A Bayesian Multimodal Framework Integrating Digital Biomarkers and Clinician-Rated Measures for Assessment of Expressive Negative Symptoms in Schizophrenia

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What is the Methodological Issue Being Addressed? Negative symptoms remain among the most disabling features of schizophrenia and are typically assessed using clinician-rated scales that require extensive training and demonstrate variable inter-rater reliability. Digital biomarkers derived from speech behavior offer objective measurement opportunities but are generally evaluated using conventional predictive modeling approaches that provide limited support for clinical decision-making. We developed a Bayesian decision analysis framework that integrates multimodal acoustic biomarkers, PANSS Expressive Negative Symptom scores, and BNSS expressive symptom ratings to estimate individualized distributions of expressive negative symptom severity. The approach supplements rather than replaces clinician-administered assessments by combining objective digital measures with established clinical rating scales to reduce subjective symptom severity estimation.

Introduction Recent studies have demonstrated associations between acoustic speech features and expressive negative symptoms, particularly alogia. However, translation of these biomarkers into clinically actionable tools remains limited. The authors prior work demonstrated that individuals with treatment-resistant schizophrenia (TRS) differed from healthy controls on acoustic features including Cepstral Peak Prominence (CPP), canonical timing alignment, reading duration, and spontaneous speech duration, and that several speech measures were associated with PANSS and BNSS expressive symptom ratings. This analysis extends those findings by evaluating whether digital biomarkers can be integrated with clinician-rated measures within a Bayesian framework to generate individualized estimates of expressive negative symptom severity while explicitly quantifying uncertainty.

Methods Data were derived from 67 TRS participants and 63 healthy controls who completed two standardized Modality virtual speech assessments. Candidate predictors included CPP, spontaneous speaking duration, reading duration, canonical timing alignment, percent pause time, and F0 variability. A Bayesian latent-variable model was constructed in which expressive negative symptom severity was treated as an unobserved clinical construct informed jointly by PANSS Expressive Negative Symptom scores (ENS), BNSS Alogia ratings, BNSS Blunted Affect ratings, and acoustic speech biomarkers. Posterior severity estimates were generated by combining clinician-rated and digital measures within a unified probabilistic framework. Model parameters were estimated using Markov Chain Monte Carlo sampling. Clinical decision thresholds were derived using a utility-based decision function that incorporated the relative costs of false-positive and

false-negative classifications. A Bayesian probit model estimated the posterior probability of clinically significant ENS: $P(Y_i=1|X_i)=\Phi(X_i\beta)$, where Y_i indicated high ENS severity and X_i represented PANSS, BNSS, CPP, F0, Speaking Duration and CTA. Posterior distributions were estimated using Markov Chain Monte Carlo sampling. Participants were classified as low, intermediate, or high severity-risk based on posterior probability thresholds: low <0.40, intermediate 0.40–0.70, and high >0.70. A utility function incorporated the relative costs of false-negative versus false-positive classification: $EU(d)=\Sigma P(\theta|X)U(d,\theta)$, and decisions were selected by maximizing expected utility.

Results The integrated Bayesian model demonstrated improved discrimination compared with speech-only clinician-rated symptom methods, with cross-validated AUC=0.88 versus 0.80 and posterior predictive accuracy of 83%. Posterior ENS severity estimates demonstrated stronger agreement with observed clinician-rated symptom severity than either clinician-rated measures or individual digital biomarkers considered independently. Integration of PANSS, BNSS, and digital biomarkers reduced posterior uncertainty by approximately 27% relative to models based solely on clinician-rated measures. Among acoustic measures, reduced CPP (posterior β=-0.41, 95% CrI [-0.63,-0.19]), reduced spontaneous speech duration (β=-0.36, 95% CrI [-0.55,-0.17]), and reduced F0 variability (β=-0.29, 95% CrI [-0.48,-0.10]) demonstrated the strongest associations with latent ENS severity. Compared with PANSS ENS scores alone, the integrated Bayesian model improved severity classification accuracy from 74% to 86% and increased cross-validated AUC from 0.79 to 0.89.

Conclusion This Bayesian framework demonstrates how digital biomarkers can augment established clinician-administered measures rather than function as stand-alone alternatives. By integrating PANSS, BNSS, and multimodal speech biomarkers within a unified probabilistic model, the approach generates individualized severity estimates, reduces uncertainty surrounding symptom assessment, and provides a transparent framework for incorporating objective behavioral measurements into clinical trials and future digital endpoint development.

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