Effect of early intervention on 5-year outcome in non-affective psychosis†

Rafael Gafoor, Dorothea Nitsch, Paul McCrone, Tom K. J. Craig, Philippa A. Garety, Paddy Power and Philip McGuire

Background
Early specialised care may improve short-term outcome in first-episode non-affective psychosis, but it is unclear if these benefits endure.

Aims
To assess the long-term effect of early intervention in psychosis.

Method
Individuals with first-episode psychosis were randomised to specialised care or care as usual (trial number: ISRCTN73679874). Outcome after 5 years was assessed by case-note review.

Results
There were no significant differences in the admission rate (coefficient 0.096, 95% CI −0.550 to 0.742, $P = 0.770$) or the mean number of bed days (coefficient 6.344, 95% CI −64.6 to 58.7, $P = 0.810$).

Conclusions
These findings that specialist intervention did not markedly improved outcome at 5 years accord with those from a larger OPUS study. The sample size of this study was small and these results should be generalised with caution. More research is needed.

Declaration of interest
None.

Specialist services aim to reduce hospitalisation in patients with psychosis by initiating treatment as soon as possible after the first episode. In the OPUS study, participants with first-episode psychosis randomised to specialist services had shorter hospital admissions at 1 year after presentation than those assigned to care as usual; however, these benefits did not endure at 2-year follow-up. The Lambeth Early Onset (LEO) trial found that individuals treated by a specialist service had lower hospital bed use at 18 months than those receiving care as usual. Whether the beneficial effects of specialist services endure in the long term is unclear. We addressed this issue by following up participants in the LEO trial 3.5 to 5 years after inception. The trial was registered with the International Standard Randomised Controlled Trial Number Register and was assigned the trial number ISRCTN73679874.

Initial study – randomised controlled trial
In 2002, 144 people presenting to psychiatric services in Lambeth, South London, with a first or second episode of non-affective psychosis were randomly allocated to either ‘specialist services’ or ‘care as usual by community mental health teams (CMHTs)’ at inception. Inception was defined as the point of first treatment for psychosis. Inclusion required an age of 16–40 years, and a presentation of a non-affective psychosis (schizophrenia, schizotypal, and delusional disorders, F20–29 in the ICD-10).

Individuals with an ‘organic’ psychosis or a primary alcohol or drug addiction were excluded. Participants were randomised by permuted random blocks of between two and six. The randomisation and concealment group allocation was carried out by sealed envelope method by the trial statistician. Follow-up interviews were conducted at 18 months (while the participant was still receiving care from the original clinical teams). Data on readmissions were obtained from centralised computer case records and from interview with psychiatric care coordinators. Follow-up information on clinical status at 18 months was collected from 131 (91%) people.

The specialist team (LEO) was a new service comprising 10 mental health professionals who delivered specialised interventions including low dose atypical antipsychotic regimens, cognitive–behavioural therapy based on manualised protocols, family counselling and vocational strategies based on established protocols. Participants in the control group received standard care from established adult general CMHTs in Lambeth. These teams had received no formal training in specialist interventions but had access to guidelines on the approach.

Although participants and clinicians were not masked to treatment arm, it is unlikely that participants had contact with other participants in the other arm. Allocation remained undisclosed until completion of the ratings. However, assessors were able to guess the arm of treatment to which 60% of participants had been allocated (95% CI 52 to 63, $z = 0.20$). Participants were analysed by intention-to-treat analysis (ITT) in the group to which they were initially randomised. Regression analyses were adjusted for variables that were unbalanced between the two groups at baseline (ethnicity, past episode and gender).

Results from the initial study
A previous study had found that individuals receiving specialist treatment had fewer admissions in the intervening 18-month review period than those assigned to care as usual: (0.4 admissions $v.$ 0.8 ($\hat{b} = 0.36$, 95% CI 0.04 to 0.66, $P = 0.030$)), but were not less likely to have ever been admitted (OR = 0.53, 95% CI 0.26 to 1.12, $P = 0.095$) or to have had shorter admissions ($\hat{b} = 19.4$, 95% CI −10.6 to 48.6, $P = 0.197$). Participants treated by the specialist team had better social and vocational functioning (mean 6.9 months in employment for the specialist group $v.$ mean of 4.2 months, $P = 0.008$), quality of life (mean score of 59.2 for specialist services $v.$ mean score of 53.3, $P = 0.010$) and medication

†See pp. 377–382, this issue.
adherence (mean adherence score of 5.4 for specialist services v.
mean score of 4.5, \( P = 0.036 \) at 18 months).

