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Version: 1.0.00
Released: 2025-09-30

Duke University Uterine Cancer Model (DU-CAM): Model Profile

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Funding

The development of this model was supported by the NIH/NCI CISNET Uterine Cancer Grant (U01CA265739).

Suggested Citation

Hazelton WD, Meyers ER, Havrilesky LJ. Duke University Uterine Cancer Model (DU-CAM): Model Profile. [Internet] Sep 30, 2025. Cancer Intervention and Surveillance Modeling Network (CISNET). Available from: https://cisnet.cancer.gov/resources/files/mpd/uterine/CISNET-uterine-du-cam-model-profile-1.0.00-2025-09-30.pdf

Version Table

Version	Date	Notes
1.0.00	2025-09-30	Initial release

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.

Model Purpose
This document describes the primary purpose of the model.

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

Assumption Overview
An overview of the basic assumptions inherent in this model.

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

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

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Model Purpose

Summary

This document describes the primary purpose of the model.

Purpose

The overarching purpose of the DU-CAM model is to create a uterine cancer natural history model that allows examination of current and future trends in incidence and mortality and allows us to estimate the impact of various population-level strategies to reduce mortality and racial disparities in outcomes for uterine cancer.

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Model Overview

Summary

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

Purpose

DU-CAM is a multistage clonal expansion (MSCE) model.
The primary purpose of the DU-CAM model is to simulate the natural history of uterine cancer while accounting for age, period, cohort, race, reproductive history, obesity, and prior hysterectomy.

Background

The incidence and mortality of uterine cancer are increasing. Uterine cancer is one of the few tumor types in which both the incidence and death rates are rising.

A number of factors drive the increasing incidence of uterine cancer:

Obesity: At the population level, the rate of obesity, the strongest risk factor for uterine cancer, is increasing substantially. The obesity rate in the U.S. is rising rapidly and driving the increasing incidence of uterine cancer. At the population level, obesity is the most important risk factor for uterine cancer. There is a dose response relationship between body weight and uterine cancer, with a 50% increase in the risk of uterine cancer for every increase of five units in body mass index (BMI).

Reproductive factors: The hysterectomy rate has declined substantially, leaving a greater number of women at risk for uterine cancer as they age. Reproductive factors, mainly acting through alterations in unopposed estrogens which drive carcinogenesis, have a strong influence on uterine cancer risk. Higher parity reduces uterine cancer risk; a pooled analysis estimated a 27% lower risk in parous compared to nulliparous women, with a significant inverse association with increasing number of live births. Age at menarche is inversely associated with risk, with a meta-analysis of eight prospective studies demonstrating a 4% decrease in risk with every 2-year delay in menarche start. Similarly, older age at menopause increases the risk of uterine cancer due to increased number of ovulatory cycles.

Racial disparities: There is a profound racial disparity in outcomes for black and white women with uterine cancer and the gap is widening. While the incidence of uterine cancer is similar for black and white women (27 cases per 100,000 women), black women are much more likely to die from uterine cancer than white women. Numerous factors contribute to the observed racial disparities in poor outcomes for black women, including an increased prevalence of high-risk tumor histologies, more advanced stage tumors at diagnosis, molecular differences in tumors, disparities in treatment quality, decreased responsiveness to treatment, and socioeconomic factors.

Given the well-documented influence of reproductive risk factors and obesity trends on uterine cancer risk, they are modeled independently in DU-CAM using an obesity and reproductive history generator.

Model Description

The DU-CAM uterine cancer model consists of a biologically based MSCE natural history model of the effects of women's reproductive history events and history of body mass index (BMI) on uterine cancer incidence and mortality. Data on women's reproductive histories and BMI status are from the National Health and Nutrition Examination Surveys (NHANES) and National Health Examination Study (NHES) including over 100,000 women in 21 studies spanning years 1960-2020.

In this work, we comprehensively model the impact of current and future trends in obesity, reproductive history, race, age, period, and birth cohort on uterine cancer incidence and mortality. We utilize a MSCE model to fit to uterine cancer incidence by AJCC stage and mortality by type (Endometrioid, Non-Endometrioid, and Sarcomas) in the Surveillance, Epidemiology, and End Results (SEER) cancer registries, including 18 registries spanning years 2000-2018.

Assumption Overview

Assumption Overview

This section describes underlying assumptions of the DU-CAM model and their implications.

Summary

The primary assumption underlying the DU-CAM model is that we can utilize women's BMI and reproductive histories from NHES and NHANES to model trends in age-specific uterine cancer incidence, survival, and mortality.

Background

Numerous studies suggest that changing uterine cancer incidence trends are associated with historical changes in the distributions of body mass index (BMI) and women's reproductive histories (RH).[1-4]

To study this in more detail, we utilize nationally representative data from the National Health and Nutrition Examination Surveys (NHANES) and National Health Examination (NHES) spanning 1959 to 2020 along with uterine cancer incidence and mortality data from the Surveillance, Epidemiology, and End Results (SEER-18) that includes 18 cancer registries [5]. The aim is to gain a better etiological understanding of the potential roles of BMI and reproductive histories on US trends for age-specific uterine cancer incidence and mortality. [6]

