BMC Psychiatry

STUDY PROTOCOL

Open Access

# PEPsy-CM study protocol: impact of a 3-year program for early psychosis based on case-management on relapse rate, a French multicenter randomized trial

Aurélie Schandrin[1*], Julie Jourdan[1], Sihame Chkair[2], Sophie Bouvet[2], Pascale Fabbro-Peray[2], Mocrane Abbar[1] and for the PEPsy-CM working group

## Abstract

**Background** Early intervention services (EIS) for early psychosis can help reduce the patient-specific and economic impacts of mental illness, but they are underdeveloped and practices are poorly harmonized in many countries.

**Methods** The aim of the study is to evaluate in France the effectiveness of a three-year Program for Early Psychosis based on Case Management (PEPsy-CM) compared to TAU in young people with a first episode of psychosis (FEP). Eligible participants are those aged between 16 and 30 years old consulting or hospitalized in mental health services for a FEP. Exclusion criteria include mental retardation, psychosis due to medication or medical condition. Four centers have so far joined the study and started recruiting. In this randomized controlled trial, the interventional group will receive TAU with the addition of intensive follow-up by a case manager, in accordance with EPPIC guidelines. The primary outcome is the percentage of participants relapsing at least once during the three-year follow-up, and time until first relapse. Secondary outcomes are relapse and hospitalization rate, adherence to care, clinical outcomes (psychotic et depressive symptoms, suicidal and aggressive behaviors, substance use), functional outcomes (living conditions, level of study or employment, social and occupational functioning), quality of life (patients and caregivers), users' satisfaction, direct and indirect costs and correct implementation of the intervention.

**Discussion** The results from this study will be invaluable in characterizing the role of early intervention and case management, and establishing optimal care protocols to treat early psychosis in France. The study has encountered problems in attracting recruiting centers often to commit to randomization. The medico-economic evaluation is a strength of the study, as economic objectives are too infrequently considered in such studies.

**Trial registration** www.clinicaltrials.gov number NCT05116514 registered on 05/10/2021

**Keywords** First Episode of Psychosis, Early Psychosis, Case-Management, Assertive Community Treatment

*Correspondence:
Aurélie Schandrin
aurelie.schandrin@chu-nimes.fr
[1] Department of Adult Psychiatry, CHU Nîmes, Univ Montpellier, Nîmes, France
[2] Department of Biostatistics, Clinical Epidemiology, Public Health and Innovation in Methodology (BESPIM), CHU Nîmes, Univ Montpellier, Nîmes, France

## Background

Psychotic disorders such as schizophrenia represent a major cause of disability in young people [1], resulting in personal and societal cost [2], and are associated with a high mortality risk [3]. For decades, specific interventions in the early stages of the illness have been recommended to promote recovery after a first episode of

© The Author(s) 2025. **Open Access** This article is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License, which permits any non-commercial use, sharing, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if you modified the licensed material. You do not have permission under this licence to share adapted material derived from this article or parts of it. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit http://creativecommons.org/licenses/by-nc-nd/4.0/.

psychosis (FEP) and reduce poor long-term outcomes [4, 5]. The value of early intervention services (EIS), based on a multimodal treatment program designed for the needs of people with early psychosis [6], has been demonstrated [7, 8]. The proven economic benefit of these services [9, 10] has led to the development of hundreds of early intervention for psychosis programs worldwide [11]. However, EIS remains underdeveloped in many countries, where changing practices face cultural, professional and economic barriers.

Implementation of EIS requires local adaptation according to the existing healthcare system. Indeed, the effectiveness of EIS is often compared to the treatment as usual (TAU) [7], which can vary between countries and must be predefined. Among the interventions recommended in EIS (e.g., case management, psychotherapy, supported employment and education, social skills training, family support), some will likely already exist in current practice, while others require development depending on local needs and system failures.

In France, many services have initiated case management for early psychosis as a basis for early intervention to bridge a missing element of the current care system [12, 13]. Indeed, case management based on the Assertive Community Treatment (ACT) model is central to EIS [8, 14, 15] and responds to specific criteria [16] with a well-established therapeutic impact. It reduces hospitalization time and improves engagement with services, independent living skills, compliance with medication and satisfaction with services [17–19]. The case manager plays a fundamental role in the process of recovery by coordinating individuals' treatment and ensuring continuity of care [20–22]. In France, there is access to local specialized consultations and to multiple interventions in the health, social and medico-social sectors. Most costs are covered by the national health care system. However, the system is complex, and lacks flexibility, coordination and continuity of care. The delays before a consultation are increasing, with months of waiting. Users, especially young people with multiple needs, can be lost and dissatisfied. The difficulty of access to care partly explains the long duration of untreated psychosis between 1 and 2 years [23, 24]. Among the young people treated for early psychosis, almost 50% are lost to follow-up during the first year after illness onset [25], with a high risk of relapse [26]. The first goal of developing case management for early psychosis in France would be to reduce the risk of relapse by providing personalized support in the community and by improving engagement and coordination of care. Pioneering teams established EIS in France between 2000 and 2010 [27, 28], but more widespread diffusion has been slow since then. The Transition network created in 2006 aims to facilitate the national dissemination of EIS and identified 18 EIS in 2018 [29] and 54 in 2023. EIS practices are heterogeneous despite all involving case management, and there is no data on the practical modalities nor their effectiveness.

Implementing this model of EIS will be supported by French health ministry recommendations, with specific funding, in particular to develop innovation and coordination of care [30–33]. In addition, case management appears to be an effective method of supporting patients in complex care situations, and is more cost-effective for the care system [34]. However, the differences between pathologies and the various forms of case management mean that studies are needed to optimize effective and efficient organization for each case.

Our study aims to evaluate the effectiveness of a three-year Program for Early Psychosis based on Case Management (PEPsy-CM) compared to TAU in a population of young people with a FEP using a randomized controlled design. The study will take place in different French mental health services. Case management for early psychosis will be practiced according to guidelines published by Early Psychosis Prevention and Intervention Center (EPPIC) in Melbourne, translated into French for the Swiss program TIPP (Traitement et Intervention dans la phase Précoce des troubles Psychotiques) [11].

The primary hypothesis is that people in the experimental group (PEPsy-CM) will have a lower rate of relapse at 3 years, defined by hospitalization in psychiatry (number of admission and beds days in hospital) and reoccurrence of positive psychotic symptoms.

The secondary hypotheses are that: a) the PEPsy-CM will reduce relapse rates by improving adherence to care (engagement, medication adherence, working alliance); b) the experimental group will have better clinical outcomes (levels of symptoms, substance use, suicidal and violent behaviors), functional outcomes (social/occupational functioning), and quality of life than the control group; c) the economic impact taking into consideration both direct and indirect costs will be in favor of the experimental program provided according to good practice recommendations whose implementation will be evaluated in each center.

## Methods

### Design

This article describes the 3rd version of the protocol, dated 18/04/2023. This study is a 1:1 parallel group randomized controlled trial (RCT) comparing case management for early psychosis (PEPsy-CM) with treatment as usual (TAU). The recruitment will be carried out over 2 years in each center and patients will be assessed every 6 months over the 3 years of intervention.

