

Incidence Patterns of Invasive and Borderline Ovarian Tumors among White Women and Black Women in the United States

Results from the SEER Program, 1978–1998

Pamela J. Mink, Ph.D., M.P.H.^{1,2}
 Mark E. Sherman, M.D.¹
 Susan S. Devesa, Ph.D.¹

¹ Division of Cancer Epidemiology and Genetics, National Cancer Institute, Rockville, Maryland.

² Division of Cancer Prevention, National Cancer Institute, Rockville, Maryland.

BACKGROUND. Malignant tumors of the ovary are the leading cause of death from gynecologic malignancies in the United States. Population-based incidence data for these neoplasms by histopathologic type and race are limited. Variation in rates may provide clues for future etiologic studies.

METHODS. The authors performed a detailed, population-based analysis of U.S. incidence rates by histologic type, race, and age for invasive ovarian tumors that were diagnosed during 1978–1998 and for borderline ovarian tumors that were diagnosed during 1992–1998 using data from the U.S. Surveillance, Epidemiology, and End Results (SEER) Program.

RESULTS. White women had significantly higher rates compared with black women of all types of epithelial tumors, with the white:black rate ratios ranging from 1.23 to 2.56. Black women had higher rates of gonadal stromal tumors. Among both white women and black women, total carcinoma rates did not change greatly from 1978–1982 to 1995–1998. Among white women, the reported incidence rates for invasive serous, endometrioid, and clear cell tumors increased during 1978–1998, whereas the rates of mucinous; papillary, not otherwise specified (NOS); and *other* epithelial tumors declined. Among black women, the reported rates of papillary, NOS tumors decreased significantly, whereas the rates of other tumor types fluctuated. Incidence rates of borderline ovarian tumors were higher among white women compared with black women and did not change significantly during 1992–1998. Serous and mucinous tumors were the predominant tumors reported for women age < 45 years, whereas serous; papillary, NOS; and *other* epithelial tumors predominated among older women.

CONCLUSIONS. Incidence rates for malignant ovarian tumors have remained relatively stable, with higher rates for white women compared with black women. The reported rates for some specific histopathologic tumor types have changed over time, in part reflecting more specific pathologic classification. The possible effect of shifting exposure prevalence on incidence patterns warrants further study.

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Ovarian cancer is the most lethal gynecologic malignancy in the United States, accounting for more deaths annually than carcinomas of the uterine cervix and corpus combined.¹ An estimated 23,300 new diagnoses and 13,900 deaths related to ovarian cancer will

Address for reprints: Pamela J. Mink, Ph.D., M.P.H., Exponent Health Group, 1730 Rhode Island Ave., NW, Suite 1100, Washington, DC 20036; Fax: (202) 293-5377; E-mail: pmink@exponent.com

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occur among women in the United States during 2002.¹ Although several risk factors and protective factors for ovarian cancer have been identified, the etiology and pathogenesis of these tumors remain obscure. Oral contraceptive use and increasing parity consistently have been associated with decreased incidence of epithelial ovarian carcinoma, whereas age and a family history of the disease have been associated with increased incidence.^{2–4} Borderline ovarian tumors (also called tumors of low malignant potential) are neoplasms of controversial biologic potential and clinical significance. These tumors appear to share a risk profile similar to that of malignant ovarian tumors, but they tend to occur at younger ages and are associated with a much better prognosis.^{5–7}

Ovarian cancer encompasses a heterogeneous group of histologic types. Weiss and colleagues⁸ reported different incidence patterns for epithelial versus nonepithelial ovarian cancer according to age, race, and marital status. However, their ability to examine differences among histopathologic subtypes of epithelial ovarian carcinoma was limited to some degree by the lack of specificity in histopathologic classification at that time. However, there was some evidence that the incidence of endometrioid and clear cell tumors differed from other epithelial tumors according to age and marital status.

To date, there have been few published descriptive studies of incidence patterns for histopathologic types of epithelial ovarian carcinoma.^{9,10} Several analytic epidemiologic studies have suggested that associations of certain risk factors with ovarian carcinoma may vary by histopathologic type.^{11–14} However, many of those studies were limited by small numbers of cases overall and by changing criteria for histopathologic classification. Two recent studies found little difference among associations of reproductive risk factors with histopathologic types of epithelial ovarian carcinoma.^{15,16}

Descriptive studies may contribute further to our understanding of ovarian carcinoma by identifying etiologically similar subtypes of ovarian carcinoma and suggesting hypotheses that may explain varying incidence rates observed among women in the United States. Using data from the U.S. population-based Surveillance, Epidemiology, and End Results (SEER) Program, we analyzed incidence trends in invasive ovarian tumors diagnosed during the period 1978–1998 according to histopathology, age, and race. We also examined SEER incidence data for borderline ovarian tumors diagnosed during the period 1992–1998.

