Ovarian cancer: Early detection isn't the answer we thought

Written by The Life Science Feed Editorial Team · Published 15 September 2026 · Edited by Mara Voss

> Ovarian cancer, often dubbed the "silent killer," frequently presents at advanced stages, leading to a grim prognosis for many women. This persistent diagnostic delay occurs despite extensive research into screening strategies aimed at earlier detection. The challenge lies in the disease's biology and the limitations of current screening modalities.

KEY TAKEAWAYS

- The Pivot: Despite significant investment in research, no population-wide screening method has demonstrated a survival benefit for ovarian cancer.
- The Data: The majority of ovarian cancer cases are still diagnosed at FIGO stage III or IV, when the disease has already spread beyond the ovaries.
- The Action: Clinicians must maintain a high index of suspicion for vague symptoms in at-risk women and advocate for prompt referral to specialist care.

Ovarian cancer is the eighth most common cancer among women globally and the leading cause of death from gynaecological malignancy. Its high mortality rate stems directly from late diagnosis, with over 70% of cases identified at advanced stages (FIGO III or IV) where the cancer has already metastasized. This late presentation severely limits treatment options and significantly impacts survival rates.

The disease typically originates in the epithelial cells lining the ovaries, fallopian tubes, or peritoneum. Symptoms are often non-specific and subtle in early stages, mimicking common benign conditions such as irritable bowel syndrome or menopause. These include abdominal bloating, pelvic or abdominal pain, difficulty eating or feeling full quickly, and urinary symptoms like urgency or frequency. The insidious onset means patients often delay seeking medical attention, and clinicians may not immediately suspect malignancy.

The Elusive Quest for Early Detection

For decades, the medical community has sought an effective screening tool for ovarian cancer, similar to mammography for breast cancer or cervical cytology for cervical cancer. The goal has been to identify the disease before symptoms appear, when surgical resection is more likely to be curative. But this has proven to be an exceptionally difficult undertaking.

Early screening efforts focused on transvaginal ultrasound (TVUS) and serum CA-125 levels. TVUS can detect ovarian masses, but it struggles to differentiate benign from malignant lesions, leading to a high rate of false positives and unnecessary surgeries. CA-125, a glycoprotein biomarker, is elevated in many ovarian cancer cases, but its sensitivity

and specificity are insufficient for population screening, particularly in early-stage disease. It can also be elevated in benign conditions like endometriosis, fibroids, or even menstruation, further complicating its utility.

Large-scale randomized controlled trials have investigated various screening algorithms combining TVUS and CA-125. These trials typically enrolled tens of thousands of asymptomatic women, often with annual screening over several years. The primary endpoint was usually a reduction in ovarian cancer mortality. But these extensive studies have consistently failed to demonstrate a significant reduction in mortality for the general population. The challenges in establishing effective screening registries for other gynaecological cancers highlight the systemic difficulties.

Why Biomarkers and Imaging Fall Short

The inherent biological characteristics of ovarian cancer contribute significantly to the failure of current screening methods. The disease is heterogeneous, comprising several distinct histological subtypes with different molecular profiles and clinical behaviors. Epithelial ovarian cancer, the most common type, includes serous, endometrioid, clear cell, and mucinous carcinomas. Each subtype may express different biomarkers or present with varying imaging features, making a single universal screening test unlikely to succeed.

High-grade serous ovarian cancer (HGSOC), the most aggressive and prevalent subtype, is often thought to originate in the fimbrial end of the fallopian tube, not the ovary itself. This understanding complicates the traditional focus on ovarian imaging. By the time these microscopic lesions grow large enough to be detected by TVUS or produce sufficient CA-125 to register as an abnormal level, the cancer has often already disseminated.

The rapid progression of some ovarian cancer subtypes also poses a challenge. Even if a screening test could detect a very early lesion, the window between detectability and advanced disease might be too short to intervene effectively. This rapid growth means that annual or biennial screening intervals might miss cancers that develop quickly between screens.

The Role of Risk Factors and Genetic Predisposition

While population-wide screening has not proven effective, targeted screening for high-risk individuals remains a critical component of ovarian cancer management. Women with germline mutations in genes like BRCA1 and BRCA2 have a significantly elevated lifetime risk of developing ovarian cancer. Other genetic syndromes, such as Lynch syndrome, also increase risk.

