Understanding Components of Duration of Untreated Psychosis and Relevance for Early Intervention Services in the Canadian Context

Comprendre les Composantes de la Durée de la Psychose Non Traitée et la Pertinence de Services D'intervention Précoce Dans le Contexte Canadien

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Abstract

Background: Clinical, functional, and cost-effectiveness outcomes from early intervention services (EIS) for psychosis are significantly associated with the duration of untreated psychosis (DUP) for the patients they serve. However, most EIS patients continue to report long DUP, while a reduction of DUP may improve outcomes. An understanding of different components of DUP and the factors associated with them may assist in targeting interventions toward specific sources of DUP.

Objectives: To examine the components of DUP and their respective determinants in order to inform strategies for reducing delay in treatment in the context of an EIS.

Methods: Help-seeking (DUP-H), Referral (DUP-R), and Administrative (DUP-A) components of DUP, pathways to care, and patient characteristics were assessed in first episode psychosis ($N = 532$) patients entering an EIS that focuses on systemic interventions to promote rapid access. Determinants of each component were identified in the present sample using multivariate analyses.

Results: DUP-H (mean 25.64 $\pm$ 59.00) was longer than DUP-R (mean $= 14.95 \pm 45.67$) and DUP-A (mean 1.48 $\pm$ 2.55). Multivariate analyses showed that DUP-H is modestly influenced by patient characteristics (diagnosis and premorbid adjustment; $R^2 = 0.12$) and DUP-R by a combination of personal characteristics (age of onset and education) and systemic factors (first health services contact and final source of referral; $R^2 = 0.21$). Comorbid substance abuse and referral from hospital emergency services have a modest influence on DUP-A ($R^2 = 0.08$). Patients with health care contact prior to onset of psychosis had a shorter DUP-H and DUP-R than those whose first contact was after psychosis onset (F(1, 498) = 4.85, $P < 0.03$ and F(1, 492) = 3.34, P < 0.07).

Conclusions: Although much of the variance in DUP is unexplained, especially for help-seeking component, the systemic portion of DUP may be partially determined by relatively malleable factors. Interventions directed at altering pathways to care

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and promote rapid access may be important targets for reducing DUP. Simplifying administrative procedures may further assist in reducing DUP.

Abrégé

Contexte : Les résultats cliniques, fonctionnels et de rentabilité des Services d'intervention précoce (SIP) pour la psychose sont significativement associés à la durée de la psychose non traitée (DPNT) pour les patients qu'ils servent. Cependant, la plupart des patients des SIP continuent de déclarer une longue DPNT alors qu'une réduction de cette DPNT peut améliorer les résultats. Une compréhension des différentes composantes de la DPNT et des facteurs qui y sont associés peut contribuer à cibler les interventions vers des sources spécifiques de la DPNT.

Objectifs : Examiner les composantes de la DPNT et leurs déterminants respectifs afin d'éclairer les stratégies visant à réduire les délais de traitement dans le contexte d'un SIP.

Méthode : La recherche d'aide (DPNT-A), la référence (DPNT-R) et les composantes administratives (DPNT-AD) de la DPNT, les trajectoires des soins et les caractéristiques des patients ont été évaluées chez les patients (N = 532) de la psychose précoce s'inscrivant dans un SIP qui met l'accent sur les interventions systémiques pour promouvoir un accès rapide. Les déterminants de chaque composante ont été identifiés dans le présent échantillon à l'aide d'analyses multivariées.

Résultats : La DPNT-A (moyenne 25,64 ± 59,00) était plus longue que la DPNT-R (moyenne 14,95 ± 45,67) et la DPNT-AD (moyenne 1,48 ± 2,55). Les analyses multivariées ont indiqué que la DPNT-A est modestement influencée par les caractéristiques des patients (diagnostic et ajustement pré-morbide; $R^2 = 0,12$); la DPNT-R par une combinaison de caractéristiques personnelles (âge au début et éducation) et de facteurs systémiques (premier contact avec les services de santé et source finale de référence) ($R^2 = 0,21$). L'abus de substances comorbide et la référence des services d'urgence hospitaliers ont une influence modeste sur la DPNT-AD ($R^2 = 0,08$). Les patients en contact avec les services de santé avant l'apparition de la psychose avaient une DPNT-A et une DPNT-R plus courtes que ceux dont le premier contact avait eu lieu après l'apparition de la psychose (F = 4,85, p <,03 et F = 3,34, <,07).

