**Introduction:** Predictors consistently associated with psychosis liability and course of illness in schizophrenia (SCZ) spectrum disorders (SSD), including the need for clozapine treatment, are lacking. Longitudinally ascertained medication use may empower studies examining associations between polygenic risk scores (PRSs) and pharmacotherapy choices.
**Objectives:** To examine associations between PRS-SCZ loading and groups with different liabilities to SSD: individuals with SSD on clozapine, individuals with SSD on other antipsychotics, their parents and siblings, and unrelated healthy controls; and between PRS-SCZ and the likelihood of receiving a prescription of clozapine relative to other antipsychotics.
**Methods: Design:** Six-year follow-up and cross-sectional observational cohort study.
**Setting:** Multi-center.
**Participants:** Individuals diagnosed with SSD using clozapine or other antipsychotics, their parents and siblings, and unrelated healthy controls.
**Exposure:** PRS-SCZ.
**Main Outcomes and Measures:** We used multinomial logistic regression to examine possible differences between groups by computing risk ratios (RRs), i.e., ratios of the probability of pertaining to a particular group divided by the probability of healthy control status. We also computed PRS-informed odd ratios (ORs) for clozapine use relative to other antipsychotics.
**Results:** PRSs-SCZ were generated for 2344 participants (mean age: 36.95 years; 42.4% female) remaining after quality control (557 individuals with SSD on clozapine, 350 individuals with SSD on other antipsychotics during six-year follow-up, 542 parents and 574 siblings of individuals with SSD, and 321 unrelated healthy controls). All RRs were significantly different from 1; RRs were highest for individuals with SSD on clozapine (RR=3.24 [95%CI 2.76-3.81], $p=2.47x10^{-46}$), followed by individuals with SSD on other antipsychotics (RR=2.30 [95%CI 1.95-2.72], $p=3.77x10^{-22}$), parents (RR=1.44 [95%CI 1.25-1.68], $p=1.76x10^{-6}$), and siblings (RR=1.40 [95%CI 1.21-1.63], $p=8.22x10^{-6}$). PRS-SCZ was positively associated with clozapine versus other antipsychotic use (OR=1.41 [95%CI 1.22-1.63], $p=2.98x10^{-6}$), suggesting a higher likelihood of clozapine prescriptions in individuals with higher PRS-SCZ.
**Conclusions:** PRS-SCZ loading differs between groups of individuals with SSD, their relatives, and unrelated healthy controls, with clozapine users being at the far end of PRS-SCZ loading. Additionally, PRS-SCZ is associated with a higher likelihood of clozapine prescribing. Our findings may inform early intervention and prognostic studies into the value of PRS-SCZ for personalized antipsychotic treatment.

