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Birth Cohort effects of other cause mortality on ovarian cancer risk among Black and White women

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B.M.,
Shandong University,
2020

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An abstract of
A thesis submitted to the Faculty of the
Rollins School of Public Health of Emory University
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Master of Public Health
in Epidemiology
2022

Abstract

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By He Tian

In the United States, Black women have a lower incidence of ovarian cancer compared to White women. Additionally, Black people are known to have higher all-cause mortality than their White counterparts. We sought to understand to what extent this difference in competing risks, other-cause mortality, may contribute to the disparity in ovarian cancer incidence between Black and White women. We built a state-transition Markov model in which we simulated counterfactual situations by varying other-cause mortality rates between Black and White women at risk of developing ovarian cancer. Applying this model, we observed the effects of altering other-cause mortality between Black and White women over a number of decades. Results indicate the racial disparity in ovarian cancer incidence between Black and White has decreased over the past decades. The incidence difference observed after varying other-cause mortality was 0.21% to 10.95% for Black women and -8.95% to -0.17% for White women. The gap between ovarian cancer incidence among Black and White women is larger in the older age groups than in younger age groups. To improve our assessment, we will need complete data from all ages for the studied time. The small sample size in older SEER data may also affect the precision of our results.

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Abstract

In the United States, Black women have a lower incidence of ovarian cancer compared to White women. Additionally, Black people are known to have higher all-cause mortality than their White counterparts. We sought to understand to what extent this difference in competing risks, other-cause mortality, may contribute to the disparity in ovarian cancer incidence between Black and White women. We built a state-transition Markov model in which we simulated counterfactual situations by varying other-cause mortality rates between Black and White women at risk of developing ovarian cancer. Applying this model, we observed the effects of altering other-cause mortality between Black and White women from 1975 to 2020. Results indicate the racial disparity in ovarian cancer incidence between Black and White has decreased over the past decades. The incidence difference observed after varying other-cause mortality was 0.21% to 10.95% for Black women and -8.95% to -0.17% for White women. The gap between ovarian cancer incidence among Black and White women is larger in the older age groups than in younger age groups. To improve our assessment, we will need complete data from all ages for the studied time. The small sample size in older SEER data may also affect the precision of our results.

Background

Ovarian cancer is the second most common gynecologic cancer in the United States. The American Cancer Society estimates about 19,880 new cases of ovarian cancer will occur in the US in 2022.[2] Ovarian cancer has the highest mortality rate compared to any other cancer of the female reproductive system.[1] In 2022 alone, approximately 12,810 women are estimated to die from ovarian cancer in the United States.[2] In the last 20 years, the annual incidence rate of ovarian cancer decreased from 14.2 to 9.8 per 100,000 and the overall death rate decreased from 9 to 6.7 per 100,000 women).[1]

Racial and ethnic differences in ovarian cancer.

From 2014 to 2018, non-Hispanic White women had the highest age-adjusted annual incidence rate of ovarian cancer (11.0 per 100,000 women)[1]; while the incidence rate among non-Hispanic Black women was lower in comparison (8.6 per 100,000 women).

A higher rate of ovarian cancer mortality is observed among non-Hispanic Whites when compared to non-Hispanic Blacks (6.9 per 100,000 women vs. 5.9 per 100,000 women).[1] However, based on cases reported by National Program of Cancer Registries (NPCR) registries from 2012-2018 and follow-up of patients through December 31, 2018, non-Hispanic Black women had a worse five-year relative survival compared to non-Hispanic White women (42.9% vs. 49.3%).[1] The average annual percent change, calculated in The Surveillance, Epidemiology, and End Results (SEER) Program 9 Delay-Adjusted ovarian cancer incidence in 2005-2014 was -1.7% for White women and -0.4% for Black women.[3] As shown, White women had a rapid decrease in both ovarian cancer incidence and mortality since 2005 compared to Black women.

Ovarian cancer prognosis is strongly associated with the stage at diagnosis, with approximately a 91.2% 5-Year relative survival for localized cancer, 73.2% for regional cancer, and 30.8% for distant cancer. However, among the newly diagnosed or incident ovarian cancer cases from 2014 to 2018, only 19.1% were found with localized cancer, 22.6% were diagnosed with regional cancer, and 52.4% were diagnosed with distant cancer[1], which means 75% of the cases were detected only after it had spread beyond the primary site.

Black women are more often diagnosed with distant-stage cancer compared to White women (54.5% vs. 52.8%), along with a notably higher proportion of unstaged cancer (7.3% vs. 5.6%).[1]

Among cases diagnosed from 2010 to 2016, the relative 5-year survival rate of distant cancer was 29%, lower than regional cancer (75%) and localized cancer (92%).[5] The higher proportion of late-stage ovarian cancer at diagnosis could explain the worse survival condition among Blacks. However, because the symptoms of early ovarian cancer are not very specific to ovarian cancer, and the tumor tissue can be easily missed during pelvic exams since the ovaries are located deep in the pelvis. There are no reliable screening methods. Therefore, we cannot improve ovarian cancer survival or racial disparities by early detection at this point.

Factors that could influence ovarian cancer incidence and survival disparities in Black and White women are not well understood. Further investigating such factors will provide a clue to reduce ovarian cancer incidence for women regardless of race. However, it is important to understand the impact of the effect of possible noteworthy competing risks, in this case, other-cause mortality. Other-cause mortality may pose an important consideration for those at risk for developing ovarian cancer. According to our research, the 5-year other-cause mortality of Black women is higher than White women in the total of 106 age- and period- combinations we studied. Within each age group, the other-cause mortality decreases over the years for Black and White women. Older women have higher other-cause mortality in the 14 age groups from 10 to 75 years old.

