[1]Boehringer Ingelheim RCV GmbH & Co KG, Vienna, Austria; [2]Graduate School of Arts and Sciences, The University of Tokyo, Tokyo, Japan; [3]Department of Psychiatry, International University of Health and Welfare, Mita Hospital, Tokyo, Japan; [4]Clinic of Psychiatry and Psychotherapy, Ludwig Maximilians University Munich, Munich, Germany; [5]Department of Psychiatry, Yale University School of Medicine, New Haven, USA and [6]Boehringer Ingelheim, Bracknell, United Kingdom
*Presenting author.

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Aims. Glutamatergic signalling deficits contribute to the neuropathology of cognitive symptoms in schizophrenia. Iclepertin (BI 425809), a glycine transporter-1 inhibitor, enhances *N*-methyl-D-aspartate receptor signalling in the brain by increasing synaptic levels of its co-agonist glycine. The Phase III CONNEX programme aims to assess the efficacy, safety and tolerability of iclepertin in improving cognition and functioning in schizophrenia.
Methods. CONNEX includes 3 randomised, double-blind, placebo-controlled parallel group trials in patients with schizophrenia from multiple centres across 41 countries in Asia, North and South America, Europe, and Asia Pacific Region (NCT04846868, NCT04846881, NCT04860830) receiving stable antipsychotic treatment. Each trial aims to recruit ~586 patients, 18–50 years old, treated with 1–2 antipsychotic medications (≥12 weeks on current drug; ≥35 days on current dose before treatment), who have functional impairment in day-to-day activities and interact ≥1 hour/week with a designated study partner. Patients with cognitive impairment due to developmental, neurological or other disorders, or receiving cognitive remediation therapy ≤12 weeks before screening will be excluded. Patients will be randomised 1:1 to once-daily oral iclepertin 10 mg (n = 293) or placebo (n = 293) for 26 weeks. Primary endpoint: change from baseline (CfB) in Measurement and Treatment Research to Improve Cognition in Schizophrenia Consensus Cognitive Battery (MCCB) overall composite T-score. Key secondary endpoints: CfB in Schizophrenia Cognition Rating Scale (SCoRS) total score and adjusted total time T-score in the Virtual Reality Functional Capacity Assessment Tool (VRFCAT).
Results. Trial completion is expected in Q1 2025. By 31/01/2024, there have been 811, 699 and 655 patients screened, 533, 474 and 458 randomised, and 320, 299 and 281 who have completed the trial medication for CONNEX-1, -2 and -3, respectively. Most patients are male (CONNEX-1: 69.3%, CONNEX-2: 69.0%, CONNEX-3: 63.3%) with similar age (mean [standard deviation; SD]) (CONNEX-1: 34.0 [8.9], CONNEX-2: 35.9 [8.4], CONNEX-3: 34.0 [8.8] years). For CONNEX-1, -2 and -3, mean (SD) duration of illness is 10.6 (8.3), 12.2 (7.9) and 9.6 (7.6) years and duration of previous schizophrenia treatment is 3.9 (4.6), 4.5 (4.9) and 3.3 (4.4) years. Baseline mean (SD) MCCB overall composite T-score (1: 28.4 [13.7], 2: 27.3 [13.8], 3: 29.7 [13.7]), SCoRS total score (1: 40.5 [11.1], 2: 39.9 [9.7], 3: 38.0 [10.0]) and VRFCAT adjusted total time T-score (1: 29.6 [22.3], 2: 30.7 [20.8], 3: 33.6 [18.1]) were similar across trials.
Conclusion. If successful, CONNEX will provide evidence for iclepertin as the first efficacious medication addressing cognitive impairments in schizophrenia.

