



Topic Exploration Report ¹

PCR-based DNA methylation tests for the detection of endometrial cancer

What is a Topic Exploration Report?

Topic Exploration Reports are not health technology assessments. These reports provide a high-level briefing on new topics submitted to Health Technology Wales and are not based on exhaustive or systematic literature searches. Instead, they rely on a focussed scan of key resources.

What evidence is used in a Topic Exploration Report?

Priority is given to summarising the most relevant or useful evidence, rather than covering all possible evidence. Information reported is typically based on abstracts and study authors' own conclusions, rather than detailed scrutiny of full texts.

What are the aims of a Topic Exploration Report?

Topic Exploration Reports offer an overview of the available evidence on a topic and aim to highlight any uncertainties or gaps in the evidence. These reports outline the quantity and type of evidence found, but no critical appraisal or formal evidence synthesis is conducted.

How should a Topic Exploration Report be used?

Topic Exploration Reports can be used to indicate what evidence may be available for a topic, and do not provide definitive guidance on how a technology should be used. The evidence presented within the reports should be interpreted with caution.

¹ [Cyfieithu dogfennau HTW wedi'u cyhoeddi o'r Saesneg i'r Gymraeg](#)
Translation of published technical HTW documents from English into Welsh

Topic exploration report number	TER667
Topic	PCR-based DNA methylation tests for the detection of endometrial cancer
Summary of findings	Uterine cancer affects around 500 females in Wales each year and is the fourth most common cancer in females in the UK. Endometrial cancer (EC) is the most common type of uterine cancer. Diagnosis of EC normally involves an initial ultrasound followed by hysteroscopy and biopsy. Non-invasive PCR-based DNA methylation tests may be an alternative detection test for endometrial cancer. Two studies evaluated the WID-qEC test. These included one prospective evaluation of the comparative diagnostic accuracy of the WID-qEC test and transvaginal ultrasound in a single centre in the UK (EPI-SURE study). The authors concluded that the WID-qEC test shows improved performance compared to standard tests and could be used to triage patients, reducing the need for invasive diagnostic assessments. Three additional diagnostic accuracy studies evaluating tests using various DNA methylation markers were also identified. No randomised evidence, systematic reviews or health technology assessments were identified. One cost-minimisation analysis using data from the EPI-SURE study reported a very high probability (>99%) of WID-qEC resulting in cost savings at an indicative price of £200. Where PCR-based DNA methylation tests may be best placed in the pathway is uncertain; as a first line triage in place of ultrasound for those with suspected EC or as part of a wider screening program. Several tests were identified which used different DNA regions and it is unclear how samples may be collected in practice.

Introduction and aims

Uterine cancer affects around 500 females in Wales each year and is the fourth most common cancer in females in the UK, accounting for 3% of female cancer deaths (Lim K 2022). Uterine cancer includes cancers that originate in the womb and endometrial cancer (EC) is the most common type. Although most are likely to occur in those who are post-menopausal, endometrial cancer can occur in those who are pre or peri menopausal.

Diagnosis of endometrial cancer requires transvaginal ultrasound and people with a thickened lining then proceed to hysteroscopy and biopsy. One in three people suffer from severe pain during outpatient hysteroscopy.

A polymerase chain reaction (PCR)-based DNA methylation test that can identify DNA biomarkers and aid the diagnosis of endometrial cancer has been developed, reducing the need for invasive diagnostic testing. The WID®-easy test is a novel PCR endometrial cancer detection test in those who are peri- and postmenopausal. Sampling is performed by means of a cervicovaginal swab and the test determines the DNA methylation status of two regions in the GYPC and ZSCAN12 genes. The WID®-easy test is currently certified as a class I medical device. The innovator states that they are working towards In Vitro Diagnostic certification.

This topic was proposed by the manufacturer of the WID®-easy test, Advanced Global Health Ltd.

Health Technology Wales researchers searched for evidence on the clinical and cost effectiveness of PCR-based DNA methylation tests to detect endometrial cancer.

Evidence overview

One piece of guidance and five individual studies were identified. One published cost-minimisation study was provided by the topic proposer. No health technology assessments or systematic reviews were found.

