How many simulations of a dynamic transmission model are enough to estimate uncertainty?

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Background

Dynamic transmission models (DTMs) are the preferred choice for simulating infectious diseases and the impact of associated interventions. DTMs typically incur substantial computational overheads and are therefore often estimated deterministically, affecting decision uncertainty in economic evaluations of interventions. The aim of this study was to explore the potential for using a curtailed probabilistic sensitivity analysis (PSA) in DTMs and to assess the precision associated with varying numbers of PSA simulations.

Methods

An age-structured DTM of varicella-zoster virus (Figure 1), developed for assessing the impact of childhood varicella (chickenpox) vaccination in Ireland, was used as a case study.

In the base case scenario, the epidemiological model run included thirty PSA simulations, where the values of four specific vaccination parameters (first-dose vaccination coverage, first-dose vaccine effectiveness, second-dose vaccine effectiveness and one-dose waning immunity) were varied. The values for the four vaccination parameters were drawn using Latin hypercube sampling (Table 1). Subsequent to the base case scenario, additional runs of the epidemiological model were conducted, where the number of PSA simulations for each run was varied and ranged from one to thirty.

The outputs on disease status for each of the epidemiological model runs were then applied to a probabilistic economic model and the outputs were summarised as a net monetary benefit (NMB). The range of NMBs for each of the model runs with different numbers of PSA simulations were compared to the model run with thirty simulations (base case scenario) to identify the point at which the estimated precision stabilised.

To assess the potential for the probabilistic economic model to mask variation in the epidemiological model results, the economic model was also run deterministically. The minimum and maximum NMBs for each model run with different numbers of PSA simulations, were compared to the model run with thirty simulations (base case scenario).

Results

While the deterministic DTM model estimates the mean NMB accurately, it does not provide precision. When PSA simulations were introduced, the epidemiological model run time ranged from over five hours, where one PSA simulation was conducted, to almost seven days, where thirty simulations were conducted. Model runs with two to four PSA simulations gave misleading estimates of the NMB mean and precision (5% to 10% error). Where the model run included five or more simulations, both the NMB mean and precision were estimated with acceptable accuracy (<3% error) (Figure 2).

When the economic model was run deterministically, results suggested that conducting 20 PSA simulations of the DTM may provide more stable results for estimating the tails of the NMB distribution (Figure 3).

Key Points

- PSA provides information to quantify the level of confidence in modelling outputs due to uncertainty in input parameters.
- This study highlights the considerable time resource required to run PSA simulations for a DTM of varicella vaccination.
- Where a limited PSA is possible (that is, with thirty or fewer simulations), fewer than five simulations can result in inaccurate estimates of the mean and or precision of the modelled outcomes.
- 20 PSA simulations of the DTM may provide the most stable results.

Figure 1 Epidemiological model structure of varicella-zoster virus and varicella vaccination