The DU-CAM natural history model relates individual reproductive and BMI histories to cellular processes that contribute to the onset and progression of uterine cancer. We model cancer development as a multistage process of cell mutations and premalignant and malignant clonal expansions. We use a two-stage clonal expansion (TSCE) model to represent pre-malignant growth up to occurrent of the first malignant cell, followed by a lag time estimate of the mean time to cancer incidence. A single-stage clonal expansion (SSCE) model represents malignant clonal growth beginning with the first malignant cell. The SSCE model combines malignant clonal growth with possible metastatic transition while calibrating by stage at incidence, while matching to the lag time estimated from the TSCE model. [7-9]

Separate models are developed by race (non-Hispanic Blacks and non-Hispanic Whites) and by uterine cancer histology (Endometriod, non-Endometriod, and Sarcomas). Age-, period-, and cohort-specific trends for each histology are fit to SEER-18 data though likelihood-based calibration of BMI and RH dose-response effects on premalignant and malignant growth determined by the TSCE and SSCE parameters. The cohort and period trends reflect changes in the distributions of women's BMI and reproductive histories across successive NHES and NHANES surveys. The DU-CAM model does not contain any additional cohort or period trends.

Assumption Listing

We assume that we can utilize women's BMI and reproductive histories from NHES and NHANES to model age-specific uterine cancer incidence, survival, and mortality data from SEER. *This is necessary because NHANES does not include enough subjects to accurately estimate cancer outcomes, and SEER does not include reproductive or BMI histories.*

We assume that women's BMI histories can be simulated based on BMI measurements done by NHANES medical professionals at a single time point by using longitudinal data from NHANES to simulate reasonable BMI lifetime trajectories that pass through the measured value for each woman at their measurement age and date.

The TSCE natural history model includes two stochastic rate-limiting mutation events. Stochastic cell division and death rates define the clonal expansion of initiated cells, and a lag time represents the mean time from first

occurrence of a malignant cell to the time of uterine cancer incidence.

The SSCE model includes stochastic rates for malignant cell division and death and possible metastatic transition. The malignant stage undergoes clonal expansion from the time of first malignant cell to detection. Stochastic size thresholds and metastatic status define the fractions of individuals diagnosed in AJCC stages I - IV.

The background rates for initiation and malignant conversion are set equal to each other. This assures mathematical identifiability of the MSCE model parameters. Growth of the population of premalignant cells (promotion) is modeled stochastically through a cell birth and death process. This process cannot be observed directly but is consistently estimated between different cohorts as the most important mechanism that regulates cancer progression and the shape of the age-specific incidence curve.

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Parameter Overview

Summary

This section describes the primary data sources and DU-CAM model parameters that were calibrated using maximum likelihood estimation (MLE) methods.

Background

The DU-CAM model is based on the Two-Stage Clonal Expansion (TSCE) model of cancer development [1-3]. The TSCE model parameters represent stochastic rates for inition of normal cells to become premalignant, and for premalignant cells to undergo clonal expansion through cell division and death and further mutation that causes malignant transformation, followed by a lag time to cancer detection. The DU-CAM model allows these cellular rates to depend through dose-response relationships on women's history of BMI and reproductive history (RH) events (ages at menarche, first and last birth, number of births, age at menopause, and age at hysterectomy, if that occurs). Data from NHANES was used to sample women's complete BMI and RH events by race, age, and birth cohort whilel calibrating the DU-CAM TSCE model to SEER incidence data by race and uterine cancer histology. By using women's complete BMI and reproductive histories we maintain the correlations between these events that together may influence the risk for uterine cancer.