Figure 1

White women other cause mortality

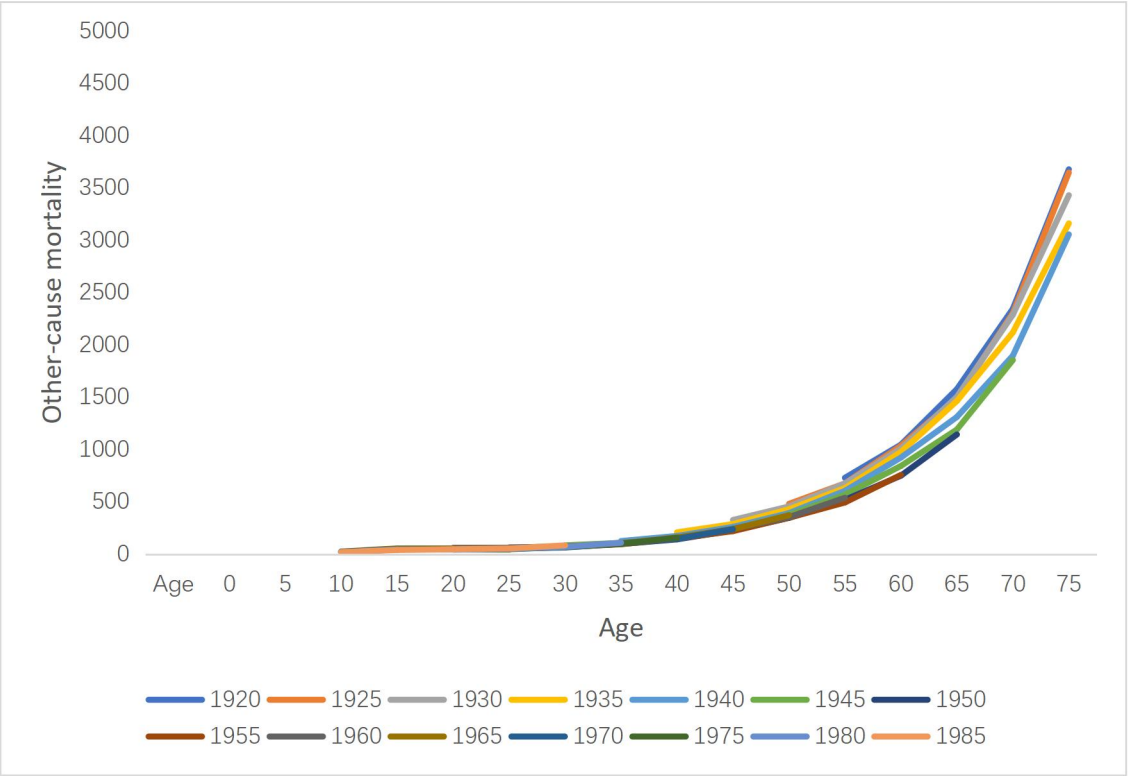
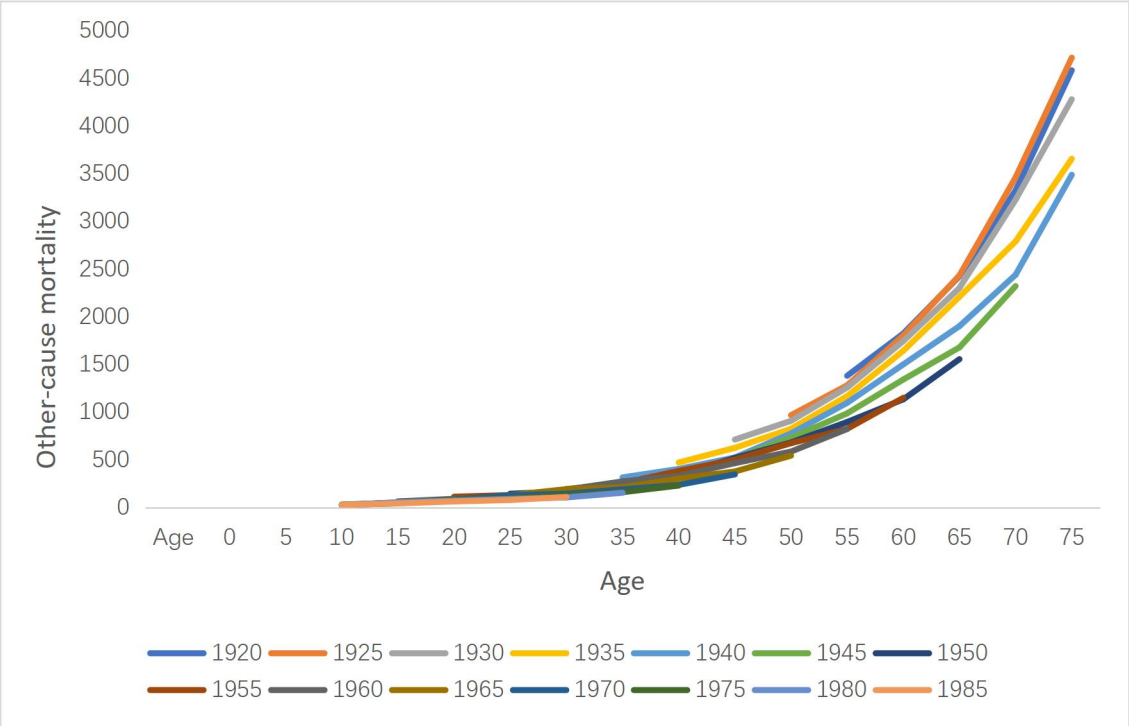


Figure 2

Black women other-cause mortality



We hypothesize that death from other causes may explain the lower incidence of ovarian cancer among Black women compared to White women. Since Black women face higher other-cause mortality, they also have less chance of developing ovarian cancer. This effect could accumulate and become much more notable in older ages. As the age-adjusted mortality rates for Black women are significantly higher than for White women,[8] it is reasonable to explore to what extent the disparity in other-cause mortality can explain the racial disparities in

In order to understand how changes in competing risk differences may lead to ovarian cancer disparities we propose a counterfactual approach to simulate the effect of other-cause mortality.

