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Author(s)	Chang, WC; Kwong, WY; Lau, SK; So, HC; WONG, SM; Chan, GHK; Jim, OTT; Hui, CLM; Chan, KW; Lee, HME; Chen, EYH
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Sustainability of treatment effect of 3-year early intervention programme for first-episode psychosis

Wing Chung Chang [1,2*], MRCPsych, FHKCPsych

Vivian Wing Yan Kwong[1], MPsyMed

Emily Sin Kei Lau[1], MSocSc(CP)

Hon Cheong So[3], MBBS, PhD

Corine Sau Man Wong[1], MsocSc

Gloria Hoi Kei Chan[1], MSSc(CP)

Olivia Tsz Ting Jim[1], BSocSc

Christy Lai Ming Hui[1], PhD

Sherry Kit Wa Chan [1,2], MRCPsych, FHKCPsych

Edwin Ho Ming Lee[1], MRCPsych, FHKCPsych

Eric Yu Hai Chen[1,2], MD

[1] Department of Psychiatry, Queen Mary Hospital

[2] State Key Laboratory of Brain and Cognitive Sciences, the University of Hong Kong

[3] School of Biomedical Sciences, the Chinese University of Hong Kong

*Corresponding author: Wing Chung Chang

Department of Psychiatry, Queen Mary Hospital, Hong Kong

Tel: (852) 22554486 Fax: (852) 28551345

Email: changwc@hku.hk

Abstract

Background

Evidence indicates that positive effects of 2-year early intervention for psychosis are not maintained after service withdrawal. Optimal duration of early intervention in sustaining initial improved outcomes remains to be determined.

Aims

To examine sustainability of positive effects of extended, 3-year early intervention for first-episode psychosis patients after transition to standard care.

Method

160 patients, who had received 2-year early intervention programme for first-episode psychosis, were enrolled to a 12-month randomised-controlled trial (NCT01202357) comparing 1-year extension of early intervention (3-year specialised treatment) with step-down care (2-year specialised treatment). Participants were followed up and reassessed 2 and 3 years after inclusion to the trial.

Results

There were no significant differences between the treatment groups in outcomes on functioning, symptom severity and service use during 2-year post-trial follow-up period.

Conclusions

Therapeutic benefits achieved by extended, 3-year early intervention were not sustainable after termination of specialised service.

Declaration of interest

None.

Introduction

Early intervention for psychosis has been the major focus in mental healthcare development worldwide in the past two decades.[1] Literature has demonstrated superiority of early intervention services over standard care in improving outcomes of patients with first-episode psychosis.[2-4] However, considerable concern is raised regarding the sustainability of therapeutic benefits of early intervention for psychosis[5,6] as there is evidence, albeit primarily based on two randomised-controlled trials (RCTs),[7-8] suggesting that positive effects achieved by early intervention may not be maintained after service withdrawal. In the Danish OPUS trial,[9] the largest RCT thus far evaluating effectiveness of integrated early intervention service for psychosis, the findings of better symptom outcome and treatment adherence for early intervention over standard care at 2 years were no longer significant after 5 and 10 years of follow-up.[7,10] Similarly, the British Lambeth Early Onset (LEO) study[11,12] found that improved 18-month outcomes on functioning, quality of life and hospitalisation resulting from early intervention were not sustained at 5 years.[8]

Of note, one important possible explanation for the lack of sustained effect of early intervention is that 2-year specialized treatment (2 years in OPUS trial; 18 months in LEO trial) is insufficient to maintain superior outcomes in first-episode psychosis after transition to standard care. Until now, empirical research evaluating the effectiveness of longer-term early intervention for psychosis is scarce,[4,13-15] and how long specialised treatment should be provided (usually offered for the first 1-2 years of illness) to consolidate and optimise the initial therapeutic gains remains unknown. One recently published RCT (namely OPUS II trial) comparing a 5-year extended early intervention with 2-year early intervention for first-episode psychosis has revealed lack of significant between-group difference in symptom and functional outcomes 5 years after service entry, though with higher client satisfaction and better working alliance in 5-year intervention group, as well as general improvement in clinical and functioning ratings for both groups over the follow-

up period.[15] There is no published RCT follow-up study examining the durability of positive effects of early intervention service with its treatment duration extended beyond 2 years. It is also worth noting that evidence supporting the effectiveness of early intervention for psychosis was mainly derived from Western countries. However, substantial variation across regions with respect to the content and intensity of early psychosis programmes, characteristics of patients enrolled and sociocultural contexts[16] limits generalisability of results and precludes direct adoption of early intervention service model by non-Western countries, including some affluent Asian communities, where public mental healthcare is often over-burdened and under-resourced.[17]