**Disclosure of Interest:** None Declared

## O0054

## Combination therapy for bipolar disorder : What to combine and which cautions to take ?

M. Gardabbou*, M. Maalej, R. Feki, I. Gassara, N. Smaoui, L. Zouari, J. Ben Thabet, S. Omri, N. Charfi and M. Maalej

psychiatry C department, Hedi Chaker, Sfax, Tunisia
*Corresponding author.
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**Introduction:** Bipolar disorder is one of the leading causes of disability among young adults. Given the heterogeneity of the disorder and the complexity of its etiopathogenesis, combination therapy is often considered as part of the treatment regimen.
**Objectives:** To assess the place of non-pharmacological interventions as a co-adjuvant to pharmacological treatment, to discuss the role of polytherapy in the management of bipolar disorder and to underline the drug to drug interactions to keep in mind.
**Methods:** We present a critical review of recent international recommendations for the management of bipolar disorder. Two main evidence-based guidelines were included: The 2020 Royal Australian and New Zealand College of Psychiatrists clinical practice guidelines for mood disorders and The 2018 Canadian Network for Mood and Anxiety Treatment.
**Results:** According to guidelines, the outcomes in bipolar disorder are improved when medication is combined with evidence-based psychological treatment and lifestyle changes. As to polytherapy, it is often recommended to maximise the treatment efficacy. Studies have shown that combination treatments tend to work faster and more effectively than monotherapy especially in episodes with higher index severity. For the management of agitation, an adjuctive treatment by Haloperidol with midazolam or promethazine can be prescribed. In acute mania, combination therapy with quetiapine, aripiprazole, risperidone or asenapine and lithium or divalproex is recommended as first-line treatment options. Combinations of mood-stabilizing drugs may be more often necessary when rapid cycling is present. In a manic episode with mixed features the use of divalproex with an atypical antipyshcotic is recommended. In bipolar I depression, lurasidone and lamotrigine are often used as adjunctive therapies. When anxious distress is present, the combination of olanzapine and fluoxetine has shown to be effective. In a depression with atypical features, tranylcypromine (IMAO) can be added to lithium, divalproex or a second generation antipsychotic for a better result. Adjunctive treatment of olanzapine with fluoxetine may be necessary in a depression with mixed features. However, in bipolar II depression and for maintenance treatment no adjunctive therapies are recommended. Finally, it is important to consider the adverse effects resulting from polytherapy. Using lithium as an adjunctive medication may increase the risk of tremor and acute dystonic reactions and can be a contributing factor for neuroleptic malignant syndrome, whereas divalproex can be an inducer or an inhibitor of some atypical antipsychotics.
**Conclusions:** Rational polytherapy allows better and faster control over symptoms of bipolar disorder and should be considered after a detailed discussion of risks and benefits.

**Disclosure of Interest:** None Declared

## O0055

## Evaluation of factors that may influence the development of chronic kidney disease in patients with bipolar disorder treated with lithium.

N. Gutiérrez Mora[1]*, J. Torres Cortés[2], I. Esteban Avendaño[2], V. Burguera Vion[3] and J. M. Montes Rodríguez[2]

[1]Hospital Universitario Ramón y Cajal, Madrid, Spain; [2]Psychiatry and [3]Nephrology, Hospital Universitario Ramón y Cajal, Madrid, Spain
*Corresponding author.
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**Introduction:** Bipolar disorder (BD) is a serious and chronic mental disease of mood. Lithium is used for treatment and studies have demonstrated that it is the most efficient drug, reducing suicide risk in a high percentage of patients. However, this drug has well known side effects, such as kidney damage. Lithium could cause chronic kidney disease, specially with the presence of other risk factors.
**Objectives:** Observational and retrospective study of creatinine levels and glomerular filtration rates observed in blood analysis (follow-up period of 11 years). Sample size of 263 patients diagnosed of BD I and BD II in treatment with lithium. We used socio-demographic (age, sex) and clinic variables (diabetes mellitus, hypertension, use of nonsteroidal anti-inflammatory drugs (NSAIDs) and/or diuretics) to generate bivariate and multivariate analysis.
**Methods:** Our main objective is to analyze the deterioration of kidney function and the development of chronic kidney disease that chronic treatment with lithium can induce in patients with BD. Our secondary objective is to determine variables which could promote the development of chronic kidney disease, and to assess if these variables could be considered as risk factors during the treatment with lithium.
**Results:** 11,3 % of patients in our study developed chronic kidney disease during monitoring. The deterioration of GFR in patients in treatment with lithium was significantly associated with female sex and NSAIDs consumption. A trend towards statistical significance was found regarding the use of diuretics (p=0,060). No statistical significance was found between diabetes mellitus, hypertension or type of BD and the deterioration of kidney function in our sample. An inverse association was found between the GFR decline and the age but no statistical significance was demonstrated.
**Conclusions:** We conclude that female sex and use of NSAIDs are predicting factors of GFR decline in patients with BD in chronic treatment with lithium. We must take into account these drugs or even avoid concomitant treatment (lithium and NSAIDs) in order to prevent chronic kidney disease. In addition to it, we should recommend careful use of diuretics during treatment with lithium because of risk of dehydration. Diabetes mellitus and hypertension have universally been associated to increase risk of development of chronic kidney disease. However, we have not found statistical significance in our study. Therefore, research should be done in order to determine specific risk factors in this group of patients and, consequently, optimize their treatment.

