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Table DS1 Characteristics of included studies

Initiative	Study design	Criteria for including patients in study evaluation	Outcomes
LEOCAT[27]	Cluster randomised trial 46 GP practices (23 on each arm) Control = standard mental health services (including EIS team) with no GP campaign 27-month study period	Age 16–35 with first-episode psychosis Treatment with antipsychotics <1 month Less than 6 months contact with mental health services No intellectual difficulties Consenting to research	DUP of referred patients Proportion of identified patients with first-episode psychosis referred directly by GP to mental health services Proportion of patients using A&E or in-patient services before referral to EIS
REDIRECT[26]	Cluster randomised trial 110 GP practices (55 on each arm) Control = standard mental health services (including EIS team) with no GP campaign 34-month evaluation period	Age 14–30 with a diagnosis of first-episode psychosis. No primary diagnosis of substance use, mood disorder or organic mental disorder; current criminal proceedings; serious concurrent physical illness; institutional residence; or intellectual difficulty	Primary outcome: number of patients with first-episode psychosis referred Secondary outcomes: DUP, number of primary care consultations in pathway to care and comparison of symptoms (PANSS scores) at admission
DETECT[23]	Two-group retrospective comparison: questionnaire sent to all 365 GPs within study catchment area. Responses from GPs receiving education intervention compared with GPs who did not	GP action for all patients with suspected first-episode psychosis evaluated	Likelihood of GP referral of patients with suspected first-episode psychosis to EIS
EPPIC 1a[21]	Historical comparison: 51 EPPIC patients admitted in 8-month period compared with 51 matched patients from 3 previous years with standard mental health services but no EIS team. Patients matched on age, gender, diagnosis, marital status and premorbid functioning	Age 16–30, with first-episode psychosis and no previous treatment for psychosis No intellectual disability, organic mental disorder, epilepsy or non-English speaking. Consent to study participation	DUP
EPPIC 1b[22]	Two-group retrospective study: 51 EPPIC patients (same sample as EPPIC 1a) Comparison = patients admitted to CMHT with first-episode psychosis within past 2 years at June 2001	EPPIC group: as EPPIC 1a Comparison group: all patients being treated by CMHT who were in first 2 years after a first episode of psychosis	DUP
TIPS a[18]	Historical comparison Comparison = standard mental health services with no EIS team. First 2 years of early detection campaign compared with a 2-year period 3 years previously	Age 15–65, with diagnosis of psychosis Previous treatment with antipsychotics <12 weeks No physical illness relating to the psychosis; no contraindications to antipsychotic medication; speaks a Scandinavian language, IQ >70 Consents to study participation	DUP
TIPS b[19]	Two-group, non-randomised prospective comparison study Comparison = standard mental health services with no EIS team 4-year study period.	As TIPS a	DUP Number of patients with first-episode psychosis referred Characteristics of patients at admission (symptoms, diagnosis, drug and alcohol use, premorbid functioning)
TIPS c[20]	Historical comparison: EIS team with early detection campaign compared with standard services including EIS team.	As TIPS a	DUP Characteristics of patients at admission (symptoms, diagnosis, drug and alcohol use, premorbid functioning)

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Table DS1 Characteristics of included studies *(continued)*

Initiative	Study design	Criteria for including patients in study evaluation	Outcomes
EPPIC 2[30]	Two-group, non-randomised prospective comparison study Comparison = EIS and mobile detection unit but no mass campaign Study period: 1 year	Age 16–30, with first-episode psychosis and no previous treatment for psychosis No intellectual difficulties, organic mental disorder; must be English speaking and have stable accommodation	DUP Characteristics of patients at admission (symptoms, diagnosis)
PEPP[29]	Historical comparison Comparison = EIS team without early detection programme Study period: 2 years pre- and post-EIS team)	Age 16–50, diagnosis of non-affective psychosis Treatment with antipsychotics < 1month Consenting to treatment in service	DUP Referral source (hospital, community health services, non-health services) Characteristics of patients at admission (symptoms, diagnosis, premorbid adjustment)
EPIP[28]	Historical comparison: 2 years of an early detection initiative compared with 1 previous year of standard services with no EIS team	First-episode psychosis No previous psychiatric consultation No physical cause for psychosis No drug-induced psychosis	DUP Referral source: number of family or self-referral, GP, counsellor, police Characteristics of patients at admission (diagnosis)

GP, general practitioner; EIS, early intervention service; DUP, duration of untreated psychosis; A&E, Accident and Emergency department; CMHT, community mental health team.

