IMPLEMENTATION OF A MICROSIMULATION MODEL FOR THE CLINICAL PATHWAY OF LIVER TRANSPLANTATION IN ITALY USING STATA/MP®

MSR143

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Introduction

Liver transplantation (LT) remains the optimal therapeutic option to address various liver diseases.[1] However, both the graft and post-transplant care impose a substantial economic burden for healthcare payers,[2-4] and therefore understanding the lifetime cost trajectories of patients undergoing transplant may be crucial in detecting cost drivers and enable the introduction of cost-saving technologies.[2]

Different simulation models are available to model the clinical pathway of transplanted patients,[5] but given the multiplicity of complications that may arise after the surgery, as well as the complexity of patients' follow-up, deterministic cohort models are inadequate to reflect the decision problems related to LT,[6] making individual-based models the most appropriate choice. This study aims to outline the implementation of a microsimulation model using the software Stata/MP® (StataCorp LP, Texas, USA) to replicate the clinical pathway of patients undergoing liver transplantation in Italy and estimate their associated lifetime costs, with respect to more traditional approaches.

Methods

In line with the methodology reported by the National Institute for Health and Care Excellence (NICE),[7] the overall process to construct the optimal model replicating the clinical pathway for patients undergoing liver transplant in Italy was developed by following a multi-step approach (*Figure 1*):

1. Initially, a targeted literature review was performed to define the clinical pathway of patients undergoing LT and, consequently, the best modeling approach to represent this clinical condition;
2. Subsequently, a pragmatic review of the scientific literature was conducted according to the PRISMA guidelines to retrieve the available information to inform the model and build a final model structure and a final version of the pathway;
3. Then, based on the modelling approach chosen in step 1 and the key components retrieved in point 2, a microsimulation model reflecting the clinical pathway was developed and implemented in Stata/MP®:
    - The model was constructed to simulate the healthcare trajectory of 10,000 individual patients who started their clinical pathway post-surgery and were followed-up until death.
    - The simulation consisted of 12 one-month cycles in the early post-transplant period and up to 44 one-year cycles subsequently, for a maximum time horizon of 45 years.
    - The modelling structure of each of the 56 cycles is presented in *Figure 2*: initially, the values of patient characteristics and unit costs values were manually inputted, and the evolution of occurrence and survival probabilities was programmed. Then, each cycle was modelled separately using an iterative approach, by updating patients' characteristics, health, and cost outcomes with respect to the previous cycle, thanks to the ability of microsimulations to track each patient's individual history.
    - To inform the initial values of inputs and their time-dependent update, costs were retrieved from the literature and National tariffs or calculated using a micro-costing approach, as appropriate, while each events' probability of occurrence was retrieved from literature and extrapolated beyond its original follow-up to cover the entire patient's life, using the fittest parametric model.
    - In each cycle, patients could be subject to different events with a time-varying probability of occurrence and were assigned the associated costs and survival probability.
4. Finally, to ensure robustness of model results, the direct healthcare lifetime cost of an average patient undergoing LT was obtained by running 1,000 simulations enhancing standard errors convergence towards 0. Moreover, a set of deterministic sensitivity analyses were conducted to furtherly test model's reliability.

Results

The microsimulation model in the present analysis proved to be easily implementable through a statistical software such as Stata/MP®. In particular, the initial programming of the evolution of each patient pathway through the model cycles allowed to smoothly modify inputs in the same section of the code, both during the model review phase and for deterministic sensitivity analyses. This feature also facilitates the replication of the model structure and results.

In terms of results regarding average total lifetime cost for a patient undergoing LT in Italy, the model successfully provided statistically stable cost estimates, proving itself as a suitable and solid method to replicate the pathway of liver transplantation patients with small enough standard errors of estimates (*Figure 3*).

The reliability of the model was further confirmed through discrete sensitivity analyses, in which variation of costs, incidence and survival inputs led to variation in results between -13% and +7% with respect to baseline estimates. Furthermore, face validity of results was assessed with Italian clinicians experts in liver transplantation, and external validation of estimates was performed with values reported in published Italian sources.

Finally, the implementation of the model proved to be highly efficient, as the average running time of each 10,000 patients' simulation was less than 4 seconds.

