Contents lists available at ScienceDirect

Journal of Affective Disorders

journal homepage: www.elsevier.com/locate/jad

Research paper

Prevalence of comorbid depression in schizophrenia: A meta-analysis of observational studies

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ARTICLE INFO

Keywords:

Depression

Prevalence

Schizophrenia

Meta-analysis

ABSTRACT

Introduction: Comorbid depressive symptoms (depression thereafter) often occur in schizophrenia and are associated with negative outcomes. This meta-analysis estimated the prevalence of comorbid depression and its associated factors in schizophrenia.

Methods: Both international (PubMed, EMBASE, PsycINFO, and Web of Science) and Chinese (WANFANG and CNKI) databases were systematically searched. Studies with data on the prevalence of comorbid depression in schizophrenia measured with the Calgary Depression Scale for Schizophrenia (CDSS) were included. Randomeffects models were used in all analyses.

Results: Fifty-three studies covering 9,879 patients were included. The pooled prevalence of comorbid depression was 28.6% (95%CI: 25.3%-32.2%). Subgroup analyses revealed that studies examining inpatients, being published in Chinese language, or those with lower CDSS cut-od values reported higher depression rates. Meta-regression analyses indicated that the rate of depression was positively associated with publication year, proportion of males, mean age, and severity of psychotic symptoms, and negatively associated with illness duration and study quality.

Conclusion: Comorbid depression is common in schizophrenia. Due to its negative impact on patients' quality of life and prognosis, regular screening and effective treatment for comorbid depression should be implemented in patients with schizophrenia.

1. Introduction

Comorbid depressive symptoms (depression thereafter) are present in all phases of schizophrenia (Naguy, 2018; Upthegrove, 2009) and correlated with higher risk of suicide (Ayesa-Arriola et al., 2015; Bagaric et al., 2013; Li et al., 2018), polypharmacy (Lako et al., 2012b), worse psychosocial functioning (Schennach-Wolff et al., 2011), and poorer quality of life (Alessandrini et al., 2016; Sim et al., 2004), and functional outcomes (Conley et al., 2007). Because comorbid depression is often under-diagnosed in schizophrenia, patients may not receive appropriate treatment (Lako et al., 2012b; Majadas et al., 2012;

Upthegrove et al., 2017).

Elucidating the pattern of comorbid depression and its correlates in schizophrenia could benefit the management and prognosis of affected patients. The prevalence of comorbid depression varies greatly across studies; for instance, one study (Dai et al., 2018) found the rate of depression measured with the 17-item Hamilton Depression Rating Scale (HAMD-17) in schizophrenia inpatients was 54.6%, while the corresponding figures were 12.9% when using the Present State Examination (PSE) (Barnes et al., 1989) and 31% in outpatients with the Calgary Depression Scale for Schizophrenia (CDSS) (Majadas et al., 2012). Discrepancies between these studies could be partially due to

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https://doi.org/10.1016/j.jad.2020.04.056

Received 9 October 2019; Received in revised form 10 March 2020; Accepted 27 April 2020 Available online 12 May 2020

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different study settings, the severity of psychotic symptoms, and assessment instruments.

Several scales have been used to assess comorbid depression in schizophrenia including generic ones, such as the HAMD and PSE, that have not been validated in schizophrenia and they are not as sensitive as schizophrenia-specific measures, such as the CDSS. The 9-item CDSS was developed to identify comorbid depression in schizophrenia; its total score ranges from 9 to 27 with a higher total score indicating more severe depression. The CDSS has satisfactory psychometric properties and has been widely used (Lako et al., 2012a; Scholes and Martin, 2013). Different CDSS cutoff values have been applied in research and clinical practice: a total score of ≥ 5 (Hani et al., 2016), ≥ 6 (Chang et al., 2015), ≥ 7 (Fountoulakis et al., 2017), >7 (Thomas et al., 2014), or ≥ 12 (Üçok et al., 2013).

The frequency of depression in schizophrenia ranges from 7% to 75% (Siris, 2000). The lack of a systematic literature search and the use of different depression measures may have contributed to the highly variable results and obscure conclusions about comorbidity rates. To date, no meta-analyses or systematic reviews have been published using schizophrenia-specific measures on comorbid depression. To address this gap, a meta-analysis of observational studies was performed on the prevalence and moderating factors of comorbid depression measured by the CDSS in schizophrenia.

2. Method

2.1. Search strategy

The principle of Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) was followed. Both international (PubMed, EMBASE, PsycINFO, and Web of Science) and Chinese (WANFANG and CNKI) databases were searched systematically and independently by two authors (WL and YY) from their inception until February 27th, 2019. The following key search terms were used: 'schizophrenia', 'schizophrenic disorder', 'disorder, schizophrenic', 'Disorders, Schizophrenic', 'schizophrenic disorders', 'dementia praecox', 'Calgary Depression Scale for Schizophrenia', and 'CDSS'. Additional publications were hand-searched from reference lists of relevant reviews and publications. The research protocol was predefined and registered with the International Prospective Register of Systematic Reviews (PROSPERO: CRD42019135031).

2.2. Study criteria and selection

Studies that fulfilled the following criteria were included: (1) patients diagnosed with schizophrenia according to international or local diagnostic criteria, such as 3rd, 4th and 5th Revisions of the Diagnostic and Statistical Manual of Mental Disorders (DSM; DSM-3, DSM-4, and DSM-5) (American Psychiatric Association, 1980, 1994, 2013), the International Statistical Classification of Diseases and Related Health Problems, 10th Revision (ICD-10) (World Health Organization, 1992), and the Chinese Classification of Mental Disorders, 3rd Revision (CCMD-3) (Psychosis Branch of Chinese Medical Association, 2001). The diagnostic criteria for schizophrenia in CCMD-3 and ICD-10 are almost the same (Chen, 2002), with high consistency (Phillips, 2001); (2) reporting prevalence of comorbid depression as measured using the CDSS with validated cutoff values; (3) peer-reviewed articles published in English or Chinese language. Studies conducted on special populations (e.g., older patients or those at high risk of suicide) (Depp et al., 2011; Lindenmayer et al., 2003; Lippi et al., 2009), case studies, and commentaries were excluded.

The literature search and selection of studies were independently performed by the same two authors (WL and YY). Eligibility of studies was determined by reading full texts of articles after screening their titles and abstracts. Any disagreements were settled by consulting the corresponding author (YTX). If multiple studies were published based on the same dataset, only those with a larger sample size were included. Therefore, some relevant studies were not included (Andrianarisoa et al., 2017; Ayesa-Arriola et al., 2014; Fond et al., 2016; Grover et al., 2018; Maggini et al., 2004; Rey et al., 2017). Additional information from the included studies was obtained by contacting first or corresponding authors by email.

2.3. Data extraction

The same two authors (WL and YY) independently extracted data including the study and patients' characteristics, the prevalence of depression, and the CDSS cut-off values, using a data collection form. Only baseline data were extracted from prospective cohort studies.

