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# Extended Diagnostic Evaluation and Neuropsychiatric Characteristics in Acute and Transient Psychotic Disorders – A Descriptive Analysis

Nima Moradzadeh<sup>1\*</sup>, Jeanett Bauer<sup>2</sup>, Dina Stenborg<sup>1</sup>, Lone Baandrup<sup>1,3</sup>

<sup>1</sup>Department Bispebjerg-Gentofte, Mental Health Centre Copenhagen, Mental Health Services of the Capital Region in Denmark

<sup>2</sup>Mental Health Services of the Capital Region in Denmark

<sup>3</sup>Department of Clinical Medicine, Faculty of Health Sciences, University of Copenhagen, Denmark

## Article Info

### Article Notes

Received: April 16, 2025

Accepted: June 20, 2025

### \*Correspondence:

\*Dr. Nima Moradzadeh, Department Bispebjerg-Gentofte, Mental Health Centre Copenhagen, Mental Health Services of the Capital Region in Denmark.

Email: [nima.moradzadeh.01@regionh.dk](mailto:nima.moradzadeh.01@regionh.dk)

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### Keywords:

Acute and Transient Psychosis

Psychosis

Affective Disorders

Schizophrenia Spectrum Disorders

## Abstract

**Background and Objectives:** Acute and transient psychotic disorders (ATPDs) constitute a frequent reason for acute hospitalization. The aim of this study was 1) to describe the value of an extended diagnostic evaluation program for first episode ATPDs and 2) to describe the short-term prognosis of transitioning to schizophrenia or affective disorder in relation to the initial symptom profile.

**Methods:** We collected medical record data from patients with consent, aged 18-65 years, and admitted due to ATPDs (ICD-10: F23.X) to an emergency psychiatry department in Copenhagen, Denmark. The extension of the diagnostic evaluation program included magnetic resonance imaging (MRI), examination of cerebrospinal fluid by lumbar puncture (LBP), and electroencephalography (EEG) if clinically indicated.

**Results:** A total of 53 patients were included. Twenty-nine (55%) were men, the mean age was 25.56 years (SD = 10.71), and the mean length of hospitalization was 32.74 days (SD = 15.39). Clinical evaluations using MRI, LBP, and EEG did not reveal abnormal findings of diagnostic significance. The clinical symptom profile was diverse but could broadly be classified as polymorphic, schizophrenia-like, or unspecified. A pattern towards short-term transitioning to affective disorder was observed among patients who initially presented with fluctuating moods. The majority of patients (53%) maintained their initial diagnosis of ATPD upon discharge.

**Conclusions:** The extended evaluation program was not of additional diagnostic value in this sample of patients with ATPDs. We observed a diverse clinical symptom profile and described patterns that were suggestive of short-term prognosis. However, further research with larger sample sizes and extended follow-up periods is needed to confirm and expand these results.

## Background

A group of acute and episodic psychoses with a usually favourable prognosis are classified as acute and transient psychotic disorders (ATPDs) (F23) in the 10<sup>th</sup> Edition of the International Classification of Mental and Behavioural Disorders<sup>1</sup> and as 'Brief Psychotic Disorder's (BPDs) in the Diagnostic and Statistical Manual of Mental Disorders (DSM-5)<sup>2</sup>. These diagnoses comprise a frequent but inhomogeneous clinical picture among acutely hospitalised patients with a prevalence rate varying between 3.9 to 9.6 per 100,000 inhabitants<sup>3</sup>.

The ICD-10 category of ATPDs includes clinical conditions with polymorphic (F23.0+1), schizophrenia-like (F23.2), or predominantly delusional (F23.3) symptoms characterised by

an acute onset of symptoms within 1-2 weeks and being associated or not with preceded acute stress, defined as events that most people would find stressful, such as bereavement, unexpected loss of partner or job, occurring less than 2 weeks before the onset of symptoms. Previous retrospective studies suggest an antecedent psychosocial stressor in 44.2% of cases<sup>4</sup>. ATPDs have a duration criterion of complete remission within three months, except if there is presence of schizophrenia-like symptoms in which the duration is limited to one month. If the disorder persists, a change in diagnostic classification will be needed. The polymorphic subgroup has a broad and variable symptomatology including delusions, hallucinations, thought disorganization, perplexity or confusion, motor symptoms and/or emotional turmoil (i.e., intense feelings of happiness and ecstasy or overwhelming and marked irritability) changing daily or even faster. The schizophrenia-like subgroup consists primarily of symptoms close to or overlapping the actual schizophrenia diagnosis<sup>1</sup>. Conversely, DSM-5 classifies BPDs as sudden-onset psychotic behaviour lasting less than one month, with possible future relapses<sup>2</sup>. BPD shares similarities with ATPDs but includes additional criteria such as disorganized speech and behaviour<sup>5</sup>.

