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# The Columbia University Uterine Cancer Model (CU-UTMO): Model Profile

## Columbia University



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### Version Table

| Version | Date | Notes |
|---|---|---|
| 1.0.00 | 2025-09-30 | Initial release |


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Readers Guide




# Reader's Guide

**Core Profile Documentation**

These topics will provide an overview of the model without the burden of detail. Each can be read in about 5-10 minutes. Each contains links to more detailed information if required.

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Model Purpose



# Model Purpose

## Summary

This document describes the primary purpose of the Columbia University uterine cancer model (UTMO).

## Purpose

The aim of this model is to be used alongside other CISNET models for comparative exercises in projecting trends in uterine cancer in the US. The guiding premise of this model has been to build on a baseline biological understanding of uterine cancer carcinogenesis, incorporating a range of data sources prioritized by quality of the data. The model estimates incidence and mortality of cancer, by AJCC stage, for both endometrioid and non-endometrioid uterine cancers in Non-Hispanic Black and White women in the US. We are in the process of incorporating uterine sarcomas into the model as well. The model can be used to evaluate cancer control and prevention strategies, changes in epidemiologic and clinical factors over time and new treatment strategies.

UTMO is also designed to project future trends, providing critical insights into how the disease might evolve over time in different demographic groups. Model outputs include sojourn time, which helps to estimate the duration of the preclinical detectable phase, along with detailed projections of incidence and mortality by AJCC stage. It also evaluates key outcomes like the 5-year survival rate, allowing for a nuanced analysis of disease progression and survival trends. These outputs are essential for comparing the long-term impact of different screening and treatment strategies on patient outcomes, further guiding policy decisions.

# Model Overview

## Summary

This document describes the primary aims and general purposes of this modeling effort.