MATERIALS AND METHODS

Data Source

The data used in this report were collected in SEER Program registries in the states of Connecticut, Iowa, New Mexico, Utah, and Hawaii and in the regional registries located in Atlanta, Detroit, San Francisco-Oakland, and Seattle. Data from these nine areas represent approximately 10% of the total U.S. population.¹⁷ Details of the SEER Program have been published.¹⁸ Although the SEER Program began reporting diagnosed malignancies in 1973, the histologic codes became more detailed with the adoption of the International Classification of Diseases for Oncology.¹⁹ Thus, we included cases who were diagnosed from January 1, 1978 through December 31, 1998. Borderline ovarian tumors were not reported to SEER until 1988, and reporting of these tumors is considered complete beginning in 1992.

Data Analysis

Incidence rates per 100,000 person-years (i.e., woman-years) were calculated by histopathologic type for invasive ovarian carcinomas diagnosed from 1978 through 1998 and for borderline ovarian tumors diagnosed from 1992 through 1998. Tumors were grouped for analysis using a modification of the classification system proposed by Berg.²⁰ Table 1 shows these groupings and the corresponding morphology codes from the second edition of the International Classification of Diseases for Oncology.²¹

Overall age-adjusted and 10-year age specific rates were standardized (direct method) to the 1970 U.S. population. Rates were calculated separately for black women and white women by histologic subtype for five periods (one 5-year period and four 4-year periods): 1978–1982, 1983–1986, 1987–1990, 1991–1994, and 1995–1998. The percent change over time was calculated by comparing 1995–1998 rates with 1978–1982 rates. The estimated annual percent change (EAPC) and corresponding *P* values were computed based on log-linear weighted regression.¹⁷ Rates were plotted on the ordinate of a semilogarithmic scale against the midpoint of the five periods on the abscissa. For borderline tumors, rates were calculated by race and histology for two periods: 1992–1995 and 1996–1998. The percent change was calculated, comparing rates between these two periods. Calculation of the EAPC required points for three periods; thus, we calculated rate ratios (RRs) and corresponding 95% confidence intervals (95% CIs) to determine whether rates of borderline tumors during the two periods differed significantly. The black:white incidence RR and the corresponding 95% CI were computed for his-

TABLE 1
International Classification of Diseases for Oncology-Second Edition Morphology Codes for Borderline and Invasive Ovarian Carcinoma

| Tumor type ICDO-2 codes | Morphology |
|---------------------------------------|--|
| Total tumors | |
| 8000-9580 | |
| Borderline ovarian tumors | |
| Serous | |
| 8442 | Serous cystadenoma, borderline malignancy |
| 8462 | Papillary serous cystadenoma, borderline malignancy |
| Mucinous | |
| 8472 | Mucinous cystadenoma, borderline malignancy |
| 8473 | Papillary mucinous cystadenoma, borderline malignancy |
| NOS | |
| 8451 | Papillary cystadenoma, borderline malignancy |
| Invasive epithelial ovarian carcinoma | |
| 8010-8580 | Excluding borderline tumor codes, (above) |
| Serous | |
| 8441 | Serous cystadenocarcinoma, NOS |
| 8460 | Papillary serous cystadenocarcinoma |
| 8461 | Serous surface papillary carcinoma |
| Mucinous | |
| 8470 | Mucinous cystadenocarcinoma |
| 8471 | Papillary mucinous cystadenocarcinoma |
| 8480 | Mucinous adenocarcinoma |
| 8481 | Mucin-producing adenocarcinoma |
| Papillary | |
| 8050 | Papillary carcinoma |
| 8260 | Papillary adenocarcinoma |
| 8450 | Papillary cystadenocarcinoma, NOS |
| Endometrioid | |
| 8380 | Endometrioid carcinoma |
| 8560 | Adenosquamous carcinoma |
| 8570 | Adenocarcinoma with squamous metaplasia |
| 8381 | Malignant endometrioid adenofibroma, malignant endometrioid cystadenofibroma |
| Clear cell | |
| 8310 | Clear cell adenocarcinoma, NOS |
| Adenocarcinoma, NOS | |
| — | All other invasive epithelial codes |
| Gonadal stromal | |
| 8590-8679 | |
| Germ cell tumors | |
| 9060-9099 | |
| Other neoplasms | |
| Malignant mixed Mullerian | |
| 8950 | Mullerian mixed tumor |
| 8951 | Mesodermal mixed tumor |
| 8980 | Carcinosarcoma, NOS |
| Other tumors, NOS | |
| — | All other ovarian malignancies excluding 9100 (choriocarcinoma) |

ICDO-2: International Classification of Diseases for Oncology-second edition; NOS: not otherwise specified.

