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Research report

The treatment of psychotic depression: Is there consensus among guidelines and psychiatrists?

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ABSTRACT

Background: Psychotic depression (PD) is a prevalent, severe, under-diagnosed and often inadequately treated mental disorder, which has received disproportionally little attention by clinicians, researchers and the pharmaceutical industry. Consequently, the evidence base for optimal clinical practice regarding PD is limited. The aim of this study was to investigate the degree of consensus among international treatment guidelines on PD and to determine whether a potential lack of consensus would be reflected in the clinical practice of Danish psychiatrists.
Methods:

1. Review and comparison of international guidelines on the treatment of PD.
2. Questionnaire based survey regarding Danish psychiatrists' treatment of PD.

Results: The nine international treatment guidelines considered in the review have contrasting opinions on the optimal treatment for PD: 6 of 9 suggest antidepressant (AD)+antipsychotic (AP) combination therapy, 3 of 9 recommend AD monotherapy and 5 of 9 find electroconvulsive therapy (ECT) equally appropriate as first line treatment. The 113 surveyed psychiatrists displayed the same lack of consensus. Their preferred treatment was either AD+AP combination therapy (42%), AD monotherapy (31%) or ECT (21%). The first line choices of ADs and APs were tricyclic antidepressants (51%) and quetiapine (62%), respectively.
Limitations: The survey data are subjected to a potential selection bias as the respondents are likely to represent the more informed fraction of psychiatrists.
Conclusions: Our results indicate that both treatment algorithms and clinical practice regarding PD are highly heterogeneous. This finding emphasizes the need for further studies on the treatment of psychotic depression.

1. Introduction

Depression with psychotic symptoms, or "psychotic depression" (PD), is characterized by the presence of hallucinations and/or delusions in conjunction with depression. PD differs from non-psychotic depression (non-PD) in a number of ways, beyond the presence of psychotic symptoms, as it has a distinct depressive symptom profile (Maj et al., 2007; Østergaard et al., 2012a, 2012b) and is associated with higher rate of recurrence (Goldberg and Harrow, 2004), more psychosocial impairment (Coryell et al., 1996), decreased quality of life (Cramer et al., 2010) and higher mortality rates (Vythilingam et al., 2003) than non-psychotic depression. PD is a prevalent condition as demonstrated by studies from both Europe and the USA, which suggest that approximately 15–20% of the cases fulfilling criteria for major depressive episode are of the psychotic subtype (Johnson et al., 1991; Ohayon and Schatzberg, 2002).

Currently PD is classified as a subtype of severe depression in both major diagnostic guidelines, namely the Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV) (American Psychiatric Association (APA), 2000) and the International Classification of Disease, 10th revision (ICD-10) (World Health Organization, 1993). As a likely consequence of the rather peripheral placement in the diagnostic manuals, PD has not been studied to the same extent

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as other mental disorders with similar prevalence (Rothschild, 2009) and remains an underdiagnosed (Rothschild et al., 2008) and probably undertreated mental disorder (Andreescu et al., 2007).

Randomized control trials (RCT) of both acute and long-term treatment of PD are rare (Meyers et al., 2006). This is probably due to a combination of many factors, i.e., the classification of PD as a sub-diagnosis of depression, difficulties inherent to the recruitment of subjects with psychotic disorders for clinical trials and a general low interest in the disorder from clinicians, researchers, and the pharmaceutical industry. As a result of this lack of RCTs, and treatment studies in general, the ensuing treatment guidelines for PD are based on relatively sparse evidence (Rothschild, 2009). This is likely to result in heterogeneous recommendations and poor consensus regarding the optimal treatment of PD in clinical practice.

The aim of this study was to investigate potential disparity in current treatment guidelines on PD and to determine whether such ambiguity would be reflected in general clinical practice and in the specific choice of psychopharmacological drugs in the treatment of PD.

2. Methods

2.1. Review of guidelines

Treatment algorithms were selected through a review of the evidence basis for PD treatment guidelines by Wijkstra et al. (2009) and in cases where they had been updated after their review, the most recent edition was considered. In addition to the guidelines from the review, the Danish algorithm for the treatment of depression in adults published by the Danish Board of Health (DNBH) (2007) was also considered due to the setting of the survey. The guidelines' recommendations regarding the use of antidepressant (AD) monotherapy, antipsychotic (AP) monotherapy, AD+AP combination therapy and electroconvulsive therapy (ECT) were assessed in order to determine the degree of consensus.

