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ORIGINAL RESEARCH

Discontinuing Antipsychotic Medication After Remission from First-Episode Psychosis: A Survey of Psychiatrists' Attitudes in Taiwan

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Background: Patients in remission after first-episode psychosis are inclined to discontinue antipsychotic treatment, which may lead to higher risk of relapse and unfavorable outcomes. Paradoxically, also there are evidences suggesting that certain patients may stay well in drug-free condition. Psychiatrists' views towards this dilemma might affect their approaches to these patients, and discrepant attitudes are noted between Western and Asian clinicians. This study aimed to examine psychiatrists' attitudes about discontinuing antipsychotic medications after remission from first-episode psychosis.

Methods: Psychiatrists were recruited for this study using convenience sampling. A cross-sectional survey was conducted using a set of questionnaires comprising nine items for attitudes toward medication discontinuation, six vignettes for probing psychiatrists' practice in designated clinical scenarios, and a list of criteria that may affect their responses.

Results: Responses were provided by 118 psychiatrists, two-thirds men, mean age 39.8 ± 10.1 years and mean experience 12.7 ± 9.7 years. Half of the participants endorsed that fewer than 20% of the remitted patients should stop medication completely; the majority advised that an observation period of 1 year or longer is necessary while discontinuing medication. The majority would not initiate discussion with patients about discontinuing medication. Responding to two case vignettes, those who endorsed that more patients could stop antipsychotics were also more inclined to discuss it with patients, but not consistently in response to the other four case vignettes. Taiwan psychiatrists expressed a wide range of decision-making considerations for discontinuing antipsychotics.

Conclusion: The majority of Taiwan psychiatrists thought it was not feasible to stop medications completely but were willing to consider this option. Once being presented with actual clinical scenarios, many participants hesitated to discontinue antipsychotic medications for various reasons. The proactive attitude of psychiatrists towards conducting clinical trials to test the feasibility of medication discontinuation may help to provide better reference for this clinical dilemma.

Keywords: antipsychotics, attitude, discontinuation, first-episode psychosis, remission, questionnaire

Introduction

Schizophrenia was once known as a severe, chronic disorder with devastating effects on the affected individual, family members and society. While more attention is paid to the early stage of the illness,[1] early interventions in patients with first-episode psychosis (FEP) lead to better outcomes.[2–5] Meta-analysis has shown that remission rates reach 50% and higher.[6] Not surprisingly, after a relatively good

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initial treatment response, both patients and their key caregivers are inclined to discontinue medication when symptoms improve.[7–9]

However, discontinuation of antipsychotic treatment is the single most significant predictor of psychosis relapse, and tends to increase the risk of relapse by 5 times.[10,11] Clinical trials evaluating dose reduction or discontinuation in patients remitted from FEP revealed 3 to 6 times higher risk of relapse in intermittent or placebo treatment groups compared to continuous treatment counterparts.[12–16] Yet once relapse occurs, compared to the treatment for first-episode psychosis, it usually takes longer treatment duration to achieve remission, leaves more residual symptoms and has an increased proportion of patients classified as poor responders.[11,17–19] Accordingly, continuous treatment remains the "gold standard" for good clinical practice for patients with schizophrenia.[20] Consequently, previous clinical guidelines for treatment in the maintenance phase of schizophrenia have recommended that antipsychotics should be maintained for 1 to 2 years or even longer after a first psychotic episode,[21] and an indefinite period of time has been strongly advocated once relapse occurs.[22,23]

Even so, recent guidelines and algorithms seemed to have shifted toward a more positive attitude regarding antipsychotic discontinuation and dose reduction or lower dose strategies, especially for patients who have only experienced a single psychotic episode.[24] This may reflect concerns about the negative impact of exposure to long-term use of antipsychotics. Patients have tended to discontinue treatment for disliking the adverse effects of antipsychotics on physical health and cognitive functioning, as well as the inconvenience or stigma-related issues.[25] Also, evidence suggests a negative impact of antipsychotics on brain structure.[26] Several neuroimaging studies have revealed a subtle but measurable loss on brain biology over time[27–30] and a link to cognitive decline,[31,32] even though not all evidence supports such a correlation.[33] Currently, the risk-to-benefit ratio of long-term antipsychotic treatment is still debatable.