## Purpose

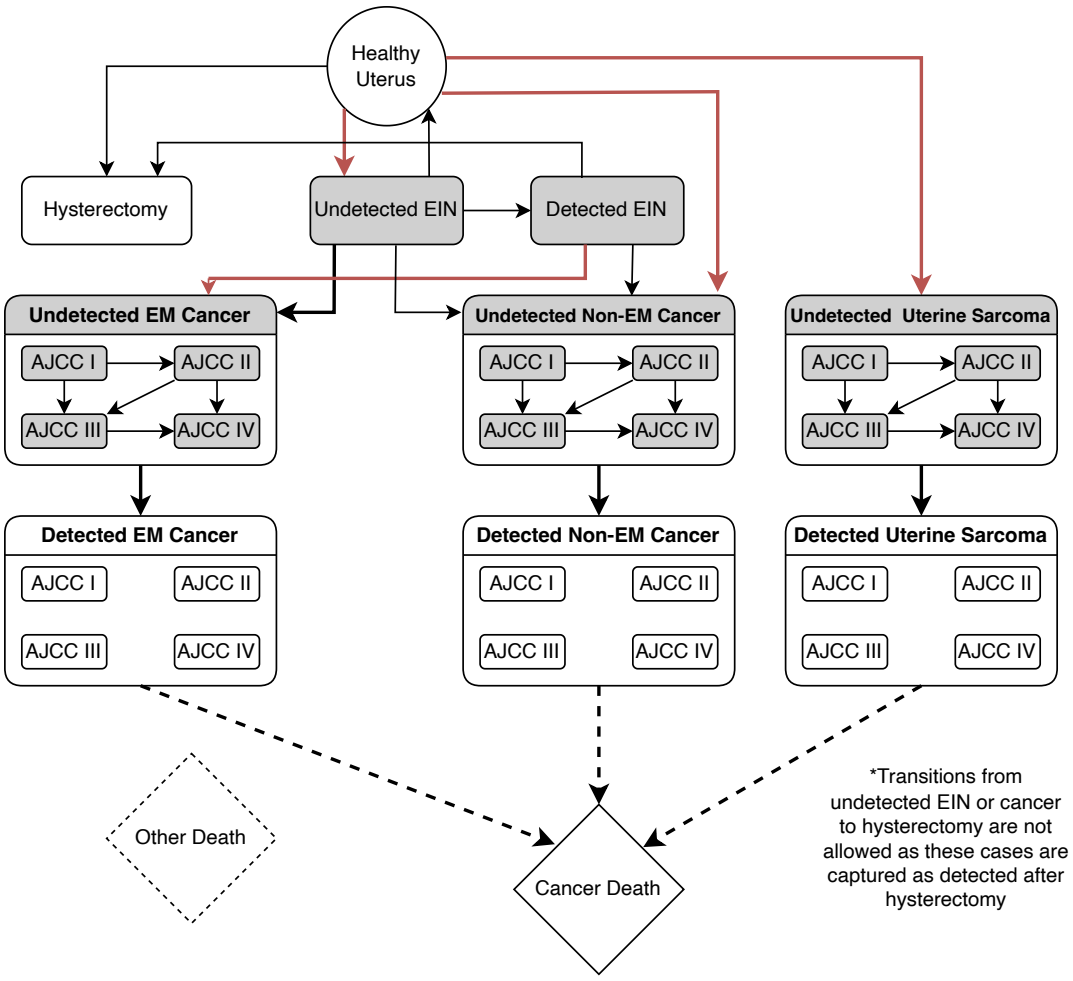
Model Purpose

## Background

Uterine cancer is the most common gynecologic malignancy in the United States, with an estimated 67,880 cases and 13,250 deaths projected in 2024[1]. The last thirty years have seen a dramatic rise in both the incidence and death rate from uterine cancer[2]. The increase in the incidence and mortality of uterine cancer is likely driven by a number of factors. Uterine cancer is predominately a disease of older women and the aging of the population in the U.S. has undoubtedly contributed to these trends[3]. Likewise, the rising rate of overweight and obesity has influenced the changing trends in uterine cancer[4]. Adipocytes produce estrogen which can stimulate the endometrium making obesity one of the strongest risk factors for uterine cancer[5]. However, the aging of the population and rising prevalence of obesity likely only explain a part of the changing trends in uterine cancer incidence and mortality. Planning for cancer control and prevention activities requires an understanding of the projected burden of a given cancer. The changing risk profile for uterine cancer in the U.S. has challenged the ability to accurately forecast the burden of the disease. UTMO is a natural history model for uterine cancer calibrated to the population-based incidence and mortality of the disease.

## Model Description

The model schematic below shows the possible states and transitions in UTMO, where solid arrows represent possible transitions, dashed arrows indicate terminal transitions, and all states are connected to ‘Other Death’. The transition probabilities between states have a complex structure of inputs and calibrated parameters (to be elaborated on later). In general, the transition probabilities vary by single year age, and 10-year birth cohort categories, the earliest cohort being 1910-1919. The state structure of the transition pathways in this model is based on an assumption of carcinogenesis of endometrioid cancers being mediated through a precancerous state, endometrial intraepithelial neoplasia (EIN). An additional crossover pathway, allowing for limited transitions from EIN and undetected EM cancer to non-endometrioid cancer is included based on the results of natural history data and a dedicated EIN precursor model, which showed up to 7% of non-endometrioid uterine cancers could occur via the same intermediary state. Due to the differing precursor structure and significantly lower incidence, sarcoma cases were excluded from the initial model. However, we are currently in the process of incorporating sarcomas, and the sarcoma pathway is also shown in the shcematic. Regression was restricted for all states except undetected EIN to healthy, as well as cancer recurrence. This improved identifiability by limiting non-primary pathways, enabling more accurate estimation of first-time cancer progression across states.




Time was incorporated into the model in two ways: age-specific transition probabilities and changing probabilities by birth cohort in 10-year groups. This captures secular trends and improves future projections. For transitions like mortality after diagnosis, where age alone wasn't sufficient, and for future screening and intervention modeling, a simple Markov model was inadequate. A patient-level microsimulation with state duration tracking was required.

The model integrates a range of data sources and literature estimates, prioritized by sample size and representativeness. Studies that did not stratify by race/ethnicity were given lower priority. CDC Wonder data and non-uterine cancer annual mortality estimates by age, birth cohort, and race/ethnicity were converted into monthly transition probabilities and directly incorporated into the model.

AJCC staging information (where available) in conjunction with historic (localized/regional/distant) data were extracted for each case listing. Multiple Imputation through Chained Equations (MICE) was used to re-classify patients with not otherwise specified histology as either endometrioid (EM) or non-endometrioid (Non-EM) and impute missing stage information based on all other available variables using the mice R package. The case listings data were then converted into incidence data, stratified by age, stage, race/ethnicity and birth cohort, and used as the primary calibration target under a mean squared error objective function. Surveillance, Epidemiology, and End Results Program (SEER) survival data were converted into duration-dependent hazard functions up to 10 years after diagnosis and imported directly at the microsimulation level.

SEER 18 case listings data was extracted with the following histology groups:

| Group | ICD Codes |
|---|---|
| Endometrioid (EM) | 8380-8383, 8480, 8570 |
| Non-Endometrioid (Non-EM) | 8020, 8050, 8260, 8310, 8441, 8460-8461, 8950-8951, 8980-8982 |
| Not otherwise specified (NOS) | 8000, 8140, 8255, 8323, 8481, 8560 |

# References

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Assumption Overview



# Assumption Overview

## Summary

An overview of the basic assumptions inherent in this model.

## Background

Due to the unavailability of data or to avoid model complexity, some assumptions about the model were made.

## Assumption Listing

**No Regression:** Regression from a higher to lower disease state was not permitted except for the regression of Undetected EIN to Healthy. Cancer recurrence is also not a part of the model with the goal of improving identifiability by limiting non-primary pathways, enabling more accurate estimation of first-time cancer progression across states. Not including regression or recurrence is an example of prioritizing model simplicity and interpretability.

**Markov Property:** Our natural history model assumes that a patient's health state is only dependent on their previous state. For example, a patient who has had stage II uterine cancer for four years has the same transition probabilities as a patient who has had stage II uterine cancer for one year (given that they have the same age, gender, cohort, etc). To account for previous states, a patient-level microsimulation is run which can account for things such as survival by years of follow-up after cancer diagnosis

**Natural History:** Our model consists of various assumptions about possible transitions that are based on the natural history of the disease:

- All cancers arise in an undetected state.
- While undetected, cancers may either persist in the given undetected stage, progress to a higher stage, or progress to a detected cancer of the corresponding stage if the tumor is identified clinically.
- Some individuals will die from other causes prior to the detection of the underlying uterine cancer.
- Obesity, survival, and hysterectomy rates are assumed not to change from their most recent available data point through 2050.

# Parameter Overview

## Summary

Describes the basic parameter set used to inform the model; more detailed information is available for each specific parameter.