### Inclusion criteria

All participants between 16 and 30 years old will be enrolled in a mental health service (consultation or hospitalization) for a FEP according to the following definition:

- Positive psychotic symptom (i.e. hallucination, delusion and/or disorganization) for at least one week, daily or at least 3 times per week for more than one hour per occasion (definition of psychosis threshold according the CAARMS (Comprehensive Assessment of At-Risk Mental States) [35, 36];

- No previous treatment for a psychotic disorder (except treatment started prior to referral for the current episode e.g. by general practitioner);

- Fulfilling criteria for DSM 5 for one of the following diagnoses:

Delusional disorder
Brief psychotic disorder (more than 7 days)
Schizophreniform disorder
Schizophrenia
Schizoaffective disorder
Substance-Induced psychotic disorder (more than 7 days)
Other specified or unspecified schizophrenia spectrum and psychotic disorder
Bipolar I and II disorder with psychotic features
Substance- induced bipolar and related disorder
Major depressive disorder with psychotic features.

Inclusion should be done within 3 months following the start of follow-up in mental health service for FEP. Individuals with co-morbid substance misuse or dependence and comorbid personality disorders will be included.

Minors (under 18 years old) may be included under a specific consent procedure involving legal representatives. Participants under curatorship need to inform their curator.

### Exclusion criteria

People unable to provide informed consent and those without sufficient command of French will be ineligible for participation. Moderate-to-severe mental retardation and medication-induced psychosis or psychosis due to medical condition will be exclusion criteria. (Participants under tutorship will also be excluded.)

### Recruitment

The trial will be conducted in different mental health services in France to recruit a large number of participants and to have a representative sample of services and clients to improve generalizability.

The centers currently involved in the study are:

- University Hospital Carémeau, Nîmes
- University Hospital La Colombière, Montpellier
- Hospital Léon-Jean Grégory, Thuir
- PEPSY Paltform, Toulouse (University Hospital Purpan, Gérard MARCHANT Hospital and Aufréry Clinic)

For recruitment, a screening of young people aged between 16 and 30 starting follow-up or having been hospitalized for the first time for a psychotic disorder is organized in each center according to local operating procedures.

### Randomization

Randomization per patient is conducted by investigator using a computerized randomization protocol (Inclusio), stratified according the center, sex, age and duration of untreated psychosis. The size of the blocks is random to keep the assignment secret. Group allocation is directly communicated to the treatment team to allow appropriate transfer decisions. Follow-up will be organized either conventionally or with a case manager who will quickly contact the person included.

### Interventions

The control intervention: treatment as usual

Patients in the control group will receive the usual follow-up in France, comprising medical appointments in the hospital or outpatient unit (medico-psychological center (CMP)) or with a private psychiatrist. Consultation frequency varies according to medical decisions. Some clients may also be followed by a referral nurse, usually from the CMP team, and/or may enroll in a day care unit. In the inpatient or outpatient mental health services, clients may receive different types of psychosocial interventions or psychotherapy, sometimes specific to youth and/or psychosis. All therapies additional to the classical medical follow-up will be collected for each participant in both groups.

The experimental intervention: case management (modified ACT) for early psychosis

The treatment in the experimental group corresponds to the usual care with the addition of intensive follow-up by a case manager in accordance with EPPIC guidelines. The intervention will be carried out according to a TIDieR-compliant checklist named PEPsy-CM checklist (Table 1) including: low caseload per case manager (20 clients or less); rapid contact after inclusion in the program; frequency of consultations adapted according to the clinical phase (weekly in the acute and early recovery phase, monthly in the recovery phase); individual

**Table 1** PEPsy-CM check-list[a]

**Items from 1 to 11 concerned general functioning of the early intervention service (EIS), to be completed with manager of EIS**:

**Item 1 Specific training of the EIS team about case management of early psychosis**

❒1 = No

❒5 = Yes, if yes specify:

**Item 2 Use of the "case management for early psychosis" manual from EPPIC translated into French by the TIPP team in Lausanne**

❒1 = No

❒5 = Yes

**Item 3 Use of specific and validated tools for psychoeducation about early psychosis**

❒1 = No

❒5 = Yes, if yes specify:

**Item 4 Use of a brochure of information about First Episode of Psychosis**

❒1 = No

❒5 = Yes, if yes specify:

**Item 5 Use of specific and validated tools for family support**

❒1 = No

❒5 = Yes, if yes specify:

**Item 6 Use of specific and validated tools for motivational interviewing**

❒1 = No

❒5 = Yes, if yes specify:

**Item 7 System of reviewing Individual Treatment Plan (ITP) every 3 months**

❒1 = No

❒5 = Yes

**Item 8 Use of an ITP model specifying the objectives of care and action plan, and also including risk assessment, recovery level assessment and relapse action plan (or equivalent)**

❒1 = No

❒5 = Yes

**Item 9 (EPPIC integrity tool item 21) Caseload per full time case manager**

❒1 = Caseload is >35 per case manager

❒2 = Caseload is between 30 and 34 per case manager

❒3 = Caseload is between 25 and 29 per case manager

❒4 = Caseload is between 21 and 24 per case manager

❒5 = Caseload is 20 or less per case manager

**Item 10 (EPPIC integrity tool item 22) Multidisciplinary case management team (SW, Psych, OT & nursing) – In addition to medical staff and consultant psychiatrist**

❒1 = Case management team has 1 discipline

❒2 = Case management team has 2 disciplines

❒3 = Case management team has 3 disciplines

❒4 = Case management team has 4 disciplines

❒5 = Case management team has 4 disciplines and makes use of specific skills.

**Item 11 (EPPIC integrity tool item 30) System to identified incomplete recovery at 3 months**

❒1 = No system in place to identify young people (YP) with incomplete recovery

❒2 = System in place to identify YP with incomplete recovery by 3 months

❒3 = System in place to identify YP with incomplete recovery by 3 months and review by senior clinician

❒4 = System in place to identify YP with incomplete recovery by 3 months and review by senior clinician and consultant psychiatrist

❒5 = System in place to identify YP with incomplete recovery by 3 months and review by senior clinician and consultant psychiatrist and use of a specific approach to enhance recovery.

**Items 12 to 35 to be completed by the case manager (CM) for each patient treated in the intervention group**:

**Item 12 (EPPIC integrity tool item 23) Time (average) to allocation to CM from acceptance and assignment to the early psychosis program**

❒1 = More than 7 days

**Table 1** (continued)

❒2 = 5-6 days

❒3 = 4 days

❒4 = 3 days

❒5 = 2 or fewer days

**Item 13 (EPPIC integrity tool item 25) Time from allocation to CM to first CM contact (average)**

❒1 = CM contacts YP more than 14 days after allocation

❒2 = CM contacts YP less than 14 days but more than 10 days after allocation

❒3 = CM contacts YP less than 10 days but more than 5 days after allocation

❒4 = CM contacts YP less than 5 days but more than 2 days after allocation

❒5 = CM contacts YP within 48 hours of allocation

**Item 14 (EPPIC integrity tool item 26) Time from allocation to first CM appointment (mean)**

❒1 = YP sees CM within 28 days of allocation

❒2 = YP sees CM within 21 days of allocation

❒3 = YP sees CM within 14 days of allocation

❒4 = YP sees CM within 10 days of allocation

❒5 = YP sees CM within 7 days of allocation

**Item 15 (EPPIC integrity tool item 27) Individual Treatment Plan (also called a care plan in some places) is developed within 4-6 weeks from allocation (should involve family and YP in development)**