2.2. Survey among Danish psychiatrists

A questionnaire was distributed to participants at the annual meeting of the Danish Psychiatric Association (DPA) in March 2011. Only psychiatrists/physicians working within the field of psychiatry (from here this group is referred to as "psychiatrists") were asked to complete the questionnaire, which was designed to obtain information that would answer the following questions within the framework of the ICD-10 definition of unipolar psychotic depression:

1. Do psychiatrists treat PD in accordance with established guidelines?
2. What are the preferred antidepressants and antipsychotics used in the treatment of PD?
3. Does suicide risk influence the choice of treatment in PD?
4. What impression do psychiatrists have of the prevalence, the suicide risk and their own knowledge of PD?
5. Are the treatment choices and the impression of PD affected by experience-level (analysis of experts versus non-experts)?

2.3. Statistical analysis

The data from the questionnaires was transferred to EpiData (EpiData-Association, 2000) to allow for statistical analysis. Questions to which the participant gave several answers (against the instructions given in the questionnaire) were treated as if they were left blank. To determine whether experience-level affected the choice of treatment an "expert group" was defined as the fraction of respondents who were trained specialists in psychiatry having treated more than 100 patients with PD. The statistical analysis was carried out using Stata11 (StataCorp, 2009). All comparisons were carried out using a two-tailed test of proportions. A significance level of 5% was used throughout.

3. Results

3.1. Review of guidelines

We assessed the first, second and third line treatment suggestions from nine treatment guidelines for psychotic depression published by the American Psychiatric Association (APA), (2010), the National Institute For Health and Clinical Excellence (NICE) (2010), the Canadian Network for Mood and Anxiety Treatment (CANMAT) (Kennedy et al., 2009; Lam et al., 2009), the Texas Medication Algorithm Project (TMAP) (Suehs, 2008), the South African Society of Psychiatrists (SASOP) (2008), the Danish Board of Health (DNBH) (2007), the Dutch National Steering Committee Multidisciplinary Guideline Development Mental Health (DNSC) (2005), the Royal Australian and New Zealand College of Psychiatrists (RANZCP) (2004) and the World Federation of Societies of Biological Psychiatry (WFSBP) (Bauer et al., 2002). An overview of this review is shown in Table 1.

The APA, CANMAT, TMAP and WFSBP guidelines have two first line treatment suggestions, namely either the combination of AD+AP or ECT. The DNBH guideline suggests either AD monotherapy or ECT as first line treatment. The SASOP and RANZCP suggest only the AD+AP combination, while the NICE and DNSC suggest only AD monotherapy as first line treatment. No guideline suggests AP monotherapy as a treatment option for PD.

The guidelines also provide some specific recommendations regarding the class of ADs and APs used in the treatment of PD. For the ADs, the DNBH, DNSC and the RANZCP advocate the use of

Table 1
1st, 2nd and 3rd line treatments of psychotic depression according to current guidelines.

Year	Guideline	Mono-AD	Mono-AP	Combination AD+AP	ECT
2010	APA (USA)	No	No	1	1
2010	NICE (UK)	1	No	2	3***
2009	CANMAT (Canada)	No	No	1	1
2008	TMAP (Texas)	No	No	1+	1
2008	SASOP (South Africa)	No	No	1*+	2
2007	DNBH (Denmark)	1**	No	2**	1
2005	DNSC (Netherlands)	1**	No	2** ◦	3***
2004	RANZCP (Australia & New Zealand)	No	No	1**	2***
2002	WFSBP (International)	No	No	1+	1

The abbreviations for the treatment options are: Mono-AD=monotherapy with an antidepressant, Mono-AP=monotherapy with an antipsychotic, Combination AD+AP=the combination of an antidepressant and an antipsychotic, ECT=Electroconvulsive Therapy. The acronyms for the treatment guidelines represent the American Psychiatric Association (APA), the National Institute of Clinical Excellence (NICE), Canadian Network for Mood and Anxiety Treatment (CANMAT), the Texas Medication Algorithm Project (TMAP), South African Society of Psychiatrists (SASOP), the Danish National Board of Health (DNBH), the Dutch National Steering Committee on Multidisciplinary Guideline Development in Mental Health Care (DNSC), the Royal Australian and New Zealand College of Psychiatrists (RANZCP) and the World Federation of Societies of Biological Psychiatry (WFSBP).