2.4. Quality assessment

Study quality was independently rated by two authors (WL and YY) using a quality assessment instrument for epidemiological studies (Parker, 2008). The assessment covered the following 6 domains: definition and representativeness of targeted population, sampling methods, response rate, definition of outcome variable, and validation of assessment instrument. Higher total scores reflected better study quality.

2.5. Statistics

Data analyses were conducted with the Comprehensive Meta-Analysis Program, Version 2.0 (CMA 2.0) (http://www.meta-analysis. com/). Considering variable demographic characteristics and sampling methods across studies, the random-effects model was applied to estimate the pooled prevalence of depression. The logit transformation was used in the CMA 2.0 to calculate the prevalence of depression in each study. The I^2 statistic was used to test heterogeneity; I^2 values > 50% were regarded as indication of high heterogeneity (Higgins et al., 2003). Potential sources of heterogeneity were examined by subgroup, meta-regression and sensitivity analyses. Subgroup analyses were conducted for categorical variables including publication language (Chinese vs. English), country (China vs. other countries), national economic level (high-income countries vs. middle-income countries) (Worldbank, 2017), study site (multicenter vs. single site), sampling method (consecutive vs. purposive vs. random sampling), sample size $(<124 \text{ vs.} \ge 124; \text{ dichotomized using the median split}), CDSS cut-off$ value (studies with cut off value of " \geq x" were grouped with those "> x-1"), diagnosis (schizophrenia alone vs. schizophrenia and other related psychotic disorders), type of patients (inpatient vs. outpatient vs. community), and phase of schizophrenia (acute vs. other stages). Metaregression analyses were conducted for continuous variables: publication year, proportion of males, mean age, mean duration of illness, quality assessment score, and the Positive and Negative Symptom Scale (PANSS) total and subscale scores. Sensitivity analyses were carried out by removing each study one by one to examine the consistency of the primary results (Higgins and Green, 2011). Publication bias was tested via Funnel plots and Begg's rank test (Begg and Berlin, 1988). Level of significance was set as P < 0.5 (two-tailed).

3. Results

3.1. Study characteristics

Study selection procedure is shown in Fig. 1. Fifty-three studies (8 in Chinese and 45 in English) involving 9,879 schizophrenia patients published between 1999 and 2018 were included in the meta-analysis. Study characteristics are presented in Supplementary Table 1. Sample sizes ranged from 39 to 1,427 with a median of 124. The mean age of patients ranged from 24.5 to 53.7 years with a median of 35.9 years. Illness duration ranged from 1.86 to 26.09 years (median=11.86

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Fig. 1. PRISMA flow chart.

years). The DSM-IV and its text version were the most used diagnostic criteria (n=39). CDSS cutoff values of $>4/\ge 5$ (n=6), $>5/\ge 6$ (n=17), $>6/\ge 7$ (n=23), >7 (n=2), and $>11/\ge 12$ (n=4) were applied in the included studies. Study quality scores ranged between 3 and 6; 46 studies (86.8%) were rated as 4 or 5 (Supplementary Table 2).

3.2. Prevalence of comorbid depression

The pooled prevalence of comorbid depression in schizophrenia was 28.6% (95%CI: 25.3%-32.2%, $I^2 = 92.30\%$); rates ranged from 4.6% (95%CI: 2.3%-8.9%) (Fountoulakis et al., 2017) to 65.1% (95%CI: 60.1%-69.8%) (Peitl et al., 2016) (Fig. 2).

3.3. Subgroup and meta-regression analyses

Table 1 displays the results of subgroup analyses. Inpatients presented with a significantly higher prevalence of depression than outpatients and community-dwelling patients (P=0.014). Studies using the cut off value of > 11 reported the lowest depression rate (15.0%, 95%CI: 10.6%-20.8%, $I^2=42.29\%$) while studies with the cut-off of > 4 had the highest rate (32.3%, 95%CI: 25.8%-39.5%, $I^2=77.44\%$) (P=0.001). Studies published in Chinese language reported higher prevalence than those in English language (P=0.038).

Meta-regression analyses revealed that publication year ($\beta = 0.022$, P < 0.001), proportion of males ($\beta = 0.015$, P < 0.001), mean age ($\beta = 0.009$, P = 0.026), and PANSS total ($\beta = 0.030$, P < 0.001) and all subscale scores (positive symptoms: $\beta = 0.047$, P < 0.001; negative

Study name

Event rate and 95% CI

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Addingson Ce Cur, 2000 0.111 0.120 0.211 0.120 0.211 0.120 0.211 0.120 0.211 0.133 0.4101 0.000 13/60 Veren et al., 2014 0.212 0.121 0.379 -3.266 0.001 9/40 Grover et al., 2017 0.228 0.182 2.50.85 0.000 55/206 Grover et al., 2017 0.287 0.315 0.322 -6.413 0.000 55/206 Grossi et al., 2017 0.286 0.257 0.315 -12.606 0.000 55/206 Varabska et al., 2016 0.290 0.291 0.377 -5.746 0.000 56/200 Varth-Reyes et al., 2011 0.303 0.242 0.377 -5.746 0.000 48/161 Adartin-Reyes et al., 2016 0.290 0.231 0.327 -5.746 0.000 66/277 Che et al., 2016 0.303 0.240 0.376 -6.145 0.000 46/14 4 Vajadas et al., 2012 0.321 0.221 -3.269<	Addinaton et al 2003	0.200	0.159	0.324	-7 218	0.000	38 / 180					
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Ceruce an, 2010 0.230 0.133 0.222 -5.063 0.1000 2.3 / 100 Varalis et al, 2012 0.267 0.211 0.323 -6.413 0.000 25 / 206 Varabska et al, 2013 0.290 0.135 -12.606 0.000 26 / 920 Varabska et al, 2016 0.290 0.231 0.377 -5.746 0.000 48 / 151 Margerial et al, 2006 0.298 0.233 0.377 -6.070 86 / 277 Attin-Reyes et al., 2011 0.301 0.242 0.367 -5.548 0.000 46 / 178 (u, 2016 0.310 0.259 0.367 -6.145 0.000 46 / 178 (u, 2016 0.311 0.242 0.367 -6.145 0.000 46 / 148 4gladas et al., 2012 0.313 0.221 0.422 -3.269 0.001 25 / 90 Kenwick et al., 2012 0.313 0.221 0.422 -3.269 0.001 25 / 90 Verewick et al., 2013 0.336 0.410 -3.862	Giuver et al., 2017	0.228	0.182	0.283	-0.349	0.000	22 / 100					
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Vrabska et al., 2018 0.290 0.195 0.407 -3.37 0.001 207 69 Wang et al., 2017 0.294 0.224 0.357 -5.746 0.000 58 / 200 Vang et al., 2017 0.294 0.223 0.373 -4.970 0.000 48 / 161 Matchin-Reye et al., 2011 0.301 0.242 0.367 -5.548 0.000 62 / 206 Mi et al., 2016 0.303 0.240 0.357 -5.099 0.000 46 / 178 Ku, 2016 0.310 0.224 0.367 -6.145 0.000 46 / 178 Ku, 2015 0.311 0.224 0.397 -4.484 0.000 25 / 80 Kunsite at l., 2012 0.310 0.224 0.412 -3.269 0.001 27 / 80 Kuch et al., 2012 0.322 0.224 0.410 -3.862 0.000 47 / 146 Gjelby et al., 2011 0.340 0.253 0.440 -3.091 0.002 33 / 97 Votot et al., 2013 0.341 <t< td=""><td>Rossi et al., 2017</td><td>0.285</td><td>0.257</td><td>0.315</td><td>-12.606</td><td>0.000</td><td>262 / 920</td><td></td><td></td><td></td><td></td><td></td></t<>	Rossi et al., 2017	0.285	0.257	0.315	-12.606	0.000	262 / 920					
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Martin-Reyes et al., 2011 0.301 0.242 0.367 -5.548 0.000 62 / 206 Mi et al., 2016 0.303 0.240 0.375 -5.099 0.000 54 / 178 (u, 2016 0.310 0.229 0.367 -6.145 0.000 86 / 277 Chen et al., 2015 0.311 0.224 0.414 -3.491 0.000 28 / 90 Michail et al., 2012 0.313 0.221 0.422 -3.269 0.001 25 / 80 venwick et al., 2012 0.322 0.251 0.402 -4.206 0.000 47 / 146 (jelby et al., 2015 0.330 0.244 0.311 -12.178 0.000 479 / 1427 Maurino et al., 2011 0.340 0.253 0.440 -3.091 0.002 33 / 97 Vote et al., 2013 0.345 0.253 0.450 -2.846 0.004 30 / 87 Ekinci et al., 2012 0.350 0.263 0.447 -2.356 0.008 37 / 102 Schennach et al., 2011 0.357 0.254 0.475 -2.366 0.006 37 / 102 <td< td=""><td>Maggini et al., 2006</td><td>0.298</td><td>0.233</td><td>0.373</td><td>-4.970</td><td>0.000</td><td>48 / 161</td><td></td><td></td><td></td><td></td><td></td></td<>	Maggini et al., 2006	0.298	0.233	0.373	-4.970	0.000	48 / 161					
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-1.00 -0.50 0.00 0.50		0.286	0.253	0.322	-10.699	0.000	3084 / 9879	I			■	
								-1.00	-0.50	0.00	0.50	

