1 Trends in Uterine Cancer Incidence in the United States: The Contribution of Age, Period and
2 Cohort Effects

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Abstract

Objective: In the U.S., uterine cancer incidence is rising, with racial and ethnic minorities experiencing the largest increases. We performed age-period-cohort analyses using novel methods to examine the contribution of age at diagnosis (age), year of diagnosis (period), and birth cohort (cohort), to trends in uterine cancer incidence.

Methods: We used uterine cancer incidence data from the Surveillance, Epidemiology, and End Result (SEER) 12 database (1992-2019), and performed hysterectomy-correction. We generated hexamaps to visualize age, period, and cohort effects, and used mutual information to estimate the percent contribution of age, period, and cohort effects, individually and combined, on uterine cancer incidence, overall and by race and ethnicity and histology.

Results: Hexamaps showed an increase in uterine cancer in later time periods, and a cohort effect around 1933 showing a lower incidence compared with earlier and later cohorts. Age, period, and cohort effects combined contributed 86.6% (95% CI: 86.4%, 86.9%) to the incidence. Age effects had the greatest contribution (65.1%, 95% CI: 64.3%, 65.9), followed by cohort (20.7%, 95% CI: 20.1%, 21.3%) and period (14.2%, 95% CI: 13.7%, 14.8%) effects. Hexamaps showed higher incidence in recent years for non-Hispanic Blacks and non-endometrioid tumors.

Conclusions: Age effects had the largest contribution to uterine cancer incidence, followed by cohort and period effects overall and across racial and ethnic groups and histologies.

Impact: These findings can inform uterine cancer modeling studies on the effects of interventions that target risk factors which may vary across age, period, or cohort.

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Introduction

Uterine cancer is the fourth most common cancer among females and the sixth most common cause of cancer-associated death in women the United States, with an estimated 66,200 new cases and 13,030 deaths in 2023.[1] The incidence of uterine cancer is increasing and expected to surpass colorectal cancer as the third leading cause of cancer in females, and fourth leading cause of cancer death by 2040.[2-4] Specifically, since 2001, uterine cancer has increased across racial and ethnic groups from 40.8 per 100,000 in 2001 to 42.9 per 100,000 in 2016 (Annual Percent Change (APC) = 0.5, p<0.001), with the largest increases observed in non-Hispanic Black, Hispanic, and Asian women.[5]

There are three main histologic types of uterine cancer: endometrioid, non-endometrioid, and sarcoma. Endometrioid cancers make up approximately 75% of all uterine cancers and have the best prognosis. Non-endometrioid cancers, which include serous and clear cell carcinomas, account for approximately 15-20% of all uterine cancers, are more aggressive, and are associated with worse outcomes. Lastly, uterine sarcomas, which arise in the myometrium, are the least common group and the least well-studied.[2,3] Non-Hispanic Black women have a two- to four-fold increased risk of developing non-endometrioid uterine cancers compared with non-Hispanic White women, which may contribute to the higher mortality observed in these women.[5]

Age-period-cohort (APC) analysis plays an important role in understanding temporal elements in epidemiology by classifying three types of time-varying phenomena: age effects, period effects, and cohort effects, birth cohort effects specifically in this analysis. Age effects are variations associated with the biological changes and social experiences of aging; period effects are variations across time that affect all age groups equally; and cohort effects are variations due to common exposures or experiences of a group of people (birth cohort) as they move

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92   through time.[6,7] APC analysis can help elucidate factors that may be contributing to observed

93   uterine cancer incidence trends. For example, changes in the prevalence of established risk

94   factors for uterine cancer, including obesity and diabetes, which increase risk, and parity and

95   hormonal contraceptive use, which decreases risk[8], may vary across age, time period, and birth

96   cohort. Further, this information can be used to predict future uterine cancer incidence and

97   prioritize interventions and populations for reducing uterine cancer risk.

98   There is limited research on age-period-cohort analyses of uterine cancer incidence in the

99   U.S. Further, given that age at diagnosis, year of diagnosis, and patient birth year are linearly

100   dependent, traditional regression models cannot effectively distinguish their relative

101   contributions to changes in incidence without additional assumptions or constraints.[9] By utilizing

102   a novel data visualization method in conjunction with a quantitative information theory-based

103   analytic approach, we are better able to capture and describe these competing temporal effects

104   which can inform model designs and targeted prevention efforts. This analysis aims to estimate

105   and compare the effects of age, period, and cohort on uterine cancer incidence in the U.S.

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107   **Materials and Methods**

108   We extracted uterine cancer incidence data from the Surveillance, Epidemiology, and

109   End Result (SEER) 12 registry database (1992-2019)[10] for patients with known age between 0

110   and 84 years. We included patients whose cancers had a primary site ICD-10 diagnosis code in

111   C54.0-C55.9. We included only cancers that had diagnostic confirmation by either microscopic

112   confirmation or positive histology. We categorized uterine cancers into the following three

113   histologic groups with respective ICD-0-3 histology codes: endometrioid: 8140, 8380-8383,

114   8480, 8570; non-endometrioid: 8000, 8020, 8050, 8255, 8260, 8310, 8323, 8441, 8460-8461,

115   8481,8560, 8950-8951,8980-8982; and sarcoma: 8800-8805, 8810-8811, 8813-8815, 8890-

116   8891, 8894-8896, 8900-8902, 8910, 8912, 8930-8931, 8933, 8935, 8990-8991. We extracted

117   the following variables from SEER: age at diagnosis, year of diagnosis, and race and ethnicity

118   defined as Non-Hispanic White, Non-Hispanic Black, Non-Hispanic American Indian/Alaska

119   Native, Non-Hispanic Asian-American/Pacific Islander, and Hispanic (all races). Although

120   hysterectomy effectively removes a woman from the at-risk population, and hysterectomy

121   prevalence in the U.S. can reach over 40%[11], information about prior hysterectomy is not

122   available in SEER. In separate analyses, we estimated hysterectomy-adjusted incidence rates

123   of uterine cancer based on age- and period-specific hysterectomy prevalence data from several

124   nationally-representative databases, including The National Hospital Discharge Survey and

125   databases from The Healthcare Cost and Utilization Project (i.e., The Naitonal Inpatient Sample,

126   State Inpatient Databases, and The State Ambulatory Surgery and Services Databases).[12]

127   We generated hexamaps to visualize the simultaneous effects of age, period, and cohort

128   on uterine cancer incidence. Hexamaps are similar to traditional heatmaps, but use hexagonal

129   instead of rectilinear tiled maps, which create equally spaced isobars for all three of the age,

130   period, and cohort axes, and enable accurate trend recognition. Color change perpendicular to

131   an isobar indicates greater effect strength.[13] (Figure 1) For age, period, and cohort effects, we

132   used age at uterine cancer diagnosis, year of uterine cancer diagnosis, and birth year, which

133   was determined by subtracting age from year, respectively.

134   Quantifying the comparative effect strengths of our collinear predictors (age, period, and

135   cohort) can be achieved by recognizing non-linear data features. Mutual information is a

136   quantity that measures non-linear associations between variables.[14] Functionally, mutual

137   information serves as a generalization of the correlation coefficient, where the reduction in

138   variance of one variable (e.g., incidence rate), due to a single observation of another variable

139   (e.g., age at diagnosis), is used to quantify the association. Thus, we used a composite

140   information theory-based metric to parse out the relative importance of age, period and cohort in

141   our observational data. The dataset is first discretized into equal width bins, with the number of

142   bins equal to the number of calendar years present in the data. This is done to avoid bias due to

143   differences in data ranges between the age at diagnosis, year at diagnosis, and birth year

144 variables.[15] Our composite measure is broken down into four percentage-based components.

145 The first is the Shannon's Entropy of the incidence with variables conditioned on the age,

146 period, and cohort variables subtracted from the unconditional Shannon's Entropy of incidence,

147 divided by the Shannon's Entropy of incidence and finally rescaled to a percentage. This serves

148 as a measure of the total amount of information contained in the predictor variables (age,

149 period, and cohort) as a percentage of the total amount of information needed to specify the

150 incidence rate. This is sensitive to the variance in the underlying incidence data. The second

151 and third components are measures of the contribution of age and period predictors. Formally,

152 this is defined as the minimum of the mutual information between incidence and predictors, and

153 the conditional mutual information between incidence and predictors when conditioned on

154 cohort. This value is then converted into a percentage of the total information contained in the

155 predictors. As age and period separately have non-zero mutual information with cohort in

156 observational data, conditioning is necessary in case the single predictor effects are mediated

157 via the cohort predictor. Practically this can be interpreted as the contribution of the predictor

158 alone to the incidence rate. The fourth component is similar to the second and third however the

159 minimum is taken out of the mutual information between incidence and cohort, the mutual

160 information conditioned on age, and the mutual information conditioned on period. This is done

161 for the same reason, to extract the contribution of cohort alone on the incidence.[16] We then

162 developed 95% confidence intervals around the mutual information contribution estimates using

163 a method developed by Stefani and colleagues.[17]

164   We estimated the percent contribution of age, period, and cohort effects to the uterine

165 cancer incidence rate, individually and combined, overall with and without hysterectomy-

166 correction. Then, using only hysterectomy-corrected uterine cancer incidence rates, we

167 generated new hexamaps and estimated the percent contribution of age, period, and cohort

168 stratified by race and ethnicity, and by histology. We also plotted hysterectomy-corrected and -

169 uncorrected incidence trends by age, period, and cohort separately (Supplemental Figures 1a-

170 1c). We analyzed all data using R Version 4.3.1.

