

First Presentation With Psychotic Symptoms in a Population-Based Sample

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Objective: Increasing evidence supports the effectiveness of comprehensive early intervention at first onset of psychotic symptoms. Implementation of early intervention programs will require population-based data on overall incidence of psychotic symptoms and on care settings of first presentation.

Methods: In five large health care systems, electronic health records data were used to identify all first occurrences of psychosis diagnoses among persons ages 15–59 between January 1, 2007, and December 31, 2013 (N=37,843). For a random sample of these putative cases (N=1,337), review of full-text medical records confirmed clinician documentation of psychotic symptoms and excluded those with documented prior diagnosis of or treatment for psychosis. Initial incidence rates (based on putative cases) and confirmation rates (from record reviews) were used to estimate true incidence according to age and setting of initial presentation.

Results: Annual incidence estimates based on putative cases were 126 per 100,000 among those ages 15–29 and 107 per 100,000 among those ages 30–59. Rates of chart review confirmation ranged from 84% among those ages 15–29 diagnosed in emergency department or inpatient mental health settings to 19% among those ages 30–59 diagnosed in general medical outpatient settings. Estimated true incidence rates were 86 per 100,000 per year among those ages 15–29 and 46 per 100,000 among those ages 30–59.

Conclusions: When all care settings were included, incidence of first-onset psychotic symptoms was higher than previous estimates based on surveys or inpatient data. Early intervention programs must accommodate frequent presentation after age 30 and presentation in outpatient settings, including primary care.

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Psychotic disorders place a substantial burden on affected individuals, their families, and society. That burden includes both high rates of disability or lost productivity and substantial excess mortality resulting from suicide and higher rates of chronic medical illness (1–3). Growing evidence supports the benefits of early intervention after first onset of psychotic symptoms. Longitudinal studies of schizophrenia consistently find that delay in receipt of effective treatment (duration of untreated psychosis) predicts poorer long-term outcome (4,5). The RAISE (Recovery After Initial Schizophrenia Episode) trial demonstrated that comprehensive early intervention for young people with new onset of non-affective psychosis improves both symptomatic and functional outcomes (6–8). Broad and effective implementation of early intervention programs for first-episode psychosis will require population-based data on overall incidence and on care settings of initial presentation.

Previous population-based studies of new-onset psychotic symptoms have yielded estimates of annual incidence ranging from as low as 15 per 100,000 to as high as 100 per 100,000; however, methods varied significantly among those studies (9–17). Higher estimates of incidence have typically

been based on ascertainment via medical records (versus recall in epidemiologic surveys), ascertainment from all care settings (versus inpatient settings or specialized treatment programs), and inclusion of patients with any psychotic symptoms (versus schizophrenia or schizophrenia spectrum disorders).

No previous research has characterized the proportions of first presentation with psychotic symptoms across all treatment settings (inpatient settings, emergency departments, mental health or chemical dependency outpatient clinics, and primary care or general medical settings). Accurate data regarding care settings of initial presentation are essential to the design of effective outreach to patients, families, and treating clinicians.

We describe a population-based study of first presentation of psychotic symptoms among members of five large health care systems serving a combined population of approximately eight million members. Comprehensive insurance claims and electronic medical records data were used to identify all first-recorded diagnoses of any psychotic disorder in this defined population. Detailed record review estimated the proportion of these diagnoses that could be

confirmed as first presentation of psychotic symptoms. These findings were used to estimate the true incidence and settings of presentation across the population of health plan members ages 15–59.

METHODS

The study was conducted in five health care systems participating in the National Institute of Mental Health–funded Mental Health Research Network: the Group Health Cooperative and the Colorado, Northern California, Northwest, and Southern California regions of Kaiser Permanente. All five systems provide prepaid comprehensive care (including general medical and specialty mental health care) to defined populations of members. Insured members are enrolled through employer-sponsored commercial insurance, individually purchased insurance, capitated Medicare programs, capitated Medicaid programs, and state- or federally subsidized insurance for low-income residents. In each health care system, members are generally representative of service area populations in terms of age, sex, and race-ethnicity (18–20).

