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Prediction of quality of life in schizophrenia using machine learning models on data from clinical antipsychotic trials of intervention effectiveness (CATIE) schizophrenia trial

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doi: 10.1192/j.eurpsy.2021.423

Introduction: Schizophrenia is a chronic and severe mental disorder. While research focus remains mainly on negative outcomes, it is questionable whether we are placing enough emphasis on improving their sense of well-being and functioning. This could be accessed through the study of the quality of life (QoL). To date, QoL prediction models mainly focused on neurocognition and psychotic symptoms, but their predictive power remained limited.
Objectives: The aim is to accurately predict the QoL within schizophrenia using unsupervised learning methods.
Methods: We computed variables from 952 patients from the CATIE study, a randomized, double-blind clinical trial for schizophrenia treatment. QoL was measured using the Heinrichs-Carpenter Quality of Life Scale and potential predictors included almost all available variables: symptoms, neurocognition, medication adherence, insight, adverse effects, etc. By optimizing parameters to reach optimal models, three linear regressions were calculated: (1) baseline predictors of 12-month QoL, (2) 6-month predictors of 12-month QoL, and (3) baseline predictors of 6-month QoL. Adjustments were made to ensure that included variables were not collinear nor redundant with QoL.
Results: Calculated models had adjusted R-squared of 0.918, 0.922 and 0.913, respectively. Best predictors were medication side effects, sociodemographic and neurocognitive variables. Low psychotic and depressive symptoms were also included, as well as lab values suggesting the absence of problems with chloremia and calcemia.
Conclusions: Calculated predictive models explain almost all subsequent QoL. It appears that physical health variables, generally omitted from mental health-related studies, have an important impact on patients' QoL. Therefore, interventions should also consider these aspects.

Disclosure: No significant relationships.
Keywords: schizophrénia; quality of life; machine learning; predictive models

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Efficacy and tolerability of lurasidone in schizophrenia: A systematic review and meta-analysis of short-term, randomized, placebo controlled trials

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doi: 10.1192/j.eurpsy.2021.424

Introduction: Lurasidone is an atypical antipsychotic approved for the treatment of patients with schizophrenia. We report on a meta-analysis focusing on both the efficacy and safety/tolerability of lurasidone in the treatment of patients with schizophrenia.
Objectives: To obtain pooled estimates from placebo-controlled clinical trials on the efficacy and safety/tolerability of lurasidone in schizophrenia.
Methods: We selected acute, randomized placebo-controlled trials of lurasidone for schizophrenia. Primary outcome for efficacy was the Positive and Negative Syndrome Scale (PANSS) change and for "acceptability" was all-cause discontinuation. Secondary outcomes included specific adverse events, body weight change, ≥7% weight gain, and glucose and lipid parameter change.
Results: Across 10 RCTs (n=3,963, age=40.5±2.3 years, males=64.7 %, trial duration=6.0 weeks), lurasidone outperformed placebo regarding the PANSS total score (N=10, n=3,354, SMD=-0.34, 95% CI: -0.47−-0.21, p<0.001). Stratifying the analysis by dose, lurasidone significantly outperformed placebo at doses 40-160 mg/day. Lurasidone was associated with significantly lower all-cause discontinuation than placebo (N=10, n=3,410, RR=0.87, 95% CI: 0.78−0.97, p=0.014). Lurasidone had significantly higher body weight change compared with placebo (N=10, n=3,359, SMD=0.17, 95% CI: 0.09−0.24, p<0.001), but without significant differences regarding ≥7% body weight gain (N=9, n=3,186, p=0.112). Lurasidone did not differ from placebo in total cholesterol (N=10, n=3,140, p=0.439), LDL-cholesterol (N=7, n=2,414, p=0.849), triglycerides (N=10, n=3,140, p=0.238), and fasting glucose change (N=10, n=3,112, p=0.633).
Conclusions: In short-term trials, lurasidone was efficacious, acceptable and safe, having minimal effect on body weight gain and glucose and lipid metabolism.

Disclosure: K. Hagi is a full time employee of Sumitomo Dainippon Phrma Co., Ltd.
Keywords: lurasidone; meta-analysis; RCT; schizophrénia

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Schizophrenia hospitalizations - a big data approach

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doi: 10.1192/j.eurpsy.2021.425

Introduction: Schizophrenia is characterized by long hospitalizations and a recurrent use of chronic and acute psychiatric care.
Objectives: The aim of this study was to analyze schizophrenia related hospitalizations in Portugal.
Methods: A retrospective observational study was conducted using a nationwide hospitalization database containing all hospitalizations registered in Portuguese public hospitals from 2008 to 2015.

