



Attrition in longitudinal studies among patients with schizophrenia and other psychoses; findings from the STRATA collaboration

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ABSTRACT

A major problem with longitudinal studies is the bias generated due to attrition, particularly apparent amongst patients suffering from psychotic disorders. Factors associated with study-participation were investigated as part of a larger research collaboration (STRATA). Out of 479 eligible participants, only 50 (10.4%) were successfully followed up. The present study investigated whether study participation differed depending on baseline characteristics. Results indicated that individuals who did not participate were more likely to report an alcohol use disorder while those who did respond were more likely to have been in full-time education for longer and be of white ethnicity. Participation did not differ depending on diagnosis, symptoms, GAF, age of onset or depression.

1. Introduction

Longitudinal studies, where participants are followed up over many years and provide data at multiple time points, contribute valuable information to our understanding of disease trajectories and prognosis prediction. They overcome many of the limitations of case-control studies and allow researchers to draw stronger conclusions on the direction of causal relationships. However, it is rare that all participants continue until the end of longitudinal studies, particularly in mental health research and research involving patients with psychosis and schizophrenia. This attrition can reduce the power of a study, violate assumptions required for statistical analysis, and bias results. Given the considerable time and funding which is required to conduct studies of this nature, it important to understand why attrition occurs, how to reduce its impact, and how to interpret results while considering attrition. Clinicians and researchers can benefit from identifying the differences between patients who complete longitudinal studies and those who do not, by applying this knowledge to both the design of longitudinal studies and recruitment strategies.

Psychotic disorders such as schizophrenia are highly debilitating disorders with a large decrease in life satisfaction and increase in mortality (Fervaha et al., 2016; Laursen, 2019). Recruitment barriers and attrition in longitudinal research are particularly prevalent among studies of psychotic disorders. For example, dropout rates of

antipsychotic medication trials have been reported to range from 36% to 90% (Gueorguieva and Rosenheck, 2012; Hofer et al., 2017; Wahlbeck et al., 2001) and between 36% and 68% in observational studies (Hengartner et al., 2017; Leanza et al., 2020). In medication trials, attrition is partly due to medication discontinuation (Hofer et al., 2017), while other common barriers in recruitment and study retainment in all types of studies range from demographic factors such as educational level, employment status, civil status as well as health factors such as smoking, alcohol consumption and physical exercise (Bjerkeset et al., 2008; de Graaf et al., 2000; Eaton et al., 1992; Nilsen et al., 2009; Tambs et al., 2009; Thygesen et al., 2008; Torvik et al., 2012; Van Loon et al., 2003). In addition, psychotic disorders are associated with study retainment issues due to symptoms of the disorders, for example suspiciousness towards researcher, lack of motivation to participate, and impaired ability to understand the content and purpose of the study (Hengartner et al., 2017; Lester and Wilson, 1999; Roberts et al., 2006).

The present study aimed to investigate predictors of re-recruitment issues in longitudinal first-episode psychosis cohort. The present study is part of one of the workstreams of STRATA (Schizophrenia: Treatment Resistance and Therapeutic Advances), where an attempt was made to recontact patients from previous first episode psychosis studies across the UK.

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2. Methods

2.1. Participants and procedure

Participants from three pre-existing longitudinal cohorts of first episode psychosis were invited to take part in STRATA (Homman et al., 2017): AESOP (Morgan et al., 2006), NIFEPS (Anderson et al., 2005), and RPGI (Casey and Corvin, 2008) (Fig. 1). Participants had taken part in at least one assessment (11–19 years previously). Participants were excluded (N=53) if they were deceased, unable to consent, or had non-identified addresses.

Ethical permission was obtained to contact participants using information collected at previous visits and to obtain up to date contact addresses. Special authority to access personal identifiable data without consent under Section 251 of NHS Act 2006 and Health Service (Control of Patient Information) Regulations 2002 was obtained from the UK Health Research Authority as no consent to be contacted at a later date had been given in the previous studies. This enabled up-to-date addresses to be obtained from the Health & Social Care Information Centre (HSCIC).

Several methods of recruitment were attempted: (in order of method used) all participants were invited via letter (two sent out) with stamped self-addressed envelope, phone calls (31.3% (N=150)) (up to two phone calls), and through their care-coordinator or consultant psychiatrist (18.3% (N=88) were contacted; 70.45% (N=62) responded), if applicable. In order to avoid issues regarding acceptance of diagnosis, invitation letters were written in a manner which did not refer to a particular mental health problem. If participants agreed to participate in the study, they had the option of taking part in the study at the research site or the researcher offered to come out to their home.

