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# Trends in the incidence of serous fallopian tube, ovarian, and peritoneal cancer in the US☆

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## HIGHLIGHTS

- The diagnosis of fallopian tube cancer increased fourfold from 2001 to 2014.
- The highest incidence of tubal cancer was seen in Whites and women ages 70–74.
- There has been increased understanding of pathology and evolving surgical paradigms.

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## ABSTRACT

*Objective.* To identify the trends in incidence of serous fallopian tube, ovarian, and peritoneal epithelial cancers in the United States.

*Methods.* Data was obtained from United States Cancer Statistics (USCS) from 2001 to 2014. All incidences are per 100,000 women. Analyses were performed using SEER*Stat and Joinpoint regression programs.

*Results.* Of the 146,470 patients with serous cancers, 9381 (6.4%) were fallopian tube, 121,418 (82.9%) were ovarian, and 15,671 (10.7%) were primary peritoneal. The study period was divided from 2001 to 2005, 2006–2010, and 2011–2014, and there was an increase in fallopian tube incidence from 0.19 to 0.35 to 0.63, with a corresponding decrease in ovarian incidence from 5.31 to 5.08 to 4.86. There was no significant change in peritoneal cancers from 0.64 to 0.69 to 0.62. The age-specific peak incidence of fallopian tube cancer was younger at age 70–74, compared to ovarian and peritoneal cancer at age 75–79. Further, the incidence of serous fallopian tube cancer was highest in Whites at 0.42, compared to Blacks at 0.24, Hispanics at 0.27, and Asians at 0.28.

*Conclusion.* From 2001 to 2014, the diagnosis of serous fallopian tube cancer increased fourfold with a corresponding decrease in ovarian cancer. The peak incidence of tubal cancer was 70–74 years with an increased incidence in Whites.

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## 1. Introduction

Ovarian cancer is the most lethal gynecologic cancer with approximately 22,440 new cases and 14,080 deaths annually in the United States [1]. Epithelial ovarian cancer accounts for 90% of cancers of the ovary, fallopian tube, and peritoneum [2]. There are currently at least five main subtypes including high and low-grade serous carcinomas, endometrioid carcinoma, clear cell carcinoma, and mucinous carcinoma. High-grade serous carcinomas are the most common type, comprising 70–80% of cases. It represents 92.0% of tubal cancers, 88.7% of peritoneal cancers, and 56.9% of ovarian cancers [3].

Traditionally, ovarian carcinomas were thought to have arisen from the ovarian surface epithelium, however there has been accumulating evidence that most extrauterine high-grade serous carcinomas originate from the fimbriated end of fallopian tubes [4–7]. Precursor lesions,

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also known as serous tubal intraepithelial carcinoma (STIC), have been implicated as the primary precursor lesion for invasive carcinomas. With ongoing advancements in the pathologic diagnosis of gynecologic cancers, the FIGO system was revised in 2012 to reflect the variation in primary site of extrauterine high-grade serous carcinomas to include ovarian, tubal, and peritoneal cancers [8]. After worldwide approval, the updated cancer staging went into effect on January 1, 2014.

With the increased attention on the fallopian tube as the probable origin of some ovarian and peritoneal cancers, there have only been a few papers analyzing the incidence of fallopian tube cancer (FTCA) over time. Most of these studies, however, examine patients in Germany and Denmark, which may not be generalizable to our population [9,10]. In the US, Usach et al. looked at the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) database and showed patients with primary peritoneal cancer were older than those with tubal or ovarian cancer [11]. Goodman and colleagues used the North American Association of Central Cancer Registries (NAACCR) database and found the incidence of disease presentation in fallopian tube, ovarian, and peritoneal cancers were similar. These patterns may support a common molecular pathogenesis, and currently all three diseases are treated as one entity. They also found an increase in FTCA by 79.3% and a decrease in ovarian cancer by 26.5% over the years 1973 to 2005. Furthermore, White women had the highest rates of all three types of carcinomas [12]. This study, however, included all subtypes of histology and had a large percentage of unclassified cases, which may skew incidence rates.

As such, we proposed a large, population-based study of 146,470 patients to assess the changes in the trends of diagnosis of fallopian tube, peritoneal, and ovarian epithelial cancers over time. More importantly, we sought to reveal the demographics and clinical presentation of those at risk for FTCA.

## 2. Methods

Data was obtained from the United States Cancer Statistics (USCS) database from the years 2001 to 2014 [13]. Because our data was extracted from a public, deidentified database, this study did not require an institutional review board approval. All women diagnosed with serous fallopian tube, ovarian, or peritoneal cancers were included. Age-group, race, region, and stage were obtained. Furthermore, the study time period was divided into 3 groups: 2001 to 2005, 2006 to 2010, and 2011 to 2014 to identify changes in diagnoses made when new publications at that time suggested a difference in ovarian cancer origin. Regions of the United States (US) were defined based on the US Department of Commerce Economics and Statistics Administration US Census Bureau consensus [14].

