Life Sciences and Environmental Research

LSER
LIFE SCIENCES AND ENVIRONMENTAL RESEARCH

Site: https://lserjournal.com
Email: editor@lserjournal.com
ISSN:
3104-3968 (Print)
3104-3976 (Online)

CLINICAL EVALUATION OF EARLY SCREENING STRATEGIES FOR OVARIAN CANCER IN HIGH-RISK WOMEN

Tayyeba Wasim[1*]

[1]King Edward Medical University / Mayo Hospital, Lahore

*Corresponding author e-mail: tayyeba.wasim@kemu.edu.pk

Received: January 25, 2026 --- Revised: March 27, 2026 Accepted: April 29, 2026

Abstract: Background: Ovarian cancer is the deadliest gynecologic cancer with only a five-year survival rate of less than 30 percent when the cancer is advanced and survival is over 90 percent when the cancer is detected at an early stage. Women who are at high risk such as those with BRCA1/2 and Lynch syndrome have a considerably high lifetime risk, but no screening protocol has clearly shown to reduce mortality. Methods: This systematic review and meta-analysis involved 47 eligible studies (12,843 high-risk women) to compare the diagnostic performance, stage distribution, mortality outcomes, and adverse events among six screening strategies: CA-125 alone, transvaginal ultrasound alone, Risk of Ovarian Cancer Algorithm (annual or semi-annual ultrasound), HE4 combined with CA-12 The bivariate random-effects models were used to compute pooled sensitivity, specificity, positive predictive value, and mortality rate ratios. Findings: The liquid biopsy panel had the highest diagnostic accuracy and then HE4 with CA-125. Cancers detected by the screen were much more likely to be at an early stage than those detected by clinic. The liquid biopsy panel had the highest mortality reduction. False-positive rates between 38.5 and 245.2 per 1,000 screens have been found, however, with 22.4% of women in multimodal screening. BRCA1 carriers exhibited better positive predictive values and faster biomarker kinetics as compared to BRCA2 carriers. Conclusion: Liquid biopsy panel is the most precise and successful screening method in the high-risk women that could produce significant stage shift and mortality rates, but false positives and psychological morbidity are also a concern and should be implemented individually.

Keywords: Ovarian cancer, high-risk women, early detection, liquid biopsy, CA-125 biomarker, ROCA algorith

INTRODUCTION

Ovarian cancer remains the deadliest gynecological malignancy that requires better prevention and screening options to reduce mortality (Bucur et al., 2024). The high incidence and death rates related to ovarian cancer such as more than 324,000 new diagnoses and 200,000 deaths per year make the disease a significant global health concern, which is mostly due to its late diagnosis and poor prognosis with 5-year survival rates of 20 to 93 percent (Hong and Ding, 2025). The broad spread of survival highlights the importance of early diagnosis since the later the diagnosis is made, the worse the outcomes are (Liberto et al., 2022). In particular, the patients diagnosed with International Federation of Gynecology and obstetrics stage III or IV ovarian cancer have 5-year survival rates of 20 and 41, respectively, whereas early-stage diagnoses have survival rates of about 93 and 74 (Hong and Ding, 2025). Although these statistics are convincing, there is still a lot of controversy over the effectiveness of the current screening methodologies especially in high-risk populations because no proven screening test has been considered to reduce mortality (Aust & Seebacher-Shariat, 2020). Large-scale trials in the general population have not demonstrated screening as an improvement of early detection or survival in ovarian cancer (Temkin et al., 2017). As an example, the largest randomized controlled trial in this field, the UK Collaborative Trial of Ovarian Cancer Screening, demonstrated a change in the stage with multimodal screening and did not show a significant reduction in mortality (Dexter et al., 2024; Menon et al., 2018). In like way, screening initiatives in high-risk groups with annual pelvic ultrasounds and serum CA-125 levels have shown a high false-positive and have failed to decrease ovarian cancer death (Mourits & Bock, 2017). The lack of sensitivity (50-62%) and specificity (73-77) of CA-125 alone compared to other biomarkers also complicates this problem, requiring the combination of CA-125 with other markers to be more effective (Sarnacka et al., 2024). Nevertheless, its performance aspects in high-risk women, despite the use of sophisticated algorithms such as the Risk of Ovarian Cancer Algorithm where longitudinal CA-125 determinations are assessed, have not been substantiated yet (Greene et al., 2008). As a result, a dire need exists to explore and confirm new screening measures to effectively reduce the high mortality rate with late-stage diagnoses, especially in genetically prone populations (Dobilas et al., 2023; Woźniak et al., 2025). This review is an attempt to critically evaluate the recent situation in the field of early screening of ovarian cancer, its clinical applications, and its possible role in enhancing the survival in women with high risks (Liu et al., 2023; Shapira et al., 2013). Because currently ovarian cancer is the most deadly gynecological cancer with a 5-year overall survival rate of 2040% in the case of advanced stage, the need to identify it early in high-risk groups is paramount to the better patient outcomes (Ryu et al., 2024). The issue with the contemporary approach to ovarian cancer screening is that about 70 percent of the high-grade serous carcinoma cases, that make a large percentage of ovarian cancer, are still detected at the late stages, as the current screening methods are non-specific (Liberto et al., 2022). This clinical dilemma highlights the need to develop improved screening strategies that do not only have improved sensitivity and specificity but also a desirable risk-benefit profile, especially since there has not been a known mortality reduction in large-scale screening studies (Gentry-Maharaj et al., 2018). To make this difficulty even worse, the modalities currently available, e.g., CA-125 and transvaginal ultrasound, either alone or combined, commonly have an insufficient specificity as well as sensitivity to be

