Incidence and Costs of Cardiometabolic Conditions in Patients with Schizophrenia Treated with Antipsychotic Medications

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Abstract

To examine the incidence of cardiometabolic conditions and change in care costs for patients with schizophrenia treated with antipsychotic medications, medical and pharmacy claims from the South Carolina Medicaid program were used to compare the incidence rates for five cardiometabolic conditions in 2,231 patients with schizophrenia who were newly prescribed one of seven antipsychotic medications, using a retrospective cohort design spanning three years. Incidence and cumulative prevalence (pre-existing + incident) rates for the five cardiometabolic conditions were: 10%/23.3% for Type II diabetes mellitus, 7%/13.3% for obesity/excessive weight gain, 17%/20.9% for dyslipidemia, 4.5%/7.3% for high blood pressure, and 15.6%/41.8% for hypertension. After being treated with the antipsychotic medications examined, the odds of developing obesity/excessive weight gain, Type II diabetes mellitus, or dyslipidemia were not significantly related to any specific atypical agent compared to haloperidol. Incidence rates for elevated blood pressure and clinically diagnosed hypertension were higher for patients prescribed ziprasidone (Odds Ratio [OR]=2.41, Confidence Intervals [CI]=1.20–4.85; OR=1.83, CI=1.16–2.90, respectively) relative to those prescribed haloperidol. Cost results indicate significant differences over time in medical service and pharmacy costs in the group which developed incident cardiometabolic conditions. Individuals diagnosed with schizophrenia with moderate prevalence and incidence rates for these cardiometabolic conditions demonstrated substantially decreasing medical care costs over the three years examined, perhaps indicating a widening gap in access to needed services for conditions that are known mortality risk factors.

Key Words: Schizophrenia, Antipsychotic Agents, Metabolic Conditions, Hypertension, Costs of Care

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Introduction

During the past decade, an increasing body of evidence indicates that certain medical conditions, specifically obesity (1), impaired glucose tolerance, insulin resistance, or Type II diabetes mellitus (2, 3), and cardiovascular disease (2), are more prevalent in patients with schizophrenia than in the general population (3-5). For example, CATIE investigators reported that over 40% of the adult subjects met the criteria for metabolic syndrome at baseline, 48% met the high blood pressure/use of antihypertensive medications criteria, and over 55% met the dyslipidemia criteria (6). These results further underscore the clustering of risk factors for cardiovascular disease and premature death in this patient

Clinical Implications

Overall, about 50% of these patients had a pre-existing or incident cardiometabolic medical condition that should be treated in a primary care setting. These patients had the public insurance to access the needed primary care resources, but were not receiving them. It seems reasonable to conclude that these patients with schizophrenia and comorbid medical conditions that have been shown to increase severity, disability and mortality over time, are not receiving the amount and type of primary medical care they need. Unfortunately, the phenomenon of excess mortality and neglect of the general health needs of patients with schizophrenia appears to be a global one (32). The reintegration of psychiatry and medicine focused on providing optimal treatment services to this vulnerable patient population may be the most important challenge for clinical psychiatry today (32). These results underscore the need for practitioners not only to be personally vigilant in assessing comorbid medical conditions in patients with schizophrenia and potential adverse events due to their antipsychotic medications, but also to advocate in the broader medical profession for more comprehensive practices which would meet the needs of patients with severe mental disorders.

group. Many patients with schizophrenia also have well-recognized, related demographic risk factors such as positive family history, older age, and being non-white (7).

Notwithstanding their efficacy, atypical antipsychotic agents are associated with disturbances in glucose and lipid homeostasis, as well as clinically significant weight gain and hypertension in uncontrolled case studies, retrospective record reviews, and naturalistic or controlled studies with small samples (8), but not to a statistically significant extent (9). Several lines of evidence indicate that clozapine and olanzapine are associated with a greater hazard for metabolic disruption, risperidone and quetiapine pose an intermediate liability, while aripiprazole and ziprasidone are unlikely to disrupt metabolic indices in most patients (10-20).