In each system, electronic medical records data (for services provided at health care system–operated facilities) and insurance claims data (for services provided by external providers and paid for by the health care system) are organized into a research virtual data warehouse (21). In this federated data structure, identifiable data remain at each health care system, but common data specifications and formats facilitate multisite research with pooled deidentified data.

Responsible institutional review boards for each system approved waivers of consent for this research use of health records data.

During the study period—January 1, 2007, to December 31, 2013—billing or encounter diagnoses were used to identify all first-occurring diagnoses of psychotic symptoms, including schizophrenia spectrum disorder (*ICD-9* codes 295.0–295.9), mood disorders with psychotic symptoms (296.04, 296.14, 296.24, 296.34, 296.44, 296.54, and 296.64), and other psychotic disorders (297.1, 297.3, 298.8, and 298.9) among health plan members ages 15 and older. Diagnoses of substance-induced psychosis were not included unless a psychosis diagnosis from the list above was also recorded.

This preliminary ascertainment of possible or putative cases included all outpatient and inpatient encounters (including general medical, emergency department, and specialty mental health encounters) by health system members, including encounters at external facilities. Patients with any of these diagnoses at any time prior to January 1, 2007, were considered preexisting diagnoses and were excluded. To ensure adequate capture of preexisting diagnoses or treatment, the sample was limited to those enrolled in the participating health plan for at least 12 months prior to first diagnosis. To exclude psychotic symptoms related to dementia, persons age 60 or older at the time of first psychosis diagnosis and those with any diagnosis of dementia or neurodegenerative disorder during or prior to the study period were excluded.

Patients in the remaining sample are hereafter referred to as “putative cases.” They were stratified by age at first presentation (15–29 or 30–59) and care setting of initial presentation (mental health inpatient stay or emergency department visit, specialty mental health outpatient visit, or general medical outpatient visit). In each stratum, the number of putative new cases per year was divided by the number of members continuously enrolled during the middle year of the study period (2010) to yield an initial estimate of annual incidence (putative new cases per 100,000 persons per year).

A random sample of approximately 1,500 putative cases (approximately 300 at each health care system) was selected for detailed medical record review to confirm the presence of psychotic symptoms and the absence of a prior diagnosis of or treatment for any psychotic disorder. Following the stratification scheme above, the total sample of putative cases selected for detailed record review included 325 patients ages 15–29 diagnosed in mental health inpatient or emergency department settings, 400 patients ages 15–29 diagnosed in mental health specialty outpatient settings, 225 patients ages 15–29 diagnosed in general medical settings, 200 patients ages 30–59 diagnosed in mental health inpatient or emergency department settings, 200 patients ages 30–59 diagnosed in outpatient mental health specialty settings, and 150 patients ages 30–59 diagnosed in general medical settings. The relative sizes of these chart review samples were based on the expected distribution of true or confirmed cases across strata.

At each health care system, two or more experienced medical record abstractors reviewed full-text electronic medical records by using a structured chart review protocol and data entry system. Abstractors examined all types of encounter notes (outpatient visits, emergency department visits, telephone contacts, hospital admission and discharge summaries, and online patient-provider messages) to confirm the presence of psychotic symptoms at time of initial recorded diagnosis and to exclude cases with documentation of diagnosis of or treatment for psychosis more than 60 days prior to the first recorded diagnosis.

All abstractors completed approximately four hours of training in use of the chart review protocol and application of criteria in the review coding instructions. Abstractors participated in biweekly conference calls during the chart review period (approximately five months) to discuss questionable ratings and to clarify coding instructions. The chart review protocol and coding manual are available on the Web site of the Mental Health Research Network (mhresearchnetwork.org).

Abstractors used data from all encounters between 60 days before and 60 days after the index diagnosis to make a categorical rating (definitely present, possibly present, or absent) for each of the characteristic symptoms of psychosis: hallucinations, delusions, disorganized speech, and disorganized or catatonic behavior. For each symptom, ratings followed descriptions in *DSM-IV* criterion A for diagnosis of schizophrenia (22). Any clear documentation of at least one

symptom was considered evidence of psychotic symptoms, regardless of duration or related functional impairment.