Parameter Listing Overview

Category	Implementation	Data source	Example
Model Inputs			
BMI at time of NHES, NHANES surveys	BMI (non-pregnant) by age, race, cohort	NHES and NHANES (1959 - 2020)	BMI(age 45) = 43 kg/m^2
Simulated age-specific BMI trajectories	BMI at ages 5, 15, ..., 85 by BMI percentile	Longitudinal & cross-sectional NHANES	BMI(age 5) = 18, BMI(age 15) = 22, ..., BMI(age 85)=34
Hysterectomy data from NHANES	Hysterectomy age by race, cohort	NHANES (1988 - 2020)	Hysterectomy at age 52
Reproductive histories from NHANES			
Age at menarche	Menarche age by race, cohort	NHANES (1988 - 2020)	Menarche at age 14
Age at first birth	First birth age by race, cohort	NHANES (1988 - 2020)	First birth at age 16
Age at last birth	Last birth age by race, cohort	NHANES (1988 - 2020)	Last birth at age 23
Number of live births	Number of live births by race, cohort	NHANES (1988 - 2020)	Number of live births = 3
Age at menopause	Menarche age by race, cohort	NHANES (1988 - 2020)	Menopause at age 46
Weight retention following childbirth(s)	Weight retention at 5, 10 years after last birth	NCHS Natality, CDC Wonder (2005 - 2023)	Increase of 1.5 BMI units by weight retention at age 33
All-cause mortality	Mortality by age, race, cohort	CDC Wonder (1968-2016)	Survival of 90.3% for NHW female at age 60 in 2020
Cancer-specific survival	10-year hazards by histology, stage, age, race	SEER (2000 - 2018)	NHW age 52 Endometrioid cancer AJCC stage 1
Calibration targets	Endometrioid (EM), Non-EM, Sarcomas		
Uterine cancer incidence	Age-specific incidence by histology, stage, race	SEER (2000 - 2018	38.8 per 100,000 at age 70 for NHB EM AJCC-I in 2015
Age at peak of EIN incidence (for EM histology)	Used to adjust lag time for for EIN in TSCE model	Semere, Obstet Gyneol. 2011, 118(1):21-28.	Median 53 years of age for EIN incidence
MLE calibration of TSCE models			
Premalignant TSCE model parameter MLEs:			
P1 background cell division rate	Maximim likelihood estimate (MLE)	SEER incidence, NHANES histories	MLE for P1 = 1.639372e+02 per year for NHW EM histology
P2 background premalignant promotion rate	Maximim likelihood estimate (MLE)	SEER incidence, NHANES histories	MLE for P2 = 1.642056e-01 per year for NHW EM histology
P3 background first and second mutation rates	Maximim likelihood estimate (MLE)	SEER incidence, NHANES histories	MLE for P3 = 1.211614e-07 per year for NHW EM histology
P4 increase in promotion rate after menarche	Maximim likelihood estimate (MLE)	SEER incidence, NHANES histories	MLE for P4 = 1.657073e+00 for NHW EM histology
P5 promotion rate during pregnancies	Maximim likelihood estimate (MLE)	SEER incidence, NHANES histories	MLE for P5 = 2.200011e+01 for NHW EM histology
P6 promotion rate after menopause	Maximim likelihood estimate (MLE)	SEER incidence, NHANES histories	MLE for P6 = 6.830476e-01 for NHW EM histology
P7 BMI promotion dose-response coefficient	Maximim likelihood estimate (MLE)	SEER incidence, NHANES histories	MLE for P7 = 4.360609e-01 for NHW EM histology
P8 BMI promotion dose-response power	Maximim likelihood estimate (MLE)	SEER incidence, NHANES histories	MLE for P8 = 1.399533e+00 for NHW EM histology
P9 lag-time from 1st malignant cell to incidence	Maximim likelihood estimate (MLE)	SEER incidence, NHANES histories	MLE for P9 = 1.224001e+00 year lagtime for NHW EM
Malignant TSCE model parameter MLEs:			
P10 background malignant cell division rate	Maximim likelihood estimate (MLE)	SEER incidence, NHANES histories	MLE for P10 = 2.190000e+02 per year for NHW EM cancer
P11 background malignant promotion rate	Maximim likelihood estimate (MLE)	SEER incidence, NHANES histories	MLE for P11 = 9.3566025e-01 per year for NHW EM cancer
P12 Stochastice size threshold AJCC I to AJCC II	Maximim likelihood estimate (MLE)	SEER incidence, NHANES histories	MLE for P12 = 8.663401e-08 threshold AJCC I to II
P13 Metastatic transition threshold	Maximim likelihood estimate (MLE)	SEER incidence, NHANES histories	MLE for P13 = 1.718970e-07 metastatic threshold
P14 Stochastice size threshold AJCC II to AJCC III	Maximim likelihood estimate (MLE)	SEER incidence, NHANES histories	MLE for P14 = 2.350917e-07 threshold AJCC II to III
P15 Stochastice size threshold AJCC III to AJCC IV	Maximim likelihood estimate (MLE)	SEER incidence, NHANES histories	MLE for P15 = 2.5853101e-07 threshold AJCC III to IV
P16 Estimated lag-time to EIN for EM histology	Maximim likelihood estimate (MLE)	SEER incidence, NHANES histories	MLE for P16 = 1.110000e+00 year lagtime for NHW EIN

Abbreviations: MLE: maximum likelihood estimate, NHW: non-Hispanic Whites, NHB: non-Hispanic Blacks, BMI: body mass index, RH: reproductive histories, NHES: National Health Examination Studies [4], NHANES: National Health And Nutrition Examination Studies [5], SEER: Surveillance, Epidemiology, and End Results cancer registries [6], NCHS: National Center for Health Statistics, CDC: Centers for Disease Control. EM: endometrioid, EIN: Endometrial Intraepithelial Neoplasia [7].

Maximum likelihood estimation (MLE) methods were utilized to calibrate the DU-CAM model by age and calendar year to 2000-2018 SEER incidence data and NHANES BMI and RH data for NHW and NHB race/ethnicity groups and EM, non-EM, and Sarcoma histology groups. We utilized a Poisson likelihod to estimate the dose-response parameter relationships between BMI and RH events to the observed race and histology-specific SEER incidence cases. These methods provided estimates relating uterine cancer incidence trends by age and year to historical changes in BMI and reproductive history trends in the US between 2000 and 2018.

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3. Hazelton WD. Longitudinal multistage model for lung cancer incidence, mortality, and CT detected indolent and aggressive cancers. Mathematical Biosciences. 2012;240(1):20–34.
4. National Center for Health Statistics (NCHS). National Health Examination Survey Data. Centers for Disease Control and Prevention (CDC). 2025;
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Component Overview

Component Overview

Summary

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

Overview

Several components are involved in construction of the DU-CAM uterine cancer model. A Population Component uses individual simulated BMI, reproductive history (RH), and other cause mortality histories to generate a simulated US population. A Natural History Component utilizes the TSCE model, previously calibrated to BMI and RH data, to estimate uterine cancer deaths in the simulated US population based on the TSCE model. A Survival-Mortality Component includes effects of the lag time from first malignant cell to uterine cancer death in the TSCE model, and adjustments for additional age, period, and birth cohort to improve the fit to US uterine cancer mortality.