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174 *Data availability*

175   The data analyzed in this study are available from the SEER database, which is

176 available from the National Cancer Institute (**https://seer.cancer.gov/data-software**/).

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178 **Results**

179   We identified 132,754 uterine cancer cases diagnosed between 1992 and 2019. The

180 number of cases increased across time periods with 45.4% of cases coming from the most

181 recent 10 years of data (2010-2019). While the greatest proportion of cases were non-Hispanic

182 White, the proportion of non-Hispanic White cases decreased over time from 78.8% in 1992-

183 2000 to 60.3% in 2010-2019. Correspondingly, the proportion of cases in all other racial and

184 ethnic groups increased over time. While the proportion of non-endometrioid cases increased

185 over time from 14.6% in 1992-2000 to 21.1% in 2010-2019, the proportion of endometrioid

186 cases slightly decreased over time from 78.4% in 1992-2000 to 72.8% in 2010-2019. The

187 proportion of local stage cancers decreased over time (73.6% in 1992-2000 and 68.4% in 2010-

188 2019) with corresponding increases in regional and distant stage disease (14.4% and 8.2% in

189 1992-2000 and 19.8% and 9.2% in 2010-2019, respectively). (Table 1)

190   The hexamaps for uterine cancer incidence overall show a strong age effect which is

191 expected, given that the majority of uterine cancers are diagnosed in postmenopausal women.

192 In order to better visualize the color gradients in women most at risk of uterine cancer, we

193 truncated the hexamaps at age 45. (Figures 2a and 2b) Consistent with prior literature on the

194   importance of using hysterectomy-corrected data to accurately estimate the uterine cancer

195   incidence in women who are at risk of the disease[3,18-21], we observed substantial differences in

196   incidence between hysterectomy-corrected and –uncorrected data, that varied across age, time

197   period, and birth cohort. (Supplemental Figures 1a-1c) However, the total contribution of age,

198   period, and cohort effects to uterine cancer incidence was similar whether using hysterectomy

199   uncorrected (86.2%, 95% CI 85.9%-86.4%) or corrected data (86.6%, 95% CI 86.4%-86.9%).

200   (Figure 2c) Using the hysterectomy-corrected data, the hexamap shows a slight cohort effect,

201   with women born around 1933 having a lower rate of uterine cancer, and a period effect with

202   higher rates in earlier and later time periods. (Figure 2b) Age effects had the greatest

203   contribution to incidence (65.1%, 95% CI: 64.3%, 65.9%), followed by cohort effects (20.7%,

204   95% CI: 20.1%, 21.3%) then period effects (14.2%, 95% CI: 13.7%, 14.8%). (Figure 2c)

205   The hexamaps also showed differences in age, period, and cohort effect contributions to

206   uterine cancer incidence by race and ethnicity. (Figures 3a-3e) The hexamap for non-Hispanic

207   White patients shows a higher incidence in earlier time periods, followed by a decrease, and

208   then a slight increase in later time periods. There was a cohort effect between birth years 1933

209   and 1938 showing a lower incidence rate. The hexamap for non-Hispanic Black patients shows

210   an increase in incidence in later time periods, particularly for women aged 60-75 years. The

211   hexamaps for Non-Hispanic AI/ANs and APIs show an increase in incidence in later time

212   periods and younger birth cohorts. The hexamap for Hispanic patients shows a slight increase

213   in incidence in later time periods, particularly for women aged 60-70 years. The contribution of

214   age, period, and cohort effects combined had the largest contribution to incidence for non-

215   Hispanic White patients (86.0%, 95% CI: 85.7, 86.4) and the smallest contribution for non-

216   Hispanic AI/ANs (78.1%, 95% CI: 72.2%, 83.4%). While age effects still had the largest

217   contribution to uterine cancer incidence for all racial and ethnic groups, it had the greatest

218   contribution for non-Hispanic White and Hispanic patients (62.5%, 95% CI: 61.4%, 63.7% and

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219   62.2%, 95% CI: 60.0%, 64.5%, respectively), and the lowest contribution for non-Hispanic

220   AI/ANs (43.2%, 95% CI: 32.4%, 56.1%). Cohort effects had the next largest contribution to

221   uterine cancer incidence for all racial and ethnic groups, but was highest for non-Hispanic

222   AI/ANs (38.2%, 95% CI: 27.7%, 50.6%) and lowest for non-Hispanic Whites (21.8%, 95% CI:

223   20.9%, 22.7%). (Figure 3f)

224   The hexamaps by uterine cancer histology show differences in incidence trends across

225   ages, periods, and cohorts. (Figures 4a-4c) The hexamap for endometrioid cancers shows a

226   period effect with an overall decreasing incidence over time, but a slight cohort effect around the

227   1938 birth year shows a lower incidence compared to the older and younger birth cohorts. The

228   hexamap for non-endometroid cancers shows a period effect with a higher incidence in later

229   time periods. Period and cohort effects were more difficult to distinguish in the hexamap for

230   sarcomas given the smaller sample size and lower incidence rate. While age effects contributed

231   the most to incidence across histologies, it had the greatest contribution for endometrioid

232   cancers (62.6%, 95% CI: 61.8%, 63.4%) and the smallest contribution for sarcomas (53.1%,

233   95% CI: 52.3%, 53.9%). Cohort effects played the next largest role in incidence across

234   histologies, contributing 35.2% (95% CI: 34.5%, 36.0%) for sarcomas, 26.6% (95% CI: 25.9%,

235   27.3%) for non-endometrioid cancers, and 22.6% (95% CI: 22.0%, 23.2%) for endometrioid

236   cancers. While period effects were similar for endometrioid and non-endometrioid cancers,

237   contributing 14.8% to the incidence rate, they had a smaller contribution for sarcomas (11.7%,

238   95% CI: 11.1%, 12.3%). (Figure 4d) Percent contribution estimates for all racial and ethnic and

239   histologic subtype groups are reported in Supplemental Table 1.

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241   **Discussion**

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243   This study evaluated the individual and total contributions of age, period, and cohort effects

244   to uterine cancer incidence using novel methodologies to both visually and computationally

245   quantify their impact. The hexamap for the overall hysterectomy-corrected uterine cancer

246   incidence displayed the increase in incidence observed in recent years[3] and highlighted a

247   cohort effect with birth cohorts around 1933 having a lower incidence compared with earlier and

248   later birth cohorts. The hexamaps further highlighted different trends across racial and ethnic

249   groups and histologic subtypes, with the higher rates in recent years more pronounced for non-

250   Hispanic Black women compared with other racial and ethnic groups, and for women with non-

251   endometrioid cancers compared with endometrioid tumors and sarcomas. These results support

252   prior research showing non-Hispanic Black women have higher rates of non-endometrioid

253   cancers compared with other racial and ethnic groups.[3] Overall, the combined contribution of

254   age, period, and cohort effects to hysterectomy-corrected uterine cancer incidence was 86.6%,

255   with age effects contributing the most (65.2%), followed by cohort (20.7%) and period (14.2%)

256   effects.

257   Recent research using SEER 18 data from 2000-2015 highlighted the rising incidence of

258   uterine cancer in the U.S., which is largely driven by increases in non-endometrioid cancers[3],

259   and our study using data from SEER 12 from 1992 to 2019 supports this with the overall and

260   histology-specific hexamaps. Further, a recent study evaluating international trends in uterine

261   cancer incidence observed a strong cohort effect in U.S. White women using SEER 9 data from

262   1978-2012, showing the highest incidence in women born around the 1920s; however, the data

263   did not have a hysterectomy-correction.[22] Similarly, in our study using hysterectomy-corrected

264   data, the hexamap for non-Hispanic White women showed the highest incidence in women born

265   between 1913-1923.

