

ORIGINAL ARTICLES

Medical Comorbidity in Women and Men with Schizophrenia

A Population-Based Controlled Study

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BACKGROUND: Persons with persistent mental illness are at risk for failure to receive medical services. In order to deliver appropriate preventive and primary care for this population, it is important to determine which chronic medical conditions are most common.

OBJECTIVE: We examined chronic medical comorbidity in persons with schizophrenia using validated methodologies.

DESIGN: Retrospective analysis of longitudinal administrative claims data from Wellmark Blue Cross/Blue Shield of Iowa.

PARTICIPANTS: Subjects with schizophrenia or schizoaffective disorder ($N=1,074$), and controls ($N=726,262$) who filed at least 1 claim for medical services, 1996 to 2001.

MEASUREMENTS: Case subjects had schizophrenia as the most clinically predominant psychotic disorder, based on psychiatric hospitalization, psychiatrist diagnoses, and outpatient care. Controls had no claims for any psychiatric comorbidity. Using a modified version of the Elixhauser Comorbidity Index, inpatient and outpatient claims were used to determine the prevalence of 46 common medical conditions. Odds ratios (ORs) were adjusted for age, gender, residence, and non-mental health care utilization using logistic regression.

RESULTS: Subjects with schizophrenia were significantly more likely to have 1 or more chronic conditions compared with controls. Adjusted OR (95% confidence interval [CI]) were 2.62 (2.09 to 3.28) for hypothyroidism, 1.88 (1.51 to 2.32) for chronic obstructive pulmonary disease, 2.11 (1.36 to 3.28) for diabetes with complications, 7.54 (3.55 to 15.99) for hepatitis C, 4.21 (3.25 to 5.44) for fluid/electrolyte disorders, and 2.77 (2.23 to 3.44) for nicotine abuse/dependence.

CONCLUSIONS: Schizophrenia is associated with substantial chronic medical burden. Familiarity with conditions affecting persons with schizophrenia may assist programs aimed at providing medical care for the mentally ill.

KEY WORDS: chronic medical condition; schizophrenia; schizoaffective disorder.

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The co-occurrence of medical illness among persons with schizophrenia has been addressed in epidemiological prevalence studies, studies reporting early or increased mor-

tality, studies reporting an increased risk for HIV, studies outlining barriers to health care delivery, and most recently with regard to the association with the development of diabetes mellitus.¹⁻¹¹ Persons with schizophrenia may have fewer medical visits, fewer documented medical problems, and be less likely to receive a detailed physical examination.⁷ Dixon et al.¹² reported that subjects in the Schizophrenia Patient Outcomes Research Team (PORT) most commonly self-reported problems with eyesight, teeth, and high blood pressure. Among persons in that sample, current medical problems independently contributed to more severe psychosis and depression.¹² The 12-month prevalence of 8 medical disorders among Medicaid beneficiaries with psychotic disorders and substance abuse disorders was significantly elevated compared with beneficiaries without these psychiatric disorders. Most recently, Sokal et al.¹¹ reported that persons with schizophrenia had greater odds of respiratory illnesses, even when controlling for smoking. Medical illnesses among persons with schizophrenia also tend to be more severe.^{11,12}

These studies support earlier literature that a significant medical burden exists for persons with schizophrenia. The results are compelling, but the significance of the findings may be restricted because of limitations in study design including (1) small nonrepresentative samples, (2) patient self-report of medical conditions, (3) cross-sectional chart reviews, and (4) poorly defined criteria for chronic medical conditions. Therefore, we conducted a population-based study, spanning multiple years, and using criteria validated for the detection of chronic medical conditions for administrative claims data. Research of this type lays the framework for refining strategies for the prevention, screening, and treatment of seriously mentally ill patients in primary care settings.

METHODS

Data Source

We conducted a population-based controlled study using a 100% sample of Wellmark Blue Cross/Blue Shield of Iowa administrative claims data from January 1, 1996 to December 31, 2001. These data are composed of inpatient and outpatient claims submitted by all health care providers and includes International Classification of Diseases (ICD-9)

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diagnostic codes and Current Procedural Terminology Codes (CPT).

