

DOES EARLY INTERVENTION FOR PSYCHOSIS WORK? An analysis of Outcomes of Early Intervention in Psychosis based on the Critical Period Hypothesis, Measured by Number of Admissions and Bed Days Used over a period of Six Years, the first three in an Early Intervention Service, The second Three in a Community Mental Health Team

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SUMMARY

Background: Early Intervention in Psychosis (EI) was introduced into the British NHS as a result of the NHS Plan, about eleven years ago. The intention was to provide the best possible care for patients with a first episode of psychosis. Recently however, long term studies over five years have suggested that early gains may be lost.

Methods and Aims: We wished to establish whether our own group of patients who had received Early Intervention continued over six years to have better outcomes than patients treated in Community Mental Health Teams. To do this we analysed statistically the data on the readmissions and bed days used by our patients over the first six years of illness.

Results: We found that patients, both in the whole two groups and in different sub-groups appeared to demonstrate a number of advantages, not always statistically significant, in favour of the EI treated team.

Discussion: In many cases, the small size of the samples may have impeded us observing statistically significant differences, however, in general, it appeared that there were a number of advantages in favour of the EI treated team.

Conclusion: Our study, though small, does appear to support the view that Early Intervention Services do improve outcomes and that some of the improvement may endure after the patient leaves EI services. Much larger studies are however required.

Key words: Early Intervention – psychosis - statistical analysis

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Introduction

Early Intervention in Psychosis (EI) was introduced into the British NHS as a result of the NHS Plan, about eleven years ago. The model of EI which was introduced into the NHS was based on the 'Critical Period Hypothesis', first developed by Max Birchwood, in Birmingham (Birchwood 1998). This hypothesis suggested that, there is often major change in the psychosocial functioning of patients with schizophreniform illnesses within the first three years of the onset, but that thereafter, the deterioration tends to plateau out. Therefore the first three years of the illness could be described as a 'critical period' during which the future course and prognosis of the illness is set. The British Early Intervention Services are designed to intervene during these first three years, beginning at the point that a first psychotic episode is identified. Hence, at the end of three years, patients are transferred from the EI service to a Community Mental Health Team for further treatment or to primary care if all symptoms have subsided and the patient has improved.

It is important for the subsequent discussion to summarise the reasons that have been put forward for working in this way and the objectives of treatment, and

hence the expected outcomes. These were summarised by Birchwood et al. in the IRIS Guidelines and have been recently restated by the present author in a review article (IRIS 1999, Agius 2010). It was felt that there is usually a long delay between the beginning of psychotic symptoms, and effective treatment, that the longer persons with psychosis remain untreated, the greater the likelihood of harm, be it physical, social or legal, that social and personal disability becomes rapidly evident in the first few years of psychosis, that early treatment with anti-psychotic drugs is known to improve the further development and prognosis of a psychotic illness, while if treatment of psychosis is delayed, there are substantially higher health care costs for the first three years after treatment is initiated, that treatment resistant symptoms tend to develop in the first three years, otherwise known as the critical period, and finally that the tendency to repeated hospital admissions began in the first three years, or critical period. Hence a rationale developed to treat patients with a first psychotic episode in a specialised manner (IRIS 1999). This rationale included the facts that it is likely that patients who have had their first episode of psychosis will recover well in the short term, that relapse during the early course of psychosis lead to an increased likelihood of further

relapses and chronic illness, that if a decline in function occurs in a psychotic illness, the decline will occur early in the illness, or even in the prodromal phase, before clear psychotic symptoms were manifested. This meant that the first three years of psychosis are a ‘critical period’ in biological terms, but the first few years of psychosis are also a ‘critical period’ from the psychosocial point of view.

Hence IRIS set out Guiding Principles for early intervention services (IRIS 1999). These were that an early psychosis service should have a youth and client centred focus, that if the patient fails to engage, his case should not be closed, that there should be an emphasis on maintaining the client’s social roles, that psychiatric treatment should be delivered in the least restrictive setting possible, so long as treatment can be delivered effectively and safely, that treatment should be delivered in such a way as to avoid stigma, that the dose of neuroleptics should be the lowest dose which will effectively treat the symptoms, and that it must be accepted that in the early phases of a psychotic illness, a definitive diagnosis may be impossible to make because of the day to day variability of symptoms, while the family must be fully involved in all aspects of the care of the patient.

Thence IRIS developed Clinical Guidelines (IRIS 1999). These were as follows:

- A strategy for early detection and assessment of frank psychosis is an essential component of early intervention;
- Following referral of the case, a key worker (otherwise called a care coordinator) should be appointed soon, in order to engage with the client and family/friends through the first three years (the critical period) within a model of assertive case engagement;
- An assessment plan and collaborative assessment of needs, which is both comprehensive and collaborative, and driven by the needs and preferences of the client and their relatives and friends should be drawn up;
- The management of acute psychosis should include low dose, preferably atypical, antipsychotics and the structured implementation of cognitive therapy;
- Family and friends should be actively involved in the engagement, assessment, treatment and recovery process;
- A strategy for relapse prevention and to counter treatment resistance should be implemented;
- A strategy to facilitate the client’s return to work and valued occupation should be developed in the critical period;
- Ensure that the basic needs of daily living- housing, money and practical support – are met;
- Assessment and treatment for co-morbidity should be undertaken in conjunction with similar processes for psychosis;

- A local strategy to promote a positive image for people with psychosis needs to be adopted.’

Thus it should be self evident from these stated objectives of early intervention that the aim is to provide optimal treatment to patients suffering from a first episode of psychosis whatever the outcome of that illness, and this hopefully improve the prognosis of the illness, not necessarily to ‘stop’ or cure psychosis. The expected outcomes of an Early Intervention Service are optimum Process outcomes over the first three years of illness, not curative outcomes.

