

SUSTAINABILITY OF TREATMENT EFFECT OF A 3-YEAR EARLY INTERVENTION PROGRAMME FOR FIRST-EPIISODE PSYCHOSIS (EASY5)

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Background

- Psychotic disorders affect 2.5-3% of the population
- Illness onset frequently at late adolescence and early adulthood
- associated with significant functional impairment and incur huge societal costs
- One of the highest disease burdens globally and locally

Rationale for Early Intervention (EI)

- Early detection to reduce treatment delay
- Phase-specific intervention in the critical period improves long-term outcome
- Evidence indicates that specialized EI service is superior to standard care in improving clinical and functional outcomes in first-episode psychosis (FEP) patients

Psychosis and Early Intervention in HK

- EASY (Early Assessment Service for Young people with psychosis) was established in 2001
- Provides specialized EI to FEP patients aged 15-25 years:
 - Community awareness programmes & Open referral system (with hotline)
 - 2y phase-specific specialized intervention with assigned case manager
- Our prior EASY evaluation study (historical control-case comparison) of 1400 patients showed that patients in EASY had lower suicide and admission rates, better functional and symptom outcomes, and fewer default and disengagement rates than standard care (Chen et al. 2011)

EASY3 study (EASY-Extension Trial)

- Funded by Commissioned Research on Mental Health Policy and Services (SMH-29)
- Aim: RCT comparing 1-year extension of EI (3-year EI) with step-down care (2-year EI) in 160 patients who had received 2-year EASY care for FEP
- Randomly allocated into: Extended EI (n = 82) vs SC (n = 78)
- This is the first RCT evaluating effectiveness of EI for FEP with its treatment duration beyond 2 years
- Outcomes:
 - patients in Extended EI group had significantly better functional outcome, fewer negative and depressive symptoms, and lower default rate than those in SC group at 1-year FU (Chang et al. 2015)