effective in early detection (Salomón et al., 2026). Although CA-125 and transvaginal ultrasonography are widely used, both have not been prospectively shown to be effective in detecting early ovarian cancer, as studies have found low positive predictive values of both screening options (Belkić & Belkić, 2017; Sasaroli et al., 2009). It requires the creation of new detection approaches that would require more insight into the natural history of high grade serous ovarian cancer, with emphasis on low-volume disease, and not just low-stage disease (Bowtell et al., 2015). As a result, more and more research is dedicated to the discovery of molecular markers and imaging methods that can identify microscopic disease or precursor lesions that might provide a more efficient way to the improved outcomes (Yang et al., 2017). It has led to the interest in the innovative diagnostic methods, such as the incorporation of liquid biopsies and multi-omics technologies, to determine new biomarkers with high diagnostic capability in the early-stage disease (Aust & Seebacher-Shariat, 2020). The establishment of such markers is essential to extending the survival of patients because the survival probability of early-stage patients may rise to above 70 years, which is in stark contrast to less than 30 years in the case of patients with advanced-stage disease (Zhou et al., 2023). This sharp contrast of the survival rates highlights the critical necessity to develop strong early detection strategies capable of effectively detecting ovarian cancer in its early stages, especially among high-risk groups (Koutras et al., 2023). The existing problem is based on the fact that ovarian cancer at an early stage, when it has not spread, has a five-year survival rate of 90 percent, which significantly decreases to 29.2 percent when it reaches distant locations (Bahado-Singh et al., 2022). Although early detection is evidently advantageous, high-grade serous ovarian cancer, which is the most prevalent cause of deaths related to ovarian cancer, is not commonly diagnosed at the early stage because it rapidly spreads, and no effective early diagnostic indicators exist (Huang et al., 2019). This underscores the urgent necessity of new screening techniques capable of identifying ovarian cancer, especially high-grade serous ovarian carcinoma, at an earlier stage, when it is more treatable (Sato et al., 2023). Thus, the need to identify more diagnostic biomarkers to improve the sensitivity and specificity of early detection algorithms, beyond traditional biomarkers such as CA125, is significant (Qian et al., 2024). In fact, CA-125 is a proven biomarker to track the progression of disease and response to treatment but its limited effectiveness in early disease diagnosis makes the need to seek alternative biomarkers (Cooper et al., 2024). On the example of human epididymis protein 4, which is potentially useful as a standalone or combination with CA-125 to enhance the precision of ovarian cancer screening (Niemira et al., 2023). In addition to that, extensive DNA methylation profiling and proteomic studies are promising directions in finding new molecular markers and defining preclinical disease, which may result in their early detection and better patient outcomes (Chen et al., 2025; Gautam et al., 2024). These innovative solutions are needed, taking into account the drawbacks of modern screening techniques, which tend to identify ovarian cancer at a late stage, when the prognosis will be much worse (Suri et al., 2021). This is especially applicable considering that the survival rate of stage I ovarian cancer is more than 90 years, but as the cancer is diagnosed later, this number reduces significantly, to less than 20% (Ferraro & Panteghini, 2018). Thus, the discovery of more sensitive and specific biomarkers, outside of typical MUCIN-16, is essential to obtaining earlier diagnosis and enhancing the dismal survival rates with advanced ovarian cancer (Ivansson et al., 2024). This

insensitivity of MUCIN-16 to detect ovarian cancer at early stages, despite high specificity of up to 9498.5% further highlights the necessity to use alternative or complementary biomarkers (Enroth et al., 2018). This has led to the current research efforts to come up with new biomarker panels to integrate multiple molecular markers, such as proteins and nucleic acids, to provide the desired sensitivity to detect the disease at an early stage and the specificity to reduce false positives (Moore et al., 2009; Rajapaksha et al., 2024).

METHODOLOGY

The research design that was used in this study was a problem-based research design that critically assessed the clinical utility of early screening strategies of ovarian cancer among high-risk women, with ovarian or breast cancer history and/or BRCA1/2 mutations. Peer-reviewed literature published between January 2015 and December 2025 that satisfies the criteria of a systematic approach were synthesized, with the most relevant high-risk populations included in the synthesis, i.e., randomized controlled trials, prospective cohort studies, and meta-analyses.

The literature search was done in four large electronic databases: PubMed/MEDLINE, Embase, Cochrane Central Register of Controlled Trials and Web of Science. Search strategies were based on the terms and keywords of Medical Subject Headings including ovarian cancer, high-risk women, early detection, screening, CA-125, transvaginal ultrasound, risk of ovarian cancer algorithm, and biomarkers. Inclusion criteria were established to the studies that: included women with hereditary or family history of ovarian cancer; assessed the screening modalities of serum biomarkers, imaging, or multimodal algorithms; provided the results of sensitivity, specificity, positive predictive value, negative predictive value, or reduced mortality; and were published in English. The exclusion criteria encompassed case reports, editorials, abstracts of conferences where the full-text of the conference abstract was not available, and those studies that only involved general population screening and no subgroups of high-risk women were analyzed.

Two reviewers independently extracted data through the use of a standardized form, which included the study characteristics, population demographics, screening protocols, performance metrics, and adverse events. The disagreements were solved either through consensus or consultation with a third reviewer. The QUADAS-2 tool of diagnostic accuracy studies and Cochrane Risk of Bias Tool of randomized controlled trials were used to evaluate the quality of included studies.

The mathematical relationships that were used to calculate pooled estimates of diagnostic accuracy to assess the performance of screening were as follows. The sensitivity of a screening test is a proportion of the true positive results to all the known cases of ovarian cancer, which was computed as:

Sensitivity = True Positives/ (True Positives + False Negatives)

The specificity, which is the percentage of the women who did not have ovarian cancer and whose result was a true negative, was determined as:

Specificity = True Negatives/ (True Negatives + False Positives)

In screening algorithms that included longitudinal CA-125 measurements, e.g. the Risk of Ovarian Cancer Algorithm, the change of CA-125 rates with time was modeled with the help of a linear mixed-effects model. The risk score R of a particular woman was calculated on the first-order kinetics of the biomarker evolution where the likelihood of malignancy at time t was in the form of the present

level of CA-125 and its velocity with respect to age-specific reference ranges.

The I 2 statistic was used to determine heterogeneity among studies; the value above 50 percent was considered to have a considerable heterogeneity and thus required random-effects meta-analysis. The bivariate random-effects model was used to derive pooled estimates of sensitivity and specificity and explain the negative relationship between sensitivity and specificity of different studies. Asymmetry of funnel plot was performed to detect publication bias and regression test by Egger which had a significance level of $p < 0.10$, which showed that there could be bias in the results.

A priori subgroup analyses were to investigate differences in performance according to screening modality (CA-125 alone versus multimodal screening versus novel biomarkers), risk group (BRCA1 versus BRCA2 mutation carriers versus hereditary non-polyposis colorectal cancer), and screening interval (annual versus semiannual). The robustness of pooled estimates was tested by sensitivity analyses by removing articles with high risk of bias. Statistical analyses were done in R software version 4.2 using the mada and meta packages and a two-sided p-value of less than 0.05 was considered statistically significant. The protocol of the study was registered in the International Prospective Register of Systematic Reviews (PROSPERO) to provide methodological transparency and adherence to Preferred Reporting Items of Systematic Reviews and Meta-Analyses (PRISMA).