❒1 = No

❒5 = Yes

**Item 16 (EPPIC integrity tool item 28) Risk assessment each appointment**

❒1 = No

❒5 = Yes

**Item 17 (EPPIC integrity tool item 29) Relapse action plan by 3 months**

❒1 = No

❒5 = Yes

**Item 18 (EPPIC integrity tool item 31) Transition from service plan established more than 3 months before discharge and involved YP and family**

❒1 = No

❒5 = Yes

**Item 19 (EPPIC integrity tool item 32) Young person's progress is reviewed every 3 months and ITP updated**

❒1 = No

❒5 = Yes

**Item 20 (EPPIC integrity tool item 33) In acute phase young person has 2 visits or contacts (phone, video call) per week**

❒1 = No

❒5 = Yes

**Item 21 (EPPIC integrity tool item 34) In early recovery YP is seen at least weekly by CM**

❒1 = No

❒5 = Yes

**Item 22 (EPPIC integrity tool item 35) In early recovery YP young is seen at least fortnightly by doctor**

❒1 = No

❒5 = Yes

**Item 23 Brochure of information about First Episode of Psychosis was handed to YP**

❒1 = No

❒5 = Yes

**Item 24 Brochure of information about First Episode of Psychosis was handed to family**

❒1 = No

❒5 = Yes

**Table 1** (continued)

❒NA = not applicable

**Item 25 Predominance of vivo contacts (visits)**

❒1 = No

❒5 = Yes

**Item 26 Predominance of contacts outside the office**

❒1 = No

❒5 = Yes

**Item 27 Evaluation of clinical recovery level**

❒1 = No

❒5 = Yes

**Item 28 Evaluation of functional recovery level**

❒1 = No

❒5 = Yes

**Item 29 Regular contacts with family**

❒1 = No

❒5 = Yes

❒NA = no family

**Item 30 Physical health monitoring**

❒1 = No

❒5 = Yes

**Item 31 Side-effects of treatment monitoring**

❒1 = No

❒5 = Yes

❒NA = no treatment

**Item 32 Support for housing**

❒1 = No

❒5 = Yes

❒NA = not necessary

**Item 33 Support for employment or education**

❒1 = No

❒5 = Yes

❒NA = not necessary

**Item 34 Psychoeducation done with or without specific tool**

❒1 = No

❒5 = Yes

**Item 35 Quality of relationship**

❒1 = Very bad

❒2 = Bad

❒3 = Acceptable

❒4 = Good

❒5 = Very good

**SCORING:** Sum of items divided by the number of items (remove items with NA or missing) with total score between 1 (poor practice) to 5 (good practice)

[a] Using items about case management of the EPPIC integrity tool (adapted to the French context and COVID period) and based on recommendations of good practice for early psychosis

treatment plan updated every 3 months with risk assessment, relapse and recovery assessment and action plan; coordination of the care and life project.

The role of the case manager will be to establish a therapeutic alliance with the client and improve their engagement in care. The case manager will be in contact with the young person during the entire three-year follow-up period, including any periods of admission, and will provide personalized support in the community. Depending on individual needs and objectives,

the case manager will also deliver psychoeducation to the patient and their family to improve their understanding about illness, medication and recovery plan. Reintegration into employment and/or educational activities will be a priority. The case manager will be in contact with all professionals involved with the client: health professionals (e.g., psychiatrist, psychologist, general practitioner, substance abuse worker) and those from the social, educational and vocational sectors.

Case managers will be predominantly nursing professionals, but may also be social workers, must have a minimum of 5 years' experience in psychiatry, with at least 3 years in the geographical area of intervention.

Case manager training will be documented via the PEPsy-CM checklist. If necessary, additional training will be offered. Study-specific training will be conducted in each centre to present the study and specific tools: case management manual, checklist and assessment tools of the implementation of the interventional model. In addition, guidelines for good practice for FEP treatment [37] will be provided to psychiatrists and the multidisciplinary team involved in the care.

**Blinding and assessments**

Evaluations and assessments are carried out at baseline, then every six months until the end of the three-year follow-up period or until withdrawal from the study, for both treatment groups (Fig. 1, Table 2).

The participants, their families and the treatment team cannot be blinded to the assignment of the treatment group. However, the assessments will be conducted in a blind manner by a clinician not involved in the participants' care and unaware of group allocation. Clinicians carrying out follow-up assessments are trained in the administration of psychometric scales and have received study-specific training according to opening of the centers. The collection of data and personal information is secure to ensure confidentiality.

Follow-up assessments will be conducted in the most suitable premises for the participants and clinicians: care units, research offices, or by videoconference if necessary. The evaluation conditions and pace will be adapted according to the acceptability of the people with the possibility of dividing the visit into several parts. A procedure will be established to optimize the follow-up of the participants without revealing the group allocation.