Nonetheless, a number of studies have been carried out to attempt to show that outcomes of patients in Early Intervention services are better than those who receive ‘Treatment as Usual’ in Community Mental Health Teams. Since at present all patients with a first episode of psychosis are referred to Early Intervention services, it is unlikely that such studies will be repeated in England. Three studies have been reported, the LEO study in Lambeth, The OPUS study from Denmark, the Moscow Research Institute study and our own study. Another study, the Moscow Research Institute study, had somewhat different goals and end points.

The Leo study from the UK has shown that the early intervention group were less likely to relapse, were re-admitted fewer times, and were less likely to drop out of the study than those receiving CMHT care. However, when adjustment was made for sex, previous psychotic episode and ethnicity, the difference in relapse rate ceased to be significant (Craig et al. 2004). At 18 months, outcomes from the participants receiving care from the Early Intervention team were significantly better for aspects of social and vocational functioning, satisfaction, quality of life and medication adherence. Symptom improvement did not differ significantly between the groups (Garety et al. 2006).

Our own group reported on sixty-two patients who had been treated for three years in an ad-hoc, assertive treatment team for patients who had suffered a first psychotic episode, and compared their outcomes to sixty-two patients who had been followed up after a first psychotic episode in a standard community mental health team (Agius et al. 2007). All patients had suffered a first or early psychotic episode. The main differences between the two teams were that the ad-hoc team was assertive in its approach, offered more structured psycho-education, relapse prevention and psychosocial interventions, and had a policy of using atypical anti-psychotics at the lowest effective dose.

There were many differences in outcome measures, at the end of three years, between the two groups. The EI patients were more likely to be taking medication at the end of three years. They were more compliant with medication. They were more likely to be prescribed Atypical Medication. The EI patients were more likely to have returned to Work or Education. The EI patients were more likely to remain living with their families.

They were less likely to suffer depression to the extent of requiring antidepressants. They committed less suicide attempts. The patients in the EI service were also less likely to suffer relapse and re-hospitalisation, and were less likely to have involuntary admission to hospital. They had systematic relapse prevention plans based on the identification of Early Warning Signs of relapse. They and their families received more psycho-education. These facts suggest that the EI patients are at the end of three years better able to manage their illness/vulnerability on their own than the CMHT patients. More patients in the EI group stopped using illicit drugs than in the CMHT group.

All the above changes were statistically significant except for the total improvement in employment status and education status, which however approached significance.

These results do suggest that an ad-hoc Early Intervention Team is more effective than standard Community Mental Health Team in treating psychotic illness.

Recently there have been further reports from the OPUS Study. This involved a 2-year assertive intervention from an Ad Hoc team, and now the team has reported on 5-year follow up once the assertive interventions had ceased at the end of the second year. The intensive early-intervention program improved clinical outcome after 2 years (Nordentoft et al. 2002, Nordentoft et al. 2006, Petersen et al. 2005, Thorup et al. 2005) but the effects did not appear to be sustained at 5 year follow up (Bertelsen et al. 2008). However the number of patients living in supported housing and number of days in hospital at 5-year follow up appeared to favour the assertive early-intervention program (Bertelsen et al. 2008). It has also been reported that the rates of recovery (defined as no psychotic or negative symptoms, living independently, GAF (f)>59, working or studying) and institutionalisation at 2 years and 5 years during this study were the same, being 18% recovery after five years, and 13% were institutionalised either at hospital or supported housing after five years. Thus it appeared that in this group, the illness did not deteriorate progressively, since no changes in the rates were seen from two to five years (Bertelsen et al. 2009). This probably shows that only a proportion of patients deteriorate progressively; previous studies suggesting that those who deteriorate form about 16% of all patients with schizophrenia. OPUS have also reported that patients who were offered inpatient rehabilitation and supportive psychotherapy used more hospital bed days and spent more time in sheltered accommodation than those who were given assertive treatment in the community. Although this was a small sample, it did suggest that patients who received assertive treatment for two years had a better quality of life over five years (Thorup et al. 2010). In general, it does then appear that assertive early intervention during the critical period offers better results than treatment as usual.

Last May, LEO reported its five year outcome data (Gafoor et al. 2010). Patients had been referred to CMHTs after 18 months of assertive treatment. LEO studied the outcomes at 5 years based on the number of Admissions and the number of Bed Days, comparing the group who had received assertive treatment from the LEO team for 18 months and where then transferred to the group who had always been treated in CMHTs.

These studies showed that there was no difference in the admission rate or in the number of bed days used after 5 years in the two groups. This led to editorial speculation in the British Journal Of Psychiatry as to the Usefulness of Early Intervention in Psychosis (Friis 2010), and it was pointed out that 'specialised treatment for people with first-episode psychosis is effective as long as the treatment continues'. 'However, at the same time the lack of long-term effect indicates that the individuals are still vulnerable even after a successful 2-year specialised treatment programme' (Friis 2010). In the same issue of the Journal, Swaran Singh (Singh 2010) argued that 'Once the early intervention 'grip is relaxed' clinical gains are lost; interventions are therefore effective only as long as actively implemented.', (Singh 2010) and furthermore 'The second possibility is that the heterogeneous trajectories of early psychosis require differentiation, with early intervention provision being tailor-made for longer periods for those with poorer early outcomes' (Singh 2010), also, 'Third, early intervention services are a complex intervention with several interacting components. We need further understanding of how this complex intervention works, i.e. what are the active 'therapeutic ingredients' within early intervention services and how these are exerting their effect. This would also inform the kind of 'maintenance' care to assure that these hard-won early gains are not lost over time' (Singh 2010).

Methods

As a contribution to this discussion we publish a statistical analysis of data from our own study. The two groups which are compared are those we have previously reported on. Each group consisted of 62 patients and have already been described (Agius et al. 2007). The Early Intervention group had received treatment for 3 years in an Early Intervention team, while the control group had received treatment only in a CMHT. After three years, the EI group patients were transferred to CMHT or in some cases to primary care. We were able to abstract data on admissions and bed days used from year 1 to year 6 from the Trust Computer. However, subsequently all data has been anonymised and it is now not possible to identify individual patients, nor was it possible to do so at the time of the analysis so that only the statistics were available when we analysed the data. Thus we carried out an anonymised audit of outcomes from our service, over the first six years, including three years in the early

intervention service and three subsequent years in Community Mental Health Teams or primary care.

