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Depressive symptoms and suicidal behavior after first-episode psychosis: A comprehensive systematic review

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ABSTRACT

Depressive symptoms and suicidal behavior are common among patients that suffered a first-episode psychosis. We searched Web of Knowledge[SM] and Pubmed® for English and Portuguese original articles investigating prevalence of depressive symptoms and/or suicidal behavior and associated factors after first-episode psychosis. We included 19 studies from 12 countries, 7 studied depressive symptoms and 12 suicidal behavior. The findings confirm that depressive symptoms and suicidal behavior have high rates in the years after first-episode psychosis. Factors identified as being associated with depressive symptoms after first-episode psychosis were anomalies of psychosocial development, poor premorbid childhood adjustment, greater insight, loss, shame, low level of continuing positive symptoms and longer duration of untreated psychosis. Suicidal behavior was associated with previous suicide attempt, sexual abuse, comorbid polysubstance use, lower baseline functioning, longer time in treatment, recent negative events, older patients, longer duration of untreated psychosis, higher positive and negative psychotic symptoms, family history of severe mental disorder, substance use, depressive symptoms and cannabis use. Data also indicate that treatment and early intervention programs reduce depressive symptoms and suicidal behavior after first-episode psychosis. Future research should overcome some methodological discrepancies that exist between studies and limit generalization of current findings.

1. Introduction

Depressive symptoms and suicidal behavior are common among patients that suffered a first-episode psychosis. Published studies revealed that depressive symptoms in patients with first-episode psychosis have prevalence from 17% to 83% (Addington et al., 1998; Bottlender et al., 2000; Romm et al., 2010). Depressive symptoms could occur in different phases of psychosis, including post-psychotic period (Birchwood et al., 2005). Depression is a well-known risk factor for suicidal behavior in psychosis with data showing that occurrence of depression in psychosis have significant correlation with suicide risk (Upthegrove et al., 2010). Suicide remains an important cause of premature death in patients with psychotic disorders (Healy et al., 2012; Laursen, 2011). In long-term follow-up studies suicide accounts for 2–5% of deaths in first-episode psychosis (Dutta et al., 2011, 2010; Palmer et al., 2005). The rate of attempted suicide in psychotic patients ranges from op10% to 50% (Aleman and Denys, 2014; Castelein et al., 2015). Individuals with first-episode psychosis have a greater risk of suicidal behavior compared with the normal population and chronic disorders (Bertelsen et al., 2007). First admissions have three times higher suicide rate than chronic schizophrenia (Palmer et al., 2005). As suicide risk peaks in the early years of psychotic disorders much attention has been given to this phase of the disorder (Palmer et al., 2005). Previous studies have been published in order to identify predictors of suicide in patients with psychotic disorders. Identifying factors associated to depressive symptoms and suicidal behavior will permit the development of preventive and treatment interventions. However, despite its prevalence, limited evidence exists regarding factors associated and interventions to reduce suicide risk among young people with first-episode psychosis.

Our aim was to perform a systematic review of the current evidence in this field of knowledge. The main objectives were (1) to assess rate of depressive symptoms and suicidal behavior (including suicidal ideation, suicide plans, suicide attempts and suicide) after first-episode psychosis and (2) to search for the most relevant demographic and clinical factors associated.