Hong Kong is among the few cities in Asia to implement early intervention service for psychosis. The intervention programme Early Assessment Service for Young People with Psychosis (EASY) was launched in 2001 and comprises community-awareness programmes, an open referral system, and a 2-year specialised intervention for young people presenting with first-episode psychosis, followed by 1-year step-down care with preserved medical follow-up but no provision of case management.[18] Evaluation of the EASY programme using historical-control methods showed that patients receiving early intervention had better functioning, milder symptom severity, fewer suicides and hospitalisations, and a lower disengagement rate than those in standard care, despite a lack of significant between-group difference in duration of untreated psychosis (DUP).[19] In an attempt to evaluate effectiveness of longer-term early intervention for psychosis, we have conducted a RCT (EASY-Extension Trial) comparing a 1-year extension of early intervention service (i.e., 3-year early intervention) with step-down care (i.e., 2-year early intervention) in a representative cohort of Chinese young patients who had completed 2-year treatment in the EASY programme for their first-episode psychosis.[13,20] This was the first reported RCT to provide evidence of the efficacy of extending an early intervention service for psychosis beyond 2 years. Our results indicated that patients receiving extended early intervention displayed significantly

better functioning, fewer negative and depressive symptoms, and lower treatment default rates than those managed by step-down care.[13]

In the current study, we aimed to address a critical question of the durability of therapeutic gains attained by extended early intervention for first-episode psychosis. To the best of our knowledge, this is the first RCT follow-up study examining the sustainability of beneficial effects of early intervention service with its treatment period extended beyond 2 years. Patients included in the EASY-Extension Trial were reassessed 1 and 2 years after completion of RCT to investigate whether better outcomes of the intervention group could be maintained after transition to generic psychiatric care.

Method

Participants

This was a 3-year follow-up of a single-blind RCT (2 years after extended early intervention ended and 5 years after entry to the EASY programme) (online Fig. DS1, Fig. 1) comparing a 1-year extension of specialised early intervention (3-year early intervention) with a step-down care (2-year early intervention) in 160 patients who had received 2 years of care from early intervention service for first-episode psychosis.[13] Participants were recruited from the EASY programme between November 2010 and August 2011 and underwent a 12-month clinical trial. Patients with DSM-IV[21] diagnosis of schizophrenia, schizophreniform disorder, schizoaffective disorder, brief psychotic disorder, delusional disorder, psychosis not otherwise specified, bipolar disorder with psychotic symptoms or depressive disorder with psychotic symptoms were included in the study. Exclusion criteria were intellectual disability, substance-induced psychosis, psychotic disorder due to general medical condition or an inability to speak Cantonese Chinese for research interview.

Details of the EASY programme have been reported elsewhere.[18] In brief, this is a publicly-funded, territory-wide service providing comprehensive assessment and early intervention for individuals aged 15 to 25 years presenting with first-episode psychosis in Hong Kong.[18] The service consists of five clinical teams with each covering a geographically-defined catchment area and comprising two psychiatrists, three case managers and one social worker. The programme adopts a phase-specific, case-management approach in which each patient is assigned a case manager who provides protocol-based psychosocial interventions,[22] taking reference to the International Clinical Practice Guidelines for Early Psychosis[23] with local cultural adaptations. This standardised intervention package is offered to all patients and their family caregivers with an aim to enhance psychological adjustment to early psychosis through in-depth engagement, comprehensive psychoeducation, adherence to medication treatment, coping and stress management, and relapse prevention.[22] As case-loads of EASY case managers (approximately 1:80) are much heavier than that of those well-established early intervention services in the West, rather than providing intensive intervention such as cognitive-behavioral therapy (CBT) or specialised family therapy, case management of the EASY programme focuses on psychoeducation and supportive care. Emphasis is also placed on enhanced support and communications with family caregivers, who have a critical role in patient management, as most patients enrolled in the programme live with their families.[18] Family counseling and caregiver support groups are arranged if indicated. Patients with additional treatment needs such as presence of residual symptoms or secondary depressive symptoms are referred to clinical psychologists for provision of CBT. The programme also closely collaborates with non-governmental organisations (NGOs) which organise community-based rehabilitation programmes and vocational training for patients recovering from early psychosis. Multi-disciplinary case reviews are held on a regular basis to closely monitor patients' clinical progress and treatment outcomes. Patients are assertively followed up for 2 years, after which they are managed by a transitional step-down clinic in the third year of treatment, whereby medical follow-up is offered by psychiatrists who have been responsible for their care in the 2-year programme but no case

management is provided (i.e., equivalent to standard psychiatric care but with 1-year continuous outpatient follow-up by psychiatrists of the EASY programme). They are then transferred to generic psychiatric services for continuous care.

In this study, participants were followed up and re-interviewed 2 and 3 years after inclusion to the trial. The study was approved by the local institutional review boards. All participants provided written informed consent. For those aged under 18 years, consent was also obtained from a parent or guardian. The trial was registered with ClinicalTrials.gov (NCT01202357).

Randomisation

Following baseline assessment, participants were randomly assigned in a 1:1 ratio to either extended early intervention (intervention group) or step-down care (control group) for the next 12 months. An allocation sequence was computer-generated with a fixed block size of four. Randomisation and concealment procedures were conducted by an independent research staff who was not involved in recruitment, clinical management and research assessments of study participants.

