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Medication strategies in first episode psychosis patients: A survey among psychiatrists

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Abstract

Aim: There is an ongoing debate regarding the optimal timing of discontinuation of antipsychotic drugs for patients with first episode psychosis. Although most guidelines recommend maintenance therapy for at least 1 or 2 years after reaching remission, study results indicate that early discontinuation may be beneficial for at least a subsample of patients. To date, little is known about which medication strategies are applied in patients recovering from a first psychotic episode. In this study, we examined the beliefs and practices of clinicians on medication discontinuation.

Methods: We performed a survey among 50 experienced Dutch psychiatrists to assess how often specific treatment strategies have been applied in the past 12 months, as well as their knowledge and expectations with respect to medication discontinuation.

Results: Psychiatrists estimated that, after remission, they continued medication at the same dose for at least 12 months in 51.2% of cases, continued in a reduced dose in 33.8% of cases and discontinued medication in 9.1% of cases after 4.4 months of remission on average. Although the medication is discontinued in only a relatively small proportion of patients, almost half of all clinicians (45.9%) used this strategy at least once in the past 12 months.

Conclusions: There is substantial practice variation in antipsychotic medication strategies after remission from a first psychotic episode. Future research on long-term effects of early medication discontinuation can guide clinicians in making evidence-based decisions when treating first-episode patients.

KEYWORDS

antipsychotic medication, discontinuation, maintenance treatment, schizophrenia

Members of the HAMLETT and OPHELIA Consortium are provided in Appendix.

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1 | INTRODUCTION

For many years, clinical guidelines on the treatment of first episode psychosis (FEP) have recommended to continue antipsychotic treatment for at least 1 or 2 years after achieving remission (Keating et al., 2017; Lehman et al., 2004). This recommendation for maintenance treatment is based on a large number of studies which show that continuation of antipsychotic medication reduces the risk of a relapse (Karson et al., 2016; Leucht et al., 2012). Although this is still the recommended treatment strategy in most international treatment guidelines today (Galletly et al., 2016; Hasan et al., 2013; Nice, 2014), there has been a change in opinion about early discontinuation of antipsychotic medication in first-episode patients, since the seminal paper of Wunderink et al. (Wunderink, 2018; Wunderink et al., 2013).

An important drawback for maintenance treatment is that antipsychotic medication can have severe side-effects affecting physical and emotional well-being as well as social and vocational functioning. From a patient perspective, in particular for remitted patients, these drawbacks may outweigh the reduced risk of relapse (Kikkert & Dekker, 2017). In addition, taking daily antipsychotic medication may give some people the feeling of still being a psychiatric patient, while being medication free feels as being truly recovered. Consequently, many patients have a strong preference themselves to discontinue their medication. Approximately 40–55% of first episode patients discontinue their medication themselves within the first year of treatment (Kamali et al., 2006; Novak-Grubic & Tavcar, 2002).

The study by Wunderink et al. indicated that early discontinuation of medication can be done safely in a subsample of patients and may result in better long term functional outcome compared to patients who continued their medication at least 12 months after remission (Wunderink et al., 2013). This study had a great impact on the clinical community and changed the opinions on maintenance treatment from several, perhaps many psychiatrists. The paper suggested that adhering to guideline recommendations may not be the best strategy for all patients if we want to find the optimal balance in well-being, functioning and relapse risk.

Whether or not early discontinuation of antipsychotic medication is beneficial for patients on the long-term is, however, an open question. First, it requires an understanding of how a patient values different outcomes such as relapse, social and societal functioning. Second, the literature is still rather inconsistent on this aspect as two studies, one RCT with a 10-year follow up (Hui et al., 2018) and one non-randomized study based on 20-year register data (Tiihonen et al., 2018), showed findings opposite to those of Wunderink. Consequently, the optimal duration of maintenance treatment with antipsychotics remains an important open question (Begemann et al., 2020; Harrow & Jobe, 2013; Hui et al., 2019; Keating et al., 2017; McGorry et al., 2013; Robinson et al., 2005; Thompson et al., 2016). This is reflected in several guidelines who provide no clear advice regarding this matter (Barnes, 2011; Buchanan et al., 2010; van Alphen et al., 2012). The absence of clear recommendations for duration of maintenance forces clinicians to rely on their own experience and judgement in deciding for which patients to discontinue or not.

