Aims. Despite considerable preclinical evidence, clinical trials assessing the effects of probiotics on individuals with major depressive disorder (MDD) are scarce. This study aimed to provide further evidence of the acceptability, tolerability and putative efficacy of probiotics in this patient group and to improve our understanding of the underlying mechanisms of action.
Methods. This double-blind randomised placebo-controlled pilot and mechanistic trial investigated the effects of an 8-week adjunctive multi-strain probiotic intervention in adults with MDD taking antidepressants. Psychiatric data and stool and blood samples were collected at baseline, week 4 and week 8. A computer-based emotion recognition task was also administered. Stool samples from 25 matched healthy controls were also obtained.
Results. 49 participants, randomised to probiotic (n = 24) or placebo (n = 25), were included in intent-to-treat analyses. Standardised effect sizes (SES) from linear mixed models demonstrated that the probiotic group attained greater improvements in depressive (HAMD week 4: SES [95%CI] = 0.70[0.01, 0.98]; IDS week 8: SES [95%CI] = 0.64 [0.03, 0.87]) and anxiety symptoms (HAMA week 4: SES [95%CI] = 0.67 [0.00, 0.95]; week 8: SES [95%CI] = 0.79 [0.06, 1.05]), compared to the placebo group. Attrition was 8% (n = 3 placebo, n = 1 probiotic), adherence was 97.2% and there were no serious adverse reactions. The probiotic modified the composition of the faecal microbiota by normalising richness and diversity towards healthy control levels. The probiotic also increased levels of specific taxa, including Bacillaceae (FDR $p < 0.05$), which correlated with reductions in anxiety scores (FDR $p < 0.05$). There was no impact of treatment on levels of inflammatory cytokines (CRP, TNFα, IL-1β, IL-6, IL-17) or BDNF. However, probiotics showed a tendency to increase positive affective bias and improved the accuracy of recognition of all emotions, except sadness.
Conclusion. Compared to placebo, the probiotic group had greater improvement in depressive and anxiety scores, from as early as 4 weeks. The acceptability, tolerability and estimated effect sizes on key clinical outcomes are promising and encourage further investigation of this probiotic as add-on treatment in MDD. The beneficial effects of probiotics in this patient group may be partially mediated by modification of the composition of the gut microbiota and improvement of affective biases, inherent to depressive disorders.

Monitoring of Inter-Dose Intervals for Long-Acting Injectable Antipsychotics: A Proposed Protocol for the MIDILIA Trial

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doi: 10.1192/bjo.2023.223

Aims. Service users taking long-acting injectable antipsychotics (LIAs) may experience recurrence of symptoms as they approach trough levels within a steady-state cycle. Limited research exists around symptom variation between peak-to-trough plasma concentrations of LIA inter-dose intervals. Different LIAs have variable rates of change in dopamine receptor occupancy during this peak-to-trough variation due to differing elimination half-lifes. It is unclear what rate of change in D_2 blockade is tolerated by patients at present, which this trial aims to determine through observing symptom severity differences during peak-to-trough variation.
Methods. A real-world observational longitudinal cohort study is proposed. Inclusion criteria would be working-age adults (18–65 years) who have received five consecutive and timely LIA administrations of a consistent drug and dose. The study would exclude anyone with significant hepatic or renal impairment, anyone on concurrent oral antipsychotic medication or anyone deemed not to yet be within steady-state plasma levels of their LIA medication.

Serum assays for drug level will be obtained at both peak and trough concentrations during an LIA cycle. Expected timings for peak levels will be determined by derived tmax values from existing pharmacokinetic literature for individual drugs. Trough levels will be taken within 24 hours of the next LIA administration being due. Plasma drug concentrations will then be used to calculate expected striatal D_2 blockade using EC_{50} values and maximal occupancy for individual drugs derived from existing PET scan data.

Symptom severity will be assessed by completing Positive and Negative Symptom Scores (PANSS) questionnaires with service users at the time of both peak and trough plasma concentrations of LIA. The difference in these scores will then be plotted alongside the difference in expected D_2 blockade derived from plasma drug concentrations.
Results. We hypothesize that the rate of D_2 occupancy change would correlate with symptom severity differences in an exponential manner, in that drugs with shorter elimination half-life would have greater difference in symptom severity between peak and trough. We expect that service users would be able to tolerate such change to a degree without significant emergence of symptoms; the trial aims to determine the threshold for what most service users can tolerate, which may then assist in guiding how to effectively reduce and discontinue medications.
Conclusion. This outlines a research protocol to monitor response to pharmacokinetic variation within inter-dose intervals of LIA medication, which may ultimately aid service users in reducing and discontinuing antipsychotics.

Psychometric Properties of the 7-Item Generalized Anxiety Disorder (Gad-7) in Nigerian Pregnant Women Attending Primary Health Care

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doi: 10.1192/bjo.2023.224

Aims. Maternal mental health is an integral component of services that should be rendered to pregnant women in addition to their physical health during their antenatal care. Mental health conditions are screened for during these visits. There is a high prevalence of anxiety disorders among this group of women. A common questionnaire used to screen for anxiety is the 7-item generalized anxiety disorder (GAD-7). However, this instrument has not been validated among pregnant women in Nigeria. We conducted research among pregnant women in Southwest Nigeria to demonstrate the psychometric properties of