

Ovarian Cancers: Evolving Paradigms in Research and Care gives a broad overview of the state of the science in ovarian cancer research, highlights major knowledge gaps, and provides recommendations to help reduce the incidence of and morbidity and mortality from ovarian cancers by focusing on promising research themes that could advance risk prediction, prevention, early detection, comprehensive care, and cure. The committee focused on identifying the research gaps that, if addressed, could have the greatest impact on reducing morbidity or mortality.

The committee identified four overarching concepts that should be applied to each recommendation in this report:

- As the most common and lethal subtype, the study of high-grade serous carcinomas needs to be given priority.
- Even so, more subtype-specific research is also needed to further define the differences among the various subtypes;
- Given the relative rarity and heterogeneity of ovarian cancers, collaborative research (including the pooling and sharing of data and biospecimen resources, such as through consortia) is essential; and
- The dissemination of new knowledge and the implementation of evidence-based interventions and practices are the final steps in the knowledge translation process.

A wide variety of stakeholders are integral to ovarian cancer research, including the U.S. Congress, federal agencies (e.g., the Centers for Disease Control and Prevention, Department of Defense, Food and Drug Administration, National Institutes of Health), private foundations, industry, academic institutions, professional societies, and advocacy groups. Most of these stakeholders are engaged in research across the care continuum, and many are both funders and performers of research. The committee therefore concluded that directing research toward the gaps identified in the recommendations is the responsibility of all stakeholders in their individual and collaborative efforts to fund, perform, or advocate for ovarian cancer research.

The following recommendations are intertwined and so need to be considered simultaneously, not sequentially. Their sequence should not be considered as priority of importance or order of implementation.

The biology of ovarian cancer

RECOMMENDATION 1

Researchers and funding organizations should design and prioritize preclinical, clinical, and population-based research agendas in the context of the different ovarian cancer subtypes. A top priority should be elucidating the cellular origins and pathogenesis of each subtype. Particular attention should be paid to

- Tumor characteristics such as microenvironment, intratumoral heterogeneity, and progression pathways;
- Development of experimental model systems that reflect ovarian cancer heterogeneity; and
- Incorporation of the multisubtype paradigm into prevention, screening, diagnosis, and treatment research.

RECOMMENDATION 2

Pathology organizations, oncology professional groups, and ovarian cancer researchers should reach consensus on diagnostic criteria, nomenclature, and classification schemes that reflect the morphological and molecular heterogeneity of ovarian cancers and promote the universal adoption of a standardized taxonomy.

Risk assessment, screening, and early detection

RECOMMENDATION 3

Researchers, public health practitioners, and clinicians should develop and implement innovative strategies to increase genetic counseling and testing, as well as cascade testing, for known germline genetic predispositions in appropriate populations (e.g., untested ovarian cancer survivors, relatives of individuals who tested positive). Furthermore, researchers, clinicians, and commercial laboratories should determine the analytic performance and clinical utility of testing for other germline mutations beyond BRCA1 and BRCA2 and the mismatch repair genes associated with Lynch Syndrome.

RECOMMENDATION 4

Researchers and funding organizations should identify and evaluate the underlying mechanisms of both new and established risk factors for ovarian cancers to develop and validate a dynamic risk assessment tool accounting for the various ovarian cancer subtypes. Furthermore, a spectrum of risk factors should be considered, including genetics, hormonal and other biological markers, behavioral and social factors, and environmental exposures.

RECOMMENDATION 5

Clinicians, researchers, and funding organizations should focus on quantifying the risk-benefit balance of nonsurgical and surgical prevention strategies for specific subtypes and at-risk populations.

RECOMMENDATION 6

Researchers and funding organizations should focus on the development and assessment of early detection strategies that extend beyond current imaging modalities and biomarkers and reflect the pathobiology of each ovarian cancer subtype.

Diagnosis and treatment

RECOMMENDATION 7

To reduce disparities in health care delivery and outcomes, clinicians and researchers should investigate methods to ensure the consistent implementation of current standards of care (e.g., access to specialist care, surgical management, chemotherapy regimen and route of administration, and universal germline genetic testing for newly-diagnosed women), that are linked to quality outcome metrics.

RECOMMENDATION 8

Clinicians and researchers should focus on improvement of current treatment strategies, including

- Development and validation of comprehensive clinical, histopathologic, and molecular characterizations that better inform precision medicine approaches for women with newly diagnosed and recurrent disease.
- Advancement in the understanding of the mechanisms of recurrent and drug-resistant (e.g., platinum resistant) disease and development of a more informative classification system;
- Identification of predictors of response to therapy and near-term indicators of efficacy.
- Determination of the optimal type and timing of surgery in women newly diagnosed with ovarian cancer and efficacy of subsequent cytoreduction procedures for women with recurrent disease.

RECOMMENDATION 9

Researchers should develop more effective pharmacologic and nonpharmacologic therapies and combinations of therapies that leverage the unique biology and clinical course of ovarian cancer. These approaches should include

- Developing immunologic and molecularly driven treatment approaches specific to the different ovarian cancer subtypes,
- Identifying markers of therapeutic resistance and exceptional response, and
- Using interdisciplinary teams to design and conduct statistically efficient and information-rich clinical studies.

Supportive care along the survivorship trajectory

RECOMMENDATION 10

Researchers and funding organizations should study the supportive care needs of patients with ovarian cancer throughout the disease trajectory, including

- Identifying the array of factors that put women at high risk for poor physical and psychosocial outcomes,
- Identifying and overcoming barriers to systematic assessment of physical and psychosocial effects of disease and treatment,
- Developing and implementing more effective supportive care and self-management interventions, and
- Defining the parameters that indicate when patients and their families would benefit from transitioning to end-of-life care.

Dissemination and implementation of knowledge

RECOMMENDATION 11

Stakeholders in ovarian cancer research, clinical care, and advocacy should coordinate efforts to develop and implement efficient, effective, and reliable methods for rapid dissemination and implementation of evidence-based information and practices to patients, families, health care providers, advocates, and other relevant parties. These efforts should include

- Researching impediments to adopting current evidence-based practices;
- Using multiple existing dissemination modalities (e.g., continuing education, advocacy efforts) to distribute messages strongly supported by the evidence base, and
- Evaluating newer pathways of dissemination and implementation (e.g., social media, telemedicine with specialists).

To download the full report and to find additional resources, visit [nas.edu/OvarianCancers](https://www.nas.edu/OvarianCancers)