* Psychotherapy in addition to combination therapy AD+AP.

** TCA is the preferred AD.

*** First line choice when severe suicidality or a threatening somatic condition is present. + Indicates atypical AP as first-line choice. ◦ Indicates first generation antipsychotic as first-line choice.

a TCA and TMAP explicitly suggests SSRI or SNRI. The remaining guidelines provide no specific advice on which AD to choose, but recommend selecting a drug based on patient characteristics. Regarding the APs, only DNSC suggests the use of typical APs while the SASOP, TMAP and WFSBP endorse the first line use of atypical AP. The remaining guidelines give no specific advice on the class of choice. Augmentation with lithium is recommended by the APA, TMAP and RANZCP guidelines when the initial pharmacological regimen fails to achieve full remission. The other guidelines do not mention lithium augmentation in the chapter dedicated to the treatment of psychotic depression and their stance in this matter is therefore somewhat unclear.

3.2. Survey respondents

Out of 250 psychiatrists attending the DPA annual meeting, and who received the questionnaire, 114 (46%) completed it. Of these, 1 had not answered any of the demographic questions. This questionnaire was therefore omitted from the statistical analysis. The demographics of the 113 participants are listed in Table 2.

The majority of the respondents were psychiatrists (trained specialists) (76%), were employed at University Hospitals (69%), working in clinical (73%) or research (11%) positions, and specialized in psychotic (42%) or affective (22%) disorders.

Table 2
Demographic data for the participating psychiatrists.

Demographic Category	$n=113$
Age (mean (SD))	51 (11)
Female sex (%)	65
Position (%)	
Psychiatrist	76
Resident	15
Pre-residency	9
Other	1
No Answer	3
Years of experience (mean (SD))	18 (10)
Primary employer (%)	
University Hospital	69
Non-university hospital	21
Psychiatric private practice	6
Other	1
No answer	3
Primary work (%)	
Clinical	73
Research	11
Administration	11
Other	1
No Answer	4
Sub-specialty (%)	
Psychotic disorders	42
Affective disorders	22
Anxiety/OCD	1
Personality disorders	4
Substance abuse	3
Eating disorders	0
Geriatric psychiatry	4
Other	11
No answer	12
Number of PD patients treated (%)	
0	1
1–25	25
26–50	16
51–75	17
76–100	8
>100	31
No answer	3

Table 3
First line treatment choice by psychiatrists for non-suicidal and suicidal psychotic depression.

Treatment choice	$n=113$ (%)	
	Non-suicidal	Suicidal
AD+AP combination	42	27*
AD monotherapy	31	9***
ECT	21	59***
AP monotherapy	4	2
Psychotherapy	0	0
Other	0	1
No answer	3	3

Statistical analysis: two-tailed test of proportions.
P-value: * <0.05, ** <0.01, *** <0.001.

3.3. Psychiatrists' preferred treatment of PD

The respondents' answers to the question regarding their first line treatment choice: *"What is your first choice of treatment for an unipolar psychotic depressive patient suffering from delusions of disease and death? The patient has no known complicating physical diseases"* are reported in Table 3.

Psychiatrists were asked to report preferred treatment for both a non-suicidal and a suicidal patient with PD. In the case of the non-suicidal patient most respondents preferred the AD+AP combination therapy (42%) followed by AD monotherapy (31%), ECT (21%) and AP monotherapy (4%). In the case of a high risk of suicide, there was a significant shift in the preferred treatment from AD+AP combination therapy (27%), AD monotherapy (9%) and AP monotherapy (1%) towards ECT (59%).

The respondents' preferred antidepressants in the treatment of PD were tricyclic antidepressants (TCA) (51%) followed by the serotonin–norepinephrine re-uptake inhibitors (SNRIs) (27%) and the selective serotonin re-uptake inhibitors (SSRIs) (12%). For the antipsychotics, quetiapine was the drug of choice by the majority (62%), followed by olanzapine (21%) and risperidone (8%). None of the psychiatrists would use a first-generation antipsychotic as their first choice.

