From Weeks to Days: A Multi-Agentic AI System for Automated Development of HTA-Ready Health Economic Models

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BACKGROUND

- Health Technology Assessment (HTA) submissions require robust economic models to demonstrate value and inform reimbursement decisions[1]
- Traditional model development is resource-intensive, typically requiring 12-16 weeks and specialized multidisciplinary expertise across:
  - ✓ Clinical & statistical inputs, transition probabilities, cycle length & time horizon[2]
  - ✓ Discounting rates, cost & utility parameters
  - ✓ VBA (Visual basic for applications) automation, validation & cross-sheet linkage
- This study presents a novel multi-agentic AI (Artificial Intelligence) system utilizing Retrieval-Augmented Generation (RAG) to automate HTA-ready health economic model development in Excel, reducing development time while preserving methodological essence and human oversight

OBJECTIVES

- To design a multi-agentic AI + RAG framework that analyses HTA model specifications and auto-builds decision-tree, Markov and hybrid economic models in Excel
- To quantify the development-time savings versus traditional manual workflows
- To validate the alignment with SME (Subject matter expert) specifications across formula accuracy, references, parameters and structure

Why AI Driven Modeling in HEOR ?

- Reimbursement timelines are compressing, and every week saved accelerates patient access
- Excel models routinely contain broken references and formula drift automated linkage audits catch these early
- Consistent sheet architecture, naming, and PSA distributions across projects and therapy areas drive meaningful standardization
- Modelers shift from typing formulas to interpreting evidence and stress-testing structure, redirecting time toward higher-value work
- Every generated formula is traceable to the prompt and retrieved reference that produced it

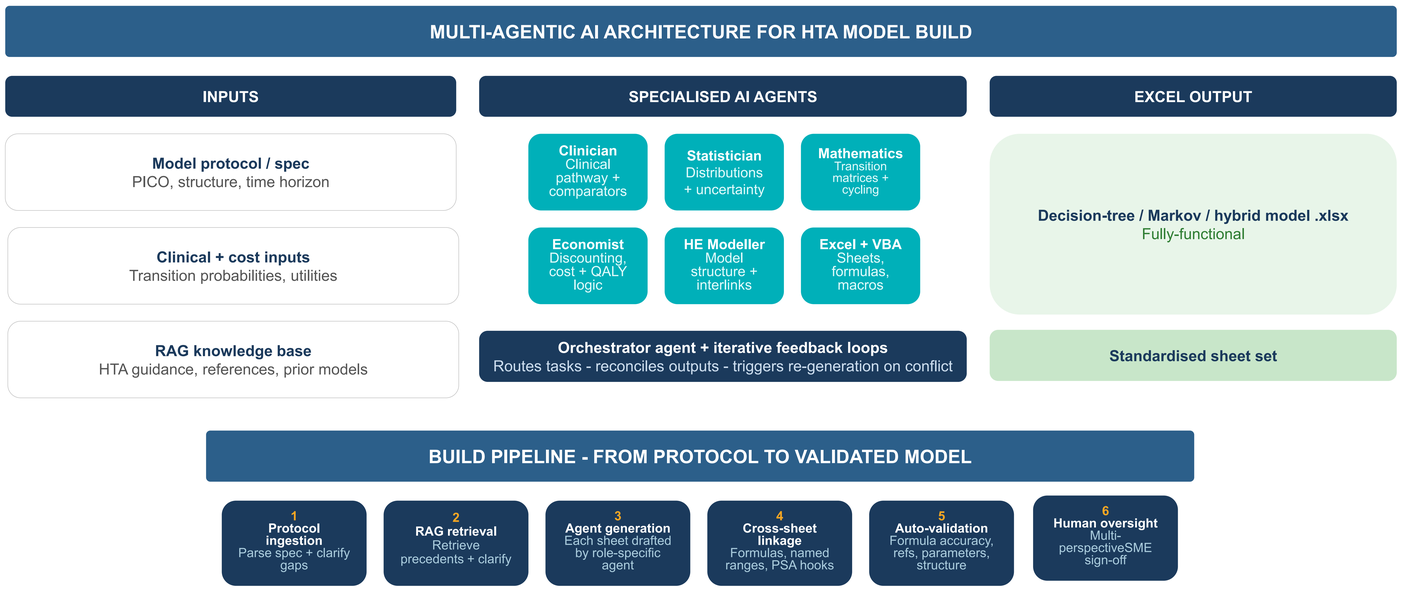
METHODS

- Multi-agent AI framework replicates a full HEOR team coordinated by a central orchestrator **(Figure 1)**
- Distinct agents cover clinical, statistical, economic, modelling, and Excel/VBA programming roles
- Validated on oncology Markov cohort models with 8-12 worksheets each
- Over several cross-sheet formulas generated with full PSA and OWSA implementation

