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Keywords: postpartum depression; zuranolone; rapid onset of action; major depressive disorder

O0093

Benzodiazepine use during cariprazine treatment in acute schizophrenia

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Introduction: Although antipsychotics are first-line treatments for schizophrenia, benzodiazepines (BZDs) are often used as concomitant medications in acutely exacerbated patients due to their anxiolytic and sedative effects. Cariprazine (CAR), a D3-preferring dopamine D2/D3 partial agonist antipsychotic, has been examined in many clinical studies for the treatment of acute schizophrenia, with and without benzodiazepines.

Objectives: To delineate the effects of benzodiazepine-use during cariprazine treatment in acute schizophrenia.

Methods: Pooled data of cariprazine-treated (1.5-6mg/day) and placebo-treated patients from four short-term, randomised, double-blind trials (NCT00404573, NCT01104766, NCT01104779, NCT00694707) were analysed. Baseline characteristics (age, duration of illness) and efficacy outcome parameters (Total and Hostility Factor Score of the Positive and Negative Syndrome Scale [PANSS]) were compared in patients receiving benzodiazepines (for more ≥ 3 consecutive days) and not receiving benzodiazepines (< 3 consecutive days).

Results: Altogether, 36.7% and 40.7% of the CAR-treated and PBO-treated patients required BZDs. BZD-taking was associated with a higher age in both the CAR-treated ($p=0.0002$) and PBO-treated ($p<0.0001$) patients, and with longer illness-duration in both treatment groups ($p<0.0001$). PANSS Total Score at baseline was similar for BZD users and non-users (CAR: LS Mean=96.36 and 96.27; PBO: LS Mean=95.55 and 96.66). Change from baseline in the PANSS Total Score was greater for patients who did not use BZD vs those who did (CAR: LS Mean= -23.8 vs LS Mean 17.2, $p<0.0001$; PBO: LS Mean= -14.0 vs LS Mean 12.9, $p=0.5776$).

Conclusions: These findings may suggest that requiring benzodiazepines is a potential indicator of longer illness duration and poorer response in acute schizophrenia.

Disclosure: I am an employee of Gedeon Richter Plc.

Keywords: benzodiazepine; cariprazine; schizophrenia; Pharmacotherapy

O0094

Characterising the evolution of antipsychotic polypharmacy and clozapine prescribing patterns in schizophrenia patients during psychiatric hospitalisations

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Introduction: A high prevalence of antipsychotic polypharmacy (APP) and low utilisation of clozapine is considered as inappropriate prescribing that can lead to suboptimal treatment, increased risk of poor response or adverse effects.

Objectives: To explore the evolution of prevalence of APP and associated factors as well as clozapine prescribing patterns between hospital admission and discharge.

Methods: We collected retrospective data on adult inpatients diagnosed with schizophrenia spectrum disorders in 2020-2021 in 6 Belgian hospitals.

Results: Of the 516 patients analysed, APP prescribing significantly increased from 47.9% on hospital admission to 59.1% at discharge. Both on admission and at discharge, APP was associated with treatment with a first-generation antipsychotic, not being treated with an antidepressant nor a mood stabilizer, high antipsychotic dosage, increased number of psychoactive cotreatments and total medicines. A lower number of comorbidities (OR=0.68, CI=0.50-0.91), no treatment with benzodiazepines (OR=0.02, CI=0.01-0.09) nor with trazodone or sedative antihistamines (OR=0.06, CI=0.01-0.03) and two or more previous antipsychotic trials (OR=4.91, CI=1.30-18.57) was associated with APP on admission only. APP at discharge was more frequent in patients with antipsychotic adverse effects (OR=2.57, CI=1.10-6.00), prior clozapine use (OR=16.30, CI=3.27-81.22) and not involuntary admitted (OR=0.26 CI=0.08-0.88). Contrary to admission, treatment with benzodiazepines was associated with APP at discharge (OR=10.9, CI=3.38-5.38). Only 9.3% of admitted patients were treated with clozapine. Although 28.1% were eligible, clozapine was introduced to 10 patients leading to 11% being discharged on it.

Conclusions: Inappropriate prescribing of antipsychotics to schizophrenia patients persist after psychiatric hospitalisations and are associated with identifiable characteristics.

Disclosure: No significant relationships.

Keywords: clozapine; Psychiatric hospitalisations; Antipsychotic polypharmacy; Clinical pharmacy

O0095

DNA methylation may mediate psychotropic drug-induced metabolic side effects: results from a 1-month observational study

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Introduction: Metabolic side effects of psychotropic medications are a major drawback to patients' effective treatment. Among the

mechanisms underlying their development, DNA methylation may be involved.