Table 4 shows how psychiatrists evaluate the prevalence of their use of various treatments in PD compared to non-PD.

The majority reported using TCA (61%), antipsychotics (96%), ECT (86%) and coercive treatment (against the patient's will) (89%) more often in the treatment of PD compared to non-PD. The opposite was the case for psychotherapy, which was reported to be used more often in non-PD than in PD by the majority of the participants (63%).

3.4. Psychiatrists' clinical impression of PD

The questionnaire also contained a number of questions, which examined the psychiatrists' impression/opinion of the prevalence, the suicide risk and their perceived knowledge of PD. The phrasing of the questions and the distribution of answers are listed in Table 5.

A large proportion (40%) of the psychiatrists had the impression that between 11–20% of severely depressed in/out-patients had psychotic symptoms, while another 36% reported the prevalence to be above 20%. The majority (70%) reported that the suicide risk was higher among PD patients than non-PD patients. Almost one fifth (19%) answered that they did not have a clear understanding of the difference between mood-congruent and mood-incongruent psychotic symptoms in PD. More than a quarter (29%) of the participants felt that their knowledge of PD was less than their knowledge of non-PD, bipolar disorder and schizophrenia.

Table 4
Psychiatrists' use of various treatments in psychotic depression compared to non-psychotic depression.

Treatment choice	$n=113$ (%)
Antidepressants	
More often	8
No difference	85
Less often	4
No answer	3
Tricyclic antidepressants	
More often	61
No difference	35
Less often	3
No answer	2
SNRI	
More often	13
No difference	61
Less often	21
No answer	4
Lithium	
More often	39
No difference	53
Less often	3
No answer	5
Benzodiazepine	
More often	39
No difference	58
Less often	0
No answer	4
Antipsychotics	
More often	96
No difference	3
Less often	0
No answer	2
ECT	
More often	86
No difference	12
Less often	1
No answer	1
Coercive treatment*	
More often	89
No difference	10
Less often	0
No answer	2
Psychotherapy	
More often	0
No difference	34
Less often	63
No answer	4

There were 3 answer possibilities for each treatment: "more often" in PD, "the same" in PD and non-PD and "less often" in PD.

* Treatment against the patient's will.

3.5. Experts versus non-experts

35 respondents fulfilled the predefined expert criteria (trained specialist in psychiatry having treated more than 100 patients with PD). In the following cases, the answers to the questions given by the non-experts and the experts, differed significantly:

Demographics: A significantly larger proportion of experts than non-experts were found to work primarily in an administrative function (23% vs. 5%, $p=0.022$).

Treatment: A greater proportion of experts than non-experts reported using TCA more often in the treatment of PD compared to non-PD (74% vs. 55%, $p=0.044$). Regarding ECT, a significantly larger proportion of the non-experts would use ECT as first-line treatment in a non-suicidal patient with PD when compared to the experts (28% vs. 6%, $p<0.001$). The preferred AD in the treatment of PD was more often a SSRI among non-experts than experts (17% vs. 3%, $p=0.0081$). For the antipsychotics, the same was the case for olanzapine (27% vs. 9%, $p=0.010$).

Table 5
Psychiatrists' clinical impression of psychotic depression.

Survey question	$n=113$ (%)
In your experience, what proportion of hospital in/out-patients with severe unipolar depression has concurrent psychotic symptoms (hallucinations, delusions or stupor)?	
$\leq 10\%$	20
11–20%	40
21–30%	18
31–50%	12
$>50\%$	7
No answer	4
Based on your clinical experience, is there a greater risk of suicide amongst patients with unipolar psychotic depression than those with unipolar non-psychotic depression?	
Yes	70
No	27
No answer	4
Do you understand the difference between mood-congruent and mood-incongruent psychotic symptoms in psychotic depression?	
Yes	80
No	19
No answer	1
Do you feel that your knowledge of psychotic depression is on par with your average level of knowledge of non-psychotic depression, schizophrenia, and bipolar disorder?	
Larger	1
The same	69
Less than	29
No answer	1

4. Discussion

This study investigated the degree of consensus regarding the optimal treatment of psychotic depression both among established international treatment guidelines and in a sample of Danish psychiatrists. The main finding was a high degree of heterogeneity both in the recommendations given by the guidelines and in the psychiatrist's preferred treatment.

