



A narrative review of intervention in first-episode affective psychoses

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ABSTRACT

While first-episode schizophrenia has received extensive attention in the literature, few studies have focused on the first episode of affective psychoses. Considering the lack of structured data regarding this diagnostic grouping commonly used in clinical settings, our aim was to scope the literature on first-episode affective psychoses to consolidate current knowledge and to identify areas to be targeted in future studies. We also planned to investigate the relevance of the “affective psychosis” concept regarding diagnostic categories and specific needs of intervention. We conducted a search on the Embase, Medline, PubMed, PsycINFO and Web Of Science databases until October 2020. We selected studies and synthesized the key findings into a narrative review regarding major topics of early intervention research: diagnostic categorization, premorbid factors, intervention, duration of untreated illness, neurobiology and neurocognition. After screening 961 titles and abstracts and 193 full-text papers, we selected 77 studies for inclusion. Our results showed heterogeneity in diagnosis-related grouping under the concept of affective psychoses, especially variability regarding the inclusion of schizoaffective disorder. Nonetheless, this concept still encompasses patients with different psychopathological and neurocognitive profiles from the non-affective patients requiring specialized intervention. This study thus provided support for the relevance of this concept as well as a need for further investigation.

1. Introduction

Early intervention in psychosis offers opportunities to improve care during the critical phase of the first few years of illness to prevent a chronic course of the disorder (Conus and McGorry, 2002). While schizophrenia spectrum disorders have received extensive attention, affective psychoses remain a neglected area of research (Berk, 2007; Chia et al., 2019; Conus et al., 2010; Conus and McGorry, 2002). Affective psychoses encompass patients who, in addition to psychotic symptoms, have a mood syndrome. This group of psychoses includes two forms of the affective disorders DSM-5 diagnostic category (major depression with psychotic symptoms and bipolar disorder with psychotic symptoms), and depending on authors also includes schizoaffective disorder, which is a mixed form between schizophrenia and bipolar disorder (Lambert et al., 2003; Malhi et al., 2008; Proctor et al., 2004; Strakowski et al., 1998), which is classified in the schizophrenia spectrum and other psychotic disorders category (American Psychiatric Association, 2013). Indeed, the large spectrum of psychotic and affective disorders overlaps when affective psychoses are concerned reflecting the dimensional nature of the disorders rather than innate and distinct

diagnostic categories (Lambert et al., 2003; Malhi et al., 2008; Proctor et al., 2004; Strakowski et al., 1998). First-episode affective psychosis thus includes patients who in addition to the onset of psychosis revealed manic, depressive, or mixed form of mood disturbance. While largely neglected in the literature, affective psychoses represent an important proportion (~30%) of the diagnoses in first-episode psychosis programs (Proctor et al., 2004), and there is a considerable risk of relapse and poor outcome if not treated adequately (Berk, 2007; Conus and McGorry, 2002; Strakowski et al., 1998).

Early intervention in affective psychoses is especially challenging considering that despite a good syndromic recovery, symptomatic and functional recoveries remain poor (Conus et al., 2006b; Strakowski et al., 1998). Furthermore, previous literature reported that patients combining mood disturbance with psychosis are at high risk of suicidal behaviour, non-adherence to treatment as well as substance abuse and may also have comorbidity leading to poor prognosis without adapted treatment (Berk, 2007; Conus et al., 2006a,b; Conus and McGorry, 2002; Smith et al., 2014; Strakowski et al., 2000; Zarate and Tohen, 2000). The common overlap between mood and psychotic symptoms in schizophrenia spectrum disorders (~30% depression; Majadas et al., 2012),

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bipolar disorder (~58% experience at least one psychotic symptom; Goodwin and Jamison, 2007), and major depressive disorder (~15% psychotic features; Johnson et al., 1991) should also urge the development of early intervention for such sensitive population. Despite these challenging issues, the early phase of affective psychoses remains understudied (Chia et al., 2019; Conus and McGorry, 2002). Moreover, affective psychoses are often included in larger studies on first-episode, failing to provide guidelines and intervention packages adapted to the specific needs of these patients (Chia et al., 2019; Marwaha et al., 2018). In addition, much of the available data on this sub-group of disorders has often focused on specific symptomatic phases, mainly first-episode mania (Chang et al., 2016; Conus and McGorry, 2002; Strakowski et al., 1996; Tohen et al., 2000a,b), and very few studies have explored the larger domain of First-Episode Affective Psychoses (FEAP).

A review of early intervention in FEAP would enable to synthesize our current scientific knowledge on this topic to fill an important research gap. Moreover, it would enable to point out the potential specific treatment needs and challenges of intervention in first-episode affective psychosis to better inform clinical practice but also to highlight issues that has to be investigated in further studies. Thus, it may be a useful study to ultimately improve outcomes for people with FEAP. In light of this, we conducted a narrative review of the literature on early intervention in FEAP. In this narrative review, we selected and synthesized the main findings of the literature on early intervention in FEAP regarding what we consider as major topics of early intervention research: 1) diagnostic categorization, 2) premorbid factors, 3) intervention, outcomes, 4) duration of untreated illness, 5) neurobiology and neurocognition.

2. Method

2.1. Data sources and search strategy

A literature search based on an exhaustive search strategy (Bramer et al., 2018) was performed in five bibliographic databases (June 2019, updated in October 2020): Embase.com, Medline Ovid SP, PubMed (not Medline), PsycINFO Ovid SP and Web Of Science. This search strategy was developed to screen most of the studies available to provide a representative review of the literature on early intervention in FEAP. The search strategies were developed in collaboration with a librarian. They were adapted to the syntax and subject headings of each database and performed without date restrictions. For the full search strategy, see appendix 1.

2.2. Study selection

We screened all studies on FEAP based on predefined inclusion criteria: (1) "Affective psychoses" including schizoaffective disorder, bipolar disorder with psychosis and major depressive disorder with psychosis; (2) first-episode psychosis including patients who met the psychosis threshold criteria for the first time; (3) early intervention including any kind of psychiatric or psychological intervention. Exclusion criteria were (1) non-affective psychosis including schizophrenia, schizophreniform disorders (2) intoxication or organic brain disease psychotic disorder (3) first-episode affective disorders without psychotic features (4) early intervention for other disorders. In the first screening on abstracts, key words, and titles, we selected studies mentioning the first episode or early intervention without specification and at least one of the affective psychoses previously mentioned. Studies on schizotypy, high-risk populations, or prodromal periods were excluded, as were studies on first-episode schizophrenia. Then, the full texts of all potentially eligible studies were reviewed. In the selection based on the full text, we removed conference abstracts and book sections to ensure that the content was a direct source of study and had been reviewed by experts. We also removed the remaining studies not mentioning results regarding affective psychoses and the first episode. One expert reviewer

in the field performed every step in the selection process and handpicked additional papers that were relevant to the subject. We only included studies in English and French.

3. Results

The screening of the electronic databases identified 961 eligible papers. Thirteen additional papers from other sources were added. Of these, 77 articles met the final criteria for inclusion after the screening and selection process (Fig. 1). We organized the results by themes that emerged from the selected papers.

3.1. Justifications for specific early intervention and challenges (Table 1)

Early intervention in FEAP seems particularly important since the delay until the introduction of an appropriate treatment after the onset and the number of manic episodes are associated with greater risk of relapse, severe cognitive deficits, and worse general outcome (Conus and McGorry, 2002). However, although some clinical cues of the very early phase of mania have been identified, the challenge in establishing early intervention strategies remains complex since no clear consensus has been established to identify the actual onset of illness (Conus, 2010). Furthermore, the identification of affective psychoses is difficult, especially bipolar disorder with insidious or depressive onset. In addition, the high prevalence of atypical features of mania during adolescence or early adulthood (with a higher prevalence of irritability rather than euphoria, for example) leads to a broad differential diagnosis with schizophrenia, personality disorders or behavioural disorders (Berk, 2007; Conus et al., 2010).

Once identified, the treatment itself is challenging as well, considering difficulties in engaging patients and the high prevalence of suicidal behaviour, comorbid substance misuse and relapses (Berk, 2007), as well as potential difficulty in parenting (Craig and Bromet, 2004).

