



## Original article

# Prediction of motivational impairment: 12-month follow-up of the randomized-controlled trial on extended early intervention for first-episode psychosis



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## ABSTRACT

**Background:** Amotivation is prevalent in first-episode psychosis (FEP) patients and is a major determinant of functional outcome. Prediction of amotivation in the early stage of psychosis, however, is understudied. We aimed to prospectively examine predictors of amotivation in FEP patients in a randomized-controlled trial comparing a 1-year extension of early intervention (Extended EI, 3-year EI) with step-down psychiatric care (SC, 2-year EI).

**Methods:** One hundred sixty Chinese patients were recruited from a specialized EI program for FEP in Hong Kong after they have completed this 2-year EI service, randomly allocated to Extended EI or SC, and followed up for 12 months. Assessments on premorbid adjustment, onset profiles, baseline symptom severity and treatment characteristics were conducted. Data analysis was based on 156 subjects who completed follow-up assessments.

**Results:** Amotivation at 12-month follow-up was associated with premorbid adjustment, allocated treatment condition, and levels of positive symptoms, disorganization, amotivation, diminished expression (DE) and depression at study intake. Hierarchical multiple regression analysis revealed that Extended EI and lower levels of DE independently predicted better outcome on 12-month amotivation. **Conclusion:** Our findings indicate a potentially critical therapeutic role of an extended specialized EI on alleviating motivational impairment in FEP patients. The longer-term effect of Extended EI on amotivation merits further investigation.

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## 1. Introduction

Negative symptoms are a core feature of psychotic disorders [1] and are associated with poor functional outcome [2,3]. Prior literature has consistently indicated that negative symptoms represent a multi-dimensional construct comprising two distinct sub-domains, namely motivational impairment (i.e., amotivation) and diminished expression (DE) [4]. Among these two sub-domains, amotivation has been found to be more prevalent and persistent over time than DE [5–7]. Recent studies have further demonstrated that amotivation is a major predictor of concurrent and longitudinal functional outcome in chronic schizophrenia

[8–13] and first-episode psychosis (FEP) [14–16], above and beyond the contributions of cognitive deficits, DE and other symptom dimensions [6,9,16].

Of note, substantial evidence has shown that a significant proportion of FEP patients exhibit pronounced functional impairment even after remission of positive symptoms [17,18]. Alternatively, recent data have revealed that negative symptoms emerged in the initial stage of psychotic illness predict severity of these symptoms at follow-up [19,20]. Given that amotivation is a key component of negative symptoms and a chief determinant of functional disability [21], it thus represents a critical therapeutic target for preventing development of persistent negative symptoms and promoting early functional recovery. Nonetheless, despite its significant clinical implications in early intervention (EI) for psychosis, very few studies have been conducted to prospectively examine predictors of amotivation in FEP [7,22,23].

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Hong Kong (HK) is among the few cities in Asia to implement a territory-wide EI service for psychosis. The program, namely Early Assessment Service for Young People with Psychosis (EASY) provides 2-year specialized EI for young people presenting with FEP in HK [24]. We have conducted a randomized-controlled trial (RCT) comparing a 1-year extension of EI (Extended EI) service with step-down psychiatric care (SC) in a representative cohort of Chinese FEP patients who had completed 2-year treatment in EASY program [25]. This is one of the first RCTs examining the effectiveness of EI program for psychosis with its treatment period extended beyond 2 years [26,27]. Results of this RCT showed that Extended EI group displayed significantly better outcomes than SC group in functioning, and negative and depressive symptoms at the end of 12-month follow-up [25].

In the current report, we sought to identify predictors of amotivation at 12-month follow-up the context of this RCT. Comprehensive evaluation encompassing premorbid adjustment, onset characteristics, baseline symptom severity and treatment-related factors including the impact of Extended EI was conducted to enable a better estimation of prediction profiles for amotivation in FEP patients.

## 2. Method

### 2.1. Participants and setting

Details of the study methodology have been reported elsewhere [25,28]. Briefly, this was a single-blind RCT comparing a 1-year extension of specialized EI (i.e., a 3-year EI service) with step-down care (i.e., a 2-year EI service) in patients who had received 2 years of treatment from EASY program. Since 2001, this publicly-funded specialized program has been providing early assessment and phase-specific intervention for all individuals aged 15 to 25 years experiencing their FEP in HK [24]. The service consisted of five clinical teams, each covering a geographically-defined catchment area and comprising two psychiatrists, three case managers and one social worker. The service adopts phase-specific case-management approach in which each patient is assigned with a case manager who provides protocol-based psychosocial interventions. Patients are assertively followed up for a period of 2 years, after which they are managed by step-down clinic in the third year of treatment without provision of case-management. They are then transferred to generic psychiatric service for continuous care [24].

