Extended early intervention versus standard psychiatric care for adults with first-episode psychosis

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KEY MESSAGES

1. Adult patients with first-episode psychosis who received 3-year extended Early Assessment Service for Young People with Psychosis (EASY) had significantly shorter treatment delay than those treated with standard psychiatric care.
2. Extended EASY programme was superior to standard care in improving functional outcome and alleviating symptom severity, in particular negative and depressive symptoms.
3. Lack of positive effect of extended EASY programme on reducing admission and suicide rates may be due to the modest sample size. Further investigation involving greater number of patients is required.

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Introduction

Psychotic disorders including schizophrenia affect 3% of the population and have high disease burden. Numerous early intervention (EI) programmes for psychosis have been established worldwide in the past two decades, based on the premise that shortening of treatment delay and provision of phase-specific treatments in the initial years of psychosis can improve long-term outcome. Prolonged duration of untreated psychosis (DUP) was associated with poorer illness outcomes.[1] A meta-analysis demonstrated that patients with first-episode psychosis (FEP) who receive EI service had better outcomes than those treated with standard psychiatric care in terms of symptom severity, functioning, hospitalisation, and service engagement.[2]

In 2001 in Hong Kong, Early Assessment Service for Young People with Psychosis (EASY) was launched. It comprised community awareness programme, an open referral system, and a 2-year specialised EI for young people aged 15 to 25 years with FEP.[3] Young patients in EI service had better functioning, milder symptom severity, fewer suicides and hospitalisations, and lower disengagement rate than those in standard care.[4] Our randomised controlled trial (SMH-29) further demonstrated superiority of extended 3-year EI over 2-year EI in improving symptom and functional outcomes in young patients with FEP.[5] Since 2011, EASY programme has been expanded to provide 3-year treatment to FEP patients aged 15 to 64 years. This study aimed to evaluate the effectiveness of extended EASY programme for adult patients with FEP.

Methods

This was a multicentre study involving seven clusters including Hong Kong West, Hong Kong East, Kowloon East, Kowloon Central, Kowloon West, New Territories East and New Territories West. The study was approved by the local institutional review boards. All subjects provided written informed consent prior to participation of follow-up interview assessment. This study used a historical-control design to compare adult patients with FEP who received 3-year extended EASY programme with those who were treated with standard psychiatric service in terms of treatment delay, pathway to care, and outcomes in functioning, symptoms, and service utilisation, based on retrospective record review and follow-up interview assessment.

We identified 160 FEP patients who enrolled to extended EASY programme (EI group) between 1 January 2012 and 30 July 2012, and 160 FEP patients who enrolled in standard psychiatric services (SC group) between 1 September 2010 and 31 March 2011 from the Psychiatric Case Register of Hospital Authority via random sampling. Inclusion criteria were Chinese adults aged 26 to 55 years presenting with FEP (ICD-10 diagnosis of schizophrenia, schizoaffective disorder, acute and transient psychotic disorders, delusional disorder or other non-organic psychotic disorders). Exclusion criteria were substance-induced psychosis, psychotic

disorders secondary to general medical condition, affective psychosis, and mental retardation.

Subjects' baseline and 3-year follow-up variables were obtained via systematic record review. Outpatient and inpatient medical records and clinical information were retrieved. Baseline data included socio-demographics, occupational status, and age at service entry. Treatment delay in the form of DUP was estimated. Positive and negative symptom levels were assessed using Clinical Global Impression-Severity of Illness Scale (CGI-S). Depressive symptoms were evaluated using CGI-S for bipolar illness. Functional outcome was evaluated using Social Occupational Functioning Assessment Scale (SOFAS). Engagement of full-time employment was assessed. Data were collected on mortality, suicide, and service utilisation including psychiatric admissions, treatment defaults, service disengagement, and antipsychotic medication dose.

