



The comparison of pharmacoeconomic and pharmacometric modeling to improve cost-effectiveness assessment of sunitinib in GIST

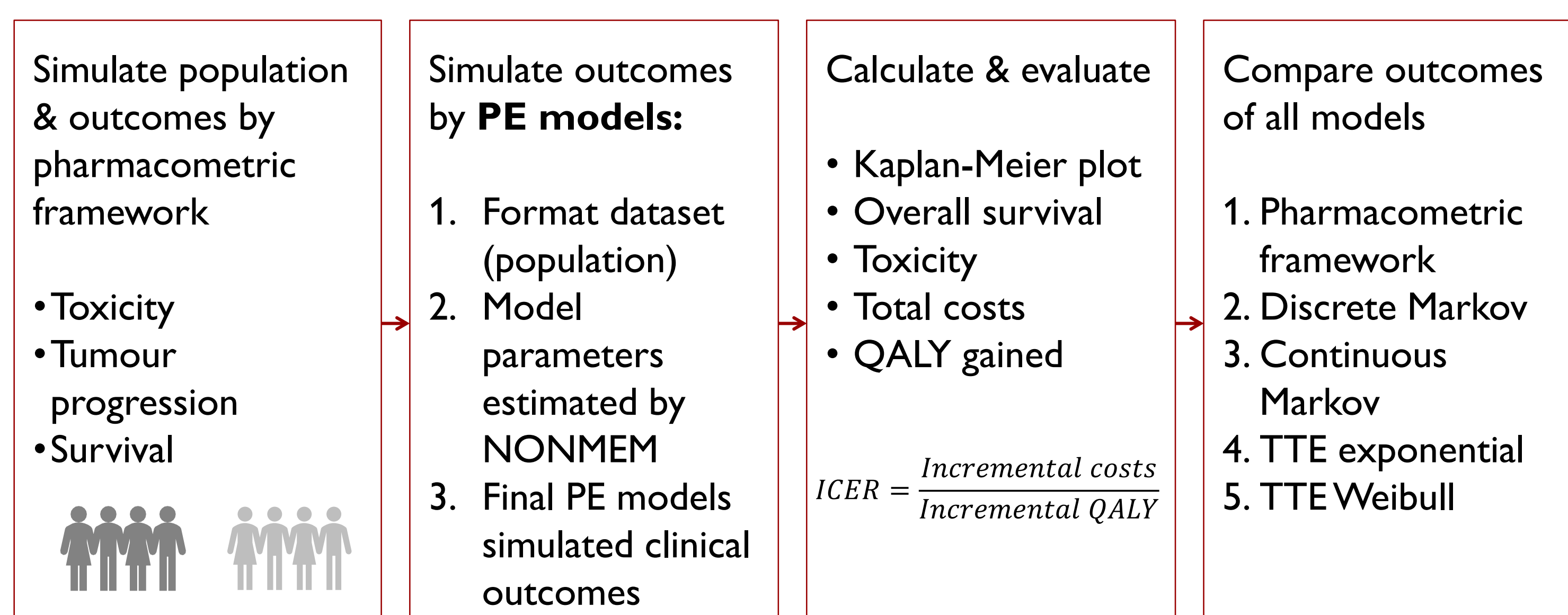
Janine Nijhuis, Maddalena Centanni, Lena E. Friberg
Department of Pharmacy, Uppsala University, Sweden

OBJECTIVES

Difficult decisions are being made balancing drug efficacy against costs. **Pharmacoeconomic (PE) models are used to inform cost-effectiveness analysis (CEA).** Differences in these models can lead to differences in outcome and influence decision making¹. Sunitinib (TKI), used in the treatment of GIST, demonstrates high variability in dose safety and efficacy, and is therefore the ideal example to demonstrate the effect of the chosen PE model on the CEA analysis ².

Aim: Compare and evaluate differences in predicted toxicity, overall survival (OS) and incremental cost-effectiveness ratio (ICER) between a pharmacometric framework and four commonly used PE models (exponential and Weibull time-to-event & continuous and discrete Markov) with a proportional odds (PO) toxicity model ^{3,4,5,6}.