3.2. Diagnostic categorization (Table 2)

3.2.1. Diagnostic issues

In 1997 in the UK, clinicians developed an observational database of an unselected population with first-episode psychosis (Proctor et al., 2004). They found an annual incidence for affective psychoses of 8.43 per 100 000 population per year, psychotic depression (19%) being the most common of these diagnoses (Proctor et al., 2004). These results highlighted the importance of affective psychoses within a cohort of first-episode psychosis. However, diagnosis is difficult to establish in first-episode patients (Radmanović, 2012) and may change within the first years (Pedrós et al., 2009) due to the emergence of mood episodes. For example, in this latter study, an initial diagnosis of schizophreniform and not otherwise specified psychotic disorders could evolve towards schizophrenia or affective psychoses over time, and none of the socio-demographic and clinical variables were significantly predictive of this evolution. Arrasate et al. (2014) suggested that affective dimensions play an important role in these diagnostic issues. Indeed, while activation dimensions predicted a diagnosis of bipolar disorder, early misdiagnosis was predicted by the presence of a depressive dimension but not by a manic dimension. To accurately differentiate psychotic disorders, Salvatore et al. (2007) suggested using psychopathological features at onset. They found four subtypes of patients including mania with psychosis (I), mixed depressive-agitated state (II), excited-hallucinatory-delusional state (III), and disorganized-catatonic-autistic state (IV). Subtypes I and III were associated with mania, II with major depression or bipolar mixed state, and IV with major depression but negatively associated with mania.

Despite these diagnostic issues, Subramaniam et al. (2007) found that schizophrenia and affective psychoses were the most stable diagnoses. This result is in line with Coentre et al. (2011), who reported no cross-diagnosis between bipolar disorder and schizophrenia or schizophreniform disorder (schizophrenia criteria for more than a month but

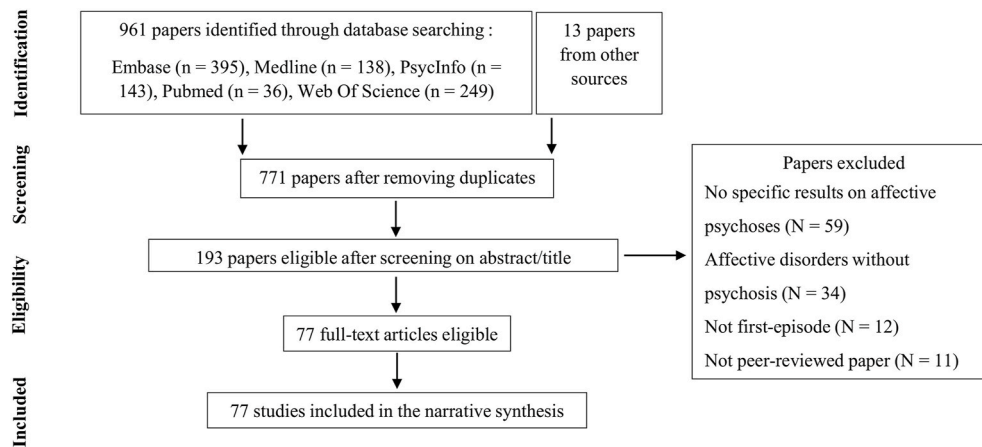


Fig. 1. Flow diagram of the process of study selection for the review.

Table 1
Summary of results on justifications for specific early intervention and challenges in first-episode affective psychoses.

Study	Method	Country	Population (N; age)	Follow-up	Key findings
Berk (2007)	Review		Bipolar disorder		<ul style="list-style-type: none"> specific challenges AP: psychotic symptoms, poor insight and rapid relapses associated with non-adherence to medication, high comorbidity with substance misuse, high risk of suicide and the impact of illness on the family the bipolar disorder onset is often insidious starting with depression atypical features of mania during adolescence or early adulthood clinical cues of mania: irritability, increase of energy, flight of thoughts, euphoria no consensus to identify the onset of illness 60% of adolescents with a first episode of mania would also have psychotic symptoms
Conus et al. (2010)	Review		Bipolar disorder		<ul style="list-style-type: none"> positive symptoms (self-recognition disorder), supposed to be specific to schizophrenia, can also be present in bipolar disorder anomalous self-experience specific to schizophrenia key manic features in first episode psychosis (irritability and increase of energy) have to be carefully differentiated from elements of behavioral disorders
Conus and McGorry (2002)	Review		First-episode mania		<ul style="list-style-type: none"> symptomatic recovery AP > NAP 40% of patients with first manic episode experience functional recovery at 24 months worse outcomes in patients with mixed episode the delay until the introduction of an appropriate treatment after the onset and the number of manic episodes associated with greater risk of disruptive effects such as relapse, severe cognitive deficits and worse general outcome earlier onset of bipolar disorder associated with greater risk of psychotic features and greater severity of symptoms, worse outcomes and more comorbidities
Craig and Bromet (2004)	Descriptive study	USA	First-admission psychosis (N = 453; 15–60 years)	24 months	<ul style="list-style-type: none"> at the entry, nearly half of females with mood disorders were parents and 29.1% of females with schizophrenia/schizoaffective the highest lifetime substance use disorder rates for mothers in the bipolar disorder group (41.9%), 37% in the major depression group 75% of fathers with bipolar disorders, and 50% with major depressive disorder lived with children at the entrance, only 5–15% of parents lived with their children at 6 months follow-up postpartum psychosis is not more frequent AP than in NAP frequent thoughts of harm regarding child requiring close attention after childbirth

Note. *AP = Affective psychoses; NAP = Non-Affective psychoses.

less than 6 months) in classifications, suggesting a good practical use of classifications in the diagnostic process. It is important to note that while assessment by a specialized professional team may ensure high diagnostic stability, a differential diagnosis between bipolar and schizoaffective disorders requires longitudinal follow-up (Schimmelmann et al., 2005; Schottle et al., 2012).

3.2.2. Differentiation between affective and non-affective psychoses

In general, presenting an affective psychosis rather than schizophrenia predicts better clinical and functional outcomes, and patients with first-episode mania may be more likely to achieve functional remission than first-episode with schizophrenia (Chang et al., 2016; Henry et al., 2010). However, contact with care usually occurs later in

adolescents with affective psychoses than those with schizophrenia (Emck et al., 2001). Other inter-group differences were reported, for example, adolescents with affective psychoses were more likely to be females and to have manic symptoms (Emck et al., 2001). They reported no differences regarding premorbid functioning and depressive symptoms. In another prospective study including both adolescents and young adults, Harris et al. (2005) found that the affective psychosis group was younger, included more females and had better psychosocial functioning than the non-affective psychosis group. Although patients with affective psychosis may recover more rapidly, they were significantly impaired overall.

Furthermore, some studies specifically differentiated subgroups of affective psychoses from other psychotic disorders. Macmillan et al.

Table 2
Summary of results on diagnostic categorization in first-episode affective psychoses.

Study	Method	Country	Population (N; age)	Follow-up	Key findings
Diagnostic issues					
Arrasate et al. (2014)	Prospective study	Spain	First-episode psychosis (N = 112; Mean age = 28.8)	5 years	<ul style="list-style-type: none"> mood dimensions, a good diagnostic tool to differentiate affective from non-affective psychoses patients with bipolar disorder scored higher on manic symptoms both at baseline and at follow-up activation dimension predicted a bipolar disorder at follow-up absence of manic and presence of depressive symptoms predicted early misdiagnosis
Coentre et al. (2011)	Restrospective study	England	First-episode psychosis (N = 148; 25.5)	24 months	<ul style="list-style-type: none"> no cross-diagnosis between bipolar disorders and schizophrenia/schizophreniform disorders confirming the existence of two distinct entities the highest agreement between classifications in affective disorders, namely in major depressive disorders with psychotic features no difference between classifications for rating psychotic depression, mania/bipolar disorder with psychosis
Schimmelmann et al. (2005)	Prospective study	Australia	First-episode psychosis (N = 492; Mean age = 22.0)	18 months	<ul style="list-style-type: none"> Schizophrenia, schizoaffective disorder, bipolar disorder were the most stable diagnoses, schizophreniform disorder were the least stable High diagnostic stability with assessment of patient and family by a specialized team Longitudinal follow-up necessary especially for diagnoses such as schizophreniform disorder and bipolar disorder
Subramaniam et al. (2007)	Prospective study	Singapore	First-episode psychosis (N = 154; 18–41 years)	24 months	<ul style="list-style-type: none"> schizophrenia and affective psychoses were the most stable diagnosis a shorter DUP predicted a diagnostic change at follow-up
Pedrós et al. (2009)	Prospective study	Spain	First-admission with acute psychosis (N = 48; Mean age = 28.1)	24 months	<ul style="list-style-type: none"> diagnosis difficult to establish in first episode patients, may change within the first years a diagnosis of schizophreniform and not otherwise specified psychotic disorders predicted an evolution toward schizophrenia and affective psychoses none of the sociodemographic and clinical variables predicted the diagnostic evolution
Proctor et al. (2004)	Epidemiological study	England	First-episode psychosis (N = 227; ≥15 years)		<ul style="list-style-type: none"> the commonest diagnoses were psychotic depression (19%) paranoid schizophrenia (11%), persistent delusional disorder (7%) and bipolar affective disorder (7.5%) annual incidence for affective psychoses of 8.43 per 100 000 population per year
Radmanović (2012)	Review		First-episode psychosis (children & adolescents)		<ul style="list-style-type: none"> distinguishing schizophrenia and bipolar disorder in psychotic adolescents is a key diagnostic issue
Schottle et al. (2012)	Epidemiological study	Australia	First-episode psychotic mania (N = 134; Mean age = 22.3)	18 months	<ul style="list-style-type: none"> schizoaffective disorder associated with longer DUP, higher illness severity and non-adherence rate at baseline, more traumatic events than bipolar disorder at follow-up, patients with bipolar disorder had better social functioning, less illness severity, more likely to achieve remission in positive symptoms, and to be employed than those with schizoaffective disorder
Affective and non-affective distinctions					
Chang et al. (2016)	Prospective study	China	First-episode mania with psychotic features and schizophrenia (N = 420; 15–25 years)	3 years	<ul style="list-style-type: none"> patients with first episode mania were younger, more likely to be hospitalized, had shorter DUP, had more severe positive symptoms and lower functioning at baseline compared to first episode schizophrenia at follow-up, patients with first episode mania, had milder positive symptom severity, higher rates of sustained employment, better functioning and functional remission than patients with first episode schizophrenia first episode of psychotic mania rather than schizophrenia predicted better clinical and functional outcomes
Emck et al. (2001)	Retrospective study	Netherlands	Early psychosis (N = 129; 12–18 years)		<ul style="list-style-type: none"> shorter DUP in adolescents with affective vs non-affective psychoses adolescents with schizophrenia have treatment contact 2 months before the onset of prodromal symptoms whereas it takes place 8 months after in affective psychoses adolescents with non-affective psychoses were more likely to be boys, had more adjustment problems at school, had more frequently drug use, as well as positive and negative symptoms no difference between groups regarding depressive symptoms but manic symptoms were more frequent in affective psychoses adolescents with affective psychoses were more likely to be girls no difference between groups on premorbid functioning
Harris et al. (2005)	Restrospective study	Australia	First-episode psychosis (N = 94; 13–25 years)		<ul style="list-style-type: none"> “mood disorder” psychosis group was younger, included more females, had a better psychosocial functioning than “schizophrenia” and “mixed” psychosis