Hospitalizations with a primary diagnosis of schizophrenia were selected and schizophrenia subtypes were grouped using the International Classification of Diseases version 9, Clinical Modification(ICD-9-CM) codes of diagnosis 295.xx.
Results: There was a total of 25,385 hospitalizations in public hospitals of Portugal between 2008 and 2015 with a primary diagnosis of Schizophrenia or other psychotic disorders. A total of 14,279 patients were hospitalized during the study period with an average of 1,78 hospitalizations episodes per patient in the 8-year interval(0.22 hospitalizations/patient/year). 68.0% of the hospitalizations occurred in male patients and the median length of stay was 18.0 days. Mean hospitalization charges were 3,509.7€ per hospitalization, summed to a total charge of 89.1M€. Throughout the study period there was a significant linear decrease in the number of hospitalizations ($r = 0.940$; $B= -47.488$; $p = 0.001$). The last year of the study(2015) had the lowest number of hospitalizations with a total of 2,958 (vs. 3,314 in 2008). When adjusted for the yearly population, there was also a decrease of the number of hospitalizations per 100,000 inhabitants from 31.39 to 28.56 hospitalizations per 100,000 inhabitants between 2008 and 2015, respectively.
Conclusions: We found differences in hospitalization characteristics by gender, age and primary diagnosis.

Disclosure: No significant relationships.
Keywords: schizophrénia; Big Data; Administrative Database

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Monitoring of antipsychotic plasma levels in the assessment of poor response and nonadherence to antipsychotics in delusional disorder

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doi: 10.1192/j.eurpsy.2021.426

Introduction: Over the last decades, antipsychotic plasma levels have been used to evaluate therapeutic response, adherence and safety of antipsychotics in schizophrenia. Their clinical utility in delusional disorder (DD) has been poorly studied.
Objectives: To investigate the relationship between plasma concentrations of risperidone (R), 9-OH-risperidone (9-OH-R) and olanzapine (OLZ), and clinical outcomes in DD.
Methods: Case-series of inpatients and outpatients with DD receiving treatment with risperidone (n=19) or olanzapine (n=2). Determination of R, 9-OH-R (active metabolite) and OLZ levels were obtained by high-performance liquid chromatography with electrochemical detection. Clinical variables such as treatment response or adverse events were recorded for all patients. These variables were correlated with two plasmatic ratios in patients treated with R: R:9-OH-R concentration ratio and total concentration-to-dose (C: D) ratio, indicating CYP2D6 activity and R elimination respectively.
Results: Twenty-one patients were included: inpatients (n=10) and outpatients (n=11). Dose range: R, 1-6 mg/day; OLZ, 5-10 mg/day. Three outpatients (R, n=2; OLZ, n=1) presented antipsychotic levels under the detection limit (non-adherence). All R patients showed CYP2D6 activity (R: 9-OH-R ratio <1). Eight patients presented C: D > 14, indicating a reduction of R elimination, which was associated with poor clinical response (n=3), adverse events (n=3) and no clinical relevance (n=2). OLZ (n=2), no association between levels and clinical outcomes.
Conclusions: The determination of antipsychotic plasma levels may be of clinical utility in the assessment of treatment resistance, antipsychotic-adverse events or non-adherence in inpatients or outpatients with DD. Therapeutic drug monitoring should be further studied in future works.

Disclosure: AGR has received honoraria, registration for congresses and/or travel costs from Janssen, Lundbeck-Otsuka and Angelini.
Keywords: Delusional disorder; Antipsychotic plasma levels; psychosis; Antipsychotics

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Ethno-psychopharmacological aspects of treatment response in patients with delusional syndrome: A systematic review

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doi: 10.1192/j.eurpsy.2021.427

Introduction: Treatment response in schizophrenia can be influenced by cultural and ethno-biological factors. However, in delusional disorder (DD), these potential influences have been poorly investigated.
Objectives: This review aims to synthesize what is known about the influence that cultural and biological factors may have on treatment response in DD.
Methods: A systematic review was performed on PubMed from inception to 2020 in keeping with PRISMA directives. Search terms: [(cultural OR ethnic* OR ethno*) AND (treatment OR therap* OR antipsychotic response) AND (delusional disorder)]. We included all studies whose objective was to explore ethno-psychopharmacological aspects of treatment response in DD.
Results: A total of 182 papers were retrieved. Four studies tested ethno-biological factors and 10 reported cultural aspects of treatment response in DD. 1. Cultural hypothesis: 3 studies reported cultural differences in diagnostic practices; in 2 studies, culturally-determined long durations of untreated psychosis (DUP) and comorbidity with mood disorders was associated with response to both antipsychotics (AP) and antidepressants (AD); 3 studies reported that response and AP dose were similar among cultures and that culturally-sensitive psychotherapy improved adherence;

https://doi.org/10.1192/j.eurpsy.2021.425 Published online by Cambridge University Press