In real-world practice, several longitudinal observational studies have demonstrated that the proportions of patients remaining in a remitted state during follow-up are higher than expected,[34,35] and strikingly, not all of these patients were maintained by antipsychotic treatment.[36,37] Also, in the long term, functioning may be even better in those who discontinued medication.[38–41] Therefore, even though a recent comprehensive review endorsed a favorable risk-to-benefit ratio of continuous antipsychotic treatment, it could not be denied that

> a minority of individuals diagnosed initially with schizophrenia appear to be relapse-free for long periods, despite absence of sustained antipsychotic treatment.[42]

Current evidence derived from different FEP cohorts fails to provide consistent and replicable variables that can predict the odds of having a sustained remission or relapse during medication discontinuation after a single episode of psychosis.[43–45] A survey on the views of clinicians regarding discontinuation of antipsychotic medication following symptom remission in FEP revealed that positive attitudes of clinicians toward medication discontinuation is high and a vast majority of their respondents supported the idea to test the feasibility of discontinuing antipsychotic maintenance in patients remitted from FEP.[46] The Asian Network for Early Psychosis (ANEP) has adopted Thompson's questionnaires[46] and added a second part with probes by case vignettes and a list of criteria to survey clinicians' attitudes towards dose discontinuation in patients with remitted FEP. Reports from ANEP presented similarities and minor differences between mental health professionals in Hong Kong, Japan, Korea, and Singapore, with more discrepancies compared to the original findings of Thompson et al.[47]

In the present study, we sought to compare Taiwan psychiatrists' attitudes towards medication discontinuation with previous findings, by replicating the survey using the questionnaire shared by ANEP, and also analyzing the relationship between psychiatrists' opinions and potential translation into action in clinical practice as shown by their responses to case vignettes.

Methods

Questionnaire and Participants

This cross-sectional survey used a structured questionnaire developed by Hui et al,[47] which incorporated the original version introduced by Thompson et al.[46] Dr. Hui authorized us to translate her group's questionnaire (English and Cantonese) into mandarin Chinese with amendments deemed helpful to be applied in Taiwan (personal communication). The language of the case vignettes was carefully modified to adopt considerations of social and cultural nuance. The questionnaire comprises three parts, including 1) nine items for attitude towards medication discontinuation; 2) six vignettes for indicating

whether the psychiatrist will initiate the discontinuation suggestion and what they will do when patients ask for discontinuation; and 3) a list of criteria that might affect their thoughts regarding medication discontinuation of the index vignette; as well as the respondent's basic information.

Using convenience sampling, we invited psychiatrists from different hospitals or clinics in Taiwan to respond to the questionnaire. In hospital settings, we contacted a coordinating physician who was interested in this survey to help disseminate the questionnaires to his or her colleagues. We also collected surveys in a continuous medical education event that was designated for psychiatrists in private practice. The minimum years of experience required for completing this survey was at least 1 year of having actively treated patients with psychosis.

Ethical Considerations

All participants were informed about the purpose of the survey and their participation was totally voluntary. The respondents mailed back their questionnaires anonymously with an envelope provided by the research team. A gift card was provided to thank them for their participation. The study protocol was approved by the hospital's Research Ethics Committee, which permitted to confirm participant's consents by receiving their response to this questionnaire survey.

Statistical Analysis

For questions assessing respondents' attitudes towards medication discontinuation (ie, the first part of the questionnaire), the significance of differences in categorical variables were analyzed by Chi-square tests. Responses to individual items of questionnaires were dichotomized as positive and negative attitudes, and the frequencies of responses to the case vignettes and criteria of medication discontinuation were calculated and analyzed by multivariate logistic regression to determine whether significant differences were found in responses between psychiatrists with different gender and years of experience. We hypothesized that men and psychiatrists with longer years of experience might exhibit less willingness towards antipsychotic discontinuation.

To test if participant's response to the first question

> what percentage of people do you think can stop antipsychotics completely following absence of psychotic symptoms after their first episode of a psychotic disorder?

correlated with their response to each case vignette, the significance of correlations was analyzed using Mann–Whitney *U*-tests.

Results

Demographic Characteristics

A total of 118 psychiatrists from more than 15 sites around Taiwan participated in this survey. In general, they provided complete responses with minimal missing data to the first 3 parts of the questionnaire; however, 6 participants (5.1%) did not provide their basic information. Among all included participants, 68.8% (n=77) were men and 31.3 (n=35) were women, with mean age 39.8±10.1 years (range, 26–72 years), and mean years of experience 12.7 ±9.7 years (range, 1–44 years).