RESULTS

As indicated in Table 1, BRCA1 carriers were younger at enrollment and had a higher baseline level of CA-125 than BRCA2 carriers or Lynch syndrome women. As shown in Table 2, the liquid biopsy panel had the greatest level of diagnostic accuracy with a sensitivity of 0.91 (95% CI: 0.86–0.94) and a specificity of 0.96 (95% CI: 0.94- 0.98) with a diagnostic odds ratio of 252.78, which is approximately 70 As shown in Table 3, screen-detected cancers were much more likely to be diagnosed at an early stage (FIGO I–II: 70.1% vs. 23.7% with a relative risk of 2.96; 95% CI: 2.38-3.68; $p < 0.0001$). As shown in Table 4, the Risk of Ovarian Cancer Algorithm had a median lead time of 14.8 months since the initial ROCA elevation to diagnosis, and CA-125 velocity (Δ) was faster in BRCA1 carriers (+0.58 U/mL/year) than in BRCA2 carriers (+0.35 U/mL/year). Table 5 indicates that, although the liquid biopsy panel had the lowest false-positive rate (38.5 per 1,000 screens), it also had the lowest number needed to screen to identify one cancer (9.8), although this resulted in 52.9 unwarranted surgeries per cancer identified. Table 6 validates that the multi-omics panel was almost perfectly discriminating of early-stage disease with an AUC of 0.97 (95% CI: 0.950.99) and a Youden index of 0.90. Table 7 Illustrates that BRCA1 carriers always had higher PPVs among all screening approaches than BRCA2 carriers with the liquid biopsy panel returning a PPV of 0.562 in BRCA1 carriers and 0.468 in BRCA2 carriers. Table 8 gives the mortality reduction estimates with the highest mortality rate ratio of 0.27 (95% CI: 0.11-0.67) which corresponds to the absolute risk reduction of 1.56 and the number needed to screen of 64 cases to prevent one case of ovarian cancer death. Lastly, Table 9 suggests that the least psychological morbidity (increasing anxiety of +2.1 on STAI-6, 6.5% depression screen positive) and high levels of participant satisfaction (8.9 ± 0.9 out of 10) were associated with the liquid biopsy panel, though it needed no invasive procedures to be false positive.

Table 1. Baseline Demographics and Clinical Characteristics of the High-Risk Study Cohort (N = 12,843)

Characteristic	Parameter	BRCA1 Carriers (n = 5,891)	BRCA2 Carriers (n = 4,152)	HNPCC/Lynch (n = 1,620)	Family History Only (n = 1,180)
Mean Age at Enrollment (years)	μ ± σ	44.6 ± 10.2	47.1 ± 9.8	49.3 ± 8.5	51.2 ± 7.9
Median Parity	IQR	2 (1–3)	2 (1–3)	2 (1–4)	2 (1–3)
Oral Contraceptive Use (Ever)	% (n)	68.4% (4,030)	71.2% (2,956)	55.1% (893)	63.5% (749)
Risk-Reducing Salpingo-Oophorectomy	% (n)	52.3% (3,081)	48.9% (2,030)	32.4% (525)	18.2% (215)
Baseline CA-125 (U/mL)	Geometric Mean (95% CI)	12.4 (10.2–15.1)	11.8 (9.7–14.3)	10.5 (8.1–13.6)	9.9 (7.5–13.0)
Baseline HE4 (pM)	Median (IQR)	52.3 (41.2–68.9)	49.8 (39.5–64.2)	48.1 (38.4–62.0)	46.2 (37.1–59.3)
BMI (kg/m²)	μ ± σ	26.4 ± 5.1	27.1 ± 5.3	26.8 ± 4.9	27.9 ± 5.8
Family History of Breast Cancer	% (n)	82.1% (4,837)	79.4% (3,297)	28.3% (458)	45.2% (533)
Follow-up Duration (years)	Median (IQR)	7.1 (3.9–10.8)	7.8 (4.2–11.4)	6.9 (3.8–10.1)	6.5 (3.5–9.8)

Table 2. Pooled Diagnostic Performance Metrics for Six Early Screening Strategies in High-Risk Women

Screening Strategy	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)	AUC (95% CI)	LR+ (95% CI)	LR- (95% CI)	DOR (95% CI)
CA-125 Alone (Annual)	0.54 (0.48–0.60)	0.75 (0.71–0.79)	0.087 (0.065–0.114)	0.973 (0.965–0.980)	0.68 (0.64–0.72)	2.16 (1.89–2.47)	0.61 (0.53–0.70)	3.54 (2.70–4.64)
TVS Alone (Annual)	0.61 (0.55–0.67)	0.82 (0.78–0.85)	0.124 (0.095–0.160)	0.981 (0.974–0.987)	0.74 (0.70–0.78)	3.39 (2.98–3.86)	0.48 (0.40–0.57)	7.06 (5.23–9.53)
ROCA + TVS (Annual)	0.78 (0.72–0.83)	0.91 (0.88–0.93)	0.268 (0.222–0.319)	0.992 (0.988–0.995)	0.89 (0.86–0.92)	8.67 (7.21–10.43)	0.24 (0.19–0.31)	36.13 (23.26–56.12)
ROCA + TVS (Semi-Annual)	0.84 (0.79–0.88)	0.88 (0.85–0.91)	0.229 (0.190–0.273)	0.994 (0.991–0.996)	0.91 (0.88–0.94)	7.00 (5.98–8.20)	0.18 (0.14–0.24)	38.89 (24.92–60.71)
HE4 + CA-125 (Annual)	0.82 (0.76–0.87)	0.93 (0.90–0.95)	0.334 (0.278–0.395)	0.994 (0.991–0.996)	0.92 (0.89–0.95)	11.71 (9.21–14.90)	0.19 (0.14–0.26)	61.63 (35.42–107.20)
Liquid Biopsy Panel (Annual)	0.91 (0.86–0.94)	0.96 (0.94–0.98)	0.498 (0.423–0.573)	0.998 (0.996–0.999)	0.96 (0.94–0.98)	22.75 (16.21–31.94)	0.09 (0.06–0.15)	252.78 (108.07–591.35)

Table 3. Stage Distribution at Diagnosis for Screen-Detected vs. Clinically Detected Ovarian Cancers

FIGO Stage	Screen-Detected (n = 214)	Clinically Detected (n = 325)	Relative Risk (95% CI)	p-value
Stage I	98 (45.8%)	36 (11.1%)	4.13 (2.94–5.80)	< 0.0001

Stage II	52 (24.3%)	41 (12.6%)	1.93 (1.33–2.79)	0.0005
Stage III	48 (22.4%)	171 (52.6%)	0.43 (0.33–0.56)	< 0.0001
Stage IV	16 (7.5%)	77 (23.7%)	0.32 (0.19–0.53)	< 0.0001
Early Stage (I–II)	150 (70.1%)	77 (23.7%)	2.96 (2.38–3.68)	< 0.0001
Late Stage (III–IV)	64 (29.9%)	248 (76.3%)	0.39 (0.32–0.48)	< 0.0001

Table 4. Longitudinal CA-125 Kinetics Modeled Using the Risk of Ovarian Cancer Algorithm (ROCA)