It is of importance that we had previously (Agius et al. 2007) reported regarding admissions that in three years, there were:

‘CMHT total admissions	137
EI total admissions	77
With	
CMHT total relapses	92
EI total relapses	129
CMHT relapses treated outside hospital	16
EI relapses treated outside hospital	63’

And statistically, ‘Regarding Relapses; CMHT (non-hospital relapses n=16, total relapses n=92) EI (non-hospital relapses n=63, total relapses n=129) A χ^2 test ($\chi^2=23.12$, $df=1$, $p<0.0001$) showed a significant relationship between whether a relapse occurred to a CMHT patient or an EI patient and whether or not this resulted in hospitalisation or not.’

Now we have been able to identify each relapse as it occurred per each year, and the number of bed days that it caused.

We have searched for statistically significant comparisons of admissions and bed days used in each year using t-tests, chi-squared tests and Mann-Whitney tests. SPSS and Graphpad Prism Software were used to carry out the analysis.

We have also examined the data in order to identify the heterogeneous trajectories of different patients with early psychosis and differentiate between them, thus identifying groups of patients who might have more favourable or poorer early outcomes. We have done this by examining the data ‘by hand’ and identifying different admission patterns among the patients on the premise that different patients will have different patterns and that those with most admissions or bed days were the ‘most ill’ and hence most likely to have poorer outcomes.

We have then used the statistical data to ‘model’ different ways of assessing the outcomes to search for statistically significant patterns which might illustrate how the illness progresses and how this influences outcome. Thus, what we have done is an audit, approved by our audit department, and some statistical modelling, using a series of figures generated anonymously.

Results

In terms of the raw data, the number of admissions and the number of bed days resulting from them are reported as follows (Tab. 1, Tab. 2.).

Table 1. Raw data of individual admissions and bed days per patient in both the early intervention (EI) and the control groups

Patients	Admissions	Control Group	Year 1	Year 2	Year 3	Year 4	Year5	Year 6
1	1	1	1			3		
2	1	2						
3	1	1						1
4	1	1	1					
5	1	1	1					
6	2					1		
7	1			1				
8	1							
9	2	1				1		
10	1	1	3					1
11	1							
12	1							2
13	1							
14	2							
15	1			1				
16	2	1						
17	1	2	1					1
18	1		1				1	
19	1		2		2			
20	1	2					2	1
21	1	2						
22	1		1					
23	1							
24	1					1		
25							1	
26	2	1	1		1			
27	1	1						
28	1							
29	1							
30	2	1						
31	1							
32	3	1						
33	2		1					
34	2					1		
35	1	3	1					1
36	1							
37	1		1					
38	1	1	2					
39	1	2	1					1
40	1							
41	1		1		1		1	1
42	1	1	1		1			1
43	2	1	2				2	
44	1	1	1					1
45	1	2			1		2	
46	1		1		1			
47	1							
48	2							
49	1	3	1				2	
50	1	2						
51	2							
52								
53								
54								
55								
56								
57								
58								
59								
60								
61								
62								
Total	63	35	27	14	11	11		

Patients Bed Days Control Group							Patients Admissions EI Group						
Patients	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	Patients	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
1	52	55	137	131			1	1		1			1
2	5	23					2	1					
3	30	16				35	3	1				2	
4	54	3	7				4	1					
5	74	292	39				5	1	1				
6	88			52			6	1					
7	14		54				7	1					
8	14						8	1	2	1	1	2	
9	88	113		11			9	1	1	1			
10	25	32	98			78	10	2		1	1		
11	124						11	1					
12	22					194	12						1
13	33						13	1					
14	52						14	1					
15	14		54				15	1		1			
16	115	27					16	1				1	
17	9	38	96			19	17	1		1			
18	4		98		62		18	2		1		1	1
19	4		28	77			19	1		1			
20	8	125			29	583	20						1
21	23	61					21	1					1
22	24		31				22	1	1	1			
23	1						23	1					
24	56			16			24	1		1		1	
25					27		25	1					
26	29	28	19	42			26	1					
27	6	64					27	1	1		1		
28	78						28	1	1	3			
29	35						29	2	1				
30	120	33					30	4	3	3	3		
31	51						31	1		1	2		
32	216	11					32	2					
33	99		17				33	1	3				
34	148			52			34	2					
35	28	75	27			45	35	1					
36	253						36	1		1			
37	17		273				37	1				1	
38	17	64	159				38					1	1
39	55	14	8			15	39	1	1	1		1	
40	6						40			1			
41	84		59	49	238	183	41	2			1		
42	1	111	64	181		76	42	1					
43	15	200	354		160		43	3	1	1	1	1	
44	25	46	13			75	44						
45	1	44		4	1240		45						
46	19		54	18			46						
47	44						47						
48	48						48						
49	6	2	328	3		245	49						
50	81	73					50						
51	41						51						
52							52						
53							53						
54							54						
55							55						
56							56						
57							57						
58							58						
59							59						
60							60						
61							61						
62							62						
Total	2456	1550	2017	636	1756	1548	Total	50	16	21	10	11	6

Patients	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
1	28		28			15
2	42					
3	3				192	
4	12					
5	60	5				
6	16					
7	4					
8	30	201	34	18	25	
9	49	97	70			
10	27		39	24		
11	40					
12						65
13	46					
14	27					
15	9		99			
16	26				838	
17	27		96			
18	240		46		38	30
19	122		8			
20						42
21	8					36
22	36	35	133			
23	17					
24	12		8		23	
25	9					
26	7					
27	1	10		86		
28	45	64	654			
29	70	95				
30	72	57	55	113		
31	29		34	112		
32	57					
33	10	34				
34	14					
35	19					
36	52		11			
37	5				37	
38					27	93
39	103	77	327		101	
40			1			
41	76			64		
42	47					
43	255	322	4	74	64	
44						
45						
46						
47						
48						
49						
50						
51						
52						
53						
54						
55						
56						
57						
58						
59						
60						
61						
62						
Total	1752	997	1647	491	1345	281

