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Early sustained recovery following first episode psychosis: Evidence from the AESOP10 follow-up study ☆

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ABSTRACT

Objective: To describe the characteristics of individuals with early sustained recovery following first episode psychosis.
Methods: Individuals with a first episode psychosis were followed-up for ten years. Comparisons were made between those with Early Sustained Recovery and those with Other Course types.
Results: Of 345 individuals, n = 43 (12.5%) had Early Sustained Recovery. They were more likely than those with Other Course types to be female (OR = 2.45; 95% CI: 1.25–4.81); employed (OR = 2.39; 95% CI: 1.22–4.69); in a relationship (OR = 2.68; 95% CI: 1.35–5.32); have a short DUP (OR = 2.86; 95% CI: 1.37–5.88); and have a diagnosis other than schizophrenia, particularly mania (OR = 6.39; 95% CI: 2.52–16.18) or brief psychosis (OR = 3.64; 95% CI: 1.10–12.10).
Conclusions: Sustained recovery from first episode psychosis occurs in a minority.

1. Introduction

A majority of individuals with a first episode psychosis experience symptom remission within the first year following contact with services (Wiersma et al., 1998; Robinson et al., 1999; Morgan et al., 2014). For some, this remission extends into sustained recovery with no subsequent psychotic episodes. For others, there will be relapse of symptoms. This can occur whether on treatment or not, though non-adherence with medication is strongly associated with relapse (Alvarez-Jimenez et al., 2012; Robinson et al., 1999). Other factors which have been identified in meta-analyses to be associated with relapse include premorbid adjustment and ongoing substance use, with some evidence for non-affective symptoms (Alvarez-Jimenez et al., 2012).

A related, but distinct, issue is whether there are useful predictors of sustained recovery following first episode psychosis. Alvarez-Jimenez et al. (2011) found that 16% of individuals aged 16–30 years with a first episode psychosis experienced only a single psychotic episode, defined as an index episode which did not exceed 12 months' duration, no further episodes, and being "virtually symptom-free and showing their premorbid personality" for a minimum of four weeks over a mean 7.5-year follow-up. Predictors of a single psychotic episode included short duration of untreated psychosis (DUP). We used the comprehensive dataset from the AESOP-10 longitudinal follow-up study of first episode psychosis in order to examine this question in a sample aged 18–64 years. We identified all individuals who achieved early sustained recovery. We aimed, first, to compare their demographic and clinical characteristics with those with other course types and, second, to describe patterns of medication use over follow-up in those with early sustained recovery.

Table 1
Demographic and clinical characteristics, and outcome measures of the Early Sustained Recovery and Other Course type individuals, showing unadjusted and adjusted odds ratios (OR) and 95% confidence intervals (CI).