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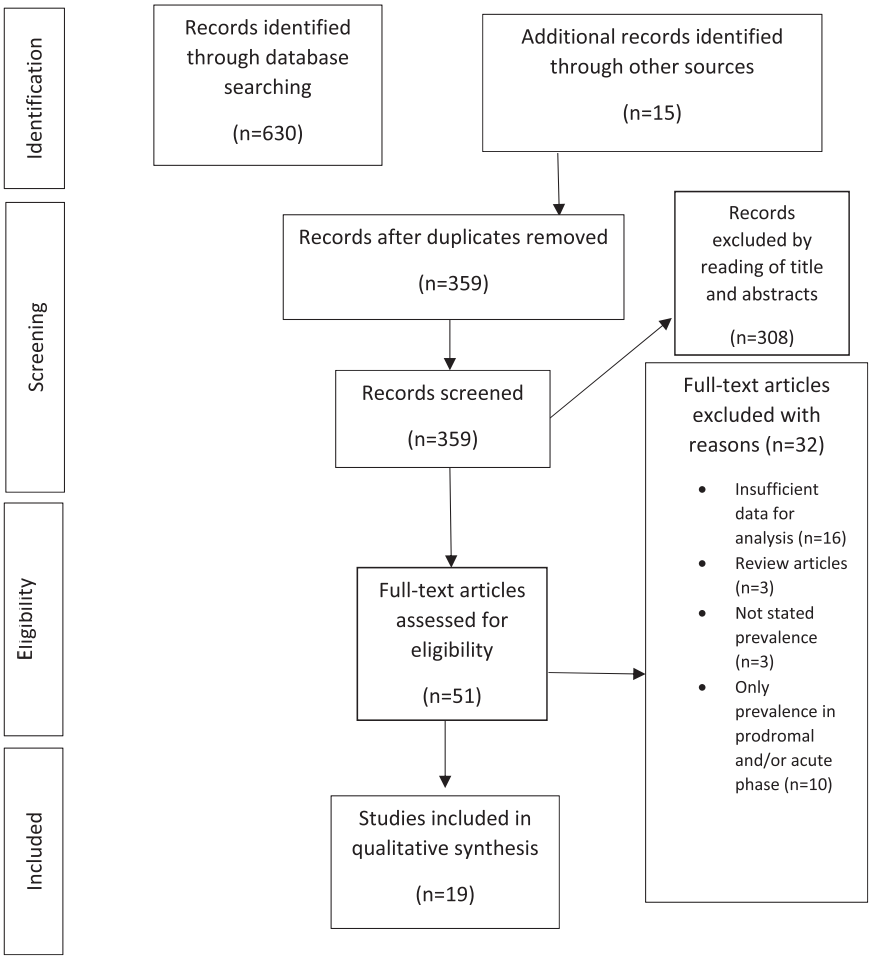

Fig. 1. Flow Chart of systematic identification of papers following PRISMA Guidance.

2. Methods

2.1. Selection procedures and data collection

2.1.1. Search strategy

A systematic literature search as described by the PRISMA statement was conducted using Web of Knowledge[SM] and Pubmed® databases to find studies that reported the prevalence and associated factors of depressive symptoms and suicidal behavior among patients that suffered a first-episode psychosis. Articles published until May 2016 and in English and Portuguese languages were considered. Search terms used to find relevant articles were 'depression' OR 'depressive' OR 'suicidal' AND 'first-episode psychosis' OR 'first-episode schizophrenia'. A secondary search was performed by reviewing reference lists of sources identified as relevant in initial search to find additional articles to the review. The articles surviving selection were fully download (PDFs) and evaluated for eligibility after full-text reading.

2.1.2. Inclusion criteria

Articles were included for the systematic rweview: (a) included affective and/or non-affective first-episode psychosis patients defined according to international standard definitions (International Classification of Diseases, Diagnostic and Statistical Manual of Mental Disorders); (b) clearly stated prevalence of depressive symptoms and/or suicidal behavior in the period after first-episode psychosis; (c) were original articles and written in English or Portuguese language.

2.1.3. Exclusion criteria

We excluded from the review: (a) duplicated reports; (b) report data on non-first episode psychosis patients; (c) did not refer clearly the prevalence of depressive symptoms and/or suicidal behavior; (d) papers with insufficient data for analysis, meta-analysis or reviews; (e) articles that studied depressive symptoms and/or suicidal behavior only in prodromal and/or acute psychotic phases; (f) articles in languages other than English or Portuguese. In case of multiple publications deriving from the same study population, we selected the articles reporting the largest or the most recent data. In case of conflict between these two last criteria, the sample size was the priority.

2.1.4. Recorded variables

We recorded the following variables from each article: authors, year of publication, country, epidemiological data of patient sample (sample size, mean age, proportion of males), clinical variables (instruments used, diagnoses included), type of study, follow-up time, main aim, prevalence of depressive symptoms and/or suicidal behavior and relevant findings.

2.2. Quality assessment

We assessed the internal validity of the included studies using the tool developed by Thomas et al. from the Effective Public Health Practice Project (EPHPP) (Thomas et al., 2004). The Cochrane Collaboration for non-randomized studies recommends this tool (Higgins and Green, 2011). It includes six components: selection bias, design,

Table 1
Characteristics of studies included in the systematic review.