Conclusions : Bien que la majorité de la variance de la DPNT soit inexpliquée, surtout pour la composante de recherche d'aide, la portion systémique de la DPNT peut être en partie déterminée par des facteurs relativement malléables. Les interventions visant à modifier les trajectoires des soins et à promouvoir l'accès rapide peuvent être des cibles importantes pour réduire la DPNT. La simplification des procédures administratives peut en outre contribuer à réduire la DPNT.

Keywords
duration of untreated psychosis, early intervention, psychosis, rapid access, pathways to care, help-seeking, treatment delay

Introduction

The relationship between the duration of untreated psychosis (DUP) and clinical, social, and functional outcomes in first episode psychosis (FEP) is a foundational evidence to support the creation and implementation of early intervention services (EIS).[1-4] Notwithstanding some ambiguity about the independence of DUP from other patient or illness characteristics (e.g., negative symptoms, premorbid adjustment), there is strong evidence that DUP has a negative impact on outcome independent of other variables and that such effect is relatively long lasting.[1-9] A recent study has questioned the impact of DUP on outcome and, therefore, of early intervention, based on the concept of "lead-time bias."[10] Apart from the conceptual elegance of lead-time bias, this study was seriously flawed on several methodological grounds, including the inappropriate use of the concept of "lead-time bias," data generated from a sample who received patchy and the quality of treatment not representative of the reality in EIS, selection of negative outcome sample, and poor quality of measurement of the key variable, DUP.[11-13] Suffering caused by prolonged exposure to psychosis alone should be worthy of intervention to reduce such exposure.

Despite the well-recognized importance of DUP, many EIS continue to report long DUP.[14,15] The strong association between DUP and outcome as well as significant interactions reported between the clinical[16] and economic[17,18] effectiveness of EIS and DUP suggest that reducing DUP would enhance the benefits of EIS. More importantly, there is indeed evidence from a study, using a parallel control design, of having experimentally reduced DUP and that such reduction in DUP leads to improvement in both short- and long-term outcomes, especially in negative symptoms and functioning.[7,8]

A methodical approach to reducing DUP would require a clear understanding of components that constitute DUP as well as what malleable or nonmalleable factors may influence each of the components.[19] Previous work has revealed that DUP is comprised of at least 2 components,[14,20,21] namely, Help-seeking DUP (DUP-H; from onset of psychotic symptoms to first service contact) and Referral DUP (DUP-R; from first help-seeking contact to referral to an EIS). It has been observed that in many jurisdictions, DUP-R is often as long as, or even longer than, DUP-H.[21-23] In addition, relatively long DUP has been reported in patients with onset before the

age of 18,[24,25] those with health services contact prior to onset of psychosis,[21,26] and others receiving mental health care at the time of onset of psychosis.[27] While DUP-H has been associated with less malleable patient characteristics (e.g., negative symptoms, poor premorbid adjustment), DUP-R has been associated with factors related to systemic pathways (e.g., type of first help-seeking contact) as well as patient characteristics (e.g., substance abuse).[20,28] These findings have emerged from relatively small sample studies. It does, however, suggest that systemic interventions designed to alter pathways to care, especially those related to the first point of contact, could reduce DUP by reducing DUP-R. As part of the total DUP, additional delays associated with administrative procedures (DUP-A; e.g., waiting lists)[15] have not been examined. Finally, studies have generally not used representative samples such as those derived from a defined catchment area.

The objectives of the present study were to examine, in a large catchment area sample: (a) the contribution of 3 different components of DUP (DUP-H, DUP-R, DUP-A) to its overall length and (b) determinants of each of the components of DUP in the patients' pathways to care to an EIS.

