Washington University
Version: 1.0.00
Released: 2025-09-30

Washington University Multiple Myeloma-Discrete Event Simulation Model (WUMM-DES): Model Profile

Washington University

Contact

Su-Hsin Chang (chang.su-hsin@wustl.edu)

Funding

The development of this model was supported by the NIH/NCI Grant U01CA265735.

Suggested Citation

Shih YH, Ji M, Huber JH, Wang M, Schoen MW, Thomas TS, Colditz GA, Li JS, Michaud TL, Chang S-H. Washington University Multiple Myeloma-Discrete Event Simulation Model (WUMM-DES): Model Profile. [Internet] Sep 30, 2025. Cancer Intervention and Surveillance Modeling Network (CISNET). Available from: https://cisnet.cancer.gov/resources/files/mpd/myeloma/CISNET-myeloma-wumm-des-model-profile-1.0.00-2025-09-30.pdf

Version Table

Version	Date	Notes
1.0.00	2025-09-30	Initial release

Other Publications

Shih YH, Ji M, Huber J, Wang M, Schoen MW, Thomas TS, Colditz GA, Li J-S, Michaud TL, Chang S-H. Burden of Monoclonal Gammopathy of Undetermined Significance and multiple myeloma: A discrete-event simulation modeling study (in preparation)

Washington University
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.

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.

Component Overview

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

Output Overview

Definitions and methodologies for the basic model outputs.

Results Overview

A guide to the results obtained from the model.

Key References

A list of references used in the development of the model.

Model Purpose

Summary

The CISNET Multiple Myeloma Incubator Program Washington University modeling group is to construct an evidence-based, calibrated, validated natural history of multiple myeloma (MM) model to evaluate MM prevention and control policies.

Purpose

Multiple myeloma (MM) is a common hematologic cancer and consistently preceded by an asymptomatic premalignant condition – monoclonal gammopathy of undetermined significance (MGUS).[1] MM incurs a significant health and economic burden to patients, family, and the entire healthcare system.[2-4] In addition, MM health disparities are well established.[5-7]

The long-term goal of the models developed by the CISNET Multiple Myeloma Incubator Program is to guide MM prevention and control policies and shift the current clinical paradigm in the management of MGUS and MM toward reducing MM burden and health disparities. We plan to comparatively model the natural disease history of MM from the development of MGUS to MM, followed by survivorship through two modeling groups (Washington University and Yale University modeling groups) under the current clinical practice: Washington University Multiple Myeloma Model (WUMM) and Yale University Multiple Myeloma Model (YUMM).

The WUMM plans to construct an evidence-based, calibrated, validated natural MM history model, which can be utilized to assess (1) the impacts of novel intervention strategies on MM prevention in high-risk patients diagnosed with MGUS, in terms of number of prevented MM cases, costs, and life years saved in high-risk MGUS patients; (2) the impacts of innovative treatment regimens on survival outcomes as well as the value of the guideline recommend therapies in MM patients; and (3) whether, under what conditions, and in which ways the goal of eliminating racial disparities can be achieved through these novel intervention strategies and treatment regimens.

References

1. Ola Landgren. Monoclonal gammopathy of undetermined significance and smoldering multiple myeloma: biological insights and early treatment strategies. Hematology 2013, the American Society of Hematology Education Program Book. American Society of Hematology Washington, DC; 2013;2013(1):478–487.
2. April Teitelbaum, Abbie Ba-Mancini, Hui Huang, Henry J Henk. Health care costs and resource utilization, including patient burden, associated with novel-agent-based treatment versus other therapies for multiple myeloma: findings using real-world claims data. The oncologist. Oxford University Press; 2013;18(1):37–45.
3. Eric M Maiese, Kristin A Evans, Bong-Chul Chu, Debra E Irwin. Temporal trends in survival and healthcare costs in patients with multiple myeloma in the United States. American Health & Drug Benefits. Engage Healthcare Communications, LLC; 2018;11(1):39.
4. Claire de Oliveira, Reka Pataky, Karen E Bremner, Jagadish Rangrej, Kelvin KW Chan, Winson Y Cheung, et al. Phase-specific and lifetime costs of cancer care in Ontario, Canada. BMC cancer. Springer; 2016;16:1–12.
5. Reference not found for key: ncicancerstatfacts2024@greenberg2012disparities.
6. Harvey Jay Cohen, Jeffrey Crawford, Murali K Rao, Carl F Pieper, Mark S Currie. Racial differences in the prevalence of monoclonal gammopathy in a community-based sample of the elderly. The American journal of medicine. Elsevier; 1998;104(5):439–444.
7. Jagat Singh, Alden W Dudley, Kimberly A Kulig. Increased incidence of monoclonal gammopathy of undetermined significance in blacks and its age-related differences with whites on the basis of a study of 397 men and one woman in a hospital setting. The Journal of laboratory and clinical medicine. Elsevier; 1990;116(6):785–789.

Washington University
Model Overview

Model Overview

Summary

In the CISNET Multiple Myeloma incubator program, the Washington University modeling group has constructed and calibrated a discrete event simulation (DES) model tailored to model the natural history of MM, from no MGUS/MM, MGUS development, progression to MM, and death for the U.S. population aged 20 years or older (WUMM-DES).

