Clear differences in ovarian cancer incidence and trends by ethnicity among Asian Americans

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A B S T R A C T

Background: Across major races in the United States (U.S.), ovarian cancer incidence is low among Asian American women. However, this observation aggregates Asian Americans as a single group despite their heterogeneity. Disaggregating the ethnic Asian population will produce more useful information to better understand ovarian cancer incidence among Asian women in the U.S.

Methods: Data from the Surveillance, Epidemiology, and End Results Program from 1990 to 2014 were used to compare age-adjusted incidence rates (AAIRs, per 100,000 women) for ovarian cancer for the six largest U.S. Asian ethnicities (Asian Indian/Pakistani, Chinese, Filipino, Japanese, Korean, Vietnamese) to non-Hispanic whites (NHWs). The race/ethnicity-specific AAIRs were calculated by time period and histotype. We examined the magnitude and direction of AAIR trends using average annual percent change (AAPC) statistics.

Results: All Asian ethnicities had significantly lower ovarian cancer incidence rates than NHWs. However, among Asian ethnicities, Asian Indians/Pakistanis had the highest rate of ovarian cancer (AAIR = 10.51, 95% CI: 9.65–11.42) while Koreans had the lowest (AAIR = 7.23, 95% CI: 6.62–7.88). Clear cell ovarian cancer had significantly higher incidence rates among Chinese, Filipino, and Japanese women than NHW women (incidence rate ratio (IRR) = 1.49, 95% CI: 1.29–1.72, IRR = 1.30, 95% CI: 1.12–1.51, IRR = 1.64, 95% CI: 1.36–1.97, respectively). Incidence trends also differed by Asian ethnicity with significant decreases only observed for Chinese (AAPC = −1.49, 95% CI: −2.22 to −0.74) and Japanese (AAPC = −1.75, 95% CI: −2.57 to −0.92).

Conclusions: Examining Asian Americans as a single group results in missed ethnic-specific disparities in ovarian cancer, hence disaggregating this heterogeneous population in future research is warranted.

1. Introduction

Ovarian cancer is the most fatal cancer of the female reproductive system, but its etiology is still poorly understood. Worldwide, ovarian cancer incidence rates are higher in Europe and North America than in Asia and Africa [1]. This may be attributable to distinct differences in ovarian cancer histotype, risk factors, and biomarkers, which have been observed between Asian women and women of European descent [2,3]. Variation in ovarian cancer incidence rates by country has also been noted within regions of the world; for example, the incidence rate in Japan is more than twice that of China [1,4,5].

There has been a growing body of literature highlighting the heterogeneity in the Asian population and the need to disaggregate the Asian ethnic groups to better understand cancer burden and develop more targeted and effective cancer control measures [6–12]. However, thus far, ovarian cancer research in the United States (U.S.) has regarded Asian Americans as a single aggregated group, which may have likely masked important ethnic-specific differences for generating new research hypotheses and identifying high-risk groups.

Hence, in the following, we present our study of subgroup differences in ovarian cancer incidence rates among the six largest Asian American ethnic groups: Asian Indian/Pakistani, Chinese, Filipino, Japanese, Korean, and Vietnamese. While it has been well-established that Asian American women as a single group have a lower rate of ovarian cancer incidence relative to non-Hispanic white (NHW) women based on findings from previous studies, we hypothesize that the rate of incidence may vary when each Asian American ethnicity is considered separately.

2. Methods

2.1. Cancer case identification

Data from the National Cancer Institute's SEER database November 2016 submission [13] were used in this analysis. All data were de-identified and coded for public use, thus this study was exempt from Institutional Review Board review. A total of 13 population-based cancer registries were included (Atlanta (metropolitan), Connecticut, Detroit (metropolitan), Hawaii, Iowa, New Mexico, Utah, New Jersey, Seattle-Puget Sound, San Francisco/Oakland, San Jose/Monterey, Los Angeles, and all remaining areas in California) representing 54% of the U.S. Asian and Pacific Islander population [14].

Ovarian cancer cases diagnosed between 1990 and 2014 were identified using International Classification of Diseases for Oncology, Third Edition (ICD-O-3), primary site: C56.9 ovary [15]. Only malignant cases with a known age at diagnosis and race/ethnicity were included in the study. These tumors were categorized by SEER historic stage (local, regional, distant, unknown), grade (low = well-differentiated, high = moderately differentiated + poorly differentiated + undifferentiated, unknown), and histotype including serous (8050, 8120, 8122, 8130, 8140, 8201, 8260, 8440–8442, 8450, 8452, 8460–8463, 9014), mucinous (8144, 8384, 8470–8472, 8480–8482, 9015), endometrioid (8290, 8380–8383), and clear cell (8005, 8310, 8313, 8443, 8444); the remaining cases that were not classified as one of these four primary histotypes (including carcinosarcomas as well as mixed, other, undifferentiated, and unspecified carcinomas) were grouped together as "other/not otherwise specified (NOS)". Nonepithelial tumors, such as germ cell and sex cord-stromal tumors, were excluded.