Authors and publish year	Country	Sample size	Age Mean (SD)	Male percent	Screening tools (depression and/or suicidal behavior)	Diagnosis	Study type/Follow-up time	Main Aim	Prevalence	Relevant findings
Depressive symptoms										
Koreen et al., 1993	USA	70	24.3 (6.0)	56%	HDRS Syndromal definition based on Research Diagnostic Criteria (RDC)	FEP: non-affective psychosis	Prospective, longitudinal/5 years	Prevalence of depressive symptoms in first-episode psychosis	Baseline: depressive symptoms (HRSD (≥15) or RDC): 75% HRSD and RDC: 22%; Follow-up: a)depression: 26%; b)Nonpsychotic ratings:4%	Depressive symptoms may represent a core part of the acute illness or may occur as a subjective reaction;
Wassink et al., 1999	USA	70	24.63 (5.23)	77.14%	CASH	FEP: non-affective psychosis	Prospective, longitudinal/5 years	Prevalence of depressive symptoms early in the course of schizophrenia	Depressive symptoms: > 50% MDD (baseline): 34.3%	Depressive symptoms are common early in the course of schizophrenia and has potential implications in diagnostic and treatment practices.
Iqbal et al., 2004	UK	29	25 (5.2)	72%	BDI	FEP: non-affective psychosis	Prospective longitudinal/ 12 months	Establish whether overgeneral memory is a feature of post-psychotic depression in FEP	PPD: 44.8%	PPD was associated with overgeneral memory and a heightened awareness of the diagnosis.
Romm et al., 2010	Norway	122	28.3 (9.2)	64%	SCID-I CDSS	FEP: non-affective psychosis	Part of ongoing longitudinal	Prevalence of MDE Demographic and clinical characteristics of patients with MDE	MDE before onset psychosis: 17%; MDE during or after onset of psychosis: 30%	Poor premorbid childhood adjustment, substance abuse and excitative symptoms at start of treatment associated with higher severity of depressive symptoms
Cotton et al., 2012	Australia	405	20.9 (3.7)	68.6%	CGI-BP	FEP: non-affective psychosis	Prospective, longitudinal/18 months	Prevalence of depressive symptoms in patients with FEP and clinical and functional characteristics of those with persistent depressive symptoms	Depression (CGI-BP depression score > 3): Baseline: 26.2% Follow-up: 14.2%	Depressive symptoms are common in patients with FES and during the first months of treatment; Greater insight into their illness was associated with depressive symptoms; Substance use was less common in those with depressive symptoms.
Upthegrove et al., 2014	UK	92	22.5 (4.89)	75%	CDSS	FEP: affective and non-affective psychosis	Prospective, longitudinal/12 months	Prevalence of depression in first-episode psychosis, its relationship to other symptom dimensions and recovery in a phase specific manner	Post psychotic depression (CDSS≥7): 37%	Loss, Shame, low level continuing positive symptoms and longer DUP were associated with post psychotic depression
Sönmez et al., 2016	Scandinavia (Norway, Denmark)	299	27.8 (9.66)	58%	PANSS depression item (g6) CDSS	FEP: non-affective psychosis	Prospective, longitudinal/10-year	Patient characteristics at baseline that predict depressive symptoms at 10 years and whether patients prone to depressive symptoms in the first year of treatment had a different prognosis in the following years	Depression (PANSS g6≥4): Baseline: 41%%; 1 year:28%; 2 years: 20%; 5 years:16%; Depression (PANSS g6≥4 and CDSS≥6): 10 years: 19%	Depressive symptoms are frequent among FEP patients at baseline but decrease after treatment. Patients with poor social functioning in childhood and alcohol use at baseline are more prone to have depressive symptoms at 10 years of follow-up.
Suicidal Behavior										
Addington et al., 2004	Canada	238	24.6 (8.33)	65.7%	Suicidality: regular clinical practice and medical records	FEP: non-affective psychosis	Prospective, longitudinal/12 months	Prevalence of suicidal behavior prior and during 1-year FEP and identify predictors	Suicide attempt during follow-up: 2.9%; Suicide: 0.4%	First-episode programs can reduce the suicidal behavior.
Clarke et al.,	Ireland	171	28.5 (11.1)	58%	Clinical interview	FEP:	Prospective,	Prevalence of suicide behavior	Attempt suicide prior	Suicide attempts prior to

(continued on next page)

