articles published within the last ten years were selected, including those with free full-text access, including books and documents, clinical trials, meta-analyses, randomized controlled trials, and systematic reviews. Only articles published in the English language were included in the selection process.

Results: The brain methylome consists of DNA methylation marks at cytosine and guanosine separated by phosphate group (CpG) sites in the brain's genome, which regulate gene expression without altering the DNA sequence. This modification influences cellular processes like gene activity, development, and memory. Dysregulation of gene expression, particularly in the prefrontal cortex (PFC), contributes to schizophrenia's pathophysiology, impacting neurotransmission, myelination, metabolism, and immune signalling.

Histone modifications (acetylation, deacetylation, methylation, phosphorylation) also regulate gene expression, with reduced Histone Deacetylase 2 (HDAC2) expression seen in the dorsolateral PFC of schizophrenia patients. Additionally, microRNAs (miRNAs) and long non-coding RNAs (lncRNAs) are implicated in gene expression dysregulation in schizophrenia, influencing processes like synaptic plasticity and neural differentiation.

Epigenetic changes in peripheral tissues, such as blood and saliva, may serve as biomarkers for schizophrenia.

A comprehensive approach integrates genotyping, epigenotyping, and deep phenotyping to enhance understanding of an individual's health and treatment responses. Early therapeutic interventions may reverse epigenetic changes, improving outcomes. Incorporating molecular endophenotypes and neuroimaging biomarkers aids in identifying schizophrenia subgroups and enhancing treatment predictions. Omics integration (genomics, transcriptomics, proteomics, metabolomics) increases the precision of schizophrenia risk stratification.

There are various advancements in DNA methylation analysis include high density CpG array system (850,000 sites), whole genome bisulphite sequencing (better resolution but costly), targeted bisulphite sequencing (cost-effective), and emerging single molecule/nanopore sequencing technologies.

Conclusion: Current research in schizophrenia reveals interactions between genetic, environmental, and epigenetic factors. While significant advancements have been made in understanding the role of DNA methylation, histone modifications, and non-coding RNAs, further studies with larger sample size and more robust structure along with using multi-omic approach are desirable for understanding the disease pathophysiology and to deliver personalized treatment.

H-MRS Correlates of Deep TMS in Schizophrenia: Insights From a Randomized Sham-Controlled Study on Negative Symptoms

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Aims: Negative symptoms of schizophrenia are disabling and often show inadequate response to antipsychotic treatment. Dysfunction in cortical regions such as the anterior cingulate cortex (ACC) and medial prefrontal cortex (mPFC) has been implicated in these symptoms. While repetitive transcranial magnetic stimulation (rTMS) has shown efficacy, deep transcranial magnetic stimulation (dTMS) offers the advantage of targeting deeper brain structures.

To assess the efficacy of high-frequency dTMS in improving negative symptoms of schizophrenia and to examine its effects as measured by proton magnetic resonance spectroscopy (h-MRS).

Methods: This sham-controlled, double-blind study randomized 46 patients with schizophrenia into active and sham dTMS groups. Participants received 10 sessions of high-frequency (10 Hz) dTMS at 100% of the resting motor threshold using an H7 coil over 2 weeks. Symptom severity was assessed using the Positive and Negative Syndrome for the Assessment of Negative Symptoms (SANS), and Clinical Global Impression (CGI) at baseline, 2 weeks, and 4 weeks post-treatment. h-MRS of the ACC and mPFC was performed at baseline and after 2 weeks of treatment.

Results: A total of 43 patients completed the study. While both groups showed improvement over time, the active dTMS group demonstrated significantly greater improvement in negative symptoms, as reflected by a reduction in SANS scores compared with the sham group ($p=0.003$) and improvement in the negative subscale of PANSS ($p=0.044$). h-MRS analysis revealed a positive correlation between ACC total N-acetylaspartate (tNAA) levels after 2 weeks of treatment and baseline SANS anhedonia subdomain scores.

Conclusion: High-frequency dTMS significantly improves negative symptoms and overall illness severity in schizophrenia. These findings highlight the potential role of dTMS as an adjunctive treatment and suggest that h-MRS may serve as a valuable biomarker for treatment response. Future studies with larger sample sizes are needed to further explore the therapeutic and neurobiological effects of dTMS.

9-Year Trajectory of Depressive and Anxiety Symptoms in Community – the Hong Kong Mental Morbidity Survey Follow Up Studies

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Aims: Depression and anxiety are common in every community. Appreciation of the long-term trajectories of these symptoms will inform more targeted interventions for reduction of disease burden. We evaluated the 7th and 9th year episode onset and remission rates of common mental disorders (CMD) in participants of the Hong Kong Mental Morbidity Survey (HKMMS) at baseline (2010–2023), who were reassessed at 7th and 9th years follow up.

Methods: The HKMMS and follow up studies were commissioned by the Medical and Health Research Fund in Hong Kong. Baseline study was conducted from 2010–2013 (n=5,719). We reassessed 1,392 subjects at 7th (2019–2021, COVID pandemic) and 9th (2020–2023, late to post-COVID) years. Depression and anxiety symptoms, episode onset and remission rates of CMD were evaluated with the Clinical Interview Schedule – Revised scores at baseline and follow up. Repeated measures ANCOVA computed factors affecting CISR scores over time.