METHODS



- Population generated: n=1000, both treatment (37.5 mg, daily) and no drug group over a time span of 102 weeks
- Pharmacometric framework describing toxicity allows dosing adjustment
- Proportional odds model was used to simulate the occurrence of toxicity in PE models
- The estimated model parameters described: OS, progression free survival and toxicity
- PE model was built in R-based package *mrqsolve* (version 1.0.3)
- A discount of 3.5% per year was applied to both costs and health outcomes (NICE⁷)

RESULTS: TOXICITY

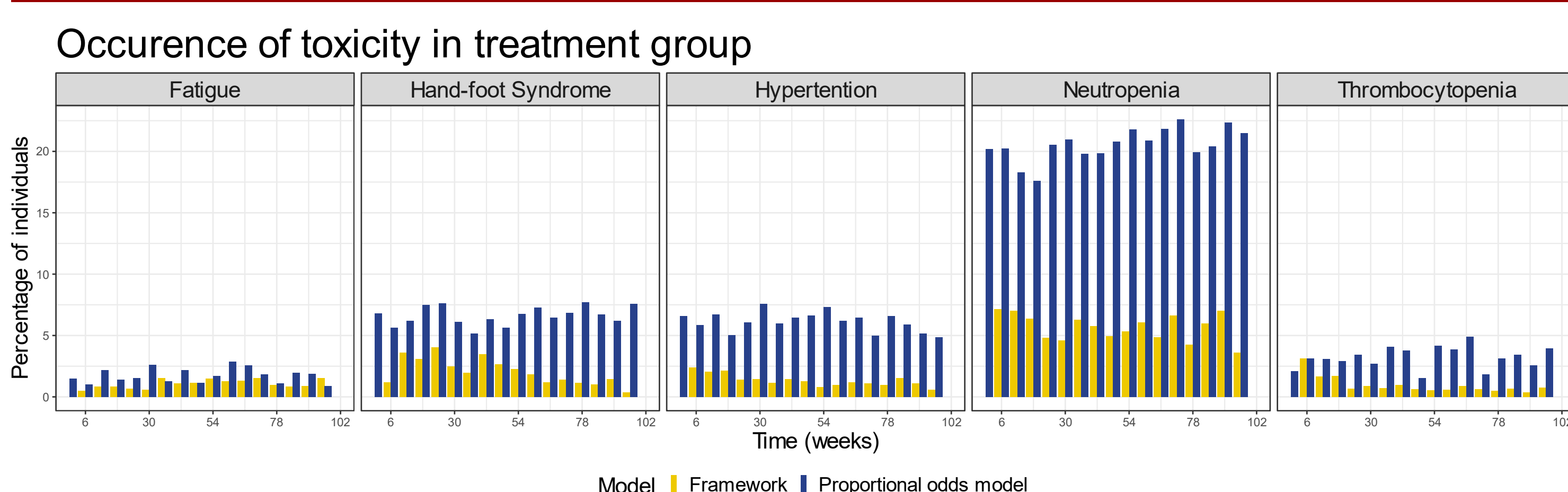


Figure 1: Occurrence of toxicity in the treatment group. Simulated by the pharmacometric framework (yellow) and the proportional odds model (dark blue) n=1000.

REFERENCES

[1] Frederix et al. Pharmacoeconomics (2014);32(1):47-61. [2] Centanni et al. Front Pharmacol (2020);11:316. [3] Chabot et al. Eur J Cancer (2008);44(7):972-7. [4] Bond et al. Health Technol. Assess (2009);13 Suppl 2:69-74. [5] Paz-Ares et al. J Clin Pharm Ther (2010);35(4):429-38. [6] Contreras-Hernández et al. (2008);98(11):1762-8. [7] (National Institute for Health and Care Excellence, 2022)