Statistics for each study

Fig. 2. Prevalence of depression in schizophrenia.

symptoms: β =0.080, *P*<0.001; general psychopathology: β =0.047, *P*<0.001) were positively associated with the prevalence of comorbid depression (Table 2). Duration of illness (β =-0.069, *P*<0.001) and study quality (β =-0.206, *P*<0.001) were negatively associated with depression rates (Table 2).

removed one by one from the analysis. The Begg's test (z=2.201, P=0.027) and funnel plot analysis revealed publication bias (Supplementary Fig. 1).

Favours A

Favours B

4. Discussion

3.4. Sensitivity analysis and publication bias

The primary results did not change significantly after studies were

To the best of our knowledge, this was the first meta-analysis that estimated the prevalence of comorbid depression in schizophrenia. The 28.6% (95%CI: 25.3%-32.2%) comorbid depression is a similar figure

Table 1

Subgroup analyses of rate of depression in schizophrenia.

Subgroups	Categories (number of studies)	Rate of depression (%)	95%	95% CI		Sample size	<i>I</i> ² (%)	P (within subgroup)	Q (P across subgroups)
Language of publication	Chinese (8)	33.2	29.9	36.8	416	1,266	39.95	0.112	4.30 (0.038)
	English (45)	27.6	23.9	31.7	2,668	8,613	93.37	< 0.001	
Country	China (10)	32.2	27.0	37.9	594	1,832	83.23	< 0.001	1.73 (0.188)
	Other countries (43)	27.7	23.8	31.9	2,490	8,047	93.23	< 0.001	
Income	High-income (27)	27.1	23.5	31.1	1,635	5,748	88.69	< 0.001	0.77 (0.380)
	Middle-income (26)	30.2	24.7	36.4	1,449	4,131	93.80	< 0.001	
Study Site	Multicenter (17)	26.1	21.8	30.9	1,332	4,618	90.29	< 0.001	0.61 (0.436)
	Single site (29)	28.7	24.1	33.8	1,314	4,244	91.22	< 0.001	
Sampling method	Consecutive (15)	27.4	23.1	32.1	619	2,135	80.81	< 0.001	2.26 (0.322)
	Purposive (1)	22.8	18.2	28.3	61	267	-	-	
	Random (3)	31.4	18.2	48.5	98	329	86.11	0.001	
Sample size*	<124 (26)	27.5	23.2	32.2	565	2,029	79.59	< 0.001	0.43 (0.511)
	≥124 (27)	29.7	25.1	34.8	2,519	7,850	95.21	< 0.001	
CDSS cut-off	>4/≥5 (6)	32.3	25.8	39.5	311	897	77.44	< 0.001	17.60 (0.001)
	>5/≥6 (17)	29.7	25.9	33.8	994	3,381	82.11	< 0.001	
	>6/≥7 (23)	29.0	23.0	35.9	1,647	4,960	95.38	< 0.001	
	>7 (2)	31.2	13.2	57.5	56	220	89.24	0.002	
	>11 or ≥12 (4)	15.0	10.6	20.8	51	351	42.29	0.158	
Diagnosis	Schizophrenia (38)	29.0	25.1	33.3	2,508	7,758	92.98	< 0.001	0.14 (0.705)
-	Schizophrenia and other related	27.6	21.7	34.3	576	2,121	89.51	< 0.001	
	psychotic disorders (15)								
Illness phase	Acute (5)	31.0	22.2	41.3	235	671	84.01	< 0.001	0.61 (0.738)
	Other status [#] (18)	29.8	22.5	38.2	1,043	3,022	95.19	< 0.001	
	Mixed (5)	25.0	15.2	38.2	153	605	89.24	< 0.001	
Patient type	Inpatients (16)	35.5	28.2	43.5	1,045	2,538	93.53	< 0.001	10.67 (0.014)
	Outpatients (11)	25.8	21.8	30.2	668	2,517	79.21	< 0.001	
	Community (1)	26.7	21.1	33.2	55	206	-	-	
	Mixed (16)	20.5	15.9	26.0	456	2,246	87.55	< 0.001	

Abbreviation: CI: confidential interval.

Containing upper middle-income and lower middle-income countries.

* Grouped by median sample size

[#] Including patients at stages of schizophrenia: chronic, stable, remitted, and residual.

Table 2

Meta-regression of rate of depression in schizophrenia.