Objectives: The aim of this study was to estimate DNA methylation changes occurring secondary to psychotropic treatment and evaluate associations between 1-month metabolic changes and baseline DNA methylation or 1-month DNA methylation changes, using an epigenome-wide approach.

Methods: Seventy-nine psychiatric patients recruited as part of PsyMetab study, who started a treatment with either an anti-psychotic, a mood stabilizer or mirtazapine were selected. Epigenome-wide DNA methylation was measured using the Illumina Methylation EPIC BeadChip at baseline and after one month of treatment.

Results: A global methylation increase was observed after 1 month of treatment, which was more pronounced in patients whose weight remained stable (i.e., <2.5% weight increase). Epigenome-wide significant methylation changes were observed at 52 loci in the whole cohort and at one site, namely cg12209987, located in an intergenic region within an enhancer, specifically in patients who underwent important early weight gain (i.e., $\geq 5\%$ weight increase) during the same period of treatment ($p < 5 \times 10^{-8}$). Multivariable analysis confirmed an association between an increase in methylation at this locus and weight gain in the whole cohort ($p = 0.004$). Epigenome-wide association analyses failed to identify any significant link between other metabolic changes (e.g. glucose or lipid levels) and methylation data.

Conclusions: These findings give new insight into the mechanisms of psychotropic drug-induced weight gain. With improved understanding of the metabolic side effects, the use of precision medicine with epigenetics may become possible

Disclosure: No significant relationships.

Keywords: psychotropic drugs; Metabolic side effects; Precision Medicine; epigenetics

Mental Health Care 2

00096

NeuroBlu: a natural language processing (NLP) electronic health record (EHR) data analytic tool to generate real-world evidence in mental healthcare

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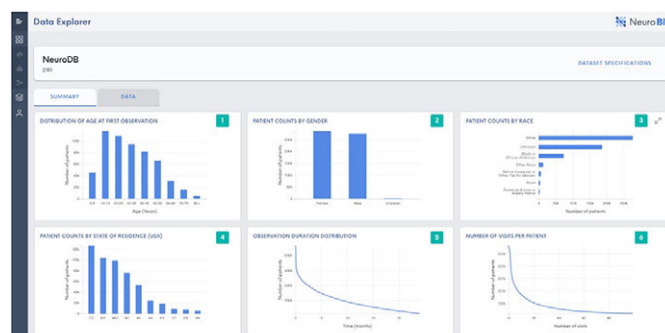
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Introduction: EHRs contain a rich source of real-world data that can support evidence generation to better understand mental disorders and improve treatment outcomes. However, EHR datasets are complex and include unstructured free text data that are time consuming to manually review and analyse. We present NeuroBlu, a secure, cloud-based analytic tool that includes bespoke NLP

software to enable users to analyse large volumes of EHR data to generate real-world evidence in mental healthcare.

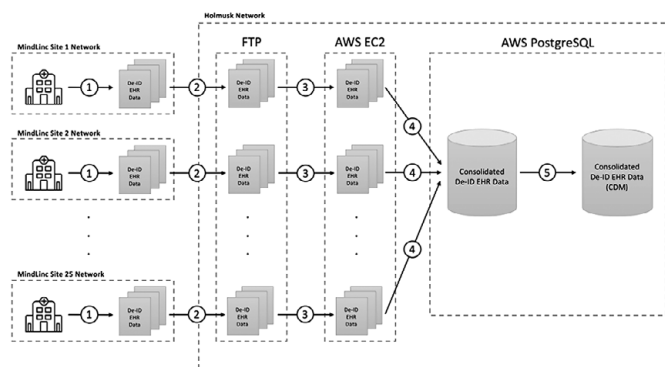


Objectives: (i) To assemble a large mental health EHR dataset in a secure, cloud-based environment.

(ii) To apply NLP software to extract data on clinical features as part of the Mental State Examination (MSE).

(iii) To analyse the distribution of NLP-derived MSE features by psychiatric diagnosis.

Methods: EHR data from 25 U.S. mental healthcare providers were de-identified and transformed into a common data model. NLP models were developed to extract 241 MSE features using a deep learning, long short-term memory (LSTM) approach. The NeuroBlu tool (<https://www.neuroblu.ai/>) was used to analyse the associations of MSE features in 543,849 patients.



Results: The figure below illustrates the percentage of patients in each diagnostic category with at least one recorded MSE feature.