Purpose

The long-term goal of this WUMM-DES model is to fill the gap in setting and prioritizing policy goals for MM prevention and control. To achieve this goal, we constructed a discrete event simulation (DES) model to simulate the natural history of MM from the development of MGUS to MM, followed by survivorship for the U.S. population. Using this model, we will then evaluate whether promising intervention strategies throughout the continuum of care will effectively prevent the devastating malignancy or improve MM survival with great value.

Background

In the CISNET Multiple Myeloma incubator program, the Washington University modeling group has constructed and calibrated a DES model tailored to model the natural history of MM, from no MGUS/MM, MGUS development, progression to MM, and death for the U.S. population aged 20 years or older (WUMM-DES), stratified by race/ethnicity and sex.

The WUMM-DES model is a stochastic model informed by real-world data to simulate the natural history of MM progression. DES models the operation of a system as a discrete sequence of well-defined events in time. It is usually a preferred model, due to its simplicity, efficiency, and flexibility, (e.g., no fixed cycle length, ability to manage multiple events simultaneously and to allow interactions between individuals).[1-4]The parameters will vary based on the characteristics of each individual, and thus the model is agent-based. Due to the long progression of asymptomatic MGUS to symptomatic MM (a feature that makes Markov models inefficient) and the unknown functional form of a mathematical equation for progression (a feature that precludes the use of system dynamics models), DES is an appropriate modeling for MGUS-MM progression.

The developed simulation modeling can be tailored to set research priorities and design clinical trials, including assessing sample sizes and power, evaluating the impact of treatment adherence of the participants, and determining the optimal treatment strategies. It can also be used to predict trial results and set policy goals.

Model Description

The theoretical model builds on natural history of MM (**Figure 1**). The WUMM-DES model targets at the U.S. general population aged over 20 years since the prevalence of MGUS for the population aged below 20 years is nearly 0%.[5] The model currently integrates three demographic factors, age, sex, and race/ethnicity and simulates the natural history of MM for four U.S. populations, including non-Hispanic white (NHW) men and women, as well as non-Hispanic Black (NHB) men and women.

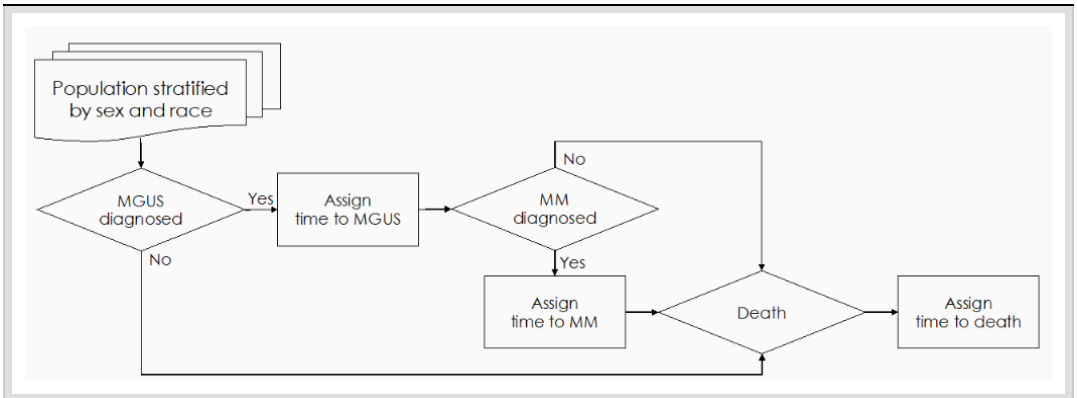

Figure 1. *WUMM-DES Model Schemepace*

Stratified by sex and race, this model starts with the population at age 20 without disease. For each population, some individuals develop MGUS, while the others do not. Some patients with MGUS progress to MM with varied time to progression depending on their characteristics, while others do not progress. All individuals, with or without MGUS and/or MM will be assigned time to all-cause death with time depending on their disease path and their individual characteristics.

References

1. Lachlan Standfield, Tracy Comans, Paul Scuffham. Markov modeling and discrete event simulation in health care: a systematic comparison. International journal of technology assessment in health care. Cambridge University Press; 2014;30(2):165–172.
2. LB Standfield, TA Comans, PA Scuffham. An empirical comparison of Markov cohort modeling and discrete event simulation in a capacity-constrained health care setting. The European Journal of Health Economics. Springer; 2017;18:33–47.
3. Sun-Young Kim, Sue J Goldie. Cost-effectiveness analyses of vaccination programmes: a focused review of modelling approaches. Pharmacoeconomics. Springer; 2008;26:191–215.
4. Jonathan Karnon. Alternative decision modelling techniques for the evaluation of health care technologies: Markov processes versus discrete event simulation. Health economics. Wiley Online Library; 2003;12(10):837–848.
5. O Landgren, BI Graubard, S Kumar, RA Kyle, JA Katzmann, K Murata, et al. Prevalence of myeloma precursor state monoclonal gammopathy of undetermined significance in 12372 individuals 10–49 years old: a population-based study from the National Health and Nutrition Examination Survey. Blood cancer journal. Nature Publishing Group; 2017;7(10):e618–e618.

