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The Early Youth Engagement (EYE-2) intervention in first-episode psychosis services: pragmatic cluster randomised controlled trial and cost-effectiveness evaluation

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Background

Early intervention in psychosis (EIP) services improve outcomes for young people, but approximately 30% disengage.

Aims

To test whether a new motivational engagement intervention would prolong engagement and whether it was cost-effective.

Method

We conducted a multicentre, single-blind, parallel-group, cluster randomised controlled trial involving 20 EIP teams at five UK National Health Service (NHS) sites. Teams were randomised using permuted blocks stratified by NHS trust. Participants were all young people (aged 14–35 years) presenting with a first episode of psychosis between May 2019 and July 2020 ($N = 1027$). We compared the novel Early Youth Engagement (EYE-2) intervention plus standardised EIP (sEIP) with sEIP alone. The primary outcome was time to disengagement over 12–26 months. Economic outcomes were mental health costs, societal costs and socio-occupational outcomes over 12 months. Assessors were masked to treatment allocation for primary disengagement and cost-effectiveness outcomes. Analysis followed intention-to-treat principles. The trial was registered at ISRCTN51629746.

Results

Disengagement was low at 15.9% overall in standardised stand-alone services. The adjusted hazard ratio for EYE-2 + sEIP ($n = 652$) versus sEIP alone ($n = 375$) was 1.07 (95% CI 0.76–1.49; $P = 0.713$). The health economic evaluation indicated lower mental healthcare costs linked to reductions in unplanned mental healthcare with no compromise of clinical outcomes, as well as some evidence for lower societal costs and more days in education, training, employment and stable accommodation in the EYE-2 group.

Conclusions

We found no evidence that EYE-2 increased time to disengagement, but there was some evidence for its cost-effectiveness. This is the largest study to date reporting positive engagement, health and cost outcomes in a total EIP population sample. Limitations included high loss to follow-up for secondary outcomes and low completion of societal and socio-occupational data. COVID-19 affected fidelity and implementation. Future engagement research should target engagement to those in greatest need, including in-patients and those with socio-occupational goals.

Keywords

Early intervention; psychosis; engagement; randomised controlled trial; cost-effectiveness.

Psychosis is associated with poor quality of life, high levels of disability, premature death and societal costs in excess of £11.8 billion per year in England.[1,2] The first 2–3 years are pivotal for long-term trajectories.[3,4] Early intervention in psychosis (EIP) services offer early detection and treatment, fewer symptoms and hospital admissions, better well-being and function, and increased cost-effectiveness compared with non-specialised treatment as usual.[5–7] NHS England require that National Institute for Health and Care Excellence (NICE)-concordant EIP services are offered to all new patients with psychosis within 2 weeks of referral.[8] Service structures aim to ensure that young people are proactively engaged to prevent inadequate care and 'falling through gaps'.[8] However, systematic reviews estimate 30% disengagement from first-episode psychosis (FEP) services, with significant costs to individuals, families, society and the National Health Service (NHS).[9] Interventions targeting disengagement are crucial for improving early psychosis outcomes; however, evidence for these is notably absent. No component of the EIP model has been demonstrated to affect engagement.[10] Our initial Early Youth Engagement (EYE) project identified risk factors for disengagement, drawing on patients' and families' views and the disengagement literature. Factors comprised (a) communication style, (b) social network engagement, (c) risk management, (d) staff knowledge and attitudes, and (e) personal experiences. Our Delphi consultation with clinicians reached consensus on components and resources to address these factors.[11] Our pilot study of the resulting team-based motivational-engagement intervention found reductions in disengagement from 24% pre-intervention to 14.5% post-intervention.[11] Qualitative data revealed effects on patients' personal recovery (social inclusion, hope, trust, goals) and engagement (communication, collaboration, family involvement), reassurance for families, and pride and professionalism for staff.[11] Data from minoritised ethnic and LGBTQ+ populations and preliminary implementation led to further training and resource refinements.[12] In the present work, we investigated whether this novel, theoretically informed, team-based motivational engagement intervention (EYE-2) was more effective than standalone standardised EIP (sEIP) for the primary outcome of prolonging engagement, and for secondary routine mental health, NHS and

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societal cost-effectiveness, and socio-occupational outcomes, over 12–26 months.

Method

Study design

This study was a multicentre, single-blind, parallel-group cluster randomised controlled trial. Clusters were UK EIP clinical teams and were allocated 1:1, stratified by site, to either EYE-2 plus sEIP or sEIP alone. Participants were followed up for between 12 and 26 months. The trial was registered prospectively (ISRCTN51629746), and the protocol and statistical analysis plan (SAP) were published before the end of data collection following trial steering committee and Data Monitoring and Ethics Committee (DMEC) approval.[13,14] Protocol changes are detailed in the Supplementary information available at https://doi.org/10.1192/bjp.2024.154 (p. 1).

Cluster and participant eligibility

Service inclusion criteria were: stand-alone service with at least two discrete teams; accepting at least 35–40 new FEP cases annually; collecting NHS England-mandated routine outcomes; geographic and population variation. Patient inclusion criteria were: consecutive referrals between mid-May 2019 and mid-July 2020; aged 14–35 years; and meeting FEP service criteria. No consent was required for the main trial, which used de-identified, routine data. All patients were therefore included. Written consent was obtained from clinicians, and from patients for the societal cost-effectiveness evaluation at 12 months.

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, revised in 2013. All procedures involving human subjects/patients were approved by London-Dulwich Research Ethics Committee (reference: 18/LO/0362 IRAS: 238744).

Randomisation and masking

Consenting teams were randomly assigned, online through Sealed Envelope™, to deliver either EYE-2 + sEIP or sEIP alone. A randomly generated sequence of teams within each site was developed by the Brighton and Sussex Clinical Trials Unit, with permuted blocks of length 2, stratified by site. Allocation was requested by trial coordinators once sites had provided consent from >80% of care coordinators and >70% of all staff for training. Research assistants, statisticians and health economists who rated or analysed primary outcomes were masked to team allocation.