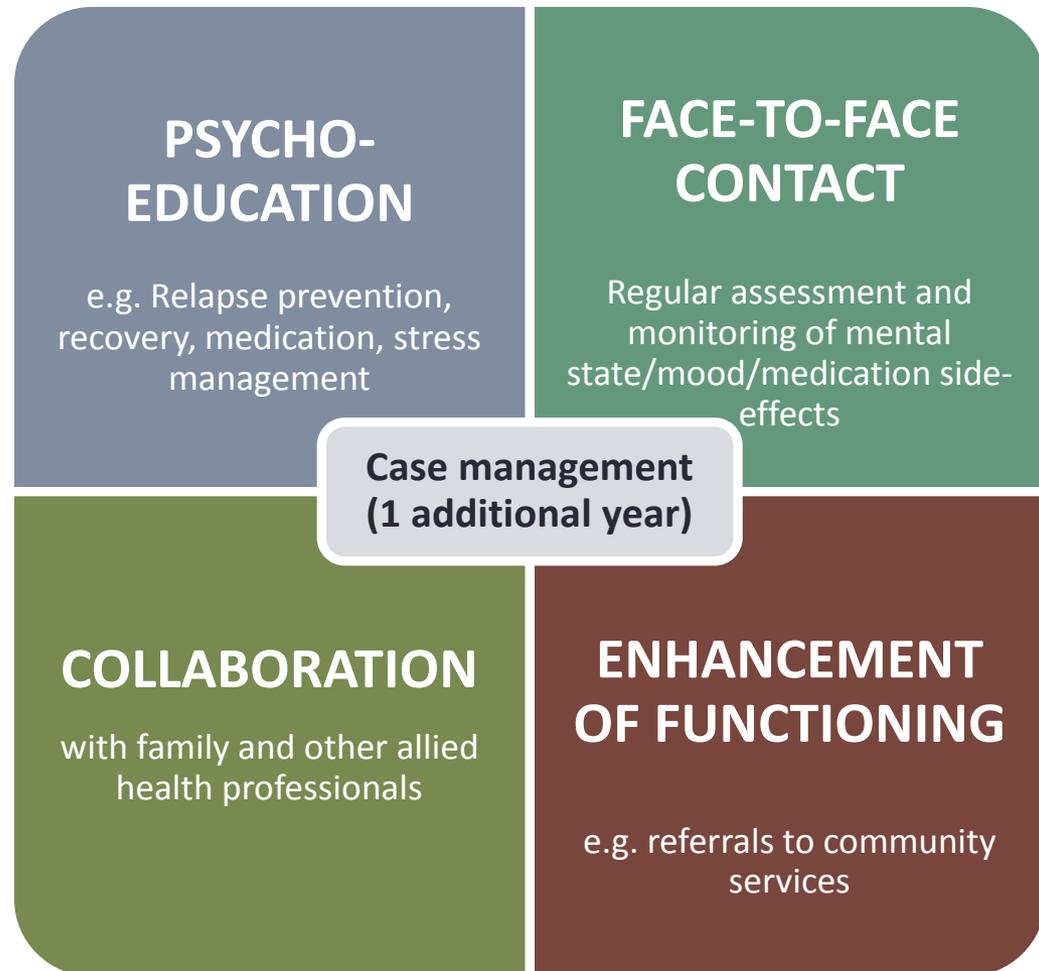
Extended EI & SC Groups

Extended EI:

- Phase-specific case management providing specialized EI service

SC:

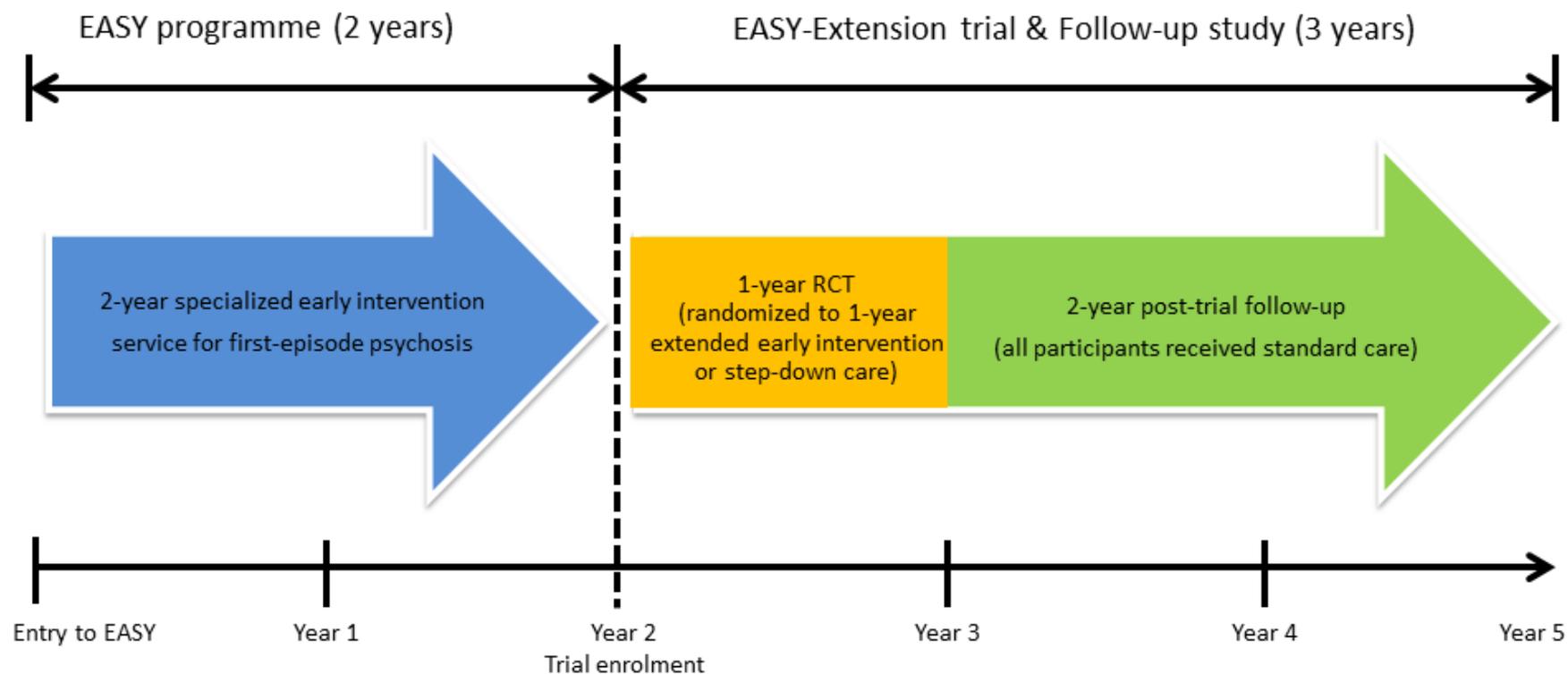
- Standard psychiatric care without case management



EASY5 study (3-year FU of EASY-Extension Trial)

