HEALTH AND MEDICAL RESEARCH FUND

Duration of early intervention for psychosis: 2 years versus 3 years

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KEY MESSAGES

1. The beneficial therapeutic gains on functional and symptom outcomes attained by an additional year of early intervention for first-episode psychosis patients could not be sustained 2 years after service withdrawal.
2. An apparent lack of efficacy of extended early intervention on maintaining better illness outcomes might be attributable to multiple factors that were not addressed by the current study and thus warrant further investigation to clarify which treatment elements might be critical in enhancing durability of early intervention for psychosis.

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Introduction

Psychotic disorders including schizophrenia constitute one of the highest disease burdens globally and locally. Numerous early intervention (EI) services targeting young people with psychosis have been established worldwide in the past two decades. Substantial evidence has indicated superiority of EI service over standard care in improving clinical and functional outcomes in first-episode psychosis (FEP) patients. Nonetheless, initial therapeutic benefits achieved by EI may not be maintained after the service is withdrawn. Increasing concern is thus raised regarding the sustainability of beneficial effects of EI service and how long EI should be provided to consolidate and optimise these initial treatment gains.

Hong Kong is among the few cities in Asia to implement EI service for psychosis. Early Assessment Service for Young People with Psychosis (EASY) provides 2-year specialised EI for young people presenting with FEP. Patients in EI service have better functioning, milder symptom severity, fewer suicides and hospitalisations, and lower disengagement rate than those in standard care, despite a lack of significant between-group difference in duration of untreated psychosis. In our previous randomised controlled trial comparing 1-year extension of EI service (extended EI) with standard care (SC) in FEP patients, the extended EI group displayed significantly better outcomes than the SC group in functioning, and negative and depressive symptoms at the end of 12-month follow-up.

In the current study, we conducted a 2-year naturalistic follow-up of our cohort with an aim to examine whether the beneficial effects of extended EI on illness outcomes could be sustained after 2 years. During this follow-up period, patients in both groups received standard psychiatric care without provision of specialised EI case management.

Methods

This was a 2-year naturalistic follow-up of our previous single-blinded randomised controlled trial (NCT01202357) comparing 1-year extension of EI service (extended EI) with standard care (SC) in FEP patients. Details of the methodology have been reported elsewhere. Briefly, a total of 160 consecutive FEP patients with a DSM-IV diagnosis of psychotic disorder were recruited from EASY between November 2010 and August 2011 and were randomly allocated to extended EI (n=82) or SC (n=78) for 1 year. Exclusion criteria were intellectual disability, substance-induced psychosis, psychotic disorder secondary to general medical condition, or an inability to speak Cantonese Chinese for research interview. In extended EI, specialised EI was continued for an additional year of case management. A trained case manager took over cases from EASY and was responsible for providing care and coordinating treatment with clinicians, allied health professionals, and community centres. Case management closely aligned with treatment protocols adopted by EASY, focusing specifically on functional enhancement by assisting patients to re-establish supportive social networks, to resume leisure pursuits, and to return to work. Continuous supportive care, psychoeducation, and stress management were also delivered to patients' caregivers by the case manager. In SC, patients received outpatient medical follow-up with limited community support that focused mainly on crisis intervention, with no case management provided. Two treatment groups did not differ from each other regarding the intensity of medical follow-up by psychiatrists, prescription of antipsychotic medications, and availability of various psychosocial interventions, and community-based services.

In the current study, the cohort were contacted for clinical and functional re-assessments. The study was approved by the local institutional review boards. All patients provided written informed consent. For those aged under 18 years, consent was also obtained from a parent or guardian.

Diagnosis of each patient was verified using Chinese-bilingual Structured Clinical Interview for DSM-IV, informant histories, and medical records. Psychopathology was assessed using Positive and Negative Syndrome Scale (PANSS) and Calgary Depression Scale. Psychosocial functioning was measured by Social and Occupational Functioning Assessment Scale (SOFAS) and Role Functioning Scale (RFS). SOFAS provided global functioning estimate of an individual participant, whereas RFS comprised four subscales for functional levels of various domains including independent living and self-care, work productivity, immediate and extended social networks. Data on socio-demographics, occupational status, service utilisation, suicidal attempt, violence, and treatment characteristics were obtained via medical record review. Complete clinical record data over the 2-year follow-up period were available to all patients for analysis.

