Insufficient Iterations and Uncertainty Probability Thresholds of Probabilistic Sensitivity Analysis in Economic Evaluation

MSR188

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BACKGROUND

- **The Problem:** Probabilistic sensitivity analysis (PSA) often relies on arbitrary iteration counts rather than formal convergence assessment in economic evaluation (EE), risking unstable and unreliable cost-effectiveness probabilities.
- **The Gap:** Even with adequate convergence, PSA results depend on a predefined probability threshold for decision-making, yet formal guidance from health technology assessment agencies remains scarce.

RESEARCH OBJECTIVE

- **Objective 1:** Verify whether PSA iterations are sufficient to yield stable uncertainty estimates.
- **Objective 2:** Assess how probability thresholds influence cost-effectiveness conclusions when using health-adjusted life years (HALYs) as the primary outcome.

METHODS

- **Search Strategy:** Full EE published between Jan 1, 2023, and Mar 18, 2025.
- **Quality Filter:** Strictly limited to journals ranked in the top 5% by Journal Impact Factor across 51 Clinical Medicine subcategories.
- **Data Extraction:** Conducted by three trained groups of independent reviewers, capturing:

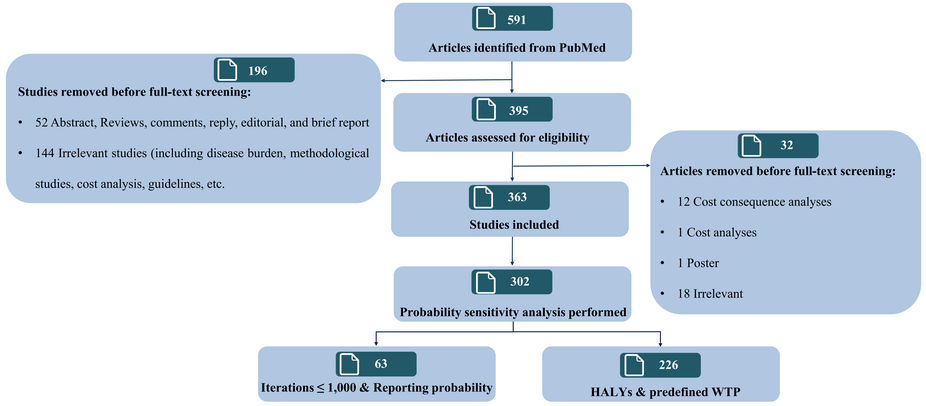
  Study Characteristics: Designs, analytical perspectives, research domains, and outcome types.

  Analytical Details: Specific PSA methods, iteration counts, and cost-effectiveness conclusions.

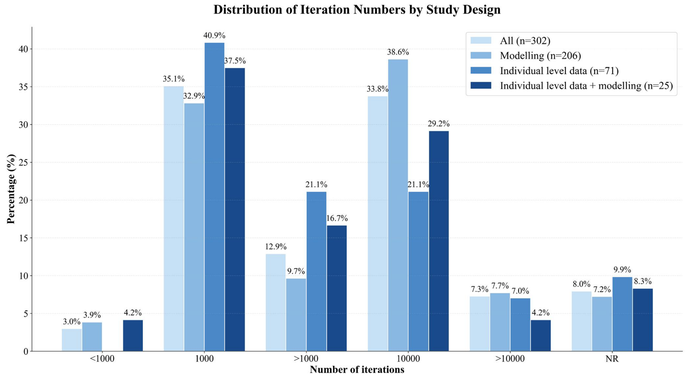
RESULTS

1. Search and Screening Results

An initial literature search identified 591 relevant articles from PubMed database, and after abstract and full-text screening according to inclusion and exclusion criteria, 363 articles were included. Of these, 302 performed PSA.

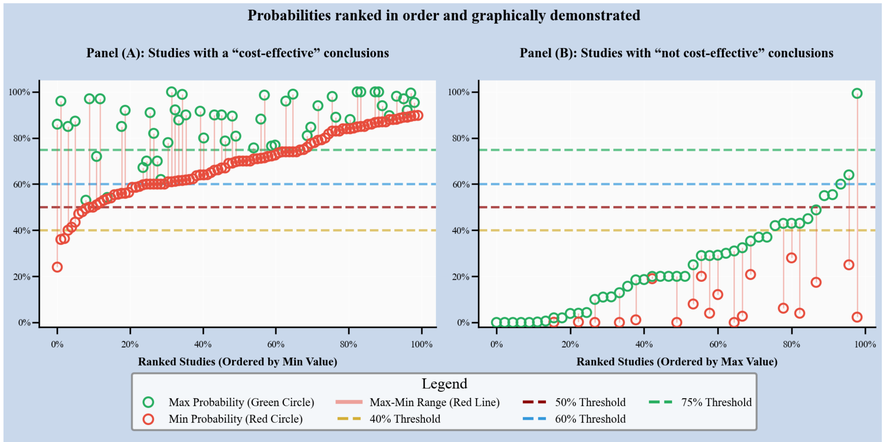


2. The Insufficient Iterations



- Across all studies (n=302), most adopted only 1,000 iterations (35.1%), followed by 10,000 iterations (33.8%).
- Individual-level data studies were most likely to use just 1,000 iterations (40.9%), while modelling studies had the highest proportion of 10,000 iterations (38.6%).
- 3.0% with fewer than 1,000 iterations exhibited risks of underestimated uncertainty analysis, particularly in EE based on individual-level data.
- **Model Convergence Validation Result:** Based on Monte Carlo Error (MCE) calculation for studies with ≤1,000 iterations, formal validation confirmed notable non-convergence problems in these studies.

3. HALYs with a Pre-defined Probability Thresholds



- **Overconfidence:** 37.4% of studies concluding cost-effective failed to meet the 75% probability threshold; 5.0% did not reach even the 50% threshold.
- **Paradoxical Rejection:** 11.1% of studies concluding not cost-effective exceeded the 50% probability threshold.

CONCLUSIONS

- **Iteration Arbitrariness & Rigor Risk**

  Empirical, arbitrary selection of 1,000 or 10,000 PSA iterations compromises methodological rigor and overall reliability of economic evaluation.

- **Threshold Consensus Gap**

  This study demonstrated that identical cost-effectiveness probabilities may yield divergent economic conclusions, driven by a lack of consensus on standardized PSA probability cutoffs.