Abstract #897

# Estimated Age-Specific Prevalence of Pathogenic Variants in Individuals with Endometrial Cancer without a Family History of Cancer

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## Background

- Uterine cancer is the most prevalent gynecologic malignancy, with endometrial carcinoma (EC) accounting for the vast majority of cases
- Prolonged unopposed estrogen exposure, resulting in endometrial proliferation, is responsible for most EC, though a fraction are due to inherited (germline) pathogenic variants (PVs)
- Guidelines recommend genetic testing for individuals at risk of carrying a PV where testing criteria are largely based on younger age at diagnosis and/or family history (FH) of cancer

**Objective:** We characterized the number of patients that may be missed by current guidelines by modeling the age-specific prevalence of PVs in patients with EC but without a FH of cancer

## Methods

- Multivariable logistic regression models were constructed to analyze PV prevalence based on age, personal cancer history, and FH in a large clinical cohort of patients referred for genetic testing using a 25-48 multigene panel
- Model-based prevalence estimates for all genes and for only EC-associated genes in patients with EC but without personal or FH are summarized across 10-year bins for age of diagnosis

## Results

- The study cohort was comprised of 30,682 individuals affected with EC: 57.1% White/Non-Hispanic; 11.9% Hispanic; 6.3% Black/African; 2.7% Asian, 10.8% Other/Multiple; and 11.2% unspecified (**Table 1**)
- The average age of EC diagnosis was 51.5 and the average age of genetic testing was 58.2 (**Table 1**)
- Across all age bins, prevalence estimates ranged from 3.5% to 9.9% and 0.9% to 7.0% when including all genes and EC-associated genes, respectively (**Table 2**)

**Table 1.** Demographics

| Demographics | |
|---|---|
| **Age of Diagnosis** - Mean (Standard Deviation) | **51.5** (14.3) |
| **Age of Testing** - Mean (Standard Deviation) | **58.2** (12.3) |
| **Ancestry** - N (%) | |
| White/Non-Hispanic | **17,525** (57.1%) |
| Hispanic | **3,643** (11.9%) |
| Black/African | **1,940** (6.3%) |
| Asian | **817** (2.7%) |
| Other/Multiple | **3,322** (10.8%) |
| None Specified | **3,435** (11.2%) |
| **TOTAL** | **30,682** |

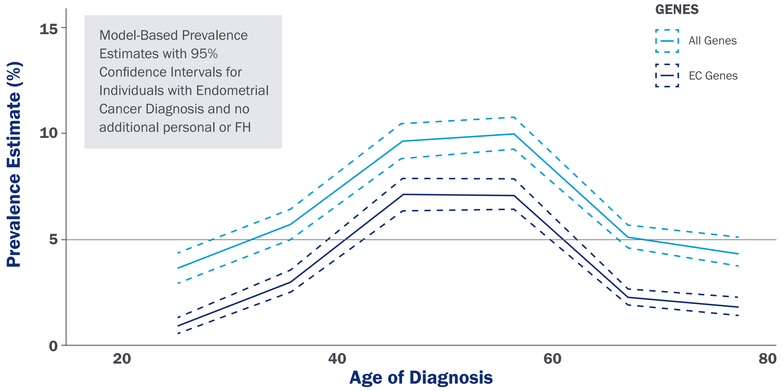
**Table 2.** Age of EC diagnosis and estimated PV prevalence (%)

| Genes | <30 | 30-39 | 40-49 | 50-59 | 60-69 | 70+ |
|---|---|---|---|---|---|---|
| **All Genes** | **3.5** | **5.6** | **9.5** | **9.9** | **5.1** | **4.3** |
| **EC Genes** | **0.9** | **2.9** | **7.0** | **7.0** | **2.2** | **1.8** |

EC-associated genes: *MLH1, MSH2, MSH6, PMS2, EPCAM, PTEN, NTHL1, STK11, TP53*

- Prevalence was highest for those diagnosed at 50-59 for all genes and was similarly high in 40-49 and 50-59 for EC-associated genes (**Table 2, Figure 1**)
- Prevalence estimates for all-genes and EC-associated genes remained consequential for those diagnosed at age 60+ (**Table 2; Figure 1**)

**Figure 1.** Prevalence estimates for all genes and EC genes




## Conclusions

- A substantial fraction of individuals with EC who may not meet guideline criteria for genetic testing likely carry PVs
- PV prevalence remains consequential for individuals diagnosed with EC at older ages
- Consideration of genetic testing at diagnosis, regardless of age, could improve patient care for individuals and families and may positively impact outcomes

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