- Previous post-RCT follow-up studies (OPUS trial, LEO trial) showed that superiority of specialized EI over standard care could not be maintained after service was withdrawn
- Key research questions: **optimal duration of EI & sustainability of positive effect of EI**
- **EASY5** study is the *first* post-RCT follow-up addressing the sustainability of positive effect of specialized EI for FEP with its treatment duration > 2 years (funded by HMRF no. 11121881)
- EASY-Extension cohort was followed up and re-interviewed 2 and 3 years after inclusion to the trial

EASY3 and EASY5



From: Chang et al. 2017. Br J Psychiatry [Epub ahead of print: doi:10.1192/bjp.bp.117.198929]

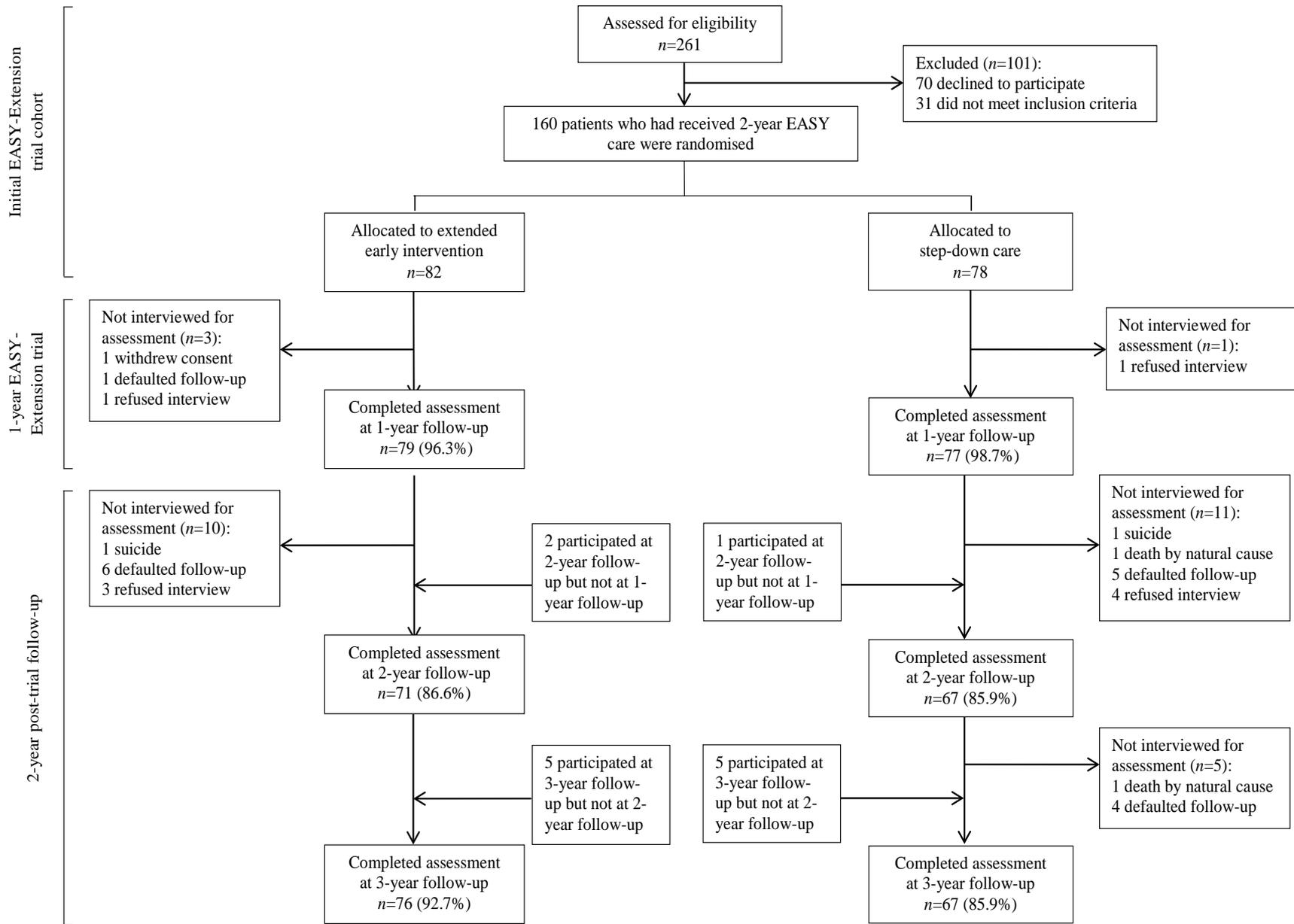


Fig. 1 Flow of patients through the study.