Cases classified as Asian Indian/Pakistani, Chinese, Filipino, Japanese, Korean, and Vietnamese were included, along with the NHW cases for comparison purposes. Asian Indians and Pakistanis were combined based on SEER coding rules for race.

2.2. Population estimates

To calculate the incidence rates, the annual at-risk population by age, sex, and ethnicity was estimated by the SEER program as described in previous publications [6,11]. Briefly, the population distributions by age, sex, and detailed/specific Asian ethnicity within the total Asian population from 1990, 2000, and 2010 Censuses of a given registry catchment area were used to disaggregate the Census Bureau's annual population estimates of the total Asian American group for the same geographic area. Due to the multiracial identification method used in the 2000 and 2010 Censuses, estimates were based on the averages of the single-race and multi-race counts. The 1991 to 1999 and the 2001 to 2009 population estimates were developed from a linear interpolation between the 1990 and 2000 estimates and the 2000 and 2010 estimates, respectively. The 2011 to 2014 population estimates were developed from a linear extrapolation of the 2000–2010 growth trends. The annual population estimates for the NHW group came directly from the same Census Bureau estimation series.

2.3. Statistical analysis

Ovarian cancer patient demographic and tumor characteristics were compared across NHWs and all six Asian American ethnicities using Chi-square tests. Chi-square tests were also performed excluding NHWs to determine if such characteristics differed across the six Asian American ethnicities only. These analyses were performed using SAS software, release 9.4 (SAS Institute, Inc., Cary, North Carolina).

Age-adjusted incidence rates (AAIRs, per 100,000 women) for overall ovarian cancer with 95% confidence intervals (CIs) were calculated for each race/ethnicity. AAIRs were also calculated for 5-year time periods (i.e. 1990–1994, 1995–1999, 2000–2004, 2005–2009, 2010–2014) as well as for each histotype (i.e. serous, mucinous, endometrioid, clear cell, other/NOS). All rates were age-adjusted to the 2000 U.S. Standard Population. In addition, overall ovarian cancer age-

Table 1
Distribution of demographic and tumor characteristics of ovarian cancer cases by race/ethnicity, 1990–2014.

Characteristic	Non-Hispanic White[*]	Asian Indian/ Pakistani[*]	Chinese[*]	Filipino[*]	Japanese[*]	Korean[*]	Vietnamese[*]	Chi-square P-value[†]	Chi-square P-value[‡]
Total:	84,416	680	1,559	1,978	1,091	552	578		
Age at diagnosis								< 0.0001	< 0.0001
< 40 years	3,340 (3.96)	91 (13.38)	134 (8.60)	168 (8.49)	61 (5.59)	47 (8.51)	68 (11.76)		
40–49 years	9,665 (11.45)	151 (22.21)	348 (22.32)	418 (21.13)	149 (13.66)	120 (21.74)	146 (25.26)		
50–59 years	17,077 (20.23)	177 (26.03)	405 (25.98)	562 (28.41)	237 (21.72)	169 (30.62)	164 (28.37)		
60–69 years	19,803 (23.46)	132 (19.41)	265 (17.00)	408 (20.63)	251 (23.01)	111 (20.11)	112 (19.38)		
70–79 years	19,572 (23.19)	91 (13.38)	231 (14.82)	294 (14.86)	240 (22.00)	60 (10.87)	54 (9.34)		
80+ years	14,959 (17.72)	38 (5.59)	176 (11.29)	128 (6.47)	153 (14.02)	45 (8.15)	34 (5.88)		
Tumor Histotype								< 0.0001	< 0.0001
Serous	50,732 (60.10)	394 (57.94)	698 (44.77)	948 (47.93)	514 (47.11)	306 (55.43)	285 (49.31)		
Mucinous	5,546 (6.57)	43 (6.32)	144 (9.24)	196 (9.91)	107 (9.81)	51 (9.24)	64 (11.07)		
Endometrioid	8,886 (10.53)	83 (12.21)	210 (13.47)	296 (14.96)	156 (14.30)	59 (10.69)	74 (12.80)		
Clear cell	3,846 (4.56)	50 (7.35)	213 (13.66)	194 (9.81)	128 (11.73)	47 (8.51)	68 (11.76)		
Other/NOS[**]	15,406 (18.25)	110 (16.18)	294 (18.86)	344 (17.39)	186 (17.05)	89 (16.12)	87 (15.05)		
Tumor Grade[***]								< 0.0001	0.14
Low	5,819 (6.89)	49 (7.21)	139 (8.92)	156 (7.89)	80 (7.33)	51 (9.24)	53 (9.17)		
High	48,643 (57.62)	408 (60.00)	898 (57.60)	1162 (58.75)	693 (63.52)	312 (56.52)	335 (57.96)		
Unknown	29,954 (35.48)	223 (32.79)	522 (33.48)	660 (33.37)	318 (29.15)	189 (34.24)	190 (32.87)		
Tumor stage								< 0.0001	0.0002
Localized	12,297 (14.57)	126 (18.53)	407 (26.11)	434 (21.94)	274 (25.11)	123 (22.28)	149 (25.78)		
Regional	5,686 (6.74)	52 (7.65)	129 (8.27)	219 (11.07)	87 (7.97)	50 (9.06)	60 (10.38)		
Distant	49,882 (59.09)	407 (59.85)	863 (55.36)	1,118 (56.52)	616 (55.46)	318 (57.61)	321 (55.54)		
Unknown	16,551 (19.61)	95 (13.97)	160 (10.26)	207 (10.47)	114 (10.45)	61 (11.05)	48 (8.30)		

Abbreviation: NOS = not otherwise specified.

