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# A comparative analysis of endometrial cancer disparities in incidence, mortality, and survival between women living in Puerto Rico, Non-Hispanic Blacks, Non-Hispanic Whites, and US Hispanics between 2000–2018

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### ABSTRACT

*Objective:* Endometrial cancer diagnosis in younger women is increasing in Puerto Rico and the United States. The study aims to evaluate the endometrial cancer trends in incidence, mortality, and survival by comparing US ethnic groups (NHW, NHB, and Hispanic) to women living in PR to assess whether disparities exist by age and stage at diagnosis on outcomes of interest.

*Methods:* We performed a secondary data analysis and comparison of the age-specific and age-adjusted incidence rates, mortality rates, and the survival of endometrial cancer in PR with that of NHB, NHW, and Hispanic using data from the PR Central Cancer Registry, the SEER Program, and PR Demographic Registry from 2000 to 2018. *Results:* PR had the highest incidence rates (41.3 per 100,000 women) of endometrial cancer, followed by NHW, NHB, and Hispanic. Women in PR younger than 65 years old had higher incidence rates of endometrial cancer than compared groups. NHB have higher overall mortality rates (12.5 per 100,000 women). Between ages 20–34 and 35–49, women in PR have the highest mortality rates, and after age 50, mortality rates are higher for NHB. *Conclusions:* Women in PR had higher endometrial cancer rates in increasing trend from 2000 to 2018 compared to similar NHB, Hispanic, and NHW cohorts. Also, women in PR experienced higher incidence and mortality rates below 50 years old among all races and ethnicities. Future studies are needed to evaluate histology, obesity trends, and the impact on the quality of life for this cohort.

# 1. Introduction

Endometrial cancer is the most common gynecologic malignancy and is the fourth most common malignancy affecting women with 66,200 estimated new cases and 13,030 estimated deaths in 2023. In addition, it is the sixth leading cause of cancer death in women in the United States, making it one of the few cancers that are increasing in incidence and mortality (Siegel et al., 2023; U.S. Cancer Statistics Working Group, 2022). Moreover, endometrial cancer is projected to become the 6th most common cancer by 2030 (Rahib et al., 2014), owing to its steady increase in incidence. Most uterine cancers are of endometrioid histology; however, other non-endometrioid histologies contribute most to mortality for affected women.

Parallel to increased rates of obesity, the incidence of endometrial cancer is also increasing. According to data from the CDC's National Program of Cancer Registries (NPCR) and the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) program, the incidence of uterine cancer has seen a 1.3% annual percent change between 2003–2019 (Institute, 2022). While the Non-Hispanic White (NHW) population has seen the smallest increase in incidence, the US Hispanic population has seen the largest, followed by Non-Hispanic American Indian/Alaska Native, Non-Hispanic Asian/Pacific Islander, and Non-Hispanic Black populations (NHB) (Institute, 2022). The data also shows that part of the burden of this increase in incidence has fallen on

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Abbreviations: (NHB), US Non-Hispanic Blacks; (NHW), US Non-Hispanic Whites; (PR), Puerto Rico; (Hispanics), US Hispanics; (SEER), Surveillance, Epidemiology, and End Results Program; (PRCCR), Puerto Rico Central Cancer Registry; (EC), Endometrial Cancer.

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age groups younger than 50 (Institute, 2022; Longo et al., 2020).

Various health disparities have been identified to disproportionally affect specific populations diagnosed with EC and determine how women experience the disease. When correcting for hysterectomies, Non-Hispanic Black female patients have the highest incidence and mortality rates (Clarke et al., 2019; Whetstone et al., 2022) and a lower survival rate when compared to White women (Whetstone et al., 2022).

Data from Ortiz et al. in 2010 on the endometrial cancer incidence, mortality, and survival rates in Puerto Rico found that age-adjusted incidence rates of endometrial cancer from 1992 to 2003 increased significantly for Puerto Ricans and non-Hispanic Blacks but remained constant for non-Hispanic Whites and Hispanics in the US (Ortiz et al., 2010). Given the rising rates of obesity and diabetes, which are associated with endometrial cancer (American Cancer Society, 2021; Raglan et al., 2019), we must continue to monitor epidemiological trends to determine whether our population has distinct epidemiological patterns and health disparities compared to NHB, NHW, and Hispanic populations.