Moderators	Number of studies	Slope	Intercept	Р						
Publication year	53	0.022	-46.032	< 0.001						
Proportion of males (%)	51	0.015	-1.737	< 0.001						
Mean age (year)	48	0.009	-1.066	0.026						
Duration of illness (year)	23	-0.069	0.244	< 0.001						
Quality score	53	-0.206	0.175	< 0.001						
Positive and Negative Symptom Scale (PANSS)										
Total score	22	0.030	-2.959	< 0.001						
Positive scale	24	0.047	-1.496	< 0.001						
Negative scale	23	0.080	-2.277	< 0.001						
General psychopathology scale	20	0.047	-2.424	< 0.001						

to the modal rate (25%) found in a previous review (Siris, 2000). Comorbid depression can have different expressions in schizophrenia: it may be related to positive symptoms in the acute phase and can remit with antipsychotic treatment (Bustamante et al., 1994; Emsley et al., 1999; Koreen et al., 1993), particularly with atypical antipsychotics (Leucht et al., 2009), or overlaps with negative symptoms in the postpsychotic or chronic phase (Majadas et al., 2012; Rabany et al., 2013). Still, depression could be present through all phases of schizophrenia as an independent and significant symptom dimension (Arabska et al., 2018; Grover et al., 2018; Upthegrove et al., 2017). As expected, in this meta-analysis depression rate was positively associated with positive, negative and general psychopathology scales of the PANSS. In addition, some studies found associations between comorbid depression, extrapyramidal symptoms (EPS) and use of antipsychotics medications (Gebhardt et al., 2008; Siris, 2000; Weng et al., 2019), which however still needs further replications, because both EPS and depressive symptoms could be the phenotype of schizophrenia and side effects of antipsychotic medications (Majadas et al., 2012; Weng et al., 2019).

Gender difference in schizophrenia has been extensively studied (Mendrek and Mancini-Marïe, 2016), but the association between comorbid depression and gender is still unclear. Significantly higher depression rates in male patients were found in some studies (Geddes et al., 1994; Hambrecht et al., 1992), while others have reported higher risk among female patients (Goldstein and Link, 1988) or no gender differences (Shtasel et al., 1992). This meta-analysis found that male patients were more likely to suffer from comorbid depression. Apart from gender, rates of comorbid depression increased with age. Stressful life events, such as chronic medical conditions and heavy occupational stress, are more common in older people, which could increase the risk of comorbid depression (Katon, 2011; Meader et al., 2011). Schizophrenia patients face higher risk of chronic diseases with increasing age due to poverty, self-neglect and long-term use of psychotropic medications (Fischer and Buchanan, 2017). In addition, work-related stress often increases in schizophrenia patients because of severe occupational dvsfunction and social isolation (American Psychiatric Association, 2013), both of which could increase the likelihood of comorbid depression with age as found in this metaanalysis.

Longer illness duration has a negative impact on cognitive deficits and social functioning in schizophrenia (Altamura et al., 2015) and is associated with higher level of self-stigma (Vrbova et al., 2016), poorer insight (Carroll et al., 1999), and demoralization (Cavelti et al., 2012), which, in turn, may raise the risk for comorbid depression (Belvederi Murri et al., 2015; Dai et al., 2018; Hill et al., 2019; López-Moríñigo et al., 2014; Majadas et al., 2012; Rapaport et al., 2002; Vidovic et al., 2016; Wang et al., 2019; Xu et al., 2018). Contrary to these findings, in this meta-analysis, longer illness duration was related to lower rates of comorbid depression. It is plausible that patients with shorter illness duration are at higher risk for comorbid depression because they have not yet adapted to negative psychosocial outcomes caused by schizophrenia.

Meta-regression analysis revealed higher rates of comorbid depression in more recent studies. This trend could be partly due to the heightened attention and recognition of comorbid depression and its negative outcomes by health professionals, patients, and their relatives (Halbreich et al., 2019; Upthegrove et al., 2017). As a result, patients with comorbid depression may be more willing to seek help from mental health services (Picco et al., 2018). Inpatients were also more likely to suffer from comorbid depression than other types of patients. Most hospitalized schizophrenia patients experience relapse and more severe psychiatric symptoms, which could be associated with an increased likelihood of comorbid depression (Geddes et al., 1994; Kessler and Lev-Ran, 2019; Siris, 2000). Studies published in Chinese reported a higher depression rate than those published in English. Six of the 8 studies in Chinese included inpatients, 1 study covered outpatients, and another comprised both in- and outpatients. Compared to outpatients, inpatients are more likely to present severe psychiatric symptoms and comorbid depression. Comorbid depression rate was also associated with different CDSS cutoff values. As expected, studies using a lower cutoff value reported a higher prevalence of depression, except for the two with a cut-off of 7, probably due to the small number of studies. Similar to other meta-analyses of epidemiological studies (Cao et al., 2017; Li et al., 2019; Zeng et al., 2019), higher rates of comorbid depression were related to lower study quality in this study. Findings of poor-quality studies are unreliable since they examined less representative samples and lower response rates.

The strengths of this meta-analysis are the large number of included studies, the cumulative sample size of 9,879 patients, and the selection of studies based on the CDSS, a schizophrenia-specific measure of depression. However, several limitations should be acknowledged. First, most studies were conducted in middle/high-income countries, which limits the generalizability of the findings to low-income countries. Second, factors related to comorbid depression in schizophrenia, for instance, the impact of substance misuse and clinical management, could not be explored due to insufficient reporting of these data. Third, highly variable comorbidity rates were observed even with applying a schizophrenia-specific depression instrument. Some authors have concluded that high heterogeneity is unavoidable in meta-analysis of epidemiological studies (Li et al., 2016; Long et al., 2014; Winsper et al., 2013). Moderator analyses in this study have attempted to identify patient characteristics and methodological factors that could account for differing depression comorbidity estimates in the literature. Fourth, due to logistical reasons, only studies published in English and Chinese were searched. Fifth, apart from validated cutoff values, certain statistical methods based on means and SDs of CDSS (http:// onlinestatbook.com/2/calculators/normal.html) (Furukawa et al., 2005) could generate prevalence of comorbid depression. However, this meta-analysis only included studies reporting prevalence of comorbid depression calculated using validated CDSS cutoff values.

In conclusion, this meta-analysis confirmed that comorbid depression is common in schizophrenia and identified several factors that are related to the frequency of comorbidity. Considering the negative effects of depression on the patients' wellbeing and prognosis, routine screening, and pharmacological (Gregory et al., 2017; Leucht et al., 2009) and psychosocial interventions (Donde et al., 2018) should be considered for patients with schizophrenia.

Role of funding

The study was supported by the National Science and Technology Major Project for investigational new drug (2018ZX09201-014), the Beijing Municipal Science & Technology Commission (No. Z181100001518005), and the University of Macau (MYRG2019-00066-FHS).

CRediT authorship contribution statement

Wen Li: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Resources, Software, Writing - original draft. Yuan Yang: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Resources, Software, Writing - original draft. Feng-Rong An: Formal analysis, Funding acquisition, Investigation, Project administration. Ling Zhang: Funding acquisition, Project administration. Gabor S. Ungvari: Writing - review & editing. Todd Jackson: Writing - original draft. Zhen Yuan: Investigation. Yu-Tao Xiang: Conceptualization, Funding acquisition, Methodology, Project administration, Resources, Supervision.