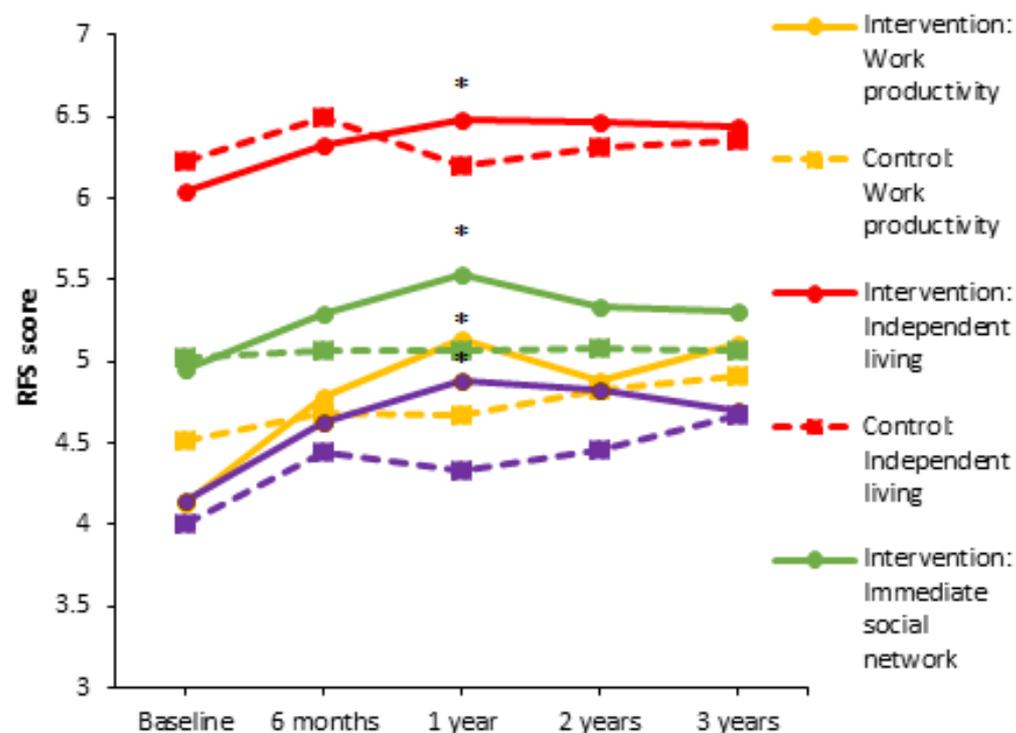
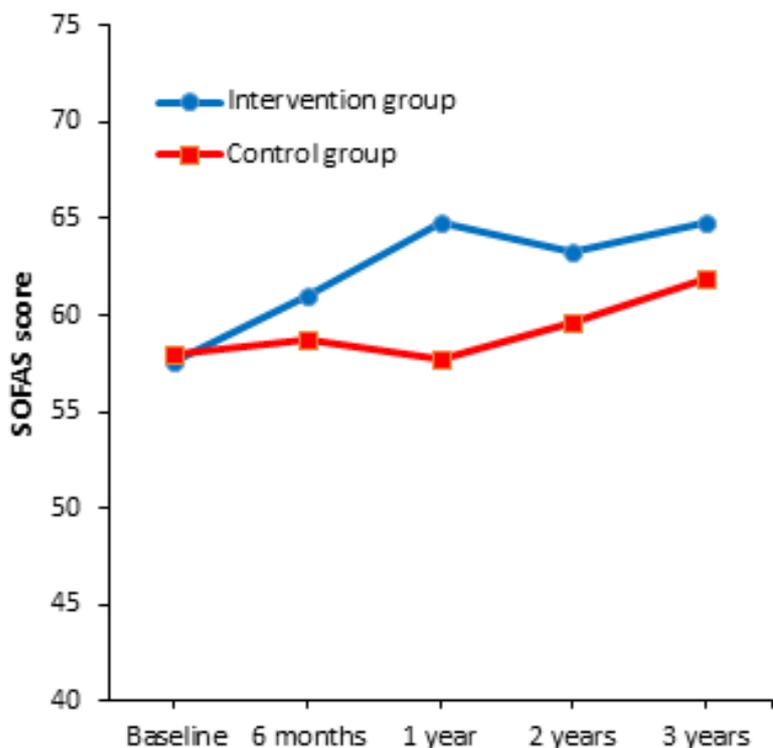
Results – Clinical Outcomes