* Number of ovarian cancer cases (percent of ovarian cancer cases).
† Across non-Hispanic whites and all six Asian ethnicities.
‡ Across the six Asian ethnicities only.
** Includes carcinosarcomas as well as mixed, other, undifferentiated, and unspecified tumors.
*** Low grade includes well-differentiated tumors only. High grade includes moderately differentiated, poorly differentiated, and undifferentiated tumors.

Table 2
Age-adjusted incidence rates by race/ethnicity and year of diagnosis, 1990–2014.

Race/Ethnicity	1990–1994		1995–1999		2000–2004		2005–2009		2010–2014		1990–2014		AAPC (95% CI)	AAPC P-value
	N	AAIR (95% CI)*	N	AAIR (95% CI)*	N	AAIR (95% CI)*	N	AAIR (95% CI)*	N	AAIR (95% CI)*	N	AAIR (95% CI)*		
Non-Hispanic White	17,594	15.99 (15.75–16.23)	17,360	15.18 (14.95–15.41)	17,318	14.50 (14.28–14.72)	16,565	13.37 (13.16–13.58)	15,579	12.08 (11.88–12.28)		14.15 (14.06–14.25)	−1.52 (−2.09 to −0.95)	< 0.0001
Asian Indian/Pakistani	56	9.31 (6.75–12.59)	84	9.23 (7.20–11.67)	127	10.90 (8.86–13.26)	166	9.71 (8.15–11.47)	247	11.34 (9.85–12.98)		10.51 (9.65–11.42)	0.95 (−0.55 to 2.47)	0.21
Chinese	196	8.49 (7.32–9.80)	274	8.83 (7.80–9.95)	348	8.90 (7.98–9.89)	344	7.09 (6.35–7.89)	397	6.95 (6.27–7.68)		7.87 (7.48–8.27)	−1.49 (−2.22 to −0.74)	0.0004
Filipino	249	9.99 (8.73–11.38)	329	10.39 (9.27–11.62)	403	10.02 (9.05–11.07)	481	9.79 (8.92–10.72)	516	8.98 (8.21–9.81)		9.73 (9.30–10.17)	−0.59 (−1.33 to 0.16)	0.12
Japanese	215	9.70 (8.40–11.16)	229	9.54 (8.31–10.91)	231	9.25 (8.06–10.58)	229	8.58 (7.45–9.84)	187	6.38 (5.44–7.46)		8.75 (8.22–9.30)	−1.75 (−2.57 to −0.92)	0.0002
Korean	61	7.02 (5.24–9.20)	78	6.28 (4.91–7.91)	103	6.80 (5.52–8.30)	138	7.46 (6.24–8.85)	172	7.91 (6.75–9.22)		7.23 (6.62–7.88)	0.94 (−0.31 to 2.20)	0.13
Vietnamese	59	10.29 (7.61–13.58)	86	8.91 (6.99–11.20)	120	9.10 (7.46–10.98)	135	7.87 (6.55–9.39)	178	8.42 (7.19–9.41)		8.64 (7.91–9.41)	−1.02 (−2.15 to 0.13)	0.079

Abbreviation: AAIR = age-adjusted incidence rate, CI = confidence interval, AAPC = average annual percent change.
* Units of per 100,000 women.

specific incidence rates (ASIRs, per 100,000 women) with 95% CIs were calculated by race/ethnicity for the age groups of < 40, 40–49, 50–59, 60–69, 70–79, and 80 + years. Age-adjusted incidence rate ratios (IRRs) with 95% CIs comparing each Asian ethnic group to NHW, based on the method described by Tiwari et al. [16], were calculated for the AAIRs by histotype and for the ASIRs. All AAIRs and ASIRs were calculated using SEER*Stat software, version 8.3.5 (http://seer.cancer.gov/seerstat/) [17].

To evaluate trends in overall ovarian cancer AAIRs from 1990 to 2014, average annual percent change (AAPC) statistics were calculated using joinpoint regression models for each race/ethnicity [18,19]. AAPC is a summary measure of trend that weights the average of the annual percent change over multiple time intervals. Trends for each tumor histotype or stage were not examined due to limited numbers of cases.

All tests of statistical significance were two-sided.

3. Results

A total of 90,854 malignant, epithelial ovarian cancer cases diagnosed between 1990 and 2014 was identified across the 13 SEER registries. The majority of cases were NHW (N = 84,416). Among the Asian American ethnic subgroups, most cases were Filipino (N = 1,978) followed by Chinese (N = 1,559), Japanese (N = 1,091), Asian Indian/Pakistani (N = 680), Vietnamese (N = 578), and Korean (N = 552).