Methods:

To address other cause mortality and assess the effect on difference in ovarian cancer in Black and White women we developed a state-transition Markov model using TreeAge Pro™ 2022 Healthcare Module (TreeAge Software Inc., Williamstown, MA, USA). In our Markov model, the life course of women was simplified in three states: alive without ovarian cancer, alive with ovarian cancer, and death due to other causes. Through this simulation model, we create cohorts of women transitioning through these three states. A birth cohort, a collection of women born in a designated five-year interval, and the transitions of women in each cohort are assessed every five years from 1975 to 2020.

Model parameters and data sources:

The transition probabilities were calculated from previously observed race-specific (Black and White) census and cancer epidemiology estimates for women born between 1920 and 1985. Year of diagnosis and age- and race-specific ovarian cancer incidence were obtained from SEER*Stat[4] (The Surveillance, Epidemiology, and End Results (SEER) Program; Supplementary Table 1 and Table 2).

Other cause mortality risk estimates were calculated using The National Vital Statistics System (NVSS) data[6] (Tables 3 and 4) and SEER program through SEER*Stat software for

population estimates.[7]

Scenarios and outcomes assessed:

The 25-year cumulative incidence of ovarian cancer for each birth cohort is calculated for counterfactual situations in addition to observed situations among Black and White women. We will set the start age to 10 groups, from 10 to 55 years old, and calculate the cumulative incidence respectively. Besides, we will visually compare the sensitivity analysis results for notable cohort effects.

Results

Among White women, as shown in Table 5, we observed the highest 25-year cumulative incidence of ovarian cancer in the group of cohorts with a start age of 55-year-old. Within this group, the 25-year cumulative incidence of ovarian cancer decreased from 1149.07 per 10,000 starting from 1920 to 954.34 per 10,000 starting from 1945. For White women, we observed the lowest 25-year cumulative incidence of ovarian cancer in the group with a start age of 10-years old, ranging from 44.24 per 10,000 starting from 1975 to 57.56 per 10,000 starting from 1965. Among Black women, the highest 25-year cumulative incidence of ovarian cancer was observed in the group with a start age of 55-year-old, ranging from 541.22 per 10,000 starting from 1935 to 820.97 per 10,000 beginning from 1930. The lowest 25-year cumulative incidence of ovarian cancer for Black women was observed in the age group with a start age of 10-years old, ranging from 32.24 per 10,000 starting from 1980 to 68.44 per 10,000 starting from 1970. Black women had a lower 25-year ovarian cancer risk compared to White women in all cohorts except for the 1970 20-year-old, 1970 15-years-old, and 1970 10-years-old cohorts. Within each age group, both Black and White women demonstrated a decreasing 25-year ovarian cancer risk along the direction of later time periods. Among women whose incidence was calculated from the same start year, women born later showed a lower 25-year ovarian cancer risk for Black and White women.

In the counterfactual simulations, our results indicated that among White women applied with Black women other-cause mortality, the 55-year-old age group had the highest 25-year

cumulative incidence of ovarian cancer, decreasing from 1046.26 per 10,000 in 1920 cohort to 893.74 per 10,000 in 1940 cohort. The group starting from 10-years-old had the lowest cumulative incidence, ranging from 44.09 per 10,000 in 1975 cohort to 57.33 per 10,000 in 1965 cohort. Appling the other-cause mortality rate for White women to Black women, the highest cumulative incidence was in the group starting from 55-year-old, ranging from 588.52 per 10,000 in 1935 cohort to 893.94 per 10,000 in 1930 cohort. The 10-year-old group showed the lowest 25-year cumulative incidence of ovarian cancer, ranging from 32.24 per 10,000 in 1980 cohort to 68.63 per 10,000 in the 1970 cohort (see Table 5).

In the 50 scenarios examined, the counterfactual White women's 25-year cumulative incidence of ovarian cancer is still higher than counterfactual Black women's except for the 1970 20-year-old, 1970 15-year-old, and 1970 10-year-old cohorts. Within each age group, both counterfactual Black and White women demonstrated a decreasing 25-year ovarian cancer risk along the direction of later time periods. The decreasing rate is still more constant for White women while fluctuating for Black women when alternating the other-cause mortality between the racial groups. Within each period group, younger-age cohorts showed a lower 25-year ovarian cancer risk for counterfactual Black and White women.

The 25-year cumulative incidence of ovarian cancer decreased when we apply the Black women other-cause mortality to White women (range (-8.95) – (-0.17) %). However, Black women demonstrated an increased risk when applied to White women other-cause mortality (range 0.21 – 10.95%) (see Table 5). As shown in supplemental Figueres 3-12 the 25-year risk difference caused by applying counterfactual other-cause mortality narrowed in later period cohorts. In the direction of decreasing age, the risk difference caused by alternating other-cause mortality also narrowed within each racial group.

Discussion

According to our simulation, the observed and counterfactual incidence of ovarian cancer decreases over the studied period (1975 – 2020) for both Black and White women. As our simulation comes close to more recent periods, the incidence difference between observed

Black and White women's ovarian cancer incidence also decreases. According to the results of our sensitivity analysis, the decreasing rate of ovarian cancer diagnosis is seen to be relatively more constant for White women while it fluctuates for Black women. The fluctuation in Black women's ovarian cancer incidence rate likely results from the smaller number of ovarian cancer cases and less stable estimates compared to White women. Another possible explanation is the early-year SEER database's data limitation since it only includes about 8.3% of the total population.[9] There was also research that showed the generalizability of SEER registries should be discussed in a disease-specific manner[10]; thus, the representativeness of the data regarding ovarian cancer is unclear and is of particular concern for Black women.

In the counterfactual scenarios, applying White women's other-cause mortality causes the ovarian cancer incidence for Black women to increase; applying Black women's other-cause mortality causes the ovarian cancer incidence for White women to decrease, which means altering other-cause mortality causes the gap between Black and White women's ovarian cancer incidence to narrow.

