Discrete Event Simulation Model for Real-World Restricted Treatment Policies in End-Stage Heart Failure

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Introduction

- Queuing is highly relevant in heart failure treatment.
- The gold standard treatment for carefully selected patients with end-stage heart failure (ESHF) is orthotopic heart transplantation (HTx). A patient's waiting list status changes based on health status (Fig 1.)
- Supportive left ventricular assist devices (LVADs) are mechanical circulatory support, used as a bridging therapy. LVADs buy the patient time whilst they wait for a suitable donor heart (Fig 2.).

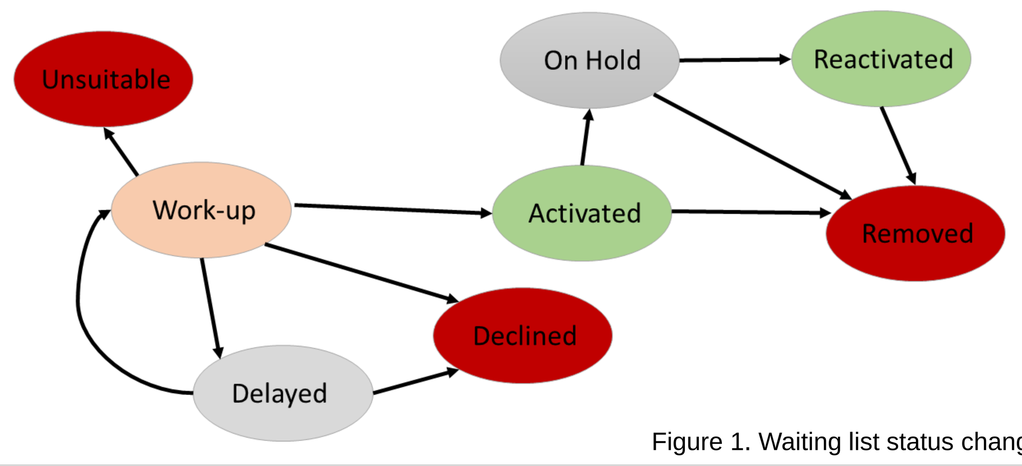

Figure 1. Waiting list status change flow-chart

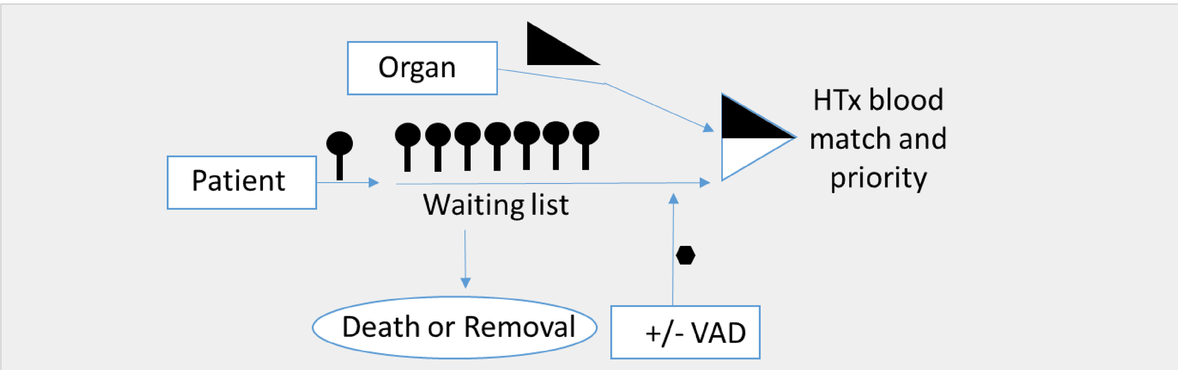

Figure 2. Schematic of HTx waiting list with/without LVAD

Objective

- Use discrete event simulation (DES) to appropriately capture the resource constraints in an economic evaluation with Patient generators (eligibility status on waiting list), Donor Organ generator and Organ Match (Fig 3).
- The "Queue model", to represent the natural history of the waiting list and incorporate allocation of LVADs and HTx, vs. "No Queue model" to reflect a typical non-constrained economic evaluation.
- The cost-effectiveness of the current ESHF policy (Policy B, "current world") compared with the previous ESHF policy without LVADs (Policy A, "previous world"). The cost-effectiveness of expanded availability of LVADs (Policy C, "increase LVADs") and HTx (Policy D, "increase HTx").