Guidance

A guideline by NICE (NG12; NICE 2015) was identified which recommends that those aged 55 years and over with unexplained post-menopausal bleeding that cannot be attributed to hormone replacement therapy be referred using the suspected cancer referral pathway (recommendation amended in 2026). It also recommends that an urgent direct access ultrasound should be considered for those with unexplained symptoms of vaginal discharge who: are presenting with these symptoms for the first time, or have thrombocytosis, or report haematuria, or those with visible haematuria, and: low haemoglobin levels, or thrombocytosis, or high blood glucose levels. For those aged under 55 the guidelines recommend considering a referral via the suspected cancer referral pathway (recommendation amended in 2026).

Individual studies

Two publications reporting the evaluation of the WID-qEC PCR-based DNA methylation (ZSCAN12 and GYPC regions) test (also known as the WID®-easy test) for people with suspected EC were identified (Evans et al. 2023, Herzog et al. 2022). The test evaluates DNA methylation in gene regions of GYPC and ZSCAN12.

Herzog et al. (2022) validated the test in 562 cervicovaginal samples using three different collection methods (cervical smear: n = 248; vaginal swab: n = 63; and self-collection: n = 251). The test detected EC with sensitivities of 97.2% in the cervical smear sample (95% CI 90.2 to 99.7), 90.1% in the vaginal swab sample (95% CI 83.6 to 94.6), and 100% in the self-collection

Evidence overview

sample (95% CI 63.1 to 100). Specificities of 75.8% (63.6 to 85.5), 86.7% (79.3 to 92.2), and 89.1% (77.8 to 95.9) were reported for each of the three sample groups, respectively. Authors report that test performance was similar across menopausal status, age, stage, grade, ethnicity, and histology.

Evans et al. (2023) reported the EPI-SURE study, which is a prospective evaluation of the comparative diagnostic accuracy of the WID-qEC test and transvaginal ultrasound. Included were 399 participants over 45 years of age with abnormal uterine bleeding who attended one tertiary gynaecological diagnostic referral centre in London, UK. A cervicovaginal sample for the WID-qEC test was obtained before standard assessment using ultrasound. The WID-qEC test was possible in 98% of the participants. A sensitivity of 90.9% (95% CI 62.3 to 98.4), a specificity of 92.1% (88.9 to 94.4), a positive predictive value of 25.6% (14.6 to 41.1), and a negative predictive value of 99.7% (98.3 to 99.9) was reported at a prespecified threshold of a summed proportional mortality ratio of 0.03 or more. The authors conclude that the WID-qEC test shows improved performance compared to standard tests and could be used to triage patients and reduce the need for invasive histological assessments.

Three additional studies were identified that evaluated different PCR tests for the detection of EC.

Cai et al. (2026) identified a three-gene methylation panel (ZNF626, GRIA4, and SPDYA) using ThinPrep Cytology Test (TCT) samples (148 samples were used for discovery/model construction and a separate cohort of 80 TCT samples for validation). In the validation cohort, for premenopausal women, the model showed a sensitivity of 90.91% and a specificity of 92.59% for benign endometrial disease. In postmenopausal women, sensitivity and specificity were 96.55% and 84.62%, respectively. A 92.86% detection rate for stage I endometrial cancer was reported.

Hu et al. (2026) evaluated a diagnostic model combining HTR1B, CELF4, and TBX5 genes. They reported 97% sensitivity and 90% accuracy from testing n = 300 endometrial samples.

Wever et al. (2023) reported a PCR-based test for nine DNA methylation markers. Paired samples (including urine, cervicovaginal self-samples and clinician taken cervical scrapes) were collected from 103 patients diagnosed with stage I to IV endometrial cancer. Results from endometrial cancer patients were compared to unpaired samples of 317 healthy controls. Sensitivities ranged from 89% to 93% at specificities of 90% to 92% for endometrial cancer detection in urine, self-samples and clinician taken scrape samples. The authors conclude that this approach has potential to screen patient populations at risk for endometrial cancer.

Economic evidence

Snowsill et al. (2026) reported a cost-minimisation analysis from the EPI-SURE study (Evans et al. 2023) evaluating WID-qEC as a first line triage test in patients aged 45 years or older undergoing urgent evaluation of abnormal uterine bleeding. A decision-analytic model was constructed using individual-level EPI-SURE data and National Health Service reference costs. At a breakeven price of £302 there was a very high probability (>99%) of WID-qEC resulting in cost savings at an indicative price of £200. A sensitivity analysis using a higher threshold for WID-qEC of £331 generated greater savings and at £150, the mean cost saving was £152 per patient.