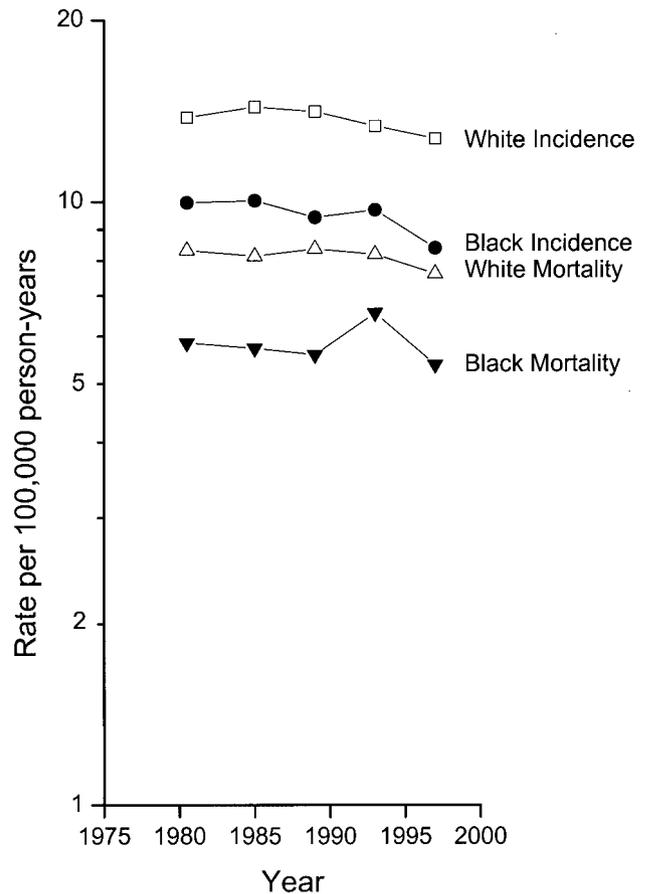


FIGURE 1. Trends in total invasive ovarian cancer incidence in the nine SEER areas and U.S. mortality rates (age-adjusted 1970 U.S. standard) by race from 1978-1982 to 1995-1998.

tologic types of invasive and borderline ovarian tumors.

Age specific incidence rates were computed in 10-year age intervals as follows: 0-4 years, 5-14 years, 15-24 years . . . 75-84 years, and ≥ 85 years. These rates were plotted as described above but with the midpoint of each age category on the abscissa.

RESULTS
Incidence of Invasive Ovarian Carcinomas

A total of 35,059 invasive ovarian malignancies that were diagnosed among black women and white women from January 1, 1978 to December 31, 1998 were reported to SEER. During that period, the total ovarian cancer incidence and mortality rates changed little, but they appear to have decreased slightly in recent years (Fig. 1). Both incidence rates and mortality rates have been approximately 40-50% higher among white women compared with black women during each period.

TABLE 2
Age-Adjusted Ovarian Carcinoma Incidence Rates per 100,000 Person-Years and White:Black Incidence Rate Ratios in Nine SEER Registries: 1978–1998

| Tumor type | White women | | Black women | | RR | 95%CI |
|--|-------------|-------|-------------|------|------|-----------|
| | Count | Rate | Count | Rate | | |
| Total invasive tumors ^a | 32,808 | 13.69 | 2251 | 9.50 | 1.44 | 1.38–1.50 |
| Epithelial | 30,171 | 12.58 | 1879 | 8.04 | 1.56 | 1.49–1.64 |
| Mucinous | 3251 | 1.38 | 257 | 1.06 | 1.29 | 1.14–1.47 |
| Serous | 10,175 | 4.38 | 569 | 2.42 | 1.81 | 1.67–1.97 |
| Papillary, NOS | 3781 | 1.55 | 232 | 1.01 | 1.53 | 1.34–1.75 |
| Endometrioid | 3543 | 1.57 | 172 | 0.75 | 2.10 | 1.80–2.45 |
| Clear cell | 1116 | 0.50 | 47 | 0.20 | 2.56 | 1.92–3.43 |
| Other epithelial | 8305 | 3.20 | 602 | 2.60 | 1.23 | 1.13–1.33 |
| Gonadal stromal | 415 | 0.18 | 89 | 0.35 | 0.53 | 0.42–0.67 |
| Germ cell | 655 | 0.34 | 108 | 0.38 | 0.90 | 0.73–1.10 |
| Other malignant neoplasms | | | | | | |
| Malignant mixed Mullerian (carcinosarcoma) | 671 | 0.27 | 55 | 0.24 | 1.11 | 0.84–1.46 |
| Others | 896 | 0.31 | 120 | 0.49 | 0.63 | 0.52–0.77 |

RR: rate ratio; 95%CI: 95% confidence interval; NOS: not otherwise specified.

^a Excluding borderline ovarian tumors.

