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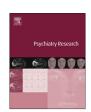
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Prevalence and predictors of medication non-adherence among Chinese patients with first-episode psychosis

Christy Lai-Ming Hui ^{a,*}, Venessa Wing-Yan Poon ^a, Vivian Shuk-Kuen Kwok ^a, Wing-Chung Chang ^a, Sherry Kit-Wa Chan ^a, Edwin Ho-Ming Lee ^a, Eric Yu-Hai Chen ^{a,b}

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ABSTRACT

Medication non-adherence is one of the major obstacles to recovery in first-episode psychosis (FEP). This study aimed to identify the predictors and rates of medication non-adherence in the first and second year after the start of treatment (baseline) in urban Chinese FEP patients. Relevant information on medication non-adherence and potential baseline predictors, including demographic variables, clinical measures, violence/suicide attempts, stressful life experiences, intervention received, and follow-up attendance, were collected from case records of 1400 FEP patients in Hong Kong. The non-adherence rate was 16.2% in year 1 and 15.4% in year 2. Regression analyses revealed the predictors for non-adherence in year 1 were no hospitalization at baseline, non-schizophrenia diagnosis, and more years of education. Predictors of non-adherence in year 2 included acute/subacute onset and older age of onset. Predictors common in both years were defaulting from psychiatric follow-up during baseline, standard psychiatric care (no early intervention), and lower positive symptoms severity at baseline. In assessing non-adherence risk and for planning phase-specific early interventions for FEP, particularly in a Chinese context, healthcare professionals should consider the common and specific predictors for non-adherence identified in the first and second years of treatment and should not overlook patients with less clinically severe symptoms.

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1. Introduction

Pharmacological treatment remains the cornerstone of clinical treatments for early-onset schizophrenia spectrum disorders. Despite the efficacy and effectiveness of antipsychotics (Lieberman et al., 2005; Sikich et al., 2008) and their strong association with relapse prevention (Robinson et al., 1999; Chen et al., 2005; Üçok et al., 2006), previous studies on schizophrenia have shown medication non-adherence rates were at least 40% in the first year and up to 75% in the second year (Coldham et al., 2002). Non-adherence to prescribed medication could have negative consequences for the patient resulting in substantial clinical and economic burdens, such as the increased need for emergency care and social care and loss of productivity (Dolder et al., 2003; Wu et al., 2005; Ekman et al., 2013; Higashi et al., 2013). In addition, first-episode psychosis (FEP) patients lack experience

E-mail address: christy@lmhui.com (C. Lai-Ming Hui).

http://dx.doi.org/10.1016/j.psychres.2015.04.047 0165-1781/© 2015 Elsevier Ireland Ltd. All rights reserved. and knowledge about psychiatric medications and their mental illness, and might undervalue the importance of continued medication adherence in relapse prevention. Therefore, identification of the risk factors of medication non-adherence is important for planning effective interventions to reduce the adverse consequences of non-adherence.

Medication adherence is the extent to which a patient's medication-taking behavior corresponds to the agreed recommendations of the healthcare provider. This is a multi-dimensional phenomenon rather than a unitary concept, which can be intermittent or continuous, while at the same time unintentional (e.g., forgetting to take medication due to cognitive impairment) or deliberate (e.g., purposefully deciding to stop medication due to lack of insight) (Acosta et al., 2012; Farooq and Naeem, 2014; Haddad et al., 2014). The pattern of medication adherence also varies in the different phases of the disorder (Robinson et al., 2002; Hui et al., 2006b; Acosta et al., 2012). Adherence behavior of first-admission patients with psychosis might differ between the period immediately after discharge and later stages of remission; for example, adherence behavior may be affected by the adverse side effects of medication at the start of treatment or the initial

^a Department of Psychiatry, University of Hong Kong, Hong Kong, China

^b State Key Laboratory of Brain and Cognitive Sciences, University of Hong Kong, Hong Kong, China

^{*}Correspondence to: Department of Psychiatry, University of Hong Kong, Queen Mary Hospital, 102, Pokfulam Road, Hong Kong, China. Tel.: +852 2255 3064; fax: +852 2855 1345.

efforts to prevent re-hospitalization (Perkins, 1999; Mojtabai et al., 2002). In the first year after presentation of FEP, antipsychotic medications are normally prescribed to clinically stabilize the symptoms. In the second year, patient management is designed to promote the habit of taking medications to prevent relapse (Ye et al., 2014). Therefore, the predictors for non-adherence and the non-adherence rates during year 1 and year 2 are likely to be different, but data on this remain sparse.

