Microsimulation Model Calibration using Incremental Mixture Approximate Bayesian Computation (IMABC)

Maria DeYoreo and Carolyn Rutter, RAND Corporation
Jonathan Ozik and Nicholson Collier, Argonne National Lab and University of Chicago

Introduction

Microsimulation Models

- Useful for estimating population-level effects of medical interventions on health outcomes by combining results from randomized controlled trials, observational studies, and expert opinion
- Characterized by simulation of individual event histories for an idealized population of interest based on mathematical models for the disease process
- These processes are not directly observable, though their outcomes are
- Calibrated MSMs an be used to make predictions about population-level trends in disease outcomes, effectiveness of interventions, and for estimating the comparative effectiveness of interventions that cannot otherwise be directly compared

MSM Calibration

- Involves selecting parameter values that result in model predictions that are consistent with observed data and expected findings
- Bayesian calibration methods focus on estimating the joint posterior distribution of model parameters given calibration targets, to capture uncertainty in the model parameters
- Calibration process can be difficult as it involves searching a high dimensional parameter space to predict many targets accurately and estimating likelihood is difficult and costly
- Calibration data are derived from published studies, and typically take the form of summary statistics (e.g., means, incidence rates)
- We assume that the data from published studies arise from known distributions, such as binomial, multinomial, or Poisson distributions, obtaining point estimates and confidence intervals for calibration targets
- Calibrating to individual-level data (reported in aggregate) requires simulating of a set of individuals that are similar to the study population based on characteristics that include age, gender, and prior screening patterns
- In total, we calibrate to 36 data points from 7 sources (registry data, epidemiological studies)

IMABC Algorithm

We develop an Approximate Bayesian Computation (ABC) algorithm that begins with a rejection-sampling ABC step, and incrementally update this initial sample by drawing from a mixture distribution centered at points that are closest to the targets. This was motivated in part by IMIS [1].

Algorithm

1. Rejection sampling ABC step: Sample $\theta_1, \ldots, \theta_{N_0}$ from the prior distribution of parameters, $\pi(\theta)$
   - Simulate calibration targets, S_{ij}, $i = 1, \ldots, N_0$, $j = 1, \ldots, J$
   - Accept θ_i if all S_{ij}, $j = 1, \ldots, J$, fall within the tolerance region (we use $(1 - \alpha_j^{(0)})$% confidence intervals for the targets O_j), and let $\delta(\theta_i, \alpha) = 1$

   For iteration $k = 1, 2, \ldots$ of the algorithm, we repeat the following steps to refine the proposal distribution and sample new points:
2. Find the best points and sample new ones:
   - Calculate the scaled distance between point estimates of the observed and simulated targets for all accepted θ_i, i.e., $\{\theta_i, i = 1, \ldots, N_k : \delta(\theta_i, \alpha_{(k-1)}) = 1\}$
   - Select the m samples of θ with the smallest scaled distance, $\theta_{(l)}$, $l = 1, \ldots, m$, and simulate new draws around each of these points using multivariate normal distributions with means $\theta_{(l)}$
3. Check to see if the tolerance can be updated to the two-sided p-value for the test of H_0: $S_{ij}^* = \hat{O}_j$, where S_{ij}^* has the median value of $|\hat{O}_j - S_{ij}|$ among accepted points
4. Determine sampling weights $w_i = \pi(\theta_i)/q_k(\theta_i)$, where q_k is a mixture distribution based on the $k+1$ iterations of the algorithm up to this point, and calculate the effective sample size (ESS) of draws from the posterior, $(\sum_{i=1}^{N_k} w_i^2)^{-1}$, where $w_i = 0$ if $\delta(\theta_i, \alpha_k) = 0$
   - If ESS$>$ N_{post} we stop and take a weighted sample from all accepted points. Otherwise, we return to step 2 and continue.

Other Implementation Details

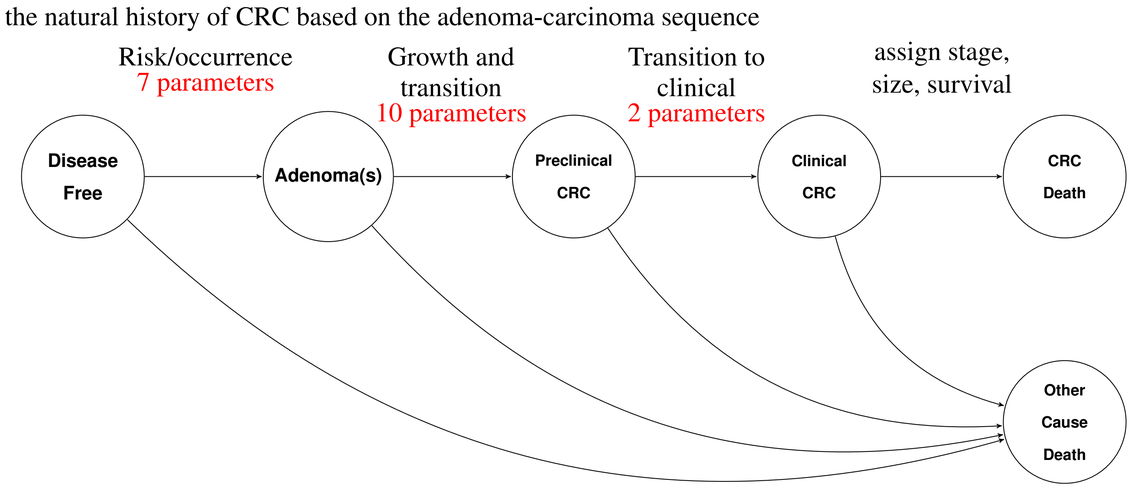
- First evaluate targets that are not time intensive to compute to avoid unnecessarily simulating the remaining, computationally intensive, targets
- Use $m = 10$ centers to take advantage of computing power and ensure exploration of space
- Let N_0 be large when using noninformative priors
- IMABC is adaptive since we start with small $\alpha^{(0)}$ (large tolerance) and update it at each iteration

Acknowledgements

The authors gratefully acknowledge the National Cancer Institute and the National Institute of Health for supporting this work. C. Rutter and M. DeYoreo were supported by NCI U01 CA199335. J. Ozik and N. Collier were supported by NIH R01 GM115839.