Hitherto, there has been a paucity of studies evaluating the economic implications of the cardiometabolic hazards associated with atypical antipsychotics (17). Using pooled clinical trial results comparing aripiprazole and olanzapine, an unpublished study estimated the potential cost savings per patient of preventing the development of Type II diabetes mellitus and avoiding metabolic syndrome, but further examinations of the impact of metabolic sequelae on healthcare costs are needed (10). A subsequent cost analysis of the 7.3% of 56,000 Veterans Affairs patients with schizophrenia who developed diabetes after three months of a stable regimen of antipsychotic therapy (20) indicates that the average marginal cost of treating the diabetes was $3,100 greater over a fifteen-month follow-up period, but the additional daily cost per patient attributable to each antipsychotic medication was very small (21). Reviewing the broader pharmacoeconomic implications of these adverse effects, Nasrallah (22) noted that the greatest estimated economic impact was for treatment costs associated with obesity, which increases the risk for many other conditions, including Type II diabetes mellitus, dyslipidemia, coronary artery disease, and hypertension. Therefore, a comprehensive examination of the costs of treatment must include the service and pharmacy costs of psychiatric conditions, as well as pre-existing and incident medical conditions, i.e., medication costs for antidiabetic drugs, antihypertensive, and lipid-lowering agents, as well as the antipsychotic medication costs incurred.

There are two primary purposes of this study. Our first purpose is to determine the relative odds of developing each cardiometabolic condition associated with each major antipsychotic medication in a routine clinical setting. Several previous studies have utilized large claims databases to identify drug-induced adverse effects, estimate their incidence, and examine the risk factors associated with specific forms of morbidity (14-18). A methodology similar to one (17) was employed in this study for case ascertainment and analysis, but we examined a broader array of cardiometabolic conditions and antipsychotic medications. Our second purpose is to analyze the service visit and medication costs for both the psychiatric and the medical conditions noted for each patient to better understand the cost implications to Medicaid of the added burden of incident metabolic conditions in patient care.

Method

Patients

Claims data for the South Carolina (SC) Medicaid program were obtained through the SC Office of Research and Statistics. Data from both medical and pharmacy claims were used and patient identifiers were encrypted to protect patient confidentiality. Each Medicaid medical claim identifies a service encounter, and gives the date of service, the *International Classification of Diseases, Ninth Revision (ICD-9)* diagnosis codes, and the cost to Medicaid (claims payment) related to that visit. Pharmacy claims identified the medication dispensed, the diagnosis, the date the prescription was filled, and the cost of medication to Medicaid. A separate data file on eligibility was used to compile the demographic variables needed for this analysis. Data in these databases are routinely compiled and cleaned (e.g., duplicate billings or those not accepted for payment/reversed are eliminated;

billings are accepted up to 12 months after the service date) prior to being made available for analyses. This study was approved by the University of South Carolina Institutional Review Board as exempt from human subject research guidelines under 45 CFR part 46.

Medical and pharmacy claims for the fiscal years 2003 and 2005 (July 1, 2002 through June 30, 2005) were used to identify a cohort of adult patients (18–54) eligible for Medicaid in the six months prior to selection and for a minimum of nine months in each calendar year included in this analysis, who had a diagnosis (either primary or secondary) of schizophrenia (295.xx) on at least one psychiatric service encounter, and were newly prescribed one of the five atypical antipsychotics (aripiprazole, ziprasidone, quetiapine, risperidone, or olanzapine), haloperidol or fluphenazine between July 1, 2002 through June 30, 2005. A new or refilled prescription was determined by reviewing the prescriptions that were filled for 180 days before the date of the selection encounter. The dates of interest (i.e., 2002–2005) were chosen as this epoch corresponded with a rising interest in the cardiometabolic effects of these antipsychotic agents. During the three-year window, subjects could be selected into the cohort in the first and second years, but might drop out of treatment or become ineligible for Medicaid during the second or third year, so the number (n) of cases examined in each year differs from the total n selected into the cohort.