(continued on next page)

Table 2 (continued)

Study	Method	Country	Population (N; age)	Follow-up	Key findings
Kapila et al. (2019)	Prospective study	England	First-episode psychosis (N = 1014; 18–35 years)	12 months	<ul style="list-style-type: none"> atypical antipsychotics were similarly used across groups but the “mood disorder” group more likely to be prescribed mood stabilizers and to be polymedicated patients with “mood disorder” psychosis may recover more rapidly but significantly impaired overall patients with manic psychosis were younger, had shorter DUP, higher level of education, compared to both depressive and schizophrenia-spectrum psychoses patients with manic psychosis had more manic symptoms, lower positive and negative symptoms at presentation than both depressive and schizophrenia-spectrum psychoses patients with depressive psychosis were older, had lower positive symptoms at baseline and were more likely to be white
Macmillan et al. (2007)	Prospective study	England	First-episode bipolar psychoses (N = 78; 14–35 years)	12 months	<ul style="list-style-type: none"> bipolar psychoses had lower level of negative symptoms, better quality of life and functioning at 3–6 months and at follow-up than other psychoses
Selvendra et al. (2014)	Descriptive study	Australia	First-episode psychosis (N = 164; 16–65 years)		<ul style="list-style-type: none"> higher proportion of depression with psychotic features in older onset patients (over 40 years), higher rates of metabolic issues (diabetes, cholesterol, lipids, weight gain) and longer DUP than other psychoses a majority of females in patients with depression with psychotic features
Sim et al. (2007)	Prospective study	Singapore	First-episode schizophrenia and schizoaffective disorder (N = 278; 18–40 years)	24 months	<ul style="list-style-type: none"> schizoaffective disorder was associated with a higher level of education, a better employment status, a shorter DUP, higher scores on general psychopathology than schizophrenia a shorter DUP was associated with better subjective quality of life.

Note. *DUP = Duration of Untreated Psychosis.

(2007) indicated that bipolar psychoses can be distinguished from other psychotic disorders based on a lower level of negative symptoms at the one-year follow-up. Kapila et al. (2019) reported that patients with manic psychosis were younger and had shorter Duration of Untreated Psychosis (DUP) compared to both depressive and schizophrenia-spectrum psychoses. They also found that they had a higher level of education and more manic symptoms but fewer positive and negative symptoms at presentation. Additionally, patients with schizoaffective disorder differed from those with schizophrenia by higher levels of education, better employment status, and shorter DUP but higher scores on general psychopathology (Sim et al., 2007). Finally, patients with depression with psychotic features were more likely to have metabolic issues and a longer DUP than those with other psychotic disorders (Selvendra et al., 2014). Depression with psychotic features may be more frequent in older-onset patients and females (Macmillan et al., 2007). Kapila et al. (2019) also reported that these patients, compared to those with manic and schizophrenia-spectrum psychosis, were older, had lower positive symptoms at baseline and were more likely to be white.

3.3. Premorbid factors (Table 3)

Regarding socio-demographic information, premorbid characteristics seem to differ between affective and non-affective psychoses. While non-affective psychosis occurred more often in economically deprived, isolated places with less racial/ethnic diversity, affective psychoses were more likely to occur in neighbourhoods with lower intragroup racial/ethnic density and higher intragroup racial/ethnic fragmentation (Richardson et al., 2018). Otherwise, affective psychoses were associated with more stable social support (DeVylder and Gearing, 2013) and with shorter help-seeking delays than non-affective psychoses (O’Callaghan et al., 2010). Among those with affective psychoses, premorbid characteristics may also depend on gender. Indeed, Cotton et al. (2013) reported that females were more likely to have experienced sexual abuse, while men were more likely to have experienced forensic issues, as well as antecedents of drug abuse (Strakowski et al., 1996).

Certain issues are highly prevalent in the history of patients with

affective psychoses and may affect the course of illness. Firstly, the prevalence of past traumatic events experienced directly and personally was very high (48%) in first-episode psychotic mania (Daglas et al., 2014). Most patients had been exposed to stressful life events during childhood or adolescence (Conus et al., 2010). A history of direct personal trauma was associated with poorer social and occupational functioning, as well as higher levels of manic, depressive and general symptoms at follow-up (Daglas et al., 2014). Although the experience of psychosis in itself can be an opportunity for growth, it is another important traumatic issue (Dunkley et al., 2007). Secondly, past substance abuse is widespread in first-episode affective psychoses and may influence the onset of illness and the time to hospitalisation (Strakowski et al., 1996). Indeed, antecedents of both alcohol and drug abuse, relative to their absence, were associated with more manic symptoms and more rapid hospitalisation in bipolar disorder (Strakowski et al., 1996). Patients with a history of alcohol abuse had a later onset than those without any past drug abuse.

3.4. Intervention (Table 4)

3.4.1. Pharmacological treatment

There are few guidelines for the treatment of first-episode mania (Power, 2015). Treatment in first-episode mania leads to full remission of the manic syndrome in most cases, but it may take longer for males, younger patients or those with psychotic features or a longer duration of untreated mania (Power, 2015). Available recommendations for the treatment of first-episode mania are similar in children and adults according to Power (2015) but with poor response rates in children. There is a stronger evidence base for the use of atypical antipsychotics than lithium in children and adolescents. Furthermore, combination therapies are more effective for severe presentations (Power, 2015). Pharmacological treatment in first-episode affective psychoses also depends on the type of episode (Douki et al., 1999). Lambert, Conus, Lambert, and McGorry (2003) recommended treating psychotic and affective syndromes as two dimensions using an accurate assessment of both. However, antipsychotics can be used as adjunctive treatment for FEAP regardless of manic or depressive aspects. Benzodiazepines can help

Table 3
Summary of results on premorbid factors in first-episode affective psychoses.