Primary outcome was psychosocial functioning as measured by SOFAS and RFS. Attrition analysis comparing completers and non-completers in terms of demographics and baseline characteristics was conducted to ensure no bias was introduced owing to loss to follow-up. Between-group comparisons on socio-demographics, clinical profiles, treatment characteristics, symptom and functioning scores at baseline were performed, as were between-group comparisons on symptom and functional outcomes at 3-year follow-up. Treatment characteristics at follow-up and outcomes on service utilisation and other clinical variables between the two groups were also compared. Repeated-measures analysis of variance followed by post-hoc within-group paired-sample *t*-tests (for those outcome variables that showed significant group x time interactions) were performed to identify any significant longitudinal changes of symptom and functioning scores across 2-year follow-up. All statistical analyses were two-tailed with the level of significance set at $P<0.05$.

Results

Of the 160 patients from the initial cohort, 143 (76 in the extended EI group and 67 in the SC group) completed clinical and functional assessments at 3-year follow-up. Four patients died, six were lost to follow-up, and seven refused to complete evaluation. Completers and non-completers were comparable with regard to demographics, baseline clinical profiles, symptom severity, and functional levels, except that completers had better social functioning (RFS immediate social network score) than non-completers. There was no significant difference in attrition rate between the extended EI and SC groups ($\chi^2=1.94$, $P=0.164$). There were no significant differences between the two groups who completed 3-year follow-up in terms of demographics, premorbid adjustment, baseline clinical profiles, symptom severity, and functioning (Table 1)

At 3-year follow-up, the extended EI and SC groups did not differ significantly regarding all functional outcome measures including SOFAS score, RFS total score, and individual RFS functional domain scores (Table 2). There were no significant between-group differences in ratings of various symptom dimensions (including positive, negative, depressive, and general symptoms), medication treatment characteristics, number of psychiatric admissions, length of inpatient stays, outpatient default rate, service disengagement, receipt of welfare allowance (Table 3). The two groups did not differ significantly in rates of relapse, suicide attempt, physical violence, or in the proportions of with all-cause mortality and completed suicides.

Repeated-measures analysis of variance revealed significant group x time interaction in SOFAS ($P<0.05$), RFS total ($P<0.01$), RFS independent living ($P<0.05$) and extended social networks ($P<0.05$) scores across 2-year follow-up period. There were no significant group x time interactions in other functional and symptom outcome variables. Post-hoc paired-sample *t*-tests revealed that patients in the extended EI group had significant reduction in RFS total score ($P<0.01$) and RFS extended social network score ($P<0.01$) over 2 years, whereas patients in the SC group had significant improvement in SOFAS score ($P<0.05$) and RFS independent living score ($P<0.05$) over 2 years.

Discussion

There were no significant between-group differences regarding outcomes on symptom severity, functional levels, and service utilisation at 3-year follow-up. The initial therapeutic gains on symptoms and functioning achieved by extended EI could not be maintained after 2 years. This is consistent with the results of two previous studies that also failed to demonstrate sustained superiority of EI over SC in functioning, symptom outcomes, and admission rate of FEP patients at follow-up after withdrawal

TABLE 1. Demographics and baseline clinical, functional, and treatment characteristics of patients who completed 3-year follow-up*

