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PREDICTING DISENGAGEMENT FROM CARE IN AN EARLY PSYCHOSIS PATIENT COHORT IN THE UNITED STATES

A Thesis Submitted to the

Yale University School of Medicine

in Partial Fulfillment of the Requirements for the

Degree of Doctor of Medicine

by

Matthew Reid Kruse

2012

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PREDICTING DISENGAGEMENT FROM CARE IN AN EARLY PSYCHOSIS PATIENT COHORT IN THE UNITED STATES.

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The current study aims to assess baseline variables which may predict disengagement from care among patients with psychosis seeking treatment at an early intervention clinic in the United States. Based on literature published at sites outside the United States, we predict that duration of untreated psychosis, global assessment of functioning, forensic history, family contact, and substance abuse are predictive of disengagement during the first year of outpatient treatment. Patients were grouped according to whether or not they disengaged from care in a one year follow-up, and compared them on the above discrete and continuous variables with chi-square analysis and Student's t-tests, respectively. Although none of the statistical tests reached significance, data trends suggest that longer duration of untreated psychosis, lower global assessment of functioning, forensic history, substance abuse, and less family contact may be associated with disengagement from care.

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Introduction

Psychotic Illness and Treatment Challenges

Schizophrenia and other psychotic disorders are a series of related, typically chronic conditions that respond best to stable, long-term treatment (1). The lifetime prevalence of any psychotic disorder is estimated to be approximately three to four percent (2), are costly to treat, and even with widespread use of antipsychotic pharmacotherapy, continue to be a major source of lifetime disability (3, 4). The exact reasons some individuals develop psychosis are still incompletely understood. Etiologically, prominent theories of schizophrenia and related psychotic illnesses include abnormal neurodevelopmental models (supported by evidence that patients may have structural brain abnormalities such as ventricular enlargement prior to onset of illness), neurodegenerative models (supported by evidence that stable schizophrenic patients who relapse following removal of antipsychotic medication often are unable to return to prior levels of wellness), and neurochemical models, with particular suspicion of dopaminergic and glutamatergic imbalance (5). Indeed, there are many forms of psychotic disorders with varied constellations of positive (such as hallucinations or disorganized thought) and negative symptoms (such as flattened affect or catatonia), likely representing a spectrum of neurobiologically distinct disorders (6). Accordingly, studies have identified a variety of risk factors associated with psychotic illness, including substance abuse (7), family history (8, 9), prenatal insults (10), and even geographic setting or culture (11, 12). Nevertheless, many authors agree that most forms of psychosis are the result of a complex interaction of genetics and environment (7, 11, 13).

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Apart from the cognitive and functional disabilities inherent to psychosis, literature has suggested that patients with a psychotic illness are at higher risk for somatic complications such as obesity, diabetes, and cardiovascular disease (14). These chronic medical conditions may help explain data showing that the life expectancy of individuals with schizophrenia or other psychotic disorders may be reduced by 15 to 25 years (14-16). There is evidence that the morbidity and mortality associated with psychotic illnesses may be intrinsically related to the biological processes underlying psychosis. A review on predisposition for metabolic syndrome and cardiovascular risk in schizophrenia suggests that present data is conflicting, but drug-naïve patients with schizophrenia may have greater baseline levels of insulin sensitivity and higher blood glucose levels than controls (17). In addition, rates of suicide and attempted suicide are particularly high among patients with psychosis, with a lifetime risk of five percent (18). Nevertheless, the impact of environmental influences cannot be ignored. First, some types of unhealthy lifestyle choices tend to occur at higher rates in these patients. A review of the literature notes that rates of smoking in patients with schizophrenia may be as high as 85% (much higher than the estimated 23% in the general population of the United States), and up to 40% of patients with schizophrenia may be smoking more than 30 cigarettes daily. Secondly, the morbidity and mortality associated with psychosis may be exacerbated by the metabolic and other systemic side effects that commonly occur with some antipsychotic medications (14, 19). Aside from the risks of medical disabilities, logistical and financial obstacles may be significant barriers to psychiatric care for patients with psychosis. A survey of patients with serious mental illness in the United States revealed that among those who did not seek desired psychiatric care, 46%

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cited lack of insurance coverage or prohibitive out of pocket expenses, and 52% had situational problems, including uncertainty of where to seek help or time constraints (20). Among a cohort of first-episode of psychosis (FEP) patients in New Haven, Connecticut, 33% of patients were uninsured at baseline, and among those who were insured, only 29% maintained coverage over the first year of psychiatric treatment. Even among those who were eligible for public insurance, 38% lost coverage over this period (21). Taken together, despite the development of multiple generations of antipsychotic medications, there remains significant room for improvement in the clinical and psychosocial interventions for patients with psychotic disorders.

Engagement and Disengagement

The previous section outlined the treatment challenges that accompany psychotic disorders, and began to address the various barriers to care facing many patients suffering from them. Unfortunately, merely connecting patients with care is inadequate, and authors agree that maintaining treatment and preventing service disengagement is critical for producing good clinical outcomes while preventing morbidity, mortality, and psychosocial decline (18, 22). Before service disengagement can be discussed further, the definition of term 'disengagement' should be examined.

Strikingly, despite a rather voluminous body of literature on the topic of disengagement from psychiatric services, there is no consensus on what constitutes "disengagement." For instance, Fischer et al. define disengagement among a cohort of patients with schizophrenia or bipolar disorder as "a period during which a cohort member had no documented contact" with his or her mental or medical healthcare providers (23). This

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study identified all disengagement periods greater than three months, but focused most of their analysis on disengagement periods of 12 months or greater. Kessler et al. defined disengagement among patients with serious mental illness as having sought psychiatric care at any time in the preceding 12 months, but not currently seeking treatment for any reason other than an improvement in symptoms (20). Olfson, meanwhile, simply defines disengagement as the discontinuation of treatment earlier than intended by a clinician (24). In an assessment of psychiatric service use of first-time patients in South Verona, Italy, Tansella provides a more formal definition of disengagement. Service use was described in terms of 'episodes of care' and 'break values' (25). A 'break value' is considered the amount of time that must pass between clinical contact before a patient can be considered disengaged from active treatment. An 'episode of care', meanwhile, is the time that passes before a patient hits a given 'break value.' They calculate patterns of service use using break periods ranging from seven days to 183 days. As would be expected, when a seven day break value was used, the median episode of care in their sample was one day. They reason that only the most acutely ill patients are seen in outpatient clinic more than once every seven days. Therefore, a seven day break value is too sensitive, producing excessive disengagement false-positives. After recalculating using various break values, they found that 90 days appeared to be the optimally sensitive and specific break value. The authors note that a 90 day break value is consistent with the clinical needs of patients, and had used this value in prior publications (25).

