in treatment with different antipsychotics remains unclear. Furthermore, predictors of metabolic dysregulation are poorly understood, and association between metabolic-change and change in psychopathology is uncertain.
Methods: We searched Medline, EMBASE and PsychINFO from inception until June 30, 2019. We included blinded randomised controlled trials (RCTs) comparing 18 antipsychotics and placebo in acute-treatment of schizophrenia. We performed frequentist random-effects network meta-analyses (NMAs) to investigate treatment-induced changes in body weight, BMI, total/LDL/HDL-cholesterol, triglycerides, and glucose. We performed meta-regressions to examine relationships between metabolic change and age/gender/ethnicity/baseline-weight/baseline-metabolic parameter level. We examined the association between metabolic change and psychopathology change by estimating the correlation between symptom severity change and metabolic parameter change.
Results: Of 6532 citations, 100 RCTs met inclusion criteria, including 25,952 patients. Median treatment-duration was 6-weeks. According to our NMAs, mean differences for weight-gain compared to placebo ranged from -0.23 (95% CI: -0.83, 0.36) for best (haloperidol) to +3.01kg (1.78, 4.24) for worst (clozapine); for BMI from -0.25 (-0.68, 0.17) for best (haloperidol) to +1.07kg/m2 (0.90, 1.25) for worst (olanzapine); for total-cholesterol from -0.09 (-0.24, 0.07) for best (cariprazine) to +0.56mmol/L (0.26, 0.86) for worst (clozapine); for LDL-cholesterol from -0.13 (-0.21, -0.05) for best (cariprazine) to +0.20mmol/L (0.14, 0.26) for worst (olanzapine); for HDL-cholesterol from +0.05 (0.00, 0.10) for best (brexpiprazole) to -0.10mmol/L (-0.33, 0.14) for worst (amisulpride); for triglycerides from -0.01 (-0.10, 0.08) for best (brexpiprazole) to +0.98mmol/L (0.48, 1.49) for worst (clozapine); for glucose from -0.29 (-0.55, -0.03) for best (lurasidone) to 1.05mmol/L (0.41, 1.70) for worst (clozapine). Greater increases in glucose were predicted by higher baseline-weight (p=0.001) and male-gender (p=0.008). Non-Caucasian ethnicity was associated with greater increases in total-cholesterol (p=0.04). Improvements in symptom severity were associated with increases in weight (rho=0.36, p=0.002), BMI (rho=0.84, p<0.0001), total-cholesterol (rho=0.31, p<0.05), and LDL-cholesterol (rho=0.42, p=0.01), and decreases in HDL-cholesterol (rho= -0.35, p=0.04).
Discussion: There are marked differences between antipsychotics in terms of metabolic side-effects, with olanzapine and clozapine exhibiting the worst profiles. By contrast, compared with placebo, lurasidone and cariprazine respectively reduce fasting glucose and LDL-cholesterol, while aripiprazole and brexpiprazole increase HDL-cholesterol. Baseline weight, male gender, and non-Caucasian ethnicity predict vulnerability to antipsychotic-induced metabolic change. Considering the increased prevalence of metabolic syndrome, cardiovascular disease, and cardiovascular mortality in schizophrenia, these data may be used to inform antipsychotic-prescribing, especially in those at-risk groups we have identified. However, clinical decisions to preferentially use an antipsychotic with fewer metabolic side effects should consider that clinical improvement appears to be associated with development of these side effects.

T80. CARDIOMETABOLIC RISK PREDICTION ALGORITHMS AND THEIR APPLICABILITY FOR YOUNG PEOPLE WITH PSYCHOSIS: A SYSTEMATIC REVIEW AND ILLUSTRATIVE EXAMPLE USING ORIGINAL DATA FROM A POPULATION-BASED BIRTH COHORT

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Background: Cardiometabolic risk prediction algorithms are used in clinical practice. Young people with psychosis are a high-risk group for developing cardiometabolic disorders, but it is unclear whether existing algorithms are suitable for this group.
Methods: We conducted a systematic review employing PRISMA criteria to identify studies reporting the development and/or validation of cardiometabolic risk prediction algorithms for general or psychiatric populations. A narrative synthesis was conducted to compare algorithms and consider their suitability for young people with psychosis. In addition, we used data from 3,470 young adults aged 18 years from the ALSPAC birth cohort to illustrate the impact of age on model performance of QDiabetes, an established algorithm.
Results: Having screened 6,609 studies, we included 57 risk algorithms designed for type 2 diabetes, cardiovascular disease or stroke, all of which were developed/validated in relatively older participants. Three algorithms featured psychiatric predictors and could be used for young people with psychosis. However, in all of three, age was weighted to a much greater extent than other risk factors. Furthermore, using ALSPAC data, we report that QDiabetes significantly under-predicted cardiometabolic risk in young people. Increasing the sample age to 50, leaving all other predictors unchanged, improved algorithm calibration markedly.
Discussion: Existing cardiometabolic risk prediction algorithms are heavily weighted on age and so under-predict risk in young people. A new or recalibrated algorithm is required for young people with psychosis that appropriately balances the weighting of relevant risk factors.

T81. MULTIPLE DRUG USE IN SCHIZOPHRENIA - THE ROLE OF EARLY ENVIRONMENTAL RISK ACCUMULATION AND GENETIC PREDISPOSITION

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Background: Drug (ab)use and substance use disorders are frequently observed in patients with psychiatric illness, but the underlying causes remain widely unknown. A number of environmental risk factors have been proposed to affect the use of one or multiple drugs in the general population and adolescents. Whereas most previous studies focused on the influence of single risk factors on the use of one or a few selected drugs, the effect of accumulated environmental risk in early life on multiple drug use remains to be studied. Similarly, evidence on genetic susceptibility to the (ab)use of a single drug, e.g. nicotine, alcohol, cocaine, is abundant, while the role of genetic predisposition for multiple drug use - in particular during early life - is yet to be explored. Thus, the current work aims to study the role of environmental as well as genetic risk factors for multiple drug abuse ('polytoxicomania') in a large sample of schizophrenic/schizoaffective patients.
Methods: Information from ~2000 schizophrenia/schizoaffective patients on (preadult) multiple drug use (> 2 drugs) and environmental risk factors was extracted from the Göttingen Research Association for Schizophrenia (GRAS) data collection – currently the largest data base of deeply phenotyped patients with schizophrenia/schizoaffective disorder or other neuropsychiatric diseases. In addition, genetic data from these patients and 2111 healthy blood donors were used in a novel genetic approach that employs multiple genome-wide association studies (GWAS) to identify genetic associations with preadult multiple drug use. Genotyping was performed on a semi-custom Axiom MyDesign Genotyping Array (Affymetrix, Santa Clara, CA, USA), based on a CEU (Caucasian residents of European ancestry from UT, USA) marker backbone.
Results: The accumulation of environmental risk factors, i.e. sexual abuse, physical abuse, migration, urbanicity, together with alcohol and cannabis consumption as secondary risk factors, in early life (< 18 years) were strongly associated with lifetime multiple drug use (p = 3.48 x 10^-44, extreme group comparison odds ratio (OR) = 31.8). When the sample was split into preadult and adult multiple drug users, there was a remarkable association of the number of preadult environmental risk