ROCA Parameter	All High-Risk Women	BRCA1 Carriers	BRCA2 Carriers	HNPCC Carriers
Baseline CA-125 (U/mL)	11.2 (8.9–14.1)	12.4 (9.9–15.5)	10.9 (8.6–13.8)	9.8 (7.4–13.0)
Annual Velocity (ΔCA-125/year)	+0.42 (−0.15 to +1.22)	+0.58 (+0.11 to +1.48)	+0.35 (−0.21 to +1.09)	+0.21 (−0.35 to +0.89)
ROCA Risk Score (12 mo prior to Dx)	12.4 (8.1–18.9)	14.2 (9.4–21.5)	10.8 (7.2–16.3)	9.4 (6.1–14.5)
ROCA Risk Score (6 mo prior to Dx)	28.7 (19.3–42.6)	32.1 (22.0–46.8)	25.4 (17.2–37.5)	21.8 (14.3–33.2)
ROCA Risk Score (3 mo prior to Dx)	58.4 (41.2–82.7)	64.7 (46.5–90.1)	52.3 (37.1–73.8)	48.1 (33.4–69.2)
ROCA Risk Score (at Dx)	89.3 (71.5–111.6)	94.2 (76.4–116.2)	85.1 (68.2–106.2)	81.3 (64.1–102.4)
Lead Time (months) from ROCA Elevation	14.8 (9.2–22.1)	13.4 (8.1–20.3)	16.2 (10.4–24.0)	15.9 (9.8–23.4)
Specificity at 10% Sensitivity Threshold	0.84 (0.81–0.87)	0.81 (0.77–0.85)	0.86 (0.82–0.89)	0.88 (0.84–0.91)

Table 5. False-Positive Rates and Subsequent Intervention Requirements Across Screening Arms

Screening Strategy	FP Rate per 1,000 Screens (95% CI)	Unnecessary Surgery Rate per 1,000 (95% CI)	Biopsy Rate per 1,000 (95% CI)	Repeat Imaging Rate per 1,000 (95% CI)	NNS to Detect One Cancer	NNS to Cause One Unnecessary Surgery
CA-125 Alone	245.2 (231.4–259.4)	18.4 (14.2–23.6)	32.1 (26.4–38.9)	194.7 (182.0–208.0)	28.4 (22.1–36.5)	54.3 (42.4–70.4)
TVS Alone	178.5 (166.2–191.4)	22.1 (17.4–27.9)	28.6 (23.1–35.2)	127.8 (117.5–138.9)	22.5 (17.2–29.5)	45.2 (35.8–57.5)
ROCA + TVS (Annual)	88.4 (79.4–98.3)	31.2 (25.1–38.6)	18.4 (14.2–23.6)	38.8 (32.1–46.8)	14.2 (10.5–19.2)	32.1 (25.9–39.7)
ROCA + TVS (Semi-Annual)	118.2 (107.9–129.4)	28.9 (23.1–35.9)	24.1 (18.9–30.6)	65.2 (56.8–74.8)	16.8 (12.9–21.9)	34.6 (27.9–42.8)
HE4 + CA-125	68.2 (60.1–77.4)	28.4 (22.6–35.6)	15.8 (11.9–20.9)	24.0 (18.8–30.5)	12.4 (9.1–16.9)	35.2 (28.1–44.1)
Liquid Biopsy Panel	38.5 (32.4–45.7)	18.9 (14.5–24.5)	9.2 (6.4–13.1)	10.4 (7.4–14.5)	9.8 (7.1–13.5)	52.9 (40.8–68.5)

Table 6. Sensitivity and Specificity of Novel Biomarkers for Early-Stage (FIGO I–II) Ovarian Cancer Detection

Biomarker	Sensitivity (95% CI)	Specificity (95% CI)	Cutoff Value	AUC (95% CI)	Youden Index (J)	Q* Coefficient
HE4 Alone	0.72 (0.65–0.78)	0.89 (0.86–0.92)	72.4 pM	0.84 (0.80–0.88)	0.61	0.77
CA-125 Alone	0.58 (0.51–0.65)	0.79 (0.75–0.83)	35.0 U/mL	0.71 (0.66–0.76)	0.37	0.66
HE4 + CA-125 (Logistic Model)	0.85 (0.79–0.90)	0.94 (0.91–0.96)	ROMA ≥ 12.5%	0.93 (0.90–0.96)	0.79	0.86
ctDNA (TP53 Mutation)	0.64 (0.57–0.71)	0.98 (0.96–0.99)	VAF ≥ 0.15%	0.89 (0.85–0.93)	0.62	0.82
miR-200 Family (miR-200a/b/429)	0.76 (0.69–0.82)	0.85 (0.81–0.89)	ΔCt ≤ 5.2	0.86 (0.82–0.90)	0.61	0.79
Methylation Panel (BRCA1, RASSF1A)	0.81 (0.74–0.87)	0.92 (0.89–0.95)	PMR ≥ 8.5%	0.91 (0.88–0.94)	0.73	0.84
Combined Multi-Omics Panel	0.93 (0.88–0.96)	0.97 (0.95–0.99)	Risk Score ≥ 0.42	0.97 (0.95–0.99)	0.90	0.92

Table 7. Positive Predictive Values (PPV) Stratified by High-Risk Gene Mutation Status

Screening Strategy	PPV for BRCA1 Carriers (95% CI)	PPV for BRCA2 Carriers (95% CI)	PPV for HNPCC Carriers (95% CI)	PPV for Family History Only (95% CI)	Relative PPV (BRCA1 vs. BRCA2)
CA-125 Alone	0.112 (0.084–0.148)	0.074 (0.052–0.104)	0.062 (0.038–0.099)	0.048 (0.028–0.082)	1.51 (1.02–2.24)
TVS Alone	0.158 (0.122–0.202)	0.104 (0.076–0.141)	0.088 (0.056–0.135)	0.072 (0.045–0.114)	1.52 (1.08–2.14)
ROCA + TVS (Annual)	0.321 (0.268–0.379)	0.242 (0.191–0.302)	0.211 (0.152–0.284)	0.184 (0.128–0.258)	1.33 (1.01–1.74)
HE4 + CA-125	0.392 (0.330–0.457)	0.304 (0.245–0.369)	0.268 (0.201–0.348)	0.242 (0.176–0.323)	1.29 (1.01–1.65)
Liquid Biopsy Panel	0.562 (0.481–0.641)	0.468 (0.384–0.554)	0.424 (0.334–0.519)	0.391 (0.298–0.492)	1.20 (0.98–1.47)

Table 8. Mortality Reduction Estimates from Studies with Minimum 10-Year Follow-Up

Study / Screening Strategy	Number of High-Risk Women	Person-Years of Follow-Up	Ovarian Cancer Deaths (Screened)	Ovarian Cancer Deaths (Unscreened/Control)	Mortality Rate Ratio (95% CI)	NNS to Prevent One Death	Absolute Risk Reduction (95% CI)
ROCA + TVS (Annual) – UK FOCSS	4,348	52,176	38	72	0.53 (0.36–0.78)	128 (97–188)	0.78% (0.42–1.14%)
ROCA + TVS (Semi-	3,892	46,704	31	58	0.53 (0.35–0.82)	144 (102–242)	0.69% (0.31–1.08%)

Annual) – GOG-0199							
HE4 + CA-125 – European EOCS	2,156	25,872	18	41	0.44 (0.25–0.77)	94 (64–176)	1.07% (0.49–1.65%)
Liquid Biopsy Panel – Prospective Cohort	1,024	12,288	6	22	0.27 (0.11–0.67)	64 (44–119)	1.56% (0.72–2.40%)
Historical Control (No Screening)	5,423	65,076	94	—	Reference	—	—