## Background

The main parameters in the model are the transition probabilities from one state to another. These parameters are calibrated and are what primarily drive the model results.

## Parameter Listing Overview

The parameters of the model are guided by the possible transitions. Refer to the schematic in Model Purpose. For each of these possible transitions, there is a certain probability of transitioning from one state to another. These parameters are the primary drivers of the model's functionality and results and are calibrated using simulated annealing.

Table 1. Input parameters and calibration targets for the natural history model

| Category | Implementation | Data Source | Example |
|---|---|---|---|
| **Model inputs** | | | |
| Obesity prevalence | Simulated BMI category by age and birth cohort | NHANES (2000–2020) [1] | 1960–1970 cohort, NH White female, age 50, 40.5% BMI ≥ 30 |
| Impact of obesity | Fixed transition risk ratio | Zhao et al. (2021) [2]; Epplein et al. (2008) [3] | BMI ≥ 25: OR = 2.7 for EMC vs. BMI < 25 |
| Hysterectomy rates | Monthly, race and age-specific | NHANES (2000–2020) [1] | NH Black women, 45–49, P = 0.002 |
| Hysterectomy mortality | Competing hazard | Wingo et al. (1985) [4] | Mortality (non-pregnancy/cancer): 6.0 per 10,000 |
| All-cause mortality | Monthly, race/cohort/age-specific | CDC WONDER (1968–2016) [5] | 1950–1960 cohort, NH White, age 55–59, P = 0.0008 |
| Cancer-specific survival | 10-year survival hazards | SEER (2000–2018) | NH White, 40–44, EM stage IV: P = 0.0078 (1st year) |
| Cancer sojourn time | Upper/lower bounds | Broder et al. (2021) [6] | Stage III–IV: median = 1.5 years |
| **Calibration targets** | | | |
| EIN incidence | Age-specific | Reed et al. (2009) [7] | Age 60–65: 28.9 per 100,000 |
| EIN progression | Undetected progression bounds | Lacey et al. (2008) [8] | 3-year risk = 8.2% |
| EIN prevalence | Age-specific | Korhonen et al. (1997) [9] | Age 45–55: subclinical = 0–2 per 3,000 |
| EM cancer prevalence | Autopsy and screening | Horwitz (1981) [10]; Göl (2001) [11] | Rate = 22–31 per 10,000 |
| Cancer incidence | Race/histology/stage/age/cohort | SEER (2000–2018) | 1940–1950 cohort, NH Black, age 70, EM I: 38.8 per 100,000 |

**Abbreviations:** EIN: endometrial intraepithelial neoplasia. EM: endometrioid. NH: non-Hispanic. Non-EM: non-endometrioid. OR: odds ratio. SEER: Surveillance, Epidemiology, and End Results.

The NHANES reproductive history [1] survey was used to extract age- and race/ethnicity-specific hysterectomy hazards which were imported directly into the model. The NHANES reproductive history survey also provided BMI category data (<25, 25–30, >30), incorporated into the microsimulation. Age-dependent odds ratios linking BMI to EIN and endometrioid cancer progression were applied based on [2]. Hysterectomy prevalence and its associated small mortality risk [4] were also included.

Cancer incidence and survival data were obtained from SEER and the literature [5,6]. SEER data were stratified by race/ethnicity, histology, stage, age, and cohort. Subclinical and clinically detected prevalence estimates came from autopsy and screening studies [7-11]. SEER data also informed survival probabilities, adjusted by race, stage, histology, and cohort.

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# Component Overview

## Summary

A description of the basic computational building blocks (components) of the model.

## Overview

The model is a state-transition microsimulation model where patients can transition to and from certain states with certain probabilities (visual in Model Overview). There are various components to the model that attempt to model the natural history of the disease as well as certain risk factors such as obesity.

## Component Listing

## Natural History Component:

The natural history component is the main component of the model. The goal of this component is to simulate the natural history of uterine cancer. The model begins at 18 years of age and uses a one-month cycle length to dynamically account for short duration changes in risk factors and health states over time. The model simulates non-Hispanic White and non-Hispanic Black women separately.

The model has four general states: healthy (unaffected), precursor lesion (endometrial intraepithelial neoplasia), cancer, and death. Individuals with uterine cancer may have two disease states. Undetected uterine cancer is based on the true presence or absence of cancer for a given tumor stage that has not yet been detected clinically or pathologically. Detected uterine cancer is also based on the true presence or absence of a cancer for a given tumor stage, but one that has been clinically identified based on a diagnostic test.

## Calibration Component:

The calibration component is primarily responsible for adjusting probabilities (besides for death and hysterectomy rates which can be derived from available data). Transition rates change based on age, race, and birth cohort, and there is not enough data to accurately capture these changes without calibration. For some of the transition probabilities, the ranges were constrained based on the literature and domain knowledge. The Surveillance, Epidemiology, and End Results (SEER) program was used to obtain cancer incidence and survival in the United States.

Calibration of UTMO was performed in two phases, a multicohort phase and a cohort-specific phase. The motivation for this methodology was to incorporate as much of the available data as possible, while being able to forecast future trends. As some target data had limited sample sizes, high variance or insufficient information to stratify by birth cohort, this information was incorporated into the multicohort phase. The parameters from the multicohort phase were then used as starting values for the cohort-specific phase, where birth cohorts were grouped into 10-year intervals beginning with 1910-1920.

