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From Evidence Synthesis to Adaptive Trials: Is EU HTA Ready for Bayesian Methods?

Background and objectives

Bayesian statistical methods offer a fundamentally different paradigm for evidence generation and inference: rather than relying solely on observed data, they formally incorporate prior knowledge and update it in light of new data to produce posterior probability distributions (figure 1). This flexibility makes them attractive in settings with limited sample sizes, adaptive trial designs, or heterogeneous evidence. Despite their increasing acceptance by regulatory authorities, their role in Health Technology Assessment (HTA) remains largely underexplored. This study examines the standing of Bayesian methods in EU HTA guidance and identifies gaps through a structured comparison with recent FDA guidance.

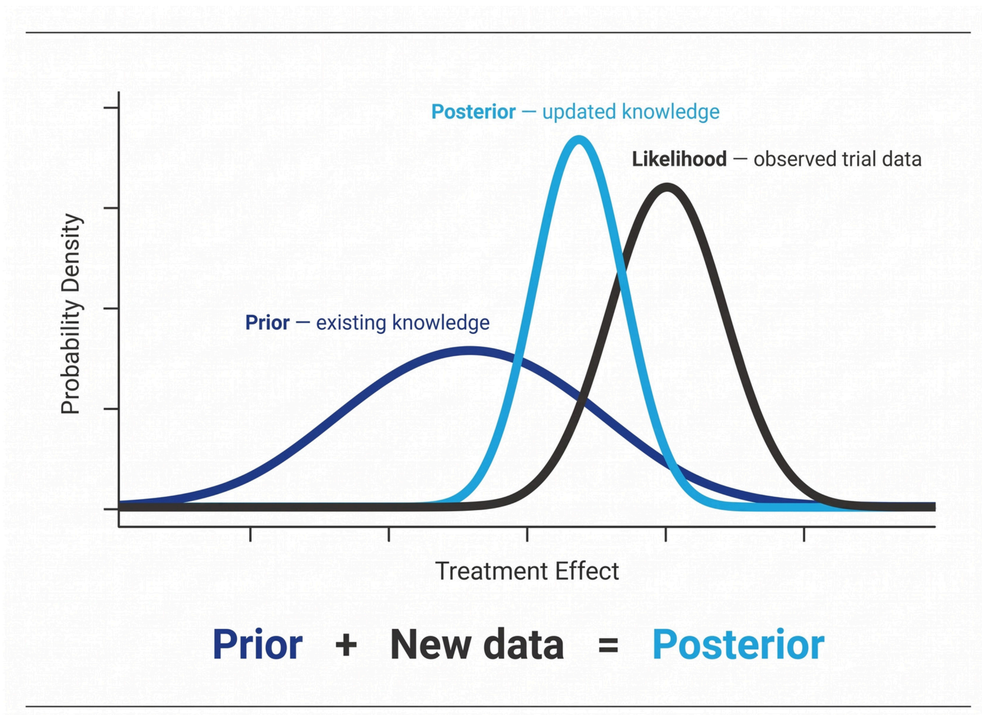


Figure 1: *Bayesian updating – from prior to posterior: How existing knowledge and new data combine into an updated estimate*

Methods

A systematic comparison of the EU HTA methodological guidelines — including the Guideline for Quantitative Evidence Synthesis (Direct and Indirect Comparisons)[1] and the Guidance on Validity of Clinical Studies[2] — was conducted against the FDA draft guidance on Bayesian methodology in clinical trials[3]. Key dimensions assessed included: permitted use cases, prior specification, evidence synthesis, adaptive designs, and transparency standards.

Results

EU HTA guidance acknowledges Bayesian methods primarily within indirect treatment comparisons and network meta-analyses, permitting informative, non-informative, and vague priors — particularly valuable in sparse-data settings. Beyond evidence synthesis, however, Bayesian approaches are notably absent: adaptive trial designs, surrogate endpoints, and real-world evidence contexts lack dedicated methodological guidance. In contrast, the FDA guidance provides a comprehensive, affirmative framework endorsing Bayesian methods for primary inference, adaptive designs, external data borrowing, pediatric extrapolation, and dose-finding, with explicit requirements for pre-specified priors, simulation-based operating characteristics, and computational transparency (figure 2).

