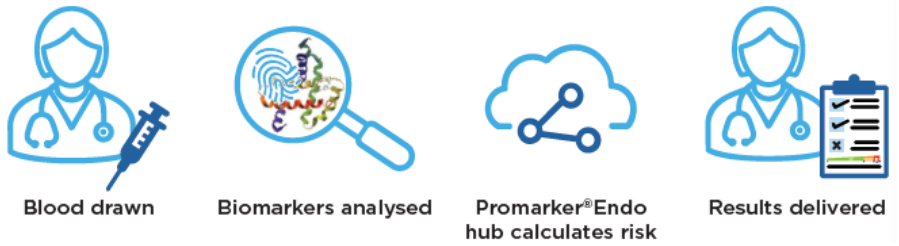
Controls:

- 95% of general population controls → low-risk
- 71% of symptomatic controls → low-risk
- <5% of controls → high-risk

PromarkerEndo Key Findings

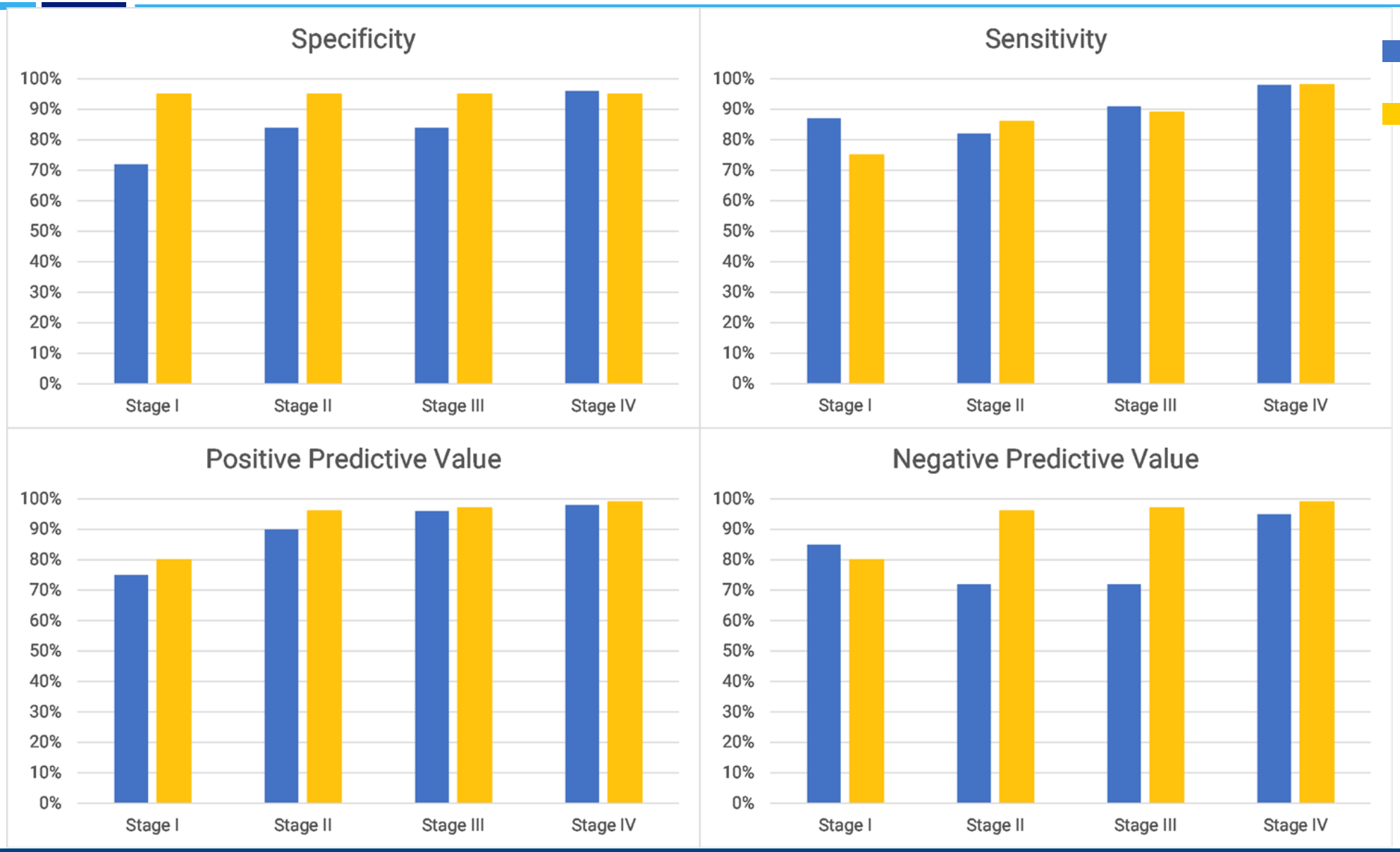
- **Optimised Statistical Approach:**
  - Sequential two-step algorithm used to calculate individual risk
  - Developed on extremes of disease, validated across all endometriosis stages

