Early detection of endometrial cancer- novel biomarkers

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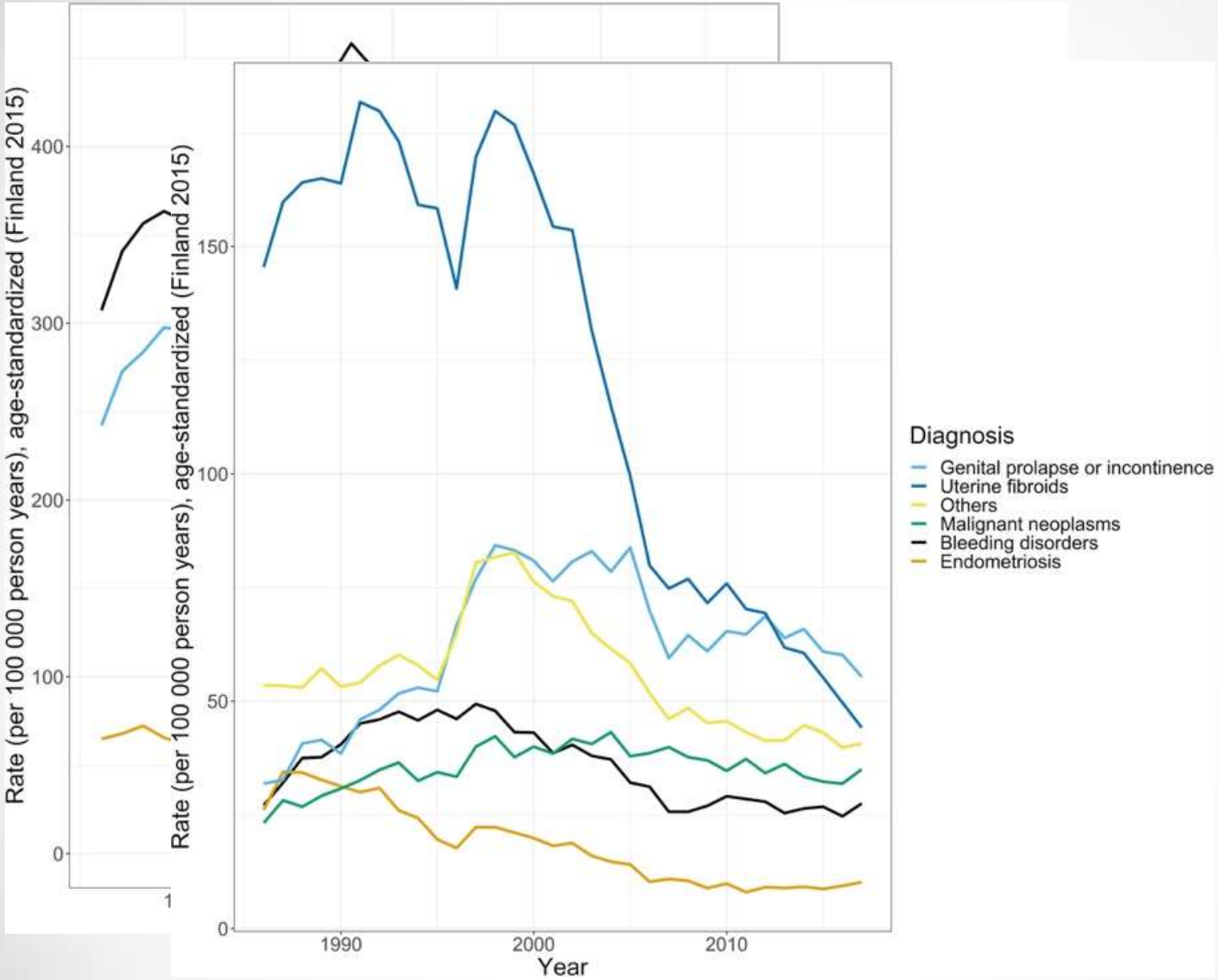
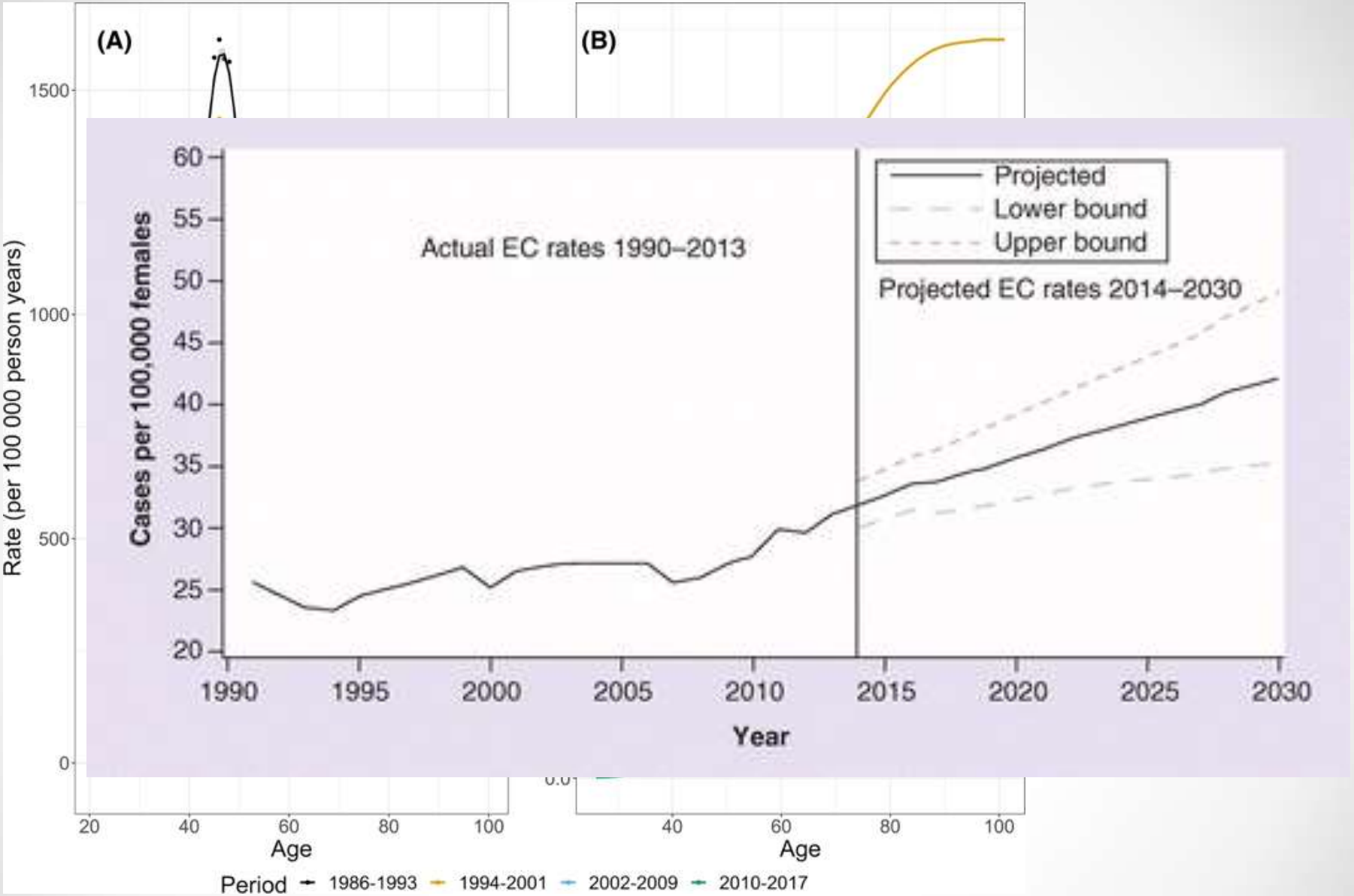
Consultant Gynaecologist