## Detection Component:

The detection component controls how individuals move from undetected to detected cancer states. Detection probabilities are governed by constraints that maintain biological plausibility and consistency with published evidence. For pre-invasive disease, detection of endometrial intraepithelial neoplasia (EIN) is constrained to always exceed the probability of regression, ensuring that progression to cancer is realistically captured. Detection of endometrioid cancer must exceed EIN detection.

For malignant states, detection rates increase across stages to reflect higher clinical detectability at more advanced stages. Detection rates for non-endometrioid cancers are constrained to be higher than for endometrioid cancers, aligning with their more aggressive natural history and shorter sojourn times. These relationships are enforced programmatically in the model's constrain logic, which adjusts transition probabilities each cycle. Broder et al. (2021)[1] provides uterine cancer sojourn time estimates, which are used to inform baseline detection rates.

## Survival Component

The survival component applies stage- and histology-specific survival probabilities to detected cases. Monthly hazards are derived from SEER's cause-specific death variable and reflect survival patterns by birth cohort, age, histology, and tumor stage for up to 120 months after diagnosis. These monthly hazards were calculated using the rstpm2 package in R. These survival hazards are directly applied in the microsimulation to ensure that modeled survival is consistent with population-based data and captures differences by race, histology, stage, age, and cohort.

# References

1. Broder MS, Ailawadhi S, Beltran H, et al. Estimates of stage-specific preclinical sojourn time across 21 cancer types. American Society of Clinical Oncology. 2021;

# Output Overview

## Summary

Definitions and methodologies for the basic model outputs.

## Overview

The uterine cancer natural history model produces key outputs that capture the burden and progression of the disease, allowing for insights into future trends and disparities across different populations. The model tracks incidence, prevalence, and mortality for uterine cancer, focusing on how these metrics evolve over time. By stratifying these results by race, age, birth cohort, and tumor histology (endometrioid vs. non-endometrioid; sarcoma to be added upon completion), the model provides an overview of how uterine cancer impacts different groups.

## Output Listing

1. Stage Distribution: The model outputs AJCC stage distribution, which is informative of cancer detection patterns by histology and can indicate screening disparities between certain groups.
2. Sojourn time: The model estimates sojourn time, which is the duration that women remain in undetected stages of uterine cancer. This is done using two different intervals: a) pre-invasive sojourn time (time between the presentation of endometrial intraepithelial neoplasia to detection) and b) malignancy sojourn time (time between first malignant cell and cancer detection). By calculating the sojourn times separately for NH White and NH Black women, we can infer how quickly uterine cancer progresses in each group.
3. Incidence: Capturing incidence in the model is important for understanding the rate at which new cases of uterine cancer are occurring. Incidence is a foundational measure for tracking the disease's spread and forecasting future trends. By including stratifications such as race, histology, and birth cohort, the model can reveal important disparities in who is getting the disease and how the incidence varies across populations.
4. 5-year survival rate: The model calculated 5-year survival rates which simulate patient outcomes after cancer diagnosis. Their survival is dependent on various factors such as tumor type, stage, race, and age.
5. Incidence-Based Mortality: The model captures incidence-based mortality within a 5-year period. This can provide a more accurate measure of cancer mortality as it links deaths to original cancer diagnosis and has a pre-specified time interval allowed between diagnosis and death, making it more interpretable.

# Results Overview

## Summary

A guide to the results obtained from the model.

## Overview

This section presents findings from the Columbia University uterine cancer model (UTMO) comparing stage distributions, incidence, and survival with SEER data to assess model alignment and validity. We also explore uterine cancer incidence by histology and BMI, stratified by race and age, and examine median ages of diagnosis. Further, sojourn times are analyzed across histological subtypes and racial groups. Lastly, results from model stress testing using the Maximum Clinical Incidence Reduction (MCLIR) methodology evaluate intervention effectiveness at different ages and cancer stages.

## Results List

Table 1. Incidence and Stage Distribution of Uterine Cancer by year of diagnosis (UTMO vs SEER)

| Incidence by Stage | Calibration Incidence (%) | | | Projection Incidence (%) | | |
|---|---|---|---|---|---|---|
| | 2000 | 2010 | 2018 | 2030 | 2040 | 2050 |
| **AJCC I** | | | | | | |
| SEER | 37.3 (75.0) | 40.8 (75.0) | 42.9 (74.5) | NA | NA | NA |
| UTMO | 33.1 (71.5) | 38.0 (71.2) | 41.8 (70.5) | 44.7 (70.0) | 48.5 (69.7) | 52.4 (68.9) |
| **AJCC II** | | | | | | |
| SEER | 3.8 (7.6) | 3.0 (5.5) | 2.6 (4.5) | NA | NA | NA |
| UTMO | 4.1 (9.0) | 4.6 (8.7) | 4.8 (8.2) | 4.9 (7.7) | 5.3 (7.6) | 5.6 (7.4) |
| **AJCC III** | | | | | | |
| SEER | 4.5 (9.1) | 6.7 (12.2) | 6.8 (11.9) | NA | NA | NA |
| UTMO | 4.7 (10.2) | 6.1 (11.3) | 7.2 (12.1) | 8.4 (13.1) | 9.4 (13.4) | 10.8 (14.2) |
| **AJCC IV** | | | | | | |
| SEER | 4.1 (8.3) | 3.9 (7.2) | 5.2 (9.1) | NA | NA | NA |
| UTMO | 4.3 (9.3) | 4.7 (8.8) | 5.4 (9.2) | 5.8 (9.2) | 6.5 (9.3) | 7.2 (9.5) |

Incidence per 100,000 in subjects 40 years of age and older (percentage of incidence per 100,000 diagnosed at each stage). Results are based on estimated incidence for non-Hispanic White and non-Hispanic Black women combined.
AJCC: American Joint Commission on Cancer. SEER: Surveillance, Epidemiology, and End Results database. UTMO: Columbia University uterine cancer model.

