

Short Communication

Cognitive complaint inversely associated to UHR transition

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ABSTRACT

The aim of this study was to identify the impact of staging on a six-months transition in Ultra-High Risk (UHR) youth.

Subjects were enrolled at assessment; evolution was monitored for six months. Clinical determinants (unusual thought content, perceptual abnormalities, cognitive complaint, etc.) were collected.

37 non-psychotic and 39 UHR subjects were included. 13 UHR (35.2 %) experienced psychotic transition, while none of non-psychotic subjects did log-rank $p < 0.001$. Self-reported cognitive complaint was inversely associated to transition OR 0.13 95 % IC [0.03–0.64]. Unusual Thought Content was associated to psychotic transition OR 8.57 95 % IC [1.17–63]. Self-reported cognitive complaint could be a protective transition marker in UHR.

The concept of Early Intervention (EI) in psychosis has been spreading worldwide since the 1980s (Watt, 1979; McGorry et al., 2018). In most cases, psychotic symptoms appear progressively. There is a clinical continuum from basic symptoms that can take the mask of anxious or depressive states (Youn et al., 2020). Prodromal symptoms then intensify until the onset of attenuated psychotic symptoms (Guo et al., 2020): the At-Risk Mental States (ARMS) or Ultra-High Risk (UHR). When psychotic symptoms reach the threshold of psychotic transition, the person experiences First Episode Psychosis (FEP). Transition rates from ARMS to FEP are 0.25 (95 % CI: 0.21–0.29) at 2.5 years (0.09 (95 % CI: 0.07–0.10) at 0.5 year, (Salazar de Pablo et al., 2021a, 2021b)).

Lower functioning at baseline is known to be a predictor (Koutsouleris et al., 2018). Some variables, such as genetic risk, higher levels of unusual thought content (UTC), higher levels of suspicion/paranoia, greater social impairment, and substance abuse, are associated with an increased risk of psychotic transition; the cumulation of some of these factors at baseline has a predictive transition hazard of about 68 to 80 % (Cannon et al., 2008).

In France, EI units have emerged since the late 2000s, such as C' JAAD (Centre Jeunes Adultes et Adolescents) in Paris (Oppetit et al.,

2018). However, in the last five years, we have witnessed an exponential growth of these units on the national territory. In Limoges (a medium-sized French city), this care service has been available since 2019. During the first three years of its existence, mostly due to COVID, help-seekers were mainly referred by adult or Child and Adolescent Psychiatry (CAP).

The aim of our study was to determine the effect of staging at assessment on a six-months psychotic transition in ARMS help-seekers and non-psychotic help-seekers. The secondary aim was to identify of the association of clinical determinants at assessment with an early psychotic transition.

We conducted a retrospective cohort study. Subjects included were assessed between January 2019 and December 2021. Participants were eligible if they met the following criteria: age between 13 and 30 years, clinical assessment using the French version of the Comprehensive Assessment of At-Risk Mental States (CAARMS) (Krebs et al., 2014). Non-inclusion criteria were the following: diagnosis of schizophrenia, psychosis, or bipolar disorder at the time of assessment, being under antipsychotic treatment, or current inability to understand or speak French. Participants were excluded if they, or their legal representatives if aged under 18, gave oral or written opposition to their data to be

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Abbreviations

ARMS	At-Risk Mental States
CAARMS	Comprehensive Assessment of At-Risk Mental States
CAP	Child & Adolescent Psychiatry
eDIP	équipe de Détection et d'Intervention Précoce
EI	Early Intervention
EHC	Esquirol Hospital Center
FEP	First Episode Psychosis
HDH	Health Data Hub
PA	Perceptual Abnormalities
THC	Tetrahydrocannabinol
UHR	Ultra-High Risk
UTC	Unusual Thought Content

collected. Inclusions were based on the population assessed during the first three years of the concrete service functioning.

Esquirol Hospital Center (EHC) is the referent psychiatric hospital in Limoges' region. The multidisciplinary EI team consists of two case managers nurses, two psychiatrists, a social worker and, since 2020, a neuropsychologist.

Follow-up is limited to three years, which corresponds to the highest risk of psychotic transition in the literature (1). If further follow-up is needed (Salazar de Pablo et al., 2021c, 2022; Fusar-Poli et al., 2020a, 2020b) the modalities are discussed with the patient and the case managers can help to organize it.

After assessment, help-seekers were divided into three categories: absence of psychotic symptoms "NoP", attenuated psychotic symptoms in their intensity or frequency "UHR", and "FEP" for those who had reached the threshold of psychotic symptoms. The interview at assessment included quantification of UTC and perceptual abnormalities (PA) symptoms absent/mild/severe using CAARMS, clinical search for depressive symptoms absent/present, self-reported cognitive complaint absent/present, active tetrahydrocannabinol (THC) use absent/present, maintained academic or vocational activity yes/no, psychiatric family history (FHP) absent/present, and referral by adult or CAP.