Through our investigation, other-cause mortality can explain the racial disparity to a certain degree but hardly serves as the leading cause of the incidence difference between Black and White women. The incidence difference caused by altering other-cause mortality increases as age increases and the studied time period in older cohorts. The result indicates potential cohort effects of other-cause mortality on ovarian cancer risk among Black and White.

Conclusion

Our research explores the extent to which the incidence difference of ovarian cancer between Black and White women can be explained by other-cause mortality. The study of the counterfactual impact of competing risks could support future exploration of the risk factors of ovarian cancer and the factors causing the incidence difference between Black and White women. This report considers cohort effects as well as the time period, which presents a

visual comparison of birth cohort effects of other-cause mortality.

By simplifying life course into three health states centering on the disease of concern, we can easily input age and race-specific census and cancer registry data and obtain incidence estimates. The way of using counterfactual simulation is intuitive, efficient, and of low cost. However, the accuracy of our simulations does depend on the accuracy and completeness of the data source. To improve our analyses, we would need complete data from all age group for the studied period. Beyond the limitation of sample size, a closer investigation into the unstable incidence change among Black women is also needed in order to address the racial disparities. Possible directions include the usage of oral contraceptives, the practice of tubal ligation, and other gene-environment interactive factors.

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Table 1

Black women ovarian cancer incidence from SEER program, per 10,000

Age	1920	1925	1930	1935	1940	1945	1950	1955	1960	1965	1970	1975	1980	1985
0														
5														
10										0.9	1.9	2	0	0
15									3.8	1.8	3.7	1.8	0	1.6
20								1	0	0.8	0.9	0	0.8	0.8
25							5.5	0.9	1.6	3.1	4.5	0.7	1.5	1.4
30						4.3	2.1	6.1	2.3	2.1	2.8	2.1	4.2	2.7
35					6.4	2.9	3.3	5.2	2.2	3.5	6.4	3.4	4.8	
40				7.9	11	5.8	4.2	4.3	5.9	12	5.7	5.5		
45			18.1	10.1	9.1	9.1	10.9	10.4	13.8	8.6	10.1			
50		12.6	16.3	14.7	25.2	13.8	16.1	16.2	20.9	16.8				
55	25.3	26.2	37.2	8.9	10	17.6	23.4	20.2	20					
60	47.5	24.2	25.5	30.1	29.4	38.7	20.9	27						
65	39.2	47.9	47.5	32.5	41	39.2	26							
70	19.9	63.8	63.5	27.7	32.8	37.2								
75	43.7	46.4	34.7	39.7	31.6									

Table 2

White women ovarian cancer incidence from SEER program, per 10,000

Age	1920	1925	1930	1935	1940	1945	1950	1955	1960	1965	1970	1975	1980	1985
0														
5														
10										0.6	0.6	0.5	0.5	1.6
15									1.7	0.9	1.8	1.8	2.4	1.8
20								1.4	2.4	2.2	1.6	1.6	2.3	2.5
25							2.3	3.6	3.3	3.5	2.4	1.9	1.4	1.1
30						4.6	4.2	3.5	3.5	4.4	2.6	3.1	3.3	3.4
35					4	5.8	7	6.3	5.8	5.2	4	4.4	4.8	
40				17.2	12.7	12.7	12.4	10.6	9.2	9.6	9	9		
45			25.5	21.5	24.3	17.2	18.2	17.5	16.1	16.6	13.5			
50		34.2	32.9	30.1	25.6	22.2	27.8	23.5	23.1	21.8				
55	39.6	41.1	39.1	37.1	32.1	36.4	30	31.9	23.7					
60	47.3	53.5	47.4	43.8	46.5	36.3	33.1	31.7						
65	56.8	51.9	52.4	46.5	38.7	40.8	39.8							
70	66.5	55.9	55.8	52.2	51.3	43.1								
75	62.2	53.5	53.4	53.1	51.2									

Table 3

Black women other-cause mortality from NVSS, per 10,000

Age	1920	1925	1930	1935	1940	1945	1950	1955	1960	1965	1970	1975	1980	1985
0														
5														
10										31.87	27.75	25.39	27.54	26.81
15									64.73	50.28	44.53	54.35	55.1	43.6
20								113.55	91.29	73.6	82.97	83.09	73.23	64.31
25							145.46	131	111.37	129.73	129.54	97.68	89.95	79.35
30						194.91	168.79	167.3	188.63	193.19	145.64	130.68	106.34	110.99
35					316.42	249.83	226.2	255.96	274.11	213.42	190.24	160.91	154.99	
40				472.37	404.87	340.92	343.37	384.08	331.37	302.79	237.75	230.57		
45			713.04	626.35	525.32	516.37	520.92	501.37	465.97	378.07	347.62			
50		968.5	909.4	826.26	777.12	731.96	682.27	675.13	586.83	544.18				
55	1,382.00	1,282.10	1,259.24	1,168.37	1,098.45	987.92	897.38	825.93	823.63					
60	1,825.40	1,803.70	1,746.43	1,644.58	1,501.48	1,343.04	1,135.04	1,150.98						
65	2,425.90	2,435.30	2,302.97	2,210.92	1,903.02	1,679.87	1,556.37							
70	3,324.50	3,463.20	3,228.55	2,791.42	2,441.33	2,322.50								
75	4,586.00	4,718.50	4,281.53	3,657.88	3,489.90									

