Ovarian Cancer Statistics, 2018

Lindsey A. Torre, MSPH1; Britton Trabert, PhD, MS, MSPH2; Carol E. DeSantis, MPH3; Kimberly D. Miller, MPH4; Goli Samimi, PhD, MPH5; Carolyn D. Runowicz, MD6; Mia M. Gaudet, PhD, MSPH7; Ahmedin Jemal, PhD, DVM8; Rebecca L. Siegel, MPH9

1Scientist, Surveillance and Health Services Research, American Cancer Society, Atlanta, GA; 2Earl Stadtman Investigator, Division of Cancer Epidemiology and Genetics, National Cancer Institute, National Institutes of Health, Bethesda, MD; 3Principal Scientist, Surveillance and Health Services Research, American Cancer Society, Atlanta, GA; 4Senior Associate Scientist, Surveillance and Health Services Research, American Cancer Society, Atlanta, GA; 5Program Director, Breast and Gynecologic Cancer Research Group, Division of Cancer Epidemiology and Genetics, National Cancer Institute, National Institutes of Health, Bethesda, MD; 6Executive Associate Dean for Academic Affairs and Professor, FL International University Herbert Wertheim College of Medicine, Miami, FL; 7Scientific Director, Behavioral and Epidemiologic Research Group, American Cancer Society, Atlanta, GA; 8Scientific Vice President, Surveillance and Health Services Research, American Cancer Society, Atlanta, GA; 9Scientific Director, Surveillance and Health Services Research, American Cancer Society, Atlanta, GA

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Corresponding author: Lindsey A. Torre, MSPH, Surveillance and Health Services Research, American Cancer Society, 250 Williams St NW, Atlanta, GA 30303; lindsey.torre@cancer.org

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Abstract: In 2018, there will be approximately 22,240 new cases of ovarian cancer diagnosed and 14,070 ovarian cancer deaths in the United States. Herein, the American Cancer Society provides an overview of ovarian cancer occurrence based on incidence data from nationwide population-based cancer registries and mortality data from the National Center for Health Statistics. The status of early detection strategies is also reviewed. In the United States, the overall ovarian cancer incidence rate declined from 1985 (16.6 per 100,000) to 2014 (11.8 per 100,000) by 29% and the mortality rate declined between 1976 (10.0 per 100,000) and 2015 (6.7 per 100,000) by 33%. Ovarian cancer encompasses a heterogenous group of malgnancies that vary in etiology, molecular biology, and numerous other characteristics. Ninety percent of ovarian cancers are epithelial, the most common being serous carcinoma, for which incidence is highest in non-Hispanic whites (NHWs) (5.2 per 100,000) and lowest in non-Hispanic blacks (NHBs) and Asians/Pacific Islanders (APIs) (3.4 per 100,000). Notably, however, APIs have the highest incidence of endometrioid and clear cell carcinomas, which occur at younger ages and help explain comparable epithelial cancer incidence for APIs and NHWs younger than 55 years. Most serous carcinomas are diagnosed at stage III (51%) or IV (29%), for which the 5-year cause-specific survival for patients diagnosed during 2007 through 2013 was 42% and 26%, respectively. For all stages of epithelial cancer combined, 5-year survival is highest in APIs (57%) and lowest in NHWs (35%), who have the lowest survival for almost every stage of diagnosis across cancer subtypes. Moreover, survival has plateaued in NHBs for decades despite increasing in NHWs, from 40% for cases diagnosed during 1992 through 1994 to 47% during 2007 through 2013. Progress in reducing ovarian cancer incidence and mortality can be accelerated by reducing racial disparities and furthering knowledge of etiology and tumorigenesis to facilitate strategies for prevention and early detection. CA Cancer J Clin 2018;68:284-296. © 2018 American Cancer Society.

Keywords: epithelial ovarian cancers, epidemiology, health disparities, ovarian neoplasms

Introduction

In 2018, there will be approximately 22,240 new cases of ovarian cancer diagnosed and 14,070 ovarian cancer deaths in the United States.1 Ovarian cancer accounts for 2.5% of all malignancies among females but 5% of female cancer deaths because of low survival rates, largely driven by late stage diagnoses.2 Improving prevention and early detection is a research priority because disease diagnosed at a local stage has a 5-year relative survival rate of 93%.2 Although advancing knowledge about ovarian cancer has previously been hindered by substantial disease heterogeneity and uncertainties about tumor tissues of origin, insight has evolved rapidly in recent years, especially for epithelial tumors, which are the most common type. This article provides an overview of ovarian cancer occurrence in the United States, by subtype when possible, including incidence, mortality, and survival rates and trends, as well as a summary of recent research on early detection strategies.
Materials and Methods

Population-based cancer incidence data in the United States are collected by the National Cancer Institute’s (NCI’s) Surveillance, Epidemiology, and End Results (SEER) program and the Centers for Disease Control and Prevention’s National Program of Cancer Registries (NPCR). The North American Association of Central Cancer Registries (NAACCR) compiles and reports incidence data from 1995 onward for registries that participate in the SEER program and/or the NPCR. These data approach 100% coverage of the US population in the most recent time period and were the source for the projected new cancer cases in 2018 and cross-sectional incidence rates by age, histology, and race/ethnicity. Some of the incidence data presented herein were previously published in volumes 1 and 2 of Cancer in North America: 2010–2014.

All invasive ovarian cancer cases were classified according to the International Classification of Diseases for Oncology, version 3 (code C56.9). Causes of death were classified according to the International Classification of Diseases. Incident cases were further grouped by histologic subtype, although this information is not available in mortality data.

Long-term incidence trends (1975–2014) were based on data from the 9 oldest SEER databases (Connecticut, Hawaii, Iowa, New Mexico, Utah, and the metropolitan areas of Atlanta, Detroit, San Francisco-Oakland, and Seattle–Puget Sound), representing approximately 9% of the US population. Beginning in 1992, data became available for Asians/Pacific Islanders (APIs), American Indians/Alaska Natives, and by Hispanic ethnicity from the SEER 13 registries (SEER 9 plus Los Angeles, San Jose–Monterey, rural Georgia, and the Alaska Native Tumor Registry), representing 13% of the US population, and were used in analyses of incidence and survival trends by race/ethnicity. Trends by histology from 1995 to 2014 are based on NAACCR data from 25 registries with complete data for the period covering 66% of the US population to maximize the number of cases in rarer subtypes. The lifetime probabilities of developing cancer and contemporary stage distribution and cause–specific survival statistics were based on data from all 18 SEER registries (SEER 13 plus Greater California, Greater Georgia, Kentucky, Louisiana, and New Jersey), covering 28% of the US population.

National mortality data were obtained from the SEER program’s SEER*Stat database, as provided by the National Center for Health Statistics. Data for APIs, for American Indians/Alaska Natives, and by Hispanic ethnicity are available from 1990. Some of the statistical information presented herein was adapted from data previously published in the SEER Cancer Statistics Review (1975–2014).

