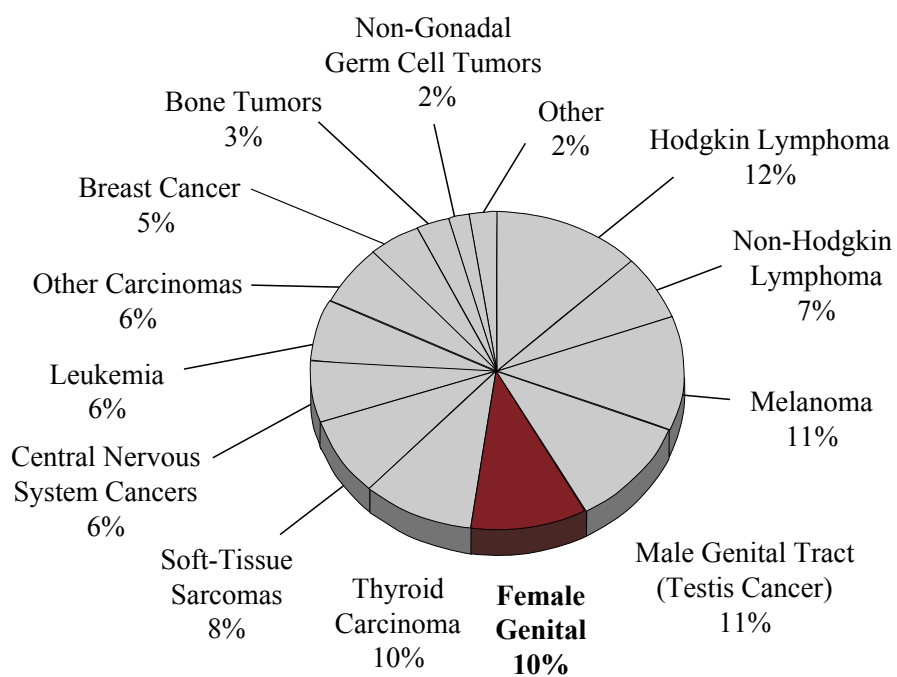


## Chapter 14

# Female Genital Tract Cancer

Cancer in 15- to 29-Year-Olds in the United States



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**HIGHLIGHTS***Incidence*

- The vast majority of genital tract tumors diagnosed in women 15 to 29 years of age are carcinomas of the cervix and corpus uteri, and carcinomas and germ cell tumors of the ovary.
- In the period 1975 to 2000, this group of cancers accounted for 13% of all malignancies in 15- to 19-year-old females, 17% in 20- to 24-year-old females, and 23% of all malignancies in 25- to 29-year-old females.
- Cervical carcinoma in 15- to 29-year-olds decreased in incidence over time from 1975 to 2000.
- The incidence of cervical cancer in 15- to 29-year-olds was higher in white non-Hispanic, Hispanic, and African American/black females than it was in other races/ethnicities.
- Cancer of the ovary occurs most frequently in Asian/Pacific Islander females and is least common in American Indian/Alaska Native females.

*Mortality & Survival*

- The 5-year survival rate for cancer of the cervix has not improved in 15- to 29-year-olds during the past quarter century.
- The 5-year survival rate for ovarian cancer has not improved in 15- to 29-year-olds during the past quarter century, in contradistinction to that for women over age 30 when diagnosed.
- In 15- to 29-year-olds, cancer of the cervix had a higher mortality rate for African Americans/blacks than for white non-Hispanics, Hispanics, or Asians/Pacific Islanders.

*Risk Factors*

- Cervical cancer in females occurs most often in those infected with human papillomavirus types 16, 18, 31, and 45.
- These malignancies are also more common in women of increased parity, those who engage in early sexual activity, have many sexual partners, use oral contraceptives, smoke, or are of lower socioeconomic status.
- The lack of adequate screening programs and poor compliance among 15- to 29-year-old women is a serious concern.
- Future use of vaccines for human papillomavirus may prevent the development of invasive cervical cancer.

**INTRODUCTION**

Among 15- to 29-year-old females, carcinomas of the uterine cervix are the most common cancer of the female genital tract, followed by ovarian cancer. Nearly all genital system tumors are carcinomas of the cervix, germ cell tumors of the ovary, and carcinomas of the ovary. Most cervical carcinomas are thought to be caused by human papillomaviruses as a result of sexual contact. With the advent of a vaccine that is highly preventive of the strains of human papillomavirus mediated by sexual contact, there is now a distinct possibility that cervical carcinoma can be largely prevented. This chapter reviews the epidemiology of cervical carcinoma and ovarian cancers in 15- to 29-year-olds in the United States, and compares the findings with those in younger and older women.