Assumption Overview

Summary

Model assumptions are based on the availability of secondary data and/or evidence supported by the literature. We made assumptions on the following aspects: risk factors, disease stages, diagnosis, MM treatment, access to care, and parametric assumptions.

Background

Model assumptions are based on the availability of secondary data and/or evidence published by the literature. The etiology of MGUS and MM is poorly known. Henceforth, only known risk factors with sufficient evidence and available data will be included in the model. Previous studies reported that risk factors for MGUS/MM include older age, black race, male sex, family history, radiation, and pesticide exposure. Among these reported risk factors, older age, black race, male sex, and family history are of sufficient evidence. Therefore, we included all but family history because data on family history are either unavailable or poorly captured. Another known and established clinical risk factors for MM -- obesity (defined as body mass index (BMI $\geq$30 kg/m^2)), will be included in the future model.

Furthermore, the disease etiology is complex. Our model currently only includes four disease stages, including no MGUS/MM, MGUS, MM, and death. Also, unlike full-blown MM, which is symptomatic, since MGUS is asymptomatic and a diagnosis does not warrant treatment, time of diagnosis of MGUS is incidental. Finally, novel (and costly) treatment regimens for MM management have emerged frequently for the past decade, improving MM survival with unknown impact on MM health disparities. We made the following assumptions.

Assumption Listing

- Only known risk factors with available data were integrated into the model, including age, race/ethnicity, sex, and obesity (with the first three already integrated in the current model and the last to be expanded).
- Smoldering MM (sMM) is a more advanced pre-malignant disease than MGUS. sMM disease stage is currently not included in the WUMM-DES.
- Data on MGUS/MM diagnosis were used to proxy MGUS/MM development. For MM, since MM is symptomatic, we assumed that the time for MM development should be sufficiently close to the time for MM diagnosis. For MGUS, since it is asymptomatic and the diagnosis is incidental, we used calibration to correct the bias.
- MM survival only depends on the characteristics of population based on the data without considering treatment regimens.
- Health insurance status,and thus access to care, is not currently considered in the model.
- Because the WUMM-DES is a lifetime horizon model, the lifetime probability of death for all individuals is equal to 1. In addition, the maximum life expectancy for the simulated individuals is 100 years.
- The probabilities and time-to-event distributions for disease progression depend on individual demographics, recognizing the inherent heterogeneity among individuals. Details can be found in Parameter Overview.

Parameter Overview

Summary

The WUMM-DES has several key parameters, including probabilities of an event and distributional parameters for time to events. These events include MGUS, MM, death. Several databases were used to estimate the parameters, including the National Health and Nutrition Examination Study (NHANES), National Health Interview Survey (NHIS), Medical Expenditure Panel Survey (MEPS), Surveillance, Epidemiology, and End Results (SEER), Veteran Health Administration (VHA), and the Centers for Disease Control and Prevention (CDC).

Background

The parameters for a DES model include the probability of an event and distributional parameters for the time to this event. The current WUMM-DES has three events: MGUS, MM, and death.

Data Sources

To ensure that our models are evidence-based and generalizable to the studied subpopulations, we populated our model using estimates derived via data from several databases representing different U.S. populations. Secondary data analyses were performed to estimate the parameters in the models. These data were also used to calibrate and validate the evidence-based models. Each database is briefly described below.

1.Three national databases that are nationally representative samples of the U.S. general population: the National Health and Nutrition Examination Study (NHANES), 1971-, the National Health Interview Survey (NHIS), 1963-, and its linked mortality data files (with mortality follow-up until end of 2015), the Medical Expenditure Panel Survey (MEPS), 1996-.

2.Surveillance, Epidemiology, and End Results (SEER) and related software, 1975-: When combined with the use of the Complete Prevalence (ComPrev) and Projected Prevalence (ProjPrev) Software, we will be able to obtain annual prevalence of MM based on the limited-duration prevalence obtained from SEER*Stat.

3.Veteran Health Administration (VHA), 1998-: VHA contains electronic health record (EHR) data for veterans utilizing the Veteran Affairs (VA) healthcare system in the entire nation and can be linked to other data, e.g., Department of Defense and Medicare. VA healthcare system provides access to all eligible veterans for a lifetime, and therefore captures the most complete longitudinal data among all databases.

4.The Centers for Disease Control and Prevention (CDC), 1999-: CDC life tables provide data on mortality and life expectancy for the U.S. generally population stratified by age, sex, and race.

Parameters

Parameters are listed in **Table 1**.

