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Authors

Hui, Christy

Wong, Charlie

Lui, Eddie

et al.

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Effects of mindfulness-based intervention in preventing relapse in patients with remitted psychosis: a randomized controlled trial

Christy Lai Ming Hui[1 ✉], Charlie Cheuk Lam Wong[1], Eddie Chi Yuen Lui[1], Tsz Ching Chiu[1], Tiffany Junchen Tao [1,2], Evie Wai Ting Chan[1], Jingxia Lin[3], Alan C. Y. Tong[4], Yi Nam Suen [5], Charles W. H. Chan[6], Wai Song Yeung[6], Edwin Ho Ming Lee[1], Sherry Kit Wa Chan [1,7], Wing Chung Chang[1,7] and Eric Yu Hai Chen[1,8]

Stress is a key factor in psychotic relapse, and mindfulness offers stress resilience and well-being benefits. This study examined the effects of mindfulness-based intervention for psychosis (MBI-p) in preventing relapse at 1 year among patients with remitted psychosis in Hong Kong. MBI-p is a newly developed manual-based mindfulness protocol and was tested to have improved well-being and clinical outcomes in a pilot study with remitted psychosis patients. In this multisite, single-blind, 1-year randomized controlled trial (RCT), 152 fully remitted patients diagnosed with schizophrenia or non-affective psychosis were randomized to receive either a 7-week MBI-p or a 7-week psychoeducation program. Outcomes were assessed before and after the intervention, and then monthly for one year. Relapse rate and severity at one year were the primary outcomes. Secondary outcomes included psychopathology, functioning, mindfulness, and psychosocial factors such as stress and expressed emotions. No significant differences were found in the rate and severity of relapse between the MBI-p and psychoeducation groups in either intention-to-treat or per-protocol analyses. While MBI-p improved observation and non-reactivity to the inner experience of mindfulness, psychoeducation was found to benefit functioning and psychosocial functioning more than MBI-p. This is the first RCT to test MBI-p's effectiveness in preventing relapse among patients with remitted psychosis in Hong Kong. We postulate that the lack of significance is due to the heightened effectiveness of psychoeducation in coping with stress during the pandemic and the multifactorial causes leading to relapse. This suggests the possibility of combining these two interventions to improve their efficacy. Trial registration: NCT04060498.

INTRODUCTION

Preventing relapse after stabilizing the first episode of psychosis is crucial. Psychotic symptom recurrence, such as delusions and hallucinations, is distressing and costly[1], with some relapses leading to treatment resistance[2]. Although antipsychotic medication can be effective, not all patients can avoid relapse. Even among those who continue their antipsychotic treatment, the relapse rate remains at 41%[3]. Interest in non-pharmacological treatments, such as cognitive-behavioral therapy (CBT), is growing. Multimodal CBT for patients, families, and group CBT have been effective and have successfully reduced relapse[4,5]. However, delivering CBT can be challenging in resource-limited settings because it needs specialized therapists. Family interventions have also shown a 20% reduction in relapse rates in schizophrenia[6]; nevertheless, routine use depends on varying family involvement and commitment.

Stress significantly affects psychosis relapse, as evidenced by prospective and retrospective studies linking life events, such as environmental changes and unemployment, to relapse prediction in schizophrenia[7–11]. These studies show that such stressful events tend to cluster in the two to four weeks immediately preceding relapse. Expressed emotion, particularly "carers' critical comments," emerged as a significant predictor of relapse[12–14]. The stress experienced by patients from life events or critical comments underscores its pivotal role in precipitating psychotic relapse, suggesting that interventions targeting stress modulation may aid in relapse prevention. Meanwhile, mindfulness is the practice of being present without judgment, often cultivated through meditation[15]. It has been linked to improved well-being[16], and is recognized as a valuable psychological intervention, known as the third wave after behavioral and cognitive interventions. Recent meta-analyses highlight its effectiveness in alleviating various psychiatric symptoms such as stress, anxiety, mood disorders, and eating disorders[17,18]. Mindfulness has also shown promise in reducing both daily and clinically relevant stresses in various populations[19–22]. Therefore, the exploration of mindfulness intervention that modulates stress may be relevant to relapse prevention in psychosis.

Mindfulness has gained popularity as a non-pharmacological treatment for psychosis. Chadwick[23] developed Person-Based Cognitive Therapy (PBCT) by combining Mindfulness-Based Stress Reduction (MBSR)[24] and Mindfulness-Based Cognitive Therapy (MBCT)[25]. Preliminary studies[26,27] and randomized controlled trials (RCTs)[28–30] suggest that PBCT helps patients respond mindfully to psychotic symptoms, reduces hospitalizations, and improves

[1]Department of Psychiatry, School of Clinical Medicine, LKS Faculty of Medicine, University of Hong Kong, Hong Kong SAR, China. [2]Department of Psychological Science, University of California, Irvine, CA, US. [3]Department of Rehabilitation Sciences, The Hong Kong Polytechnic University, Hong Kong SAR, China. [4]Department of Applied Social Sciences, The Hong Kong Polytechnic University, Hong Kong SAR, China. [5]School of Nursing, LKS Faculty of Medicine, University of Hong Kong, Hong Kong SAR, China. [6]Department of Psychiatry, Pamela Youde Nethersole Eastern Hospital, Hong Kong SAR, China. [7]State Key Laboratory of Brain and Cognitive Sciences, University of Hong Kong, Hong Kong SAR, China. [8]Orygen National Center of Excellence in Youth Mental Health, University of Melbourne, Melbourne, Australia. ✉email: christy@lmhui.com

functioning. However, these protocols are relatively complicated and require intensive training. Therefore, we aimed to test a simplified, manual-based mindfulness protocol—the mindfulness-based intervention for psychosis (MBI-p)[31]. MBI-p focuses on simplicity for facilitators and patients and uses acceptance and embracing attitudes for fear and sadness. Tong et al.[31] developed the protocol using a systematic approach, drawing from multiple sources such as MBSR[24], the works of Thich Nhat Hanh[32], and Rezek[33]. The content, number, and duration of the sessions were refined through three pilot trials before finalization. The ultimate aim is to help patients achieve a greater sense of peace and calm and facilitate managing everyday stress and conflicts (for more detailed information on the content and development of the manual and protocol, see Tong et al.[31]). The pilot study involving 14 patients with remitted schizophrenia revealed that after seven weeks of MBI-p, the severity of psychotic and depressive symptoms and the mental component of life quality improved[31]. Patients provided positive feedback and experienced positive changes after MBI-p training. Additionally, a meta-analytic review investigating the efficacy of mindfulness meditation in Chinese patients with psychosis found that it improved their mindfulness levels with improvements in well-being and clinical outcomes[34].