**METHODS, CLASSIFICATION SYSTEM, AND BIOLOGICAL IMPLICATIONS**

In the International Classification of Childhood Cancer (ICCC), malignant germ cell tumors are described in category IX as *Germ-Cell, Trophoblastic and other Gonadal Neoplasms*. Within this classification, there is no distinction between those germ cell tumors that occur in males versus those that develop in females. (The ICCC group also includes intracranial and intraspinal germ-cell tumors (category IX(a)).) Hence for female genital tract tumors, the ICCC was not used and the analysis is based on the topography and morphology information from the International Classification of Diseases for Oncology (ICD-O).

The female genital tract includes the ovaries, fallopian tubes, uterus (body/corpus and cervix), vagina and vulva.

Within the ICD-O, the topographic sites of the female genital tract are the vulva (C51.0-C51.9), vagina (C52.9), cervix uteri (C53.0-C53.9), corpus uteri (C54.0-C54.9), uterus NOS (C55.9), ovary (C56.9), fallopian tube (C57.0), and other specified and unspecified sites of female genital tract (C57.1-C57.9). The ICD-O morphology categories include carcinomas and adenocarcinomas (8010-8041, 8140, many others). Also included are malignant gonadal neoplasms [malignant thecomas (8600), malignant granulosa cell tumors (8620), malignant androblastomas (8630), Sertoli cell carcinoma (8640, and malignant Leydig cell tumor (8650)]. The germ cell neoplasms span categories 9060 to 9085 and include dysgerminoma (9060-9063), germinoma (9064), embryonal carcinoma (9070), endodermal sinus (yolk sac) tumor (9071), polyembryoma (9072), and teratoma/teratocarcinoma (9080-9083), and mixed germ cell tumor (9085).

Most cancers of the genital tract in 15- to 29-year-old females occur within the ovary and uterine cervix. Hence, this chapter focuses on cancer at these two sites. As explained in the *Methods* chapter, data are presented for 15- to 29-year-olds with comparisons to the age groups 0 to 15 years and 30 to 44+ years, as appropriate. For some analyses the entire age range from birth to 85+ years is included. The absence of data in any figure or table within this chapter means that too few cases were available for analysis; it does not mean that the rate or change in rate was zero.

Since the ICC was set up as a classification for childhood cancer, it does not have a separate category for female genital cancer or for specific sites such as ovary and cervix uteri. Topography and histology from ICD-O can be used to examine differences among young females with cancer of the genital tract compared to older patients, but it is not expected to capture the intermediate biology of these cancers in females aged 15 to 29, which is at a transition point from pediatric to adult features.

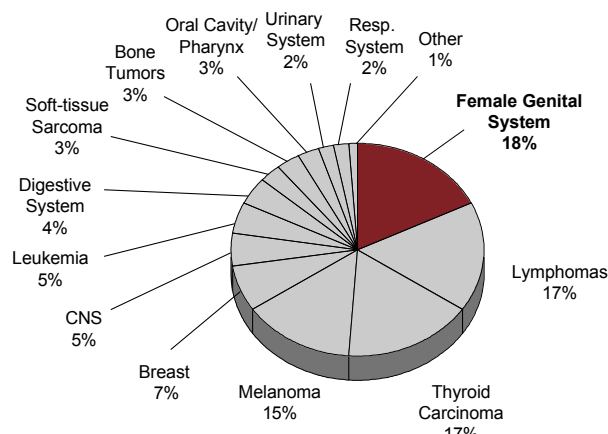
**INCIDENCE**

In the United States, genital tract tumors accounted for 17.8% of all invasive cancers in females 15 to 29 years of age who were diagnosed between 1975 and 2000 at SEER sites (Figure 14.1). In the year 2000, approximately

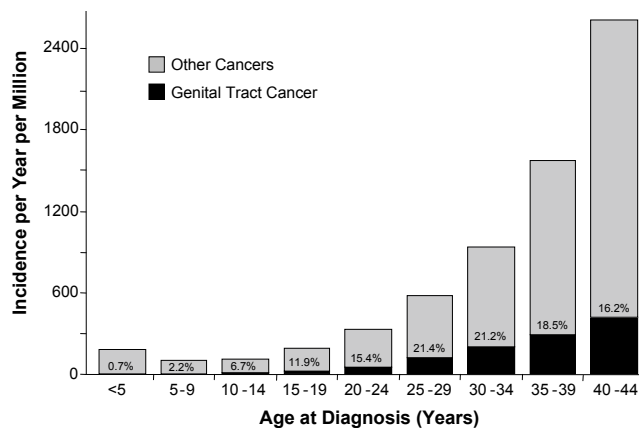
1,700 U.S. women aged 15 to 29 years were diagnosed to have a genital tract cancer (Table 14.1). Among 15- to 19-year-old females, the proportion of all invasive cancers that were genital tract tumors was 11.9%. Among 20- to 24-year-olds, the proportion was 15.4%, and among 25- to 29-year-olds it was 21.4% (Figure 14.2).

*Age-Specific Incidence*

The most common cancers in females 10 to 44 years of age are shown in Figure 14.3, each as a proportion of all cancers that occurred in women during 1975 to 2000. In 25- to 29-year-olds, genital tract tumors peaked as a proportion of all cancer and accounted for more cancers than any other category. In the 15- to 24-year age group, the genital-tract-cancer proportion was third to melanoma and thyroid malignancies.