Study	Method	Country	Population (N; age)	Follow-up	Key findings
Socio-economic factors					
Cotton et al. (2013)	Prospective study	Australia	First-episode psychotic mania (N = 118; Mean age = 22.4)	18 months	<ul style="list-style-type: none"> males were more likely to have past history of substance use and forensic issues females were more likely to have experienced sexual abuse at service entry, males had more substance use issues (cannabis) but were more likely to stop substance use during treatment than females. Males had also a more severe form of illness and poorer functioning at follow-up, men were more likely to live with their families and there were no gender differences regarding psychopathology or functioning bipolar disorder and manic symptoms associated with more stable social support
DeVylder and Gearing (2013)	Retrospective study	Canada	First-episode psychosis adolescents (N = 84; Mean age = 14.7)		
O'Callaghan et al. (2010)	Retrospective study	Ireland	First-episode psychosis (N = 142; 16–65 years)	18 months	<ul style="list-style-type: none"> AP associated with shorter help-seeking delays both in the prodromal and psychotic phases than NAP
Richardson et al. (2018)	Epidemiological study	England	First-episode psychosis (N = 631; Mean age = 23.8)		<ul style="list-style-type: none"> reduced risk of AP associated with higher intragroup racial/ethnic density and lower intragroup racial/ethnic fragmentation.
Trauma					
Conus et al. (2010)	Prospective study	Australia	First-episode psychotic mania (N = 118; Mean age = 22.4)	18 months	<ul style="list-style-type: none"> 80% first-episode psychotic mania experienced stressful life events during childhood or adolescence 24.9% of sexual or physical abuse history, and 29.8% of females sexually abused Patients sexually or physical abused had poorer functioning and higher rates of forensic history, more likely to disengage from treatment and less likely to live with their family history of sexual or physical history was not associated with poorer symptomatic or functional outcome
Daglas et al. (2014)	Prospective study	Australia	First-episode psychotic mania (N = 65; Mean age = 21.60)	12 months	<ul style="list-style-type: none"> very high prevalence (48%) of past traumatic events experienced directly and personally no difference on global functioning at discharge patients with past history of direct-personal trauma had poorer social and occupational functioning, higher levels of manic, depressive and general symptoms at follow-up
Dunkley et al. (2007)	Qualitative study	Australia	First-episode psychosis (Bipolar I disorder) (N = 2; 22 and 25 years)		<ul style="list-style-type: none"> the experience of psychosis, treatment, symptoms, loss of control, powerlessness, the impact on relationships and insight on illness are traumatic the experience of psychosis can be an opportunity of growth regarding appreciation of life, deeper relating to others, enhanced perceptions of personal strength, and creation of new opportunities
Substance abuse					
Strakowski et al. (1996)	Retrospective study	USA	First-episode psychotic mania (N = 59; Mean age = 25)		<ul style="list-style-type: none"> past alcohol abuse was associated with later onset than those without any drug abuse both antecedent of alcohol and drug abuse were associated with more manic symptoms and more rapid hospitalization than those without any substance abuse antecedents men were more likely than females to have an antecedent of drug abuse

Note. *AP = Affective psychoses; NAP = Non-Affective psychoses.

with behavioural disturbances, agitation and insomnia. If psychotic symptoms persist, it is recommended to first switch to another atypical antipsychotic and continue with the mood stabilizer.

Furthermore, Conus, Berk, and McGorry (2006) concluded that mood stabilizers, in contrast to antipsychotics, were often not prescribed in first-episode mania with psychotic features. They also highlighted poor treatment adherence in first-episode mania. Moreover, although atypical antipsychotics constitute a promising alternative to typical neuroleptics in acute mania, their prescription requires high awareness regarding side effects. Salvatore, Drevets, Henter, Zarate, and Manji (2008b) reported that both valproate and olanzapine are efficient pharmacological strategies in FEAP. Finally, Conus et al. (2015) showed that olanzapine and combined chlorpromazine and lithium had similar safety profiles, although olanzapine showed a higher rate and earlier occurrence of mania remission.

Recently, Chia and colleagues' (2019) manuscript, in addition to mentioning a lack of specific guidelines for first-episode mania patients, summarized current knowledge. It put forward that (a) a combination of mood stabilizers and atypical antipsychotics should be used, (b) past occurrences of manic or hypomanic episodes should always be investigated in first-episode depression patients, (c) lithium acts as a first-line mood stabilizer, followed by valproate as second-line treatment, and (d)

risperidone, quetiapine, ziprasidone, and aripiprazole are the recommended atypical antipsychotic medications. They also mentioned the absence of recommendations regarding the duration of maintenance treatment. As maintenance treatment in first-episode mania, Jauhar et al. (2019) recommended lithium but raised concerns regarding tolerability and adherence.

3.4.2. Psychosocial interventions

Psychosocial interventions are essential to reduce residual symptoms, prevent recurrence of mood episodes, improve psychosocial functioning, and to sustain remission in first-episode mania (McMurrich et al., 2012; Power, 2015). The development of a clear care package of early intervention and further professional training on the identification and management of FEAP are required (Marwaha et al., 2018). It is also necessary to develop psychoeducation and psychological interventions targeting engagement, the development of insight, adherence to treatment, comorbidities such as substance abuse, social phobia, self-esteem, and vocational recovery strategies that take into account the effect of illness on age-appropriate developmental tasks (Douki et al., 1999). Therefore, previous studies explored the implementation of psychosocial interventions.

Macneil et al. (2012) tested a manualized psychological

Table 4
Summary of results on intervention in first-episode affective psychoses.

Study	Method	Country	Population (N; age)	Follow-up	Key findings
Pharmacological treatment					
Chia et al. (2019)	Review		Bipolar disorder		<ul style="list-style-type: none"> • A lack of differentiation first vs multiple episodes in guidelines • For a first episode psychotic mania or depression, a combination of mood stabilizers and atypical antipsychotics is the first-line treatment • Past manic or hypomanic episodes should be explored in case of a first episode depression • The first-line mood stabilizer is lithium carbonate, sodium valproate the second-line • Second generation antipsychotics recommended are risperidone, quetiapine, ziprasidone, and aripiprazole • In case of inadequate response, switching to another second-generation antipsychotic and optimizing psychosocial intervention
Conus et al. (2006a)	Review		Bipolar disorder		<ul style="list-style-type: none"> • A lack of guidelines regarding the duration and dose of maintenance treatment • mood stabilizers often not prescribed in first-episode mania with psychotic features contrary to antipsychotics • treatment with mood stabilizers is stopped very early and treatment adherence is poor in first-episode mania • characterizing mania and depression leading to bipolar disorders to reduce delay before introducing appropriate treatment atypical antipsychotics, a promising alternative to typical neuroleptics in acute mania, but their prescription requires awareness regarding side effects (extra-pyramidal syndromes, tardive dyskinesia)
Conus et al. (2015)	RCT	Australia	First-episode psychotic mania (N = 74; Mean age = 21.5)	8 weeks	<ul style="list-style-type: none"> • similar safety profile of olanzapine and chlorpromazine plus lithium • higher rate and earlier occurrence of mania remission with olanzapine
Daglas et al. (2016)	RCT	Australia	First-episode mania (N = 34; Mean age = 21.41)	12 months	<ul style="list-style-type: none"> • for most cognitive domains, similar effects of treatment with lithium vs quetiapine • better improvement in phonemic fluency when participants were treated with lithium vs quetiapine
Douki et al. (1999)	Review		First-episode psychosis		<ul style="list-style-type: none"> • a manic episode can be treated with both mood stabilizers and antipsychotics or with antipsychotics • a depressive episode can be treated with both antidepressants and antipsychotics
Jauhar et al. (2019)	Review		First-episode mania		<ul style="list-style-type: none"> • pharmacological treatment for acute mania should consider recommendations for established illness • lithium may be the gold standard treatment for maintenance treatment • for individuals with concerns regarding adherence and tolerability with lithium, low-dose antipsychotics may be more tolerable with less propensity for weight gain • maintenance treatment should be based on natural course of illness considering previous mood symptoms, and taking into account variability in efficacy of antipsychotic medication as maintenance treatment
Lambert et al. (2003)	Review		First-episode psychosis		<ul style="list-style-type: none"> • treating psychotic and affective syndromes as two dimensions with accurate assessment of both, subtyping regarding the course and psychosocial features • antipsychotics the most commonly prescribed adjunctive treatment in FEAP which can be introduced regardless of manic or depressive aspect • Benzodiazepines added for behavioral disturbances, agitation and insomnia • for long-term treatment, antipsychotic treatment should be discontinued for 6–8 weeks until the full remission of the affective syndrome in bipolar disorder, a schizoaffective disorder should be treated with a combination of mood stabilizer and atypical antipsychotic • if psychotic symptoms persist, first switch to another atypical antipsychotic and continue with the mood stabilizer
Power (2015)	Review		Bipolar disorder		<ul style="list-style-type: none"> • treatment in first-episode mania lead to full remission in 6 weeks in 50% of cases, take longer for males, younger patients or those with psychotic features or a longer duration of untreated mania • patients with adult onset had achieved remission by 1 year in 90% of cases, adolescents in 85% of cases • lithium, valproate or atypical antipsychotic remain the first line of treatment • phase-specific pharmacological treatment would be useful • combination therapy is more efficacious for severe presentation • similar treatment in children and adults, but poor response rates in children • in children and adolescents, atypical antipsychotics have a stronger evidence base than lithium. Lamotrogine is not recommended (risk of fatal skin rashes), little evidence in favor of valproate or carbamazepine, risperidone is approved for a brief use with greater safety concerns
Salvadore et al. (2008b)	Review		Bipolar disorder		<ul style="list-style-type: none"> • Valproate (mood stabilizer) and olanzapine (atypical antipsychotic) efficient pharmacological strategy and commonly used in first-episode AP
Zarate and Tohen (2000)	Prospective study	USA	First-episode psychosis (N = 158; Mean age = 30.6)	6 months	<ul style="list-style-type: none"> • Lower antipsychotic medication exposure in manic patients than in nonaffective psychotic patients at follow-up • Manic patients more likely to be treated with mood stabilizer than nonaffective psychotic patients • Manic patients more likely to receive lower doses of antipsychotics at discharge, at follow-up than the nonaffective group, and if recovered