For both ATPDs and BPDs it is mandatory to exclude organic or medical conditions that could cause the psychosis. These include medication-induced psychoses, drug-induced psychoses, and psychoses caused by organic factors such as metabolic, endocrinological, infectious, or neoplastic causes. International clinical guidelines recommend a full assessment of the first episode of psychosis including somatic and neurological examination, routine blood tests, urine drug screen, and if indicated by the clinical presentation brain imaging with magnetic resonance imaging (MRI) (or computed tomography (CT) if not available), examination of cerebrospinal fluid, and electroencephalography (EEG)<sup>6</sup>. In Denmark, the basic somatic evaluation of patients with psychosis includes objective somatic and neurological examinations, routine blood tests and other laboratory tests as indicated. MRI and lumbar puncture (LBP) are not performed routinely in all patients admitted with ATPDs, but such procedure has been recommended by the national German guidelines<sup>7</sup>.

Since the development of the ICD-10 category ATPDs, a new research field of autoimmune inflammatory encephalitis (AIE) has evolved. It constitutes a secondary and organic cause of ATPD and should be classified as such. Recent research has shed light on the similarity between AIEs and ATPDs in their initial symptomatology. Both conditions often present with an acute onset of polymorphic psychotic symptoms, which may subsequently evolve to include neurological manifestations such as catatonia, seizure, dyskinesia, and autonomic instability<sup>8</sup>. The most frequent

type of AIE, that in >85% of cases present with an initial clinical picture indistinguishable from ATPDs, is the anti-N-methyl-D-aspartate receptor encephalitis (anti-NMDA-R)<sup>9</sup>.

As of now it is still unclear whether some cases of AIE might be missed among patients classified with ATPDs due to insufficient laboratory evaluation in patients not presenting with symptoms resembling an underlying organic cause. However, a few previous studies have found that around 4%<sup>9,10</sup> of hospitalized patients presenting with ATPDs have an underlying somatic cause based on an extended diagnostic evaluation program including cerebrospinal fluid (CSF) analysis. These findings underscore the importance of comprehensive assessments and the potential overlap between ATPDs and some organic syndromes including AIE, necessitating further exploration in clinical practice and research.

The existing literature suggests that ATPDs constitute a composite category of mental disorders, affecting more frequently females during early to middle adulthood, and associated with an increased risk of mortality from both natural causes and suicide<sup>11</sup>. Transition rate within ATPDs to schizophrenia spectrum disorders or affective disorders vary considerably. Castagnini, Munk-Jørgensen and Bertelsen, 2016<sup>12</sup> conducted an analysis of short-term prognosis, revealing that 59.6% of individual retained their initial diagnosis, while 27.7% progressed to affective psychoses and 12.8% to schizophrenia or schizoaffective disorders within a one-year follow-up period. Moreover, a recent meta-analysis of 25 studies including 13,507 patients with ATPDs across a follow-up period of 6.3 years revealed that 55% did not develop any other mental health disorder, 25% developed schizophrenia or related disorders, 12% affective disorders, and 6% other ICD-10 categories<sup>13</sup>.

The following risk factors for transitioning to schizophrenia have been reported: younger age, male sex, and longer first admission to hospital<sup>14,15</sup>.

We report here the results of a descriptive longitudinal study examining 1) the value of an extended diagnostic evaluation program for people presenting with ATPDs and 2) the short-term prognosis of transitioning from ATPDs to schizophrenia or affective disorder in relation to the initial symptom profile.

## Methods

### Design and Study Population

This research project is a descriptive longitudinal study that was carried out at Mental Health Centre Copenhagen which is the largest psychiatric hospital in the urban area of Copenhagen in Denmark. All patients admitted to the emergency department at Mental Health Centre Copenhagen under the picture of ATPD and meeting the inclusion criteria were offered an extended evaluation program. Inclusion

criteria were defined as hospitalized patients with acutely developed psychotic symptoms and age 18-65 years. Participants were excluded if they 1) had previously been diagnosed with schizophrenia spectrum disorder (F2X), bipolar affective disorder (F31.X), depression with psychotic symptoms (F32.3, F33.3), 2) presented with other obvious causes of the psychotic condition including medication-induced psychosis, drug-induced psychosis, and psychosis of metabolic or endocrinological origin. Contraindications for MRI did not exclude the patient from the remainder of the evaluation program.

The basic diagnostic evaluation that was already routinely performed included a clinical unstructured interview in the emergency department upon admission, followed by a comprehensive review by the attending physician the subsequent day, somatic and neurological examinations, as well as routine laboratory tests comprising haematology, c-reactive protein (CRP), renal and liver function tests, electrolytes, blood glucose, thyroid stimulating hormone (TSH), calcium, and folate. Urine tests were also performed for drug screening. In addition, the extended evaluation program included a full MRI of the brain, urine dipstick analysis for infections, cerebrospinal fluid examination (CSF), and an EEG if clinically indicated.

We obtained informed written consent from the participants to register and analyse their clinical data in accordance with Danish regulation. Patients who did not want to or who were not able to provide informed consent were still offered the extended evaluation program, but their data could not be included for analysis according to Danish regulations.

