

disease emerges. The distal deletion (distal of LCR22D) comprises the MAPK1-gene and is typical associated with conotruncal defects. The rare central deletion (LCR22B-D) encompasses the CRKL-gene and is predominantly associated with urogenital anomalies. 22q11DS also differs in its neuropsychiatric profile: the common deletion is accompanied by schizophrenia-like psychoses and autism spectrum disorders, the distal by anxiety disorders, and the central by autistic-like behaviours.

**Methods:** Thirty-three patients with genetically proven 22q11DS were referred for detailed neuropsychiatric analysis and treatment advice.

**Results:** Apart from two patients with distal and one with central deletion, common deletion was detected in 30 patients. They presented with a highly variable level of intellectual disability. Those with the common deletion had a history of relapsing schizophrenia-like psychoses and partial non-response to conventional antipsychotics. In most, anxieties and mood instability were manifest as well. In two patients with a common deletion, early Parkinson disease was present. The two patients with a distal deletion predominantly showed anxiety symptoms, while the behaviour of the patient with a central deletion was characterized by symptoms from the autism spectrum. Most patients with a common deletion could successfully be treated with clozapine or quetiapine, often in combination with valproic acid. One patient with distal deletion showed full remission upon treatment with citalopram (the second refused such a pharmacological intervention). The behaviour of the patient with central deletion improved upon contextual measures only.

**Conclusion:** The genetic subtype of 22q11DS enables targeting of the treatment strategy avoiding unnecessary and mostly unsuccessful pharmacological interventions.

**Policy of full disclosure:** None.

#### P-02-011

##### New 1,5-benzodiazepin-2-ones with anticonvulsant and tranquilizer activity

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**Objective:** Benzodiazepines (BDZs) represent an important class of pharmaceuticals and possess sedative, hypnotic, anxiolytic, anticonvulsant, miorelaxant, amnesic, antimicrobial and antitumor activities. BDZ-based sedatives and hypnotics are among the most prescribed drugs in the community. We analyzed structures of 50 FDA approved drugs containing 1,4- and 1,5-benzodiazepine subunits and found that many compounds include N-alkylamide fragment. Aim: creation of a family of new BDZ-based alkyl derivatives and an assessment of their biological activity spectrum.

**Methods:** Organic synthesis and nuclear magnetic resonance (NMR) spectroscopy, in vivo (white mice) and in silico (PASS, docking) studies.

**Results:** We have tested three different one-pot methods for the synthesis of N-alkyl-1,5-benzodiazepine-2-ones. We found that all three are effective for the appropriate cases and provide desired products within 70–95% yield. We synthesized a family of 25N-alkyl-1,5-benzodiazepine-2-ones and evaluated their biological potential in silico using PASS and molecular docking approaches. In silico screening of the synthesized compounds showed their high tranquilizing and anticonvulsant potential coupled with strong probability levels of inhibition of amine dehydrogenase, taurine dehydrogenase, gluconate 2-dehydrogenase and glycosylphosphatidylinositol phospholipase D. According to the molecular docking studies, the highest binding affinity to human serum albumin was observed for N-allyl derivative (−9.8 kcal/mol), which is slightly better than for Diazepam

(−9.7 kcal/mol). The two in vivo tested compounds showed high levels of antihypoxic (156–199% to the control group of animals), tranquilizing (412% to the control group of animals) and anticonvulsant (337–398% to the control group of animals) activity compared to the reference drug Diazepam.

**Conclusion:** The new compounds were fully characterized using IR, <sup>1</sup>H NMR, <sup>13</sup>C NMR, COSY, NOESY, HSQC, HMBC spectroscopy and X-ray diffractometry techniques. We envision that synthetic and biological studies of the novel 1,5-BDZs can be further expanded toward a greater scope and utility.

**Policy of full disclosure:** None.

#### P-02-012

##### Pitfalls of managing schizophrenia

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**Objective:** Attaining stability with schizophrenia by titration of medications can take time. Here we present a patient and discuss about the pitfalls in treating schizophrenia ranging from therapeutic failure, psychosocial issues and ethical issues.

**Methods:** A 26 year old female schizophrenia patient develops a relapse secondary to defaulting medications. Her relapse symptoms were isolating herself from family and paranoia towards parents. She also suffered from auditory hallucinations and persecutory delusions. On admission patient was recommenced on her IM Fluvoxol; which was progressively increased and augmented with three other oral antipsychotics over a duration of 4 months. There was minimal response from the patient in spite of being on a regime of Aripiprazole 30 mg, Olanzapine 20 mg and Fluvoxol 60 mg. Family refused ECT and decision made to commence patient on Clozapine; after atypical antipsychotics were ineffective. Whilst on Clozapine there was mild improvement in her symptoms; unfortunately mother was keen for DAMA and transfer of care to a private psychiatrist in view of slow improvement. On discussion with the mother this request was refused and patient was held involuntary for treatment under the Mental Health Care in view of risk to herself and mother threatening DAMA. 2 days later at a further family conference; family were adamant for discharge. They were not keen for home leave or follow-up in outpatient clinic. After a prolonged discussion with family, decision was made to DAMA, stop clozapine and a detailed memo provided to private psychiatry team for follow-up.

**Results:** This case outlines many of the pitfalls in treating Schizophrenia. In this case a considerable amount of time was taken to titrate medications and stabilize patient, unable to utilize treatment modalities such as ECT with only clozapine being effective. This case also highlights the need for engaging family early for psycho social interventions.