Declaration of Competing Interest

The authors declare that they have no conflicts of interest concerning this paper.

Acknowledgments

None.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jad.2020.04.056.

References

- Alessandrini, M., Lançon, C., Fond, G., Faget-Agius, C., Richieri, R., Faugere, M., Metairie, E., Boucekine, M., Llorca, P.M., Auquier, P., Boyer, L., 2016. A structural equation modelling approach to explore the determinants of quality of life in schizophrenia. Schizophr. Res. 171, 27–34. https://doi.org/10.1016/j.schres.2016.01.012.
- Altamura, A.C., Serati, M., Buoli, M., 2015. Is duration of illness really influencing outcome in major psychoses? Nord. J. Psychiatry 69, 403–417. https://doi.org/10.3109/ 08039488.2014.990919.
- American Psychiatric Association, 1980. Diagnostic and Statistical Manual of Mental Disorders, Third Edition (DSM-3). APA, Washington, DC.
- American Psychiatric Association, 1994. Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-4). APA, Washington, DC.
- American Psychiatric Association, 2013. Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5). APA, Washington, DC.
- Andrianarisoa, M., Boyer, L., Godin, O., Brunel, L., Bulzacka, E., Aouizerate, B., Berna, F., Capdevielle, D., Dorey, J.M., Dubertret, C., Dubreucq, J., Faget, C., Gabayet, F., Llorca, P.M., Mallet, J., Misdrahi, D., Rey, R., Richieri, R., Passerieux, C., Schandrin, A., Tronche, A.M., Urbach, M., Vidailhet, P., Schurhoff, F., Fond, G., 2017. Childhood trauma, depression and negative symptoms are independently associated with impaired quality of life in schizophrenia. Results from the national FACE-SZ cohort. Schizophr. Res. 185, 173–181. https://doi.org/10.1016/j.schres.2016.12.021.
- Arabska, J., Łucka, A., Strzelecki, D., Wysokiński, A., 2018. In schizophrenia serum level of neurotrophin-3 (NT-3) is increased only if depressive symptoms are present. Neurosci. Lett. 684, 152–155. https://doi.org/10.1016/j.neulet.2018.08.005.
- Ayesa-Arriola, R., Alcaraz, E.G., Hernández, B.V., Pérez-Iglesias, R., López Moríñigo, J.D, Duta, R, David, A.S, Tabares-Seisdedos, R, Crespo-Facorro, B, 2015. Suicidal behaviour in first-episode non-affective psychosis: specific risk periods and stage-related factors. Eur. Neuropsychopharmacol. 25, 2278–2288. https://doi.org/10.1016/j. euroneuro.2015.09.008.
- Ayesa-Arriola, R., Moríñigo, J.D.L., David, A.S., Pérez-Iglesias, R., Rodríguez-Sánchez, J.M., Crespo-Facorro, B., 2014. Lack of insight 3 years after first-episode psychosis: An unchangeable illness trait determined from first presentation? Schizophr. Res. 157, 271–277. https://doi.org/10.1016/j.schres.2014.05.011.
- Bagaric, D., Brecic, P., Ostojic, D., Jukic, V., Goles, A., 2013. The relationship between depressive syndrome and suicidal risk in patients with acute schizophrenia. Croat. Med. J. 54, 436–443. https://doi.org/10.3325/cmj.2013.54.436.
- Barnes, T.R., Curson, D.A., Liddle, P.F., Patel, M., 1989. The nature and prevalence of depression in chronic schizophrenic in-patients. Br. J Psychiatry: J. Ment. Sci. 154, 486–491. https://doi.org/10.1192/bjp.154.4.486.
- Begg, C.B., Berlin, J.A., 1988. Publication bias: a problem in interpreting medical data. J. R. Stat. Soc. Ser. A Stat. 151, 419–445. https://doi.org/10.2307/2982993.
- Belvederi Murri, M, Respino, M, Innamorati, M, Cervetti, A, Calcagno, P, Pompili, M, Lamis, D.A, Ghio, L, Amore, M, 2015. Is good insight associated with depression among patients with schizophrenia? Systematic review and meta-analysis. Schizophr. Res. 162, 234–247. https://doi.org/10.1016/j.schres.2015.01.003.
- Bustamante, S., Maurer, K., Loffler, W., Hafner, H., 1994. Depression in the early course of schizophrenia. Fortschr. Neurol. Psychiatr. 62, 317–329. https://doi.org/10.1055/ s-2007-999063.