### Data Collection and Analysis

We analysed the included patient sample by systematically reviewing medical records from the first week of admission to categorize the clinical picture presented by each of the patients into subset of groups representing the subcategories of ICD-10's ATPD, F23.x. Using this approach in combination with an overview of stability versus change of diagnosis from baseline (diagnosis at the time of admission) to follow-up (diagnosis at discharge), we were able to describe how the initial clinical picture might influence the short-term prognosis of transitioning into schizophrenia or affective disorder, i.e., from admission to discharge during the initial hospitalization. Both the admission diagnosis and the discharge diagnosis reported for this study was validated by an experienced psychiatrist based on medical record data. Data were analysed using descriptive statistics.

### Results

A total of 53 patients were included in the sample from August 26, 2016, to January 2, 2023.

### Demographic and Clinical Characteristics

Table 1 presents the sociodemographic characteristics. The sample comprised 29 men (55%) and 24 women (45%). The mean age was 25.56 years (SD = 10.71). Most participants were of European origin (77%), with a smaller proportion representing African, Asian/Middle Eastern, and mixed ethnic backgrounds.

Regarding educational attainment, a third (N=16; 30%) of the participants had only completed primary school whereas more than half of the participants (N=34; 64%) had higher levels of education including high school, vocational education, and a bachelor's or master's degree.

Table 2 shows the clinical characteristics of the study population. All patients included were diagnosed with ATPD of which the unspecified subtype (F23.9) was the most common (N=31; 58%), followed by other ATPDs (F23.8) (N=6; 11%). An overweight of females (2:5 ratio, m:f) received an initial diagnosis of acute polymorphic psychotic disorder (F23.0 and F23.1), while males (4:1 ratio, m:f) were more frequently diagnosed with acute schizophrenia-like disorders (F23.2). The discharge diagnosis varied with ATPD, unspecified (F23.9) remaining the most prevalent (N=16; 30%), followed by bipolar affective disorder (F31.x) (N=8; 15%).

The admission length ranged from 1 to 164 days with mean length of admission of 32.74 days (SD=15.39). Approximately one third of the patients (N=15; 28%) reported current substance use and one-third (N=20; 38%) had a previous psychiatric contact, diagnosis, or treatment. Most previous contacts were for the treatment of depression, with a few patients diagnosed or treated for post-traumatic stress disorder (PTSD), attention deficit hyperactive disorder (ADHD), and autism spectrum disorder.

**Table 1:** Socio-demographic characteristics of the study population

Variables		N = 53 (%)
Sex	Male	29 (55)
	Female	24 (45)
Age (years)	18-30	29 (55)
	31-50	19 (36)
	>51	5 (9)
Ethnic status	White	41 (77)
	African	3 (6)
	Asian/ Middle Eastern	5 (9)
	Mixed	4 (8)
Highest level of completed education	Primary school	16 (30)
	High school	7 (13)
	Vocational education	7 (13)
	Bachelor's degree	9 (17)
	Master' degree	11 (21)
	Other	3 (6)

**Table 2:** Clinical characteristics and laboratory findings of the study population

Variables		N = 53 (%)
<b>Admission diagnosis</b>	F23.0	4 (8)
	F23.1	3 (6)
	F23.2	5 (9)
	F23.3	4 (8)
	F23.8	6 (11)
	F23.9	31 (58)
<b>Discharge diagnosis</b>	F10-F19	5 (9)
	F20.0-20.9	3 (6)
	F22.0-22.9	4 (8)
	F23.0-23.1	5 (9)
	F23.2	3 (6)
	F23.3	1 (2)
	F23.8	3 (6)
	F23.9	16 (30)
	F30-F39	13 (25)
<b>Admission length</b>	1-10 days	5 (9)
	11-30 days	20 (38)
	31-60 days	19 (36)
	61-90 days	5 (9)
	>90 days	4 (8)
<b>Current substance use</b>	Yes	15 (28)
	No	38 (72)
<b>Previously treated for a mental health disorder – GP or psychiatrist</b>	Yes	20 (38)
	No	33 (62)
<b>Neurological examination</b>	Within normal limits	47 (89)
	Abnormal	1 (2)
	Not examined	5 (9)
<b>Blood samples</b>	Within normal limits	24 (45)
	Elevated infection count	18 (34)
	Other anomalies	11 (21)
<b>Urine stick with culture and sensitivity</b>	Positive	7 (13)
	Negative	21 (40)
	Not examined	25 (47)
<b>Urine drug screen</b>	Positive	9 (17)
	Negative	16 (30)
	Not examined	28 (53)
<b>MRI</b>	Positive	18 (34)
	Negative	31 (58)
	Not examined	4 (8)
<b>CSF</b>	Positive	2 (3)
	Negative	21 (40)
	Not examined	30 (57)
<b>EEG</b>	Positive	0 (0)
	Negative	9 (17)
	Not examined	44 (83)