We expect that, as a result of these conflicting findings and patient interests, large differences in medication prescription patterns have arisen between clinicians who treat FEP patients. Several studies have shown a distinct discrepancy between clinical guidelines and clinical practice with respect to dosing or polypharmacy (Correll & Gallego, 2012; Fisher et al., 2014; Fleischhacker & Uchida, 2014), as well as considerable variation in prescribing patterns among countries and clinicians (Bitter et al., 2003; Patel et al., 2014).

Thompson examined clinicians' views towards discontinuation in first episode patients (2016) and concluded that they are much less conservative than most current guidelines. Of doctors 49% expressed to be extremely happy to put their patient forward for a guided discontinuation trial, and doctors estimated that 20–40% of their patients could stop medication following remission. Moreover, Hui et al., 2018 examined Asian psychiatrists' attitudes towards discontinuation in first episode patients. Psychiatrists estimated that 1–19% of remitted patients can discontinue medication. Thompson and Hui both found that psychiatrists, on average, think that patients should remain on antipsychotic medication for 1–2 years following remission. Notably, although this was the most common response, it was only given by 29 and 30% of clinicians, meaning the majority of clinicians did not agree. However, to the best of our knowledge, no study has specifically investigated patterns in prescription behaviour of antipsychotic maintenance treatment for FEP patients.

1.1 | Aims of the study

The objective of this study is to examine psychiatrists' medication strategies in patients who have remitted from a first psychosis.

2 | METHODS

2.1 | Population

This study was performed in the Netherlands, the country where the Wunderink study was performed and where its results were very influential. We designed a questionnaire directed at Dutch psychiatrists concerning medical treatment of first episode patients. Psychiatrists were recruited by an e-mail send to all members of the Dutch Association for Psychiatry (NVvP) asking to them to fill out an Online questionnaire, in the period between September 2018 and March 2019. The NVvP has approximately 3500 members covering more than 90% of psychiatrists currently working in the Netherlands.

2.2 | Instruments

We drafted scenarios which are representative for cases in regular clinical practice. Clinicians were asked how they usually acted in any of those cases and to rate the importance of a variety of factors for making that decision. It is unlikely that, faced with a certain scenario,

clinicians always respond in a similar fashion as each client and his or her circumstances is unique. Therefore, we did not ask clinicians which single strategy they would prefer given a certain situation but to give an estimate of how often they applied specific strategies in the past year given this specific scenario. The cases presented referred to different phases in the treatment of patients who experience a first psychotic episode: (1) after remission, (2) after 12 months of stable remission, (3) during phasing out of medication. Finally, we asked clinicians about their knowledge and expectancies with respect to medication discontinuation. The questionnaire can be found in the Appendices.

2.3 | Statistical analyses

All analyses were performed using SPSS Statistics for Microsoft Windows version 26. In Tables 1 and 2, mean percentages of patients are based on the percentage of patients that clinicians estimated to have treated with that particular strategy. It, therefore, does not take into account the size of the caseload of each clinician, as this was not known. Mean start of medication reduction, dosage reduction and duration of phasing out was calculated in the same way.

3 | RESULTS

A total of 52 respondents filled out the questionnaire. Two respondents were not psychiatrists and were for that reason removed from the database. The remaining sample consisted of 50 Dutch psychiatrists. Respondents had a mean age of 49.4 years (SD = 10.7), 50% were woman and respondents had been working as a psychiatrist for 14.8 (SD = 10.6) years on average. All clinicians had at least 1 year of working experience in treating FEP's and most clinicians (82%) had 6 years or more of experience in working with FEP. The majority of mental healthcare institutes in the Netherlands do not have dedicated FEP teams. In our sample, 20% of respondents worked in a dedicated FEP team, but—as mentioned above—all had experience in treating

FEP's. Other characteristics of respondents can be found in the Table S1.