Overview

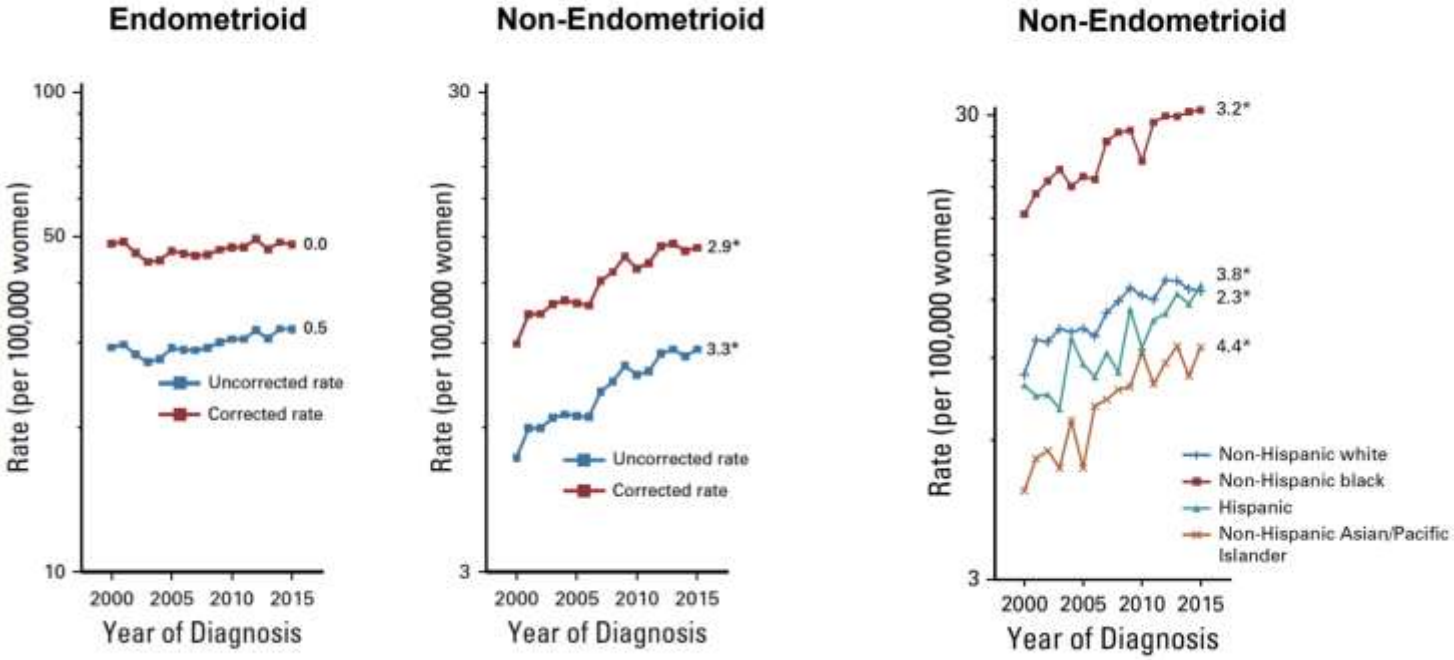
- Current trends in surgical gynaecology
- Global challenges for cancer services
- Current detection methods- challenges and system adaptability
- Leverage on modern, on the spot diagnostic testing
- Merge and grow
- Future collaborations
- Discussions


Rate (per 100 000 person years), age-standardized (Finland 2015)
400
300
200
100
0
Rate (per 100 000 person years), age-standardized (Finland 2015)
150
100
50
0
1990
2000
2010
Year
Diagnosis
Genital prolapse or incontinence
Uterine fibroids
Others
Malignant neoplasms
Bleeding disorders
Endometriosis


(A)
(B)
Rate (per 100 000 person years)
1500
1000
500
0
20
40
60
80
100
Age
Period
1986-1993
1994-2001
2002-2009
2010-2017
Cases per 100,000 females
60
55
50
45
40
35
30
25
20
Actual EC rates 1990–2013
Projected
Lower bound
Upper bound
Projected EC rates 2014–2030
1990
1995
2000
2005
2010
2015
2020
2025
2030
Year