Procedures

All teams received a half-day training in routine data collection. EYE-2 teams then received 1.5 days training from the lead researcher, the Patient and Public Involvement (PPI) lead, a research assistant, and one or two local patients or carers. Booster training was delivered approximately 6 monthly, initially in-person and then online.

The EYE-2 intervention was distinct from standardised care in providing an engagement-focused theoretical model, manualised training, targeted approaches and psychoeducational tools, co-produced with patients and families. The intervention was delivered over the whole period, alongside sEIP, by lead practitioners, with social groups provided by a combination of PPI leads, lead practitioners and research assistants. The intervention addressed engagement through three core therapeutic processes: (a) a motivational therapeutic alliance, focused on patient treatment goals; (b) broad systemic (social) support from families, friends and peers for treatment goals; and (c) psychoeducation, using the EYE-2 resources (booklet series, website) systematically to collaboratively promote treatment goal choices.

Teams in the comparison arm delivered a standarised stand-alone sEIP only, comprising early detection; assertive engagement; work with diagnostic uncertainty; positive risk-taking; person, family and recovery focus; and NICE-recommended medication, cognitive–behavioural, family, physical and vocational interventions.[15]

Outcomes

The primary outcome was time to disengagement in days, from the date of allocation to the lead practitioner to the date of last contact following either refusal to engage or lack of response to EIP contact for 3 consecutive months. This definition and the follow-up timeframes of 12–26 months are widely used in engagement research.[9,16,17] For participants who remained engaged at the end of follow-up or were lost to follow-up, time to disengagement was censored. Primary outcome (engaged, disengaged, lost to follow-up) and time to event were double-rated by a masked research assistant and independent clinician, using a detailed protocol and case-note data. Discrepancies were treble-rated by a third rater to reach consensus.

Secondary outcomes were mandated by NHS England and comprised (a) health and well-being measured by the Health of the Nation Outcome Scales (HoNOS) total, subscale and symptom scores;[18] (b) recovery measured by the Process of Recovery Questionnaire (QPR) total score;[19] (c) subjective quality of life and treatment satisfaction scores (DIALOG QoL and DIALOG TS, respectively)[20] collected by trained EIP clinicians or research assistants at 0, 6, 12, 18 and 24 months. Only data from 0–12 months were used for this investigation. Death, unplanned service use (days in hospital, emergency presentations, section 136 use) and number of NICE guideline interventions received were recorded by research assistants using case-note data. Data completeness and quality were enhanced through training, manuals and monitoring. Serious adverse events were defined using standard criteria as those that resulted in death, were life-threatening, required hospital admission, or resulted in persistent or significant disability or incapacity. Eight criteria were prespecified for relatedness to the trial. Only events that were rated as at least possibly serious and at least possibly related to the trial were recorded. See the protocol for further information.[13]

The economic evaluation investigated the incremental costs of mental health service contacts associated with EYE-2 compared with sEIP, measured using case-note data which were available for all patients. A probabilistic incremental cost-effectiveness analysis was carried out from a mental health service perspective using HoNOS scores to measure patient outcomes. This analysis included intervention costs associated with EYE-2 delivery. A secondary economic analysis investigated differences in mental health plus wider care system costs (societal costs), as well as socio-occupational outcomes (days in stable accommodation, employment, education and training), based on data collected retrospectively from all consenting participants at 12 months by research assistants masked to group allocation, using the Adult Service Use Schedule, and costs in British Pounds derived from 2021–2022 national reference costs according to the Health Economic Analysis Plan. No discounting was needed as all the analyses happened within 12 months.

For the trial process evaluation, all lead practitioners were invited to complete a bespoke questionnaire to determine fidelity to the EYE-2 model at early-, mid- and late-intervention time points. A composite mean fidelity score was calculated for each

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clinician and team by averaging clinicians' scores for use of booklets, websites and social groups. Scores ranged from 0 (not used) to 4 (used with 76–100% of patients). The average lead practitioner case-load was obtained using the national EIP triangulation tool.[21]

Statistical analysis

The study was powered to detect differences corresponding to 12-month disengagement rates of 25% *v.* 15% with 90% power and a 5% significance level. The 25% rate was based on 30% disengagement rates of FEP patients from all service types and 24–25% disengagement from stand-alone EIP services, including our pilot study.[9,11,13,14] The 10% reduction was derived from our pilot data.[11,13,14] Simulations confirmed that ten teams per arm with 950 participants in total across 20 teams would be sufficient. See the published protocol and SAP for assumptions and simulations.[13,14]

Analyses were performed in Stata version 17.1 or later. Baseline characteristics were summarised overall and by arm. Intention-to-treat principles were followed, and estimates, 95% confidence intervals and *P*-values were reported for comparisons between arms. Time to disengagement was known or censored for all participants and modelled with treatment allocation, site, age at allocation to lead practitioner and HoNOS substance misuse score at baseline as fixed effects. The SAP specified Cox regression with a gamma-distributed shared frailty to allow for team clustering and a permutation test to obtain a true *P*-value.[22] However, clustering was negligible, so a multivariable Cox regression without clustering or permutation test was used. The proportional hazards assumption was assessed using Schoenfeld residuals.