Table 2. Total admissions and bed days in the two groups per year over six years

Admissions						
	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Control	63	35	27	14	11	11
EI	50	16	21	10	11	6

Bed Days						
	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Control	2456	1550	2017	636	1756	1548
EI	1752	997	1647	491	1345	281

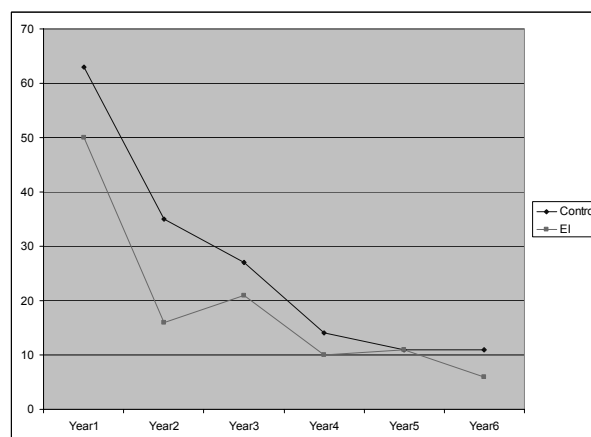


Figure I. Admissions per Year

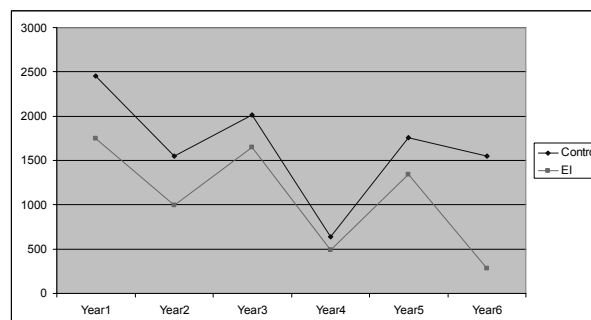


Figure II. Bed Days per Year

Patterns were noted in how there are heterogeneous trajectories of early psychosis which can be differentiated on the basis of different admission rates. Hence different groups can be identified with poorer or more favourable outcomes as follows:

- There were less admissions in the EI group compared to control in year 1; year 2; year 3; year 4; year 6; and in year 5 numbers were equal in both groups;
- 43 EI patients Vs 51 control patients had at least 1 admission in the follow up period;
- 19 EI patients had no admissions at all compared to 11 control patients;
- There was a general trend over the years to have decreasing total number of patient admission in both groups;
- 2 patients in EI group had their first admission in year 6;

- 1 patient in EI group had their first admission in year 5; then a further admission in year 6;
- 1 patient in EI group had their first admission in year 3;
- In the control group only 1 patient had their first admission in year 5;
- 12 EI patients had 1 admission in year 1 then no more admissions at all (Vs 10 in the control group);
- 2 EI patients had 2 admission in year 1 then no further admission at all (Vs 3 in control group);
- There is a group of possibly “more unwell” or “chronic” subtype of patients in the EI group:
 - 1 Patient had 4 admissions in year 1; 3 in year 2; 3 in year 3; 3 in year 4;
 - 1 patient had 1 admission in year 1; 2 in year 2; 1 in year 3; 1 in year 4; 2 in year 5;
 - 1 patient had 3 admissions in year 1; 1 in year 2; 1 in year 3; 1 in year 4; 1 in year 5.

Statistical Analysis and Interpretation for EI vs Control group data

We carried out chi-squared tests between EI and control groups with respect to:

1. Number of admissions in each year
2. Any admissions in each year (yes/no)
3. Number of bed days in each year grouped into none, 1 – 30 and more than 30.

These showed significant differences between the two groups for:

1. number of admissions in year 2 only (chi-squared test for linear association =5.11; p=0.024)
2. any admission in year 1 (Fisher’s exact test p=0.045) and year 2 (Fisher’s exact test p=0.016)
3. grouped number of bed days in year 1 (chi-squared test for linear association=4.25; p=0.039) and year 2 (chi-squared test for linear association =4.90; p=0.027)

We also carried out two-tailed student t-tests and Mann-Whitney tests to compare EI with the control group with respect to the number of admissions in each year and number of bed days in each year. The t-tests showed significant differences between the two groups for number of admissions in year 2 only (p=0.023).

The Mann-Whitney tests show significant differences between the two groups for both the number of admissions (p=0.041) and the number of bed days in year 1 (p=0.049) and again the both the number of admissions (p=0.009) and the number of bed days in year 2 (p=0.018).

Discussion

The most important result which arises from the above analysis is that Early Intervention can be shown to reduce admissions to hospital more than treatment in

CMHTs as usual by some statistical tests during the first two years of the intervention. In our previous publication, quoted above, we showed that over a three year period, Early Intervention led to significantly fewer admissions than Treatment as usual in a CMHT, hence it appears that the ‘statistically significant difference’ is in the first two years of the intervention. This is consonant with the findings from LEO and OPUS, which showed better results in the first 18 months and first 2 years than treatment as usual. However the assumption has been that, when subsequently, five year outcomes for both studies showed a loss of statistical significance in the measured outcomes of both studies, this was due to the transition of Patients to CMHTs, and hence the loss of assertive intervention. However, since in our study, statistical significance is lost during the third year, while assertive intervention is still going on, we must consider another possibility; that the inexorable advance of the illness does, once it has started, outstrip any protective effect that assertive intervention may assert. On the other hand, these results are in fact consonant with all the outcomes expected by an EI service, as described above; optimal process outcomes will be provided by an EI service, but they will not prevent all relapses and readmissions, nor would we expect that all residual symptoms will be prevented, indeed, even on the third year, we had in our previous report pointed out that some of our patients, while being able to function, and even attend university and qualify, did, none the less, continue to suffer positive symptoms of schizophrenia.