**Follow-up study**

In 2005, the above participants were retrospectively assessed
during an 18-month period (3.5 to 5 years after inception). The primary (null) hypothesis was that there would be no difference in
the odds of having ever been admitted in the 18 months prior
to this second assessment. The secondary (null) hypotheses were
that the relative admission rates and the length of bed occupancy
during this period would be the same for both groups.

Ethical permission for this study was given by the Institute of Psychiatry at the Maudsley (Kings College London, University of London). Ethical permission for the analysis of the data was given by the ethical committee of the London School of Hygiene and Tropical Medicine, University of London. Clinical ethical permission for participants to be traced, contacted and inter-
viewed was given by the South London and Maudsley NHS Mental Health Trust (SlaM).

We assumed that the relative reduction in the rate of ever
having been admitted would decrease by 10% in the next 5 years
as the effects of specialist services waned; there are no comparative admission data currently available at 5 years for individuals who
were exposed to specialist services as this is the first follow-up
study of such a randomised cohort. Using data from clinical audit,
the rate of ever having been admitted for individuals in ‘care as
usual’ CMHTs is approximately 65% over 18 months at 5-year
follow-up. We assumed a relative reduction in the rate of ever
having been admitted of 23% between the two groups and a rate
of 46% of ever having been admitted (for people who had been
randomised to the specialist group) over the 18-month period
leading up to 5 years post first admission. At a power of 80%
and an alpha of 0.05, we determined that 234 people would be
required in total to find a difference between the two groups if
one existed. If all 144 individuals had been traced, the study would
have a power of 56% of discovering a difference between the
groups if such a difference existed at an alpha of 0.05. This study
was underpowered but it is no longer possible to increase the
sample size given that it would be unethical to randomise
individuals again to care as usual. This follow-up study (although
imperfect) provides the best evidence currently available in the
clinical circumstances.

An extensive sequential tracing algorithm was used to find
participants: individuals were traced using electronic patient
records held by the local National Health Service (NHS) trust,
the NHS Strategic Tracing Service (NSTS), land registry records,
general practitioner (GP) records, the UK register of deaths or
via the last known relative. We were not able to access prison
records or Home Office immigration records for deported
individuals. Migrants and prisoners may have had worse
prognoses and more admissions than other people; differential
loss to follow-up for this subgroup may have resulted in an
‘emigration bias’.\(^{11–15}\) Follow-up was not masked to intervention
differences as individuals often disclosed their treatment on interview
and treatment group was apparent on review of the notes. Poor
concealment was also an issue in the original LEO trial (as
discussed above). To reduce the chance of information bias, dates
of recorded admissions and the number of documented
admissions were used as the primary sources for data collection.
Information was verified by reference to written material or by
reference to the team treating the individual.

All traced participants were successfully contacted (including
those living overseas), and all agreed to provide follow-up
information. Individuals were given information about the study
on the telephone and this was followed up by written materials
where requested. Participants were interviewed on the telephone
or in person (whichever method they preferred). Figure 1 shows
that of the original 144 participants who were randomised, 99
(69%) were traced and contacted. In comparison, Nordentoft et
al in their 5-year follow-up study of service interventions
in Denmark were able to contact 301 participants (55%) out of an
incipient cohort of 547.\(^{16}\)

To remove the potential influence of differential access to
home treatment teams on hospital admission rates (as it is often
considered as an alternative to admission), all home treatment team
events were counted as equivalent to an admission. Where the
home treatment team care was provided in isolation, the case
was recorded as an admission with the length of home treatment
counting as the length of hospital admission. In some cases,
individuals initially receiving home treatment teams were then
admitted: in this case, home treatment and hospital admission
were counted as a single admission event. The total time of
admission was the time in hospital plus the time with home
treatment teams. The same algorithm was used for individuals
who were discharged from the ward directly to home treatment
teams.