All incidence and death rates were age–standardized to the 2000 US standard population and expressed per 100,000 population, as calculated by NCI’s SEER*Stat software (version 8.3.4). Whenever possible, cancer incidence rates were adjusted for delays in reporting, which have the greatest impact on the most recent data years and occur because of a lag in case capture or data corrections. The annual percent change in rates was quantified using NCI’s Joinpoint Regression Program (version 4.5.0.1). The probability of developing cancer was calculated using the NCI’s DevCan software (version 6.7.5).

Selected Findings

Ovarian Cancer Occurrence Overall

This section presents overall incidence and mortality statistics for ovarian cancer. While it is generally more appropriate to provide information separately by histologic subtype, combined incidence allows comparison with other major cancer sites, with ovarian cancer mortality, which is unavailable by subtype, and with historic data, because of temporal changes in tumor classification. Information for specific cancer subtypes is presented in the section below.

Contemporary incidence and mortality

The average lifetime risk of developing ovarian cancer is 1.3%, the equivalent of 1 in 78 women (Table 1). The average annual ovarian cancer incidence rate in the United States was 11.5 per 100,000 women during 2010 through 2014. Incidence rates in non-Hispanic white (NHW) women (12.0 per 100,000), who have the highest rates, are 30% higher than those in non-Hispanic black (NHB) women (9.4 per 100,000) and API women (9.2 per 100,000), who have the lowest rates (Fig. 1). Racial/ethnic differences in ovarian cancer risk at the population level are partially explained by the prevalence of risk factors. Reduced risk is associated with higher parity, use of oral contraceptives, tubal ligation, and oophorectomy, whereas...
menopausal hormone use increases risk. However, the source of most of the variation remains unknown. As with incidence, mortality rates are highest in NHW women (7.9 deaths per 100,000) and lowest in API women (4.4 per 100,000) (Fig. 1). NHB women have the second highest mortality rates (6.6 deaths per 100,000 women) despite relatively low incidence rates, likely due in part to a lower likelihood of receiving optimal treatment and more comorbidities compared with other women.

**Trends in incidence and mortality**

Ovarian cancer incidence has been decreasing since the mid-1980s, largely driven by declines in whites that accelerated during the past decade. Overall, the incidence rate dropped 29%, from 16.6 per 100,000 in 1985 to 11.8 per 100,000 in 2014. However, trends differ by age. Among whites and blacks ages 65 years and older, incidence rates increased from 1975 until around 1990 before beginning to decline (Fig. 2). This increase may be related to decreasing parity during the early to mid-20th century; invasive epithelial ovarian cancer risk is reduced by about 20% with the first childbirth and by about 10% with each additional birth. The rapid decline among white women in recent years may be caused in part by decreased use of menopausal hormones after publication of a landmark report in 2002 linking them to increased breast cancer risk. Women who have ever used menopausal hormones (estrogen alone or estrogen combined with progesterone) have a 20% higher risk of developing ovarian cancer versus never-users, with a stronger risk among recent users; current users and those who have stopped within 5 years have an excess risk of about 40%. Risk is increased even with short-term menopausal hormone use and remains elevated for at least 10 years after discontinuation.

In contrast, incidence among women younger than 65 years has generally declined at a continuous rate since at least 1975 (Fig. 2). This is likely because of uptake of oral contraceptives, which confer a substantial risk reduction and also likely contributed to the recent declines in older women. Among women who use oral contraceptives for a total of 5 to 9 years, the risk is reduced by about 35%, with the protective effect persisting with diminishing strength for at least 30 years after discontinuation.

The mortality rate for ovarian cancer declined 33% between 1976 (10.0 per 100,000) and 2015 (6.7 per 100,000) because of reductions in incidence and improvements in treatment. Age-specific mortality trends closely mirror those of incidence because of generally low survival (Fig. 2). Death rates declined during the most recent 10 years of data (2006 to 2015) by about 2% annually in Hispanics and NHWs and by 1% annually in NHBs and APIs, but remained stable in American Indians/Alaska Natives (Table 2).

**Ovarian Cancer Subtypes**

**Overview**

Ovarian cancer encompasses a heterogenous group of malignancies differentiated by cell/site of origin, pathologic grade, risk factors, prognosis, and treatment. Epithelial cancers are most common among women of all racial/ethnic groups, accounting for 90% of all cases (Fig. 3). Epithelial cancers are classified by tumor cell histology as serous (52%), endometrioid (10%), mucinous (6%), or clear cell (6%), with one-quarter classified as more rare or unspecified subtypes. Epithelial malignancies are further grouped as type I or type II based on clinicopathologic factors, with the primary distinguishing molecular factor being marked genetic instability in type II versus type I. Type I ovarian cancers are generally large, unilateral, cystic tumors at diagnosis with indolent behavior. They are thought to usually develop from extratubal benign lesions that embed in the ovary and subsequently undergo a series of mutations resulting in malignant transformation. In this way, low-grade serous carcinomas are thought to originate from benign deposits of fallopian tube epithelium in the ovaries (endosalpingiosis); endometrioid and clear cell carcinomas from benign foci of endometrial tissue in the ovaries (endometriosis); and most mucinous carcinomas from benign foci of transitional epithelium from the tuboperitoneal junction. Type I ovarian cancers are considered low grade, with the

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**FIGURE 1. Ovarian Cancer Incidence and Mortality Rates by Race and Ethnicity, United States, 2010 to 2014.**

Rates are per 100,000 and age adjusted to the 2000 US standard population. Persons of Hispanic origin may be of any race; American Indians/Alaska Natives and Asians/Pacific Islanders include those of Hispanic and non-Hispanic origin. Sources: Incidence: NAACCR, 2017. Mortality: US mortality data, National Center for Health Statistics, Centers for Disease Control and Prevention, 2017. Data for American Indians/Alaska Natives are based on Contract Health Service Delivery Area (CHSDA) counties.
exception of clear cell carcinomas, and account for only a small fraction of ovarian cancer deaths.\textsuperscript{29}

Type II epithelial cancers are high grade and characterized by involvement of both ovaries, aggressive behavior, late stage at diagnosis, and low survival.\textsuperscript{29} They are thought to originate as fallopian tube fimbriae carcinomas that spread to the ovaries and/or peritoneum.\textsuperscript{29,32} Women with these cancers often present with extensive extraovarian disease and ascites. Type II cancers are primarily high-grade serous carcinomas, the most common epithelial subtype, but also include carcinosarcomas and undifferentiated carcinomas.\textsuperscript{29} It is notable that although tumor grade is important
in clinical practice, it is not a robust independent prognostic indicator. Moreover, grade is not a reliable metric for population-based cancer epidemiology research because of the high proportion of inaccurately recorded and unknown grade, including up to one-third of epithelial cancers, in cancer registry data (see Supporting Fig. 1). As a result, while many epidemiologic studies stratify by grade, caution should be used in interpreting these results.

Nonepithelial cancers are typically less aggressive than epithelial malignancies. Germ cell and sex cord-stromal tumors make up the majority of nonepithelial cancers but account for only 3% and 2%, respectively, of all ovarian cancers (Fig. 3). Sex cord-stromal tumors arise from various connective tissue cell types, including granulosa, Sertoli, and/or Leydig cells. Other nonepithelial ovarian cancers include small cell carcinoma (hypercalcemic and nonhypercalcemic types) and ovarian sarcoma.