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Table 4 (continued)

Study	Method	Country	Population (N; age)	Follow-up	Key findings
Psychosocial interventions					<ul style="list-style-type: none"> • No difference between groups regarding the frequency of antipsychotic medication use • necessary to develop psycho-education and psychological interventions targeting engagement, development of insight, adherence to treatment, comorbidities (substance abuse), social phobia, self-esteem, vocational recovery strategies and that would consider the effect of illness on age-appropriate developmental tasks • the manualized psychological intervention for bipolar disorder had a significant effect on depressive and general symptoms but not on manic symptoms, improved significantly social and occupational functioning after 18 months, no significant effect regarding number or type of relapses • sufficient knowledge about AP • the development of clear package in early intervention of AP and more training required • Important to establish a good therapeutic alliance for treatment adherence and psychoeducation for patients and their relatives • observance is one main challenge considering the severity of a first episode requiring biotherapy, and the young addict population affected • psychosocial interventions reduce residual symptoms, prevent recurrence from mood episodes, improve psychosocial functioning • pharmacotherapy showed good results for acute episodes but not for sustained remission • mindfulness-based intervention may improve symptomatology, functioning, emotion regulation, and reduced the psychological distress of the onset of mania and/or psychosis • it may be a feasible, well-tolerated, and effective approach • psychological interventions promote recovery, reduce risk of relapses and secondary morbidity in first-episode mania • psychoeducation, cognitive behavioral therapy (CBT) have shown good results in bipolar disorder, especially early in the course of illness, and with young people • In young people, adding CBT to medication reduces risk of relapse and is cost saving • family interventions reduce rates of mania and depression at 12 months follow-up for young people with a bipolar disorder • psychotherapy, self-help resources (books) provide useful support • young first-episode people need practical advice to re-establish a daily routine, long term-recommendations should include information about drugs, alcohol, stimulants, steroids, childbirth and reducing risk for one's children • the Internet is an effective way of delivering individualized intervention, improves social connectedness, reduces depressive symptoms and showed high uptake to the program • better clinical and functional outcomes in bipolar disorder than schizoaffective disorder to integrated and individualized case management intervention
Douki et al. (1999)	Review		First-episode psychosis		
Macneil et al. (2012)	RCT	Australia	First-episode mania (N = 40; Mean age = 21.5)	18 months	
Marwaha et al. (2018)	Qualitative study	England	Staff of an intervention service		
Maurel et al. (2010)	Review		First-episode mania		
McMurrich et al. (2012)	Review		First-episode mania		
Perlini et al. (2020)	Review		Early psychosis		
Power (2015)	Review		Bipolar disorder		
Vallarino et al. (2015)	Review		Bipolar disorder		

Note. *AP = Affective psychoses; NAP = Non-Affective psychoses.

intervention. They found that this intervention improved depressive and general symptoms but not manic symptoms. It also improved social and occupational functioning after 18 months. Perlini et al. (2020) reported that mindfulness-based intervention may also be effective, especially to reduce distress associated with the onset of mania and/or psychosis. Furthermore, psychoeducation, Cognitive Behavioural Therapy (CBT), and family interventions have shown good results in bipolar disorder, especially in the early course of illness, and with young people (Power, 2015). Otherwise, Vallarino et al. (2015) suggested the Internet as a suitable way of delivering individualized interventions.

In addition to psychotherapy, self-help resources, practical advice to re-establish a daily routine, and long-term recommendations may be crucial in FEAP (Power, 2015). Not only does psychosocial intervention requires several therapeutic tools, but also a good therapeutic alliance for treatment adherence combined with psychoeducation for patients and their relatives (Maurel et al., 2010). However, some differences between bipolar and schizoaffective disorders in therapeutic response, especially to integrated and individualized case management intervention, suggests the necessity of more intense care for schizoaffective disorder (Vallarino et al., 2015).

3.5. Outcomes (Table 5)

3.5.1. Symptoms

Some studies investigated symptomatic differences within affective psychoses. In a study on first-episode mania, Azorin et al. (2012) pointed out that people with a unique episode can be distinguished from those experiencing multiple episodes by more psychotic and fewer depressive symptoms but not by temperament and anxiety. In contrast, higher level of anxiety, and especially social anxiety, distinguished patients with unipolar depression from those with bipolar disorder (Scott et al., 2013). Sub-groups differences within bipolar I manic patients on mood symptoms (depressive, manic, mixed) expressed at onset were also observed (Azorin et al., 2011).

Otherwise, symptomatic recovery seems challenging in affective psychoses. Although a majority of adolescents or adults with affective psychoses achieved syndromal recovery (8 weeks without a depressive or manic episode), they did not achieve symptomatic recovery (8 contiguous weeks with minimal affective symptoms) within 2 years after a first episode (Salvadore, Drevets, Henter, Zarate and Manji, 2008a). A more frequent and rapid syndromic recovery was associated with full compliance (Strakowski et al., 1998). However, although the development of insight has a large impact on hospital admission (Ramu et al., 2019), it may partially improve the course of symptoms in FEAP (Smith

Table 5
Summary of results on outcomes in first-episode affective psychoses.

Study	Method	Country	Population (N; age)	Follow-up	Key findings
Symptoms					
Azorin et al. (2011)	Retrospective study	France	First-episode bipolar I disorder (N = 1008; Mean age = 42.9)		<ul style="list-style-type: none"> patients with manic onset had a hyperthymic temperamental predisposition, had a first episode triggered by substance abuse, an illness course with pure, severe and psychotic mania. patients with depressive onset had a first episode triggered by stress and alcohol, had an illness course with more episodes, cyclicity, suicide attempts, anxious comorbidity and residual symptoms patients with mixed episode at onset shared characteristics with both manic and depressive onset but had more mixed episodes and cyclothymic temperament
Azorin et al. (2012)	Retrospective study	France	First- and multiple-episode mania (N = 1090; 18–65 years)		<ul style="list-style-type: none"> people with first episode mania had more psychotic and fewer depressive symptoms but were comparable to multiple episode patients regarding temperament and anxiety the prodromal phase of first episode mania was characterized by a shorter delay before correct diagnosis, greater substance use, being not divorced, greater stressors before current mania, a prior diagnosis of an anxiety disorder, lower levels of depression during index manic episode, more suicide attempts in the past year
Ramu et al. (2019)	Prospective study	England	First-episode psychosis (N = 2026; both children and adults)	from 12 to 60 months	<ul style="list-style-type: none"> poor insight was positively associated with age 16–35, bipolar disorder, history of cannabis use, and negatively associated with white ethnicity and depression poor insight was significantly associated for higher levels of outcomes (number of psychiatric hospital admission, legally enforced admission, number of unique antipsychotics prescribed, number of inpatient days) at follow-up
Salvatore et al. (2007)	Prospective study	USA	First-episode psychosis (N = 377; Mean age = 30.8)	24 months	<ul style="list-style-type: none"> Psychopathological features gathered into four factors: mania with psychosis (I), mixed depressive-agitated state (II), excited-hallucinatory-delusional state (III), disorganized-catatoniac-autistic state (IV) Factors I and III were associated with mania, II with major-depression or bipolar mixed-state, IV with major depression and negatively with mania
Salvadore et al. (2008a)	Review		Bipolar disorder		<ul style="list-style-type: none"> A majority of adolescents or adults with affective psychoses achieve syndromal recovery (8 weeks without a depressive or manic episode) but not symptomatic recovery (8 contiguous weeks with minimal affective symptoms) within 2 years after a first episode
Scott et al. (2013)	Retrospective study	Australia	Bipolar disorder and unipolar depression (N = 308; Mean age = 19.4)		<ul style="list-style-type: none"> comparable psychological distress, depressive symptoms, current role impairment, neuropsychological dysfunction, and alcohol or substance misuse between both groups the unipolar depression group showed higher level of social anxiety reported bipolar patients were more likely to have a family history of bipolar or psychotic disorder as well as substance misuse but not depressive disorders
Smith et al. (2014)	Prospective study		First-episode psychotic mania (N = 83; Mean age = 21.5)	18 months	<ul style="list-style-type: none"> poor functioning, great severity of manic and overall symptoms were associated with poor insight at baseline level of insight at baseline did not predict symptomatology or functioning at follow-up
Strakowski et al. (1998)	Prospective study	USA	First-episode affective psychosis (N = 109; Mean age = 26)	12 months	<ul style="list-style-type: none"> full compliance was associated with more frequent and rapid syndromic recovery, and was more common in white patients, and in patients without substance abuse delayed symptomatic recovery in patients with substance abuse higher socio-economic status was associated with both symptomatic and functional recovery good premorbid function was associated with functional recovery only 35% of patients achieved functional recovery Mood-incongruent psychosis was associated with longer time exhibiting psychotic symptoms, poorer overall functioning than mood-congruent psychosis The two sub-groups had similar percent of weeks with affective symptoms or syndromes
Strakowski et al. (2000)	Prospective study	USA	First episode mania (N = 42; 16–45 years)	8 months	<ul style="list-style-type: none"> only 35% of patients achieved functional recovery Mood-incongruent psychosis was associated with longer time exhibiting psychotic symptoms, poorer overall functioning than mood-congruent psychosis The two sub-groups had similar percent of weeks with affective symptoms or syndromes
Functioning					
Abdel-Baki et al. (2013)	Descriptive study	Canada	First-episode psychosis (N = 97; 18–30 years)	Over 60 months	<ul style="list-style-type: none"> AP vs NAP were more likely to have a productive occupation at follow-up prior employment predicted better occupation at follow-up
Berge et al. (2016)	Prospective study	Spain	First-episode psychosis (N = 140; Mean age = 25.4)	24 months	<ul style="list-style-type: none"> affective psychoses and non-affective psychoses did not differ in terms of days until the first relapse and global functioning at follow-up
Conus et al. (2006b)	Prospective study	Australia	First-episode psychotic mania (N = 87; Mean age = 22.1)	12 months	<ul style="list-style-type: none"> 90% of syndromic and 60% of symptomatic recovery at 6 and 12 months A majority of patients both at 6 months (66%) and at 12 months (61%) fail to get back to their premorbid functioning