3.1 | Strategies after achieving remission

Clinicians reported that they continued the antipsychotic medication for at least 12 months in, on average, 51.2% of their patients who had achieved remission after a first episode (see Table 1). In addition, clinicians reported that they reduced the dosage to an average of half the initial dose in a third of their patients (33.8%), and discontinued the medication in 9.1% of their patients. Dosage reduction or completely phasing out of medication was, on average, initiated 4.2 and 4.4 months after remission is reached.

Nine clinicians indicated that they used alternative strategies. Some mentioned switching to another agent or to initiate a psychosocial intervention. Several clinicians did not mention any particular medication strategy here but only asserted that it depends on a variety of circumstances.

The majority of clinicians (81.1%) responded that they utilized various strategies in the past year depending on the situation, instead of using one particular strategy in all of their patients. Most clinicians (91.9%) answered that they applied medication continuation in at least one of their patients, while 81.1% applied dosage reduction and 45.9% applied phasing medication out completely within the first year.

In case a patient prefers to discontinue medication early, although this conflicts with the advice of the clinician, clinicians reported they nonetheless went along with an attempt to reduce or discontinue the medication in 57.9% of cases.

3.2 | Strategies 12 months after remission

At the time patients have been in remission for 12 months, clinicians responded that they continued the medication in 33.1% of cases. See Table 2. In these cases, on average, the medication was continued for

TABLE 1 Clinicians estimate of the medication strategies they applied in the past 12 months in their first episode patients who responded to medication and achieved remission. Patients may or may not still experience some remaining positive symptoms but this does not affect functioning

	Strategy applied	Start of medication reduction	Dosage reduction	Duration of phasing out period
	Mean percentage of patients (SD)	Mean months after remission (SD)	Mean percentage of initial dose (SD)	Mean weeks (SD)
Continue medication for at least 1 year (in the dosage in which remission was achieved)	51.2 (32.0)			
Reduce dosage	33.8 (25.0)	4.2 (2.4)	48.0 (16.0)	8.9 (7.0)
Phase medication out to zero	9.1 (12.2)	4.4 (2.4)		14.9 (11.2)
Something else	5.9 (13.2)			

TABLE 2 Clinicians estimate of the medication strategies they applied in the past 12 months in their first episode patients who responded to medication and have been in stable remission for 12 months. Patients may or may not still experience some remaining positive symptoms but this does not affect functioning

	Strategy applied	Start of medication reduction	Dosage reduction	Duration of phasing out period
	Mean percentage of patients (SD)	Mean months after remission (SD)	Mean percentage of initial dose (SD)	Mean weeks (SD)
Continue medication (in the dosage in which remission was achieved)	33.1 (25.6)			
Reduce dosage	33.8 (21.3)	14.0 (4.7)	49.6 (15.7)	11.1 (10.4)
Phase medication out to zero	30.6 (25.0)	12.2 (0.8)		14.3 (9.5)
Something else	2.6 (8.2)			

almost 2 years after remission (mean = 23.3; SD = 6.2 months). Clinicians also reported that they continued the medication with a reduced dosage of, on average, half (49.6%) the initial dose in 33.8% of patients. They estimated that medication was discontinued in 30.6% of patients.

Also, during this phase, most clinicians (90.3%) indicated that they utilized more than one of the above strategies in their patients. Medication continuation, dosage reduction and discontinuation were reported to occur at least once during the past year by respectively 83.9, 87.1 and 80.6% of clinicians.