2.2. Instruments used

Informed consent was taken at the time of the interview, including consent to be contacted again for possible participation in further studies. The study procedure included a structured interview, in which data were collected on personal contact details, demographic data, hospitalisation history, medication history, substance use, psychotic

symptoms (Positive and Negative Syndrome Scale (PANSS)), depression (Becks Depression Inventory (BDI)) and Global functioning (Global Assessment of Functioning (GAF)). Participants were asked to provide a blood or urine sample. The interview took about 1 h. The participant was reimbursed £10 on completion of the study, and all their travel expenses were reimbursed.

2.3. Statistical analyses

Completers (completed the study), decliners (declined participation) and non-responders (did not respond) were compared on baseline measures using chi-square analyses and a one-way ANOVA, where appropriate. If significant differences were observed multinomial logistic regression was used for post-hoc analyses. Site was entered as a covariate into all analyses as response rate differed significantly between sites ($\chi^2=21.55, p<.001$). Statistical analyses were performed in STATA 14. Alpha level was 0.05.

3. Results

3.1. Participants

A total of 479 participants were eligible for STRATA, 183 females and 296 males. Out of the 479 participants 428 were recontacted (Fig. 1), which of 11.7% (n=50) completed the study. Ethnicity was not recorded in the NIFEPS study although the great majority were white British or Irish. Among the remaining two studies (AESOP and RPGI), 62.17% were of white ethnicity, 26.49% were of black ethnicity, 6.49% were of Asian ethnicity, and the remaining 4.85% were of 'mixed' or 'other' ethnicity.

3.2. Group differences

Some baseline characteristics differed significantly between participants who completed, declined and did not-respond to the invitation, while some did not. Characteristics which did not significantly differ between groups were age, gender, age of onset, living and employment status, diagnosis, all substance use apart from alcohol, GAF, BDI, and

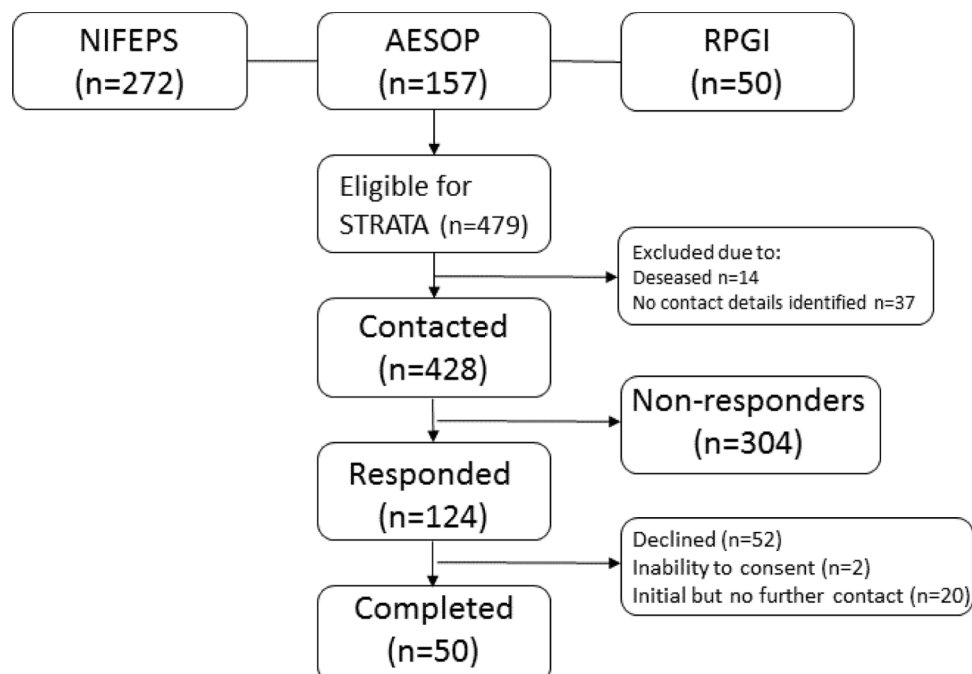


Fig. 1. Flow chart of STRATA recruitment and participation.

PANSS (apart from grandiosity) (see supplementary material). Characteristics which did differ across groups were ethnicity ($\chi^2=16.80$, $p=.002$), AUD ($\chi^2=8.14$, $p=.02$), education ($F(2, 396)=2.86$, $p=.05$), marital status ($\chi^2=10.74$, $p=.03$), PANSS symptom of grandiosity ($F(6, 237)=2.20$, $p=.04$), and being prescribed clozapine or not ($\chi^2=6.25$, $p=.04$). Completers were more likely to be of White ethnicity, be married, and less likely to have reported AUD at baseline. Decliners were more likely than non-responders to have been prescribed clozapine. Non-responders reported lower levels of education compared to completers. Post hoc analyses did not reveal significant differences between groups on grandiosity.