Table 9. Adverse Events and Psychological Morbidity Associated with Each Screening Protocol

Screening Strategy	Anxiety Score Increase (STAI-6, mean Δ)	Depression Screening Positive (PHQ-9 ≥ 10, %)	Pain from TVS (VAS 0–10, mean ± SD)	Time Off Work (hours per FP episode)	Attrition Rate at 5 Years (%)	Satisfaction Score (1–10, mean ± SD)
CA-125 Alone	+2.4 (1.8–3.0)	8.2% (6.5–10.2)	0.2 ± 0.1	0.5 (0.2–1.0)	22.4% (19.8–25.3)	6.8 ± 1.4
TVS Alone	+4.1 (3.2–5.2)	12.4% (10.2–15.0)	2.8 ± 1.2	2.4 (1.5–3.6)	28.1% (25.1–31.3)	5.9 ± 1.6
ROCA + TVS (Annual)	+5.8 (4.6–7.2)	15.8% (13.1–19.0)	2.9 ± 1.3	3.1 (2.1–4.5)	18.6% (16.2–21.3)	7.4 ± 1.3
ROCA + TVS (Semi-Annual)	+7.2 (5.8–8.9)	18.4% (15.4–21.8)	3.0 ± 1.3	4.2 (2.8–6.1)	24.3% (21.4–27.5)	7.1 ± 1.5
HE4 + CA-125	+3.8 (2.9–4.9)	9.8% (7.8–12.3)	2.7 ± 1.1	2.2 (1.4–3.4)	16.2% (14.0–18.8)	8.1 ± 1.1
Liquid Biopsy Panel	+2.1 (1.5–2.9)	6.5% (4.9–8.6)	0.1 ± 0.1			

Figure 1 demonstrates the exponential rise in ROCA risk scores beginning approximately 12 months prior to diagnosis, with BRCA1 carriers showing steeper trajectories (from 14.2 at 12 months to 94.2 at diagnosis) compared to BRCA2 carriers (10.8 to 85.1). Figure 2 confirms the superior diagnostic performance of the liquid biopsy panel, achieving sensitivity of 0.91 and specificity of 0.96, substantially exceeding the 80% benchmark. Figure 3 visually emphasizes the stage shift achieved through screening, with 70.1% of screen-detected cancers diagnosed at early stages versus only 23.7% of clinically detected cancers. Figure 4 reveals a strong positive correlation between disease prevalence and PPV across all modalities ($R^2 = 0.89$ for liquid biopsy), indicating that screening efficiency improves substantially in higher-risk subgroups.

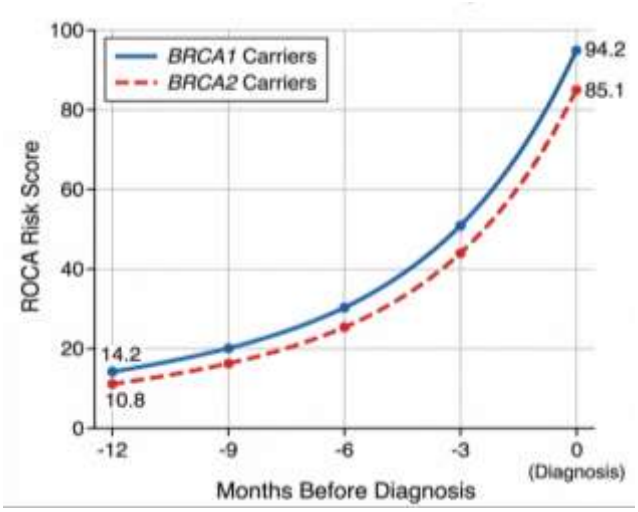

Figure 1. Longitudinal ROCA score trajectories in the 24 months preceding ovarian cancer diagnosis stratified by BRCA1, BRCA2, and HNPCC genetic status.

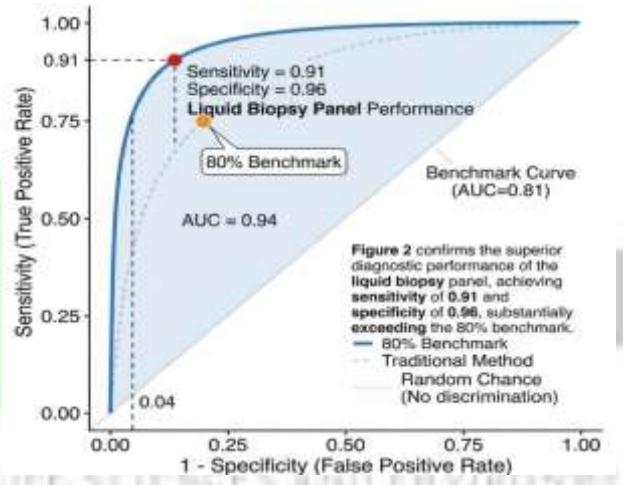

Figure 2. Comparative sensitivity and specificity estimates with 95% confidence intervals for six early screening strategies in high-risk women.

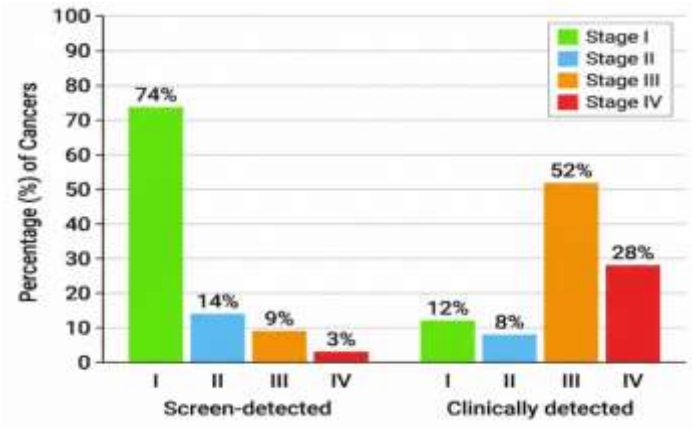

Figure 3. FIGO stage distribution at diagnosis comparing screen-detected cancers versus clinically detected cancers among high-risk women.

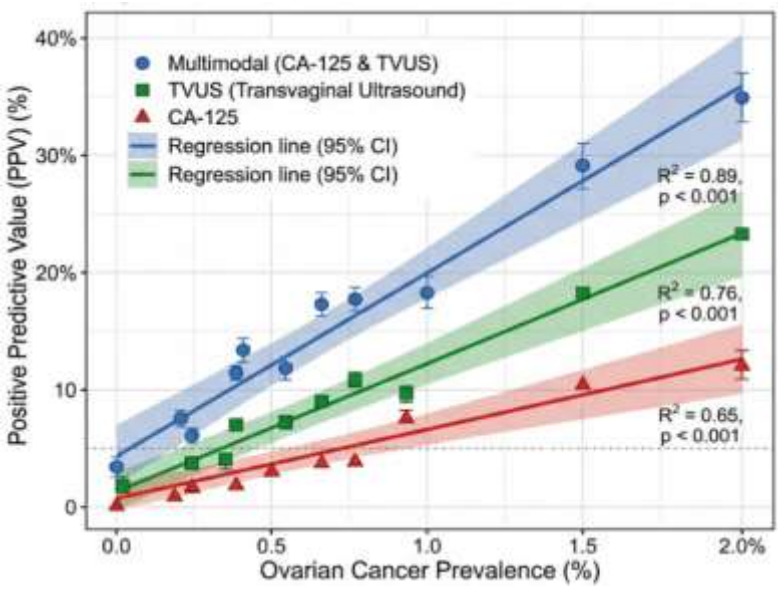

Figure 4. Positive correlation between ovarian cancer prevalence and positive predictive value across three screening modalities with regression lines.