266   The total contribution of age, period, and cohort effects to uterine cancer incidence of 87%

267   that we observed suggests that approximately 13% of the total contribution is due to other

268　factors that do not vary across age, period, or birth cohort. This aligns with research showing

269　approximately 10% of uterine cancers are hereditary, including both familial (family history of

270　uterine cancer) and genetic (Lynch Syndrome) factors.[23] When comparing across histologies,

271　we observed that endometrioid cancers had the highest total contribution of age, period, and

272　cohort effects to incidence (86.5%), followed by non-endometrioid (85.3%), and sarcomas

273　(80.2%), suggesting that there may be underlying risk of these aggressive tumors that is

274　constant and not influenced by period or cohort effects. For example, a study by Long *et al*.

275　observed a greater proportion of cancer predisposition pathogenic variants in Type II compared

276　with Type 1 uterine cancers.[24] Lastly, we observed differences in the total contribution of age,

277　period, and cohort effects to incidence across racial and ethnic groups, with non-Hispanic White

278　patients having the highest contribution (86.0%) and non-Hispanic AI/AN having the lowest

279　contribution (78.1%), however, the confidence intervals were wide for the non-Hispanic

280　American Indian/Alaskan Natives due to a smaller sample size.

281　　　Similar to most cancers, age is a strong risk factor for uterine cancer, and our study

282　highlights its impact on uterine cancer incidence showing age effects had the largest

283　contribution to incidence compared with cohort and period effects. The median age at uterine

284　cancer diagnosis is 63 years, with approximately 79% of all uterine cancers being diagnosed in

285　women aged 55 years and older.[25] Further, we showed that the risk of uterine cancer increases

286　more than 8-fold between the ages of 45 and 75 years. (Supplemental Figure 1a). Not

287　surprisingly, age had a far greater effect on the incidence of uterine cancer than either period or

288　cohort effects.

289　　　Historically, endometrioid uterine cancers have been thought to be estrogen-dependent and

290　associated with obesity and other reproductive and hormonal risk factors, while non-

291　endometrioid uterine cancers have been thought to be estrogen-independent and associated

292　with distinct molecular abnormalities.[26] However, recent research suggests that obesity may be

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293   related to both endometrioid and non-endometrioid uterine cancers.[26,27] In the U.S., while

294   obesity rates have increased over time, there are also differences across ages and birth cohorts

295   with the highest obesity prevalence observed in women 60-69 years born in 1950, and the

296   second highest obesity prevalences observed in women 50-59 years born in 1940 and 1960

297   and women 40-49 years born in 1970.[28] Further, obesity rates differ by race and ethnicity with

298   non-Hispanic Black women having the highest obesity prevalence (56.9%) and non-Hispanic

299   Asian women having the lowest obesity prevalence (17.1%) in 2017-2018.[29] Thus, obesity may

300   be one modifiable risk factor contributing to the observed age, period, and cohort effects on the

301   uterine cancer incidence rate.

302   Other hormonal risk factors for uterine cancer have changed over time and vary by race and

303   ethnicity, including parity and use of hormonal contraceptives and postmenopausal hormone

304   replacement therapy (HRT), and may play a role in the contribution of both period and cohort

305   effects to uterine cancer incidence.[30,31] In the U.S., the total fertility rate has decreased over

306   time between 2010 and 2021. In 2021, Native Hawaiian or Other Pacific Islander women had

307   the highest fertility rate, and Asian women had the lowest.[32] In the U.S., oral contraceptive use

308   peaked in the early 1970's[33] which may have contributed to the lower incidence observed in the

309   hexamaps among the 1933 birth cohort. Overall, the use of hormonal contraceptives has

310   declined in the U.S. between 2000 and 2017, primarily driven by a reduction in oral

311   contraceptive use. While there has been an increase in the use of intrauterine devices, rates are

312   still lower than oral contraceptives. Further, non-Hispanic Whites had the highest rates of

313   hormonal contraceptive use compared to minority populations.[34] Postmenopausal HRT,

314   particularly estrogen-only formulations, have been associated with an increased risk of uterine

315   cancer[8], and trends in use have changed over time. Our finding in non-Hispanic Whites that

316   women born between 1913-1923 had the highest uterine cancer incidence may, in part, be

317   explained by the push for women to use unopposed estrogen for menopause in the 1960's

318 before research was published showing an association between unopposed estrogen use and

319 increased risk of uterine cancer in the mid-1970's.[35,36] In the 1990's, research then showed the

320 risk of uterine cancer could be reduced by lowering the dose of estrogen and combining it with

321 progesterone.[36,37] However, following the early stop of the Women's Health Initiative trial over

322 safety concerns of estrogen-progestin therapy, there was a dramatic reduction in the prevalence

323 and initiation of HRT.[38,39] Further, HRT initiation rates vary across racial and ethnic groups with

324 non-Hispanic Whites having the highest rates of HRT initiation both pre- and post-WHI. Further,

325 the decline in HRT initiation post-WHI was greatest in non-Hispanic White patients and lowest in

326 Hispanic patients.[38,39]

327   Our study had several strengths. We used data from SEER, which is a longitudinal

328 population-based cancer registry with microscopically confirmed uterine cancer cases. We

329 performed a hysterectomy correction on the incidence rate, which allowed us to evaluate

330 incidence trends accurately over time and across racial and ethnic groups. We used a novel

331 methodology to visually and empirically evaluate the total and individual contributions of age,

332 period, and cohort effects to the uterine cancer incidence rate, which could be used in future

333 age-period-cohort analyses. We examined our results by race and ethnicity and histologic

334 subtype to evaluate the potential differing contributions of risk factors that vary across age, time

335 period, and birth cohort in these different groups.

336   Our study also had limitations. While we used nationally representative data to obtain

337 hysterectomy prevalence estimates for our hysterectomy correction, our incidence data came

338 from SEER 12 which only accounts for 12.2% of the U.S. population and may not be

339 representative of the total population.[25] The hexamaps were difficult to interpret for subgroups

340 with small sample sizes, such as American Indian/Alaskan Natives and sarcomas. Further, the

341 percent contribution estimates for American Indian/Alaskan Natives had wide confidence

342 intervals.

343   Overall, we observed differences in uterine cancer incidence rates across age, time period,

344   and birth cohort. Further, we observed differences in the individual and combined percent

345   contribution of age, period, and cohort effects to uterine cancer incidence overall, and across

346   racial and ethnic groups and histologic subtypes. These findings add to and expand the limited

347   literature on age-period-cohort analyses for uterine cancer incidence in the U.S., by including

348   data on race and ethnicity and histology, and estimating the contribution of each effect to the

349   incidence rate. The findings of our study can be used in several ways to reduce uterine cancer

350   incidence. Specifically, they can be used to inform model decision-making, such as whether a

351   uterine cancer model should be cohort-specific. Further, these findings can be used in modeling

352   studies of uterine cancer incidence to accurately estimate the effects of interventions or public

353   health measures that target risk factors that may vary across age groups, time periods, or birth

354   cohorts. For example, using these results, researchers could explore key ages to target for a

355   new screening modality or target intervention, and to see how the resulting impact may change

356   over time. These results can help prioritize investment in research and interventions that will

357   have the largest impact on reducing uterine cancer incidence. Further, this work highlights

358   differences in age, period, and cohort effects on uterine cancer incidence across racial and

359   ethnic groups and can inform disparities research. Lastly, our findings on the percent

360   contribution of age, period, and cohort effects can be used for accurate forecasting of uterine

361   cancer incidence.

362   Conflicts of Interest

363   Dr. Wright has received royalties from UpToDate and research support from Merck. Dr. Elkin

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365   Author Contributions

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479

480   **Figure 1**. Illustration of a hexagonal heatmap (hexamap) depicting the age, period, and cohort

481   isolines

482   **Table 1**. Baseline characteristics of uterine cancer cases in SEER 12 (1992-2019)

483   **Figure 2a.** Hexamap for the uterine cancer incidence rate (per 100,000) overall without

484   hysterectomy correction (SEER 12)

485   **Figure 2b.** Hexamap for the uterine cancer incidence rate (per 100,000) overall with

486   hysterectomy correction (SEER 12)

487   **Figure 2c.** Percent contribution to the incidence rate for age, period, and cohort effects

488   individually and combined stratified by hysterectomy correction

489   **Figure 3a.** Hexamap for the uterine cancer incidence rate (per 100,000) in Non-Hispanic White

490   women (SEER 12)

491   **Figure 3b.** Hexamap for the uterine cancer incidence rate (per 100,000) in Non-Hispanic Black

492   women (SEER 12)

493   **Figure 3c.** Hexamap for the uterine cancer incidence rate (per 100,000) in Non-Hispanic

494   American Indian/Alaska Native women (SEER 12)

495   **Figure 3d.** Hexamap for the uterine cancer incidence rate (per 100,000) in Non-Hispanic Asian

496   and Pacific Islander women (SEER 12)

497   **Figure 3e.** Hexamap for the uterine cancer incidence rate (per 100,000) in Hispanic women

498   (SEER 12)

499   **Figure 3f.** Percent contribution to the uterine cancer incidence rate for age, period, and cohort