Table 1 shows encouraging alignment between Columbia's uterine cancer stage distribution and SEER, with UTMO closely matching SEER's data in most categories. For Stage I, UTMO reports 3-4% fewer cases than SEER, demonstrating a strong similarity. In Stage II, UTMO slightly overrepresents cases. For Stage III and Stage IV, UTMO's data aligns closely with SEER. In Stage IV, UTMO's results are more similar to SEER's, with just a slight 0.3% difference in 2018. Overall, UTMO's data is highly comparable to SEER's, indicating a strong alignment in stage distribution.

Table 2. Sojourn Times (Months) Stratified by Race and Histology

| Type of Sojourn Time | Histology | NH Black Mean | NH Black SD | NH White Mean | NH White SD |
|---|---|---|---|---|---|
| Pre-invasive | Endometrioid | 127.6 | 105.1 | 97.8 | 72.9 |
| | Non-endometrioid | 27.1 | 54.6 | 52.3 | 73.0 |
| Malignancy | Endometrioid | 22.4 | 19.7 | 21.9 | 19.8 |
| | Non-endometrioid | 8.2 | 6.6 | 8.7 | 6.6 |

Two sojourn times were estimated from model outputs by race and histology: 1) pre-invasive sojourn time, which reflects the time from first pre-invasive lesion (undetected EIN state) to detected cancer, and 2) malignancy sojourn time, which reflects the time from first malignant cell (undetected cancer) to clinically detected cancer (Table 3). The sojourn time was shorter for non-endometrioid compared to endometrioid cancers. For example, the malignancy sojourn time for endometrioid uterine cancer was 22.4 months in Black women compared to 21.9 months in White women. The corresponding sojourn times for non-endometrioid tumors were 8.2 and 8.7 months, respectively.

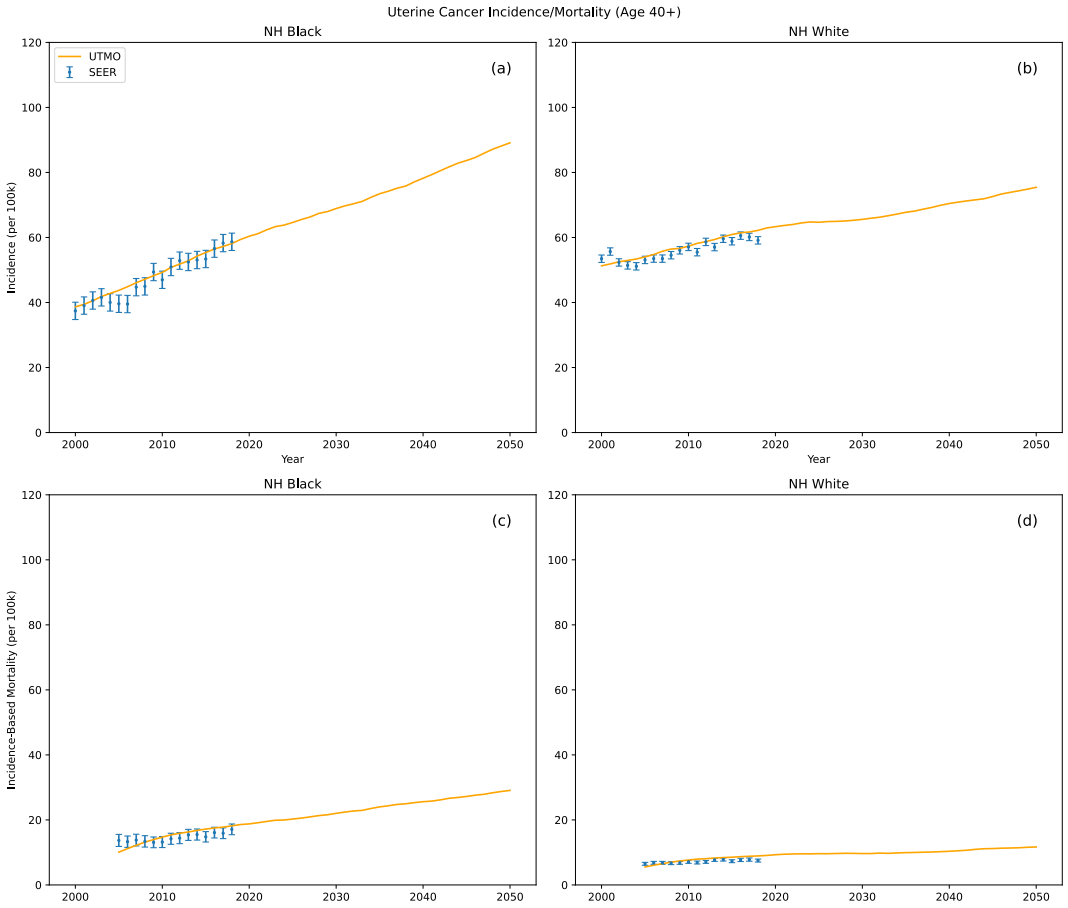


**Figure 1.** Projected age adjusted uterine cancer incidence and incidence-based mortality among women aged 40+ stratified by race and ethnicity to 2050. A. Incidence in Black women. B. Incidence in White women. C. Incidence-Based Mortality in Black women. D. Incidence-Based Mortality in White women

Table 3. Observed and projected incidence and mortality 5-year survival of uterine cancer overall and stratified by histology.

