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/sex/ethnicity/baseline-weight/baseline-metabolic parameter level. We examined the association between metabolic change and psychoticophopathy 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 -10mmol/L (-0.33, 0.14) for worst (amisulpride); for triglycerides from -0.01 (-0.10, 0.08) for best (brexpiprazole) to +0.96mmol/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-induced metabolic change. 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 schizophrenia/schizoaffective patients.

**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**

Agnes Steixner-Kumar*1, Jan Seidel1, Vinicius Daguan-Gastald1, Martin Begemann1, Hannelore Ehrenreich1

1Max Planck Institute of Experimental Medicine, Göttingen

**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 schizophrenia/schizoaffective patients.

**Methods:** Information from ~2000 schizophrenia/schizoaffective patients on (pre)adult 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 factors...
factors with preadult multiple drug use (p = 1.12 x 10^-25, OR = 243.6). Furthermore, preadult environmental risk accumulation strongly predicted onset of multiple drug use in adulthood (> 18 years; p = 6.27 x 10^-18, OR = 19.4). The application of the novel genetic approach yielded 35 single-nucleotide variants (SNPs) that potentially confer susceptibility to preadult multiple drug use. Out of these, 14 were located in gene-coding regions. Interestingly, 9 of these genes are implicated in neuronal development/function or metabolite transport/transformation. Additional gene-based analyses identified another 4 genes relevant for metabolite transport/transformation as well as 4 genes that play a role in hypoxia signaling.

Discussion: The present results show that an accumulation of environmental risk factors during early life (< 18 years) is a strong predictor of multiple drug use during adolescence and later life. These findings suggest that exposure to accumulated environmental risk during early life is not only associated with violent aggression – as previously reported by our lab – but is also an important predictor of multiple drug use. Moreover, we present first evidence of a genetic susceptibility to preadult multiple drug use, which will benefit from future replication in suitable samples of patients with mental illness or the general population.

T82. THE IMPACT OF SMOKING ON LIFE EXPECTANCY IN PSYCHOTIC DISORDERS, AN ELECTRONIC CASE REGISTER COHORT STUDY.

Edward Chesney1, Deborah Robson1, Rashmi Patel1, Hitesh Shetty2, Sol Richardson2, Chin-Kuo Chang3, Philip McGuire1, Ann McNeill1

1Institute of Psychiatry, King’s College London; 2BRC Nucleus, South London and Maudsley NHS Foundation Trust; 3University of Taipei

Background: Schizophrenia, schizoaffective disorder and bipolar affective disorder are associated with a life expectancy at birth that is 10–20 years shorter than in the general population. The prevalence of cigarette smoking in people with these disorders is very high, but the extent to which this accounts for differences in mortality is unclear. We addressed this issue by examining the effect of smoking on life expectancy and survival in a large electronic healthcare database of patients receiving secondary mental healthcare in South East London.

Methods: Data on all patients with a diagnosis of schizophrenia, schizoaffective disorder or bipolar affective disorder from 1st January 2007 to 31st December 2018 was obtained. Smoking status was determined using unstructured text data extracted from electronic health records. Chiang’s method of abridged life tables was used to calculate estimates of life expectancy at birth according to gender and most commonly recorded smoking status. Cox proportional hazards models were used to estimate mortality risk and adjusted for a broad range of demographic and clinical variables.

Results: 21,588 patients were included in the study of which 20,155 (93.4%) were classified as either smokers (16,717 [77.4%]) or non-smokers (3,438 [15.9%]). 2,434 (11.3%) participants died by the end of the observation period. In female patients, life expectancy at birth was 67.6 years in current smokers (95% CI: 64.4 to 68.8) and 74.9 years in non-smokers (95% CI: 72.8 to 77.0). In male patients, life expectancy at birth was 63.5 years in current smokers (95% CI: 62.5 to 64.5) and 68.5 years in non-smokers (95% CI: 64.4 to 72.6). Adjusted survival models showed that current smoking was associated with an increased risk of death, in both females (aHR = 1.42; 95% CI: 1.21–1.66) and males (aHR = 1.49; 95% CI: 1.25–1.79).