Epithelial Ovarian Cancer Occurrence

Incidences

Epithelial ovarian cancer incidence varies by age and race/ethnicity. The age distribution for serous carcinoma, the most common epithelial subtype, is older than that for other subtypes, peaking in the seventh versus the fifth decade of life (Fig. 4). Serous carcinoma incidence is highest in NHWs (5.2 per 100,000) and lowest in APIs and NHBs (3.4 per 100,000) (Table 3). NHW women also have the highest rate of endometrioid carcinoma, alongside APIs (1.1 per 100,000). API women also have the highest rate of clear cell carcinoma (1.0 per 100,000), about twice that of women in other racial/ethnic groups. Notably, clear cell carcinoma incidence in API women also peaks at a younger age compared to women of other racial/ethnic groups (Fig. 4).

| TABLE 2. Trends in Ovarian Cancer Mortality Rates by Age and Race/Ethnicity, United States, 1992 to 2015 |
|-----------------------------------------------|----------------|----------------|----------------|----------------|
| TREND 1 | TREND 2 | TREND 3 |
| YEARS | APC 95% CI | YEARS | APC 95% CI | YEARS | APC 95% CI |
| All races | | | | | |
| All ages | 1992-1998 | -1.2 a (-1.8 to -0.6) | 1998-2003 | 0.6 (-0.5 to 1.7) | 2003-2015 | -2.3 a (-2.5 to -2.1) |
| <65 y | 1992-1998 | -2.3 a (-3.2 to -1.3) | 1998-2002 | 0.5 (-2.1 to 3.3) | 2002-2015 | -2.7 a (-3.0 to -2.4) |
| ≥65 y | 1992-2005 | 0.0 (-0.2 to 0.3) | 2005-2015 | -2.2 a (-2.6 to -1.9) | |
| Non-Hispanic white | | | | | |
| All ages | 1992-2005 | -0.2 (-0.5 to 0.0) | 2005-2015 | -2.5 a (-2.8 to -2.1) | |
| <65 y | 1992-2005 | -1.1 a (-1.4 to -0.7) | 2005-2015 | -3.1 a (-3.6 to -2.5) | |
| ≥65 y | 1992-2005 | 0.3 a (0.0 to 0.5) | 2005-2015 | -2.2 a (-2.5 to -1.8) | |
| Non-Hispanic black | | | | | |
| All ages | 1992-2015 | -1.0 a (-1.3 to -0.8) | |
| <65 y | 1992-2015 | -1.3 a (-1.6 to -1.0) | |
| ≥65 y | 1992-2015 | -0.9 a (-1.1 to -0.6) | |
| Asian/Pacific Islander | | | | | |
| All ages | 1992-2015 | -0.6 a (-1.0 to -0.2) | |
| <65 y | 1992-2015 | -1.0 a (-1.6 to -0.5) | |
| ≥65 y | 1992-2006 | 1.9 a (0.6 to 3.1) | 2006-2015 | -2.9 a (-4.5 to -1.3) | |
| American Indian/Alaska Native | | | | | |
| All ages | 1992-2015 | -0.0 (-1.1 to 1.0) | |
| <65 y | 1992-2015 | -1.3 (-3.0 to 0.4) | |
| ≥65 y | 1992-2015 | 0.5 (-0.9 to 1.9) | |
| Hispanic | | | | | |
| All ages | 1992-2006 | -0.1 (-0.7 to 0.6) | 2006-2015 | -1.8 a (-2.9 to -0.8) | |
| <65 y | 1992-2015 | -0.9 a (-1.2 to -0.6) | |
| ≥65 y | 1992-2015 | -0.7 a (-1.2 to -0.3) | |

95% CI indicates 95% confidence interval; AAPC, average annual percent change over the most recent data years; APC, annual percent change. Based on incidence rates age adjusted to the 2000 US standard population. aThe APC or AAPC is significantly different from zero (P < .05). Source: NCHS, 2017. Data for American Indians/Alaska Natives are based on Contract Health Service Delivery Area (CHSDA) counties. Data for Hispanics exclude Oklahoma and New Hampshire. Trends were analyzed using the Joinpoint Regression Program, version 4.5.0.1, allowing up to 4 joinpoints.
High rates of clear cell and endometrioid carcinoma in Asian women have been previously documented in the United States and Eastern Asia, although the reasons remain unknown. Endometriosis is most strongly associated with these subtypes; however, it is unclear whether the relationship is causal or a result of shared risk factors, and whether the prevalence of this condition is higher among Asian women. Genetic and reproductive/hormonal factors may also contribute. NHBs have the lowest incidence rates for all epithelial subtypes (Table 3). Reasons for the lower rates among NHBs are unknown, even when accounting for prevalence of protective factors, such as fallopian tube ligation, which is associated with a roughly 30% reduced risk of ovarian cancer.

Declines in endometrioid and serous carcinoma incidence rates of 3.7% and 1.0% per year, respectively, since 2000 (Table 4) may be linked to reductions in the use of menopausal hormone therapy, which is associated specifically with these subtypes. Mucinous carcinoma incidence decreased by greater than 5% annually from 1995 to 2009, likely because of improvements in laboratory methods to recognize metastases to the ovary, which can mimic primary mucinous carcinoma, and perhaps declines in smoking, which increases risk only for this subtype. However, the incidence of mucinous carcinoma has been stable since 2009, as has the incidence of clear cell carcinoma since at least 1995. Rates for other epithelial cancers combined have declined rapidly in recent years because of ongoing efforts to improve classification, which may have attenuated decreasing trends for some subtypes. Future trends will be similarly impacted by advances in the understanding of ovarian cancer biology. For instance, because many epithelial cancers are now recognized to originate in the fallopian tubes, high-grade serous carcinoma is increasingly being classified as cancer of the fallopian tube rather than of the ovary, although the accuracy thereof requires further research.

**Stage at diagnosis and survival**

Stage at diagnosis varies substantially by epithelial subtype (Fig. 5). Most serous carcinomas are diagnosed at stage III (51%) or IV (29%), reflecting the aggressive nature of predominant high-grade serous carcinomas. In contrast, the majority (58% to 64%) of endometrioid, mucinous, and clear cell carcinomas are diagnosed at stage I, similar to nonepithelial tumors. Consequently, the 5-year cause-specific survival for serous carcinoma is 43%, compared with 82%, 71%, and 66% for endometrioid, mucinous, and clear cell carcinoma, respectively (Table 5).

Survival also varies by race/ethnicity (Table 5). For example, 5-year cause-specific survival for serous carcinoma is 47% to 48% in NHW, API, and Hispanic women compared with 36% in NHB women (Table 5). Indeed, serous carcinoma survival is lowest among NHB women for every stage of diagnosis, likely due in part to lower receipt of guideline-adherent treatment. Furthermore, NHBs have among the lowest stage-specific survival across
epithelial cancer subtypes. The relatively high survival in APIs for epithelial cancers overall reflects their low incidence of serous carcinoma as well as high survival across subtypes (Table 5). Reasons for this survival advantage are unknown but may include better response to treatment. Overall 5-year cause-specific epithelial cancer survival in
NHW women has improved from 40% for cases diagnosed from 1992 to 1994 to 47% for cases diagnosed from 2007 to 2013. In contrast, 5-year survival in NHB women remained around 35% over the same period. Slower dissemination of treatment advances, including less access to optimal debulking surgery and intraperitoneal chemotherapy, may have contributed to the stagnation.