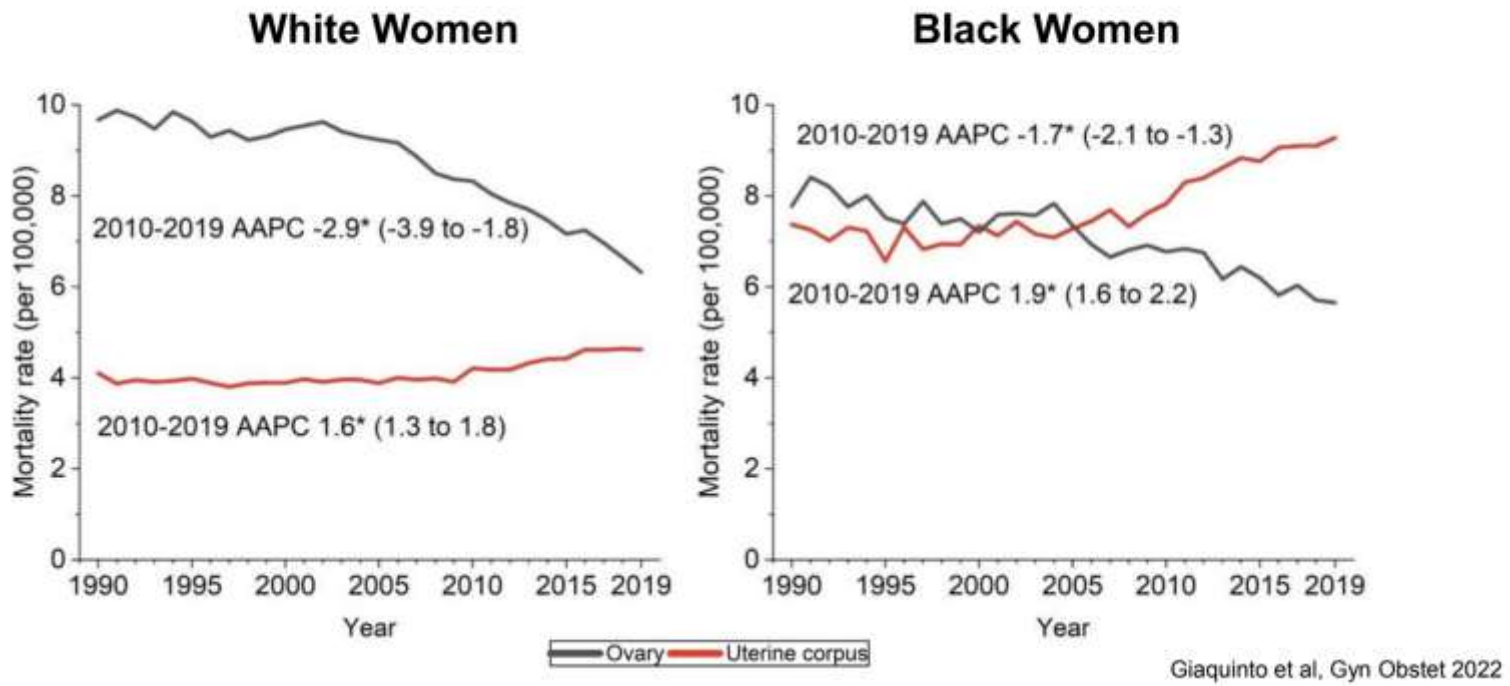
Endometrial cancer – a very fast growing problem

Endometrial cancer incidence



Clarke et al, JCO 2019

Endometrial cancer mortality rates



Giaquinto et al, Gyn Obstet 2022

DOI: 10.1111/tog.12781
The Obstetrician & Gynaecologist
http://onlinetog.org

Education

The blind spot: value-based health care in obstetrics and gynaecology

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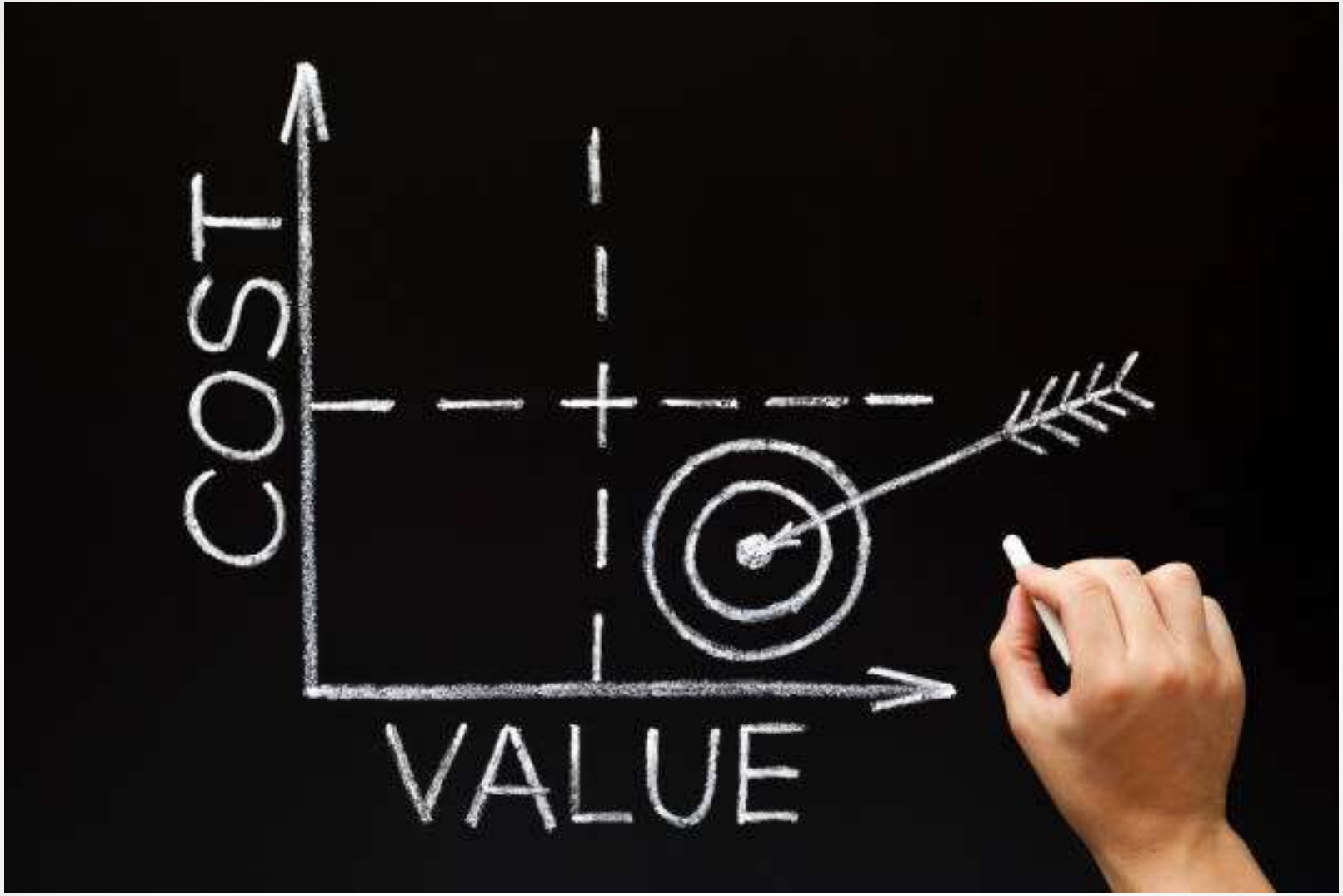
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Journal of Advanced Nursing