A second finding arises, which favours Early Intervention over Treatment as Usual in Our Sample.

This is that over six years, 19 patients in the EI group (30.65%) and 11 patients in the Control Group (17.74%) never had an admission over six years (Figure 1). Hence there is twice as much a possibility of not ever having an admission in the EI group than in the Control Group. According to the results of a chi-squared test, this difference is real (odds ratio= 0.49) however, it did not reach statistical significance (p>0.05). The strong value of the odds ratio suggests a hint that EI is overall protective in terms of having no admissions at all but perhaps the small size of our cohorts hinders the result from becoming statistically significant.

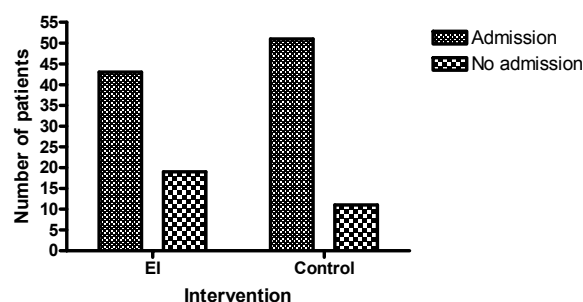


Figure 1. Number of patients without any admission over the six-year period

Again this is consonant with the consequence of the expected process outcomes of the Early Intervention service. This effect was maintained for these patients for three years after they were transferred from the EI service to the CMHTs. However, this finding could be explained by selection of less serious cases in the EI group, although this was not our intention. We only reported the outcomes of the patients referred by other doctors to the EI service. Nor did we specifically seek out more difficult patients to be used as the control group. Our recruitment procedures are described in our previous publication (Agius et al. 2007).

Hence, and given the different patterns of admission/relapse within the patients of both groups, it is necessary to further study the effect of the EI service intervention on patients who tend to have more relapses (and hence are presumably 'more ill') and compare this to treatment as usual.

In the Control Group, out of 62 patients, 50 suffered admissions in years 1 to 3 (82.26%), while 23 suffered admissions in years 4 to 6 (37.10%). In all except one patient, all patients in the Control group who had admissions in years 4 to 6 also had had at least one admission in years 1 to 3.

In the EI Group, out of 62 patients, 40 suffered admissions in years 1 to 3 (69.35%), while 18 suffered admissions in years 4 to 6 (29.03%). In all except one patient, all patients in the EI group who had admissions in years 4 to 6 also had had at least one admission in years 1 to 3.

Given the above, we carried out a chi-squared test to investigate whether 40 (the number of patients in EI group who had admissions in years 1-3) is significantly lower than 50 (the number of patients in Control group who had admissions in years 1-3) (Figure 2). Indeed we found that this difference was statistically significant (Odds ratio=0.36; p=0.018).

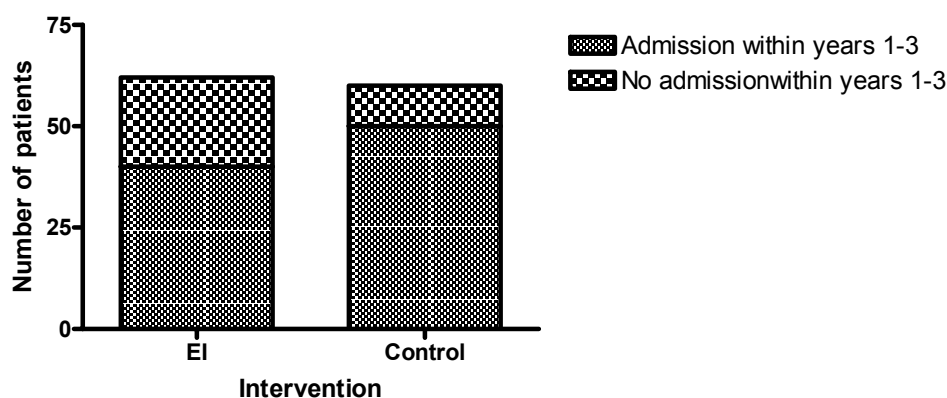


Figure 2. Number of patients with at least 1 admission over years 1-3

Furthermore, when the same subgroup of patients, with at least one admission over years 1-3, was compared for the number of bed days rather than admissions using a non-parametric Mann-Whitney t-test to compare medians, statistical significance was once again obtained. This suggested that on average, individual patients in the EI group were admitted with a significantly lower number of total bed days than patients in the control group (p=0.018).

In contrast to years 1-3, when the same statistical analysis was carried out to compare the two treatment subgroups over years 4-6 statistical significance was lost both in terms of number of patients with at least one admission and the number of bed days for this subgroup of patients. Nevertheless, hints of protective effects emerged as suggested by the chi-squared test results despite lack of statistical significance (odds ratio=0.69) when comparing the number of patients in the EI group to those in the control group who had at least one admission in years 4-6.

Additional subgroups of patients were identified.

In both groups, some patients suffered multiple admissions during the first three and last three years.

We believe that these patients represent a more severely ill subgroup and thus, we investigated a possible protective effect of the EI intervention in two ways in these more seriously ill groups.

1. Arguably, the most severely ill patients are those who have had more than one (2 or more) admissions in years 4-6.

In the control group, 9 patients had more than one admission in years 4-6. Of these, 8 had more than one admission years 1-3.; the other patient had one admission in years 1-3.

In the EI group, 7 patients had more than one admission in years 4-6. Of these all but 1 had more than one admission in years 1-3. The final patient had no admissions in years 1-3.

These findings are consonant with the critical period hypothesis; multiple admissions in the first 3 years predispose to multiple admissions in the subsequent three years.

The difference between the two groups, according to a chi-squared test, was not significant in this aspect.