An "early" psychotic transition was defined by the appearance/worsening of the attenuated psychotic symptoms (according to the CAARMS threshold) in the following six months, for included NoP and UHR subjects. Psychiatric records were searched for psychotic transition and, if present, the time since assessment (expressed in days). The date of entry into the study was the date of the CAARMS assessment. If transition occurred, the date was the date the transition was documented in the patient's medical record.

Data were collected between 1 January and 30 June 2022. The list of the subjects assessed was obtained via the "program for medicalization of information systems". Each patient's file was searched and identified using the patient's identification code in EHC. Data were collected by a psychiatrist specialized in EI.

The study was submitted to the Health Data Hub (HDH), as the research is conducted on collected data and does not involve any intervention on patients. The Data Protection Officer supports the declaration to HDH, in accordance with the General Data Protection Regulation.

Quantitative variables were presented as mean \pm SD. Qualitative variables were presented in percentages. Kolmogorov-Smirnov test was applied to identify the normal distribution of quantitative variables. To identify the impact of staging on an early psychotic transition, a survival curve using Kaplan-Meier method was applied for NoP and UHR groups, and a comparison has been conducted with a log-rank test. A p -value < 0.05 was considered statistically significant. Analyses were performed using SPSS software version 28.0.0.0.

76 subjects, 37 NoP, and 39 UHR were included. Sociodemographic

description of the population at assessment is available in our related paper (Hamdan et al., 2023). No early transition event was documented in the NoP subjects. In the UHR, 13 subjects (35.2 %) reached the threshold of a psychotic episode six months after assessment. The median time between assessment and transition was 68 days 95 % IC [8; 193]. The log-rank test showed a significant difference between the two groups evolution $p < 0.001$.

Fig. 1 shows survival curves comparing psychotic transition between the two groups.

Logistic regression was used on two groups: 13 transitioned versus 63 non-transitioned. Cognitive complaints were inversely associated with transition OR 0.13 95 % IC [0.03–0.64]. The presence of UTC was associated with psychotic transition OR 8.57 95 % IC [1.17–63]. Neither PA nor other variables showed a significant association (Table 1).

We wanted the referral to our team to be direct for help-seekers and general practitioners, but the Covid crisis had changed our plans, and we initially focused on intra-hospital communication. While all referred patients were assessed, those without psychotic symptoms were referred to other care teams, with whom we share the same hospital records. None of the NoP subjects had a documented transition at six months. In the UHR, 33.3 % reached the threshold of the psychotic stage, which is a high rate compared to the actual transition rate of 9 % at six months (Salazar de Pablo et al., 2021a, 2022; Fusar-Poli et al., 2020b). This could be the result of more severe symptoms in this population, which was exclusively referred by psychiatric services.

However, the main finding of this study is the association between self-reported cognitive complaints and psychotic transition in the UHR population. Neurocognitive dysfunction is recognized as a potential predictor in ARMS (Catalan et al., 2021), as well as poorer metacognition (Barbato et al., 2014). Cognitive biases are known to be significant in UHR and FEP subjects (Bolt et al., 2019; Guo et al., 2020) and severity of cognitive basic symptoms might be associated with higher risk of transition (Youn et al., 2020; Seidman et al., 2016). However, we did not find any study in the literature supporting that reduced self-awareness of cognitive impairment may be associated with transition.

In characterized schizophrenia, awareness of cognitive impairments does not correlate with deficits. In 2008, Medalia et al. (Medalia and Thysen, 2008) established that less than half of schizophrenia patients with cognitive deficits were aware of them. Self-misperceptions of deficits are known to have a functional impact in schizophrenia subjects (Gould et al., 2015), and introspective accuracy appears to be worsened by psychotic symptoms (Morgan et al., 2022). However, in the early stages, insight dimensions like self-reflectiveness are less affected than in more advanced stages (Preti et al., 2022), with a hypothesized progressive gradient from early stages to more serious ARMS, to FEP (Xu et al., 2022). Thus, insight into cognitive issues may be a protective marker for psychotic transition.

Presence of UTC is known to distinguish ARMS who transitioned from other clinical outcomes (Addington et al., 2015), so the difference between UTC and PA was not surprising. If attenuated psychotic symptoms are now established as a confirmed risk of transition, less typical symptoms such as anxiety and depression are reasons for referral to EI services, confirming the polymorphic presentation of help-seekers (Rice et al., 2019).