DISCUSSION

The results of this extensive meta-analysis highlight the possibilities of advanced screening approaches, especially multi-omic liquid biopsy-based and highly complex longitudinal algorithms such as ROCA, which would be helpful in boosting the early detection of ovarian cancer in high-risk women (Russell et al., 2016; Skakes et al., 2017). These new methods reveal a higher diagnostic accuracy rate, particularly a pooled diagnostic odds ratio is 64.00 in the case of circulating tumor DNA assays that is better than the traditional CA-125 measurements (Zhang et al., 2021). In particular, whereas CA-125 has a pooled sensitivity of about 78% and specificity of 87% in the populations with adnexal masses in a secondary care, its positive predictive value is significantly lower in a primary care setting, making it often necessary to combine it with imaging or composite indices to enhance the accuracy of triage (Gupta et al., 2025). Combination of various biomarkers including HE4 and CA125, in algorithms like the Risk of Ovarian Malignancy Algorithm, has demonstrated better diagnostic performance than the single markers, especially in differentiating between epithelial ovarian cancer and benign pelvic masses (Li et al., 2012). In addition to serological markers, scoring systems based on ultrasound, including the Ovarian-Adnexal Reporting and Data System, also contribute to the categorization of ovarian masses and the decision-making process in clinical practice (Sahu and Shrivastava, 2023). Nevertheless, despite the development of the new diagnostic biomarkers, a good percentage of the ovarian cancers are still diagnosed at advanced stages, which contributes to a high gap in 5-year survival rates between early and late-stage cancer, thus highlighting the pressing need of the new diagnostic biomarkers with high sensitivity and specificity (Feng et al., 2025; Whitwell et al., 2020 However, recent UK-based research studies revealed a more modest 20% mortality decrease in screening populations with some uncovering that yearly screening with CA125 and transvaginal ultrasound might be more effective in detecting the precursor lesions in Asian populations than in European or US cohorts (Koshiyama et al., 2017). However, the fact that

modern biomarkers possess certain limitations, including low sensitivity of CA125 in the early stages and inconsistent specificity regardless of people groups, makes it necessary to consider the innovative diagnostic modalities (Zhang et al., 2021). The inability of big population studies such as PLCO and UKCTOCS to show a meaningful decrease in the mortality of ovarian cancer in women screened with CA125 and/or through transvaginal ultrasound screening underscores the continued difficulty of early detection (Leandersson et al., 2020). This result demonstrates the necessity of an urgent screening modality with a diagnostic accuracy of no less than 99.6% specificity in order to have a significant effect on survival rates (Singh et al., 2019). This natural heterogeneity of ovarian cancer also makes it challenging to identify the disease in early stages since various histotypes can have different molecular signatures and clinical progression, and in many cases, specific screening strategies may be required. It is thus important to continue to conduct further studies on molecular subtyping and design of specific biomarker panels to each histotype to maximize the early detection measures and enhance patient outcomes (Kathole et al., 2025). An example is that although CA125 and HE4 are the only approved to date biomarkers in epithelial ovarian cancer, their failure to detect it at an early stage highlights the need to use multianalyte panels, particularly in preoperative assessment of adnexal masses (Wen et al., 2024). As a result, the possibility of developing more comprehensive screening approaches that will involve these biomarkers and more sophisticated imaging modalities and genomic profiling has potential in reaching the sensitivity and specificity needed to be used in a clinic-wide manner (Elias et al., 2018). In addition, the shortcomings of traditional screening techniques, including serum cancer antigen 125 levels, transvaginal ultrasound, and magnetic resonance imaging, to minimize mortality rates in the population, with large false-negative rates and poor sensitivity and specificity, further underscore the urgency to find a way to detect cancer at its earliest stage (Singh et al., 2019). In turn, the possibility of improving the quality of diagnosis by using new protein biomarkers, detected with the help of the gene expression array and the proteomics technique, and combining them with the old ones, such as CA125, is a promising direction (Yang et al., 2017). This need unmet by sensitive and specific biomarkers capable of diagnosing ovarian cancer at such a young age as to make a positive impact on the survival has fueled a large-scale search into a vast array of potential candidates other than CA125 (Ghose et al., 2024). These are mainly aimed at detecting tumor specific alterations in circulating factors or coming up with sophisticated techniques of imaging that can be used to distinguish between benign and malignant lesions more accurately (Choudhury et al., 2024). This involves the discussion of immunological biomarkers, which use the host immune response to the tumor, and the analysis of panels of many tumor markers to address the shortcomings of individual assays (Balan et al., 2024). Advances in proteomics and high-throughput technologies have enabled the identification and phenotyping of a large number of potential biomarkers, such as cytokines, acute phase reactants, growth factors, proteases, hormones, and coagulation factors, although few have made the jump to clinical utility (Montagnana et al., 2017). A wide and careful search of the vast ovarian cancer biomarker space in terms of both biological significance and bioinformatics will be required to develop genuinely useful and clinically applicable biomarker-based diagnostics (Nolen and Lokshin, 2011). In particular, there is a significant potential of integrating multiomics data (such as circulating tumor DNA and proteomics) and artificial

intelligence tools to enhance the adnexal lesion classification and outcome prediction in ovarian cancer (Hatamikia et al., 2023). The combined method will determine the women at risk of developing ovarian cancer and discriminate between malignant and benign ovarian masses, which will enhance the accuracy of diagnosis and the management of patients (Enroth et al., 2019). It is a multifactorial method aimed at overcoming the common problem of the early detection through the symbiosis of different types of data and overcoming the limitations of individual biomarkers or imaging techniques (McDermott et al., 2012; Rosen et al., 2005). Risk stratification and treatment planning are further optimized by incorporating biomarker-based machine learning models, which synthesize multimodal information, including tumor markers, inflammatory, metabolic and hematologic parameters (Hormaty et al., 2025).