Given the significant improvement of well-being in the pilot study, we aim to further test the long-term impact and efficacy on relapse prevention of MBI-p. To date, only a few studies have explored the long-term effects of mindfulness-based intervention (MBI) and its role in relapse prevention in remitted psychosis patients specifically in Chinese population[34]. Longitudinal studies, with follow-up periods ranging from 6 months to 24 months, found significant impact of MBI on improving clinical symptoms for early psychosis, but remission status of the sample is unknown, and the sample is likely to have a mixture of active and remitted patients[35–37]. Most importantly, they tended to measure overall clinical outcome instead of relapse. Meanwhile, only one study has specifically focused on relapse rate and found that MBI is significantly better than treatment as usual (TAU) at post-intervention[38]. Yet, no longer follow-up was available, and definition of relapse was unclear. Despite the success in soothing clinical symptoms of active psychosis, MBI's long term impacts and efficacy in preventing relapse remains uncertain.

In this study, we primarily examined whether MBI-p could reduce relapse after one year. We then investigated whether MBI-p could reduce stress and depressive symptoms and improve functioning and life quality at post-intervention and one-year follow-up. One year was chosen as the study duration because previous research indicates that significant changes can be observed within a minimum of six months[37]. Additionally, it provides sufficient time for relapse to be detected, as demonstrated by naturalistic studies examining relapse rates following first-episode psychosis (FEP) in Hong Kong[39,40].

METHODS

Study design and participants
This study was a single-blind, multisite RCT on MBI's effectiveness in preventing relapse in patients with remitted psychosis. Recruitment took place between October 2019 and May 2023. In total, 152 eligible patients were consecutively recruited from two general adult outpatient clinics and two Early Assessment Services for Young People with Psychosis (EASY) outpatient psychiatric clinics, located at Queen Mary Hospital and Pamela Youde Nethersole Eastern Hospital in Hong Kong. EASY provides specialized psychiatric care for young individuals with FEP for the first three years, with extended follow-up when necessary, covering approximately seven million people in Hong Kong. As a result, the sample includes not only early psychosis cases but also a mix of patients with varying durations of illness.

Recruited patients were randomized to receive either a 7-week MBI-p or a 7-week psychoeducation program. This study was reported according to Consolidated Standards of Reporting Trials (CONSORT) reporting guideline. The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. The study was approved by the Institutional Review Board of each participating site and registered at ClinicalTrials.gov (NCT04060498) before trial commencement. All participants provided written informed consent.

The study comprised the following time points: baseline (before intervention), after the 7-week intervention, and monthly for the remaining one year following intervention. At each time point, participants completed clinical, cognitive, and psychosocial assessments via either Zoom or face-to-face interviews. Relapse was assessed during the intervention and monthly during the one-year follow-up period. Patients were excluded if they relapsed during the study.

Inclusion criteria were as follows: (1) age 18–55 years; (2) full symptomatic remission for at least six months (Positive and Negative Syndrome Scale: delusion ≤2, conceptual disorganization ≤3, hallucination ≤2, suspiciousness ≤4, unusual thought content ≤3); and (3) sufficient proficiency in Chinese to understand verbal instructions and provide informed consent. Exclusion criteria were as follows: (1) known diagnosis of intellectual disability, (2) organic brain disorder, (3) current or previous use of illicit drugs, (4) substance-induced psychosis or alcohol intake in excess of five standard units per day, and (5) practice of mindfulness and meditation exercises more than twice a week over the past month.

Sample size
Naturalistic studies in Hong Kong report relapse rates of 16–20% within the first year and 16–40% within the first three years of FEP[39,40]. Additionally, the only study comparing relapse rates between TAU and MBI found a relapse rate of 13.3% in the intervention group over one month[38]. Based on these findings, the proposed sample size was 144 patients (72 per treatment group), estimated on a power of 80% and a 0.05 alpha to detect 1-year relapse rates of 15% in the mindfulness group and 35% in the psychoeducation group. Considering a 5% dropout rate, the estimated sample size was 152 patients (76 per treatment group).

Randomization and blinding
Patients were individually randomized into one of two parallel groups: 7-week MBI-p and 7-week psychoeducation. The investigator generated a randomization sequence using a computer with a fixed block size of four without stratification at an intervention-to-control ratio of 1:1. The investigator does not participate in any data obtaining or analysis to prevent bias. The first project staff enrolled patients at psychiatric clinics, and the investigator conducted randomization. During randomization, each patient was consecutively assigned a unique Project ID and treatment arm according to the randomization list. In this single-blind study, investigators, patients, and the first project staff were aware of the treatment arms. However, all subsequent baseline and monthly outcome assessments were conducted by a second-project staff member blinded to the randomization of the treatment and block size.

Intervention
As some patients were recruited from the EASY outpatient clinics, these patients underwent the EASY early intervention. EASY is a 3-year service targeting at those who have experienced their first episode of psychosis in Hong Kong. Specialized multidisciplinary mental health teams offered phase-specific interventions focusing

on intensive case management and promoting recovery and functional improvement. EASY's reach extends through a robust media campaign and screening hotline system[41]. While the other patients did not receive the EASY interventions, we did not document any additional psychological interventions received by these patients.

Mindfulness intervention group. The mindfulness group underwent MBI-p for seven weeks. MBI-p, a low-intensity protocol-based mindfulness program, aims to enhance patient peace, calmness, and stress management (refer to Tong et al.'s pilot study[31] for details). Our facilitators were master's level psychology graduates trained by two investigators (Tong and Lin). Seven 1.5-hour online group sessions were conducted due to the COVID-19 pandemic, covering engagement, mindfulness practices, daily life applications, and consolidation of learning. Facilitators used adaptations such as mindful outdoor-walking audio for online sessions.

Mindfulness practice encourages participants to respond with clarity to stress reactions and let go of clinging to emotions, thus, fostering a decentered awareness. The program addressed nonjudgment by guiding participants to accept judgments as part of themselves, thereby enhancing stress reactivity through desensitization. Group discussions involved reflection on coping reactions through Socratic discussions.

To support mindfulness practice beyond the sessions, participants received information on mindfulness benefits and a WhatsApp booklet for recording their practices and changes after each session. Moreover, a link to a 3-to-9-min audio of daily mindfulness meditations was sent after every session. Weekly sessions included participants sharing their practice experiences, and monthly booster messages on WhatsApp served as reminders of post-intervention self-practice.

