

PRESENTER NOTES

Ovarian Cancers: Evolving Paradigms in Research and Care

KEY MESSAGES FOR HEALTH CARE PROFESSIONALS

SLIDE 1

This is an overview of the state of the science of ovarian cancer research, with an emphasis on key messages for health care professionals and their patients, based on a consensus report from the National Academies of Sciences, Engineering, and Medicine, *Ovarian Cancers: Evolving Paradigms in Research and Care*. To learn more about the report, please visit nationalacademies.org/OvarianCancers.

SLIDE 2

Ovarian cancer is relatively uncommon, yet it is one of the deadliest 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. In spite of the relatively low incidence of ovarian cancer in the United States, it is the fifth leading cause of cancer deaths among American women.

SLIDE 3

Given the public health burden of ovarian cancer, the Centers for Disease Control and Prevention (CDC) asked the National Academies to convene an expert committee to examine the state of the science in ovarian cancer research, identify major knowledge gaps about the biology and treatment of ovarian cancer, and consider opportunities to advance ovarian cancer research. The congressionally mandated report makes recommendations to reduce the incidence of ovarian cancer and to lessen the morbidity and mortality from the disease, highlighting promising research themes that could advance progress in the care of women diagnosed with or at risk for ovarian cancer.

SLIDE 4

Although recent years have seen many promising advances in cancer research, there are surprising gaps in the fundamental knowledge about ovarian cancer. This has impeded progress in the prevention, early detection, treatment, and management of ovarian cancers.

The committee concluded that the failure to reduce morbidity and mortality from ovarian cancers during the past several decades is likely due to several factors, including:

- A lack of research focusing on the subtypes of ovarian cancer
- A lack of precision medicine approaches to address the heterogeneity of ovarian cancer
- Lack of research on survivorship, including supportive care and long-term disease management
- An incomplete understanding of the risk factors for ovarian cancer
- Lack of validated and effective screening and early detection tools
- Variation in the delivery of care for women with ovarian cancer

SLIDE 5

The committee developed a conceptual model to illustrate that research gaps exist across the entire continuum of ovarian cancer care—from prevention and early detection through long-term survivorship. The model highlights several critical areas of research that span all phases of the continuum (biology, research design, intervention development, disparities, and supportive care).

Four overarching concepts were highlighted to improve the evidence base for ovarian cancer:

- As the most common and lethal subtype, the study of high grade serous carcinoma needs to be given priority;
- More subtype-specific research is also needed to further define the differences among the various subtypes;
- Collaborative research (including the pooling and sharing of data and biospecimen resources, such as through consortia) is essential; and
- Key to progress in ovarian cancer research is the dissemination and broad implementation of new knowledge and evidence-based practices.

SLIDE 6

“Ovarian cancer” is a generic term used for any primary malignant tumor of the ovary. However, the term does not reflect the complexity and heterogeneity of the disease. Instead, “ovarian cancerS” may be a better term because it emphasizes the numerous subtypes of the disease.

The ovaries are composed of a variety of cell types, and ovarian cancer can arise from any of these cells. However, more than 85 percent of ovarian cancers are classified as ovarian cancers with epithelial differentiation (or ovarian carcinomas), and most ovarian cancer-related deaths are due to ovarian carcinomas.

Furthermore, recent evidence suggests that many ovarian carcinomas do not arise in the ovary per se. Instead, they may originate in other tissues, such as the fallopian tubes, and then metastasize to the ovaries.

SLIDE 7

Ovarian carcinomas themselves are heterogeneous and include several different subtypes. More than 70 percent of ovarian carcinomas are also the most lethal type: high-grade serous carcinomas. Given the heterogeneity of ovarian cancers, it is essential that the initial diagnosis be accurate.

SLIDE 8

Most women with ovarian cancer—60 percent—are diagnosed with advanced-stage disease. This is one of the chief causes of the significant morbidity and mortality from ovarian cancer.

A major challenge of early detection is that there is currently no accurate and reliable test to screen asymptomatic women for early ovarian cancer. Although some biomarker tests and imaging technologies have been shown to detect more ovarian cancers at earlier stages of the disease, these methods also have high false positive rates, and to date they have not demonstrated a significant impact on mortality from ovarian cancer.