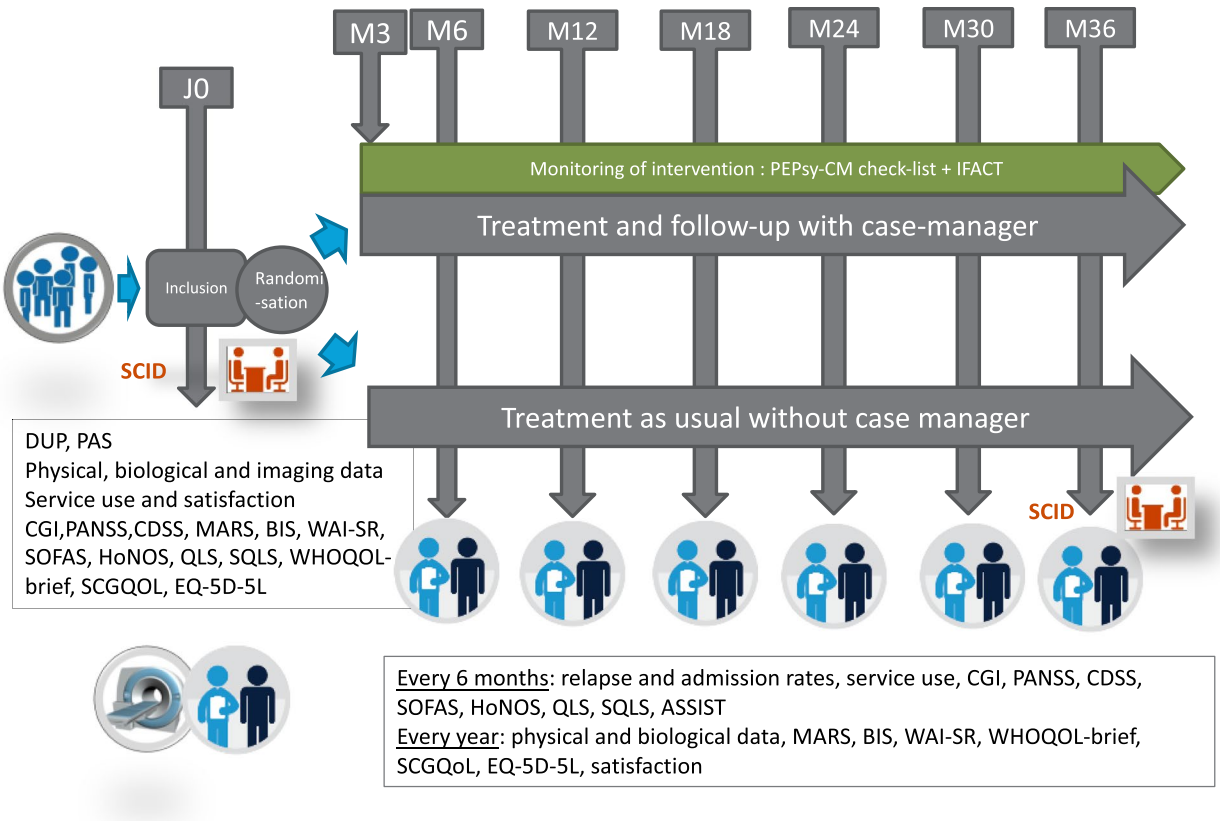


**Fig. 1** Time schedule of inclusion, assessments and visits for participants

**Table 2** Assessment list

| Assessment | Baseline | Follow-up visits | | Discharge |
|---|---|---|---|---|
| **Timeline (Day=D, Month=M)** | **D0** | **M6,18,30** | **M12, M24** | **M36** |
| Diagnoses (Structured Clinical Interview for DSM)<br>Duration of untreated psychosis (DUP) | ✓✓ | | | ✓ |
| Premorbid Adjustment Scale (PAS) | ✓ | | | |
| Physical, biological and imaging data | ✓ | | ✓ | ✓ |
| Medication and psychosocial interventions | ✓ | ✓ | ✓ | ✓ |
| Number of admission and beds days at psychiatric hospital | ✓ | ✓ | ✓ | ✓ |
| Service use : % of presence to consultation, disengagement with service | ✓ | ✓ | ✓ | ✓ |
| Psychopathology<br>. Clinical Global Impression (CGI)<br>. Positive and Negative Symptom Scale (PANSS)<br>. Calgary Depression Scale for Schizophrenia (CDSS) | ✓✓<br>✓ | ✓<br>✓<br>✓ | ✓✓<br>✓ | ✓<br>✓<br>✓ |
| Adherence to care<br>. Medication Adherence Rating Scale (MARS)<br>. Working Alliance Inventory-Short Revised (WAI-SR)<br>. Birchwood Insight Scale (BIS) | ✓<br>✓<br>✓ | | ✓<br>✓<br>✓ | ✓<br>✓<br>✓ |
| Functioning<br>. Socio-demographic data<br>. Social and Occupational Functioning Assessment Scale (SOFAS)<br>. Health of the Nation Outcome Scales (HoNOS) | ✓<br>✓<br>✓ | ✓<br>✓ | ✓<br>✓ | ✓<br>✓<br>✓ |
| Quality of life<br>. Quality of Life Scale (QLS)<br>. Schizophrenia Quality of Life Scale R4 (SQLS)<br>. World Health Organization Quality of Life brief (WHOQoL brief)<br>. EuroQol-5D 5 level version (EQ-5D-5L)<br>. Caregiver schizophrenia quality of life questionnaire for families (S-CGQOL) | ✓<br>✓<br>✓<br>✓<br>✓ | ✓<br>✓ | ✓<br>✓<br>✓<br>✓<br>✓ | ✓<br>✓<br>✓<br>✓<br>✓ |
| Alcohol, Smoking and Substance Involvement Screening Test (ASSIST) | ✓ | ✓ | ✓ | ✓ |
| Users satisfaction : participants, families<br>. Client Satisfaction Questionnaire (CSQ)<br>. Satisfaction Questionnaire focus on case management in PEPsy-CM group | .<br>✓<br>✓ | | ✓<br>✓ | ✓<br>✓ |
| Case management in PEPsy-CM group<br>. PEPsy-CM check-list, client version | ✓ | ✓+ M3 | ✓ | ✓ |
| Implementation model<br>. PEPsy-CM check-list, center version<br>. Index of Fidelity to Assertive Community Treatment (IFACT) | At baseline and every year in each center throughout the duration of the study | | | |

Accidental unblinding will be reported by the evaluator. Adverse events or unintended effects of trial interventions or trial conduct are reported.

Financial compensation is provided for participants for follow-up visits at the rate of 30 € per visit.

## Outcomes

Patients will be described according the socio-demographic data. The Structured Clinical Interview for DSM (SCID) [38, 39] will be used to determine the diagnoses and the DUP. The Premorbid Adjustment Scale (PAS) [40, 41] will be evaluated at baseline in addition to the collection of the history of the personal and family medical history. The initial medical assessment (biological assessment, brain imaging, neurological and cognitive examination) will be collected retrospectively from the medical file alongside an inventory of drug treatments and psychosocial interventions received. These data will be updated throughout the follow-up.

The group receiving PEPsy-CM will be compared to the control group on the following outcomes.

### Primary outcome

The primary outcome is the percentage of participants who relapsed at least once during the three-year follow-up and time until first relapse. Relapse is defined by the admission in psychiatric hospital (excluding any hospitalization prior to initiation of the PEPsy-CM intervention) with a diagnosis of psychotic disorder and/or the return of positive psychotic symptoms for a period of at least one week and using the Positive and Negative Symptoms Scale (PANSS) [42, 43] with at least 4 in severity at item P1 "delusion" or P2 "conceptual disorganization" or P3 "hallucinatory behavior" (after remission of the FEP).

Data concerning admission at hospital will be collected from French national health databases (SNIIRAM and PMSI) including for participants lost to follow-up.

### Secondary outcomes

i) Relapse and hospitalization rate: number of relapses, number of admissions and bed-days in psychiatric hospital during the three-year follow-up.
ii) Adherence to care: service use (attendance at consultations with psychiatrist and referent caregivers) and engagement in care (disengagement period with service is defined as "an unplanned break of at least 30 days in treatment or between treatment regimens or status" [17]); medication adherence rating scale (MARS) [44, 45]; working alliance inventory (WAI) [46, 47]; awareness of illness and necessity of treatment according the Birchwood Insight Scale (BIS) [48].
iii) Clinical outcomes: clinical global impression (CGI) [49]; psychotic symptoms assessed by the PANSS (relapse defined previously; remission of the FEP defined by less than 4 in severity at item P1 "delusion", P2 "conceptual disorganization", P3 "hallucinatory behavior"; total remission defined according consensus criteria [50] by less than 4 in severity at item P1, P2, P3, N1 "blunted affect", N4 "passive/apathetic social withdrawal", N6 "lack of spontaneity and flow of conversation", G5 "mannerisms and posturing" and G9 "unusual thought content" during the past six months); depressive symptoms and suicidal thoughts assessed by the Calgary Depression Scale for Schizophrenia (CDSS) [51, 52], reported suicidal and aggressive behaviors; substance use evaluated using the Alcohol, Smoking and Substance Involvement Screening Test (ASSIST) [53].
iv) Functional outcomes: living conditions, level of study and/or employment; Social and Occupational Functioning Assessment Scale (SOFAS) [54]; Health of the Nation Outcome Scales (HoNOS) [55, 56].
v) Quality of life of the clients: Quality of Life Scale (QLS) interviewer administered evaluation [57, 58]; Schizophrenia Quality of Life Scale Revision 4 (SQLS-R4) [59]; World Health Organization Quality of Life brief (WHOQOL brief) [60] and EuroQol-5D 5 level version (EQ-5D-5L) [61] as self-report evaluation; Caregiver schizophrenia quality of life questionnaire (S-CGQoL) for the families [62] .
vi) User satisfaction: satisfaction of clients and their families according the Client Satisfaction Questionnaire [63, 64] and a qualitative evaluation in the experimental group using a custom questionnaire.
vii) Implementation of the PEPsy-CM in each center and per client in the experiment group: development and evaluation of the intervention using the PEPsy-CM checklist (table 1) according to the TIDieR checklist (template for intervention description and replication) based on the Index of Fidelity to Assertive Community Treatment (IFACT) and on the EPPIC Model Integrity Tool, items 21 to 35 "case management and continuity of care".