Table 1: Parameters and data sources

Parameter	Event	Source	Year
Probability			
P_G	No MGUS to MGUS	VHA	2000-2022
P_{M1}	MGUS to MM for MGUS at [20,50)		
P_{M2}	MGUS to MM for MGUS at [50,65)		
P_{M3}	MGUS to MM for MGUS at [65,75)		

P_{M4}	MGUS to MM for MGUS at [75,100)		
Time-to-event distribution			
$F_G(t)$	No MGUS to MGUS	VHA	2000-2022
$F_{M1}(t)$	MGUS to MM for MGUS <50		
$F_{M2}(t)$	MGUS to MM for MGUS at [50,65)		
$F_{M3}(t)$	MGUS to MM for MGUS at [65,75)		
$F_{M4}(t)$	MGUS to MM for MGUS at [75,100)		
$F_{D,H}(t)$	No MGUS to death	CDC Life Table	2002
$F_{D,G}(t)$	MGUS to death	CDC Life Table, Ji et al., 2023	2002, 1999-2004
$F_{D,M}(t)$	MM to death	CDC Life Table, SEER	2002, 2000-2019

1. Parameters were initially estimated from the VHA data, including the probability of no MGUS to MGUS (P_G) and its corresponding time-to-event distribution (F_G). To account for age-specific progression rates, the progression of MGUS to MM was stratified into four age groups based on the age at which MGUS was diagnosed: 20-49, 50-64, 65-74, and 75-100 years. The probabilities of MGUS progression to MM for these age groups are represented as P_{Mi}, $i = 1, 2, 3, 4$, respectively, along with their corresponding time-to-event distributions $F_{M1}(t)$, $i = 1, 2, 3, 4$,respectively.[1]

   Due to the imbalanced sample sizes for gender in the VHA data, these parameters were obtainedsolely based on race. To ensure parameters are representative of for each subpopulation, calibration was conducted. The parameters obtained from the VHA data were served as the starting values and were calibrated using both national estimates of MGUS prevalence and MM incidence for each subpopulation. The time-to-event distributions were presented as cumulative density functions (CDFs).

   The distribution for time (from age 20)-to-MGUS, $F_G(t)$, were assumed to be piece-wise linear with five parameters based on empirical CDF curves.

$$F_G(t) = \begin{cases} \frac{p_1 \cdot (t-20)}{30} & \text{if } t \in [20, 50] \\ \frac{(p_2 - p_1) \cdot (t-50)}{15} + p_1 & \text{if } t \in [50, 65] \\ \frac{(p_3 - p_2) \cdot (t-65)}{15} + p_2 & \text{if } t \in [65, 75] \\ \frac{(p_4 - p_3) \cdot (t-75)}{15} + p_3 & \text{if } t \in [75, 85] \\ \frac{(p_5 - p_4) \cdot (t-85)}{15} + p_4 & \text{if } t \in [85, 100] \end{cases}$$

   The distributions for time-from-MGUS-to-MM, F_{Mi}, were estimated by Gamma distribution,

   $F_{Mi}(t) = \frac{\gamma(a_{Mi}, b_{Mi} t)}{\Gamma(a_{Mi})}$,

   $\gamma(s, x) = \int_0^x t^{s-1} e^{-t} dt$,

$\Gamma(s) = \int_0^\infty t^{s-1}e^{-t}dt$,

where $i = 1, 2, 3, 4$ for the five age groups, $\Gamma(a_{Mi})$ is the gamma function, and $\gamma(a_{Mi}, b_{Mi}t)$ is the incomplete gamma function. Therefore, the mean and variance of time from MGUS to MM are $\frac{a_{Mi}}{b_{Mi}}$ and $\frac{a_{Mi}}{b_{Mi}^2}$, respectively.

2. Parameters for mortality include time to death for (a) no MGUS $F_{D,H}(t)$, (b) MGUS $F_{D,G}(t)$, and (c) MM $F_{D,M}(t)$.
Because the WUMM-DES is a lifetime horizon model, the lifetime probability of death for all individuals is equal to 1.

   a. For each subpopulation, $F_{D,H}(t)$ were estimated from the CDC life tables, reflecting the mortality rates of the general population.

   b. We obtained estimates for $F_{D,G}(t)$ from a published study by our team: hazard ratios (HR) for death comparing MGUS population to no MGUS population in the United States: 1.21, 1.17, and 1.16 for MGUS at age 50 to 69, 70 to 79, and ≥80 years, respectively[1] Assuming theevent times in each age interval is an exponential distribution, the probability to death can be expressed as $1 - e^{-\lambda}$, where λ is the mortality rate. Therefore, the probability from MGUS diagnosis to death at time t is, $p_{D,G}(t) = 1 - (1 - p_{D,H}(t))^{HR(t)}$, where $P_{D,H}$(t) is the probability of death among general population at time t. Therefore,

$F_{D,G}(t) = 1 - \exp\left(\int_0^t \frac{HR(t)f_{D,H}(t)}{F_{D,H-1}}dt\right)$, where $f_{D,G}(t) = \frac{dF_{D,H}(t)}{dt}$
$F_{D,M}(t) = 1 - RS(t)$

Derivation of $F_{D,G}(t)$:

