

supported by translational models of this disease, even if the antipsychotics derived from this conceptual framework are not yet available on the market. However, the need for new pathogenesis models for schizophrenia and new generations of antipsychotics is acute, therefore, an exploration of the antipsychotics in the pipeline could be helpful in understanding the current stage of research in schizophrenia.

Objectives: To assess the evidence supporting the potential benefits of new antipsychotics in the pipeline.

Methods: A literature review was performed through the main electronic databases PubMed, Cochrane, Clarivate/Web Of Science, and EMBASE) and clinical trials repositories (US National Library of Medicine and World Health Organization Clinical Trials Registry Platform) using the search paradigm “antipsychotics” AND “schizophrenia” AND “non-dopaminergic” AND “non-glutamatergic”. All papers published between January 2010 and September 2022 were included.

Results: Xanomeline/trospium (xanomeline is a muscarinic M1/M4 receptor agonist at the central nervous system, while trospium limits its peripheral effects) was efficient for schizophrenia in one phase III clinical trial. Pimavanserin (a selective 5HT_{2A} inverse agonist and antagonist) was efficient in improving negative symptoms of schizophrenia in a phase II trial. Roluperidone (a 5HT_{2A} and σ_2 receptor antagonist) has been associated with favorable results in phase III clinical trials, mainly on negative symptoms of schizophrenia. SEP-363856 is a TAAR-1 agonist and 5HT_{1A} agonist, currently explored in phase III clinical trials for schizophrenia. MK-8189 is a phosphodiesterase 10A inhibitor, investigated in phase III clinical trials for schizophrenia.

Conclusions: Based on the retrieved data in the literature, multiple mechanisms, other than glutamatergic and dopaminergic pathways, are currently being investigated, and many of the antipsychotics based on these mechanisms are in the advanced stage of research. This is important not only for the clinical need to find more efficient and tolerable drugs for patients with schizophrenia but also because they may shed new light on the pathogenesis of this disease.

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EPP0896

Defining the therapeutic reference range for cariprazine

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Introduction: According to the Consensus Guideline, the “therapeutic reference range” (TRR) defines ranges of drug blood concentrations that specify a lower limit below which a drug-induced therapeutic response is unlikely to occur and an upper limit above which tolerability decreases or the therapeutic improvement ceases. The TRR can be obtained from concentration measurements (trough (pre-dose) plasma concentration under steady-state conditions) in studies at therapeutically effective doses.

Objectives: The aim is to examine the TRR for cariprazine (CAR: 1.5 mg/day to 6 mg/day) in schizophrenia studies.

Methods: The population based TRR for CAR is derived by PK/PD evaluation from phase 2/3 schizophrenia efficacy studies with sparse PK sampling. The population PK simulated TRR is compared to the actually measured values obtained from two PK studies. As the two active metabolites of cariprazine also contribute to the drug effect, plasma exposure is given for Total cariprazine (CAR + DCAR + DDCAR) and the parent drug (CAR).

Results: PK/PD analyses demonstrated an increase in efficacy with increasing exposure. These efficacy results are related to Total cariprazine trough concentrations of ca. 30 nM and 100 nM that determine the lower and upper TRR limits. For the parent drug, the pre-dose mean plasma concentration at 6 mg/day was between 5.7-10 ng/mL in different studies, while at 1.5 mg/day it was 1.9 ng/mL.

Conclusions: The TRR of the trough plasma levels at steady state is ca. 30 – 100 nM for Total cariprazine and ca. 2-10 ng/mL for the parent drug (unchanged drug) for schizophrenia treatment.

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Suicidology and suicide prevention 03

EPP0897

Efficacy of a regional systems intervention for suicide prevention (SUPREMOCOL) in Noord-Brabant, the Netherlands

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Introduction: Worldwide, annually more than 800,000 suicides occur. In the Netherlands, suicide rates rose from 8.6 per 100,000 in 2007 to 11.4 per 100,000 in 2016. Rates in the province of Noord-Brabant were consistently higher than the national average. Noord-Brabant is a province in the south of the Netherlands covering an area of over 4700 km² with 2.5 million inhabitants. Although Noord-Brabant has five specialised mental healthcare institutions (SMHIs), and 90% of suicides are deemed related to mental disorders, 60% of those who died by suicide did not receive mental health treatment. However, with good access to treatment, suicide could be preventable.

Objectives: To evaluate whether the systems intervention compared to the regular care approach led to a reduction in suicides in Noord-Brabant. We aimed to attain a reduction in suicides of at least 20%.

Methods: Co-design and development of a digital monitoring system and decision aid. Stepwise implementation per subregion of the systems intervention by the five specialized mental healthcare institutions (SMHIs) and their chain partners. Pre-post analysis for the whole province (Exact Rate Ratio Test, Poisson count).

