Notable Differences between CRC-AIM and CRC-SPIN

There are two fundamental differences between CRC-AIM and CRC-SPIN.

The first is in overall approach. CRC-SPIN is a continuous-time microsimulation model, in which the natural history processes that describe an individual's adenoma-carcinoma sequence are generally expressed as continuous cumulative distribution functions (CDFs). As a result, CRC-SPIN generates events in an individual's life that can be precisely expressed within an arbitrarily small unit of time.

In contrast, CRC-AIM features a cycle-based approach, in which event probabilities—namely adenoma generation and transition into preclinical cancer—are assigned at the beginning of a cycle and depend on the pre-defined cycle length. This approach is commonly used to develop microsimulation models (eg, by TreeAge Pro, a popular modeling software) and reflects more classic, canonical ways of structuring and considering microsimulations. A cycle-based approach can facilitate collaboration among clinicians and researchers who do not have a substantial background in programming. One consequence is that it does not allow for either the generation of multiple adenomas in the same year or an individual transitioning across "health states" in the same year (eg, an adenoma transitioning to both preclinical and clinical CRC). However, the probability of multiple health state transitions occurring within the same year has been quantified in a CRC-SPIN publication and was found to be exceedingly small.[1]

The second difference relates to microsimulation model calibration. Calibration is the process of deriving model parameters that allow the model to replicate expected or observed data, referred to as calibration targets.[1] The CRC-SPIN model uses a

Bayesian calibration method, which offers two advantages over non-Bayesian methods[1]: (1) posterior model parameters can be explicitly influenced by prior knowledge such as expert opinion or empirical data, which is incorporated as prior distributions; and (2) the uncertainty of modeled outcomes can be quantified as prediction intervals by sampling across the joint posterior distribution of model parameters.

Calibration may be implemented as an automated statistical procedure to update a model's parameters and can be performed for various reasons, including incorporating new empirical evidence, modifying prior distribution(s) (for Bayesian models) and/or calibration targets, or updating poorly performing statistical distributions within the model (eg, for CRC-SPIN v2.x[2]). After calibration is performed, when a Bayesian microsimulation model is executed, parameters are sampled across the joint posterior distribution. This parameter sampling generates an estimate for each model parameter (23 for CRC-SPIN) and the natural history of individuals—often millions of individuals—are simulated. The parameters are then resampled and another set of individuals are simulated. This process is repeated for hundreds or thousands of samples of the joint posterior distribution. The average outcome across all draws is often reported as the point-prediction, and prediction intervals for the outcome can be estimated using percentile methods to indicate uncertainty in model predictions. The process is similar in concept to a probabilistic sensitivity analysis.

CRC-AIM does not implement a Bayesian calibration component, although we may incorporate a formal calibration component into future versions of the model. Bayesian calibration methods for complex microsimulations are computationally costly

to perform and, once calibrated, Bayesian microsimulation models are computationally costly to execute. After we recognized that certain model parameters had to be recalibrated (see “CRC-AIM Recalibration”), we estimated a single set of these best-fitting parameters using Latin Hypercube sampling methods to generate a parameter space and a Gaussian process framework to perform parameter optimization. This optimization framework can be suitable for computer simulations that yield little to no variation in outcome given the same set of inputs, as long as a sufficiently large simulation size is used. We selected particular natural history outcomes from CRC-SPIN as calibration targets to help ensure comparability between CRC-SPIN and CRC-AIM.

References

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