Results: The IVW MR method provided strong evidence of a casual effect of genetically instrumented neuroticism on risk of schizophrenia ($p < 0.001$). This causal association was also evident when using the median weighted approach ($p = 0.004$) but evidence was weaker when using the weighted mode ($p = 0.719$) and MR Egger approaches ($p = 0.439$). The MR Egger intercept provided weak evidence of presence of horizontal pleiotropy ($p = 0.067$), however, the I2GX statistic indicated potential violation of the no measurement error MR assumption. There was also evidence of a causal effect of schizophrenia on neuroticism (IVW $p = 0.001$, weighted median $p = 0.017$, weighted mode $p = 0.018$) however, again, the I2GX statistic indicated potential violation of the no measurement error MR assumption.

Discussion: Assuming certain MR assumptions are met, our results provide evidence of a bi-directional causal association between neuroticism and schizophrenia suggesting a genetic overlap rather than a uni-directional causal association, however, the impact of feedback loops between exposure and outcome cannot be addressed. Although there was evidence of horizontal pleiotropy between neuroticism and schizophrenia, evidence of violation of the no measurement error indicates that the MR Egger results should be interpreted with caution.

F139. INCLINATION OF STIGMA TOWARD SCHIZOPHRENIA, ATTENUATED PSYCHOSIS, PSYCHOTIC-LIKE EXPERIENCES AND DEPRESSION AMONG DIFFERENT SUBPOPULATIONS IN TAIWAN

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Background: Stigma toward mental illness may lead to delayed detection, impaired treatment adherence, and poorer recovery. The fear of being labeled as at risk of psychosis can be barriers to early identification of putative prodromal subjects. Compounded by an intriguing feature, psychotic-like experience with no apparent impact on functioning, we wonder if people will generalize their prejudice and discrimination towards schizophrenia to subjects with subthreshold psychotic symptoms.

Methods: A cross-sectional survey using a structuralized questionnaire modified from a previous study conducted by the Hong Kong University Early Psychosis research team was employed. Participants were recruited from various channels; including laypersons in general population invited after their attending talks about mental health topics, patients with mental illness and their key caregivers of 2 hospitals, and mental health professionals. The key component of this questionnaire is comprised by 4 case vignettes describing the symptoms and disabilities of patients with attenuated psychosis syndrome (APS), schizophrenia, depression, and psychotic-like experiences (PLE), respectively; followed by 2 sets of questions using 4-point Likert scale with 19 and 21 items for each set to measure social distance as a proxy for discrimination and prejudices. Basic demographic information, including age, gender, education level, current occupation, and previous contact with persons with mental illness were also collected.

Results: A total of 354 subjects completed this survey, including 239 lay publics, 32 psychiatric patients, 29 patient’s main caregivers, and 54 mental health professionals. Stigmas, especially prejudice, toward PLE are significantly higher in the patient group compared to the other 3 groups. Prejudice, but not discrimination, toward depression is significantly lower in professionals group. Stigmas toward schizophrenia and APS are in general not significantly different among groups, although the general public showed marginally higher scores in discrimination compared to the patient group. In each individual group, the patterns of attitude reflecting discrimination and prejudice are almost identical; that is, highest toward schizophrenia, followed by APS and depression (almost equivalent to each other), and lowest toward PLE, except the patient group which failed to reveal significant differences in ratings of 4 clinical case vignettes.

Discussion: APS seems to be a clinical entity too new to be judged. The majority of participants, except the patient group, reported a similar gradient of stigma toward different clinical severities. Such a result is consistent with previous studies that APS shared similar level of stigma with depression, not as high stigma as towards schizophrenia, but higher than PLE. Interestingly, patients with psychosis might have assimilated PLE to symptoms of schizophrenia based on their personal experiences, so they might have overrated the severity of subjects with PLE.

F140. HOMICIDES OF PHYSICIANS AND MENTAL HEALTH WORKERS

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Background: Violence towards mental health care workers, and towards physicians in general, is a common occupational hazard. The goal of this work was to determine to what extent violence escalates to actual homicides, both for mental health workers and for physicians in general. Characteristics of the victims, the perpetrators and of the methods of homicide were examined in order to formulate recommendations for violence assessment and safety measures in healthcare settings.

Methods: A systematic search for accounts describing homicides of mental health workers between 1981 and 2014, and for physicians between 1981 and 2017 was conducted. Cases of homicides committed by patients, family members of patients, and co-workers of the victims were included. Cases of homicide that occurred in correctional setting, or in agencies not focused on health care (such as child protective services) were excluded. News outlet accounts, internet sources, and the medical literature was searched for details of these cases. Data that were extracted included demographic details on victims and perpetrators, scene and method of homicide, presence of psychiatric diagnoses and prior treatment, and disposition of the perpetrators.

Results: Results obtained for mental health workers has been published previously1. Thirty-three homicides of mental health workers were found and examined. Young women caseworkers who were unaccompanied during visits to residential treatment facilities were the most common victims. Men with a diagnosis of schizophrenia were the most common perpetrators. The most likely method of homicide was gunshot. Perpetrators often had a prior history of violence, criminal charges, involuntary hospitalization and nonadherence to medications. Thirty cases of homicides of physicians were found and examined. Psychiatry was the single most likely specialty of the victims (37%). Most homicides occurred in physician offices (33%). The most common psychiatric diagnosis of the perpetrators was schizophrenia (17%), but many other diagnoses were identified, and 33% of perpetrators could not be assigned a diagnosis. The most common method of homicide was again by gunshot.