3.3 | Strategies during or after medication discontinuation

During the process of gradually reducing the medication dosage, several warning signs may provide reasons for clinicians to recommend a dosage increase. As expected, most clinicians (94.4%) responded that they will advise a dose increase if the patient has a relapse. Increase in positive symptoms and deterioration of social functioning are important signs to advise a dose increase for respectively 55.6 and 48.6% of clinicians. For most clinicians (ranging from 70.3 to 51.4%) more subtle signs such as agitation, sleeping problems, restlessness, mood changes/emotional instability and anxiety are only cause to increase the dosage when other signs are also present. See the Table S2 for further details.

In case the dose has been increased as a response to worsening of positive symptoms during phasing out, 43.2% of clinicians advise to continue the medication in this increased dose when a patient responds well to this. In contrast, 54.1% of clinicians advise to try to resume phasing out at a later stage.

3.4 | Clinicians knowledge and beliefs

The majority of clinicians (67.6%) expect that patients, who start phasing medication out 3–6 months after remission, will have more relapses on the long term compared to continuation treatment of at least 12 months. Some clinicians (21.6%) expect however that these

patients will have the same number of relapses while less relapses are expected by 2.7% of clinicians. With respect to functioning, 32.4% of clinicians expect patients to have worse longer term personal, social and societal functioning when medication is discontinued after 3–6 months of remission. In contrast, 29.7% of clinicians expect functioning to be better, 18.9% thinks it will be similar and 18.9% does not know what to expect.

Most clinicians expressed the need for guidelines that can help identify patients who are more likely to discontinue medication successfully. Although less urgent, the majority of clinicians also finds it useful to have guidelines on what to do when symptoms return during phasing out of medication and how to discontinue medication. See Table 3.

4 | DISCUSSION

In this study, we examined which medication continuation and discontinuation strategies were applied by Dutch psychiatrists when treating patients who have recovered from a first psychotic episode. We expected that clinicians do not always comply with treatment guidelines and sometimes discontinue medication early, which was confirmed by our results. Based on self-report of 50 experienced Dutch psychiatrists, we found that medication is continued for at least 12 months after remission in 51.2% of patients in the same dose and that dosage is reduced in 33.8% of patients to, on average, half the initial dose. These are the most common strategies yet in 9.1% of patients medication was reported to be discontinued after 4.4 months of remission on average. Although this is a relatively small proportion of patients, almost half of all clinicians (45.9%) used this strategy at least once in the past 12 months.

We conclude that in 42.9% of patients the medication was discontinued within the first year after remission or continued in a strongly reduced dose which is not in line with most clinical guidelines (Galletly et al., 2016; Hasan et al., 2013; Nice, 2014). It is important to note that these results show how often these strategies have been applied in real cases during the past year according to the psychiatrists. As such, they do not necessarily reflect the strategy preferred by the clinician but the strategy which emerged from shared decision

TABLE 3 Clinicians need for guidelines related to medication phasing out

Guidelines on how to:	How much need		
	None or a little %	Average %	Much %
Identify patients that will be most likely to successfully discontinue their medication (e.g., patient- and environmental characteristics, risk factors)	13.5	21.6	64.9
Act when symptoms increase or return during phasing out of medication	29.7	43.2	27.0
Discontinue antipsychotic medication, such as dosing schedules	37.8	35.1	27.0

making which also factors in the patients' preferences and circumstances.

The recommendation given by a clinician depends on his or her beliefs about early medication discontinuation in first episode patients. However, this may vary substantially among clinicians, as we found that they have contrasting expectancies when it comes to the effects on relapse risk, but also regarding the effects on personal, social and societal functioning. These opinions reflect different findings in the literature, which also show strong contrasts (Hui et al., 2018; Tiihonen et al., 2018; Wunderink, 2018). Also, they confirm findings from Thompson et al. (2016) who found that clinicians thought that 20–40% of patients could stop medication following remission and 71.4% of doctors thought that quality of life for patients who continued their medication was worse compared to those who stop (Thompson et al., 2016).

After the first 12 months of remission, which is the recommended duration of maintenance medication in most guidelines, we found that medication was reported to be discontinued in only 30.6% of stable remitted patients. In the remaining two-thirds of patients (66.9%) medication discontinuation was not deemed feasible or patients may have been reluctant to do so.