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EMPIRICAL RESEARCH QUALITATIVE OPEN ACCESS

Women's Experience and Management of Cancer-Related Fatigue and Psychological Distress During Treatment for Gynaecological Cancer: A Qualitative Study

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Keywords: cancer-related fatigue | gynaecological cancer | nursing | psychological distress | qualitative approaches | symptom experience | symptom management

EC Detection - Sonography

Threshold, mm	% (95% CI) Sensitivity	Specificity
Black women		
≥3	51.1 (49.6-52.6)	55.0 (54.5-55.5)
≥4	47.5 (46.0-49.0)	64.9 (64.4-65.3)
≥5	43.7 (42.3-45.2)	74.1 (73.7-74.5)
White women		
≥3	89.5 (89.1-89.8)	25.7 (25.6-25.9)
≥4	87.9 (87.6-88.3)	42.7 (42.5-42.9)
≥5	86.0 (85.6-86.4)	58.5 (58.3-58.7)

Double-layer endometrial thickness measurements on TVS with a cut off of ≥4 mm should be investigated

-British Gynaecological Cancer Society

Sensitivity of endometrial biopsy when compared to histology form hysterectomy specimens

Open access Original research

BMJ Open

Diagnostic accuracy of endometrial sampling tests for detecting endometrial cancer: a systematic review and meta-analysis

Up to 23% of endometrial cancers are potentially missed by endometrial sampling (D&C)

For each cancer detected, 72 hysteroscopies have to be performed!

Table 2 histopa

Index test							ty / ce
All tests	cancer		to 0.863)	to 0.994)	123.000)	0.335)	
	Atypical hyperplasia	10 (1390)	0.760 (0.639 to 0.849)	0.978 (0.953 to 0.989)	36.100 (16.400 to 69.700)	0.250 (0.155 to 0.368)	High

LR, likelihood ratio.

Sensitivity of endometrial biopsy when compared to histology from hysterectomy specimens

Garuti et al. Gynecological Surgery (2020) 17:10
https://doi.org/10.1186/s10397-020-01077-0

Gynecological Surgery

ORIGINAL ARTICLE Open Access

Hysteroscopic view with targeted biopsy in the assessment of endometrial carcinoma. What is the rate of underestimatated diagnosis? The results of a multicenter Italian trial

Giancarlo Garuti[1], Stefano Angioni[2*], Liliana Mereu[3], Stefano Cabolari[4], Luca Mannini[5], Federica Scrimin[6], Paolo Casadio[7], Davide De Alberti[8], Luigi Nappi[9], Enrico Busato[10], Francesco P. G. Leone[11], Gaetano Perrini[12], Vito Cela[13] and Massimo Luerti[14]

24% of endometrial cancers are potentially missed by hysteroscopy guided biopsy

Abstract

Objective: In the last two decades, many reports demonstrated the unreliability of endometrial biopsy pathology showing an AH (atypical hyperplasia) to exclude a synchronous EEC (endometrioid endometrial carcinoma), with an underestimation of EEC in up to 50% of women endometrial pathology. However, a recent meta high rate of failure with respect to dilatation an instead of concurrent EC. The aim of this study sampling in diagnosing EEC.