# 2. Methods

# 2.1. Data collection and Sources

For the purposes of this Manuscript, Puerto Rico, a non-incorporated territory of the United States and geographically located in the Caribbean, is considered separately as differences in ethnicity, geography, and complex Latino, afro-descendant, and European inheritance patterns exist. United States (US) is defined as the continental US, Alaska, and Hawaii. PR data is not included in our data or any of our references that are referred to as US.

The endometrial cancer incidence and mortality data were analyzed from 2000 to 2018 for both the PR and the US populations to include the most recent data from the 2000 s and provide continuity of previously documented trends from 1992 to 2003 (Ortiz et al., 2010). For the survival analysis, the time frame was from 2010 to 2014, with a follow-up to 2019.

Incidence data for Puerto Rico was obtained from the Puerto Rico Central Cancer Registry (PRCCR). The Puerto Rico Central Cancer Registry (PRCCR) has been part of the CDC's National Program of Cancer Registry and uses the SEER and the North American Association of Central Cancer Registries standards for coding the data and is fully compatible with both SEER and NAAACR data. All cancer cases are coded using the Third Edition of the International Classification of Disease for Oncology (ICD-O-3). The PRCCR has a completeness of more than 95% annually since 2010, which has been achieved through electronic mandatory reporting. The states included in the SEER data are the 50 states and the District of Columbia. Data from Puerto Rico is not included in the SEER database used for this study's analysis. The SEER database that provides Puerto Rico data does not include race/ethnicity, limiting our study aims. For Puerto Rico, the incidence cases file population of 2017 were restricted to the first 6 months of the year (January to June). Cases from July to December were excluded due to the population change after Hurricane Maria. (Torres-Cintrón et al., 2021).

The incidence data of the United States (NHB, NHW and Hispanics) was obtained from the Surveillance, Epidemiology, and End Results (SEER) Program (Registries, 2020). The population source for the rates calculation was the Vintage 2019 estimates series for the Population Division of the United States Census Bureau. The mortality information for Puerto Rico was obtained from the Demographic Registry of Puerto Rico of the Puerto Rico Department of Health. The mortality data for US ethic groups was obtained from the SEER program.

Women older than 19 years at the time of diagnosis with a microscopically confirmed primary endometrial carcinoma were included in this analysis with the following primary sites codes: C54 Corpus Uteri and C55.9 Uterus NOS, with histologically confirmed codes from 8000 to 8933. This study was approved by the Institutional Review Board of the Comprehensive Cancer Center of the University of Puerto Rico protocol number 2021–04-46.

# 2.2. Statistical Analysis

Incidence and mortality rates were calculated per 100,000 women 20 years and older and age-adjusted to the 2000 US Standard Population with a 95% interval for all the mutually exclusive racial/ethnic groups: PR, NHW, NHB, and Hispanics.

The Annual Percent Change (APC) was calculated and estimated using the SEER Software and NCI Joinpoint Regression software program (version 4.9.1.0). For the confidence interval the parametric method and permutation model test were selected. The input data file used contains counts per the independent variable of year of diagnosis or death, racial/ethnic populations, and standard population. The APC represented the magnitude of the identified trend over time and was determined to be significant if different from zero at an alpha level of 0.05. The specific methodology and permutation tests of the Statistical Software has been previously described (Kim et al., 2000).

Descriptive epidemiology for incidence includes stratifications by age, and stage at diagnosis. Age-groups were divided as follows: 20–34 years, 35–49 years, 50–64 years, 65–79 years, and 80 years and older. Stage at diagnosis was described as localized, regional, distant, and unstaged.

# 2.3. Survival

The 5-year relative survival rates were calculated for cases diagnosed between 2010 and 2014 with follow up to 2019 for the Puerto Rico population.

#### 3. Results

Between the years 2014–2018, women in Puerto Rico showed the highest incidence rates (41.3 per 100,000 women) of endometrial cancer among all ethnic and racial groups, while Hispanic women had the lowest incidence rates (34.2). When evaluating findings by age groups, women in Puerto Rico younger than 65 years old had higher incidence rates of endometrial cancer than NHW, NHB and Hispanic. When stratified by stage at diagnosis, women in Puerto Rico had the lowest incidence rates (2.1) of distant stage at diagnosis when compared with NHW (3.1), Hispanic (3.6) and NHB (6.7) and the highest for localized stage (27.5) compared to NHW (27.3), Hispanic (22.8), and NHB (20.7).