Treatment

Participants in both treatment conditions were managed by psychiatrists from their respective EASY clinical teams during a 12-month period of RCT. After completion of the trial, all participants were transferred to standard psychiatric services for continuous care.

Extended early intervention

Specialised early intervention was continued in the form of an additional year of case management. A trained case manager took over cases from the EASY programme and was responsible for providing care and coordinating treatment with clinicians, allied health professionals and NGOs to

all participants in this group (n=82) (i.e., a case-load comparable to the EASY programme). Case management closely aligned with the EASY treatment protocols, focusing specifically on functional enhancement by assisting participants to re-establish supportive social networks, resume leisure pursuits and return to work. Additionally, continuous supportive care, psychoeducation, coping and stress management were delivered to family caregivers of each participant in the intervention group by the case manager. Biweekly clinical supervision was provided to case manager by senior psychiatrists who had extensive experience in early intervention for psychosis.

Step-down care

Step-down care provided outpatient medical follow-up with limited community support which focused mainly on crisis intervention. The two treatment groups did not differ from each other with respect to the intensity of medical follow-up by psychiatrists, prescription of antipsychotic medications and availability of various psychosocial interventions and community-based services.

Assessment

Diagnosis of each participant was ascertained in consensus meetings attended by a senior psychiatrist and research assistants using all available information encompassing the entire follow-up period, including the Chinese-bilingual Structured Clinical Interview for DSM-IV (CB-SCID)[24] (conducted at baseline, 1 and 3-year follow-up), informant histories and medical records. Premorbid functioning was measured with the Premorbid Adjustment Scale (PAS)[25] at study entry. The Interview for the Retrospective Assessment of the Onset of Schizophrenia (IRAOS)[26] was employed at baseline to determine DUP, age and mode of onset of psychosis. Psychopathology was assessed at baseline, 1, 2 and 3-year follow-up using the Positive and Negative Syndrome Scale (PANSS)[27] and the Calgary Depression Scale (CDS).[28] Psychosocial functioning was measured with the Social and Occupational Functioning Assessment Scale (SOFAS)[29] and the Role Functioning Scale (RFS).[30] The SOFAS provided global functioning estimate of an individual participant, whereas the

RFS, which comprised four subscales, was used to assess functional levels of various domains including work productivity, independent living and self-care, and immediate and extended social networks. Occupational status was also assessed. Functional evaluation was conducted at baseline, at 6 months, 1, 2, and 3 years after study entry.

Follow-up information on service use including hospitalisation, defaults in outpatient appointments and service disengagement, treatment characteristics including use of second-generation antipsychotic and dose of antipsychotic medication (chlorpromazine equivalent doses[31] were computed for analysis), and other clinical outcome measures including relapse, all-cause mortality and suicide were obtained via systematic record review using outpatient and inpatient case-notes as well as computerised clinical information from the hospital database. Data on mortality and cause of death were also verified with the Coroner's Register. Complete clinical record data over 2-year post-trial follow-up period were available to all participants for analysis.

Trained research assistants masked to treatment allocation administered all assessments. Videotaped interviews of 10 cases were independently rated by all research assistants for interrater reliability evaluation. Intra-class correlation coefficients (ICCs) for PANSS general psychopathology, positive and negative symptom subscales, and CDS total score were 0.92, 0.95, 0.79 and 0.96, respectively, indicating good inter-rater reliability. Satisfactory level of concordance was also observed in functional measures, with ICCs for SOFAS and RFS total scores being 0.91 and 0.86, respectively.

Statistical analysis

Statistical analyses were performed on an intention-to-treat (ITT) basis. Primary outcome was psychosocial functioning as measured by SOFAS and RFS. Secondary outcome measures included symptom severity, service use and other clinical variables. We estimated sample size based on

SOFAS as this was a key outcome measure of the study. To detect clinically meaningful 5-point difference in SOFAS, with a power of 0.8 and an alpha of 0.05, and to allow for 20% dropout rate, a total of 160 participants were required for the study. Potential attrition bias was examined by comparing between patients who participated in 3-year follow-up assessment and those who did not regarding sociodemographic factors, baseline clinical profiles, symptom and functional scores at entry, and treatment characteristics,. To determine group differences in functional and symptom outcomes during 2-year post-trial follow-up, a series of linear mixed models (LMMs) with repeated measures (using data from baseline and all follow-up time-points) were performed. Implementation of LMM analyses is recommended as a preferred statistical method of outcome analysis in clinical trials as these models can address missing outcome data by allowing the analysis of all available data on the assumption that data are missing at random.[32] In our models, treatment group, time and group x time interaction were treated as fixed factors, and unstructured covariance structure was employed. Interaction terms between treatment group and time were used to estimate whether longitudinal changes of outcome variables across 3-year follow-up differed between the two groups. Between-group comparisons on functional and symptom outcomes at individual follow-up time-points were analysed based on estimated mean differences and *P* values of difference derived from LMMs. In addition, comparisons between treatment groups based on completers-only analyses on functional and symptom outcomes at 2 and 3-year follow-up were conducted. Treatment characteristics, service use and other clinical outcome variables during 2-year post-trial follow-up were also compared between the two groups. DUP was log-transformed due to its skewed distribution. All statistical analyses were two-tailed with significance level set at $P<0.05$. Statistical analyses were performed with IBM SPSS Statistics 24.0.