NH Black Women

| Outcome | 2000 | 2010 | 2018 | 2030 | 2040 | 2050 |
|---|---|---|---|---|---|---|
| **Incidence per 100,000 (40+)** | | | | | | |
| Overall (SEER) | 36.0 (33.4, 38.6) | 45.5 (42.9, 48.1) | 56.8 (54.2, 59.4) | - | - | - |
| Overall (UT-MO) | 35.5 (32.1, 38.9) | 46.9 (43.5, 50.3) | 56.6 (53.2, 60.0) | 65.5 (62.1, 68.9) | 75.6 (72.2, 79.0) | 86.9 (83.5, 90.3) |
| Endometrioid (SEER) | 23.5 (22.1, 24.9) | 30.7 (29.3, 32.2) | 34.2 (32.8, 35.7) | - | - | - |
| Endometrioid (UT-MO) | 23.0 (21.2, 24.8) | 29.6 (27.9, 31.4) | 35.2 (33.4, 37.0) | 39.3 (37.5, 41.1) | 44.7 (42.9, 46.5) | 50.5 (48.7, 52.3) |
| Non-Endometrioid (SEER) | 12.5 (11.2, 13.8) | 14.8 (13.5, 16.0) | 22.5 (21.2, 23.8) | - | - | - |
| Non-Endometrioid (UT-MO) | 12.5 (10.9, 14.1) | 17.2 (15.6, 18.8) | 21.4 (19.8, 23.0) | 26.2 (24.6, 27.8) | 30.9 (29.3, 32.5) | 36.3 (34.7, 37.9) |
| **5-Year Survival (%)** | | | | | | |
| Overall (SEER) | 66.5 (62.1, 70.5) | 68.5 (65.3, 71.6) | 69.1 (66.1, 71.8) | - | - | - |
| Overall (UT-MO) | 71.4 (69.5, 73.3) | 67.2 (65.4, 69.0) | 67.1 (65.3, 68.9) | 66.7 (65.2, 68.3) | 64.3 (62.8, 65.7) | 68.2 (67.0, 69.5) |
| Endometrioid (SEER) | 81.8 (75.4, 86.2) | 84.5 (80.9, 87.5) | 86.5 (83.3, 89.1) | - | - | - |
| Endometrioid (UT-MO) | 88.8 (87.2, 90.5) | 86.5 (84.8, 88.2) | 86.4 (84.7, 88.2) | - | - | - |
| Non-Endometrioid (SEER) | 38.4 (30.0, 46.7) | 39.0 (32.4, 45.5) | 42.9 (37.3, 48.4) | - | - | - |
| Non-Endometrioid (UT-MO) | 44.5 (41.2, 47.8) | 40.2 (37.3, 43.2) | 37.5 (34.5, 40.5) | 41.7 (39.3, 44.0) | 40.5 (38.3, 42.6) | 43.2 (41.2, 45.1) |

NH White Women

| Outcome | 2000 | 2010 | 2018 | 2030 | 2040 | 2050 |
|---|---|---|---|---|---|---|
| **Incidence per 100,000 (40+)** | | | | | | |
| Overall (SEER) | 52.1 (51.0, 53.2) | 55.9 (54.8, 57.0) | 57.7 (56.6, 58.9) | - | - | - |
| Overall (UT-MO) | 48.0 (46.3, 49.7) | 54.4 (52.7, 56.2) | 59.7 (57.9, 61.4) | 63.6 (61.9, 65.3) | 68.7 (67.0, 70.4) | 74.2 (72.5, 75.9) |
| Endometrioid (SEER) | 43.6 (42.7, 44.6) | 48.2 (47.3, 49.2) | 49.2 (48.3, 50.2) | - | - | - |
| Endometrioid (UT-MO) | 41.0 (39.5, 42.5) | 46.7 (45.2, 48.2) | 51.2 (49.8, 52.7) | 54.5 (53.0, 56.0) | 58.8 (57.3, 60.3) | 63.4 (61.9, 64.9) |
| Non-Endometrioid (SEER) | 8.5 (8.3, 8.7) | 7.7 (7.4, 7.9) | 8.5 (8.3, 8.8) | - | - | - |
| Non-Endometrioid (UT-MO) | 7.0 (6.8, 7.3) | 7.8 (7.5, 8.0) | 8.4 (8.2, 8.7) | 9.1 (8.8, 9.3) | 9.9 (9.6, 10.1) | 10.8 (10.6, 11.1) |
| **5-Year Survival (%)** | | | | | | |
| Overall (SEER) | 86.6 (85.7, 87.5) | 86.6 (85.8, 87.4) | 89.0 (85.1, 86.8) | - | - | - |
| Overall (UT-MO) | 86.3 (85.0, 87.5) | 85.7 (84.4, 87.0) | 85.7 (84.4, 87.0) | 85.1 (83.9, 86.3) | 85.1 (83.9, 86.2) | 83.8 (82.6, 84.9) |
| Endometrioid (SEER) | 91.5 (90.5, 92.5) | 92.5 (91.7, 93.2) | 92.2 (91.4, 92.9) | - | - | - |
| Endometrioid (UT-MO) | 92.3 (91.2, 93.3) | 92.4 (91.3, 93.4) | 92.6 (91.5, 93.6) | - | - | - |
| Non-Endometrioid (SEER) | 50.0 (45.6, 54.3) | 50.0 (46.0, 53.8) | 52.4 (48.4, 55.9) | - | - | - |
| Non-Endometrioid (UT-MO) | 50.5 (45.6, 55.4) | 52.8 (48.3, 57.3) | 45.9 (41.2, 50.7) | 48.4 (44.1, 52.7) | 51.6 (47.6, 55.6) | 45.5 (41.7, 49.3) |