Subjects were contacted for follow-up interview assessment. Diagnosis was made according to ICD10 Diagnostic Criteria for Research,[33] based on structured diagnostic interview, medical records, and informant history. Family history of psychotic disorder and past history of substance abuse were ascertained. Premorbid Adjustment Scale was used to measure premorbid functioning. Age of psychosis onset, first-episode status, and DUP were measured and verified. Help-seeking and referral patterns were examined. Positive and negative symptom severity was evaluated using Positive and Negative Syndrome Scale. Depressive symptoms were measured by Calgary Depression Scale for Schizophrenia. Psychosocial functioning was measured by SOFAS and Role Functioning Scale. The Chinese version of SF-12 was used to measure subjective quality of life. Antipsychotic-induced motor side-effects were examined by Simpson-Angus Scale, Barnes Akathisia Scale, and Abnormal Involuntary Movement Scale.

Psychosocial functioning was the primary outcome measure. Between-group comparisons were made using Chi-squared test and independent t-test as appropriate. Analysis of covariance was used for variables that were significantly different between groups, adjusting for the effect of DUP on outcomes. The level of statistical significance was set at $P<0.05$.

Results

The EI and SC groups were comparable regarding demographics and baseline clinical, functional, and treatment characteristics, as well as non-participation rate for follow-up interview assessment. Of 320 patients, 251 were interviewed 48.3±3.1 months after service entry (Table 1).

EI patients had significantly shorter DUP than SC patients although there was no significant difference with respect to the proportion of patients receiving inpatient treatment upon entry (Table 2). EI patients had significantly lower mean CGI-S positive symptom levels in the first and second year of follow-up than SC patients. EI patients attained significantly higher mean SOFAS scores in the first, second, and third year of follow-up, and had longer cumulative full-time employment than SC patients. There was a trend that EI patients were less likely to disengage from service. After controlling for

TABLE 1. Baseline characteristics of patients with first-episode psychosis

Variables	Early intervention (n=160)*	Standard care (n=160)*	t/χ^2	P value
Male gender	66 (41.3)	61 (38.1)	0.33	0.57
Age at service entry, y	37.6±8.5	39.2±8.0	1.75	0.08
Full-time employed at entry	20 (12.5)	27 (16.9)	1.22	0.27
Age at psychosis onset, y	36.6±8.9	37.3±8.2	-0.72	0.47
Psychiatric diagnosis			2.19	0.14
Schizophrenia-spectrum disorder	130 (81.2)	119 (74.4)		
Other non-affective psychoses	30 (18.8)	41 (25.6)		
Clinical Global Impression – Severity Scale				
Positive symptom score	5.1±1.2	5.4±1.0	-1.67	0.09
Negative symptom score	2.6±1.3	2.7±1.5	-0.68	0.50
Depression score	2.0±1.3	1.9±1.2	0.83	0.41
Social and Occupational Functioning Assessment Scale score	41.8±12.6	40.7±11.5	0.79	0.43
On antipsychotic medication	159 (99.4)	156 (98.1)	1.03	0.37
Chlorpromazine equivalent dose, mg	146.1±102.1	172.2±225.2	-1.32	0.19

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

TABLE 2. Treatment delay and 3-year outcome based on retrospective medical record review