Methods

Settings and Study Population

This study was conducted at Prevention and Early Intervention for Psychosis Program (PEPP)-Montreal, an EIS for a catchment area of 300,000 English/French-speaking residents in South-West Montreal and covered the period from 2003 to 2016. No major alterations were made to the model of care during this period. The inclusion criteria are age 14 to 35 years, nonaffective or affective psychotic disorder, not having received antipsychotics for ≥ 30 days since the onset of psychosis, and an IQ ≥ 70. The exclusion criteria are symptoms of psychosis secondary to a medical disorder (e.g., epilepsy) and substance-induced psychosis. Patients with concurrent substance abuse/dependence disorders are included. Eligible patients are offered 2 years of treatment. PEPP-Montreal is the only such service available for patients with FEP in the catchment area.

An open referral system with no restrictions on the source of referral and offer of an assessment by a rapid-access clinician (RAC, nonphysician) within 72 hours following the receipt of the referral are designed to facilitate rapid access.[29] The program delivers workshops on early identification of psychotic symptoms to staff in emergency services, primary care, mental health clinics, and community/educational institutions within its catchment area. An established protocol for emergency/hospital staff facilitates rapid assessment of potential FEP patients. Every case assessed by the RAC is reviewed the same day with a program psychiatrist to facilitate quick acceptance. All accepted patients are assigned a case manager and a psychiatrist and invited to participate in an evaluation protocol. The study was approved by the institutional ethics review board as part of

a longitudinal study of FEP and EIS. All patients who agreed to participate provided written informed consent.

Circumstance of Onset and Relapse Schedule

Patients were administered the Circumstance of Onset and Relapse Schedule (CORS),[21,30] a retrospective semi-structured interview for assessment of longitudinal course preceding and following onset of psychosis and pathway to care. The dates of onset of any psychiatric symptoms, first health care contact for a mental health problem, onset of threshold-level psychotic symptoms for a duration of at least 1 week, first mental health contact after onset of psychosis, referral to the EIS, assessment for suitability for the EIS, and admission to the EIS were recorded. Information on each component of DUP derived from the CORS for each patient was reviewed to arrive at consensus on key variables of interest between trained research staff and experienced program psychiatrists. We have previously reported high rates of inter-rater reliability (Intraclass correlation coefficient = 0.86 to 0.93) between raters on different components of DUP.[31]

DUP

DUP-Total: Time between the onset of psychosis and acceptance to the EIS.

DUP-H: Time between the onset of psychosis and the first service contact after onset.

DUP-R: Time between first service contact after onset and referral to PEPP-Montreal.

DUP-A: Time between receipt of referral and time of acceptance to the EIS, defined as assignment of a case manager.

Symptoms and functioning: Positive and negative symptoms were assessed with the Scale for Assessment of Positive Symptoms[32] and the Scale of Assessment for Negative Symptoms,[33] respectively, at entry to the program covering the preceding 1 month. Global functioning was measured with the Social and Occupational Functioning Assessment Scale[34] (SOFAS); the degree of social contact with the social subdomain and level of educational/vocation with the educational/vocational subdomain of Strauss Carpenter Scale,[35] respectively.

Premorbid social and educational functioning was assessed with the Premorbid Adjustment Scale,[36] for childhood and early adolescence only, to avoid an overlap with the age at onset of psychosis during late adolescence.

Primary diagnosis (psychosis) and comorbid diagnosis (substance abuse/dependence) were determined using the Structured Clinical Interview for *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition.*[37] Psychotic disorders included nonaffective (schizophrenia, schizophreniform disorder, schizoaffective disorder, delusional disorder, brief psychotic disorder, psychosis Not otherwise specified) and affective psychoses (bipolar or depressive disorders with psychotic features). An insidious mode of

Table 1. Independent Predictors of DUP in Multivariate Analyses.