Table DS2 Quality of included studies

Study	Selection bias	Allocation bias	Confounders	Data collection methods	Withdrawals	Analysis	Intervention integrity
LEOCAT[27]	Strong	Strong Cluster randomisation by statistician independent of study team (method not stated)	No differences between groups measured prior to intervention	Strong Data collection tools stated DUP defined	Weak DUP data gathered for 71/197 eligible patients (only patients who saw GP during period of DUP included in analyses)	Study size informed by power calculation DUP data was log transformed to account for skew	58/62 eligible GP practices participated
REDIRECT[26]	Moderate Some inclusion criteria beyond clinical target population (e.g. no criminal proceedings or institutional residence)	Strong Cluster randomisation: masked allocation using computer algorithm	Included practices stratified by list size and PCT	Strong Data collection tools stated DUP defined	Weak for DUP data gathered for 83/179 eligible patients Strong for number of referrals	Study size informed by power calculation Method of analysis/account for skew in DUP data not reported Primary outcome stated in advance	62/93 intervention group GPs received education session; 43/92 attended any follow-up session
DETECT[23]	Strong Only GP outcomes measured; all GPs in catchment area included	Weak Retrospective comparison of two self-selecting groups	No differences between groups measured prior to intervention	Weak, unpublished questionnaire	Weak 126/348 GPs returned questionnaires	No primary outcome stated in advance	All GPs received information pack. Only 48% of respondents had attended an information session
EPPIC 1a[21]	Weak Additional exclusion criteria for study beyond standard service requirements. Matched control sample constituted 51/200 admissions during study period	Weak Historical comparison	No comparison of area variables Patients matched on demographic/clinical variables	Strong Data collection tool stated and DUP defined	Strong DUP data gathered for 102/102 patients	Log transformation and non-parametric tests used to account for skew in DUP data	n/a
EPPIC 1b[22]	Weak As EPPIC 1b + comparison group only includes patients still known to CMHT 2 years after entry into treatment	Weak Two-group retrospective study	No differences between groups measured prior to intervention. 8-year gap between data collection period for EPPIC group (1993) and comparison group (2001)	Weak Different data collection methods for study arms DUP not defined for comparison group	Moderate DUP data gathered for 53/68 eligible patients in comparison group	No statistical analysis; descriptive data only	n/a
TIPS a[18]	Moderate Some exclusion criteria beyond service requirements (e.g. must speak Scandinavian language)	Weak Historical comparison	No differences between groups measured prior to intervention Population reported as stable	Moderate DUP defined Assessment involved patient and family: assessment tool not reported	Weak Number of eligible patients not included in study not reported. Overall 4-year TIPS inclusion = 53/100 patients with first-episode psychosis	Non-parametric test used to account for skew in DUP data	Mass campaign implemented

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Table DS2 Quality of included studies *(continued)*

Study	Selection bias	Allocation bias	Confounders	Data collection methods	Withdrawals	Analysis	Intervention integrity
TIPS b[19]	Moderate As TIPS a	Moderate Two-group natural experiment	Differences between groups measured Some significant differences found: urban living, rates of immigration, educational attainment – but not accounted for in analyses	Moderate As TIPS a	Moderate DUP data gathered for 281/380 patients	Non parametric test of median DUP data	Mass campaign implemented
TIPS c[20]	Moderate As TIPS a	Weak Historical comparison	No differences between groups measured prior to intervention	Moderate As TIPS a	Moderate DUP data collected for 183/229 eligible patients	Non-parametric test used to account for skew in DUP data	Mass campaign implemented
EPPIC 2[30]	Moderate Some inclusion criteria beyond service requirements (stable accommodation, English speaking)	Moderate Two-group natural experiment	Areas reported as demographically similar regarding population, gender, average income, education and employment levels	Strong Data collection tool stated and DUP defined	Strong DUP data collected for 98/120 eligible patients	Log transformation and non-parametric tests used to account for skew in DUP data	Mass campaign implemented: possibility of leakage across to control area acknowledged
PEPP[29]	Strong	Weak historical comparison	No changes to healthcare delivery during the study period; no other comparison of areas reported	Moderate DUP defined Unpublished assessment tool used, based on patient, family and professionals' reports	Strong DUP data collected for 169/188 patients	Non-parametric test used to account for skew in DUP data	Mass campaign implemented
EPIP[28]	Strong No inclusion criteria beyond service requirements reported	Weak historical comparison	No differences between groups measured prior to intervention	Weak DUP unclearly defined, no assessment tool reported DUP based on interviews with patient and primary caregiver	Weak Proportion of eligible patients included in study not reported	Non-parametric test used to account for skew in DUP data	Mass campaign implemented

DUP, duration of untreated psychosis; GP, general practitioner; PCT, primary care trust; n/a not applicable; CMHT, community mental health team.