Psychoeducation group. Each psychoeducation session lasted 1.5 h and was held once a week for seven weeks. It included topics on psychosis' signs and symptoms, etiology of psychosis, pharmacological and non-pharmacological treatment, healthy living tips such as stress management and exercise, and communication skills. Like the MBI group, our facilitators were master's-level psychology graduates who had been trained by our investigators. They were also encouraged to engage with participants during each session.

Outcome assessments

Primary outcome. The primary relapse outcome was the presence of all the following conditions for at least one week: (1) an increase in at least one of the following Positive & Negative Syndrome Scale (PANSS)[42] items (delusion, hallucinatory behavior) to a score of ≥3; (conceptual disorganization, unusual thought content) to a score of ≥4; (suspiciousness) to a score of ≥5; (2) Clinical Global Impression (CGI) Severity of Illness[43] scale rated ≥3; and (3) CGI Improvement scale rated ≥5. A binary relapse variable was created to represent whether the patient experienced relapse during the follow-up period. Furthermore, continuous variables were also created for individual relapse item scores (e.g., PANSS delusion, PANSS hallucinatory behavior, and PANSS conceptual disorganization). Relapse was assessed before (baseline) and after seven weeks of intervention; thereafter, monthly until one-year post-intervention. Patients experiencing a relapse at any month during the one-year follow-up period signified study termination.

Secondary outcomes. Basic demographic information, including age, sex, years of education, employment status, duration of untreated psychosis, and diagnosis, was obtained at baseline. Psychopathology, functioning, cognitive functioning, psychosocial well-being, and mindfulness were measured before and after

intervention; thereafter, monthly for one year.

PANSS measured positive and negative symptoms. The Calgary Depression Scale for Schizophrenia (CDSS)[44] measured depressive symptoms, the Modified Medication Adherence Rating Scale[45] measured treatment adherence, and the List of Threatening Experiences[46] assessed stressful life events. Functioning was measured using the Social and Occupational Functioning Assessment Scale[47], Role-Functioning Scale[48], and Social Functioning Scale[49], while life quality was measured using the 12-Item Short-Form Health Survey[50]. Psychosocial factors, such as expressed emotion, resilience, and perceived risk of relapse, were measured using the Expressed Emotion Scale[51], Connor-Davidson Resilience Scale -10 items[52], and Perceived Recovery Inventory[53]. Neurocognitive performance was assessed using the visual pattern test and letter-number span. Mindfulness was measured using the Five-Facet Mindfulness Questionnaire (FFMQ)[54]. Scale details are provided in Supplementary List 1.

Statistical analysis

All statistical analyses were conducted using IBM® SPSS® version 28.0.1.0. All enrolled participants were included in the intention-to-treat (ITT) analysis of relapse prevention at one year. We performed a per-protocol (PP) sensitivity analysis on patients who had completed all seven sessions of either intervention. To explore the predictive nature of the intervention group (MBI-p vs. psychoeducation) for relapse at the one-year post-intervention mark, logistic regression was used for the categorical outcome variable (relapsed vs. no relapse), whereas linear regression determined the continuous outcome variables (e.g., individual relapse item score). Age was included as a covariate in the regression analysis because it showed marginal significance in the preliminary analysis when comparing the demographic information between the two groups. The relapse status of patients who dropped out before the intervention ($n = 20$) was assessed using the Clinical Management System (CMS). Relapse was defined as the deterioration of symptoms meeting the relapse criteria within one year of their baseline assessment date, as documented in their CMS case notes.

A linear mixed-effects model (LMM) analyzed the secondary outcomes (e.g., psychopathology, functioning, cognitive functioning, and life quality). We compared baseline data with post-intervention (i.e., short-term impacts) and with one-year follow-up outcomes (long-term impacts). This analysis adopted the ITT approach enrolling all participants in this study, regardless of their dropout or relapse status. Data were collected from patients who had dropped out during the study. LMM assessed the interaction effect of interventions (MBI-p vs. psychoeducation) and time (baseline vs. post-intervention or baseline vs. one-year follow-up), controlling for age. For all analyses, a two-sided p-value was calculated and a value of less than 0.05 was considered significant.

RESULTS

Recruitment outcome

Of 152 participants, 77 were in the MBI-p and 75 in the psychoeducation group. Ten patients withdrew before intervention in both interventions. During the intervention, three participants withdrew from MBI-p, one relapsed, and two withdrew from psychoeducation. During the one-year follow-up, 10 patients relapsed, 12 withdrew from MBI-p, 6 relapsed, and 17 withdrew from the psychoeducation program (Fig. 1).