**Nonepithelial Ovarian Cancer Occurrence**

Compared with epithelial cancers, nonepithelial malignancies have a younger age distribution, especially germ cell tumors (Fig. 6). The incidence of sex cord-stromal tumors is highest among NHBs at every age of diagnosis (Fig. 6), with an overall rate (0.5 per 100,000) 5-fold higher than that among APIs (0.1 per 100,000), who have the lowest rate (Table 3). In contrast, rates of germ cell tumors are highest in Hispanics (0.5 per 100,000) and lowest in American Indians/Alaska Natives (0.2 per 100,000). Whereas the incidence of germ cell tumors has remained stable since at least 1995, rates of sex-cord stromal tumors increased by 2.3% annually from 2004 to 2014 (Table 4). Reasons for this increase are unknown because risk factors for these cancers are poorly understood. The majority of sex-cord stromal (64%) and germ cell (57%) tumors are diagnosed at stage I (Fig. 5), for which 5-year cause–specific survival is 98% and 99%, respectively (Table 5). Survival for these tumors remains relatively high even for stage IV disease, at 41% and 69%, respectively.

**Familial Risk and Risk Reduction**

The strongest risk factor for ovarian cancer is a family history of breast or ovarian cancer. 44 The risk of developing invasive epithelial ovarian cancer is increased by approximately 50% among women who have a first-degree relative with a history of ovarian cancer and by 10% among those who have a first-degree relative with breast cancer. 19 It is estimated that approximately 18% of epithelial ovarian cancers, particularly high–grade serous carcinomas, are caused by inherited mutations that confer elevated risk, the majority in the BRCA1 or BRCA2 gene. 54 Mutations in BRCA1

| TABLE 3. Ovarian Cancer Incidence Rates\(^a\) by Race/Ethnicity and Histology, United States, 2010 to 2014 |
|-----------------------------------------------|
| **EPITHELIAL** | **ALL EPITHELIAL SUBTYPES** | **SEROUS** | **ENDOMETROID** | **MUCINOUS** | **CLEAR CELL** | **SEX CORD-STROMAL** | **GERM CELL** |
| All races | 9.4 | 4.9 | 1.0 | 0.6 | 0.6 | 0.3 | 0.4 |
| Non-Hispanic white | 10.0 | 5.2 | 1.1 | 0.7 | 0.6 | 0.2 | 0.3 |
| Non-Hispanic black | 6.9 | 3.4 | 0.5 | 0.4 | 0.1 | 0.3 | 0.4 |
| American Indian/Alaska Native | 8.3 | 4.3 | 0.9 | 0.5 | 0.4 | 0.3 | 0.2 |
| Asian/Pacific Islander | 7.8 | 3.4 | 1.1 | 0.6 | 0.1 | 0.1 | 0.4 |
| Hispanic | 8.1 | 4.0 | 0.8 | 0.5 | 0.4 | 0.2 | 0.5 |

\(^a\)Per 100,000, age adjusted to the 2000 US standard population. Persons of Hispanic origin may be of any race; American Indians/Alaska Natives and Asians/Pacific Islanders include those of Hispanic and non-Hispanic origin. Data for American Indians/Alaska Natives are based on Contract Health Service Delivery Area (CHSDA) counties. Source: NAACCR, 2017.

| TABLE 4. Trends in Ovarian Cancer Incidence Rates by Histology, United States, 1995 to 2014 |
|-----------------------------------------------|
| **TREND 1** | **TREND 2** | **TREND 3** |
| **YEARS** | **APC** | **95% CI** | **YEARS** | **APC** | **95% CI** | **YEARS** | **APC** | **95% CI** | **2005-2014 AAPC** |
| Epithelial | 1995-2000 | −1.2\(^a\) | (−1.8 to −0.6) | 2000-2014 | −2.1\(^a\) | (−2.2 to −1.9) | | | | −2.1\(^a\) |
| Serous | 1995-2000 | 0.9 | (−0.2 to 2.0) | 2000-2014 | −1.0\(^a\) | (−1.2 to −0.8) | | | | −1.0\(^a\) |
| Endometrioid | 1995-2000 | −1.5 | (−3.1 to 0.2) | 2000-2014 | −3.2\(^a\) | (−4.0 to −3.3) | | | | −3.2\(^a\) |
| Mucinous | 1995-2009 | −5.3\(^a\) | (−5.6 to −5.0) | 2009-2014 | −0.0 | (−1.9 to 1.9) | | | | −2.4\(^a\) |
| Clear cell | 1995-2014 | −0.1 | (−0.4 to 0.2) | | | | | | | −0.1 |
| Other | 1995-2005 | −3.1\(^a\) | (−3.5 to −2.7) | 2005-2008 | −0.6 | (−5.5 to 4.5) | 2008-2014 | −5.5\(^a\) | (−6.4 to −4.7) | −3.9\(^a\) |
| Germ cell | 1995-2014 | 0.4 | (−0.1 to 0.9) | | | | | | | 0.4 |
| Sex cord-stromal | 1995-2004 | −1.9 | (−4.0 to 0.3) | 2004-2014 | 2.3\(^a\) | (0.5 to 4.0) | | | | 2.3\(^a\) |

95% CI indicates 95% confidence interval; AAPC, average annual percent change over the most recent data years; APC, annual percent change. Based on incidence rates age adjusted to the 2000 US standard population. \(^a\)The APC or AAPC is significantly different from zero \(P < .05\) Source: NAACCR, 2017. Trends were analyzed using the Joinpoint Regression Program, version 4.5.0.1, allowing up to 3 joinpoints.
and BRCA2 account for almost 40% of ovarian cancer cases in women with a family history of the disease. Rare moderate penetrance gene mutations for epithelial ovarian cancer include those in BRCA1-interacting protein C-terminal helicase 1 (BRIP1), RAD51 paralog C (RAD51C), and RAD51D. There are also more common low-penetrance gene variants that potentially result in a substantial number of cancers because of their ubiquity. Nonepithelial cancers are often associated with non-BRCA1/BRCA2 gene mutations, including in forkhead box L2 (FOXL2) for adult-type granulosa cell tumors and dicer 1, ribonuclease III (DICER1) for Sertoli-Leydig tumors. Because of the relatively high prevalence of identified genetic mutations, the National Comprehensive Cancer Network recommends genetic testing for all women diagnosed with ovarian cancer to inform their medical and reproductive decisions and those of their relatives. The identification of additional genes associated with increased risk and their potential utility in a clinical setting for risk prediction continues to evolve.