F10-F19: Mental and behavioural disorders due to psychoactive substance use

F20.0-20.9: Schizophrenia

F22.0-22.9: Persistent delusional disorders

F23.0: Acute polymorphic psychotic disorder without symptoms of schizophrenia

F23.1: Acute polymorphic psychotic disorder with symptoms of schizophrenia

F23.2: Acute schizophrenia-like psychotic disorder

F23.3: Other acute predominantly delusional psychotic disorders

F23.8: Other acute and transient psychotic disorders

F23.9: Acute and transient psychotic disorder, unspecified

F30-F39: Mood (affective) disorders

## Laboratory and Imaging Findings

Table 2 shows that neurological examinations were generally without abnormal findings (N=47; 89%), with only a single case (2%) presenting dysdiadokokinesia of the tongue, which did not result in further examinations or changes in treatment. Blood samples revealed various findings outside the reference limits, including elevated infection counts (N=18; 34%) and other anomalies (N=11; 21%) such as cases with elevated liver counts, reduced potassium, and folate. None of them resulted in further examinations. Urine tests for infection showed both positive mixed floral results (N=7; 13%) and negative (N=21; 40%) results, however, a large proportion of cases (N=25; 47%) were not examined. Urine toxicology screenings also yielded positive (N=9; 17%) and negative (N=16; 30%) results, with a significant proportion (N=28; 53%) not examined. Of the positive tests, delta-9-tetrahydrocannabinol (THC) were detected in six cases, 3,4-methylenedioxymethamphetamine (MDMA) in a single case, and gamma-hydroxybutyrate (GHB) in a single case. These findings did not lead to exclusion of the patients from the study because only a sporadic use of drugs was reported and therefore not considered as the main causing agent of the acute psychotic episode.

MRI were performed in most patients (N=49; 92%), with 18 cases (34%) showing positive results and 31 (58%) showing negative results. Eleven (61%) of the cases presenting positive findings showed individual subcortical gliosis changes which were not attributed pathological significance and resulted in no further examinations. Furthermore, two cases were observed with cysts without compression, one case with cerebellar and cortical atrophy, and one case with a vestibular schwannoma, also not resulting in further examinations. CSF examinations were less frequently performed (N=23; 43%), and only two cases (4%) showed positive findings, both with elevated glucose, one of them with additionally reduced albumin, protein, and IgG. None of the cases showed antibodies against NMDA-receptors and therefore did not result in further examinations. EEG was only performed in a total of 9 patients (17%). One of these patients was admitted with muscle twitching suspected to be a possible seizure, while another patient was admitted after being found unresponsive on the ground. The remaining patients who underwent EEG had no apparent symptoms or neurological findings that would suggest abnormalities on EEG but were still examined as a part of the comprehensive diagnostic package. The rest of the patients (N=44; 83%) did not undergo EEG either because there was no clinical suspicion of brain pathology or because they refused the examination.

**Table 3:** Characteristics of the clinical picture of the patient sample divided into ICD-10's F23.x subcategories

	N	Clinical picture
F23.0-23.1	7	The central feature was a polymorphic, fluctuating picture with shifting emotions. Often, there was bizarre behaviour, perplexity, and anxiety. Some of the patients in this group exhibited catatonic symptoms such as mutism. Sleep disturbances and hallucinations in multiple modalities were common. Patients often displayed aggression.
F23.2	5	The clinical picture was characterized by delusions, typically of persecutory nature. Often, there was a sense of mistrust and guarded attitude. Some of the patients exhibited first-rank symptoms.
F23.3	4	The clinical picture was dominated by delusions, primary of persecution and surveillance, some of the patients hallucinated as well.
F23.8	6	Besides psychotic symptoms, mainly delusions, all the patients simultaneously presented symptoms consistent with either elevated (3) or lowered (3) mood. Symptoms were e.g., erethism, aggressive or flirtatious behaviour, pressured speech, hyperactivity, inhibition, anxiety, and somatic delusions. The clinical pictures did not justify a diagnosis of mania or depression and appeared somewhat uncharacteristic early in the hospitalization. However, four of the patients were discharged with a diagnosis of mood disorder.
F23.9	31	The clinical picture in this group was diverse and initially somewhat uncharacteristic. Eight of the patients presented mixed symptoms with a partially polymorphic character. Perplexity and confusion were seen in most cases as well as severe aggression and bizarre behaviour. Other presenting symptoms were catatonia, visual hallucinations, disorganized speech, derealization and disturbed perception. Seven of the patients presented some degree of schizophrenia-like symptoms, e.g., disorganized speech, thought broadcasting, delusions of control, and thought withdrawal. Most of these patients had long admissions with emerging symptoms of schizophrenia, two of them discharged with a F20.x diagnosis. One died shortly after discharge. Most of these patients did not have a history of mental illness. Five patients had been exposed to stressful life events prior to admission (e.g., birth of child, moving from home, loss of near relative). Six of the patients were discharged with a diagnosis of mania or bipolar disorder.