**Disclosure of Interest:** None Declared

## O0056

## Meta-analysis of the variability in the individual response to pharmacological treatments for mania in bipolar disorder

G. Anmella[1]*, M. De Prisco[2], V. Oliva[2], M. Sanabra[2], L. Fortea[3], M. Ortuño[3], G. Fico[2], A. Murru[2], E. Vieta[2], D. Hidalgo-Mazzei[2], A. Solanes[3] and J. Radua[3]

[1]Hospital Clínic de Barcelona, Barcelona, Spain; [2]Hospital Clínic de Barcelona, Barcelona and [3]Imaging of Mood- and Anxiety-Related Disorders (IMARD) group, IDIBAPS, Barcelona, Spain
*Corresponding author.
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**Introduction:** Many studies have investigated whether there exist predictors of good response to antimanic drugs in bipolar disorder (BD). However, these factors predict response or only indicate benign illness course.
**Objectives:** To shed some light on the topic, we tested whether the response to antimanic drugs showed any variability beyond that expected by the effects of illness course and placebo.
**Methods:** We included all double-blind, placebo-controlled RCTs of oral pharmacotherapies targeting adult patients with acute bipolar mania from 1991 to 2020. The primary outcome was the variance of the improvement in manic symptoms in treated individuals compared to placebo. The effect size was the log variability ratio (logVR). We performed a random-effects meta-analysis, including assessments of heterogeneity, sensitivity/cumulative/subgroup analyses, and meta-regression.
**Results:** 42 RCTs (46 comparisons) from a total of 8,438 BD patients with acute mania (53.7% male, mean age=39.3; 5,563 treatment/2,875 control groups) were included in the analysis. Individuals in active treatment groups did not show variability in the response beyond that observed in individuals under placebo (VR=1; 95% C.I.=0.97,1.03; p-value=0.97). No heterogeneity was detected between the studies ($I^2$=0%; $tau^2$=0%; Q=29.21; df=45; p-value=0.97). Results were similar in the leave-one-out/cumulative/subgroup analyses. Meta-regression did not show influences by age, sample size, sex, severity of manic symptoms at baseline, or clinical features (rapid cycling, mixed or psychotic features).
**Conclusions:** This meta-analysis shows no evidence of differences in the individual response to treatments. These findings suggest that the average treatment effect is a reasonable assumption for the individual BD patient with acute mania. The presented article adds evidence to the equivalent results in schizophrenia-spectrum disorders, clinical high-risk state for psychosis, and major depressive disorder, not supporting classification in responders vs. non-responders. However, these findings should be balanced with results from other fields supporting such classification.

**Disclosure of Interest:** None Declared

## O0057

## Mindfulness, Attention, and Impulsivity in Bipolar Disorder

N. E. Fares-Otero*, B. Solé, S. Martin-Parra, F. Piazza, J. Sanchez-Moreno, E. Vieta and A. Martinez-Aran

Psychiatry and Psychology, Bipolar and Depressive Disorders Unit, Hospital Clínic of Barcelona, Institute of Neurosciences, Barcelona, Spain
*Corresponding author.
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**Introduction:** Bipolar disorder (BD) is a chronic mental disorder characterized by mood instability[1]. BD is further related to neurocognitive and functional disruptions that remain remarkably stable even when patients are euthymic, leading to poor well-being and quality of life. Mindfulness means paying attention on purpose, in the present moment, and involves different facets such as observing, describing, acting with awareness, non-judging and non-reacting of inner experience. It remains unclear whether mindfulness and its specific facets are differentially associated with different aspects of attention and trait impulsivity in individuals with BD.