- Cao, X.L., Wang, S.B., Zhong, B.L., Zhang, L., Ungvari, G.S., Ng, C.H., Li, L., Chiu, H.F., Lok, G.K., Lu, J.P., Jia, F.J., Xiang, Y.T., 2017. The prevalence of insomnia in the general population in China: a meta-analysis. PLoS One 12https://doi.org/10.1371/ journal.pone.0170772. e0170772.
- Carroll, A., Fattah, S., Clyde, Z., Coffey, I., Owens, D.G.C., Johnstone, E.C., 1999. Correlates of insight and insight change in schizophrenia. Schizophr. Res. 35, 247–253. https://doi.org/10.1016/S0920-9964(98)00142-X.
- Cavelti, M., Kvrgic, S., Beck, E.-M., Rüsch, N., Vauth, R., 2012. Self-stigma and its relationship with insight, demoralization, and clinical outcome among people with schizophrenia spectrum disorders. Compr. Psychiatry 53, 468–479. https://doi.org/ 10.1016/j.comppsych.2011.08.001.
- Chang, W.C., Cheung, R., Hui, C.L.M., Lin, J.X., Chan, S.K.W., Lee, E.H.M., Chen, E.Y.H., 2015. Rate and risk factors of depressive symptoms in Chinese patients presenting with first-episode non-affective psychosis in Hong Kong. Schizophr. Res. 168, 99–105. https://doi.org/10.1016/j.schres.2015.07.040.
- Chen, Y.F., 2002. Chinese Classification of mental disorders (CCMD-3): towards integration in international classification. Psychopathology 35, 171–175. https://doi. org/10.1159/000065140.
- Conley, R.R., Ascher-Svanum, H., Zhu, B., Faries, D.E., Kinon, B.J., 2007. The burden of depressive symptoms in the long-term treatment of patients with schizophrenia. Schizophr. Res. 90, 186–197. https://doi.org/10.1016/j.schres.2006.09.027.
- Dai, J., Du, X., Yin, G., Zhang, Y., Xia, H., Li, X., Cassidy, R., Tong, Q., Chen, D., Teixeira, A.L., Zheng, Y., Ning, Y., Soares, J.C., He, M.X., Zhang, X.Y., 2018. Prevalence, demographic and clinical features of comorbid depressive symptoms in drug naive patients with schizophrenia presenting with first episode psychosis. Schizophr. Res. 193, 182–187. https://doi.org/10.1016/j.schres.2017.06.029.
- Depp, C.A., Cardenas, V., Harris, S., Vahia, I.V., Patterson, T.L., Mausbach, B.T., 2011. Psychopathological and functional correlates of behavioral activation and avoidance in schizophrenia. J. Nerv. Ment. Dis. 199, 861–865. https://doi.org/10.1097/NMD. 0b013e3182349cb7.
- Donde, C., Vignaud, P., Poulet, E., Brunelin, J., Haesebaert, F., 2018. Management of depression in patients with schizophrenia spectrum disorders: a critical review of international guidelines. Acta Psychiatr. Scand. 138, 289–299. https://doi.org/10. 1111/acps.12939.
- Emsley, R.A., Oosthuizen, P.P., Joubert, A.F., Roberts, M.C., Stein, D.J., 1999. Depressive and anxiety symptoms in patients with schizophrenia and schizophreniform disorder. J. Clin. Psychiatry 60, 747–751. https://doi.org/10.4088/jcp.v60n1105.
- Fischer, B.A., Buchanan, R.W., 2017. Schizophrenia in adults: clinical manifestations, course, assessment, and diagnosis. UpToDate, Waltham, MA. https://www.uptodate. com/contents/schizophrenia-in-adults-clinical-manifestations-course-assessmentand-diagnosis.
- Fond, G., Godin, O., Brunel, L., Aouizerate, B., Berna, F., Bulzacka, E., Capdevielle, D., Chereau, I., Dorey, J.M., Dubertret, C., Dubreucq, J., Faget, C., Gabayet, F., Le Strat, Y., Micoulaud-Franchi, J.M., Misdrahi, D., Rey, R., Richieri, R., Passerieux, C., Schandrin, A., Schürhoff, F., Tronche, A.M., Urbach, M., Vidalhet, P., Llorca, P.M., Leboyer, M., Aouizerate, B., Berna, F., Blanc, O., Brunel, L., Bulzacka, E., Capdevielle, D., Chereau-Boudet, I., Chesnoy-Servanin, G., Danion, J.M., D'Amato, T., Deloge, A., Delorme, C., Denizot, H., De Pradier, M., Dorey, J.M., Dubertret, C., Dubreucq, J., Faget, C., Fluttaz, C., Fond, G., Fonteneau, S., Gabayet, F., Giraud-Baro, E., Hardy-Bayle, M.C., Lacelle, D., Lançon, C., Laouamri, H., Leboyer, M., Le Gloahec, T., Le Strat, Y., Llorca, P.M., Metairie, E., Misdrahi, D., Offerlin-Meyer, I., Passerieux, C., Peri, P., Pires, S., Portalier, C., Rey, R., Roman, C., Sebilleau, M., Schandrin, A., Schürhoff, F., Tessier, A., Tronche, A.M., Urbach, M., Vaillant, F., Vehier, A., Vidailhet, P., Vilá, E., Yazbek, H., Zinetti-Bertschy, A., 2016. Peripheral sub-inflammation is associated with antidepressant consumption in schizophrenia. Results from the multi-center FACE-SZ data set. J. Clin. Psychopharmacol. 191, 209–215. https://doi.org/10.1016/j.jad.2015.11.017.
- Fountoulakis, K.N., Popovic, D., Mosheva, M., Siamouli, M., Moutou, K., Gonda, X., 2017. Mood symptoms in stabilized patients with schizophrenia: a bipolar type with predominant psychotic features? Psychiatr. Danubina. 29, 148–154. https://doi.org/10. 24869/psyd.2017.148.
- Furukawa, T.A., Cipriani, A., Barbui, C., Brambilla, P., Watanabe, N., 2005. Imputing response rates from means and standard deviations in meta-analyses. J. Clin. Psychopharmacol. 20, 49–52. https://www.ncbi.nlm.nih.gov/pubmed/15602117.
- Gebhardt, S., Hartling, F., Hanke, M., Theisen, F.M., von Georgi, R., Grant, P., Mittendorf, M., Martin, M., Fleischhaker, C., Schulz, E., Remschmidt, H., 2008. Relations between movement disorders and psychopathology under predominantly atypical antipsychotic treatment in adolescent patients with schizophrenia. Eur. Child Adolesc. Psychiatry 17, 44–53. https://doi.org/10.1007/s00787-007-0633-0.
- Geddes, J., Mercer, G., Frith, C.D., MacMillan, F., Owens, D.G., Johnstone, E.C., 1994. Prediction of outcome following a first episode of schizophrenia: a follow-up study of Northwick Park first episode study subjects. Br. J Psychiatry: J. Ment. Sci. 165, 664–668. https://doi.org/10.1192/bjp.165.5.664.
- Goldstein, J.M., Link, B.G., 1988. Gender and the expression of schizophrenia. J. Psychiatr. Res. 22, 141–155. https://doi.org/10.1016/0022-3956(88)90078-7.
- Gregory, A., Mallikarjun, P., Upthegrove, R., 2017. Treatment of depression in schizophrenia: systematic review and meta-analysis. Br. J Psychiatry: J. Ment. Sci. 211, 198–204. https://doi.org/10.1192/bjp.bp.116.190520.
- Grover, S., Dua, D., Chakrabarti, S., Avasthi, A., 2018. Factor analysis of symptom dimensions (psychotic, affective and obsessive compulsive symptoms) in schizophrenia. Asian J. psychiatry 38, 72–77. https://doi.org/10.1016/j.ajp.2017.10.028.
- Halbreich, U., Schulze, T., Botbol, M., Javed, A., Kallivayalil, R.A., Ghuloum, S., Baron, D., Moreira Almeida, A, Musalek, M, Fung, W.L.A, Sharma, A, Tasman, A, Christodoulou, N, Kasper, S, Ivbijaro, G, 2019. Partnerships for interdisciplinary collaborative global well-being. Asia Pac. Psychiatry 11https://doi.org/10.1111/ appy.12366. e12366.

- Hambrecht, M., Maurer, K., H\u00e4fner, H., 1992. Gender differences in schizophrenia in three cultures. Soc. Psychiatry Psychiatr. Epidemiol. 27, 117–121. https://doi.org/ 10.1007/bf00788756.
- Hani, Y., Ghuloum, S., Mahfoud, Z., Opler, M., Khan, A., Yehya, A., Abdulhakam, A., Hammoudeh, S., Al-Mujalli, A., Elsherbiny, R., Al-Amin, H., 2016. Validation of the arabic version of calgary depression scale for schizophrenia. PLoS One 11https://doi. org/10.1371/journal.pone.0162304. e0162304.

Higgins, J.P., Green, S., 2011. Cochrane Handbook for Systematic Reviews of Interventions. John Wiley & Sons.