Among women with BRCA1 or BRCA2 mutations, the risk of developing ovarian cancer by age 80 years is 44% and 17%, respectively. While these mutations are rare in the general population (less than 1%), they are more common in certain ethnic or geographically isolated groups, such as those of Ashkenazi (Eastern European) Jewish descent (about 2%). The US Preventive Services Task Force recommends that primary care providers evaluate the potential risk for BRCA1 or BRCA2 mutations among women who have a family history of breast, ovarian, tubal, or peritoneal cancer using one of several available screening tools (eg, BRCAPRO or BOADICEA). Women with a positive screen should receive genetic counseling and, if indicated, BRCA1/BRCA2 genetic testing.

For women who have a BRCA1 or BRCA2 mutation, risk-reducing bilateral salpingo-oophorectomy decreases the risk of ovarian cancer by about 80% and is recommended by the American College of Obstetricians and Gynecologists and the Society of Gynecologic Oncology once childbearing is complete. Bilateral salpingectomy alone for premenopausal, high-risk women is not currently recommended; however, clinical trials are underway. The National Comprehensive Cancer Network also recommends consideration of bilateral salpingo-oophorectomy for women ages 45 to 50 years who are carriers of BRIP1, RAD51C, and RAD51D mutations. The American College of Obstetricians and Gynecologists and the Society of Gynecologic Oncology suggest that women with BRCA1 or BRCA2 mutations consider use of oral contraceptives, which reduce risk of ovarian cancer by about 50% among high-risk women. Although there has been concern that this would further increase breast cancer risk, to date, no clear significantly increased risk with modern oral contraceptive use has been shown in these women.

Lynch syndrome (hereditary nonpolyposis colon cancer) is a rare hereditary condition associated with an increased risk of colorectal, endometrial, ovarian, and other cancers. Families with

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**FIGURE 5.** American Joint Committee on Cancer Sixth Edition Stage Distribution (%) for Ovarian Cancer by Histology, United States, 2007 to 2013. Source: SEER 18 Registries, National Cancer Institute, 2017.
Lynch syndrome are mainly characterized by a germline mutation in a DNA mismatch-repair gene (eg, mutL homolog 1 \([MLH1]\), mutS homolog 2 \([MSH2]\), \([MSH6]\), or PMS1 homolog 2 \([PMS2]\)). Women with Lynch syndrome have an approximately 8% risk of developing ovarian cancer (usually nonserous epithelial tumors) by age 70 years \(^7\) compared with 0.7% in the general population. \(^1\) The National Comprehensive Cancer Network recommends consideration of hysterectomy along with bilateral salpingo-oophorectomy for women with Lynch syndrome who have completed childbearing. \(^6\)

### Early Detection and Screening

Epithelial ovarian cancer is usually advanced by the time it is diagnosed because early stages of the disease have no obvious symptoms and to date, the efficacy of screening has not been demonstrated in prospective randomized controlled trials. The most common sign of advanced disease is swelling of the abdomen caused by ascites. \(^7\) However, studies indicate that some women experience persistent, nonspecific symptoms in the months before diagnosis, including back pain, abdominal distension, pelvic or abdominal pain.

### TABLE 5. Five-Year Cause-Specific Survival (%) for Ovarian Cancer by Race/Ethnicity, AJCC Stage\(^a\), and Histology:
United States, 2007 to 2013

| EPITHELIAL ALL EPITHELIAL SUBTYPES | SEROUS | ENDOMETRIOID | MUCINOUS | CLEAR CELL | SEX CORD-STROMAL | GERM CELL |
|---------------------------------|--------|--------------|----------|------------|------------------|-----------|
| All races                        |        |              |          |            |                  |           |
| All stages                       | 47     | 43           | 82       | 71         | 66               | 88        | 94        |
| Stage I                          | 89     | 86           | 95       | 92         | 85               | 98        | 99        |
| Stage II                         | 71     | 71           | 84       | 69         | 71               | 84        | 93        |
| Stage III                        | 41     | 42           | 59       | 30         | 35               | 61        | 90        |
| Stage IV                         | 20     | 26           | 29       | 13         | 16               | 41        | 69        |
| Non-Hispanic white               |        |              |          |            |                  |           |
| All stages                       | 47     | 47           | 82       | 72         | 67               | 88        | 94        |
| Stage I                          | 89     | 86           | 94       | 94         | 86               | 100       | 99        |
| Stage II                         | 72     | 73           | 82       | 69         | 68               | 78        | 84        |
| Stage III                        | 40     | 42           | 58       | 32         | 36               | 61        | 93        |
| Stage IV                         | 20     | 25           | 27       | 10         | 22               |           |           |
| Non-Hispanic black               |        |              |          |            |                  |           |
| All stages                       | 35     | 36           | 77       | 50         | 39               | 85        | 88        |
| Stage I                          | 81     | 78           | 93       | 80         | 53               | 95        | 97        |
| Stage II                         | 58     | 57           | 91       |           |                  |           |           |
| Stage III                        | 36     | 40           | 55       |           |                  |           |           |
| Stage IV                         | 13     | 16           |           |           |                  |           |           |
| Asian/Pacific Islander           |        |              |          |            |                  |           |
| All stages                       | 57     | 47           | 84       | 79         | 70               | 94        | 95        |
| Stage I                          | 89     | 80           | 95       | 93         | 87               | 87        | 100       |
| Stage II                         | 76     | 76           | 89       |           |                  | 83        |           |
| Stage III                        | 45     | 47           | 77       |           |                  | 24        | 24        |
| Stage IV                         | 25     | 30           |           |           |                  |           |           |
| Hispanic                         |        |              |          |            |                  |           |
| All stages                       | 52     | 48           | 82       | 71         | 62               | 90        | 95        |
| Stage I                          | 91     | 90           | 99       | 90         | 84               | 98        | 99        |
| Stage II                         | 68     | 65           | 87       |           |                  |           |           |
| Stage III                        | 45     | 48           | 49       | 41         | 38               |           |           |
| Stage IV                         | 24     | 31           | 40       | 23         | 0                |           |           |

\(^a\)American Joint Committee on Cancer (AJCC) Cancer Staging Manual, 6th edition. \(^b\)This statistic is not shown due to fewer than 25 cases. American Indians/Alaska Natives are not shown due to sparse data. Source: SEER 18 Registries, National Cancer Institute, 2017.
difficulty eating or feeling full quickly, vomiting, indigestion, altered bowel habits, or urinary urgency or frequency. Women who experience such symptoms daily for more than a few weeks should seek prompt medical evaluation. Women who have nonepithelial tumors often present with more specific early signs, including irregular vaginal bleeding. Additionally, sex cord-stromal tumors often produce sex hormones, which may affect menstruation and/or cause male physical characteristics, such as a deep voice or body hair. Currently, there is no recommended screening test for ovarian cancer, although large-scale randomized clinical studies to identify effective screening modalities are ongoing. The Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial, which assessed the use of transvaginal ultrasound (TVU) and a fixed cut-point (≥ 35 U/mL) in the tumor marker cancer antigen 125 (CA 125) for early detection, did not observe a reduction in ovarian cancer mortality after up to 19 years of follow-up. The UK Collaborative Trial of Ovarian Cancer Screening, another large randomized trial based in the United Kingdom, evaluated TVU combined with a risk algorithm incorporating changes in CA 125 levels and found reduced mortality in average-risk women after 15 years. However, the use of secondary analysis to reach these results has been a matter of active debate; further years of follow-up may clarify the potential benefits of this screening method. On the basis of these studies, the US Preventive Services Task Force continues to recommend against screening for ovarian cancer. Identifying an effective screening method is complicated by accumulating evidence that ovarian cancer, particularly aggressive high-grade serous carcinoma, begins as a microscopic lesion in the fallopian tube that is undetectable with current strategies. For women who are at high risk, a thorough pelvic examination in combination with TVU and a blood test for changes in the level of the tumor marker CA 125 may be offered, although this strategy has not proven effective in reducing ovarian cancer mortality.