Epithelial tumors accounted for 92% and 83% of ovarian invasive tumors among white women and black women, respectively (Table 2). Of these, serous carcinomas were the most common, accounting for about one-third of all epithelial carcinomas. Mucinous; papillary, not otherwise specified (NOS); and endometrioid carcinoma rates were lower, and clear cell carcinomas were the rarest.

The white:black incidence RR for the period 1978–1998 was 1.44 (95%CI, 1.38–1.50) for invasive ovarian tumors overall and 1.56 (95%CI, 1.49–1.64) for epithelial carcinomas (excluding borderline tumors) (Table 2). The rates for all histopathologic types of carcinoma were significantly higher among white women compared with black women, with the white:black RRs for serous tumors (RR, 1.81), endometrioid tumors (RR, 2.10), and clear cell tumors (RR, 2.56) especially elevated. The incidence of gonadal stromal tumors, by contrast, was significantly lower among white women compared with black women (RR, 0.53; 95%CI, 0.42–0.67). For germ cell and malignant mixed Mullerian tumors, the rates for white women and black women were similar.

The incidence rates for carcinoma fell 9.87% among white women and 12.70% among black women from 1978–1982 to 1995–1998 (Table 3). Although much rarer, gonadal stromal tumor rates decreased 43% for white women and 35% for black women over this period. Rates of these tumors fluctuated for black women due to small numbers. There was a nonsignificant decrease in rates of germ

cell tumors for women of both races, whereas rates of *other* ovarian neoplasms increased among white women.

Among white and black women, rates of papillary carcinoma decreased more than 70% over the entire study period (Fig. 2). Among white women, the incidence rate for serous tumors increased 32.25%, from 3.59 to 4.85 per 100,000 person-years from 1978–1982 to 1995–1998, and rates for mucinous carcinomas declined. Among black women, the rates for serous and mucinous carcinomas fluctuated but did not change significantly overall. The decline in the incidence rates for papillary carcinoma among white women was countered by an increase in serous carcinomas, although this increase appeared to level off over the last two periods, whereas the rates for papillary carcinoma continued to drop. Among black women, the significant decline in papillary carcinomas did not appear to be offset by increases in mucinous or serous carcinomas, which did not change significantly. Rates of endometrioid and clear cell tumors increased overall between 1978–1982 and 1995–1998, but the increase was not monotonic, and the EAPC approached statistical significance ($P = 0.07$) only for clear cell tumors among white women. For both black women and white women, the steepest increase in the incidence of endometrioid carcinoma occurred between the first two periods. Rates for *other* epithelial tumors decreased for white women and increased for black women, but these changes were marginally significant only for white women.

TABLE 3
Age-Adjusted Ovarian Cancer Incidence Rates per 100,000 Person-Years by Race in Nine SEER Registries for Five Periods

