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Visually modelling the cost-effectiveness of AML treatment strategies

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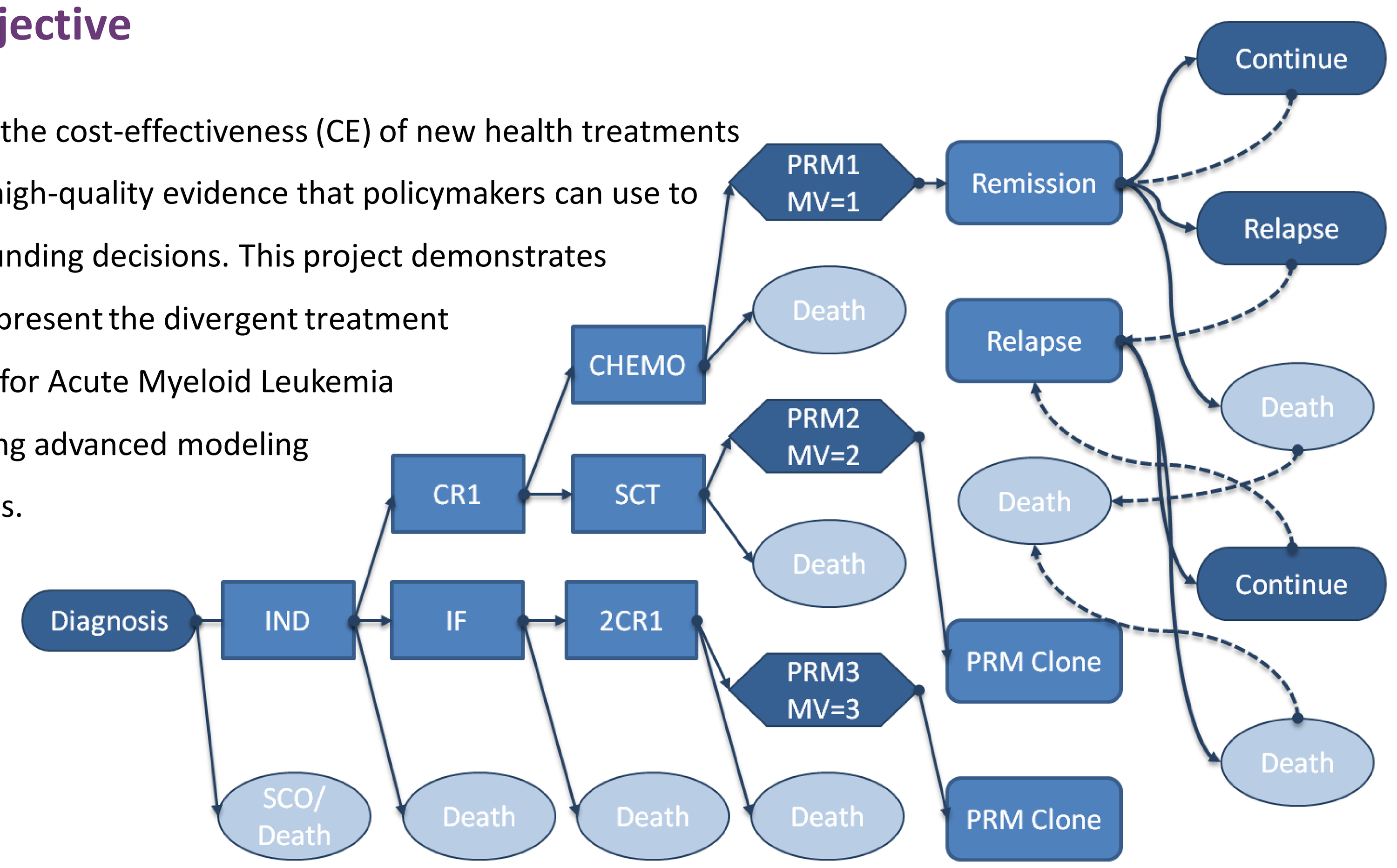
The objective

Modeling the cost-effectiveness (CE) of new health treatments provides high-quality evidence that policymakers can use to support funding decisions. This project demonstrates how to represent the divergent treatment pathways for Acute Myeloid Leukemia (AML) using advanced modeling techniques.



Decision tree model

Figure 1. The possible outcomes of an AML diagnosis are visually represented. Straight lines are for observed average rates of transition from our sample. Curved lines are for calculated probabilities of transition after a patient achieves remission.