**Figure 14.1:** Cancer Incidence in 15- to 29-Year-Old Females



**Figure 14.2:** Incidence of Genital Tract Cancer Relative to All Cancer in Females, U.S., SEER 1975-2000

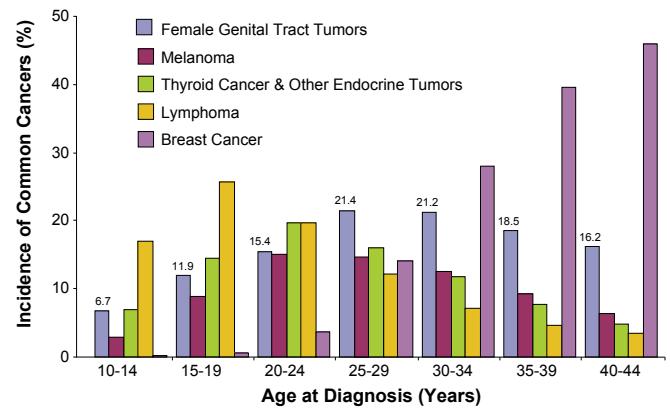
The most common genital tract tumor occurring in females 15 to 29 years of age was carcinoma of the uterine cervix. Cancer of the ovary (germ cell tumors and carcinoma) was second in incidence in this age group, in contrast to being the most predominant genital tract tumor, by far, among 5- to 14-year-olds (primarily germ cell type) (Figure 14.4).

From 1975 to 2000, cervical carcinoma accounted for 22% of the genital tract tumors in females 15 to 29 years of age (Figure 14.4). Ovarian tumors accounted for 18% of the genital tract tumors in adolescent and young adult females during this same era (Figure 14.4). In the year 2000, nearly 800 U.S. women 15 to 29 years of age were diagnosed to have a cervical carcinoma, and approximately 525 were diagnosed to have cancer of the ovary (Table 14.1).

*Gender-Specific Incidence*

The age dependence of genital tract malignancies in females contrasts sharply with that of males. This is dramatically apparent when the incidence of genital tract tumors in one gender is compared with the other, as in Figure 14.5. In the 15- to 29-year age group, genital tract cancer incidence was higher in males than females. From ages 30 to 50, however, there was a strikingly higher

female:male ratio of genital tract tumors that peaked at 3.7 between 40 and 45 years of age. Under age 30 and over age 50, there was a higher male:female ratio, primarily due to testicular cancer in young males and prostate cancer in older males. In the 15- to 29-year age group, testicular cancer accounted for 11% of all invasive cancers, which is similar to the corresponding value of 10% for female genital tract cancer.



**Figure 14.3:** Common Cancers in 10- to 44-Year-Old Females as a Proportion of All Cancer, SEER 1975-2000

**Table 14.1:** Incidence of Female Genital Tract Cancer in Persons Younger Than 30 Years of Age, U.S., 1975-2000

AGE AT DIAGNOSIS (YEARS)	<5	5-9	10-14	15-19	20-24	25-29
U.S. population, year 2000 census (in millions), females	9.365	10.026	10.008	9.829	9.276	9.583
<b>ALL FEMALE GENITAL TRACT CANCER</b>						
Average incidence per million, 1975-2000, SEER	1.0	2.1	7.3	22.7	50.4	122.6
Average annual % change in incidence, 1975-2000, SEER	^	^	0.2%	-0.3%	-1.9%	-1.0%
Estimated incidence per million, year 2000, U.S.	1.1	1.0	7.4	16.5	50.1	111.1
Estimated number of persons diagnosed, year 2000, U.S.	10	11	74	162	465	1064
<b>CARCINOMA OF THE UTERINE CERVIX</b>						
Average incidence per million, 1975-2000, SEER	0	0.1	0.3	3.3	23.2	78.0
Average annual % change in incidence, 1975-2000, SEER	^	^	^	^	-1.9%	-1.0%
Estimated incidence per million, year 2000, U.S.	0	0	0	2.2	14.8	66.0
Estimated number of persons diagnosed, year 2000, U.S.	0	0	0	22	137	632
<b>CANCER OF THE OVARY</b>						
Average incidence per million, 1975-2000, SEER	0.2	1.8	6.4	15.3	19.0	27.0
Average annual % change in incidence, 1975-2000, SEER	^	^	0.3%	-0.1%	-1.7%	-1.7%
Estimate incidence per million, year 2000, U.S.	0	1.0	7.4	13.2	26.2	15.7
Estimated number of persons diagnosed, year 2000, U.S.	0	11	74	130	243	151