SEER: Surveillance, Epidemiology, and End Results database.
UT-MO: Columbia University uterine cancer model.
* 2013 was the last year with 5-year survival data from SEER 18.

The incidence and mortality for uterine cancer have gradually increased over time for both White and Black women (Figure 2, Table 3). Our model closely fit SEER incidence and mortality data available through 2018. For uterine cancer incidence, our model has a square root normalized SSE (NSEE), a measure of average variance from the target, of 0.064 in White women and 0.084 in Black women. For uterine cancer incidence-based mortality, our model has an NSSE of 0.124 in White women and 0.333 in Black women. These results demonstrate excellent model validity.

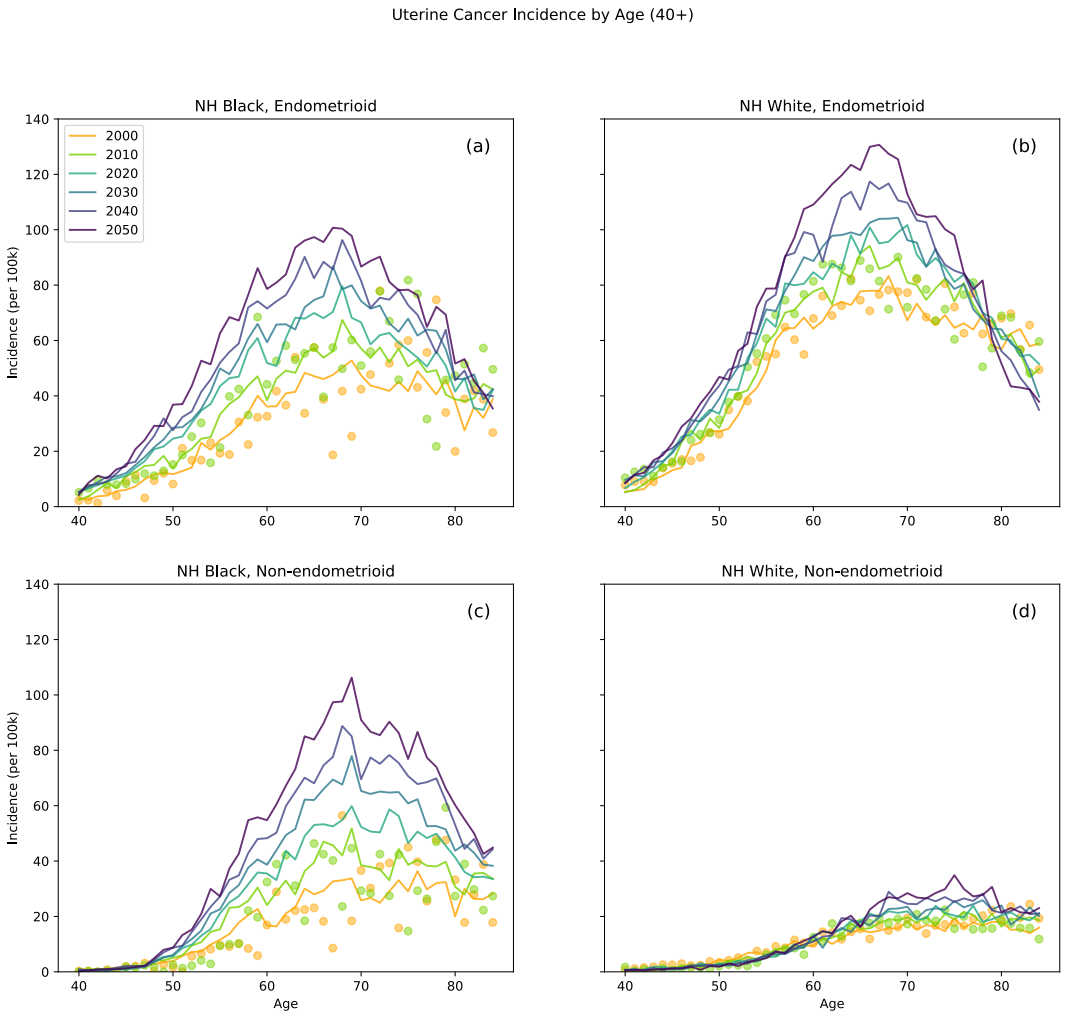


**Figure 2.** Histology-specific uterine cancer incidence stratified by race and ethnicity and birth cohort among women aged 40+. A. Endometrioid cancer in Black women. B. Endometrioid cancer in White women. C. Non-endometrioid cancer in Black women. D. Non-endometrioid cancer in White women.

