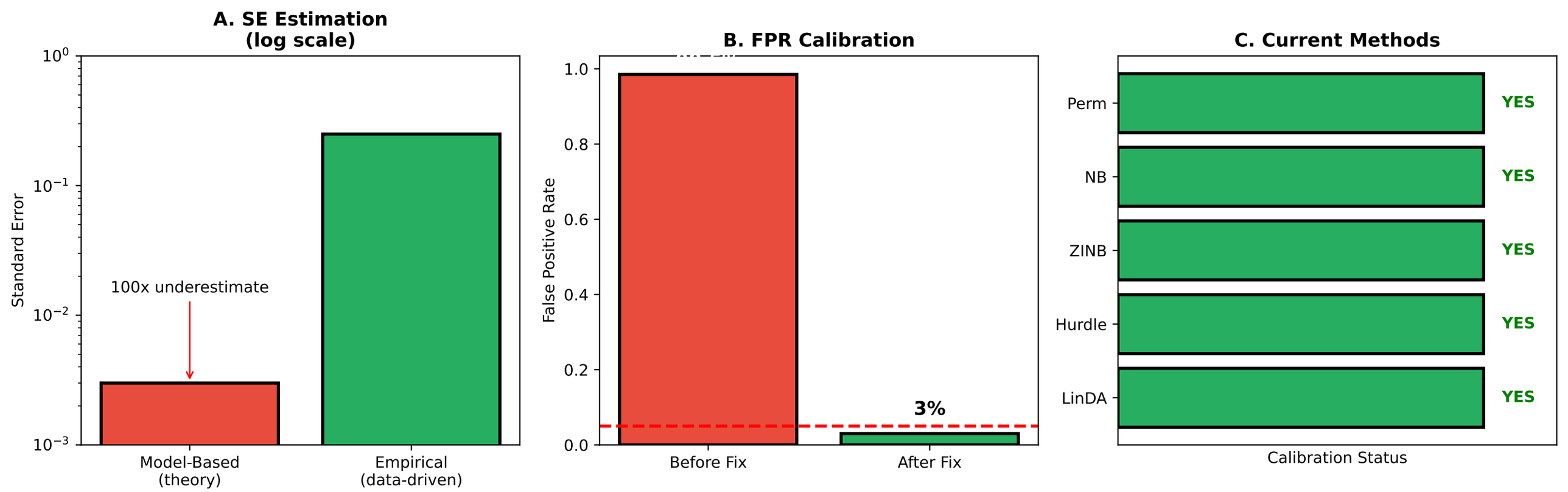

Key Finding: Theoretical variance formulas severely underestimate uncertainty for microbiome data (100x). Solution: Use empirical variance estimation. All current methods are properly calibrated with FPR < 5%.