Abstractors used data from the same period to determine whether treating providers clearly attributed psychotic symptoms to a specific general medical condition (for example, hallucinations clearly attributed to delirium related to acute medical illness). Given high rates of substance use among those experiencing a first episode of psychosis (23–25), symptoms were not discounted or excluded because of co-occurring use or abuse of alcohol or drugs, even if treating providers attributed symptoms to substance use. However, symptoms were excluded if clearly attributed by treating providers to adverse effects of prescribed drugs used within prescribed limits (for example, symptoms attributed to corticosteroids prescribed to treat general medical illness).

Records of all encounters more than 60 days prior to first diagnosis were used to identify prior diagnosis of or treatment for psychotic symptoms. Abstractors made categorical ratings (definitely present, possibly present, or definitely absent) regarding chart documentation of prior diagnosis or treatment. Our aim was to identify the first clinical presentation with psychotic symptoms rather than the first onset of symptoms or first mental health contact for diagnosis other than psychosis. Consequently, the following were not considered indicators of prior diagnosis of or treatment for psychosis: patients' recall of prior psychotic symptoms without documentation of prior professional diagnosis or treatment, prior treatment with antipsychotic medication not specifically prescribed for psychotic symptoms, or prior diagnosis of mood disorder (including bipolar disorder) without documented psychotic symptoms.

For all ratings, abstractors submitted brief (up to 100 words) deidentified verbatim quotations from clinical notes to support the final rating. The principal investigator (GES) reviewed these quotations and adjudicated all symptoms classified as possibly present, all symptoms classified as explained by medical diagnosis, and all cases classified as having possible or definite prior diagnosis or treatment. Following this adjudication, final criteria for confirmation as a true case of first-episode psychosis included the following: chart notes clearly documented at least one *DSM-IV-TR* criterion A symptom of schizophrenia within 60 days before or after the first recorded diagnosis, criterion A symptoms that were not clearly attributed to a general medical disorder or to an adverse effect of prescribed medication, and chart notes that did not describe diagnosis of or treatment for psychotic symptoms more than 60 days prior to the first recorded diagnosis. All putative cases satisfying these criteria were considered confirmed cases.

At each health care system, 10% of records were rereviewed by a second reviewer blinded to initial review results. In this rereview sample, the kappa statistic for chance-corrected agreement between blinded pairs of abstractors for final classification was .88 (range of .78–.93 among five health care systems).

Descriptive analyses examined incidence rates based on putative cases and confirmation rates based on chart reviews

in each of the six strata described above. The 95% confidence intervals for rates were estimated without continuity correction (26). Initial estimated incidence rates (based on putative cases) were multiplied by confirmation rates (confirmed cases/putative cases) to yield final estimates of true incidence rates in each stratum.

RESULTS

Across all health care systems, electronic health records and insurance claims identified 109,687 individuals with first diagnoses of any psychotic disorder during the study period. Restriction to those ages 15–59 and enrolled in the participating health system for at least 12 months prior to the first diagnosis reduced this sample to 56,470. Exclusion of those with any diagnosis of dementia or neurodegenerative disease during the study period yielded a final sample of 37,843 putative cases over seven years. First recorded diagnosis was a schizophrenia spectrum disorder for 7% (N=2,649), mood disorder with psychosis for 19% (N=7,190), and other psychotic disorder for 74% (N=28,004).

Table 1 displays the distribution of cases across strata as well as estimated incidence rates based on putative cases (prior to chart review confirmation). The proportion of putative cases presenting in mental health inpatient or emergency department settings was 21% among those ages 15–29 and 23% among those aged 30–59. The proportion of putative cases presenting in primary care or other outpatient general medical settings was 33% among those aged 15–29 and 42% among those aged 30–59. Initial incidence rates and distribution of care settings of presentation were generally similar across the five health care systems (data available on request). Source of insurance coverage at first presentation was employer-sponsored for 85% (N=32,167), Medicare or Medicaid for 10% (N=3,784), and individually purchased insurance for 5% (N=1,892).

Among 1,500 putative cases selected for chart review, records were available for 1,337 (89%). For the remaining putative cases, participating systems did not receive records from external facilities. Results of reviews for putative cases with available records are shown in Table 2. The proportion of putative cases confirmed ranged from 84% among younger patients initially diagnosed in mental health inpatient or emergency department settings to 19% among older patients diagnosed in other outpatient settings. Failure to confirm criterion A symptoms for schizophrenia was the most common reason for nonconfirmation; however, among older patients initially diagnosed in primary care, the proportion excluded because of documented prior diagnosis or treatment was 25%. Stratum-specific and overall confirmation rates were generally similar across health care systems (details available on request).

