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LETTER TO THE EDITOR

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Ensuring transparency and clinical utility in SMA noninvasive prenatal diagnosis

To the Editor,

We read the article by Li H et al. on proband-independent NIPD for SMA [1]. This first-trimester, haplotype-based approach is a significant advance. To ensure its clinical adoption, two methodological issues must be addressed.

First, the Bayesian Factor (BF) framework lacks transparency, preventing independent validation. The diagnostic call depends entirely on a BF model using fixed thresholds (BF ≥10, ≤0.1), yet the manuscript omits the model's likelihood, priors, and—critically—empirical justification for these thresholds. In clinical genomics, using uncalibrated heuristic thresholds is discouraged, as it can lead to misinterpretation, especially in complex regions like *SMN1/SMN2* [2]. Full disclosure of the statistical model and calibration data is essential for replication.

Second, incomplete reporting overstates the 100% accuracy claim and limits clinical utility. Reporting 76/76 concordance without its 95% confidence interval (95.2–100%) omits precision. More importantly, the absence of performance stratified by fetal fraction (e.g. in the critical <4% range) or informative SNP count obscures the test's true operating limits. This contravenes STARD guidelines for diagnostic accuracy studies, which mandate such disaggregated data to define reliable clinical use [3].

These issues are intrinsically linked: an opaque model and incomplete reporting together undermine the study's clinical translatability and trustworthiness for multi-center validation. Addressing them is urgent. With the 2023 FDA approval of a prenatal SMA treatment trial and global policy shifts towards early intervention [4], establishing transparent, robust NIPD methods is critical to ethically integrate diagnosis with new therapeutic pathways.

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References

[1] Li H, Gao S, Li S, et al. Proband-independent noninvasive prenatal diagnosis for spinal muscular atrophy: early detection paving the way for early prenatal treatment. Ann Med. 2026;58(1):2610892. doi:10.1080/07853890.2025.2610892.

[2] Pritchard AJ, Xian Lim KM, Smith G, et al. A framework for bioinformatic reporting in prenatal sequencing: insights from a systematic review. Prenat Diagn. 2026. doi:10.1002/pd.70085.
[3] Bossuyt PM, Reitsma JB, Bruns DE, et al. STARD 2015: an updated list of essential items for reporting diagnostic accuracy studies. BMJ. 2015;351:h5527. doi:10.1136/bmj.h5527.
[4] Shaikh R, Sethu P, Shanmugam J, et al. Concurrent diagnosis of spinal muscular atrophy and trisomy 21: value of comprehensive analysis in prenatal genetic testing. Clin Chim Acta. 2026;580:120723. doi:10.1016/j.cca.2025.120723.

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