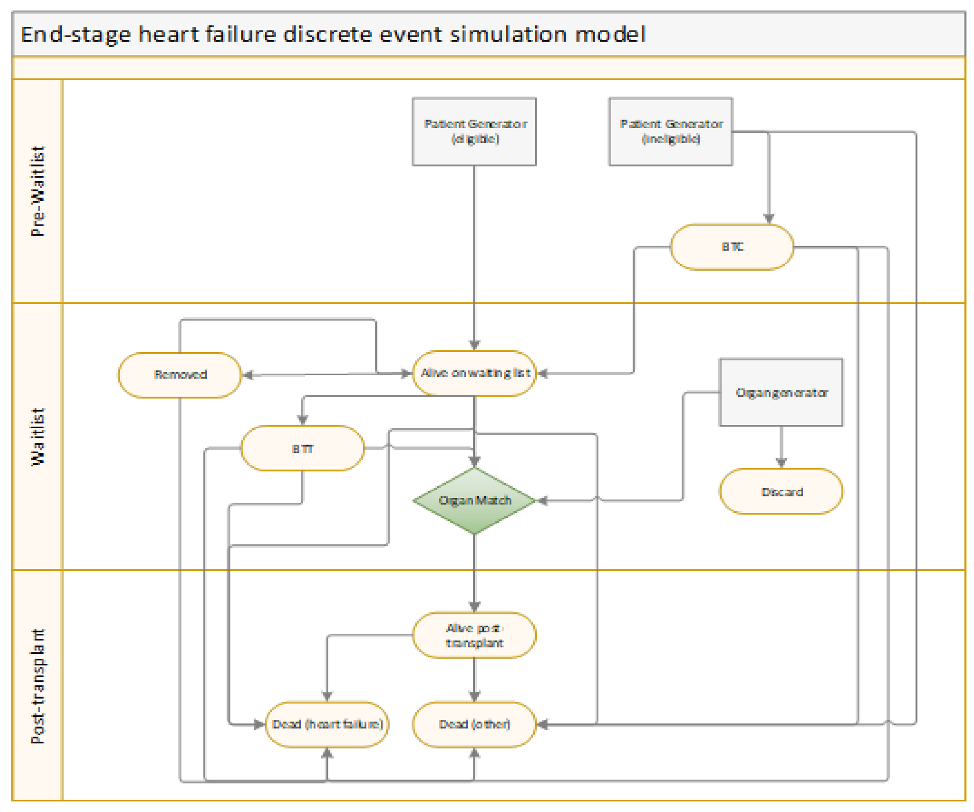

Figure 3. Flow-chart design of discrete event simulation model

Method

A cost utility analysis, based on a DES model using the agent-based simulation software AnyLogic® (V8, St Petersburg, Russia) (Tab 1).

- Individual patient data (n=77) sourced from St. Vincent's Hospital Sydney, AUS and published registries
- 20 years time horizon and costed at $AUD2019 from a healthcare system perspective.
- Costs and benefits were discounted by 5% per annum in line with Australian economic evaluation guidelines.
- Random numbers used to implement the selection from distributions. The model agent (patient or organ) arrival rates followed a Poisson distribution. A fixed seed was applied.
- Quality of life – utility values (Göhler et al. 2009) by New York Heart Association (NYHA) functional classification of disease and event.

Model structure

- The DES components in AnyLogic ® (Table 1) as applied in:
- Queue model including Source for ineligible and waitlist (prevalent or new) patients, LVAD and donor organ arrival. LVAD implant for ineligible patient (Match BTC), LVAD implant for eligible patient (Match BTT), Match HTx (Fig 4). The No Queue model excluded LVAD and donor organ arrival and the corresponding Match (BTC, BTT, HTx).
- Each event modifies the current flow of patients on the waiting list and the number of patients that are eligible for LVAD implant or HTx.

Table 1: Components of a DES in AnyLogic®

Component	Description
Source	Agents consume resources or experience events arrive in the model
Parameter	Attributes of entities
Delay	Stochastically delays patients for a given amount of time.
Match	Synchronises two streams of agents by matching pairs according to a given criteria. The agents that have not been matched are stored in two queues (one for each stream). Once the new agent arrives at either of the input ports, it is checked for match against all agents in the queue for the other stream. If the match is found both agents exit the Match object at the same time.
Combine	Waits for two agents to arrive and outputs a new agent
Select Output	Routes incoming agents to one of up to 5 output ports depending on probabilistic or deterministic conditions.
Sink	Disposes agents
Wait	A buffer or queue of agents allowing for manual retrieval.

