Aims: Clozapine is the only evidence-based medication for treatment-resistant schizophrenia and is associated with reductions in relapse, suicide risk, and all-cause mortality.Nevertheless, its use is restricted by concerns about adverse effects, particularly neutropenia and agranulocytosis, which often result in permanent discontinuation under current UK monitoring rules.

Emerging evidence and regulatory changes, particularly in the United States and Europe, suggest that Clozapine re-challenge may be safe in selected patients following careful individualised risk–benefit assessment. However, Clozapine re-challenge remains uncommon in the UK.

Methods: We completed a retrospective case series of patients who underwent Clozapine re-challenge within TEWV NHS Trust.Using CPMS data and clinical records, patients who stopped Clozapine due to neutropenia between 1994 and 2024 were identified. We then checked the data of patients who were re-challenged with Clozapine in detail. Extracted data included demographic characteristics, severity and duration of neutropenic episodes, time to neutropenia following Clozapine initiation, interval between discontinuation and re-challenge, re-challenge strategies (including use of lithium and/or G-CSF) and clinical outcomes.

Successful re-challenge was defined as continued Clozapine treatment without recurrent red blood results requiring permanent discontinuation.

Results: We found that thirteen (46%)out of twenty-eight patientswho discontinued Clozapine due to neutropenia underwent re-challenge.

Eight patients (61.5%) were successfully re-challenged and maintained on Clozapine.

Five re-challenges were unsuccessful and three of which were associated with recurrent severe neutropenia.

No fatalities occurred following Clozapine re-challenge.

Most cases of Clozapine re-challenge were undertaken using Clozapine alone, without adding lithium or G-CSF.

With the exception of two cases, all index neutropenic events occurred beyond the first year of Clozapine treatment, ranging from 17 months to 20 years.

Neither the severity nor the timing of the initial neutropenic episode reliably predicted the rechallenge outcome.

Conclusion: Clozapine re-challenge was successful in a majority of patients, with no deaths observed. Neither severity nor timing of the index neutropenic episode reliably predicted the re-challenge outcome. Therefore,Clozapine re-challenge should be cautiously considered in selected patients, particularly where no effective alternatives exist.

These findings highlight the need for a more flexible and evidence based guidance for Clozapine monitoring and re-challenge.

Abstracts were reviewed by the RCPsych Academic Faculty rather than by the standard *BJPsych Open* peer review process and should not be quoted as peer-reviewed by *BJPsych Open* in any subsequent publication.

Clozapine-Associated Neutropenia in a Middle Eastern Population: Incidence, Predictors, and the Role of Benign Ethnic Neutropenia

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Aims: Clozapine-associated neutropenia occurs in approximately 3.8% of patients globally, with agranulocytosis reported in around 0.9%. Benign ethnic neutropenia (BEN), which is prevalent among Arab and African populations, complicates interpretation of haematological monitoring and may lead to unnecessary treatment interruption. Despite the high representation of BEN-susceptible ethnicities in Gulf populations, regional data on clozapine haematological safety are lacking. This study aimed to estimate the incidence of clozapine-associated neutropenia, identify clinical predictors, and evaluate the role of baseline absolute neutrophil count (ANC) in risk stratification.

Methods: A retrospective cohort study was conducted including all patients prescribed clozapine at a tertiary psychiatric hospital in the United Arab Emirates between January 2018 and July 2024. A total of 184 patients were followed over 228.1 patient-years, comprising 3,907 ANC measurements. Neutropenia was defined as ANC $<2.0 \times 10^9$/L and categorised as mild (1.5–2.0), moderate (1.0–1.5), severe (0.5–1.0), or agranulocytosis (<0.5). Cox proportional hazards regression was used to identify predictors of neutropenia. Receiver operating characteristic (ROC) analysis assessed the discriminatory performance of baseline ANC.

Results: Twenty patients (10.9%; 95% CI 7.1–16.2%) developed neutropenia, corresponding to an incidence rate of 9.74 per 100 patient-years (95% CI 5.95–15.05). Most events were mild (n=19, 10.3%), and no cases of agranulocytosis were observed. Patients of Arab or African ethnicity had significantly higher neutropenia rates compared with other ethnic groups (16.2% vs 1.6%; odds ratio 11.5, 95% CI 1.5–87.5; p=0.001). Baseline ANC emerged as the only independent predictor of neutropenia (hazard ratio 0.15, 95% CI 0.07–0.31; p<0.001), with each unit increase associated with an 85% reduction in risk. Baseline ANC demonstrated excellent discriminatory ability (AUC 0.92, 95% CI 0.86–0.97), with an optimal threshold of 3.3×10^9/L (sensitivity 85%, specificity 87.4%). Clozapine was continued in 80% of affected patients, with no permanent discontinuations due to haematological events.

Conclusion: This first Middle Eastern study of clozapine haematological safety demonstrates neutropenia rates comparable to international data and no observed agranulocytosis. Baseline ANC provides excellent risk stratification, while higher neutropenia rates in Arab and African patients likely reflect benign ethnic neutropenia rather than true drug toxicity. These findings support continued clozapine treatment with appropriate monitoring and highlight the need for ethnicity-informed interpretation of haematological results in diverse populations.

No financial sponsorship was received for this project.

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Computational Modelling and Analysis of Ligand Interactions With the Dopamine Transporter

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Aims: This study aimed to computationally investigate interactions between DAT and a range of ligands across different conformational states using molecular docking and structural modelling, with the goal of identifying residues associated with ligand binding and potential conformational specificity.