In this real-world trial, secondary routine data were mostly collected outside prespecified windows of −2 to +4 weeks owing to clinical service pressures. Data were swapped to the nearest interim (pseudo) time point (3 or 9 months), except HoNOS data, which were collected at baseline and included as covariates. For QPR and DIALOG, data could be collected after the true baseline and reassigned to the closest empty time point, so the baseline score was included in the outcome variables and the true baseline was assumed to be equal between groups. An interaction between treatment allocation and time was included, but not a treatment allocation main effect, which would compare outcomes at baseline. HoNOS, QPR and DIALOG were analysed using mixed-effects linear regression analysis of all non-missing data, with site and age at allocation to lead practitioner as fixed effects and individual as a random effect. Treatment effect was estimated at each time point. The HoNOS analysis was adjusted for HoNOS score at baseline. Analyses of QPR and DIALOG included baseline as an additional time point, owing to data collection after the true baseline, but the treatment effect at baseline was constrained to zero. Robust standard errors were estimated, as assumptions of normality of residuals were not appropriate. Unobserved participant data were assumed to be missing at random, and sensitivity analysis was used to examine the effects of missing data by imputing 12-month outcomes.[23–26] Individual missing question items were replaced for QPR and the DIALOG QoL domain with the relevant average score for a participant if more than 80% of items were completed by that participant. Missing values were not replaced for DIALOG TS, as this comprised only three questions. Sensitivity analyses for HoNOS, QPR and DIALOG explored the impact of (a) data collected within planned time frames only; (b) HoNOS data collected by lead practitioner only; and (c) baseline data collected before versus after the first UK COVID-19 lockdown (23 March 2020), with pooled estimates from each pair of models using a fixed-effects meta-analysis.

Subgroup analyses were conducted for the primary outcome using interaction terms for treatment allocation with factors hypothesised to influence implementation (average lead practitioner case-load) or engagement (substance misuse, symptom severity, ethnicity, educational attainment, socioeconomic deprivation, gender) and for secondary outcomes with factors affecting implementation.

Multivariable Poisson regression (for nights in hospital) and logistic regression (owing to low numbers of accident and emergency department (A&E) visits) were fitted respectively with robust standard errors. Section 136 was not modelled owing to its rarity. We report the estimated incidence rate ratio for the treatment effect and its 95% confidence interval and include fixed effects for site, treatment allocation, baseline HoNOS score and age.

For the economic evaluation, generalised linear models were fitted, and cost differences were identified using a trial allocation dummy variable. Covariate adjustments included site fixed effects and baseline HoNOS scores. Sampling error was accounted for using probabilistic analysis implemented through boot-strap resampling and repeated estimation of cost and outcome models on each bootstrap sample replication. The distribution of jointly estimated incremental costs and outcomes were used for the cost-effectiveness analysis. Mean values were used as 'best-estimates' of cost and outcome differences. Probabilities derived from the bootstrap distribution of estimates were used to assess uncertainty around mean estimates. Missing case-note and self-report data were assumed to be missing-at-random and imputed through multiple imputation methods (Supplementary information, p. 1).

Results

Eleven teams were randomised to deliver EYE-2 + sEIP, and nine to deliver sEIP alone; 3816 patients were referred during the identification period from 13 May 2019, and 1027 (652 EYE-2; 375 sEIP) met eligibility criteria (Fig. 1). Forty per cent (1525 patients) were assessed as not having FEP. However, this proportion varied widely by team (16.6–66.1%), with acceptance rates by team ranging from 9.5–42.5%. Twenty-one per cent of patients in each arm were lost to follow-up, mostly owing to migration to another mental health service (11%) or mutually agreed discharge (almost 5%). The mean age was 25 years, with more men than women, and more White British compared with other ethnicities. Most patients were educated to age 18 years. Participant characteristics were relatively well balanced between trial arms (Table 1). Levels of deprivation and ethnicity other than White were slightly higher, whereas levels of educational attainment were slightly lower in EYE2 + sEIP versus sEIP. Of the 272 staff in EYE-2 teams and 190 staff in sEIP teams, 204 (75%) and 132 (70%) attended training, including 116 (85%) and 71 (82%) lead practitioners (Supplementary information, p. 1).

Disengagement ratings were 85% concordant between the first and second masked raters, with remaining cases agreed through consensus. The median time to disengagement was 258 days. Disengagement was lower than expected, at 16% in the EYE-2 + sEIP and 15.7% in the sEIP group (Fig. 2 and Supplementary information, p. 2). Multivariable Cox regression was fitted to 1005 participants, adjusting for site, age and baseline substance use. Twenty-two participants were excluded owing to missing baseline substance use. The adjusted hazard ratio for EYE-2 + sEIP to sEIP alone was 1.07 (95% CI 0.76–1.49; $P = 0.71$). The point estimate indicated a marginally higher observed risk of earlier disengagement in the EYE-2 + sEIP group. The confidence interval ruled out a reduction of more than 24% in the risk of earlier disengagement in the intervention arm. Sensitivity analyses (Supplementary information, p. 3)