4.1. Review of guidelines

The nine different treatment guidelines, covering four continents and spanning eight years, each represent one of two central views on the appropriate first line pharmacological treatment of psychotic depression, these being either AD monotherapy or AD+AP combination therapy. The guidelines are based largely on the same body of literature. However, the DNBH, DNSC and NICE favor AD monotherapy, as they seem to give more weight, than the remaining guidelines, to the 2005 Cochrane review of pharmacological treatment for psychotic depression. The Cochrane review proved AD+AP combination therapy to be more effective than AP monotherapy, but not more effective than AD monotherapy (Wijkstra et al., 2005). Accordingly, some of the authors behind the Cochrane review (Wijkstra et al., 2009), have later systematically reviewed the evidence basis of the treatment guidelines for PD and ranked NICE highest based on the AGREE rating system (Brouwers et al., 2010).

Among the guidelines, there are also discrepancies regarding the suggested first line AD and AP. The TMAP advocates the first-line use of SSRI/SNRI, while the DNBH, the DNSC and the RANZCP recommend the use of a TCA as first line AD. The remaining guidelines suggest choosing an AD based on the individual patient characteristics. The choice of a TCA as first line AD by the DNBH and the DNSC is probably related to the fact that these two guidelines also advocate AD monotherapy. According to the Cochrane review from 2005, TCA is more effective than other

AD monotherapies in the treatment of PD (Wijkstra et al., 2005). Regarding the antipsychotics, only the DNSC specifically advocates the use of a typical AP as first line, possibly due in part to the findings of Spiker et al. (1985). While the APA, RANZCP and TMAP advocate lithium augmentation in the treatment of PD when the initial pharmacological treatment does not achieve remission, the remaining guidelines do not specifically discuss this aspect. The use of lithium augmentation in PD is only supported by a relatively limited body of evidence (Rothschild, 2009). ECT is advocated by most guidelines as being at least equally effective to the suggested pharmacological first line treatment. Only NICE, RANZCP and DNSC place ECT as a third and final option to be used when other treatments have failed, or if acute response is required due to medical comorbidities or suicidality.

The conclusion of this review is that the recommendations given in the various guidelines are quite heterogeneous—particularly regarding the optimal pharmacological treatment of PD (monotherapy with AD versus AD+AP combination therapy). This is probably due to the relatively limited evidence base on the topic. The Cochrane review from 2005 states that the lack of statistical evidence for the superior efficacy of the AP+AD combination therapy coupled with well-known AP side effects constitutes continuing with AD monotherapy as the first line treatment (Wijkstra et al., 2005). However, since the publication of the Cochrane review three RCTs on the pharmacological treatment of PD have been conducted. Two of these studies point to the superiority of combination therapy compared to monotherapy: venlafaxine and quetiapine versus venlafaxine alone (Wijkstra et al., 2010) and olanzapine and sertraline versus olanzapine alone (Meyers et al., 2009), while the third study, comparing amitriptyline and haloperidol versus trimipramine, shows equal effect (Kunzel et al., 2009). A very recent meta-analysis by Farahani and Correll, which takes these studies into account, concludes that the combination of AP+AD is significantly more effective than not only AP monotherapy, but now also AD monotherapy in the acute management of PD (Farahani and Correll, 2012). Future revisions of treatment guidelines on PD should take the recent evidence of the superiority of the AD+AP combination into account. However, it must be noted that until now, no RCTs have clearly demonstrated that the combination of an atypical AP and a SSRI/SNRI is more effective than TCA monotherapy. The only study, which has tested these two regimens against one another did not find a significant difference in response (primary outcome), but did detect a difference in remission (*post hoc* outcome), favoring the combination of venlafaxine and quetiapine over imipramine monotherapy. This underlines, that the meta-analyses on AD+AP combination treatment versus AD or AP monotherapy in PD should be interpreted in the light of a very important methodological limitation: There are numerous ways of combining an AD and an AP and only a very limited number of these combinations have been tested in RCTs. The meta-analyses cited in this paper rely on the assumption that the effect of the combinations can be compared and summed (class-effect), despite the use of entirely different ADs and APs in the individual studies. When considering the heterogeneity of the pharmacological mechanisms of various ADs and APs this assumption is questionable. Therefore, more head to head studies of specific AD+AP combinations are warranted, e.g., comparing the combinations of sertraline+olanzapine (Meyers et al., 2009) and fluoxetine +olanzapine (Rothschild et al., 2004) to the combination of venlafaxine+quetiapine (Wijkstra et al., 2010). In these trials, combination therapy has already been proven more effective than olanzapine and venlafaxine monotherapies, but the superior AD+AP regimen has yet to be identified. Furthermore, the efficacy of a combined treatment with TCA and a second generation AP (SGA) in comparison with TCA monotherapy has never been studied in psychotic depression. As the most recent Cochrane review found TCA to be more effective than other AD monotherapies (Wijkstra et al., 2005), a trial comparing the combination of TCA and an atypical AP to TCA monotherapy would be of interest, as well as a head to head comparison of SSRI/SNRI and SGA versus TCA+SGA. In addition, given quetiapine's potential value as a monotherapy in the treatment of non-psychotic unipolar and bipolar depression (Chiesa et al., 2012; Pae et al., 2010), studies of its role in the treatment of PD are highly relevant.

