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INCIDENCE AND PRESENTATION OF FIRST-EPIISODE PSYCHOSIS IN A POPULATION-BASED SAMPLE

Gregory E Simon, MD, MPH¹, Karen J Coleman, PhD², Bobbi Jo Yarborough, PhD³, Belinda Operskalski, MPH¹, Christine Stewart, PhD¹, Enid Hunkeler, MA⁴, Frances L Lynch, PhD, MSPH³, David Carrell, PhD¹, and Arne Beck, PhD⁵

¹Group Health Research Institute, Seattle, WA

²Kaiser Permanente Southern California Department of Research and Evaluation, Pasadena, CA

³Kaiser Permanente Center for Health Research, Portland, OR

⁴Kaiser Permanente Division of Research, Oakland, CA

⁵Kaiser Permanente Colorado Institute for Health Research, Denver, CO

Abstract

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 regarding overall incidence of psychotic symptoms and care settings of first presentation.

Methods—In five large healthcare systems, electronic health records data were used to identify all first occurrences of psychosis diagnoses among people aged 15 through 59 between 1/1/2007 and 12/31/2013. For a random sample of these putative cases, 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—Incidence estimates based on putative cases were 126 per 100,000 per year among those aged 15 to 29 and 107 per 100,000 among those aged 30–59. Rates of chart review confirmation ranged from 84% among those aged 15–29 diagnosed in emergency department or inpatient settings to 19% among those aged 30 to 59 diagnosed in general medical outpatient visits. Estimated true incidence rates were 86 per 100,000 per year among those aged 15 to 29 and 46 per 100,000 in those aged 30 to 59.

Conclusions—Including all care settings, total incidence of first-episode psychosis is higher than previous estimates based on surveys or inpatient data. Early intervention programs must accommodate frequent presentation after age 30 and presentation in outpatient, including primary care, settings.

Corresponding author address: Gregory E Simon, Group Health Research Institute, 1730 Minor Ave., Seattle, WA 98101. Phone: 206-287-2900. simon.g@ghc.org.

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Psychotic disorders place a substantial burden on affected individuals, their families, and broader society. That burden includes both high rates of disability or lost productivity and substantial excess mortality due both to suicide and higher rates of chronic medical illness 1–3.

Growing evidence supports the benefits of early intervention following first onset of psychotic symptoms. Longitudinal studies consistently find that delay in receipt of effective treatment (i.e. duration of untreated psychosis) predicts poorer long-term outcome 4, 5. The RAISE (Recovery After Initial Schizophrenia Episode) trial demonstrated that comprehensive early intervention 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 regarding overall incidence and common care settings of first presentation.

Previous population-based studies of first-episode psychosis have yielded estimates of annual incidence ranging from as low as 15 per 100,000 to as high as 100 per 100,000, but methods have 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 cases with any psychotic symptoms (versus schizophrenia or schizophrenia-spectrum disorders).

No previous research has characterized the proportions of first psychotic episodes presenting 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 here a population-based study of first-onset psychotic symptoms among members of five large healthcare systems serving a combined population of approximately 8 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 and to estimate the proportion of these recorded diagnoses that could be confirmed as valid by detailed record review. These findings were used to estimate the true incidence and settings of presentation across the population of health plan members aged 15 to 59.

METHODS

The study was conducted in five healthcare systems participating in the National Institute of Mental Health-funded Mental Health Research Network: Group Health Cooperative and the Colorado, Northern California, Northwest, and Southern California regions of Kaiser Permanente. All five healthcare systems provide pre-paid 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 healthcare system, members are generally representative of service area populations in terms of age, sex, and race/ethnicity^{18–20}.

In each healthcare system, electronic medical records data (for services provided at healthcare system-operated facilities) and insurance claims data (for services provided by external providers and paid for by the healthcare system) are organized into a research virtual data warehouse²¹. In this federated data structure, identifiable data remain at each healthcare system, but common data specifications and formats facilitate multi-site research using pooled de-identified data.

Responsible Institutional Review Boards for each healthcare system approved waivers of consent for this research use of health records data.

During the study period of 1/1/2007 to 12/31/2013, billing or encounter diagnoses from all outpatient and inpatient encounters (including general medical, emergency department, and specialty mental health encounters) in each health system were used to identify all first-occurring diagnoses of any psychotic disorder (including schizophrenia-spectrum disorder, mood disorders with psychotic symptoms, and other psychotic disorders) among health plan members aged 15 or older. Eligible ICD9 codes for new psychosis diagnosis included 295.0 through 295.9, 296.04, 296.14, 296.24, 296.34, 296.44, 296.54, 296.64, 297.1, 297.3, 298.8, or 298.9. Those with any of these diagnoses at any time prior to 1/1/2007 were considered pre-existing diagnoses and were excluded. To ensure adequate capture of pre-existing 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, those aged 60 or older at 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. These putative cases were stratified according to age at diagnosis (15–29 or 30–59) and care setting of initial diagnosis (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 1500 putative cases (approximately 300 at each healthcare system) was selected for detailed medical record review to confirm presence of psychotic symptoms and absence of 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 aged 15–29 diagnosed in mental health inpatient or emergency department settings
- 400 patients aged 15–29 diagnosed in mental health specialty outpatient settings
- 225 patients aged 15–29 diagnosed in general medical settings

- 200 patients aged 30–59 diagnosed in mental health inpatient or emergency department settings
- 200 patients aged 30–59 diagnoses in mental health specialty outpatient settings
- 150 patients aged 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 healthcare system, two or more experienced medical record abstractors reviewed full-text electronic medical records 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 or treatment for psychosis more than 60 days prior to the first recorded diagnosis.

