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New report finds 'surprising gaps' in knowledge of ovarian cancers

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Ovarian cancer should not be categorized as a single disease, but rather as a constellation of different cancers involving the ovary, yet questions remain on how and where various ovarian cancers arise, says a new congressionally mandated report from the National Academies of Sciences, Engineering, and Medicine. The report presents research opportunities that if addressed could have the greatest impact on reducing the number of women who are diagnosed with or die from ovarian cancers.

Each year in the United States, more than 21,000 women are diagnosed with ovarian cancer, and more than 14,000 women die from the disease. It is the fifth leading cause of cancer deaths among women, with a five-year survival rate of less than 46 percent. The five-year survival rate has increased over the years, though; between 1975 and 1977, only 36 percent of women diagnosed with ovarian cancer lived five years or more. However, five-year survival rates decreased for black women, from 42 percent between 1975 and 1977 to 36 percent between 2005 and 2007. Often called a silent killer, ovarian cancer has no distinct symptoms in the early stages of the disease, and an effective screening test is unavailable. Roughly two-thirds of women are diagnosed at an advanced stage when the cancer has already spread beyond the ovary, of which less than 30 percent survive past five years.

"While progress has been made in ovarian cancer research over the past few decades, much remains to be learned," said Jerome F. Strauss III, chair of the committee that carried out the study and wrote the report,

and executive vice president for medical affairs and dean of Virginia Commonwealth University School of Medicine, Richmond. "The more that is understood about the basic biology of various types of ovarian cancers, such as where they originate in the body, the more rapidly we can move toward advances in prevention, screening, early detection, diagnosis, treatment, and supportive care."

The committee found recent evidence that suggests many ovarian cancers arise in other tissues besides the ovary, such as the fallopian tubes, which eventually metastasize to the ovary, or they arise from cells that are not considered intrinsic to the ovary. Furthermore, researchers do not have a complete understanding of how each subtype of ovarian cancer progresses. The committee recommended that researchers and funding organizations design and prioritize research agendas to take into account the different ovarian cancer subtypes, and a top priority in research should be to determine the cellular origins and how the disease develops.

Better methods for identifying high-risk women could facilitate the prevention or early detection of ovarian cancers, the committee said. A family history of ovarian cancer, specific inherited genetic mutations, and certain hereditary cancer syndromes have strong links with risk for ovarian cancers. The BRCA1 and BRCA2 genes, also associated with increased risk for breast cancer, are among the most recognizable ovarian cancer risk-related genes. Several other risk-related genes have also been identified but are less studied. Multiple professional groups recommend that all women diagnosed with an invasive ovarian cancer receive genetic testing and counseling for a variety of reasons, including to choose appropriate therapies, assess other health risks, and determine the risk for family members. Counseling and testing may also be appropriate for family members or other women considered at high risk. However, genetic counseling and testing for women at risk has not been universally adopted. The committee called for the development and

implementation of innovative strategies to increase genetic counseling and testing as well as testing relatives for known inherited genetic predispositions to the disease. Furthermore, researchers, clinicians, and commercial laboratories should determine the analytic performance and clinical utility of testing for other gene mutations beyond BRCA1 and BRCA2.

Nevertheless, the majority of women with an ovarian cancer do not have an inherited gene mutation or a significant family history, and the current understanding of risk factors has limited utility in accurately predicting risk at the individual level. The committee called for the identification and evaluation of a range of potential risk factors for ovarian cancers in addition to genetics - including hormonal, behavioral, social, and environmental factors - in order to develop a risk assessment tool that accounts for the various ovarian cancer subtypes.

Regarding screening for ovarian cancers, current imaging technologies are effective at detecting pelvic masses but are limited in their sensitivity to detect small, early lesions. Efforts to improve early detection through technology are hampered by an incomplete understanding of how the cancer cells form and where they begin. Current screening methods have not had a substantial impact on overall death rates for general or high-risk populations. The committee recommended that researchers and funding organizations focus on the development and assessment of early detection strategies that extend beyond current imaging technologies and biomarkers.

For treatment, most women with newly diagnosed ovarian cancer undergo surgery to remove as much of the visible tumor as possible and determine a specific diagnosis. Survival time is markedly better for women who have complete tumor removal, yet great variability exists in the extent of tumor removal. For women in whom an optimal removal is not feasible, or who are unable to undergo surgery, neoadjuvant

chemotherapy can reduce tumor size and facilitate subsequent surgical resection. While the majority of women respond well to initial treatments, most will experience a recurrence of ovarian cancer, and virtually all recurrent ovarian cancers ultimately become resistant to current drug therapies. The committee said there is a need for better tools to predict near- and long-term response to treatments for both newly diagnosed and recurrent cancers.

While clinicians should have better ways to select the most appropriate treatment for individual patients, they also require more treatment options, and the development of better treatments depends in large part on the clinical trials system. At present, clinicians have few options for drug therapy, and the long-term efficacy of these agents is limited by a high rate of drug resistance. A better understanding of the diversity of ovarian cancers will offer the potential for targeted treatments. Innovative early phase clinical trial designs that incorporate biomarkers predictive of efficacy are needed to help identify which cancer subtypes are likely to be responsive to specific new therapies. The committee called for researchers to develop more effective therapies and combinations of therapies that take into account the unique biology and clinical course of the different subtypes of ovarian cancer.

The committee found considerable variability in the quality of care provided to women with ovarian cancers nationwide. Several organizations have developed national standard-of-care guidelines for the assessment and treatment of women with both newly diagnosed and recurrent ovarian cancers, but less than one-half of women with ovarian cancer receive such care. Being treated by a gynecologic oncologist and having treatment in a high-volume hospital or cancer center are the two most significant predictors of whether a woman with ovarian cancer will receive the appropriate standard of care and have better health outcomes, but access to such care can be a challenge. To reduce disparities in care, the committee recommended that clinicians and

researchers investigate methods to ensure the consistent implementation of current standards of care - such as access to specialists, surgical management, a chemotherapy regimen, and universal genetic testing.

The knowledge base on ovarian cancers has advanced, but not all stakeholder groups are receiving important messages, which may contribute to the current variability in the delivery of the standard of care. The committee recommended that stakeholders in ovarian cancer research, clinical care, and advocacy coordinate the efforts to develop and implement efficient, effective, and reliable methods for the rapid dissemination and implementation of evidence-based information and practices to patients, families, health care providers, advocates, and other relevant parties.

More information: www.nap.edu/catalog/21841/ovar … in-research-and-care

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