



## Prospective relationship between duration of untreated psychosis and 13-year clinical outcome: A first-episode psychosis study



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### ABSTRACT

**Background:** The adverse effects of a long duration of untreated psychosis (DUP) have been explored in numerous short-term studies. These studies support the development of early interventions that reduce treatment delay and promote recovery. However, the enduring impact of DUP is largely unknown, partly due to the paucity of prospective long-term studies. Although the DUP–outcome relationship is commonly assumed to be linear, the threshold effect has not been adequately examined.

**Objective:** To explore the relationship between DUP and long-term symptomatic remission.

**Methods:** This was a prospective study of a cohort of 153 first-episode psychosis patients in Hong Kong at the 13-year follow-up. The patients were categorized into short ( $\leq 30$  days), medium (31–180 days) and long ( $> 180$  days) DUP groups.

**Results:** The long-term outcome was ascertained in 73% of the patients. Nearly half of the patients (47%) fulfilled the criteria for symptomatic remission. The short DUP group experienced a significantly higher remission rate over the course of the illness. The odds of long-term symptomatic remission was significantly reduced in the medium DUP (by 89%) and long DUP (by 85%) groups compared with the short DUP group. Further analysis showed that DUP had a specific impact on negative symptom remission.

**Conclusion:** The findings support the threshold theory that DUP longer than 30 days adversely impacts the long-term outcome. The present study is one of the few studies that confirmed the enduring impact of DUP on long-term outcomes based on well-defined criteria and adequate statistical adjustment.

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### 1. Introduction

The duration of untreated psychosis (DUP) is one of the most widely studied risk factors associated with poor outcomes such as treatment response, positive symptoms, negative symptoms and functioning (Marshall et al., 2005; Perkins et al., 2005). The effect of DUP on the outcome was supported by evidence from numerous short-term studies, but the follow-up periods in these studies were 2 years or less. In agreement with the critical period hypothesis for patients with first-episode psychosis (Birchwood, 1999), these studies supported the development of early detection programmes that aim to shorten treatment delay and

improve long-term recovery. Despite the general acceptance of early interventions for first-episode psychosis patients, the enduring impact of DUP remains unclear, which is partly due to the lack of prospective studies with longer follow-up periods. Potentially, the adverse impact of DUP may be gradually weakened by other intervening factors over the course of the illness. Alternatively, this adverse impact would not manifest during the early stage because the majority of the patients with early psychosis respond well to medications (Chang et al., 2012). Our understanding of the impact of the association between DUP and long-term outcome is very limited. Our existing knowledge about the relationship between DUP and long-term symptomatic remission has been based mainly on a few prospective studies. Many of these studies were limited by the different pre-treatments, the poorly defined pre-treatment variables and the lack of key covariate adjustments, especially premorbid adjustment (Table 1). The relationship between DUP and

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**Table 1**  
Summary of prospective long-term studies ( $\geq 10$  years) examining the relationship between DUP and long-term outcome.

Study (year)	The pre-treatment variable	Definition	Long-term outcome as predicted by a longer DUP predicted	Remarks
Huber et al. (1980)	Treatment during their initial psychotic episodes	“Treated” or “non-treated” with electroconvulsive or psychopharmacological therapy during the initial psychotic episode	Uncharacteristic and characteristic residues	Results not adjusted for any covariates
Tsoi and Kua (1992)	Pre-admission duration of illness	Method to determine the time of the onset of illness was unclear	“Poor outcome” (based on treatment and severity of psychotic symptoms)	Results not adjusted for any covariates
Thara and Eaton (1996)	Duration of illness	Duration of illness before first contact with treatment facility; method to determine the time of the onset of illness was unclear	Poorer outcome (based on psychotic symptoms and course)	Unclear reference group. Results controlled for the effect of onset type but not premorbid adjustment.
Harrison et al. (1996)	Duration of untreated illness prior to contact with the services	Method to determine the time of the onset of illness was unclear	A range of poorer clinical and functional outcomes	Unknown magnitude of association. Results controlled for the effect of onset type but not premorbid adjustment.
Wiersma et al. (1998)	Delayed mental health treatment	The outbreak of psychosis to the initiation of mental health treatment. Subjects were categorized into “delayed” or “prompt” treatment group. Unclear cutoff value.	Shorter time for full remission and longer duration of first episode	Results controlled for the effect of premorbid functioning and onset type.
Wiersma et al. (2000)	Psychosis without treatment/DUP	The estimated onset of psychotic symptoms to the first contact with a mental health professional	Higher level of disability	Insignificant bivariate relationship with outcome. No multiple regression was performed.
Bottlender et al. (2003)	First psychotic symptoms to first admission	The onset of psychotic symptoms to the first psychiatric admission; assessed by clinical interview.	Lower GAS and higher severity on SANS, PANSS positive subscale and PANSS general psychopathology.	Adjusted for only onset type. Premorbid adjustment had insignificant bivariate relationship with outcome, and thus was not used as a covariate. Categorisation of DUP did not account for very short duration.
Kurihara et al. (2005)	DUP	Unclear	Did not predict PANSS severity and social adjustment	Results not controlled for the effect of premorbid adjustment
White et al. (2009)	DUP	The onset of first psychotic symptoms to index admission	Greater outcome symptom burden	Results controlled for the effect of premorbid adjustment
Hegelstad et al. (2012)	DUP	The onset of the first psychotic symptoms to the start of first adequate treatment	A higher proportion of patients from the early detection group had recovered relative to those from the usual-detection group	Comparison of results between subjects in the early detection group and usual-detection group. Results not controlled for the effect of premorbid adjustment
Hill et al. (2012)	DUP	The onset of the first psychotic symptom to the start of antipsychotic treatment	More severe positive and negative symptoms and a range of functional measures	Results controlled for the effect of premorbid adjustment

DUP = duration of untreated psychosis; GAS = Global Assessment Scale; PANSS = Positive and Negative Syndrome Scale; SANS = Scale for the Assessment of Negative Symptoms.

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