Demographic information

We examined participants' basic demographic information ($n = 152$) in both intervention groups. Participants in the MBI-p group (M = 40.16, SD = 9.43) were slightly older than those in the
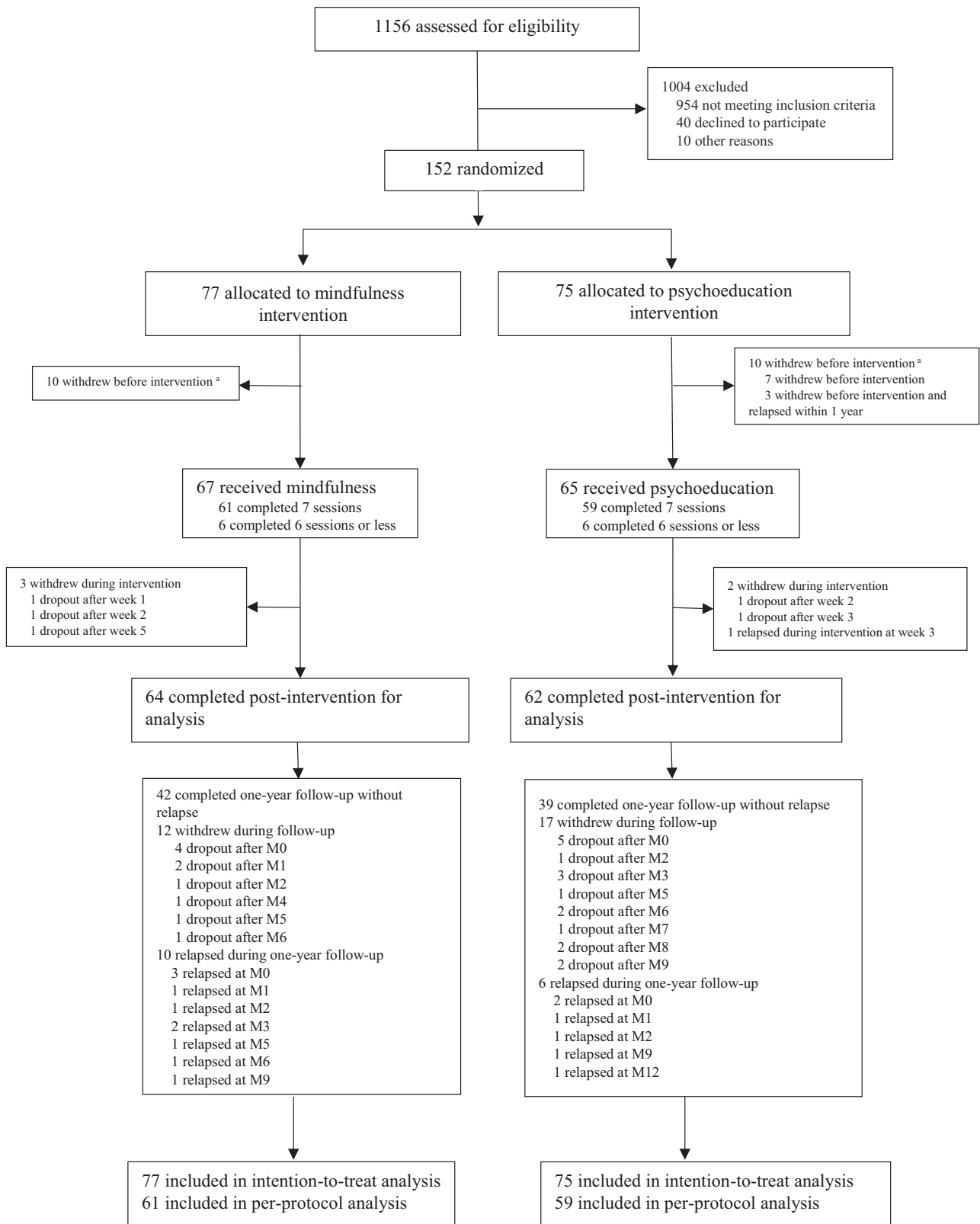
Fig. 1 Enrollment and outcomes. [a]The relapse status of patients who dropped out before the intervention (n = 20) was assessed using the Clinical Management System (CMS). Relapse was defined as the deterioration of symptoms meeting the relapse criteria within one year of their baseline assessment date, as documented in their CMS case notes. For the rest of the patients (n = 132), relapse status was assessed from monthly assessment based on the deterioration of symptoms meeting the relapse criteria. The relapse criteria was the presence of all the following conditions for at least one week: (1) an increase in at least one of the following PANSS27 items (delusion, hallucinatory behavior) to a score of ≥3; (conceptual disorganization, unusual thought content) to a score of ≥4; (suspiciousness) to a score of ≥5; (2) Clinical Global Impression (CGI) Severity of Illness29 scale rated ≥3; and (3) CGI Improvement scale rated ≥5. Continuous variables were also created for individual relapse item scores (e.g., PANSS delusion).

Table 1. Comparisons of basic demographics at baseline between MBI-p and Psychoeducation groups.

Variables, mean (SD)	All ($n = 152$)	MBI-p ($n = 77$)	Psychoeducation ($n = 75$)	Statistics	p-value
Age	38.77 (9.03)	40.16 (9.43)	37.35 (8.42)	$t = 1.936$	0.055
Male (n, %)	52 (34.2%)	26 (33.8%)	26 (34.7%)	$X^2 = 0.014$	0.907
Schizophrenia (n, %)	93 (61.2%)	48 (62.3%)	45 (60.0%)	$X^2 = 0.087$	0.767
Single (n, %)	110 (75.3%)	53 (72.6%)	57 (78.1%)	$X^2 = 0.590$	0.442
Years of education	13.49 (2.98)	13.41 (3.16)	13.57 (2.81)	$t = -0.327$	0.744
Employed (n, %)	107 (70.4%)	51 (66.2%)	56 (74.7%)	$X^2 = 1.296$	0.255
Birth in HK (n, %)	122 (80.3%)	59 (76.6%)	63 (84.0%)	$X^2 = 1.305$	0.253
Alcohol use[a] (n, %)	135 (88.8%)	69 (89.6%)	66 (88.0%)	$X^2 = 0.099$	0.753
Drug use[a] (n, %)	7 (4.6%)	5 (6.5%)	2 (2.7%)	$X^2 = 1.267$	0.442
Smoking (n, %)	11 (7.2%)	6 (7.8%)	5 (6.7%)	$X^2 = 0.072$	0.789
DUP, days (median, IQR)	38.00 (8.00–160.00)	32.50 (7.00–166.75)	45.00 (13.00–155.00)	$Z = -0.646$	0.518
Duration of illness ≤5 years (n, %)	34 (22%)	14 (18.2%)	20 (26.7%)	$X^2 = 1.613$	0.204
Medication adherence behavior[b]	3.70 (0.40)	3.70 (0.37)	3.70 (0.42)	$t = 0.043$	0.965

IQR interquartile range, *SD* standard deviation, *n* number, *DUP* duration of untreated psychosis.
[a]This refers to if the patient has ever tried alcohol/ drugs throughout their lifetime.
[b]Medication adherence behaviors are self-reported by patients using the Medication Adherence Rate Scale, which captures both intentional (e.g., deliberate decision to stop taking medication) and unintentional (e.g., forgetting to take medication) actions.

psychoeducation group (M = 37.35, SD = 8.42; $p = 0.055$). Owing to its marginal significance, age was treated as a covariate in subsequent analyses. Other demographic variables such as sex, diagnosis, marital status, years of education, and untreated psychosis (DUP) were not significantly different (Table 1). Our sample consists of patients with varying durations of illness, with only 22% classified as being in early psychosis, defined as having an illness duration of less than five years. There was no significant difference between the intervention groups in the proportion of early psychosis patients ($p = 0.204$). Additionally, relapse rates did not differ based on the duration of illness (Supplementary Table 1).

Participants in both groups completed almost all intervention sessions (83%) with no significant difference in the proportion of lessons attended by the two groups (Supplementary Table 2).