- Higgins, J.P., Thompson, S.G., Deeks, J.J., Altman, D.G., 2003. Measuring inconsistency in meta-analyses. BMJ 327, 557–560. https://doi.org/10.1136/bmj.327.7414.557. Clinical research ed.
- Hill, H., Killaspy, H., Ramachandran, P., Ng, R.M.K., Bulman, N., Harvey, C., 2019. A structured review of psychiatric rehabilitation for individuals living with severe mental illness within three regions of the Asia-Pacific: implications for practice and policy. Asia Pac. Psychiatry 11https://doi.org/10.1111/appy.12349. e12349.
- Katon, W.J., 2011. Epidemiology and treatment of depression in patients with chronic medical illness. Dialogues Clin. Neurosci. 13, 7–23. https://www.ncbi.nlm.nih.gov/ pmc/articles/PMC3181964/.
- Kessler, T., Lev-Ran, S., 2019. The association between comorbid psychiatric diagnoses and hospitalization-related factors among individuals with schizophrenia. Compr. Psychiatry 89, 7–15. https://doi.org/10.1016/j.comppsych.2018.12.004.
- Koreen, A.R., Siris, S.G., Chakos, M., Alvir, J., Mayerhoff, D., Lieberman, J., 1993. Depression in first-episode schizophrenia. Am. J. Psychiatry 150, 1643–1648. https://doi.org/10.1176/ajp.150.11.1643.
- Lako, I.M., Bruggeman, R., Knegtering, H., Wiersma, D., Schoevers, R.A., Slooff, C.J., Taxis, K., 2012a. A systematic review of instruments to measure depressive symptoms in patients with schizophrenia. Compr. Psychiatry 140, 38–47. https://doi.org/10. 1016/j.jad.2011.10.014.
- Lako, I.M., Taxis, K., Bruggeman, R., Knegtering, H., Burger, H., Wiersma, D., Slooff, C.J., 2012b. The course of depressive symptoms and prescribing patterns of antidepressants in schizophrenia in a one-year follow-up study. Eur. Psychiatry 27, 240–244. https://doi.org/10.1016/j.eurpsy.2010.10.007.
- Leucht, S., Corves, C., Arbter, D., Engel, R.R., Li, C., Davis, J.M., 2009. Second-generation versus first-generation antipsychotic drugs for schizophrenia: a meta-analysis. Lancet North Am. Ed. 373, 31–41. https://doi.org/10.1016/S0140-6736(08)61764-X.
- Li, A., Huang, X., Zhu, T., 2018. A systematic analysis of online broadcasts of suicidality in China. Asia Pac. Psychiatry 10https://doi.org/10.1111/appy.12302. e12302.
- Li, X.H., Zhong, X.M., Lu, L., Zheng, W., Wang, S.B., Rao, W.W., Wang, S., Ng, C.H., Ungvari, G.S., Wang, G., Xiang, Y.T., 2019. The prevalence of agranulocytosis and related death in clozapine-treated patients: a comprehensive meta-analysis of observational studies. Psychol. Med. 1–12. https://doi.org/10.1017/ s0033291719000369
- Li, Y., Cao, X.L., Zhong, B.-L., Ungvari, G.S., Chiu, H.F.K., Kelly, Y.C.L., Zheng, W., Correll, C.U., Xiang, Y.-T., 2016. Smoking in male patients with schizophrenia in China: a meta-analysis. Drug Alcohol Depend. 162, 146–153. https://doi.org/10. 1016/j.drugalcdep.2016.02.040.
- Lindenmayer, J.P., Czobor, P., Alphs, L., Nathan, A.M., Anand, R., Islam, Z., Chou, J.C.Y., InterSe, P.T.S.G., 2003. The InterSePT scale for suicidal thinking reliability and validity. Schizophr. Res. 63, 161–170. https://doi.org/10.1016/s0920-9964(02) 00335-3.
- Lippi, G., Smit, D.J., Jordaan, J.C., Roos, J.L., 2009. Suicide risk in schizophrenia a follow-up study after 20 years Part 2: symptomatology and pharmacotherapy. S. Afr. J. Psychiatr. 15, 79–85. https://www.researchgate.net/publication/288659738_ Suicide_Risk_in_Schizophrenia_a.g.follow-up_study_after_20_years_Part_2_ Symptomatology_and_pharmacotherapy.
- Long, J., Huang, G., Liang, W., Liang, B., Chen, Q., Xie, J., Jiang, J., Su, L., 2014. The prevalence of schizophrenia in mainland China: evidence from epidemiological surveys. Acta Psychiatr. Scand. 130, 244–256. https://doi.org/10.1111/acps.12296.
- López-Moríñigo, J.D., Wiffen, B., O'Connor, J., Dutta, R., Di Forti, M, Murray, R.M, David, A.S, 2014. Insight and suicidality in first-episode psychosis: understanding the influence of suicidal history on insight dimensions at first presentation. Early Interv. Psychia. 8, 113–121. https://doi.org/10.1111/eip.12042.
- Maggini, C., Raballo, A., Salvatore, P., 2004. Depressive and basic symptoms in schizophrenia. Neurol. Psychiatry Brain Res. 11, 1–6. https://doi.org/10.1176/ajp.156.11. 1736.
- Majadas, S., Olivares, J., Galan, J., Diez, T., 2012. Prevalence of depression and its relationship with other clinical characteristics in a sample of patients with stable schizophrenia. Compr. Psychiatry 53, 145–151. https://doi.org/10.1016/j. comppsych.2011.03.009.
- Meader, N., Mitchell, A.J., Chew-Graham, C., Goldberg, D., Rizzo, M., Bird, V., Kessler, D., Packham, J., Haddad, M., Pilling, S., 2011. Case identification of depression in patients with chronic physical health problems: a diagnostic accuracy meta-analysis of 113 studies. Br. J. Gener. Pract.: J. R. Coll. Gener. Pract. 61, e808–e820. https://doi. org/10.3399/bjgp11X613151.
- Mendrek, A., Mancini-Marïe, A., 2016. Sex/gender differences in the brain and cognition in schizophrenia. Neurosci. Biobehav. Rev. 67, 57–78. https://doi.org/10.1016/j. neubiorev.2015.10.013.
- Naguy, A., 2018. Depression in schizophrenia a good or bad omen? Asia Pac. Psychiatry 10https://doi.org/10.1111/appy.12312. e12312.
- Parker, G., 2008. Technical report for SCIE research review on the prevalence and incidence of parental mental health problems and the detection, screening and reporting of parental mental health problems. Soc. Policy Res. Unit. Univ. York. https://www.york.ac.uk/inst/spru/research/pdf/SCIEReview1.pdf.
- Peitl, V., Vidrih, B., Karlović, Z., Getaldić, B., Peitl, M., Karlović, D., 2016. Platelet serotonin concentration and depressive symptoms in patients with schizophrenia.

Psychiatry Res. 239, 105–110. https://doi.org/10.1016/j.psychres.2016.03.006.