### Economic analysis

The medico-economic objective is to estimate the efficiency of the PEPsy-CM strategy compared with the TAU.

This evaluation includes:

- The three-year incremental cost-utility ratio defined by the ratio of the cost difference from the community perspective (care system, out-of-pocket expenses and informal carers) between the two strategies divided by their difference in QALYs (quality-ajusted life year). This ratio measures the cost per life-year gained in full health. This indicator is obtained by weighting the time spent in each health state by the utility of that health state, measured by the (EQ-5D-5L) [61], and reassessed annually from inclusion until the last follow-up at 3 years.
- The amount of expenditure to be planned for the implementation of the strategy evaluated at national level (assessment of financial sustainability) is assessed to estimate the budgetary impact of generalizing the proposed experimental strategy.

The economic data covers direct medical and non-medical costs: hospital stays, home nursing care, convalescence stays, transport costs, drug prescriptions, medical consultations and examinations. Daily benefits linked to work absence for patients and their family carers will also be collected.

These data will be collected from the French national health database called (SDNS) [65] to obtain a complete picture of the care provided to patients and their most active carers, and to estimate disease burden.

The liquidation period (or reimbursement period) chosen is 6 months for each patient and carer in order to guarantee more than 98% of care reimbursements without over-penalizing the study in terms of analysis time.

Out-of-pocket expenses are estimated by taking into account fee overruns and the costs of complementary medicine; the costs of informal carers are estimated using the replacement cost method.

Finally, the cost of the PEPsy-CM strategy corresponds to the cost of setting up this new organization. It

is estimated from the healthcare system and healthcare establishment perspectives:

- From the healthcare system perspective, for reimbursed procedures, these are the additional consultations required as a result of case management. Ancillary costs will be considered, including logistical costs: car, telephone, travel and visits to patients and their families, various forms of support, etc. These have been estimated at €13,000 per person per year (Ministry of Social Affairs and Health, n.d.).

- From the healthcare establishment perspective, this involves a full-time care coordinator post, which will be estimated in the experimental arm on the basis of the average gross annual salaries of this category of staff (nurse or social worker). Staff training costs will also be estimated.

#### Power and sample size

Without intervention, the relapse rate is between 43% [26] and 51.8% [66] at 2 years, and around 54% at 3 years [26]. In EIS, the 2-year relapse rate in Canada is 29.7% [67], amounting to a reduction of 13.3 to 22.1% in the relapse rate. Relapse is defined in these studies by the admission in psychiatric hospital and/or return of positive psychotic symptoms.

In order to be clinically significant, we set a target of 20% reduction in relapse rate at 3 years, according our composite primary outcome (relapse defined by hospitalization in psychiatry and/or return of positive psychotic symptoms). With a power of 85%, taking into account 15% of dropouts and a bilateral alpha risk of 5%, 128 patients are needed in each group, for 256 patients in total.

#### Participant follow-up and withdrawal

Each participant is contacted every 6 months for the follow-up visit, even if they missed the previous visit, unless they withdrew from the study.

At each visit, participant continuation of care with their referral team will be reported without compromising blinding. Discontinuing or modifying allocation intervention are notified. A participant may stop their care yet still attend study assessment visits, and vice versa.

If a patient drops out of study follow-up but continues to consent to using their data, medical files for their case will be accessed to obtain outcome measure data. Data concerning admission at hospital will also be collected from French national health databases SNIIRAM and PMSI, even if participants are lost to follow-up.

#### Statistical analyses

The quantitative variables will be described by their mean, standard deviation, median and interquartile range and the qualitative variables will be described by their number and percentage.

The duration of the follow-up period without recurrence of the psychotic episode will be evaluated in the two groups using the Kaplan Meier method and compared by a Log Rank test. This analysis will be supplemented by modeling taking into account potential "cluster" effects. We will use multi-level mixed effects models to evaluate the effect of the treatment (fixed effect) taking into account random factors (cluster effects) on the results describing the recurrence of the psychotic episode.

The quantitative variables will be compared between the two groups using a Student or Mann Whitney test, depending on the distribution of the variables. A mixed multiple linear regression model will complete the analysis if necessary to take into account the "cluster" effect.

The temporal evolution of data from the MARS, BIS, WAI-RS, CGI, PANSS, CDSS, SOFAS, HoNOS, QLS, SQLS-R4, WHOQOL-brief, EQ-5D-5L, S-CGQoL questionnaires will be compared between the two groups by a linear mixed model for repeated longitudinal data.

All analyzes will be carried out on the Intention to Treat (ITT) population. The significance level will be set at $p < 0.05$ (two-sided). Statistical analysis will be performed with R 4.1.2 software or later version (R Development Core Team, (2021). R Foundation for Statistical Computing, Vienna, Austria). No interim analysis is planned.

For the medico-economical objectives, the analysis will be based on the methodology described in the French Health Authority (Haute Autorité de Santé) guide [68] to economic evaluation for 2020. The cost/utility ratio will be estimated using cumulative cost and utility functions. The result will be represented on the four-quadrant cost-effectiveness plan. Several methods will be used to represent the uncertainty associated with the point estimate of the ratio:

- the acceptability curve represents the probability that the PEPsy-CM strategy will be cost-effective compared with the TAU strategy, as a function of the pay.

- the cloud of points (obtained by bootstrap) in the cost-effectiveness plane and their confidence ellipses. The probability of belonging to each quadrant will be deduced.

A sensitivity analysis will be carried out to assess the robustness of the results and incorporate the uncertainty of the model parameters. For this, deterministic and stochastic Monte Carlo simulations will be proposed.

Finally, the experimental strategy will be considered efficient if the cost-utility ratio is significantly lower than the community's willingness to pay.

For the budget impact analysis, a description of the calculations used will be provided. The estimated differences in euros will be presented both in monetary terms

and as a percentage difference. These costs will be broken down by expenditure item and, where applicable, by avoided care procedure. Finally, a sensitivity analysis will be carried out on the hypothetical elements to limit the biases associated with uncertainty. The analysis will be based on the methodology described in the 2016 French Health Authority guide on budget impact analysis and the French Health Economists Council (Collège des économistes de la santé) guide.

#### Research council and monitoring

The coordinating investigator of the study was trained in 2019 at Orygen within the EPPIC program. During this year, an expert advisory committee was created and consulted to establish the study protocol and, if necessary, during the course of the study.

