A Generalizable Discrete Event Simulation Framework to Assess Clinical and Economic Impact of Prescription Protocol Revisions

MSR3

HEALTHINK
Medical Research & Innovation

P. STAFYLAS[1,2], C. TYCHALA[1], A. GEORGIOU[2], K. KAPARIS[2], D. PANAGIOTAKOS[3], Z. STEFANIDOU[4], C. STAFYLAS[1,5], K. AVGITIDOU[1], VH ALETRAS[2]

[1] HealThink, Thessaloniki, Greece, [2] Department of Business Administration, University of Macedonia, Thessaloniki, Greece, [3] Department of Nutrition and Dietetics, School of Health Sciences and Education, Harokopio University, Athens, Greece, [4]ELPEN Pharmaceutical SA, Athens, Greece, [5] School of Informatics, Aristotle University of Thessaloniki, Thessaloniki, Greece.

INTRODUCTION

- National Prescription Protocols (NPP) and Clinical Guidelines (CG) are frequently revised in response to emerging clinical evidence. However, such revisions often lack a structured, quantitative evaluation of their real-world clinical and economic impacts. As a result, changes intended to improve care may also accelerate the growth of healthcare expenditure, with uncertain or contested benefits for society.[1]
- Computer-based simulation modelling provides a unique opportunity to address this issue. By enabling stakeholders to virtually replicate healthcare systems, simulation allows decision-makers to test new care models before they are implemented. This not only reduces the risks associated with adopting unproven policies but also encourages widespread involvement from healthcare professionals and administrators, ensuring that reforms are based on real-world considerations and consensus.[2,3]

OBJECTIVE

- To develop and validate a dynamic, generalizable methodological framework to evaluate the impact of NPP/CG revisions on population health outcomes, healthcare utilisation, and budgetary consequences - supporting evidence-based policy decisions across different therapeutic areas.

METHOD

- A targeted review of ISPOR-SMDM Modelling Good Research Practices and related literature was conducted to identify best practices in healthcare modelling.[1-4]
- Discrete-event simulation (DES) was chosen for its capacity to model patient-level heterogeneity, event sequencing, and dynamic treatment effects over time (Table 1).[3,4]
- A modular, generalisable DES framework was developed to simulate individual patient journeys in continuous time, incorporating explicit events, queues, and resource constraints, enabling evaluation of NPP/CG revisions under alternative policy scenarios.
- The framework integrates local epidemiological data, real-world treatment patterns, and cost inputs to improve relevance and accuracy.
- The model was built using Simul8 software (SIMUL8 Corporation, Boston, MA, USA), chosen for its process-centric architecture and established use in healthcare settings.
- To enhance applicability and transferability, the conceptual design is based on cardiovascular disease (CVD) management, given its significant burden and fiscal impact across Europe (approximately €282 billion annually; 11% of health expenditure).[5] This use case offers realistic pathways, events, and resource considerations; however, specific case study results are not included in this poster.
- Model transparency, calibration, internal validation, and scenario-based uncertainty analyses were conducted following established best practice standards.[6,7,8]

Table 1. Comparison of Simulation Modelling Approaches in Health Economics

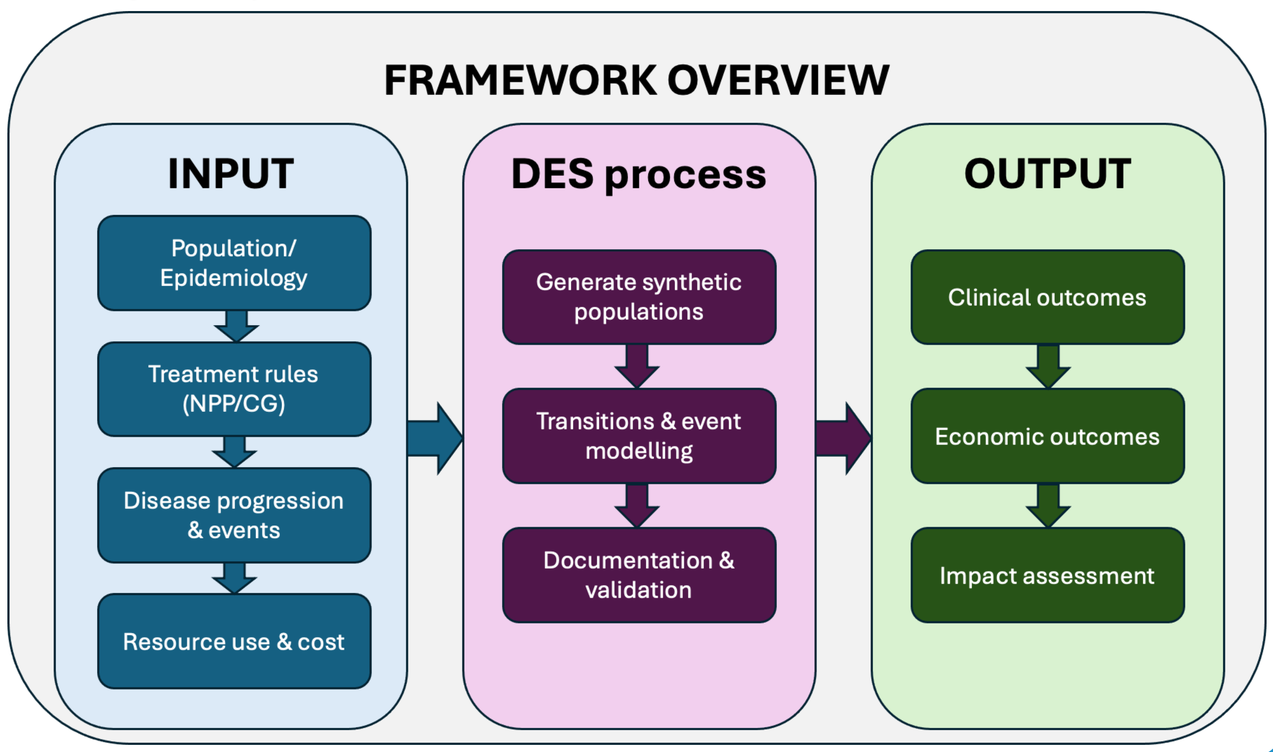
Simulation Model Type	Description	Strengths	Limitations	Typical Applications	Benefits of Discrete Event Simulation (DES)
Markov Cohort Models	Population-level state-transition models over fixed cycles	Simple, transparent, widely used	Limited patient heterogeneity, Markovian (memoryless) assumptions	Chronic disease modeling, cost-effectiveness analysis	Cannot capture individual patient history and time-to-event variability, less realistic for dynamic treatment protocols
Monte Carlo Simulation	Uses repeated random sampling to estimate probabilistic outcomes	Flexible uncertainty analysis, generates distributions	Not a discrete-event model; often combined with other methods	Probabilistic sensitivity analysis, risk assessment	Often integrated within other models, lacks pathway/timing specificity on its own
System Dynamics	Models system flows and feedback loops via differential equations	Good for aggregate-level dynamics, policy impact	Limited individual-level detail	Population health, policy scenario modeling	Not patient level, unsuitable for discrete events and resource queues
Agent-Based Modeling (ABM)	Models autonomous agents interacting on micro and macro levels	Captures emergent phenomena, behavior dynamics	High complexity, data demanding	Behavioral interventions, infectious disease spread	High computational complexity, less common in HTA
Discrete Event Simulation (DES)	Models individual events and resource interactions over continuous time	Captures complex timing, patient heterogeneity, resource constraints, queues	More complex to develop, data intensive	Healthcare resource use, complex pathways, policy analysis	Models individual trajectories with event-based timing, accommodates patient heterogeneity and dynamic treatment rules, integrates resource constraints and real-world service capacity