	Adjusted β	SE	t-score	P value
Duration of untreated psychosis-Help-seeking (DUP-H)[a]				
Type of psychotic disorder	−1.19	0.24	−4.92	**<0.01**
Early adolescent social PAS score	1.27	0.51	2.47	**0.01**
Duration of untreated psychosis-Referral (DUP-R)[b]				
Age at onset of FEP	−0.10	0.03	−3.12	**<0.01**
Total SOFAS score	−0.02	0.01	−1.92	
				0.06
Educational/vocational SCS score	−0.21	0.10	−2.19	
				0.03
Type of first pathway contact	−2.02	0.40	−5.11	
				<0.01
Source of referral to EIS	−0.85	0.32	−2.67	
				0.01
Duration of untreated psychosis-Administrative (DUP-A)[c]				
Gender	0.22	0.13	1.76	0.08
Diagnosis of substance abuse/dependence disorder	0.37	0.12	3.23	**<0.01**
Source of referral to EIS	−0.44	0.13	−3.30	**<0.01**

Note. DUP = duration of untreated psychosis; EIS = early intervention services; FEP = first episode psychosis; PAS = premorbid adjustment scale; SANS = Scale for Assessment of Negative Symptoms; SAPS = Scale for Assessment of Positive Symptoms; SCS = Strauss-Carpenter Scale; SE = standard error; SOFAS = Social and Occupational Functioning Assessment Scale.

[a]Stepwise linear regression model included the following independent variables: gender, ethnicity, age at onset of FEP, mode of onset of FEP, early adolescent social PAS score, early adolescent academic PAS score, type of psychotic disorder, diagnosis of substance abuse/dependence disorder, total SAPS score, total SANS score, total SOFAS score, social SCS score, and education/vocation SCS score; adjusted $R^2 = 0.12$.

[b]Stepwise linear regression model included the following independent variables: gender, ethnicity, age at onset of FEP, mode of onset of FEP, early adolescent social PAS score, early adolescent academic PAS score, type of psychotic disorder, diagnosis of substance abuse/dependence disorder, total SAPS score, total SANS score, total SOFAS score, social SCS score, and education/vocation SCS score, first pathway contact, and source of referral to EIS; adjusted $R^2 = 0.19$.

[c]Gender, ethnicity, age at onset of FEP, mode of onset of FEP, early adolescent social PAS score, early adolescent academic PAS score, type of psychotic disorder, diagnosis of substance abuse/dependence disorder, total SAPS score, total SANS score, total SOFAS score, social SCS score, and education/vocation SCS score, and source of referral to EIS; adjusted $R^2 = 0.08$.

Values in bold are lower than the significance threshold set at $\alpha < 0.05$.

onset of FEP was defined as a prodromal length >30 days, consistent with previous reports.[38]

Pathway variables: We identified *first point of contact* following onset of psychosis and the *final contact* (referral source) that led to referral to the EIS. For predictors of components of DUP, we combined the type of contact variables into "medical" (emergency services/inpatient unit, psychiatrists, or family physician) versus nonmedical (psychologists, social worker, school counsellor, clergy, or other). For the referral source, we created categories of hospital-based emergency services/inpatient unit versus other (community mental health services, primary care, community social services, educational institutions, student health services, and family/self). These definitions for pathway-related variables were based on the findings from a past systematic review.[39] *Demographic* variables included age, sex (male, female), ethnicity (regrouped as White vs. non-White), educational status, relationship, and living status.

Data Analysis

We used *t*-tests for independent samples for normally distributed data, Mann-Whitney tests for data not distributed normally, chi-square tests for binary variables (Fisher exact test for cell counts < 5), Kruskal-Wallis test for ordinal variables, and point-biserial correlation coefficients to examine associations between components of DUP with binary variables and spearman correlations for their relationships with continuous variables. Natural log transformation was performed on DUP variables to normalize the distribution for our linear regression models. For additional analysis, data on patients who had contact with health services *prior* to onset of psychosis (pre-onset contact) were compared with those whose first health contact was only *after* the onset of psychosis (post-onset contact).

Independent variables as putative predictors were selected from our literature review for stepwise linear regression models (see Table 1),[14,24,26,36,37,39-42] Any additional variables identified on univariate analyses were added to the putative predictors listed. Each stepwise linear regression model used backward elimination. Interactions were tested in each of these models and Variance inflation factor tests were performed to detect multicollinearity. All statistical tests were performed using STATA version 13.0. Significance was set at $\alpha < 0.05$.

Results

Study Population

Of the 747 patients admitted to the EIS between 2003 and 2016, 569 (76.2%) consented to participate in the full research protocol. Of these, 37 were excluded due to history of a

Table 2. Descriptive Analysis of FEP Patients Who Accessed an EIS for Psychotic Disorders.