Population

The eligible study population included all subjects ages 18 to 64 who filed at least 1 claim for medical service during the study period, 1996 to 2001. All subjects were residents of Iowa and were classified as residing in a rural or urban county based on the metropolitan statistical area definition.¹³ The basic medical insurance coverage was similar among subjects, with only a small proportion (<10%) enrolled in a managed care plan.

The case population was composed of subjects diagnosed with schizophrenia (ICD-9 295.0 to 295.3, 295.5 to 295.6, 295.8 to 295.9) or schizoaffective disorder (ICD-9 295.7) in the inpatient or outpatient setting during 1996 to 2001. These diagnoses will be described as schizophrenia throughout the remainder of the text. Subjects were included provided that schizophrenia was the most clinically predominant disorder, regardless of whether other mental disorders (e.g., depression) were also present. The most clinically predominant disorder was determined by the number of claims for schizophrenia based on the following criteria: (1) number of hospitalizations for the given condition, and then (2) number of psychiatrist visits for the condition, then (3) number of any other outpatient claims for the condition. Subjects with claims for both schizophrenia and bipolar disorder were included if schizophrenia was more predominant than bipolar disorder.

The control population consisted of men and women who had no mental disorder claims during 1996 to 2001.

Comorbidity

The Elixhauser Comorbidity Index was used to assess medical comorbidity using inpatient and outpatient claims data.¹⁴ The Elixhauser index was first used to describe chronic medical conditions most commonly occurring in hospitalized persons. As modified and validated by Klabunde, comorbid outpatient conditions were also counted if the condition occurred either in the inpatient setting or in 2 or more outpatient claims coded in a period of no fewer than 30 days during 1996 to 2001.¹⁵ This time period was used to ensure that acute or miscoded outpatient comorbidities were not included in the total comorbidity count. Twenty-six comorbidities were selected from the Elixhauser Comorbidity index based on prevalence in the general population and prior research on medical co-morbidity in schizophrenia. Using the same methodology, we also examined twelve additional medical co-morbidities prevalent in the adult population (stroke, ischemic heart disease, hyperlipidemia, pancreatitis, hepatitis C, other viral hepatitis, backache, arthritis, asthma, accidents/injuries, benign prostatic hyperplasia, and headache), and 5 specific comorbidities unique to women's health care (cystitis, mammary dysplasia, endometriosis, inflammatory disease of the ovary, and disorders of menstruation). Finally, we included nicotine, polysubstance, and alcohol abuse/dependence conditions as comorbidities, given the likelihood of these conditions to complicate the course of underlying medical illness.

Statistical Analyses

Demographic and clinical characteristics were analyzed using χ^2 tests for categorical variables and *t* tests for continuous variables. Demographic variables included gender, age, urban or rural residence, number of months eligible for medical care as calculated from the first medical claim date to the last medical claim date, and number of nonmental health care visits. Membership files with actual dates of enrollment in Blue Cross/Blue Shield were unavailable. Comorbidity was further categorized as the presence of 0, 1, 2, 3+ total conditions described above.

Logistic regression was used to calculate odds ratios (ORs) and 95% confidence intervals (CI) for each of the 46 comorbidities examined. Odd ratios were adjusted for gender, age, residence (rural vs urban), and nonmental health care utilization. Odd ratio for comorbidities specific to 1 gender (e.g., benign prostatic hyperplasia, cystitis) were not adjusted for gender. We adjusted for utilization by controlling for the number of known nonmental health encounters in order to take into account potential differences in diagnostic patterns attributed to contact with a provider during the time of observation from the first to the last known claim. All statistical tests were 2 sided, with an α of 0.05. All analyses were performed with SAS version 8.2.¹⁶ Only adjusted findings are reported.

The Institutional Review Boards at Indiana University and the University of Iowa approved this study.

RESULTS

Overall, 569 (53%) women and 505 (47%) men were identified with schizophrenia. The mean age of the cases was 40.2 years (SD, 11.9 years). Persons with schizophrenia had significantly more months of follow-up, more overall health care visits, and were only slightly more likely to live in urban settings than controls, persons without schizophrenia (Table 1). Over 33% of cases had 3 or more medical comorbidities, nearly 3 times more than controls (33.2% vs 12.1%, respectively).