Conclusions

A microsimulation method on Stata/MP® implemented with a multi-step approach effectively modeled the complex clinical pathways of patients undergoing liver transplantation. This method successfully replicated individual patient healthcare trajectories, ensuring statistically stable estimates and presenting a robust alternative to conventional cohort modeling techniques.

Figure 1. ***Steps performed for microsimulation model development***

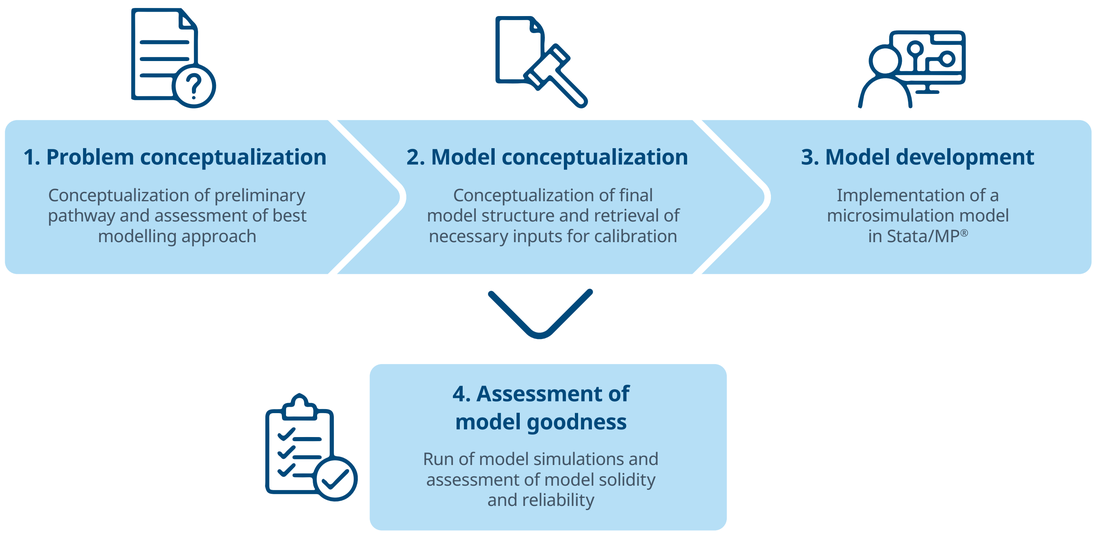


Figure 2. ***Modelling approach for each individual cycle within each simulation***