| Histologic type | 1978-1982 ^a | | 1983-1986 | | 1987-1990 | | 1991-1994 | | 1995-1998 | | Percent change | EAPC | P value |
|--|------------------------|-------|-----------|-------|-----------|-------|-----------|-------|-----------|-------|----------------|--------|---------|
| | Count | Rate | Count | Rate | Count | Rate | Count | Rate | Count | Rate | | | |
| White women | | | | | | | | | | | | | |
| Invasive carcinoma ^b | 6615 | 12.81 | 5755 | 13.26 | 5960 | 13.01 | 5984 | 12.31 | 5857 | 11.54 | - 9.87 | - 0.65 | 0.11 |
| Mucinous | 831 | 1.60 | 685 | 1.60 | 641 | 1.39 | 577 | 1.23 | 517 | 1.05 | - 34.40 | - 2.54 | 0.01 |
| Serous | 1799 | 3.59 | 1738 | 4.12 | 2035 | 4.59 | 2248 | 4.83 | 2355 | 4.85 | 35.25 | 1.84 | 0.02 |
| Papillary | 1305 | 2.51 | 893 | 2.02 | 723 | 1.52 | 520 | 1.00 | 340 | 0.65 | - 74.30 | - 7.44 | < 0.01 |
| Endometrioid | 656 | 1.34 | 663 | 1.63 | 677 | 1.60 | 774 | 1.69 | 773 | 1.62 | 20.79 | 1.00 | 0.15 |
| Clear Cell | 181 | 0.37 | 193 | 0.48 | 233 | 0.56 | 244 | 0.55 | 265 | 0.56 | 51.73 | 2.28 | 0.07 |
| Other Epithelial | 1843 | 3.40 | 1583 | 3.40 | 1651 | 3.36 | 1621 | 3.01 | 1607 | 2.81 | - 17.20 | - 1.17 | 0.04 |
| Gonadal stromal | 118 | 0.24 | 91 | 0.22 | 78 | 0.19 | 64 | 0.14 | 64 | 0.14 | - 43.40 | - 3.74 | 0.01 |
| Germ cell | 173 | 0.36 | 125 | 0.35 | 124 | 0.34 | 119 | 0.32 | 114 | 0.34 | - 6.10 | - 0.50 | 0.07 |
| Other ovarian neoplasms | | | | | | | | | | | | | |
| Malignant Mixed Mullerian (carcinosarcoma) | 94 | 0.17 | 122 | 0.27 | 140 | 0.31 | 147 | 0.29 | 168 | 0.33 | 93.16 | 3.14 | 0.07 |
| Others | 136 | 0.24 | 141 | 0.29 | 154 | 0.29 | 205 | 0.32 | 260 | 0.40 | 62.64 | 2.80 | 0.01 |
| Black women | | | | | | | | | | | | | |
| Invasive carcinoma ^b | 377 | 8.23 | 351 | 8.69 | 357 | 7.88 | 407 | 8.20 | 387 | 7.18 | - 12.70 | - 0.78 | 0.17 |
| Mucinous | 49 | 1.05 | 68 | 1.66 | 46 | 0.92 | 54 | 0.97 | 40 | 0.75 | - 28.30 | - 3.02 | 0.27 |
| Serous | 125 | 2.66 | 80 | 1.94 | 96 | 2.10 | 136 | 2.82 | 132 | 2.42 | - 8.99 | 0.25 | 0.85 |
| Papillary | 79 | 1.75 | 51 | 1.27 | 53 | 1.19 | 22 | 0.46 | 27 | 0.48 | - 72.30 | - 7.71 | 0.02 |
| Endometrioid | 21 | 0.46 | 36 | 0.93 | 31 | 0.71 | 42 | 0.86 | 42 | 0.81 | 74.02 | 1.88 | 0.40 |
| Clear cell | 7 | 0.16 | 6 | 0.13 | 6 | 0.13 | 16 | 0.33 | 12 | 0.20 | 25.83 | 3.60 | 0.34 |
| Other epithelial | 96 | 2.15 | 110 | 2.76 | 125 | 2.83 | 137 | 2.77 | 134 | 2.51 | 16.98 | 0.65 | 0.52 |
| Gonadal stromal | 22 | 0.44 | 23 | 0.53 | 8 | 0.17 | 19 | 0.34 | 17 | 0.29 | - 34.60 | - 3.15 | 0.28 |
| Germ cell | 29 | 0.48 | 18 | 0.35 | 26 | 0.51 | 19 | 0.35 | 16 | 0.23 | - 52.60 | - 3.36 | 0.17 |
| Other malignant neoplasms | | | | | | | | | | | | | |
| Malignant mixed Mullerian (carcinosarcoma) | 8 | 0.18 | 9 | 0.23 | 14 | 0.31 | 11 | 0.24 | 13 | 0.26 | 46.57 | 1.66 | 0.36 |
| Others | 28 | 0.63 | 10 | 0.24 | 26 | 0.56 | 31 | 0.58 | 25 | 0.45 | - 29.70 | - 0.78 | 0.77 |

EAPC: estimated annual percent change.

^a Note that this period covers 5 years.^b Excluding borderline ovarian tumors.

Incidence of Borderline Ovarian Tumors

The incidence rates for borderline ovarian tumors were compared by race (Table 4) and for two periods (1992-1995 vs. 1996-1998). The total incidence rate for borderline tumors was significantly higher among white women compared with black women (RR, 1.61; 95%CI, 1.37-1.90) as were the specific rates for mucinous and serous tumors (Table 4). The white:black RR was greatest for borderline mucinous tumors (RR, 2.35; 95%CI, 1.69-3.27). The incidence rates for all borderline tumors changed little during the two periods. The age-adjusted rates for all borderline tumors among white women were 2.49 and 2.52 per 100,000 person-years for the periods 1992-1995 and 1996-1998, respectively. The comparable rates for black women were 1.61 and 1.46, respectively. The rates for the two periods did not differ significantly for any histologic type of borderline tumor for women of either race (data not shown).

Age Specific Incidence of Ovarian Carcinoma

Figure 3 displays age specific incidence curves for invasive ovarian carcinomas in 10-year age groups for black women and white women. The incidence rates for each histologic type increased rapidly with age starting in early adulthood. Among white women, mucinous, serous, endometrioid, and *other* carcinomas were rare before ages 35-44 years (incidence rates < 1.0 per 100,000 person-years); and papillary and clear cell carcinomas were rare before ages 45-54 years. Among black women, serous tumors were rare before ages 35-44 years; and mucinous, papillary, endometrioid, and *other* epithelial tumors were rare before ages 45-54 years. Clear cell tumors were rare for most age groups, and age specific patterns were unstable for black women. The rates for most tumor types leveled off and even decreased after approximately age 60 years; the rates for *other* carcinomas, however, continued to increase until age \geq 85 years.