Nevertheless, literature reviews have suggested that in general, psychiatric patients in the United States have a disengagement rate of about 20% (24). Among patients with psychosis, a systematic review uncovered estimates of disengagement rates ranging from

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24 to 90%. The average rate of disengagement among the 86 studies analyzed, weighted for sample size, produced an estimate of 26% disengagement rate. The definition of disengagement in this review cannot be defined, as rates of disengagement were assessed according to the definition used in each study included in the meta-analysis. (26)

Predicting Disengagement

Even if there is ongoing disagreement in the literature on what constitutes disengagement, and what the true rate of disengagement is among various patient populations, there have been factors associated with greater risk for disengagement from care both in cases of psychotic illness as well as in general psychiatric populations. Namely, younger age (24, 27), living apart from family (28, 29), lack of insurance (30), forensic history (29, 31), less use of available services (27), longer duration of untreated psychosis (DUP) (32), lower baseline global assessment of functioning (GAF) (28), lack of insight (33), and persistent substance abuse (24, 28, 29) often correlate with higher rates of service disengagement.

In addition to these factors, early stage of treatment is a particularly critical time for preventing disengagement from care. Data has shown that first-time psychiatric patients are almost six times more likely to drop out of treatment if they have had fewer than three clinical visits, with authors hypothesizing that once rapport and trust is established over time, risk of disengagement decreases (24). Among patients with psychotic illnesses, side effects of antipsychotic medication, which may occur early in treatment, could be contributing the high rates of disengagement early in treatment. One study demonstrated that a 12 week course of some antipsychotics in treatment naive adolescents produced

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significant weight gain and triglyceride elevation that was not observed in unmedicated controls (34). These side effects may provide incentives for patients to disengage from care and discontinue medication during the first few weeks of treatment if a strong therapeutic relationship has yet to be established. The Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) study indeed demonstrated that among an array of first- and second-generation antipsychotics, 74% of patients discontinued their antipsychotic medication within 18 months, often due to side effects or perceived lack of efficacy (19).

Duration of Untreated Psychosis

Of the factors listed above, much emphasis has been placed in the literature on DUP, defined as the lapse in time between the onset of psychosis and the start of treatment. DUP receives emphasis not only as a predictor of disengagement, and poor clinical outcomes, but also as a valuable tool for examining the natural progression of psychotic illness (35-37). An examination of DUP in patients living in Nova Scotia, Canada showed that longer DUP is associated with more severe negative symptoms and social withdrawal at baseline, in addition to more severe positive symptoms and lower GAF scores six months into treatment (35). Similarly, Schimmelmann et al. demonstrated that longer DUP is associated with worse illness severity, positive symptom remission rate, and general functioning after 18 months of treatment (37). A meta-analysis of 26 studies demonstrated that DUP correlated significantly with worse depression, anxiety, positive and negative symptoms, social functioning, and overall quality of life 12 months into treatment (32).

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Conversely, a study of first-episode schizophrenia patients in West London found only older age to be significantly associated with DUP longer than 26 weeks. They found some data trends linking longer DUP and more errors on a computerized neurocognitive task, as well as longer duration of untreated illness (but not DUP) with poorer initial response to antipsychotics. (Duration of untreated illness was defined as DUP plus the length of any prodromal symptoms.) Though the sample size was limited (n = 53), the authors were nevertheless skeptical that untreated psychosis may be conferring any inherent challenges to treatment once a connection to care is established. Instead, they hypothesize that longer DUP may be linked to confounding variables such as social isolation or less socially-conspicuous negative symptomology which may prolong the time to seeking treatment (38). Polari et al. stress that poor adherence to medication while attending medical appointments might be considered part of the DUP period, potentially accounting for some of the variation in findings on the effect of DUP in studies that might not necessarily be measuring this metric (36).

First-Episode Psychosis and Early Intervention

The potential importance and benefits of limiting DUP, combined with the insight that several predictors of disengagement, including younger age and early treatment phase, tend to co-segregate in patients with first-episode psychosis (FEP), has rendered this population of particular importance to investigators interested in optimizing outcomes in patients with psychotic illness. A survey in the U.K. of patients with FEP found that the 67% were between 16 and 30 years old, 86% were unemployed, and 72% had discontinued education by the age 16 (39). Sixty-two percent of a FEP cohort in Australia was found to have a substance use disorder at baseline assessment (40). These

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demographic and socioeconomic trends in FEP underscore concerns that intervention should be initiated as early as possible to prevent the medical, psychiatric, and psychosocial decline that is common in this population by the time care is initiated (14, 41).

Aside from establishing care, the particularly high risk of disengagement within the first two appointments of care following discharge from an emergency department or inpatient psychiatric unit has prompted investigators to stress that it is critical to establish a strong clinical relationship as early as possible (24). This insight, combined with the challenges in treating FEP discussed, has inspired a growing number of specialized early intervention clinics aimed at initiating treatment as early as possible in the course of any psychotic illness, either in the prodromal phase (prior to the onset of frank psychosis) or as soon as possible after the onset of psychosis, effectively reducing DUP (42).

One of the flagship programs studying the effects of specialized early intervention in FEP was the Buckingham study, established in 1984. The program was established in rural England to improve the recognition and prompt treatment of patients in the earliest stages of serious mental illness, employing several key strategies. Initial psychiatric evaluations were performed at a location convenient to the patient. Primary care providers were given additional training and screening tools to improve their detection of serious mental illness during routine checkups. Specialized psychiatric consultations were made readily available, often performed collaboratively with a patient's primary care provider (43).