Table 1 *(continued)*

Authors and publish year	Country	Sample size	Age Mean (SD)	Male percent	Screening tools (depression and/or suicidal behavior)	Diagnosis	Study type/Follow-up time	Main Aim	Prevalence	Relevant findings
2006						affective and non-affective psychosis	longitudinal/4 years	and associated factors	presentation: 10%; Follow-up attempt suicide: 18.2%	presentation were associated with longer DUP
Follow-up suicide: 3%										
Bertelsen et al., 2007	Denmark	547	26 (6.3)	59%	Suicide attempts and ideation based on self-reporting; Suicide: Death register and death certificates	FEP: non-affective psychosis	Randomized controlled trial/5 years	Rates of suicide and predictive factors of suicidal behavior	Suicide: 1.3%	Depressive and psychotic symptoms (especially hallucinations) predicted suicidal plans and attempts, and persistent suicidal behavior and ideation were associated with high risk of attempted suicide
Robinson et al., 2009	Australia	661	ns (15–29)	65.65%	Patient medical record	FEP: affective and non-affective psychosis	Retrospective/18 months	Prevalence and predictors of suicide and suicide attempts before and during the first 18 months of treatment	Suicide attempt prior to entry: 14.3%; Suicide attempt during treatment: 8.7%; Suicide: 0.9%	Predictors of suicide attempt were: previous attempt, sexual abuse, comorbid polysubstance, greater insight, lower baseline functioning and longer time in treatment.
Dutta et al., 2010	UK	2723	33.6 (SD ns)	55.2%	Death certificates	FEP: affective and non-affective psychosis	Retrospective /mean follow up: 11.5 years	Rate of deaths by suicide	Suicide: 1.9% Proportionate mortality: 11.9%	The highest risk of suicide occurs soon after presentation but risk is elevated even a decade or longer later.
Fedyszyn et al., 2012	Australia	180 (cases:72; controls:108)	19.56 (2.73)	56.1%	Medical files CAD-SAS	FEP: affective and non-affective psychosis	Case-control study (retrospective)/18 months	1)Determine the relative importance of baseline, past and recent variables to prediction of suicidal behavior; 2)Identify recent characteristics that exert most influence on suicide risk levels	Suicidal attempt: 11.9%	Recent negative events and recent non-suicidal self-injurious behavior were strongest predictors of suicide-related behaviors during treatment for FEP
Mitter et al., 2013	Singapore	1397	27.7 (6.6)	50.8%	Medical records	FEP: affective and non-affective psychosis	Prospective longitudinal/2 years	Prevalence of suicides and associated risk factors	Suicide: 1.9%	Older patients with longer DUPs, higher PANSS positive and negative scores and better functioning appear to be at higher risk of suicide
Björkenstam et al., 2014	Sweden	2819	22.6 (ns)	58%	Death Register	FEP: affective and non-affective psychosis	Longitudinal, prospective study (cohort study)/not applicable	Prevalence of suicide and associated risk factors	Suicide: 4.29%	Impulsive behavior such as self-harm and family history of severe mental disorder or substance use are risk factors for suicide in first-episode psychosis
Ayesa-Arriola et al., 2015	Spain	397	28.94 (9.46)	56.9%	Medical records	FEP: non-affective psychosis	Longitudinal, prospective/3 years	Determine and characterize the highest risk period for suicide	Suicide attempts: 10.83% Suicide: 1.51%	Greatest suicide risk was found during the month before and 2 months after first contact; Severity of depressive symptoms and cannabis use are predominant risk factos across time
Chang et al.,	Hong-Kong	700	21.2 (3.4)	51.4%	Medical file review	FEP:	Longitudinal,	Prevalence and predictors of	Baseline (Suicide attempt	Previous suicide attempt,

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Table 1 *(continued)*

Authors and publish year	Country	Sample size	Age Mean (SD)	Male percent	Screening tools (depression and/or suicidal behavior)	Diagnosis	Study type/Follow-up time	Main Aim	Prevalence	Relevant findings
2015						affective and non-affective psychosis	Prospective/3-year	suicidal behavior	prior treatment): 10.6%; Follow-up: Suicidal behavior: 10%; suicide: 1%	history of substance abuse and poorer baseline functioning were associated with an increased risk for suicidal behavior after treatment initiation
Barret et al., 2015 CDSS item 8 (current suicidality)	Norway Follow-up suicidal behavior (suicidal CDSS item 8: 1–3): 20%	146	Ns (18–65)	62.3%	SCID-I interview (suicide attempts) Gaining insight during treatment was associated with reduced risk for suicidality; More depressive episodes before study entry, longer DUP, more suicide attempts six months prior to follow-up and depression at follow-up are predictors of suicidality at follow-up	FEP: non-affective psychosis	Prospective longitudinal/one year	Predictors of suicidality focusing on the relationship between insight and suicidality		Baseline suicidal behavior: 37%
Castelein et al., 2015	Netherlands	424	28.5 (9)	71.2%	Patient file search	FEP: affective and non-affective psychosis	Retrospective	Change in suicide risk comparing with a study made two decades ago; Identify predictors of suicide risk	Suicide: 2.4%	Higher age predict suicide Significant reduction in the suicide rate was found for people with psychosis over the past two decades

CAD-SAS: Classification Algorithm for the Determination of Suicide Attempt and Suicide; CASH: Comprehensive Assessment of Symptoms and History; CDSS: Calgary Depression Scale for Schizophrenia; CGI-BP: Clinical Global Impressions Scale – Bipolar Disorder; DSM-IV: Diagnostic and Statistical Manual of Mental Disorders, 4th Edition; FEP: first-episode psychosis; HDRS: Hamilton Rating Scale for Depression; ICD-10: International Classification of diseases, 10th Edition; PPD: Post-psychotic depression; SCID-I: Structured Clinical Interview for DSM-IV.