Diagnoses were assigned at a median time of 5.3 years and
were made using a notes-based diagnostic tool, the operational
criteria OPCRIT checklist\(^{17}\) for psychotic and affective illness,
which provided diagnoses according to the ICD–10 system.\(^{4}\)

Analyses were performed using STATA release 9 on Windows
Vista. Linear regression models were employed to assess the
relationship between initial randomisation group and outcome
variables. There were two potential sources of confounding: failure
of randomisation to produce balanced groups in the original LEO
trial and differential contactability between treatment arms.

<table>
<thead>
<tr>
<th>Fig. 1 Participant flow.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Reasons for exclusion:</strong> not resident in Lambeth, too old or too young (n = 38); did not meet diagnostic criteria (n = 90); already engaged with services (n = 35); lost before confirmed (n = 10).</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Potential participants (n = 319)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants randomised (n = 144)</td>
</tr>
<tr>
<td>Excluded (n = 175)</td>
</tr>
<tr>
<td>Allocated to specialist services (n = 71)</td>
</tr>
<tr>
<td>Allocated to standard care (n = 73)</td>
</tr>
<tr>
<td>No reported deaths</td>
</tr>
<tr>
<td>1 reported death</td>
</tr>
<tr>
<td>Participants uncontactable (n = 26)</td>
</tr>
<tr>
<td>Participants uncontactable (n = 18)</td>
</tr>
<tr>
<td>Participants followed up (n = 45) 63% of original cohort</td>
</tr>
<tr>
<td>Participants followed up (n = 54) 74% of original cohort</td>
</tr>
</tbody>
</table>
(Details of the strategy for analysis for confounding and the results of these analyses are contained in the online supplement.) A sensitivity analysis was performed to assess the robustness of the findings when participants who could not be traced were assigned extreme values.

### Results

Figure 1 shows the participant flow for both the original trial in 2000 and during the 18-month period of follow-up (i.e. 3.5 to 5 years after inception). One person died due to accidental causes. Of those who had been randomised to care as usual, 15 (28%) v. 15 (33%) of those who had been allocated to the specialist team had been discharged to their GP (Pearson \( \chi^2 = 0.359, P = 0.549, \text{d.f.} = 1 \)). The length of time for which individuals were with their GP after discharge from services was highly skewed. Participants in specialist services who had been discharged to their GP spent a median of 0 days (IQR = 0–826) with their GP v. a median of 0 days (IQR = 0–264) for those randomised to care as usual. There was no significant difference in the length of time spent with their GP for either group (Mann–Whitney \( U = 1147.5, Z = -0.571, P = 0.568 \)). Participants treated by the specialist service were followed up by psychiatric services for a median of 1778 days (IQR = 1152–2030) after first randomisation v. a median of 1887 days (IQR = 1640–2034) for those randomised to care as usual. There was no statistically significant difference in the length of time spent in psychiatric services for either group (\( U = 1077.5, Z = -0.973, P = 0.330 \)). Individuals randomised to specialist services spent a median of 861 days in the specialist service (IQR = 720–1027). In total, 99 participants (70%) were successfully traced from the original cohort. By comparison, Nordentoft et al. in their 5-year follow-up were able to contact only 301 participants (55%) of an incipient cohort of 547, underscoring the difficulties of follow-up in this cohort.

The follow-up participants were representative of the original LEO sample (Table 1). Contactable participants were not significantly different in baseline clinical variables from those who were traced (see online supplement). Analysis for confounding (see online supplement for details) identified that ‘ever having been discharged from psychiatric services to a GP’ was a confounder in the relationship between whether of not a participant could be contacted and the main outcome of ever having been admitted. We also adjusted for imbalances in baseline variables: gender, previous psychotic episodes and ethnic group.