Table 1 shows the percentage of ovarian cancer cases by age at diagnosis and tumor characteristics for each race/ethnicity. There was a significant difference in histotype distribution when comparing across NHWs and all six Asian American ethnicities together (p < 0.0001) (Table 1). Although serous tumors constituted the majority of ovarian cancer diagnoses for all women, clear cell tumors accounted for less than 5% of all NHW cases in comparison to 13.66% and 11.76% of all Chinese and Vietnamese cases, respectively; however, they only accounted for 7.35% of Asian Indian/Pakistani cases, which was lowest among the Asian subgroups (Table 1). In addition, there were fewer low-grade ovarian cancers regardless of race/ethnicity although the tumor grade distribution varied with NHWs having the lowest percent of low-grade tumors (6.89%) and Koreans having the highest percent (9.24%) (Table 1). We also noted a significant difference in the distribution of tumor staging when we compared across NHWs and the six Asian American ethnicities together (p < 0.0001) and across the six Asian subgroups only (p = 0.0002); localized and regional tumors constituted 21.31% of NHW ovarian cancer cases and 26.18% of Asian Indian/Pakistani ovarian cancer cases, yet they accounted for over 31% for the other five Asian subgroups (Table 1). Lastly, all Asian American ovarian cancer cases were diagnosed at younger ages than NHW cases; 65.40% of ovarian cancer diagnoses among Vietnamese were under the age of 60 versus 35.64% among NHWs (Table 1). There was also significant variation in the age distribution of ovarian cancer cases across the six Asian American subgroups (p < 0.0001) (Table 1).

Incidence of ovarian cancer was significantly lower in all Asian American ethnicities relative to NHWs (p < 0.0001) (Table 2, Fig. 1). However, among the Asian ethnicities, Asian Indians/Pakistanis had the highest incidence rate (10.51, 95% CI: 9.65–11.42) and Koreans had the lowest incidence rate (7.23, 95% CI: 6.62–7.88) (Fig. 1). When we examined incidence trends, we observed a significant decrease only among NHW (AAPC = −1.52, 95% CI: −2.09 to −0.95), Chinese (AAPC = −1.49, 95% CI: −2.22 to −0.74), and Japanese (AAPC = −1.75, 95% CI: −2.57 to −0.92) women (Table 2). Decreasing trends were observed for Filipino and Vietnamese women as well, but neither AAPC was statistically significant (AAPC = −0.59, 95% CI: −1.33 to 0.16 and AAPC = −1.02, 95% CI: −2.15 to 0.13, respectively) (Table 2, Fig. 2). Koreans and Asian Indians/Pakistanis, on the other hand, showed a non-significant increase in ovarian cancer incidence (AAPC = 0.94, 95% CI: −0.31 to 2.20 and AAPC = 0.95, 95% CI: −0.55 to 2.47, respectively) (Table 2, Fig. 2).
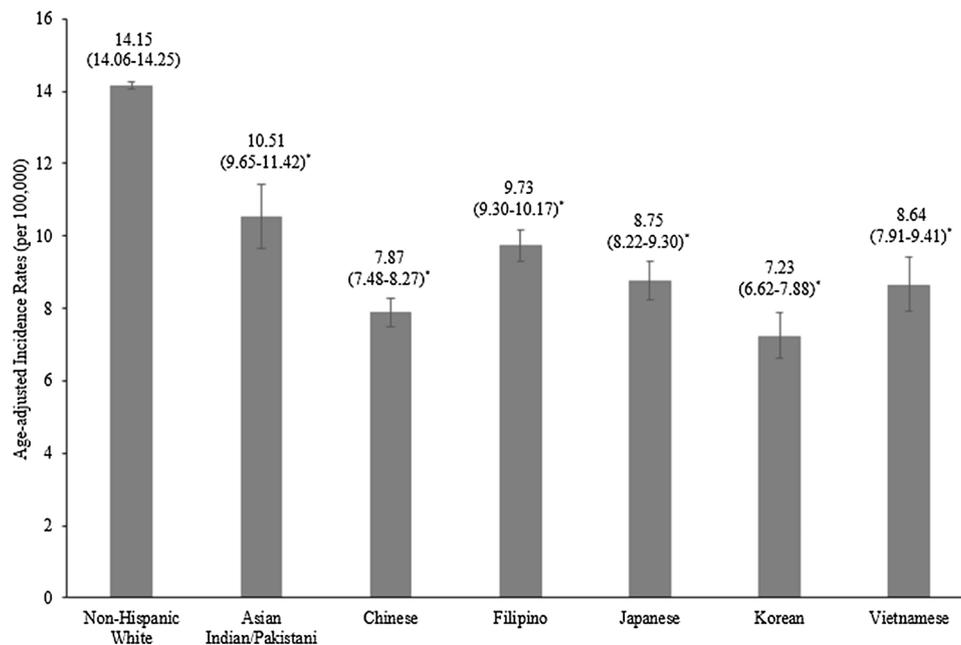
Fig. 1. Age-adjusted incidence rates for ovarian cancer by race/ethnicity, 1990–2014. The error bars represent 95% confidence intervals. Note: * indicates statistical significance at a p < 0.0001 level with non-Hispanic Whites as the reference.
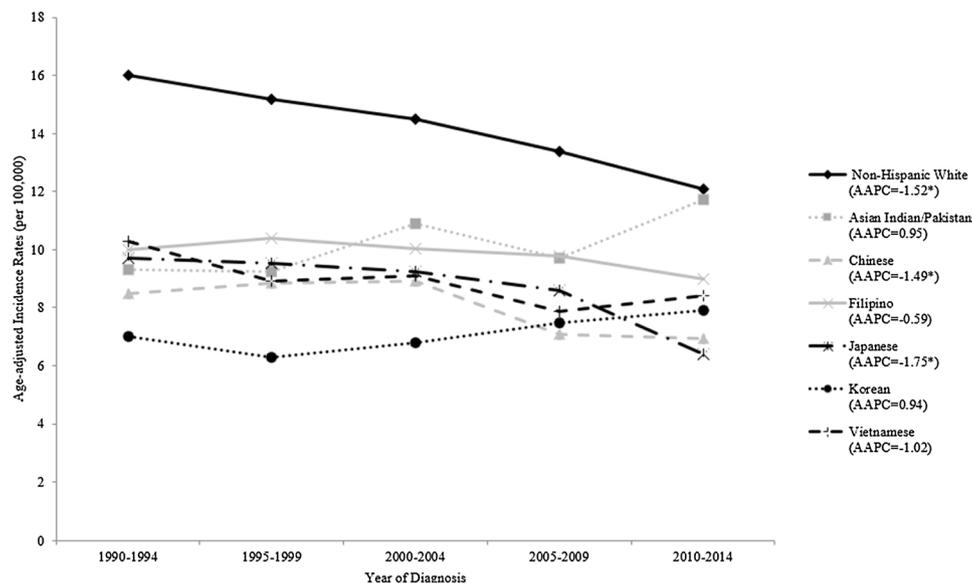