Let $T_{D,G}$ be the random variable denoting the time of death from MGUS and $f_{D,G}$ and $F_{D,G}$ be the probability density and cumulative distribution functions of $T_{D,G}$, respectively, then the hazard rate of death from MGUS is defined by $h_{D,G}(t) = -\frac{f_{D,G}(t)}{1-F_{D,G}(t)}$. Hence, it satisfies $h_{D,G}(t) = \frac{d}{dt}\log(1 - F_{D,G}(t))$, which also holds for the hazard rate of death from health $h_{D,H}(t)$ with $F_{D,G}(t)$ replaced by $F_{D,H}(t)$, the cumulative distribution function of the time of death from health. The hazard ratio is then defined by $HR(t) = \frac{h_{D,G}(t)}{h_{D,H}(t)}$, so that

$\frac{d}{dt}\log(1 - F_{D,G}(t)) = HR(t)\left(-\frac{f_{D,G}(t)}{1-F_{D,G}(t)}\right)$, which yields
$F_{D,G}(t) = 1 - \exp\left(-\int_0^t \frac{HR(t)f_{D,G}(t)}{F_{D,G}(t)-1}dt\right)$.

Derivation of $F_{D,M}(t)$:

Let $T_{D,M}$ be the random variable characterizing the time of death after MM is diagnosed, then its cumulative distribution function $F_{D,M}(t)$ gives the probability of death from MM in t years or less. By the definition of $RS(t)$ as the percentage of patients surviving MM for t years or more (from the SEER database), we obtain $RS(t) = 1 - F_{D,M}(t)$.

References

1. Mengmeng Ji, John H Huber, Martin W Schoen, Kristen M Sanfilippo, Graham A Colditz, Shi-Yi Wang, et al. Mortality in the US populations with monoclonal gammopathy of undetermined significance. JAMA oncology. American Medical Association; 2023;9(9):1293–1295.

Component Overview

1. Simulation Overview

Summary

We describe microsimulation/Monte Carlo simulation and detail for each component/step of the simulation of the constructed WUMM-DES model.

Overview

We performed Monte Carlo simulations using a hypothetical subpopulation aged 20 years with a size of 100,000. For each subpopulation, we first determined whether an individual in this population has an event by comparing the probability P with a random number ($\widehat{P}$), drawn from a uniform distribution $U[0,1]$. If $\widehat{P} < P$, the individual experiences an event; otherwise, the individual does not experience the event. For individuals experiencing an event, their time to such event was determined by another random number from $U[0,1]$ to compare to the CDF for the time-to-event (F) to identify the time corresponding to the random number.

Component Listing

- Progression from no MGUS/MM to MGUS: Within a hypothetical subpopulation aged 20 years without MGUS/MM (n=100,000), we first determined whether an individual in this population develops MGUS by comparing the probability P_G with a random number ($\widehat{P}_G$) drawn from $U[0,1]$. If $\widehat{P}_G < P_G$, the individual develops MGUS; otherwise, the individual dies without MGUS or MM (see below for time to death). For individuals who were determined to develop MGUS, their time to MGUS was determined by another random number, $\widehat{F}_G$, drawn from $U[0,1]$ to compare to F_G to identify T_G, where $T_G = F_G^{-1}(\widehat{F}_G)$. The age at MGUS was then determined by $A_G = 20 + T_G$.

- Progression of MGUS to MM: For those with MGUS, whether an individual develops MM was determined by comparing the probability P_M, where P_M varies with age at MGUS (20-50, 50-64, 65-74, and 75-100), with a random number ($\widehat{P}_M$) drawn from $U[0,1]$. If $\widehat{P}_M < P_M$, the individual develops MM; otherwise, the individual dies without MM (see below for time to death). For individuals who were determined to develop MM, their time to MM was further determined by another random number, $\widehat{F}_M$, drawn from $U[0,1]$ to compare to F_M to identify T_M, where $T_M = F_M^{-1}(\widehat{F}_M)$. The age at MM was then determined by $A_M = A_G + T_M$.

- Death: Age at death was determined by $F_{D,H}$, $F_{D,G}$, and $F_{D,M}$.
  - For individuals without MGUS/MM, their life expectancy was determined by a random number, $\widehat{F}_{D,H}$, drawn from $U[0,1]$ to compare to $F_{D,H}$ to identify $T_{D,H}$, where $T_{D,H} = F_{D,H}^{-1}(\widehat{F}_{D,H})$. The age at death was then determined by $A_H = 20 + T_{D,H}$.
  - For individuals with MGUS without progressing to MM, their life expectancy was determined by a random number, $\widehat{F}_{D,G}$, drawn from $U[0,1]$ to compare to $F_{D,G}$ to identify $T_{D,G}$, where $T_{D,G} = F_{D,G}^{-1}(\widehat{F}_{D,G})$. The age at death for individuals with MGUS without progressing to MM was then determined by $A_{DG} = A_G + T_{D,G}$.
  - For individuals with MM, their life expectancy was determined by a random number, $\widehat{F}_{D,M}$, drawn from $U[0,1]$ to compare to $F_{D,M}$ to identify $T_{D,M}$, where $T_{D,M} = F_{D,M}^{-1}(\widehat{F}_{D,M})$. The age at death for individuals with was then determined by $A_{DM} = A_M + T_{D,M}$.