Table 2 shows the cross-sectional differences between the two groups during the 18-month follow-up (i.e. from 3.5 to 5 years post-inception) at baseline. There was no difference in the chances of any admission, the number of admissions or the number of bed days used during the follow-up period. We noted that there was an increase in the number of admissions during the follow-up period relative to the initial review period. This increase was attributable to an increased admission rate for each individual relative to that during the initial follow-up period. Thus, during the second follow-up period, 21% of people were not admitted, 49% were admitted once, 20% were admitted twice and 8% were admitted three or more times. The reason for the increased number of admissions during this period is unclear. It may reflect changes in service structures over the period of the study, and/or a change in the pattern of service use or need as psychotic illnesses become more chronic.

Regression modelling was employed to estimate effect size of interventions and to allow for adjustment with potential confounding factors.

Although the data were not normally distributed, because the data from the original LEO trial used a parametric analysis, we replicated this analysis so that the results during the initial and subsequent18-month periods could be more directly compared.

Data on number and length of admission during the 18-month period leading to 5 years were highly skewed. The median number of admissions was identical in both groups (median 0, IQR = 0–1). The mean number of bed days was 42.25 days (s.d. = 112.8, median 0, IQR = 0–31.0) and 51.41 days (s.d. = 125, median 0, IQR = 0–38.0) in the ‘specialist services’ and ‘care as usual’ groups respectively.

Table 3 shows the relationship between outcome and randomisation group for crude and adjusted regression modelling. There were no significant differences between the two groups in terms of any of the outcome measures before and after adjusting for confounders.

### Sensitivity analysis

In total, 26 participants in the specialist services arm and 18 people in the care as usual arm could not be traced at 5-year follow-up. We performed sensitivity analyses on the data from these missing individuals to examine the robustness of the finding from the initial logistic regression model that there was no group difference in ever having been admitted (see online supplement). We calculated that the finding of no observed differences in the odds of being admitted between the two groups would only be reversed if at least 80% of those who were missing from the specialised care group and had been admitted as well as if 20% of missing participants from the care as usual group had also ever been admitted (see online supplement). This is an unlikely scenario and uncontactable individuals in the specialised care arm would have to have been twice as likely to have ever been

### Table 1

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Original cohort baseline characteristics (n = 144)</th>
<th>Baseline characteristics of participants traced 5 years later (n = 99)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at baseline, years: median (IQR)</td>
<td>25 (21.0–25.0)</td>
<td>25.0 (20–25)</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>93 (65)</td>
<td>60 (60)</td>
</tr>
<tr>
<td>Ethnicity, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>45 (31)</td>
<td>28 (28)</td>
</tr>
<tr>
<td>Black British</td>
<td>16 (11)</td>
<td>15 (15)</td>
</tr>
<tr>
<td>Black Caribbean</td>
<td>22 (15)</td>
<td>15 (15)</td>
</tr>
<tr>
<td>Black African</td>
<td>41 (28)</td>
<td>25 (25)</td>
</tr>
<tr>
<td>Mixed</td>
<td>12 (8)</td>
<td>9 (9)</td>
</tr>
<tr>
<td>Other</td>
<td>8 (6)</td>
<td>7 (7)</td>
</tr>
<tr>
<td>Single, n (%)</td>
<td>100 (69)</td>
<td>69 (69)</td>
</tr>
<tr>
<td>First episode, n (%)</td>
<td>113 (78)</td>
<td>73 (73)</td>
</tr>
<tr>
<td>Living situation, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Family</td>
<td>77 (54)</td>
<td>65 (65)</td>
</tr>
<tr>
<td>Alone</td>
<td>41 (28)</td>
<td>26 (26)</td>
</tr>
<tr>
<td>Other</td>
<td>24 (17)</td>
<td>8 (8)</td>
</tr>
<tr>
<td>Employment, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Full time</td>
<td>17 (12)</td>
<td>8 (8)</td>
</tr>
<tr>
<td>Part time</td>
<td>9 (6)</td>
<td>7 (7)</td>
</tr>
<tr>
<td>Unemployed</td>
<td>90 (63)</td>
<td>53 (53)</td>
</tr>
<tr>
<td>Migrant, n (%)</td>
<td>56 (39)</td>
<td>38 (38)</td>
</tr>
</tbody>
</table>

a. Percentages based on traceable population of 99.

b. Inclusion criteria for the incipient cohort allowed participants to have had a previous psychotic episode, providing it had been untreated and the individual had subsequently disengaged from clinical services.
c. Living with friends or living in a hostel.
admitted as those from the specialised care arm who were traced. We discounted the scenarios where all or none of those people who could not have been traced had been admitted in either arm as being unlikely.