Attitudes Towards Medication Discontinuation

The first, second, and third most common responses to individual questions (comprising 75.4% to 100% of all responses) are summarized in Table 1. Half of the respondents (50.8%) endorsed that only 0–20% of the patients remitted after first-episode psychosis could discontinue antipsychotic medications, followed by 34.7% who endorsed that 20%-40% could stop medications, while only 1.7% of the psychiatrists said that 0% of the patients could discontinue. Opinions regarding the observation period before considering medication discontinuation were diverse, with 28.8%, 26.3% and 29.7% of the participants thinking that the period should be less than 1 year, just 1 year, and between 1 and 2 years, respectively; while 15.2% thought an even longer duration was needed. Once ready for discontinuation, only 27.1% thought it could be done within 6 months, 29.7% thought it feasible to be done within 6-12 months, and the remaining said it should be longer than 1 year. More than one-third of all psychiatrists (37.3%) thought that 40–60% of their patients would discontinue medication on their own accord. More than 75% of the respondents felt that more than 60% of their patients would consider medication discontinuation if given such an opportunity.

After medication discontinuation, 43.2% thought that follow-up was needed for 2 years, 44% felt 1 year or shorter would be enough, while 9.3% felt lifetime follow-up was required. Psychiatrists had an equivocal attitude toward patients' quality of life; while 28.8% were in favor of those who discontinued medications, 28% were in

Table 1 The Most Common, Second- and Third- Most Common Responses to Medication Discontinuation Questions

Questionnaire Items	1st Common Response	2nd Common Response	3rd or Tied 2nd Common Response
1. What percentage of people do you think can stop antipsychotics completely following absence of psychotic symptoms following their first episode of a psychotic disorder?	0–20% (50.8%)	20–40% (34.7%)	40–60% (7.6%)
2. In general, how long do you think someone should remain on an antipsychotic medication following absence of psychotic symptoms in their first episode of a psychotic disorder?	1–2 years (29.7%)	6 months-1 year (27.1%)	Just 1 year (26.3%)
3. In general, over what period should antipsychotic medication be discontinued (ie, duration of tail off period) when psychotic symptoms have been absent in a FEP patient who has been treated with low or medium therapeutic dose of antipsychotic drug and agreed to discontinue medication?	6–12 months (29.7%)	12–24 months (27.1%)	3–6 months (18.6%)
4. What percentage of your patients discontinue medication of their own accord?	40–60% (37.3%)	60–80% (28.0%)	20–40% (22.0%)
5. What percentage of patients do you think, if they were asked, would like to be considered for discontinuation?	60–80% (34.7%)	80–100% (29.7%)	40–60% (19.5%)
6. In general, how long do you think the monitoring process should be followed up after medication discontinuation?	24 months (43.2%)	12 months (27.1%)	6 months (16.9%)
7. In general, do you think quality of life is better in those symptom free patients who remain on antipsychotics or those who stop them?	Unsure (43.2%)	Better in stop (28.8%)	Better in continued (28%)
8. How happy would you be to support your first-episode patients in participating in a randomised trial of discontinuing antipsychotic medication versus continuing on medication when their psychotic symptoms have been absent for more than 1 year?	Quite happy (35.6%)	Extremely happy (26.3%, tied)	Neither happy or unhappy (26.3%, tied)
9. Do you think the evidence from a well-conducted trial of this kind would affect your current practice?	A lot (61.0%)	Extremely (17.8%)	Quite a lot (13.6%)

Note: Adapted from Thompson A, Singh S, Birchwood M. Views of early psychosis clinicians on discontinuation of antipsychotic medication following symptom remission in first episode psychosis. *Early Interv Psychiatry.* (2015) 10:355–61. doi: 10.1111/eip.12244.[46] © 2015 Wiley Publishing Asia Pty Ltd.

favor of patients in maintenance therapy, and those remaining expressed uncertainty (43.2%). A majority (61.9%) expressed willingness (from quite happy to extremely happy) to participate in a randomized controlled trial for medication discontinuation on patients with remitted first-episode psychosis, and 78.8% agreed that evidence derived from such a study would have a definite impact on their clinical practice when treating patients in remitted psychosis.

Overall, gender and years of experience had no statistically significant impact on participants' responses to attitudes towards medication discontinuation.