Table 2
Studies quality assessment according to EPHPP tool for quantitative studies (Thomas et al., 2004).

Study	Selection bias	Design	Confounders	Blinding	Data collection methods	Withdrawals and drop-outs	Total
Koreen et al. (1993)	Weak	Moderate	Moderate	Moderate	Strong	Strong	Moderate
Wassink et al. (1999)	Weak	Moderate	Moderate	Moderate	Strong	Weak	Weak
Iqbal et al. (2004)	Weak	Moderate	Moderate	Moderate	Strong	Weak	Weak
Romm et al. (2010)	Weak	Moderate	Moderate	Moderate	Strong	Not applicable	Moderate
Cotton et al., 2012	Weak	Moderate	Moderate	Moderate	Strong	Moderate	Moderate
Upthegrove et al. (2014)	Weak	Moderate	Weak	Moderate	Strong	Strong	Weak
Sönmez et al. (2016)	Weak	Moderate	Moderate	Moderate	Strong	Weak	Weak
Addington et al. (2004)	Weak	Moderate	Weak	Moderate	Strong	Strong	Weak
Clarke et al. (2006)	Weak	Moderate	Moderate	Strong	Moderate	Weak	Weak
Bertelsen et al. (2007)	Weak	Strong	Moderate	Moderate	Strong	Strong	Moderate
Robinson et al. (2009)	Weak	Weak	Moderate	Moderate	Strong	Strong	Weak
Dutta et al. (2010)	Weak	Weak	Strong	Moderate	Strong	Strong	Weak
Fedyszyn et al. (2012)	Weak	Moderate	Moderate	Moderate	Strong	Strong	Moderate
Mitter et al. (2013)	Weak	Moderate	Strong	Moderate	Moderate	Strong	Moderate
Björkenstam et al. (2014)	Strong	Moderate	Strong	Moderate	Strong	Strong	Strong
Ayesa-Arriola et al. (2015)	Weak	Moderate	Strong	Moderate	Strong	Moderate	Moderate
Chang et al., 2015	Weak	Moderate	Strong	Moderate	Strong	Strong	Moderate
Barret et al., 2015	Weak	Moderate	Strong	Moderate	Strong	Moderate	Moderate
Castelein et al. (2015)	Weak	Weak	Not applicable	Moderate	Strong	Moderate	Weak

Strong = No weak ratings, Moderate = One weak rating, Weak ≥ 2Weak ratings.

confounders, blinding, data collection methods, withdrawals and drop-outs. Each component has to be rated as “strong”, “moderate” or “weak” according to a standardized guide and dictionary. All six components made the overall rating of each study. Studies with no “weak” ratings and at least four “strong” ratings are considered strong. Those with less than four “strong” ratings and one “weak” rating are considered “moderate”. Those with two or more “weak” ratings are considered weak.

3. Results

3.1. Flow of included studies

Search results are summarized in the Prisma Flow Chart in Fig. 1. A total of 630 studies were identified through the search strategy from databases. Fifteen additional studies that met the inclusion criteria were found through a manual search of the reference section for relevant additional studies. Three hundred and fifty-nine articles remain after exclusion of duplicate articles. Three hundred and eight articles were excluded by reading of the title and abstracts. Thirty-two articles were excluded with reasons: 16 with insufficient data for analysis, 3 non-systematic review articles, 3 not stated prevalence rate of depression and/or suicidal behavior and 10 articles that only studied prodromal and/or acute psychotic phase. Finally, we included 19 articles in the systematic review (Table 1).

3.2. Quality assessment

The general quality of studies included was “weak” to “moderate”, with only one study “strong” (Björkenstam et al., 2014) (Table 2). Only Björkenstam et al. (2014) studied data from a nationwide cohort. The remaining studies selection bias was the rule because information was obtained from samples from clinical centers, mainly single-center and two-center and thus not representative of the target population. Two publications did not report conflicts of interest or statements about funding or grants (Iqbal et al., 2004; Sönmez et al., 2016).