Results: The SUPREMOCOL systems intervention consisted of four pillars, which were all supported by a digital decision aid

and monitoring system. This was provided via a desktop computer with a secured login. The data were kept on a secured encrypted server. The number of professionals accessing the system was limited to two per SMHI or other chain partner. They could only see patients in their subregion, not in the whole of the province. The pillars of our systems intervention for suicide prevention are:

1. Swift identification of people at risk for suicide by triage on the spot after a non-fatal suicide attempt.
2. Provision of swift access to specialised mental health care for those at risk
3. Accommodating transitions in care following a collaborative care approach
4. Prevention of suicidal attempts after discharge or treatment dropout by 12 months telephone follow-up.

Suicide rates dropped 17.8% ($p=0.013$) from baseline (2017) to implementation in 2018 and 2019. This is a significant reduction ($p=0.043$) compared to the non-significant drop in the rest of the Netherlands. Suicide rates dropped further by 21.5% ($p=0.002$) in 2021. Noord-Brabant also dropped in the relative rank of the number of suicides, from second place in 2015 to third in 2018.

Conclusions: During the SUPREMOCOL systems intervention, over a period of 4 years, there was a sustained and significant reduction of suicides in Noord-Brabant. We attained a reduction of 21,5% in total. Noord-Brabant dropped in the relative rank of the number of suicides, from second place in 2015 to third in 2018. This is a result that warrants further research and implementation into system interventions for suicide prevention with digital support such as SUPREMOCOL.

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EPP0898

Suicide and Violence against Women in Azerbaijan: Risk Factors and Barriers for Seeking Mental Healthcare

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Introduction: Azerbaijan ranks among the top 3 countries with the highest rates of suicide in the Muslim world. Yet, research indicates an underestimate of risk due to cultural stigma related to suicidal behavior that may influence reporting and given that many Muslim-majority countries, where populations exceed 100 million, do not report any data on suicide rates. Violence against women also occurs at alarming rates in Azerbaijan and is a significant risk factor for suicide.

Objectives: We examine perspectives towards suicide and violence against women and barriers to care among key stakeholders.

Methods: Thirty qualitative interviews and 4 semi-structured focus groups were held with female survivors of suicide and mental health professionals working with individuals at risk of suicide to assess for perspectives on suicide and violence against women, factors influencing help-seeking, and the nature of existing resources.

Results: Most participants viewed suicide (83%) and violence against women (73%) as problems. Nevertheless, 33% reported negative stereotypes regarding suicide and 50% reported psychological treatment as unaccepted in Azerbaijan. Findings highlight that domestic violence is the strongly identified as risk factor for suicide among women in Azerbaijan. Stigma and related cultural values regarding gender norms are significant contributors to violence against women and suicide. Existing services are under-recognized and perceived of as unavailable or insufficient.

Conclusions: Employing a social determinants of health lens, multi-level programming is needed that spans micro (individual level supports), mezzo (family level supports), and macro (advocacy and outreach) levels to support a comprehensive strategy that beings with prevention and extends to address intervention, management, and capacity building to halt the increasing rates of suicide and deter violence against women.

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EPP0900

Psychopathological symptoms as clinical phenotypes in suicide attempters: relation in terms of suicidal ideation, suicidal related behaviors and medical damage of the attempt

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Introduction: Suicide behaviour is a complex and multifactor concept that includes different risk factors. According with literature a dimensional concept of illness could help to understand this complexity and clarify clinical aspects of suicide risk.

Objectives: The aim of this study is to identify different profiles of symptoms in a sample of suicide attempters and the relationship between this profiles and suicide behaviour in terms of outcome: presence and intensity of suicidal ideation, presence and number of attempts and severity of the medical damage in the current attempt.

Methods: 634 patients were recruited at the psychiatry emergency of eight public general hospitals in Spain between November 2020 until February 2022 in the SURVIVE protocol. The patients were assessed in 15 days using a battery of clinical tools that includes Brief Symptom Inventory, a sociodemographic interview, Mini Clinical Interview and C-SSRS, ACSS and BIS-11 scales. Latent profile analysis was applied to obtain profile symptoms. Logistic and multivariant regression was used to obtain data about outcome.

Results: Three clinical profiles of psychiatric symptoms were described in suicide attempters ($p < 0.01$): high symptoms (HS) (45.02%), moderate symptoms (MS) (42.5 %) and low symptoms (LS) (12.48%). Significant differences were found between classes in four symptom domains (Figure 1): anxiety, obsessive-compulsive, sensitivity, and somatization ($p < 0.01$). Participants of the HS class showed higher values in relation with the BSI summary indexes, and more diagnoses, higher levels of suicidal ideation and suicidal related behaviour as well as higher acquired capability for suicide.