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Table 5 (continued)

Study	Method	Country	Population (N; age)	Follow-up	Key findings
Henry et al. (2010)	Prospective study	Australia	First-episode psychosis (N = 651; Mean age = 28.7)	7 years	<ul style="list-style-type: none"> Age at intake, family history of affective disorder, illicit drug use, functional recovery at 6 months predicted functional recovery at 12 months better global and psychosocial functioning and quality of life in affective psychoses than in schizophrenia at follow-up, no difference regarding vocation (time living independently, work status)
Ratheesh et al. (2017)	Prospective study	Australia	First-episode mania (N = 117; Mean age = 21.4)	18 months	<ul style="list-style-type: none"> premorbid social adjustment predicted short to medium term interpersonal functioning premorbid adjustment was not associated with illness severity at follow-up premorbid academic adjustment correlated with vocational functioning
Shinn et al. (2017)	Descriptive study	USA	First-episode psychosis (N = 92; Mean age = 21.4)	30 months	<ul style="list-style-type: none"> patients with affective psychoses had better premorbid functioning, baseline indices of severity between groups were similar, the retention rate was lower in the not otherwise specified (NOS) group than in affective psychoses primary psychosis groups and affective psychoses or NOS groups had a majority of individuals who dropped out of treatment early While most patients attained syndromal recovery, only one third of them recovered functionally Low initial depression severity, functional recovery by 6 months, short length of stay, and age of onset of 30 years or older were associated with syndromal recovery Age of onset of 30 years or older, and short length of stay were associated with functional recovery
Tohen et al. (2000a)	Prospective study	USA	First episode major affective disorders with psychotic features (N = 219; Mean age = 34.1)	24 months	<ul style="list-style-type: none"> Syndromal recovery rates were the highest in the major affective disorder sub-group (81%), followed by non affective acute psychoses (74%), schizoaffective disorders (70%), and the lowest were for schizophrenia (36%) Functional recovery was associated with syndromal recovery, shorter hospitalization normalized to year, and older age at onset Two third of patients who had attained syndromal recovery did not achieved functional recovery at follow-up
Tohen et al. (2000b)	Prospective study	USA	First-episode psychosis (N = 296; Mean age = 31.9)	6 months	<ul style="list-style-type: none"> Syndromal recovery rates were the highest in the major affective disorder sub-group (81%), followed by non affective acute psychoses (74%), schizoaffective disorders (70%), and the lowest were for schizophrenia (36%) Functional recovery was associated with syndromal recovery, shorter hospitalization normalized to year, and older age at onset Two third of patients who had attained syndromal recovery did not achieved functional recovery at follow-up
Physical health Archie et al. (2015)	Retrospective study	Canada	First-episode affective psychoses (N = 53; Mean age = 23.8)		<ul style="list-style-type: none"> a probability of 75% to develop an abnormal lipid test within the first 18 months after receiving antipsychotic medications the median time to develop an abnormal lipid test was 8 months for men and 12 months for females
Strassnig et al. (2017)	Prospective study	USA	First-episode bipolar disorder and schizophrenia (N = 233; 15–60 years)	20 years	<ul style="list-style-type: none"> early overweight was a predictor of eventual obesity around 50% of patients with bipolar disorder were obese at follow-up but greater prevalence of obesity in schizophrenia bipolar patients experience a later development of obesity than in schizophrenia, probably due to their lower initial BMI, suggesting more time to intervene to prevent weight gain

Note. *AP = Affective psychoses; NAP = Non-Affective psychoses.

et al., 2014). Finally, symptomatic recovery was correlated with higher socioeconomic status (Strakowski et al., 1998) and may be more difficult in patients with mood incongruent symptoms (Strakowski et al., 2000) and substance abuse.

3.5.2. Functioning

While most patients with a first-episode mania achieve syndromic recovery, most of them fail to recover at the functional level (Conus et al., 2006b; Tohen et al., 2000a,b). Previous literature thus identified some factors that may affect functional recovery, among those an age of onset over 30 years and a short length of stay (Tohen et al., 2000). At 12 months, it was predicted by age at intake, familial antecedents of affective disorder, illicit drug use and functional recovery at 6 months (Conus et al., 2006b). However, although premorbid social adjustment predicted short-to medium-term interpersonal functioning in first-episode mania, functioning at the 18-month follow-up was not predicted by premorbid adjustment (Ratheesh et al., 2017).

Elsewhere, previous literature compared affective and non-affective psychoses in terms of functional adjustment. In a first-episode psychosis cohort, Shinn et al. (2017) found that patients with affective psychoses had better premorbid functioning than those with other psychotic disorders. Moreover, Abdel-Baki et al. (2013) found a higher rate of productive occupation at the 5-year follow-up in the affective than the non-affective psychosis sub-group. Although Henry et al. (2010)

reported a better global and psychosocial functioning in those with affective than those with non-affective psychoses at 7-year follow-up, they found no difference regarding vocation. Berge et al. (2016) also did not find any inter-group differences on global functioning after 2 years.

3.5.3. Physical health

Very few studies have reported results regarding physical health in FEAP. Early overweight was a predictor of obesity (Strassnig et al., 2017). At a 20-year follow-up, approximately 50% of patients with bipolar disorder were obese, but the prevalence of obesity was greater in patients with schizophrenia, and those with bipolar disorder experienced a later development of obesity. Furthermore, Archie et al. (2015) highlighted that there was a 75% probability of developing an abnormal lipid test result within the first 18 months after receiving antipsychotic medication, with men showing a shorter median time to develop this than females.

3.6. Duration of untreated illness (DUI) (Table 6)

In general, diagnoses of affective psychoses and psychotic mania, but not of psychotic depression, have been associated with a shorter DUP in comparison to schizophrenia (Basu et al., 2015; Bhui et al., 2014; Large et al., 2008). The Nottingham Onset Schedule was reported to be an easy and reliable standardized tool to measure DUP (Singh et al., 2005).

Table 6
Summary of results on DUI (Duration of Untreated Illness) in first-episode affective psychoses.

