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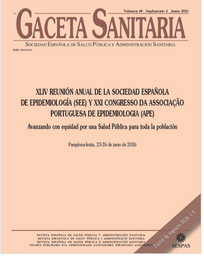

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359 - A NOVEL BOOTSTRAP-BASED APPROACH FOR ESTIMATING BIOMARKER CUT-OFFS

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Resumen

Background/Objectives: Selecting appropriate biomarker cut-off values is critical for clinical diagnosis and treatment decisions, yet defining reliable and reproducible thresholds remains challenging. Dichotomizing continuous variables leads to information loss, and traditional approaches are often data-dependent, limiting generalizability. Moreover, many methods prioritize statistical criteria with limited consideration of clinical relevance and uncertainty.

Methods: We propose a novel cut-off selection method that evaluates the full biomarker range by assessing discriminatory capacity using a log-binomial model. To enhance robustness and stability, a bootstrap resampling procedure is applied to estimate the empirical distribution of candidate optimal cut-offs. Model likelihood, assessed via the Akaike Information Criterion, is used for selection instead of p-values. Visualization of the bootstrapped distribution enables identification of optimal threshold ranges and assessment of precision and bias, explicitly incorporating uncertainty into cut-off estimation. Performance is evaluated using sensitivity, specificity, positive and negative predictive values, and accuracy, with 95% confidence intervals (CIs), and compared with established approaches such as the Youden Index and the minimum p-value method. Evaluation is conducted through simulation studies and real-world data applications. Simulations assume normally distributed biomarkers with varying disease prevalences and effect sizes (null, moderate, and large).

Results: Under a null effect, the proposed method does not identify spurious cut-offs, demonstrating protection against false thresholds and improved stability. In moderate effect scenarios with low prevalence, it identifies meaningful cut-offs and improves accuracy (0.75 [0.72; 0.78]) compared with other methods, which range from 0.61 [0.58; 0.63] to 0.71 [0.69; 0.74]. With moderate effects and medium prevalence, results are comparable to the minimum p-value method but with higher accuracy and narrower CIs. For large effect sizes, the method consistently identifies clinically relevant thresholds and outperforms alternatives. Notably, in low-prevalence, large-effect scenarios, accuracy reaches 0.84 [0.80; 0.86], compared with 0.69 [0.66; 0.73] to 0.80 [0.76; 0.83] for other methods.

Conclusions/Recommendations: This bootstrap-based approach yields more stable and informative cut-offs by formally incorporating uncertainty and enabling detection of multiple optimal thresholds. It performs consistently across diverse scenarios and supports exploration of the full cut-off distribution. Further simulations and real-data applications are warranted to assess generalizability.