Estimated true incidence rates (incidence rates based on putative cases multiplied by stratum-specific confirmation rates) are shown in Table 3. Estimated true incidence was approximately twice as high among patients ages 15–29 as

among those ages 30–59. Across both age groups, approximately one-third of true or confirmed cases presented were first diagnosed in mental health inpatient or emergency department settings, and approximately half were initially diagnosed in outpatient mental health specialty settings.

DISCUSSION

In this large, population-based sample, we estimated that the rate of first presentation of psychotic symptoms was approximately 86 per 100,000 person-years among those ages 15–29 and 46 per 100,000 person-years among those ages 30–59. Although incidence was lower in the older age group, the population at risk at ages 30–59 was twice as large as that at ages 15–29. Consequently, nearly half of first diagnoses occurred among those ages 30–59. Only about one-third of first presentations occurred in emergency departments or inpatient mental health facilities, with half occurring in outpatient mental health settings and the remainder in primary care or other outpatient settings.

We should acknowledge some important limitations of these data and methods. First, our sample was limited to people enrolled in large health care systems. Although the sample included those insured by Medicare, Medicaid, and other programs for low-income persons, it did not include those with no insurance coverage. Onset of psychotic symptoms could be higher among those without insurance or in populations with higher rates of Medicaid or Medicare insurance. We should distinguish, however, between insurance coverage at time of diagnosis and loss of insurance coverage as a result of chronic psychosis. Although ongoing psychosis might lead to loss of insurance coverage, that phenomenon would not be expected to affect coverage prior to first presentation—especially among young people insured via parents or guardians. Second, our methods did not capture those with new psychotic symptoms who never sought health care or those who sought care but were not recognized as having psychotic symptoms. Transient or less severe symptoms would more often be missed. We would, however, expect to identify missed diagnoses that later escalated to the point of requiring care. Both of these limitations would be expected to cause underestimation of true incidence rates in the entire population.

Third, records were not available for approximately 10% of putative cases. If confirmation rates were much lower in that group with missing records, our estimates of true incidence might be slightly inflated. Fourth, our methods identified first presentation with psychotic symptoms rather than first onset of symptoms. The incidence and settings of first clinical presentation, however, are most relevant for service planning. Fifth, low rates of mental health inpatient and emergency department presentations in our sample may

TABLE 1. Crude incidence of first psychosis diagnoses in five health care systems, by age group and care setting of presentation

Age group and setting	N of first-recorded diagnoses, 2007–2013	Population at risk in 2010	Annual incidence rate (per 100,000)	95% CI
Ages 15–29				
Inpatient or emergency department	2,837	1,487,032	27	25–30
Outpatient mental health specialty	5,876	1,487,032	56	53–60
Other outpatient	4,391	1,487,032	42	39–45
Total	13,104	1,487,032	126	120–132
Ages 30–59				
Inpatient or emergency department	5,806	3,298,367	25	23–27
Outpatient mental health specialty	8,511	3,298,367	37	35–39
Other outpatient	10,422	3,298,367	45	43–47
Total	23,409	3,298,367	107	104–111

reflect relatively easier access to outpatient mental health care in integrated health care systems. Presentation to emergency department or inpatient settings might be more common among the uninsured and those with other forms of health insurance.

The incidence rates we estimated are markedly higher than previously reported rates based on diagnoses from inpatient settings or specialized treatment centers (9,13). Given that a significant proportion of first presentations occurs in primary care or general medical settings (27,28), service planning should consider incidence rates across all settings.