In the endometrial cancer incidence data analysis stratified by age groups, the group of Puerto Rican women aged 20–34 years has an APC of 5.02% (p < 0.05), the highest percentage change among ethnic groups between the years of 2000–2018. In addition, Puerto Rican women have the highest increase in incidence of endometrial cancer across all age groups compared to all races and ethnicities evaluated, most significantly, however, in women between the ages of 35–49 years (6.96%, p < 0.05)) (Table 1). Puerto Rican women aged 50–64 years old, continue to present increasing incidence rates between 2000 and 2018 with an APC of 5.87% (p < 0.05).

As for the mortality rate, black women continue to have the highest rates (12.5 per 100,000 women) when compared with Hispanic, USW, and Puerto Rican women with the mortality rate being highest among Black females aged 65–79 years of age (49.5). Mortality rates for women in Puerto Rico are similar to NHW (6.8 and 6.4, respectively) and higher than Hispanic (5.7). Hispanic and NHW present a significant increase in mortality rates between ages 35–79. The greatest increase for Hispanic at ages 50–64 with a rate of 8.3 per 100,000 and APC of 2.57% (p < 0.05) and for NHW at ages 65–79 with a rate of 22.5 for every 100,000 and APC of 2.46% (p < 0.05). Table 2

During the 2000–2018 period, the largest increase in mortality rates was seen in NHB aged 35–49 years (APC = 3.15, p < 0.05) at a lower

#### Table 1

Descriptive epidemiology of endometrial cancer incidence in Puerto Rico and the United States: 2000 - 2018.

Characteristics	Puerto Rico		US Overall		Hispanic		NHB		NHW	
	No.(%)	Rate	No.(%)	Rate	No. (%)	Rate	No.(%)	Rate	No.(%)	Rate
Incidence	3,067 (100)	41.3	74,281 (100)	37.7	10,300 (100)	34.2	8,197 (100)	37.9	48,103 (100)	38.6
Age at diagnosis										
20-34 years	97(3.2)	7.0	1,267(1.7)	2.8	439(4.3)	3.7	148(1.8)	2.6	476(1.0)	2.2
35–49 years	440(14.3)	28.6	7,858(10.6)	17.5	2,042(19.8)	19.2	697(8.5)	12.6	3,749(7.8)	16.6
50-64 years	1,303(42.5)	78.7	32,859(44.2)	71.5	4,746(46.1)	65.4	3,627(44.2)	66.5	20,765(43.2)	73.9
65–79 years	1,068(34.8)	89.1	26,774(36.0)	102.2	2,631(25.5)	84.2	3,215(39.2)	122.2	18,893(39.3)	107.4
80 + years	159(5.2)	37.2	5,523(7.4)	58.6	442(4.3)	45.3	510(6.2)	65.6	4,220(8.8)	63.1
Stage										
Localized	2,031(66.2)	27.5	50,530(68.0)	25.7	6,964(67.6)	22.8	4,518(55.1)	20.7	33,879(70.4)	27.3
Regional	552(18.0)	7.2	14,307(19.3)	7.2	1,942(18.9)	6.7	1,913(23.3)	9.0	8,972(18.7)	7.1
Distant	160(5.2)	2.1	7,001(9.4)	3.5	1,021(9.9)	3.6	1,447(17.7)	6.7	3,870(8.0)	3.1
Unstaged	323(10.5)	4.4	2,438(3.3)	1.2	373(3.6)	1.2	319(3.9)	1.5	1,378(2.9)	1.1
Age Specific Trend	(APC) (%)									
20–34 years	5.02*		/		4.84*		2.36*		2.20*	
35–49 years	6.96*		/		2.74*		2.34*		0.97*	
50-64 years	5.42*		/		2.63*		2.79*		2000-2003: -1.10	
									2003-2009: 1.95*	
									2009-2018: 0.12	
65–79 years	3.63*		2000-2008: 0.28		-		2.36*		2000-2004: -2.64	
			2008-2011: 8.51						2004-2018: 1.71*	
			2011-2018: 1.33*							
80 + years	1.14		-		0.05		0.96		2000-2013: -1.72	
									2013–2018: 1.34	

\*APC: Annual Percent Change with statistical significance (p < 0.05).

/:Analysis not performed.