	Extended early intervention (n=76)	Standard care (n=67)	t or χ^2	P value
Male gender	52.6 (40)	52.2 (35)	0.002	0.963
Age at entry, y	20.1±3.0	20.4±3.5	0.5	0.632
Tertiary educational level or above	25.0 (19)	29.9 (20)	1.3	0.535
Premorbid Adjustment Scale				
Social score	0.42±0.14	0.44±0.17	0.9	0.375
Academic score	0.40±0.12	0.42±0.16	1.1	0.273
Age at onset, y	20.1±3.0	20.4±3.5	0.5	0.632
Log duration of untreated psychosis	1.9±0.69	1.9±0.75	0.5	0.612
Psychiatric diagnosis			0.4	0.833e
Schizophrenia-spectrum disorders	84.2 (64)	83.6 (56)		
Affective psychosis	10.5 (8)	9.0 (6)		
Other non-affective psychoses	5.3 (4)	7.5 (5)		
Positive and Negative Syndrome Scale				
Positive symptom score	9.3±3.3	8.9±2.6	3.2	0.455
Negative symptom score	11.3±4.7	12.1±5.0	1.3	0.351
General psychopathology score	24.3±7.5	24.3±6.3	0.08	0.936
Calgary Depression Scale total score	2.8±3.2	2.7±3.3	-0.3	0.830
Social and Occupational Functioning Assessment Scale score	57.9±14.7	58.9±13.4	0.4	0.665
Role Functioning Scale				
Work productivity	4.2±1.8	4.7±1.4	1.7	0.094
Independent living	6.1±1.1	6.3±0.8	1.6	0.120
Immediate social network	5.0±1.2	5.1±1.3	0.6	0.574
Extended social network	4.2±1.4	4.1±1.5	0.3	0.741
Use of second-generation antipsychotic	80.3 (61)	86.6 (58)		
Chlorpromazine equivalent dose, mg	310.1±256.9	302.0±249.3	-0.2	0.849

* Data are presented as mean±standard deviation or No. (%) of participants

of EI service. Our longitudinal analyses revealed that this might be attributed to functional decline of patients in the extended EI group as well as gradual functional improvement of patients in the SC group over the 2-year follow-up period. However, changes in raw functioning scores during follow-up were very small and thus such significant differences might not necessarily equate with clinically significant and relevant changes in real-world settings. In addition, patients in the extended EI group still exhibited better (though not significantly) functional levels in both global ratings and across individual functional domains than those in the SC group.

There are several possible explanations for the lack of sustained effects of extended EI on functional outcome at 3-year follow-up. It might be that 3-year duration of specialised EI for FEP is insufficient and therefore not an optimal period for sustained therapeutic effects on functional outcome to take place. A relatively high caseload (1 case manager to 82 patients) of a 1-year extension of EI might represent inadequate treatment in maintaining the initial therapeutic gains. Enhanced SC via recent improvement in local community psychiatric services in Hong Kong might dilute the impact of extended EI on longer-term outcomes. The comparatively shorter duration of untreated psychosis (median, 13 weeks) of our cohort might obscure potential positive effects of extended EI on longer-term outcome in a subgroup of patients who have prolonged untreated initial psychosis. In fact, a large-scale case-control study examining the medium- and long-term effects of early detection on FEP patients has demonstrated that patients with shorter duration of untreated psychosis had significantly better clinical and functional outcomes than those with longer duration of untreated psychosis at 5- and 10-year follow-up. It is thus plausible that complementing specialised EI care with early detection (shortening of treatment delay) might enhance the durability of therapeutic gains attained by extended EI.

There is substantial variation in EI services

TABLE 2. Clinical and functional outcomes in the two treatment groups at 1-year and 3-year follow-up*

	1-year follow-up			3-year follow-up		
	Extended early intervention (n=79)	Standard care (n=77)	P value	Extended early intervention (n=76)	Standard care (n=67)	P value
Positive and Negative Syndrome Scale						
Positive symptom score	8.3±2.5	8.6±2.9	0.500	9.9±3.4	10.2±3.6	0.577
Negative symptom score	8.5±2.5	9.9±3.9	0.009	12.0±4.0	11.9±4.0	0.941
General psychopathology score	19.2±3.7	21.1±5.1	0.010	21.2±5.4	22.1±4.6	0.304
Calgary Depression Scale total score	0.9±1.6	1.9±2.8	0.005	1.6±2.3	2.04±2.8	0.271
Social and Occupational Functioning Assessment Scale score	64.8±13.1	57.9±12.7	0.001	64.8±13.7	61.9±12.5	0.187
Role Functioning Scale						
Total score	22.1±3.2	20.3±3.7	0.002	21.5±3.2	21.0±3.2	0.302
Work productivity	5.1±1.4	4.7±1.5	0.045	5.1±1.5	4.9±1.4	0.436
Independent living	6.5±0.6	6.2±1.0	0.036	6.4±0.6	6.3±0.7	0.390
Immediate social	5.5±0.9	5.1±1.0	0.002	5.3±0.9	5.0±0.9	0.152
Extended social	4.9±1.0	4.3±1.3	0.004	4.7±0.9	4.7±1.0	0.803
Full-time work	58.2±46	48.1±37	0.273	56.6±43	47.8±32	0.292
Treatment characteristics						
Use of second-generation antipsychotic	81.8 (63)	77.2 (61)	0.805	82.9 (63)	83.6 (56)	0.913
Chlorpromazine equivalent dose, mg	322.2±275.8	301.0±295.2	0.618	364.9±281.0	296.5±261.7	0.142