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Evaluation of the TRANSFORM Pilot Training Program for Community Health Workers and Traditional and Faith-Based Healers in Bangladesh

Dr Tanjir Rashid Soron[1,2]*, Dr Kazi Shammin Azmery[1], Dr Farzana Akter[1], Dr Belaluzzaman Rana[1] and Dr Maksudur Rahman[1]

[1]Telepsychiatry Research and Innovation Network Ltd, Dhaka, Bangladesh and [2]NiHealth Ltd, Dhaka, Bangladesh
*Presenting author.

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Aims. In the densely populated Korail slum of Bangladesh, there is a critical gap in mental health care provision and utilization that was revealed in our ethnographic study. We observed the pivotal role of Community Health Workers (CHWs), Medicine Sellers, and Traditional and Faith-Based Healers (TFHs) in the existing health care service delivery. Moreover, we explored the opportunity to collaborate with them to ensure universal access to biomedical care for serious mental disorders in this slum. As a part of this collaborative approach, we aimed to train these 4 key stakeholders through co-designed training programs that were codeveloped through extensive community engagement including 5 co-designing workshops and 2 writing workshops with them. Furthermore, we refined the initial training program by an expert committee and stakeholders. This training program was piloted to find out the acceptability, feasibility, impact, challenges and areas of improvement.
Methods. We followed mixed-methods approach to evaluate the 3-day pilot training with 20 participants at Mirpur, Dhaka. In quantitative part of evaluation we used a) pre and post test assessment that has been carefully designed to assess knowledge, skills, communication, attitudes and motivation, b) session specific questionnaire to find out feedback of the content, activities and time sensitivity of the session, anonymous feedback forms.

In the qualitative part, we conducted a) focus group discussions (FGDs) after completion of training with each group, b) observational notes from each session for deeper understanding.
Results. The pilot training engaged a diverse group of 20 participants and their age ranged from 24 to 52 years, representing 11 different organizations. Though most of the participants were working in the health sector for a long time, we found more than 10% of the participants believed there was no effective biomedical care for the serious mental disorder during pretesting. However, their perception changed during the training. The role playing and case scenario was the most engaging and enjoyable part. We found the participants considered their knowledge regarding the mental health increased up to 80% from their baseline. Our research team also found the increased number of referrals to the biomedical care from the community after the pilot training.
Conclusion. The increased motivation and sense of responsibility reported by participants underscore the training program's effectiveness and the experience and learning from this pilot helped us to further refinements of the training program for the traditional and faith based healer, community health workers and medicine to transform the mental health scenario in Bangladesh.

Menopause and Risk-Taking Behaviours: A Cross-Sectional, Online Survey

Dr Dan Reisel*, Ms Aini Kamal, Dr Sarah Glynne and Dr Louise Newson

Newson Health, Stratford-upon-Avon, United Kingdom
*Presenting author.

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Aims. Limited data suggest that negative mood symptoms in the menopause transition may be associated with a higher prevalence of alcohol misuse and other risk-taking behaviours in menopausal women. Excessive alcohol consumption can exacerbate menopausal symptoms, reduce quality of life and is associated with chronic morbidity that overlaps with the consequences of long-term oestrogen deficiency (such as osteoporosis and cardiovascular disease). The aim of this survey was to explore the impact of mental ill-health on alcohol consumption and gambling habits in menopausal women.
Methods. We constructed an anonymous survey consisting of multiple-choice and free-text questions. The survey was distributed online via social media channels on the 22 August 2023 and was open for 6 weeks. All perimenopausal and menopausal women were invited to participate. Responses were collected using the Qualtrics survey platform and analysed in Excel for descriptive statistics.
Results. 1,178 responses were submitted. One in three women reported drinking more alcohol during the perimenopause/menopause; 15% of women drink more than the recommended maximum of 14 units per week, and 24% (286) are spending up to £50 per week on alcohol. 70% (332) cited anxiety, stress, and/or depression as the reason for their increased alcohol consumption, whilst 29% (135) said they drank to alleviate menopause symptoms. Further, 5% (54) of respondents admitted gambling more since the onset of perimenopause/menopause; 43% (27) said it was due to anxiety, stress, and/or depression, whilst 13% (9) said they do so to help manage their menopause symptoms.
Conclusion. This anonymous, cross-sectional survey found evidence of an association between menopause and addiction. Increased awareness of this association should facilitate earlier recognition and more timely access to support and effective treatment for addiction, including hormone replacement therapy to treat menopausal symptoms that may underlie and/or exacerbate unhealthy lifestyle behaviours.