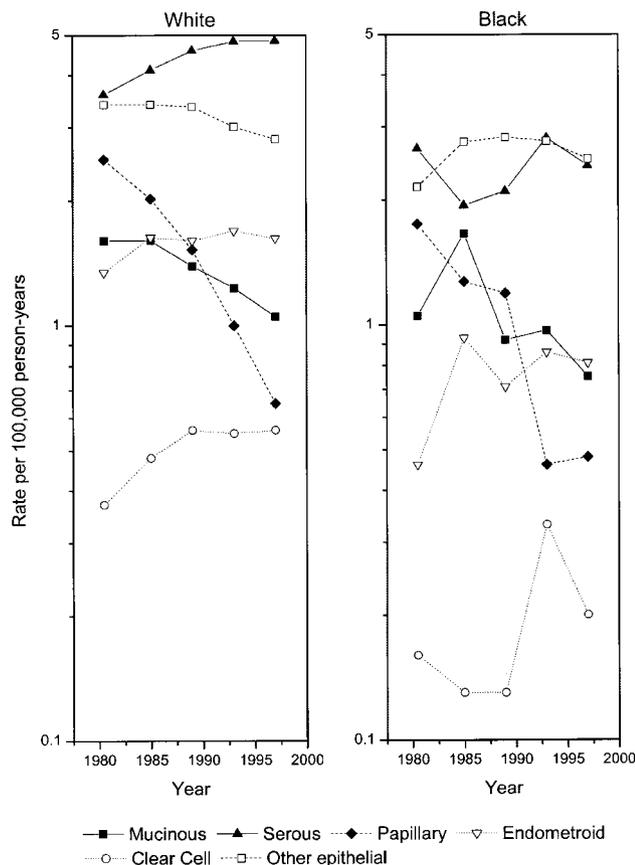


FIGURE 2. Trends in epithelial ovarian cancer incidence rates (age-adjusted U.S. standard) in the nine SEER areas by race and histologic type from 1978–1982 to 1995–1998.

TABLE 4
Age-Adjusted Incidence Rates per 100,000 Person-Years and White: Black Incidence Rate Ratios for Nine SEER Registries: Ovarian Borderline Malignancies, 1992–1998

| Tumor type | White women | | Black women | | RR | 95%CI |
|-------------------------|-------------|------|-------------|------|------|-----------|
| | Count | Rate | Count | Rate | | |
| Borderline malignancies | | | | | | |
| Total | 2,054 | 2.50 | 157 | 1.55 | 1.61 | 1.37–1.90 |
| Mucinous | 756 | 0.92 | 37 | 0.39 | 2.35 | 1.69–3.27 |
| Serous | 1259 | 1.53 | 115 | 1.10 | 1.39 | 1.15–1.68 |
| Other | 39 | 0.05 | 5 | 0.05 | 0.92 | 0.36–2.33 |

RR: rate ratio, 95%CI: 95% confidence interval.

Serous tumors were the predominant tumor type for most age groups, representing approximately one-third of all carcinomas among women age \geq 45 years. Among women age \leq 45 years, serous and mucinous carcinoma were predominant; whereas serous, papillary, and *other* epithelial tumors predominated after age 65 years. Among both black women and white

women, the rate of increase between age 30 years and age 70 years was less rapid for mucinous carcinomas compared with other carcinomas. The peak ages for each epithelial histologic subtype for black women and white women were within 10 years of each other.

Both serous and mucinous borderline tumors increased in incidence with advancing age, peaking among white women at ages 45–54 years, earlier than their malignant counterparts (data not shown). Age specific incidence rates of all borderline tumors for black women were highest among women between ages 45 years and 74 years. Data for black women were too sparse to permit further analysis.

Gonadal stromal tumors were very rare, particularly before age 45 years (data not shown). Incidence rates for these tumors rose to 0.42–0.50 per 100,000 person-years for women ages 45–74 years, then declined slightly. Similarly, malignant mixed Mullerian tumors (carcinosarcomas) were rare before age 45 years, but the incidence rates then rose rapidly and reached their peak among women ages 65–84 years. In contrast to most ovarian tumors, the occurrence of germ cell tumors peaked in young women (ages 15–24 years) and dropped substantially after age 35 years (data not shown).

DISCUSSION

Analysis of SEER data for over 35,000 invasive ovarian tumors revealed that incidence rates have remained relatively stable overall during the period 1978–1998 in the United States, with evidence of a recent slight decline. Carcinomas accounted for 92% of all malignant tumors among white women and 83% of all malignant tumors among black women. The overall incidence rate for carcinoma during this 20-year period was 13.69 per 100,000 person-years among white women and 9.50 per 100,000 person-years among black women.