Areas of uncertainty

The WID®-easy test is currently certified as a class I medical device. The innovator states that they are working towards In Vitro Diagnostic certification. The regulatory status of the other tests identified is uncertain.

There is a lack of comparative evidence and no RCTs were identified.

It is unclear whether the test is proposed for use as a wider population screening tool or as a diagnostic test for those with suspected EC, in place of, e.g. ultrasound.

It is unclear how samples would be collected in clinical practice (e.g. via cervical smear tests, an additional clinically delivered test or collected by the patient themselves).

The PCR tests identified used a variety of genes as biomarkers to identify EC.

Literature search results

Health technology assessments and guidance

NICE. (2015). NICE Guideline. Suspected cancer: recognition and referral. National Institute for Health and Care Excellence. Available at: <https://www.nice.org.uk/guidance/ng12/chapter/Recommendations-organised-by-site-of-cancer#gynaecological-cancers> [Accessed].

Individual studies

Cai Y, Chen S, Wu Z, et al. (2026). Systematic Multiplatform Discovery of Methylation Markers Enables Non-Invasive Early Detection of Endometrial Cancer. *Cancer Sci.* 117(5): 1412-21. <https://doi.org/10.1111/cas.70346>

Hu M, Kang L, Huang L, et al. (2026). DNA Methylation of Combined Gene Markers in Cytological Specimens for Endometrial Cancer Screening. *Diagn Cytopathol.* 54(5): 342-50. doi: <http://doi.org/10.1002/dc.70081>

Wever BMM, van den Helder R, van Splunter AP, et al. (2023). DNA methylation testing for endometrial cancer detection in urine, cervicovaginal self-samples and cervical scrapes. *Int J Cancer.* 153(2): 341-51. <http://doi.org/10.1002/ijc.34504>

Supplied by topic proposer

Herzog C, Marín F, Jones A, et al. (2022). A Simple Cervicovaginal Epigenetic Test for Screening and Rapid Triage of Women With Suspected Endometrial Cancer: Validation in Several Cohort and Case/Control Sets. *J Clin Oncol.* 40(33): 3828-38. <https://doi.org/10.1200/JCO.22.00266>

Evans I, Reisel D, Jones A, et al. (2023). Performance of the WID-qEC test versus sonography to detect uterine cancers in women with abnormal uterine bleeding (EPI-SURE): a prospective, consecutive observational cohort study in the UK. *Lancet Oncol.* 24(12): 1375-86. [http://doi.org/10.1016/s1470-2045\(23\)00466-7](http://doi.org/10.1016/s1470-2045(23)00466-7)

Snowsill TM, Sleigh S, Barrett J, et al. (2026). Cost-Minimization Analysis of the Women's Cancer Risk Identification-Quantitative Polymerase Chain Reaction Test for Endometrial Cancer Epigenetic Biomarker Compared With Transvaginal Ultrasound for Triaging Abnormal Uterine Bleeding. *Value Health.* <http://doi.org/10.1016/j.jval.2026.03.2235>

Background information

Lim K. (2022). All Wales Guideline for the Management of Uterine Cancer. NHS Wales Cancer Network. Available at: <https://performanceandimprovement.nhs.wales/functions/networks-and->

Date of search	22/06/26
Concepts used	Uterine cancer; endometrial cancer; polymerase chain reaction; PCR; diagnostic

Proposed research question and evidence selection criteria (if selected)

Proposed Research question	What is the clinical and cost effectiveness of PCR-based DNA methylation tests in the detection of endometrial cancer?
----------------------------	--

	Inclusion criteria	Exclusion criteria
Population	People with suspected endometrial cancer	Wider population
Intervention	PCR-based DNA methylation tests (specific DNA regions would need to be confirmed)	
Comparison/Comparators	Ultrasound	
Outcome measures	Health related QoL Resource use Economic outcomes Diagnostic accuracy outcomes (compared to histopathology) Time to diagnosis Time to treatment Overall survival	

Proposed speciality	Cancer
---------------------	--------