Neurodevelopmental Disorders and Their Association With Neurodegenerative Disorders: A Systematic Narrative Review

Dr Rebecca Restorick[1,2]*, Dr Huw Dunstall[3] and Dr Katja Umla-Runge[2]

[1]NHS Borders, Selkirk, United Kingdom; [2]Cardiff University, Cardiff, United Kingdom and [3]Swansea Bay UHB, Swansea, United Kingdom
*Presenting author.

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Aims. Neurodevelopmental disorders (NDDs), such as dyslexia, dyspraxia, and dyscalculia affect cognitive function and therefore share symptomology with neurodegenerative disorders, such as Alzheimer's disease, vascular dementia, and frontotemporal lobe dementia. The primary aim of this narrative systematic review is to ascertain if there is an association between NDDs and neurodegenerative disorders. Secondary aims are what the prevalence of NDDs within a dementia population is and what effect these early life learning disorders have on patients as they get older. It was hypothesised that NDDs would overestimate the severity of cognitive impairment, thereby increasing the severity of dementia staging, and impacting patient care.
Methods. Using a Population, Exposure, Comparator, Outcome, Setting, and Study design (PECOS) framework, keywords of "dementia", "dyslexia", "Dyspraxia/clumsy child syndrome/developmental apraxia/motor learning difficulty/disorder of attention and motor perception" and "dyscalculia/mathematical learning disability" were searched for on 4 databases (SCOPUS, OVID, Cochrane Central Register of Controlled Trials and Web of Science) from January 1, 1960 – June 10, 2022. Studies were included if they discussed both neurodegenerative and neurodevelopmental disorders or compared an intervention typically used in one disorder on the other (e.g., dementia intervention being used on neurodevelopmental disorder). Studies were excluded from grey literature articles, or if they only discussed a neurodevelopmental or neurodegenerative disorder without reference to the other, or if it included acquired, rather than neurodevelopmental dyslexia, dyscalculia, or dyspraxia.
Results. A total of 8 studies were included for narrative synthesis. The main finding was an association between dyslexia and both Alzheimer's disease and frontotemporal dementia. Many studies suggested this was due to a genetic phenotype that caused a vulnerability in the language regions of patients' cortices. There was also evidence of structural changes associated with NDDs and increased levels of grey and white matter atrophy in dementia subtypes, particularly in the language areas of the brain.
Conclusion. Due to screening and consequently formal diagnosis of neurodevelopmental disorders only recently coming into education systems, many adults currently attending memory clinics did not have a formal diagnosis. As there was limited research on dyspraxia and dementia, partly due to limited research into dyspraxia itself and without a standardized diagnostic tool for adolescents and adults, further research is needed in this area. The hypothesis of NDDs increasing the severity of dementia staging was also not supported by the literature results, and on the contrary, some studies suggested greater global preservation of cognitive function in patients with NDDs and dementia.

Decrypting the Thalamic Subnuclei and Functional Composites in Adolescents With Psychotic Experiences

Dr Sahar Riaz*, Michael O'Connor, Anurag Nasa, Dr Mary Cannon and Dr Darren Roddy

Royal College of Surgeons in Ireland, Dublin, Ireland
*Presenting author.

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Aims. The thalamus, a dual grey matter formation within the diencephalon is thought to be involved in psychosis. It consists of distinct nuclei with specific functions. To date no study has investigated the volumes of the thalamic nuclei in young adolescents with Psychotic Experiences (PEs).