Table 4

White women other-cause mortality from NVSS, per 10,000

Age	1920	1925	1930	1935	1940	1945	1950	1955	1960	1965	1970	1975	1980	1985
0														
5														
10										24.19	21.91	19.74	18.7	18
15									51.95	54.02	46.65	45.73	43.68	39.2
20								58.97	57.21	49.39	46.38	43.74	42.73	46.12
25							63.05	58.09	52.7	54.28	52.06	46.84	50.42	53.56
30						83.17	72.4	66.68	68.46	72.36	63.07	67.52	69.22	83.25
35					124.57	107.42	96.09	94.42	104.45	99.61	99.65	97.99	108.46	
40				207.89	173.41	153.96	140.69	148.52	151.79	159.61	146.95	155.75		
45			326.15	286.44	259.69	238.04	226.26	219.44	241.21	237.75	237.04			
50		480	455.07	427.63	391.53	374.06	345.94	347.21	352.89	371.43				
55	729.2	675.7	675.24	630.55	604.41	567.94	518.85	493.26	538.39					
60	1,045.70	1,034.50	1,008.20	975.6	922.43	842.24	749.3	756.75						
65	1,576.40	1,490.50	1,502.52	1,463.22	1,310.62	1,190.33	1,143.04							
70	2,344.50	2,303.70	2,287.97	2,118.47	1,896.19	1,854.42								
75	3,677.40	3,646.50	3,429.89	3,160.42	3,055.13									

Table 5

Estimated 25-year cumulative incidence of ovarian cancer across Markov models varying other-cause mortality

Birth cohort	Start Age	White (White_Mort)	White (Black_Mort)	Black (Black_Mort)	Black (White_Mort)	White % Difference	Black % Difference
1920	55	1149.07	1046.26	691.18	752.91	-8.95	8.93
1925	50	1056.59	974.51	686.78	759.23	-7.77	10.55
	55	1097.40	1002.28	790.17	876.70	-8.67	10.95
1930	45	908.96	850.23	618.27	663.50	-6.46	7.31
	50	1016.30	941.80	765.39	834.53	-7.33	9.03
	55	1062.22	976.47	820.97	893.94	-8.07	8.89
1935	40	708.07	672.77	320.00	338.08	-4.99	5.65
	45	829.04	780.58	412.87	441.98	-5.85	7.05
	50	941.62	879.34	472.09	508.58	-6.61	7.73
	55	1001.35	928.85	541.22	588.52	-7.24	8.74
1940	35	475.50	457.08	289.27	299.22	-3.87	3.44
	40	669.76	639.24	385.24	402.96	-4.56	4.60
	45	779.99	740.60	499.30	529.67	-5.05	6.08
	50	877.06	823.85	585.86	624.55	-6.07	6.60
	55	954.34	893.74	584.36	626.79	-6.35	7.26
1945	30	305.15	297.05	170.74	175.38	-2.66	2.72
	35	455.04	439.05	229.36	237.72	-3.51	3.64
	40	594.60	570.00	382.75	401.91	-4.14	5.00
	45	714.63	679.88	517.87	548.14	-4.86	5.85
	50	814.77	771.97	624.68	662.64	-5.25	6.08
1950	25	216.88	212.41	125.80	128.15	-2.06	1.86
	30	340.09	330.83	173.59	178.75	-2.72	2.97
	35	462.35	446.90	269.46	279.84	-3.34	3.85
	40	582.13	559.34	346.08	361.18	-3.92	4.36
	45	700.60	669.78	437.69	458.13	-4.40	4.67
1955	20	125.48	123.56	85.42	86.57	-1.53	1.35
	25	204.24	199.77	129.96	132.60	-2.19	2.03
	30	300.19	291.36	201.03	206.69	-2.94	2.81
	35	434.83	419.01	262.64	272.70	-3.64	3.83
	40	551.67	529.60	356.61	372.76	-4.00	4.53
1960	15	82.75	82.12	48.88	49.16	-0.75	0.57
	20	119.63	118.04	58.34	59.25	-1.33	1.55
	25	186.46	182.67	123.88	126.74	-2.03	2.31
	30	281.69	274.10	213.37	219.77	-2.69	3.00
	35	377.15	366.09	294.16	303.59	-2.93	3.21
1965	10	57.56	57.33	43.09	43.22	-0.39	0.30
	15	80.26	79.72	55.69	56.03	-0.67	0.61
	20	123.12	121.65	104.63	106.12	-1.19	1.43
	25	193.32	189.96	141.88	144.30	-1.74	1.71

	30	281.26	275.54	205.82	210.09	-2.04	2.07
1970	5	33.32	33.25	54.58	54.70	-0.21	0.22
	10	44.73	44.58	68.44	68.63	-0.33	0.28
	15	61.52	61.16	90.25	90.79	-0.59	0.60
	20	96.91	95.83	99.51	100.51	-1.11	1.00
	25	155.03	152.85	143.78	145.54	-1.40	1.23
1975	0	19.24	17.84	16.56	17.86	-7.29	7.80
	5	29.85	29.78	22.40	22.43	-0.22	0.13
	10	44.24	44.09	32.77	32.86	-0.34	0.26
	15	63.50	63.16	39.44	39.67	-0.54	0.59
	20	98.90	98.04	57.26	57.81	-0.87	0.96
1980	0	26.12	24.63	8.07	8.56	-5.71	6.00
	5	34.35	34.28	16.38	16.42	-0.21	0.24
	10	49.23	49.09	32.10	32.24	-0.28	0.44
	15	70.46	70.18	55.67	55.96	-0.39	0.52
1985	0	29.69	28.18	10.91	11.49	-5.09	5.37
	5	36.36	36.32	18.88	18.91	-0.13	0.17
	10	51.73	51.64	32.23	32.29	-0.17	0.21

Figure 3

The 25-year cumulative incidence of ovarian cancer in cohorts born from 1920 to 1940