In the adjusted analyses, persons with schizophrenia had increased ORs for conditions spanning nearly every organ system, and markedly higher ORs for substance abuse and dependence including alcohol 12.57 (95% CI 10.16 to 15.55), nicotine 2.77 (2.33 to 3.44), and illicit substances 35.42 (28.35 to 44.27) (Table 2). Our findings confirm prior reports that

Table 1. Demographic Characteristics of Women and Men with Schizophrenia Compared with Controls

	Cases (N=1,074)	Controls (N=726,262)
Age, mean (SD)*	40.2 (11.9)	37.7 (12.8)
# Nonmental health care visits, mean (SD)*	14.5 (19.2)	6.4 (9.8)
Length of follow-up (months), mean (SD)*	39.8 (24.6)	26.8 (23.8)
Rural residence, n (%)	592 (55.1)	402,674 (55.4)
Women, n (%)	569 (53.0)	381,116 (52.5)
Number of comorbidities†		
0	311 (29.0)	397,257 (54.7)
1	211 (19.7)	155,720 (21.4)
2	196 (18.3)	85,460 (11.8)
3+	356 (33.2)	8,782 (12.1)

**P* < .0001, based on the *t*-test.

†*P* < .0001, based on the χ^2 statistic.

Table 2. Prevalence and Adjusted Odds Ratios for Medical Conditions in Women and Men with Schizophrenia Compared with Controls

	n (%)		OR (95% CI) [†]
	Cases (N=1,074)	Controls* (N=726,262)	
Cardiovascular			
Hypertension	177 (16.5)	66,575 (9.2)	0.99 (0.81 to 1.20)
Ischemic heart disease	25 (2.3)	13,567 (1.9)	0.86 (0.56 to 1.31)
Hyperlipidemia	135 (12.6)	55,495 (7.6)	0.86 (0.69 to 1.06)
Congestive heart failure	16 (1.5)	3,117 (0.4)	2.38 (1.42 to 4.01)
Cardiac arrhythmias	39 (3.6)	8,740 (1.2)	1.92 (1.37 to 2.70)
Peripheral vascular disorder	10 (0.9)	2,519 (0.4)	1.92 (1.01 to 3.65)
Stroke	14 (1.3)	3,187 (0.4)	2.11 (1.22 to 3.65)
Neurological			
Paralysis	11 (1.0)	812 (0.1)	6.66 (3.64 to 12.18)
Other neurological disorders	82 (7.6)	4,674 (0.6)	9.67 (7.66 to 12.21)
Headache	129 (12.0)	41,234 (5.7)	1.37 (1.12 to 1.69)
Pulmonary			
COPD	116 (10.8)	25,894 (3.6)	1.88 (1.51 to 2.32)
Asthma	54 (5.0)	12,542 (1.7)	1.80 (1.34 to 2.42)
Endocrine			
Diabetes w/out complications	61 (5.7)	17,205 (2.4)	1.62 (1.23 to 2.14)
Diabetes w/complications	23 (2.1)	4,401 (0.6)	2.11 (1.36 to 3.28)
Hypothyroidism	102 (9.5)	18,168 (2.5)	2.62 (2.09 to 3.28)
Obesity	49 (4.6)	7,828 (1.1)	2.73 (2.01 to 3.71)
Weight loss	3 (0.3)	345 (0.1)	3.96 (1.26 to 12.45)
Renal			
Renal failure	10 (0.9)	1,514 (0.2)	2.94 (1.55 to 5.57)
Fluid and electrolyte disorders	74 (6.9)	7,632 (1.1)	4.21 (3.25 to 5.44)
Gastrointestinal			
Liver disease	12 (1.1)	1,281 (0.2)	4.42 (2.47 to 7.89)
Pancreatitis	9 (0.8)	1,058 (0.2)	4.00 (2.06 to 7.79)
Viral/infectious			
Hepatitis C	7 (0.7)	492 (0.1)	7.54 (3.55 to 15.99)
Hematology/oncology			
Deficiency anemias	48 (4.5)	9,164 (1.3)	1.90 (1.38 to 2.62)
Musculoskeletal			
Arthritis	54 (5.0)	15,939 (2.2)	1.40 (1.04 to 1.89)
Other			
Accidents and injuries	358 (33.3)	145,431 (20.0)	1.19 (1.03 to 1.37)
Genital			
Cystitis	6 (1.1)	1,094 (0.3)	2.30 (1.01 to 5.22)
Inflammatory disease of ovary	33 (5.8)	9,676 (2.5)	1.52 (1.05 to 2.22)
Disorders of menstruation	61 (10.7)	19,330 (5.1)	1.50 (1.12 to 2.00)
Drug abuse/dependence			
Alcohol	102 (9.5)	6,176 (0.9)	12.57 (10.16 to 15.55)
Nicotine	94 (8.8)	19,008 (2.6)	2.77 (2.23 to 3.44)
Illicit	95 (8.9)	2,011 (0.3)	35.42 (28.35 to 44.27)