However, to our surprise, when we compared the number of bed days in the same subgroup of patients with two or more admissions in years 4-6, the median number of bed days for each patient, was significantly lower in the EI group than the controls (Mann Whitney test; $p=0.0357$). In the same subgroup, the comparisons of number of bed days for each patient in years 1-3 and over the entire six-year period yielded no statistically significant results. This is extremely interesting as it suggests a protective effect of EI with regards to reduced number of bed days that only applies to the period of years 4-6 when the EI patients have been transferred back to CMHT. *It could, of course be argued that more efficient methods of managing beds might have been introduced over the years of the study, including early discharge with the support of crisis teams, which were historically introduced at the same time as EI services, and this might in part account for this finding.*

The second subgroup for investigation was as follows:

2. In the EI Group, out of 23 patients with two or more admissions in years 1-3, 14 (60.87%) went on to have no admission in years 4-6.

In the control Group, out of 37 patients that had two or more admissions in years 1-3, only 10 (27.03%) had no further admission in years 4-6.

We compared the two subgroups using a chi-squared test to discover that the difference was highly statistically significant (odds ratio=4.2; $p=0.009$) suggesting that an EI service intervention carried out during years 1-3 has a protective effect that for severe cases (as arbitrarily defined by two or more admissions in years 1-3) lasts through years 4-6 i.e. even after it has ended (Figure 3). *Such a protective effect might possibly in part be due to patients learning how to control their symptoms more effectively as a result of the psycho-education imparted during the EI intervention.*

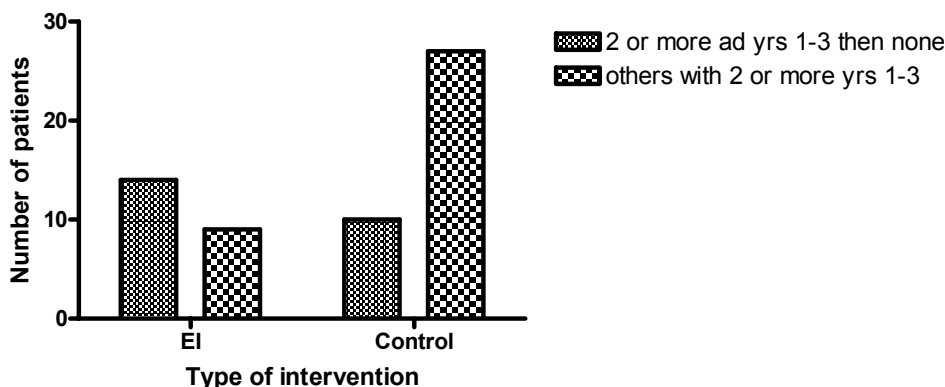


Figure 3. Number of patients with two or more admissions in years 1-3 that had no further admissions in years 4-6 shown in two different diagrammatic ways

For the comparison between the number of patients with two or more admissions in the entire six-year period (26 out of 62 in the EI group and 35 out of 62 in the control group), the chi-squared test again gave slight hints of a protective effect (odds ratio=0.56) but without reaching statistical significance.

When the same analysis was carried out for the subgroup of patients that was theoretically less ill i.e. had 1 or less admissions in years 1-3 and then went on to have no admissions in years 4-6 (13 out of 20 in the EI group and 10 out of 12 in the control group) statistical significance was lost despite the favourable odds ratio (0.37) of the chi-squared test suggesting a hint of protection from EI once more. Overall, these results show that severely ill patients seem to benefit more from the EI than less serious cases; this benefit lasting through years 4-6.

Finally it is of interest regarding the Critical Period Hypothesis that, out of those patients that were admitted at any time at least once over the six-year period, 4 (9.30%; $n=43$) patients in the EI group and 1 (1.96%; $n=51$) patient in the control group had their first

admission in years 4-6, when the critical period was over. The chi-squared test was not statistically significant but the odds ratio (5.2) was, not surprisingly, strongly in favour of the EI group. *It is known from our previous publication that Duration of Untreated Psychosis in our patients was long (Agius et al. 2007), however, it is certainly possible that some of the EI patients began to receive treatment earlier in the illness than did the control group patients, and this may account for their not requiring admission in the early years of treatment.*

We also carried out some more conventional analyses as shown below.

Total admissions over the entire six-year period numbered 161 for the control group and 114 for the EI group (Figure 4). When we compared mean and median admissions between all 62 patients from each of the two groups over years 1-6, statistical significance for this difference was obtained both with an unpaired student t-test ($p=0.04$) and even more strongly with a Mann-Whitney test ($p=0.01$).

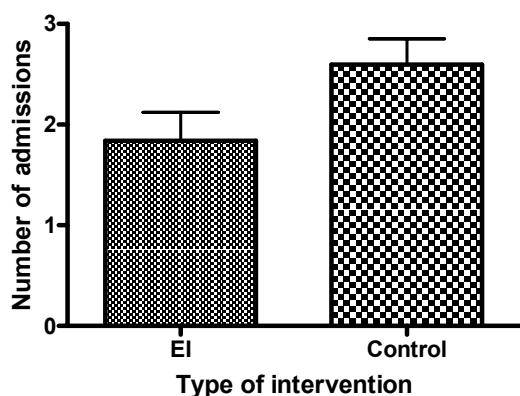


Figure 4. Average number of admissions per patient over 6 years

The same analysis was carried out for years 1-3 and subsequently years 4-6.

In the first 3 years there were a total of 125 admissions in the control group compared to only 87 in the EI group (Figure 5). This difference was statistically significant both with the unpaired t-test ($p=0.03$) and even more with the Mann-Whitney test ($p=0.006$).

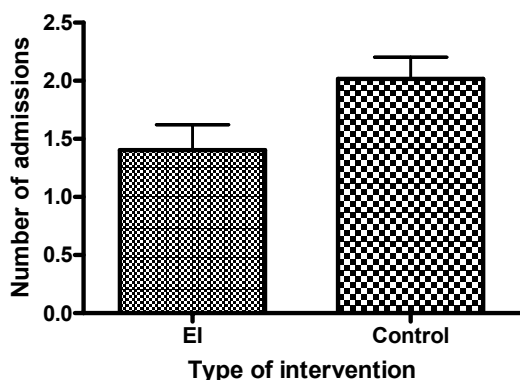


Figure 5. Average number of admissions per patient over years 1-3

Within years 4-6, there were 27 admissions in the EI group and 36 admissions in the control group (Figure 6). Interestingly, statistical significance was lost no matter whether the test was parametric or non-parametric.