All abstractors completed approximately 4 hours of training in use of the chart review protocol and application of criteria in the review coding instructions. Abstractors participated in bi-weekly conference calls during the chart review period (approximately 5 months) to discuss questionable ratings and clarify coding instructions. The chart review protocol and coding manual are available at 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, absent) for each of the characteristic symptoms of psychosis as defined by DSM-IV Criterion A for diagnosis of schizophrenia: hallucinations, delusions, disorganized speech, and disorganized or catatonic behavior²². Any clear documentation of at least one of these characteristic symptoms was considered evidence of psychosis, without respect to duration or related functional impairment.

Abstractors used data from the same period to determine whether treating providers considered symptoms of psychosis to be clearly attributable to a specific general medical condition (e.g. hallucinations clearly attributed to delirium related to acute medical illness). Given high rates of substance use among those experiencing first episode of psychosis^{23–25}, symptoms were not discounted or excluded due to 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 (e.g. 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 psychosis. Abstractors made categorical ratings (definitely present, possibly present, 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:

- Notation of prior psychotic symptoms without documentation of prior professional diagnosis or treatment
- Prior treatment with antipsychotic medication not specifically prescribed for psychotic symptoms
- Prior diagnosis of mood disorder (including bipolar disorder) without documented psychotic symptoms

For all ratings, abstractors submitted brief (up to 100 words) de-identified verbatim quotations from clinical notes to support the final rating. The principal investigator (GS) 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:

- Chart notes clearly documented at least one DSM-IV TR Criterion A symptom of schizophrenia within 60 days before or after first recorded diagnosis.
- Criterion A symptoms were not clearly attributed to general medical disorder or adverse effect of prescribed medication
- Chart notes 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 healthcare system, 10% of records were re-reviewed by a second reviewer blinded to initial review results. In this re-review sample, kappa statistic for chance-corrected agreement between blinded pairs of abstractors for final classification was 0.88 (range among 5 healthcare systems was 0.78 to 0.93).

Descriptive analyses examined incidence rates based on putative cases and confirmation rates based on chart reviews in each of the six strata described above. 95% confidence intervals for rates were estimated without continuity correction²⁶. 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 healthcare 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 aged 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. 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 inpatient or emergency department settings was 21% among those aged 15–29 and 23% among those aged 30–59. The proportion of putative cases presenting in primary care or other 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 healthcare systems (data available on request).

Among 1500 putative cases selected for chart review, records were available for 1337 (89%). For the remaining putative cases, participating healthcare 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 settings to 19% among older patients diagnosed in primary care. Failure to confirm Criterion A symptoms for schizophrenia was the most common reason for non-confirmation, but the proportion excluded because of documented prior diagnosis or treatment was 25% among older patients initially diagnosed in primary care. Stratum-specific and overall confirmation rates were generally similar across healthcare 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 those aged 15–29 as among those aged 30–59. Across both age groups, approximately one third of true or confirmed cases presented were first diagnosed in mental health inpatient settings and approximately half were initially diagnosed in mental health specialty outpatient settings.

DISCUSSION

In this large, population-based sample, we estimate that the incidence of first-episode psychotic symptoms is approximately 86 per 100,000 person-years among those aged 15 to 29 and 46 per 100,000 person-years among those aged 30 to 59. While incidence is lower in the older age group, the population at risk aged 30 to 59 was twice as large as that aged 15 to 29. Consequently, nearly half of first diagnoses occurred among those aged 30 to 59. Only approximately one-third of first-episode psychosis cases were initially diagnosed in acute-care settings (emergency departments or inpatient facilities).

We should acknowledge some important limitations of these data and methods. First, our sample is limited to people enrolled in large healthcare systems. While the sample does include those insured by Medicare, Medicaid, and other low-income programs, it does not include those with no insurance coverage. Incidence of psychosis could be higher among those without insurance. We should distinguish, however, between insurance coverage at time of diagnosis and loss of insurance coverage due to chronic psychosis. While ongoing psychosis might lead to loss of insurance coverage, that phenomenon would not be expected to affect coverage prior to diagnosis – especially among young people insured via parents or guardians. Second, our methods would not capture people with new psychotic symptoms who never seek health care or those who seek care but are not recognized as having psychotic symptoms. Transient or less severe symptoms would more often be missed. We

would, however, expect to identify those “missed” diagnoses that later escalate to the point of requiring care. Both of these two limitations would be expected to cause under-estimation 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, low rates of inpatient and emergency department presentations in our sample may reflect relatively easier access to outpatient mental health care in integrated healthcare 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 estimate are markedly higher than those previously reported based on diagnoses from inpatient settings or specialized treatment centers^{9, 13}. Ascertainment from all care settings serving a defined population seems necessary given that a significant proportion of first psychotic episodes present in primary care or general medical settings^{27, 28}.