Data from Canada and northwestern European countries, as well as data from the United States, suggest that ovarian carcinoma incidence and mortality rates may be declining in recent decades among younger women but not (or to a lesser degree) among older women.^{10,22–29} Patterns of parity and oral contraceptive use have changed over the past 40 years. The interplay between increasing risk due to declining parity and a protective effect of increased use of oral contraceptive use over time has been suggested as an explanation for observed declining ovarian carcinoma rates among younger women (age 35–59 years) in the United States during 1970–1995.³⁰

Differences and variations in incidence patterns among histologic types of carcinomas may provide etiologic clues. Because epidemiologic data have sug-

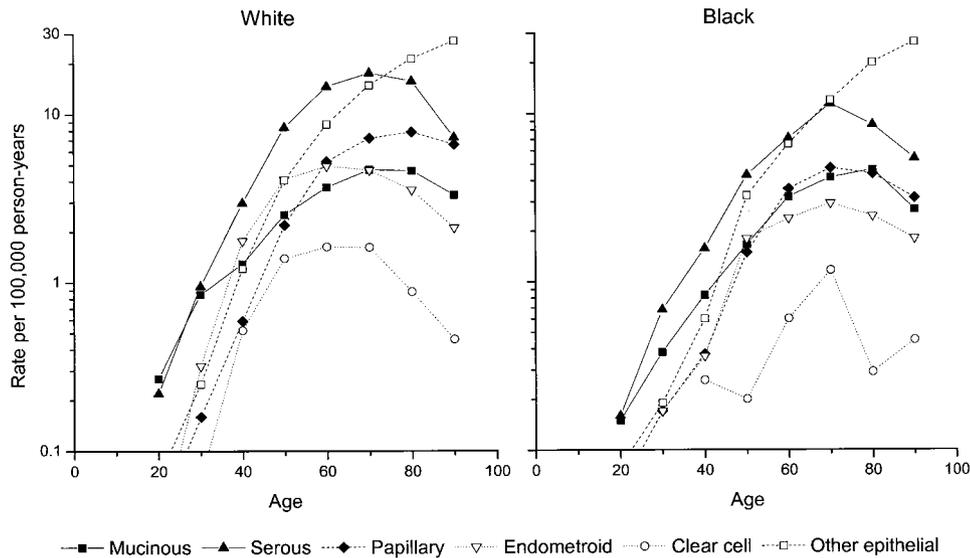


FIGURE 3. Epithelial ovarian cancer incidence in the nine SEER areas by race, histologic type, and 10-year age groups (age-adjusted 1970 U.S. standard), 1978–1998.

gested etiologic differences among histologic types, particularly between mucinous tumors and nonmucinous tumors,^{11–14} it is plausible that incidence patterns may differ accordingly. Although little overall change was observed when rates of epithelial tumors were considered as a group, there were apparent differences in reported diagnoses over time among histologic types. Our data showed that the reported rates of invasive serous carcinomas increased, whereas the rates for mucinous carcinomas and papillary carcinomas, NOS decreased among white women over the study period. Although there were no statistically significant changes in the rates for endometrioid or clear cell carcinomas over the entire 20-year period, the rates seemed to have increased between the periods 1978–1982 and 1995–1998.

A recent report of histology specific incidence rates in Canada during 1969–1993 also observed increases in age-adjusted rates for serous, endometrioid, and clear cell tumors.¹⁰ However, unlike the current study, Canadian rates of mucinous tumors did not change. A previous U.S. study reported that the relative frequency of endometrioid and clear cell carcinoma doubled between the periods 1969–1971 and 1975–1977.⁹ The increases we observed occurred during the next contiguous period (1978–1982), perhaps reflecting a continuation of the trend observed by those authors. We speculate that the observed increase in endometrioid ovarian tumors in particular, like the increase in endometrioid endometrial tumors that occurred in the U.S. during the early to middle 1970s, may be related to the use of unopposed estrogen by postmenopausal women. This hypothesis is supported by recent data linking the use of meno-

pausal estrogen replacement therapy with ovarian carcinoma mortality in a large cohort study.³¹

The decline in the reported incidence of papillary carcinoma, NOS most likely reflects increased specificity of histologic typing by pathologists.^{32–35} This decline may account for a significant proportion of the observed increase in serous carcinoma secondary to a shift in pathologic classification. We speculate that the increased specificity in reporting has been prompted by recognition among clinicians that the pathogenesis and behavior of ovarian tumors may vary by type. The observed decline in the incidence of mucinous carcinomas partly may reflect increased accuracy in the diagnosis of mucinous gastrointestinal tumors metastatic to the ovary. The differential diagnosis of mucinous tumors occurring in the ovary has received increasing attention among pathologists, and diagnostically useful immunohistochemical panels have been developed to distinguish primary ovarian tumors from secondary (metastatic) tumors.^{36–38} The decline in the incidence of mucinous carcinomas may also be related to decreasing smoking prevalence among U.S. women. Cigarette smoking has been associated with increased risk of mucinous ovarian tumors in recent epidemiologic studies.^{11,39,40}

Our data show a significant excess of invasive carcinomas of all histopathologic types among white women compared with black women, with the highest white:black rate ratios observed for clear cell and endometrioid carcinomas. This excess was also observed in a SEER analysis of relative frequency of these two types of carcinoma for white women compared with black women during 1973–1987.⁴¹ It is notable that the incidence rates for endometrioid endometrial carci-

noma also are higher among white women compared with black women,¹⁷ which may reflect similarities in etiology for these homologous ovarian and endometrial tumors. However, the rates for other types of endometrial tumors, including clear cell and serous tumors, are higher among black women compared with white women.