3.3. Study characteristics and outcome measures

We included 7 articles that studied depressive symptoms (Cotton et al., 2012b; Iqbal et al., 2004; Koreen et al., 1993; Romm et al., 2010; Sönmez et al., 2016; Upthegrove et al., 2014; Wassink et al., 1999) and 12 articles that studied suicidal behavior (Addington et al., 2004; Ayesa-Arriola et al., 2015; Barrett et al., 2015; Bertelsen et al., 2007; Björkenstam et al., 2014; Castelein et al., 2015; Chang et al., 2014; Clarke et al., 2006; Dutta et al., 2010; Fedyszyn et al., 2012; Mitter et al., 2013; Robinson et al., 2009). The main outcome measures were prevalence of depressive symptoms and/or suicidal behavior and associated factors during the first years after first-episode psychosis. Main exclusion criteria were the presence of organic brain disorder and intellectual disability.

A total of 11490 patients were included, sample size ranged from 29 to 2819 patients, with mean age from 19.56 to 33.6 years, with male percentage from 50.8% to 77.14%. Fourteen studies were longitudinal/prospective, 3 retrospectives, 1 retrospective case-control and 1 randomized controlled trial. In longitudinal studies the follow-up time was between 12 months and 10 years.

The instruments used to measure depressive symptoms were Calgary Depression Scale for Schizophrenia (CDSS), Hamilton Depression Rating Scale (HDRS), Beck Depression Inventory (BDI) and Clinical Global Impression for Bipolar Disorder (CGI-BP). Suicidal behavior was mostly assessed by review of medical files. Death certificates confirmed suicide more frequently (Table 3).

3.4. Depressive symptoms

3.4.1. Prevalence

The reported prevalence of depressive symptoms after first-episode psychosis among the studies included ranged from 14.15% and 44.80%. All studies found significant rates with prevalence of depressive symptoms on different times of follow-up ranging from 12 months to 10 years. Studies evidenced that depressive symptoms diminished with follow-up time and treatment. However, Sönmez et al. (2016) clearly demonstrated that depressive symptoms progressively decrease with treatment but still significant even 10 years after first-episode psychosis (Sönmez et al., 2016). Using The Positive and Negative Syndrome Scale (PANSS) depression item (g6 ≥ 4) at baseline, at 1 year, at 2 years at 5 years and at 10 years authors found prevalence of depressive symptoms respectively 41%, 28%, 20%, 16% and 19%.

3.4.2. Correlates and risk factors

Many factors were identified as being associated with depressive symptoms after first-episode psychosis: anomalies of psychosocial development (Iqbal et al., 2004; Sönmez et al., 2016), poor premorbid childhood adjustment (Romm et al., 2010), greater insight (Cotton et al., 2012b), loss (Upthegrove et al., 2014), shame (Upthegrove et al.,

Table 3
Major measurement tools for depressive symptoms and suicidal behavior used in the studies.

Measure	Population	Items (n)	Scoring	Range	Interpretation	Cut-off
Depressive symptoms						
Beck Depression Inventory (BDI)	Adults and adolescents	21	0–3	0–63	0–13: minimal depression 14–19: mild depression 20–28: moderate depression 29–63: severe depression	≥14
Calgary Depression Scale for Schizophrenia (CDSS)	Adults and adolescents diagnosed with schizophrenia	9	0 to 3	0–27	≥5: depression	≥5
Clinical Global Impression for Bipolar Disorder (CGI-BP)	Adults	6	1 to 7 (items I, II, III)	Not applicable	Depression	> 3 (depression item)
Hamilton Depression Rating Scale (HDRS)-17 items	Adults	17	0 to 2 or 3 or 4	0–52	Depression	> 17
Positive and Negative Syndrome Scale (PANNS) (depression item)	Adults and adolescents	30 (including one of depression in general psychopathology subscale)	1 to 7	Not applicable	Depression	≥4 (depression item)
Suicidal behavior						
Beck Scale for Suicide ideation (BSSI)	Adults and adolescents	21	0 to 2 (items 1–19)	0–38	Higher scores indicate greater severity of suicidal ideation	ns
Beck Suicidal Intent Scale (SIS)	Patients who attempt suicide but survive	15 (with more 5 items not included in final score)	1 to 3	15–45	15–19: low intent 20–28: medium intent ≥29: high intent	≥20

2014), low level of persistent positive symptoms (Upthegrove et al., 2014) and longer DUP (Upthegrove et al., 2014). Regarding substance use the results were divergent some studies showed that substance abuse was associated with depressive symptoms after first-episode psychosis (Romm et al., 2010; Sönmez et al., 2016) and 1 study found substance use less common in those patients with depressive symptoms (Cotton et al., 2012b).

3.4.3. Treatment

No specific treatment or intervention studies were found regarding depressive symptoms after first-episode psychosis. Some samples studied were included in early intervention programs as treatment for first-episode psychosis (Cotton et al., 2012b; Iqbal et al., 2004; Upthegrove et al., 2014). Also Koreen et al. (1993) studied prospectively 70 patients with first-episode psychosis with a follow-up to 5 years and received usual treatment. Authors concluded that since depressive symptoms mostly resolved as the psychosis remitted, antidepressant therapy should be used only in that patients in whom depression persists (Koreen et al., 1993).