	Study sample (N = 532)
Age at admission into EIS (mean ± SD)	23.55 ± 4.61 years
Gender (n men, %)	370 (70%)
Ethnicity (n White, %)	323 (64%)
Relationship status (n single, %)	468 (90%)
Education status (n completed high school or more, %)	336 (66%)
Living status (n someone, %)	419 (82%)
Age at onset of FEP (mean ± SD)	22.65 ± 4.73 years
Mode of onset (n insidious, %)	396 (79%)
Early adolescent social PAS score (mean ± SD)	0.23 ± 0.22
Early adolescent academic PAS score (mean ± SD)	0.34 ± 0.24
Diagnosis of nonaffective psychotic disorder (n, %)	365 (70%)
Diagnosis of current/past substance abuse/ dependence (n, %)	257 (53%)
SAPS total score (mean ± SD)	34.15 ± 15.08
SANS total score (mean ± SD)	24.71 ± 13.72
SOFAS total score (mean ± SD)	41.29 ± 13.25
SCS social score (mean ± SD)	2.21 ± 1.39
SCS educational/vocational score (mean ± SD)	1.88 ± 1.25
DUP-Total (mean ± SD, med)	42.50 ± 81.16, 14.07
DUP-H Mean (mean ± SD, med)	25.64 ± 59.00, 6
DUP-R Mean (mean ± SD, med)	14.95 ± 45.67, 1
DUP-A Mean (mean ± SD, med)	1.48 ± 2.55, 1

Note. DUP = duration of untreated psychosis; DUP-A = duration of untreated psychosis-Administrative; DUP-H = duration of untreated psychosis-Help-seeking; DUP-R = duration of untreated psychosis-Referral; EIS = early intervention service for psychotic disorders; FEP = first episode of psychosis; med = median; PAS = premorbid adjustment scale; SANS = Scale for Assessment of Negative Symptoms; SAPS = Scale for Assessment of Positive Symptoms; SCS = Strauss-Carpenter Scale; SD = standard deviation; SOFAS = Social and Occupational Functioning Assessment Scale.

previous episode of psychosis upon further inquiry. Our study sample characteristics of 532 FEP patients are presented in Table 2. Patients were prescribed antipsychotic medication within a mean of 10.25 days (standard deviation [SD] 31.82) prior to initial assessment at PEPP-Montreal.

Different Components of DUP

We observed that the magnitude of DUP was greatest for DUP-H, followed by DUP-R and DUP-A, in that order. However, in all components, the means are large and distribution skewed, while medians are comparable, implying that the differences can be attributed to a small proportion of patients with very long DUP (Table 2). A comparison across 4 time periods (2003 to 2006, 2007 to 2010, 2011 to 2014, 2015 to 2016) revealed a significant decrease in mean DUP-A from 2.3 weeks; SD 3.79, in the period 2003 to 2006 to 1.12 weeks, SD 1.2, in 2015 to 2016; $F(3) = 9.59$, $P < 0.001$.

Health Care Contact and Referral to the EIS

Data for the type of first successful help-seeking contact following onset of psychosis were available on 377 patients. Data were missing for the rest because either the dates or the nature of first contact could not be accurately ascertained (Table 3). For most patients, the first such contact was either with hospital services (emergency; $N = 185$, 49.07%) or with a nonmedical health, social services worker or an educational counsellor ($N = 109$, 28.91%) and less commonly with a family physician ($N = 30$, 7.96%). A comparison of the 377 patients with and 155 without these data revealed no differences on any demographic or clinical variables, including DUP (see Supplementary Table 1).

For the final contact resulting in referral to the EIS, almost two-third of patients (327/525) used a hospital-based service (mostly emergency).

Comparison of Patients Who Seek Help Prior to Onset of Psychosis (N = 198, 37.7%) and Those Whose First Contact is Post-Onset (N = 327, 63.2%)

Almost half of the "pre-onset contact" group had their first contact with community, social, and educational services, while the first contact with services for the "post-onset contact" group was mostly with hospital-based services (emergency). For the final source of admission to the EIS, there was no difference between the 2 groups (Table 4).