We examined the stability of the initial diagnosis of ‘non-affective psychosis’ that had been made 5 years previously when the participants took part in the original LEO study. Data were extracted from case notes and used in the OPCRIT algorithm to produce ICD–10 diagnoses. Table 4 shows the ICD–10 diagnostic category assigned by OPCRIT at the time of follow-up. The median time from entry into the study to diagnosis was 64.2 months (5.3 years) (IQR = 58.3–64.2 months). Of those who could be accorded a diagnosis at follow-up, more than 85% of them continued to be diagnosed with a psychotic illness.

### Discussion

#### Limitations

The power of the study to detect statistically significant differences between the two groups was low. However, this is not surprising given that the benefits of specialised services did not persist during the period of 3.5 to 5 years post-inception and relative differences between the two groups became smaller. Only a restricted range of clinical outcomes were assessed and potential benefits in other outcome domains may persist.

The study was conducted in an urban population with a relatively high incidence of psychosis, and high levels of poverty, unemployment and illicit drug use. The risk of developing psychosis and of relapsing after a first episode in this population may not be representative of the UK overall. Given these limitations, the results of this study should be generalised to other populations with caution.

#### Clinical implications

Although there is good evidence that specialised intervention in first-episode psychosis improves outcomes in the first 1–2 years, the extent to which these benefits persist in the longer term remains unclear, particularly after the specialised intervention is withdrawn.
Funding

This study was funded by the Medical Research Council (UK) via a Clinical Research Training Fellowship to the lead author.

References


Ian Curtis

Geoff Dickens and Marco Picchioni

18 May marks the 30th anniversary of the suicide of Ian Curtis, lead singer of Joy Division, who was just 23 when he hanged himself. Curtis’s work comprises little more than two dozen songs recorded over 3 years but it remains disproportionately influential. A lineage can be traced from Joy Division through Siouxsie and the Banshees, The Cure, U2, through to contemporary artists such as Interpol and Editors.

Prescribed barbiturates for his poorly controlled epilepsy, Curtis was hospitalised following an overdose 6 weeks before his death. He self-discharged the next day to front the band at a chaotic gig. Curtis’s last show at Birmingham University, 2 weeks before his suicide, was featured posthumously on the Joy Division album Still; his state of mind. Curtis had already told his wife that his life’s end was near and that he wanted to leave the band and ‘join a circus’.

Thirty years on, Curtis’s fame outshines that achieved in his brief lifetime. Best known for the single Love will Tear Us Apart, released a month after his death – the song features in Rolling Stone’s top 500 songs of all time, with Curtis the subject of two feature films, numerous books, documentaries and reissued discs.
Details of analysis to identify confounders

Imbalances in initial Lambeth Early Onset (LEO) trial

Factors that were unbalanced at baseline (due to failure of randomisation to produce balanced groups when using small sample sizes) between the two randomised groups were entered into the regression model. This adjustment was performed by the first LEO study and we replicate this analysis to increase comparability of the two studies. Both crude and adjusted ratios are given as adjusting for variables that are known to be unbalanced at baseline and could potentially introduce error into the analyses. Randomisation potentially removes confounding for both known and unknown confounders but may have been ineffectual in the original LEO study because of insufficient size. Adjusting for imbalances in known confounders could potentially introduce confounding by creating imbalances in unknown confounders.