Our case definition included all patients with new onset symptoms, including those with co-occurring substance use disorders and those with prior diagnoses of mood disorder. Some of these patients might later be determined to have substance-induced psychotic symptoms or primary diagnoses of mood disorder rather than schizophrenia-spectrum disorders. Our findings, however, 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}. Delivery of early intervention services should not be delayed pending definitive diagnosis^{4, 5}. Attempts to exclude patients with mood disorders or substance-induced psychotic symptoms from early intervention programs may be problematic. 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 or substance-induced psychoses to shift toward schizophrenia-spectrum diagnoses^{24, 25, 29, 30}.

We should acknowledge that ascertainment from all care settings and use of a broad case definition could identify a large number of people with transient or self-limited symptoms³¹. Additional epidemiologic research is necessary to examine whether specific clinical characteristics or patterns of presentation indicate a favorable enough prognosis that comprehensive early intervention programs are not necessary.

The high proportion of true cases in this sample presenting after age 30 contrasts with conventional wisdom that first onset of psychosis typically occurs at younger ages⁹. Most early intervention programs have focused on adolescents and young adults⁶. Our finding that almost half of true new cases present after age 30 may reflect our study methods, especially the inclusion of cases with established diagnoses of mood disorder followed by first onset of psychotic symptoms. Nevertheless, other population-based studies have also found that up to half of first psychotic episodes occur after age 30^{10, 25}.

Our findings have several important implications for the design of early intervention programs. First, capacity of these programs must be substantial in order to accommodate all

US residents who experience first onset of psychotic symptoms. Applied to the entire US population³², our incidence estimates would predict approximately 56,000 new cases per year among those aged 15–29 and an additional 58,000 among those aged 30–59. For perspective, this compares to approximately 130,000 new cases of colon cancer diagnosed annually in the US³³. Second, outreach efforts certainly cannot be limited to mental health inpatient facilities. Instead, outreach must extend to half of first psychosis episodes presenting in outpatient mental health settings and one fifth presenting in other general medical settings, including primary care. Finally, early intervention programs must consider the needs and preferences of middle-aged patients who account for up to half of people with new-onset psychotic symptoms.

CONCLUSIONS

When including data from all care settings, total incidence of first-episode psychosis is higher than previous estimates based on surveys or inpatient data. Early intervention programs must accommodate frequent presentation after age 30 and presentation in outpatient, including primary care, settings.

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Table 1

Crude incidence of first psychosis diagnoses in five healthcare systems by age group and care setting of presentation.

	# of First Recorded Diagnoses (2007 thru 2013)	Population at Risk (in 2010)	Annual Incidence Rate (per 100,000)	95% Conf. Interval
Age 15 to 29				
Inpatient or ER	2837	1,487,032	27	25 – 30
Outpatient MH Specialty	5876	1,487,032	56	53 – 60
Other Outpatient	4391	1,487,032	42	39 – 45
Total Age 15 to 29	13,104	1,487,032	126	120–132
Age 30 to 59				
Inpatient or ER	5806	3,298,367	25	23 – 27
Outpatient MH Specialty	8511	3,298,367	37	35 – 39
Other Outpatient	10,422	3,298,367	45	43 – 47
Total Age 30 to 59	23,409	3,298,367	107	104 – 111

Table 2
Chart review confirmation of new onset psychotic symptoms by age group and care setting of presentation

	Number Reviewed	Symptoms Not Confirmed	Prior Diagnosis or Treatment	Confirmed New Case	95% Conf. Interval
Age 15 to 29					
Inpatient or ER	288	33 (11%)	14 (5%)	241 (84%)	79%–88%
Outpatient MH Specialty	385	71 (18%)	15 (4%)	299 (78%)	74%–82%
Other Outpatient	195	93 (48%)	10 (5%)	92 (47%)	40%–54%
Age 30 to 59					
Inpatient or ER	119	32 (27%)	9 (8%)	78 (66%)	57%–74%
Outpatient MH Specialty	177	64 (36%)	12 (7%)	101 (57%)	50%–64%
Other Outpatient	173	96 (55%)	44 (25%)	33 (19%)	13%–25%

Table 3

Adjusted incidence of first presentation of psychotic symptoms by age group and care setting of presentation

	Incidence of Putative Cases (per 100,000)	Confirmed by Record Review	Estimated True Incidence Rate (per 100,000)	Estimated Proportion of First Presentations
Age 15 to 29				
Inpatient or ER	27	84%	23	26%
Outpatient MH Specialty	56	78%	44	51%
Other Outpatient	42	47%	20	23%
Total Age 15 to 29			86	100%
Age 30 to 59				
Inpatient or ER	25	66%	17	36%
Outpatient MH Specialty	37	57%	21	46%
Other Outpatient	45	19%	9	19%
Total Age 30 to 59			46	100%

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