Materials and methods: A multicenter, retrosp December 2018 in 14 Italian gynecological unit identified as those women in whom either a p preoperative hysteroscopy assessment with en primary outcome, we calculated the sensitivity driven sampling in the diagnostic workup of E

Results: Nine hundred forty-eight patients (age 65.83 ± 10.43) resulted eligible for analysis. Hysteroscopy view showed a sensitivity of 54.2%, a specificity of 47.2%, and an accuracy of 54% in the diagnosis of EC. Moreover, hysteroscopic view was significantly able to distinguish carcinoma from hyperplasia ($p < 0.001$). We evidenced an important difference of the results comparing the centers involved. Hysteroscopy-driven biopsy presented a sensitivity of 76.2%, a specificity of 52.8%, and an accuracy of 75.3%. AH pathology was reported in 19% of the cases.

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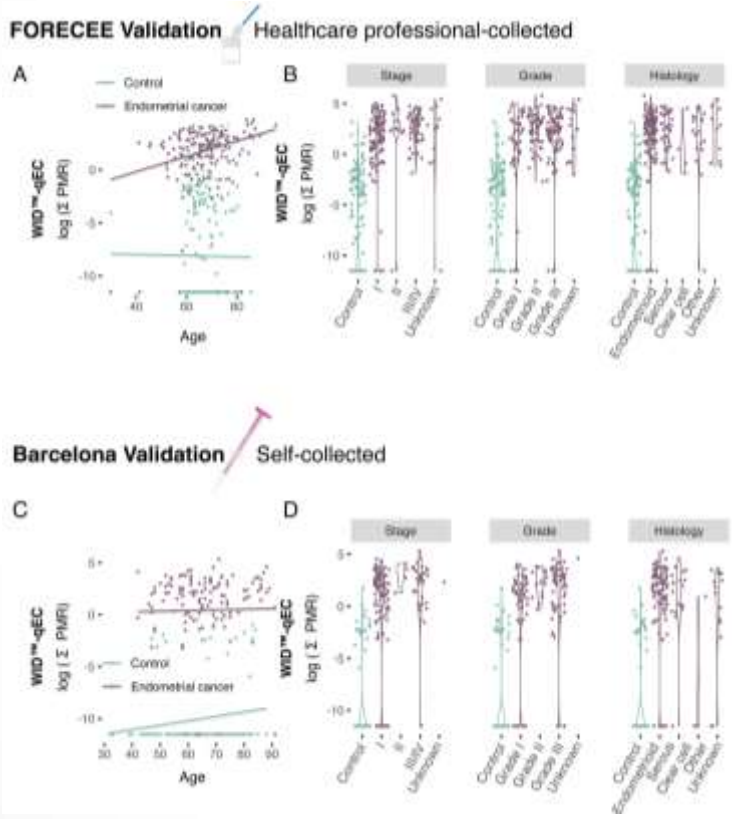
WID-easy = WID-qEC

- The WID®-can test is referred to in the scientific literature as the WID-qEC DNA methylation test
- Epigenetic test for the detection and prediction of endometrial cancer
- Based on a vaginal swab and examines DNA methylation in the COL2A1 and ZSCAN12 genes

WID-easy initial validation



	FORECEE Validation	Barcelona Validation
Pre-menopause		
Cancer cases – n	5	6
Controls – n	1	18
Sensitivity – % (95% CI)	80 (28-99)	100 (54-100)
Specificity – % (95% CI)	100 (3-100)	78 (52-94)
Post-menopause		
Cancer cases – n	188	117
Controls – n	194	98
Sensitivity – % (95% CI)	97 (93-99)	90 (83-95)
Specificity – % (95% CI)	74 (67-80)	88 (80-94)
Endometrioid histology		
Cancer cases – n	124	94
Controls – n	195	120
Sensitivity – % (95% CI)	96 (91-99)	91 (84-96)
Specificity – % (95% CI)	74 (67-80)	87 (79-92)
Serous histology		
Cancer cases – n	35	19
Controls – n	195	120
Sensitivity – % (95% CI)	100 (90-100)	95 (74-100)
Specificity – % (95% CI)	74 (67-80)	87 (79-92)

Herzog et al, JCO 2022

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ARTICLES · Volume 24, Issue 12, P1375-1386, December 2023 · *Open Access* Download Full Issue