-: Data was unable to be analyzed by Jointpoint Program.

# Table 2

Descriptive epidemiology of endometrial cancer mortality in Puerto Rico and the United States: 2000 - 2018.

Characteristics	Puerto Rico		US Overall		Hispanic		NHB		NHW	
	No.(%)	RateAPC	No.(%)	RateAPC	No.(%)	RateAPC	No.(%)	RateAPC	No.(%)	RateAPC
Mortality	607 (100)	6.80.80	52,660 (100)	6.91.97*	4,144 (100)	5.72.84*	10,188 (100)	12.51.94*	36,359 (100)	6.41.84*
Age at death										
20-34 years	9(1.5)	0.6	208(0.4)	0.1	51(1.2)	0.2	33(0.3)	0.1	107(0.3)	0.1
35–49 years	56(9.2)	3.22.08*	2,115 (4.0)	1.32.50*	401(9.7)	1.42.50*	409(4.0)	1.93.15*	1,121(3.1)	1.21.58*
50-64 years	159(26.2)	8.61.61	14,490(27.5)	8.31.92*	1,403(33.9)	7.32.57*	3,296(32.4)	15.22.31*	9,055(24.9)	7.41.20*
65–79 years	269(44.3)	20.60.67	23,911(45.4)	24.62.47*	1,618(39.0)	19.51.98*	4,933(48.4)	49.51.67*	16,610(45.7)	22.52.46*
80 + years	114(18.8)	23.1	11,936 (22.7)	31.40.73	671(16.2)	24.50.42	1,517(14.9)	47.1	9,466(26.0)	31.10.73
		-0.96						-0.02		

\*APC: Annual Percent Change with statistical significance (p < 0.05).

incidence rate of 1.9. In the same age group, mortality rates for Puerto Rican women also increased significantly (APC = 2.08, p < 0.05), as well as for NHW and Hispanic. It should be noted that between ages 20–34 and 35–49, women in PR have the highest mortality rates of 0.6 and 3.2 per 100,000 at an increasing annual percent change of 2.08% for the 35–49 age group among all ethnic and racial groups (p < 0.05). Table 2

Of note, an increase in the incidence rates of endometrial cancer was observed for women in Puerto Rico in all age groups. However, in the group of 80 + the increase was not statistically significant compared to all other races and ethnicities in the US (Table 1).

# 4. Discussion

This study shows that Puerto Rican women between the ages of 20 and 64 years have a greater incidence rate of Endometrial Cancer when compared to Hispanic, NHB, and NHW, which suggests the presence of factors that might increase the risk of developing EC earlier in life. One pivotal factor is obesity. In 2013 a study found that 77.4% of the PR population is either overweight or obese, with lower-income and non-smoking women being the group with the highest obesity rate (Pérez et al., 2013). More recently, the CDC BRFSS published data from 2021

stating that the Obesity Rate among female participants in Puerto Rico was 37.5% vs. an overall US prevalence of 33.7% (Centers for Disease Control and Prevention, 2023). This, in association with the growing prevalence of obesity overall (Registries, 2020; Pérez et al., 2013) and among younger age groups (Agha and Agha, 2017), can help explain the growing incidence of endometrial cancer that is particularly affecting the PR population as people experience obesity for longer periods of time.

In addition, the decrease in fertility rate (Ellison-Barnes et al., 2021), therefore an increase in nulliparity, can also contribute to the increasing incidence of endometrial cancer and greater estrogenic exposure. The influence of obesity increasing infertility may also contribute to endometrial cancer incidence.

In the incidence data analysis by age groups considering all endometrial cancer histology types, the group of Puerto Rican women ages 20–34 years has a statistically significant annual percent incidence rate change of 5.02%, the highest percentage change among ethnic groups between the years of 2000–2018. This suggests a steeper increase in new cases among younger patients. This association was also observed in a study published in 2010 that analyzed data from Puerto Rican patients diagnosed with Endometrial Cancer (Ortiz et al., 2010), which found that women between the ages of 20 and 34 years old showed to have the fastest increase in incidence with an APC of 9.2%. Importantly, the author mentions careful interpretation of the APC due to the small number of cases in the studied sample from 1992 to 2003. For comparison, the sample size of this study contains more cases for each ethnic group: PR 97, Hispanic 439, NHW 476 and NHB 148. Therefore, confirming the previously seen association of increasing incidence rates in comparison with NHB and NHW which remains at a lower APC of 2.36% and 2.2% in comparison with 2010 by Ortiz et al. data of APC 10.5% and 6.4% respectively. The Hispanic trend in incidence rates is like the PR trend with an APC of 4.84%.