500   effects individually and combined stratified by race and ethnicity

501   **Figure 4a.** Hexamap for the incidence rate (per 100,000) of Endometrioid uterine cancers

502   (SEER 12)

503   **Figure 4b.** Hexamap for the incidence rate (per 100,000) of Non-Endometrioid uterine cancers

504   (SEER 12)

505   **Figure 4c.** Hexamap for the incidence rate (per 100,000) of Sarcoma uterine cancers (SEER

506   12)

507   **Figure 4d.** Percent contribution to the uterine cancer incidence rate for age, period, and cohort

508   effects individually and combined stratified by histology

Figure 1.
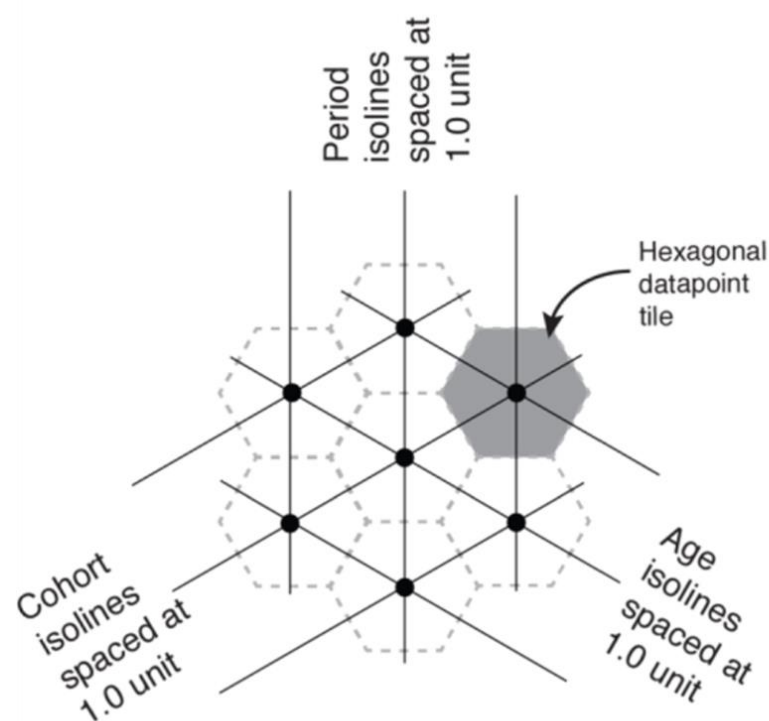
Figure 2a.
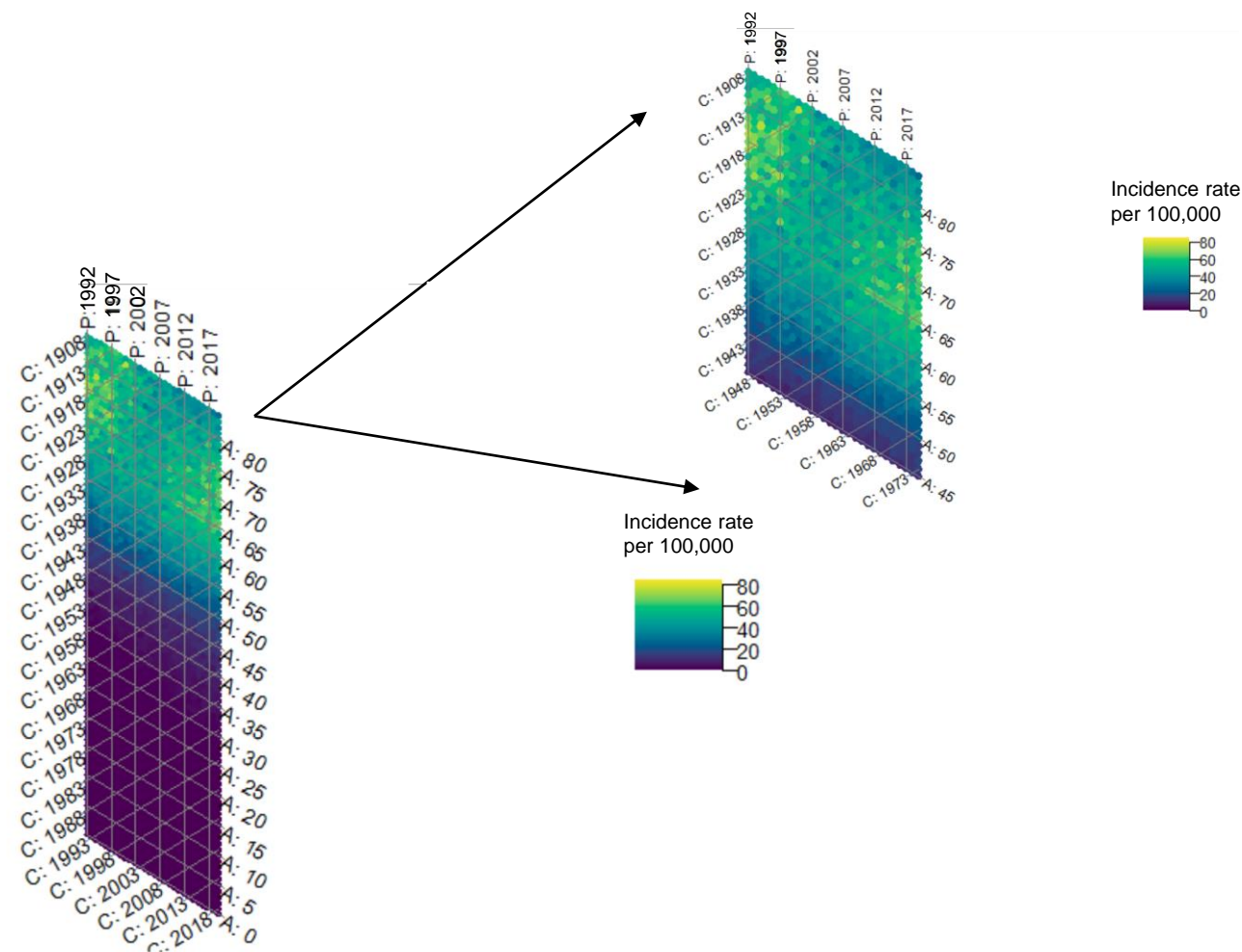
*Abbreviations: C = Cohort; P = Period; A = Age