Our technical approach

- ➢ Following a conceptual map of the modeling requirements for AML treatment, we programmed in TreeAge software a model that contains a decision tree and Markov models at the right of the decision tree "branches."
- ➢ The Markov transition probabilities were calculated using Stata-based survival analysis on our outcomes data.
- ➢ The impact of parameter instability was evaluated using probabilistic sensitivity analysis, discussed further at right.

The Markov model

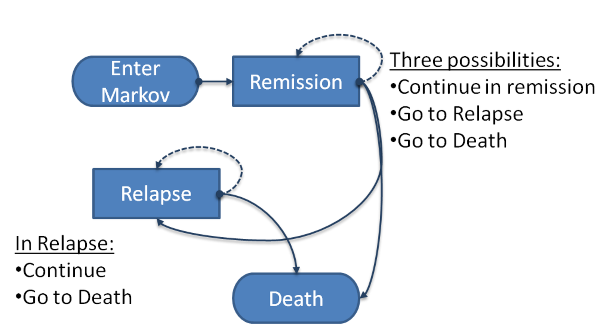
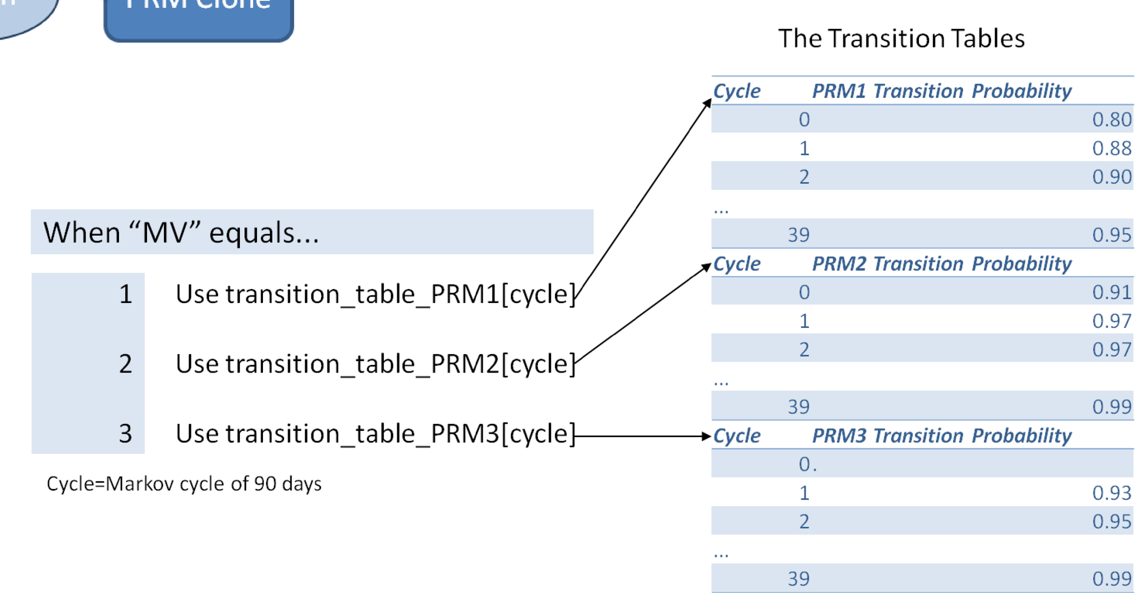


Figure 2. Here simulation subjects begin the model process in remission and move between three health states according to transition probabilities for the current cycle of time.

Table 1. Model health states with definitions

Diagnosis	Patient is diagnosed with AML
IND	Patient receives induction chemotherapy
SCO/Death	Patient bypasses induction chemotherapy
CR1	Patient achieves complete remission achieved after consolidation therapy
CHEMO	Patient receives consolidation chemotherapy after CR1
SCT	Patient receives stem cell transplant after CR1
PRM1	Patient is 90 days disease-free after consolidation chemotherapy
PRM2	Patient is 90 days disease-free after stem cell transplant
PRM3	Patient is 90 days disease-free after achievng 2CR1
IF	Patients are in this state if the fail to achieve remission after induction therapy
2CR1	Patient achieves remission after second induction chemotherapy treatment
Remission	Patient has had no disease recurrence
Remission Continue	Patient remains in Remission state at cycle end
Relapse	Patient experiences disease recurrence
Relapse Continue	Patient remains in Relapse state at cycle end
MV	Markov variable, used by arrays to assign correct values to Markov models
Clone	Clone of PRM1 model using MV=2 or 3 values