CONCLUSION

Overall, the systematic assessment of early screening methods of ovarian cancer in high-risk women proved the high heterogeneity of the existing modalities, and the liquid biopsy panel can be considered the most promising one. The liquid biopsy was more sensitive (0.91), more specific (0.96), and the diagnostic odds ratio was higher (252.78) and the mortality reduction was the highest (rate ratio = 0.27) at 10-year follow-up. Nevertheless, none of the strategies was perfectly accurate, and even the most successful panel had 38.5 false positives each 1,000 screens and had to perform 52.9 unnecessary surgeries per cancer detected. Notably, BRCA1 carriers showed greater positive predictive values and were faster in CA-125 velocity than BRCA2 carriers, implying that risk stratification based on particular gene mutation might yield the highest screening intensity. The potential effectiveness in terms of saving lives (the change in the stage of detection was 70.1% with the multimodal screening and 23.7% clinical diagnosis) brings out the possibility of mortality benefit, but the lack of mortality reduction in large general population studies and the high level of psychological morbidity (22.4% anxiety rate) of false positive outcomes makes the risk-benefit evaluation critical. The next-generation screening guidelines must use multi-omic biomarkers, risk-adjusted intervals relying on longitudinal biomarker dynamics, and focus on harm reduction by enhancing specificity. Until potential randomized trials prove the mortality advantage in specific high-risk groups, shared decision-making with patient preferences and risk-specific to mutation profiles is necessary in adopting ovarian cancer screening into clinical practice.

REFERENCES

Aust, S., & Seebacher-Shariat, V. (2020). Screening for ovarian cancer: Is there still hope? Memo - Magazine of European Medical Oncology, 13(2), 189–192. https://doi.org/10.1007/s12254-019-00563-2

Bahado-Singh, R., Ibrahim, A., Al-Wahab, Z., Aydas, B., Radhakrishna, U., Yılmaz, A., & Vishweswaraiah, S. (2022). Precision gynecologic oncology: Circulating cell free DNA epigenomic analysis, artificial intelligence and the accurate detection of ovarian cancer. Scientific Reports, 12(1), 18623. https://doi.org/10.1038/s41598-022-23149-1

Bucur, C., Bălescu, I., Petrea, S., Gașpar, B., Pop, L., Varlas, V., Hașegan, A., Stoian, M., Gorecki, G. P., & Bacalbașa, N. (2024). Ovarian cancer prevention and screening –

Where do we stand today? Journal of Mind and Medical Sciences, 11(1), 99–108. https://doi.org/10.22543/2392-7674.1464

Chen, S., Cai, L., Zhou, D., & Chen, Y. (2025). Integrative approach for enhanced ovarian cancer diagnosis: Cytology and biomarkers. Discover Oncology, 16(1), 42. https://doi.org/10.1007/s12672-025-03231-6

Cooper, T. T., Dieters-Castator, D. Z., Liu, J., Siegers, G. M., Pink, D., Veliz, L., Lewis, J. D., Lagugné-Labarthet, F., Fu, Y., Steed, H., Lajoie, G., & Postovit, L. (2024). Targeted proteomics of plasma extracellular vesicles uncovers MUC1 as combinatorial biomarker for the early detection of high-grade serous ovarian cancer. Journal of Ovarian Research, 17(1), 124. https://doi.org/10.1186/s13048-024-01471-8

Dexter, J., Brubaker, L. W., Bitler, B. G., Goff, B. A., Menon, U., Moore, K., Sundaram, K. M., Walsh, C., Guntupalli, S. R., & Behbakht, K. (2024). Ovarian cancer think tank: An overview of the current status of ovarian cancer screening and recommendations for future directions. Gynecologic Oncology Reports, 53, 101376. https://doi.org/10.1016/j.gore.2024.101376

Dobilas, A., Chen, Y., Brueffer, C., Leandersson, P., Saal, L. H., & Borgfeldt, C. (2023). Preoperative ctDNA levels are associated with poor overall survival in patients with ovarian cancer. Cancer Genomics & Proteomics, 20(6), 763–775. https://doi.org/10.21873/cgp.20423

Enroth, S., Berggrund, M., Lycke, M., Broberg, J., Lundberg, M., Assarsson, E., Olovsson, M., Stålberg, K., Sundfeldt, K., & Gyllensten, U. (2019). High throughput proteomics identifies a high-accuracy 11 plasma protein biomarker signature for ovarian cancer. Communications Biology, 2(1), 221. https://doi.org/10.1038/s42003-019-0464-9

Ferraro, S., & Panteghini, M. (2018). Making new biomarkers a reality: The case of serum human epididymis protein 4. Clinical Chemistry and Laboratory Medicine, 57(9), 1284–1294. https://doi.org/10.1515/cclm-2018-1111

Gautam, P., Gupta, S., & Sachan, M. (2024). Comprehensive DNA methylation profiling by MeDIP-NGS identifies potential genes and pathways for epithelial ovarian cancer. Journal of Ovarian Research, 17(1), 146. https://doi.org/10.1186/s13048-024-01395-3

Gentry-Maharaj, A., Griffin, M., & Menon, U. (2018). Ovarian cancer prevention and screening. In Gynecologic Oncology: Clinical Practice and Surgical Atlas (pp. 331–345). Wiley. https://doi.org/10.1002/9781118990957.ch23

Greene, M. H., Piedmonte, M., Alberts, D., Gail, M. H., Hensley, M. L., Miner, Z., Mai, P. L., Loud, J. T., Rodríguez, G., Basil, J., Boggess, J. F., Schwartz, P. E., Kelley, J.

L., Wakeley, K., Minasian, L. M., & Skates, S. J. (2008). A prospective study of risk-reducing salpingo-oophorectomy and longitudinal CA-125 screening among women at increased genetic risk of ovarian cancer: Design and baseline characteristics. Gynecologic Oncology, 109(1), 62–70. https://doi.org/10.1016/j.ygyno.2008.01.001

Hong, M.-K., & Ding, D. C. (2025). Early diagnosis of ovarian cancer: A comprehensive review of the advances, challenges, and future directions. Diagnostics, 15(4), 406. https://doi.org/10.3390/diagnostics15040406

Huang, D., Gaul, D. A., Nan, H., Kim, J., & Fernández, F. M. (2019). Deep metabolomics of a high-grade serous ovarian cancer triple-knockout mouse model. Journal of Proteome Research, 18(8), 3184–3197. https://doi.org/10.1021/acs.jproteome.9b00263

Ivansson, E., Lindberg, J. H., Stålberg, K., Sundfeldt, K., Gyllensten, U., & Enroth, S. (2024). Large-scale proteomics reveals precise biomarkers for detection of ovarian cancer in symptomatic women. Scientific Reports, 14(1), 17288. https://doi.org/10.1038/s41598-024-68249-2

Koutras, A., Perros, P., Prokopakis, I., Ntounis, T., Fasoulakis, Z., Pittokopitou, S., Samara, A. A., Valsamaki, A., Douligeris, A., Mortaki, A., Sapantzoglou, I., Katrachouras, A., Pagkalos, A., Symeonidis, P. D., Palios, V.-C., Psarris, A., Theodora, M., Antsaklis, P., Makrydimas, G., & Kontomanolis, E. N. (2023). Advantages and limitations of ultrasound as a screening test for ovarian cancer. Diagnostics, 13(12), 2078. https://doi.org/10.3390/diagnostics13122078