Figure 2b.
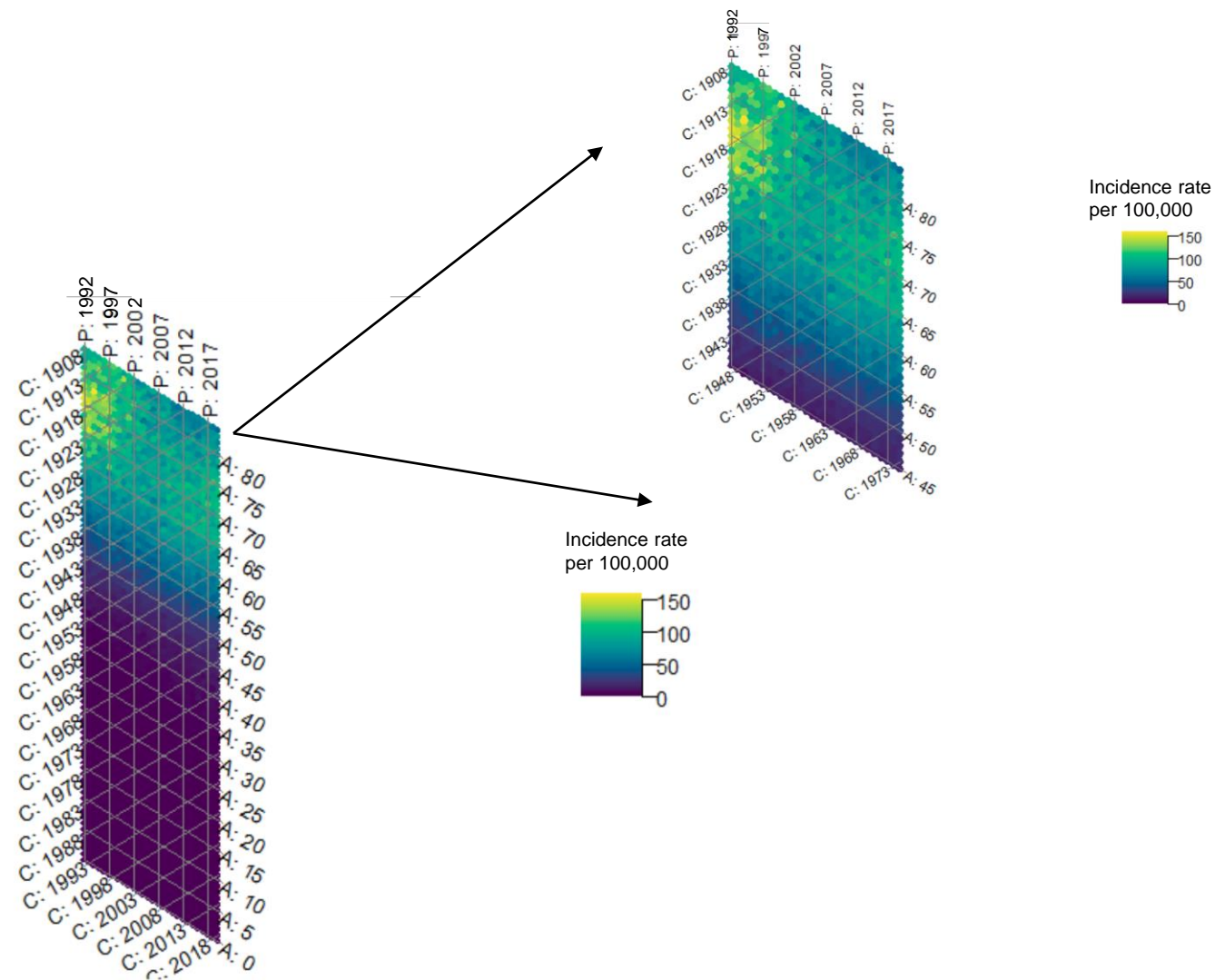
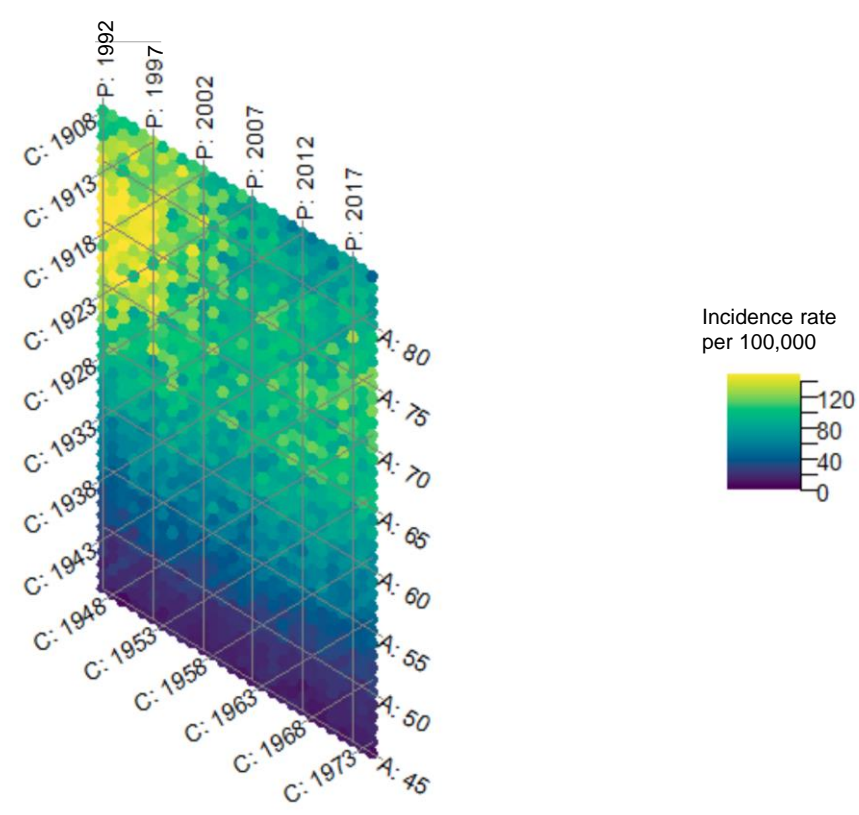*Abbreviations: C = Cohort; P = Period; A = Age

Figure 2c.
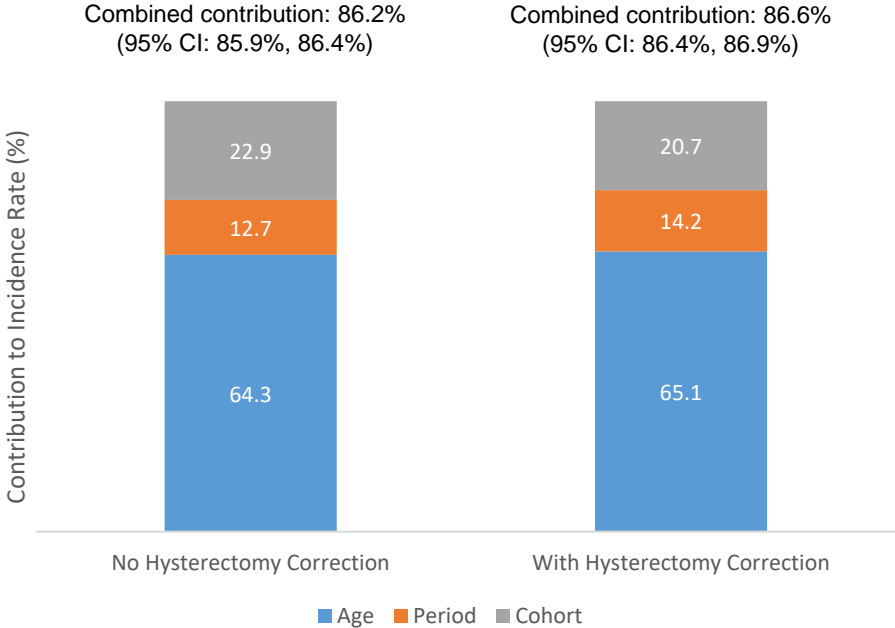
*No Hysterectomy Correction:
  Cohort: 22.9 (95% CI: 22.4, 23.5)
  Period: 12.7 (95% CI: 12.3, 13.2)
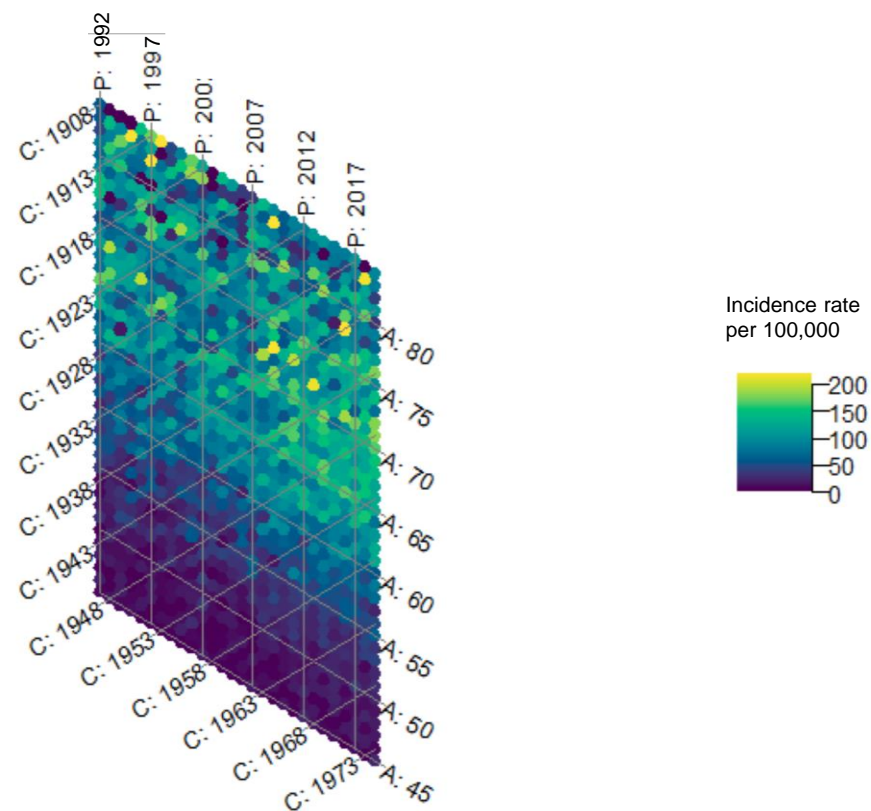 Age: 64.3 (95% CI: 63.6, 65.1)