Results

The participant flow through the study is presented in Fig. 1. A total of 160 patients were enrolled and randomly assigned to intervention group (n=82) and control group (n=78). Table S1 shows baseline characteristics of 160 participants included in the trial and reveals no significant between-group difference in sociodemographic profile or baseline clinical, functional and treatment characteristics. A total of 138 (intervention group: n=71, 86.6%; control group: n=67, 85.9%) and 143 patients (intervention group: n=76, 92.7%; control group: n=67, 85.9%) participated in 2 and 3-year follow-up assessment, respectively. There was no significant difference between the two groups in participation rate at 2-year (P=0.90) and 3-year (P=0.16) follow-up. For those who had completed 3-year follow-up, no significant between-group difference was observed in sociodemographic and other baseline characteristics (online Table DS2). Attrition analysis at 3-year follow-up demonstrated no significant difference between participants and non-participants in sociodemographic characteristics or baseline clinical, functional and treatment variables, with the exception of RFS immediate social network score (participants had higher scores than non-participants, P=0.03). At the end of 3-year follow-up, 4 participants were deceased (intervention group: n=1; control group: n=3, P=0.36), with 2 died of suicide and 2 of natural causes (Fig. 1, Table 2).

Functional outcomes

Table 1 presents observed means (SDs) as well as estimated mean differences and P values of difference from LMMs at 1, 2 and 3-year follow-up for functional outcomes. There were no significant differences between the two groups in any of the functional measures at 2 and 3-year follow-up. Similarly, comparisons based on completers-only analyses demonstrated lack of significant between-group differences in ratings of all functional measures at 2 and 3-year follow-up, with the exception that intervention group had significantly higher RFS extended social network score than control group at 2-year follow-up (online Table DS3). Longitudinal analysis over 3-year follow-up showed significant group x time interactions in SOFAS score (P<0.01), and RFS work

productivity score (P<0.01), independent living score (P<0.01) immediate social network score (P=0.03), extended social network score (P=0.01) and total score (P<0.01). This indicates that significant differential courses of functioning over 3 years in treatment groups appeared to be driven mostly by between-group differences in the first year of follow-up (i.e., a 12-month trial period). A graphical illustration of the longitudinal trajectories of functional measures across 3-year follow-up in treatment groups is shown in Fig. 2.

Symptoms and other secondary outcomes

Comparisons based on both LMMs and completers-only analyses revealed no significant differences between the two groups in outcomes on positive symptoms, negative symptoms, depressive symptoms and PANSS general psychopathology scores at 2 and 3-year follow-up (Table 2, online Table DS4). There were no significant between-group differences in medication treatment characteristics, length of inpatient stay, employment outcome, and rates of relapse, psychiatric admission, outpatient treatment defaults and service disengagement across 2-year post-trial follow-up period (Table 2).

Discussion

The aim of the current study was to examine the sustainability of superior functional and clinical outcomes of 1-year extended early intervention to step-down care (3-year versus 2-year early intervention service) in first-episode psychosis patients 1 and 2 years after the service ended. We found that there were no significant differences between the treatment groups in outcomes on functioning, symptom severity and service use during 2-year post-trial follow-up period. Although significant time x intervention interaction effects were observed across 3-year follow-up in various functional measures, these findings appeared to be driven mainly by group differences occurred in the first year of follow-up when extended specialised treatment was actively implemented. Our

results thus indicate that despite extending early intervention service to 3-year duration, superior outcomes achieved by specialised treatment still could not be maintained after transition to generic psychiatric service.

Of note, however, our negative findings concur with the results of two previous RCT follow-up studies, namely the OPUS and LEO trials[7,8] which also failed to demonstrate sustained superiority of early intervention over standard care in most treatment outcomes after service withdrawal. Alternatively, despite lack of statistically significant between-group differences in functional ratings and employment outcome at post-trial follow-up, our results showed that patients randomised to intervention group exhibited higher scores than those allocated to control group in global functioning and most individual functional domains. Additionally, patients receiving extended early intervention attained higher full-time employment rate and longer cumulative duration in full-time work than those managed by step-down care by the end of 3-year follow-up. Hence, this indicates that, overall, the intervention group still compared favorably with the control group in longer-term functional outcome, with the former having slightly better functioning, albeit statistically nonsignificant, than the latter 2 years after service termination. It is also worth noting that although intervention group exhibited functional decline in RFS domains of social networks after service withdrawal, improvement in work productivity and independent living was largely maintained. Subsequent loss of significant group difference in functioning was also partly due to gradual functional improvement in control group during the post-trial follow-up.