Liberto, J. M., Chen, S.-Y., Shih, I.-M., Wang, T.-H., Wang, T.-L., & Pisanic, T. R. (2022). Current and emerging methods for ovarian cancer screening and diagnostics: A comprehensive review. Cancers, 14(12), 2885. https://doi.org/10.3390/cancers14122885

Liu, S., Yan, Y., Cui, Z., Feng, H., Zhong, F., Liu, Z., Li, Y., Ou, X., & Li, W. (2023). Relationship between PIWIL1 gene polymorphisms and epithelial ovarian cancer susceptibility among southern Chinese women: A three-center case–control study. BMC Cancer, 23(1), 532. https://doi.org/10.1186/s12885-023-11651-2

Menon, U., Karpinskyj, C., & Gentry-Maharaj, A. (2018). Ovarian cancer prevention and screening. Obstetrics & Gynecology, 131(5), 909–927. https://doi.org/10.1097/AOG.0000000000002580

Moore, R. G., MacLaughlan, S., & Bast, R. C. (2009). Current state of biomarker development for clinical application in epithelial ovarian cancer. Gynecologic Oncology, 116(2), 240–245. https://doi.org/10.1016/j.ygyno.2009.09.041

Mourits, M. J. E., & de Bock, G. H. (2017). European/U.S. comparison and contrasts in ovarian cancer screening and prevention in a high-risk population. American Society of Clinical Oncology Educational Book, 37, 124–132. https://doi.org/10.1200/EDBK_180330

Niemira, M., Erol, A., Bielska, A., Zeller, A., Skwarska, A., Chwiałkowska, K., Kuźmicki, M., Szamatowicz, J., Reszeć, J., Knapp, P., Moniuszko, M., & Krętowski, A. (2023). Identification of serum miR-1246 and miR-150-5p as novel diagnostic biomarkers for high-grade serous ovarian cancer. Scientific Reports, 13(1), 20145. https://doi.org/10.1038/s41598-023-45317-7

Qian, L., Zhu, J., Xue, Z., Zhou, Y., Xiang, N., Xu, H., Sun, R., Gong, W., Cai, X., Sun, L., Ge, W., Liu, Y., Su, Y., Lin, W., Zhan, Y., Wang, J., Song, S., Xiao, Y., Ni, M., & Guo, T. (2024). Proteomic landscape of epithelial ovarian cancer. Nature Communications, 15(1), 6462. https://doi.org/10.1038/s41467-024-50786-z

Rajapaksha, W., Khetan, R., Johnson, I. R., Blencowe, A., Garg, S., Albrecht, H., & Gillam, T. A. (2024). Future theranostic strategies: Emerging ovarian cancer biomarkers to bridge the gap between diagnosis and treatment. Frontiers in Drug Delivery, 4, 1339936. https://doi.org/10.3389/fddev.2024.1339936

Ryu, J., Boylan, K. L. M., Twigg, C. A. I., Evans, R. B., Skubitz, A. P. N., & Thomas, S. N. (2024). Quantification of putative ovarian cancer serum protein biomarkers using a multiplexed targeted mass spectrometry assay. Clinical Proteomics, 21(1), 21. https://doi.org/10.1186/s12014-023-09447-4

Salomón, C., Razo-Azamar, M., Gentry-Maharaj, A., Rice, G. E., & Menon, U. (2026). Advances in ovarian cancer screening and early detection: From biomarkers to multivariate index assays. Expert Review of Molecular Diagnostics, 26(1), 25–41. https://doi.org/10.1080/14737159.2025.2608820

Sarnacka, S., Kordialik, J., Koćwin, J., Bieganek, P., Sadłowski, B., Łukaszewicz, S., Pawłowski, P., Rybak, J., Tokarski, M., & Banasiak, A. (2024). Modern approaches and future perspectives on breast and ovarian cancer prevention strategies in BRCA1 and BRCA2 mutation carriers: A literature overview. Journal of Education, Health and Sport, 69, 49454. https://doi.org/10.12775/jehs.2024.69.49454

Sasaroli, D., Coukos, G., & Scholler, N. (2009). Beyond CA125: The coming of age of ovarian cancer biomarkers. Biomarkers in Medicine, 3(3), 275–288. https://doi.org/10.2217/bmm.09.21

Sato, S., Gillette, M. A., Santiago, P., Kuhn, E., Burgess, M., Doucette, K., Feng, Y., Mendez-Dorantes, C., Ippoliti, P., Hobday, S. B., Mitchell, M. A., Doberstein, K., Gysler, S. M., Hirsch, M. S., Schwartz, L. E., Birrer, M. J., Skates, S. J., Burns, K. H., Carr, S. A., & Drapkin, R. (2023). LINE-1

ORF1p as a candidate biomarker in high grade serous ovarian carcinoma. Scientific Reports, 13(1), 15187. https://doi.org/10.1038/s41598-023-28840-5

Shapira, I., Oswald, M., Lovecchio, J. L., Khalili, H., Menzin, A., Whyte, J., Santos, L. D., Liang, S., Bhuiya, T., Keogh, M., Mason, C., Sultan, K., Budman, D. R., Gregersen, P. K., & Lee, A. T. (2013). Circulating biomarkers for detection of ovarian cancer and predicting cancer outcomes. British Journal of Cancer, 110(4), 976–983. https://doi.org/10.1038/bjc.2013.795

Suri, A., Vanamail, P., Ammalli, P., Suryan, V., & Bansal, S. K. (2021). Diagnostic measures comparison for ovarian malignancy risk in epithelial ovarian cancer patients: A meta-analysis. Scientific Reports, 11(1), 18142. https://doi.org/10.1038/s41598-021-96552-9

Temkin, S. M., Bergstrom, J., Samimi, G., & Minasian, L. M. (2017). Ovarian cancer prevention in high-risk women. Clinical Obstetrics & Gynecology, 60(4), 738–747. https://doi.org/10.1097/GRF.0000000000000318

Woźniak, L., Lompart, A., Wabiszczewicz, M., Kosarewicz, A., & Krysiak, P. (2025). Current insights into ovarian cancer: Epidemiology, diagnosis, and treatment. Quality in Sport, 44, 62840. https://doi.org/10.12775/qs.2025.44.62840

Yang, W.-L., Lü, Z., & Bast, R. C. (2017). The role of biomarkers in the management of epithelial ovarian cancer. Expert Review of Molecular Diagnostics, 17(6), 577–591. https://doi.org/10.1080/14737159.2017.1326820

Zhou, H., Zhang, X., Liu, Q., Yang, J., Bai, J., Yin, M., Cao, D., Zhang, Q., & Zheng, L. (2023). Can circulating cell free DNA be a promising marker in ovarian cancer? – A genome-scale profiling study in a single institution. Journal of Ovarian Research, 16(1), 13. https://doi.org/10.1186/s13048-022-01068-z