When total bed days were compared similar trends were obtained as to those above for admissions.

In the entire six-year period, there were 6513 bed days counted for patients within the EI group as opposed to 9963 for the admitted control group patients (Figure 7). In contrast to the results for average admissions though, for bed days, statistical significance was not obtained when the means were compared by an unpaired student t-test but only when a Mann-Whitney test was used to compare medians ($p=0.01$).

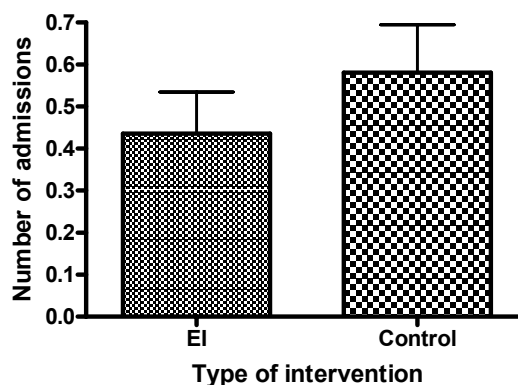


Figure 6. Mean number of admissions per patient over 6 years

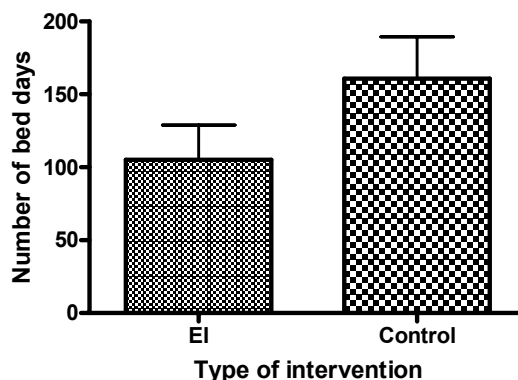


Figure 7. Average number of bed days per patient in all 6 years

The same was true for average (or total) number of bed days over years 1-3 where statistical significance was only obtained when medians were compared by Mann-Whitney test ($p=0.003$) (Figure 8). This highlights the possibility of the small size of our sample hindering the quality of our results.

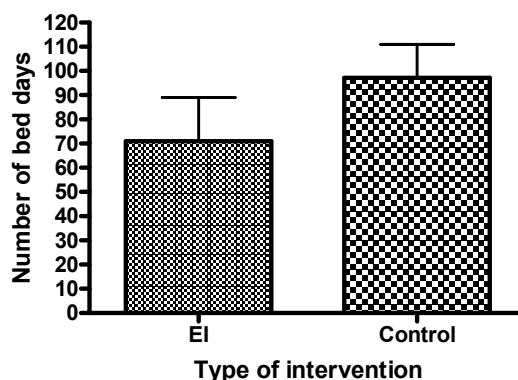


Figure 8. Average number of bed days per patient over years 1-3

The difference between the EI and control groups in terms of average number of bed days per patient showed no statistical significance over years 4-6.

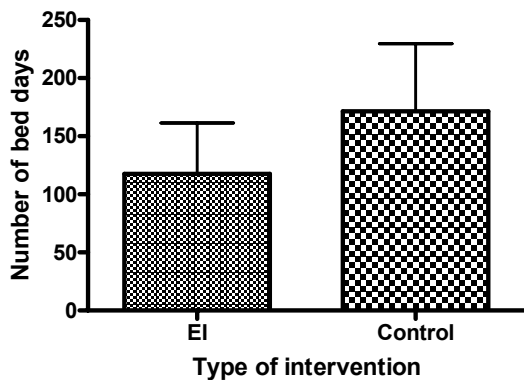


Figure 9. Average number of bed days per patient over years 4-6

Finally we compared the average number of bed days per admission (rather than per patient) between the two treatment groups.

For all 6 years the average number of bed days per admission was statistically significant only when the Mann-Whitney test was used ($p=0.04$) (Figure 10a).

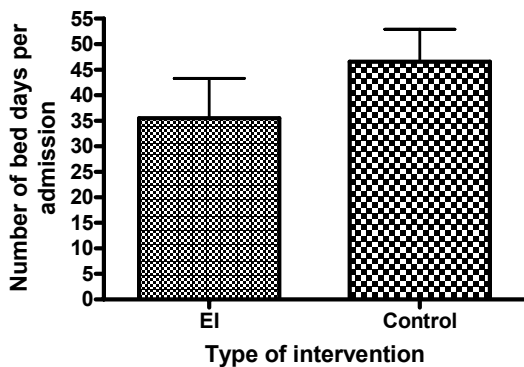


Figure 10a. Average number of bed days per admission over all 6 years

It should be noted that this comparison includes patients with no admissions in both groups. These patients were each allocated an average of zero days per admission. If patients without any admissions are excluded, $P=0.22$ with Mann-Whitney, that is, statistical significance is lost if patients without any admissions are excluded. See graph below (Figure 10b).

For years 1-3 statistical significance was obtained using both the unpaired t test for means ($p=0.04$) and the Mann-Whitney test for medians ($p=0.008$) (Figure 11a).

Statistical significance was lost again when patients who had never had any admissions at all over the years 1-3 were not included in the comparison (Figure 11b). The Graph was changed but not reversed as in years 4-6 (see later).

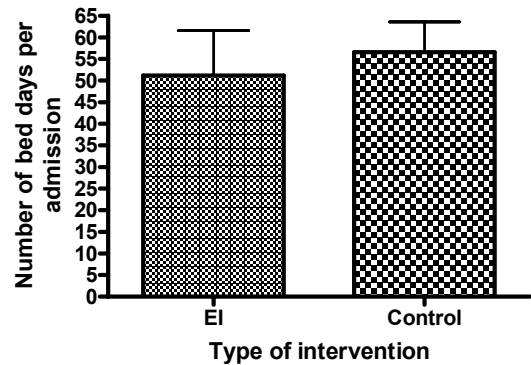


Figure 10b. Average number of bed days per admission per patient over all 6 years; patients with no admissions in years 1-6 excluded.