Variables	Early intervention	Standard care	t/χ^2	P value
Inpatient treatment upon service entry	78 (48.8)	91 (56.9)	2.12	0.15
Duration of untreated psychosis, d	353.7±545.9	620.7±1045.8	-	-
Log duration of untreated psychosis	2.0±0.8	2.3±0.8	-2.40	0.017
Clinical Global Impression – Severity Scale				
Year 1	(n=151)	(n=141)		
Positive symptom score	2.2±0.9	2.7±1.2	-4.04	<0.001
Negative symptom score	2.1±1.1	2.3±1.2	-1.42	0.16
Depression score	1.4±0.7	1.5±0.7	-0.85	0.40
Year 2	(n=148)	(n=134)		
Positive symptom score	1.4±0.7	1.7±0.9	-2.46	0.02
Negative symptom score	1.8±1.1	2.0±1.1	-1.65	0.10
Depression score	1.2±0.5	1.2±0.5	-1.48	0.14
Year 3	(n=143)	(n=132)		
Positive symptom score	1.5±0.8	1.6±0.9	-1.07	0.29
Negative symptom score	1.7±1.1	1.9±1.1	-1.64	0.10
Depression score	1.1±0.5	1.2±0.5	-1.20	0.23
Social and Occupational Functioning Assessment Scale				
Year 1	51.2±9.6 (n=151)	48.2±9.6 (n=141)	2.66	0.01
Year 2	56.2±9.9 (n=148)	52.0±9.6 (n=134)	3.72	<0.001
Year 3	57.4±10.3 (n=143)	52.1±9.3 (n=132)	4.53	<0.001
Months in full-time work in 3 years	11.5±14.0 (n=143)	8.0±12.7 (n=132)	2.34	0.02
Relapse of psychotic episodes	55 (36.9)	44 (31.7)	0.88	0.35
All-cause mortality	2 (1.3)	5 (3.1)	1.31	0.45
Suicide	2 (1.3)	2 (1.3)	0.00	1.00
Service utilisation over 3 years				
Psychiatric hospitalisation	94 (60.7)	100 (65.8)	0.88	0.35
Length of hospital stay, d	41.9±72.3	53.0±101.6	-1.11	0.27
Default in outpatient appointment	67 (41.9)	72 (45.0)	0.32	0.57
Service disengagement	17 (10.6)	28 (17.5)	3.13	0.08
Length of service stay, mo	33.8±7.6	31.8±10.1	1.92	0.06
Chlorpromazine equivalent dose, mg				
Year 1	306.5±218.7	299.6±221.1	0.26	0.80
Year 2	338.5±267.3	312.6±216.2	0.85	0.40
Year 3	351.0±327.5)	353.0±293.7	-0.05	0.96

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

the effect of DUP, better outcomes in EI patients remained significant in terms of positive symptoms and SOFAS. No significant differences were noted in rates of relapse, mortality, suicide, admission, and treatment defaults.

EI and SC patients were comparable in terms of patterns of first help-seeking action and referral source (Table 3). EI patients had shorter (not significantly) DUP, help-seeking delay, and referral delay than SC patients. Upon follow-up assessment, EI patients demonstrated significantly less severe positive symptoms, negative symptoms, general psychopathology, and depressive symptoms than SC patients. EI patients displayed significantly higher Role Functioning Scale total score and immediate and extended social network scores, and SF-12 physical domain score than SC patients. Better outcomes in EI patients remained significant after controlling for the effect of DUP, with the exception of positive symptom severity.