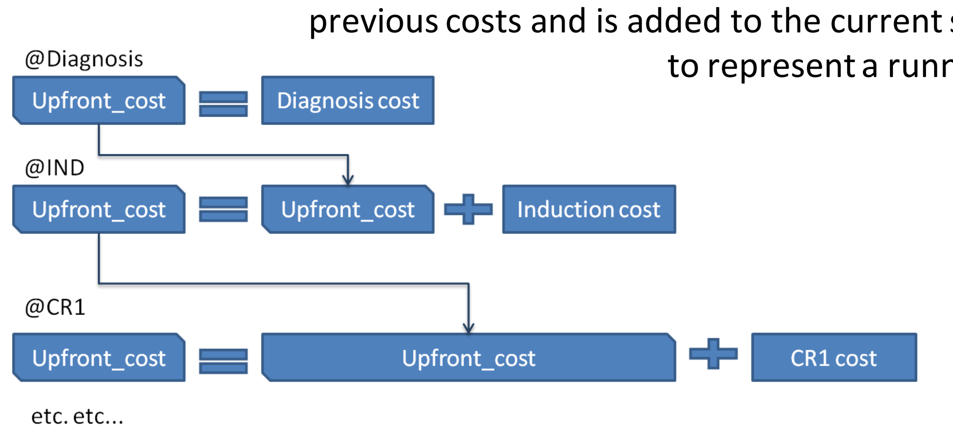


Array variables with table "look-ups"

Figure 4. Each PRM group is assigned a value of MV. Those three values are placed in variable which is defined as a list or "array"; each list item is defined with a table. The cycle of the Markov process determines which table value is used in the calculation of that cycle.

Recursive cost variables

Figure 3. Costs in the upfront model are defined with "Upfront_cost", a recursive variable that includes all previous costs and is added to the current state cost to represent a running total.



Hypothesizing disease pathways...

Data : at the patient level

- ➢ We used comprehensive patient-level cost and outcomes data from Vancouver General Hospital.

Cost-effectiveness analysis

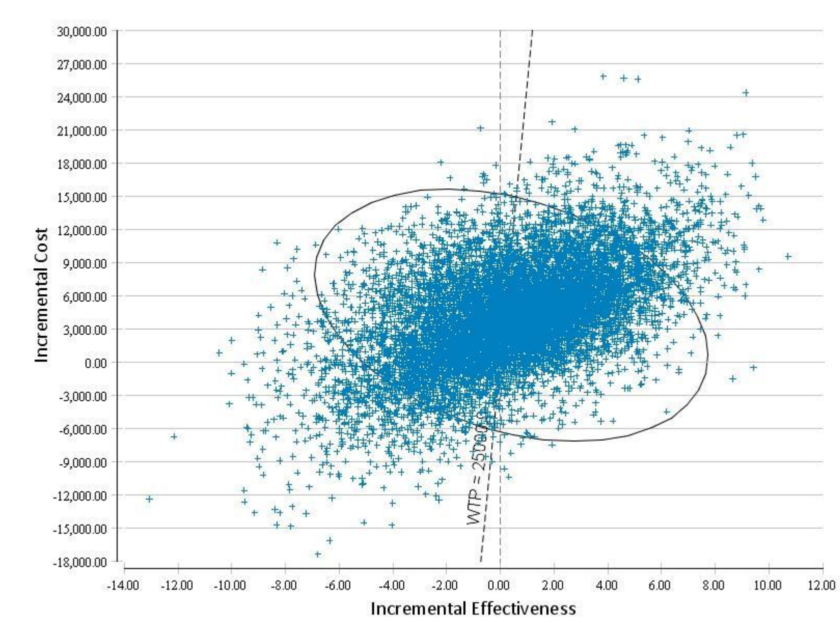
- ➢ With tables of cycle-specific costs and outcomes data, we programmed a comprehensive AML decision model.
- ➢ Cost variables were attached to every health state that subjects experience in the model.
- ➢ Outcomes awarded and costs picked up in the Markov models were discounted into the future.
- ➢ An incremental cost-effectiveness ratio (ICER) was calculated to compare costs (C) and effects (E) for the treatment (1) and comparator (2) interventions: ICER=(C1-C2)/(E1-E2)
- ➢ The model was tested and validated probabilistically and was used to develop scenarios relevant to AML diagnosis and treatment and policy.