- The aforementioned process was repeated for each of the four subpopulations. For each subpopulation, we obtained model outputs including prevalence of MGUS, incidence of MM, median age at MGUS/MM, and life expectancy for no MGUS/MM, MGUS without MM, and MM.
- For each subpopulation, the process was repeated for 1,000 times to compute the means, standard errors, and 95% confidence intervals.

2. Calibration Overview

Summary

We provide an overview of the calibration process employed to ensure the accuracy and reliability of the WUMM-DES model. In this process, we fine-tuned the model parameters, including the probability of no MGUS to MGUS, MGUS to MM, and corresponding time-to-event distribution parameters, with the objective to minimize the difference between the simulated outcomes and the real-world data, thus ensuring the model validity.

Overview

For each subpopulation, we targeted the following key parameters for calibration:

1. Probability of developing MGUS in individuals without MGUS/MM (P_G)
2. Parameters for the CDF of time from no MGUS/MM to MGUS (F_G)
3. Probability of developing MM in individuals with MGUS for each of the four age groups: 20-49, 50-64, 65-74, and 75-100 (P_{Mi}, $i = 1, 2, 3, 4$)
4. Parameters for the CDF of time from MGUS to MM (F_{Mi}, $i = 1, 2, 3, 4$)

The calibrated parameters and their corresponding intervals are outlined in **Table 2**.

Table 2: Uncertain parameters for calibration

Symbol	Description	Interval
P_G	Probability of no MGUS to MGUS	$(0, 0.5]$
$a_{G1}, a_{G2}, a_{G3}, a_{G4}, a_{G5}$	Fitting parameters for no MGUS to MGUS (F_G)	$(20, 100]$
$P_{M1}, P_{M2}, P_{M3}, P_{M4}$	Probability of MGUS to MM	$(0, 0.5]$
$a_{M1}, a_{M2}, a_{M3}, a_{M4}$	Fitting parameters for MGUS to MM	$(0, 5]$
$b_{M1}, b_{M2}, b_{M3}, b_{M4}$	($F_{M1}, F_{M2}, F_{M3}, F_{M4}$)	$(0, 3]$

We used age-specific MGUS prevalence and MM incidence for calibration. Age-specific MGUS prevalence with one-year age intervals from age 54 to 80 was estimated from the NHANES 1999 to 2004. Age-specific MM incidence with five-year age intervals from age 20 to 80 were obtained from SEER 2013 to 2018.

These data were compared to the same outputs, i.e., age-specific MGUS prevalence with one-year age intervals from age 54 to 80 ($M = 37$), and age-specific MM incidence with five-year age intervals from age 20 to 80 ($N = 12$), from the simulation. We then performed an optimization to minimize the sum of the squared errors (SS) with respect to the target parameters listed in **Table 2**. The error was defined as the differences between the simulated prevalence/incidence outputs or the prevalence/incidence data.

$$\min_{\substack{P_G, a_{G1}, \cdots, a_{G5}, \\ P_{M1}, \cdots, P_{M4}, \\ a_{M1}, \cdots, a_{M4}, \\ b_{M1}, \cdots, b_{M5},}} SS = \sum_{i=1}^{M} \left| \text{Pre}_{\text{Model},i} - \text{Pre}_{\text{NHANES},i} \right|^2 + \sum_{i=1}^{N} \left| \text{Inc}_{\text{Model},i} - \text{Inc}_{\text{SEER},i} \right|^2$$

subject to:

$$0 < P_G \leq 0.5$$

$$20 \leq a_{G1} \leq a_{G2} \leq a_{G3} \leq a_{G4} \leq a_{G5} \leq 100$$

$$0 < P_{Mi} \leq 0.5, \;\; i = 1, 2, 3, 4$$

$$0 < a_{Mi} \leq 5, \;\; i = 1, 2, 3, 4$$

$$0 < b_{Mi} \leq 3, \;\; i = 1, 2, 3, 4$$

The upper bounds for the constraints were informed by empirical data.

The calibration results can be found in Results Overview.

Output Overview

Summary

We define the outputs generated by MM-DES model, including MGUS prevalence, MM incidence, life expectancy, and life years lost.

Overview

- MGUS prevalence: Prevalence is defined as the proportion of a population who have a specific characteristic in a given time period.[1] In the WUMM-DES model, we evaluated age-specific MGUS prevalence with one-year age intervals from age 54 to 80,

$$Pre_i = \frac{\#\ of\ people\ with\ MGUS\ at\ age\ i}{Total\ \#\ of\ people\ alive},\ \ i = 54,\ 55, \cdots, 80.$$

- MM incidence: Incidence is defined as the number of cases of disease having their onset during a prescribed period of time, which is often expressed as a rate.[2] In the WUMM-DES model, we evaluated age-specific MM incidence with five-year age intervals from age 20 to 80,

$$Inc_i = \frac{\#\ of\ people\ with\ MM\ onset\ between\ age\ [i, i+5)}{Total\ \#\ of\ people\ at\ risk},\ \ i = 20, 25, \cdots, 80.$$

- Life Expectancy (LE): Life expectancy is defined as the average number of years of life a person who has attended a given age can expect to live.[3] In the WUMM-DES model, we evaluate life expectancy with 10-year age group across three different conditions for each subpopulation: people without MGUS/MM, those with MGUS onset but no MM development, and those with MM onset.