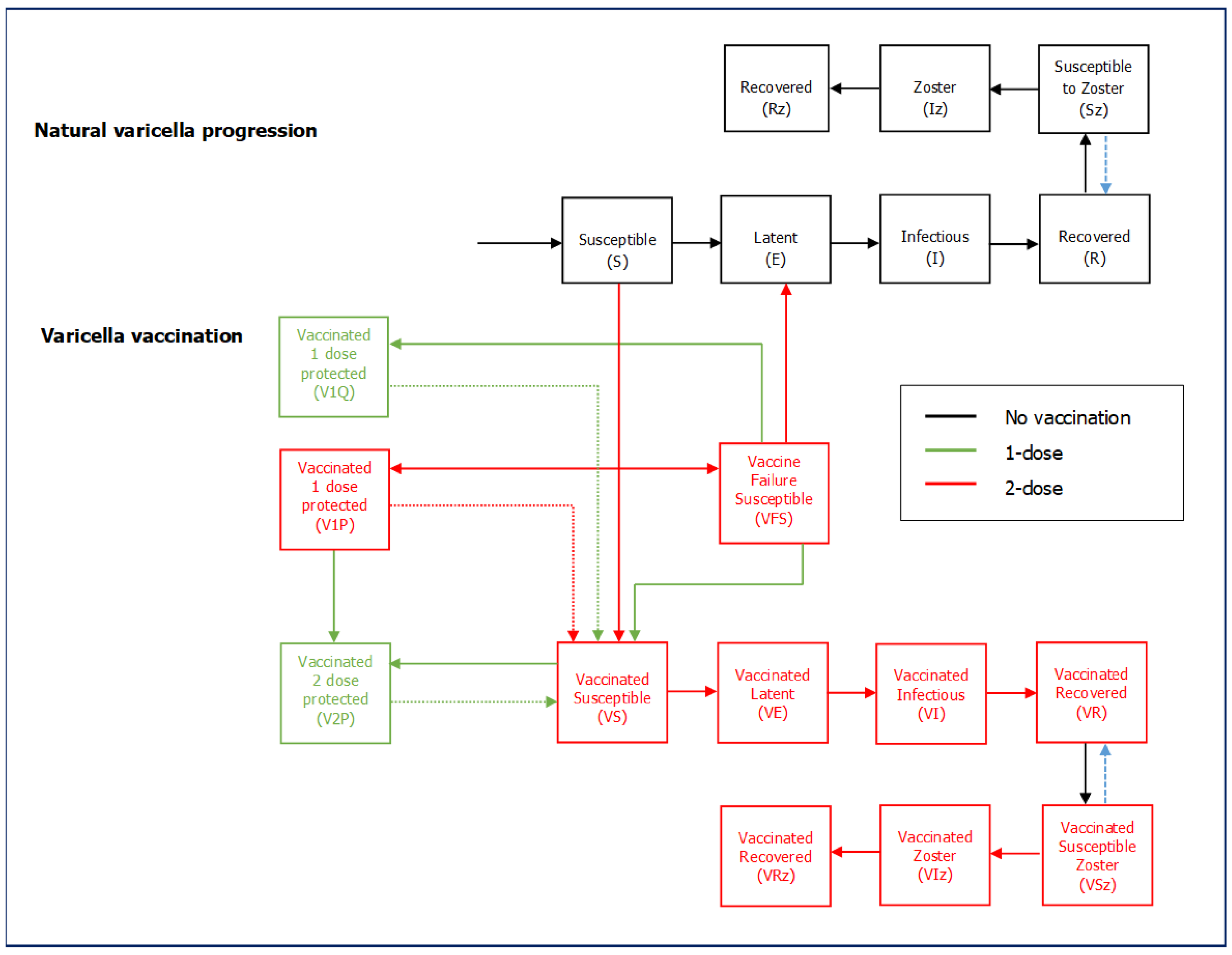
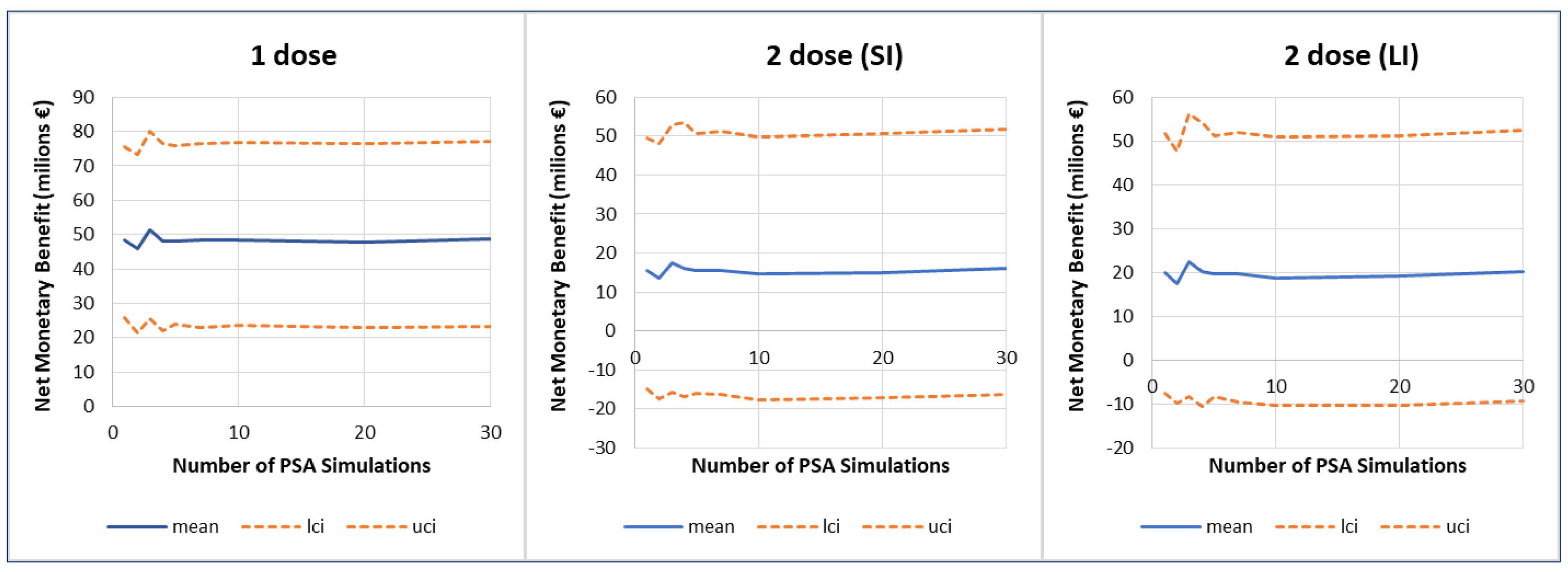