Our findings, on the one hand, seem to support the proposition that positive effects of early intervention persist only as long as the service continues.[33] This may further suggest that specialised treatment programmes do not alter the early course of illness in first-episode psychosis patients and hence lack the lasting influence on longer-term outcome. On the other hand, a number of factors might contribute to an apparent loss of therapeutic benefits attained by extended early intervention,

particularly on functional outcome, over the subsequent 2 years after transition to generic psychiatric care. First, it might be possible that 3-year duration of early intervention for psychosis is still insufficient to maintain initial functional gains after specialised service ended. Substantial evidence has also shown that a significant proportion of first-episode psychosis patients experience persistent functional impairment even in the presence of clinical remission.[34-36] A longer period of early intervention encompassing the entire hypothesised critical period (i.e., up to 5 years after onset of psychosis)[37] might be required to achieve sustained functional improvement (please refer to two RCTs evaluating effectiveness of 5-year early intervention service for psychosis, namely the Danish OPUS II trial and the Canadian trial).[14,15] Second, treatment intensity level of our early intervention might be significantly compromised by a high patient-to-case manager ratio, rendering it inadequate to maintain longer-term beneficial effects. Conversely, as our service is constrained by low resources and high case-loads as compared to those well-established early psychosis progrmames implemented in some Western countries, our results should be generalised to other populations with caution. Third, recent enhancement of community psychiatric services in Hong Kong[38] might, however, dilute the positive effect of extended intervention on longer-term outcomes through an overall improvement in treatment efficacy of generic psychiatric care received by participants during the post-trial period. This may in fact echo the recent findings of OPUS II trial which suggested that the lack of superior effect of 5-year extended intervention might partly be attributable to the high quality of standard community care provided to the control group.[15] Fourth, the potential disruptive effects of transfer of care from specialised early intervention to generic service, with subsequent withdrawal of case management and change of clinician for psychiatric follow-up, would likely lead to patients' perceived sense of loss,[7] diminished treatment alliance[10] and limited care coordination with significantly reduced multidisciplinary inputs. This may thus result in functional deterioration. In fact, our findings are partially in keeping with this postulation as functional decline in various domains, in particular immediate and extended social networks of our cohort over the 2-year post-trial period mainly took place in the first year after service

termination. A recent naturalistic study further revealed that extended continuity of care up to 5 years with lower treatment intensity after initial 2-year intensive specialised intervention prevented loss of therapeutic gains on symptom and functional outcomes at 5-year follow-up in first-episode psychosis patients.[39] Fifth, it is plausible that the comparatively briefer DUP (median DUP: 13 weeks) of our cohort might obscure the potential differential effects of extended intervention on longer-term outcomes between patients with short and prolonged untreated initial psychosis. Evidence from a recent RCT (RAISE study in United States) has demonstrated that among first-episode psychosis patients who were allocated to 2-year comprehensive treatment programme, those with shorter DUP had significantly better symptom outcome and quality of life at 2-year follow-up than the counterparts with prolonged DUP and those randomised to standard care.[40] Reassessment of the RAISE study cohort will help clarify whether such differential treatment effect on patients with varying DUP would be critical in determining the durability of therapeutic benefits achieved by early intervention service.

The strengths of the study included low dropout rate (89.4% of the initial cohort completed 3-year follow-up assessment), lack of differential attrition between treatment groups, masking of research staff assessing outcomes to treatment allocation, 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 use and other clinical variables for all participants. Several methodological limitations, however, warrant consideration in interpreting the study results. First, as the sample was recruited from the EASY programme, which treated patients aged 15-25 years only, our results may not be generalisable to people who are older at onset of psychosis. Second, data regarding the inputs of community psychiatric care and clinical psychologists after transition to generic service were not available, and thus precluded us from estimating the potential confounding effect of enhanced community service and provision of CBT on clinical and functional outcomes at post-trial follow-up.

This was the first RCT follow-up study examining the durability of treatment effects of extending an early intervention service for psychosis beyond 2 years. Our results indicate that superior symptom and functional outcomes attained by 3-year extended early intervention (versus 2-year early intervention) were not sustained after service withdrawal, even though initial improvement in some functional domains seem to be largely maintained during post-trial follow-up. Aside from a genuine lack of efficacy of specialised intervention on maintaining positive effects in first-episode psychosis patients, an absence of significant outcome difference between treatment groups at post-trial follow-up might also be attributable to an array of factors, which nonetheless, could not be adequately addressed by the current study. Further investigation is warranted to clarify the roles of treatment delay, treatment intensity levels (e.g. case-load per case manager) and length of specialised service (e.g. 5-year intensive programme or extended continuity of care by a step-down service with lower treatment intensity) in determining the sustainability of early intervention on outcome improvement. Given the heterogeneous outcome trajectories in first-episode psychosis, a universal provision of specialised service to all patients for an extended period might not be the most cost-effective approach in optimising long-term outcome. Future research is required to identify a subgroup of patients who may benefit most from extended intervention. More studies should also be conducted to delineate which specific treatment elements, from an integrated, multi-component early intervention service, should be offered for an extended duration so as to maintain longer-term therapeutic benefits.