Relapse outcome
At the one-year follow-up, 10 (13.0%) participants in the mindfulness group and 10 (13.3%) in the psychoeducation group relapsed. Both MBI-p and psychoeducation showed similar rates of relapse at one year (Odds ratio = 1.064, 95% CI [0.410, 2.762], $p = 0.889$), and severity of relapse, as indicated by the total and five individual relapse item scores (i.e., PANSS Delusion, Conceptual Disorganization, Hallucination, Suspiciousness/Persecution, and Unusual Thought Content) at one-year follow-up (p-values of 0.256–0.937). PP analysis showed consistent results (p-values of 0.072–0.837) with the ITT approach (Table 2).

Psychopathological comparisons
Post-intervention, the interaction effect on the CDSS was significant, in which MBI-p showed a more severe CDSS score, whereas psychoeducation showed an improvement ($p = 0.024$). At the one-year follow-up, the PANSS total score ($p = 0.037$) was significantly different; both interventions showed a more severe score, but MBI-p showed greater deterioration (Table 3).

Functioning, cognitive functioning, and life quality comparisons
Several significant interaction effects were observed after the intervention. MBI-p showed a reduction in social activities but

psychoeducation showed an increase ($p = 0.005$), and this effect persisted at the one-year follow-up ($p = 0.005$; Table 3). MBI-p also presented a more severe hostility score for expressed emotions but a lower score for psychoeducation ($p = 0.031$). Although this did not persist at the one-year follow-up, the overall expressed emotion was significantly decreased in psychoeducation, but not in MBI-p ($p = 0.046$). Resilience increased significantly in psychoeducation but decreased in MBI-p ($p = 0.036$); however, this effect did not persist. Patients in the psychoeducation group showed a significant reduction in perceived risk of relapse, but MBI-p score increased ($p = 0.035$) post-intervention (Table 4).

Mindfulness comparisons
Several interaction effects were observed after intervention. The results revealed that MBI-p enhanced observing ($p = 0.047$) and non-reactivity to inner experiences ($p = 0.007$), whereas psychoeducation led to a decline in these facets. However, a decline in description ($p = 0.001$) and acting with awareness ($p < 0.001$) was found in MBI-p, whereas psychoeducation improved these facets. The effects of observing, acting with awareness, and non-reactivity to inner experiences persisted at the one-year follow-up (Table 4).

DISCUSSION
We found that MBI-p did not prevent relapse or improve clinical symptoms better than psychoeducation but demonstrated a similar effect on mindfulness facets as Tong et al.'s pilot study. Psychoeducation shows promising benefits in enhancing secondary outcomes such as functioning and life quality among these patients.

MBI-p on relapse prevention
We found no significant differences in relapse rates or severity between the MBI-p and psychoeducation groups. Thus, MBI-p does not offer added benefits in reducing relapse rates or severity of psychoeducation among remitted patients with psychosis at the one-year mark. Few longitudinal studies have explored the long-term effects of MBI on patients with psychosis[34]. For instance, only one study examined MBI's impact on relapse and found it significantly better than TAU[38]. However, these findings' generalizability is uncertain owing to the treatment-group format

Table 2. Predictability of intervention group on relapse using logistic regression and linear regression for intention to treat (n = 152) and per protocol (n = 120).

Outcome, mean (SD)[a]	Intervention				Analysis[bc]			
	MBI-p (n = 77)		Psychoeducation (n = 75)		Intention-to-treat		Per-protocol	
	Baseline	Termination	Baseline	Termination	Estimate/B (95% CI)	p-value	Estimate (95% CI)	p-value
Relapse (n, %)	N/A	10 (13.0%)	N/A	10 (13.3%)	1.064 (0.410, 2.762)	0.899	0.507 (0.160, 1.607)	0.248
Relapse item score total	5.34 (0.88)	6.42 (2.94)	5.25 (0.84)	6.25 (3.09)	−0.054 (−1.030, 0.923)	0.914	−0.718 (−1.685, 0.249)	0.144
PANSS P1-Delusion	1.00 (0)	1.30 (0.95)	1.00 (0)	1.23 (0.94)	−0.046 (−0.352, 0.259)	0.765	−0.244 (−0.554, 0.067)	0.123
PANSS P2-Conceptual disorganization	1.16 (0.54)	1.38 (0.87)	1.13 (0.50)	1.36 (0.86)	0.011 (−0.270, 0.293)	0.937	−0.074 (−0.387, 0.238)	0.639
PANSS P3- Hallucination	1.00 (0)	1.14 (0.56)	1.00 (0)	1.21 (0.78)	0.086 (−0.133, 0.304)	0.440	−0.093 (−0.279, 0.093)	0.325
PANSS P6- Suspiciousness/ Persecution	1.10 (0.45)	1.31 (0.91)	1.07 (0.41)	1.15 (0.65)	−0.148 (−0.405, 0.109)	0.256	−0.276 (−0.578, 0.025)	0.072
PANSS G9-Unusual thought content	1.08 (0.39)	1.29 (0.86)	1.05 (0.32)	1.31 (0.87)	0.044 (−0.236, 0.324)	0.755	−0.031 (−0.330, 0.268)	0.837
CGI								
Severity of Illness	1.01 (0.11)	1.34 (0.95)	1.03 (0.16)	1.40 (1.17)	0.073 (−0.275, 0.420)	0.681	−0.229 (−0.550, 0.092)	0.160
Improvement Scale	4 (0)	4.17 (0.52)	4 (0)	4.21 (0.62)	0.052 (−0.135, 0.238)	0.586	−0.097 (−0.280, 0.086)	0.295

CGI Clinical Global Impression Scale, *PANSS* Positive and Negative Syndrome Scale, *SD* standard deviation, *n* number, *N/A* Not applicable.
[a]Raw mean calculated based on the indicated sample size.
[b]Intention-to-treat analysis includes every randomized participant (n = 152); per-protocol analysis includes participants who completed the entire intervention (n = 120).
[c]Age is included as a covariate in both binary logistic and linear regression.

not being specified and the relatively short illness duration in their sample (1.49 years). This lack of comparability suggests the need for replication studies to confirm MBI-p's effectiveness in relapse prevention in patients with psychosis.

Two possible explanations for these nonsignificant results exist. First, our study directly compared MBI-p with psychoeducation without TAU. This could potentially obscure MBI-p's effects, hampering determining its efficacy in relapse prevention. A meta-analysis examining digital-psychological intervention on depressive symptoms has shown that control groups involving psychoeducational material produce a moderate effect immediately after the intervention[55]. Moreover, MBI, CBT, and psychoeducation have similar effects in reducing depressive symptoms, suggesting that these interventions exert similar degrees of impact[56]. Second, most of our interventions took place during the COVID-19 pandemic. This contributes to enhancing psychoeducational efficacy. Hui et al.[57] found that patients with FEP were more likely exposed to stressors such as financial difficulties and job termination during the pandemic and poorer medication compliance. This suggests that our psychoeducational intervention had a greater positive impact on the sample as it focused on enhancing patients' understanding of pharmacological treatment and its side effects, as well as stress management and exercise. This could render the relapse prevention effects comparable between the two interventions.