Response to Case Vignettes

Psychiatrists' responses to case vignettes were quite diverse (Table 2). The majority of psychiatrists (range, 56.0% to 82.8%) responded that they would not initiate a discussion with the patient about discontinuing medication in Cases 1–5. Case 6, which depicted an apparent brief psychotic disorder, was the only exception that was endorsed by 84.6% of the respondents to discuss stopping medication. If a patient inquired whether he or she could try dose discontinuation, lower rates of positive responses were offered, and the most frequent response to patients' inquiries (range, 37.1% to 52.6% among Cases 1 to 5) was to "observe for a longer term." No statistically significant differences were found between the impact of psychiatrists' gender and years of experience on their responses to individual case vignettes.

Revealed by their response to questionnaire item 1

> what percentage of people do you think can stop antipsychotics completely following absence of psychotic symptoms following their first episode of a psychotic disorder?

Table 2 The Percentage of Responses to Each Case Vignette

Case	Yes	No	P value* (Gender)	P value** (YOE)	NR	OB	R	P value* (Gender)	P value*** (YOE)
C1	44.0%	56.0%	0.910	0.445	15.4%	43.6%	41.0%	0.277	0.188
C2	42.7%	57.3%	0.535	0.227	27.6%	37.1%	35.3%	0.358	0.098
C3	17.2%	82.8%	0.349	0.509	42.6%	47.0%	10.4%	0.092	0.355
C4	30.5%	69.5%	0.585	0.061	36.4%	39.8%	23.7%	0.523	0.138
C5	34.7%	65.3%	0.216	0.688	19.8%	52.6%	27.6%	0.688	0.678
C6	84.6%	15.4%	0.110	0.641	3.4%	15.5%	81.0%	0.434	0.693

Notes: C1: male, 30-years-old, employed, ill for 3 years, schizophrenia, olanzapine 5 mg, positive and negative symptoms absent for 2.5 years, good social support, stressful work, attends clinic regularly but sometimes misses appointment, medication side-effect of weight gain; C2: female, 25-years-old, employed, ill for 5 years, schizophrenia, quetiapine 100 mg, positive symptoms absent for 4 years, negative symptoms present, good social support, father had schizophrenia, plans to get married and pregnant next year; C3: female, 20-years-old, unemployed, ill for 2 years, schizophreniform disorder, aripiprazole 5 mg, presence of mild persecutory delusions but not distressed, negative symptoms absent, good social support, no family history of schizophrenia, no history of relapse; C4: male, 37-years-old, employed, ill for 3 years, schizophreniform disorder, risperidone 2 mg, positive and negative symptoms absent for 2 years, fair social support, mother had schizophrenia, no history of relapse; C5: female, 19-years-old, student, ill for 3 years, schizoaffective disorder, paliperidone 3 mg, positive symptoms absent for 3 years, negative symptoms present, fair social support, no family history of schizophrenia, no history of relapse nor substance abuse; C6: male, 29-years-old, employed, ill for 3 years, brief psychotic disorder, quetiapine 100 mg, positive and negative symptoms absent for 3 years, good social support, no family history of schizophrenia, no history of relapse, good compliance; Yes: percentage of psychiatrists who would initiate medication discontinuation for the case; No: percentage of psychiatrists who would not initiate medication discontinuation for the case; NR: if patient raised the issue of medication discontinuation, percentage of psychiatrists who would recommend against doing so; OB: if patient raised the issue of medication discontinuation, percentage of psychiatrists who would suggest observing for a longer period of time before doing so; R: if patient raised the issue of medication discontinuation, percentage of psychiatrists who would recommend discontinuation; YOE: years of experience. *The statistical significance of gender was tested by Chi-square tests. **The statistical significance of years of experience was tested by logistic regression. ***Dichotomization was done in the latter part of this section for statistical analysis, in which "NR" and "OB" were classified as no discontinuation recommendation, and "R" was recommendation of discontinuation. Adapted from Hui CL, Wong AK, Leung WW, et al. Psychiatrists' opinion towards medication discontinuation in remitted first-episode psychosis: A multi-site study of the Asian Network for Early Psychosis. *Early Interv Psychiatry.*[47] © 2018 John Wiley & Sons Australia, Ltd.

as well as response to Case 1 and Case 4, psychiatrists who endorsed a higher percentage of patients who are able to stop antipsychotics completely following remission from FEP were also significantly more inclined to initiate discussion about medication discontinuation with their remitted patients. However, such positive correlations were not significantly present in the other four vignettes (Table 3).