Confounders in second trial

Potential confounders were chosen after review of the literature identified variables that could potentially be related to both outcome and chance of being traced for the LIFE study. As contactability lies on the causal pathway between exposure and outcome of interest, confounders of the relationship between contactability and outcome are very likely to also act in the relationship between randomisation group and outcomes. The following confounders were identified: ethnicity; gender; age; duration of untreated psychosis; whether or not the person was in a relationship at baseline; whether or not the person was working at baseline; whether or not the person was in education at baseline; migrant status.

Although the list is not exhaustive, these factors had the strongest relationship with outcomes of those considered. Specialist psychiatrists were consulted about other factors they considered important. The following factors are therefore also considered: discharge to general practitioner; and total time with psychiatric services. Cannabis misuse at baseline was a potential confounder but could not be assessed as this information had not been collected in the original study. Duration of untreated psychosis is a potential confounder and was recorded at baseline. However, the recorded values were judged to have poor reliability and so were not used in further analyses.

All potential confounders were entered sequentially into a logistic regression model to ascertain strength of relationship with contactability at follow-up. Any variables thus identified were considered as potential confounders. There was insufficient sample size to examine the potential role for interaction between variables that were entered one at a time. Relationship with outcome (where known for participants) was similarly assessed by sequential entry of any variables identified in the first analysis into a logistic regression model with ‘ever been admitted’ as the primary outcome of interest.

Table DS1 shows the results of modelling for an association between contactability and the potential confounding variables.

Details of statistical modelling for missing data-sensitivity analysis

We were not able to contact 30% of participants. It is possible that this cohort may have had a systematically better or worse outcome than those who had been traced and thus the overall results obtained may have been biased. We modelled for missing data from uncontactable participants using sensitivity analyses in which we considered the possibilities of this missing cohort having different admission rates from those who had been contactable. The underlying assumption is that the missing individuals were ‘not missing at random’ (i.e. that missingness was not as a result of completely random loss of data (which would be termed ‘missing completely at random’). Examples of mechanisms underlying missingness are demonstrated in Appendix DS1.

For missing ‘not at random’ data we assume that participants who were not followed up were less or more likely not to have ever been admitted potentially because they had the best or worse outcomes after the end of the LEO study. Data were modelled using a complete data-set that included both values of ‘missing’ as well as predicted outcome values.

Sensitivity analysis was employed to assess the robustness of the outcomes by randomly substituting possible outcome values for missing data. A fixed proportion of data from uncontactable participants was randomly chosen to be assigned the most severe outcome (ever admitted to hospital), whereas the missing data from the other participants was simultaneously assigned the best outcome (i.e. ‘not admitted’). An alternative strategy would have been to set a proportion of the missing values to ‘admitted’ while simultaneously setting the other missing values to ‘missing’.

This analysis was not selected as the odds ratios thus produced for each permutation are less directly comparable.

Initially, 20% of patients for whom outcome data were missing in the care as usual arm were randomly selected and assigned the worse outcome value (ever admitted in the follow-up period). Participants were randomly selected by the computer programme STATA on Windows Vista. The subsequent odds ratio and 95% intervals of uncertainty of ever been admitted by randomised group were then calculated. This procedure was carried out 100 times and the average odds ratio and the associated 95% intervals of uncertainty were reported. Next, the percentage of missing data for the care as usual arm was increased by 20% and the odds ratio recalculated as before. This procedure was continued in intervals of 20% until all of the care as usual participants for whom data were missing had been assigned to the worst outcome. Then, 20% of participants for whom data were missing in the specialist care arm were randomly assigned the worst outcome and resultant mean odds ratios and associated 95% intervals of uncertainty were calculated after 100 iterations of each of the possible six groups of ‘care as usual’ participants with missing data (i.e. those with 0%, 20%, 40%, 60%, 80% and 100% of missing data randomly assigned to the worst outcome).

The participants in the specialist care arm were randomly rescored ten times and the resultant odds ratios of ever being admitted calculated for each category of participant in the care as usual arm with missing data for each selection. The percentage of individuals in the specialist group with missing data were increased by another 20% and the odds ratios recalculated until 100% of the missing data in the specialist group had been assigned the worst outcome.