^ Too few for a reliable estimate

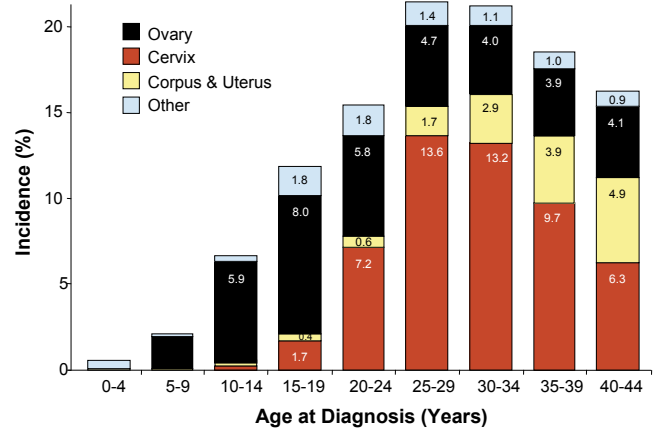
*Racial/Ethnic Differences in Incidence*

In 15- to 29-year-olds, the incidence of cervical cancer during 1992 to 2002 was higher in white non-Hispanic, Hispanic, and African American/black females than it was in females of other races/ethnicities (Figure 14.6). Among females over 30 years of age, however, Hispanics had the highest incidence of cervical cancer (Figure 14.6), a pattern that became more prominent with increasing age (data not shown).

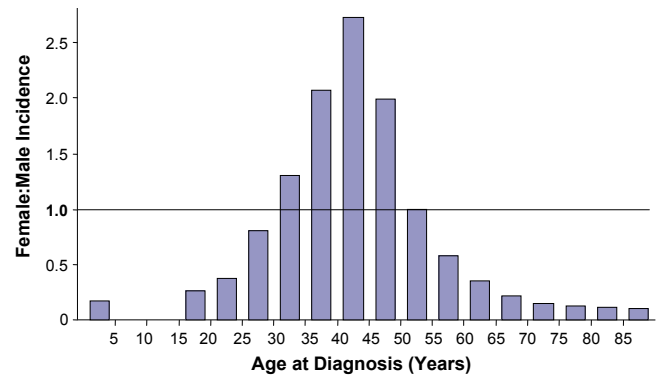
Cancer of the ovary, however, occurred most frequently in Asian/Pacific Islander females and was distinctly less common in American Indian/Alaska Native females (Figure 14.7). Among females over 30 years of age, however, non-Hispanic whites had the highest incidence of ovarian cancer, a difference that became more prominent with increasing age (data not shown).

*Trends in Incidence*

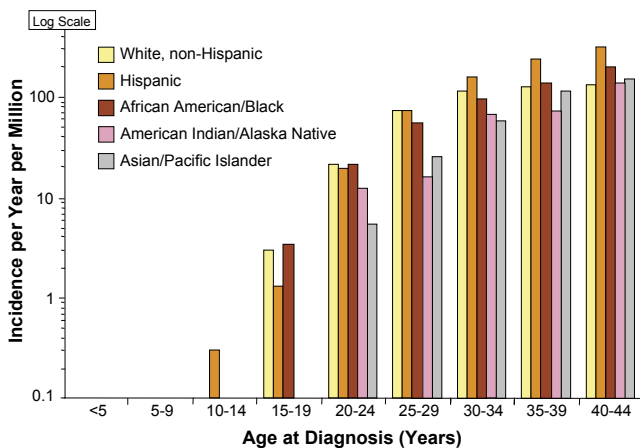
The incidence of cancer of the cervix was 33.6 per year per million in 15- to 29-year-olds; this increased dramatically for those over 30 years of age (Figure 14.8). Over time, however, the incidence of cervical cancer declined slightly in the 20- to 24-year-old group (Figure 14.9), a trend that was also noted in older age groups. This reduction in incidence is attributable to a decline in the incidence of squamous cell carcinoma of the cervix, although the incidence of adenocarcinoma of the cervix actually increased.<sup>1</sup>



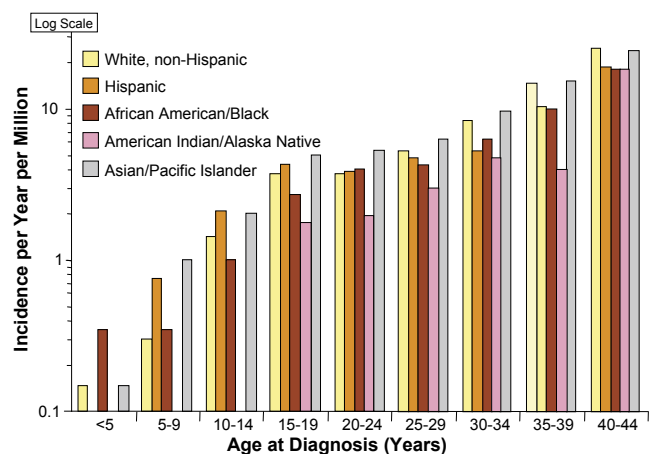
**Figure 14.4:** Incidence of Female Genital Tract Tumors as a Proportion of All Cancer, by Age and Tumor Type, SEER 1975-2000