4.2. Psychiatrists' preferred treatment of PD

In accordance with the general finding of superior efficacy of the AD+AP combination in the literature, our survey showed that most respondents would treat non-suicidal psychotic depression with this regimen. However, there was a considerable proportion (31%) that would choose AD monotherapy. This tendency to omit APs in the treatment of PD has been described previously (Andreescu et al., 2007).

When examining specific choices of antidepressants more than 50% of the respondents would choose a TCA. A SNRI was the second most chosen. The choice of a TCA reflects the recommendations given in the Danish guideline on the treatment of depression in adults (Danish Board of Health(DNBH), 2007), where TCA monotherapy is advocated as the first line antidepressant for the treatment of PD.

The favored antipsychotic by the Danish psychiatrists was quetiapine, followed by olanzapine and risperidone. All three are discussed in the literature on PD and are considered to be valid treatment options (Goto et al., 2006; Meyers et al., 2009; Wijkstra et al., 2010). In a study examining the use of antipsychotics in the treatment of schizophrenia in Denmark, quetiapine, risperidone and olanzapine were the three most prescribed antipsychotics (Nielsen et al., 2010). Consequently it seems likely that Danish psychiatrists prefer some APs compared to others "across" disorders involving psychotic symptoms. Notably, none of the participants in the survey would administer a classical AP as first line treatment of PD. A similar tendency was seen in the study on the pharmacological treatment of schizophrenia (Nielsen et al., 2010). If we assume that Danish psychiatrists would use their "preferred" AD (TCA) and AP (quetiapine) in combination when treating PD, it is noteworthy that this specific combination has never been tested in a clinical trial.

In the case of a high risk of suicide among patients with PD, ECT became the preferred first line treatment compared to AD monotherapy and AD+AP combination therapy. NICE, SASOP, DNSC and RANZCP all advocate this same hierarchy. ECT is suggested as first line treatment option by APA, CANMAT, TMAP, DNBH and WFSBP, even without the presence of suicidality or acute somatic deterioration as it is both fast acting and highly effective in PD (Birkenhager et al., 2003; Loo et al., 2010; Petrides et al., 2001).

The Danish psychiatrists' more prevalent use of TCA, antipsychotics and ECT in the treatment of PD compared to non-PD is in accordance with the recommendations given in the guideline by the DNBH (2007). The psychiatrists also reported that they use coercive treatment more often in PD compared to non-PD. We are not aware of any other studies assessing this aspect, but speculate that the combination of "lack of insight" and suicidality, which are cardinal features in PD (Rothschild, 2009), may underlie this finding.

4.3. Psychiatrists' clinical impression of PD

There was a high degree of consensus regarding the participating psychiatrists' perception of the prevalence of the psychotic subtype among in/out patients with severe depression. More than 60% believed the prevalence was $\leq$20%. However, this is a rather low estimate compared to a number of studies, which report prevalence rates in the range of 18–53% among in/outpatients with major depression depending on the exact clinical setting and the age of the

patients (Rothschild, 2009). The low estimate of the prevalence of PD by the respondents supports previous findings indicating that the disorder is frequently missed in clinical practice (Rothschild et al., 2008).