- Phillips, M.R., 2001. Characteristics, experience, and treatment of schizophrenia in China. Dialogues Clin. Neurosci 3, 109–119. https://www.ncbi.nlm.nih.gov/pmc/articles/ PMC3181649/.
- Picco, L., Abdin, E., Pang, S., Vaingankar, J.A., Jeyagurunathan, A., Chong, S.A., Subramaniam, M., 2018. Association between recognition and help-seeking preferences and stigma towards people with mental illness. Epidemiol. Psychiatr. Sci. 27, 84–93. https://doi.org/10.1017/s2045796016000998.
- Psychosis Branch of Chinese Medical Association, 2001. The Chinese Classification and the Diagnose Criterion of Mental Disorder (CCMD-3)(in Chinese). Shandong Technology Press.
- Rabany, L., Weiser, M., Levkovitz, Y., 2013. Guilt and depression: two different factors in individuals with negative symptoms of schizophrenia. Eur. Psychiatry 28, 327–331. https://doi.org/10.1016/j.eurpsy.2012.02.008.
- Rapaport, M.H., Judd, L.L., Schettler, P.J., Yonkers, K.A., Thase, M.E., Kupfer, D.J., Frank, E., Plewes, J.M., Tollefson, G.D., Rush, A.J., 2002. A descriptive analysis of minor depression. Am. J. Psychiatry 159, 637–643. https://doi.org/10.1176/appi.ajp.159. 4.637.
- Rey, R., D'Amato, T., Boyer, L., Brunel, L., Aouizerate, B., Berna, F., Capdevielle, D., Chereau, I., Chesnoy-Servanin, G., Denizot, H., Dorey, J.-M., Dubertret, C., Dubreucq, J., Faget, C., Gabayet, F., Lancon, C., Mallet, J., Misdrahi, D., Passerieux, C., Schandrin, A., Schürhoff, F., Urbach, M., Vidailhet, P., Llorca, P.-M., Fond, G., 2017. Nicotine dependence is associated with depression and childhoot rauma in smokers with schizophrenia: Results from the FACE-SZ dataset. Eur. Arch. Psychiatry Clin. Neurosci. 267, 567–577. https://doi.org/10.1007/s00406-017-0779-9.
- Schennach-Wolff, R., Obermeier, M., Seemüller, F., Jäger, M., Messer, T., Laux, G., Pfeiffer, H., Naber, D., Schmidt, L.G., Gaebel, W., Klosterkötter, J., Heuser, I., Maier, W., Lemke, M.R., Rüther, E., Klingberg, S., Gastpar, M., Möller, H.J., Riedel, M., 2011. Evaluating depressive symptoms and their impact on outcome in schizophrenia applying the Calgary Depression Scale. Acta Psychiatr. Scand. 123, 228–238. https:// doi.org/10.1111/j.1600-0447.2010.01608.x.
- Scholes, B., Martin, C., 2013. Measuring depression in schizophrenia with questionnaires. J. Psychiatr. Ment. Health 20, 17–22. https://doi.org/10.1111/j.1365-2850.2012. 01877.x.
- Shtasel, D.L., Gur, R.E., Gallacher, F., Heimberg, C., Gur, R.C., 1992. Gender differences in the clinical expression of schizophrenia. Schizophr. Res. 7, 225–231. https://doi. org/10.1016/0920-9964(92)90016-x.
- Sim, K., Mahendran, R., Siris, S.G., Heckers, S., Chong, S.A., 2004. Subjective quality of life in first episode schizophrenia spectrum disorders with comorbid depression. Psychiatry Res. 129, 141–147. https://doi.org/10.1016/j.psychres.2004.07.007.
- Siris, S.G., 2000. Depression in schizophrenia: perspective in the era of "atypical" antipsychotic agents. Am. J. Psychiatry 157, 1379–1389. https://doi.org/10.1192/apt. bp.108.005629.

- Thomas, N., Ribaux, D., Phillips, L.J., 2014. Rumination, depressive symptoms and awareness of illness in schizophrenia. Behav. Cogn. Psychother. 42, 143–155. https://doi.org/10.1017/S1352465812000884.
- Üçok, A., Karadayi, G., Emiroğlu, B., Sartorius, N., 2013. Anticipated discrimination is related to symptom severity, functionality and quality of life in schizophrenia. Psychiatry Res. 209, 333–339. https://doi.org/10.1016/j.psychres.2013.02.022.
- Upthegrove, R., 2009. Depression in schizophrenia and early psychosis: implications for assessment and treatment. Adv. Psychiatr. Treat. 15, 372–379. https://doi.org/10. 1192/apt.bp.108.005629.
- Upthegrove, R., Marwaha, S., Birchwood, M., 2017. Depression and schizophrenia: cause, consequence, or trans-diagnostic issue? Schizophr. Bull. 43, 240–244. https://doi. org/10.1093/schbul/sbw097.
- Vidović, D., Brecic, P., Vilibic, M., Jukic, V., 2016. Insight and self-stigma in patients with schizophrenia. Acta Clin. Croat. 55, 23–28. https://doi.org/10.20471/acc.2016.55. 01.4.
- Vrbova, K., Prasko, J., Holubova, M., Kamaradova, D., Ociskova, M., Marackova, M., Latalova, K., Grambal, A., Slepecky, M., Zatkova, M., 2016. Self-stigma and schizophrenia: a cross-sectional study. Neuropsychiatr. Dis. Treat. 12, 3011–3020. https:// doi.org/10.2147/NDT.S120298.
- Wang, Y.C., Lin, Y.T., Liu, C.M., Hwang, T.J., Hsieh, M.H., Chien, Y.L., Hwu, H.G., Liu, C.C., 2019. Stigmas toward psychosis-related clinical features among the general public in Taiwan. Asia Pac. Psychiatry. https://doi.org/10.1111/appy.12370. e12370.
- Weng, J., Zhang, Y., Li, H., Shen, Y., Yu, W., 2019. Study on risk factors of extrapyramidal symptoms induced by antipsychotics and its correlation with symptoms of schizophrenia. Gen. Psychiatr. 32https://doi.org/10.1136/gpsych-2018-100026. e100026.
- Winsper, C., Ganapathy, R., Marwaha, S., Large, M., Birchwood, M., Singh, S.P., 2013. A systematic review and meta-regression analysis of aggression during the first episode of psychosis. Acta Psychiatr. Scand. 128, 413–421. https://doi.org/10.1111/acps. 12113.
- World Health Organization, 1992. The ICD-10 Classification of Mental and Behavioural Disorders: Clinical Descriptions and Diagnostic Guidelines. World Health Organization, Geneva.
- Worldbank, 2017. New country classifications by income level: 2017–2018. Available at. http://databank.worldbank.org/data/download/site-content/CLASS.xls.
- Xu, Y.M., Li, F., Liu, X.B., Zhong, B.L., 2018. Depressive symptoms in Chinese male inpatients with schizophrenia: Prevalence and clinical correlates. Psychiatry Res. 264, 380–384. https://doi.org/10.1016/j.psychres.2018.04.016.
- Zeng, L.N., Yang, Y., Feng, Y., Cui, X., Wang, R., Hall, B.J., Ungvari, G.S., Chen, L., Xiang, Y.T., 2019. The prevalence of depression in menopausal women in China: a metaanalysis of observational studies. J. Affect. Disord. 256, 337–343. https://doi.org/10. 1016/j.jad.2019.06.017.