Fig. 2. Age-adjusted incidence rates for ovarian cancer by race/ethnicity and time period, 1990–2014. Note: AAPC = average annual percent change; * indicates statistical significance at a p < 0.05 level.

Table 3 presents ovarian cancer AAIRs by histotype and race/ethnicity. All six Asian American ethnic groups showed a significant lower incidence of serous and endometrioid ovarian cancer relative to NHWs (Table 3). However, incidence of the clear cell histotype was statistically significantly higher in Chinese, Filipino, and Japanese women when compared to NHW women (IRR = 1.49, 95% CI: 1.29–1.72, IRR = 1.30, 95% CI: 1.12–1.51, IRR = 1.64, 95% CI: 1.36–1.97, respectively) (Table 3). This increased clear cell incidence when compared to the NHWs was not observed among Asian Indian/Pakistani (IRR = 0.92, 95% CI: 0.67–1.24) and Korean (IRR = 0.81, 95% CI: 0.59–1.09) women.

Lastly, the ASIRs for NHWs were statistically significantly higher than the ASIRs for all Asian American ethnic groups after age 50 with the exception of Asian Indians/Pakistanis in the 80 + years group (Table 4). Asian Indian/Pakistani women also constituted the only

Asian American ethnic group whose age-specific incidence patterns notably increased after age 50 (Fig. 3). Prior to age 50, the ASIRs across all Asian American ethnicities were comparable to NHWs with the exception of Koreans who had statistically significantly lower ASIRs for the < 40 years and 40–49 years groups (IRR = 0.68, 95% CI: 0.50–0.91 and IRR = 0.69, 95% CI: 0.57–0.83, respectively) (Table 2, Fig. 3).

4. Discussion

Our analysis comprehensively examines ovarian cancer among the six largest ethnic groups of the Asian American population. We observed significant differences in ovarian cancer tumor characteristics, incidence rates and trends not only between Asian subgroups and NHWs, but also across the various Asian ethnicities, highlighting the heterogeneity of ovarian cancer incidence rates among Asian

Table 3

Age-adjusted incidence rates of ovarian cancer by histotype and race/ethnicity, 1990–2014.