DUP-H was significantly longer for "post-onset contact" group compared to those in the "pre-onset" group ($Z = 2.733$, $P = 0.006$). Of the "pre-onset contact" patients, those involved in care around the time of onset of psychosis had shorter total DUP and DUP-H compared to those not involved in such care ($Z = 3.126$, $P = 0.0018$; Table 4).

Predictors of Components of DUP

Univariate analyses

DUP-H. Female sex ($r = 0.11$; 95% confidence interval [95% CI], 0.00 to 0.20) or affective psychosis ($r = 0.25$; CI, 0.16 to 0.33) was associated with a shorter DUP-H (Supplementary Table 2), while a longer DUP-H was related to earlier age at onset of psychosis ($\rho = -0.09$, $P = 0.04$), poor early adolescent social ($\rho = 0.19$, $P < 0.01$) or academic ($\rho = 0.14$, $P < 0.01$) adjustment, a greater severity of negative symptoms ($\rho = 0.16$, $P < 0.01$), fewer social contacts ($\rho = -0.21$, $P < 0.01$), and lower education/vocational level ($\rho = -0.12$, $P = 0.01$).

DUP-R. Referral from emergency service ($r = 0.23$) and first pathway contact with a physician were associated with shorter DUP-R (Supplementary Table 3), while an earlier age at onset of FEP ($\rho = -0.18$, $P < 0.01$), a greater severity of negative symptoms ($\rho = 0.13$, $P < 0.01$), poorer degree of social contacts ($\rho = -0.12$, $P = 0.01$), and lower education/vocational level ($\rho = -0.13$, $P = 0.01$) were significantly

Table 3. First Contact and Final Source of Referral to EIS.

	First contacts with helping professional			Source of referral		
	Before psychosis $N = 187$ (49.6%)	After psychosis $N = 190$ (50.4%)	Total $N = 377$	With pre-onset contact $N = 198$ (37.7%)	Only post-onset contact $N = 327$ (62.3%)	Total $N = 525$
Family physician or pediatrician	19 (10.16)	11 (5.79)	30 (7.96)	1 (0.51)	2 (0.61)	3 (0.57)
Hospital services/emergency room	53 (28.34)	132 (69.47)	185 (49.07)	141 (71.21)	250 (76.45)	391 (74.48)
Psychiatrist	19 (10.16)	9 (4.74)	28 (7.43)	4 (2.02)	7 (2.14)	11 (2.10)
PEPP-CAYR	0 (0.00)	5 (2.63)	5 (1.33)	0 (0.00)	0 (0.00)	0 (0.00)
Community or school counsellor, psychologist, social worker	87 (46.52)	22 (11.58)	109 (28.91)	30 (15.15)	41 (12.54)	71 (13.52)
Other	9 (4.81)	11 (5.79)	20 (5.31)	22 (11.11)	27 (8.26)	49 (9.33)

Note. EIS = early intervention services; PEPP-CAYR = Prevention and Early intervention Program for Psychoses and Clinic for Assessment of Youth at Risk.

Table 4. Analysis of Variance (Mann-Whitney Test): DUP Length (Weeks) for Patients with Health Care Contact Before Onset of Psychosis (Pre-onset Contact) versus Those with Health Care Contact Only After Onset of Psychosis (Post-onset Contact).

		N	Mean (SD), Median	Z	P
DUP-H	Pre-onset contact	217	19.08 (41.39), 5	2.73	0.006
	Post-onset contact	283	30.77 (69.27), 6		
DUP-R	Pre-onset contact	214	10.69 (29.50), 1	−1.17	0.24
	Post-onset contact	280	18.26 (54.80), 1		
DUP-A	Pre-onset contact	216	1.37 (2.20), 1	−1.64	0.10
	Post-onset contact	298	1.55 (2.77), 1		
DUP-Total	Pre-onset contact	211	33.10 (53.30), 12.71	5.03	0.02
	Post-onset contact	277	49.70 (96.66), 14.43		

Note. DUP-A = duration of untreated psychosis-Administrative; DUP-H = duration of untreated psychosis-Help-seeking; DUP-R = duration of untreated psychosis-Referral; DUP-T = duration of untreated psychosis-Total; SD = standard deviation.

associated with a longer DUP-R. All the associations above are of modest magnitude.