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

Iona Evans, PhD [a,*] · Daniel Reisel, PhD [a,*] · Allison Jones, BSc [a,*] · Alba Bajrami, MBBS [b,*] · Simrit Nijjar, MBBS [b] · Sarah Annie Solangon, MBBS [b] · Rupali Arora, MD [c] · Elisa Redl, MSc [d,e] · Lena Schreiberhuber, MSc [d,e] · Isma Ishaq-Parveen [d] · Julia Rothärmel, MSc [d] · Chiara Herzog, PhD [d,e] · Prof Davor Jurkovic, PhD [b] · Prof Martin Widschwendter, MD [a,d,e,f,g] ✉ Show less

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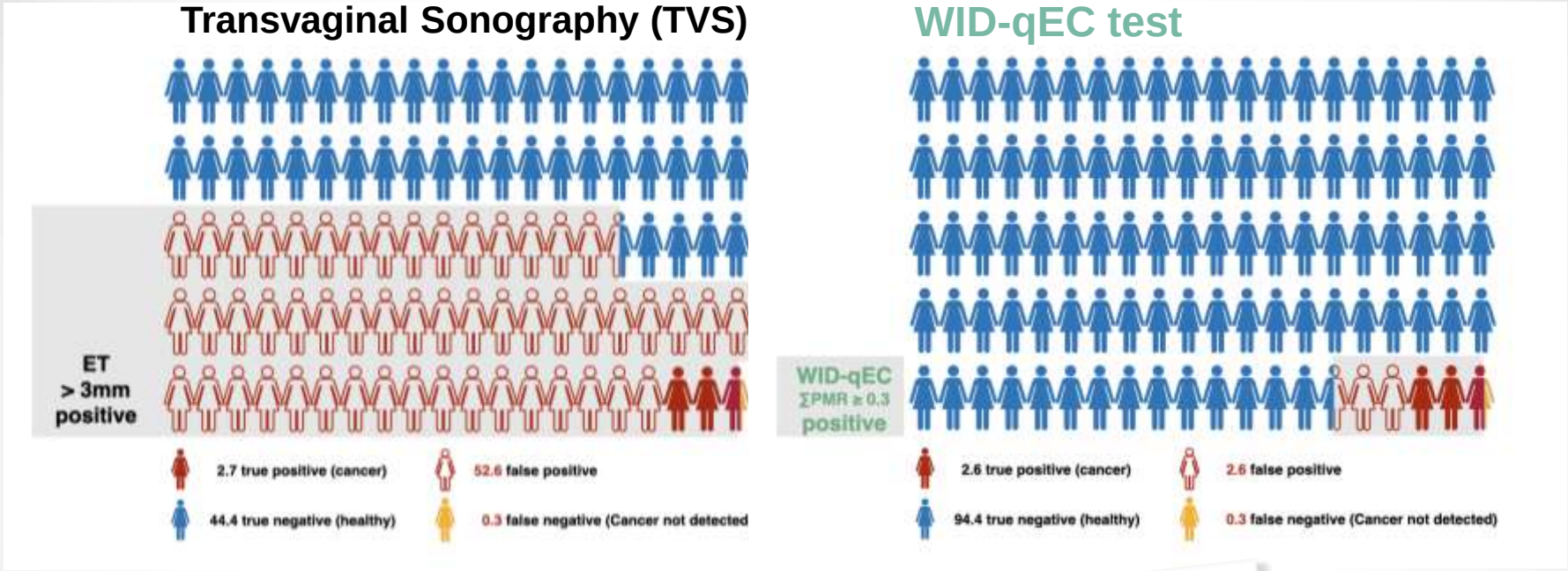
	Endometrial thickness (n=369)				Pattern recognition (n=366)	WID-qEC (n=378)	
	>3 mm	≥4·5 mm	≥5 mm	≥4·5 mm or polyp, or both	Suggestive of cancer	≥0·03 ΣPMR	≥0·3 ΣPMR
Population prevalence (number of cancer cases out of total individuals with available test)	11 (3%)	11 (3%)	11 (3%)	11 (3%)	11 (3%)	11 (3%)	11 (3%)
Sensitivity (95% CI)	90·9% (62·3–98·4)	90·9% (62·3–98·4)	72·7% (43·4–90·3)	90·9% (62·3–98·4)	63·6% (35·4–84·8)	90·9% (62·3–98·4)	90·9% (62·3–98·4)
Specificity (95% CI)	45·8% (40·7–51·0)	79·1% (74·5–82·9)	81·0% (76·6–84·7)	61·7% (56·6–66·6)	99·2% (97·5–99·7)	92·1% (88·9–94·4)	97·3% (95·1–98·5)
Positive predictive value (95% CI)	4·9% (2·7–8·8)	11·8% (6·5–20·3)	10·5% (5·4–19·4)	6·8% (3·7–12·1)	70·0% (39·7–89·2)	25·6% (14·6–41·1)	50·0% (29·9–70·1)
Negative predictive value (95% CI)	99·4% (96·6–99·9)	99·6% (98·0–99·9)	99·0% (97·0–99·7)	99·5% (97·5–99·9)	98·9% (97·1–99·6)	99·7% (98·3–99·9)	99·7% (98·4–100·0)