Each expert was approached for a specific area of the study:

Case management: Shona Francey (Orygen), Nadir Mebdouhi (CHUV Lausanne)
Medical management: Brian O'Donoghue (Orygen)
Fidelity to the model: Eoin Killackey (Orygen)
Trial methodology: Sue Cotton (Orygen)
International context: Patrick McGorry (Orygen), Philippe Conus (CHUV Lausanne)

The research department of the study sponsor University Hospital Carémeau of Nîmes provide a data monitoring of each center including data entry, coding, security and storage. An audit of the progress of the trial is planned with the participation of investigators and sponsors. An inspection can also be carried out by a competent authority.

#### Trial status

Of the nine centers screened to participate, four PEPsy-CM centers were successfully opened: one in 2021, two in 2022 and one in 2024. These centers have a current average fidelity score of 4.06 on the PEPsy-CM checklist (5 as the maximum score meaning "good practice" of case management) and a score of 0.71 according the IFACT (score between 0 "poor practice" to 1 "best practice"). The centers could not be opened at the same time. Each center needed a specific adaptation to the research project, which required a prior evaluation of the organization of each center and a specific training in the research protocol. This implementation was therefore carried out center by center by the principal investigator and the project research team.

During the implementation of the project within the centers, there was a change in practices due to the project, which is a bias and improved certain point: systematic screening of people with FEP in inpatient and outpatient units, choice of people included according to objective and fixed criteria, self-evaluation of the case management practice using the PEPsy-CM check-list. Finally, recruiting has prompted some services to expand their service reach across larger geographical areas.

Five of the centers screened declined participation mostly due to concerns about the randomization of treatment. Randomization was perceived as a loss of opportunity for patients assigned to the TAU group, since TAU differs according to the geographical areas with sometimes long waiting times or poorly adapted care for young people with FEP. Among these centers' practices in case management for early psychosis, four completed the PEPsy-CM checklist, with an average score of 3.28.

In march 2024, 74 participants have been recruited and are randomized with n=36 in the experimental PEPsy-CM group and n=38 in the TAU group.

In view of the delay in recruitment, the planned inclusion period of 2 years has been extended to 4 years, which has been validated by the ethics committee. The screening of new centers continues.

## Discussion

This study aims to evaluate the effects of a new practice of case management for early psychosis. Early intervention and the practice of case management both have been demonstrated to have benefits [7, 21, 34], but this has been evaluated against a different TAU than that currently used in France. France has one of the highest rates of psychiatrists per inhabitant: 22.9 per 100 000 inhabitants [69]. The care is covered by national health care system without advance payment, and is often fully reimbursed, in public hospitals, emergencies and in private clinics or practices.

The Ministry of Health and the psychiatric services promote the emergence of specific and innovative care such as EIS with case management [70, 71]. It is therefore essential to establish which outcomes are improved by these interventions. Should TAU prove to be just as effective or more effective in certain areas, this will also support the importance of maintaining sufficient means in the usual care service while developing more specialized and innovative care units.

Some centers have refused to participate due the difficulty of integrating a RCT and evaluations in a care service where it is difficult to set up new practices. Moreover, some teams are convinced of the superior efficiency of their practice compared to the TAU, hence the impossibility of considering a randomization. Another frequent obstacle was simultaneous research projects on early intervention in France, which cannot recruit at the same time in the centers [72]. Indeed, there are currently more

than 50 EIS, highlighting the positive dynamic in France with other national projects. Ever more tools are being developed in French and recommendations for good national practices are emerging [73].

Within this positive dynamic, and despite the obstacles, it is essential to assess the effectiveness and impact of the practice of case management in France. Many centers claim to practice case management, but no study has yet described the practices and their impact on the mental health of users. Moreover, although the profession of case manager is developing, it struggles to be recognized [74].

The study is thus continuing despite recruitment difficulties, and the ethics committee has granted an extension of inclusion of interested centers. The objective is to assess the effectiveness of our practices, to better describe and treat the population of young French people with FEP. The medico-economic evaluation is also essential to objectively establish financial priorities in the light of this data.

Finally, focusing the evaluation on the practice of case management will allow evaluation of this therapy independently of other possible interventions. To date, case management for early psychosis according to the recommendations is rarely practiced outside EIS, but this study raises the possibility of developing it more widely within traditional ambulatory follow-up services. Data from this study will be invaluable for reflecting on these questions and establishing optimal care protocols to treat early psychosis in terms of medical, functional and personal recovery.

**Abbreviations**

| | |
|---|---|
| ACT | Assertive Community Treatment |
| ASSIST | Alcohol, Smoking and Substance Involvement Screening Test |
| BIS | Birchwood Insight Scale |
| CAARMS | Comprehensive Assessment of At-Risk Mental States |
| CGI | Clinical global impression |
| CDSS | Calgary Depression Scale for Schizophrenia |
| EIS | Early intervention services |
| EPPIC | Early Psychosis Prevention and Intervention Center |
| EQ-5D-5L | EuroQol-5D 5 level version |
| FEP | First episode of psychosis |
| HoNOS | Health of the Nation Outcome Scales |
| ITT | Intention to treat |
| MARS | Medication adherence rating scale |
| PANSS | Positive and Negative Symptoms Scale |
| PMSI | Programme de médicalisation des systèmes d'information |
| QALY | Quality-adjusted life year |
| QLS | Quality of Life Scale |
| S-CGQoL | Caregiver schizophrenia quality of life questionnaire |
| SNIIRAM | Système national d'information inter-régimes de l'Assurance maladie |
| SOFAS | Social and Occupational Functioning Assessment Scale |
| SQLS-R4 | Schizophrenia Quality of Life Scale Revision 4 |
| TAU | Treatment as usual |
| TIDieR | Template for intervention description and replication |
| WAI | Working alliance inventory |
| WHOQOL brief | World Health Organization Quality of Life brief |

**Acknowledgments**
We would like to thank all participants already involved in this study. We also thank the research management team involved in the project: Anissa Megzari for his support in project coordination, Pierre Rataboul for help drafting the protocol, Camille Briand for editing eCase Report Form, Léonie Gazel for regulatory assistance, Lorrie Lafuente for data monitoring and Sarah Kabani for editing the manuscript. Finally we express our thanks the case managers involved in the study: G. Gaffet, S. Henry, A. Honrubia, C. Marty, V. Uriot, N. Yang, V. Mottet, N. Salinier, K. Allix, L. Serres, S. Beaufort, C. Marchant, M. Lescure, I. Melon, A. Moreira

**Authors' contributions**
A. S. is the main author of this paper and of the study protocol for which she is the coordinating investigator. M. A. participated in the development of the study protocol and the paper. P. F.-P. is the protocol methodologist for this study and the paper. S. C. and S. B. are the methodologists of the medico-economic part of the protocol of this study and this paper. J. J. participated in the conduct of the study and proofread the paper.

**Funding**
This study obtained the funding agreement in December 2018 as part of the research programs on the performance of the healthcare system, programs organized by the general management of the healthcare offer of the French Ministry of Solidarity and Health. The study funders have not and will not play any role in the study design, collection, management, analysis and interpretation of data, the writing of the report or the decision to publish. The study sponsor is the University Ethics approval and consent to participate Hospital Carémeau of Nîmes.