**Figure 14.5:** Incidence of Genital Tract Cancer, Female:Male Ratio, SEER 1975-2000



**Figure 14.6:** Incidence of Cervical Cancer in Females by Race/Ethnicity, SEER 1992-2002



**Figure 14.7:** Incidence of Ovarian Cancer in Females by Race/Ethnicity, SEER 1992-2002

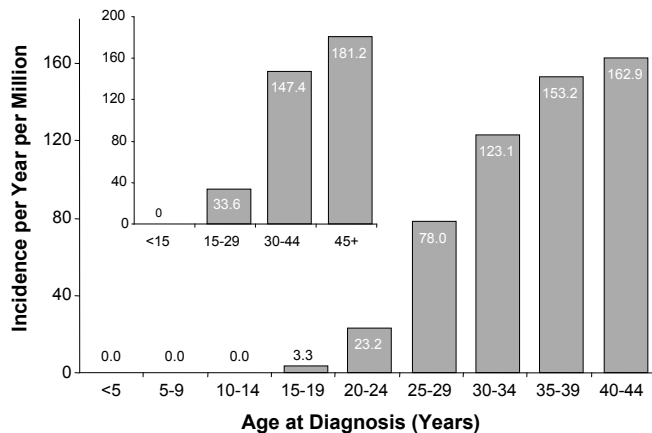


Figure 14.8: Incidence of Cervical Cancer, SEER 1975-2000

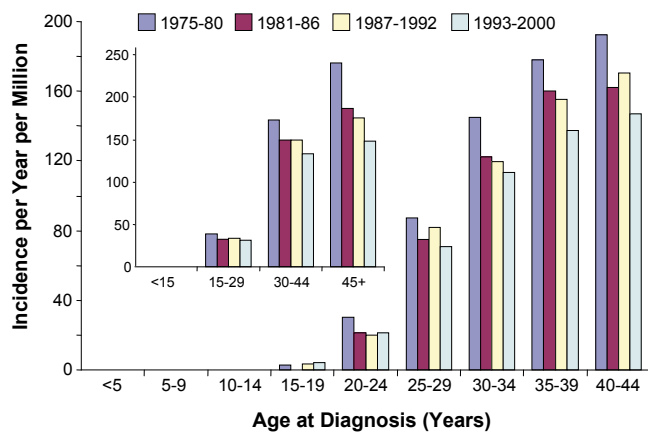


Figure 14.9: Incidence of Cervical Cancer by Era, SEER

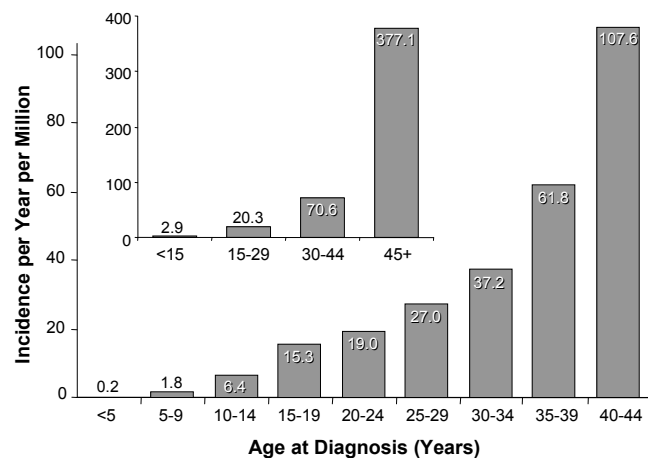


Figure 14.10: Incidence of Ovarian Cancer, Excluding Borderline Histology, SEER 1975-1999

The incidence of cancer of the ovary is depicted in Figure 14.10. In 15- to 29-year-olds the incidence was 20.3 per year per million, but this increased dramatically to 377 per year per million in adults over 45 years of age.

OUTCOME

Mortality

The U.S. mortality for cervical carcinoma from 1975 to 2000 is shown in Figure 14.11. In the 15- to 19-year age group, the death rate was 0.1 deaths/year/million; in 20- to 24-year-olds the rate was 1.9 deaths/year/million, and in 25- to 29-year-olds it was 8.4 deaths/year/million, reflecting increasing incidence. The African American/black population had the highest mortality for cervical carcinoma at all ages (Figures 14.12 and 14.13). Among 15- to 29-year-olds, Asians/Pacific Islanders had the lowest mortality (Figure 14.13). The mortality differential in African Americans/blacks, relative to other races/ethnicities, was greater than the corresponding difference in incidence.

Mortality for cancer of the ovary in persons younger than age 45 is shown in Figure 14.14. The pattern reflects the incidence-versus-age profile. Mortality according to race/ethnicity (Figure 14.15) was generally similar among adolescents and young adults and reflective of the incidence patterns. American Indians/Alaska Natives were an exception, in that 20- to 39-year-olds had a disproportionately higher death rate in comparison to incidence (Figure 14.7).