It is common for patients to develop physical or psychiatric symptoms following decrease or withdrawal of antipsychotic medication (Cerovecki et al., 2013; Salamon & Hamilton, 2014). Some of these signs can indicate an emerging relapse and some may be due to rebound phenomena of the reduction of the medication itself. Although the response to any of these signs will depend on a variety of factors, we found discrepancies between clinicians whether or not a specific warning sign, such as deterioration of social functioning, agitation or sleeping issues, justifies the recommendation for a dosage increase. With the exception of a psychosis, warning signs in this questionnaire will bring some clinicians to increase the medication dose while others will not.

If positive symptoms increase during medication reduction, it is important to distinguish a true relapse from discontinuation syndromes such as withdrawal and rebound symptoms or supersensitivity syndromes (Chouinard & Chouinard, 2008; Moncrieff, 2006). Although this is difficult based on the initial clinical presentation, it has been argued that symptoms caused by medication withdrawal, in contrast to a relapse, generally subside quickly after a dose increase

(Cerovecki et al., 2013; Chouinard & Chouinard, 2008). If so, it seems justified to continue to taper the medication down once the patient has been stabilized. We found that in such a scenario approximately half of clinicians (54%) indeed prefer to resume medication reduction at a later stage while 43% is reluctant to do so and prefers to continue the increased dose. This reflects the difficult balance between reducing the risk of a relapse on the one hand and to avoid long-term use of antipsychotic medication on the other. Also, these differences in medication strategies seem to underline our finding that 70% of clinicians expressed a need for guidelines on how to deal with reoccurring or increasing symptoms during or after tapering of the medication.

Although the focus of this paper was on first episode patients, medication reduction or discontinuation is also a relevant issue for patients who have had more than one psychotic episode. We included two questions about this and found that in the past 12 months, an average of 41% of patients with two or more episodes indicated that they wanted to reduce or discontinue their medication. An actual attempt to reduce or discontinue medication was undertaken in 22% of patients.

Our results provide insight into clinicians' beliefs and their preferred strategies. Although this is an important and sometimes decisive factor in clinical practice, the actual strategy needs to be tailored to preferences and circumstances of the individual patient. Some patients may accept a higher relapse risk if this makes them feel less affected or restricted by side-effects, while others do not.

Only a small number of the clinicians we approached filled out the questionnaire. As the questionnaire focused on treatment of FEP's, clinicians who do not treat this patient category may have declined participation. At face value, mean age, sex, working experience and work setting seem representative for clinicians working with FEP's. As such we propose that current findings may reflect the average opinion and practice of clinicians working with FEP's. Some figures are based on psychiatrists' retrospective estimates of treatment strategies they applied in the past 12 months and may be subject to error. Also, we realize that the scenarios which we presented in the questionnaire lack the complexity of real life cases. Clinicians may differ in their interpretation of scenarios based on the patient population one is accustomed to. Finally, the situation in the Netherlands may differ from that in other countries as the Dutch Wunderink study has inspired many clinicians to taper off medication in an earlier stage.

In conclusion, our results demonstrate that medication is discontinued in only 9.1% of patients within the first year. But even among patients who have been in stable remission for 1 year, the number of patients who remain on medication seems rather high. Although it is common to reduce the dosage, clinicians seem rather cautious in their decision to discontinue medication. This seems to be in contrast with earlier findings that many patients prefer to stop their medication (Kamali et al., 2006; Novak-Grubic & Tavcar, 2002). Also, we found substantial variation in beliefs and practice concerning preferred medication strategies. These differences are in line with the expressed needs for guidelines on this topic. Fortunately, several discontinuation trials are ongoing which may help guide optimal duration of maintenance treatment following remission after a first psychotic episode (Begemann et al., 2020; Moncrieff et al., 2019; Stürup et al., 2017; Weller et al., 2019).

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CONFLICT OF INTEREST

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

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APPENDIX A.

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