Histotype	Race/Ethnicity	N	AAIR (95% CI)[*]	IRR (95% CI)	IRR P-value
Serous	Non-Hispanic White	50,732	8.45 (8.37–8.52)	1.00	–
	Asian Indian/Pakistani	394	6.24 (5.57–6.95)	0.74 (0.66–0.82)	< 0.0001
	Chinese	698	3.57 (3.31–3.85)	0.42 (0.39–0.46)	< 0.0001
	Filipino	948	4.71 (4.41–5.03)	0.56 (0.52–0.60)	< 0.0001
	Japanese	514	3.96 (3.62–4.33)	0.47 (0.43–0.51)	< 0.0001
	Korean	306	4.05 (3.60–4.54)	0.48 (0.43–0.54)	< 0.0001
	Vietnamese	285	4.37 (3.85–4.93)	0.52 (0.46–0.58)	< 0.0001
Mucinous	Non-Hispanic White	5,546	1.00 (0.97–1.03)	1.00	–
	Asian Indian/Pakistani	43	0.57 (0.39–0.79)	0.57 (0.39–0.79)	0.0004
	Chinese	144	0.72 (0.60–0.85)	0.72 (0.60–0.85)	0.0001
	Filipino	196	0.96 (0.83–1.10)	0.96 (0.83–1.11)	0.59
	Japanese	107	0.94 (0.76–1.14)	0.94 (0.76–1.14)	0.58
	Korean	51	0.61 (0.46–0.81)	0.62 (0.46–0.82)	0.0003
	Vietnamese	64	0.87 (0.67–1.13)	0.88 (0.67–1.13)	0.34
Endometrioid	Non-Hispanic White	8,886	1.60 (1.57–1.63)	1.00	–
	Asian Indian/Pakistani	83	1.00 (0.79–1.26)	0.63 (0.49–0.79)	< 0.0001
	Chinese	210	1.02 (0.89–1.17)	0.64 (0.55–0.73)	< 0.0001
	Filipino	296	1.40 (1.24–1.57)	0.87 (0.77–0.98)	0.022
	Japanese	156	1.35 (1.15–1.59)	0.85 (0.72–1.00)	0.047
	Korean	59	0.71 (0.54–0.92)	0.45 (0.34–0.58)	< 0.0001
	Vietnamese	74	1.01 (0.79–1.27)	0.63 (0.49–0.80)	< 0.0001
Clear cell	Non-Hispanic White	3,846	0.69 (0.67–0.71)	1.00	–
	Asian Indian/Pakistani	50	0.64 (0.47–0.85)	0.92 (0.67–1.24)	0.66
	Chinese	213	1.03 (0.90–1.18)	1.49 (1.29–1.72)	< 0.0001
	Filipino	194	0.90 (0.78–1.04)	1.30 (1.12–1.51)	0.0007
	Japanese	128	1.13 (0.94–1.35)	1.64 (1.36–1.97)	< 0.0001
	Korean	47	0.56 (0.41–0.75)	0.81 (0.59–1.09)	0.18
	Vietnamese	68	0.89 (0.69–1.13)	1.29 (0.99 –1.65)	0.052
Other/NOS[†]	Non-Hispanic White	15,406	2.42 (2.38–2.46)	1.00	–
	Asian Indian/Pakistani	110	2.07 (1.66–2.55)	0.86 (0.68–1.05)	0.15
	Chinese	294	1.53 (1.36–1.72)	0.63 (0.56–0.71)	< 0.0001
	Filipino	344	1.76 (1.58–1.97)	0.73 (0.65–0.81)	< 0.0001
	Japanese	186	1.36 (1.17–1.58)	0.56 (0.48–0.65)	< 0.0001
	Korean	89	1.30 (1.03–1.61)	0.54 (0.43–0.66)	< 0.0001
	Vietnamese	87	1.50 (1.18–1.87)	0.62 (0.49–0.77)	< 0.0001

Abbreviation: AAIR = age-adjusted incidence rate, IRR = incidence rate ratio, CI = confidence interval, NOS = not otherwise specified.

[*] Units of per 100,000 women.

[†] Includes carcinosarcomas as well as mixed, other, undifferentiated, and unspecified tumors.

Americans, as well as the need for ethnic-specific cancer statistics and research for Asian Americans, as previously noted by previous studies for other cancer sites [6,11].

Although all Asian American ethnic groups had a lower incidence rate of ovarian cancer relative to NHWs, there are some very interesting findings of unique incidence patterns associated with certain ethnic groups. For example, in our analysis, Asian Indian/Pakistani women showed a higher ovarian cancer incidence rate than other Asians and had a lower percentage of the clear cell tumor that is known to be more common among Asians [3,20,21]. Genetics may play a role in such observations, since previous phylogenetic work has presented Asian Indians/Pakistanis as distinct from other Asian ethnicities and more closely related to Caucasians [22]. This could explain why Asian Indian/Pakistani women's ovarian cancer incidence rates and percent distributions of tumor characteristics, such as stage and histotype, were more comparable to those for NHWs.

In agreement with existing literature, we found that Chinese, Filipino, and Japanese women indeed had higher incidence of clear cell ovarian cancer. Endometriosis could partly explain this given that it is a strong risk factor for the clear cell histotype [23]. Miyazawa reported the highest hospital admission rates for endometriosis among Japanese women in comparison to non-Japanese Asian ethnicities and non-Asian races [24]. Similarly, a retrospective cohort study based on electronic medical records of infertility clinic patients observed women of Filipino and Japanese origin to be more likely to have endometriosis than NHW women [25]. Given that endometriosis is also a risk factor for endometrioid ovarian cancer, we would expect to see a higher incidence of the endometrioid histotype among these Asian American ethnic groups in our results. However, this was not observed, which may be due to other ovarian cancer etiologic factors with histotype-specific effects.

The ASIRs for all Asian American ethnic groups were statistically significantly lower than those of NHWs after age 50, which has been observed in previous work [26]. Again, the age-specific incidence pattern for Asian Indians/Pakistanis appeared to diverge from the other Asian subgroups since their ASIRs continued to increase after age 50 mimicking that of NHWs (Fig. 3). Given the timing of these observations, the racial/ethnic differences in these patterns may be related to menopause given that menopausal symptoms, lifestyles, and behaviors during and after the menopause transition have been shown to differ by race/ethnicity [27,28], and such factors could differentially impact disease incidence. For example, differences in the prevalence of postmenopausal hormone therapy use by race has been noted, with White women being more commonly prescribed hormone therapy than other races [29]. Also, the specific effect of hormone therapy and other factors on ovarian cancer risk could vary by race; Peres et al. found significant heterogeneity in the association between reproductive, hormonal, and lifestyle factors and ovarian cancer by race, such as parity being more protective for Asian women [30]. Such variation across the Asian ethnic groups is likely, but there is limited reporting on this, highlighting the need for greater diversity in clinical and epidemiologic studies.