*Other comorbidities with nonsignificant odds ratios not listed in Table 2 include valvular disease, pulmonary circulation disorders, peptic ulcer disease, AIDS, lymphoma, metastatic cancer, nonmetastatic cancer, rheumatoid arthritis, coagulopathy, blood loss anemia, other hepatitis, backache, benign prostatic hyperplasia, mammary dysplasia, endometriosis.

[†]Adjusted for age, gender (except gender-specific comorbidities), residence (rural/urban), and number of nonmental health care visits.

conditions related to tobacco use are more likely, including peripheral vascular disease (OR 1.92, CI 1.01 to 3.65), stroke (OR 2.11, 95% CI 1.22 to 3.65), chronic obstructive pulmonary disease (OR 1.88, 95% CI 1.51 to 2.32), and asthma (OR 1.80, 95% CI 1.12 to 1.69). Although a higher percentage of persons with schizophrenia had ischemic heart disease (2.3% vs 1.9%, respectively) and hypertension (16.5% vs 9.2%, respectively) than controls, the adjusted ORs for these conditions were not significant.

Several conditions not previously reported were found to occur at increased odds in this population. For instance, not only do persons with schizophrenia have increased odds for diabetes, they also have increased odds of complications because of diabetes compared with controls (OR 2.11, 95% CI 1.36 to 3.28). In addition, persons with schizophrenia have increased odds of hypothyroidism (OR 2.62%, 95% CI 2.09 to 3.28), liver disease (OR 4.42%, 95% CI 2.47 to 7.89), and

pancreatitis (OR 4.00%, 95% CI 2.06 to 7.79) as well as markedly increased odds of hepatitis C (OR 7.54%, 95% CI 3.55 to 15.99). However, these findings must be taken in the context of the elevated odds of polysubstance and alcohol abuse. Finally, renal failure (OR 2.94%, 95% CI 1.55 to 5.57) and fluid and electrolyte disorders (OR 4.21%, 95% CI 3.25 to 5.44) also occurred at increased odds. Notable conditions not occurring at increased odds in persons with schizophrenia included hypertension, ischemic heart disease, hyperlipidemia, other hepatitis, and malignancies.

DISCUSSION

Our results are consistent with those from prior studies: persons with schizophrenia have significant increased medical comorbidity for conditions related to modifiable behaviors (e.g., chronic obstructive pulmonary disease), as well as con-

ditions that may influence the course of mental symptoms (e.g., hypothyroidism). We add to prior studies by identifying increased risk for conditions not previously reported, such as deficiency anemias, hypothyroidism, neurological disorders, and fluid and electrolyte conditions. It is possible that such conditions were diagnosed in this insured population because subjects had greater financial access to physician and diagnostic services than the uninsured or underinsured who have previously been studied. It is also noteworthy that the ORs for ischemic heart disease and hypertension were not elevated, given the increased odds for nicotine abuse. We speculate that this is likely because of underdiagnosis of these conditions in this population.

Finally, compared with controls without mental illness, persons with schizophrenia were more likely to have a greater number of conditions spanning several disease categories including cardiovascular, pulmonary, neurological, and endocrine diseases. One-third of this young population (average age 40 years) had 3 or more chronic comorbidities, and only 29% of persons with schizophrenia compared with 54% of controls had *no* claims for comorbidities.