Notably, our overall relapse rate (10%) is lower than the expected relapse rates for both intervention groups (15% and 35%). Several factors may explain the reduced number of relapses observed in this study. Firstly, research has shown that patients within Chinese populations tend to have higher compliance rates, with 70–80% displaying positive adherence behaviors and attitudes[58,59], resulting a lower relapse risk. Secondly, our sample excludes patients with substance abuse, which may contribute to the lower relapse rate observed compared to studies in Western populations. Lastly, while our expected relapse rate was based on the first-year relapse rates of the FEP population[39,40] and Wang et al.'s (2016)[38] findings, our sample includes patients with varying illness durations, many of whom are relatively more stable. In fact, early psychosis only takes up to 22% of our sample. Interestingly, relapse rates did not differ based on illness duration (see Supplementary Table 1), suggesting that MBI-p may have a similar effect in both early and late-stage psychosis.

Furthermore, relapse can be influenced by various factors, including medication discontinuation, poor adjustment before the onset of illness, and critical comments from caregivers[12]. Medication is considered a significant factor in relapse[3]. However, it can be argued that the measure of medication adherence used in our study might not be sufficient to fully account for its potential confounding effect on relapse. On the other hand, the complexity of preventing relapse suggests that relying solely on one intervention may be insufficient. For instance, despite efforts to mitigate relapse through early intervention programs for psychosis, these often yield limited success[60,61]. MBI-p primarily focuses on stress management through mindfulness techniques, which may not comprehensively address all aspects relevant to relapse prevention. A recent review indicated that MBCT may offer a more comprehensive approach than MBSR alone. MBCT typically incorporates psychoeducation aimed at preventing depressive relapse and provides insights tailored to conditions such as schizophrenia[62]. This suggests that integrated interventions such as MBCT could offer more robust strategies for preventing relapse in psychosis.

MBI-p on secondary outcomes

MBI-p had a less beneficial impact on secondary outcomes than psychoeducation, likely because of the different aspects of mindfulness that each group enhanced. MBI-p enhances

Table 3. Comparative analysis of psychopathology, functioning, and cognitive functioning between the MBI-p and Psychoeducation groups using the Linear Mixed Effect Model.

Outcomes, mean (SD)[a]	MBI-p (n = 77)			Psychoeducation (n = 75)			Intervention* Time Interaction[b]			
							Baseline Vs Post-intervention		Baseline Vs Termination	
	Baseline (n = 77)	Post-intervention (n = 64)	Termination (n = 64)	Baseline (n = 75)	Post-intervention (n = 62)	Termination (n = 62)	Estimate (95% CI)	p-value	Estimate (95% CI)	p-value
Psychopathology										
PANSS										
Total	35.09 (5.02)	39.86 (8.15)	41.50 (9.31)	34.73 (4.63)	37.47 (4.86)	37.61 (4.44)	−1.657 (−3.725, 0.411)	0.116	−2.359 (−4.577, −0.142)	**0.037***
Positive	7.44 (1.06)	7.81 (2.73)	8.77 (3.51)	7.39 (1.10)	7.55 (1.16)	7.69 (1.49)	−0.196 (−0.904, 0.513)	0.586	−0.677 (−1.526, 0.173)	0.118
Negative	8.49 (2.80)	8.70 (3.22)	8.95 (3.57)	8.59 (2.68)	8.47 (2.57)	8.10 (2.47)	−0.147 (−0.947, 0.653)	0.717	−0.604 (−1.653, 0.445)	0.257
General psychopathology	19.16 (3.37)	19.80 (4.87)	20.20 (5.02)	18.76 (3.47)	18.11 (2.64)	18.52 (2.55)	−1.120 (−2.443, 0.202)	0.096	−0.814 (−2.085, 0.458)	0.208
CDSS	1.96 (2.28)	2.14 (2.75)	1.91 (2.64)	2.00 (2.47)	1.26 (1.76)	1.47 (1.92)	−0.913 (−1.704, −0.122)	**0.024***	−0.628 (−1.496, 0.240)	0.155
Medication compliance										
Attitude	3.29 (0.59)	3.39 (0.3)	3.39 (0.64)	3.50 (0.57)	3.55 (0.54)	3.49 (0.67)	0.002 (−0.130, 0.134)	0.976	0.010 (−0.151, 0.171)	0.902
Behavior	3.70 (0.37)	3.63 (0.37)	3.69 (0.40)	3.70 (0.42)	3.70 (0.40)	3.72 (0.47)	0.105 (−0.002, 0.212)	0.055	0.028 (−0.115, 0.171)	0.696
Functioning and life quality										
RFS	20.09 (2.31)	19.97 (1.93)	20.04 (2.31)	20.12 (2.33)	20.40 (2.54)	20.40 (2.42)	0.277 (−0.289, 0.843)	0.578	0.133 (−0.595, 0.860)	0.719
SOFAS	67.92 (9.08)	67.48 (10.05)	70.42 (9.89)	68.15 (11.42)	69.73 (11.02)	72.46 (11.75)	1.572 (−1.230, 4.373)	0.270	1.024 (−1.978, 4.026)	0.501
Social functioning										
Social engagement	6.22 (2.25)	5.98 (2.24)	6.61 (2.20)	6.49 (2.03)	6.52 (2.17)	6.89 (2.01)	0.311 (−0.371, 0.992)	0.369	0.128 (−0.515, 0.772)	0.694
Relationships	5.91 (1.83)	5.91 (1.98)	6.05 (1.91)	5.67 (1.57)	5.50 (1.91)	5.57 (1.68)	−0.139 (−0.561, 0.283)	0.516	−0.317 (−0.751, 0.117)	0.151
Social activities	15.62 (7.42)	14.70 (6.48)	14.11 (6.72)	16.33 (7.08)	17.71 (6.12)	15.82 (5.80)	2.600 (0.815, 4.386)	**0.005***	2.601 (0.808, 4.395)	**0.005***
SF-12										
Physical	15.71 (2.65)	15.95 (2.59)	15.80 (3.16)	16.38 (2.59)	16.54 (2.49)	16.47 (2.64)	0.007 (−0.685, 0.698)	0.984	−0.048 (−0.805, 0.709)	0.901
Mental	20.26 (3.58)	20.09 (3.55)	20.65 (3.85)	20.77 (3.83)	20.63 (4.18)	20.98 (3.97)	0.348 (−0.909, 1.606)	0.585	0.157 (−0.976, 1.291)	0.784
Neurocognitive										
Visual pattern test										
Total correct items	20.41 (6.66)	21.87 (7.35)	24.29 (7.10)	20.65 (7.47)	22.65 (6.79)	24.05 (6.35)	1.052 (−0.717, 2.820)	0.241	−0.321 (−2.462, 1.820)	0.767
Longest item passed	9.44 (2.41)	9.82 (2.71)	10.51 (2.55)	9.32 (2.78)	10.19 (2.48)	10.47 (2.38)	0.417 (−0.356, 1.190)	0.288	0.122 (−0.685, 0.929)	0.765
Letter-number span										
Total correct items	13.38 (4.13)	14.52 (3.74)	16.31 (4.45)	14.55 (3.50)	15.49 (4.19)	16.59 (3.63)	−0.335 (−1.522, 0.852)	0.578	−0.976 (−2.266, 0.314)	0.137
Longest item passed	5.64 (3.37)	5.54 (1.23)	6.11 (1.34)	5.55 (1.01)	5.87 (1.20)	6.07 (1.10)	0.420 (−0.419, 1.259)	0.324	0.075 (−0.843, 0.992)	0.873