It has been noted that incidence rates of ovarian cancer has either remained unchanged or only slightly decreased among the aggregated Asian American women, contrary to the significantly greater decline that has been observed among NHW women [31–34]. However, when

Table 4
Age-specific incidence rates of ovarian cancer by race/ethnicity, 1990–2014.

Age Group	Race/Ethnicity	N	ASIR (95% CI)[*]	IRR (95% CI)	IRR P-value
< 40 years	Non-Hispanic White	3,340	1.33 (1.28–1.38)	1.00	–
	Asian Indian/Pakistani	91	1.26 (1.01–1.56)	0.95 (0.76–1.18)	0.69
	Chinese	134	1.13 (0.95–1.34)	0.85 (0.71–1.01)	0.066
	Filipino	168	1.40 (1.20–1.63)	1.05 (0.90–1.23)	0.54
	Japanese	61	1.22 (0.93–1.57)	0.92 (0.70–1.18)	0.57
	Korean	47	0.91 (0.67–1.21)	0.68 (0.50–0.91)	0.008
	Vietnamese	68	1.32 (1.03–1.68)	1.00 (0.77–1.27)	0.99
40–49 years	Non-Hispanic White	9,665	13.26 (13.00–13.53)	1.00	–
	Asian Indian/Pakistani	151	12.05 (10.20–14.14)	0.91 (0.77–1.07)	0.26
	Chinese	348	10.92 (9.80–12.13)	0.82 (0.74–0.92)	0.0003
	Filipino	418	13.33 (12.08–14.67)	1.01 (0.91–1.11)	0.94
	Japanese	149	10.60 (8.97–12.45)	0.80 (0.68–0.94)	0.006
	Korean	120	9.18 (7.61–10.98)	0.69 (0.57–0.83)	< 0.0001
	Vietnamese	146	12.58 (10.62–14.80)	0.95 (0.80–1.12)	0.56
50–59 years	Non-Hispanic White	17,077	27.42 (27.01–27.84)	1.00	–
	Asian Indian/Pakistani	177	21.00 (18.02–24.33)	0.77 (0.66–0.89)	0.0003
	Chinese	405	16.98 (15.37–18.72)	0.62 (0.56–0.68)	< 0.0001
	Filipino	562	22.04 (20.25–23.94)	0.80 (0.74–0.87)	< 0.0001
	Japanese	237	19.25 (16.86–21.87)	0.70 (0.61–0.80)	< 0.0001
	Korean	169	17.51 (14.97–20.35)	0.64 (0.55–0.74)	< 0.0001
	Vietnamese	164	18.91 (16.12–22.04)	0.69 (0.59–0.80)	< 0.0001
60–69 years	Non-Hispanic White	19,803	43.03 (42.43–43.63)	1.00	–
	Asian Indian/Pakistani	132	25.62 (21.42–30.42)	0.60 (0.50–0.71)	< 0.0001
	Chinese	265	17.44 (15.40–19.69)	0.41 (0.36–0.46)	< 0.0001
	Filipino	408	24.06 (21.78–26.53)	0.56 (0.51–0.62)	< 0.0001
	Japanese	251	24.23 (21.32–27.42)	0.56 (0.50–0.64)	< 0.0001
	Korean	111	18.31 (15.06–22.07)	0.43 (0.35–0.51)	< 0.0001
	Vietnamese	112	22.15 (18.22–26.67)	0.51 (0.42–0.62)	< 0.0001
70–79 years	Non-Hispanic White	19,572	55.55 (54.78–56.34)	1.00	–
	Asian Indian/Pakistani	91	38.20 (30.70–46.97)	0.69 (0.55–0.85)	0.0002
	Chinese	231	23.19 (20.29–26.38)	0.42 (0.37–0.48)	< 0.0001
	Filipino	294	29.69 (26.38–33.30)	0.53 (0.47–0.60)	< 0.0001
	Japanese	240	27.66 (24.27–31.40)	0.50 (0.44–0.57)	< 0.0001
	Korean	60	17.74 (13.52–22.87)	0.32 (0.24–0.41)	< 0.0001
	Vietnamese	54	21.01 (15.75–27.45)	0.38 (0.28–0.49)	< 0.0001
80+ years	Non-Hispanic White	14,959	56.87 (55.96–57.80)	1.00	–
	Asian Indian/Pakistani	38	44.42 (31.35–61.09)	0.78 (0.55–1.07)	0.14
	Chinese	176	30.58 (26.23–35.45)	0.54 (0.46–0.62)	< 0.0001
	Filipino	128	27.75 (23.14–33.02)	0.49 (0.41–0.58)	< 0.0001
	Japanese	153	26.60 (22.55–31.16)	0.47 (0.40–0.55)	< 0.0001
	Korean	45	29.20 (21.29–39.08)	0.51 (0.37–0.69)	< 0.0001
	Vietnamese	34	29.69 (20.55–41.50)	0.52 (0.36–0.73)	< 0.0001