Our study also has several limitations. Data were extracted retrospectively from medical records, which may introduce information bias. Depression, anxiety, and adverse childhood experiences were identified clinically, but not assessed with scales. Self-reported cognitive complaints were also subjectively assessed, and patients did not undergo a neuropsychological test battery. In addition to the fact that 6 months is not enough time to assess the global proportion of psychotic transition, the sample size was not assessed beforehand, which prevents us from drawing general conclusions.

Therefore, a prospective cohort will be conducted in the EI population to better understand the relationship between these variables and psychotic transition.

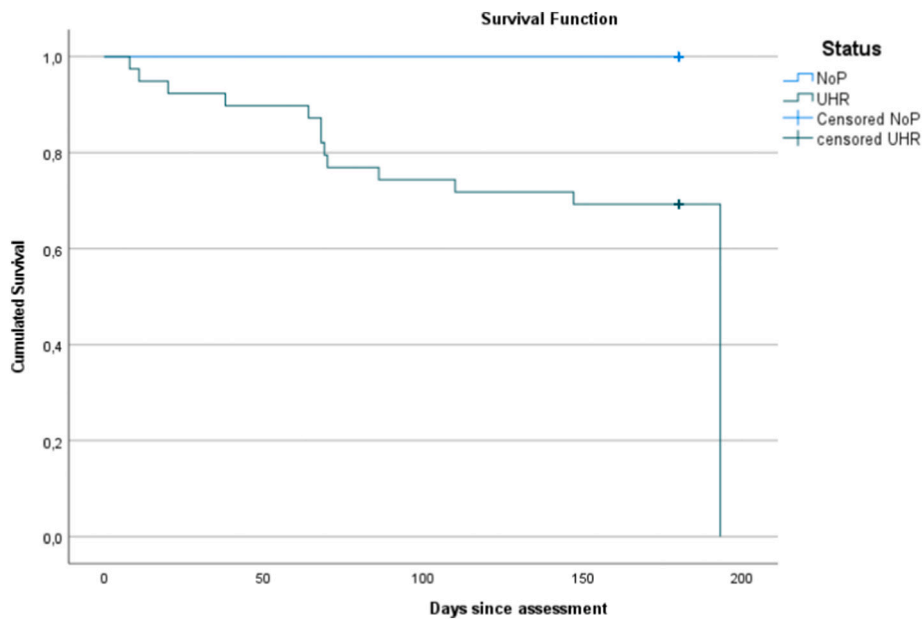


Fig. 1. Survival curves comparing the psychotic transitions in NoP and UHR subjects.

Table 1

OR associated to clinical characteristics when comparing transitioned to non-transitioned subjects. Values marked in bold are significant.

Variables	β -coefficient	Wald	p-value	Exp β (OR)	95 % CI exp. β
Age	-0.004	0.001	0.98	1.004	[0.74–1.36]
Gender	1.02	0.99	0.32	2.76	[0.38–20.29]
Adult psychiatric referral	-0.26	0.05	0.83	0.77	[0.08–8.00]
Depressive symptoms	-0.13	0.03	0.87	0.88	[0.17–4.41]
Cognitive complaint	-2.04	6.3	0.01	0.13	[0.03–0.64]
Unusual thought content	2.15	4.46	0.04	8.57	[1.17–63]
Perceptual abnormalities	0.34	0.15	0.7	1.4	[0.25–7.72]
Maintained activity	0.35	0.18	0.68	1.42	[0.27–7.4]
THC	0.62	0.35	0.56	1.86	[0.24–14.68]
FHP	-1.034	0.814	0.242	0.36	[0.06–2.01]

Ethics approval statement & clinical trial registration

This study was submitted to Health Data Hub (HDH), as the research is conducted on collected data and does not imply intervention on patients. Thus, the French law allows data treatment without submission to an Ethics Committee. The Data Protection Officer (DPO), in accordance with General Data Protection Regulation (GDPR) supports the declaration to HDH.

Declaration of generative AI and AI-assistance technologies in the writing process

The authors did not use AI or AI-assistance technologies in the writing process.

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CRedit authorship contribution statement

Mirvat Hamdan-Dumont: Writing – original draft, Validation, Project administration, Methodology, Investigation, Formal analysis, Conceptualization. **Laurent Lecardeur:** Writing – review & editing, Validation, Methodology. **Marine Habert:** Writing – review & editing, Validation, Methodology. **Jérémy Couturas:** Writing – review & editing, Validation. **Mireille Okassa:** Writing – review & editing, Validation. **Aurélien Lacroix:** Writing – review & editing, Validation, Methodology. **Benjamin Calvet:** Writing – review & editing, Validation, Supervision, Methodology, Formal analysis, Conceptualization.

Declaration of competing interest

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