* Data are presented as mean±standard deviation or No. (%) of participants

TABLE 3. Service utilisation and other clinical outcomes in the two treatment groups during follow-up*

	During 1-year follow-up			During 2-year follow-up		
	Extended early intervention (n=82)	Standard care (n=78)	P value	Extended early intervention (n=82)	Standard care (n=78)	P value
Service utilisation						
Psychiatric admission	15.9 (13)	10.4 (8)	0.353	17.1 (14)	16.7 (13)	0.945
Length of admission, d	7.4±20.6	3.5±12.8	0.146	131.5±139.7	174.3±259.0	0.594
Loss to follow-up	18.3 (15)	33.3 (26)	0.029	31.7 (26)	41. (32)	0.220
Service disengagement	3.7 (3)	5.1 (4)	0.650	6.1 (5)	7.7 (6)	0.690
Receipt of welfare allowance	23.8 (19)	12.8 (10)	0.076	39.0 (32)	41.0 (32)	0.796
Outcome						
Relapse	15.9 (13)	19.2 (15)	0.574	25.6 (21)	37.2 (29)	0.115
Suicide attempt	0 (0)	0 (0)		1.2 (1)	1.3 (1)	0.972
Physical violence	3.7 (3)	1.3 (1)	0.336	6.1 (5)	7.7 (6)	0.517
All-cause mortality	0 (0)	0 (0)		1.2 (1)	3.8 (3)	0.287
Suicide	0 (0)	0 (0)		1.2 (1)	1.2 (1)	1.000

* Data are presented as mean±standard deviation or No. (%) of participants

across different regions regarding the content and intensity of service provided, and characteristics of patients enrolled including age range and diagnostic distribution. Given that our findings were based on EI service of comparatively low resources and high caseloads relative to those well-established early psychosis programmes implemented in some Western countries, generalisation of our results to other populations should be made cautiously.

There are several limitations to the study. The sample was recruited from the EASY programme that provided early intervention to patients aged 15 to 25 years only. Our results may not be generalisable to those with older age at onset of psychosis. Data regarding the inputs of community psychiatric services in standard care received by patients during the follow-up period were not available, thereby precluding us from estimating the potential confounding (and possibly the diluting effect) of enhanced community care on clinical and functional outcomes at 3-year follow-up. Nonetheless, the strengths of the current study included lack of differential attrition between treatment groups, blinding of research staff involving outcome assessments to treatment allocation, low dropout rate (89.4% of the cohort completed 3-year follow-up reassessment), comprehensive evaluation of functional outcomes encompassing both global functioning and various specific functional dimensions, and availability of complete clinical record data regarding medication treatment, service utilization, and other clinical variables of all patients.

Conclusion

There were no significant differences between the extended EI and SC groups in clinical and functional outcomes at 3-year follow-up. The beneficial treatment effects attained by 1-year extended EI could not be sustained after 2 years in Chinese FEP patients. However, caution should be exercised in interpretation and generalisation of our negative findings to EI services owing to the methodological limitations as well as substantial variation across regions in terms of sociocultural and mental health service contextual factors. In addition, the failure to demonstrate superiority of extended EI on longer-term outcomes might be attributable to an array of factors that could not be adequately addressed by the naturalistic follow-up design. Future research should clarify the differential impacts of treatment intensity (eg caseload), individual intervention elements, treatment delay, as well as the length of service on the durability of EI on long-term outcomes in FEP patients. This may inform further development and enhancement of the EI service model for patients with FEP.

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