Component Listing

Population component

The National Health and Examination Survey (NHANES) and National Health Examination Study (NHES) comprise a series of population-based cross-sectional surveys of approximately 100,000 women in 21 studies with individual sampling weights to provide a representative sample of the US population that have been collected from 1960 -2020 and include periodic longitudinal follow up surveys of participants. Pertinent data include medical examinations, BMI, race, ethnicity, birth year, age at menarche, age at menopause, hysterectomy status and age, and use of hormonal medications.

The Surveillance, Epidemiology, and End Results (SEER) Program is an authoritative source of information on cancer incidence and survival in the United States. The SEER Program collects and publishes cancer incidence and survival data from population-based cancer registries covering approximately 48% of the U.S. population. SEER 17 (previously 18*) is available for cases diagnosed from 2000 through the current data year and includes expanded races.

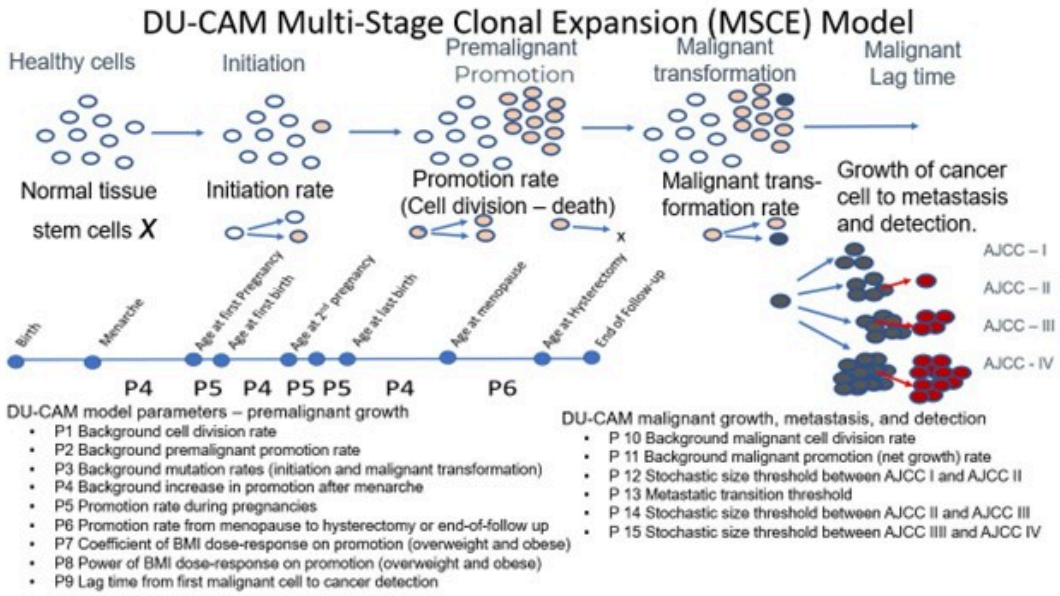
Hysterectomy incidence is currently incorporated into DU-CAM from NHANES (stratified by age, race, and BMI). Subsequent updates to DU-CAM will use data from the National Hospital Discharge Survey (NHDS), National Inpatient Sample (NIS), and National Ambulatory Surgery Sample (NASS), allowing stratification by age, indication for hysterectomy, race, and geographic region.

Reproductive and Obesity History Generator Component

NHANES surveys include a single BMI measurement. In order to generate individual BMI histories, patients are matched based on birth cohort, ages at live births, and age at menarche/menopause and NHANES BMI measurement at study age and date to generate individual BMI trajectories based on longitudinal data that all pass through the measured BMI value.

Natural History Component

DU-CAM is designed as a multistage clonal expansion (MSCE) model, with a two-stage component with lag time initially fit to SEER incidence, followed by a single stage model of malignant growth and metastasis to fit to the SEER AJCC stage I - IV distributions. The models are informed by a reproductive and obesity history “generator” and then calibrated to observed cancer registry incidence, and further modified to generate stage-dependent detection rates.



Modeling endometrial cancer incidence:

Because the reproductive histories and obesity profiles in NHANES are derived from a cross-sectional sampling with individual sampling weights, they are representative of the US population. Endometrial cancer incidence derived from SEER data is also cross-sectional and representative and was mapped/calibrated to obesity and RH profiles based on birth cohort, age, and race/ethnicity.

The nascent model is calibrated to age-specific incidence in SEER. Risk per birth cohort differs by age. Future projections of risk to 2050 are based on projecting reproductive history and BMI trends in NHANES observed between 2000 and 2020 to extend to the future date of 2050.

Race and histologic type were modeled independently.

Of note, DU-CAM models the natural history of uterine cancer using 3 parallel disease cohorts: (1) Endometrioid uterine cancers, (2) High-risk carcinomas: uterine papillary serous carcinomas (UPSC), clear cell carcinomas (CCC), and carcinosarcomas (MMT); and (3) leiomyosarcomas (LMS). Our model includes AJCC stages I – IV.

Survival-Mortality Component

Stage-dependent malignant growth and detection are modeled using a 1-stage clonal expansion model. DU-CAM is then recalibrated to BMI and reproductive histories.

We also use women's histories from NHANES to calibrate to uterine cancer mortality using a separate MSCE model, and are currently working on fitting to 1-, 5-, and 10-year survival by histological subtype age, and birth cohort based on SEER data.

Output Overview

Summary

Definitions and methodologies for the basic model outputs.

