AI-Supported Pre-Mortem Analysis for HEOR Strategies: Lessons from Project Management Science

MSR30

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KEY MESSAGE

What if AI could critique your HTA strategy before the reviewer does? We propose a framework pairing AI-generated failure scenarios with expert filtering across four risk domains: turning pre-mortem analysis from a team exercise into a structured, repeatable HEOR strategy tool.

BACKGROUND

- Pre-mortem analysis asks a team to assume a plan has already failed, then work backwards to explain why, surfacing risks while they can still be acted on.
- Prospective hindsight raises correct identification of reasons for a future outcome versus a conventional "what could go wrong?" review, and it removes the social cost of dissent.[1]
- Healthcare already applies prospective risk analysis to clinical processes (HFMEA, FMEA), yet HEOR strategy like evidence generation plans, modelling approaches, HTA submissions, is rarely subjected to structured pre-emptive critique.[2]

POST-MORTEM
After failure. Explains a decision already made and paid for.

PRE-MORTEM
Before commitment. Can still change the decision.

More than 40% of EMA-approved medicines are not recommended by NICE[3]

Modelling issues account for ~37% of NICE and ~41% of SMC economic uncertainties[4]

A dossier takes 12–24 months to build : the fatal flaw surfaces far too late

OBJECTIVES

1 **PRIMARY** Apply pre-mortem methodology to HEOR strategy development, using AI-supported scenario generation to anticipate methodological, evidence and HTA risks earlier in the decision lifecycle.

2 **SECONDARY** Develop a reusable risk-domain taxonomy for categorising and reviewing the generated failure modes.

3 **SECONDARY** Assess, through expert review, the plausibility and usefulness of the risks identified.

METHODS

- A conceptual framework was developed integrating classical pre-mortem methodology with AI-supported scenario generation, applied to HEOR strategies including evidence generation plans, modelling approaches and HTA submission strategies.

1 **DECOMPOSE THE STRATEGY** — HUMAN + AI -LED
Assumptions and decision points made explicit: population and subgroups, comparator, endpoints and surrogates, data sources, extrapolation and model structure, utilities, timelines.

2 **GENERATE FAILURE SCENARIOS** — AI-LED
A proprietary AI tool adopts prospective hindsight, e.g., "the strategy has failed, explain why", grounded in historical HTA decisions, methodological guidance and documented HEOR risks. Deliberately divergent.

3 **CATEGORISE INTO RISK DOMAINS** — AI-LED
Outputs mapped to four example domains: evidence sufficiency, methodological alignment, stakeholder interpretation and implementation feasibility.

4 **EXPERT REVIEW** — HUMAN-LED
Each risk assessed for plausibility (a real mechanism of failure here?) and usefulness (does knowing it change what we would do?). Generic or implausible scenarios discarded.

5 **MITIGATION PLANNING** — HUMAN-LED
Retained risks translated into pre-emptive actions: added scenario analyses, revised comparators, indirect comparison, early scientific advice, earlier clinician engagement.

PROPOSED FRAMEWORK

4 risk domains structuring every generated failure mode

5 workflow from strategy decomposition to mitigation planning

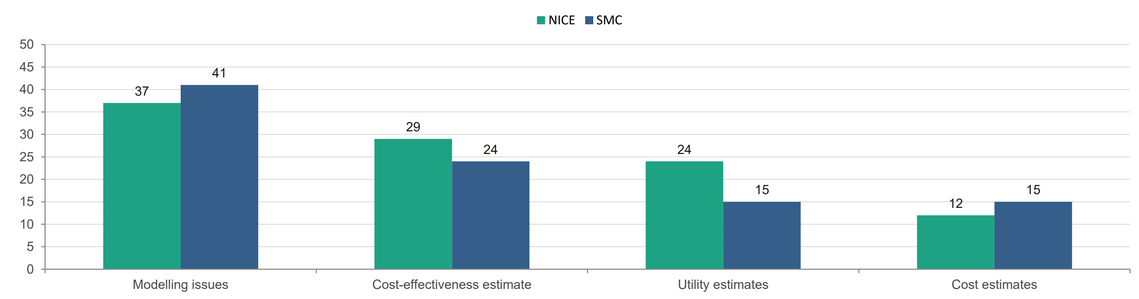
HITL Human-in-the-loop; prioritisation and contextual judgement remained human-led

Examples of Failure Modes

Risk domain	Representative failure modes surfaced
Evidence sufficiency	Overreliance on immature survival data; surrogate endpoints without validated linkage; single-arm evidence with no acceptable comparator; no direct head-to-head comparison
Methodological alignment	Trial endpoints misaligned with HTA expectations; indefensible extrapolation choices; structural weaknesses in modelling assumptions; comparator not reflecting real practice; utilities not generalisable
Stakeholder interpretation	Vulnerabilities in the value narrative; insufficient clinician and patient input on unmet need and severity; assumptions likely to be reinterpreted unfavourably at review
Implementation feasibility	Data access and registry readiness; analytic and resource capacity; timeline dependencies compressing quality assurance before submission

A broad range of failure modes was surfaced across all four domains; experts reported the principal value was making implicit assumptions explicit.

Independently reported economic uncertainties raised in appraisal (%)



Convergence check: the domains the pre-mortem surfaced most were modelling and cost-effectiveness assumptions, which are the same ones that dominate real appraisal uncertainty.[4]

DISCUSSION

- The contribution is coverage and candour, not prediction: AI can hold far more prior appraisal outcomes and documented pitfalls in working memory than any single reviewer, and has no investment in the plan being critiqued: the exact bias a pre-mortem exists to defeat.[1]
- Limitations follow from the method's own logic. Presuming failure can surface threats that are not real; outputs are unranked and uncalibrated, with no probability attached; and generative systems can produce plausible but unfounded scenarios.
- Expert curation, disclosure of AI assistance and human-led prioritisation are therefore structural requirements rather than optional additions.[5,6]

CONCLUSION

AI-supported pre-mortem analysis offers a structured approach to proactively identifying HEOR strategy risks before downstream investment and submission. The underlying AI tool is also used for broader HEOR model interpretation and validation.

Combined with expert interpretation it may enhance strategic robustness, reduce late-stage HTA failure and support more resilient evidence generation planning. Future work could include retrospective validation against known HTA outcomes and the addition of a risk prioritisation layer.

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