Once patients were identified as potentially in the early stages of schizophrenia, specialized treatment interventions were immediately implemented. First, patients were

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educated on all parameters of their illness, with an emphasis on the good prognosis that may be achieved with stable, long-term treatments. Second, sources of a patient's stressors were identified, especially in cases where precipitating life events were suspected to have triggered psychiatric symptoms, and stress management was instituted with an intensity appropriate to a particular patient's needs. Finally, these psychosocial interventions were complemented by low-dose antipsychotic medication, targeted at the correction of a particular deficit, such as insomnia or thought disturbances, and discontinued when the target symptom had resolved. Once prodromal symptoms had resolved, primary care providers took responsibility for close, long-term monitoring for any signs of relapse (43).

Many of the key features of the Buckingham study have been implemented in later early intervention programs, including lower-dose antipsychotics, comprehensive case management, supportive psychotherapy, psychoeducation for patients and families, and group cognitive-behavioral therapy (41, 44-46).

The rationale behind the continued and growing support for specialized early intervention clinics for FEP is multifaceted. First, early specialized intervention may help prevent functional decline and improve clinical outcomes, applying a preventive philosophy to psychosis treatment. By asserting more intensive outpatient follow-up early in the course of illness, the degenerative neurobiological changes that have been hypothesized to accompany untreated psychosis may be avoided (5). In addition, patients with FEP often report adverse events in the time leading up to their first connection with psychiatric care. One survey revealed that significant functional disability develops over the course of untreated psychosis, and 14% of FEP patients in Melbourne attempted suicide prior to

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treatment (41). A review by Goff et al. also points out that rates of infectious disease, including influenza, HIV, and hepatitis C is particularly high among individuals with serious mental illness, due in large part to unhealthy lifestyle habits that occur with higher frequency in this patient population. Findings such as these provide a compelling argument for earlier, more assertive intervention driven by the ideals of preventive care (14). A comparison of early specialized versus standard treatment for FEP patients in Denmark suggests that the specialized approach produced superior positive and negative symptom relief at one and two years into treatment. In addition, the group receiving specialized treatment demonstrated lower rates of substance abuse, and greater service engagement (46). A similar study of 144 first- and second-episode psychosis patients by the Lambeth Early Onset team in the U.K. failed to find a significant advantage for specialized treatment in symptom reduction at 18 months, but did report that specialized treatment produced superior measures of quality of life and global functioning at 18 months (47). Psychiatric patients with access to dual modality treatment, including both pharmacotherapy and talk therapy, have been shown to be less likely to dropout from care (30). In addition, Iyer et al. demonstrated that aside from symptom relief, patients with FEP in Chennai, India most frequently cited vocational, educational, and interpersonal improvement as their highest priority goals for treatment. By emphasizing these global issues in treatment through modalities including vocational rehabilitation and family education, early intervention clinics may be aligning themselves more closely with a patient's personal goals, helping build strong therapeutic alliances more efficiently (45). This may help explain an analysis of an early intervention clinic in the U.K. which revealed lower dropout rates than standard treatment controls (44).

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Economically, early intervention may yield additional benefit, especially in terms of cost-effectiveness of treatment, more optimal allocation of scarce resources, and improved educational and vocational outcomes. As mentioned previously, early intervention clinics aim to provide more intensive outpatient care with an emphasis on crisis prevention. An analysis of patients with psychosis in the U.K. demonstrated that while 86% of FEP patients were unemployed at initiation of treatment, unemployment reached 100% in patients with a second episode of psychosis (39). If patients are identified and treated earlier, the psychosocial decline associated with more severe cases of psychosis may theoretically be prevented, reducing rates of unemployment.

A cost-effectiveness analysis was performed at an early intervention for psychosis clinic in Milan, Italy. In both groups, treatment was administered for approximately five years, and both groups demonstrated significant clinical improvement, as measured by the Health of Nation Outcome Scales (HoNOS), an inventory measuring a variety of clinical and social outcomes relevant to psychotic illness. The average daily costs of treatment in the early intervention group and the standard care group were similar (€22.60 and €23.00 per patient, respectively), but the specialized treatment group demonstrated a larger absolute decrease in the HoNOS measure of illness severity. The authors concluded that specialized treatment is cheaper per unit of improvement in symptoms and global functioning (€4802 versus €9871 per unit reduction in severity on the HoNOS) . They additionally noted that more expensive outpatient interventions such as psychotherapy rendered specialized treatment more expensive in the first two years of treatment, but became less expensive than standard treatment in the last three years, likely due to a trend in fewer admissions to and shorter stays in inpatient care facilities (though this data trend

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fell short of statistical significance). Standard care, meanwhile, became linearly more expensive, on average, over the five year course of treatment, again, potentially due to greater use of inpatient psychiatric services among this patient group (48). Indeed, analyses of early intervention clinics in Melbourne, Australia (49) and the U.K. (44) demonstrated statistically significant reductions in hospitalization rate compared to standard treatment controls.

It may be too soon to draw definitive conclusions on the benefits of early intervention clinics. A recent Cochrane Review article found that specialized early intervention for FEP did improve compliance with treatment, but failed to find statistically significant benefits on other outcome metrics, including hospitalization, relapse, and suicide. The authors, however, noted the limited number of studies from which to draw conclusions, and underscored the importance for more, higher-powered studies to more fully elucidate potential benefits of early intervention, and whether these benefits are maintained over time (50).

Criticism of Early Intervention

Despite the urging for more data and the efforts on the parts of investigators, the movement towards earlier intervention for psychosis is not without its critics. Pelosi et al. argue that intervention earlier in the course of illness – particularly during the prodromal phase of psychosis – will lead to a greater number of patients being inappropriately treated for a psychosis who would never have developed the illness, noting that symptoms of a prodromal psychotic illness are far more common than psychotic illnesses themselves. Aside from the risks of treating patients prior to full onset of psychosis, he

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additionally notes that some patients with psychosis will improve spontaneously without treatment, with earlier interventions at greater risk of providing unnecessary treatment to these patients (51, 52).