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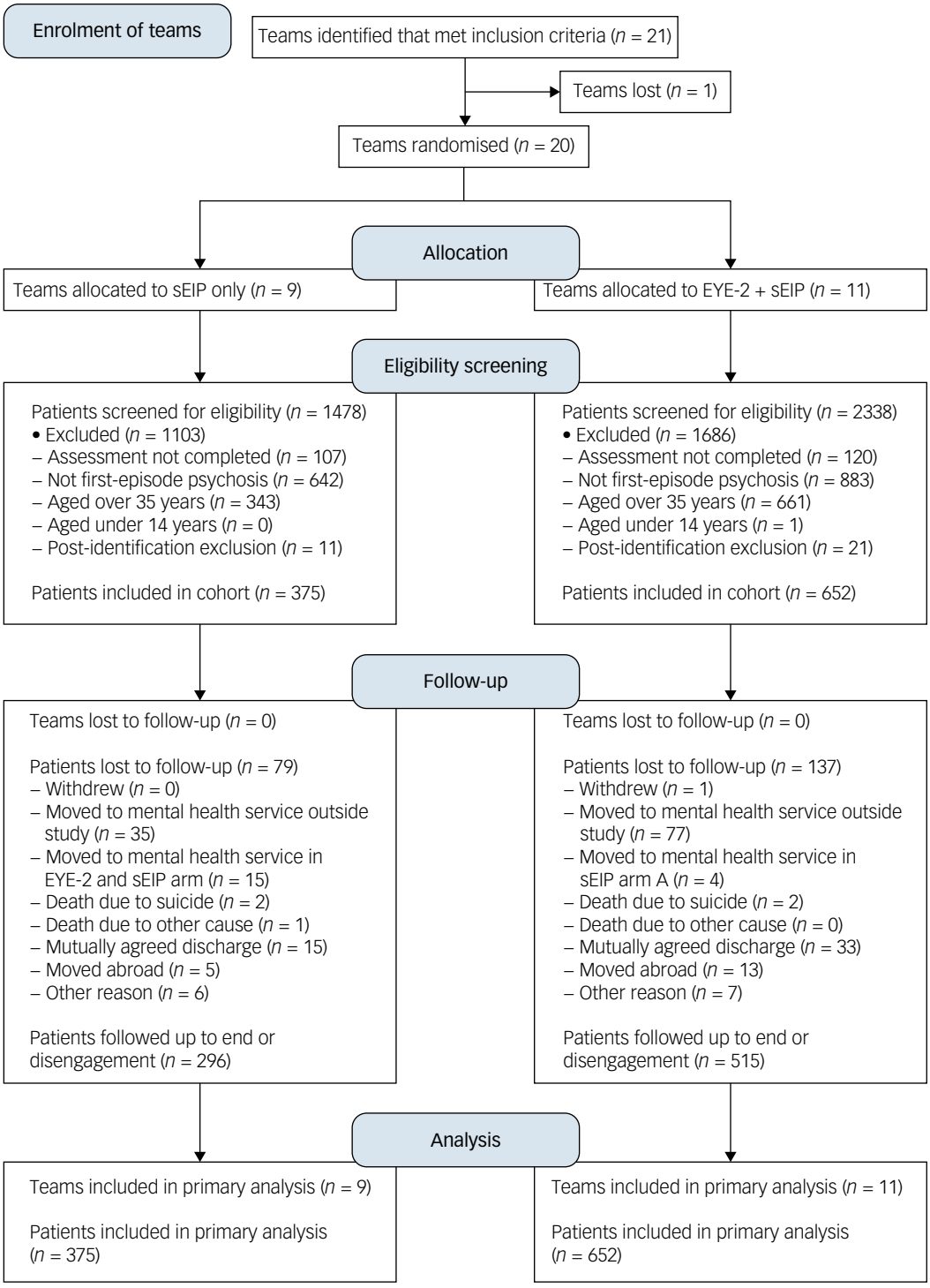

Fig. 1 Study CONSORT diagram. sEIP, standard early intervention in psychosis; EYE-2, Early Youth Engagement.

were consistent with the primary analysis, and subgroup analyses revealed no interactions with any factor predicted to affect engagement.

HoNOS, QPR and DIALOG data collected within and outside data collection windows and a visual summary example of data reallocation are presented in the Supplementary information (pp. 4–5). Secondary 12-month data were either collected or unavailable owing to loss to follow-up for 79.2% of HoNOS, 49.4% of DIALOG and 50.6% of QPR data (Supplementary information, p. 6). HoNOS, QPR and DIALOG descriptive data, adjusted coefficients (mean difference in score by arm) over time and as derived from models are presented in the Supplementary information (pp. 7–12). Linear mixed-effects regression models were fitted for HoNOS, recovery (QPR), quality of life (DIALOG QoL) and treatment satisfaction (DIALOG TS). The adjusted coefficients did not favour either arm for any score or timepoint ($P > 0.10$ for all outcomes; Supplementary information, pp. 13–14). HoNOS and DIALOG TS generally improved from baseline to 6 months, whereas recovery (QPR) and DIALOG QoL improved across all time points in both arms (Supplementary information, p. 15). Conclusions were not robust to departures from the missing-at-random assumption (Supplementary information, pp. 16–19).

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Table 1 Descriptive statistics of baseline participant characteristics by intervention arm and overall

	sEIP only			EYE-2 + sEIP			Overall		
	Mean	s.d.	*n*	Mean	s.d.	*n*	Mean	s.d.	*n*
Age, years	24.9	5.5	375	25.2	5.4	652	25.1	5.4	1027
HoNOS symptoms score at baseline (range 0 to 12)	5.6	2.4	360	5.3	2.4	615	5.4	2.4	975
	Median	IQR	*n*	Median	IQR	*n*	Median	IQR	*n*
Duration of untreated psychosis (days)	77.0	32.0 to 242.0	297	76.0	27.0 to 294.0	517	77.0	29.0 to 264.0	814
Indices of multiple deprivation decile	4.0	2.0 to 7.0	372	3.0	2.0 to 5.0	644	4.0	2.0 to 6.0	1016
	n	%		*n*	%		*n*	%	
Substance use (HoNOS question 3)									
No problem	202	54.9		367	57.6		569	56.6	
Minor problem requiring no action	41	11.1		68	10.7		109	10.8	
Mild problem but definitely present	59	16.0		124	19.5		183	18.2	
Moderately severe problem	55	14.9		65	10.2		120	11.9	
Severe to very severe problem	11	3.0		13	2.0		24	2.4	
Total	368	100.0		637	100.0		1005	100.0	
Indices of multiple deprivation decile (binary)									
Low (6 to 10)	136	36.6		167	25.9		303	29.8	
High (1 to 5)	236	63.4		477	74.1		713	70.2	
Total	372	100.0		644	100.0		1,016	100.0	
Ethnicity									
White British	165	44.4		228	35.5		393	38.7	
White Irish	1	0.3		4	0.6		5	0.5	
Any other White background	38	10.2		65	10.1		103	10.1	
White and Black Caribbean	2	0.5		9	1.4		11	1.1	
White and Black African	6	1.6		19	3.0		25	2.5	
Any other mixed background	17	4.6		23	3.6		40	3.9	
Indian	7	1.9		11	1.7		18	1.8	
Pakistani	15	4.0		14	2.2		29	2.9	
Bangladeshi	2	0.5		2	0.3		4	0.4	
Any other Asian background	21	5.6		32	5.0		53	5.2	
Black Caribbean	8	2.2		25	3.9		33	3.3	
Black African	32	8.6		79	12.3		111	10.9	
Any other Black background	21	5.6		81	12.6		102	10.0	
Chinese	2	0.5		2	0.3		4	0.4	
Any other ethnic group	15	4.0		21	3.3		36	3.5	
Not stated	20	5.4		28	4.4		48	4.7	
Total	372	100.0		643	100.0		1015	100.0	
Ethnicity (binary)									
Any white background	204	58.0		297	48.3		501	51.8	
Any mixed, Black, Asian, or other background	148	42.0		318	51.7		466	48.2	
Total	352	100.0		615	100.0		967	100.0	
Gender									
Male	253	67.5		400	61.3		653	63.6	
Female	122	32.5		247	37.9		369	35.9	
Non-binary/not specified	0	0.0		5	0.8		5	0.5	
Total	375	100.0		652	100.0		1027	100.0	
Education level									
No educational awards received	36	13.1		79	16.3		115	15.2	
GCSE grade A-G NVQ level 1 or 2, etc.	79	28.8		132	27.2		211	27.8	
A-Level, NVQ level 3, BTEC, etc.	100	36.5		148	30.5		248	32.7	
Undergraduate, NVQ level 4 or 5, BTEC HND, foundation degree, etc.	54	19.7		107	22.1		161	21.2	
Postgraduate (Masters), MCGI, Diploma, Doctoral, FCGI, etc.	5	1.8		19	3.9		24	3.2	
Total	274	100.0		485	100.0		759	100.0	