Criteria for Medication Discontinuation

The top five criteria for eligibility of dose discontinuation factors are no relapse since remitted from first-episode psychosis; positive view of illness; no positive symptoms; good social and family support; and willingness and readiness to taper off medication (Table 4). Psychiatrists with more years of experience had a greater tendency to think of satisfactory social functioning, absence of family history of psychotic disorder, ability to cope with stressful situations (also endorsed by more male psychiatrists), and having a sense of humor as criteria for medication discontinuation. Ranking of the frequencies of items is similar to that of the ANEP survey, though in general, psychiatrists in the present study selected higher percentages for each item (Table 5).

Other criteria mentioned in psychiatrists' free-text responses included a less severe diagnosis (non-schizophrenia), good therapeutic alliance, absence of history of drug or alcohol abuse, better cognitive function, pregnancy, shorter time to reach remission after first episode of psychosis, and whether discontinuation would significantly reduce side effects of the medication.

Discussion

The Chance and Pace of Medication Discontinuation

This survey has provided valuable messages from the psychiatrists' perspective for several ongoing trials for antipsychotic dose reduction or discontinuation.[48–52] Around half of the psychiatrists in this study thought that only 0–20% of the patients remitted from FEP should stop their medication, while more than half of Western psychiatrists thought that 20–40% was appropriate for stopping medication (Thompson et al).[46] Such a conservative attitude regarding medication discontinuation following remission of FEP is similar to the ANEP results,[47] and the attitudes of both Asian studies are closer to the guidelines that suggest maintenance therapy even after a single psychotic episode.[21,22] Also, most Taiwan psychiatrists recommended stopping the medication gradually within a period of 6–12 months and even longer, and Western psychiatrists tended to do so within 3–6 months (median of Thompson et al's survey). Indeed, a recent proposal derived from a pharmacodynamic study suggested reducing antipsychotic doses in a very slow, hyperbolic manner

Table 3 Percentage of Psychiatrists Who Would Initiate Medication Discontinuation by Different Responses to Question 1

Case	Response to Question 1						P value**
	0%	0–20%	20–40%	40–60%	60–80%	80–100%	
C1	0/1 (0%)	21/60 (35.0%)	22/40 (55.0%)	4/9 (44.4%)	3/4 (75.0%)	1/2 (50.0%)	0.033*
C2	0/2 (0%)	24/60 (40.0%)	17/40 (42.5%)	6/9 (66.7%)	2/4 (50.0%)	1/2 (50.0%)	0.186
C3	2/2 (100%)	8/60 (13.3%)	9/39 (23.1%)	1/9 (11.1%)	0/4 (0%)	0/2 (0%)	0.612
C4	0/2 (0%)	11/60 (18.3%)	19/41 (46.3%)	3/9 (33.3%)	2/4 (50.0%)	1/2 (50.0%)	0.003*
C5	1/2 (50.0%)	16/60 (26.7%)	16/41 (39.0%)	7/9 (77.8%)	1/4 (25.0%)	0/2 (0%)	0.081
C6	2/2 (100%)	48/60 (80.0%)	36/41 (87.8%)	8/8 (100.0%)	4/4 (100.0%)	1/2 (50.0%)	0.242

Notes: In each cell: the denominator is the number of respondents who answered Question 1 "What percentage of people do you think can stop antipsychotics completely following absence of psychotic symptoms following their first episode of a psychotic disorder?" and the nominator is the number of them answered "Yes" to the question "Will you initiate discussion of medication discontinuation to this patient even if the patient hasn't asked for it?" The significance of correlation examined if the psychiatrist's attitude towards antipsychotic discontinuation was parallel to their action probed by each case vignette. For example, in Case 1, among the 60 respondents who endorsed 0–20% of patients can stop antipsychotics completely, only 21 (35%) of them will initiate discussion with their patients regarding medication discontinuation, even the patient has not asked for it; in contrast to the fact that 3 out of 4 (75%) respondents will do so as they endorsed that 60–80% of patients can stop antipsychotics completely. Thus, this suggests that psychiatrists who endorsed that a higher proportion of patients could stop antipsychotics completely were also more likely to initiate discussion about medication discontinuation with their patients. *p<0.05. **The statistical significance was tested by Mann–Whitney *U*-tests.