	Other Course type (n = 302) no (%) or mean (SD)	Early Sustained Recovery (n = 43)	Unadj. OR	95% CI	p	Adj. OR (1)[a]	95% CI	p
Demographic								
Study Centre								
London	188 (62.3)	27 (62.8)	1.00	–	–	1.00	–	–
Nottingham	114 (37.7)	16 (37.2)	0.98	0.51–1.89	0.95	0.98	0.50–1.93	0.96
Sex								
Men	173 (57.3)	15 (34.9)	1.00	–	–	1.00	–	–
Women	129 (42.7)	28 (65.1)	**2.50**	**1.28–4.88**	**0.007**	**2.45**	**1.25–4.81**	**0.009**
Age								
16–29	158 (52.3)	20 (46.5)	1.00	–	–	1.00	–	–
30–64	144 (47.7)	23 (53.5)	1.26	0.67–2.39	0.48	1.15	0.60–2.21	0.67
Ethnicity								
White British	125 (41.4)	21 (48.8)	1.00	–	–	1.00	–	–
Other	177 (58.6)	22 (51.2)	0.74	0.39–1.40	0.36	0.72	0.37–1.39	0.33
Relationship status[b]								
Single	217 (75.3)	21 (51.2)	1.00	–	–	1.00	–	–
In a relationship	71 (24.7)	20 (48.8)	**2.91**	**1.49–5.68**	**0.002**	**2.68**	**1.35–5.32**	**0.005**
Employment[c]								
Unemployed	179 (60.3)	16 (37.2)	1.00	–	–	1.00	–	–
Employed	118 (39.7)	27 (62.8)	**2.56**	**1.32–4.96**	**0.005**	**2.39**	**1.22–4.69**	**0.01**
Education[d]								
University	34 (11.7)	5 (11.6)	1.00	–	–	1.00	–	–
Further	81 (27.9)	13 (30.2)	1.09	0.36–3.30	0.88	1.31	0.43–4.04	0.64
GCSE	75 (25.9)	13 (30.2)	1.18	0.39–3.57	0.77	1.48	0.48–4.60	0.49
No qualifications	100 (34.5)	12 (27.9)	0.82	0.27–2.49	0.72	0.95	0.31–2.93	0.92
Clinical								
Diagnosis								
Schizophrenia	145 (48.0)	9 (20.9)	1.00	–	–	1.00	–	–
Mania	32 (10.6)	15 (34.9)	**7.55**	**3.04–18.78**	**0.001**	**6.39**	**2.52–16.18**	**0.001**
Depression	44 (14.6)	7 (16.3)	2.56	0.90–7.28	0.08	2.17	0.74–6.34	0.16
Schizoaffective	14 (4.6)	3 (7.0)	3.45	0.84–14.24	0.09	3.18	0.76–13.26	0.11
Brief	20 (6.6)	5 (11.6)	**4.03**	**1.23–13.23**	**0.02**	**3.64**	**1.10–12.10**	**0.04**
Other	47 (15.6)	4 (9.3)	1.37	0.40–4.66	0.61	1.32	0.39–4.50	0.66
Dimensions[g]								
Reality distortion	3.8 (2.8)	2.9 (2.5)	0.87	0.76–1.00	0.05	0.88	0.76–1.01	0.07
Negative	1.3 (1.9)	0.5 (1.2)	**0.70**	**0.51–0.95**	**0.02**	**0.72**	**0.54–0.98**	**0.04**
Disorganised	1.3 (1.9)	0.5 (1.2)	0.86	0.57–1.29	0.46	0.88	0.58–1.34	0.55
Mania	1.5 (2.5)	2.4 (3.1)	1.12	1.00–1.25	0.05	1.10	0.98–1.23	0.12
Depression	1.2 (1.8)	1.6 (1.8)	1.11	0.94–1.33	0.23	1.10	0.92–1.31	0.30
Mode of onset[e]								
Acute	109 (41.6)	23 (57.5)	1.00	–	–	1.00	–	–
Insidious	153 (58.4)	17 (42.5)	0.53	0.27–1.03	0.06	0.59	0.30–1.19	0.14
DUP[f]								
Long	151 (51.9)	11 (25.6)	1.00	–	–	1.00	–	–
Short	140 (48.1)	32 (74.4)	**3.13**	**1.49–6.25**	**0.002**	**2.86**	**1.37–5.88**	**0.005**
Symptom severity[g]	8.5 (4.6)	8.0 (4.8)	0.97	0.90–1.05	0.50	0.97	0.90–1.05	0.49
Mode of admission								
Community treatment	94 (31.1)	14 (32.6)	1.00	–	–	1.00	–	–
Voluntary admission	96 (31.8)	13 (30.2)	0.91	0.41–2.04	0.82	0.81	0.36–1.85	0.62
Compulsory admission	112 (37.1)	16 (37.2)	0.96	0.45–2.06	0.92	0.86	0.39–1.88	0.70
Lifetime alcohol use[h]								
No misuse/dependence	233 (82.6)	38 (92.7)	1.00	–	–	1.00	–	–
Misuse/dependence	49 (17.4)	3 (7.3)	0.38	0.11–1.27	0.11	0.47	0.14–1.59	0.22
Lifetime illicit drug use[i]								
No misuse/dependence	217 (77.8)	31 (79.5)	1.00	–	–	1.00	–	–
Misuse/dependence	62 (22.2)	8 (20.5)	0.90	0.40–2.08	0.81	1.30	0.53–3.23	0.57
Outcomes								
Treatment at 12 months[j]								
On treatment	128 (50.8)	29 (85.3)	1.00					
Not on treatment	124 (49.2)	5 (14.7)	**0.17**	**0.06–0.45**	**0.001**	**0.18**	**0.07–0.48**	**0.001**
Full recovery at follow up[k]								
Clinical only	26 (11.3)	16 (45.7)	1.00					
Clinical and functional	205 (88.7)	19 (54.3)	**0.15**	**0.07–0.33**	**0.001**	**0.14**	**0.06–0.32**	**0.001**

Bold indicates significance at p > 0.05 level.

[a] Adjusted for, as appropriate, sex and age (as continuous variable).
[b] Missing, 16.
[c] Employed or economically inactive missing, 5.
[d] Missing, 12.
[e] Missing, 43.
[f] Missing, 26.
[g] Missing, 34.
[h] Missing, 22.
[i] Missing, 27.
[j] Missing, 59.
[k] Missing, 79.

2. Materials and methods

2.1. Setting

AESOP-10 is a follow-up at approximately 10 years of a cohort of individuals with a first episode of psychosis identified in the South East London and Nottingham centres of the AESOP study (Kirkbride et al., 2006). Full methods are detailed in Morgan et al. (2014).