F23.0: Acute polymorphic psychotic disorder without symptoms of schizophrenia

F23.1: Acute polymorphic psychotic disorder with symptoms of schizophrenia

F23.2: Acute schizophrenia-like psychotic disorder

F23.3: Other acute predominantly delusional psychotic disorders

F23.8: Other acute and transient psychotic disorders

F23.9: Acute and transient psychotic disorder, unspecified

## Clinical Presentation and Diagnostic Transition

### Initial Clinical Presentation

The clinical presentation of the patient sample, as outlined in Table 3, highlights a diverse symptomatology within distinct ICD-10 ATPD categories. These categories encompass a broad spectrum of symptoms including delusions, hallucinations, disorganized speech, emotional disturbances, and motor symptoms.

Among patients classified under polymorphic or unspecified diagnostic categories (F23.0, F23.1, F23.8 and F23.9), a significant proportion exhibited mood disorder symptoms, with a notable prevalence among those falling into the F23.8 and F23.9 categories. The F23.8 category demonstrated a unique presentation characterized by psychotic symptoms alongside fluctuations in mood, the latter being related to a subsequent diagnosis of mood disorders. Patients within the F23.9 category displayed diverse symptom profiles, including schizophrenia-like symptoms and mixed features, often resulting in diagnostic challenges and varied outcomes upon discharge.

### Diagnostic Changes from Admission to Discharge

Analysing the diagnostic changes from admission to discharge, as depicted in Table 4, sheds light on the dynamic nature of diagnostic processes in psychiatric care.

Approximately half of the patients experienced diagnostic revisions during their hospitalization (N=25, 47%), underscoring the complexity of psychiatric diagnoses and the need for ongoing evaluation. Transitional patterns were observed, with notable proportions of patients transitioning to schizophrenia (N=3, 6%), the broader group of schizophrenia-spectrum disorders (N=6, 13%), or affective disorders (N=13, 25%), highlighting the evolving nature of diagnostic categorizations.

## Discussion

In this study, we set out to achieve two primary objectives: 1) to investigate whether an extended evaluation program would improve the quality of the diagnostic evaluation of ATPDs, and 2) to investigate whether the initial clinical picture during admission was related to the short-term prognosis of transitioning to schizophrenia or affective disorders.

Our findings as determined through the descriptive analysis of the study sample showed that ATPDs primarily affected individuals between the ages of 18-30 (55%) and 31-50 (36%), with a slightly higher proportion of male patients diagnosed (55%). Notably, an overweight of females (2:5 ratio) received a diagnosis of acute polymorphic psychotic disorder (F23.0 and F23.1), while males (4:1 ratio) were

**Table 4:** Short-term prognosis of transitioning (%) into schizophrenia (F20.x), schizophrenia-spectrum disorders (F2x), or affective disorder (F3x) based on difference in admission diagnosis vs diagnosis at discharge

Diagnosis at admission	Total	Stable diagnosis from admission to discharge	Revised diagnosis at discharge	Transitioning (%) from each subgroup	Total transitioning (%)
F23.0-23.1	7	5	F30.2 (1) F31.2 (1)	F30.x: 14% F31.x: 14%	<b>F20.x: 6%</b> <b>F2x: 13%</b> <b>F30.x: 6%</b> <b>F31.x: 15%</b> <b>F3x: 25%</b>
F23.2	5	1	F20.0 (1) F22.0 (1) F22.9 (1) F31.9 (1)	F20.x: 20% F2x: 60% F31.x: 20%	
F23.3	4	3	F12.5 (1)		
F23.8	6	2	F31.2 (1) F31.9 (1) F32.3 (1) F33.2 (1)	F31.x: 33% F3.x: 66%	
F23.9	31	17	F12.5 (3) F19.5 (1) F20.0 (1) F20.9 (1) F22.9 (2) F30.2 (1) F30.9 (1) F31.1 (1) F31.2 (2) F31.5 (1)	F20.x: 6% F2x: 13% F30.x: 6% F31.x: 13% F3x: 19%	

F2x: Schizophrenia-spectrum disorders (F20.x, F22.x, and F25.x)

F23.0: Acute polymorphic psychotic disorder without symptoms of schizophrenia

F23.1: Acute polymorphic psychotic disorder with symptoms of schizophrenia

F23.2: Acute schizophrenia-like psychotic disorder

F23.3: Other acute predominantly delusional psychotic disorders

F23.8: Other acute and transient psychotic disorders

F23.9: Acute and transient psychotic disorder, unspecified

F30.2: Mania with psychotic symptoms

F30.9: Manic episode, unspecified

F31.1: Bipolar affective disorder, current episode manic without psychotic symptoms

F31.2: Bipolar affective disorder, current episode manic with psychotic symptoms

F31.5: Bipolar affective disorder, current episode severe depression with psychotic symptoms

F31.9: Bipolar affective disorder, unspecified

F32.3: Severe depressive episode with psychotic symptoms

F33.2: Recurrent depressive disorder, current episode severe without psychotic symptoms

more frequently diagnosed with acute schizophrenia-like disorders (F23.2). This finding agrees with prior research, underscoring the tendency for females to manifest polymorphic symptomatology<sup>16</sup> and for males to exhibit characteristics of schizophrenia-like presentations<sup>17</sup>.