CDSS Calgary Depression Scale for Schizophrenia, LMM Linear Mixed Effect Model, n number, PANSS Positive and Negative Syndrome Scale, PSP Personal and Social Performance Scale, RFS Role-Functioning Scale, SANS Scale for Negative Symptoms, SAPS Scale for Positive Symptoms, SD standard deviation, SF-12 12-item Short-Form Survey, SOFAS Social and Occupational Functioning, YMRS Young Mania Rating Scale.
*p < 0.05, bold and asterisked.
[a]Raw mean calculated based on the indicated sample size.
[b]Age is included as covariate.

Table 4. Comparative analysis of psychosocial and mindfulness components on before and after intervention between the MBI-p and Psychoeducation groups using the Linear Mixed Effect Model.

| Outcomes, mean (SD)[a] | MBI-p (n = 77) | | | Psychoeducation (n = 75) | | | Intervention* Time Interaction[b] | | | |
| | | | | | | | Baseline Vs Post-intervention | | Baseline Vs Termination | |
	Baseline (n = 77)	Post-intervention (n = 64)	Termination (n = 64)	Baseline (n = 75)	Post-intervention (n = 62)	Termination (n = 62)	Estimate (95% CI)	p-value	Estimate (95% CI)	p-value
Psychosocial										
Stressful life events										
Severity	8.26 (11.69)	6.66 (9.62)	2.82 (4.13)	9.15 (13.98)	7.83 (12.84)	5.15 (10.32)	−0.143 (−5.063, 4.778)	0.954	1.405 (−3.106, 5.915)	0.539
Number of SLEs	2.63 (3.14)	2.25 (2.96)	1.09 (1.40)	2.71 (3.66)	2.53 (3.69)	1.80 (3.03)	0.099 (−1.243, 1.440)	0.885	0.630 (−0.535, 1.794)	0.287
Expressed emotion										
Total	22.85 (8.67)	21.93 (8.15)	22.55 (8.04)	25.88 (10.88)	23.95 (11.17)	22.73 (10.91)	−1.698 (−3.906, 0.509)	0.131	−2.297 (−4.557, −0.038)	**0.046***
Hostility	8.37 (3.78)	8.47 (3.59)	7.96 (3.54)	9.26 (4.21)	8.47 (4.35)	7.71 (3.74)	−1.043 (−1.990, −0.096)	**0.031***	−0.939 (−1.930, 0.051)	0.063
Criticism	6.52 (2.66)	6.29 (2.43)	6.54 (2.52)	7.62 (3.49)	7.07 (3.60)	7.05 (3.40)	−0.647 (−1.411, 0.117)	0.096	−0.505 (−1.293, 0.284)	0.208
Over-involvement	7.95 (3.31)	7.16 (3.05)	8.11 (3.27)	9.00 (3.94)	8.41 (4.12)	7.96 (4.19)	0.008 (−0.890, 0.905)	0.986	−0.963 (−1.988, 0.063)	0.066
Resilience	23.24 (7.21)	21.71 (6.68)	23.44 (7.09)	24.35 (8.59)	25.25 (7.55)	26.65 (7.41)	2.305 (0.156, 4.455)	**0.036***	0.652 (−1.732, 3.036)	0.590
Perceived risk of relapse	24.74 (25.78)	25.98 (22.17)	N/A	23.94 (22.14)	19.76 (21.07)	N/A	−7.201 (−13.890, −0.512)	**0.035***	N/A	N/A
Mindfulness										
FFMQ										
Total	122.50 (14.15)	121.55 (12.85)	124.75 (15.24)	124.02 (9.78)	125.47 (10.29)	125.52 (11.20)	2.632 (−0.333, 5.598)	0.081	−0.416 (−3.835, 3.002)	0.810
Observing	20.11 (6.28)	21.32 (5.16)	21.80 (5.86)	21.27 (5.36)	21.02 (5.25)	20.72 (5.68)	−1.542 (−3.064, −0.020)	**0.047***	−1.911 (−3.347, −0.476)	**0.009***
Describing	25.55 (5.43)	25.36 (4.84)	26.80 (5.34)	25.40 (5.17)	26.97 (4.79)	26.65 (5.65)	1.962 (0.768, 3.156)	**0.001***	−0.340 (−1.166, 0.987)	0.614
Acting with awareness	29.17 (5.41)	26.80 (4.47)	28.10 (4.83)	28.63 (5.15)	29.20 (5.05)	30.28 (5.08)	3.310 (1.523, 5.097)	**<0.001***	3.359 (1.943, 4.775)	**<0.001***
Non-judging of inner experience	29.56 (5.87)	28.18 (4.82)	28.63 (4.87)	28.92 (5.48)	29.10 (5.81)	29.30 (5.84)	1.305 (−0.306, 2.916)	0.111	0.915 (−0.479, 2.309)	0.197
Non-reactivity to inner experience	18.12 (5.26)	19.67 (3.93)	19.41 (4.46)	19.80 (4.96)	19.18 (4.59)	18.57 (4.69)	−2.056 (−3.546, −0.565)	**0.007***	−2.454 (−3.865, −1.042)	**<0.001***

FFMQ Five Facets Mindfulness Questionnaire, *LMM* Linear Mixed Effect Model, *n* number, *SD* standard deviation, *SLE* Stressful life event.