Conclusions

Ovarian cancer mortality decreased by greater than 30% since the mid-1970s because of reductions in incidence and improvements in treatment in recent decades. Still, fewer than one-half of women survive beyond 5 years after diagnosis because of the predominance of aggressive high-grade serous carcinomas and the absence of specific early symptoms and effective early detection strategies. Notably, risk factors for high-grade serous carcinoma remain largely unknown, stymying prevention efforts. Survival rates have improved only slightly over the past 3 decades among NHWs and have remained stagnant among NHBs, likely because of differential access to high-quality treatment. Moreover, NHB women experience the lowest survival for almost every stage of diagnosis across cancer subtypes. Further research is needed to more specifically determine the reasons for this disparity and to advance understanding of the disease in order to identify modifiable risk factors, develop effective early detection methods, and improve treatment.

References

1. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2018. CA Cancer J Clin. 2018;68:7-30.
2. Howlader N, Noone AM, Krapcho M, et al. eds. SEER Cancer Statistics Review, 1975-2014. Bethesda, MD: National Cancer Institute; 2017. seer.cancer.gov/csr/1975_2014/. Accessed March 1, 2018.
3. Surveillance, Epidemiology, and End Results (SEER) Program. SEER*Stat Database: North American Association of Central Cancer Registries (NAACCR) Incidence Data-Cancer in North America (CINAC) Analytic File, 1995-2014, for Expanded Races, Custom File With County, American Cancer Society Facts and Figures Projection Project (which includes data from the Centers for Disease Control and Prevention).
Prevention’s National Program of Cancer Registries [NPCR], the Canadian Counsel of Cancer Registry’s Provincial and Territorial Registries, and the National Cancer Institute’s SEER Program, certified by NAACCR as meeting high-quality incidence data standards for the specified time periods. Bethesda, MD: National Cancer Institute; 2016.

4. Copeland G, Lake A, Firth R, et al. eds. Cancer in North America: 2010-2014. Volume One: Combined Cancer Incidence for the United States, Canada and North America. Springfield, IL: North American Association of Central Cancer Registries Inc; 2017.

5. Copeland G, Lake A, Firth R, et al. eds. Cancer in North America: 2010-2014. Volume Two: Registry-specific Cancer Incidence in the United States and Canada. Springfield, IL: North American Association of Central Cancer Registries Inc; 2017.

6. Adamo M, Dickie, L, Ruhl J. SEER Program Coding and Staging Manual 2016. Bethesda, MD: US Department of Health and Human Services, National Institutes of Health, National Cancer Institute; 2016.

7. World Health Organization, International Agency for Research on Cancer. International Classification of Diseases for Oncology, 3rd ed. Geneva, Switzerland: World Health Organization; 2000. codes.iarc.fr/. Accessed March 1, 2018.

8. World Health Organization. International Classification of Diseases, 10th revision. Geneva, Switzerland: World Health Organization; 2013. who.int/classifications/icd/en/. Accessed March 1, 2018.

9. Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov). SEER*Stat Database: Incidence-SEER 9 Regs Research Data with Delay-Adjustment, Malignant Only, Nov 2016 Sub (1975-2014) <Katrina/Rita Population Adjustment--Linked To County Attributes-Total US, 1969-2015 Counties. Bethesda, MD: National Cancer Institute, Division of Cancer Control and Population Sciences, Surveillance Research Program; 2017.

10. Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov). SEER*Stat Database: Incidence-SEER 13 Regs Research Data with Delay-Adjustment, Malignant Only, Nov 2016 Sub (1992-2014) <Katrina/Rita Population Adjustment--Linked To County Attributes-Total US, 1969-2015 Counties. Bethesda, MD: National Cancer Institute, Division of Cancer Control and Population Sciences, Surveillance Research Program; 2017.

11. Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov). SEER*Stat Database: Invasive, SEER 18 Regs Research Data - Hurricane Katrina Impacted Louisiana Cases, Nov 2016 Sub (2000-2014) <Katrina/Rita Population Adjustment--Linked To County Attributes-Total US, 1969-2015 Counties. Bethesda, MD: National Cancer Institute, Division of Cancer Control and Population Sciences, Surveillance Research Program; 2017.

12. Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov). SEER*Stat Database: Mortality-All COD, Total US (1969-2015) <Early release with Vintage 2015 Katrina/Rita Population Adjustment--Linked To County Attributes-Total US, 1969-2015 Counties. Bethesda, MD: National Cancer Institute, Division of Cancer Control and Population Sciences, Surveillance Research Program; 2017. Underlying mortality data provided by the National Center for Health Statistics (www.cdc.gov/nchs).

13. Surveillance Research Program, National Cancer Institute’s SEER*Stat software (seer.cancer.gov/seerstat), version 8.3.4. Bethesda, MD: National Cancer Institute; 2017.

14. Statistical Methodology and Applications Branch, Surveillance Research Program, National Cancer Institute. Joinpoint Regression Version 4.5.0.1 [software program]. Bethesda, MD: National Cancer Institute; 2017.

15. Surveillance Research Program, Statistical Methodology and Applications, National Cancer Institute. DevCan: Probability of Developing or Dying of Cancer Software, version 6.7.5 [software program]. Bethesda, MD: National Cancer Institute; 2017. Surveillance.cancer.gov/devcan/. Accessed March 1, 2018.

16. Cibula D, Widschwendter M, Majek O, Dusek L. Tubal ligation and the risk of ovarian cancer: review and meta-analysis. Hum Reprod Update. 2011;17:35-50.

17. Collaborative Group on Epidemiological Studies of Ovarian Cancer, Beral V, Doll R, Hermon C, Peto R, Reeves G. Ovarian cancer and oral contraceptives: collaborative reanalysis of data from 45 epidemiological studies including 23,257 women with ovarian cancer and 87,303 controls. Lancet. 2008;371:303-314.

18. Collaborative Group on Epidemiological Studies of Ovarian Cancer, Beral V, Gaitskell K, et al. Menopausal hormone use and ovarian cancer risk: individual particip-ant meta-analysis of 52 epidemiological studies. Lancet. 2015;385:1835-1842.

19. Wentzensen N, Poole EM, Trabert B, et al. Ovarian cancer risk factors by histologic subtype: an analysis of the Ovarian Cancer Cohort Consortium. J Clin Oncol. 2016;34:2888-2898.