Discussion: Smoking may account for a substantial proportion of the reduced life expectancy in patients with psychiatric disorders. Interventions to reduce tobacco smoking in patients with psychosis may therefore improve life expectancy in this group.

T83. SUBSTANCE-INDUCED PSYCHOSIS LINKED TO BOTH INFECTIONS AND SCHIZOPHRENIA

Carsten Hjorthøj1, Marie Starzer2, Michael Benros3, Merete Nordenboft1

1Copenhagen University Hospital, Mental Health Centre Copenhagen. The Lundbeck Foundation Initiative for Integrative Psychiatric Research (iPSYCH); 2Copenhagen University Hospital, Mental Health Center Copenhagen, Copenhagen Research Center for Mental Health - CORE; 3Mental Health Centre Copenhagen

Background: Substance-induced psychosis is an under-researched phenomenon, and little is known about its etiology (other than exposure to substances) and long-term prognosis. In this presentation, we aim to present results from two recent studies, one of which was recently published and the other is currently in the process of being analyzed. The first study investigates rates and predictors of conversion from substance-induced psychosis; the second study investigates the association between severe infections and substance-induced psychosis, including the contribution of infections on conversion to schizophrenia.

Methods: Both studies utilized the nationwide Danish registers. In study 1, we included all people diagnosed with substance-induced psychosis from 1994 to 2014 (n=6,788). These were followed using the Kaplan-Meier method and Cox proportional hazards regression to estimate rates and predictors of conversion to schizophrenia or bipolar disorder. In study 2, we included the entire Danish population born since 1981 (n=2,256,779). These were followed in Cox proportional hazards regression models, linking hospital-requiring infections as time-varying covariates to development of substance-induced psychosis. In further analyses, we followed those who had developed substance-induced psychosis to determine whether infections would influence the risk of converting to schizophrenia.

Results: Study 1: Overall, 32.2% (95% CI 29.7–34.9) of patients with a substance-induced psychosis converted to either bipolar or schizophrenia-spectrum disorders. The highest conversion rate was found for cannabis-induced psychosis, with 47.4% (95% CI 42.7–52.3) converting to either schizophrenia or bipolar disorder. Young age was associated with a higher risk of converting to schizophrenia. Self-harm was significantly linked to a higher risk of converting to both schizophrenia and bipolar disorder.

Study 2: Infections increased the risk of substance-induced psychosis (HR=1.30, 95% CI 1.22–1.39) in the fully adjusted model. Hepatitis was the infection most strongly associated with substance-induced psychosis, at HR=3.42 (95% CI 2.47–4.74). Different sites of infections showed associations with different types of substance-induced psychosis. Finally, hepatitis increased the risk of conversion to schizophrenia with HR=1.87 (95% CI 1.07–3.26).

Discussion: Substance-induced psychosis is strongly associated with the development of severe mental illness, and a long follow-up period is needed to identify the majority of cases. Infections appear to play a role in the etiology of substance-induced psychosis which is very similar to the role infections play in the etiology of schizophrenia. This lends strong support to the existence of an immune-related component to psychosis in general, and not just to schizophrenia.

T84. PREMORBID ADJUSTMENT AND IQ IN PATIENTS WITH FIRST-EPILOGUE PSYCHOSIS: A MULTISITE CASE-CONTROL STUDY OF THEIR RELATIONSHIP WITH CANNABIS USE

Abstract not included.

T85. LIVING WITH PSYCHOSIS IN LATER LIFE

Cherrie Galletty1, Shuichi Suetani1, Duncan McKellar1, David J. Castle3

1The University of Adelaide; 2Queensland Centre for Mental Health Research; 3Older Persons’ Mental Health Service, Northern