The extended evaluation program included additional clinical and paraclinical assessments, such as brain MRI, urine dipstick analysis, lumbar puncture (LBP), and EEG when clinically indicated. Among those who completed these assessments, the majority showed unremarkable findings: neurological and haematological examinations were largely within normal limits, and 40% of those tested had negative urine cultures. MRI was performed in 92% of patients, with 34% showing structural abnormalities – most commonly subcortical gliosis – but none were deemed of diagnostic significance or linked to the psychotic episode. Consistent with previous systematic reviews<sup>18</sup>, structural

anomalies were occasionally detected, but rarely resulted in further clinical intervention, as the abnormalities could not be attributed to the patient’s psychotic symptoms. However, a recent systematic review<sup>19</sup> highlights that patient’s experiencing first-episode psychosis exhibit cortical thinning in areas crucial for emotional processing and higher executive functions. These morphological changes appear to escalate over time following the initial psychotic episode. The review indicates that cortical volume loss may serve as a marker for psychotic disorders; however, it does not point to a specific aetiology. Therefore, differentiating between psychotic disorders based solely on cortical volume loss remains challenging. It is, however, essential to further investigate the potential implications of the observed MRI abnormalities and their relationship with the development and prognosis of ATPDs, initially with a bigger sample size, preferably in combination with functional MRI scans.

Only 43% underwent LBP, with 2 (3%) cases showing elevated CSF glucose, again without clinical implications. No case of AIE were found.

These findings suggest that, in this patient sample, structural or infectious causes of psychosis were not evident through extended testing. However, a large proportion of patients did not undergo urine dipstick testing (47%) or urine toxicology screening (53%), limiting the ability to assess potential substance-induced psychosis. This gap likely reflects the guarded, suspicious behaviour often seen in acutely psychotic individuals, which can make compliance with invasive or perceived intrusive tests difficult. Furthermore, 30 patients (57%) did not undergo LBP. Several factors contributed to this lack of compliance with the extended evaluation programme, most notably that patients enrolled in the study did not accept to have LBP performed due to their distressed and often paranoid condition. If there are no abnormal neurological clinical findings and thus no suspicion of AIE or other serious neurological conditions, it is not possible to perform paraclinical examinations forcefully against the patients' will according to Danish legislation. Consequently, a diagnostic grey zone remains, particularly regarding unverified drug use or other undetected somatic contributors, highlighting the dual challenge of incomplete data and limited yield from extended diagnostics.

Our study's results also revealed that a substantial proportion of patients (58%) were classified under the F23.9 category, labelled as 'unspecified'. This high prevalence likely reflects the diagnostic challenges posed by a multifaceted and often uncharacterized clinical presentation in this subgroup. Patients in the F23.9 category exhibited a broad range of symptoms including perplexity, severe aggression, bizarre behaviour, visual hallucinations, disorganized speech, derealization, and catatonia. In several cases, symptoms evolved during admission, making early classification difficult. Notably, seven patients in this group demonstrated schizophrenia-like features such as thought broadcasting and delusions of control; two of them were ultimately discharged with a schizophrenia diagnosis. Additionally, six patients were discharged with affective disorder diagnoses, further underscoring the heterogeneity within this subgroup. The frequent assignment of F23.9 may thus reflect both the evolving nature of symptomatology during acute psychosis and the limitations of categorical diagnostic systems in capturing such clinical complexity at admission.

Our descriptive analysis of the prognostic value of the initial clinical picture revealed that 53% of patients maintained their initial diagnosis at discharge, while 47% had a change of diagnosis. Of particular interest is the subgroup that transitioned to affective disorders and schizophrenia. We observed that thirteen (25%) patients

transitioned to affective disorders, while three (6%) patients transitioned to schizophrenia (ICD-10: F20.x) and seven (13%) patients to schizophrenia-spectrum disorders (F20.x, F22.x and F25.x). Collecting and extracting our data showed a probable pattern suggesting that patients discharged with an affective disorder often exhibited symptoms throughout their initial hospitalization characterized by fluctuating and shifting mood, some of which exhibited either elevated or lowered mood, and a majority found within the 'unspecified' subgroups of F23.8-9. On the other hand, patients discharged with a schizophrenia diagnosis tended to have longer admission lengths, initially uncharacteristic symptoms but in time emerging schizophrenia-like symptoms throughout their hospitalization. These patients were predominantly also found within same subgroups of F23.8-9.

Based on our data, which aligns with previous research projects such as those by Castagnini et al. (2016)<sup>12</sup> and supported by subsequent findings from Rutigliano et al. (2018)<sup>20</sup> and Koparal et al. (2024)<sup>21</sup>, approximately 25% of patients initially diagnosed with ATPD were discharged with an affective disorder. These studies also reported diagnostic transitions towards mood disorders in 20-30% of cases, highlighting a recurrent pattern across cohorts. This alignment suggests a potentially identifiable subgroup within ATPD patients – particularly those with early mood instability – who may benefit from closer monitoring for affective trajectories.