3.5. Suicidal behavior

3.5.1. Prevalence

The prevalence of suicide attempts after first-episode psychosis ranged from 2.9% to 18.2% and suicide from 0.4% to 4.29% in studies included. One study that measured suicidal behavior as whole (including suicidal ideation, suicide plan and/or suicide attempt) found a prevalence of 20% (Barrett et al., 2015).

3.5.2. Correlates and risk factors

As in depressive symptoms, a heterogeneity of factors associated with suicidal behavior (including suicide) were studied and found significant: previous suicide attempt (Barrett et al., 2015; Björkenstam et al., 2014; Chang et al., 2014; Fedyszyn et al., 2012; Robinson et al., 2009), sexual abuse (Robinson et al., 2009), comorbid polysubstance use (Robinson et al., 2009), lower baseline functioning (Chang et al., 2014; Robinson et al., 2009), longer time in treatment (Robinson et al., 2009), recent negative events (Fedyszyn et al., 2012), older patients (Castelein et al., 2015; Mitter et al., 2013), longer DUP (Barrett et al., 2015; Mitter et al., 2013), higher positive and negative psychotic symptoms scores (Mitter et al., 2013), family history of severe mental disorder (Björkenstam et al., 2014), substance use (Björkenstam et al., 2014; Chang et al., 2014), depressive symptoms (Ayesa-Arriola et al., 2015; Barrett et al., 2015), cannabis use (Ayesa-Arriola et al., 2015). Concerning insight the results were divergent with one study revealing that gaining insight during treatment was associated with reduced risk for suicidality (Barrett et al., 2015) and other showing that greater insight was predictor of suicidal behavior after first-episode psychosis (Robinson et al., 2009).

3.5.3. Treatment

Two studies make conclusions about treatment regarding suicidal behavior after first-episode psychosis. Bertelsen et al. (2007) researched treatment intervention in suicidal behavior in first-episode psychosis. It studied suicide rate and predictive factors of suicidal behavior in first-episode psychosis patients comparing treatment as usual and an early intervention program. Results showed lower probability of death by suicide in the specified treatment compared with standard treatment (Bertelsen et al., 2007). Also Addington et al. (2004) studied 290 first-episode psychosis patients in Canada in a longitudinal prospective study with a follow-up of 1-year. Authors concluded that first-episode psychosis programs can reduce suicidal behavior (Addington et al., 2004).

4. Discussion

This is the first systematic review to summarize the available research of depressive symptoms and suicidal behavior and associated factors in the period after affective and/or non-affective first-episode psychosis. We included articles from 12 countries all over the world with 11490 patients. Seventeen (almost 90%) of the articles included were published in the past 12 years, attesting to the increase interest in depressive symptoms and suicidal behavior following first-episode psychosis in recent years. We found convincing evidence that depressive symptoms and suicidal behavior have high rates in the years after first-episode psychosis. There is a high heterogeneity across individual studies regarding factors associated to depressive symptoms and suicidal behavior which difficult robust evidence. All studies included had a majority of males in first-episode psychosis samples, ranging from 50.8% to 77.14%. This is in line with some studies suggesting higher incidence of psychotic disorders in men (Castle et al., 1993; Lewine et al., 1984).

Our results should be interpreted with caution as significant methodological limitations condition generalization of the findings. Majority of the studies included only non-affective psychotic patients which is quite artificial in the early phase of psychotic disorders namely because of the diagnostic instability (Heslin et al., 2015; Tohen et al., 2016). It is quite easy to hypothesize that including also affective psychotic patients the rates of depressive symptoms and suicidal behavior will be different and more approximate to daily clinical practice. Other significant limitation from results of different studies are the instruments used namely to measure depressive symptoms. The use of different instruments certainly affects different prevalence of depressive symptoms found. Also different cut-offs were used for the same instrument which limits comparisons between studies. For example, to evaluate depression Upthegrove and al. in 2014 (Upthegrove et al., 2014) used a cut-off of 7 (depression CDSS $\geq$ 7) in CDSS, with the same instrument Sönmez et al. in 2016 used the cut-off of 6 (depression CDSS $\geq$ 6) (Sönmez et al., 2016). For evaluation of suicidal behavior, the most used method was the analysis of medical records for suicide attempts and death certificates for suicide which are more reliable. One study evaluated suicidal behavior using item 8 from CDSS (Barrett et al., 2015).

