Edges between PHQ9 and environmental factors were mediated by loneliness (UCLA). Poor architectural conditions (REAT) were linked positively with neighborhood belonging and adversely with social cohesion. Living in UA was negatively related to PHQ9, PHQ5 (eating control), and PHQ2, social cohesion, and green area distance, while positively to PHQ7 (problems with being focused), poor physical health, REAT, and neighborhood belonging (Figure 1).
Conclusions: Living in a city is negatively related to the most central depression symptoms. Even though social cohesion is negatively linked to UA, neighborhood belonging is higher in more urbanized areas.
The balance between detrimental environmental factors and those that protect mental health requires a better understanding of the interaction between urban living and depression.

Disclosure of Interest: None Declared

O0096

Brain magnetic resonance imaging outperforms clinical severity ratings in the prediction of treatment outcomes in major depressive disorder

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Introduction: Major depressive disorder (MDD) is a prevalent and disabling condition. Approximately 30-50% of patients do not respond to first-line medication or psychotherapy. Therefore, several studies have investigated the predictive potential of pretreatment severity rating or neuroimaging features to guide clinical approaches that can speed optimal treatment selection.
Objectives: To evaluate the performance of 1) severity ratings (scores of Hamilton Depression/Anxiety Scale, illness duration, and sleep quality, etc.) and demographic characteristic and 2) brain magnetic resonance imaging (MRI) features in predicting treatment outcomes for MDD. Second, to assess performance variations among varied modalities and interventions in MRI studies.
Methods: We searched studies in PubMed, Embase, Web of Science, and Science Direct databases before March 22, 2023. We extracted a confusion matrix for prediction in each study. Separate meta-analyses were performed for clinical and MRI studies. The logarithm of diagnostic odds ratio [log(DOR)], sensitivity, and specificity were conducted using Reitsma's random effect model. The area under curve (AUC) of summary receiver operating characteristic (SROC) curve was calculated.
Subgroup analyses were conducted in MRI studies based on modalities: resting-state functional MRI (rsfMRI), task-based fMRI (tbfMRI), and structural MRI (sMRI), and interventions: antidepressant (including selective serotonin reuptake inhibitors [SSRI]) and electroconvulsive therapy (ECT). Meta-regression was conducted 1) between clinical and MRI studies and 2) among modality or intervention subgroups in MRI studies.
Results: We included ten studies used clinical features covering 6494 patients, yielded a log(DOR) of 1.42, AUC of 0.71, sensitivity of 0.61, and specificity of 0.74. In terms of MRI, 44 studies with 2623 patients were included, revealing an overall log(DOR) of 2.53. The AUC, sensitivity, and specificity were 0.89, 0.78, and 0.75.
Studies using MRI features had a higher sensitivity (0.89 vs. 0.61) in predicting treatment outcomes than clinical features ($P < 0.001$). RsfMRI had higher specificity (0.79 vs. 0.69) than tbfMRI subgroup ($P = 0.01$). No significant differences were found between sMRI and other modalities, nor between antidepressants (SSRIs and others) and ECT. Antidepressant studies primarily identified predictive imaging features in limbic and default mode networks, while ECT mainly focused on limbic network.
Conclusions: Our findings suggest a robust promise for pretreatment brain MRI features in predicting treatment outcomes in MDD, offering higher accuracy than clinical studies. While tasks in tbfMRI studies differed, those studies overall had less predictive utility than rsfMRI data. For MRI studies, overlapping but distinct network level measures predicted outcomes for antidepressants and ECT.

Disclosure of Interest: None Declared

O0097

Rapid reduction of depressive symptoms with minimal dissociation: results from the KET01-02 and KET01-03 trials with oral prolonged-release (PR) ketamine KET01

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Introduction: Current ketamine-based therapies for treatment-resistant depression (TRD) often induce dissociative effects. A novel oral PR ketamine formulation (KET01) results in a low and delayed peak concentration of ketamine, high hydroxynorketamine concentration, and is associated with limited dissociative properties.
Objectives: To investigate efficacy, safety, and pharmacokinetics of KET01 in TRD.
Methods: KET01-02 was a randomized, double-blind phase 2 trial in outpatients with TRD comparing adjunct 120 mg (n=42) or 240 mg (n=40) oral KET01 once-daily for 3 weeks to placebo (PBO, n=40). The primary endpoint was change from baseline in the MADRS mean score on Day 21. KET01-03 was a randomized, double-blind, cross-over phase I trial in 26 healthy volunteers comparing single doses of 240 mg oral KET01 and 84 mg an approved intranasal formulation of eketamine. The primary endpoint was maximum change of Clinician-Administered Dissociative States Scale (CADSS) score from baseline.
Results: KET01-03 trial; the mean (±SD) maximum change of CADSS score within 24 hours after dosing was 29.6±12.5 for intranasal eketamine and 0.7±1.7 for KET01 (p<0.00000000001). KET01-02 trial; no differences in CADSS score (range: 0.2 to 1.3), and heart rate and blood pressure were observed between the groups on Day 1 and beyond. 10%, 12%, and 15% of patients in