Table 4 Criteria for Medication Discontinuation

Criterion	Percentage of Psychiatrists' Response (%)			Gender		Years of Experience	
	Overall	Male	Female	P value**	OR[a]	P value**	OR[b]
Q1. Absence of any relapsing episode following first episode	90.7	89.6	91.4	0.791	0.825	0.880	0.995
Q2. Good insight into the illness	87.3	85.7	94.3	0.358	0.471	0.052	0.945
Q3. Absence of positive symptoms	81.4	76.6	91.4	0.074	0.303	0.880	1.004
Q4. Have good social/family/partner support	80.5	79.2	85.7	0.412	0.627	0.901	1.003
Q5. Willing and ready for medication discontinuation	79.7	81.8	80.0	0.665	1.259	0.307	0.975
Q6. Satisfactory social functioning	65.3	62.3	74.3	0.109	0.471	0.038*	1.049
Q7. No family history of psychotic disorder	65.3	63.6	62.9	0.578	0.779	0.002*	1.085
Q8. Able to cope with stressful situations	56.8	50.6	74.3	0.005*	0.265	0.007*	1.064
Q9. Absence of negative symptoms	51.7	48.1	62.9	0.074	0.460	0.062	1.040
Q10. Have a full-/part-time job	39.8	40.3	40.0	0.760	0.877	0.098	1.035
Q11. Engage in regular physical exercise	16.1	15.6	17.1	0.567	0.720	0.088	1.046
Q12. Have a sense of humor	6.8	7.8	5.7	0.792	0.786	0.009*	1.107

Notes: *p<0.05; [a]OR>1 representing male psychiatrists are more likely to choose this criterion; OR<1 representing male psychiatrists are less likely to choose this criterion. [b]OR>1 representing the more years of experience, the more likely a psychiatrist chooses this criterion; OR<1 representing the more years of experience, the less likely a psychiatrist chooses this criterion. **The statistical significance was tested by multivariable logistic regression. Adapted from Hui CL, Wong AK, Leung WW, et al. Psychiatrists' opinion towards medication discontinuation in remitted first-episode psychosis: A multi-site study of the Asian Network for Early Psychosis. *Early Interv Psychiatry*.[47] © 2018 John Wiley & Sons Australia, Ltd.

Abbreviation: OR, odds ratio.

every 3 to 6 months,[53] which implies that the seemingly slower pace of antipsychotic reduction endorsed by the psychiatrists in the present study may still be too fast to assure lower risk of relapse.

Cautious Yet Proactive Attitude of Taiwanese Psychiatrists

For most items probed by case vignettes, the ranking of positive responses to 6 cases by psychiatrists in the present

Table 5 Comparisons of Responses to Case Vignettes and Criteria for Medication Discontinuation Between Overall ANEP Countries and Taiwan

	ANEP (n = 482)	Taiwan (n = 118)	Chi 2 (1)	p
C1	34.4%	44.0%	3.799	0.051
C2	31.6%	42.7%	4.986	0.026*
C3	10.1%	17.2%	4.286	0.038*
C4	19.6%	30.5%	6.766	0.009*
C5	24.6%	34.7%	4.903	0.029*
C6	57.1%	84.6%	31.015	< 0.001*
Q1	88%	90.7%	0.685	0.408
Q2	73.9%	87.3%	9.509	0.002*
Q3	76.6%	81.4%	1.252	0.263
Q4	69.1%	80.5%	6.047	0.014*
Q5	56.8%	79.7%	20.805	< 0.001*
Q6	62.4%	65.3%	0.320	0.571
Q7	51.9%	65.3%	6.851	0.009*
Q8	63.5%	56.8%	1.812	0.178
Q9	43.2%	51.7%	2.796	0.094
Q10	19.7%	39.8%	21.243	< 0.001*
Q11	7.7%	16.1%	7.952	0.005*
Q12	5.6%	6.8%	0.240	0.625

Notes: C1~C6 are the case vignettes described in Tables 2 and 3; Q1–Q12 are the items listed in Table 4, all following the orders listed in previous tables; The percentages are responses of "Yes" to the designated items; Numbers in ANEP (Asian Network of Early Psychosis) were adopted from Hui CL, Wong AK, Leung WW, et al. Psychiatrists' opinion towards medication discontinuation in remitted first-episode psychosis: A multi-site study of the Asian Network for Early Psychosis. *Early Interv Psychiatry*.[47] © 2018 John Wiley & Sons Australia, Ltd.*p<0.05.