**Policy of full disclosure:** No conflict of interest.

#### P-03 Outcome and stigma

##### P-03-001

##### Predictors of remission in late-life schizophrenia: a 5-year follow-up study in a Dutch psychiatric catchment area

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**Objective:** To date reported symptomatic remission rates in schizophrenia vary largely, ranging from 25 to 50%, and consensus on

predictors of remission is lacking. We conducted this research to expand our knowledge on the longitudinal course of remission in late-life schizophrenia. We hypothesized to find higher remission rates at follow-up, because of treatment and social interventions. Next, we hypothesized that findings of putative baseline predictors would be in line with previous cross-sectional findings of schizoaffective disorder, adherence to psychiatric service, and better social functioning to be associated with remission.

**Methods:** 5-Year follow-up course trajectories of symptomatic remission were examined in a catchment area based group of 77 older Dutch patients (mean age 66 years) with schizophrenia and schizoaffective disorder. A modified version of the Remission in Schizophrenia Working Group criteria was used to determine remission status. Next, in individuals who did not fulfill remission criteria at baseline ( $n = 56$ ), predictors of remission at 5-year follow-up were analyzed with multivariable regression analyses.

**Results:** We found a 22% increase in remission over the 5-year period (27% at baseline, 49% at follow-up). Of all participants, 23% was in remission at both assessments, while 47% was in non-remission at both assessments. 26% of the participants changed from non-remission at baseline to remission at follow-up, while only 4% of remitted persons at baseline demonstrated a non-remitted state at follow-up. Predictors of remission were a lower total PANSS-score at baseline and a diagnosis of schizoaffective disorder (vs. schizophrenia).

**Conclusion:** Remission was an attainable goal for almost half of all older persons with schizophrenia at 5-year follow-up. With a lower intensity of psychotic symptoms and being diagnosed with schizoaffective disorder emerging as the only predictors of remission, there remains a clear need to search for modifiable predictors of remission.

*Policy of full disclosure:* None.

#### P-03-002

##### **Predictors of remission in the acute treatment of first-episode schizophrenia involuntarily hospitalized and treated with an algorithm-based pharmacotherapy: secondary analysis of an observational study**

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**Objective:** Early symptom resolution predicts symptomatic remission and recovery at the maintenance treatment phase in first-episode schizophrenia. However, little is known about predictors of symptomatic remission in the acute treatment of severely ill patients with first-episode schizophrenia. We conducted a secondary analysis of our retrospective observational study that examined the response, remission and treatment-resistance rates in seriously ill patients with first-episode schizophrenia involuntarily hospitalized and treated with an algorithm-based pharmacotherapy.

**Methods:** We conducted a retrospective chart review of 131 patients admitted involuntarily between October 2012 and October 2015. Our algorithm aimed to delay olanzapine, standardize medications, and suggest initiation of clozapine after failure (non-response or intolerance) of third-line antipsychotic treatment. The duration of each adequate antipsychotic treatment at optimal dosage was 4 weeks or more. Remission was defined using the symptom-severity component of the consensus remission criteria. Univariate tests and logistic regression model were applied to identify significant predictors of remission at discharge.

**Results:** 74 patients (56%) were remitters at discharge. Non-remitters were hindered from becoming remitters mainly by the presence of negative symptoms. Univariate tests revealed several differences between remitters and non-remitters such as gender, duration of

untreated psychosis, negative symptoms at baseline, early response, non-response to first-line trials, and duration of hospitalization. There were no differences in first-line antipsychotics, dosages of antipsychotics at time of response, and adherence rates to algorithm-based pharmacotherapy. A shorter duration of untreated psychosis, early response, and lower negative symptoms at baseline were identified as independent contributors to remission at discharge.

**Conclusion:** Predictors of short-term remission in severely ill patients with first-episode schizophrenia involuntarily hospitalized were consistent with those in non-severely ill patients included in clinical trials. The importance of early intervention and a specific and adequate treatment of negative symptoms is also highlighted.

*Policy of full disclosure:* None.

#### P-03-003

##### **The time-course of negative symptoms and their relationships with social functioning and quality of life of first episode schizophrenia patients: a prospective 11–15 year follow-study**

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**Objective:** Negative symptoms have been found to have adverse effects on functioning and quality of life. These symptoms can be present at the early and later stages of the illness, however their progression over time is much less recognized. The aim of this study was to clarify a longitudinal course of negative symptomatology in first episode schizophrenia and to determine its relationships with short- and long-term social functioning and quality of life.

**Methods:** Fifty six patients with a first episode were followed for a 11–15 year period and examined at 1 month after a first psychiatric hospitalization (Time 1), 12 months after Time 1 (Time 2), and 4–6 years (Time 3), 7–11 years (Time 4) and 12–15 years (Time 5) after Time 1. Negative symptoms were assessed with the PANSS Negative Factor according Marder et al. (1997), social functioning with Social Functioning Scale (SFS), quality of life with WHOQoL-Bref.

**Results:** The means ( $\pm$ SD) of the negative symptoms scale were 16.8 (9.2), 17.1 (9.6), 21.4 (10.4), 21.5 (9.9) and 21.3 (10.7). There were differences in symptom severity between Time 1, Time 2 and Time 3, Time 4, Time 5 ( $p = 0.009$ ). There were no differences between the two first examinations and the three last examinations. At Time 1 there were significant correlations between negative symptoms and SFS ( $r = -0.65$ ) and WHOQoL ( $r = -0.59$ ). At Time 5, the correlation coefficients were:  $-0.76$  and  $r = -0.60$ , respectively.

**Conclusion:** The severity of negative symptoms tends to be stable during the first year after the first episode of psychosis and then increases remaining stable for the next years. The results confirm that the negative symptoms have a significant adverse impact on functioning and quality of life irrespective of the stage of schizophrenia.

*Policy of full disclosure:* None.

#### P-03-004

##### **A description of physical health outcomes in a first episode psychosis cohort over 20 years**

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**Objective:** The findings of increased risk of physical health problems in those with schizophrenia and other psychoses, has deemed the