The risk of transitioning to schizophrenia from the initial diagnosis has also been analysed. A clear pattern emerged among patients who presented with schizophrenia-like symptoms, categorizing them under the F23.2 subgroup, that one in five patients (20%) received a discharge diagnosis of schizophrenia (F20.x) and three out of five patients (60%) received a discharge diagnosis within what we earlier defined as schizophrenia-spectrum disorders (F20.x, F22.x, and F25.x). In contrast, only two patients from the remaining subcategories (comprising a total of 48 patients) were discharged with a diagnosis of schizophrenia. This indicated that patients initially placed in the F23.2 subgroup, characterized by persistent psychotic symptoms, persecutory delusions, mistrust, and guarded behaviour, may represent a clinical phenotype with a higher likelihood of early diagnostic transition towards schizophrenia-related outcomes.

These findings are consistent with those reported by Castagnini et al. (2016)<sup>12</sup>, who found that 12.8% of ATPD patients transitioned to schizophrenia or schizoaffective disorder within a one-year follow-up period. While our follow-up period only spans the initial hospitalization, our observed 13% transition rate to schizophrenia-spectrum disorders and 6% to schizophrenia specifically mirrors their long-term data from 2022, finding that 25% of ATPD

patients transitioned to schizophrenia-spectrum disorders over a 6.3-year period, suggesting that early diagnostic patterns, particularly those found in the F23.2 subgroup, may already signal future trajectories. However, the value of the initial clinical picture to predict transitioning to schizophrenia-spectrum disorders must be further explored in larger studies and with extended follow-up.

### Limitations of the Study

Our study faced limitations, most importantly the small sample size caused by difficulties obtaining informed consent from this acutely affected patient population. Likewise, number of screened but not included patients was not recorded. This lack of registration was due to the study being conducted as an integrated part of clinical practice. Additionally, no information was obtained about genetics or familial predisposition, which could have been relevant for assessing the potential risk of psychopathology.

Despite the limitations of the study, the results provide valuable insights into the demographic and clinical characteristics of patients with ATPDs. The inclusion of additional clinical and paraclinical tests as part of the extended evaluation program, particularly MRI, showed that there might be potential underlying organic pathology associated with ATPDs. However, further research with larger sample sizes and longitudinal follow-up is needed to validate and expand upon these findings.

Despite the comprehensive nature of the extended diagnostic evaluation program, our study did not find critical implications for diagnosis or patient management. Instead, it underscored the challenges associated with obtaining patient compliance with such extensive assessments. Our study did not contain results from the time after discharge where continued focus on the need for further diagnostic evaluation depending on the clinical picture might be relevant.

### Conclusion

Our study results highlight the clinical heterogeneity and diagnostic instability of ATPDs during initial hospitalization. While the extended diagnostic evaluation program including MRI, EEG, and CSF analysis did not yield findings of diagnostic significance in most cases, it underscored challenges in patient compliance and limited additional value of extended diagnostic evaluation as routine procedure. Nearly half (47%) of the patients experienced a diagnostic shift during admission, most often towards affective (25%) or schizophrenia-spectrum (13%) disorders. These findings suggest that early symptom profiles, particularly mood fluctuations or schizophrenia-like features, may hold short-term prognostic relevance. Future research with larger samples and longer follow-up is warranted to validate these trajectories and clarify the

role of comprehensive somatic assessment in first-episode psychosis.

### Ethical Considerations

We obtained informed written consent from the participants to register and analyse their clinical data in accordance with Danish regulation.

Approval was waived by the Ethics Committee for scientific research because they did not consider the study a biochemical research project.

Participants with a lived experience were not involved in the planning or conduct of the project.

### Funding

There was no specific funding for this study.

### Conflict of Interest

The authors report no conflicts of interest.