TABLE 3. Treatment delay and outcome based on interview assessment

Variables	Early intervention (n=130)*	Standard care (n=121)*	t/χ^2	P value
First help-seeking action			0.97	0.62
Community non-medical sector	49 (38.0)	39 (32.5)		
Community medical sector	34 (26.4)	32 (26.7)		
Non-community medical sector	46 (35.6)	49 (40.8)		
Referral source			4.66	0.10
Community non-medical sector	8 (6.3)	17 (14.1)		
Community medical sector	20 (15.9)	22 (18.2)		
Non-community medical sector	98 (77.8)	82 (67.7)		
Inpatient status upon service entry	70 (53.9)	69 (48.8)	0.26	0.61
Duration of untreated psychosis, d	375.8±565.8	635.2±1136.1	-	-
Log duration of untreated psychosis	2.1±0.8	2.2±0.8	-1.54	0.13
Help-seeking delay, d	330.7±534.4	67.4±1088.3	-	-
Log help-seeking delay	2.0±0.8	2.1±0.9	-1.29	0.20
Treatment delay, d	45.7±118.4	68.5±286.4	-	-
Log treatment delay	0.7±0.9	0.7±0.9	-0.36	0.72
Positive and Negative Syndrome Scale				
Positive symptom score	8.7±3.2	9.6±3.8	-2.13	0.03
Negative symptom score	10.8±5.7	13.4±8.0	-2.91	0.01
General psychopathology	19.4±4.0	24.4±8.9	-5.59	<0.001
Calgary Depression Scale for Schizophrenia score	1.8±3.0	2.8±3.7	-2.28	0.02
Social and Occupational Functioning Assessment Scale score	59.0±11.4	57.3±12.1	1.16	0.25
Role Functioning Scale score	22.4±3.3	21.3±4.0	2.30	0.02
Work productivity	5.1±1.9	4.9±1.9	0.65	0.52
Independent living	6.8±0.5	6.6±1.0	1.94	0.06
Immediate social network	5.7±1.1	5.4±1.2	2.70	0.01
Extended social network	4.7±0.9	4.4±1.2	2.59	0.01
Full-time employed at follow-up	41 (31.5)	42 (34.7)	0.29	0.59
SF-12 physical domain score	49.0±7.1	46.4±8.1	2.47	0.01
SF-12 mental domain score	48.0±9.2	46.5±11.7	1.06	0.29
On antipsychotic medication	122 (93.8)	112 (93.3)	0.03	0.87
Chlorpromazine equivalents at follow-up, mg	416.0±595.3	387.2±307.4	0.46	0.65
Simpson-Angus Scale score	0.2±1.0	0.5±1.6	-1.64	0.10
Barnes Akathisia Rating Scale score	0.1±0.5	0.2±0.7	-1.29	0.20
Abnormal Involuntary Movement Scale score	0.3±1.8	0.3±1.1	0.27	0.79

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

Discussion

Compared with SC patients, EI patients had significantly shorter DUP, lower levels of negative and depressive symptoms, and better functional outcome in follow-up assessment. EI patients demonstrated shorter (not significantly) help-seeking and referral delays than SC patients. Nonetheless, patterns of first formal help-seeking action and referral source were similar between groups. EI patients displayed better functional outcome and attained higher SF-12 physical domain score. EI patients displayed lower negative and depressive symptom levels. This is of critical clinical significance, as negative symptoms are associated with poor functional outcome and limited response to pharmacotherapy. Depressive symptoms frequently occur in people with psychotic disorders and are associated with heightened suicide risk.

Contrary to past studies reported that patients received EI service had fewer admissions than those

in standard care, we found no significant group difference in hospitalisation outcome over 3-year treatment period. This may be due to difference in caseloads between EASY programme and EI services in Western countries. Our EASY programme has a higher patient-to-case manager ratio that may lower the capacity of EI service in reducing readmission. The modest sample size might also contribute to null findings owing to compromised statistical power to detect subtle but significant difference. This also applies to examination of rates of mortality and suicide. Consistent with most prior EI research, our EI patients had lower service disengagement rate than SC patients (at trend-wise significance).

There are several limitations in the study. Interview assessment could not be conducted at service intake; data at baseline and during 3-year treatment period were based on medical record review, which might be biased by documentation quality. Measurement of treatment delay is retrospective with potential recall bias. Outcomes on hospitalisation and mortality were likely to be underpowered and should be treated with caution. Generalisation of our results to other populations should be cautious because our findings were based on EI service of comparatively low resources and high caseloads, relative to well-established EI services implemented in Western countries.

Conclusion

Extended EASY programme is superior to standard care in reducing treatment delay, improving negative and depressive symptom outcomes, and enhancing functioning in adult patients with FEP. Further investigation with a larger sample size is required to examine the effectiveness of extended EASY programme in reducing rates of admission, mortality, and suicide. Future research clarifying potential differential treatment effects of extended EASY programme on FEP patients at various age groups should be conducted to streamline service delivery and optimise outcomes. Reassessment is warranted to examine whether positive effects achieved by extended EASY programme could be maintained after service withdrawal.

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