Pelosi additionally notes that the growing number of early intervention clinics may be diverting the limited resources of the already strained mental healthcare infrastructure away from the majority of patients with a long history of psychotic illness to better fit the needs of a select few early in the course of illness. Furthermore, he suggests that by discharging patients to standard care following a finite course of treatment during more critical periods of intervention (often the first few years following onset of psychosis), early intervention clinics are providing the very same fragmented care that they were designed to avoid (51, 52). Finally, some in the psychiatric community question whether the selection criteria of many early intervention clinics, such as limited duration of psychotic illness and little-to-no prior courses of antipsychotic medication, may be introducing a selection bias for patients with better prognoses or who may have spontaneously improved without intervention. Aside from providing inappropriate treatment, such recruitment practices may in fact be skewing data towards better outcomes, obscuring the true benefit of specialized early intervention (53). The concerns regarding early intervention are certainly valid. Even as the behavioral and neurologic antecedents to schizophrenia and other psychotic illnesses become more refined, there remains a considerable challenge in predicting future cases of psychotic illnesses with much specificity. Some authors note, however, that this lack of specificity may actually potentiate the benefit of early intervention through prevention of behaviorally or biologically related conditions such as bipolar disorder, as long as the dangers of

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treatment are minimized (54). As long as antipsychotic medication remains a treatment mainstay, however, side effects of intervention will continue to be a legitimate concern. In a review of the literature on metabolic side effects of antipsychotic medication in FEP patients, Foley and Morley found that significant increases in weight, insulin resistance, cholesterol, and fasting glucose could be present within six to eight weeks (55). On the other hand, the multiple modality treatments for psychosis characteristic of early intervention, with a use of lower-dose antipsychotic medication, may reduce the risks of extra-pyramidal symptoms or metabolic side effects of treatment (56). In a review on the use of antipsychotic medication in FEP, Francey et al. even suggest that psychosocial interventions alone may be sufficient in the treatment of some cases of early psychosis, evading their cardiovascular risks completely (57). Furthermore, Conus et al. note that FEP patients have typically experienced significant social and psychiatric decline prior to engagement with an early intervention clinic. As a result, they suggest treatment during the prodrome of psychosis may be necessary to truly optimize outcomes, and treating only after the onset of a full psychosis, as critics of early intervention recommend, may be too late (41). Concerns regarding the fragmented care of patients discharged from specialized treatment to standard care following the critical period of illness has been examined by several studies. A two year early intervention (OPUS trial) in Denmark found that the clinical benefits of specialized treatment at two years were no longer present in at a five year follow-up (58). A clinic in Canada, however, provides specialized FEP care for five years, though with much lower intensity after the second year of treatment, and found persistent improvement in symptoms at a five year follow-up, lending support for the need of longer continuity of care in early intervention clinics (59). In a separate follow-up assessment of Canadian FEP patients discharged to standard care following three

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years of specialized intervention, Addington and Addington find that patients maintained benefits on metrics of positive symptoms, and continued improvement in negative symptomology and quality of life scales over a four- to five-year follow-up period. (Although, only approximately half of patients could be followed up following discharge, potentially biasing results towards patients who retained higher functioning.) (60)

Even though the rationale and promise of early intervention clinics has its critics, a growing number of elements of specialized early intervention are becoming validated by experts. The Schizophrenia Patient Outcomes Research Team (PORT) treatment recommendations is a review published periodically which analyzes the current literature to assess which psychosocial interventions for schizophrenia are supported by evidence, and makes recommendations for standard treatments. In the 2009 update of PORT, they recommend the use of Assertive Community Treatment involving a multidisciplinary treatment team and higher frequency of contact between patients and clinicians. Also recommended is a broader treatment focus, emphasizing vocational and interpersonal skills, access to cognitive behavioral therapy, and family education. At the time of writing the 2009 PORT recommendations, there was insufficient evidence for the authors to officially endorse psychosocial treatments for recent onset schizophrenia. They nevertheless express optimism for this intervention, noting the early intervention data is "witnessing substantial progress," and note that their inability to officially endorse early intervention was "primarily due to small numbers of studies for any given intervention and some inconsistencies among the findings" (1).

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Early Intervention in the United States

Helping to answer the call for more data regarding early intervention for psychosis, the Specialized Treatment Early in Psychosis (STEP) program at the Connecticut Mental Health Center in New Haven, CT, is an NIH-funded pilot program that aims to investigate the effects of multidisciplinary, evidence-based intensive outpatient intervention in the United States. Briefly, its focus is to replicate and further elucidate the benefit of early intervention in psychosis in a cohort of FEP patients in the United States using a pragmatic randomized controlled trial paradigm (described in detail in the following methods section).

STEP is one of the first specialized early intervention in psychosis clinics in the United States (61). As noted previously, the benefit of the psychiatric interventions assessed by early intervention clinics may vary between geographic regions due to variances in standard care protocols, making extrapolation of currently available data to the United States unreliable and necessitating replication studies (62).

Statement of Purpose

The current study aims to explore data on disengagement from an early intervention psychosis clinic in the northeast United States. Our first aim is to begin elucidating the effects of early intervention in the United States, where there is currently little published data, focusing on predictors of disengagement in an FEP cohort. The fragmented care that is typically available to patients in the US, particularly in psychiatric populations, renders engagement in a strong, long-lasting connection to a mental healthcare facility of particular importance (62, 63). We will explore whether previously identified predictors

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of disengagement can be replicated in our patient sample. Specifically, we hypothesize that younger age, longer DUP, lower baseline GAF, forensic history, less family contact, and substance abuse will associate with higher rates of service disengagement. In addition, as many studies on disengagement from service seem to rely on varied or even vague definitions of disengagement (64), we hope to contribute data centered on a clinically reasoned, objectively measurable definition of disengagement.

Method

Setting

The current study was conducted at Connecticut Mental Health Center (CMHC), a publicly-owned mental health treatment facility that operates as part of the Connecticut Department of Mental Health and Addiction Services (DMHAS). CMHC and much of its clinical staff are additionally affiliated with the Yale University School of Medicine. CMHC provides inpatient and outpatient mental health care to uninsured or publicly insured-patients over the age of 18 living in New Haven, CT and surrounding communities, representing a catchment of approximately 200,000 eligible individuals (61).