No professional organization recommends screening for ovarian cancers in the general population, and health care professionals should not offer screening tests of unproven value to asymptomatic women.

SLIDE 9

Researchers have identified several factors associated with either an increased or decreased risk of developing ovarian cancer. These patterns of association are inconsistent and can vary among ovarian cancer subtypes; more research is needed to clarify the associations of these various risk factors. However, most of the identified risk factors are associated with the less common, less lethal ovarian cancer subtypes rather than with high-grade serous carcinomas.

SLIDE 10

A family history of ovarian cancer and certain genetic mutations and hereditary cancer syndromes have strong associations with risk for ovarian cancer. Family history is linked to an increased risk for all ovarian cancer subtypes and most strongly linked with risk for high grade serous carcinomas; up to 25 percent of women have a germline mutation of certain genes known to be associated with increased ovarian cancer risk.

Women in families with several cases of ovarian carcinoma usually have mutations in the BRCA1 or BRCA2 genes, which, along with the DNA mismatch repair genes associated with Lynch syndrome, are consistently associated with ovarian cancer risk. (BRCA mutations are also associated with increased risk of breast cancer. DNA mismatch repair gene mutations are also associated with increased risk of colorectal cancer.) Several other genes associated with ovarian cancer risk have been identified, but those are less well-studied.

SLIDE 11

Genetic counseling services can provide evaluations of personal and family history for possible hereditary cancer syndromes, consideration of diagnoses, genetic testing if indicated and available, recommendations for the prevention and management of cancer, and information for at-risk relatives.

SLIDE 12

There are a number of medical interventions you can consider to reduce the risk of ovarian cancer, including modulation of female hormone cycles as well as the surgical removal or modification of gynecological tract components. Surgical interventions include bilateral salpingo-oophorectomy, oophorectomy, bilateral salpingectomy with ovarian retention, hysterectomy, and tubal ligation.

Some women may benefit from risk reduction interventions, but the risks and benefits of these options need to be considered for each person. For example, risk-reducing surgeries and the use of oral contraceptives need to be weighed against potential complications and long-term health risks (e.g., stroke risk, risk for other cancers, surgical complications, and overall mortality).

SLIDE 13

Several medical professional groups have established guidelines for the initial assessment, referral, and treatment of women with suspected ovarian cancer.

The diagnosis of ovarian cancer can be challenging, because the symptoms of the disease often mimic common, nonspecific symptoms that can be associated with a variety of other health conditions. Symptoms of ovarian cancer include bloating, pelvic and abdominal pain, difficulty eating, and urinary symptoms. Improved awareness of the signs and symptoms of ovarian cancer among health care professionals and better communication between health care professionals and patients is needed.

It is crucial that women with suspected ovarian cancer be carefully examined to help determine appropriate clinical management. In addition to symptom recognition, the clinical presentation of ovarian cancer can also include detection of a pelvic mass on physical exam, concerns raised with diagnostic testing, and incidental findings from a previous surgery, imaging test, or tissue biopsy. For women with late-stage ovarian cancer, diagnosis can also be challenging because it can mimic gastrointestinal tumors at initial presentation.

Components of the diagnostic workup can include

- assessment of family history of breast or ovarian cancer
- abdominal/pelvic exam, imaging
- blood tests
- avoidance of needle aspiration in women with presumed early-stage disease to prevent tumor rupture and spread.

SLIDE 14

Most women with newly diagnosed ovarian cancer undergo primary debulking surgery (PDS) to remove as much of the grossly visible tumor as possible (cytoreduction), as well as to make it possible to determine a specific diagnosis (e.g., subtype, staging). Survival is markedly better for women who have complete (or optimal) tumor resection, yet great variability exists in the extent of tumor resection. For women in whom an optimal resection is not thought to be feasible, or who are unable to undergo PDS due to comorbidities, neoadjuvant chemotherapy can reduce tumor size and facilitate subsequent resection. After surgery, women typically receive multiple cycles of chemotherapy.

