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How do participants in clinical trials compare with other patients with schizophrenia?

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ABSTRACT

We aimed to explore the clinical relevance of a multicentre, pragmatic randomised trial of antipsychotic reduction in people diagnosed with schizophrenia or psychosis The sample recruited for the antipsychotic reduction study (n = 69 people) was compared with the population of patients with an eligible diagnosis undergoing treatment in the same service (n = 3067 people), using routinely-collected, anonymised data. The trial sample was found to resemble the wider population in terms of the number of past admissions, the likelihood of having been subject to legal detention and the level of risk the patient was perceived to pose to themselves or others. There was a lower proportion of people from minority ethnic backgrounds in the trial sample. The results provide some reassurance that trial recruits were similar to the wider population in terms of the severity of their condition and did not comprise a highly select sample of people with milder problems. The different ethnic composition of the research sample is consistent with other research.

1. Introduction

As in other areas of medicine, there is a longstanding concern that randomised trials of mental health interventions are not applicable to real life clinical populations [1,2]. Research suggests that compared to the wider population of people who use mental health services, study participants are more likely to be young, male, white, have less severe conditions and fewer medical complications [2–4]. Where experimental interventions involve some risk, or when there are strong beliefs in the efficacy of one type of treatment, it may be particularly difficult to recruit people who are comparable to the wider population. Clinicians and patients may, therefore, regard the research findings as irrelevant.

The current study set out to compare the characteristics of participants recruited to a multicentre, pragmatic randomised trial of antipsychotic reduction with those of the population from which they were drawn. The trial, known as the RADAR trial (Research into Antipsychotic Discontinuation and Reduction), compared a supported programme of antipsychotic reduction and discontinuation to maintenance therapy in people with recurrent episodes of schizophrenia or psychosis [5]. The potential risks involved in antipsychotic discontinuation, and the existence of highly polarised views about the value of long-term antipsychotic medication might restrict recruitment more than most studies in the area. Hence it is important to establish the clinical relevance of the results, especially since this is the first trial to evaluate a gradual programme of antipsychotic reduction in this population and therefore has significant implications for clinical practice.

2. Methods

In the RADAR trial, participants randomised to the antipsychotic reduction arm undertook a gradual and flexible reduction of their antipsychotic medication in collaboration with their treating psychiatrists. The aim was to discontinue antipsychotics completely if the reduction proceeded smoothly and if this was the wish of the participant. Participants randomised to the maintenance arm were requested not to reduce the dose of their antipsychotic unless they experienced signifi-

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cant adverse effects. The primary outcomes of the trial were social functioning and severe relapse.

Inclusion criteria for the trial included being aged over 18; having a clinical diagnosis of schizophrenia, schizoaffective disorder, delusional disorder or other non-affective psychosis and having had more than one previous episode or a single episode lasting more than one year. Exclusion criteria were as follows:

- Lacking capacity to consent
- Not speaking sufficient English to understand trial procedures
- Being on a legal order that includes a requirement to take antipsychotic medication
- A clinician considers there to be a serious risk of harm to self or others
- Having been admitted to inpatient care or had treatment from a crisis of home treatment team within the last month
- Being pregnant or breast feeding
- Taking part in another drug or medical device trial

There were no restrictions on people with comorbid substance misuse, physical health difficulties, or other psychiatric comorbidities.

The sample recruited at the largest study site was compared with the population of patients undergoing treatment in the same service using CRIS software. This software was introduced to parts of the UK health service in order to harmonise clinical records and facilitate research [6]. All participants in the RADAR trial gave informed consent to the use of their data. No ethical approval was required for the use of CRIS data since this is routinely collected, anonymised and no identifying information was provided.

All patients with a diagnosis listed in the inclusion criteria for the RADAR trial who were born before 2000 and currently under the service were identified. Data were extracted on age, gender and ethnicity. The severity of people's underlying condition was assessed by looking at the number of prior admissions to the local area psychiatric hospital, legal detentions and risk ratings made by clinical staff since 2007 (the year in which the electronic record system became available). The same information was collected from the electronic clinical records of the study sample. Logistic regression analyses and t-tests were performed to compare the total service population with an inclusion diagnosis and the trial sample, using the SPSS statistical software package v27.

3. Results

The total service population who had a diagnosis that made them eligible for inclusion in the RADAR trial consisted of 3067 patients. The sample recruited for the trial at this site was 69 people. Table 1 outlines the characteristics of the sample and test statistic.

The age of the sample population was broadly reflective of the total service population of people with psychotic disorders, with both groups having a mean age of 51. There was a slightly lower proportion of women in the trial sample compared to the total population, but the difference was not statistically significant.

Due to the small numbers in many of the original ethnicity categories, these were combined into two categories consisting of “white” and non-white”. The study sample had a statistically significantly lower proportion of non-white participants than that in the total service population.