Study	Method	Country	Population (N; age)	Follow-up	Key findings
Basu et al. (2015)	Retrospective study	Singapore	First-episode psychosis (N = 794; Mean age = 27.1)	24 months	<ul style="list-style-type: none"> • affective psychoses was associated with shorter DUP than schizophrenia spectrum and delusional disorders
Bhui et al. (2014)	Retrospective study	England	First-episode psychosis (N = 480; 18–64 years)	24 months	<ul style="list-style-type: none"> • affective psychoses and psychotic mania but not psychotic depression associated with a shorter DUP in comparison to schizophrenia
Dagani et al. (2017)	Meta-analysis		Bipolar disorder (N = 9415)		<ul style="list-style-type: none"> • the delay between the onset and management of bipolar disorder was 5.8 years but there was high heterogeneity between samples • a longer interval in studies defining the onset as the first episode and management as age at diagnosis
Large et al. (2008)	Meta-analysis		Psychosis (N = 9870)		<ul style="list-style-type: none"> • affective psychoses associated with a shorter DUP than schizophrenia • necessary to examine DUP separately affective (DUP proportion of less than a week) and non-affective (length of DUP) psychosis
Malik et al. (2010)	Experimental study	Pakistan	First-episode psychosis (N = 60; Mean age = 26)		<ul style="list-style-type: none"> • no significant differences in emotion recognition between diagnostic categories • longer DUP was associated with more difficulties in facial emotion recognition and patients with schizoaffective disorders had longer DUP than those with substance-induced psychosis
Malla et al. (2014)	Quasi-experimental study	Canada	First-episode psychosis (N = 295; 14–30 years)		<ul style="list-style-type: none"> • patients with longer DUP more likely to have more severe positive symptoms • Test of a targeted intervention (intensive training and education regarding early signs of FEP and benefits of early intervention) to reduce DUP. Results showed an increase in the proportion of patients referred to the early intervention service especially for those with affective psychoses
Singh et al. (2005)	Psychometric study	England	First-episode psychosis (N = 20; Mean age = 25)		<ul style="list-style-type: none"> • The Nottingham Onset Schedule, a reliable and easy to use scale to measure onset in psychosis • shorter DUP in AP than in schizophrenia • longer onset in schizophrenia than in AP

Note. *DUP = Duration of Untreated Psychosis; AP = Affective psychoses; FEP = First-Episode Psychosis.

However, the definition of the DUI or DUP may vary across studies, which affects the results. Indeed, in a meta-analysis including studies on bipolar disorders with or without psychosis, the delay between the onset and management of illness was 5.8 years, but there was a high degree of heterogeneity between samples (Dagani et al., 2017). Studies defining the onset as the first episode and management of illness as the age at diagnosis found longer intervals.

Reducing DUI is a major challenge in early intervention, and some studies have explored its impact and possible specific interventions. Considering the central role of emotional disturbances in patients with psychosis associated with interpersonal problems, Malik et al. (2010) investigated the impact of DUP on emotion recognition. They found that a longer DUP was associated with more difficulties in facial emotion recognition. Moreover, Malla et al. (2014) implemented a targeted intervention to reduce DUP. Interestingly, the impact on DUP was significant. Indeed, they showed an increase in the proportion of patients referred to early intervention services, especially for those with affective psychoses.

3.7. Neurobiology and neurocognition (Table 7)

3.7.1. Neurocognitive and neurostructural abnormalities

Previous literature has suggested important neurocognitive impairments associated with affective psychoses. In line with this, patients with FEAP show impaired psychomotor speed, attention, working memory, verbal learning, visual and verbal memory, and cognitive flexibility (Daglas et al., 2016; Lee et al., 2014; Olvet et al., 2013). While Lee et al. (2014) suggested that these deficits were not mood-state dependent, Sax et al. (1998) found that attentional impairments were associated with mania and did not persist after 2 months. Furthermore, these neurocognitive deficits, especially those regarding attentional performance, did not differ between diagnostic categories within affective psychoses (Sax et al., 1998). Nonetheless, although this is non-specific to affective psychoses, verbal memory deficits at baseline predicted more negative symptoms which in turn predicted poorer functioning at one year follow-up (Buck et al., 2020).

Regarding neurostructural abnormalities, Kozicky et al. (2016) showed that changes in grey matter loss did not differ between patients and healthy controls after a year. However, patients with recurrent

manic episodes had greater grey matter loss than healthy controls, especially in left frontal and bilateral temporal regions that are important for emotion regulation. They also had greater loss of grey matter volume in bilateral frontal, temporal and left parietal regions than those with sustained remission. Moreover, Hirayasu et al. (1998) mentioned that patients with affective psychosis, similarly to those with schizophrenia, presented significantly less left than right asymmetry in the posterior amygdala-hippocampal complex. Finally, Salvatore et al. (2008a) mentioned an abnormal decrease in grey matter volume in the cingulate gyrus in first-episode affective psychoses. Additionally, those with a family history of mood disorders showed a reduction in left subgenual anterior cingulate cortex volume.

3.7.2. Differences in neurocognition between affective and non-affective psychoses

Some studies have compared the neuropsychological aspects of affective and non-affective psychoses. Amoretti et al. (2018) examined cognitive reserve in FEP patients to compare inter-group differences in brain capacity for dealing with pathology to minimize symptoms. Patients with affective psychoses had higher cognitive reserve than those with non-affective psychoses.

Elsewhere neuropsychological functioning differences have been investigated, showing a tendency for patients with schizophrenia to have more severe neurocognitive deficits than patients with bipolar disorder (Olvet et al., 2013). However, bipolar disorder associated with psychosis may lead to a greater frequency and severity of cognitive impairment, similar to schizophrenia syndrome. In line with the above review suggesting neurocognitive similarities between schizophrenia and affective psychoses, Torrent et al. (2018) did not find any neuropsychological differences between those with affective and non-affective psychoses at 2-year follow-up. Finally, Lee et al. (2015) also did not find inter-group differences in neuropsychological changes.

4. Discussion

Our aim was to synthesize current knowledge and to identify specificities of FEAP regarding what we consider important topics of FEP early intervention research such as diagnostic categorization, premorbid factors, intervention, outcomes, duration of untreated illness,

Table 7
Summary of results on neurobiology and neurocognition in first-episode affective psychoses.

Study	Method	Country	Population (N; age)	Follow-up	Key findings
Amoretti et al. (2018)	Prospective study	Spain	First-episode psychosis (N = 247 patients vs 205 healthy controls; Mean age = 25.2)	24 months	<ul style="list-style-type: none"> people with affective psychoses had higher cognitive reserve (including premorbid IQ, education-occupation, leisure activities) than those with non-affective psychoses in the affective psychosis subgroup, people with low cognitive reserve were more likely to have a lower socio-economic level as well as a lower level of education than those with high cognitive reserve. People with high cognitive reserve had also better functioning and global cognition at follow-up, a better verbal memory both at baseline and at follow-up.
Buck et al. (2020)	Prospective study	Canada	First-episode psychosis (N = 435 patients, vs 138 controls; Mean age = 23.9)	12 months	<ul style="list-style-type: none"> verbal memory deficits in first-episode psychosis vs healthy controls verbal memory was worst in males than females in both affective and non-affective psychosis at baseline better baseline verbal memory predicted better functioning at follow-up, mediated through fewer negative symptoms at baseline
Daglas et al. (2017)	RCT	Australia	First-episode mania (N = 40 first-episode mania vs 21 healthy controls; Mean age = 21.32)		<ul style="list-style-type: none"> patients with first-episode mania had significantly a lower full-scale IQ score, more difficulties in processing speed, verbal learning and memory, working memory and cognitive flexibility than healthy controls
Hirayasu et al. (1998)	Prospective study	USA	First-episode psychosis (N = 33 first-episode vs 18 healthy controls; Mean age = 24.8)		<ul style="list-style-type: none"> both the patients with schizophrenia and those with affective psychosis had significantly less left than right asymmetry of the posterior amygdala-hippocampal complex
Kozicky et al. (2016)	Prospective study	Canada	First-episode mania (N = 41 first-episode mania vs 25 healthy controls; Mean age = 22.9)	12 months	<ul style="list-style-type: none"> the grey matter loss change did not differ between patients and healthy controls at follow-up patients with recurrence of manic episode had greater grey matter loss than healthy controls, especially in left frontal and bilateral temporal regions that are important for emotion regulation patients with recurrence had also greater loss of grey matter volume in bilateral frontal, temporal and left parietal regions than those with sustained remission there was no significant difference in grey matter volume between sustained-remission patients and healthy controls symptoms severity associated with poor performance in executive functions predicted lower functioning at follow-up
Lee et al. (2014)	Meta-analysis		First-episode bipolar disorder		<ul style="list-style-type: none"> medium to large deficits in psychomotor speed, attention and working memory, and cognitive flexibility smaller deficits in verbal learning and memory, attentional switching, and verbal fluency no difference on visual learning and memory functioning compared to controls cognitive deficits are not mood-state dependent
Lee et al. (2015)	RCT	Australia	First-episode psychosis (N = 311; 12–35 years)	Between 12 and 36 months	<ul style="list-style-type: none"> neuropsychological changes did not differ between diagnostic categories neuropsychological functioning remained stable excepting verbal memory improved at follow-up verbal memory improvement associated with a decrease of positive and negative residual symptoms
Olvet et al. (2013)	Review		Bipolar disorder		<ul style="list-style-type: none"> visual, verbal, and working memory deficits were consistently higher in first episode mania than in healthy controls. Both groups were comparable regarding premorbid and current IQ patients with schizophrenia tend to have more severe neurocognitive deficits as well as lower premorbid and current IQ than patients with bipolar disorder bipolar disorder with psychotic symptoms associated with more severe and frequent cognitive deficits.
Torrent et al. (2018)	Prospective study	Spain	First-episode psychosis (N = 192; 7–35 years)	24 months	<ul style="list-style-type: none"> less perseverative errors in affective than in non-affective psychoses at baseline no neuropsychological differences between groups at follow-up
Salvadore et al. (2008a)	Review		Bipolar disorder		<ul style="list-style-type: none"> an abnormal decrease in grey matter volume in the cingulate gyrus for first-episode affective psychoses First-episode affective psychoses with family history of mood disorders had reduction in left subgenual anterior cingulate cortex volume
Sax et al. (1998)	Prospective study	USA	First-episode affective psychosis (N = 27 FEAP vs N = 31 healthy controls; Mean age = 25.5)	2 months	<ul style="list-style-type: none"> No difference on attentional performance between diagnostic categories (depression with psychotic features, schizoaffective disorder, bipolar disorder) Worse attentional performance at baseline but no difference at follow-up in FEAP vs healthy controls Attentional performance correlated with manic state