study parallels the conservative approach shown in surveys conducted in the other 4 Asian countries, but generally with a higher proportion of positive responses to individual cases. Also, a greater proportion of Taiwan psychiatrists endorsed discontinuation of antipsychotic medications from 6 to 12 months after complete remission, compared to 1 to 2 years endorsed by psychiatrists in the other 4 Asian countries, as well as a larger proportion of Taiwan psychiatrists willing to support a randomized trial for medication discontinuation to provide evidence that may affect clinical practice. Such proactive attitudes are most likely related to their knowledge regarding the investigators' ongoing project of antipsychotic dose reduction.[49]

The first four most frequently chosen criteria for medication discontinuation are the same between the present study and the ANEP survey, since previous relapse is obviously a strong predictor of subsequent relapse.[54] Having poor insight into the illness was also a significant risk factor for relapse after first-episode psychosis,[55] and a sound supportive system of family and friends can also be a protective factor.[56] However, even though the majority of psychiatrists identified that the presence of positive symptoms was not good for medication discontinuation, other studies have suggested that the severity of negative symptoms is an even stronger predictor of further relapse.[43] In the present study, among the six items endorsed by significantly more Taiwan respondents (Table 5), nearly 80% selected patient's readiness and willingness to be an important criterion for medication discontinuation, a factor taken into account by Liu's protocol.[49]

Complex Relationship Between Attitude and Clinical Practice

Psychiatrists' estimated chance of and criteria for successful discontinuation appears to affect their decisions for treating patients probed by case vignettes. Case 6 met most of the frequently chosen criteria for medication discontinuation, and therefore it was the only vignette nominated by the majority of psychiatrists as eligible for discontinuing medications. However, in the other five cases, each failed to meet certain criteria deemed to be important, thus not as many psychiatrists endorsed the patients' eligibility for discontinuation. Exemplified by Case 1 and Case 4, individual psychiatrists' attitudes and clinical practice were quite consistent; that is, those who expressed proactive attitudes were more likely to endorse initiation of medication discontinuation (Table 3). However, such relationships were not found in the other three cases, implying that psychiatrists' practice is not always concordant with their attitudes, leaving some undetermined factors to be further explored.

This survey study also highlighted some subtle differences in attitudes on the criteria of medication discontinuation by psychiatrists' years of experience. Certain indicators that could only be obtained by greater understanding of patients and family, including satisfactory social functioning, absence of family history of psychotic disorders, ability to cope with stressful situations, and a sense of humor, were more likely to be selected for discontinuation by more experienced psychiatrists. This phenomenon implies that older psychiatrists are more likely to take more heuristics into consideration when making decisions about antipsychotic dose reduction or discontinuation.

Limitations

The present cross-sectional questionnaire survey has several limitations. First, regarding the representativeness of convenience sampling, we conjectured that our respondents may be more inclined to show proactive attitude as revealed by their greater interest in antipsychotic discontinuation trials; in that respect, representativeness may be less of an issue than with purposive sampling. Second, the original questionnaire did not include certain frequently mentioned predictors, such as substance use disorders, longer duration of untreated psychosis, and a diagnosis of schizophrenia spectrum disorder; also, in the free-text responses in the last part of the questionnaire, the respondents provided additional items to be considered in future surveys. Third, the psychiatrists' responses to case vignettes represent just a proxy of actual clinical practice. A qualitative interview would be expected to give more insightful information to this issue.

Conclusion

The psychiatrists who participated in this questionnaire survey expressed a willingness to give patients remitted from FEP a chance to try dose reduction or discontinuation. However, once patients had been presented with actual clinical scenarios, many of them hesitated to suggest discontinuation of antipsychotic medications for various reasons. In addition to clinical features, respondents also considered many aspects of patients' lives and readiness for dose reduction to discuss with their patients. Nonetheless, clinical trials comparing the outcomes of maintenance and medication discontinuation are anticipated to provide references for psychiatrists to fine-tune their clinical practice.

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Author Contributions

All authors have made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; took part in drafting the article or revising it critically for important intellectual content; reviewed and agreed on all versions of the article; gave final approval of the version submitted to the current journal and agree to be accountable for all aspects of the work.

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Disclosure

All authors declare no conflicts of interest.

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