sEIP, standardised early intervention in psychosis service; EYE-2, Early Youth Engagement intervention; HoNOS, Health of the Nation Outcome Scales; IQR, interquartile range; MCGI, Level 7 Diploma of Membership of the City and Guilds of London Institute; FCGI, Level 8 Fellowship of the City & Guilds of London Institute.

Sensitivity analyses for HoNOS, QPR and DIALOG suggested that findings were not affected by the COVID-19 pandemic or by variations in timing or method of data collection. However, QPR and DIALOG COVID-19 sensitivity analyses excluded participants without baseline measures and so involved smaller samples than the main analyses; in addition, dichotomising participants with baseline assessment either side of the first lockdown date was a blunt approach to assess the impact of COVID-19, given that 12–16 months of the EYE-2 intervention occurred during COVID-19. Subgroup analyses revealed weak evidence that EYE-2 + sEIP performed slightly less well than sEIP alone in improving recovery in teams with low average case-loads, with no other case-load effects on secondary outcomes. The difference in QPR score between arms in the low compared with the high average case-load group was −3.53 (95% CI −7.00 to −0.55, $P = 0.046$); this was a small difference and the opposite of the anticipated effects for both EYE-2 and lower case-load, which are expected to aid clinicians to promote recovery, so it may have been a chance observation. Visual summaries of primary and secondary analyses are included in the Supplementary information (pp. 20–21).

In terms of service use, 42% of the sample had at least one hospital admission, 20% had at least one A&E visit and 4% had section 136 use. Proportions were similar across arms, although the median number of nights in hospital for people who were

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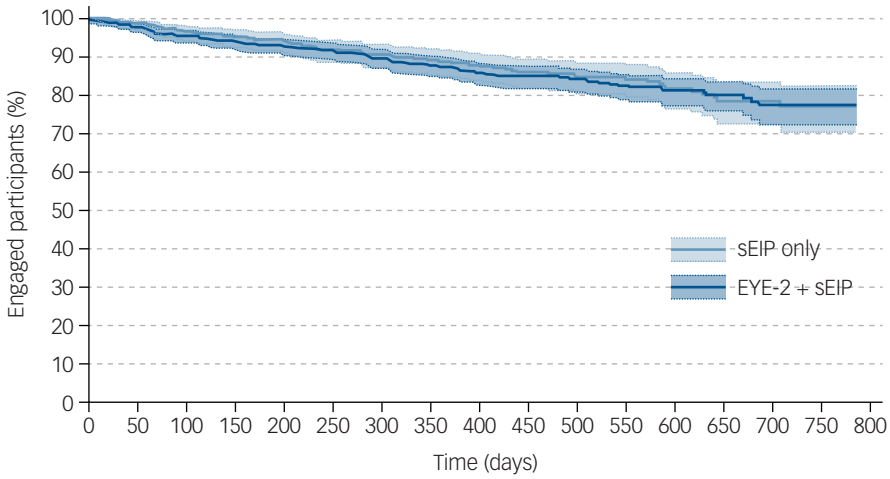

Fig. 2 Kaplan–Meier plot of time to disengagement (in days) by intervention arm with 95% confidence intervals. sEIP, standard early intervention in psychosis service; EYE-2, Early Youth Engagement intervention.

admitted was lower in the EYE-2 (26 nights) arm compared with sEIP (33 nights) (Supplementary information, p. 22). Models were fitted to 866 participants, adjusting for site, age and substance use: 161 participants were excluded owing to missing nights in hospital and A&E outcomes ($n = 139$), substance use at baseline ($n = 17$) or both ($n = 5$). The robust Poisson regression model for number of nights in hospital revealed a slightly lower incidence rate ratio for EYE-2 + sEIP, but there was insufficient evidence of any difference between arms (adjusted incidence rate ratio for EYE-2 + sEIP versus sEIP: 0.83 (95% CI 0.61–1.13, $P = 0.23$)). According to the logistic regression model for A&E visits ($N = 174$ with ≥1 visit versus 709 with no A&E visit), the odds of at least one A&E visit were slightly lower in the EYE-2 arm, but there was insufficient evidence of any difference between arms (adjusted odds ratio for EYE-2 + sEIP versus sEIP: 0.81 (95% CI 0.57–1.17, $P = 0.26$)). Four patients (0.4%) died during the 12 months: three (0.8%) in the sEIP arm (two by suicide) and one (by suicide; 0.2%) in the EYE-2 arm, and one person died by suicide in the EYE-2 arm after 12 months. The median number of NICE-recommended interventions received per participant was five in each arm (Supplementary information, p. 23). Medication, physical health assessments, care planning, and vocational and family support were most common, followed by cognitive–behavioural therapy. The low proportions of patients in receipt of some interventions may have reflected delivery during COVID-19 and in the first 12 months of service use.