neurobiology and neurocognition. Our findings showed psychopathological and neurocognitive differences between affective and non-affective psychosis suggesting the need for developing specific intervention strategies for FEAP. However, most studies did not include schizoaffective disorder in the affective group considering its

schizophrenic appearance or only included it in first-episode mania studies. Considering its affective dimension, either depressive or manic, which requires mood treatment strategies, it would be important to include such diagnostic category to further investigate FEAP and to develop clinical guidelines. Finally, the literature on early intervention

in FEAP remains sparse suggesting the need for further studies to better understand the challenges of such clinical entity and to explore whether specific intervention strategies would improve outcomes.

Our review of the literature on FEAP highlighted differences between affective and non-affective psychoses. Especially, although symptomatic recovery in affective psychosis may be more frequent than in non-affective psychosis (Conus and McGorry, 2002), the development of specific interventions is required. Indeed, the previous literature has highlighted major challenges associated with affective psychoses such as suicidal risk, non-adherence to treatment, and substance abuse (Berk, 2007; Strakowski et al., 1996). The results also pointed out that early intervention in FEAP is particularly important because most people with delayed treatment will experience multiple relapses, increasing the risk of damaging effects (Conus and McGorry, 2002). However, identifying affective psychoses at onset is particularly difficult because of overlapping symptomatology with both depression and schizophrenia (Berk, 2007; Conus, 2010). It is especially complex with psychotic patients presenting depressive but no manic or only hypomanic symptoms (Arrasate et al., 2014). There are thus many challenges with current diagnostic practice and difficulties related to differential diagnosis. A useful way of differentiating affective from non-affective psychoses may be activation (Arrasate et al., 2014). Psychopathological features at onset may also enable subtyping (Salvatore et al., 2007). However, further investigation on affective psychoses is required to address identification issues associated with the presence of a depressive dimension without mania. Finally, due to the highlighted challenges specific to FEAP, it is important to focus interventions on the development of insight, comorbidities, therapeutic engagement, educational and vocational counselling, and follow-up through age-appropriate developmental tasks (Berk, 2007; Douki et al., 1999; Ramu et al., 2019). In order to cope with such specific challenges, further studies are however required to investigate potential internal differences within affective psychoses to develop more adaptive intervention strategies.

Despite the few guidelines for intervention in FEAP, the previous literature provided some recommendations. Namely, pharmacological treatment first requires accurate assessments of both psychotic and affective dimensions (Douki et al., 1999; Lambert et al., 2003). Moreover, combining mood stabilizers with atypical antipsychotics remains the most effective strategy to deal with FEAP. Benzodiazepines can also be included in cases of behavioural disturbances, agitation or insomnia. While mood stabilizers like lithium are recommended during the maintenance phase (Jauhar et al., 2019), antidepressants should only be cautiously introduced due to the risk of manic relapse. To avoid relapses during the maintenance phase, psychosocial intervention is essential. Psychoeducation and psychotherapy, especially CBT and mindfulness-based intervention, have been reported to be effective (Douki et al., 1999; Maurel et al., 2010; Perlini et al., 2020; Power, 2015). Finally, self-help resources and daily routine recommendations may be helpful tools for young people (Power, 2015).

The consulted literature also provides some interesting potential targets for early interventions in FEAP, namely premorbid history and socio-demographic factors. Indeed, although premorbid history is mainly characterized by good socio-professional adaptation and functioning, there is a high prevalence of past traumatic events linked to poor outcomes (Conus et al., 2010; Daglas et al., 2014). It is therefore crucial to accurately explore past personal trauma (potential or acknowledged) and to develop psychotherapeutic tools to focus early intervention on traumatic experience. Otherwise, considering the high rate of parenthood among those with FEAP, there is a clear need to develop family interventions and psychoeducation to protect children from the adverse effects of their parents' illness (Abdel-Baki et al., 2013).

Furthermore, despite a lack of literature on remission that would require further investigation, some studies have highlighted key findings on outcomes, which may provide opportunities to accurately monitor care in FEAP. While FEAP is often associated with shorter DUP and

better socio-professional and global functioning recovery than non-affective psychoses (Shinn et al., 2017; Sim et al., 2007), it can induce severe deficits, especially in cases of multiple episodes (Conus, 2010). It is especially important to consider that relapses are frequent and that symptomatic recovery (8 contiguous weeks with minimal affective symptoms) and functional recovery remain challenging (Conus et al., 2006b; Salvatore et al., 2008a; Tohen et al., 2000a,b). Preventing relapses requires both psychosocial and pharmacological intervention with a good therapeutic alliance to prevent non-adherence to treatment (Maurel et al., 2010). Finally, subtyping affective psychoses patients using affective symptoms may improve intervention monitoring (Azorin et al., 2011, 2012; Scott et al., 2013; Selvendra et al., 2014).

Considering neurocognition, the previous literature has consistently reported deficits in psychomotor speed, verbal and working memory in those with FEAP compared to healthy controls (Buck et al., 2020; Daglas et al., 2017; Lee et al., 2014; Olvet et al., 2013; Torrent et al., 2018). Verbal memory should be carefully assessed, especially in males (Buck et al., 2020), because of its impact on negative symptoms, and thus on functional recovery which remains challenging in FEAP (Conus et al., 2006b). Furthermore, the impact of illness on cognition may depend on cognitive reserve; thus, it may be useful to subtype patients regarding their cognitive reserve (Amoretti et al., 2018). It should be noted that the studied samples did not include the whole spectrum of affective psychoses. It is therefore important to confirm these results in a cohort that includes every FEAP diagnostic category. While these cognitive deficits were independent of mood-state (Olvet et al., 2013), grey matter loss was more prominent in patients with recurrent manic episodes (Kozicky et al., 2016). It remains unclear how neurocognitive deficits and grey matter loss are linked, as well as how relapse impacts neurocognition and grey matter loss. These questions require further investigation.

While this narrative review adequately presents current knowledge on FEAP, it has limitations. First, the literature on FEAP remaining scarce, this review included studies on various topics which did not enable us to provide clear and straightforward guidelines for early intervention in FEAP. Secondly, the selection process was conducted by one person alone, and it may therefore lack the reliability of multiple ratings. Third, despite a rational selection process, as a narrative review, we selectively reviewed data/papers that is less likely to be both transparent and reproducible as a systematic review would be. Fourth, we were not able to peer-review our search strategy, we might thus fail to screen all the existing studies in the literature as a proper scoping review search strategy would do.

5. Conclusion

Affective psychoses require specific treatment to prevent adverse development of illness. Despite few clear guidelines emerging, our synthesis identified some recommendations for early intervention in FEAP. Our review also highlighted the lack of accurate tools to characterize the early course of affective psychoses. Through this review, we identified the specific needs of FEAP patients, but research remains sparse in this field, suggesting that further investigation is required, especially in cohort including every FEAP diagnostic category.

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Declaration of competing interest

The authors declare that they have no conflict of interest.

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Appendix A. Supplementary data

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