*p < 0.05, bold and asterisked.

[a]Raw mean calculated based on the indicated sample size.

[b]Age is included as covariate.

observation and non-reactivity to inner experiences, whereas psychoeducation elevates descriptions and acts with awareness. This aligns with the literature reporting stable effects on non-reactivity but not on describing skills[63–66]. Our MBI-p program prioritized awareness over verbal expressions, whereas psychoeducation emphasized social support and communication. Despite the generally positive impacts of MBI on psychosis, we postulate that differing focuses of interventions and pandemic-related challenges influence secondary outcomes such as functioning and life quality.

Psychopathology. Our findings revealed a significant interaction effect in PANSS at the one-year follow-up. Although the difference in relapse rates between the interventions was not statistically significant, the MBI-p group had a slightly greater relapse severity, leading to higher PANSS scores. This contrasts with Tong et al.'s pilot study, which showed significant PANSS improvement. This result was arguably driven by a significant improvement in the general psychopathology score, whereas the positive and negative symptom scores only mildly contributed to this effect. This suggests that MBI-p may have little effect on the reduction of psychotic symptoms in remitted patients.

In the post-intervention assessment, CDSS scores indicated that depressive symptoms worsened in the MBI-p group but improved in the psychoeducation group, with no long-term effects observed. MBI-p may have heightened awareness of negative emotions, as indicated by increased scores in the "observing" facet of the FFMQ following MBI-p. Initial negative experiences during mindfulness practice are common[67–69]. Despite this discomfort, MBI often lead to positive self-care practices and overall positive impacts. Mindfulness is a process of reconnecting with difficult thoughts and emotions, initially causing discomfort but ultimately resulting in greater self-awareness and well-being[67,68]. Conversely, psychoeducation likely provides practical coping mechanisms that enhance mental well-being during a pandemic.

Functioning, cognitive functioning, and life quality. We found significant interactive effects on functional and life quality outcomes, particularly social activities, hostility in expressed emotions, resilience, and perceived risk of relapse. MBI-p is generally less beneficial than psychoeducation.

Psychoeducation has led to short- and long-term improvements in social activities because of its focus on effective communication and healthy lifestyle habits through social support. Conversely, while MBI-p focuses on the individual practice of mindfulness, it might be more susceptible to the pandemic's adverse impact, including reduced social connectivity and more stressful life events[47]. This may account for the decrease in psychosocial functioning in the MBI-p group.

Improved "observing" skills in MBI-p may heighten awareness of internal and external stimuli, impacting functioning. Post-intervention, the MBI-p group experienced an increased hostile attitude from the caregiver and perceived risk of relapse, whereas reductions were noted in the psychoeducation group. This heightened awareness is typical in mindfulness learning, but participants often adapt to these emotions through mindfulness techniques over time[68]. Our findings showed that the MBI-p group experienced slightly fewer negative emotions from others at the one-year follow-up. Moreover, the increased awareness of relapse risk in MBI-p participants (25.98%) aligned more closely with actual relapse rates in Hong Kong, indicating a more realistic perception of relapse[70]. Psychoeducation provides practical coping mechanisms, enhancing resilience and managing negative attitudes or relapse triggers better than MBI-p.

Limitation
Several limitations may have impacted the results of this study. Firstly, the sample size and follow-up duration might have been insufficient to detect relapse events effectively. However, there is a possibility that longer follow-up period could potentially dilute the intervention's impact, given the relatively low intensity of MBI. Secondly, relapse is influenced by various factors, including stress and medication adherence. One limitation of this study is that, although medication adherence behavior was measured, we did not record patients' actual medication dosages. Additionally, demographic comparisons between the two groups indicated that age was nearly significant. While age did not significantly contribute to relapse in this study, this finding suggests that the stratification process during randomization could be improved. Thirdly, our study included a mix of patients with both early-stage and longer-duration psychosis, some of whom underwent EASY interventions while others did not. Although our analysis showed that the MBI-p intervention appears to have a similar effect across stages, a large proportion of the sample had lived with the illness for more than five years, leading to a more stable cohort. Future studies may wish to focus on a more vulnerable and specific stage of psychosis, such as early psychosis, to better examine the intervention's effects. Forth, limited information was also gathered regarding patients' acceptance and commitment to mindfulness practices. For example, we did not adequately document patients' perspectives on mindfulness before the intervention or the frequency and intensity of mindfulness practice after the intervention and during the follow-up period. Despite monthly reminders, this limited monitoring raises concerns about the extent of patients' engagement with mindfulness outside the intervention sessions. To better understand the impact of mindfulness on relapse rates among patients with psychosis, future studies should more rigorously track the frequency and intensity of mindfulness practice, as well as to control for patients' history of other psychological interventions outside of the study. Furthermore, the study period overlapped with the COVID-19 pandemic, during which patients may have experienced additional benefits from psychoeducation. Replicating this study is recommended, and future research should include a TAU group to allow for a more robust comparison.

CONCLUSION
MBI in this study emphasized simplicity and acceptance to address fear and sadness, aiming to cultivate peace and calm while aiding in managing daily stress. Although effectiveness in preventing relapses remains uncertain, our findings indicate its lasting effect on certain mindfulness aspects. This protocol serves as a guide for future implementation, ensuring consistency even with personnel changes. We also developed supporting materials, including presentation slides, practice scripts, audio tapes, and participant booklets to facilitate ease of delivery and training. This analysis underscores the importance of targeted education within interventions, particularly during challenging periods such as the COVID-19 pandemic, to improve functioning and symptoms and create a more supportive environment for participants.

Importantly, our study highlights the varied effects of interventions on functioning and life quality in individuals with psychosis. Psychoeducation offers better support and practical skills and improves social engagement, resilience, and coping with relapse-related factors more effectively than MBI-p. These findings emphasize the need for tailored interventions to address holistic well-being in mental healthcare.

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Dr Hui had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Concept and design: Hui, Lin, Tong, Chen. Acquisition, analysis, or interpretation of data: Hui, Wong, Lui, Chiu, Evie WT Chan, Tao. Drafting of the manuscript: Hui, Wong, Chiu. Critical review of the manuscript for important intellectual content: All authors. Statistical analysis: Hui, Wong, Chiu, Suen. Obtained funding: Hui.

COMPETING INTERESTS

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Correspondence and requests for materials should be addressed to Christy Lai Ming Hui.

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