Table DS3 Results from included studies (duration of untreated psychosis (DUP) and referral numbers)

Study	Mean (s.d.) DUP			Median DUP		Other DUP results	Number of referrals
	Intervention	Control	Significance	Intervention	Control		
GP education LEOCAT[27]	240 (537) days ($n = 36$)	245 (527) days ($n = 35$)	Not significant			No significant difference between groups in mean days from first contact with GP to referral to or to assessment by mental health services, but significantly fewer patients in the intervention group (6% *v.* 27%) experienced delays of longer than 6 weeks	
REDIRECT[26]	247 (454) days ($n = 47$)	234 (290) days ($n = 36$)	Not significant	56.5 days	71 days	Mean days from first help-seeking to reaching EIS significantly smaller in intervention arm ($P = 0.002$) Intervention mean: 143 days (s.d. = 193) Control mean: 367 days (s.d. = 389) Other service delay measures show no significant difference	Intervention: 97 referrals Control: 82 referrals No significant difference
Service configuration EPPIC 1[21]	191 (484) days ($n = 51$)	236.6 (703) days ($n = 51$)	Significantly greater mean DUP in intervention sample (using log-transformed and non-parametric tests) despite smaller mean. *P* value not reported	52 days	30 days		
EPPIC 1[22]	191 (484) days ($n = 51$)	469 (953) days ($n = 53$)	No test of statistical significance	52 days	90 days		
Multifocus initiatives EPPIC 2[30]	314 (559) days ($n = 40$)	254 (380) days ($n = 58$)	No significant difference in mean or median results	50 days	104 days	No significant difference in proportion of patients with DUP < 1 year but significantly more patients in intervention group with long DUP (>3 years)	No data presented but authors report probable greater increase in cases in intervention region during study period
TIPS[18]	26 weeks ($n = 60$)	114 weeks ($n = 43$)	Mean DUP significantly shorter in intervention group ($P = 0.005$)	5 weeks	26 weeks		
TIPS[19]			Median DUP significantly shorter in intervention group ($P = 0.003$). Intervention area was significantly associated with shorter DUP in linear regression	5 weeks	16 weeks	No significant difference in numbers of patients with long DUP (>2 years)[50]	186 eligible patients from intervention regions (incidence over 4 years 50:100 000) 194 eligible patients from control regions (incidence 66:100 000) No test of significance reported
TIPS[20]	26 (59) weeks ($n = 108$)	105 (276) weeks ($n = 75$)	Mean DUP significantly shorter in intervention group ($P<0.005$)	5 weeks	15 weeks		
PEPP[29]			No significant difference in median DUP	24 weeks ($n = 84$)	22 weeks ($n = 85$)	More patients in intervention group with very short (<12 weeks) and very long (>2 years) DUP, more patients in control group with medium DUP. Significance of differences not tested No significant change in DUP following discontinuation of the intervention[51]	Annual treated incidence rate: intervention group, 27.5:100 000; control group, 26:100 000 No test of significance reported
EPIP[28]	13 (26) months ($n = 287$)	32 (59.3) months ($n = 107$)	Median DUP significantly shorter in intervention group ($P = 0.002$)	4 months	12 months		

GP, general practitioner; EIS, early intervention service.

Additional references

50 Friis S, Vaglum P, Haahr U, Johannessen JO, Larsen TK, Melle I, et al. Effect of an early detection programme on duration of untreated psychosis. Part of the Scandinavian TIPS study. *Br J Psychiatry* 2005; **187** (suppl 48): s29–32.

51 Cassidy C, Schmitz N, Norman R, Manchanda R, Malla A. Long-term effects of a community intervention for early identification of first-episode psychosis. *Acta Psychiatr Scand* 2008; **117**: 440–8.