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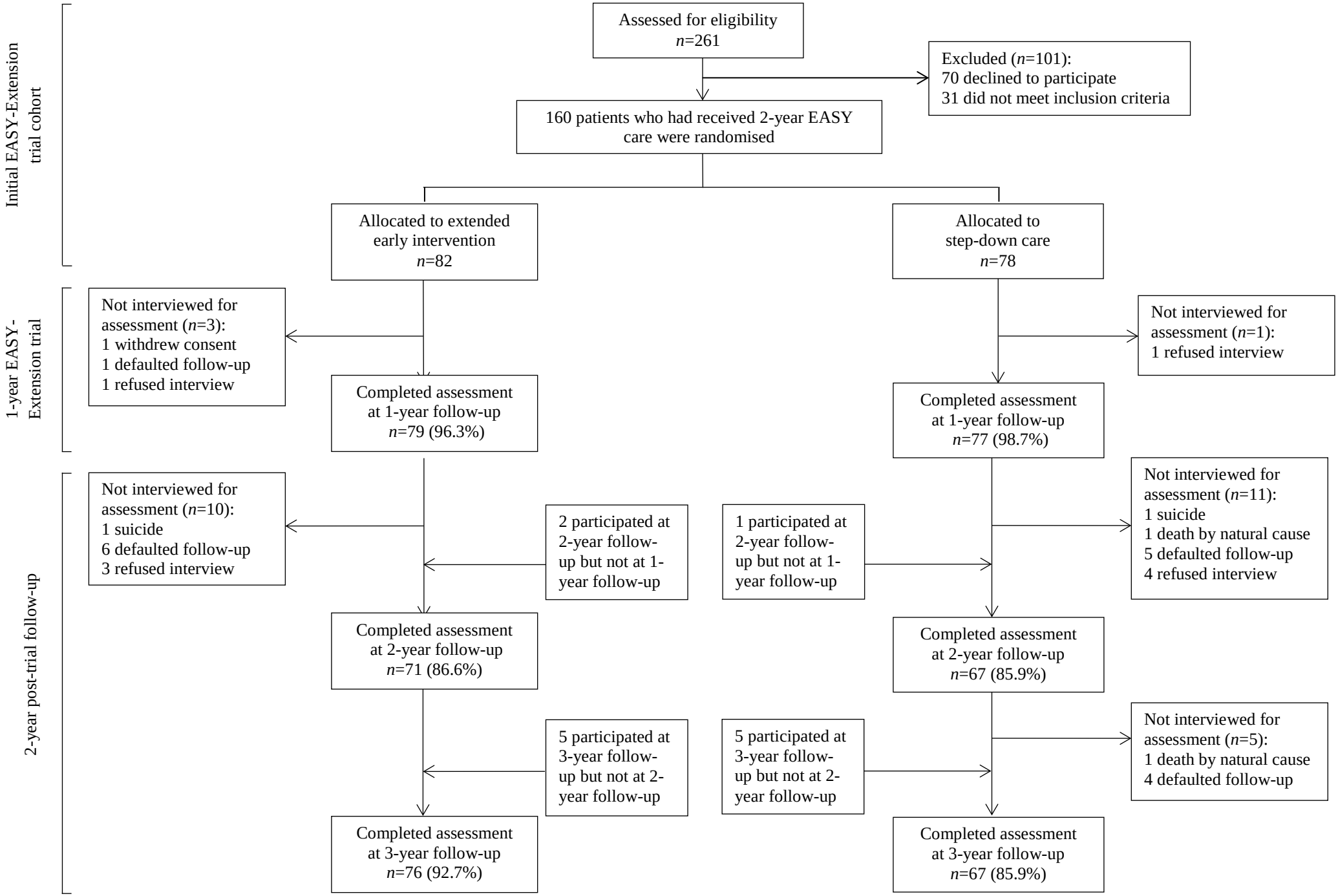

Fig. 1 Flow of patients through the study.