Our case definition included all patients with new-onset symptoms and excluded only those for whom psychotic symptoms were clearly attributed to substance use or a general medical condition. Those with some co-occurring substance use disorders and those with prior diagnoses of a mood disorder were included. Some of these patients might later be determined to have substance-induced psychotic symptoms or primary diagnoses of a mood disorder rather than schizophrenia spectrum disorders. We believe that these broad inclusion criteria are directly relevant to planning and implementing early intervention programs. Mood symptoms and co-occurring substance use are common among patients with new-onset psychotic symptoms (23–25). Initial diagnostic classification among schizophrenia spectrum disorders, mood disorders, and substance use disorders may change significantly over time, with a general tendency for initial diagnoses of mood disorder (especially bipolar mood disorder) or substance-induced psychoses to shift toward schizophrenia spectrum diagnoses (24,25,29–31). If we hope to minimize duration of untreated psychosis (4,5), it may not be possible to delay early intervention pending definitive diagnosis.

It is not clear whether all persons identified by our methods would require or benefit from early intervention services. Ascertainment from all care settings and use of a broad case definition could identify a large number of

TABLE 2. Chart review confirmation of new-onset psychotic symptoms, by age group and care setting of presentation

Age group and setting	N reviewed	Symptoms not confirmed		Medically explained		Prior diagnosis or treatment		Confirmed new case		
		N	%	N	%	N	%	N	%	95% CI
Ages 15–29										
Inpatient or emergency department	288	32	11	1	<1	14	5	241	84	79–88
Outpatient mental health specialty	385	71	18	0	–	15	4	299	78	74–82
Other outpatient	195	93	48	0	–	10	5	92	47	40–54
Ages 30–59										
Inpatient or emergency department	119	30	25	2	2	9	8	78	66	57–74
Outpatient mental health specialty	177	64	36	0	–	12	7	101	57	50–64
Other outpatient	173	95	55	1	1	44	25	33	19	13–25

persons with transient or self-limited symptoms (32). Approximately one-fifth of our sample received mood disorder diagnoses at initial presentation, and patients with primary mood diagnoses were excluded from the RAISE early intervention trial. It is not clear, however, whether those likely to experience persistent nonaffective psychosis (compared with those with true mood disorders and those likely to recover spontaneously) can be accurately identified at first presentation. Additional epidemiologic research is necessary to identify useful predictors of need for more intensive treatment.

The large proportion of true cases in this sample presenting after age 30 contrasts with conventional wisdom that first onset of psychosis typically occurs at younger ages (9). Most early intervention programs have focused on adolescents and young adults (6). Our finding that almost half of true new cases presented after age 30 may reflect our study methods, especially the inclusion of presentations in general

population (34), our incidence estimates would predict approximately 56,000 new first presentations of psychotic symptoms among those ages 15–29 and an additional 58,000 among those ages 30–59. For perspective, this is similar to the number of new cases of colon cancer diagnosed annually in the United States—approximately 130,000 (35). Second, outreach or engagement efforts certainly cannot be limited to mental health inpatient facilities. Instead, outreach must extend to half of first presentations occurring in outpatient mental health settings and one-fifth occurring in other outpatient general medical settings, including primary care. Third, early intervention programs should consider the needs and preferences of middle-aged patients who account for up to half of persons with new-onset psychotic symptoms.

Finally, additional population-based research is necessary to clarify the specific clinical populations likely to benefit from early intervention services. Identifying all first presentations with any symptoms of psychosis almost certainly identifies some patients likely to recover spontaneously, including patients with substance-induced psychotic symptoms. But deferring comprehensive intervention until prognosis is clear could have the undesired effect of prolonging duration of untreated psychosis. Consequently, there is a critical need to identify accurate prognostic indicators present at first clinical presentation.

TABLE 3. Adjusted incidence of first presentation of psychotic symptoms, by age group and care setting of presentation

Age group and setting	Incidence of putative cases per 100,000	Confirmed by record review	Estimated true incidence rate (per 100,000)	Estimated proportion of first presentations
Ages 15–29				
Inpatient or emergency department	27	84	23	26
Outpatient mental health specialty	56	78	44	51
Other outpatient	42	47	20	23
Total			86	100
Ages 30–59				
Inpatient or emergency department	25	66	17	36
Outpatient mental health specialty	37	57	21	46
Other outpatient	45	19	9	19
Total			46	100

CONCLUSIONS

When data from all care settings were included, incidence of psychotic symptoms was higher than previous estimates based on surveys or inpatient data. Planning for early intervention programs must accommodate frequent presentation after age 30 and presentation in outpatient settings, including primary care.

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