**Data availability**
No datasets were generated or analysed during the current study.

## Declarations

**Ethics approval and consent to participate**
The project has been approved by a Research Ethics Committee, committee for the protection of persons (CPP) Ile de France I. It was designed in line with the Declaration of Helsinki and registered at www.clinicaltrials.gov, NCT05116514. All changes to the protocol will be submitted for ethical approval and then forwarded to investigators and participants. Additionally, during the funding process, the protocol has undergone independent peer review.
Participants are informed by investigators about the trial and about the voluntary nature of their participation with both written and verbal communications. Participants are only randomized following the provision of informed consent. Persons in mandatory care, often in inpatient unit, can consent to the study if their clinical condition allows it according to medical and participant evaluation. For minors, their consent and the consent of the two legal guardians are necessary. The choice of the treatment according to the randomization is explained to the participants as well as their families.
If an ancillary or post-trial study is developed, it will be submitted for ethical approval.

**Consent for publication**
Participants who give their informed consent for this study are informed of the use of their data for publication purposes. Any written or oral communication of the results of the research must receive the prior agreement of the coordinating investigator and the sponsor.

**Competing interests**
The authors declare no competing interests.

Received: 9 June 2024 Accepted: 6 May 2025
Published online: 15 May 2025

**References**

1. Gore FM, et al. Global burden of disease in young people aged 10–24 years: a systematic analysis. The Lancet. 2011;377:2093–102.
2. Kahn RS, et al. Schizophrenia Nat Rev Dis Primer. 2015;1:15067.

3. Schoenbaum M, et al. Twelve-Month Health Care Use and Mortality in Commercially Insured Young People With Incident Psychosis in the United States. Schizophr Bull. 2017;43(6):1262–72.
4. McGorry PD, Edwards J, Mihalopoulos C, Harrigan SM, Jackson HJ. EPPIC: an evolving system of early detection and optimal management. Schizophr Bull. 1996;22:305–26.
5. Edwards J, McGorry PD. Implementing early intervention in psychosis: A guide to establishing psychosis services. Prim Care Companion J Clin Psychiatry. 2003;5(4):187.
6. Iyer SN, Malla AK. Early intervention in psychosis: concepts, current knowledge and future directions. Sante Ment Que. 2014;39:201–29.
7. Correll CU, 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;75:555–65.
8. Nordentoft M, Rasmussen JO, Melau M, Hjorthøj CR, Thorup AAE. How successful are first episode programs? A review of the evidence for specialized assertive early intervention. Curr Opin Psychiatry. 2014;27:167–72.
9. Tsiachristas A, Thomas T, Leal J, Lennox BR. Economic impact of early intervention in psychosis services: results from a longitudinal retrospective controlled study in England. BMJ Open. 2016;6: e012611.
10. Mihalopoulos C, Harris M, Henry L, Harrigan S, McGorry P. Is early intervention in psychosis cost-effective over the long term? Schizophr Bull. 2009;35:909–18.
11. McGorry PD, Killackey E, Yung A. Early intervention in psychosis: concepts, evidence and future directions. World Psychiatry Off J World Psychiatr Assoc WPA. 2008;7:148–56.
12. Petitqueux-Glaser C, Acef S, Gozlan G. Case management, patient accompaniment and continuity of care. Soins. Psychiatr. 2009;265:18–21.
13. Lecardeur L, Meunier-Cussac S, Dollfus S. Mobile Intensive Care Unit: A case management team dedicated to early psychosis in France. Early Interv Psychiatry. 2018;12:995–9.
14. Jørgensen P, et al. Early detection and assertive community treatment of young psychotics: the Opus Study Rationale and design of the trial. Soc Psychiatry Psychiatr Epidemiol. 2000;35:283–7.
15. Lutgens D, et al. A five-year randomized parallel and blinded clinical trial of an extended specialized early intervention vs regular care in the early phase of psychotic disorders: study protocol. BMC Psychiatry. 2015;15:22.
16. McGrew JH, Bond GR, Dietzen L, Salyers M. Measuring the fidelity of implementation of a mental health program model. J Consult Clin Psychol. 1994;62:670–8.
17. Dieterich M, et al. Intensive case management for severe mental illness. Cochrane Database Syst Rev. 2017;1:CD007906.
18. Smith L, Newton R. Systematic review of case management. Aust N Z J Psychiatry. 2007;41:2–9.
19. Rosen A, Teesson M. Does case management work? The evidence and the abuse of evidence-based medicine. Aust N Z J Psychiatry. 2001;35:731–46.
20. Orygen, The National Centre of excellence in Youth Mental Health. Early Psychosis Guidelines Writing Group and EPPIC National Support Program, Australian Clinical Guidelines for Early Psychosis. edition 2016.
21. Bonsack C, Conus P. Le case management clinique en santé mentale. Santé Ment. 2017;216:24–31.
22. Conus P, Polari A, Bonsack C. Intervention dans la phase précoce des troubles psychotiques: objectifs et organisation du programme TIPP (Traitement et intervention dans la phase précoce des troubles psychotiques) à Lausanne. Inf Psychiatr. 2010;86:145–51.
23. Fond G, et al. Risk factors for increased duration of untreated psychosis Results from the FACE-SZ dataset. Schizophr Res. 2018;195:529–33.
24. Souaiby L, et al. Individual factors influencing the duration of untreated psychosis. Early Interv Psychiatry. 2018. https://doi.org/10.1111/eip.12562.
25. Capdevielle D, et al. A multi-dimensional approach to insight and its evolution in first-episode psychosis: A 1-year outcome naturalistic study. Psychiatry Res. 2013;210:835–41.
26. Alvarez-Jimenez M, et al. Risk factors for relapse following treatment for first episode psychosis: A systematic review and meta-analysis of longitudinal studies. Schizophr Res. 2012;139:116–28.
27. Gut-Fayand A. A French experience: the Evaluation Center for young adults and adolescents. L'Encephale. 2008;34(Suppl 5):S175–178.
28. Oppetit A, et al. The C'JAAD: a French team for early intervention in psychosis in Paris. Early Interv Psychiatry. 2016. https://doi.org/10.1111/eip.12376.
29. Gozlan G, Meunier-Cussac S, Lecardeur L, Duburcq A, Courouve L. Early intervention in first psychotic episodes in France: mapping of specialized programs in 2017. Inf Psychiatr. 2018;94:393–401.
30. Ministry of Social Affairs and Health in France. Psychiatry and Mental Health Plan 2011–2015. edition 2011.
31. Ministry of Social Affairs and Health in France. Five-Year Strategy for the Development of Medico-Social Services – Mental Disability Component. 2016.
32. Laforcade M. Report on mental health. Regional Health Agency of Nouvelle-Aquitaine. 2016.
33. Ministry of Social Affairs and Health in France. Decree No. 2018-125 on the Framework for Health System Innovation Pilots under Article L. 162-31-1 of the Social Security Code. 2018.
34. Klaehn A-K, Jaschke J, Freigang F, Arnold M. Cost-effectiveness of case management: a systematic review. Am J Manag Care. 2022;28:e271–9.
35. Yung AR, et al. Mapping the Onset of Psychosis: The Comprehensive Assessment of At-Risk Mental States. Aust N Z J Psychiatry. 2005;39:964–71.
36. Krebs M-O, et al. Assessment of mental states at risk of psychotic transition: validation of the French version of the CAARMS. L'Encéphale. 2014;40:447–56.
37. Conus P, Maire A, Polari A. Case Management in Early Psychosis: A Manual. French translation adapted from the original text produced by EPPIC (Early Psychosis Prevention and Intervention Centre, Orygen).
38. Spitzer, R. L., Williams, J. B., Gibbon, M. & First, M. B. The Structured Clinical Interview for DSM-III-R (SCID). I: History, rationale, and description. Arch Gen Psychiatry. 1992;49:624–629.
39. First MB, Williams JBW, Karg RS, Spitzer RL. User's guide for the SCID-5-CV Structured Clinical Interview for DSM-5® disorders: Clinician Version (SCID-5-CV). Am J Psychiatry. 2016.
40. van Mastrigt S, Addington J. Assessment of premorbid function in first-episode schizophrenia: modifications to the Premorbid Adjustment Scale. J Psychiatry Neurosci JPN. 2002;27:92–101.
41. Cannon-Spoor HE, Potkin SG, Wyatt RJ. Measurement of premorbid adjustment in chronic schizophrenia. Schizophr Bull. 1982;8:470–84.
42. Kay SR, Flszbein A, Opfer LA. The positive and negative syndrome scale (PANSS) for schizophrenia. Schizophr Bull. 1987;13:261.
43. Lançon C, Auquier P, Nayt G, Reine G. Stability of the five-factor structure of the Positive and Negative Syndrome Scale (PANSS). Schizophr Res. 2000;42:231–9.
44. Thompson K, Kulkarni J, Sergejew A. Reliability and validity of a new Medication Adherence Rating Scale (MARS) for the psychoses. Schizophr Res. 2000;42:241–7.
45. Fond, G. et al. Validation study of the Medication Adherence Rating Scale Results from the FACE-SZ national dataset. Schizophr Res. 20217;182:84–89.
46. Munder T, Wilmers F, Leonhart R, Linster HW, Barth J. Working Alliance Inventory-Short Revised (WAI-SR): psychometric properties in outpatients and inpatients. Clin Psychol Psychother. 2010;17:231–9.
47. Corbière M, Bisson J, Lauzon S, Ricard N. Factorial validation of a French short-form of the Working Alliance Inventory. Int J Methods Psychiatr Res. 2006;15:36–45.
48. Birchwood M, et al. A self-report Insight Scale for psychosis: reliability, validity and sensitivity to change. Acta Psychiatr Scand. 1994;89:62–7.
49. Guy, W. Clinical Global Impressions, ECDEU Assessment Manual for Psychopharmacology, revised (DHEW Publ. No. ADM 76-338). National Institute of Mental Health, Rockville, 1976, 218–222.
50. Andreasen NC, et al. Remission in schizophrenia: proposed criteria and rationale for consensus. Am J Psychiatry. 2005;162:441–9.
51. Addington D, Addington J, Maticka-Tyndale E. Assessing depression in schizophrenia: the Calgary Depression Scale. Br J Psychiatry. 1993;22:39–44.
52. Bernard D, Lançon C, Auquier P, Reine G, Addington D. Calgary Depression Scale for Schizophrenia: a study of the validity of a French-language version in a population of schizophrenic patients. Acta Psychiatr Scand. 1998;97:36–41.
53. Khan R, et al. Validation of the French version of the alcohol, smoking and substance involvement screening test (ASSIST). Eur Addict Res. 2011;17:190–7.
54. Rybarczyk, B. Social and Occupational Functioning Assessment Scale (SOFAS). in Encyclopedia of Clinical Neuropsychology (eds. Kreutzer, J. S., DeLuca, J. & Caplan, B.) 2313–2313 (Springer New York, 2011). https://doi.org/10.1007/978-0-387-79948-3_428.