- Life Years Lost (LYL): Life years lost, or years of life lost, estimates the number of years that individuals who died would have lived if they had not experienced a specific condition. It provides a measure of the impact of premature mortality on a population. [4] In the WUMM-DES model, we defined as LE without MGUS/MM minus LE at MGUS/MM.

References

1. National Cancer Institute. Mental Health information Statistics, what is prevalence . 2024.
2. National Center for Health Statistics, Division of analysis and epidemiology. 1CDC: Centers for Disease Control and Prevention. . 2024.
3. National Center for Health Statistics, Division of analysis and epidemiology. 1CDC: Centers for Disease Control and Prevention. . 2024.
4. Troy Quast, Ross Andel, Sean Gregory, Eric A Storch. Years of life lost associated with COVID-19 deaths in the United States. Journal of Public Health. Oxford University Press; 2020;42(4):717–722.

Results Overview

Summary

We summarize the key results generated from the WUMM-DES model. Furthermore, it quantifies the differences across various demographic subpopulation in terms of life expectancy (LE) and life years lost (LYL).

Results List

Calibration

We conducted 1,000 simulations for each subpopulation using the calibrated parameters outlined in the Calibration Overview. In each simulation, the model output was compared to the national data to obtain the difference. We then computed the mean squared errors (MSEs) across the 1,000 simulations. We plotted MGUS prevalence (**Figure 2**) and MM incidence (**Figure 3**) to visually present the calibration results in comparison to the data from the NHANES (1999-2004) and SEER (2013-2018) data. The calibrated results closely approximate both the MGUS prevalence and MM incidence. **Table 3** presents the MSEs of the simulated MGUS prevalence and MM incidence compared to NHANES and SEER data.

Table 3: Mean squared errors (MSE) for NHB men and women, NHW men and women

	NHW men	NHB men	NHW women	NHB women
MGUS prevalence MSE (%)	1.64	11.8	0.88	3.52
MM incidence MSE (cases per 100,000)	19.6	3.17	12.7	22.0

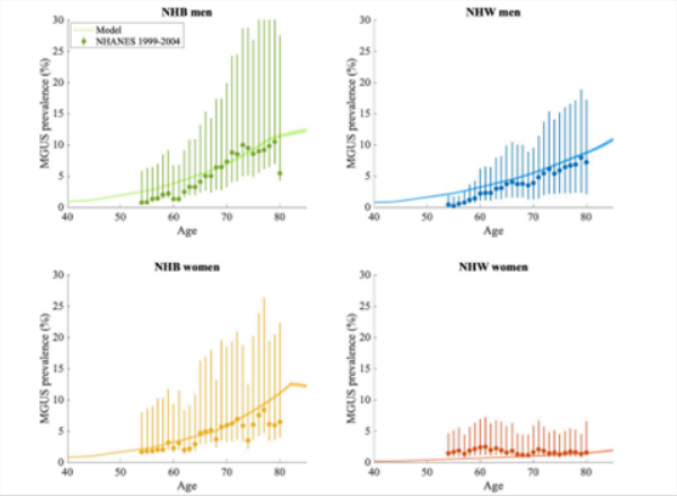

Figure 2. MGUS prevalence for NHB men and women, NHW men and women: calibrated data and 95% CI versus data estimated from NHANES 1999-2004

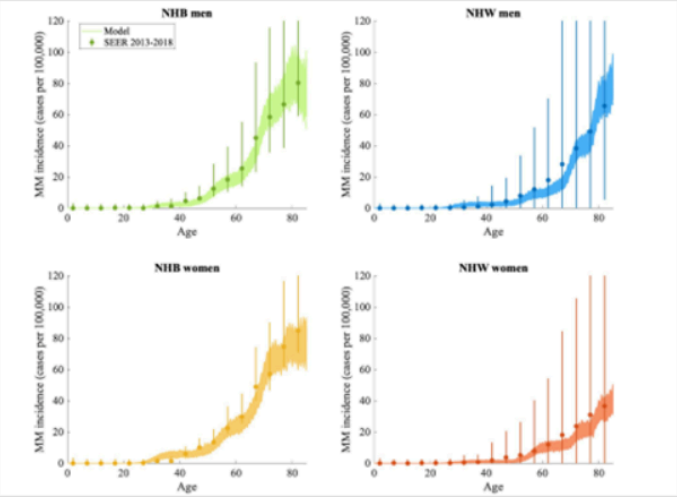

Figure 3. MM incidence for NHB men and women, NHW men and women: calibrated data and 95% CI versus data obtained from SEER 2013-2018

Simulation

The simulation was conducted on the calibrated model 1,000 times for each subpopulation and the means, standard errors, and 95% confidence intervals from these simulations.

We present age-specific incidence (**Figure 2**), LE at MGUS/MM, and LYL associated with MGUS/MM (see **Figure 2** and **Figure 3**). Results show that NHW men and women exhibited longer LEs compared to their NHB counterparts for those diagnosed with MGUS/MM. For both NHW and NHB patients, women exhibited higher LYL after MM diagnosis compared to men.