Early detection review – electronic search terms: MEDLINE search

exp schizophrenia/ OR exp paranoid psychosis/ OR (schizo$ or psychotic$ or psychosis or psychoses or hebephreni$ or oligophreni$).hw,id,tw OR ((chronic$ or sever$) adj5 mental$ adj5 (ill$ or disorder$)).tw

AND

((duration and (((long$ or delay$ or not$1 or wait$) adj2 treat$) or untreat$ or un treat$)) or DUP$1).tw OR ((decreas$ or lessen$ or lower$ or minim$ or prevent$ or reduc$ or shorten$) and (((long$ or delay$ or not$1 or wait$) adj2 treat$) or un?treat$)).tw OR early diagnosis/ or exp early intervention/ or "early intervention (education)"/ OR (early adj3 (detect$ or intervent$ or diagnos$ or recogni$)).tw OR (client education or health education or health promotion or patient education or psychoeducation).sh,id. Or ((communit$ or health) adj3 (educat$ or promot$)).tw OR ((communit$ adj2 awareness) or ((health or wellness) adj campaign$)).tw OR prodrom$.tw OR early onset.tw

AND

A. [Systematic review filter] (literature searching or (systematic review$ or metaanal$ or meta anal$)).sh,id. OR ((analy$ or assessment$ or evidence$ or methodol$ or qualitativ$ or quantativ$ or systematic$) adj5 (overview$ or review$)).tw. or ((analy$ or assessment$ or evidence$ or methodol$ or quantativ$ or qualitativ$ or systematic$).ti. and review$.ti,pt.) or (systematic$ adj5 search$).ti,ab. OR ((electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw,sh. or (bids or cochrane or index medicus or isi citation or psyclit or psychlit or scisearch or science citation or (web adj2 science)).tw. or cochrane$.sh.) and (review$.ti,ab,sh,pt. or systematic$.ti,ab.) OR (metaanal$ or meta anal$ or metasynthes$ or meta synethes$).ti,ab. OR (research adj (review$ or integration)).ti,ab. OR reference list$.ab. OR bibliograph$.ab. OR published studies.ab. OR relevant journals.ab. OR selection criteria.ab. OR (data adj (extraction or synthesis)).ab. OR (handsearch$ or ((hand or manual) adj search$)).ti,ab. OR (mantel haenszel or peto or dersimonian or der simonian).ti,ab. OR (fixed effect$ or random effect$).ti,ab. OR (systematic$ or meta$).pt. or (literature review or meta analysis or systematic review).md. OR ((pool$ or combined or combining) adj2 (data or trials or studies or results)).ti,ab.

OR

B. [Randomised controlled trial filter] exp clinical trials/ or exp controlled clinical trials/ or (crossover procedure or double blind procedure or placebo or randomization or random sample or single blind procedure).sh OR exp clinical trial/ or cross-over studies/ or double-blind method/ or random allocation/ or randomized controlled trials as topic/ or single-blind method/ OR exp clinical trials/ or (placebo or random sampling).sh,id. OR exp clinical trials/ or (crossover design or double-blind studies or single-blind studies or random assignment or triple-blind studies).sh. or random sample.hw. OR (clinical adj2 trial$).tw. OR (crossover or cross over).tw OR (((single$ or doubl$ or trebl$ or tripl$) adj5 (blind$ or mask$ or dummy)) or (singleblind$ or doubleblind$ or trebleblind$)).tw. OR (placebo$ or random$).mp. OR (clinical trial$ or random$).pt. or treatment outcome$.md.

OR

C. [Observational study filter] (clinical study or cohort analysis or correlational studies or cross sectional studies or epidemiologic studies or family study or longitudinal study or nonconcurrent prospective studies or prospective study or retrospective study).sh OR exp case control studies/ OR "epidemiological study".id or "empirical study".md OR ((cross sectional or epidemiologic$ or observational) adj (study or studies)).tw OR (case control or cohort$1 or cross sectional or followup$ or follow up$ or followed or longitudinal or retrospective).tw OR (case$ or cohort$ or follow-up$ or follow up$ or longitudinal$ or prospective$ or retrospectiv).tw

OR

D. [Grey literature filter] limit to (congresses or government publications or technical report) AND ((abstract report$ or book$ or conference paper$ or dissertation$ or government publication$ or pamphlet$ or report$ or theses$).sh. or "policy and procedure manauls"/)) OR ((book$ or brochure$ or dissertation$ or pamphlet$ or report$ or thesis$ or theses$).tw)

Table DS4 Measurement of duration of untreated psychosis (DUP) in included studies