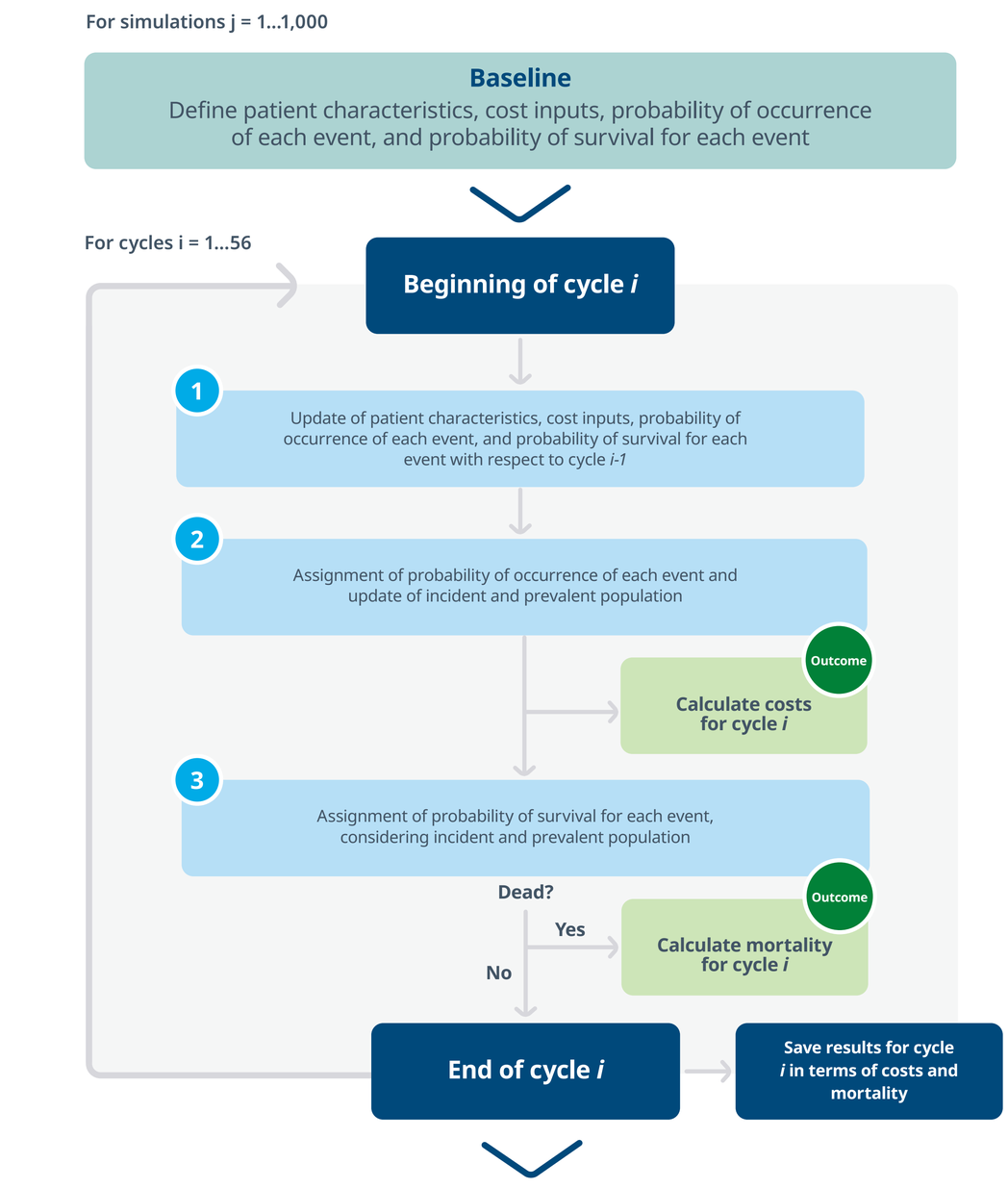
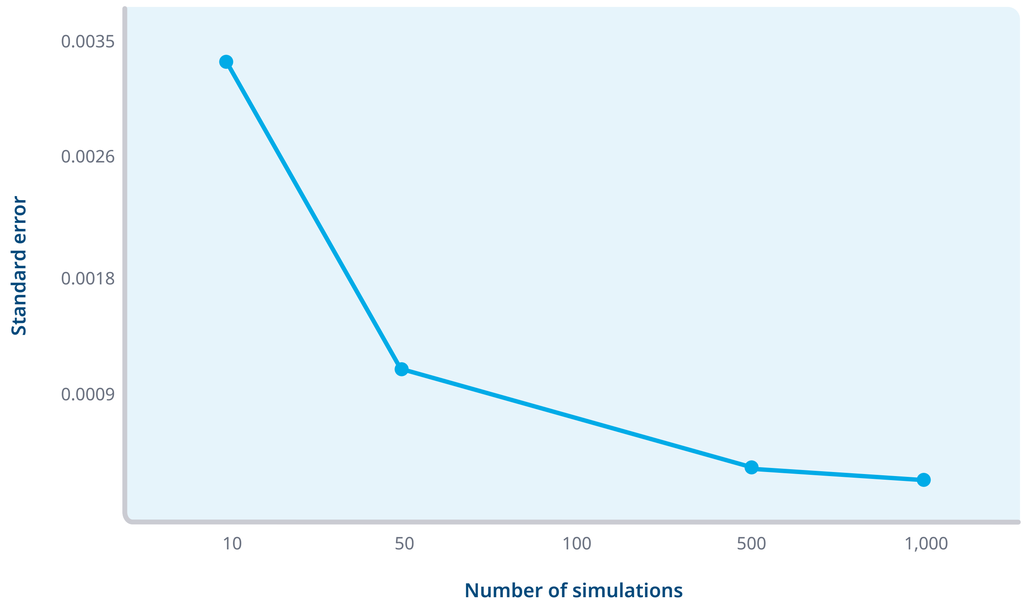


Figure 3. ***Standard error of model result, by number of simulations***



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