Clinical data was obtained from the Specialized Treatment Early in Psychosis (STEP) at CMHC, an NIH-funded pilot program designed to investigate the clinical and economic benefit of evidence-based interventions early in the course of psychosis. STEP was designed as a pragmatic randomized controlled trial that enrolled all patients early in the course of a psychotic illness (61). To be eligible for enrollment in STEP, patients have be over 18 years of age, currently suffering from first episode of psychosis (FEP), and have

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fewer than eight weeks of lifetime treatment with an antipsychotic medication. Patients need not be eligible for public-sector care, and those with co-morbid psychiatric illnesses are eligible as long as there is no developmental or intellectual disability present. Once enrolled in STEP, patients are assigned to either STEP treatment at CMHC or randomized out to a control "treatment as usual" (TAU) group, receiving care at either CMHC or with a private mental health practitioner. Patients enrolled to receive care from STEP do so free of charge. The length of treatment is determined individually by each patient's symptom profile, response to treatment, and clinical needs.

The majority of patients enrolled in the STEP study are recruited either by referral from Yale Psychiatric Hospital following admission or from regional hospitals.

STEP employs several treatment strategies for early psychosis patients. Aside from standard antipsychotic pharmacotherapy, patients also have access to group cognitive-behavioral therapy. Individual case managers assist patients with the educational and vocational difficulties that are common among patients with psychotic illnesses. In addition, assertive interventions, including frequent clinical contact with a primary clinician (typically a social worker or psychiatric nurse) as well as phone and written appointment reminders to patients, aim to decrease clinical drop-out from care. After enrollment in the STEP study, outcome data is gathered on each patient at baseline and 6 month intervals (61). Data collected is described in more detail in a later section.

Patients

The current study examines patients enrolled in the experimental arm of STEP treatment. In accordance with STEP's research protocol, all patients were between ages 18 and 45 at

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time of enrollment in STEP, suffering from a first episode of a psychotic illness. Appropriate diagnosis for inclusion in STEP was determined by guidelines published in the DSM-IV-TR (6), as assessed by clinical evaluation and the Structured Clinical Interview for DSM-IV (SCID) and chart review by a psychiatrist or psychologist on staff at STEP. Exclusion criteria include evidence for substance-induced psychosis, prior episodes of diagnosed psychosis, or prior antipsychotic pharmacotherapy of greater than eight weeks (61). All patients were retrospectively evaluated over a period of one year following enrollment in STEP. Patients enrolled for less than one year at the time of analysis, or for whom complete clinical records were not available, were excluded.

Assessment of Service Disengagement

Patients were classified as having either remained engaged or disengaged over the first year of STEP treatment. Disengagement was defined as having been out of contact with all STEP service providers for a period of 3 months or greater during their first year of outpatient follow-up, even if they did eventually return to care. Clinical contact was assessed by chart review. Attendance to appointments was confirmed by clinic notes, and non-attendance was confirmed by lapses in progress notes and records indicating missed appointments. Engagement was tracked with a one month resolution. In cases of service disengagement, the month of the last appointment attended was considered the month when disengagement occurred.

The one year follow-up period and current definition of disengagement were chosen for several reasons. First, as noted, literature suggests that the earliest stages of clinical care following a first episode of psychosis may be the most critical period for establishment of

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a strong therapeutic relationship and optimizing clinical and functional outcomes (24), so the decision was made to focus on the first year of treatment. From a treatment standpoint, a period of no clinical contact of three months or greater within the first year of care following FEP would not be consistent with the assertive treatment modality employed by STEP, and we considered a three month absence a reasonable indicator of a patient's failure to attend scheduled appointments. Our three month definition of disengagement is additionally supported by the above-mentioned analysis by Tansella, et al. which suggests a shorter period may be too sensitive, inappropriately labeling active patients as disengaged, and longer periods may inappropriately label patients who only sporadically attend appointments, as fully engaged (25). In addition, the primary importance for investigating predictors of and reducing rates of disengagement is to improve outcomes by effecting greater continuity of care (64). Therefore, we consider any instances of disengagement an indicator that a patient is not receiving optimal continuity of care, and have classified patients as disengaged even if they eventually return to care during the one year follow-up period. As the current study is not concerned with patients who involuntarily disengage from services, patients who move away, become incarcerated, or expire during the one year follow-up period have been excluded.

Measures

Patients enrolled in STEP are evaluated at baseline. Measures include basic demographics including age and address, current and past medications, medical history, the Structured Clinical Interview for DSM-IV Axis I Disorders, Clinician Version (SCID-CV) (65), Positive and Negative Syndrome Scale (PANSS) (66), Columbia Suicide Severity Rating Scale (C-SSRS) (67), Global Assessment of Functioning Scale (GAF)

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(6), Heinrich's Quality of Life (QOL) (68), Alcohol Use and Drug Use Scales (AUS/DUS) (69), Abnormal Involuntary Movement Scale (AIMS) (70), modified Social Functioning Scale (71), and a modified Service Use and Resources Form (SURF) (72). Patients receive follow-up measures every six months, for which they are compensated 50 dollars. All evaluations are adminstered by a trained STEP affiliated clinician. These measures provided the demographic, educational, GAF, symptom profile, and forensic data employed in the current study. Service use was gathered from the modified SURF scale and medical chart review. These measures are repeated every six months if the patient is still in contact.

Statistical Analysis

Patients were grouped as being "engaged" or "disengaged" according to criteria described earlier in the methods section. We used Student's t-test to measure differences between these two populations on several continuous metrics, including age, duration of untreated psychosis (DUP), and baseline Global Assessment of Functioning (GAF). Differences in discrete variables, including level of family contact, forensic history, and baseline substance abuse were assessed by chi-square analysis. Family contact was converted to an indicator variable of 0, 1, or 2. Family status of "0" indicates that the patient has no contact with his or her family at the time of baseline assessment, "1" indicates the patient is in contact with his or her family but does not reside with them, and "2" indicates that the patient is currently residing with his or her family. In cases where a patient becomes disengaged, service utilization is calculated only for the months leading up to, but not including, the final month of engagement. We additionally assessed substance abuse at baseline and at 6 months, as prior literature has found a stronger

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correlation between persistent substance abuse and disengagement than baseline substance abuse (28), though our analysis focuses on baseline substance abuse, since our focus is primarily in predicting risk of disengagement upon initiation of care

All statistical analyses were performed using SPSS (IBM Corporation).