20. Wu AH, Pearce CL, Tseng CC, Pike MC. African Americans and Hispanics remain at lower risk for ovarian cancer than non-Hispanic whites after considering nonge-netic risk factors and oophorectomy rates. Cancer Epidemiol Biomarkers Prev. 2015;24:1094-1100.

21. Long B, Chang J, Ziogas A, Tewari KS, Anton-Culver H, Brinton LA, et al. Impact of race, socioeconomic status, and the health care system on the treatment of advanced-stage ovarian cancer in California. Am J Obstet Gynecol. 2015;212:468.e1-468.e9.

22. Bristow RE, Powell MA, Al-Hammadi N, et al. Differences in ovarian cancer care quality and survival according to race and socioeconomic status. J Natl Cancer Inst. 2013;105:823-832.

23. Yang HP, Anderson WF, Rosenberg PS, et al. Ovarian cancer incidence trends in relation to changing patterns of menopausal hormone therapy use in the United States. J Clin Oncol. 2013;31:2146-2151.

24. Sopik V, Iqbal J, Rosen B, Narod SA. Why have ovarian cancer mortality rates declined? Part I. Incidence. Gynecol Oncol. 2015;138:741-749.

25. Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov). SEER*Stat Database: Mortality-All COD, Total US (1990-2015) <Early release with Vintage 2015 Katrina/Rita Population Adjustment--Linked To County Attributes-Total US, 1969-2015 Counties. Bethesda, MD: National Cancer Institute, Division of Cancer Control and Population Sciences, Surveillance Research Program; 2017. Underlying mortality data provided by the National Center for Health Statistics (www.cdc.gov/nchs).

26. National Academies of Sciences, Engineering, and Medicine. Ovarian Cancers: Evolving Paradigms in Research and Care. Washington, DC: The National Academies Press; 2016.

27. Bray F, Loos AH, Tognazzi S, La Vecchia C. Ovarian cancer in Europe: cross-sectional trends in incidence and mortality in 28 countries, 1953-2000. Int J Cancer. 2005;113:977-990.

28. Barnholtz-Sloan JS, Schwartz AG, Qureshi F, Jacques S, Malone J, Munkarah AR. Ovarian cancer: changes in patterns at diagnosis and relative survival over the last three decades. Am J Obstet Gynecol. 2003;189:1120-1127.

29. Kurman RJ, Shah IeM. The dualistic model of ovarian carcinogenesis, revised, expanded. Am J Pathol. 2016;186:733-747.

30. Pearce CL, Rossing MA, Lee AW, et al. Combined and interactive effects of environmental and GWAS-identified risk factors in ovarian cancer. Cancer Epidemiol Biomarkers Prev. 2013;22:880-890.

31. Prat J. New insights into ovarian cancer pathology. Ann Oncol. 2012;23(suppl 10):x111-x117.

32. Kurman RJ. Origin and molecular pathogenesis of ovarian high-grade serous carcinoma. Ann Oncol. 2013;24(suppl 10):x16-x21.

33. Matsuno RK, Sherman ME, Visvanathan K, et al. Agreement for tumor grade of ovarian carcinoma: analysis of archival tissues from the Surveillance, Epidemiology, and End Results Residual Tissue Repository. Cancer Causes Control. 2013;24:749-757.

34. Peres LC, Cushing-Haiguen KL, Kobel M, et al. Invasive epithelial ovarian cancer survival by histotype and disease stage. J Natl Cancer Inst. Apr 28 2018:djy071-djy071.

35. Coburn SB, Bray F, Sherman ME, Trabert B. International patterns and trends in ovarian cancer incidence, overall and by histologic subtype. Int J Cancer. 2017;140:2451-2460.

36. Matz M, Coleman MP, Sant M, et al. The histology of ovarian cancer: worldwide distribution and implications for international survival comparisons (CONCORD-2). Gynecol Oncol. 2017;144:405-413.

37. Peres LC, Risch H, Terry KL, et al. Racial/ethnic differences in the epidemiology of ovarian cancer: a pooled analysis of 12 case-control studies [published online ahead of print March 23, 2018]. Int J Epidemiol. doi: 10.1093/ije/diy054.

38. Park HK, Ruterbusch JJ, Cote ML. Recent trends in ovarian cancer incidence and relative survival in the United States by race/ethnicity and histologic subtypes. Cancer Epidemiol Biomarkers Prev. 2017;26:1511-1518.

39. Guo SW, Zilberberg MD, Hummelshoj L. Endometriosis and ovarian cancer. Lancet Oncol. 2012;13:e189-190; author reply e190.
40. Ness RB. Endometriosis and ovarian cancer: thoughts on shared pathophysiology. Am J Obstet Gynecol. 2003;189:280-294.

41. Nezhat FR, Pejovic T, Reis FM, Guo SW. The link between endometriosis and ovarian cancer: clinical implications. Int J Gynecol Cancer. 2014;24:623-628.

42. Pearce CL, Templeman C, Rossing MA, et al. Association between endometriosis and risk of histological subtypes of ovarian cancer: a pooled analysis of case-control studies. Lancet Oncol. 2012;13:385-394.

43. Jacoby VL, Fujimoto VY, Giudice LC, Kuppermann M, Washington AE. Racial and ethnic disparities in benign gynecologic conditions and associated surgeries. Am J Obstet Gynecol. 2010;202:514-521.

44. Jones MR, Kamara D, Karlan BY, Pharoah PDP, Gayther SA. Genetic epidemiology of ovarian cancer and prospects for polygenic risk prediction. Gynecol Oncol. 2017;147:705-713.

45. Lee KR, Young RH. The distinction between primary and metastatic mucinous carcinomas of the ovary: gross and histologic findings in 50 cases. Am J Surg Pathol. 2003;27:281-292.

46. Collaborative Group on Epidemiological Studies of Ovarian Cancer. Beral V, Gaittelli K, et al. Ovarian cancer and smoking: individual participant meta-analysis including 28,114 women with ovarian cancer from 51 epidemiological studies. Lancet. 2012;379:946-956.

47. Liao CL, Chow S, Chen LM, Kapp DS, Mann A, Chan JK. Trends in the incidence of serous fallopian tube, ovarian, and peritoneal cancer in the US [published online ahead of print March 4, 2018]. Gynecol Oncol. doi:10.1016/j.ygyno.2018.01.030.

48. Trabert B, Coburn SB, Mariani A, et al. Reported incidence and survival of fallopian tube carcinomas: a population-based analysis from the North American Association of Central Cancer Registries [published online ahead of print December 21, 2017]. J Natl Cancer Inst. doi:10.1093/jnci/djx263.

49. Bandera EV, Lee VS, Rodriguez-Rodriguez L, Powell CB, Kushi LH. Racial/ethnic disparities in advanced ovarian cancer survival and adherence to treatment guidelines. Obstet Gynecol. 2015;125:833-842.

50. Aranda MA, McGory M, Sekeris E, Maggard MA, G. Zingmond DS. Do racial/ethnic disparities exist in the utilization of high-volume surgeons for women with ovarian cancer? Gynecol Oncol. 2008;111:166-172.