Simulating uncertainty...

With Probabilistic Sensitivity Analysis (PSA)

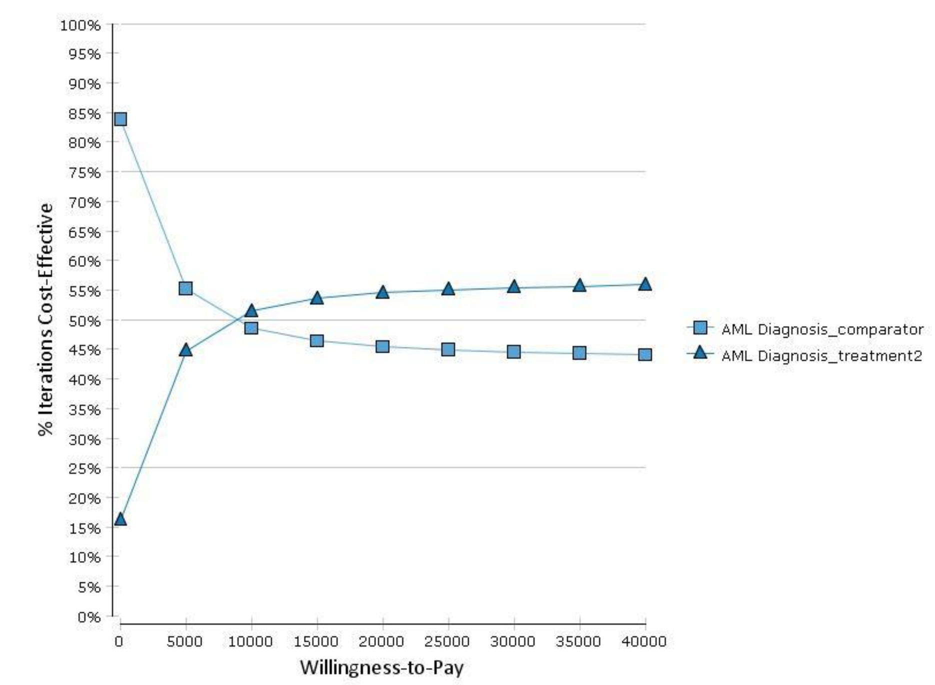
- ➢ Sensitivity analysis shows how the model results change at different levels of model variables. For example if a model's data inputs are based on assumptions, such as those coming from expert opinion, they may contain more uncertainty than observed data.
- ➢ In this PSA we used our data as mean values for distributions that correspond to the variable category (Gamma for costs, Beta and Dirichlet for effectiveness).
- ➢ We then set the model to run many times, using at each run or "iteration" a different and random draw from the included distributions that are centered on our data values.
- ➢ Each iteration of the PSA produces an ICER: the comparator's costs and outcomes are subtracted from the treatment option (presumably more costly).

Premilinary PSA results



Scatterplot with ellipse

Figure 5. Here each point is one of the PSA ICERs. Points to the right of the WTP line are cost-effective. The ellipse represents the confidence interval; it contains 95% of the ICER points.



Aggregate CE acceptability curve

Figure 7. Shows what percent of iterations are cost-effective at different levels of willingness-to-pay (WTP).

Incremental CE plot report

Table 2. Shows by proportion where iteration ICERs fall on the four quadrants of the cost-effectiveness plane.

INCR-EFF	INCR-COST	QUADRANT	INCR-CE	PROPORTION
IE>0	IC<0	IV	Superior	0.0284
IE>0	IC>0	I	ICER<25000.0	0.5207
IE<0	IC<0	III	ICER>25000.0	0.0013
IE>0	IC>0	I	ICER>25000.0	0.0197
IE<0	IC<0	III	ICER<25000.0	0.1323
IE<0	IC>0	II	Inferior	0.2976
IE=0	IC=0	origin	0/0	0

Our conclusions

- ➢ The model estimates a hypothetical patient's life expectancy as well as the cost associated with fulfilling that expectation.
- ➢ It shows with reasonable certainty that the diagnostic intervention may be considered cost effective at WTP thresholds of $100,000/LYG.

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Genome BritishColumbia

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