55. Wing J, Curtis R, Beevor A. HoNOS: Health of the nation outcome scales. Rep Res Dev Lond R Coll Psychiatr. 1996;172:11–8.
56. Lauzon S, et al. Validation of the French version of the Health of the Nation Outcome Scales (HoNOS-F). Can J Psychiatry Rev Can Psychiatr. 2001;46:841–6.
57. Heinrichs DW, Hanlon TE, Carpenter WT. The Quality of Life Scale: an instrument for rating the schizophrenic deficit syndrome. Schizophr Bull. 1984;10:388–98.
58. Simon-Abbadi S, Guelfi JD, Ginestet D. Psychometric qualities of the French version of the Heinrichs quality of life rating scale. Eur Psychiatry J Assoc Eur Psychiatr. 1999;14:386–91.
59. Lançon C, Reine G, Simeoni M-C, Aghababian V, Auquier P. Development and validation of a self rating quality of life scale: the S-QoL. L'Encephale. 2007;33:277–84.
60. World Health Forum. What quality of life? The WHOQOL Group World Health Organization Quality of Life Assessment. World Health Forum. 1996;17:354–6.
61. Rabin R, de Charro F. EQ-5D: a measure of health status from the EuroQol Group. Ann Med. 2001;33:337–43.
62. Richieri R, et al. A preliminary validation of a new French instrument to assess quality of life for caregivers of patients suffering from schizophrenia. L'Encephale. 2011;37:425–32.
63. Attkisson CC, Zwick R. The client satisfaction questionnaire Psychometric properties and correlations with service utilization and psychotherapy outcome. Eval Program Plann. 1982;5:233–7.
64. Attkisson CC, Greenfield T. The client satisfaction questionnaire (CSQ) scales. In book: Outcome Assessment in Clinical Practice Publisher: Baltimore, MD: Williams & Wilkins Editors: Sederer LL, Dickey B. 1995:2–10.
65. Tuppin P, et al. Value of a national administrative database to guide public decisions: From the système national d'information interrégimes de l'Assurance Maladie (SNIIRAM) to the système national des données de santé (SNDS) in France. Rev Epidemiol Sante Publique. 2017;65(Suppl 4):S149–67.
66. Cougnard A, et al. Pattern of health service utilization and predictors of readmission after a first admission for psychosis: a 2-year follow-up study. Acta Psychiatr Scand. 2006;113:340–9.
67. Malla A, et al. Factors influencing relapse during a 2-year follow-up of first-episode psychosis in a specialized early intervention service. Psychol Med. 2008;38:1585–93.
68. French National Authority for Health. Methodological Guide – Methodological Choices for Economic Evaluation. 2011.
69. Statista Daily Data. Infographic: European Countries with the highest number of psychiatrists. 2019. https://fr.statista.com/infographie/11425/les-pays-europeens-qui-comptent-le-plus-de-psychiatres.
70. Bellivier F. L'individualisation d'un programme de développement spécifiquement dédié à la santé mentale. Inf Psychiatr. 2023;99:143–143.
71. Ministry of Social Affairs and Health in France. Psychiatry and Mental Health Plan 2018-2023. edition 2018.
72. Institut de Psychiatrie GDR 3557. Projets de recherche, réseau Transition. Institut de Psychiatrie https://institutdepsychiatrie.org/reseau-transition/projets-de-recherche/.
73. Lecardeur, L. Troubles psychotiques : protocoles d'intervention précoce | Livre | 9782294761799. Elsevier Masson SAS https://www.elsevier-masson.fr/troubles-psychotiques-protocoles-dintervention-precoce-9782294761799.html (2019).
74. Bartoli A, Sebai J, Gozlan G. Les case-managers en santé mentale : des professionnels en quête de définition. Manag Avenir Santé. 2020;6:83–104.


## Publisher's Note

A list of authors and their affiliations appears at the end of the paper.