Research indicates that the period of major risk to depression and suicidal behavior is the few months after first-episode psychosis (Ayesa-Arriola et al., 2015; Cotton et al., 2012a; Dutta et al., 2010) with a reduction with follow-up and treatment but even with long period of follow-up the rates are high. For example Sönmez et al. (2016) studied 299 first-episode psychosis patients with a follow-up of 10 years. It was found a prevalence of depressive symptoms of 41% at baseline and 19% at 10-year follow-up (Sönmez et al., 2016).

Studies researched different factors regarding correlates and risk factors to depressive symptoms and/or suicidal behavior after first-episode psychosis. Comparison of the findings was not possible because results are limited to few articles. The major factors associated with depressive symptoms after first-episode psychosis were anomalies/difficulties in psychosocial and functioning in childhood in 3 studies (Iqbal et al., 2004; Romm et al., 2010; Sönmez et al., 2016) and substance and alcohol use in 2 studies (Romm et al., 2010; Sönmez et al., 2016). The most consistent factors associated with suicidal behavior after first-episode psychosis were previous suicidal attempts found in 7 studies (Barrett et al., 2015; Bertelsen et al., 2007; Björkenstam et al., 2014; Chang et al., 2014; Clarke et al., 2006; Fedyszyn et al., 2012; Robinson et al., 2009), depressive symptoms in 3 studies (Ayesa-Arriola et al., 2015; Barrett et al., 2015; Bertelsen et al., 2007) and longer DUP in 3 studies (Barrett et al., 2015; Clarke et al., 2006; Mitter et al., 2013).

Previous studies referred that etiology of depressive symptoms in the period after first-episode psychosis may represent a core part of the acute illness or it is associated with the subjective reaction to psychosis and its deficits impacting in daily life activities (Ventriglio et al., 2016). In line with this hypothesis is the included study made by Koreen et al. in 1993 in USA (Koreen et al., 1993). Independently of the etiology of depressive symptoms, studies demonstrate that depression diminished with antipsychotic treatment (Koreen et al., 1993; Sönmez et al., 2016).

The research for treatment of depressive symptoms and/or suicidal behavior after first-episode psychosis is very limited. Some authors conclude that early intervention programs reduced suicidal behavior after first-episode psychosis (Addington et al., 2004; Bertelsen et al., 2007). The only randomized controlled trial published was the included study of Bertelsen et al. (2007) made in Denmark as part of the OPUS Trial (Bertelsen et al., 2007). This is a longitudinal, prospective study with 5-year follow-up of 547 patients with first-episode schizophrenia spectrum psychosis in Denmark. Integrated treatment including assertive community treatment model with family involvement and social skills training was compared with standard treatment at a community mental health center. Suicidal behavior and clinical and social status were assessed using validated interviews and rating scales. Authors found a suicide rate of 1.3% during follow-up. Results showed lower probability of death by suicide in the integrated treatment compared with standard treatment. These results underline the importance of dissemination of specific programs on early intervention in first-episode psychosis patients worldwide.

Few limitations of this review exist. We did not perform a meta-analysis of the findings, which may have added additional information. Different methodologies (sample, study type, instruments used etc.) of studies jeopardizes meta-analysis construction. It also has to be considered that the quality assessment with EPHPP was “weak” for a substantial part of the studies included. Main reasons were selection bias, low evidence level of study design and bias caused by uncontrolled confounding variables. We also compared rates and risk factors for depression and suicidal behavior in studies that used different methodologies that certainly gave different results. Two major differences between studies were diagnoses included (affective *versus* non-affective psychosis) and instruments used to measure depressive symptoms. Also majority of the included studies were from Europe, USA and other developed countries which could restrict the generalization of findings. The exact time when the depressive symptoms found begun are not possible to determine in some papers. We could speculate that in some researches depressive symptoms could have begun not after the first-episode psychosis but in the prodrome or during acute phase of first-episode psychosis and continue in the period after first-episode psychosis. Finally, papers written in other languages than English and Portuguese were not included and therefore some interesting researches may have not been considered.

5. Conclusions

The current systematic review provides convincing evidence that depressive symptoms and suicidal behavior have high rates in the first years after first-episode psychosis. There is a high heterogeneity of factors associated studied between studies. Treatment and early intervention programs can reduce depressive symptoms and suicidal behavior. Some methodological limitations in published studies limit generalization of the findings. Future studies should include more often affective psychosis, more than one center, other countries than Europe and USA/Canada and adequate sample sizes for more meaningful results. Data suggest that there is an opportunity to intervene and reduce depressive symptoms and suicidal behavior after first-episode psychosis.

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