For the economic evaluation, descriptive cost data and adjusted differences in mental health service costs are presented in the Supplementary information (pp. 24–26). Mean costs were estimated to be £1280 lower for unplanned mental health service contacts (95% CI −£4126 to –£1566) and £25 lower for planned contacts (95% CI −£173 to £122) for EYE-2 participants. The average total cost of all contacts (planned and unplanned) was £788 lower in the EYE-2 arm (95% CI −£3571 to £1994). The probability that these costs were higher in the EYE-2 arm was 28.8%. For the cost-effectiveness analysis, adjusted differences in HoNOS scores were 'inverted' so that positive differences indicated a better mental health state for intervention participants. The differences in mean values for cost (−£788) and outcome (0.13 on HoNOS) point to EYE-2 'dominating' usual care (lower cost, superior outcome) (Supplementary information, p. 27). There was uncertainty in this finding, with 43.4% probability of EYE-2 dominance, 14.1% probability of usual care dominance, 27.8% probability of lower total cost but poorer clinical outcome with EYE-2, and 14.7% probability of better clinical outcomes but higher cost with EYE-2. Societal and socio-occupational data were collected from 232 consenting participants: 456 did not consent, and 339 were lost to follow-up or not approached. Consent rates were proportionate to the sample size in each arm. The subsample interviewed had a similar mean age (25.4 years) and baseline HoNOS score (5.6) but a higher proportion of White ethnicity (59.7%) and fewer males (59.5%) compared with the whole sample. The expected total societal cost per participant was £526 lower for EYE-2, with a 43% probability of this outcome (Supplementary information, p. 28). The EYE-2 intervention was associated with, on average, 5.73 more days in stable independent accommodation, 7.56 more days in employment, and 30 more days in education and training, with probabilities ranging from 77% to 99% (Table 2).

High fidelity to the EYE-2 intervention was expected, with clinicians using resources with at least 75% of their patients, represented by a score of 3 or above. However, median scores of 2–2.3 out of 4 revealed moderate fidelity, with clinicians using EYE-2 resources with approximately half their EYE-2 patients. Only 64% (7/11) of teams reported scores of 3 or more, and fidelity decreased from early to late intervention in most (83%) teams; this was linked to challenges during COVID-19 (Supplementary information, p. 29).

Table 2 Socio-occupational outcomes: adjusted differences

	Adjusted difference in mean days (expected value)	95% CI	Probability mean days higher for intervention participants (%)	*N*[a]
Stable independent living arrangements	5.73	−1.79 to 13.25	98	232
Paid and unpaid employment	7.56	−35.64 to 50.76	77	232
Education and training	27.59	1.52 to 53.68	99	232

a. All models based on imputed data samples (using multiple imputation methods).

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No serious adverse events were recorded that were at least possibly related to the trial.

Discussion

We found no evidence for superiority of EYE-2 + sEIP over sEIP with respect to time to disengagement over 12–26 months or secondary mental health outcomes: 15.9% of patients disengaged across arms. The economic evaluation indicated lower mental healthcare costs linked to shorter admissions, slightly lower societal costs, and more days in education, training, employment and stable accommodation with EYE-2. The impacts on unplanned crisis care and socio-occupational outcomes were consistent with the focus of EYE-2 on engagement in crises and to support goals. The findings for societal and socio-occupational outcomes must be viewed cautiously as only 22% consented to provide data.

The lack of intervention effects on outcomes may have resulted from low overall disengagement rates, consistent with our own recent meta-analysis[27] and possibly resulting from high-quality stand-alone service delivery, improved NHS England standards[8] and increased stringency in EIP acceptance criteria. Implementation was also substantially affected by COVID-19. Social engagement stopped entirely, before restarting in a limited online format; goal-focused therapeutic alliance was affected by restrictions on socio-occupational activities, online consultations and personal protective equipment; and psychoeducation was hampered by an inability to access resources, although this was partially ameliorated by use of the EYE-2 website (Supplementary information, p. 31). Only those seen face to face in crisis and those who engaged effectively online potentially received the intervention as planned.

This is the largest study to date to investigate disengagement from EIP services, the only evaluation of an intervention to reduce disengagement, and the largest longitudinal cohort of EIP patients in more than a decade. The whole-population cohort comprised all new FEP patients from 20 EIP teams across five representative NHS sites (nine trusts) in England (Supplementary information, p. 31), comprising approximately 10% of new FEP patients in England in this period. The sample was similar in size and demographics to the national EDEN sample, but it comprised a whole population and had higher representation of minority ethnic populations (48.2% *v.* 27%).[28] We found improvements in mental health, well-being, social function and treatment satisfaction in the first 6 months, as well as continuous improvement, consistent with recovery models, in recovery and subjective quality of life over 12 months, in both the EYE-2 and sEIP teams. Hence, stand-alone EIP services achieve positive outcomes and low disengagement but may be more cost-effective and have better societal and socio-occupational outcomes, with an added engagement approach.

EIP team acceptance rates were very low (9.5%) in some services owing to stringent exclusion of specific diagnoses and early non-engagers; 40% of patients did not meet service inclusion criteria, 40% had an in-patient admission at or within 12 months of acceptance, and 5% were discharged by mutual agreement. These figures are concerning, as patients with initial non-engagement, other diagnostic comorbidities and early discharge may present later with greater severity or as in-patient admissions.[29] Just over 12% migrated across (10.9%) or out of the country (1.8%), many returning home after onset, raising the possibility that migration and isolation from supportive social networks contribute to onset of psychosis in young people, even within the UK.[30] We should consider how best to support young people who do not engage from the outset, are isolated, present with psychosis in the context of mood disorders or request early discharge.

