An Outline for 'Research into Antipsychotic Discontinuation and Reduction' (RADAR): A Randomised Controlled Trial.

By Zoë Haime, Lisa Grünwald, Jesutofunmi Aworinde and Dr Joanna Moncrieff.
Research and Development Department at North East London NHS Foundation Trust.

RADAR
Research into Antipsychotic Discontinuation And Reduction

Rationale

- Antipsychotics have been found to be helpful in the acute phase of Schizophrenia, less is known about long term use.
- **Side effects** have been reported in conjunction with antipsychotic use, these include tardive dyskinesia, weight gain, hyperprolactinaemia, sedative effects and memory problems.
- Additionally, serious **physical health problems** have been linked with long-term antipsychotic use, including: Diabetes, Cardiac Death, and Hyperlipidaemia.
- There is also evidence that antipsychotics may effect social and neuropsychological functioning (Faber et al, 2011).
- In a study led by Wunderink et al (2007) looking at reduction vs. maintenance of antipsychotics in **Early Intervention** patients, relapse occurred in 43% of those randomised to the reduction group, at 18months after treatment implementation.
- At long-term follow-up (7 years) there was **no difference in relapse rates between groups**, and **significant improvements in neurocognitive and social functioning** (Figure 1.) (Wunderink et al 2013)

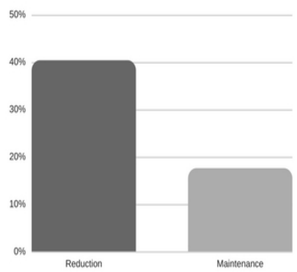
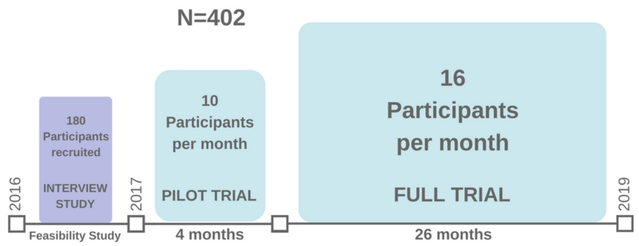


Figure 1. 7yr Follow-up Recovery Rates in Reduction (40.4%)Vs. Maintenance (17.6%) Groups. (Wunderink et al, 2013).

Methodology

Sample

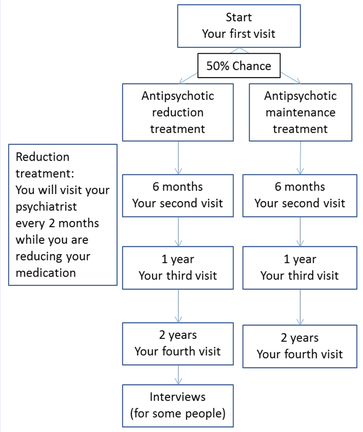
- Recruitment of participants will be from community teams in participating NHS Trusts across a number of UK sites (currently NELFT and ELFT for the pilot).



Design

- Multi site, pragmatic, two arm, open, parallel group, single blind individually randomised controlled trial..
- Researchers conducting follow-up assessments will be blinded to treatment allocation.
- Participants will be randomised to an Antipsychotic intervention group, either: **Reduction and Discontinuation** or **Maintenance**

The Participant Journey



Baseline Visit
- The initial assessment where consent will take place.
- The assessment involves questionnaires, PANNS assessment, and neuropsychological function tests.

Randomisation
- Randomisation will take place using a remote computerised system.
- Randomisation will place participants in either the reduction/discontinuation group, or the maintenance group.
- Randomisation will be completed by unblinded researchers.

Follow-up
- The study is designed to have as a long of a follow-up period as possible.
- Follow-up assessments will follow similar protocol to baseline.

Exclusion Criteria

- Home Treatment Team, Crisis, or Inpatient care in the last month
- On Section/Community Treatment Order (CTO)
- At risk of self to harm or others
- Pregnant or breast-feeding

Inclusion Criteria

- Over 18 years old
- Diagnosis of Schizophrenia, Schizoaffective, Delusional Disorder or Non-affective
- More than one previous episode of relapse or psychotic exacerbation, or a single episode lasting more than one year
- Taking antipsychotic medication

Interventions

Antipsychotic Reduction/Discontinuation Group:
- Individualised antipsychotic reduction plan based on initial antipsychotic regime
- Dose will be reduced incrementally every 2 months over a 12 month period with the aim of stopping or reducing to minimum dose
- Relapse prevention plan will be designed collaboratively with all patients The intervention protocol will include guidance on how to manage increased symptoms and relapse and there will be close liaison between research staff and clinical staff about monitoring and managing symptoms and relapse.

Antipsychotic Maintenance Group:
- Patients will continue on their current dose of antipsychotic medication.
- Minor dose adjustments may be made to manage side effects.

Analysis

- The primary outcome of **Social Functioning** will be measured by the Social Functioning Scale (**SFS**, Birchwood et al, 1990)
- Additional outcomes: Relapse (as measured by service use), Symptomology (**PANNS**, Kay et al 1987), Quality of Life (**MANSA**, Priebe et al, 1999). Side Effects (**GASS**, Waddell&Taylor, 2008), Body Weight, Sexual Dysfunction (**ASEX**. McGahuey et al 2000), Recovery (**QPR**, Law et al 2014), Employment, and Economic Analysis.
- **Neuropsychological Function** will be measured using various tasks to evaluate memory, learning, visual attention and motor speed.
- The information will be analysed using **Generalised Mixed Models**, accounting for baseline and treatment periods.
- Relapse will be compared between the randomised groups using Cox Constant Proportional Hazards Model. Secondary outcomes will be analysed using analogous methods.

Aims

- To evaluate the **benefits and risks** of a supported programme of antipsychotic dose reduction and discontinuation compared with continuous maintenance antipsychotic treatment in people with a Schizophrenia Spectrum Disorder.
- The Primary outcome will be a measure of **Social Functioning.**
- Follow-up is for two years following the initial intervention.

> **"I don't find antipsychotics to be helpful for myself. I don't like the side effects which are bad memory, dribbling, getting the shakes [and] sleeping in."**

Quote from trial participant.

@RADARprogramme

Contact us:
radar@nelft.nhs.uk

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