Overview

Calibration Data

- NHANES reproductive histories**
    - Age at menarche
    - Age at first birth
    - Age at last birth
    - Number of live births
    - Age at hysterectomy
    - Age at menopause
    - BMI
- SEER-18 uterine cancer incidence
    - Endometrioid
    - Non-Endometrioid
    - Sarcomas
- SEER-18 AJCC stage distributions and survival by histology
    - AJCC - I
    - AJCC - II
    - AJCC – III
    - AJCC – IV
- SEER-18 Uterine cancer mortality – all histologies

Output Listing

Outputs of the DU-CAM model include:

- EM, non-EM, and sarcoma uterine cancer incidence for NHB and NHW women that are calibrated to SEER-18 data between years 2000 and 2018, with projections to 2050.
- Endometrial intraepithelial neoplasia (EIN) that is a precursor for EM cancer incidence for NHB and NH for years 2000 - 2050.
- AJCC stage distributions at incidence for EM, non-EM, and sarcomas by race/ethnicity for years 2000 - 2050.
- Age-specific incidence-based mortality for EM, non-EM, and sarcomas for NHB and NHW for years 2000 - 2050.
- Age-specific attributable risks for BMI and reproductive histories as etiological risk factors in uterine cancer incidence by race/ethnicity and histology.
- Estimates of the age-specific impact on uterine cancer incidence of hysterectomies by race/ethnicity and histology.

Results Overview

Results Overview

This section describes results from fitting the DU-CAM model to uterine cancer incidence and mortality.

Summary

We used maximum likelihood estimation (MLE) methods to optimize the DU-CAM model fit age-specific uterine cancer incidence from SEER-18 across birth cohorts spanning years 2000-2018. Separate models were fit for non-Hispanic Whites (NHW) and non-Hispanic Blacks (NHB) and by histology: endometrioid (EM), non-EM, and sarcomas. The general age incidence trends depend on the TSCE model parameters. Differences by cohort and period arise through dose-response relationships for BMI and reproductive histories (RH) that modify the TSCE model parameters. Women undergoing hysterectomy were modeled as not being subsequently at risk for uterine cancer.

Overview

To identify the best fitting model for each race and histology, we optimized and compared over 20 different dose-response models influencing the TSCE model parameters. Each model was fit to histology-specific uterine cancer incidence from SEER-18. The different models assumed alternative dose-response relationships for the TSCE model parameters based on contemporaneous nationally-representative women's BMI and reproductive histories (RH) from NHANES. The RH events included ages at menarche, pregnancies defined by first and last birth, menopause, and hysterectomy, if it occurred.
Model comparisons were done using the Akaike Information Criterion (AIC) which adjusts the model likelihood scores based on the number of model parameters [1].

After identifying the best fitting TSCE model for each race and histology, we fit a single-stage clonal expansion (SSCE) model to represent the growth, metastatic transformation, and stage distribution at incidence observed in SEER-18, while matching to the estimated lag time estimated earlier from the TSCE model. Histology-specific cancer stage was classified according to the staging manual of the American Joint Committee on Cancer (AJCC), 7th edition, as AJCC stages I-IV.

Uterine cancer incidence-based mortality in the DU-CAM model was calculated for years 2000-2018 based on DU-CAM incidence and monthly histology-specific SEER-18 survival data.

Results List

In comparing over 20 different BMI and RH dose-response models for each race and histology, we identified the best fitting model based on AIC. We found a high degree of consistency for best fitting model by race and histology. For all histologies (EM, non-EM, and sarcoma), the best fitting models included a linear dose-response relationship for BMI influencing malignant conversion, and a piecewise-constant dose-response for RH intervals influencing premalignant promotion. However, for NHB EM, we found an additional significant linear dose-response relationship for BMI affecting initiation.

Figure 1 shows model fits by race for EM cancers. The difference in incidence by year are attributable to the effects of BMI and RH influencing the TSCE model rates, as described above.

Figure 2. shows predictions for endometrial intraepithelial neoplasia (EIN), a precursor to EM cancers. EIN was modeled as a secondary result of fitting the DU-CAM model to EM cancer incidence by adjusting lag time used in the TSCE model to approximate the observed age-specific peak in EIN incidence around ages 50-54.

Figure 3 shows model fits by race for non-EM cancers. Rates for non-EM cancers are increasing more rapidly among NHB than NHW women. Mortality rates tend to be higher for non-EM cancers than for EM cancers.

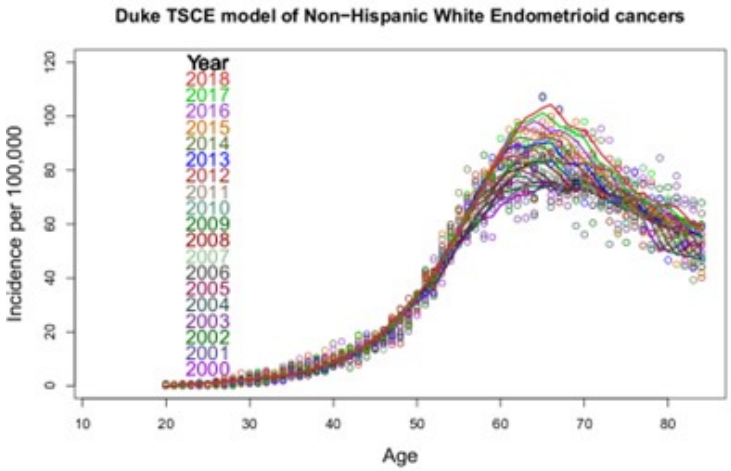
Figure 4 shows model fits by race for sarcomas. Sarcomas occur less frequently than other uterine cancers and tend to have poor survival.