Microsimulation Model

Colo**R**ectal **C**ancer **S**imulated **P**opulaton **I**ncidence and **N**atural history model (CRC-SPIN) describes the natural history of CRC based on the adenoma-carcinoma sequence



1. **Adenoma occurrence**: modeled with a nonhomogeneous Poisson process with risk having age and sex effects
2. **Adenoma growth**: Janoshek growth curve, time to reach 10 mm has Frèchet distribution allowing for slow growing adenomas
3. **Transition to preclinical cancer**: Lognormal distribution for transition from adenoma to preclinical cancer with mean function of sex, location, age
4. **Transition to clinical cancer**: Weibull distribution with location-dependent parameter for transition from preclinical to clinical cancer (sojourn time)

Once clinically detectable, simulate stage and size based on Surveillance, Epidemiology, and End Results (SEER) data from 1975-1979, with survival time simulated based on a Cox proportional hazards model estimated using SEER data on cancer survival

CRC-SPIN Calibration Results

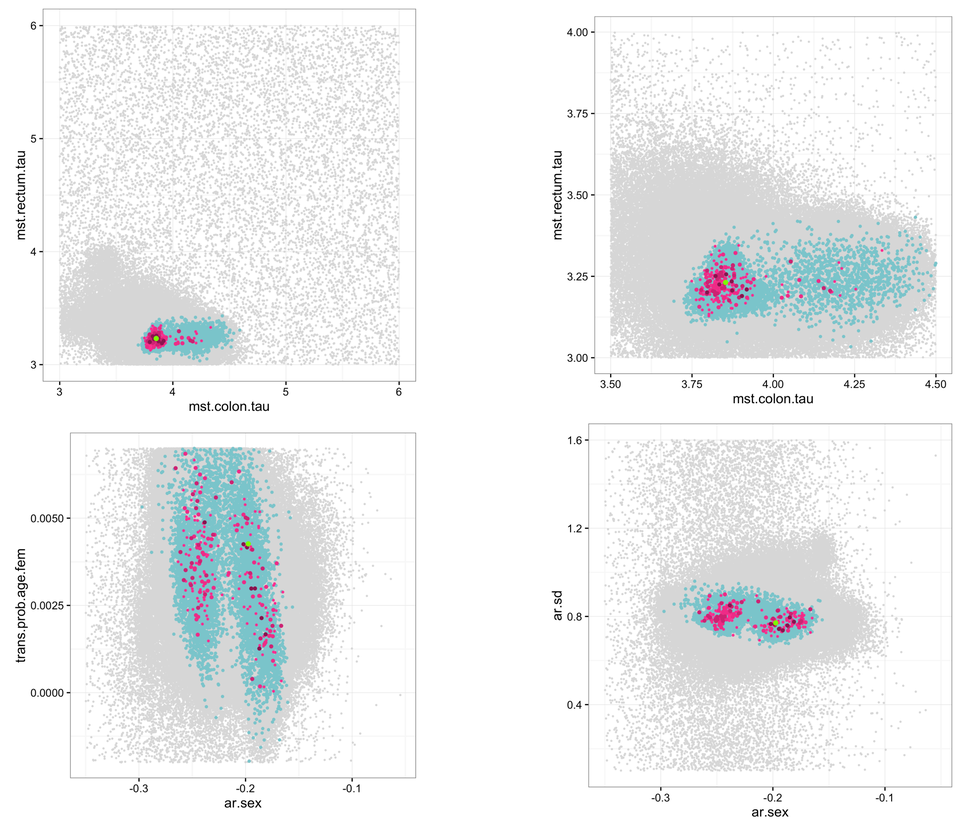


Figure 1: Scatterplots of samples of parameters θ drawn via IMABC. Blue points correspond to all samples drawn at the most recent iteration, pink points represent all accepted points (with darker colors corresponding to simulated calibration data points that are closer to the targets), and gray corresponds to all points sampled up to the current iteration.

Conclusions and Future Work

- Previous work used MCMC for MSM calibration [2] which had a number of drawbacks
- The proposal distribution we use consists of a mixture of normal distributions, which allows us to take advantage of parallelized code, is useful in capturing multimodality, and ensures we are exploring the parameter space fully
- Future work will provide guidance on efficient algorithm implementation: Number of initial draws, centers (mixture components), draws per center, number of embedded simulations...

References

[1] A. Raftery and L. Bao. Estimating and projecting trends in HIV/AIDS generalized epidemics using incremental mixture importance sampling. *Biometrics*, 66:1162–1173, 2010.

[2] C M Rutter, D L Miglioretti, and J E Savarino. Bayesian calibration of microsimulation models. *JASA*, 104:1338–1350, 2009.