Abbreviation: ASIR = age-specific incidence rate; IRR = incidence rate ratio, CI = confidence interval.
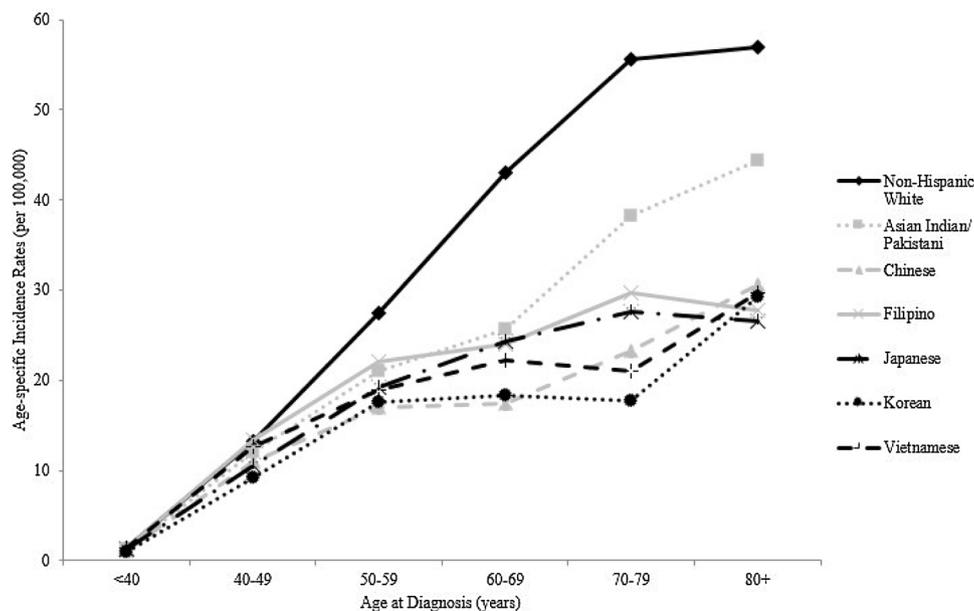 * Units of per 100,000 women.

Fig. 3. Age-specific incidence rates for ovarian cancer by race/ethnicity, 1990–2014.

we disaggregate the Asian American population, we observed incidence to be significantly decreasing for Chinese and Japanese women as well. Interestingly, increases in ovarian cancer incidence have been reported in both China [35,36] and Japan [37–39]. However, those living in the U.S. are likely to be different from those living in their native countries with respect to socioeconomic and lifestyle factors [26], as the ovarian cancer incidence differential between Japanese American and Chinese American women is much less than the reported two-fold between Japan and China [1,4,5]. Redaniel et al. also found significant ovarian cancer survival differences between Philippine residents and Filipino-Americans [40], underlying possible environmental mediations.

The lack of readily available cancer data, as well as population data, by detailed Asian ethnicity coupled with the rareness of ovarian cancer are often why most ovarian cancer research evaluates Asians in the aggregate. By leveraging the population-based SEER registry database, we are able to provide valuable insights into ovarian cancer incidence patterns and trends among the heterogeneous Asian American population with disaggregated ethnic groups. A limitation of such population-based studies is possible misclassification of race/ethnicity given that this information is primarily based on medical records [41]. However, studies comparing administrative databases to self-report have shown low misclassification even when specific Asian ethnicities were considered [42,43]. The agreement between our findings and supporting literature adds to our confidence in the quality of data used in the analysis. In addition, we did not correct for salpingo-oophorectomy in our rate calculations, which underestimates the true incidence of ovarian cancer. However, prior incidence correction by Merrill that took into account the impact of this surgical procedure on ovarian cancer rates showed the biggest impact on NHWs and the smallest impact on Asians, suggesting an even greater disparity between the two [44]. Ethnic-specific salpingo-oophorectomy rates would be useful given that they may differ by Asian American subgroup, which could explain some of our findings despite salpingo-oophorectomy's small impact on Asians as a whole. However, current data on this is sparse, hence future work in this area could refine our understanding of ovarian cancer incidence rates among the Asian American ethnic populations.

The ovarian cancer disparities revealed by our analysis further underscore the need for disaggregated Asian American cancer studies to more accurately understand disease burden and generate etiologic hypotheses. They also provide needed information for developing more targeted ovarian cancer educational outreach and intervention strategies. Future research should take advantage of the ethnic diversity in the Asian American community to advance cancer research that can benefit public health in not only the U.S., but also the world.

Authorship contribution statement

A.W.L. and L.L. conceived and designed the study. A.W.L and E.E.N. analyzed the data. A.W.L. drafted the manuscript. All authors contributed to data interpretation as well as the critical revision and final approval of the manuscript.

Declaration of competing interest

The authors have no conflicts of interest to disclose.

Acknowledgements

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