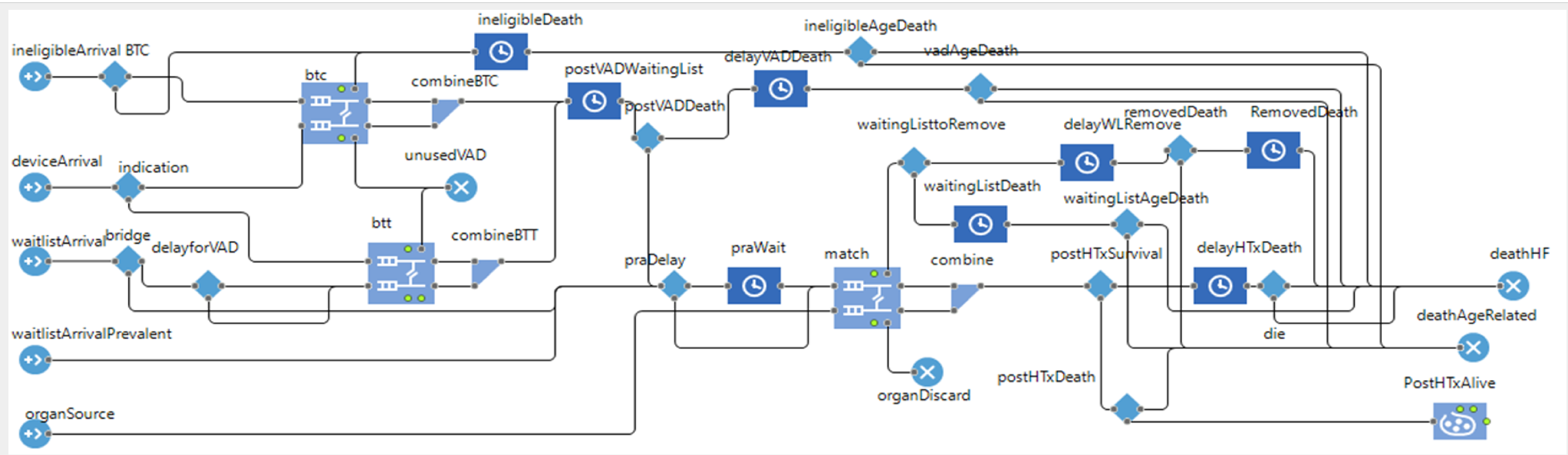

Figure 4: Model Structure – Queue

Results

- In a comparison against the previous ESHF policy (Policy A), i.e. prior to the introduction of LVADs. The Queue model for Policy B vs. Policy A produced an ICER of AUD$179,450 per QALY gained whilst the No Queue model produced an ICER of AUD$209,171 per QALY gained. The incremental cost was larger but also accompanied by larger incremental gains. This resulted in a lower (better) ICER per QALY gained in the No Queue model vs. the Queue model. In the Queue model, Policy C provides LVADs to patients at a faster rate; however, there is no corresponding increase in the available supply of donor hearts.
- An incremental analysis was conducted for the Queue model and the interventions were ranked from least costly to most costly: Policy A < Policy D < Policy B < Policy C. In the Queue and No Queue model, Policy C is a dominated option (Fig 5 and Fig 6). This means that Policy B is cheaper and produces more QALYs than Policy C in both models.