SLIDE 15

Despite the high response rate to initial treatment, most women with ovarian cancer will experience a recurrence of the disease, resulting in a cycle of repeated surgeries and additional rounds of chemotherapy. The rate of relapse is highly dependent on the initial stage at diagnosis, the histologic type, and the presence of residual disease at the time of primary or interval debulking.

Although many women with recurrent ovarian cancer will be symptomatic or have detectable signs of recurrence, some women are now being monitored for recurrence based on diagnostic testing, such as rising CA-125 levels or imaging. However, there is limited information to assess whether earlier diagnosis of recurrence improves overall survival. Early identification of recurrence might improve the effectiveness of secondary cytoreduction, but it may also negatively impact quality of life without providing a survival benefit. Thus, more research is needed to evaluate strategies for monitoring recurrence.

SLIDE 16

Several medical professional groups have developed clinical practice guidelines for the treatment of women with both newly diagnosed and recurrent ovarian cancers. Women who receive care in accordance with these guidelines have considerably better outcomes (e.g., longer survival and fewer surgical complications). However, more than half of women with ovarian cancer do not receive care that adheres to these guidelines.

The considerable variability in the quality of care provided to women with ovarian cancer nationwide is influenced by a number of factors. The most significant predictors of receiving guideline-concordant ovarian cancer care are: (1) treatment provision by a gynecologic oncologist (versus a general gynecologist or general surgeon) and (2) a high-volume treatment setting (versus a low-volume hospital or cancer center). Treatment by gynecologic oncologists in high-volume settings is associated with better outcomes.

Factors that significantly predict that women will not receive care consistent with national guidelines include: advanced age at diagnosis, the presence of one or more treatment-limiting comorbidities, non-white race, and lower socioeconomic status.

SLIDE 17

The committee emphasized that supportive (or palliative) care be integrated throughout the disease course, including concurrently with cancer-directed therapies, even when the goal of therapy is cure. Women with ovarian cancer can live for years, even with recurrent disease, and can enjoy substantial benefits from supportive care in terms of both symptom relief and life prolongation. Supportive care is especially important for women diagnosed with ovarian cancers because the majority these women do not fit neatly into the traditional definition of survivorship. Women with ovarian cancer experience survivorship as part of the long-term management of active disease and often undergo active disease-directed treatment until the end of their lives.

For this reason, these patients require early and ongoing supportive care to ensure that aggressive, life-extending treatments are enhanced by multidisciplinary supportive care that maximizes their quality of life. Health care professionals should continually assess physical and psychological symptoms of women with ovarian cancer, and ensure that a patient's care plan is aligned with her goals, values, and preferences.

SLIDE 18

Because most ovarian cancer research focuses on improving diagnosis and disease-directed treatment, there is a dearth of information about how to best support women living with ovarian cancer and improve their quality of life. Research is often insufficiently detailed to distinguish how supportive care needs vary among women with ovarian cancer based on individual characteristics such as age, race, ethnicity, tumor subtype, or point in the cancer care trajectory.

SLIDE 19

Health care professionals can convey key messages to help improve the lives of women diagnosed with or at risk for ovarian cancer. Some of those messages include:

- **Ovarian cancer is not just one disease.** There are many subtypes of ovarian cancer, each with different risk factors and biological behavior.
- **Women can become more aware of the risk factors and symptoms commonly associated with ovarian cancer.** Health care professionals can also direct patients toward online sources of ovarian cancer information, including the websites of the National Cancer Institute, the Centers for Disease Control and Prevention, and the CDC's Inside Knowledge campaign.
- **Women can consider interventions to reduce their risk of ovarian cancer. Health care professionals and patients should discuss these options, including the potential risks and benefits of each option.**

SLIDE 20

- **All women diagnosed with invasive ovarian cancer should receive genetic counseling and testing.**
- **First-degree relatives (parents, siblings, and children) of women with ovarian cancer should seek genetic counseling to determine whether genetic testing is warranted.**
- **Women with ovarian cancer should receive supportive care alongside disease-directed care.**

SLIDE 21

To learn more and to download a free copy of the report of the National Academies of Sciences, Engineering, and Medicine, please visit nationalacademies.org/OvarianCancers.