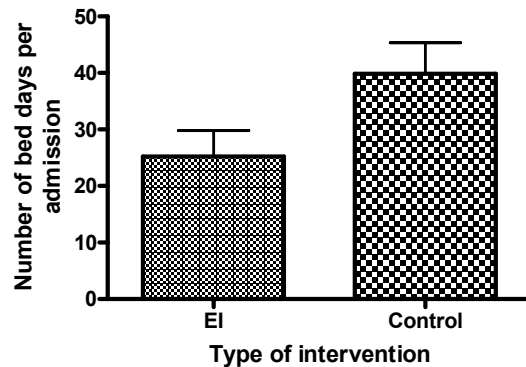


Figure 11a. Average number of bed days per admission per patient over years 1-3 patients with no admissions included

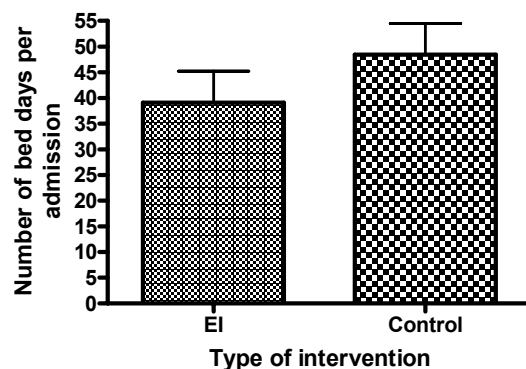


Figure 11b. Average number of bed days per admission per patient over years 1-3; patients with no admissions in any year excluded

When we compared the average number of bed days per admission (rather than per patient) between the two treatment groups for years 4-6 no statistical significance was obtained even when no admissions were included in the comparison (Figure 12a).

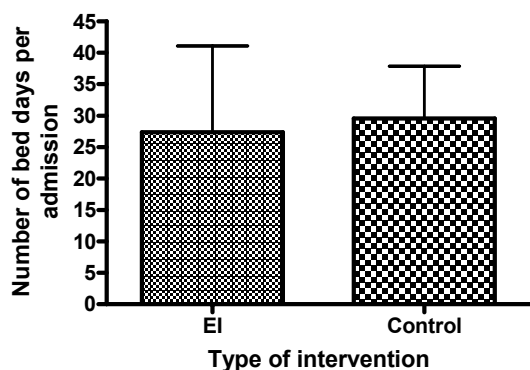


Figure 12a. Average number of bed days per admission per patient over years 4-6; all patients included.

Similarly, when patients who had no admissions in years 4-6 were excluded, there was no statistical significance found. However there was a reversal change in the graph, as shown below (Figure 12b). This suggests that in our sample, the EI patients spend more days per admission in hospital, despite having a reduced number of admissions.

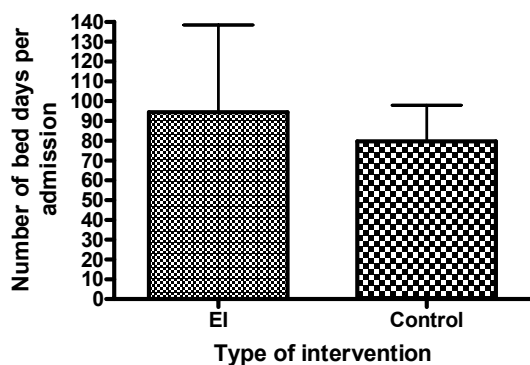


Figure 12b. Average number of bed days per admission per patient over years 4-6; patients without admissions excluded.

Conclusion

There seems to be a statistically significant advantage in patients with a first episode of psychosis being treated in an ad Hoc EI service during the first two years of the service. That significance is lost after this is probably due to the progress of the illness with ongoing loss of grey matter and brain plasticity as demonstrated in recent MRI studies of brains in different stages of schizophrenia. It does appear in our sample, that the assertive approach used in EI services does reduce the deterioration, in that there is a greater likelihood of patients in EI services not needing admission at all over six years than there is with treatment as usual, also, fewer patients require admissions in years 4-6 in patients first treated in EI services than in

Treatment as Usual in CMHTs, and this effect appears to continue into the sixth year of the service.

It is important to note that the average duration of untreated psychosis of our initial sample of patients was long (Agius et al. 2007), and therefore we had attributed our success in improving outcomes of psychosis treatment in our initial study to the assertive approach used, including the use of psycho-education and psychosocial interventions. Therefore the results in the present study must, where they favour EI, be also attributed to the same effects and also the effects of parallel reforms in mental health services, including the gradual introduction of early discharge policies, and the use of crisis/home treatment teams to facilitate these policies and reduce admissions. All these changes are interdependent and are part of a single redesign of community mental health services introduced into England over the last ten years. One might surmise that a change in one part of the system will affect the other parts. One might also surmise that, given the known improvement in mental health outcomes in first episode psychosis if the Duration of Untreated Psychosis is reduced (Marshall et al. 2005), our present results would have been enhanced if the DUP of our patients were greater; thus we suggest that there may be two components to the effect of EI services; that attributable to reduced DUP and that attributable to the functioning of the EI team itself.

One final consideration needs to be made; despite any residual advantages after Early Intervention has ended, it is necessary to consider whether functional outcomes and quality of life can remain optimal once the assertive intervention has ended. This goes beyond the presently studied outcomes of readmissions and bed days. Of interest in this regard is a study by Zaytseva (Zaytseva et al. 2008, Zaytseva et al. 2009), who reports that if the assertive approach is continued till year 5, then the functional outcomes of the treatment are not lost, in important contrast to the reports from the LEO and OPUS studies.

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