Ovarian Cancers: Evolving Paradigms in Research and Care

Although recent years have seen promising advances in cancer research, there remain surprising gaps in the fundamental knowledge about and understanding of ovarian cancer, including basic biology, risk factors, diagnosis, delivery of care, and survivorship. Ovarian cancer is relatively uncommon, yet it is one of the deadliest cancers. Symptoms such as bloating, pelvic or abdominal pain, and urinary symptoms can be nonspecific, so they are often not initially seen as indicating a serious illness. Late diagnosis and a high rate of recurrence are major factors contributing to the high mortality rate.

Ovarian cancer is not just one disease; rather, it is a constellation of distinct types of cancer involving the ovary. Epithelial cancers (carcinomas) represent 85 percent of malignant ovarian tumors and are responsible for most ovarian cancer–related deaths. Ovarian carcinomas are further classified into different subtypes, the most common subtype being high-grade serous carcinoma (HGSC). Recent evidence suggests that many ovarian carcinomas do not arise in the ovary per se. Instead, they may arise from cells that are not considered intrinsic to the ovary, or from other tissues and then metastasize to the ovary.

With support from the Centers for Disease Control and Prevention (CDC), the Institute of Medicine (IOM) of the National Academies of Sciences, Engineering, and Medicine convened an expert committee to examine and summarize the state of the science in ovarian cancer research, to identify key gaps in the evidence base, and to identify opportunities for advancing ovarian cancer research. The resulting report, *Ovarian Cancers: Evolving Paradigms in Research and Care* gives a broad overview of ovarian cancer research 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.
FIGURE Continuum of Research to Advance Ovarian Cancer Prevention and Care

To guide its deliberative process, the committee developed a conceptual model to identify research gaps across the continuum of ovarian cancer care and in critical areas of cross-cutting research. Colored figures represent phases of the ovarian cancer care continuum where research can be focused. Black boxes indicate critical areas of ongoing cross-cutting research that span these phases.

AREAS OF RECOMMENDATION

The committee identified four overarching concepts to be applied to each recommendation:

- 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 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.
- The dissemination of new knowledge and the implementation of evidence-based interventions and practices are the final steps in the knowledge translation process.
The Biology of Ovarian Cancer

Ovarian cancer research is complicated by the significant degree of heterogeneity of ovarian carcinomas, both within and between subtypes, yet clinicians and researchers tend to combine them in many types of research. In spite of recent advances, the incomplete understanding of the basic biology of each subtype, including origin and pathogenesis, is an impediment to advances in prevention, screening and early detection, diagnosis, treatment, and supportive care.

Gaps in the understanding of ovarian cancer biology have also prevented the emergence of uniform standards for describing the characteristics of the subtypes. The implementation of a single, uniformly applied nomenclature and classification scheme with standardized diagnostic criteria is essential and will serve as the necessary foundation for all future research in ovarian cancer. Achieving this consensus will be complex and will require the efforts of multiple stakeholders engaged in an iterative process.

Risk Assessment, Screening, and Early Detection

Better methods for identifying women at high risk could facilitate the prevention or early detection of ovarian cancers. A family history of ovarian cancer and certain genetic mutations and hereditary cancer syndromes have strong associations with risk for ovarian cancer. Genetic counseling and testing are recommended for all women with an invasive ovarian cancer and for certain high-risk women, but barriers prevent widespread referral to these services. Several nongenetic factors are also associated with either an increased or decreased risk for developing ovarian cancer; however, patterns of association are inconsistent. Research is needed to determine the significance of known risk factors, and to identify potential new risk factors. Women known to be at high risk may benefit from nonsurgical and surgical preventive measures, but the risk–benefit ratios of these measures need to be better defined for different subtypes and at-risk populations.

Current approaches for early detection of ovarian cancers, including assaying for biomarkers and use of imaging technologies, have resulted in more ovarian cancers being detected at earlier stages, but to date have not had a substantial impact on overall mortality. While research on refining current methods of early detection may be fruitful, distinct multimodal approaches will likely be needed to detect each of the various subtypes at its earliest stages.

Diagnosis and Treatment

Newly diagnosed ovarian cancers are now being more accurately and consistently staged, and a wider variety of treatment options exist. Still, clinicians have few options for drug therapy, and the long-term efficacy of these agents is limited by a high rate of drug resistance. Further, most women will experience a recurrence of the disease, resulting in repeated surgeries and additional rounds of chemotherapy. While women who receive care in accordance with national clinical practice guidelines have considerably better clinical outcomes—including improved survival—less than one-half of women with ovarian cancer receive such care. More research is needed on the barriers to receiving the standard of care and on the use of quality metrics to help drive continuous quality improvement.

A better understanding of the diversity of ovarian cancers offers the potential for targeted treatments. Precision medicine approaches can be used to match individual patients to specific procedures and treatments, to predict therapeutic efficacy, and to inform the development of new and better treatments. Patient preferences also need to be considered in assessing the effectiveness of and tolerance to new therapies. Further, little research exists on nonpharmacologic therapies and interventions that might affect response to treatment. A variety of approaches needs to be evaluated, including new therapeutic combinations and formulations, and nonpharmacologic interventions.
Supportive Care Along the Survivorship Trajectory
Most ovarian cancer research focuses on disease treatment rather than on how to improve the management of the acute and long-term physical and psychosocial effects of diagnosis and treatment across the trajectory of survivorship. For women with ovarian cancer, shared decision making and the management of the physical and psychosocial effects may be neglected in the effort to urgently address the typically advanced stage of disease at diagnosis. Current research provides little insight as to which women are most likely to suffer physical and psychosocial effects, or the best approaches for managing these effects. These research gaps may be informed by more effective assessment of patient-reported symptoms and outcomes, especially on the outcomes that are most important to patients, such as improved quality of life. Finally, as many women with ovarian cancer continue active treatment until the end of their lives, researchers should help better define when disease-focused treatments are unlikely to be effective, and the focus might need to shift to end-of-life care.

Dissemination and Implementation of Knowledge
While the knowledge base on ovarian cancers has advanced, not all stakeholder groups are receiving important messages. This may contribute to the variability seen in the delivery of the standard of care which, in turn, affects outcomes. Dissemination of new information among multiple stakeholders—patients, families, health care providers, industry, payers, media, and advocacy groups—is critical.

CONCLUSION
While progress has been made in understanding ovarian cancers over the past few decades, much remains to be learned, especially about the origins and mechanisms of development—fundamental knowledge that could change paradigms for prevention, screening and early detection, and treatment. Improved communication is also needed to recognize ovarian cancer as a constellation of many types of cancer involving the ovary. A focus on distinct areas of research within and across the continuum of ovarian cancer care will help improve the lives of all women at risk for or diagnosed with an ovarian cancer.