In the second step, the selection process was reversed and 20% of people in the specialist arm with missing data were randomly selected to have the worst outcome. The procedure for the initial sensitivity analysis was then repeated until all of the participants with missing data (in both arms) were again eventually assigned to the worst outcome.

In the third step, the results from the first and second iterations were compared to see if they differed significantly. In
Mechanisms of missingness

Assumption of missingness

Missing completely at random (MCAR)

Mechanism of missingness

An example of a MCAR mechanism would be if a completely random process underlies the missingness of data (i.e., data lost in transit).

If data are MCAR, then approximately equivalent results would be obtained by performing the analyses if those units with complete data give valid inferences.

This is not a valid analysis for this data-set as the missing data are not due to MCAR mechanisms.

Missing at random (MAR)

This assumption would be valid if there were predictor of missingness. Statistical analysis of this data-set identified no predictors of missingness and thus this assumption is not valid for this data-set.

No missing at random (NMAR)

This is the most suitable analysis if the assumptions for MCAR and MAR are not met and is used in the analysis of this data-set.

Additional references


Table DS1 Regression models to assess relationship of potential confounders with contactability

<table>
<thead>
<tr>
<th>Variable</th>
<th>Contactable</th>
<th>Not contactable</th>
<th>OR (or regression coefficient) of being contactable</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethnicity, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>27 (27)</td>
<td>16 (32)</td>
<td>1.196&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.59–2.42</td>
<td>0.620</td>
</tr>
<tr>
<td>Black</td>
<td>28 (29)</td>
<td>10 (22)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caribbean</td>
<td>26 (27)</td>
<td>16 (35)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Black African</td>
<td>4 (4)</td>
<td>0 (0)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mixed/other</td>
<td>13 (13)</td>
<td>4 (9)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>60 (61)</td>
<td>33 (72)</td>
<td>0.559</td>
<td>0.258–1.21</td>
<td>0.141</td>
</tr>
<tr>
<td>In a relationship, n (%)</td>
<td>19 (19)</td>
<td>22 (48)</td>
<td>3.343</td>
<td>1.16–9.66</td>
<td>0.026&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Working, n (%)</td>
<td>15 (15)</td>
<td>11 (23)</td>
<td>1.822</td>
<td>0.758–4.38</td>
<td>0.180</td>
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<tr>
<td>Employment, n (%)</td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Full time</td>
<td>8 (8)</td>
<td>9 (20)</td>
<td>1.13&lt;sup&gt;c&lt;/sup&gt;</td>
<td>0.549–2.32</td>
<td>0.743</td>
</tr>
<tr>
<td>Part time</td>
<td>7 (7)</td>
<td>2 (4)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unemployed</td>
<td>81 (83)</td>
<td>35 (73)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not migrant, n (%)</td>
<td>57 (58)</td>
<td>18 (39)</td>
<td>0.331</td>
<td>0.158–0.689</td>
<td>0.003&lt;sup&gt;d&lt;/sup&gt;</td>
</tr>
<tr>
<td>Discharge to GP&lt;sup&gt;e&lt;/sup&gt;</td>
<td></td>
<td></td>
<td>0.048</td>
<td>0.005–4.04</td>
<td>0.005&lt;sup&gt;e&lt;/sup&gt;</td>
</tr>
<tr>
<td>Log of total time with psychiatric services&lt;sup&gt;f&lt;/sup&gt;</td>
<td>4.05</td>
<td>1.20–13.7</td>
<td>0.024&lt;sup&gt;f&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age at baseline, years: median (IRQ)</td>
<td>25.0 (20.0–31.3)</td>
<td>27.0 (22.0–30.0)</td>
<td>0.964</td>
<td>0.930–1.04</td>
<td>0.583&lt;sup&gt;f&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

a. Recategorised as White or other. White is the reference category.

b. There was no significant association between 'being in a relationship' and the outcome of 'ever been admitted' (OR = 0.542, 95% CI 0.113–2.59; P = 0.443). Being in a relationship was not further analysed as a potential confounder.

c. Odds of contactability for unemployed v. those who were employed.

d. There was no significant association between being a migrant and the outcome of 'ever been admitted' (OR = 1.12, 95% CI 0.449–2.82, P = 0.743). Being in a migrant was not further analysed as a potential confounder.