A total of 160 patients with a DSM-IV diagnosis of psychotic disorder were recruited from EASY program between November 2010 and August 2011, randomly allocated to Extended EI ( $n = 82$ ) or SC ( $n = 78$ ), and followed up for 12 months. Exclusion criteria were intellectual disability, substance-induced psychosis or psychotic disorder due to general medical condition. Participants in both treatment conditions were managed by psychiatrists from their respective EASY clinical teams. In Extended EI condition, specialized EI was continued in the form of an additional year of case-management. A trained case manager took over cases from EASY program and was responsible for providing care and coordinating treatment with clinicians, allied health professionals and community centers. Case-management provided closely aligned with treatment protocols adopted by EASY program, focusing specifically on functional enhancement by assisting subjects to re-establish supportive social networks, to resume leisure pursuits and to return to work. Continuous supportive care, psychoeducation, and stress management were also delivered to subjects' caregivers by case manager. Participants allocated to SC received outpatient medical follow-up with limited community support, which focused mainly on crisis intervention, and no case-management was provided. Two treatment groups did not differ

from each other regarding the intensity of medical follow-up by psychiatrists, prescription of antipsychotic medications, and availability of various psychosocial interventions and community-based services [25].

In this report, we focused on investigating predictors of amotivation in 156 subjects of the initial cohort who had completed follow-up assessments. The study was approved by the local institutional review boards. All participants provided written informed consent. For those aged under 18 years, consent was also obtained from a parent or guardian.

### 2.2. Assessment

Diagnosis of each participant was ascertained using all available information including Chinese-bilingual Structured Clinical Interview for DSM-IV (CB-SCID) [29], informant histories and medical records. Premorbid functioning was measured with the Premorbid Adjustment Scale (PAS) [30]. The Interview for the Retrospective Assessment of the Onset of Schizophrenia (IRAOS) [31] was employed to determine duration of untreated psychosis (DUP) and age at onset of psychosis. Psychopathology was assessed using Positive and Negative Syndrome Scale (PANSS) [32] and Calgary Depression Scale (CDS) [33]. Measurement of negative symptoms was divided into two distinct sub-domains, i.e., amotivation and DE scores using PANSS based on previous factor-analytic studies [12,34]. Amotivation score was derived by summing the PANSS items N2 (emotional withdrawal), N4 (passive social withdrawal) and G16 (active social avoidance), while DE score was the sum of items N1 (blunted affect), N3 (poor rapport), N6 (lack of spontaneity) and G7 (motor retardation). Intra-class correlation coefficients for PANSS general psychopathology, positive and negative symptom subscales, and CDS total score were 0.92, 0.96, 0.91 and 0.89, respectively, indicating good inter-rater reliability. Medication Adherence Rating Scale (MARS) [35] was applied to assess treatment adherence. Psychopathological assessment was conducted at study entry and at 12 months.

### 2.3. Statistical analysis

The primary analyses focused on identifying predictors of amotivation at 12-month follow-up. First, associations of amotivation score at 12 months with demographics, premorbid functioning, clinical variables at study intake encompassing onset characteristics, diagnosis and symptom severity, allocated treatment condition (i.e., Extended EI vs. SC) and other treatment-related variables including medication adherence were examined using correlation analyses (by Pearson's product-mean correlation coefficients) and independent t-tests as appropriate. Then, those variables that were found to be statistically significant in preceding analyses were included in a hierarchical multiple regression model to determine the predictors of and their independent contributions to amotivation at follow-up. Multicollinearity of predictor variables in a multiple regression model was evaluated using a measure of variance inflation factor (VIF). Our results on VIFs of predictive variables ranged between 1.02–1.61, indicating minimal multicollinearity (VIF = 1 indicates no multicollinearity and VIF > 10 indicates serious multicollinearity) [36]. The level of statistical significance was set at  $P < 0.05$ .

## 3. Results

### 3.1. Characteristics of the sample

Of 156 subjects, 51.9% were male. The mean age of the sample at study intake was 22.9 years ( $SD = 3.2$ ) and the median DUP was 13 weeks (mean = 36.5,  $SD = 53.0$ ). Diagnoses of the cohort were

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