RESULTS

- The simulation framework was developed with a modular architecture, allowing updates or replacements of core components without the need for a complete system redesign.
- It is organised around three main pillars (Input / DES process and Output), comprising ten functional building blocks, each addressing a specific aspect of the disease pathway and policy evaluation (Figure 1).
- The framework effectively captured complex treatment pathways and population-level dynamics across different cardiovascular risk groups.
- Scenario analyses demonstrated that modest protocol changes, such as increased statin use, led to measurable reductions in cardiovascular event rates and healthcare costs. Detailed results are presented in HSD89 poster.
- The dyslipidemia case study demonstrated feasibility and policy relevance, while also highlighting limitations related to the availability of real-world data (RWD).
- A comprehensive validation plan is currently ongoing, pending external validation with RWD (Figure 2).

Figure 2. The ongoing validation plan

Figure 1. The framework's modular architecture



CONCLUSIONS

- The proposed framework is a **robust, dynamic, and highly flexible methodological tool** for **quantifying the clinical and economic impact of CG/NPP revisions prior to real-world adoption**, directly supporting early health technology assessment (HTA), informed reimbursement decision-making, and protocol optimisation.
- Its modular architecture enhances **scalability and transferability**, enabling rapid **adaptation across therapeutic areas, patient populations, and diverse health technologies**, as demonstrated by its application in cardiovascular disease management.
- **Integration of local real-world data and epidemiological sources** improves the relevance and utility for health policy and budget planning.
- **Full methodological alignment with key international standards** (ISPOR, SMDM, NICE, EU HTA) ensures credibility and broad acceptance in HTA processes.
- While initial case studies have confirmed technical feasibility and added value, broader external validation using independent real-world datasets is ongoing. **Future work will focus on establishing generalizability and practical application across further disease areas and technology types**.

REFERENCES

1. Tay CT, et al. Key standards and principles for developing evidence-based clinical guidelines: balancing health professional, patient, funder, and government needs. Fertil Steril. 2025;123:561-568.
2. Karnon J, et al. Modeling using Discrete Event Simulation: A Report of the ISPOR-SMDM Modeling Good Research Practices Task Force-4. Value Health. 2012;15(6):821-827.
3. Vázquez-Serrano JI, et al. Discrete-Event Simulation Modeling in Healthcare: A Comprehensive Review. Int J Environ Res Public Health. 2021;18(22):12262.
4. Salleh S, et al. Simulation modelling in healthcare: An umbrella review of systematic literature reviews. Pharmacoeconomics. 2017;35:937-949. doi:10.1007/s40273-017-0523-3.
5. Luengo-Fernandez R, et al. Economic burden of cardiovascular diseases in the European Union. Eur Heart J. 2023;44(45):4752–4762. doi:10.1093/eurheartj/ehad644
6. Eddy DM, et al. Model Transparency and Validation: A Report of the ISPOR-SMDM Modeling Good Research Practices Task Force-7. Value Health. 2012;15(6):843-850.
7. Monks T, et al. Strengthening the reporting of empirical simulation studies: Introducing the STRESS guidelines. J Simulation. 2019;13(1):55-67.
8. Marshall DA, et al. Applying dynamic simulation modeling methods in health care delivery research: the SIMULATE checklist. Value Health. 2015;18(5):516-529.

CONTACT INFORMATION

Dr. Panos Stafylas, MD, MSc, PhD,
Scientific Director HealThink
Thessaloniki, Greece
Panos@healthink.info

HEALTHINK
Medical Research & Innovation