Limitations

Although the real-world pragmatic trial design is a strength in terms of generalisability, limitations included missing routine secondary data and modest implementation, affected by COVID-19. Secondary data completion was nevertheless higher owing to the whole-population sample compared with the previous largest cohort, in which only 49% of patients consented to provide data.[28]

Summary

This is the largest real-world whole-population investigation of disengagement, effectiveness and cost-effectiveness in EIP services and the first to evaluate a disengagement-focused intervention. The EYE-2 intervention is a low-cost therapeutic model with psychoeducational resources, co-produced with patients, carers and clinicians, that is safe, well liked and easy to use to engage new patients. We found no evidence that the EYE-2 intervention is superior to stand-alone sEIP services in improving time to disengagement or secondary mental health outcomes, but disengagement was low overall. The EYE-2 intervention added to sEIP services may be more cost-effective with better societal and socio-occupational outcomes, but the findings for the latter outcomes should be viewed cautiously owing to low sample sizes. Study outcomes may be specific to stand-alone services adhering to an EIP model. New services internationally and those looking to reconfigure should consider carefully the potential impact of non-standard EIP models on disengagement, health, and societal and cost outcomes. Future research should investigate core components that maximise engagement across EIP models, and in target populations at greatest risk for disengagement, presenting in crisis and with socio-occupational goals.

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Supplementary material

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Data availability

Fully anonymised data will be available from K.G. upon reasonable request, subject to submission and approval of a research proposal and review and contract with Sussex Partnership NHS Foundation Trust, following the publication of all results of this study. Owing to the personal nature of case note data pertaining to engagement or disengagement, these data will only be made available in a suitable abbreviated form to ensure anonymity. Analytic code will be available from C.J., S.B., R.H. and A.H. upon reasonable request. Trial materials can be obtained from K.G. on reasonable request. Intervention resources are also available at www.likemind.nhs.uk.

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Author contributions

K.G. led the design and coordination of the study, contributed to data analysis and interpretation, and wrote the report. C.J. contributed to the design of the study, conducted the analysis and drafted the initial results. N.Y. contributed to the design of the study, conducted the health economic analysis and contributed to drafting of the results. A.H. contributed to the design of the study, co-developed and oversaw the health economic analysis, and drafted the initial results. C.M. contributed to the design of the study and co-led the process evaluation with K.G. S.B. contributed to the design of the study, co-developed and oversaw the analysis. R.H. contributed to the design of the study, conducted power calculations and oversaw the SAP. S.R., P.P., B.L., L.J., P.F., J.H., M.P. and E.P. contributed to the design and were responsible for site management and supervision. H.L. contributed to the design of the study and supported site management and supervision. S.N. and J.P. were responsible for site management and supervision. R.d.V. contributed to the design. T.M. led on all aspects of PPI. G.B., J.G. and R.W. were the trial managers and oversaw all aspects of supervision and delivery. I.A. was the trial manager with oversight of data and site management. R.T. contributed to the design of the study and led on all aspects of PPI. D.F. and P.G. contributed to the design of the study and the interpretation of the results. A.O.D. and S.C. contributed to the design of the study and the study set-up. R.J. advised on the health economic analysis. All authors had full access to all the data in the study, reviewed the paper for important scientific content and had final responsibility for the decision to submit the manuscript for publication.

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Declaration of interest

K.G. has received NIHR funding for previous research and has received funding from the University of Sussex, Sussex Partnership Foundation Trust and South-East Network for Social Sciences for work linked to this project. She has received funding for a conference presentation from Boehringer Ingelheim. R.J. is a general practitioner and was the local clinical commissioning group clinical lead until June 2021. S.R. has received consultancy fees and honoraria from various industry providers, does medicolegal work and sits on an industry advisory Board. P.P. has received NIHR funding, industry funding, book loyalties and honoraria from universities for lectures and presentations. P.F. has received previous NIHR research funding and is clinical advisor to the National Clinical Audit of Psychosis. He sat on Health Technology Assessment prioritisation and funding panels. P.G. has received funding from NIHR and Wellcome and is a member of an expert international advisory committee. D.F. has received previous NIHR research funding. T.M. has received previous NIHR research funding. E.P. has received funding from the Medical Research Council and NIHR. L.J. has received funding from NIHR for research and has received book royalties and payment for workshops. S.B. has received previous NIHR funding. C.M. has received financial reimbursement for travel to present on Normalisation Process Theory. K.G., S.C., S.N., L.J., M.P., J.P. and A.O.D. either currently work or have previously worked in EIP services, and B.L. and P.F. have been regional EIP leads.

Transparency declaration

The lead author and manuscript guarantor (K.G.) affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

References

1 Rossler W, Salize HJ, van Os J, Riecher-Rossler A. Size of burden of schizophrenia and psychotic disorders. *Eur Neuropsychopharmacol* 2005; **15**(4): 399–409.

2 The Schizophrenia Commission. *The Abandoned Illness: A Report by the Schizophrenia Commission*. Rethink Mental Illness, 2012 (https://www.rethink.org/media/2629/the-abandonned-illness_tsc_executive_summary_14_nov.pdf).

3 Birchwood M, Fiorillo A. The critical period for early intervention. *Am J Psychiatr Rehabil* 2000; **4**(2): 182–98.

4 Perkins DO, Gu H, Boteva K, Lieberman JA. Relationship between duration of untreated psychosis and outcome in first-episode schizophrenia: a critical review and meta analysis. *Am J Psychiatry* 2005; **162**: 1785–804.

5 Correll CU, Galling B, Pawar A, Krivko A, Bonetto C, Ruggeri M, et al. Comparison of early intervention services vs treatment as usual for early-phase psychosis: a systematic review, meta-analysis, and meta-regression. *JAMA Psychiatry* 2018; **75**(6): 555–65.