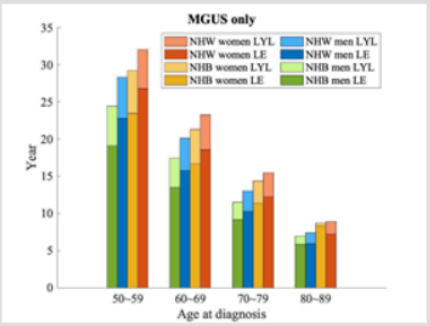

Figure 4. Life expectancy (LE) and life years lost (LYL) for NHB men and women, NHW men and women after MGUS diagnosis.

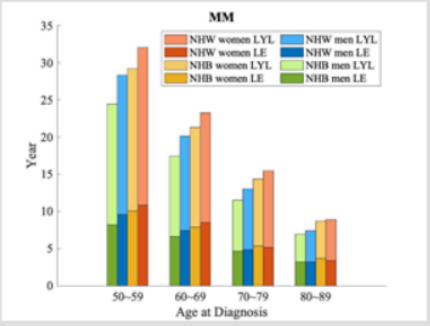

Figure 5. Life expectancy (LE) and life years lost (LYL) for NHB men and women, NHW men and women after MM diagnosis.

Washington University
Key References

Key References

National Center for Health Statistics, Division of analysis and epidemiology. 1CDC: Centers for Disease Control and Prevention. . 2024.

National Center for Health Statistics, Division of analysis and epidemiology. 1CDC: Centers for Disease Control and Prevention. . 2024.

Harvey Jay Cohen, Jeffrey Crawford, Murali K Rao, Carl F Pieper, Mark S Currie. Racial differences in the prevalence of monoclonal gammopathy in a community-based sample of the elderly. The American journal of medicine. Elsevier; 1998;104(5):439–444.

Mengmeng Ji, John H Huber, Martin W Schoen, Kristen M Sanfilippo, Graham A Colditz, Shi-Yi Wang, et al. Mortality in the US populations with monoclonal gammopathy of undetermined significance. JAMA oncology. American Medical Association; 2023;9(9):1293–1295.

Jonathan Karnon. Alternative decision modelling techniques for the evaluation of health care technologies: Markov processes versus discrete event simulation. Health economics. Wiley Online Library; 2003;12(10):837–848.

Sun-Young Kim, Sue J Goldie. Cost-effectiveness analyses of vaccination programmes: a focused review of modelling approaches. Pharmacoeconomics. Springer; 2008;26:191–215.

Ola Landgren. Monoclonal gammopathy of undetermined significance and smoldering multiple myeloma: biological insights and early treatment strategies. Hematology 2013, the American Society of Hematology Education Program Book. American Society of Hematology Washington, DC; 2013;2013(1):478–487.

O Landgren, BI Graubard, S Kumar, RA Kyle, JA Katzmann, K Murata, et al. Prevalence of myeloma precursor state monoclonal gammopathy of undetermined significance in 12372 individuals 10–49 years old: a population-based study from the National Health and Nutrition Examination Survey. Blood cancer journal. Nature Publishing Group; 2017;7(10):e618–e618.

Eric M Maiese, Kristin A Evans, Bong-Chul Chu, Debra E Irwin. Temporal trends in survival and healthcare costs in patients with multiple myeloma in the United States. American Health & Drug Benefits. Engage Healthcare Communications, LLC; 2018;11(1):39.

National Cancer Institute. Mental Health information Statistics, what is prevalence . 2024.

Claire de Oliveira, Reka Pataky, Karen E Bremner, Jagadish Rangrej, Kelvin KW Chan, Winson Y Cheung, et al. Phase-specific and lifetime costs of cancer care in Ontario, Canada. BMC cancer. Springer; 2016;16:1–12.

Troy Quast, Ross Andel, Sean Gregory, Eric A Storch. Years of life lost associated with COVID-19 deaths in the United States. Journal of Public Health. Oxford University Press; 2020;42(4):717–722.

Jagat Singh, Alden W Dudley, Kimberly A Kulig. Increased incidence of monoclonal gammopathy of undetermined significance in blacks and its age-related differences with whites on the basis of a study of 397 men and one woman in a hospital setting. The Journal of laboratory and clinical medicine. Elsevier; 1990;116(6):785–789.

Lachlan Standfield, Tracy Comans, Paul Scuffham. Markov modeling and discrete event simulation in health care: a systematic comparison. International journal of technology assessment in health care. Cambridge University Press; 2014;30(2):165–172.

LB Standfield, TA Comans, PA Scuffham. An empirical comparison of Markov cohort modeling and discrete event simulation in a capacity-constrained health care setting. The European Journal of Health Economics. Springer; 2017;18:33–47.

April Teitelbaum, Abbie Ba-Mancini, Hui Huang, Henry J Henk. Health care costs and resource utilization, including patient burden, associated with novel-agent-based treatment versus other therapies for multiple myeloma: findings using real-world claims data. The oncologist. Oxford University Press; 2013;18(1):37–45.