On average, participants in the trial and members of the general service population had been admitted to hospital for a mental health problem twice since 2007. A slightly lower proportion of the trial sample had had no admissions during this period. Around half of both groups had been legally detained at least once. A slightly lower proportion of the trial sample had ever been rated as being ‘high risk’. There were no statistically significant differences between the trial sample and the total service population on any of these measures.

Table 1
Comparison of characteristics of whole service population and trial sample.

	Whole service population (N = 3067)	Trial sample (N = 69)	Odds Ratio or mean difference (95% confidence intervals)
Age (mean, s.d.)	51 (15.9)	50.9 (11.7)	−0.11 years (−3.9 – 3.7)
Gender (% women)	1294 (42.4)	26 (37.7)	1.2 (0.7 – 1.9)
Ethnicity (% non-white)	1608 (52.4)	23 (33.3)	2.2 (1.3–3.7)*
Number of psychiatric hospital admissions since 2007 (mean, s.d.)	2 [3]	2 (1.8)	−0.04 (−0.7 - 0.7)
No psychiatric hospital admissions since 2007 (number, %)	1014 (33.1)	17 (24.6)	0.7 (0.9 – 1.2)
Legally detained at least once since 2007 (number, %)	1531 (49.9)	37 (53.6)	1.2 (0.7 – 1.9)
Risk (rated ‘high risk’ at any point since 2007; number, %)	1140 (37.2)	20 (29)	0.7 (0.4 – 1.2)

Statistical significance of odds ratios was calculated using Fisher's Exact test; mean difference using a *t*-test.
*$p < 0.05$.

4. Discussion

4.1. Limitations

The information available on the control sample was limited to what is routinely collected and categorised on the CRIS system. Hence it was not possible to compare the study population and the overall population on measures of severity of psychopathology, medical comorbidities, drug or alcohol use, treatments received or specific risk behaviours. Data on inpatient admissions, legal detention and the risk ratings that were used as an indication of severity were only available from 2007, when the electronic medical records system was introduced.

It was not possible to subtract the sample recruited for the trial from the overall sample. Therefore, we could not compare the trial sample to the rest of the local eligible population, but only to the total eligible population. Therefore, the two groups were not independent of each other which is required for the tests applied, although the number of people in the recruited sample was small enough that this should not have influenced results substantially.

4.2. Findings

The eligibility criteria for the RADAR trial were intended to be as broad as possible, but other research has found that this does not prevent clinicians and patients selecting who is put forward for research. People from non-white ethnic backgrounds were less likely to be recruited into the trial, but women were not significantly underrepresented in the trial sample unlike much other research in this population [7]. The trial sample resembled the wider population in terms of the number of past admissions, the likelihood of having been subject to legal detention and the level of risk the patient was perceived to pose to themselves or others. This provides some reassurance that trial recruits were similar to the wider population in terms of the severity of their condition and did not comprise a highly select sample of people with milder problems. This is likely because the RADAR trial was a pragmatic trial with broad inclusion criteria, exclusions were minimised and clinicians involved were generally supportive of the trial's aims. The fact that almost half the sample had been legally detained in hospital in the preceding 10 years indicates that the trial sample, like the local service population, showed significant psychiatric morbidity.

Difficulties recruiting people from non-white ethnic backgrounds are well recognised in mental health and other areas of medical re-

search [8–10]. Reasons include lack of resources, training and commitment by research teams as well as cultural differences, a lack of trust in services, fear of stigma and practical or financial difficulties among potential participants [11–13]. It is known that black African and Caribbean participants, in particular, have higher refusal rates to take part in mental health research than their white counterparts [12], which is relevant because they have higher rates of diagnosis of psychosis [14] and legal detention [15]. The lack of funding for interpreters is likely to have contributed to the lower rates of recruitment into the RADAR trial sample, since the catchment area for recruitment includes areas with a high proportion of non-native English speakers [16].

5. Conclusion

These results challenge the perception that clinical trials necessarily recruit people who are less unwell or impaired than the wider patient population [2]. In line with other research, this study highlights the importance of finding new ways to engage people from ethnic minority backgrounds in research studies [17].

CRediT author statement

Robert Freudenthal: conceptualisation, methodology, project administration, investigation, writing-original draft, writing– review and editing, **Louise Marston**: methodology, formal analysis, writing– review and editing, **Jacki Stansfeld**: investigation, formal analysis, writing– review and editing, **Stefan Priebe**: methodology, writing – review and editing, **Joanna Moncrieff**: conceptualisation, methodology, writing – review and editing, supervision.

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Declaration of competing interest

JM is a co-applicant on another NIHR-funded study, she is co-chair person of the Critical Psychiatry Network, a member of the Council for Evidence-based Psychiatry and has recently published a book on psychiatric drugs entitled *A Straight-Talking Guide to Psychiatric Drugs*. No other authors have anything to declare. JM is Chief investigator of the RADAR programme, and SP is Co-chief investigator.

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