6 Puntis S, Minichino A, De Crescenzo F, Harrison R, Cipriani A, Lennox B. Specialised early intervention teams for recent-onset psychosis. *Cochrane Database Syst Rev* 2020; **11**: CD013288.

7 Aceituno D, Vera N, Prina AM, McCrone P. Cost-effectiveness of early intervention in psychosis: systematic review. *Br J Psychiatry* 2019; **215**(1): 388–94.

8 NHS England, National Collaborating Centre for Mental Health and National Institute for Health and Care Excellence. *Implementing the Early Intervention in Psychosis Access and Waiting Time Standard: Guidance*. NHS England, 2016.

9 Doyle R, Turner N, Fanning F, Brennan D, Renwick L, Lawlor E, et al. First episode psychosis and disengagement from treatment: a systematic review. *Psychiatr Serv* 2014; **65**(5): 603–11.

10 Williams R, Ostinelli E, Agorinya J. Comparing interventions for early psychosis: a systematic review and component network meta-analysis. *eClinicalMedicine* 2024; **70**: 102537.

11 Greenwood K, Chandler R, Labuschagne K, Peters E, Alford K, deVisser R, et al. The development and piloting of an early youth-engagement (EYE) model to improve engagement of young people in first episode psychosis services: a mixed methods study. *Early Interv Psychiatry* [Epub ahead of print] 22 Oct 2024. Available from: https://doi.org/10.1111/eip.13623.

12 Rathod S, Phiri P, de Visser R, Moore S, Au-Yeung K, Collier O, et al. Applying the cultural adaption framework to the Early Youth Engagement (EYE-2) approach to early intervention in psychosis. *Br J Clin Psychol* 2023; **62**(3): 537–55.

13 Greenwood K, Webb R, Gu J, Fowler D, deVisser R, Bremner S, et al. The Early Youth Engagement in first episode psychosis (EYE-2) study: pragmatic cluster randomised controlled trial of implementation, effectiveness and cost-effectiveness of a team-based motivational engagement intervention to improve engagement. *Trials* 2021; **22**(1): 272.

14 Jones C, Bremner S, Hooper R, Gu J, Bartl G, Greenwood K. Statistical analysis plan for the early youth engagement in first episode psychosis (EYE-2) study: a pragmatic cluster randomised controlled trial of implementation, effectiveness and cost-effectiveness of a team-based motivational engagement intervention to improve engagement. *Trials* 2021; **22**: 732.

15 Bertolote J, McGorry P. Early intervention and recovery for young people with early psychosis: consensus statement. *Br J Psychiatry* 2005; **187**(S48): s116–9.

16 Turner M, Smith-Hamel C, Mulder R. Prediction of twelve-month service disengagement from an early intervention in psychosis service. *Early Interv Psychiatry* 2007; **1**: 276–81.

17 Conus P, Lambert M, Cotton S, Bonsack C, McGorry PD, Schimmelmann BG. Rate and predictors of service disengagement in an epidemiological first-episode psychosis cohort. *Schizophr Res* 2010; **118**: 256–63.

18 Wing JK, Beevor AS, Curtis RH, Park SGB, Hadden J, Burns A. Health of the Nation Outcome Scales (HoNOS). Research and development. *Br J Psychiatry* 1998; **172**(1): 11–8.

19 Neil ST, Kilbride M, Pitt L, Nothard S, Welford M, Sellwood W, et al. The questionnaire about the process of recovery (QPR): a measurement tool developed in collaboration with service users. *Psychosis* 2009; **1**(2): 145–55.

20 Priebe S, Golden E, McCabe R, Reininghaus U. Patient-reported outcome data generated in a clinical intervention in community mental health care – psychometric properties. *BMC Psychiatry* 2012; **12**: 113.

21 National Health Service (NHS). *Early Intervention in Psychosis Triangulation Tool*. NHS, n.d. (https://future.nhs.uk/system/login?nextURL=%2Fconnect%2Eti%2FEIPtriangulationtool%2Fview%3Fexp%3Dc1%26objectId%3D13093520 [accessed 15 Aug 2022]).

22 Heß S. Randomisation inference with Stata: a guide and software. *Stata J* 2017; **17**(3): 630–51.

23 Little RJ, D'Agostino R, Cohen ML, Dickersin K, Emerson SS, Farrar JT et al. The prevention and treatment of missing data in clinical trials. *N Engl J Med* 2012; **367**(14): 1355–60.

24 White IR, Horton NJ, Carpenter J, Pocock SJ. Strategy for intention to treat analysis in randomised trials with missing outcome data. *BMJ* 2011; **342**: d40.

25 Wood AM, White IR, Thompson SG. Are missing outcome data adequately handled? A review of published randomized controlled trials in major medical journals. *Clin Trials* 2004; **1**(4): 368–76.

https://doi.org/10.1192/bjp.2024.154 Published online by Cambridge University Press

26 Morris TP, Kahan BC, White IR. Choosing sensitivity analyses for randomised trials: principles. *BMC Med Res Methodol* 2014; **14**: 11.

27 Robson E, Greenwood K. Rates and predictors of disengagement and strength of engagement for people with a first episode of psychosis using early intervention services: a systematic review of predictors and meta-analysis of disengagement rates. *Schizophr Bull Open* 2022; **3**: 1.

28 Birchwood M, Lester H, McCarthy L, Jones P, Fowler D, Amos T, et al. The UK national evaluation of the development and impact of early intervention services (the national EDEN studies): study rationale, design and baseline characteristics. *Early Interv Psychiatry* 2014; **8**(1): 59–67.

29 Pelosi AJ, Arulnathan V. Neglecting the care of people with schizophrenia: here we go again. *Psychol Med* 2023; **53**(4): 1137–42.

30 Gayer-Anderson C, Morgan C. Social networks, support and early psychosis: a systematic review. *Epidemiol Psychiatr Sci* 2013; **22**(2): 131–46.

https://doi.org/10.1192/bjp.2024.154 Published online by Cambridge University Press