Research Approval and Collaboration

The STEP research protocol and all associated data analysis included in the current study was approved by the Human Investigation Committee at Yale University School of Medicine, New Haven, CT. All participants provided written informed consent authorizing use of clinical and demographic data for analyses. The current study was conceptualized by Matthew Kruse, Dr. Vivek Phutane, and Dr. Vinod Srihari. Mr. Kruse and Dr. Phutane gathered all clinical data and performed the statistical analysis. Mr. Kruse composed the initial and final versions of the current thesis, and Drs. Phutane and Srihari reviewed the first draft.

Results

Tables 1 and **2** display the investigated variables of the patient groups including age and gender. The mean age of patients in the current study was relatively young in both groups at approximately 20 years. The "engagement" group ages ranged from 17 to 30. The "disengagement" group ages ranged from 17 to 28. The patient population was

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predominantly male (32 out of 39, or 82%).

		Mean (S.D.)	t	Sig. (2-tailed)
Age (Years)	Engagement Group	20.30 (7.94)	0.149	0.883
	Disengagement Group	20.58 (2.59)		
DUP (Weeks)	Engagement Group	21.50 (23.33)	0.776	0.443
	Disengagement Group	27.95 (28.17)		
Baseline GAF	Engagement Group	35.70 (6.46)	-1.157	0.256
	Disengagement Group	32.47 (10.40)		

Table 1. Continuous variables and t-test results.

All patients in the current study carried a clinical diagnosis of schizophrenia, schizophreniform disorder, schizoaffective disorder, or psychosis not otherwise specified.

Disengagement Rate

Among the 39 patients examined in the current study, 19 (49%) disengaged over the course of the first year. Among patients in the disengagement group, the most likely time for initial disengagement to occur was within the first three months of outpatient care, representing nine of 19 (36.8%) disengagement cases. Overall, the average time to initial disengagement was 3 months. Among the 19 patients who disengaged, 5 (26.3%) reinitiated clinical contact at some point before the end of the year follow-up. **Figure 1** demonstrates a relatively steep drop-off of engagement in the initial months of our follow-up period.

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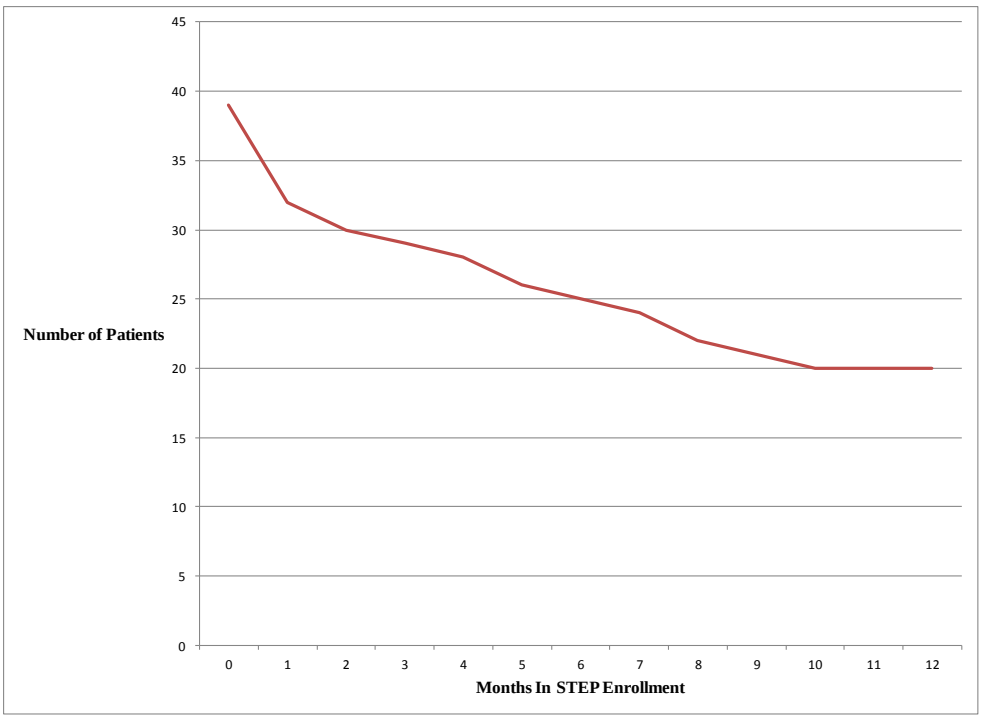

Figure 1. Patients with no disengagement periods in first year of treatment

Predictive Variables

Neither group demonstrated significant difference on any of the continuous variables examined, including age (t = 0.15; p = 0.88), clinic visits per month of engagement **(**t = 1.75; p = 0.09**)**, DUP (t = 0.78; p = 0.443) or baseline GAF (t = -1.16; p = 0.26) **(Table 1)**. Similarly, none of the discrete variables were significantly different between the engagement and disengagement groups, including gender (χ^2 = 0.24; p = 0.62), contact with family (χ^2 = 3.7; p = 0.16), forensic history (χ^2 = 1.76; p = 0.18), or baseline substance abuse (χ^2 = 1.25; p = 0.264) **(Table 2)**. It was not clear whether these variables followed a normal distribution, but replication with non-parametric statistical tests did not yield different results.

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	Engaged	Disengaged	Chi-Square	Sig. (2-sided)
Male	17 (43.6%)	15 (38.5%)	0.242	0.622
Female	3 (7.8%)	4 (10.3%)		
Living Alone, No Contact	1 (2.6%)	4 (10.3%)	3.729	0.155
Living Alone with Contact	2 (5.1%)	4 (10.3%)		
Living with Family	17 (43.6%)	11 (28.2%)		
Forensic History	2 (5.1%)	5 (12.8%)	1.761	0.184
No Forensic History	18 (46.2%)	14 (35.9%)		
Substance Abuse (baseline)	8 (20.5%)	11 (28.2%)	1.249	0.264
No Substance Abuse (baseline)	12 (30.8%)	8 (20.5%)		

Table 2. Discrete variables and chi-square results.