- **Enhanced Diagnostic Performance:**
  - PromarkerEndo accurately distinguishes endometriosis from both symptomatic and general population controls
  - Reliable across all stages, including early-stage (Stage I / minimal)
  - Successfully separates stage I endometriosis from symptomatic controls
  - Improved performance over the Prototype Test, especially for early-stage disease



	All Stages	**Stage I** Minimal	**Stage II** Mild	**Stage III** Moderate	**Stage IV** Severe
Endo Cases	436	228	64	57	87
Controls	268	268	268	268	268
PromarkerEndo					
AUC	**0.92**	**0.89**	**0.93**	**0.94**	**0.98**
Sensitivity	83%	75%	86%	89%	98%
Specificity	95%	95%	95%	95%	95%
NPV	75%	80%	96%	97%	99%
PPV	96%	80%	96%	97%	99%
Prototype					
AUC		**0.85**	**0.90**	**0.91**	**0.997**
Sensitivity		87%	82%	91%	98%
Specificity		72%	84%	84%	96%
NPV		85%	72%	72%	95%
PPV		75%	90%	96%	98%

PromarkerEndo Key Findings by Stage



From Prototype Test to Real-World Solution

Early Development:

- Three separate prototype models created for specific clinical comparisons:
  - Endometriosis vs. general population controls
  - Stage II–IV vs. symptomatic controls
  - Stage IV vs. symptomatic controls

Clinical Practice:

- People present with non-specific symptoms, disease status unknown, models need to be generalisable
- Highly stratified models are not practical for initial diagnosis

Current Solution:

- PromarkerEndo consolidates previous models into a single universal test
- Applicable to all symptomatic individuals, potential application in fertility care
- Provides a simple risk score: low, moderate, or high

Clinical Value:

- Enables early, non-invasive assessment to support timely triage and referral
- Aims to reduce diagnostic delays and improve care pathways

Limitations: predominantly European ethnicity, possibility of undiagnosed endometriosis in general population controls

Promarker®Endo
powered by Proteomics International

Launching CY2025

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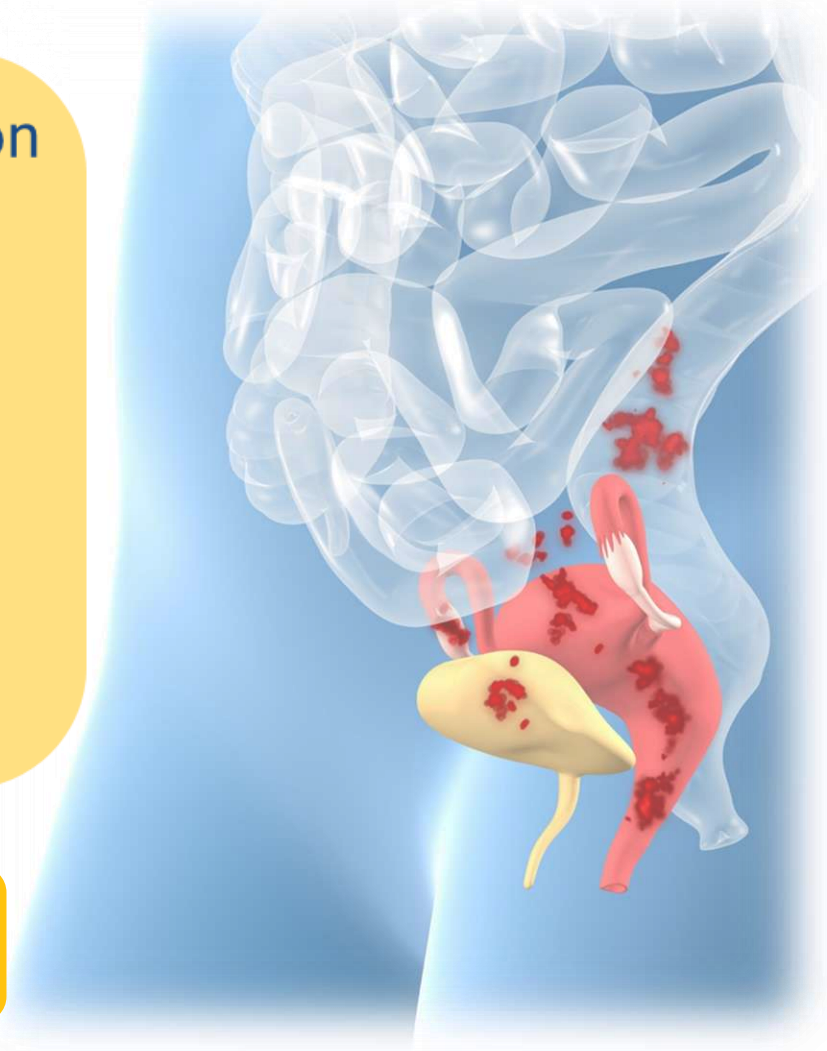

Use of this test is subject to country-specific regulatory approval