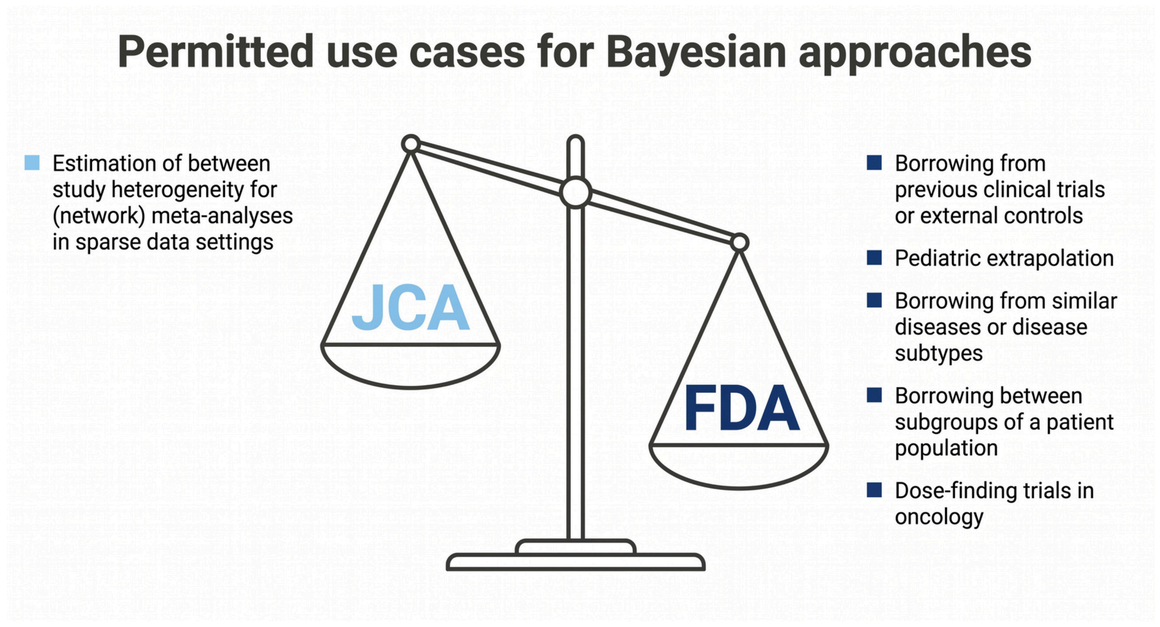


Figure 2: *Bayesian methods: JCA vs. FDA*

Conclusion

While EU HTA guidance acknowledges Bayesian methods in evidence synthesis, it lags behind the FDA's proactive framework. Bayesian adaptive trials may represent an opportunity for further methodological development, particularly for rare diseases and ATMPs — the populations currently in JCA scope (figure 3). Aligning EU HTA methodology with FDA standards could enhance evidence quality, reduce development burdens, and improve patient access to innovative therapies.

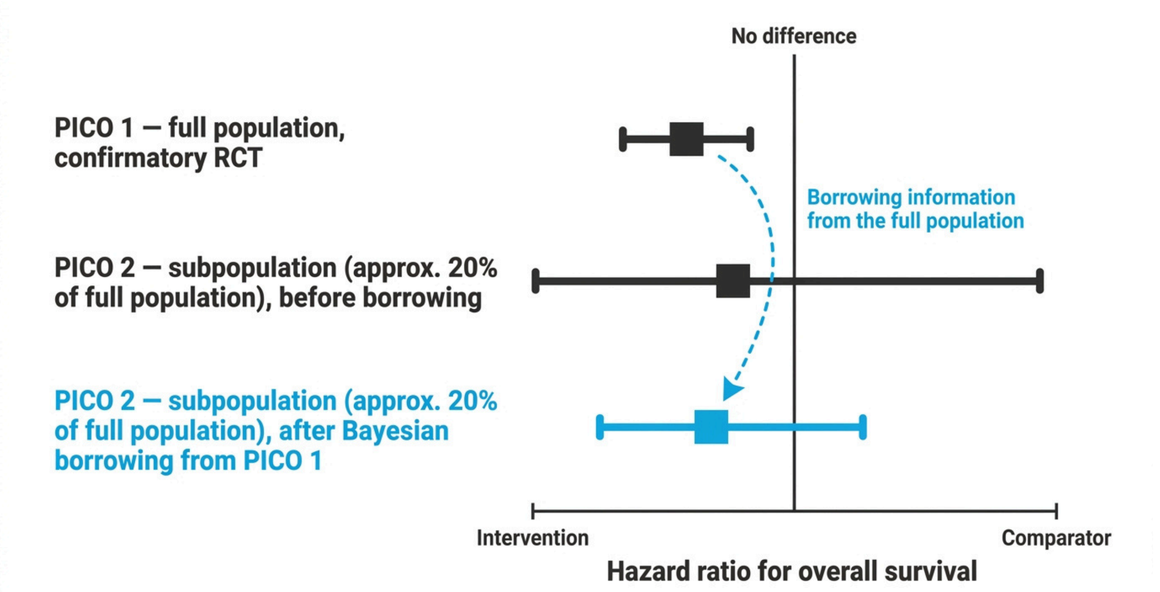


Figure 3: *Hypothetical example where borrowing from the full population of an RCT (PICO 1) helps achieve more reliable results in a small subpopulation to answer PICO 2*

References

1. Member State Coordination Group on Health Technology Assessment (HTA Coordination Group, HTACG). Methodological Guideline for Quantitative Evidence Synthesis: Direct and Indirect Comparisons. March 2024
2. Member State Coordination Group on Health Technology Assessment (HTA Coordination Group, HTACG). Guidance on the Validity of Clinical Studies for Joint Clinical Assessments. July 2024
3. U.S. Food and Drug Administration (FDA), Center for Drug Evaluation and Research (CDER) / CBER. Use of Bayesian Methodology in Clinical Trials of Drug and Biological Products; Draft Guidance for Industry. January 2026

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