Although there were no significant differences in the two groups for any of the variables examined, some patterns emerged upon review of our data. The mean DUP was slightly higher in the disengagement group (27.95; $\sigma = 28.17$) than the engagement group (21.5; $\sigma = 21.5$) though standard deviations were large, and statistical significance was not achieved. The mean baseline GAF was higher in the engagement group (35.7; $\sigma = 6.46$) than the disengagement group (32.47; $\sigma = 10.4$), but again not significantly so. In addition, the disengagement group seemed to have less contact with family. Of the five patients in the current sample who live alone with no contact with family, four (80%) were in the disengagement group. Of the six patients who live alone yet maintain contact with family, four (66%) were in the disengagement group. Among the remaining 28 patients who live with family, only 11 (39%) of them disengaged from care. Despite a lack of statistical significance, all of these factors trended in the direction that we would have predicted from the literature (24, 28, 29, 32).

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Discussion

Specialized treatment for first episode psychosis is a growing trend internationally, with mixed yet promising data being published from clinics in locations including Australia (28), Canada (60), and the U.K. (47). Strengths of the current study include being among the first examinations of disengagement patterns associated with specialized early psychosis interventions in the United States. Our data and current definition of disengagement strives to maximize accuracy in identifying truly disengaged patients based on clinical attendance data, supported by prior disengagement analyses (25). Furthermore, our presentation of the data and unambiguous definitions of disengagement aims to facilitate future meta-analyses as more data is published on patient cohorts in the United States.

Key Findings

None of the variables examined in the current study were significantly different between the two groups examined in the current study. The lack of significance may have resulted from insufficient statistical power caused by a relatively small sample size.

Although we did not uncover any variables that were significantly associated with disengagement in the first year of outpatient follow-up in FEP, the data on DUP, baseline GAF, connection with family, forensic history, and substance abuse trended in the same direction as would have been predicted in the literature. This consistency across all variables with previously published findings discussed in our introduction suggests our data trends may not be spurious findings, and may be an indicator of a type II statistical error stemming from an underpowered analysis.

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Age

We failed to find any relationship between age and disengagement patterns in the current study. The mean ages of the engagement and disengagement groups were very similar (20.30 and 20.58 years, respectively). The standard deviation in the ages, conversely, were strikingly dissimilar between the engagement and disengagement groups (7.94 and 2.59 years, respectively). A post-hoc Levene's Test for Equality of Variances on the age variable was performed, revealing the variances to be significantly different ($F = 5.28$; $p = 0.027$). This data may suggest a unimodal disengagement risk over the age range of the current patient sample. In other words, those patients either at the lower or higher end of the current age distribution may be more prone to stay engaged in care, while those in the middle are at a relatively higher risk of dropout. Reasons for this distribution would be merely speculative at this point. Although literature reviews on schizophrenia have linked younger age to higher rates of disengagement, it might be reasonable to suggest that the risk of disengagement by younger patients may be overcome by the protective factor of living with parents (a high likelihood in the younger patients in the current study who are under 20 years old) (22). Older patients, meanwhile, may be more likely to remain engaged for the same reasons proposed by earlier studies, such as a correlation of later onset FEP with lower severity of illness or greater insight (30, 39). Our findings raise the possibility of a critical age of onset for psychosis that renders patients at a higher risk for disengagement, arising from the aggregate clinical and demographic factors that co-segregate with that particular age range. On the other hand, if the predictive power of age is merely a result of co-segregation of other factors, a direct measurement of those other factors may be a more powerful measure for risk of service disengagement.

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Forensic History

Only two patients in the engagement group have a forensic history, as compared to five in the disengagement group, a trend consistent with prior associations of forensic history with disengagement (31). It is still unclear why forensic history is associated with disengagement from healthcare services, though Lecomte et al. suggest that individuals who have a history of exposure to violence, abuse, or other forms of trauma are more likely to commit crimes themselves later in life. These same individuals, as a result of traumatic exposures, may develop impaired interpersonal dynamics, including an inherent mistrust of the status and authority of a healthcare provider. Hence, a history of trauma may be the confounding variable linking forensic history with service disengagement (31).

Social Support

A trend in family contact is consistent with the literature on disengagement patterns in psychiatric patient populations. Four patients in the disengagement group (21%) live alone with no contact with family. Meanwhile, only one patient in the engagement group (5%) lives alone with no contact with family. It is plausible that patients living alone with no contact with family may have difficulty establishing or maintaining relationships. These difficulties could extend beyond family or social circles, and form a barrier to establishing strong therapeutic relationships with healthcare providers. Alternatively, patients that have fewer social contacts may experience logistical impediments to care, including fewer social contacts to help remember appointments or greater difficulty arranging for transportation. The latter hypothesis introduces legitimate concerns about

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why some patients may disengage from care. Patients who do not have access to transportation, or must financially support themselves and cannot take time off work, may stop showing up to appointments even if a strong therapeutic relationship is established. As one may suspect, an assessment of barriers to care in the United States revealed such difficulties to be common. Specifically, among individual with serious mental illness who recognized a need for psychiatric treatment, 52% reported prohibitive logistical barriers, such as being unsure where to seek help, or not having the time to attend appointments (31). Accordingly, the ease with which patients can attend appointments should be assessed by clinicians early in a course of treatment. The current study did not examine the reasons patients dropped out of treatment. Future studies with this and other data sets should explore the reasons care was discontinued, to assess any barriers to care that may be present and provide strategies to further improve engagement.