Table DS4 Symptom 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)	<i>P</i>
PANSS positive symptoms				
1-yr follow-up	8.3 (2.5)	8.6 (2.8)	-0.59 (1.58 – -0.40)	0.240
2-yr follow-up	10.1 (3.7)	10.3 (3.7)	-0.27 (-0.92 – 0.39)	0.422
3-yr follow-up	9.9 (3.4)	10.2 (3.6)	-0.24 (-0.75 – 0.26)	0.346
PANSS negative symptoms				
1-yr follow-up	8.5 (2.5)	9.8 (3.8)	-0.63 (-1.91 – -0.65)	0.033
2-yr follow-up	12.1 (5.1)	11.3 (4.5)	0.78 (-0.09 – 1.65)	0.079
3-yr follow-up	12.0 (4.0)	11.9 (4.0)	0.26 (-0.53 – 1.05)	0.520
PANSS general psychopathology				
1-yr follow-up	19.2 (3.7)	21.1 (5.0)	-1.80 (-3.44 – -0.16)	0.031
2-yr follow-up	21.3 (4.3)	21.9 (4.0)	-0.15 (-1.28 – 0.98)	0.795
3-yr follow-up	21.2 (5.4)	22.1 (4.6)	-0.28 (-1.01 – 0.45)	0.446
CDS total score				
1-yr follow-up	0.9 (1.6)	1.8 (2.7)	-0.92 (-1.77 – -0.07)	0.034
2-yr follow-up	1.7 (2.3)	2.7 (2.9)	-0.51 (-1.10 – 0.07)	0.086
3-yr follow-up	1.6 (2.3)	2.0 (2.8)	-0.16 (-0.53 – 0.21)	0.385

CI, confidence interval; CDS, Calgary Depression Scale; PANSS, Positive and Negative Syndrome Scale.

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

Results – Psychosocial Functioning



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Results – Service Utility and Others

Service utility and treatment characteristics of the two study groups during 2-year post-trial follow-up period				
Variables	Intervention group	Control group	<i>t</i> or χ^2	<i>P</i>
Service use outcomes during follow-up^b				
Psychiatric hospital admission, % (<i>n</i>)	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, % (<i>n</i>)	31.7 (26)	41. (32)	1.502	0.220
Service disengagement, % (<i>n</i>)	6.1 (5)	7.7 (6)	0.2 ^c	0.762
Other outcome measure during follow-up				
Relapse of psychotic episode ^b , % (<i>n</i>)	25.6 (21)	37.2 (29)	2.5	0.115
All-cause mortality ^b , % (<i>n</i>)	1.2 (1)	3.8 (3)	1.1 ^c	0.358
Suicide ^b , % (<i>n</i>)	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 , % (<i>n</i>)	56.6 (43)	46.3 (31)	1.6	0.218
Treatment characteristics at follow-up^d				
Antipsychotic treatment at 2-year follow-up, % (<i>n</i>)				
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, % (<i>n</i>)				
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

Summary of study results

- No significant between-group differences at 2 and 3 years in outcomes on functioning and symptom severity
- No significant between-group differences on service utilization (e.g. length of inpatient stay, admission and default rates etc.) over the 2-year post-trial period
- Therapeutic benefits achieved by the Extended EI were not sustainable after termination of specialized service

Interpretation

- This may suggest that specialized EI cannot alter early course of psychotic illness, i.e., lacking lasting influence on longer-term outcome after service termination
- Yet, other possible explanations should be considered:
 - 3-year EI may not be optimal for sustained effect
 - Insufficient treatment intensity (high patient-to-case manager ratio of 1:80)
 - Dilution effect by recent enhancement of community psychiatric services in generic care
 - Disruptive effect upon transition from EI to generic service
 - Relatively short DUP in our cohort may obscure longer-term effect of Extended EI on outcomes

Implications and future directions

- Absence of significant group difference on 3-year outcomes might not necessarily indicate lack of efficacy of EI for FEP on longer-term outcome
- An array of factors must be clarified esp. roles of treatment intensity (caseload), DUP, length of EI in determining sustainability of EI effect
- whether universal provision of EI to all FEP patients (one size unlikely fits for all) for an extended period is the most cost-effective approach
- The need to identify a *subgroup of patients* benefit most from extended EI &
- To delineate which *specific treatment elements* from EI should be offered for an extended duration so as to maintain longer-term beneficial effect

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