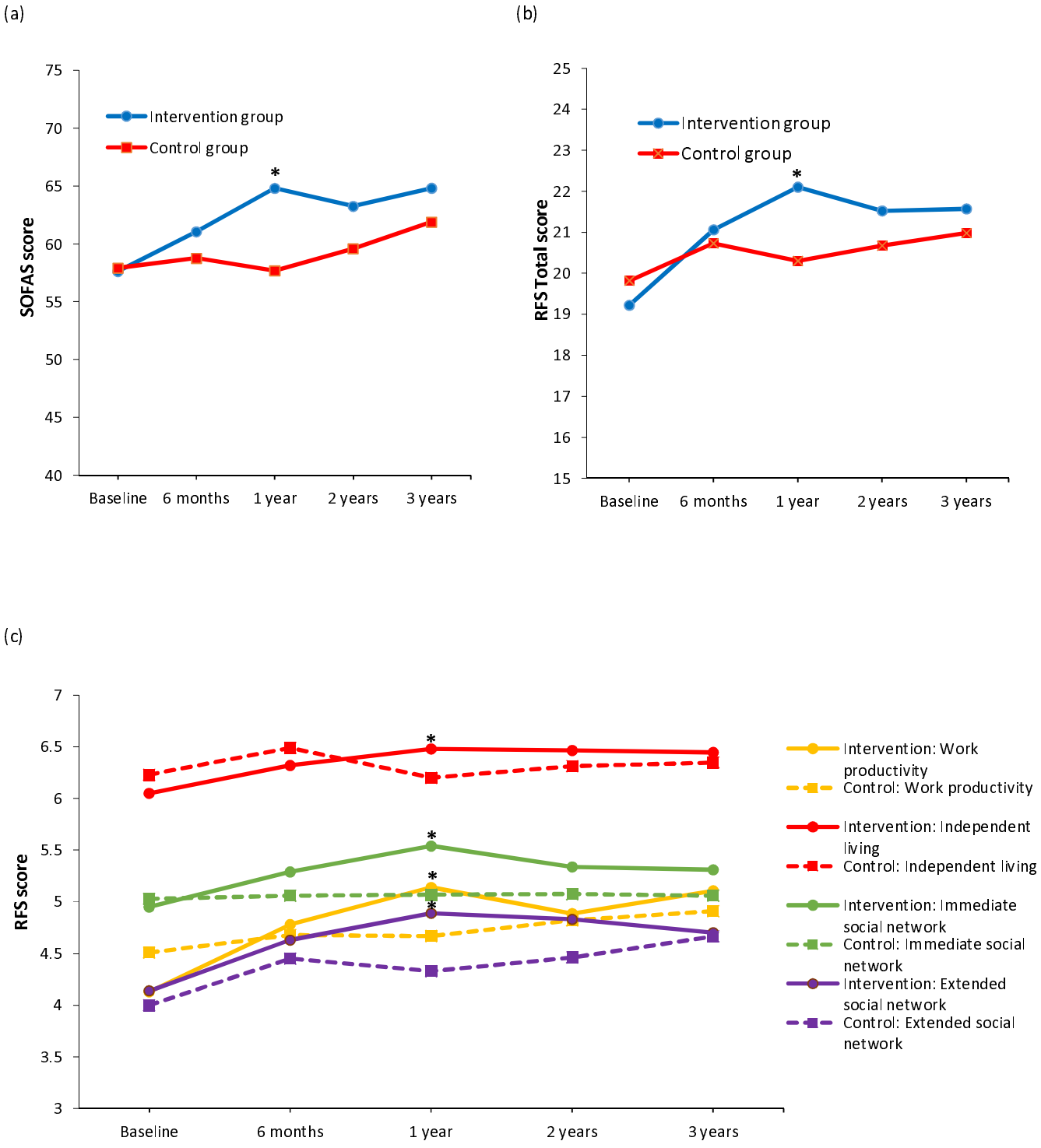

Fig. 2 Longitudinal change in functioning scores across 3-year follow-up in the extended early intervention and step-down care control groups: (a) change in Social and Occupational Functioning Assessment Scale (SOFAS) score; (b) change in Role Functioning Scale (RFS) total score; (c) change in RFS sub-domains score.
*****P<0.05

Table 1 Functional outcomes at 1, 2 and 3-year follow-up of the two study groups[a]

Variables	Intervention group mean (s.d.)	Control group mean (s.d.)	Estimated mean difference[a] (95% CI)	*P*
SOFAS score				
1-yr follow-up	64.8 (13.1)	57.9 (12.7)	3.57 (1.14 – 5.99)	0.004
2-yr follow-up	63.3 (13.6)	59.6 (12.1)	1.28 (-0.31 – 2.88)	0.113
3-yr follow-up	64.8 (13.7)	61.9 (12.5)	-1.11 (-1.04 – 3.27)	0.311
RFS work productivity				
1-yr follow-up	5.1 (1.4)	4.7 (1.5)	0.44 (-0.16 – 0.72)	0.002
2-yr follow-up	4.9 (1.5)	4.8 (1.4)	0.15 (-0.01 – 0.30)	0.060
3-yr follow-up	5.1 (1.5)	4.9 (1.4)	0.17 (-0.07 – 0.41)	0.173
RFS independent living				
1-yr follow-up	6.5 (0.6)	6.2 (1.0)	0.23 (0.06 – 0.39)	0.007
2-yr follow-up	6.5 (0.5)	6.3 (0.7)	0.11 (0.01 – 0.23)	0.071
3-yr follow-up	6.4 (0.6)	6.3 (0.7)	0.08 (-0.02 – 0.18)	0.112
RFS immediate social network				
1-yr follow-up	5.5 (0.9)	5.1 (1.0)	0.27 (0.07 – 0.47)	0.008
2-yr follow-up	5.3 (0.8)	5.1 (0.9)	0.15 (-0.04 – 0.34)	0.117
3-yr follow-up	5.3 (0.9)	5.0 (1.0)	0.08 (-0.01 – 0.17)	0.059
RFS extended social network				
1-yr follow-up	4.9 (1.0)	4.3 (1.3)	0.20 (0.04 – 0.45)	0.010
2-yr follow-up	4.8 (0.9)	4.5 (1.1)	0.08 (-0.06 – 0.22)	0.268
3-yr follow-up	4.7 (0.9)	4.7 (1.0)	0.01 (-0.21 – 0.20)	0.959
RFS total score				
1-yr follow-up	22.1 (3.2)	20.3 (3.7)	1.16 (0.59 – 1.74)	< 0.001
2-yr follow-up	21.5 (3.3)	20.7 (3.2)	0.44 (-0.13 – 1.01)	0.126
3-yr follow-up	21.5 (3.2)	20.9 (3.2)	0.35 (-0.23 – 0.95)	0.251