Substance Abuse

At baseline assessment, eight patients in the engaged population reported some element of substance abuse. By six months, this number had increased to 12 (data not shown). Prior literature has shown that persistent substance abuse (but not baseline substance abuse) is associated with greater risk of disengagement from treatment (24), and lower rates of positive symptom remission (40). One explanation for this phenomenon is that patients who continue to abuse substances throughout their course of treatment may be less receptive to the advice of their healthcare providers, leading to poorer medication compliance and eventual discontinuation of clinical care. Alternatively, patients with persistent substance abuse may be self-medicating due to greater severity of illness or poor response to treatment. These patients may perceive formal medical care as being

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less beneficial, which has been shown to increase the likelihood of disengagement (64). In the current study, the rate of substance abuse increased in the patients that remained engaged in treatment. It is unclear why this pattern was observed. On one hand, all of the patients in the current study are undergoing a first-episode of illness. It is possible that while adjusting to their illness, some patients might be predisposed to substance abuse as a form of self-medication, as speculated above. Indeed, a similar increase in substance abuse was noted in the disengagement group (11 patients at baseline, up to 14 at six months) (data not shown). The similar pattern between the engagement and disengagement groups might suggest that risks of substance abuse may be related to the inherent nature and symptoms of psychotic disorders rather than the external factors examined in the current study. Alternatively, as with the other comparisons in the current study, there is a chance that a limited sample size may lead to underpowered analysis, obscuring patterns that may otherwise be present.

DUP

There was a trend for higher DUP in the disengagement group in the current dataset. Although this difference was not significant, the data was in the direction we would have predicted from prior literature (32). As with many variables associated with disengagement from care, authors have speculated on why this relationship may exist, but the precise dynamics are still unclear. As noted before, some investigators speculate that schizophrenia and related disorders may reflect a neurodegenerative process which would be exacerbated by prolonged DUP and produce greater treatment and engagement challenges at baseline (5). Others hold that DUP may be confounded by associations with

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other variables that independently predict delays in seeking treatment and poor engagement in services, such as poor social supports (38).

Baseline GAF

GAF is a subjective numeric scale used by mental health professionals to assess how well patients manage daily obligations and stressors, including social functioning, psychological coping, and vocational or educational performance (6). It is perhaps not surprising that prior studies have linked lower GAF scores to higher rates of disengagement, as difficulty or unwillingness in maintaining a relationship with mental health clinicians is precisely the type of poor functioning GAF is meant to measure. Similarly, by virtue of the metrics that it measures, GAF may correlate with illness severity. The alignment of GAF with both disengagement and illness severity may explain at least a portion of the correlation of disengagement with worse clinical outcomes. In agreement with previous studies on disengagement (28), our data trends suggest that lower GAF may be associated with higher disengagement rates in our patient population. As with other variables currently studied, a repeated study with a larger sample may yield a statistically significant relationship.

Limitations

Many of the studies on specialized psychiatric cohorts, including FEP patients receiving specialized early intervention, are limited by sample size. The current study is similarly limited by a sample of only 39 patients. In addition, much of the literature on service disengagement is plagued by the current disagreement on what constitutes disengagement, as illustrated earlier. Because our data was collected retrospectively,

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some measures that would have made some of our analyses more meaningful could not be collected. Although methods for determining disengagement vary, most definitions discussed so far are based on the presence (or not) of clinical contact. Meanwhile, some argue that measuring disengagement should be much more nuanced. Some authors have noted that service disengagement is a product of the complex interactions of a patient's attitudes towards his or her illness, clinicians, and treatment (73).

The Service Engagement Scale is a metric developed for objectively and thoroughly measuring engagement with services at community mental health centers. The scale measures engagement as a function of several metrics, including the ease with which patients can attend appointments, the perceived role of a patient in his or her care, a patient's perceived need or desire to seek help, and a patient's willingness to follow clinical advice and take medication. Evaluation of the scale has demonstrated that it is a highly reliable and valid measure of service engagement among patients with schizophrenia seeking treatment at a community mental health center (73).

It is imperative that future studies examining disengagement begin adopting more consistent, reliable, and thorough measures of engagement and disengagement, allowing for more meaningful meta-analyses and data interpretation. In addition, adopting a more quantitative, nuanced measure of engagement may allow for more sensitive and specific stratification of patients according to engagement levels, improving the allocation of resources and outreach measures to those patients who will benefit most (73), or even boosting statistical power of future disengagement studies employing relatively small sample sizes. The current study was limited by not employing such a measure of disengagement, and while we used a working definition that we believed would

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maximize our ability to identify patients who are truly disengaged from care, it's possible that the use of SES would have provided a superior measure. Additionally, our definition of disengagement allowed for a potential third group of patients: those who disengage from care but eventually return. It may be worthwhile in future studies with larger populations to either exclude these patients, or analyze them as a behaviorally distinct third group to uncover predictive variables with greater power.

Finally, because we were primarily interested in the earlier, more critical periods for establishing clinical contact, we limited follow-up to one year. While likelihood of disengagement decreases as length of consistent clinical contact increases (24), we may have uncovered higher rates of disengagement had we examined service use over a longer period.

Conclusions

Specialized early intervention in psychosis is a growing trend in psychiatry, driven by the potential for superior clinical outcomes and more efficient allocation of economic resources. Much of the data on the benefit of early intervention is drawn from patient populations in Australia, Europe, and Canada. Even with a lack of statistical power, it appears that the factors that correlate with service disengagement in these countries may be similarly predictive in the United States. Specifically, patients with lower baseline GAF, longer DUP, forensic history, and less family contact may be more likely to discontinue treatment for psychotic illness in the first year of initial outpatient treatment.

Early intervention clinics hoping to improve rates of service use do so via assertive treatment methods, including frequent contact with case workers, letter and telephone

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reminders of appointments, and vocational assistance. By identifying factors at baseline that associate with service disengagement, early intervention clinics will be able to channel limited resources to those patients who are at higher risk of discontinuing care. Future studies should seek to analyze the predictive power of these and other factors with larger patient samples in the United States. More research should also assess which interventions improve service use among at-risk patients, allowing for even more efficient allocation of limited resources in these specialized clinics. Finally, future studies should compare the clinical and functional outcomes of patients who disengage from care those versus who do not. Although it is reasonable to suggest that a lack of regular contact with healthcare providers may lead to worse outcomes in patients with psychosis, additional data on the outcomes associated with disengagement is warranted, particularly in the unique healthcare infrastructure of the United States. Such associations would be beneficial in assessing the benefit of early intervention and other strategies to improve clinical engagement.

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