Methods: Recent Cryo EM structures of DAT representing inward-facing and outward-facing conformations were obtained from the Protein Data Bank and prepared using MODELLER.Eight compounds (Amphetamine, Buproprion, Methamphetamine, Modafinil, Methylphenidate, Mephedrone, Vanoxerine and Nortriptyline) were categorised based on binding preferences. Molecular docking was performed using Cresset Flare, generating ten poses per compound, which were ranked using Lead Finder scores. The lowest-energy protein-ligand interactions were visualised with VMD and further analysed using Schrodinger Maestro and Nanome VR.
Results: In the inward-facing conformation, conserved interacting residues across compounds included Val328, Tyr156, Phe326, and Val152. In the outward-facing conformation, conserved residues included Tyr156, Val152, Ala423, Asp79, Phe320, Phe76, Phe326, Ser149, and Ser422. Asp79 and Val328 were observed to participate in interactions that differed between conformational states.
Conclusion: These results identify recurring residues involved in ligand interactions with DAT and suggest conformation-dependent interaction patterns that may be relevant to transporter modulation. Future work will build on these docked complexes using molecular dynamics simulations with AI-guided analysis of protein dynamics to support drug discovery efforts aimed at the development of novel treatments for stimulant use disorder.

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Repurposing Serotonin-Norepinephrine-Dopamine Reuptake Inhibitors for the Treatment of Stimulant Use Disorder

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Aims: Stimulant use disorder is associated with increasing morbidity, mortality, and high relapse rates, yet there is currently no approved pharmacotherapy. Relapse vulnerability is increasingly recognised as arising from dysregulation across dopaminergic, serotonergic, and noradrenergic neurocircuitry. Serotonin-Norepinephrine-Dopamine Reuptake Inhibitors (SNDRIs) modulate these monoaminergic pathways and represent a mechanism-informed pharmacological strategy. This review aimed to evaluate the neurobiological rationale, translational potential, and emerging clinical feasibility of repurposing SNDRIs for stimulant use disorder.
Methods: A review was conducted integrating preclinical neuropharmacological evidence, human neuroimaging and behavioural studies, and clinical trial data examining monoamine transporter modulation. Evidence relating to dopamine transporter (DAT), serotonin transporter (SERT), and norepinephrine transporter (NET) function was analysed to evaluate reinforcement neurobiology, relapse vulnerability, pharmacokinetic characteristics, and clinical safety data from candidate SNDRIs including dasotraline, centanafadine, and ansofaxine.
Results: Psychostimulant reinforcement is strongly associated with DAT occupancy and dopamine elevation within mesolimbic reward circuitry. However, relapse vulnerability is increasingly linked to serotonergic and noradrenergic dysregulation contributing to stress sensitivity, affective instability, and cue-driven drug seeking. Preclinical evidence demonstrates that NET inhibition reduces stress-induced and cue-mediated stimulant seeking, while SERT modulation influences impulsivity and negative affective states associated with relapse. SNDRIs produce sustained, moderate monoaminergic modulation that normalises hypodopaminergic states observed during stimulant withdrawal without producing rapid dopamine elevations associated with abuse liability. Pharmacokinetic data demonstrates extended elimination half-lives supporting once-daily dosing and improved treatment adherence. Clinical trials investigating SNDRIs in attention-deficit/hyperactivity disorder and major depressive disorder demonstrate favourable tolerability and sustained monoaminergic modulation in human populations. Advances in transporter structural modelling and computational pharmacology support the use of dynamic transporter-ligand profiling to stratify therapeutic development and improve prediction of abuse liability.
Conclusion: SNDRIs demonstrate mechanistic plausibility and clinical feasibility as candidate pharmacotherapies for stimulant use disorder. Multi-transporter modulation may address both reward-driven reinforcement and relapse-related neuropsychiatric processes. However, current evidence remains indirect and derived primarily from mechanistic, preclinical, and non-addiction clinical populations. Targeted, stratified clinical trials in stimulant use disorder populations are required before treatment recommendations can be made.

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Olanzapine Use in Children and Adolescents With Anorexia Nervosa: A Narrative Synthesis of Efficacy, Safety and Applicability to UK Practice

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Aims: Anorexia nervosa (AN) is a severe psychiatric disorder with the highest mortality of any mental illness. While psychological therapies such as family therapy remain first-line, up to 30% of adolescents experience partial or non-recovery, prompting interest in adjunctive pharmacological options. Olanzapine, an atypical antipsychotic associated with reduced cognitive rigidity and anxiety and with restorative weight gain, is increasingly used off-label in adolescent AN despite limited evidence and lack of NICE endorsement. This review aimed to synthesise international evidence on olanzapine use in under-18s with AN, evaluating efficacy, safety, tolerability and applicability to UK NHS practice.
Methods: A systematic literature search was conducted across multiple bibliographic databases to identify peer-reviewed studies examining olanzapine use in patients under 18 years with anorexia nervosa for the period 2000 – 2025. Eligible study designs included randomised controlled trials (RCTs), open-label and observational studies, case series, audits and clinical guidelines. Findings were synthesised narratively to assess clinical outcomes, adverse effects and implementation within UK Child and Adolescent Mental Health Services (CAMHS).
Results: Thirty-six studies met inclusion criteria. Evidence from adolescent RCTs was limited and underpowered, demonstrating modest effects on weight restoration and variable psychological