DUP-A. Being female ($r = 0.10$, Supplementary Table 2) and a higher SOFAS score showed a marginally significant association with a longer DUP-A ($\rho = 0.09$, $P = 0.05$).

Multivariate Analyses

DUP-H. Affective psychosis diagnosis was related to a shorter DUP-H (adjusted $\beta = -1.19$; standard error [SE] = 0.24, t-score $= -4.92$, $P < 0.01$) and lower social premorbid functioning to a longer DUP-H (adjusted $\beta = 1.27$ [SE = 0.51],

$t = 2.47$, $P = 0.01$; Table 1. The model accounted for 12% of the variance in the length of DUP-H (adjusted $R^2 = 0.12$).

DUP-R. An earlier age at onset of FEP was associated with a longer DUP-R (adjusted $\beta = -0.10$ [SE = 0.03], t-score $= -3.12$, $P < 0.01$), while higher level of education/vocation (adjusted $\beta = -0.21$ [SE = 0.10], t-score $= -2.19$, $P = 0.03$), physician as the first pathway contact (adjusted $\beta = -2.02$, [SE = 0.40], t-score $= -5.11$, $P < 0.01$), or being referred from emergency services/inpatient units (adjusted $\beta = -0.85$ [SE = 0.32], t-score $= -2.67$, $P = 0.01$) were associated with a shorter length of DUP-R. The model accounted for 21% of outcome variance (adjusted $R^2 = 0.21$).

DUP-A. Substance abuse/dependence disorder was associated with a longer DUP-A (adjusted $\beta = 0.37$ [SE = 0.12], $t = 3.23$, $P < 0.01$), while referral from emergency services/inpatient units was linked to a shorter length of DUP (adjusted $\beta = -0.44$ [SE = 0.13], $t = -3.30$, $P < 0.01$), the model accounting for 8% of variance (adjusted $R^2 = 0.08$).

Discussion

Our results derived from a large catchment area-based treated incidence sample of FEP patients confirm that both help-seeking and referral processes contribute to the DUP; and that the administrative component, while small, also contributes to the overall delay. DUP-H, the longest component, was independently associated with diagnosis (shorter with affective vs. nonaffective) and poor social premorbid adjustment (longer).[20,42] This suggests that in patients with affective psychosis, a distinct change in behavior may facilitate early help-seeking while behavior indicative of early signs of psychosis (e.g., increased withdrawal) may be relatively imperceptible in the context of poor social premorbid adjustment. The latter may be hard for family and friends to attribute to mental illness in general and, even less, to a specific set of disorders such as psychoses.

Unlike many previous studies,[21-23] DUP-R in our study was significantly shorter than DUP-H. This may be attributed partly to the focus on reducing DUP-R through promoting rapid access.[29] The EIS being situated in the same institution as the only psychiatric emergency service in the catchment area, the RAC being the first point of contact in the EIS and an established protocol for facilitating rapid access for emergency staff, may have facilitated a short DUP-R. However, entry through a hospital emergency may still be undesirable due to potential for a traumatic experience for a young treatment naive patient as well as an increased risk of hospitalization.[26] An awareness, on the part of local social, community, and medical services, of the rapid access intervention may also explain that, unlike a previous study,[21] patients who were engaged in active health care contact, at the time of onset of psychosis, had shorter DUP-R than those not engaged in such contact.

Although most EIS have an open referral policy, the majority of patients are referred from key points of contact within the health care system. Systemic delay (DUP-R), in general, could be positively influenced by the ability of the first point of contact in making a referral directly to the EIS without additional encounters. In our study, very few patients had their first contact with a family physician, and often the first contact was with hospital-based (e.g., emergency department) or social and community services. However, when the first contact was made with a physician, the trajectory of referral to the EIS was shorter than if the first contact was with a nonmedical service. The low frequency of first contact with a physician undermines this potential. This may reflect the system of primary health care in Québec being organized as health and social service community clinics (CLSC), staffed largely by nonmedical personnel and not uncommonly without a family physician. In addition, over 40% of the population (15 to 49 years) in Montreal are not registered with a family physician.[43] Our results are in contrast to 40% of FEP patients making their first contact with a family physician in an Ontario sample[21] from a similar EIS, although there too entry to the EIS did not usually result from the first contact and mostly followed the psychiatric emergency route.

