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INTRODUCTION

Meta-analyses frequently combine studies measuring the same outcome (e.g., pain relief) using different scales (e.g., Numeric Rating Scale [NRS], Brief Pain Inventory [BPI]). While **standardized mean differences (SMDs)** enable synthesis across scales, they express effects in standard deviations (SDs)—units that **lack clear clinical interpretation**. Determining whether an effect is clinically meaningful requires comparison to the **Minimal Clinically Important Difference (MCID)**. However, **both the treatment effect and MCID involve inherent uncertainty** that must be addressed.

OBJECTIVE

To provide **novel methodological procedures** for evaluating the **clinical significance of treatment effects** using a **probabilistic framework** that accounts for **uncertainty in both the effect estimate and the clinical threshold**.

RESULTS

Estimated probabilities ranged from **1.90% to 22.41%** across scenarios, all remaining **<25%**, indicating the treatment effect **consistently falls short of the clinical significance threshold** (Table 1).

Distributional assumptions (normal vs. Beta) had **minimal impact** (~0.1 percentage points). Sensitivity analysis with **higher MCID uncertainty (CV=40%)** increased probability by approximately **10 percentage points**. Analytical distributions for each scenario are presented in Figure 1.

Table 1. Numerical Results for Different Analytical Scenarios Accounting for Parameter Uncertainty

Analysis	Distributional Assumptions	Probability% (95% CrI)
Primary	Normal vs. Normal (CV=20%)	13.33% (0.69%, 45.32%)
Fixed MCID	Normal vs. Fixed (-2.00)	1.90% (0.00%, 1.90%)
SA1: Beta distribution	Beta vs. Normal (CV=20%)	13.47% (0.82%, 43.59%)
SA2: MCID CV=40%	Normal vs. Normal (high uncertainty)	22.41% (6.21%, 47.19%)

Crl: Credible Interval; CV: Coefficient of Variation; MCID: Minimal Clinically Important Difference; SA: Sensitivity Analysis

METHODS

We illustrate these procedures using an example treatment effect of A vs. B = **-0.60** for pain relief (95% CI: **-0.86 to -0.34**).

