

TITLE: From Hunch to Hedge: Applying Bayesian Thinking in Clinical Development Where It Matters Most

AUTHOR: Kevin Kunzmann, Boehringer Ingelheim Pharma GmbH & Co. KG

ABSTRACT: A positive proof-of-concept (PoC) result is often treated as a major de-risking milestone in drug development, yet substantial uncertainty about late-stage success typically remains. This talk examines the apparent paradox through a Bayesian lens, focusing on the conditional probability of Phase III success given a positive PoC result that is key to late-stage drug development efficiency.

To this end, Post-PoC success is decomposed into two principal drivers: the probability of late-stage success for a truly viable compound and the positive predictive value of PoC - the probability that a PoC-positive compound is genuinely viable. Under two transparent approximations - little late-stage success without viability and limited additional information from PoC once viability is known - the post-PoC success probability is approximately the product of these quantities.

The framework highlights an important practical conclusion. Late-stage operating characteristics are often constrained by regulatory requirements and therefore offer limited scope for improving post-PoC success probability. By contrast, the positive predictive value of a PoC design can be influenced through endpoint and population choice to maximize transportability of the treatment effect to late-stage, sample size, decision thresholds, specificity, and go/no-go rules. Low prior viability and imperfect PoC specificity can keep the PoC positive predictive value surprisingly low even when sensitivity appears strong. This shows that Bayesian thinking is at the core of increasing late-stage efficiency in drug development and moving from hunch to hedge.

The derived approximation is intended as a transparent tool for communication, intuition, and back-of-the-envelope plausibility checks - not as a substitute for decision analysis. Exact calculation or simulation remains appropriate for program and portfolio optimization.

References

- Browner WS, Newman TB. Are all significant p values created equal?: The analogy between diagnostic tests and clinical research. JAMA. 1987;257(18):2459–2463. doi:10.1001/jama.1987.03390180077027.
- Pater JL, Willan AR. Clinical trials as diagnostic tests. Controlled Clinical Trials. 1984;5(2):107–113. doi:10.1016/0197-2456(84)90117-X.
- Sailer O, Kunzmann K. What drug do we want to develop? Interpretation of results from proof-of-concept trials and de-risking of phase 3. Poster P064, PSI 2026.
- Kirchner M, Kieser M, Götte H, Schüler A. Utility-based optimization of phase II/III programs. Statistics in Medicine. 2016;35(2):305–316. doi:10.1002/sim.6624