The impact of medical comorbidity in schizophrenia is significant because medical comorbidity affects quality of life and delivery of psychiatric and medical services. Dixon et al. reported that not only did persons with clinically diagnosed schizophrenia sampled from a variety of community and treatment settings have at least 1 medical problem, these persons also had worse perceived physical health status, more psychosis, more depression, and a greater likelihood of suicide attempt. Medical comorbidity can either cause or exacerbate the psychotic illness.¹⁷ Because medical conditions may go unrecognized in this population, it is possible that unrecognized medical conditions contribute to prolonged hospitalizations and treatment failure.¹⁷⁻²⁰

Primary care and behavioral health providers dealing with apparent exacerbations of mental illness in their patients with schizophrenia may need to consider whether symptoms are being driven by undiagnosed medical conditions. Unfortunately, failure to treat medical conditions in persons with schizophrenia is a common problem,^{17-19,21} and these patients are more likely to report substantial barriers to care including economic barriers and delays in seeking care.¹⁰ Even among insured persons with mental disorders, risks for delaying care or not receiving needed care are substantial.²² Reasons include failure of psychiatric providers to ask about medical issues and patient inability to identify primary care provider by name.²³ Recognition of treatment barriers has led to calls for integration of physical and mental health treatment services,^{12,22,24-28} and integrated services have been successfully demonstrated in inpatient settings, outpatient clinics, detoxification units, and smoking cessation programs.²⁸⁻³¹

Furthermore, primary care providers may play an essential role in providing care to persons with schizophrenia, and may be first in line to assess medical conditions, especially in homeless shelters, walk-in clinics, or emergency treatment venues. Our results may guide the evaluation of persons with schizophrenia. For instance, the high rates of alcohol and polysubstance abuse increase the likelihood that presenting signs and symptoms of worsening psychosis may be related to substance intoxication, withdrawal, or medical conditions (e.g., hypothyroidism, congestive heart failure, diabetes). These findings also indicate that systems of care for primary

and secondary prevention are important, especially for conditions related to smoking and infection.

Our study has several important strengths. Unlike studies conducted in a single hospital or clinic setting, our study analyzed a large population-based sample of adults. The data represent practice patterns of a diverse group of physicians in a wide geographical area. Because these subjects were commercially insured, the findings represent a population rarely studied, the commercially insured chronically mentally ill. We examined 6 years of claims data, with a follow-up period of approximately 40 months for subjects with schizophrenia. The use of rigorous case-finding methodology further ensures specificity of the schizophrenia-spectrum diagnoses and the generalizability of these findings to other men and women having schizophrenia. The use of the Klabunde comorbidity measure also ensures that the medical conditions are likely to be valid.

The limitations of this work should also be considered. First, this study included insured adults from Iowa, a racially homogeneous state. These results are generalizable to similarly insured populations but may not apply to racial and ethnic minorities and the uninsured. Second, limitations inherent to the analysis of claims data may have affected our results. Subjects who did not visit health care providers during the study period are not represented and could have only been captured if enrollment data were available. Thus, the "true" rates of comorbidity may be different from those reported. Physician failure to bill for services or failure to code medical diagnoses may have resulted in lower than expected rates of comorbidity. We have no reason to suspect that this differentially affected either the cases or controls. However, physician failure to provide needed medical assessments of persons with schizophrenia may have resulted in lower rates of claims for specific medical diagnoses. Subjects with multiple insurers may also have resulted in lower than expected rates of service receipt represented in these data. Differences because of disparate length of follow-up were controlled for in the adjusted analyses. Yet, it is possible that persons with schizophrenia had longer follow-up times for fear of losing health benefits.²² Finally, we had limited access to data regarding tobacco use, and risk for some conditions may be changed if tobacco use were entered into statistical models. However, logistic models controlling for smoking did not change the elevated risk for respiratory conditions in the Sokal et al.¹¹ study.

In summary, this research contributes to the growing literature on medical and psychiatric comorbidity by describing a commercially insured population of men and women with schizophrenia compared with contemporaries without administrative claims for mental illness. Using rigorous methodology, we confirmed the findings of prior studies (e.g., increased comorbid diabetes) and extended these studies by identifying other comorbid medical conditions (e.g., hypothyroidism, anemia) in persons with schizophrenia. Our findings support the development and dissemination of coordinated medical and psychiatric systems of care, especially those directed at detection and the primary and secondary prevention of these medical conditions.

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