The model performed well when additionally stratified by histology and age (Figure 2), while recognizing the additional noise present in single-age observations. The model-predicted median age of diagnosis across all cohorts for EM cancer was 65.4 and 65.7 for White and Black women respectively (compared to actual median ages of 65.7 and 66.9). The predicted median age of diagnosis for non-EM cancer was 70.7 and 68.9 for White and Black women respectively (compared to actual median ages of 70.7 and 69.7).

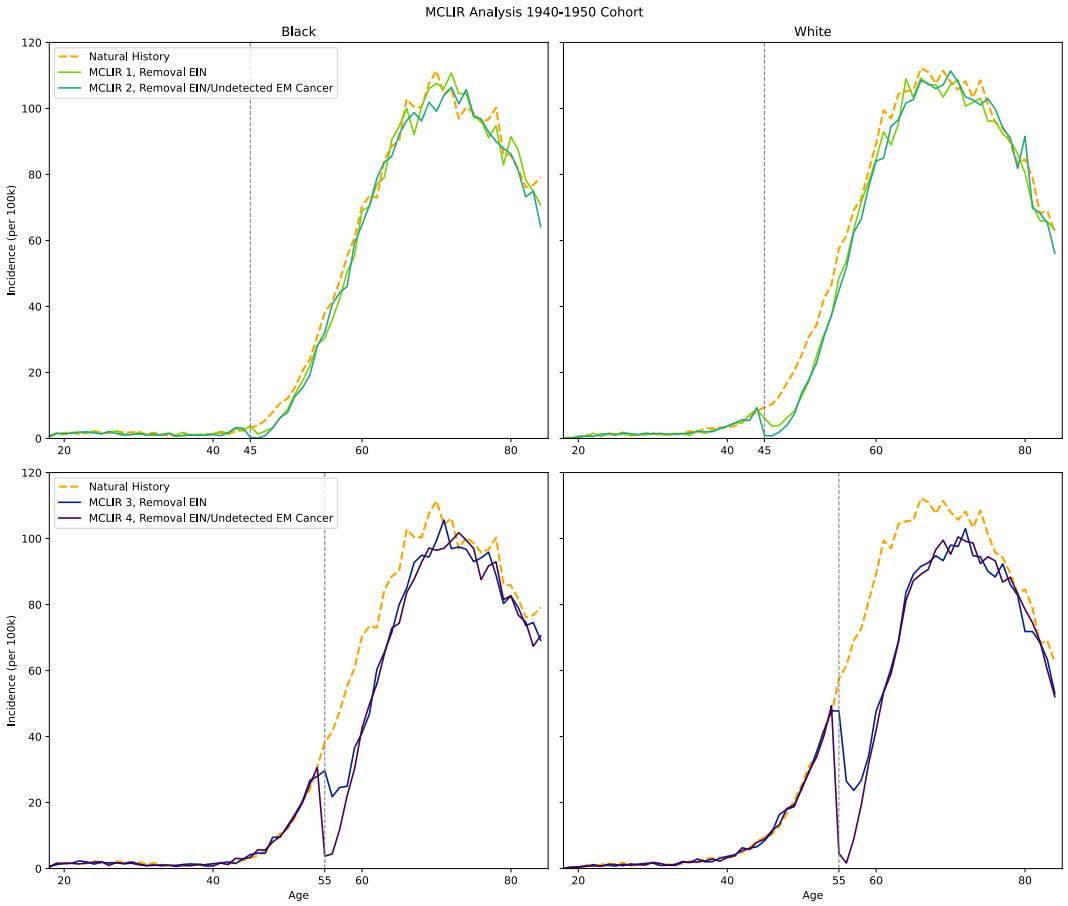


**Figure 3.** Sensitivity analysis using maximum clinical incidence reduction (MCLIR)[1] scenario analysis in the birth cohort of 1940-1950.
A. Removal of undetected endometrial intraepithelial neoplasia (scenario 1) or undetected endometrioid cancer (scenario 2) in 45-year-old Black patients.
B. Removal of undetected endometrial intraepithelial neoplasia (scenario 1) or undetected endometrioid cancer (scenario 2) in 45-year-old White patients.
C. Removal of undetected endometrial intraepithelial neoplasia (scenario 3) or undetected endometrioid cancer (scenario 4) in 55-year-old Black patients.
B. Removal of undetected endometrial intraepithelial neoplasia (scenario 3) or undetected endometrioid cancer (scenario 4) in 55-year-old White patients.

Results from stress testing of the model using the MCLIR methodology are shown in Figure 3. Scenarios 1 and 2 were applied for women at age 45 and eliminated further risk for patients with undetected EIN alone (scenario 1) or undetected EIN and endometrioid tumors (scenario 2). For both White and Black women there was a decline in cancer incidence starting at age 45 and lasting up to 7 years and 8 years, respectively. Women 55 years of age for scenario 3 (removal of undetected EIN alone) and scenario 4 (removal of undetected EIN and endometrioid tumors) saw a decline in cancer incidence lasting up to 15 and 16 years for White and Black women respectively. The magnitude of decline and the absolute number of cases eliminated was larger when the intervention was applied at 55 compared to 45 years of age. This indicates that potential screening and intervention options are more effective when targeting women aged 55 than those aged 45.

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