e. Discharge to general practitioner (GP) and time in psychiatric services not measured at baseline.

f. Being discharged to a GP was also strongly related to the outcome 'ever been admitted' (OR = 0.124, 95% CI 0.027–0.569, P = 0.007). This variable was included in future analyses as a potential confounder.

g. The total length of time spent in psychiatric care was highly skewed. Time was therefore log adjusted. The log of time ranged from 4.40 to 7.70 (mean 7.33, s.d. = 0.485). The relationship between contactability and the log of total time spent in psychiatric care is presented. Graphical analysis showed six outliers below the median. Statistical analysis of the relationship with the outliers removed did not alter the odds ratio significantly. However, log of total time spent in psychiatry (entered as a continuous variable) was not significantly associated with the outcome and so was not considered further as a potential confounder (OR = 1.74, 95% CI 0.834–3.67, P = 0.036).

h. There was a relatively small age span between the oldest and youngest participants. We therefore treated the potential relationship between odds of being contactable and age as linear; it is unlikely that the odds of being contactable would change significantly over such a relatively small age range.

Appendix DS1
Table DS2  Sensitivity analysis for ever been admitted (odds ratio (OR) of ever being admitted with 95% interval of uncertainty)\(^a\)

<table>
<thead>
<tr>
<th>Percentage of missing participants in specialist care assigned to 'admitted'</th>
<th>0% ((n = 0))</th>
<th>20% ((n = 4))</th>
<th>40% ((n = 7))</th>
<th>60% ((n = 11))</th>
<th>80% ((n = 14))</th>
<th>100% ((n = 18))</th>
</tr>
</thead>
<tbody>
<tr>
<td>0% ((n = 0))</td>
<td>1.26</td>
<td>1.63</td>
<td>2.07</td>
<td>2.44</td>
<td>2.89</td>
<td>3.26</td>
</tr>
<tr>
<td>20% ((n = 5))</td>
<td>0.549–2.89</td>
<td>0.733–3.62</td>
<td>0.956–4.50</td>
<td>1.14–5.23</td>
<td>1.36–6.10</td>
<td>1.56–6.84</td>
</tr>
<tr>
<td>40% ((n = 10))</td>
<td>0.460–2.31</td>
<td>0.615–2.89</td>
<td>0.802–3.59</td>
<td>0.959–4.17</td>
<td>1.14–4.87</td>
<td>1.30–5.45</td>
</tr>
<tr>
<td>60% ((n = 16))</td>
<td>0.370–1.92</td>
<td>0.530–2.40</td>
<td>0.691–2.98</td>
<td>0.827–3.46</td>
<td>0.990–4.04</td>
<td>1.13–4.52</td>
</tr>
<tr>
<td>80% ((n = 22))</td>
<td>0.318–1.48</td>
<td>0.426–1.85</td>
<td>0.537–2.29</td>
<td>0.666–2.67</td>
<td>0.797–3.11</td>
<td>0.907–3.48</td>
</tr>
<tr>
<td>100% ((n = 26))</td>
<td>0.287–1.31</td>
<td>0.383–1.64</td>
<td>0.501–2.03</td>
<td>0.599–2.36</td>
<td>0.718–2.75</td>
<td>0.817–3.08</td>
</tr>
</tbody>
</table>

\(^a\) Grey shaded area identifies analyses that would have resulted in a change in the conclusion, i.e. that the efficacy of the intervention had been diluted. The white area identifies sensitivity analyses that would have made no difference to the overall conclusions.

Fig. DS1  Schematic analysis for potential confounds.
Effect of early intervention on 5-year outcome in non-affective psychosis
Rafael Gafoor, Dorothea Nitsch, Paul McCrone, Tom K. J. Craig, Philippa A. Garety, Paddy Power and Philip McGuire
Access the most recent version at DOI: 10.1192/bjp.bp.109.066050

Supplementary Material
Supplementary material can be found at:
http://bjp.rcpsych.org/content/suppl/2010/05/04/196.5.372.DC1

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