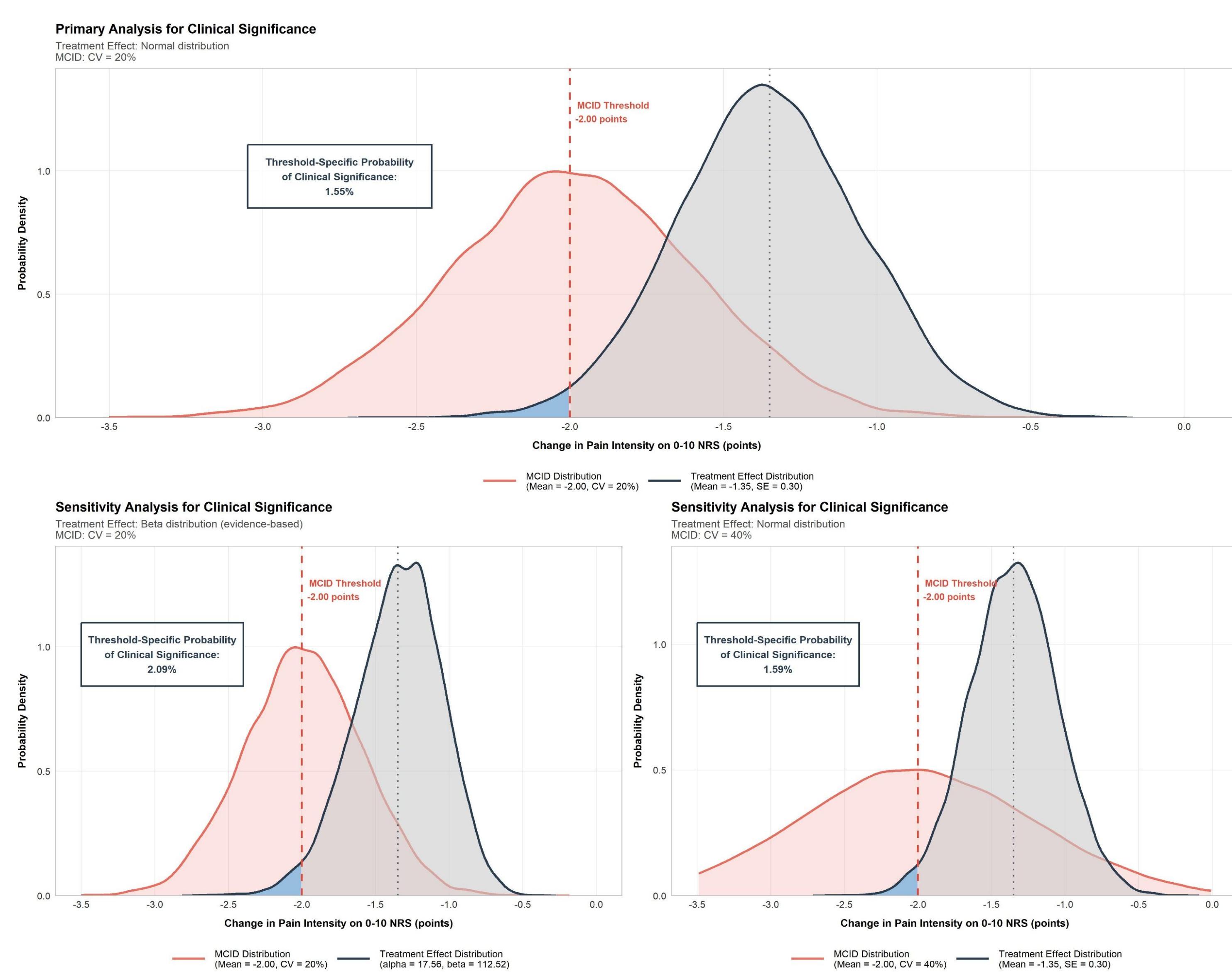
Step 1: Translate **SMD to NRS-specific units** (range: 0–10 points) using an external SD reference¹

Step 2: Parameterize MCID by selecting a point estimate (**2-point reduction on NRS** represents clinically significant improvement^{2,3}) with a **coefficient of variation of 20%** (SD = 0.40)

Step 3: Conduct **distributional comparison** (primary analysis). Generate **10,000 random draws** from both treatment effect and MCID distributions, then calculate the **proportion where the effect exceeds MCID**. Iterate this process **1,000 times** to capture parameter uncertainty.

Step 4: Perform **sensitivity analyses**: (1) apply evidence-based **Beta distribution** for treatment effect, and (2) increase **MCID uncertainty (CV = 40%)**

Figure 1. Distributional Comparison Between Treatment Effect and MCID.



Blue shaded area represents the proportion achieving clinically significant improvement using a fixed MCID threshold.

CONCLUSIONS

This **probabilistic framework** directly addresses the **communication challenge in meta-analyses** that use standardized mean differences. By translating **SMDs to scale-specific units** and **comparing them against established clinical thresholds**, we provide stakeholders with:

- (1) **Interpretable metrics** clinicians can discuss with patients
- (2) **Evidence-based probabilities** for clinical decision-making **beyond statistical significance**
- (3) **Transparent uncertainty quantification** in both effects and thresholds

CONTACT INFORMATION

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For a more detailed explanation of the analytical approach, use the attached QR code to visit the GitHub repository of the poster.



REFERENCES

¹Daly C, Welton NJ, Dias S, Anwer S, Ades AE. Meta-Analysis of Continuous Outcomes: Guideline Methodology Document 2. NICE Guidelines Technical Support Unit, 2021. 49 p.

²Farrar JT, et al. Clinical Importance of changes in chronic pain intensity measured on an 11-point numerical pain rating scale. *Pain*. 2001;94(2):149-158

³Dworkin RH, et al. Interpreting the clinical importance of treatment outcomes in chronic pain clinical trials: IMMPACT recommendations. *J Pain*. 2008;9(2):105-121