Past research has suggested that medication non-adherence in psychosis was associated with a large number of variables at the patient, illness, medication, and environmental levels (e.g., Fenton et al., 1997; Lacro et al., 2002; Higashi et al., 2013). However, these findings were mixed and inconclusive, possibly due to differences between studies such as the criterion thresholds used to define non-adherence and the methodologies used for the assessments (Novak-Grubic and Tavcar, 2002; Dolder et al., 2003; Farooq and Naeem, 2014). The operational definition of non-adherence also varies in the literature. Most previous research conceptualized adherence in relation to an all-or-nothing dichotomy, and some viewed complete adherence and non-adherence as opposite ends of a spectrum (Julius et al., 2009). Furthermore, methods used for the evaluation of non-adherence can be objective (e.g., pill count, blood or urine analysis, and electronic monitoring devices) or subjective (e.g., patient reports, significant other reports, and chart reviews) (Velligan et al., 2006; Acosta et al., 2012). Since these methods each have their own advantages and disadvantages, a universal problem in the field has always been the lack of a universal "yardstick" for the measurement of adherence (Haddad et al., 2014). For example, clinical ratings and carer reports can be easy and efficient to conduct but may not be entirely accurate, whereas urine and blood serum level tests are relatively more accurate but are costly and best suited only to "yes or no" determinations (Donohoe, 2006). Methods involving patient reports and medical record reviews are relatively easy and inexpensive to administer and thus remain the most commonly used strategy for assessing medication adherence (Velligan et al.,

The vast majority of previous studies on medication nonadherence were conducted in Western settings. However, there is little information available on the applicability of the rates and predictors of non-adherence from studies on Western populations to FEP patients in the Chinese population. Stigmatization is known to be more severe in collectivistic Chinese societies and its negative effect on adherence has been previously demonstrated (Fung et al., 2010; Lam et al., 2010). Family contribution to continued medication adherence has also been reported (Fancher et al., 2014). Extrapolated predictors and adherence rates may be unreliable due to differences in cultures. Studies on nonadherence have been conducted in both urban and rural areas of China. Xiang et al. (1994) reported at least 53% of rural schizophrenia outpatients in China had irregular adherence or discontinued their medication. Xiong et al. (1994) reported the nonadherence rate was 41% in urban schizophrenia outpatients in China during a 2-year follow-up. Hui et al. (2006a) found the nonadherence rate was 26% among schizophrenia outpatients in Hong Kong. Most of the existing non-adherence data for Chinese FEP patients were presented in intervention evaluation studies as a measurement of outcome. However, only a handful of studies on non-adherence to medication have been conducted, and these studies had relatively small sample sizes. The predictors of nonadherence in Chinese FEP patients remain largely unknown, and further exploration is warranted.

The present study was part of a retrospective cohort study which evaluated the outcome of 1400 Chinese FEP patients in Hong Kong receiving phase-specific early intervention or standard psychiatric care (without early intervention) (Chen et al., 2011).

We aimed to explore the potential predictors of non-adherence during the first and the second year of treatment in urban Chinese FEP patients using case record reviews. Potential predictors include demographic variables, clinical factors and symptom severity during initial treatment of FEP (baseline), the type of treatment received at baseline (phase-specific early intervention or standard psychiatric care), violence or suicide attempts at baseline, psychiatric follow-up attendance at baseline, and stressful life experience during the course of untreated psychosis.

2. Methods

2.1. Study setting

In our study, we explored the potential predictors of medication adherence in FEP patients in the first two years upon presentation for treatment at baseline. The data presented in this study was obtained from a larger cohort study which aimed to determine the effectiveness of the phase-specific early intervention program, Early Assessment Service for Young people with psychosis (EASY), in Hong Kong (Chen et al., 2011). EASY is a territory-wide early intervention service launched in 2001 that targets young people aged 15 to 25 with FEP (Chen, 2004; Wong et al., 2012). Patients in the program are managed by a multi-disciplinary team of clinicians and professionals. A designated case manager, who has specialized training in early intervention for psychosis, is assigned to each patient. The service provides individualized phase-specific case management and assertive follow-up for 2 years.

Prior to the introduction of EASY, patients received standard psychiatric care from general psychiatric teams who did not have specialized training in early intervention for psychosis; and support and intervention from general community psychiatric nurses, clinical psychologists, and social workers were offered as needed (Chan et al., 2014). This form of routine management was characterized by its high service volume and brief consultation times (Hui et al., 2008). Patients usually received inpatient treatment for a first presentation of psychotic symptoms with relatively sparse outpatient follow-up and little psychosocial support.

2.2. Participants

A total of 1400 cases were identified from the psychiatric case register (PsyCIS) in Hong Kong, of which 700 were consecutive patients participating in the EASY programme between 2001 and 2003 and 700 were consecutive patients receiving standard psychiatric care between 1998 and 2001 (prior to the launch of EASY). Patients from the two groups were individually matched for gender, age ($\pm\,3$ years), and diagnosis (Chen et al., 2011). To minimize potential cohort effects, samples were chosen with close temporal proximity.

Inclusion criteria for the study were any of the following diagnoses according to the International Classification of Diseases and Related Health Problems Tenth Revision (ICD-10): schizophrenia (code F20), acute and transient psychotic disorders (code F23), schizoaffective disorders (code F25), psychosis not otherwise specified (code F28 or F29), and affective disorders with psychotic features (codes F30.2, F31.2, F31.5, F32.3 or F33.3). Exclusion criteria included those with a history of psychiatric treatment for more than 1 month before first presentation, significant organic condition, drug-induced psychosis, or mental retardation. Informed consent was obtained from patients before recruitment into the study. The study was approved by the institutional review board and ethics committees of the corresponding study sites.

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