

## STATISTICAL ANALYSIS PLAN

**Title:** Multimodal Biomarker Predictors of Relapse in Major Depressive Disorder: A Hybrid Retrospective–Prospective Cohort Study

**NCT Number:** Not yet available

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## Statistical Analysis Plan

### Analysis Block 1: MDD Biomarkers (Baseline)

**Groups:** Recurrent vs. Non-recurrent vs. Healthy

- ANOVA or Kruskal–Wallis
- Post-hoc: Tukey/Bonferroni
- Genotype: Chi-square

Goal: Identify baseline biomarker differences distinguishing recurrent MDD phenotype.

### Analysis Block 2: Longitudinal Change (Prospective Group)

Model:

**Biomarker Group (Relapse/No Relapse) × Time (T0 vs T2) + Random Intercept (Subject)**

Using Repeated Measures ANOVA or Linear Mixed Models.

**Expected pattern:**

- Non-relapsers: abnormal at T0 → normalized at T2 → similar to healthy
- Relapsers: abnormal at T0 → remain abnormal at T2

### Analysis Block 3: Early Predictors (T0 → T1)

- $\Delta P300$  and  $\Delta AEEG$  % improvement
- Logistic regression for relapse prediction
- Point-biserial correlations with relapse

### Analysis Block 4: Decision Algorithm Development

**Normalization Index (NI):**

For each biomarker at T2:

$$Z\text{-score} = (\text{Patient T2} - \text{Healthy\_Mean}) / \text{Healthy\_SD}$$

**ROC Analysis:**

- Predictor: NI
- Outcome: Relapse (Yes/No)
- $AUC > 0.80 \rightarrow$  strong predictor
- Cut-off = optimal Youden threshold

**Example Interpretation:**

“If P300 latency > 320 ms at medication discontinuation, relapse risk = 85%.”