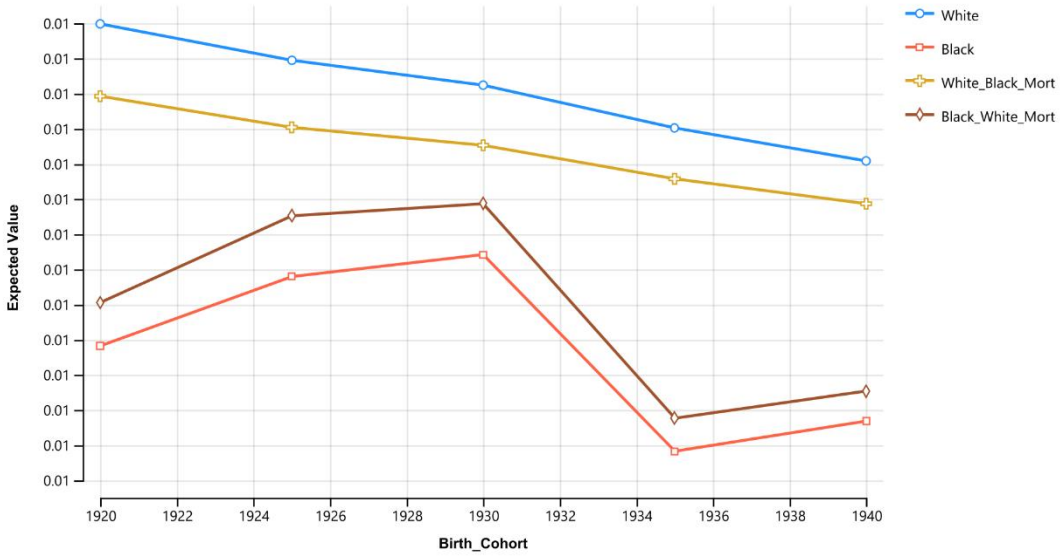

Figure 4

The 25-year cumulative incidence of ovarian cancer in cohorts born from 1925 to 1945

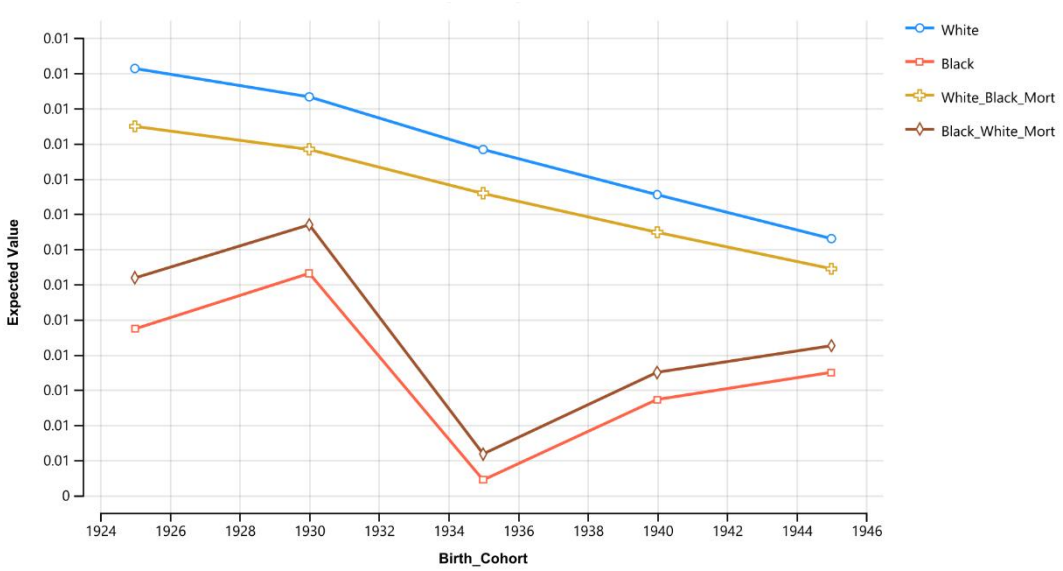

Figure 5

The 25-year cumulative incidence of ovarian cancer in cohorts born from 1930 to 1950

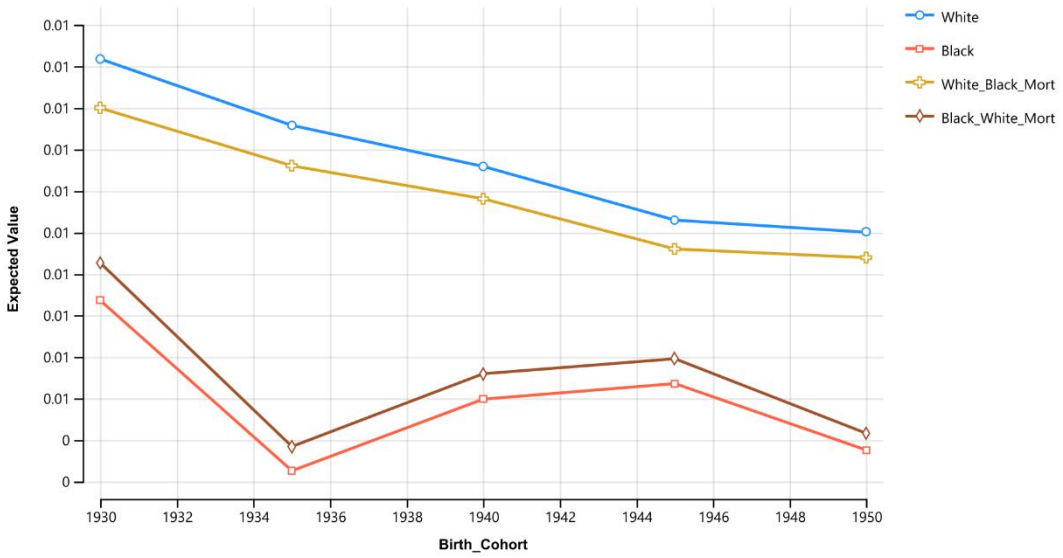

Figure 6

The 25-year cumulative incidence of ovarian cancer in cohorts born from 1935 to 1955