In addition, Puerto Ricans have a higher rate of diagnosing EC at a localized stage while NHB have the highest rate of discovering the diagnosis having distant metastasis. Table 3. This discrepancy is one of the contributing factors that lead to the poorer outcomes seen in the NHB population concerning EC. This is exemplified through the fact that the NHB population counts with the highest overall mortality rate due to EC compared to all other ethnic groups. However, when analyzed by age group, Puerto Rican patients aged 20–49 years are more likely to die from EC than young NHB, NHW, or Hispanic patients of the same ages. This points to what can be an important indicator of health disparities that lead to increased incidence and mortality rates in young Puerto Rican females. These disparities may include difficult access to medical attention, low socioeconomic status, increased obesity rates at younger ages, or host inherent biologic factors that might increase the prevalence of higher-risk ECs.

The overall survival rate (RSR) at 5 years for the PR population was 79.9%, which is 1.5% greater than the one obtained from data from 1992 to 2003 (Ortiz et al., 2010), which might indicate that, at present, there is a greater survival rate despite increasing incidence. Table 3. According to the SEER program, the overall survival rate in the United States from 2012 to 2018 was 81.3%. Literature from 2018, reports worse survival outcomes for NHB younger than 50 years (81.5%) compared with NHW (90.6%) for stage IB tumors and presentation with more aggressive non-endometrioid types. This difference in survival persisted when comparing NHW and NHB women with stage III Tumors (Ortiz et al., 2010).

This study reveals a substantial health disparity among young Puerto Rican females with greater endometrial cancer incidence rates and an increased risk of dying from EC compared to Hispanic, NHW, and NHB. This sheds light on the importance of further research to characterize what are the contributing risk factors that are making our young population more vulnerable to endometrial cancer and to promote educational campaigns focused on the prevention of risk factors and early detection of this disease since there is deficient public awareness of obesity as a risk factor for endometrial cancer.

Multiple surgeries performed for benign indications decrease women at risk of developing endometrial cancer, providing a more accurate denominator for incident rates. One limitation of this study is that the analysis is not corrected by hysterectomy rate. More studies are needed to investigate the BMI of patients diagnosed with endometrial cancer, the prevalence of other known risk factors for endometrial cancer, and a clinical correlation with pathology biomarkers and the gynecologist index of suspicion and consideration of indications to perform endometrial sampling procedures in view of the epidemiologic data of susceptibility in a younger cohort.

#### CRediT authorship contribution statement

Ana Rosario-Santos: Conceptualization, Methodology, Project administration, Visualization. Carlos R. Torres-Cintrón: Methodology, Software, Formal analysis. Ana G. López-Rexach: . Paulina Gonzalez-Carcache: Conceptualization. Guillermo Tortolero-Luna: Conceptualization, Methodology, Project administration, Visualization, Supervision. Sharee Umpierre: Conceptualization, Methodology, Project administration, Visualization, Supervision.

# Table 3

1-, 3-, and 5-year relative survival rate (RSR) of endometrial cancer: 2010–2014 (follow up to 2019).

Total cases	1-year RSR (95% CI)	3-year RSR (95% CI)	5-year RSR (95% CI)
Overall –	91.80	82.91	79.91
2,561	(90.60-92.87)	(81.26-84.46)	(78.09-81.63)
Stage			
Localized –	96.58	92.27	90.01
1,636	(95.45–97.49)	(90.61-93.72)	(88.09–91.74)
Regional – 567	90.71	74.17	69.67
	(87.85–92.98)	(70.11–77.83)	(65.33–73.66)
Distant – 151	57.00	30.15	23.04
	(48.61–64.56)	(22.89–37.77)	(16.50-30.29)
Unstaged –	82.32	71.25	69.44
207	(76.21-87.09)	(64.18–77.32)	(62.08–75.88)

Notes: Year of diagnosis 2010–2014 (follow up to 2019 mortality cutoff). Only includes first primary cases (sequence 0 or 1) with microscopic diagnosis confirmation and age at dx between 20 and 99 years old.

## **Declaration of Competing Interest**

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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