METHODS

- Performance benchmarked across 6 dimensions structure, linkage, distributions, parameters, naming, and VBA providing a reproducible quality standard
- RAG grounds every agent in an indexed corpus of ~350 HTA and pharmacoeconomic documents, ensuring outputs are anchored to evidence rather than inference[3]
- Corpus spans NICE, CADTH, and ICER guidance alongside trial reports and annotated Excel templates, covering the breadth of international HTA requirements[4]
- Every agent issues a structured retrieval query before generating any output, creating a disciplined evidence-first workflow at each stage of model construction
- All formulas and assumptions trace back to a retrieved reference, providing a fully auditable link between model inputs and the evidence base that informed them
- Build inputs comprise three structured sources model protocol and specification, clinical and cost data, and a RAG knowledge base of HTA guidance and prior models ensuring every agent operates from a complete and evidence-grounded foundation

Figure 1: Iterative feedback loop - Detect issue - Re-prompt agent - Re-validate



- Clinician agent defines clinical pathways, health states, and comparators directly from the model protocol and PICO framework
- Statistician agent assigns beta, gamma, and Dirichlet distributions to uncertain parameters, underpinning PSA and uncertainty analyses
- Mathematician agent builds transition matrices with half-cycle correction applied, ensuring methodologically sound patient flow across health states
- Economist agent assembles discounting, cost, and QALY (Quality-Adjusted Life Year) logic consistent with HTA conventions using retrieved unit cost and utility evidencing the entire model
- Health economic Modeler agent defines sheet architecture, model structure, and cross-sheet interlinks to produce a consistent, submission-ready workbook layout
- Excel/VBA agent generates the final .xlsx complete with named ranges, data validation, formulas, and macros as a fully functional model file
- Orchestrator agent routes tasks across all agents, reconciles outputs, and triggers targeted re-generation on validation failure without rebuild
- Auto-validation runs independently after model assembly, checking formula syntax, cross-sheet reference integrity, and distribution mapping before any human review is initiated
- Human oversight is embedded as the final pipeline stage, with multi-perspective SME sign-off required before the model is accepted as submission-ready
- The full build pipeline follows a deterministic six-step sequence: protocol ingestion, RAG retrieval, agent generation, cross-sheet linkage, auto-validation, and human oversight
- An iterative feedback loop operates throughout the pipeline, detecting issues, re-prompting the relevant agent, and re-validating until all quality thresholds are met

RESULTS

- Across three validation cases, AI-generated models demonstrated strong alignment with SME specifications and a step-change reduction in development time **(Table 1)**

-75% DEV TIME 15-16 wks to 3-4 wks

65-70% SME ALIGNMENT across 3 validation cases

82% FORMULA ACCURACY via linkage audit

80% USER SATISFACTION 5 Health economists

Figure 2: Percentage wise performance matrix

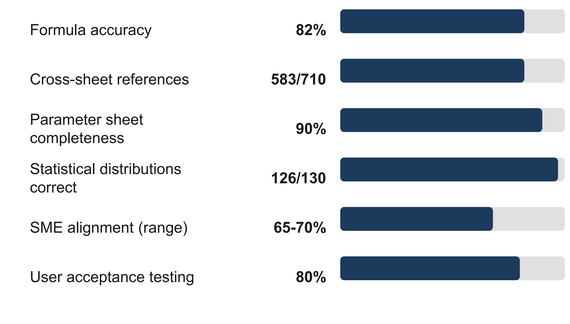


Table 1: Performance of AI-RAG at section level

Validation dimension	Result	Status
Formula linkage accuracy	82% (583/710)	Pass
Parameter sheet completeness	~90%	Pass
Statistical distribution assignment	96% (126/130)	Pass
Structural assessment	Aligned	Pass
SME specification alignment	65-70%	Review
VBA automation	Partial	Review

- Formula linkage achieved 82% accuracy with 583 of 710 cross-sheet references successfully validated **(Figure 2)**
- Statistical distribution assignment reached 96% correctness across 126 of 130 parameters
- Structural alignment passed across all three validation cases with consistent architecture throughout
- VBA automation was partially successful; PSA and OWSA macros require further refinement

CONCLUSIONS

- ❖ The framework delivered a 75% reduction in model development time, reducing a 15-16 weeks manual workflow to 3-4 weeks
- ❖ Formula linkage of 82% and distribution assignment of 96% demonstrated that AI-generated models can meet HTA-grade technical standards
- ❖ Structural alignment was consistent across all three oncology validation cases, confirming that the framework produces standardized, reproducible workbook
- ❖ The SME role fundamentally shifts from model builder to reviewer and decision-maker, redirecting expert time toward interpretation and evidence appraisal

LIMITATIONS

- ❖ Validated on oncology Markov models only; generalizability to partitioned survival, microsimulation, or non-oncology settings remains untested.
- ❖ VBA automation for PSA and OWSA macros achieved partial success; manual refinement still required for complex scenario analyses
- ❖ An 82% formula linkage accuracy indicates that approximately 18% of cross-sheet references require SME validation, reinforcing the role of the system as a decision-support tool that complements, rather than replaces, expert oversight.
- ❖ RAG corpus limited to English-language HTA guidance; multi-jurisdiction or non-English submissions not yet supported

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