2.2. Cases

Inclusion criteria: aged 16–64 years with a first episode of psychosis; resident within the study catchment areas. Exclusion criteria: evidence of psychotic symptoms precipitated by an organic cause; transient psychotic symptoms resulting from acute intoxication as defined by ICD–10 (WHO, 1993); previous contacts with mental health services for psychosis; moderate/severe learning difficulties, or IQ < 50 (WHO, 1993).

2.3. Follow-up

Cases were followed-up ten years after first contact with mental health services. Of 532 incident cases, 458 remained after removing those who had died, emigrated, or been excluded (Morgan et al., 2014). Full ethical approval was provided by the local research ethics committees.

2.4. Measures

2.4.1. Baseline

Clinical and demographic data were collected from interview, informants, and clinical records. The SCAN version 2 (WHO, 1992) was used to assess symptom presence and severity. This was used in conjunction with other clinical information (excluding diagnosis) to assign ICD-10 (WHO, 1993) psychotic diagnoses within research-team consensus meetings. The Personal and Psychiatric History Schedule (WHO, 1996) was used to determine DUP, defined as the period from onset of psychosis to first contact with mental health services. Onset of psychosis was defined as the presence for one week or more of psychotic symptoms (Morgan et al., 2006).

2.4.2. Follow-up

The WHO Life Chart Schedule (Harrison et al., 2001) was used to collate information at follow-up. It comprises four main areas: symptoms; treatment; residence; and work. It was adapted to include additional information on service use, including use of prescribed medication. Course of illness was categorised as follows: Early Sustained Recovery (remission within six months and no further psychotic episodes over 10-year follow-up) and Other Course comprising episodic (no episode longer than six months' duration), continuous (no remission longer than six months' duration) and intermediate (neither episodic nor continuous).

2.5. Statistical analyses

Conducted using SPSS Statistics Version 22 (IBM 2013). Categorical variables were analysed using logistic regression. Comparisons were made between the Early Sustained Recovery and Other Course groups, adjusting for age and sex.

3. Results

3.1. Demographic and clinical characteristics

Of the 458 baseline cases, useable information on clinical course and outcome was available for 345 (75.3% of 458): Early Sustained Recovery (ESR) (n = 43; 12.5%) and Other Course (OC) (n = 302; 87.5%). OC comprised episodic n = 69 (20%), continuous n = 80 (23.2%), and intermediate n = 153 (44.3%). Median age at baseline for the total sample was 29.0 (range 16–62) (mean = 30.5 ± 10.2(SD)) years. Median age for the ESR group was 30.0 (range 17–56) (mean = 31.8 ± 10.5(SD)) years, and for the OC group 29.0 (range 16–62) (mean = 30.4 ± 10.1 (SD)) years (MWU = 5994.5, p = 0.42).

ESR individuals were predominantly women (65.1%) and employed (62.8%) (Table 1). They were more likely than OC to be in a relationship (OR = 2.68; 95% CI: 1.35–5.32) and to have a short DUP (OR = 2.86; 95% CI: 1.37–5.88). They were more likely at baseline to have a diagnosis other than schizophrenia, with the evidence being most robust for mania (OR = 2.39; 95% CI: 1.22–4.69) and for brief psychosis (OR = 2.39; 95% CI: 1.22–4.69). ESR individuals had fewer negative symptoms (OR = 0.72; 95% CI: 0.54–0.98) and, more tentatively, fewer symptoms of reality distortion (OR 0.88; 95% CI 0.76–1.01) and more manic symptoms (OR 1.10; 95% CI 0.98–1.23). There was no strong evidence of differences between groups in age, study centre, ethnicity, educational level attained, mode of onset, symptom severity at first episode psychosis, non-hospitalisation at first episode psychosis, compulsory treatment at first episode psychosis, or lifetime alcohol or illicit drug misuse (Table 1). A logistic regression model of ESR on gender and diagnosis demonstrated that gender was no longer a significant predictor, while mania and brief psychoses each significantly predicted ESR (Table 2).

3.2. Medication use during follow-up

ESR individuals were less likely to be taking treatment at 12 months post-first episode psychosis (OR = 0.18; 95% CI: 0.07–0.48). They were more likely to be in full functional recovery at follow-up (OR = 7.17; 95% CI: 3.17–16.18) (Table 1). Patterns of taking treatment differed between the groups (X^2 = 98.61, p = 0.001) (Table 3): 95% of ESR individuals took antipsychotic treatment at the time of first episode psychosis; 17.9% restarted treatment at some later point during the follow-up; and 74.4% stopped and never restarted. The median duration of treatment was 53 days (SD: 276.7; range: 0–1393; mean: 154.2). Around 20% took treatment for 14 days or less. Only one individual took treatment throughout follow-up.

Treatment during follow-up for conditions other than psychosis was received by 19 (44.2%) for hypomania with or without depression; 7 (16.3%) depression; 1 post-traumatic stress disorder; and 1 alcohol abuse. A further 7 (16.3%) reported periods of depression with or without anxiety for which they did not seek treatment. Nine (20.9%) made attempt(s) to kill (7) or harm themselves (2) over the follow-up period, based on the individual's reported intent.