With Hysterectomy Correction:
  Cohort: 20.7 (95% CI: 20.1, 21.3)
  Period: 14.2 (95% CI: 13.7, 14.8)
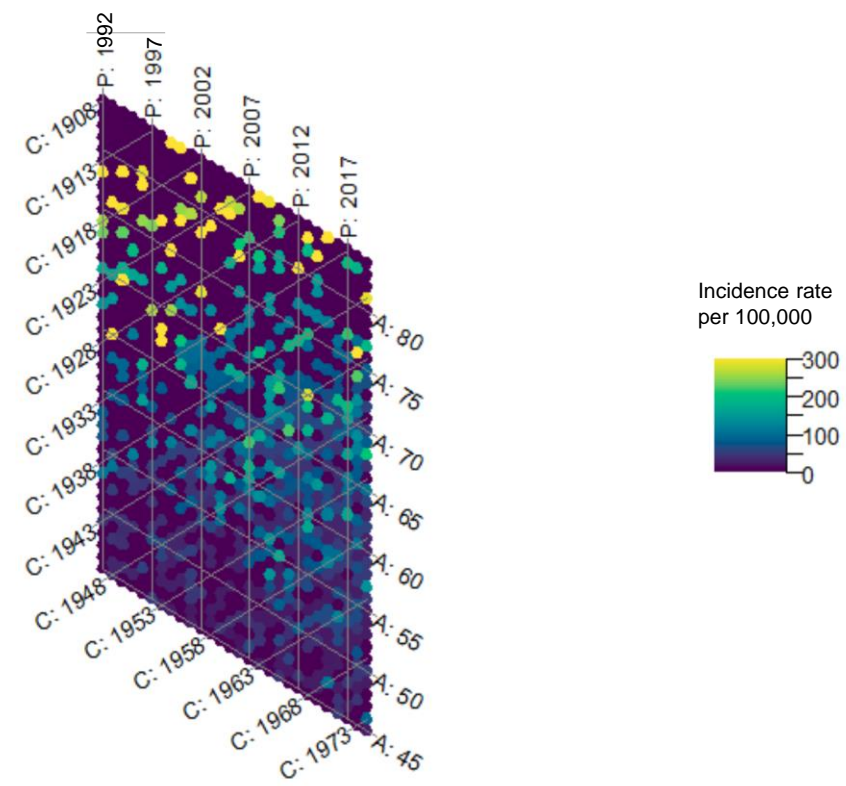 Age: 65.1 (95% CI: 64.3, 65.9)

Figure 3a.

*Abbreviations: NH = Non-Hispanic; C = Cohort; P = Period; A = Age
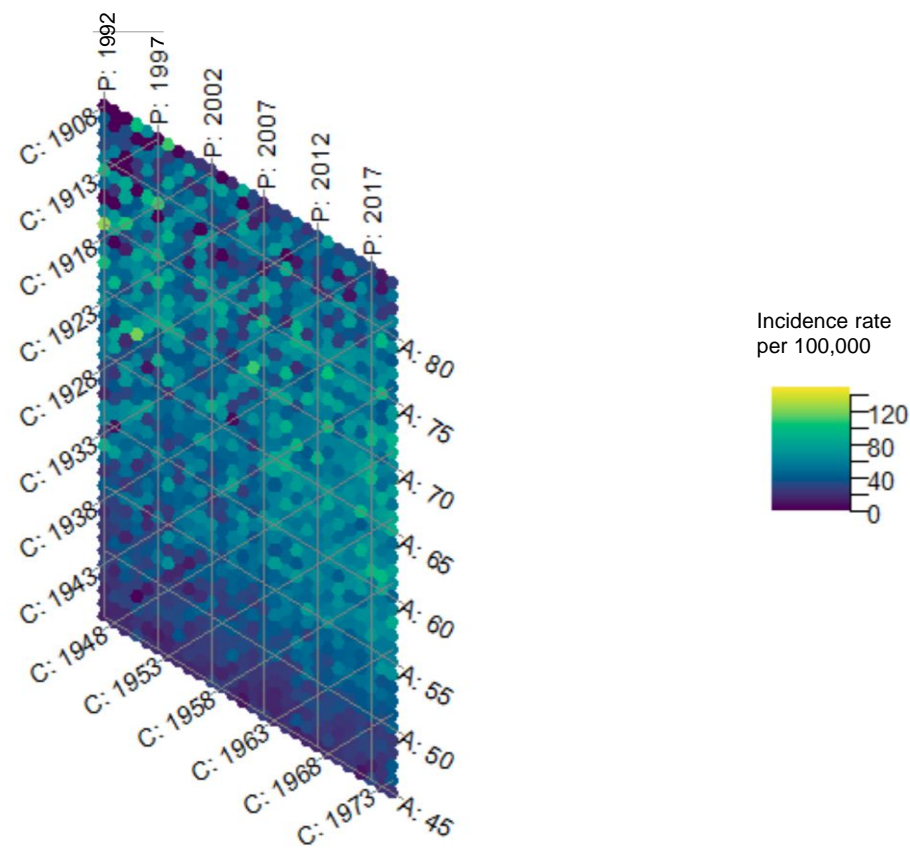
Figure 3b.

*Abbreviations: NH = Non-Hispanic; C = Cohort; P = Period; A = Age
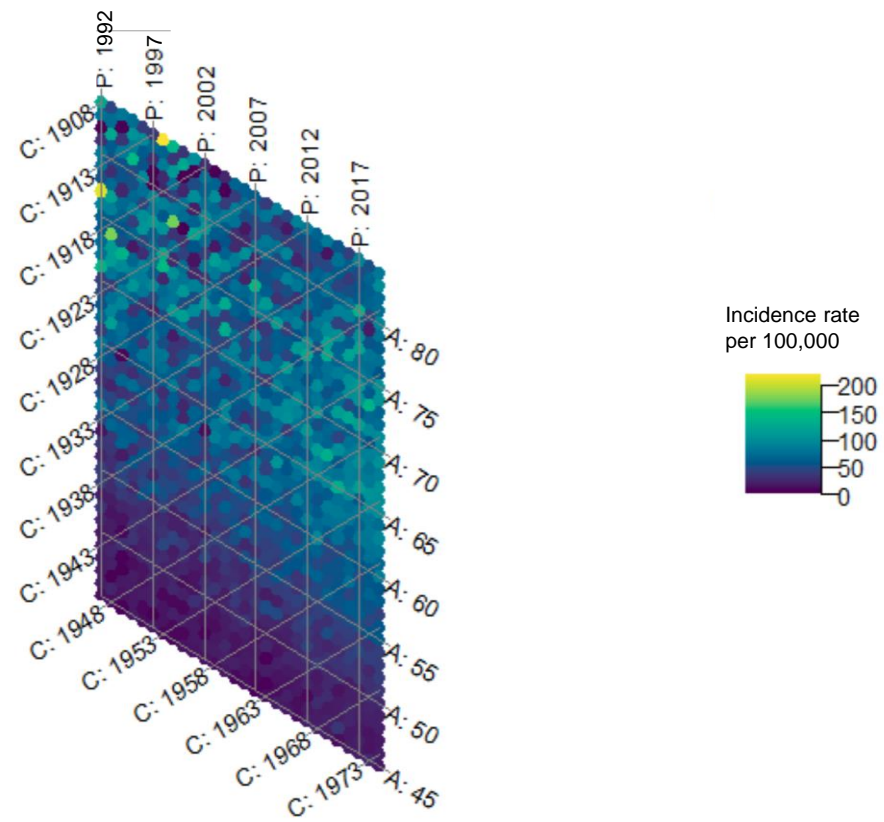
Figure 3c.