Table 1 Range of parameter values drawn using Latin hypercube sampling for probabilistic sensitivity analysis simulations

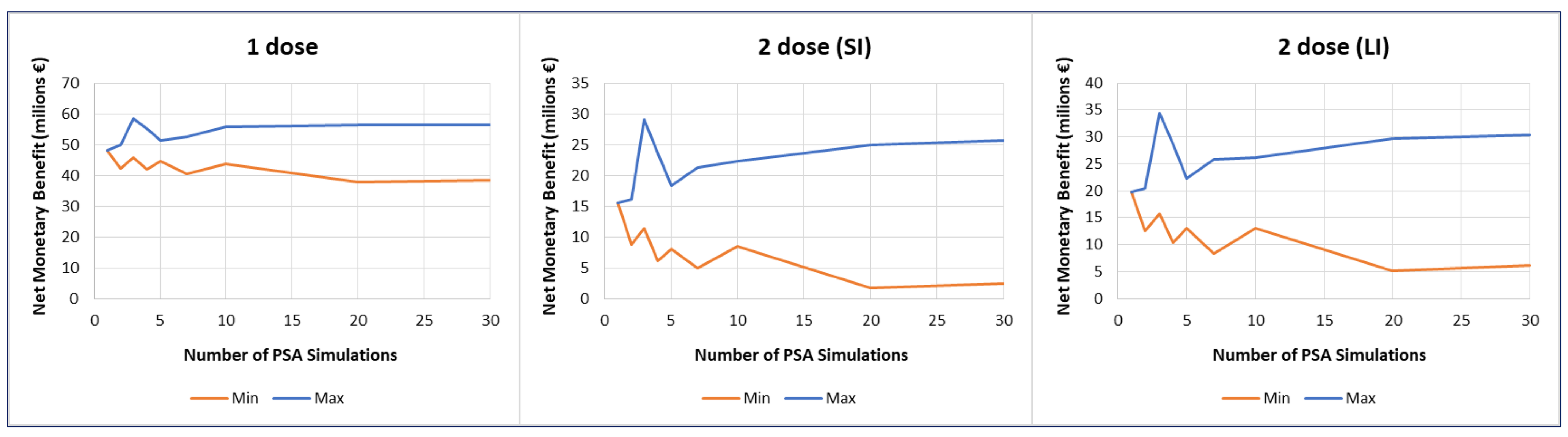
Number of PSA simulations	First-dose vaccination coverage	First-dose vaccine effectiveness	Second-dose vaccine effectiveness	One-dose waning immunity
1	0.88	0.74	0.67	0.04
2	0.84 – 0.89	0.74 – 0.75	0.63 – 0.68	0.04 – 0.05
3	0.87 – 0.92	0.67 – 0.82	0.64 – 0.69	0.03 – 0.05
4	0.83 – 0.90	0.70 – 0.85	0.59 – 0.74	0.03 – 0.06
5	0.83 – 0.91	0.66 – 0.81	0.63 – 0.73	0.03 – 0.05
7	0.84 – 0.91	0.64 – 0.84	0.60 – 0.72	0.03 – 0.05
10	0.84 – 0.93	0.61 – 0.82	0.57 – 0.73	0.03 – 0.06
20	0.80 – 0.91	0.61 – 0.88	0.59 – 0.75	0.02 – 0.07
30	0.82 – 0.93	0.61 – 0.88	0.59 – 0.76	0.02 – 0.07

Figure 2 Mean net monetary benefit for probabilistic economic model by number of PSA simulations and vaccination strategy



Key: lci - lower confidence interval; LI – long interval; PSA - probabilistic sensitivity analysis; SI – short interval; uci - upper confidence interval

Figure 3 Minimum and maximum net monetary benefit for deterministic economic model by number of PSA simulations and vaccination strategy



Key: LI – long interval; PSA - probabilistic sensitivity analysis; SI – short interval