4. Discussion

One in eight individuals with first episode of psychosis recovered early and never experienced a recurrence over ten-year follow-up. This is important and relevant to clinical decision-making following first episode psychosis, when a key question raised is: what is the risk of relapse (or continued symptoms) following a single episode of

Table 2
Logistic regression model of early sustained recovery on gender and diagnosis.

Independent variable	Odds ratio ± 95% CI[a]	p
Female gender	1.91 (0.95–3.84)	0.07
Diagnosis		**0.03**
Mania	6.38 (2.52–16.14)	**<0.001**
Depression	2.25 (0.78–6.48)	0.13
Schizoaffective	3.24 (0.78–13.51)	0.11
Brief	3.67 (1.11–12.19)	**0.03**
Other	1.32 (0.39–4.52)	0.65

Bold indicates significance at p > 0.05 level.
[a] Odds ratios and 95% Confidence Intervals for each variable as an independent predictor of early sustained recovery.

Table 3
Patterns of treatment in the Early Sustained Recovery and Other Course type groups.

	Other Course type (n = 302)	Early Sustained Recovery (n = 43)	Statistic, p-value
Antipsychotic medication (n; %)[a]			$X^2 = 98.61$, p = 0.001
Took treatment at first episode psychosis and continued throughout follow-up	50 (20.2)	1 (2.6)	
Took treatment at first episode psychosis, stopped treatment and later restarted	136 (54.4)	7 (17.9)	
Took treatment at first episode psychosis, stopped treatment and never restarted	28 (11.2)	28 (71.8)	
Did not take treatment at first episode psychosis, but later took treatment	34 (13.6)	1 (2.6)	
Never took treatment	1 (0.4)	2 (5.1)	

[a] Missing n = 59.

psychosis? Our findings suggest around 88% (or 7 in 8). Early sustained recovery was more common among women of any age, those with a short DUP, those with a diagnosis other than schizophrenia, and those who had good premorbid function, as evidenced by being employed and in a relationship. Half the group had an affective psychosis, in keeping with evidence that affective disorders generally follow more favourable trajectories than non-affective disorders (Bottlender et al., 2010). Of note, in the logistic regression model of early sustained recovery on gender and diagnosis, the effect of gender was explained by diagnosis, with mania and brief psychoses significantly predicting early sustained recovery.

Only 15% of individuals with early sustained recovery were taking treatment by 12 months post-first episode psychosis, despite 95% being initiated on an antipsychotic. These data pertain to a second clinical question: for how long should antipsychotic treatment be maintained? Some argue that, "treatment discontinuation should not be a part of routine clinical care" (Emsley et al., 2013). Others make the case that there is little evidence that antipsychotic medications reduce or eliminate psychosis (Harrow et al., 2014): over 20-year follow-up >70% of schizophrenia patients continuously prescribed antipsychotics experienced psychotic symptoms at the majority of follow-up assessments. Further concerns associated with long-term treatment include its potential cumulative detrimental effects on physical health and brain structure (Murray et al., 2016).

Only one individual with early sustained recovery did not attempt a trial off antipsychotic treatment, that is, remained on treatment throughout follow-up. It is clear, however, that in a minority there is sustained recovery without treatment: 74.4% of our sample stopped antipsychotic treatment and never restarted. There is a known paradox in discontinuation studies: while up to 50% of patients with schizophrenia relapse by 6–10 months following discontinuation, those who remain stable during the first few months post-discontinuation are much less likely to relapse subsequently (Viguera et al., 1997). This is made more likely where withdrawal from treatment is gradual rather than abrupt (Viguera et al., 1997). We argue, therefore, that where an individual has sustained a period of remission, reduction and/or gradual discontinuation of antipsychotic treatment are legitimate management options, albeit with significant associated risks. If low-grade symptoms recur, treatment can be reintroduced. Indeed, this is the most likely explanation for our finding that seven (18%) individuals with early sustained recovery restarted treatment at some later point during the follow-up despite never again meeting criteria for a further psychotic episode.

Finally, regular monitoring should remain a mainstay of treatment. Despite achieving sustained recovery from psychosis, 40% of the individuals with early sustained recovery experienced considerable psychiatric morbidity over 8-year follow-up, with over 40% receiving treatment (not antipsychotic) for other conditions, and 20% self-harming or attempting suicide.

In conclusion, our naturalistic study of outcomes following first episode psychosis provides evidence that in a minority there is early sustained recovery. This is more likely in women of all ages, those

with good premorbid adjustment, and those with brief or affective psychotic symptoms. Due consideration should be given to the risks and benefits of continued treatment in those with sustained symptomatic remission.

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