*Abbreviations: NH = Non-Hispanic; AI/AN = American Indian/Alaskan Native; C = Cohort; P = Period; A = Age
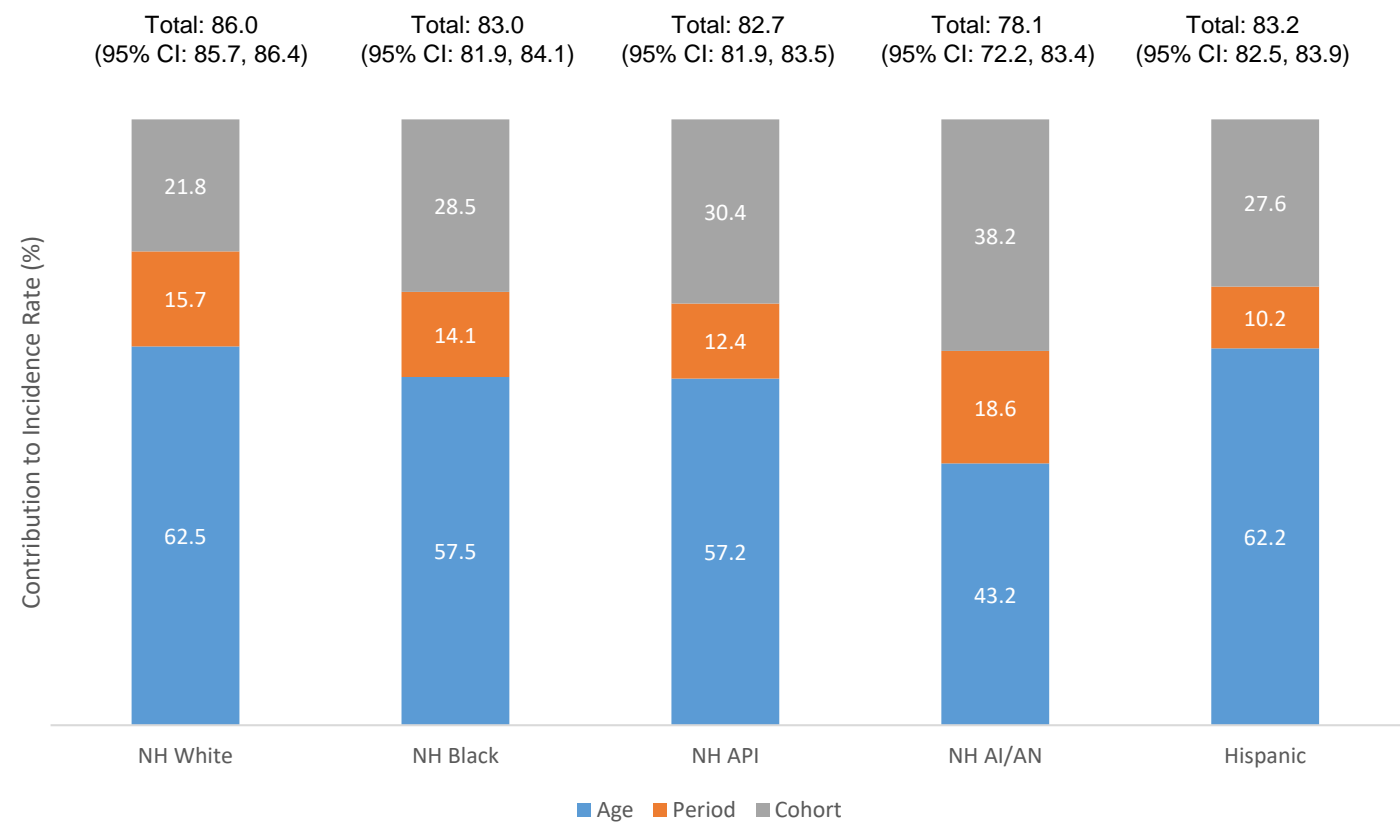
Figure 3d.

*Abbreviations: NH = Non-Hispanic; API = Asian/Pacific Islander; C = Cohort; P = Period; A = Age
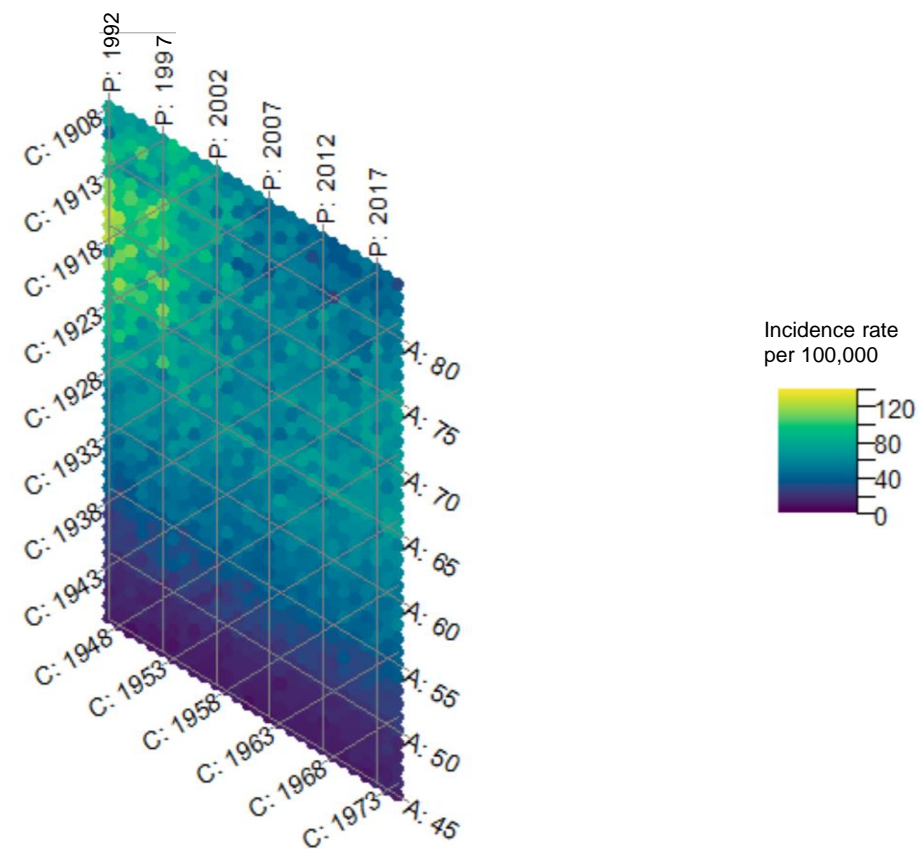
Figure 3e.

*Abbreviations: C = Cohort; P = Period; A = Age

Figure 3f.

Total: 86.0
(95% CI: 85.7, 86.4)

Total: 83.0
(95% CI: 81.9, 84.1)

Total: 82.7
(95% CI: 81.9, 83.5)

Total: 78.1
(95% CI: 72.2, 83.4)

Total: 83.2
(95% CI: 82.5, 83.9)

Contribution to Incidence Rate (%)

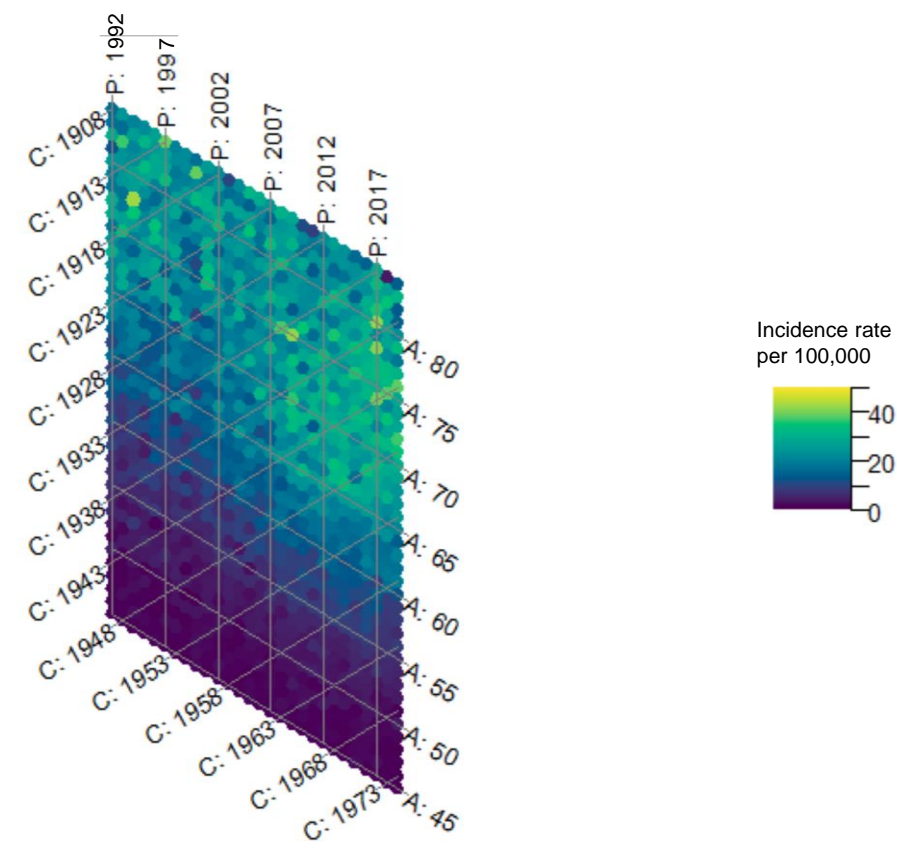| | NH White | NH Black | NH API | NH AI/AN | Hispanic |
Cohort	21.8	28.5	30.4	38.2	27.6
Period	15.7	14.1	12.4	18.6	10.2
Age	62.5	57.5	57.2	43.2	62.2

■ Age ■ Period ■ Cohort

*NH White:
  Cohort: 21.8 (95% CI: 20.9, 22.7)
  Period: 15.7 (95% CI: 14.8, 16.5)
  Age: 62.5 (95% CI: 61.4, 63.7)

NH Black:
  Cohort: 28.5 (95% CI: 25.9, 31.1)
  Period: 14.1 (95% CI: 11.8, 16.4)
  Age: 57.5 (95% CI: 54.3, 60.7)

NH API:
  Cohort: 30.4 (95% CI: 28.7, 32.3)
  Period: 12.4 (95% CI: 10.9, 13.9)
  Age: 57.2 (95% CI: 55.2, 59.3)

NH AI/AN:
  Cohort: 38.2 (95% CI: 27.7, 50.6)
  Period: 18.6 (95% CI: 9.6, 29.2)
  Age: 43.2 (95% CI: 32.4, 56.1)