Discussion: Homicides of mental health workers, and of physicians generally, are rare events that emerge from a background of common aggression and violence in healthcare settings. Many of these homicides may have been preventable. Strategies to identify violence risk and to train acute care staff in possible prevention measures, as well as some policy and training measures will be discussed.

F141. DUTY TO WARN FOR POTENTIAL RISK OF PSYCHOLOGICAL HARM: A CASE REPORT

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Background: Under the current ethical and legal standards physicians are expected to breach confidentiality when a third party is at risk. However, the law has mainly focused on risk of bodily harm and there is no legal
Muscarinic M1 binding potential (BPND) was measured in this study was to evaluate the effect of patient and disease characteristics, and matched controls. Administration of xanomeline, a M1/4 agonist in patients with schizophrenia resulted in improved learning and memory scores and decreased psychotic symptom severity. Therefore, the current study sought to examine alterations in muscarinic M1 receptor signaling in relation to cognitive functioning in medication free subjects with psychotic disorders and matched controls.

Methods: Data were taken from a COMT genotype and response to cognitive remediation study of schizophrenia in the United States conducted between 07/2005 and 10/2015 for inpatients with schizophrenia who were also participating in psychiatric rehabilitation. Patients with and without relapse 2 years following completion of the study were compared on clinical, demographic, cognitive, functional and COMT genotype characteristics. The COMT gene rs4680 polymorphism was genotyped using a DNA sequence detection system. Relapse or events identified as treatment failures include: arrest, psychiatric re-hospitalization, suicide, discontinuation of antipsychotic treatment due to inadequate efficacy, treatment supplementation with another antipsychotic due to inadequate efficacy, discontinuation of antipsychotic treatment due to safety or tolerability, or increase in the level of psychiatric services. Baseline (end of study, start of 2-year follow-up) predictors of subsequent relapse were also assessed. Univariate Analysis and Cox’s regression was used to examine the effect of potential predictors on outcome.

Results: Of 140 subjects with eligible data, 91 (65.00%) relapsed during the 2-year follow-up period. Patients who relapsed were younger (< 45 years), higher number of previous hospitalizations, shorter chronicity of illness (< 10 years), PANSS baseline score of >4 on the core PANSS items (conceptual disorganization, hallucinatory behavior, suspiciousness, unusual thought content), higher negative symptom factor, substance use, PSP score of < 60 and lower MCCB composite T score (> 2 SD below the mean). Univariate analysis shows that COMT rs4680 gene variants were different between relapse and stable groups. The COMT rs4680 gene had an interaction with PANSS baseline core item scores suggesting the promise to provide neurofunctional biomarkers for improved diagnosis, prognosis, and optimized treatment of schizophrenic and affective disorders. These findings from functional neuroimaging studies may help to foster the development of precision medicine in psychiatry.

F142. THE USE OF NEUROIMAGING MARKERS IN STRATIFIED DIAGNOSIS AND THERAPY OF SCHIZOPHRENIC AND AFFECTIVE DISORDERS

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Background: Neuroimaging techniques have been developed as important tools to investigate brain dysfunctions that underlie mental disorders. In particular, modern functional magnetic resonance imaging (fMRI) holds the promise to provide neurofunctional biomarkers for improved diagnosis, prognosis, and optimized treatment of schizophrenic and affective disorders. Methods: Neurofunctional connectivity MRI using advanced experimental paradigms permits targeted investigation of the functional integrity of brain systems involved in the pathomechanisms of schizophrenic and affective disorders. From these investigations, pathophysiological relevant neuroimaging biomarkers can be derived for differential diagnosis and tailored treatment selection.

Results: Possible neuroimaging biomarkers will be presented for the prediction of development and clinical course of schizophrenic and affective disorders as well as for the prediction of individual treatment responses. Further, recent neuroimaging findings on possible pathophysiological subtypes of schizophrenic and affective disorders will be discussed.

Discussion: These findings from functional neuroimaging studies may help to foster the development of precision medicine in psychiatry.

F144. MUSCARINIC M1 RECEPTOR SIGNALLING UNDERLYING COGNITION IN PSYCHOTIC DISORDERS

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Background: Antipsychotic treatment has failed to improve cognitive deficits associated with psychotic disorders. This has led to an increased interest to revisit earlier implications from post-mortem studies that lowered muscarinic M1 receptor signaling may underlie these symptoms. This receptor is highly expressed in important regions for cognition such as the dorsolateral prefrontal cortex (DLPFC) and hippocampus, and administration of anti-muscarinic agents gives induce cognitive deficits in healthy volunteers. Administration of xanomeline, a M1/4 agonist in patients with schizophrenia resulted in improved learning and memory scores and decreased psychotic symptom severity. Therefore, the current study sought to examine alterations in muscarinic M1 receptor signaling in relation to cognitive functioning in medication free subjects with psychotic disorders and matched controls.

Methods: Muscarinic M1 binding potential (BPND) was measured using single photon emission computed tomography (SPECT) with the M1 selective radiopharmaceutical 123I-iododextemizide in the DLPFC and hippocampus in the psychotic group. Pharmacological functional magnetic resonance imaging (phMRI) with the M1 antagonist biperiden was used to assess differences in functional response on