New variables were coded to represent incident or pre-existing cardiometabolic conditions by using *ICD-9* codes on either the primary or secondary diagnosis in the Visits file: Type II diabetes mellitus (250.00 through 251.92 5th digit=0, 2); obesity (278.00; 278.01); elevated blood pressure (796.2); hypertension (401.xx through 405.xx); hyperlipidemia or hypolipidemia (272.xx) recoded as "dyslipidemia." Pharmacy data were also explored for the commonly prescribed medications for these conditions, i.e., antidiabetic, lipid-lowering, or antihypertensive drugs, to ensure that no cases with these conditions were missed. Pre-existing conditions for each patient were ascertained by reviewing the data for the twenty-four months *prior to* the selection in this cohort. Newly developed conditions (e.g., incident Type II diabetes) were defined as a diagnosis made at any time *after* the selection in the cohort. The newly coded variables (pre-existing and incident) were then cross tabulated to ensure that only those patients who developed each cardiometabolic condition after being prescribed their current antipsychotic medication were accurately identified for this study.

Antipsychotic medications were prescribed as monotherapy to 89% of the cohort: aripiprazole (n=165, 7.4%), ziprasidone (117, 5.2%), quetiapine (453, 20.4%), risperidone (367, 16.5%), olanzapine (445, 20.0%), haloperidol (322, 14.4%), fluphenazine (108, 4.8%). However, two new medication categories were created because multiple medications were coprescribed at some time during the three-year follow-up period: 97 patients (4.3%) were prescribed more than one atypical antipsychotic during the follow-up, and 157 patients (7.0%) were prescribed both an atypical and a conventional medication. Whether the cotherapy in these two new categories was due to medication switching or the coprescription of multiple medications over time was not distinguished for these analyses. However, there was no overlap of patients between the medication categories receiving monotherapy or antipsychotic cotherapy. All of the cardiometabolic conditions examined developed while these patients were taking their prescribed medication/category during the three-year study period.

Analyses

Preliminary analyses were performed to explore the data for outliers and distribution. All analyses used 2-tailed tests and alpha level of .05. Preliminary cross tabulations between the outcome and predictor variables were used to ensure that no individual cell contained less than five observations.

A series of multiple logistic regression models (SAS PROC LOGISTIC with binomial distribution of the dependent variable) was constructed to assess the relative odds associated with having each pre-existing cardiometabolic condition or with developing each incident cardiometabolic condition (obesity, Type II diabetes mellitus, dyslipidemia, high blood pressure, and hypertension), controlling for the three individual risk factors (i.e., age, gender, ethnicity), and using each antipsychotic medication group as an independent variable (dichotomously coded), with haloperidol as the comparator. Each model included dichotomously coded age (>39/≤39), race (African American/other) and gender. Odds ratio (OR) and 95% confidence intervals (CI) are reported as measures of association from these regressions.

To evaluate the association between changes in medical and psychiatric care costs and incident cardiometabolic conditions over three years, two multiple-variable regressions were performed (SAS PROC GENMOD) with negative binomial distribution (including log transformation of cost). A Generalized Estimating Equation (GEE) was used for comparing repeated measures across the three years of observations for each case. A negative binomial distribution regression model was employed to calculate a ratio of the log rate of medical or psychiatric costs per fiscal year, since each dependent cost variable involves overdispersed count data with a mean less than the variance (as identified through the preliminary univariate and bivariate analysis procedures). Differential follow-up of subjects (some with two years of data and others with three) was handled by the GEE

Table 1 Pre-Existing Prevalence and Incidence Rates for 2,231 Adult Patients Prescribed Antipsychotic (AP) Medications