51. Bristow RE, Chang J, Ziegas A, Campos B, Chavez LR, Anton-Culver H. Sociodemographic disparities in advanced ovarian cancer survival and adherence to treatment guidelines. Obstet Gynecol. 2015;125:833-842.

52. Aranda MA, Mcgory M, Sekeris E, Maggard MA, G, Zingmond DS. Do racial/ethnic disparities exist in the utilization of high-volume surgeons for women with ovarian cancer? Gynecol Oncol. 2008;111:166-172.

53. Bristow RE, Chang J, Ziegas A, Randall LM, Anton-Culver H. High-volume ovarian cancer care: survival impact and disparities in access for advanced-stage disease. Gynecol Oncol. 2014;132:403-410.

54. Fairfield KM, Murray K, LaChance JA, et al. Intraperitoneal chemotherapy among women in the Medicare population with epithelial ovarian cancer. Gynecol Oncol. 2014;134:473-477.

55. Norquist BM, Harrell MI, Brady MF, et al. Inherited mutations in women with ovarian carcinoma. JAMA Oncol. 2016;2:482-490.

56. Alspok K, Fereday S, Meldrum C, et al. BRCA2 mutation frequency and patterns of treatment response in BRCA2 mutation-positive women with ovarian cancer: a report from the Australian Ovarian Cancer Study Group. J Clin Oncol. 2012;30:2654-2663.

57. Ramsay SJ, Song H, Dicks E, et al. Germline mutations in the BRIP1, BARD1, PALB2, and BRIP1 genes in women with ovarian cancer [serial online]. J Natl Cancer Inst. 2015;107:dxv214.

58. Song H, Dicks E, Ramsay SJ, et al. Contribution of germline mutations in the RAD51B, RAD51C, and RAD51D genes to ovarian cancer in the population. J Clin Oncol. 2015;33:2901-2907.

59. Heravi-Moussavi A, Anglesio MS, Cheng SW, et al. Recurrent somatic DICER1 mutations in nonneoplastic ovarian cancers. N Engl J Med. 2012;366:234-242.

60. Shah SP, Kobel M, Senz J, et al. Mutation of FOXL2 in granulosa-cell tumors of the ovary. N Engl J Med. 2009;360:2719-2729.

61. Van Nieuwenhuyzen E, Lambrechts S, Lambrechts D, Leunen K, Amant F, Vergote I. Genetic changes in nonneoplastic ovarian cancer. Expert Rev Anticancer Ther. 2013;13:871-882.

62. Daly MB, Pilarski R, Axilbund JE, et al. Genetic/Familial High-Risk Assessment: Breast and Ovarian, Version 2.2015. J Natl Compr Canc Netw. 2016;14:153-162.

63. Kuchenbaecker KB, Hopper JL, Barnes DR, et al. Risks of breast, ovarian, and contralateral breast cancer for BRCA1 and BRCA2 mutation carriers. JAMA. 2017;317:2402-2416.

64. Gabai-Kapara E, Lahad A, Kaufman B, et al. Population-based screening for breast and ovarian cancer risk due to BRCA1 and BRCA2. Proc Natl Acad Sci U S A. 2014;111:14205-14210.

65. US Preventive Services Task Force. Final Recommendation Statement. BRCA-Related Cancer: Risk Assessment, Genetic Counseling, and Genetic Testing, Version 3.2017.

66. Committee on Practice Bulletins-Gynecology, Committee on Genetics, Society of Gynecologic Oncology. Practice Bulletin No 182: Hereditary- Breast and Ovarian Cancer Syndrome. Obstet Gynecol. 2017;130:e110-e126.

67. Walker JL, Powell CB, Chen LM, et al. Sociodemographic and Genetic Risk Assessment for the prevention of ovarian cancer. Cancer. 2015;121:2108-2120.

68. Daly MB, Pilarski R, Berry M, et al. NCCN Guidelines Insights: Genetic/Familial High-Risk Assessment: Breast and Ovarian, Version 2.2017. J Natl Compr Canc Netw. 2017;15:9-20.

69. Friebel TM, Domchek SM, Rebbeck TR. Modifiers of cancer risk in BRCA1 and BRCA2 mutation carriers: systematic review and meta-analysis [serial online]. J Natl Cancer Inst. 2014;106:duo91.

70. Moorman PG, Havrilesky LJ, Giersch JM, et al. Oral contraceptives and risk of ovarian cancer and breast cancer among high-risk women: a systematic review and meta-analysis. J Clin Oncol. 2013;31:4188-4198.

71. Bonadonna V, Bonaiti B, Olschwang S, et al. Cancer risks associated with germline mutations in MLH1, MSH2, and MSH6 genes in Lynch syndrome. JAMA. 2011;305:2304-2310.

72. Ketabi Z, Bartumia K, Bernstein I, et al. Ovarian cancer linked to Lynch syndrome typically presents as early-onset, non-serous epithelial tumors. Gynecol Oncol. 2011;121:462-465.

73. Goff BA, Mandel LS, Melancon CH, Muntz HG. Frequency of symptoms of ovarian cancer in women presenting to primary care clinics. JAMA. 2004;291:2705-2712.

74. Bankhead CR, Collins C, Stokes-Lampard HJ, et al. Identifying symptoms of ovarian cancer: a qualitative and quantitative study. BJOG. 2008;115:1008-1014.

75. Hamilton W, Peters TJ, Bankhead C, Sharp D. Risk of ovarian cancer in women with symptoms in primary care: population based case-control study [serial online]. BMJ. 2009;339:b2998.

76. Boussios S, Zarkavilos G, Seraj E, Zeredes I, Tatsi K, Pentheroudakis G. Non-epithelial ovarian cancer: elucidating uncommon gynaecological malignancies. Anticancer Res. 2016;36:5031-5042.

77. Schultz KA, Harris AK, Schneider DT, et al. Ovarian sex cord-stromal tumors. J Oncol Pract. 2016;12:940-946.

78. Pinsky PF, Yu K, Kramer BS, et al. Extended mortality results for ovarian cancer screening in the PLCO trial with median 15years follow-up. Gynecol Oncol. 2016;143:270-275.

79. Jacobs UJ, Menon U, Ryan A, et al. Ovarian cancer screening and mortality in the UK Collaborative Trial of Ovarian Cancer Screening (UKCTOCS): a randomised controlled trial. Lancet. 2016;387:945-956.

80. Nard SA, Sopik V, Giannakeas V. Should we screen for ovarian cancer? A commentary on the UK Collaborative Trial of Ovarian Cancer Screening (UKCTOCS) randomized trial. Gynecol Oncol. 2016;141:191-194.

81. US Preventive Services Task Force, Grossman DC, Curry SJ, et al. Screening for ovarian cancer: US Preventive Services Task Force recommendation statement. JAMA. 2018;319:588-594.

82. Berchuck A, Havrilesky LJ, Kauff ND. Is there a role for ovarian cancer screening in high-risk women? J Clin Oncol. 2017;35:1384-1386.

83. Rosenthal AN, Fraser LSM, Philipston S, et al. Evidence of stage shift in women diagnosed with ovarian cancer during phase II of the United Kingdom Familial Ovarian Cancer Screening Study. J Clin Oncol. 2017;35:1411-1420.