All incidences reported are per 100,000 and age-adjusted to the 2000 US Standard Population. Case numbers and incidence rates were provided for each cancer based on the data from the USCS database. Case numbers describe the absolute number of patients with the disease. Incidence rates provide an insight to the change in the number of new disease cases. Trends in incidence were described using annual percent change (APC). This allowed for more consistent comparison between each cancer type [15]. For example, a rare cancer and a common cancer may both change at 1% per year, however the rare cancer and the common cancer would not change in the same increments on an absolute scale. Thus, APC was used to simplify comparison between fallopian tube, ovarian, and peritoneal cancer. Analyses were performed using SEER*Stat Software, Version 8.3.4, released March 23, 2017 [16]. Trend analyses were performed using Joinpoint Trend Analysis Software, Version 4.5.0.1, released June 21, 2017 [17,18].

## 3. Results

### 3.1. Patient demographics

Of 146,470 women diagnosed with non-uterine serous epithelial cancers, 9381 (6.4%), 121,418 (82.9%), and 15,671 (10.7%) were fallopian tube, ovarian, and peritoneal in origin. The majority of all serous cancers occurred in the 65–69 year old age group. Of these, 74.3% were high grade, 3.75% were low grade, and 21.96% were unknown. With serous FTCA, the highest numbers occurred in the 65–69 age group. Similarly, the highest numbers in peritoneal cancer occurred in the 65–69 age group. Ovarian cancer had the most case numbers in the 60–64 age group. Stage was defined as localized (7.13%), regional (18.11%), distant (72.39%), and unknown (2.37%). Whites, Blacks, Hispanics, and Asian/Pacific Islanders comprised 82.79%, 6.51%, 6.97%, and 2.81% of patients, respectively (Table 1). There was significant regional variation in incidence for all three cancers. 33.36%, 23.33%, 21.72% and 21.59% resided in the South, Midwest, West, and Northeast regions of the US.

### 3.2. Trends

After dividing the study group into 3 time periods from 2001 to 2005, 2006–2010, and 2011–2014, we found the incidence in each time period of fallopian tube cancer increased from 0.19 to 0.35 to 0.63 with a concurrent decrease in ovarian cancer from 5.31 to 5.08 to 4.86. There was no significant change in the incidence of peritoneal cancer from 0.64 to 0.69 to 0.62 (Fig. 1). The APC in diagnosis of FTCA was 7.56%, 18.26%, and 4.94%, respectively. There was an APC decrease in ovarian cancer diagnosis of −1.12%, −1.62%, and −0.58% in this same period. Peritoneal cancer had an APC of 6.49%, −0.53% and −2.89%.

A further analysis of the trend in carcinoma diagnoses using Joinpoint was performed to test if the apparent change in trends were statistically significant. Joinpoint analysis demonstrated an increase in fallopian tube diagnosis of 8.66% from 2001 to 2006 and a further increase of 17.51% from 2006 to 2012. Ovarian cancer consistently declined by 0.96% during the study period. Peritoneal cancer displayed an increase by 7.51% from 2001 to 2004 and ultimately a decrease by 3.14% after 2008 (Fig. 2).

Given the association between FTCA and high grade serous ovarian cancer with BRCA mutations, we performed a subset analysis limited to pathology-confirmed, high grade serous cancers. In this subset of patients, we found that the incidence of FTCA increased from 0.16 to 0.30 to 0.54 over the 3 time periods with a corresponding decrease of ovarian cancer from 3.94 to 3.84 to 3.48 (Fig. 3). To further decrease the

**Table 1**
Patient demographic features, race, and regional distribution.

| USCS (2001–2014) | Patient number (%) | Age-adjusted incidence (per 100,000) |
|---|---|---|
| Total | 146,470 (100) | 6.12 |
| Fallopian tube | 9381 (6.40) | 0.39 |
| Ovarian | 121,418 (82.90) | 5.08 |
| Peritoneal | 15,671 (10.70) | 0.65 |
| Grade | | |
| High grade | 108,824 (74.30) | 4.54 |
| Low grade | 5487 (3.75) | 0.24 |
| Unknown | 32,159 (21.96) | 1.34 |
| Stage | | |
| Localized | 10,439 (7.13) | 0.44 |
| Regional | 26,527 (18.11) | 1.11 |
| Distant | 106,032 (72.39) | 4.42 |
| Unknown | 3472 (2.37) | 0.14 |
| Race | | |
| White | 121,267 (82.79) | 6.65 |
| Black | 9532 (6.51) | 3.86 |
| Hispanic | 10,216 (6.97) | 4.87 |
| Asian/Pacific Islander | 4111 (2.81) | 3.95 |
| Other | 1344 (0.92) | 8.91 |
| Region | | |
| Northeast | 31,629 (21.59) | 6.66 |
| Midwest | 34,172 (23.33) | 6.29 |
| South | 48,859 (33.36) | 5.61 |
| West | 31,810 (21.72) | 6.32 |

Note: incidence rates are per 100,000 and age-adjusted to the 2000 U.S. standard.

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