Following informed consent and assent, endoxifen was initiated at 8 mg/day and gradually titrated to 24 mg/day, while aripiprazole was continued at 5 mg/day. Clinical response and tolerability were monitored over 12 months.

Results: Over one year of treatment, the patient demonstrated sustained reductions in impulsivity, hyperactivity, repetitive behaviours, and anger outbursts, with notable improvements in behavioural regulation and overall family functioning. The medication was well tolerated, with no significant metabolic, neurological, or systemic adverse effects, and adherence remained satisfactory throughout follow-up.

Conclusion: Endoxifen showed favourable efficacy and tolerability in managing behavioural dysregulation in an adolescent with ID who was refractory or intolerant to conventional psychotropics. Targeting PKC-mediated pathways may represent a promising therapeutic strategy for impulsivity and aggression in neurodevelopmental disorders. Larger controlled studies are needed to establish safety and long-term efficacy.

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The Impact on Relapse Rates of Switching From Oral Therapy to Long-Acting Injectable Antipsychotics in the Treatment of Psychosis: A Real-World Retrospective Study

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Aims: In a community mental health setting, we studied real-world relapse rates in patients with a history of psychosis, before and after switching from oral antipsychotics to a long-acting injectable antipsychotic (LAIA). We also aimed to evaluate the relevance of metabolic/demographic factors in relapse rate.

Methods: Twenty-five individuals with a past history of psychosis and variable medication concordance who were switched from oral antipsychotics to LAIAs were included in the study. Oral agents were converted to olanzapine equivalents whilst LAIA generics were converted to flupenthixol depot equivalents. The depot equivalent oral dose of olanzapine was calculated, assuming an oral bioavailability of 40%. Relapse-rates occurring over the time periods on oral therapy were compared with rates occurring following initiation of LAIAs. Relapse was defined as any psychiatric hospital admission.

A multivariable Poisson regression model including drug formulation/age/sex/smoking status/BMI were fitted with follow-up time as an offset to estimate adjusted incidence rate ratios and associations with relapse outcomes.

Results: The mean±SD age of the 25 individuals was 50.6±13.9 years whilst 12 (60%) were male. Mean BMI of males/females was 28.1±9.3 kg/m^2/ 32±6.4 kg/m^2(higher in women) respectively. 65% of patients received either flupenthixol or zuclopenthixol depot with next most common depot being Risperidal Consta. The median (IQR) of daily oral olanzapine equivalent was 10mg (6.9 – 20.0mg)/day and after switching to depot was 16.0mg (5.4 – 40.7mg)/day. The 4-week depot equivalent dose for services users switched to depot was flupenthixol 480mg (200 – 1220mg) / 4-weeks.

Following adjustment for age/sex/smoking status/BMI, relapse rates were significantly lower during LAIA treatment compared with oral treatment (incidence rate ratio [IRR] 0.13, 95% CI 0.08–0.22, p<0.001). Thus depot antipsychotics were associated with an 87% reduction in relapse rates compared to oral therapy. Male sex/younger age/lower BMI were independently associated with higher relapse rates (Exp (beta) 1.9/0.98/0.94 respectively (p<0.05)).

Conclusion: In this real-world community mental health setting, this study highlights that depot antipsychotics provide a dramatic and sustained reduction of 87% in relapse rate for individuals with a history of psychosis. These findings support early prescription of LAIAs in prevention of psychosis relapse. Further evaluation is warranted to elucidate the potential of LAIAs as a treatment option after first presentation of psychosis.

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Can Pharmacogenomic Testing Aid Psychiatric Medication Prescriptions?

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Aims: Various antipsychotics and antidepressants have pharmacogenomic guidelines available from international sources, recommending dose adjustments and/or alternative drug selection based on a patient's genetic profile. However, pharmacogenomic implementation remains limited in UK healthcare.

Methods: Genetics and Environment in Mental Health Study (GEMS) is a prospective study of pharmacogenomic testing in psychosis; the first in the UK. Adults taking an antipsychotic medication have been recruited across England. Participants provided a DNA sample for genotyping on a multi-gene panel, selected from evidence-based pharmacogenomic guidelines. Pharmacogenomic reports, displaying the participants' genetic profile and any alterations to usual prescribing guidelines were delivered to the prescribing clinician. Any changes to the participants' prescription were at the discretion of the clinician.

Results: A diverse sample of 584 people taking an antipsychotic medication has been recruited so far, consisting of participants aged 18-82 years, with an even split of male and female participants, and 32.5% of the sample from Black, Asian, and Minority Ethnic (BAME) backgrounds.

Across the four genes with pharmacogenomic guidelines in psychiatry (*CYP2D6*, *CYP2C19*, *CYP2B6*, and *CYP3A4*), 90.4% of the sample carried at least one actionable variant. At the time of recruitment, 20.9% of participants carried a pharmacogenomic variant that (based on current guidelines) was actionable for the antipsychotic and/or antidepressant they were currently prescribed. By medication class, 6.8% were taking an antipsychotic and 15.1% were taking an antidepressant for which they had a pharmacogenomic recommendation. A further 69.5% of the sample would have a recommendation for at least one antipsychotic or antidepressant medication.

Based on the estimated population prevalence of pharmacogenomic actionable variants and prescription data in England, approximately

45% of people would be expected to carry an actionable variant for antipsychotic medications and at least 61% would be expected to carry an actionable variant for antidepressants. This equates to approximately 285,000 people currently taking an antipsychotic medication that could have a pharmacogenomic recommendation and at least 4.2 million people taking an antidepressant with a pharmacogenomic recommendation in England.

Conclusion: Pharmacogenomics has the potential to personalise medication prescriptions and improve patient outcomes. Workforce training and implementation barriers present a challenge. However, in line with the NHS 10 Year Plan goal of 50% of healthcare interventions being genomics-informed by 2035, psychiatry is one of the most promising areas for the implementation of pharmacogenomic-guided prescribing.

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