Hispanic:
  Cohort: 27.6 (95% CI: 25.8, 29.4)
  Period: 10.2 (95% CI: 8.7, 11.7)
  Age: 62.2 (95% CI: 60.0, 64.5)
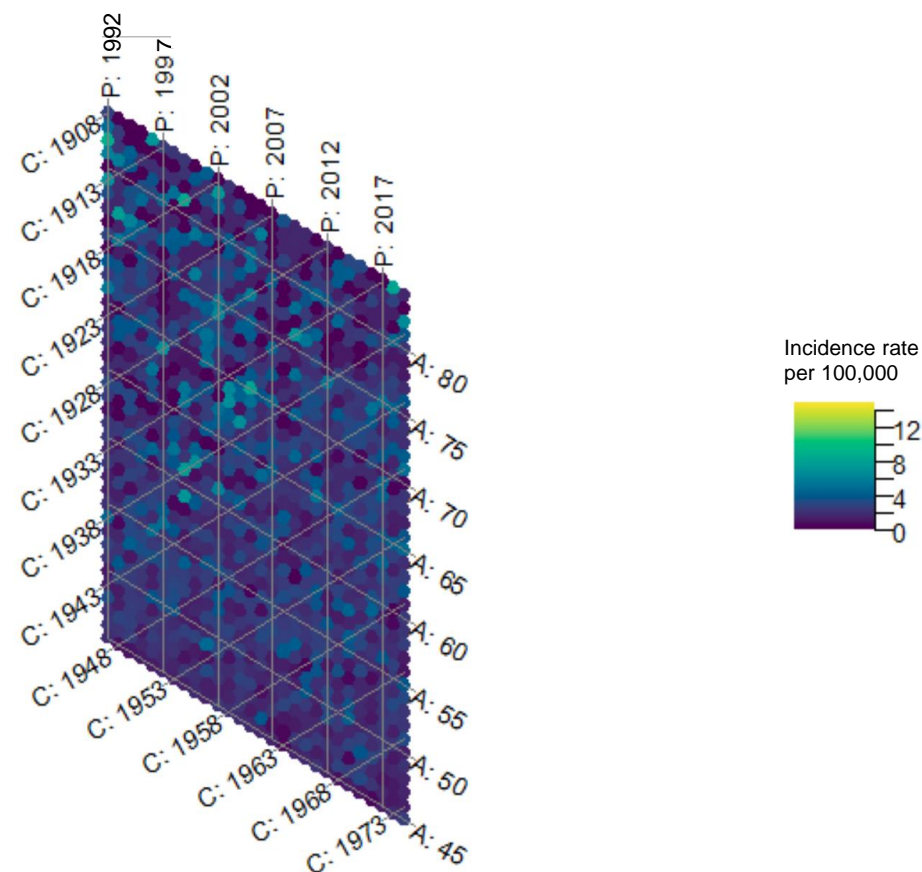
Figure 4a.

*Abbreviations: Em = Endometrioid; C = Cohort; P = Period; A = Age
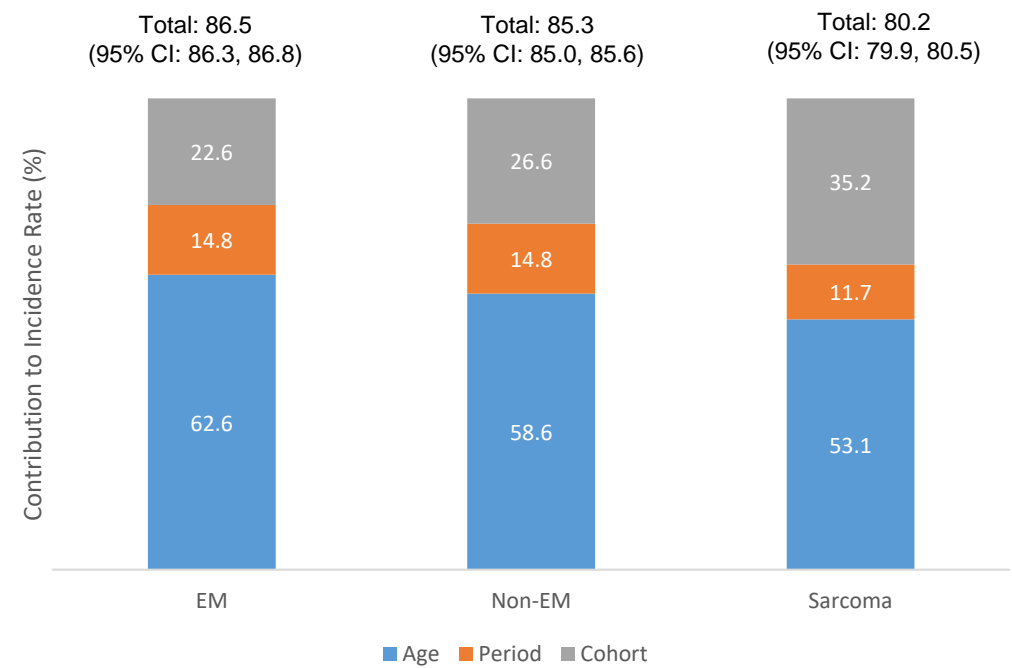
Figure 4b.

*Abbreviations: NonEm = Non-Endometrioid; C = Cohort; P = Period; A = Age

Figure 4c.

*Abbreviations: C = Cohort; P = Period; A = Age

Figure 4d.

*Endometriod:
  Cohort: 22.6 (95% CI: 22.0, 23.2)
  Period: 14.8 (95% CI: 14.2, 15.4)
  Age: 62.6 (95% CI: 61.8, 63.4)

Non-Endometriod:
  Cohort: 26.6 (95% CI: 25.9, 27.3)
  Period: 14.8 (95% CI: 14.2, 15.5)
  Age: 58.6 (95% CI: 57.5, 59.4)

Sarcoma:
  Cohort: 35.2 (95% CI: 34.5, 36.0)
  Period: 11.7 (95% CI: 11.1, 12.3)
  Age: 53.1 (95% CI: 52.3, 53.9)

Table 1. Baseline characteristics of uterine cancer cases in SEER 12 (1992-2019)

Baseline Characteristics	Year at Diagnosis							
	Overall 1992-2019		1992-2000		2001-2009		2010-2019	
	N	%	N	%	N	%	N	%
Age at diagnosis (years)	132,754	100.0	33,219	25.0	39,216	29.5	60,319	45.4
0-10	4	0.0	0	0.0	2	0.0	2	0.0
11-20	30	0.0	9	0.0	9	0.0	12	0.0
21-30	969	0.8	213	0.7	266	0.7	490	0.9
31-40	5196	4.3	1,274	4.2	1,593	4.4	2,329	4.2
41-50	15657	12.8	4,147	13.6	5,163	14.4	6,347	11.4
51-60	37929	31.0	7,909	25.9	12,213	34.0	17,807	32.0
61-70	40887	33.5	9,303	30.5	10,848	30.2	20,736	37.2
71-80	26168	21.4	8,442	27.6	7,122	19.8	10,604	19.0
81-84	5914	4.8	1,922	6.3	2,000	5.6	1,992	3.6
Race and Ethnicity								
NH White	89,459	67.4	25,919	78.0	27,163	69.3	36,377	60.3
NH Black	9,840	7.4	1,756	5.3	2,726	7.0	5,358	8.9
NH AI/AN	1,118	0.8	181	0.5	342	0.9	595	1.0
NH API	15,050	11.3	2,624	7.9	4,329	11.0	8,097	13.4
Hispanic	16,610	12.5	2,649	8.0	4,488	11.4	9,473	15.7
Histology								
Non-Endometriod	24,727	18.6	4,855	14.6	7,157	18.3	12,715	21.1
Endometriod	99,195	74.7	26,043	78.4	29,243	74.6	43,909	72.8
Sarcoma	6,055	4.6	1,540	4.6	1,912	4.9	2,603	4.3
Other	2,777	2.1	781	2.4	904	2.3	1,092	1.8
Region								
Northeast	16,745	12.6	4,584	13.8	5,228	13.3	6,933	11.5
Midwest	14,014	10.6	3,843	11.6	4,276	10.9	5,895	9.8
South	9,370	7.1	1,985	6.0	2,548	6.5	4,837	8.0
West	92,625	69.8	22,807	68.7	27,164	69.3	42,654	70.7
Summary Stage								
Local	92,948	70.0	24,447	73.6	27,243	69.5	41,258	68.4
Regional	23,822	17.9	4,790	14.4	7,076	18.0	11,956	19.8
Distant	12,098	9.1	2,730	8.2	3,829	9.8	5,539	9.2
Unstaged/Unknown	3,886	2.9	1,252	3.8	1,068	2.7	1,566	2.6