For all histologies, we found that BMI contributes more than RH to age-specific risk at earlier ages, while RH contributes more to uterince cancer risk at older ages.

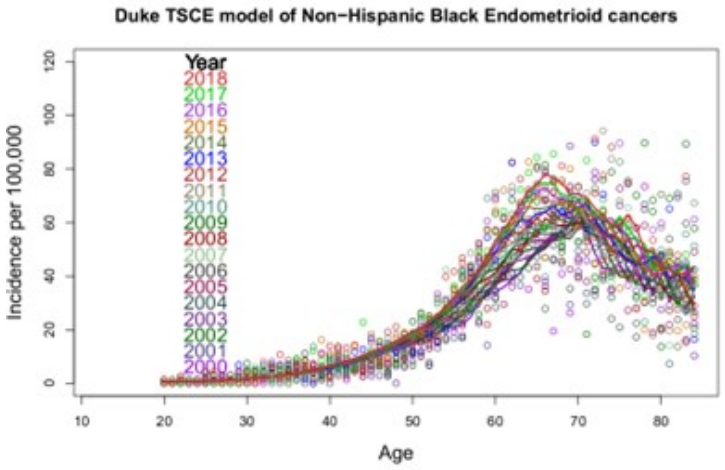
Fit/Figures

1. Calibration of DU-CAM model of endometrioid (EM) cancers to reproductive history and SEER incidence for endometrioid cancers. SEER EM incidence data by year are shown by colored circles and MSCE model fits are shown by corresponding colored lines.

   1a. NH White EM

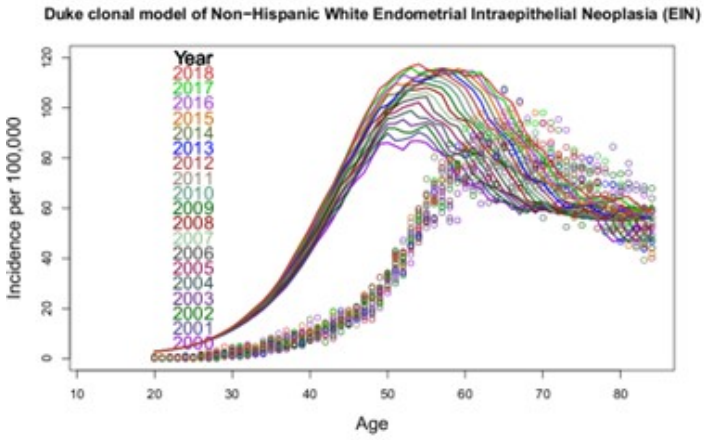


   1b. NH Black EM

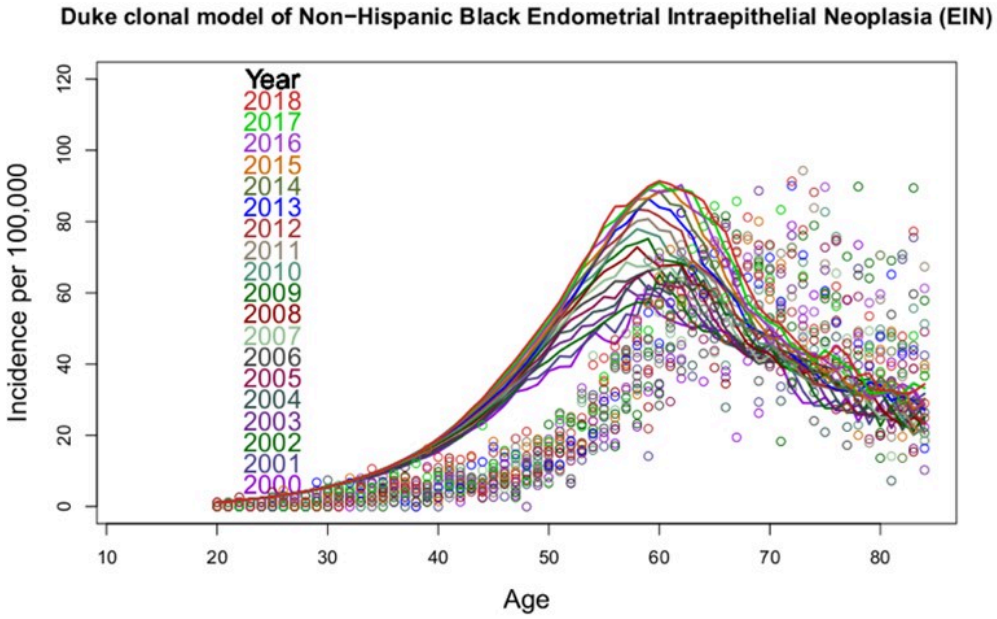


2. EIN prediction.
   SEER incidence data by year are shown by colored circles. Likelihood-based prediction of earlier EIN (a precursor to EM cancers) are shown by corresponding colored lines. EIN is potentially detectable prior to cancer diagnosis (as shown below).