ΣPMR=sum of the percentage of fully methylated reference.

Table 3: **Performance characteristics of sonographic assessments and the WID-qEC test in women with a final diagnosis**



Rate of false positive women decreased by 95%
(from 52.6% for ET to 2.6% for WID-qEC)

Evans, Reisel, Jones, Bajrami et al, Lancet Oncol 2023

WID-easy Overview

	Sum	PBM[1] Cohort	ForeCee[1] Case-Control	Barcelona[1] Case-Control	Karolinska[1] Cohort	Hall[2] Cohort	Hall[2] Case-Control	EpiSure[3] Cohort	Copan[4] Case-Control	Ghana[5] Cohort
		Real Life	Endometrial Cancer	Endometrial Cancer	Endometrial Cancer	Real Life	Cervical Cancer	Real Life	Endometrial & Cervical Cancer	Real Life
Collection Device		Cotton swab	Cervex/ThinPrep	Evalyn Brush Self sample	Cervex/ThinPrep	Cervex/SurePath	Cervex/ThinPrep	Cervex/ThinPrep	Copan/eNat	Cervex/ThinPrep
Remarks		PMB	AUB	AUB	Cervical Screening (asymptomatic); EC diagnosed within 1 year after sample collection	General Hospital Cohort, various conditions		True cohort of ALL women presenting with AUB in one UK diagnostic centre	AUB	True cohort of ALL women presenting with AUB in African diagnostic centres
Participants	1,399	63	137	251	37	304	51	378	102	76
Cancer	324	8	71	131	22	6	23	12	28	23
No Cancer	1,075	55	66	120	15	298	28	366	74	53
Sensitivity		100%	97.2%	90.1%	90.9%	100%	100%	90.9%	92.9%	100%
95% CI		(83.1% - 100%)	(90.2% - 99.7%)	(83.6% - 94.6%)	(70.8% - 98.9%)	(54.1% - 100%)	(85.2% - 100%)	(82.3% - 98.4%)	(75.0% - 98.8%)	(58.1% - 100%)
Specificity		89.1%	75.8%	86.7	100%	84.6%	92.9%	97.3	98.6%	76.1%
95% CI		(77.8% - 95.9%)	(83.6% - 85.5%)	(79.3% - 92.2%)	(81.9% - 100%)	(80% - 88.5%)	(76.5% - 99.1%)	(95.1% - 98.5%)	(91.7% - 99.9%)	(80.9% - 86.9%)
PPV		45.4%	28.4%	40.1%		9 %	47.2%	50.0%	68%	38.9%
95% CI		(27.4% - 60.2%)						(29.9% - 70.1%)		(18.3% - 63.9%)
NPV		98.3%	99.6%	98.9%		99.7%	99.4%	99.7%	99.8%	100%
95% CI		(92.3% - 99.4%)						(98.4% - 100%)		(87.7% - 100%)
Comments			Case/control, PPV/NPV modelled; no 95%CI	Case/control, PPV/NPV modelled; no 95%CI	Samples form health cohort in advance of diagnosis, no PPV/NPV	Case/control, PPV/NPV modelled; no 95%CI	Case/control, PPV/ NPV modelled; no		Case/control, PPV/NPV modelled; no 95%CI	

[1] Herzog et al, J Clin Oncol 2022
[2] Schreiberhuber et al, Int J Cancer 2023
[3] Evans et al, Lancet Oncol 2023
[4] Illah et al, Int J Cancer 2024
[5] submitted and under review

Interpretation The WID-qEC test delivers fast results and shows improved performance compared with a combination of imaging index tests. Triage of women with abnormal uterine bleeding using the WID-qEC test could reduce the number of women requiring histological assessments for identification of potential malignancy and specifically reduce the false positive rate.

Post COVID Era

- Cancer diagnostics- evolving field
- Internet 1995- small town
- COVID 2019- small village
- Collaboration without borders

Thank you

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