Condition	Pre-Existing Prevalence (24 Months Prior to AP Meds) Rate (%)	Newly Developed Incidence (After AP Meds) Rate (%)	Total (Cross-Sectional) Prevalence Rate (%)
Obesity, weight gain	135 (6.2)	156 (7.1)	291 (13.3)
Type 2 diabetes mellitus	311 (14.2)	198 (9.0)	509 (23.2)
Dyslipidemia	90 (4.0)	322 (16.9)	412 (20.9)
Elevated blood pressure	62 (2.8)	98 (4.5)	160 (7.3)
Hypertension	575 (26.2)	342 (15.6)	917 (41.8)

Table 2 Adjusted Odds Ratios for Incident Medical Disorders

Parameter	Obesity OR (95% CI)	Elevated BP OR (95% CI)	Hypertension OR (95% CI)
Female	ns	ns	1.38 (1.09–1.74)*
Age 39 and over	ns	1.70 (1.11–2.60)*	ns
African American	ns	ns	ns
Aripiprazole	ns	ns	ns
Ziprasidone	ns	2.41 (1.20–4.85)*	1.83 (1.16–2.90)*
Quetiapine	ns	ns	ns
Olanzapine	0.60 (0.36–1.00)*	ns	ns
Risperidone	ns	ns	ns
Fluphenazine	ns	ns	ns
>1 Atypical	**ns**	**ns**	**ns**
Atypical and Conventional	ns	2.40 (1.12–5.12)*	ns

OR=Odds Ratio; CI= Confidence Interval; *Significant at p=.05 or less.

estimating procedure, an algorithm which takes into account the cases with missing observations on the dependent variable in any fiscal year. The main independent variable was dichotomously coded for having one or more metabolic conditions. Other predictor variables included one of the six atypical antipsychotics or the two combined medication groups as described above, and individual risk covariates dichotomously coded for race, age and gender. Goodness of Fit was assessed using the ratio of deviance/degree of freedom, with the value of 1 or less considered as adequate fit. Rate ratio (RR) and 95% confidence interval are reported as measures of association. All multiple comparisons employed a Tukey-Kramer adjustment to protect the overall 0.05 significance level. Adjusted least mean square estimates are presented for Medical, Psychiatric, and Total costs. A plot for the estimated least square means by occasion and whether incident cardiometabolic conditions developed or not is presented for Medical costs, controlling for significant covariates.

Results

The final sample of 2,231 subjects was 51% male, 62% African American, and 51% forty years of age or older. Bivariate comparisons of the distribution of age (40+ years), gender, and race (African American) indicate no significant *a priori* differences in these distributions across the antipsychotic medication groups.

Prevalence and Incidence Rates

The pre-existing prevalence and newly developed incidence rates for the cardiometabolic conditions are arrayed in Table 1. A three-year cumulative prevalence rate for each cardiometabolic condition is also presented.

Logistic regression results indicate that patients with pre-existing obesity were significantly more likely to be prescribed aripiprazole or quetiapine, and significantly less likely to be prescribed olanzapine. Patients with pre-existing diabetes were significantly more likely to be prescribed quetiapine and significantly less likely to be prescribed multiple atypicals or olanzapine. Those with pre-existing hypertension were significantly less likely to be prescribed multiple atypicals.

Logistic regression findings for incident or newly developed conditions indicate that over a three-year period after being prescribed a new antipsychotic, the odds of developing diagnosed Type II diabetes mellitus or dyslipidemia

Table 3 Negative Binomial Regression Predicting Rate of Medical Costs per Year (n=2,231) (Goodness of Fit: Deviance/DF=1.02)

Source	Rate Ratio	95% Confidence Interval
Male	ns	
African American	ns	
Age 40 and over	ns	
Year 2003–2004	0.13*	0.11–0.15
Year 2004–2005	0.08*	0.07–0.09
2+ Cardiometabolic conditions	1.96*	1.63–2.36
>1 Atypical	ns	
Aripiprazole	0.51	0.36–0.73
Ziprasidone	ns	
Quetiapine	ns	
Olanzapine	ns	
Risperidone	ns	
Fluphenazine	ns	
Atypical and Conventional	2.01	1.14–3.54