Results from post hoc multivariate analysis (Table 1) were in line with previous results, however, marital status, clozapine prescription and PANSS grandiosity were no longer significant predictors of participation.

4. Discussion

The present study investigated baseline factors associated with attrition rates in a follow up study on first episode psychosis called STRATA. Only 11% of eligible participants took part in STRATA even though several measures were taken in order to avoid attrition. Furthermore, the present study did differentiate between participants who did not respond and those who declined, a differentiation rarely made.

Overall, eligible participants did not differ on many factors directly associated with psychosis, including symptoms of psychosis, diagnosis, depression, GAF, and age of onset. It is possible that the recruitment methods used have captured a representative sample regarding these factors or alternatively, that these factors are not the main predictors of attrition. However, the present findings did indicate that the completed sample is under-representative of individuals with baseline AUD, poor education, and of minority ethnicities; findings in line with previous studies (Souto Melo and Crosland Guimarães, 2005; Tambs et al., 2009; Üçok et al., 2007; Warden et al., 2007). Overall, the study indicates, in line with previous studies, that individuals who do participate report a more stable life situation (longer education, lower AUD, higher GAF, lower PANSS symptoms), while non-participants were associated with more adverse life situations (AUD, lower education, being of ethnic minority) (Clark et al., 1997; Hawkins et al., 1992; Keyes and Hasin, 2008; McLeod and Kessler, 1990).

Based on the present study, we recommend that future studies (i) take consent for participation in possible follow up studies (ii) attempt to keep track of participants change in contact details, possibly through their care-provider (iii) offer a large enough compensation as incentive to participate and a smaller incentive to simply respond to why participation is not of interest (iv) when possible, use care-provider/clinician for contact due to ease and possible trust issues in unknown individuals of research team (v) write study invitation letters to apply to both those who currently have and have had symptoms (vi) use appropriate channels to increase uptake in groups of risk of attrition such as ethnic minorities, AUD and lower education. However, we wish to add two considerations as limitations to this list. First, not all eligible participants may be in contact with a care provider, in particular if they had improved since the initial study and were no longer in care of need. Secondly, the present study was undertaken several years after the initial studies, and it is possible that participants did not recall their participation in the initial study.

4.1. Limitations

While the present study highlights possible bias caused by attrition in STRATA, there are also several limitations which should be considered. First, baseline was measured several years ago, making it likely for major changes to have taken places in participants lives. Secondly, it may have been off-putting for participants to give blood even though it

Table 1

Multinomial logistic regression analyses of significant variables impacting participation.

	Multivariate analyses (RRR= (CI), $p=$)		
	A	B	C
Education	0.78 (.65–.95) .013	1.02 (.86–1.22) .79	1.12 (.93–1.27) .30
Marital status	0.68 (.41–1.33) .14	0.97 (.53–1.74) .91	1.52 (.91–2.55) .11
Ethnicity (Black)	3.54 (1.04–3.41) .001	6.11 (2.03–7.42) .001	1.74 (.98–4.60) .24
Grandiosity	0.94 (.73–1.20) .62	1.03 (.72–1.35) .95	1.05 (.84–1.32) .65
Clozapine	1.71 (.16–3.11) .65	2.35 (.07–1.73) .20	2.49 (.15–1.68) .26
AUD	4.72 (1.51–14.73) .007	4.87 (1.06–14.13) .04	0.74 (.98–6.60) .88

A=Non-responders compared to completers

B=Decliners compared to completers

C=Decliners compared to non-responders

AUD=Alcohol Use Disorders

was not a strict requirement. Finally, the aim of STRATA was not to look at predictors of non-adherence. If this was the case, it would have been of interest to ask participants who did take part why they decided to do so.

5. Conclusions

Conclusively, the present study shows that attrition is a major obstacle in longitudinal psychiatric research on first episode psychosis. The present study indicates possible bias regarding attrition rates on AUD, ethnicity, and years of education but not on symptoms, GAF, age of onset and depression.

CRediT authorship contribution statement

L.E. Homman: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Visualization, Writing – original draft, Writing – review & editing. **S.E. Smart:** Data curation, Investigation, Writing – review & editing. **F. O’Neill:** Project administration, Supervision, Writing – review & editing. **J.H. MacCabe:** Funding acquisition, Conceptualization, Project administration, Supervision, Writing – review & editing.

Declaration of Competing Interest

The authors declare that they have no conflict of interest.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:[10.1016/j.psychres.2021.114211](https://doi.org/10.1016/j.psychres.2021.114211).

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