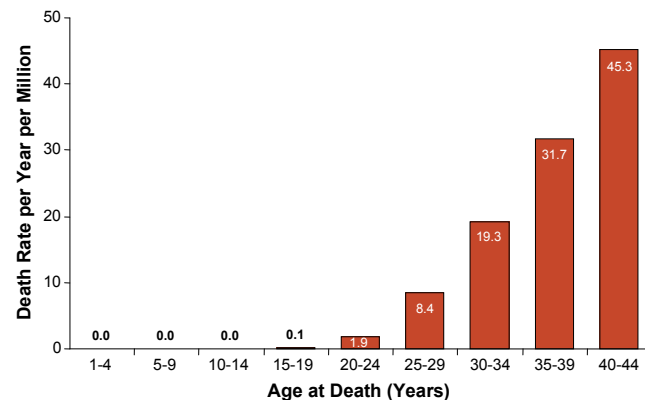


Figure 14.11: National Mortality for Cervical Carcinoma, U.S., 1975-2000

*Survival*

The 5-year survival rate of women diagnosed between 1975 and 2000 with cervical carcinoma was 91% in 15- to 19-year-olds, 89% in 20- to 24-year-olds, and 87% in 25- to 29-year-olds (Figure 14.16). The survival rate in older patients plummeted as a function of age.

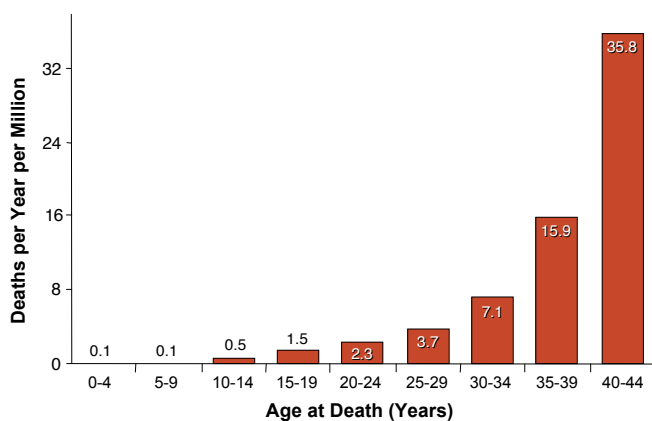
The 5-year survival rate of women diagnosed between 1975 and 2000 with cancer of the ovary was between 83% and 87% for the 5-year age intervals between 15- and 29-years of age (Figure 14.17). In older patients, the survival rate declined dramatically as a function of age, and at a steeper slope than that of cervical carcinoma.

*Trends in Survival*

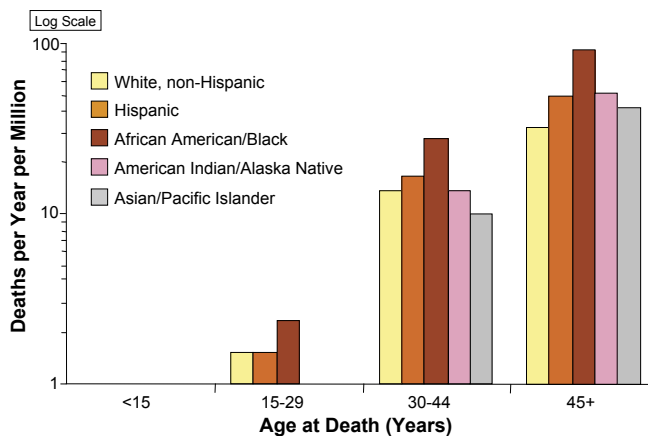
Figure 14.18 depicts the change in 5-year survival rates for carcinoma of the cervix as a function of era, from 1975 to 1998. According to these data, there was no improvement in survival over the last quarter century among 15- to 29-year-olds with cervical carcinoma. Figure 14.19 shows analogous data for ovarian cancer, and similarly indicates that there was no improvement in the 5-year survival rate among 15- to 29-year-olds with ovarian cancer, in contradistinction to the improvement in survival noted for women older than 30 years when diagnosed with ovarian cancer.

**RISK FACTORS**

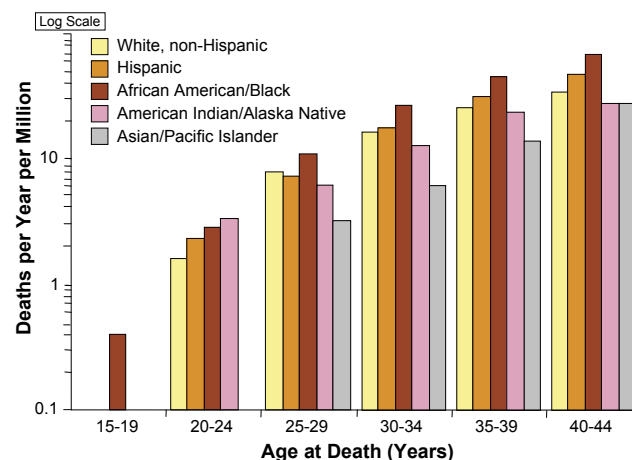
The risk of developing ovarian carcinoma is influenced by genetic, hormonal, and environmental factors.