CI, confidence interval; RFS, Role Functioning Scale; SOFAS, Social and Occupational Functioning Assessment Scale.

[a] Estimated mean difference and *P* values were derived from linear mixed models for repeated measurements (at baseline, at 6-month, 1-year, 2-year and 3-year follow-up).

Table 2 Clinical and service use outcomes of the two study groups during 2-year post-trial follow-up period

Variables	Intervention group	Control group	*t* or χ^2	*P*
Symptom severity at follow-up[a], mean (s.d.)				
PANSS positive symptom score				
2-year follow-up	10.1 (3.7)	10.3 (3.7)	-0.5	0.649
3-year follow-up	9.9 (3.4)	10.2 (3.6)	-0.6	0.577
PANSS negative symptom score				
2-year follow-up	12.1 (5.1)	11.3 (4.5)	0.9	0.355
3-year follow-up	12.0 (4.0)	11.9 (4.0)	0.1	0.941
PANSS general psychopathology score				
2-year follow-up	21.3 (4.3)	21.9 (4.0)	-0.9	0.364
3-year follow-up	21.2 (5.4)	22.1 (4.6)	-1.0	0.304
CDS total score				
2-year follow-up	1.7 (2.3)	2.7 (2.9)	-2.3	0.024
3-year follow-up	1.6 (2.3)	2.0 (2.8)	-1.1	0.271
Service use outcomes during follow-up[b]				
Psychiatric hospital admission, % (*n*)	17.1 (14)	16.7 (13)	0.0	0.945
Length of hospital stay, days: mean (s.d.)	131.5(139.7)	174.3(259.0)	0.5	0.594
Default in outpatient appointment, % (*n*)	31.7 (26)	41. (32)	1.502	0.220
Service disengagement, % (*n*)	6.1 (5)	7.7 (6)	0.2[c]	0.762
Other outcome measure during follow-up				
Relapse of psychotic episode[b], % (*n*)	25.6 (21)	37.2 (29)	2.5	0.115
All-cause mortality[b], % (*n*)	1.2 (1)	3.8 (3)	1.1[c]	0.358
Suicide[b], % (*n*)	1.2 (1)	1.3 (1)	0.0[c]	1.000
Total months in full-time work[a], mean (s.d.)	12.9 (10.0)	11.8 (10.1)	0.6	0.519
Full-time work at 3-year follow-up[a], % (*n*)	56.6 (43)	46.3 (31)	1.6	0.218
Treatment characteristics at follow-up[b]				
Antipsychotic treatment at 2-year follow-up, % (*n*)				
Not on antipsychotic	16.0 (13)	6.6 (5)	3.6[c]	0.181
Use of FGA	8.6 (7)	7.9 (6)		
Use of SGA	75.3 (61)	85.5 (65)		
Antipsychotic treatment at 3-year follow-up, % (*n*)				
Not on antipsychotic	11.1 (9)	12 (9)	0.23[c]	0.911
Use of FGA	8.6 (7)	6.7 (5)		
Use of SGA	80.2 (65)	81.3 (61)		
CPZ equivalent dose, mg: mean (s.d.)				
2-year follow-up	333.3 (344.2)	308.2 (290.6)	0.5	0.584
3-year follow-up	364.9 (281.0)	296.5 (261.7)	1.5	0.142

CDS, Calgary Depression Scale; CPZ, chlorpromazine; FGFA, first-generation antipsychotic; PANSS, Positive and Negative Syndrome Scale; SGA, second-generation antipsychotic.

[a] 71 participants in intervention group and 67 participants in control group were assessed at 2-year follow-up. 76 participants in intervention group and 67 participants in control group were assessed at 3-year follow-up.

[b] Complete clinical record data were available for all participants.

[c] Fisher's exact test was applied as the assumption of chi-square test was not met.