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RESULTS: OS and ICER

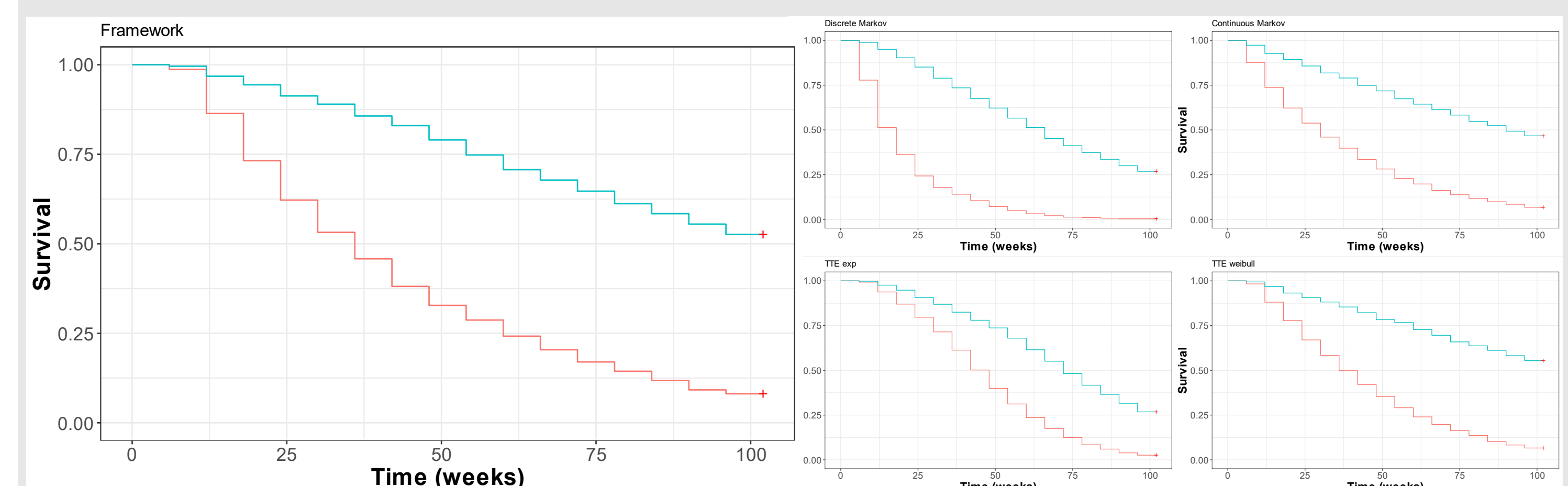


Figure 2: Kaplan-Meier plot of population over a time span of 102 weeks. Simulated survival of the **treatment (blue)** and **no drug (red)** group are visualised per model. Each cycle consists of 6 weeks.



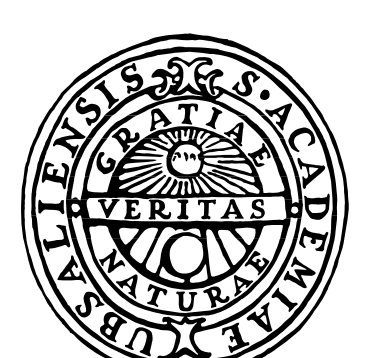
Figure 3: Distribution of cost-effectiveness per individual. Incremental effect in QALY gained and incremental costs in total costs over 102 weeks in euros, comparison is made between treatment and no drug group.

Table 1: Outcomes of CEA per model, all values include discount and are given as comparison between treatment and no drug. The QALY gained is given as difference between the treatment group and no drug group (n=1000). The total costs are given as difference between the two groups and over the 102 week time span in euros.

	Pharmacometric Framework	Discrete Markov	Continuous Markov	TTE exponential	TTE Weibull
Effect (QALY gained)	464	496	454	305	434
Cost (Additional costs)	61,947,138	53,018,274	59,894,119	57,284,541	65,073,439
ICER (cost per QALY gained)	133,646	106,991	131,953	187,697	149,811

CONCLUSION

- As expected, PO models for toxicity assume a stable frequency while the PK/PD framework better captures the potential time-varying changes in toxicity.
- The exponential TTE and discrete Markov model underestimate the OS, most likely due to model rigidity, while the overall QALY gained differs largely due the difference in the shape of the survival curve between the no drug and treatment group.
- The final ICER predictions demonstrated large deviations from the framework value, indicating that the PE model structures have a high influence on sunitinib CEA.



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