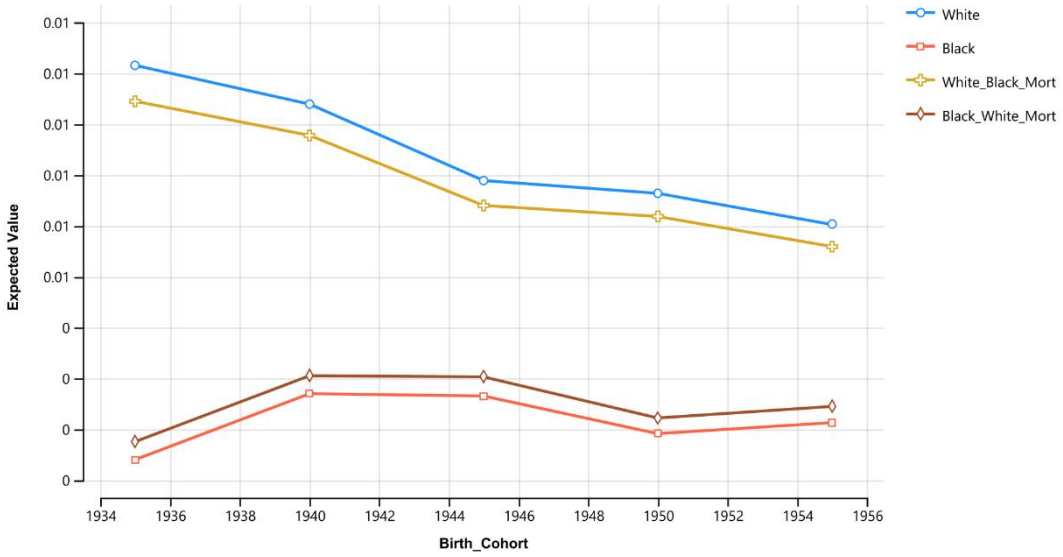

Figure 7

The 25-year cumulative incidence of ovarian cancer in cohorts born from 1940 to 1960

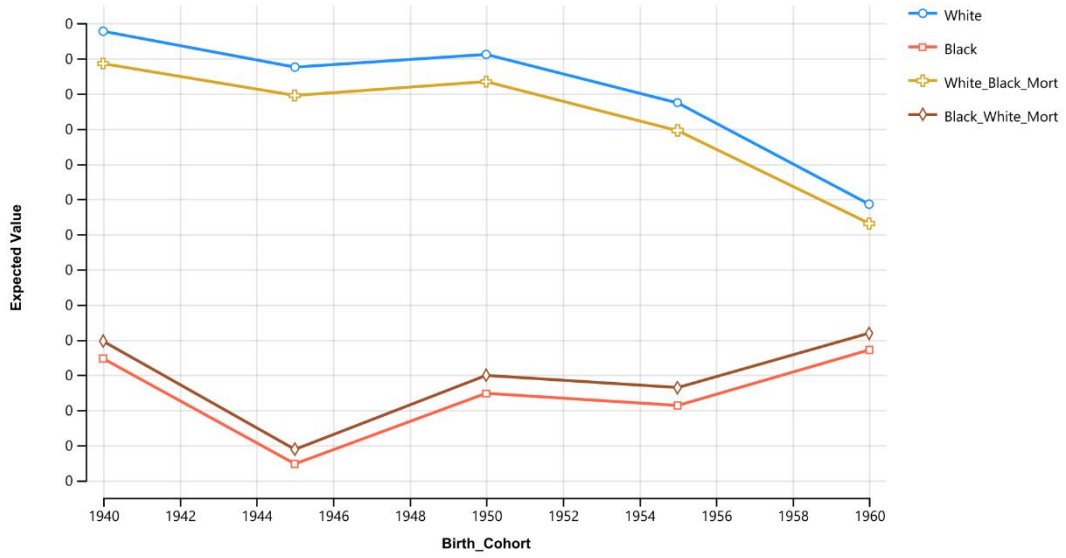

Figure 8

The 25-year cumulative incidence of ovarian cancer in cohorts born from 1945 to 1965

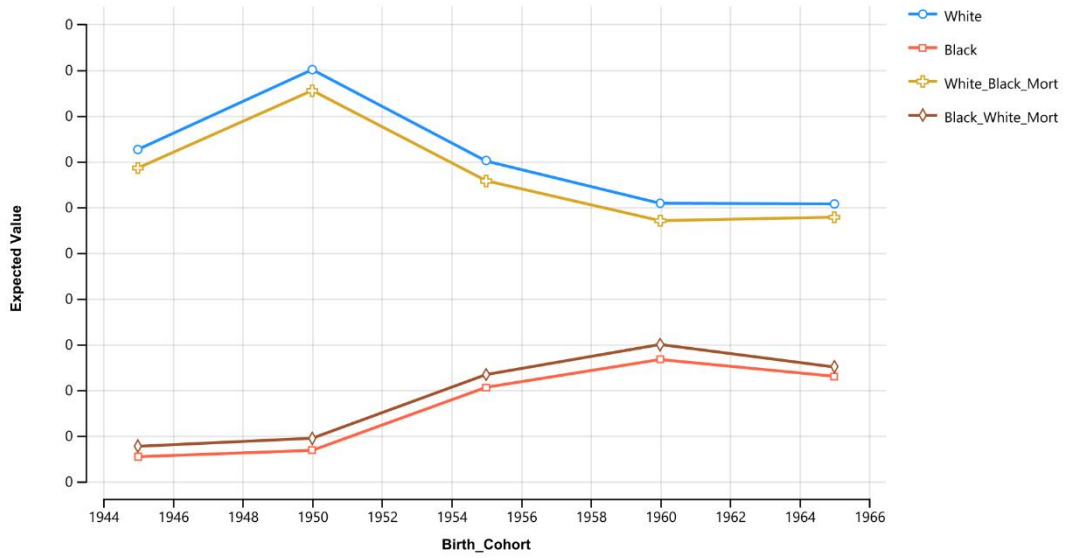

Figure 9

The 25-year cumulative incidence of ovarian cancer in cohorts born from 1950 to 1970