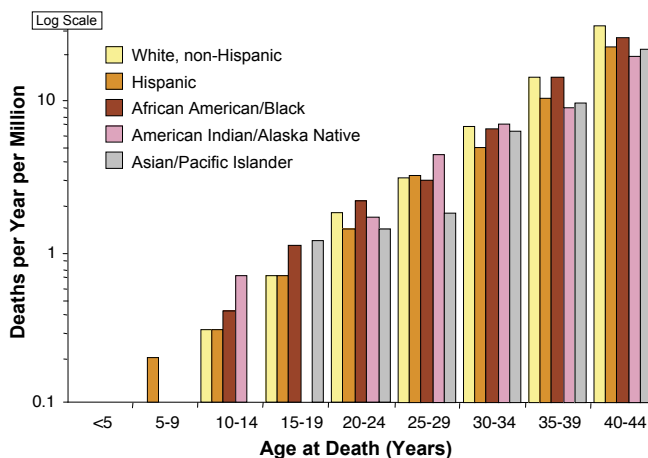
**Figure 14.14:** National Mortality for Ovarian Cancer, U.S., 1975-2000



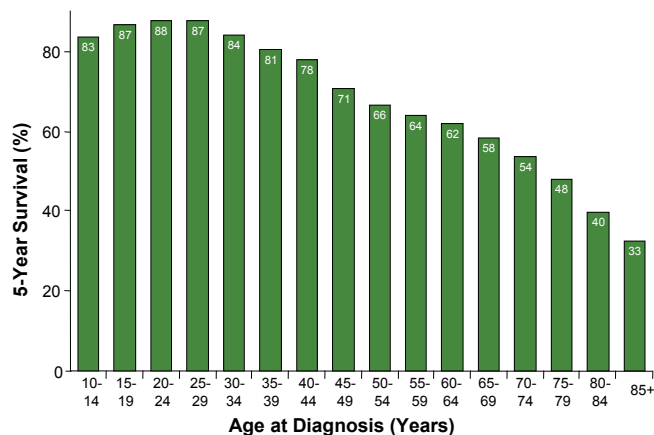
**Figure 14.12:** National Mortality for Cervical Carcinoma in Females, by Race/Ethnicity, SEER 1992-2002



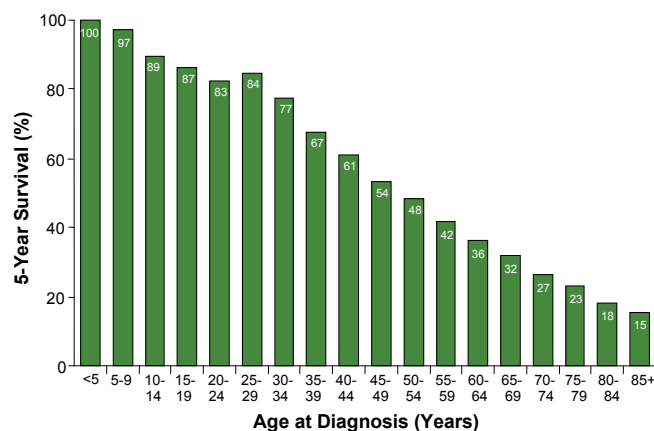
**Figure 14.13:** National Mortality for Cervical Carcinoma by Race/Ethnicity, U.S., 1975-2000



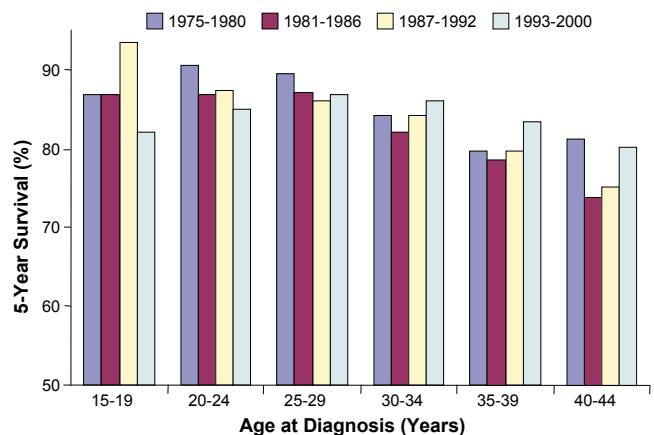
**Figure 14.15:** National Mortality for Ovarian Cancer by Race/Ethnicity, U.S., 1990-2000