For these high-risk women, current guidelines recommend intensive surveillance, often involving annual or semi-annual CA-125 measurements and TVUS. But even in this high-risk group, the efficacy of screening in preventing mortality is debated. Many clinicians advocate for risk-reducing salpingo-oophorectomy (RRSO) once childbearing is complete, as this surgical intervention is the most effective way to reduce ovarian cancer risk in mutation carriers. This surgical approach, however, is not without its own set of considerations, including surgical menopause and its associated health implications.

The lack of a reliable screening test means that clinical suspicion remains paramount. GPs and specialists must be acutely aware of the subtle symptoms of ovarian cancer, especially in women over 50 or those with a family history. Persistent, unexplained abdominal symptoms warrant thorough investigation, including physical examination, imaging, and appropriate laboratory tests. For a comprehensive overview of oncology practice, the Oxford Handbook of Oncology (4th ed) provides a valuable reference.

The Path Forward: New Avenues of Research

Research continues into novel biomarkers and imaging techniques. Efforts are underway to identify multi-biomarker panels that could improve sensitivity and specificity beyond CA-125. These panels often combine CA-125 with other proteins, such as HE4 (human epididymis protein 4), to create risk algorithms. While some of these panels show promise in differentiating benign from malignant pelvic masses, their utility for asymptomatic population screening is still under investigation.

Liquid biopsies, which analyze circulating tumor DNA (ctDNA) or circulating tumor cells (CTCs) in blood, represent another exciting area of research. These technologies could theoretically detect cancer at its earliest stages by identifying genetic mutations or cellular abnormalities shed by tumors. But the technical challenges of detecting minute quantities of tumor material in early-stage disease are substantial. The sensitivity required for effective screening is far greater than what is needed for monitoring established disease or detecting recurrence.

Imaging advancements, including diffusion-weighted MRI and PET scans, are also being explored, but their cost and accessibility make them unsuitable for population-wide screening. These modalities are currently reserved for diagnostic work-up or staging in symptomatic patients. The fundamental problem remains: ovarian cancer often does not produce a detectable signal until it has already progressed. This is a stark contrast to lung cancer screening, where low-dose CT has shown a clear mortality benefit in high-risk smokers.

The persistent challenge of late diagnosis underscores the urgent need for continued research into the fundamental biology of ovarian cancer. Understanding the earliest molecular events that drive tumor initiation and progression could unlock new targets for detection. Without a deeper understanding of these mechanisms, screening efforts will likely continue to chase a moving target. The focus must shift from simply detecting a mass to identifying the earliest molecular signatures of disease. This is a complex undertaking, but one that holds the greatest promise for improving outcomes for women.

> **CLINICAL IMPLICATIONS**
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> The ongoing failure to establish effective population-wide screening for ovarian cancer means clinicians cannot rely on a test to catch this disease early. This places a significant burden on primary care and general gynaecology to recognize the subtle, often vague symptoms that might indicate malignancy. A high index of suspicion, particularly in postmenopausal women or those with a family history, is not merely good practice, it is the only current strategy.
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> Referral pathways must be streamlined for women presenting with persistent, unexplained abdominal or pelvic symptoms. Delays in specialist assessment can directly translate to worse outcomes. While CA-125 and TVUS have limitations as screening tools, they remain valuable in the diagnostic work-up of symptomatic patients, guiding further investigation and referral.
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> For women with known genetic predispositions, such as BRCA1/2 mutations, the discussion around risk-reducing salpingo-oophorectomy should be proactive and thorough. This surgical option, while significant, offers the most robust protection against ovarian cancer in this high-risk group. It is a conversation that requires careful consideration of individual patient circumstances, including age, reproductive plans, and personal preferences.
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> The pharmaceutical industry and academic researchers must continue to invest in novel biomarker discovery

> and advanced imaging techniques. The current toolkit is simply inadequate. Until a truly effective early detection method emerges, the onus remains on vigilant clinical practice and rapid access to specialist care to mitigate the devastating impact of this disease.

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