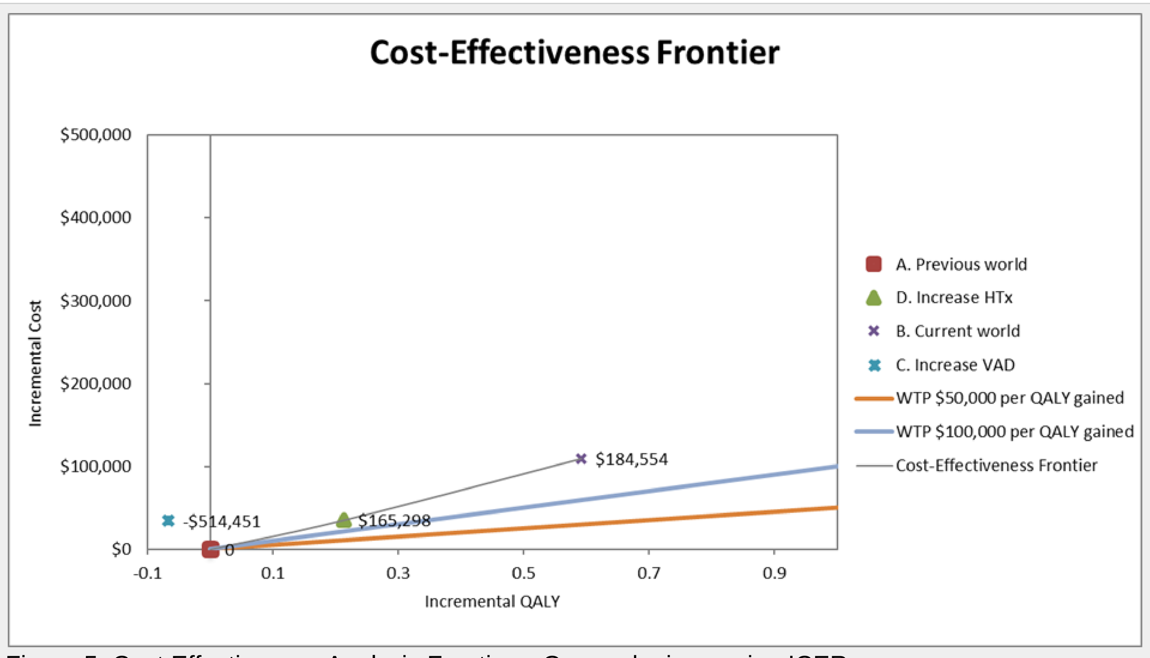

Figure 5: Cost Effectiveness Analysis Frontier – Queue, by increasing ICER
Note: Policy C is a dominated option.

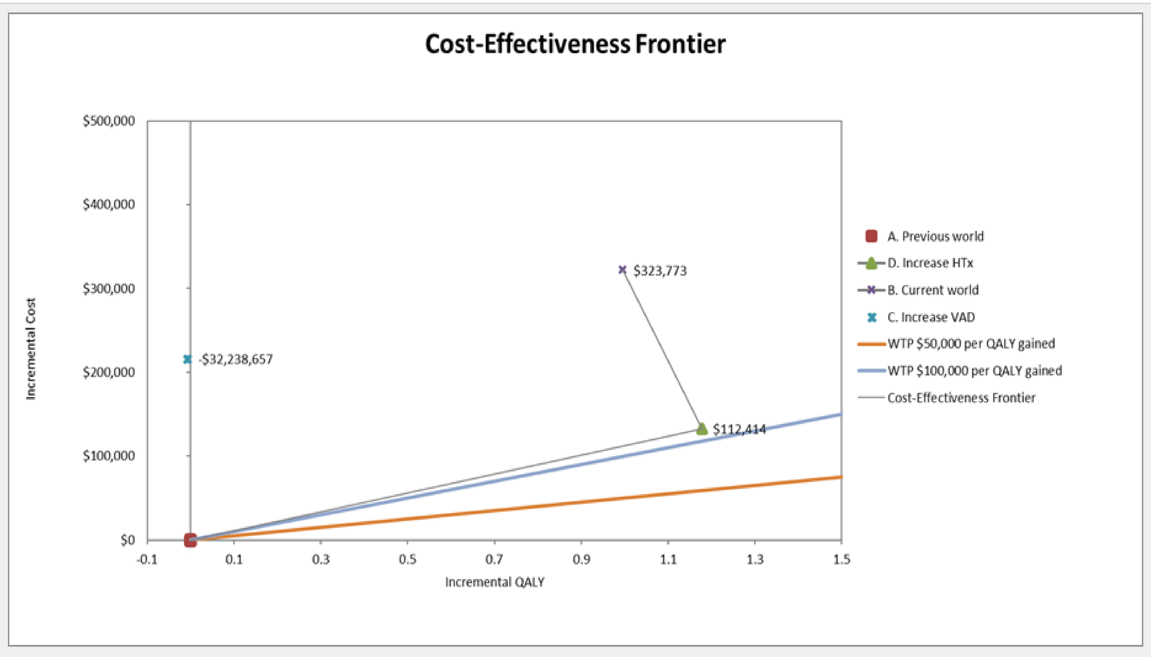

Figure 6: Cost Effectiveness Analysis Frontier – Queue, by increasing ICER

Discussion and conclusion

The Queuing model reflects patients competing for resources (LVADs and HTx) as well as the interaction between the patient and the donor organ via the matching algorithm. These results demonstrate the importance of considering resource allocation decisions in HTA, specifically when policies are supply-restricted. The organ donation policy in Australia is resource-constrained with a HTx matching algorithm driving time spent on the heart transplant waiting list.

Abbreviations: AUD = Australian Dollar; AUS = Australia; BTC = bridge to candidacy; BTT = bridge to transplant; HTx = heart transplant; ICER = incremental cost-effectiveness ratio; LVAD = left ventricular assist device; NYHA = New York Heart Association; QALY = quality-adjusted life year; VAD = ventricular assist device; WTP = willingness-to-pay

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