**Figure 14.16:** 5-Year Survival for Cervical Carcinoma, SEER 1975-2000



**Figure 14.17:** 5-Year Survival for Ovarian Cancer, SEER 1975-2000



**Figure 14.18:** 5-Year Survival for Cervical Carcinoma by Era, SEER

Approximately 5-10% of women have a genetically acquired risk of ovarian cancer due to inherited mutations in the BRCA1 or BRCA2 tumor suppressor genes; there is an increased incidence of these mutations in the Ashkenazi Jewish population.<sup>2,3</sup> The overall risk of developing ovarian carcinoma for those with BRCA1 mutations is 20-60% and for those with BRCA2 mutations, 10-35%.<sup>2</sup> Several studies have reported that women with ovarian cancer and BRCA mutations may survive longer than women with sporadic ovarian cancer,<sup>2,4,5</sup> possibly due to an improved tumor response to platinum-based chemotherapy.<sup>4</sup>

Over the last 30 years, the highest incidence of ovarian carcinoma has occurred in Norway, Sweden and Israel.<sup>6</sup> Studies have linked this higher incidence with occupational/environmental exposures, increased body mass index and low physical activity, and BRCA mutations.<sup>7-9</sup>

Conditions that delay or suspend ovulation—such as oral contraceptive use, pregnancy, and lactation—reduce the risk of ovarian cancer.<sup>2,10,11</sup>

The most important risk factor for cervical cancer is human papilloma virus (HPV) infection; HPV DNA can be found in 95-100% of cervical cancers. HPV has multiple types, both oncogenic and non-oncogenic, and many cervical cancers reveal multiple HPV types.<sup>12</sup> HPV types 16, 18, 31, 33 and 45 are those most associated with invasive cervical cancers; these strains take longer to clear than other non-pathogenic strains.<sup>13-15</sup> Recent vaccines have been developed for types 16 and 18, which account for approximately 70% of HPV cases associated with cervical cancer.<sup>16</sup> Since peak infection occurs in the adolescent and young adult years, clinical trials are ongoing to determine the efficacy of these vaccines when initiated in adolescence. Other preventative methods such as screening programs for older women should also lower the risk of developing invasive cervical cancer.<sup>17</sup>

Co-risk factors for cervical carcinoma include sexual activity at an early age, multiple sexual partners, sexually transmitted disease, high parity, smoking, long-term oral contraceptive use, and low socioeconomic status.<sup>14,15,18-25</sup>

Human immunodeficiency virus is felt to affect the disease progression of HPV and the incidence of cervical carcinoma.<sup>12,25</sup> When at-risk populations are adequately



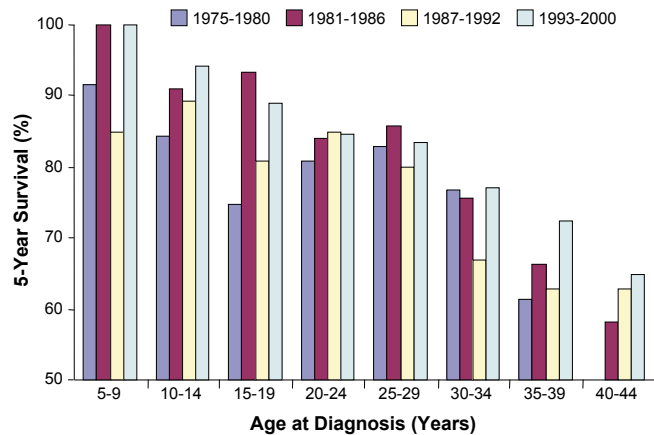


Figure 14.19: 5-Year Survival for Ovarian Cancer by Era, SEER

monitored with available and accepted screening programs, favorable changes in incidence have been noted.<sup>12</sup>

There is preliminary evidence that male circumcision may decrease the incidence of HPV infection as well as the incidence of cervical carcinoma in female partners.<sup>21,22</sup> Those with strict religious beliefs governing sexual behavior have a lower incidence of HPV infection and a lower incidence of cervical carcinoma.<sup>12</sup>

## SUMMARY

Genital tract tumors account for nearly one-fourth of invasive cancers in adolescent and young adult females.<sup>26</sup> The ratio of male-to-female cancer also changes within this age group. Under age 30, testicular

cancer in males exceeds the incidence of gynecological cancer in females. After age 50, the high incidence of prostate cancer increases the ratio of male-to-female genital tract tumors.

The predominant genital tract cancers in 15- to 29-year-old females are carcinomas of the cervix and carcinomas and germ cell tumors of the ovary. Within the classification of cervical carcinoma, the incidence of squamous cell carcinoma has decreased since 1975 in this age group, but especially in 25- to 29-year-olds, whereas the incidence of adenocarcinoma has increased.

Cervical carcinoma is one of the few cancers than can be successfully identified at a pre-invasive stage in the 15- to 29-year age group by the use of screening methods (Pap smears). Yet there is little evidence, in contradistinction to older patients, that survival from cervical carcinoma has improved in young adults during the past quarter century. The recent development of vaccines for two of the most common HPV types offers reason to hope that cervical cancer can be successfully prevented in the majority of women. In the near term, screening programs help identify cervical dysplasia so treatment can be initiated prior to the development of invasive disease. Such screening programs should be made accessible to all women, and at-risk groups should be educated about their use. With such programs and the eventual vaccination of adolescents, invasive cervical cancer may become a disease of the past.

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