2a. NH White EIN

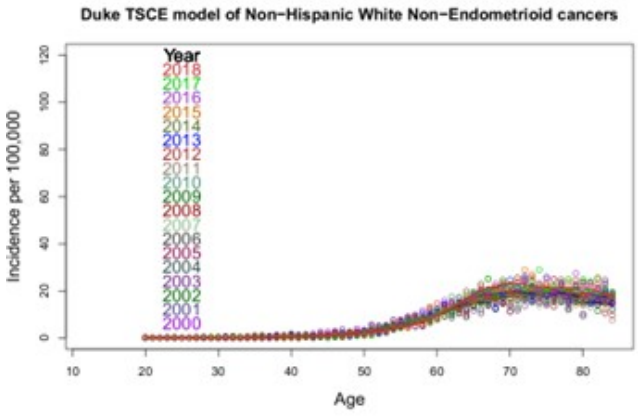


2b. NH Black EIN

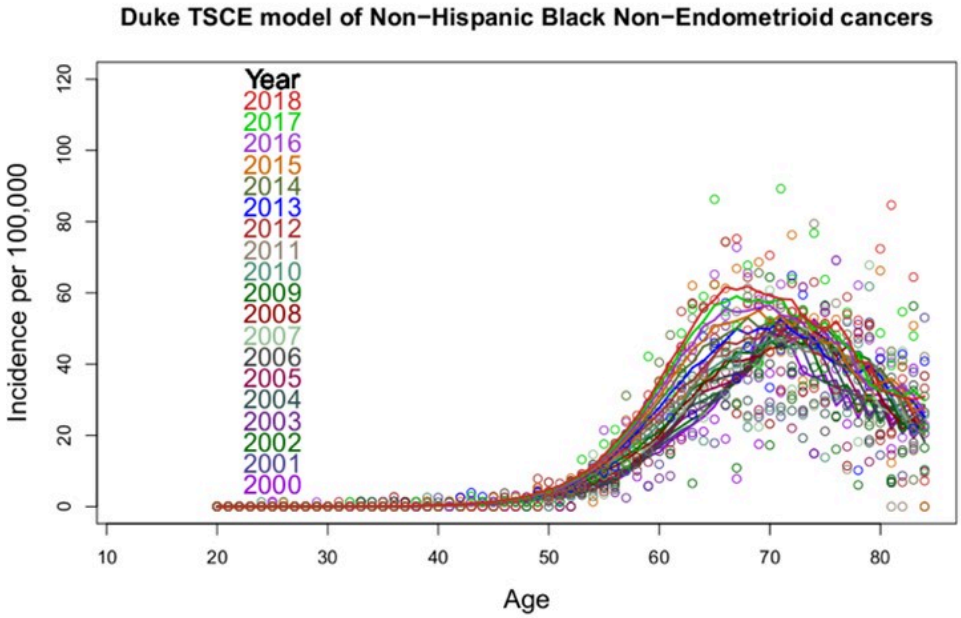


3. Calibration of DU-CAM TSCE of non-endometrioid (non-EM) cancers to reproductive history and SEER incidence. SEER non-EM incidence data by year are shown by colored circles and MSCE model fits are shown by corresponding colored lines.