Results: At 7th year, episodes onset rates of CMD in BL normal (n=832, CISR =<5) and BL subsyndromal (n=332, CISR 6–11) were 8.2% and 26.5% respectively. The corresponding figures were 7.9% and 22.3%. Remission rates of CMD from BL (n= 228) to 7th and 9th years were 39.9% and 50.4%. Repeated measure ANCOVA identified a significant time effect with increase in CISR scores at 7th ($p<0.001$) and decrease from 7th to 9th year ($p<0.001$). Women had higher CISR at all time points, interaction with time was not significant. Younger age groups (BL 18–44) reported more CISR symptoms at 7th year and greater drop at 9th year. Older adults with physical comorbidity had a trend for increase symptoms over time.
Conclusion: In this 9 year follow up study of adults in Hong Kong, episode onsets are related to baseline CISR scores, indicating that psychological symptoms confer long-term risks for deterioration. Conversely, a significant proportion of CMD improved with time. The time frames for assessments unintentionally fell into active COVID pandemic (7th) with social distancing measures, and late to post-COVID pandemic (9th) with lifting of COVID social distancing measures. Our repeated measures evaluation suggested that younger adults are possibly more reactive to environmental stresses. Primary care interventions should consider the age factor into design.

Cost-Effectiveness of the Interventions for Severe Mental Illness (SMI) in Low and Middle-Income Countries (LAMICs): A Systematic Review

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Aims: Despite the high prevalence of mental illnesses, particularly Severe Mental Illness, there is limited literature on the cost-effectiveness of available interventions in low- and middle-income countries. Therefore this review aimed to assess the cost-effectiveness of the pharmacological and psychosocial interventions for Severe Mental Illness (SMI) in Low and Middle-Income Countries (LMICs).
Methods: Based on PRISMA guidelines through electronic searches (Medline, CINAHL, APA PsycINFO, Embase, Cochrane Central Register of Controlled Trials, and Global Index Medicus), we identified cost-effectiveness studies conducted between January1980 and April 2024. Studies included whether they focused on people with schizophrenia, bipolar disorders and depression with psychosis, assessed any interventions (pharmacological or psychosocial), and reported cost-effectiveness outcomes based on predefined criteria, specifically presented as incremental cost-effectiveness ratio (ICER) values. Screening and data extraction were performed using a pre-specified criterion. ECOBIAS and JBI tools were used for quality assessment.

The analysis was confined to a narrative synthesis due to the substantial variations in methods adopted for ICER calculations and the inherent complexity of model-based studies. Protocol was registered on the PROSPERO having registration # *CRD42024513743.*
Results: Out of the 6905 studies identified, 20 met the inclusion criteria for data extraction. Most of the studies (18/20) were based on the economic model, predominantly the Markov Model (11/18). Most of the studies were conducted in upper-middle-income countries (13/20). Atypical or second-generation antipsychotics were the major group evaluated in most of the studies. The cost-effectiveness of olanzapine was assessed in the highest number of studies (10/20), followed by risperidone. "Family intervention" was the predominant psychosocial intervention and was evaluated in three studies. Ten studies reported ICER in terms of cost/QALYs gained, while 6/20 studies reported cost/DALYs averted. The remaining studies assessed cost-effectiveness in the context of cost savings against the Positive and Negative Symptoms scale.

Cost-effectiveness was evaluated based on the quadrants of the cost-effectiveness plane in which the ICER values fell. In upper-middle-income countries, atypical such as amisulpride, lurasidone, aripiprazole orally disintegrating tablets (ODT) and olanzapine with any psychosocial interventions were cost-effective strategies. In contrast, risperidone with Family Interventions was reported as the cost-effective strategy in lower-middle-income countries.
Conclusion: Most studies have found that combining atypical antipsychotics with psychosocial interventions is a cost-effective approach. However, significant variations in ICER calculations, differences in methods used to assess QALYs/DALYs, and the complexity of model-based studies make it challenging to generalize these findings to other clinical settings.

Cannabis-Based Medicinal Products in the Treatment of Post-Traumatic Stress Disorder in Children and Young People: A Literature Review

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Aims: Post-traumatic stress disorder (PTSD) is a condition that may develop following exposure to a highly threatening or horrific event or series of events. PTSD can affect people across all age groups with extensive impact on functioning and is often associated with psychoactive substance misuse. Cannabis is one of the most abused psychoactive substances worldwide, with users reporting anxiolytic benefits. Cannabis-based medicinal products (CBMPs) have gained more attention and interest over the past few years due to changes in the legislation around cannabis worldwide. Research has shown cannabis-based medicinal products to be effective in treating several medical conditions. Observational studies in adult populations indicate some therapeutic promise for CBMPs in PTSD, but these results are not generalizable to younger populations.

The authors aimed to complete a search of the literature for any evidence of the benefit of cannabis-based medicinal products in treating children and young people diagnosed with PTSD.
Methods: A comprehensive search of databases, including Medline, Embase, PsycINFO, CINAHL, Cochrane Library, and Google Scholar, from their inception until September 2024, was conducted using medical subject headings and keywords: "Post-traumatic stress disorder", "Medical Marijuana", "Cannab*", "Canab*", "THC*".

The authors limited their search to papers involving children and young people under 18 years of age. Three of the 105 papers