First contact with a *nonmedical* service was shown to delay final referral to the EIS. Nonmedical parts of primary care (CLSC) as well as other community health and education sectors could be important targets for improving early case identification of psychosis while promoting the local EIS. It may, however, be difficult to sensitize even professionals in the health and education sectors specifically about psychosis.[44] Therefore, while continuing to improve the overall mental health literacy of the population, it may be more efficient to focus on improving the skills for early case identification of all mental disorders among health care and educational sector workers, who are often the first point of contact for individuals with emerging psychotic symptoms. Such training will also need to impart the knowledge that patient characteristics such as an early age at onset of

psychosis[24] and those with poor social relationships are likely at higher risk of delay in being referred to an EIS. Such dissemination of knowledge would need to be accompanied by direct access to a designated EIS clinician (e.g., the RAC) for all potential sources of referral, including social and community services, educational counsellors, as well as family and potential patients. It may be important to find ways toward greater involvement of family physicians in such training by addressing issues related to the fee-for-service system of remuneration, as such activities remain nonreimbursable.

Our observations regarding the portion of delay in treatment (DUP-A) that appears to be procedural have not received much attention in the past although it contributes significantly to delay in entering EIS in some settings.[45] Most of the variance in DUP-A is unexplained. Our findings show only a modest delay is encountered by patients with a comorbid diagnosis of substance abuse, while entry through the emergency shortens such delay. Given the high rate (40% to 60%) of concurrent substance abuse with FEP and their eligibility for treatment in the EIS, separating these cases from those for whom the psychotic symptoms may be regarded as purely drug induced may be difficult in addition to requiring several days of inpatient or outpatient observation. The modest delay may also be associated with greater difficulty in engaging some patients due to initial hesitation to accept treatment. Simplifying admission procedures and improving clinicians' skills for assessment and treatment of substance abuse, drug intoxication, and family engagement are likely to assist in this process. It is noteworthy that in our study this delay was reduced significantly over a number of years, possibly through improved skills and a general realization that most drug-induced psychoses turn out to be comorbid conditions of substance abuse and psychosis.[46,47]

The strengths of our study include a large sample of FEP patients derived from a catchment area with no competing service and hence close to an epidemiological treated incidence sample, who had little or no prior exposure to treatment and who had been extremely well characterized on demographic, pathways to care, and clinical variables. A high proportion (75%) of all patients seeking treatment were included and all assessments were conducted with standard instruments with sound psychometric properties. The proportion of variance explained by factors associated with each of the components of DUP was relatively modest. The nature of factors that explain at least 21% of variance in the systemic component of DUP (DUP-R) may suggest a greater malleability of the latter to interventions such as those that could shorten pathways to care. Given the relatively large proportion of unexplained variance, especially in DUP-H, it is likely that unexplored local cultural and systemic factors may play a significant role in determining the length of all components of DUP. If the DUP-R is particularly long, an attention to the factors identified here as well as further exploration of local factors may assist in designing appropriate interventions to reduce DUP. Our findings need to be

interpreted in the context of extensive efforts at reducing DUP inherent to the program, especially through rapid access. These findings may, however, be applicable to other EI services but not to settings of regular care. The extensive use of hospital emergency services remains a concern to be addressed even though it may reduce DUP when rapid access to an EIS is available.

Data availability statement

The principal author was also the principal investigator of the study and hence was responsible for designing the study as well as supervising all data collection and analyses. All other investigators had equally full access to the data.

Declaration of Conflicting Interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: AM served as a research consultant to and gave lectures at conferences supported by Lundbeck and Otsuka and was on an advisory board meeting for the same 2 companies for which he received honoraria. RJ served as a speaker and member of advisory board committees for Pfizer, Janssen, BMS, Sunovian, Myelin, Otsuka, Lundbeck, shire, and Perdue. He also received grants from Janssen, BMS, Otsuka, Lundbeck, Astra Zeneca, and HLS, within the last 3 years, unrelated to the submitted work.

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Supplemental Material

Supplemental material for this article is available online.

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