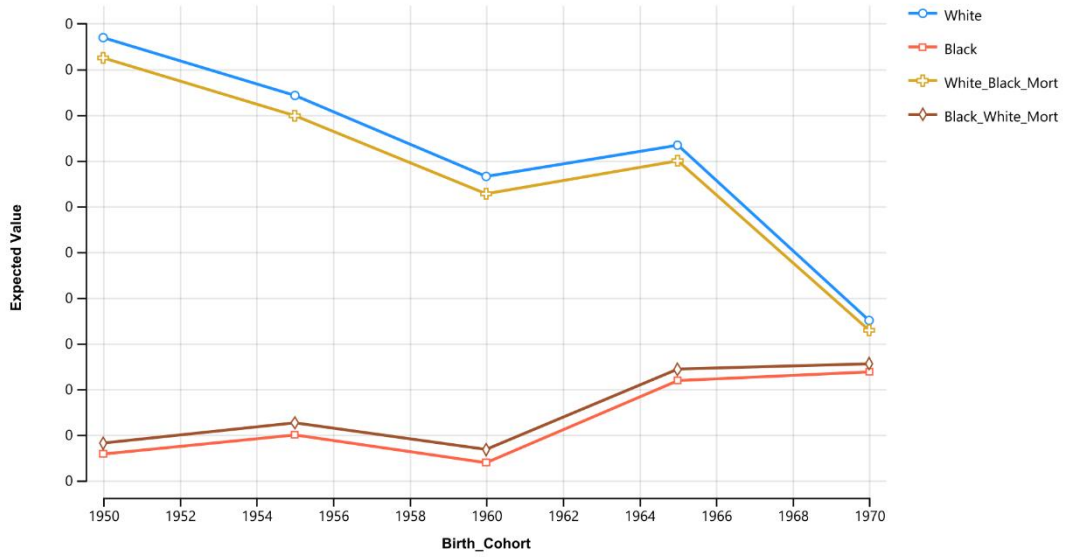

Figure 10

The 25-year cumulative incidence of ovarian cancer in cohorts born from 1955 to 1975

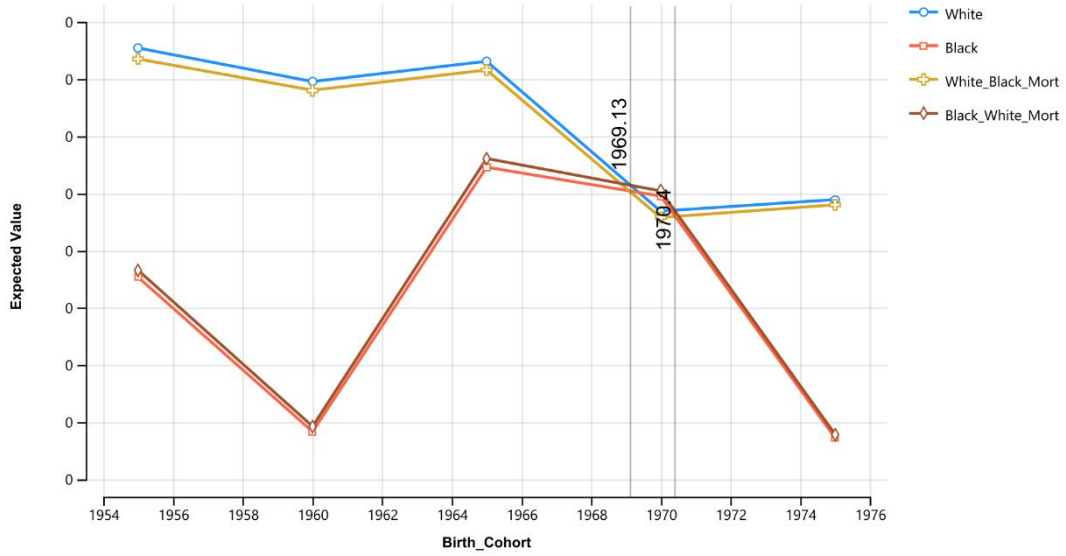

Figure 11

The 25-year cumulative incidence of ovarian cancer in cohorts born from 1960 to 1980

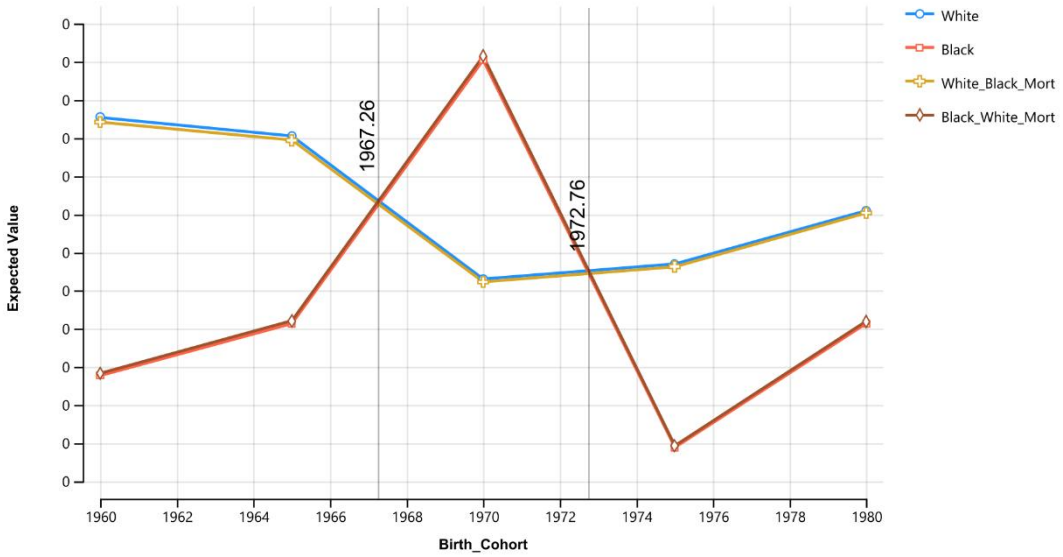

Figure 12

The 25-year cumulative incidence of ovarian cancer in cohorts born from 1965 to 1985