### References

1. WHO. ICD-10 Version:2016. [online] 2023. Available at: <https://icd.who.int/browse10/2016/en#/F20-F29> [Accessed 18 July 2023].
2. American Psychiatric Association (APA). Diagnostic and Statistical Manual of Mental Disorders: DSM-5 [online]. 5th edn. Washington, D.C.: American Psychiatric Publishing, 2013. Available at: <https://doi.org/10.1176/appi.books.9780890425596> [Accessed 31 May 2025].
3. Malhotra S, Sahoo S, Balachander S. Acute and Transient Psychotic Disorders: Newer Understanding. *Curr Psychiatry Rep*. 2019; 21(11): 113. <https://doi.org/10.1007/s11920-019-1099-8>
4. Mishra KK, Patil V, Sathe HS, et al. Clinical features and outcomes in acute psychosis: A retrospective hospital-based study in rural patients of central India. *Ind Psychiatry J*. 2023; 32(2): 297-301. doi: 10.4103/ipj.ipj\_139\_22. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10756627/>
5. Stephen A, Lui F. Brief Psychotic Disorder. In: StatPearls. [online] Treasure Island (FL): StatPearls Publishing; 2023. Available at: <http://www.ncbi.nlm.nih.gov/books/NBK539912/> [Accessed 18 July 2023].
6. Keepers GA, Fochtmann LJ, Anzia JM, et al. The American Psychiatric Association Practice Guideline for the Treatment of Patients with Schizophrenia. *Am J Psychiatry*. 2020; 177(9): 868-872. <https://doi.org/10.1176/appi.ajp.2020.177901>
7. DGPPN e.V. (ed.) for the Guideline Group. S3 Guideline for Schizophrenia. Abbreviated version (English), 2019, Version 1.0, last updated on 29 December 2019, available at: <https://www.awmf.org/leitlinien/detail/ll/038-009.html>
8. Endres D, Leypoldt F, Bechter K, et al. Autoimmune encephalitis as a differential diagnosis of schizophreniform psychosis: clinical symptomatology, pathophysiology, diagnostic approach, and therapeutic considerations. *Eur Arch Psychiatry Clin Neurosci*. 2020; 270(7): 803-818. <https://doi.org/10.1007/s00406-020-01113-2>
9. Pavál D, Gherghel-Pavál N, Căpățînă OO, et al. The Importance of Cerebrospinal Fluid Investigation in First-episode Psychosis. *Yale J Biol Med*. 2023; 96(1): 125-126. <https://doi.org/10.59249/OAMT2710>
10. Kranaster L, Koethe D, Hoyer C, et al. Cerebrospinal fluid diagnostics in first-episode schizophrenia. *Eur Arch Psychiatry Clin Neurosci*. 2011; 261(7): 529-530. <https://doi.org/10.1007/s00406-011-0193-7>

11. Castagnini A, Galeazzi GM. Acute and transient psychoses: clinical and nosological issues. *BJPsych Adv*. 2016; 22(5): 292-300. <https://doi.org/10.1192/apt.bp.115.015198>
12. Castagnini AC, Munk-Jørgensen P, Bertelsen A. Short-term course and outcome of acute and transient psychotic disorders: Differences from other types of psychosis with acute onset. *Int J Soc Psychiatry*. 2016; 62(1): 51-56. <https://doi.org/10.1177/0020764015590493>
13. Castagnini A, Foldager L, Caffo E, et al. The predictive validity and outcome of ICD-10 and DSM-5 short-lived psychotic disorders: a review and meta-analysis. *Eur Arch Psychiatry Clin Neurosci*. 2022; 272(7): 1157-1168. <https://doi.org/10.1007/s00406-021-01356-7>
14. Queirazza F, Semple DM, Lawrie SM. Transition to schizophrenia in acute and transient psychotic disorders. *Br J Psychiatry*. 2014; 204: 299-305. <https://doi.org/10.1192/bjp.bp.113.127340>
15. Castagnini AC, Fusar-Poli P. Diagnostic validity of ICD-10 acute and transient psychotic disorders and DSM-5 brief psychotic disorder. *Eur Psychiatry*. 2017; 45: 104-113. <https://doi.org/10.1016/j.eurpsy.2017.05.028>
16. Castagnini A, Foldager L, Berrios GE. Acute Polymorphic Psychotic Disorder: Concepts, Empirical Findings, and Challenges for ICD-11. *J Nerv Ment Dis*. 2018; 206(11). <https://doi.org/10.1097/NMD.0000000000000882>
17. Castagnini A, Foldager L. Epidemiology, course and outcome of acute polymorphic psychotic disorder: implications for ICD-11. *Psychopathology*. 2014; 47(3): 202-206. <https://doi.org/10.1159/000357784>
18. Forbes M, Stefler D, Velakoulis D, et al. The clinical utility of structural neuroimaging in first-episode psychosis: A systematic review. *Aust N Z J Psychiatry*. 2019; 53(11): 1093-1104. <https://doi.org/10.1177/0004867419848035>
19. Matéos M, Hanafi R, Mathys L, et al. Advanced imaging in first episode psychosis: a systematic review. *J Neuroradiol*. 2023; 50(5): 464-469. <https://doi.org/10.1016/j.neurad.2023.04.001>
20. Rutigliano G, Merlotti E, Pelosi A, et al. Long-term outcomes of acute and transient psychotic disorders: the missed opportunity of preventive interventions. *Eur Psychiatry*. 2018; 50: 1-7. <https://pubmed.ncbi.nlm.nih.gov/29787962/>
21. Koparal B, Onur E, Demirci U, et al. Diagnostic stability of acute and transient psychotic disorder: a 5-year retrospective cohort study. *Düşünen Adam: The Journal of Psychiatry and Neurological Sciences*. 2024; 37(1): 17-25. <https://dusunenadamdergisi.org/storage/upload/pdfs/1734519115-en.pdf>