The vast majority of the Danish psychiatrists believed that the suicide risk was more pronounced amongst patients with PD compared to non-PD. This is in accordance with most studies on this subject (Johnson et al., 1991; Park et al., 2010; Wenzel et al., 2011), although no firm conclusion has been made to the incidence difference or lack thereof (Rothschild, 2009).

Almost 20% of the psychiatrists participating in our survey reported that they did not have a clear understanding of the distinction between mood-congruent and mood-incongruent psychotic symptoms in PD. This is obviously problematic as the ICD-10 allows this subtyping of PD. Some studies have indicated that mood-incongruence predicts a more severe course of disease (Coryell and Tsuang, 1985; Coryell et al., 1982), but this remains controversial (Maj et al., 2007). However if we are to clarify the prognostic significance of mood-congruence vs. mood-incongruence it is essential that clinicians feel confident when distinguishing between the two. The upcoming ICD-11 should address this issue and provide clear definitions on this aspect. The criteria for mood-congruence/incongruence proposed for the DSM-5 (American Psychiatric Association (APA), 2011) appear to be very straightforward, easy to apply and could readily be implemented in the ICD-11, which would also serve the purpose of decreasing the boundaries between the two diagnostic systems (Østergaard et al., 2012b). Future studies should aim to outline differences in the optimal treatment of mood-congruent versus mood-incongruent psychotic depression, along with the prognostic significance of these subgroups.

In relation to the lack of understanding of mood-congruence, the respondents also reported that their general knowledge of PD was less than that of non-PD, bipolar disorder and schizophrenia. This finding emphasizes the need for increased focus on PD in order to improve diagnostic sensitivity and treatment of the disorder.

4.4. Differences between experts and non-experts

The higher preference for the treatment of PD with SSRI, olanzapine and ECT among non-experts when compared to the experts may reflect that this younger fraction of physicians, mainly working at university hospital settings (74%) are more likely to be informed on the results from recent treatment studies, which favor the combination of SSRI+olanzapine (Meyers et al., 2009; Rothschild et al., 2004) and ECT (Birkenhager et al., 2003; Fink, 2003; Petrides et al., 2001). Furthermore, the current administrative function of many experts (23%) may also contribute to these differences as these psychiatrists will have less time available/allocated for clinical practice and consequently a lesser need to be informed on the latest results from clinical studies and their impact on the treatment algorithms.

4.5. Limitations

The questions posed in our survey were tested for clarity prior to the survey, yet there were 5 questionnaires on which some participants noted their confusion about the wording of the questions or a lack of answer choices. However, more than 95% of the participants did not report any difficulties regarding the completion of the questionnaire.

Our results are also limited by a potential selection bias as only 114 of 250 attending psychiatrists at the annual meeting completed the questionnaire. Furthermore the 250 attendees represent a minority of the 1080 members of the Danish Psychiatric Association. However, the main-finding of the present study, namely that of considerable ambiguity in the treatment of PD among Danish psychiatrists, is probably only underestimated by this bias as the participants at the DPA annual meeting are likely to represent a more well-informed fraction of the field.

5. Conclusions

The main finding of this study on the treatment of PD is the high degree of heterogeneity found both in the recommendations given by major established treatment guidelines and in the treatment regimens preferred by Danish psychiatrists. The lack of consensus is most likely due to the relatively limited evidence base on this topic and emphasizes the need for further studies on the treatment of psychotic depression.

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Conflict of interest

A.K.K. Leadholm and P. Bech declare no conflict of interest. A.J. Rothschild has received grant support from the National Institute of Mental Health, Cyberonics, Takeda, and St. Jude Medical and has served as a consultant to Allergan, Eisai Medical, GlaxoSmithKline, Eli Lilly, Noven Pharmaceuticals, Pfizer, Shire Pharmaceuticals and Takeda. W.A. Nolen has received grants from the Netherlands Organization for Health Research and Development, the European Union, the Stanley Medical Research Institute, Astra Zeneca, Eli Lilly, GlaxoSmithKline; and received honoraria/speaker's fees from Astra Zeneca, Pfizer, Servier and Wyeth; and has served in advisory boards for Astra Zeneca, Pfizer and Servier. P. Munk-Jørgensen has received non-conditional education grants from Astra Zeneca, Janssen-Cilag, Servier and Bristol-Myers Squibb. S.D. Østergaard has until April 2011 received honoraria from Janssen-Cilag.

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