3a. NH White Non-EM

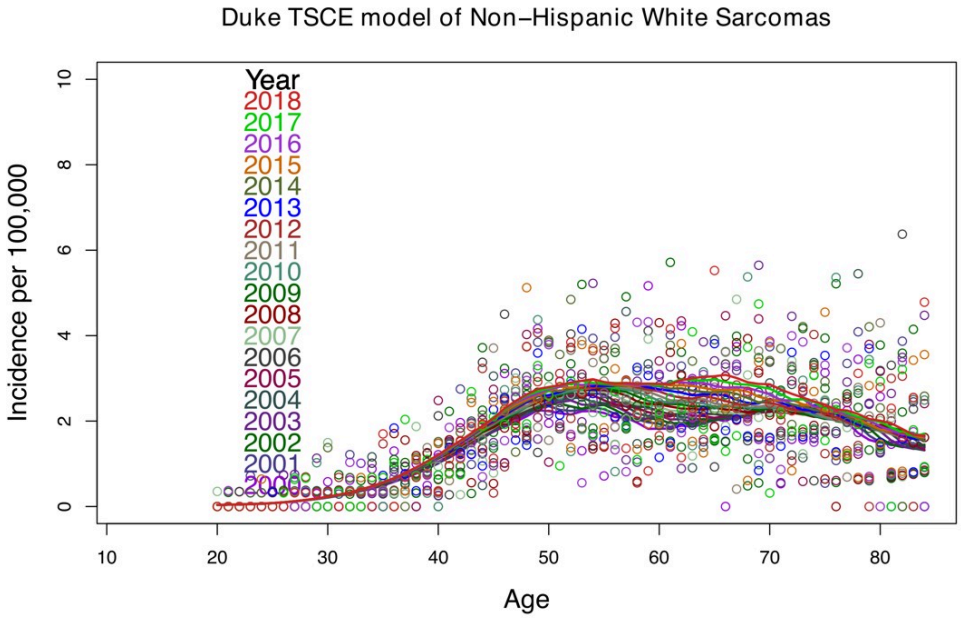


3b. NH Black Non-EM

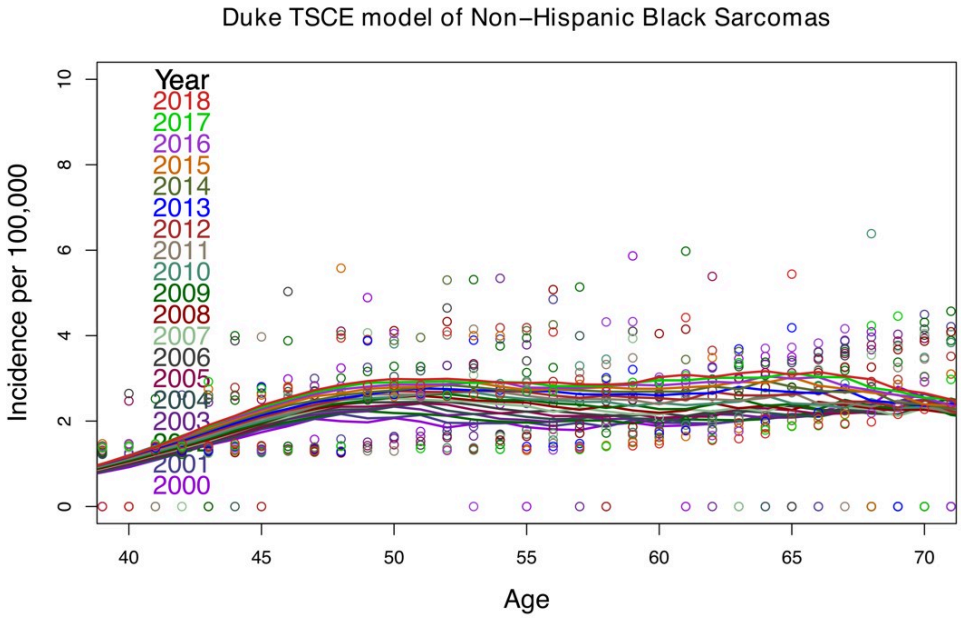


4. Calibration of DU-CAM TSCE of uterine sarcomas to reproductive history and SEER incidence. SEER sarcoma incidence data by year are shown by colored circles and MSCE model fits are shown by corresponding colored lines.

4a. NH White



4b. NH Black



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Duke University
Natural History
Component

DukeHealth

Natural History Component

Summary

Women's history of BMI and reproductive events are recognized as important risk factors in uterine cancer.

Overview

The DU-CAM model is informed by women's natural histories of BMI and reproductive history events as risk factors for uterine cancer.

Detail

We harmonized data on women's individual histories of BMI and reproductive events by race/ethnicity using US representative data from NHANES surveys between 1991 and 2020. These thousands of individual histories were utilized to inform the natural history of uterine cancer cellular progression from normal tissue by initiating mutations that generate premalignant cells. Premalignant cells undergo clonal expansion and malignant transformation to generate clonally expanding malignancies that may progress to cancer incidence and mortality.

By using full individual histories from women we are able to capture the complex correlations between BMI and and reproductive history events, (including ages at menarche, pregnancies associated with first and last birth, menopause, and hystorectomies) that contribute to uterine cancer progression. Changes by birth cohort and calendar year in the joint distributions of BMI and reproductive history events are captured by successive NHANES surveys, allowing modeling of current and future uterine cancer trends by histology and race/ethnicity.

Duke University
Population Component

Population Component

Summary

We utilize population data on uterine cancer incidence from SEER, and contemporaneous data on women's BMI and reproductive histories from NHES and NHANES.

Overview

A large fraction of uterine cancer incidence in the US is available from the SEER-18 cancer registries, while US representative data on women's BMI and reproductive histories is available from NHES and NHANES.

Detail

To study the relationships between uterine cancer incidence and women's BMI and reproductive histories, we need extensive US population-representative data of both types. SEER data is the best available large data source for uterine cancer incidence, survival, and mortality, but it does not include information on women's BMI or reproductive histories. NHES and NHANES survey data spanning 1959 - 2020 is one of the best available sources of BMI and reproductive histories, but it is not large enough to provide sufficient uterine cancer incidence or mortality. The DU-CAM model links the two data sets to infer mechanistic associations between BMI and reproductive histories with uterine cancer incidence between 2000 and 2018.

Duke University
Reproductive and Obesity History Generator Component

Reproductive and Obesity History Generator Component

Summary

The DU-CAM model utilizes inputs on women's obesity and reproductive histories to model the etiology of uterine cancer and predict future trends.

Overview

US representative data on reproductive histories and obesity were generated by extracting and harmonizing individual level records from NHES and NHANES survey data spanning 1959 - 2020.

Detail

There are complex correlations between BMI and different components of women's reproductive histories. It would be difficult to model these correlations in separate models of BMI and ages of reproductive history events. Instead we capture these correlations and inform the DU-CAM model by utilizing thousands of individual BMI and reproductive histories from NHANES.

Duke University
Survival-Mortality
Component

Survival-Mortality Component

Summary

The DU-CAM model utilizes incidence-based cancer mortality methodology.

Overview

The DU-CAM model provides a mechanistic model for uterine cancer incidence by race/ethnicity and histology in relation to women's BMI and reproductive histories. We utilize SEER-18 survival data by histology to calculate incidence-based cancer mortality.

Detail

We utilize 10-year monthly survival from SEER-18 by race/ethnicity and histology tp predict histology specific uterine cancer mortality between years 2000-2018, while predicting mortality out to year 2050.

However the DU-CAM incidence calibration began in year 2000, so we do not have complete incidence data to predict cancer mortality for the first ten years between 2000 and 2010. To fill in this interval, we assumed that incidence trends remained fixed between years 1990 and 2000.

Key References

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