## O092

### Maternal antenatal depression is associated with metabolic alterations that predict birth outcomes, neurodevelopment and mental health of the child

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doi: 10.1192/j.eurpsy.2025.346

**Introduction:** Evidence regarding metabolic alterations associated with maternal antenatal depression (AD) is limited, and their role as potential biomarkers improving the prediction of AD and adverse child birth, neurodevelopmental, and mental health outcomes remains unexplored.
**Objectives:** To identify metabolic measures associated with AD.
To test whether the metabolic measures associated with AD increased the amount of variance explained in AD over its risk factors.
To test whether the identified metabolic measures increased the amount of variance explained in child gestational age and weight at birth, developmental milestones at ages 2.3-5.7 years and any mental or behavioral disorder by the ages of 13.1-16.8 years over AD, sex, and age.
To replicate the findings in an independent cohort.
**Methods:** In a cohort of 331 mother-child dyads, we applied elastic net regression to study associations between AD (history of medical register diagnoses and/or Center of Epidemiological Studies Depression Scale score during pregnancy≥20) and 95 metabolic measures analyzed three times during pregnancy. Child birth and mental health outcomes were extracted from national registers and child neurodevelopmental outcomes were mother-reported.
**Results:** Elastic net regression identified 15 metabolic measures that collectively explained 25% ($p<0.0001$) of variance in AD, including amino and fatty acids, glucose, inflammation, and lipids. These metabolic measures increased the variance explained in AD over its risk factors (32.3%,$p<0.0001$ vs. 12.6%,$p=0.004$), and in child gestational age (9.0%,$p<0.0001$ vs. 0.7%, $p=0.34$), birth weight (9.0%,$p=0.03$ vs. 0.7%, $p=0.33$), developmental milestones at the age of 2.3-5.7 years(21.0%,$p=0.002$ vs. 11.6%,$p<0.001$) and any mental or behavioral disorder by the age of 13.1-16.8 years (25.2%,$p=0.03$ vs. 5.0%,$p=0.11$) over AD, child sex and age. These findings replicated in the independent cohort.
**Conclusions:** AD is associated with alterations in 15 metabolic measures, which collectively improve the prediction of AD over its risk factors, and birth, neurodevelopmental and mental health outcomes of the child over AD. These metabolic measures may become biomarkers identifying at-risk mothers and children for personalized interventions.

**Disclosure of Interest:** None Declared

## O093

### Difficult-to-Treat Depression: Effectiveness, Functionality, and Quality of Life—Preliminary Results from a Real-World Prospective Cohort under Esketamine Treatment in Spain after 3-Month Follow-Up

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doi: 10.1192/j.eurpsy.2025.347

**Introduction:** Major depressive disorder (MDD) is one of the most prevalent and disabling mental health conditions globally. Approximately one-third to half of MDD patients, suffer from difficult-to-treat depression (DTD), a condition marked by persistent symptoms that do not respond to multiple standard treatments. DTD is often associated with comorbid physical and psychiatric conditions leading to chronic disability and a reduced quality of life. The complexity of DTD poses a considerable challenge in clinical practice, underscoring the need for innovative treatment options.
**Objectives:** Despite the demonstrated efficacy of esketamine in controlled clinical trials, real-world evidence is limited. This study aimed to address this gap by assessing the effectiveness of esketamine in routine clinical practice in DTD patients.
**Methods:** This prospective, naturalistic, open-label, observational study was conducted at Marqués de Valdecilla University Hospital in Cantabria, Spain. It included 33 patients diagnosed with DTD, comprising both unipolar and bipolar depression, as well as persistent depressive disorder (see table 1). Esketamine was administered intranasally in doses ranging from 56 mg to 84 mg, across three phases: induction, consolidation, and maintenance. Treatment effectiveness was measured using the MADRS, Clinical Anxiety Scale (CAS), and Clinical Global Impression (CGI). Functionality and quality of life were assessed with the Brief Functioning Scale (FAST) and the EQoL-5D (ESH). Assessments were conducted at baseline, 1-month, and 3-month. Data analysis was performed using SPSS v26, with repeated measures ANOVA and Pearson's $\chi^2$ tests employed to evaluate changes over time.
**Results:** The final analysis included 33 patients with DTD and long-lasting current MDD episodes (table 2). Baseline MADRS scores indicated severe depression (39.12 ± 6). Significant reductions in MADRS scores were observed at both one month (21.61 ± 11.15) and 3-month (19.70 ± 11.65) compared to baseline. At 3-month, 54.5% of patients achieved a ≥50% reduction in MADRS scores, and 30.3% reached remission (MADRS < 12). Similar improvements were seen in anxiety (CAS) and health status (ESH) scores, with significant reductions noted over time.