Initiative	Definition of onset of illness	Definition of start of treatment	Measurement instrument / information sources	Data reported
LEOCAT[27]	Two definitions used: 'traditional DUP' – time from first psychotic symptom; and 'contemporary DUP' –time from unremitting psychotic symptoms for 1 week, using CAARMS criteria[52]	Two definitions used: 'traditional DUP'– first contact with mental health services; and 'contemporary DUP' – the commencement of antipsychotic medication (greater than 50% treatment adherence for a minimum of 1 month)	Combined DUP, pathway to care and service receipt measure.[53] Information gathered from patient, carer and clinician	Mean DUP Mean service delay (time from first contact with GP to assessment by mental health services) 'Contemporary DUP' used in main analyses
REDIRECT[26]	First week with psychotic symptoms scoring 4 or above on PANSS[54] positive symptoms	Start of adequate antipsychotic medication or hospital admission Criteria defined by Larsen et al[55]	Semi-structured interview based on checklist[56] Patient interviewed; no other sources stated	Mean DUP Median DUP Mean interval from initiation of help-seeking to reach early intervention service Mental health service delay (first contact with mental health services to contact with EIS)
EPPIC 1a[21]	Onset of sustained symptoms at threshold level	Initiation of treatment Both operationalised in Royal Park Multi Diagnostic Instrument for Psychosis (RPMIP): good interrater reliability established[57]	RPMIP[57] Interview with patient and other informant (usually family member)	Mean DUP (EPPIC 1a & 2) Median DUP (EPPIC 1a & 2) Number of patients with DUP <1year; 1–3 years; >3 years (EPPIC 2)
EPPIC 2[30]				
EPPIC 1b[22]	Not defined	Not defined	As EPPIC 1a for EPPIC group No assessment instrument reported for comparison group: source = case notes	Mean DUP Median DUP
TIPS a & c[18,20]	Onset of psychotic symptoms (first week with symptoms corresponding to a PANSS score of 4 or above for positive symptoms)	Start of treatment (start of antipsychotic medication or hospital admission or psychotherapy for psychosis)	Use of assessment instrument not reported All available data sources used including interviews with patient and relatives	Mean DUP Median DUP
TIPS b[19]	As above	As above	As above	Median DUP Number of patients with long DUP (>2 years)[40]
PEPP[29]	Onset of psychotic symptom (corresponding to structured clinical interview for DSM–IV thresholds)	Start of adequate treatment (taking antipsychotics for 1 month or until treatment response)	CORS (Circumstances of Onset and Relapse Schedule) – unpublished instrument based on IRAOS[58] All sources used to calculate DUP including patient, family and involved professionals' reports	Median DUP Number of patients with DUP 0–12 weeks; 13–26 weeks; 27–52 weeks; >52 weeks
EPIP[28]	Onset of psychotic symptoms (no severity or duration specified)	The time when a diagnosis and treatment (unspecified) were established	None stated Information from patient and primary carer	Mean DUP Median DUP

GP, general practitioner; EIS, early intervention service.

Additional references

52 Yung A, Yuen H, McGorry P, Phillips L, Kelly D, Dell'ollio M. Mapping the onset of psychosis – the comprehensive assessment of at-risk mental states. *Aust N Z J Psychiatry* 2005; **39**: 964–71.

53 Power P, Russell M, Fisher H. The measurement of duration of untreated psychosis (DUP): a new rating scale that combines DUP with pathways to care and service receipt. *Schizophr Res* 2004; **70** (suppl): 137.

54 Kay S, Opler L, Fishbein A. *A Positive and Negative Syndrome Scale (PANSS) Rating Manual.* Multi-Health Systems, 1992.

55 Larsen T, Johannessen J, Opjoerdsmoen S. First-episode schizophrenia with long duration of untreated psychosis. Pathways to care. *Br J Psychiatry* 1998; **172** (suppl 33): 45–52.

56 Beiser M, Erickson D, Fleming J, Iacono W. Establishing the onset of psychotic illness. *Am J Psychiatry* 1993; **150**: 1349–54.

57 McGorry P, Singh B, Copolov D, Kaplan I, Dossetor C, van Riel R. Royal Park Multidiagnostic Instrument for Psychosis: Part II. Development, relaibility and validity. *Schizophr Bull* 1990; **16:** 517–36.

58 Hafner H, Riecher-Rossler A, Hambrecht M, Maurer K, Meissner S, Schmidtke A, et al. IRAOS: an instrument for the assessment of onset and early course of schizophrenia. *Schizophr Res* 1992; **6**: 209–23.