Previous studies of U.S. populations have demonstrated consistently higher incidence rates of malignant ovarian tumors among white women compared with women in other racial and ethnic groups.^{8,41–44} Two studies have addressed the question of whether differences in reproductive patterns account for the black-white variation in incidence rates.^{45,46} Although increasing parity, oral contraceptive use, hysterectomy, and tubal ligation have been associated with reduced risk of ovarian carcinoma in both black women and white women, differences in the distribution of these factors did not fully explain the observed differences in incidence in either study. A family history of ovarian cancer has been associated with increased risk of the disease among white women but not among black women.⁴⁶ However, only a small percentage of women with ovarian cancer have disease that is associated with family history, suggesting that additional unidentified factors also must contribute to the observed racial variation in the incidence of epithelial ovarian carcinoma. Reasons for lower rates among other racial and ethnic groups have not been studied well.

Age specific carcinoma rates varied by histologic type. Incidence rates for these tumors generally increased with age, with rates of endometrioid and clear cell tumors among white women peaking at approximately age 60 years before declining. Rates for serous, mucinous, and papillary tumors peaked at approximately age 70 years before leveling off and/or declining; whereas rates for other epithelial tumors increased monotonically with age through the highest age group for both races. The age patterns we observed generally were consistent with the patterns reported in Canada and northern Europe, countries that, like the United States, have high rates of ovarian carcinoma compared with other parts of the world.^{10,22,23,25,26} Similarly, ovarian cancer incidence rates in those countries have not changed dramatically over the past 2–3 decades.

Borderline tumors occurred less frequently compared with their invasive counterparts, with overall rates of 2.50 for white women and 1.55 for black women. Among borderline tumors, mucinous neoplasms had the highest white:black RR (RR, 2.35); whereas, among invasive carcinomas, serous tumors had the highest white:black ratio (RR, 1.81), and the

white:black RR for invasive mucinous tumors was lower, although it remained statistically significant (RR, 1.39). Because it is believed that risk factors for invasive and borderline tumors generally are similar,^{5,6} this difference in RRs according to race was somewhat surprising.

Rates of all borderline tumors were similar in the two periods. However, the relatively small numbers and the shorter period for which data were available limits our interpretation of temporal patterns of borderline tumors. Rates of borderline tumors as a group peaked at 2.80 per 100,000 person-years for white women ages 45–54 years and then declined.

The observed decline in gonadal stromal tumors largely reflects reporting of granulosa cell tumors, which account for the bulk of these neoplasms. Among white women, the incidence rates of gonadal stromal tumors declined significantly during this 20-year period, whereas the decline in germ cell tumors was smaller and marginally significant. Rates of these two tumors also declined in black women, but the changes were not statistically significant. Gonadal stromal tumors were almost twice as common among black women compared with white women, and rates for germ cell tumors did not differ significantly by race. Studies of risk factors for gonadal stromal tumors have been few and inconsistent,^{47,48} and future studies are needed to confirm our findings and to evaluate reasons for the observed differences by race. In general, the contrasting white:black RRs for epithelial tumors and nonepithelial tumors are consistent with presumed differences in the risk factors for these tumor types.

The strengths of this study include completeness of reporting of diagnoses to the SEER registries, microscopic confirmation of histopathologic subtypes, and more patients and more years of data than previous U.S. studies. However, changing histopathologic classification over time limited our ability to determine the degree to which changing incidence rates may reflect changing prevalence of important etiologic factors. In addition, there was no central pathology review for this study. Analyses of ovarian carcinoma by histopathologic type are challenging, because these tumors are often large at detection and show mixed patterns of differentiation and/or solid areas of undifferentiated growth. Finally, the limited number of patients and years of available data for borderline tumors did not allow us to examine temporal patterns of these tumors conclusively.

These data illustrate the importance of specific and consistent classification of tumors in analyzing and interpreting descriptive data. This also is applicable to the interpretation of data from etiologic studies

of histology specific ovarian tumors. Further analysis of SEER data may provide a clearer picture regarding the incidence patterns of histopathologic types of ovarian tumors as pathologic classification continues to improve. Although the SEER Program will discontinue formal surveillance of borderline tumors, we hope that some registries may elect to continue tracking these neoplasms so that long-term population-based data remain available for researchers.

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