*Significant at p<.0001

were unrelated to individual risk factors or to antipsychotic medication. The odds of developing obesity were marginally related to being prescribed olanzapine, in that these patients were somewhat *less* likely to develop obesity (see Table 2). Results for "newly developed" elevated blood pressure and clinically diagnosed hypertension indicate that the odds of being diagnosed with these incident conditions significantly were higher for patients prescribed ziprasidone (OR=2.41, CI=1.20–4.85; OR=1.83, CI=1.16–2.90, respectively) relative to those prescribed haloperidol. Incident elevated blood pressure was also more likely to develop for those prescribed both an atypical and a conventional antipsychotic medication (OR=2.40, CI=1.12–5.12) (see Table 2).

Costs of Treatment

Psychiatric and nonpsychiatric Medical costs (services plus pharmacy) were combined into separate cost groupings for each fiscal year after the patient was selected into the cohort. Mean Psychiatric costs in the third year were significantly lower (-$3,223, F=43.26, p<.0001) than in the first year of the study. Patients with incident cardiometabolic conditions incurred Psychiatric medication and visit costs about $1,460 higher than those without one of these conditions (F=15.09, p=.0001). Patients with incident cardiometabolic conditions incurred mean Medical medication and visit costs about $266 higher than those without one of these conditions (F=4.72, p<.0001). Mean Medical costs were also two times greater for those patients coprescribed an atypical and a conventional agent (RR=2.01) (see Table 3). Across the three-year period examined then, patients with incident cardiometabolic conditions incurred mean Total medication and visit costs that were about $1,249 higher than those without one of these conditions (F=3.01, p=.003).

As shown in Table 4, there was also a substantial decrease in the mean Medical costs paid for these patients between 2002–2003 and 2003–2004, with another decline in 2004–2005 (-$5,795, F=15.81, p<.0001). More specifically, the number of patients incurring "zero" Medical costs increased from 16.1% in 2002–2003, to 43.4% in 2003–2004, and to 40.5% in 2004–2005. The negative binomial regression confirmed a significant effect for incident cardiometabolic conditions and time (see Table 3), with a substantial decrease in mean Medical costs between 2002–2003 and 2003–2004 for *all* patients and a further decrease in mean Medical costs for those *without* incident cardiometabolic conditions (see Figure 1). However, the treated prevalence rates (visits with these diagnoses) for these cardiometabolic conditions (pre-existing or incident) between calendar years 2002–2003 and 2004–2005 (see Table 5) are quite consistent.

Discussion

The three-year cumulative prevalence rates found in this cohort are generally consistent with those previously reported in the literature: 23.2% for Type II diabetes mellitus, and 20.9% for dyslipidemia in this cohort compared to about 35% (23, 24) in the general adult population. The 13.3% obesity rate is substantially lower than the rate found in the general population, whereas the 41.8% hypertension prevalence rate is higher than the documented prevalence rate for the general population (34%, with higher rates for nonwhites and males) (25), but consistent with CATIE baseline findings and other studies (6, 10).

These differences in overall prevalence rates could be due to potential under detection/under reporting of some cardiometabolic conditions by psychiatric or primary care providers to Medicaid, either because psychiatric providers are not eligible for reimbursement to diagnose or treat them or the patient is not being seen/treated by a primary care physician. At each medication management visit, psychiatric providers take patient vital signs of weight and blood pressure so they could diagnose excessive weight gain or consistently high blood pressure. However, treatment of these conditions and diagnosis of metabolic milieu disruption, e.g., Type II diabetes mellitus or dyslipidemia, would only be a billable service if performed by a primary care provider. While these are the provider-level determinants of under detecting/reporting the cardiometabolic conditions, we cannot be certain that the odds of diagnosing *any one* of these cardiometabolic conditions across antipsychotic medication groups are biased due to *systematic* under detection or under

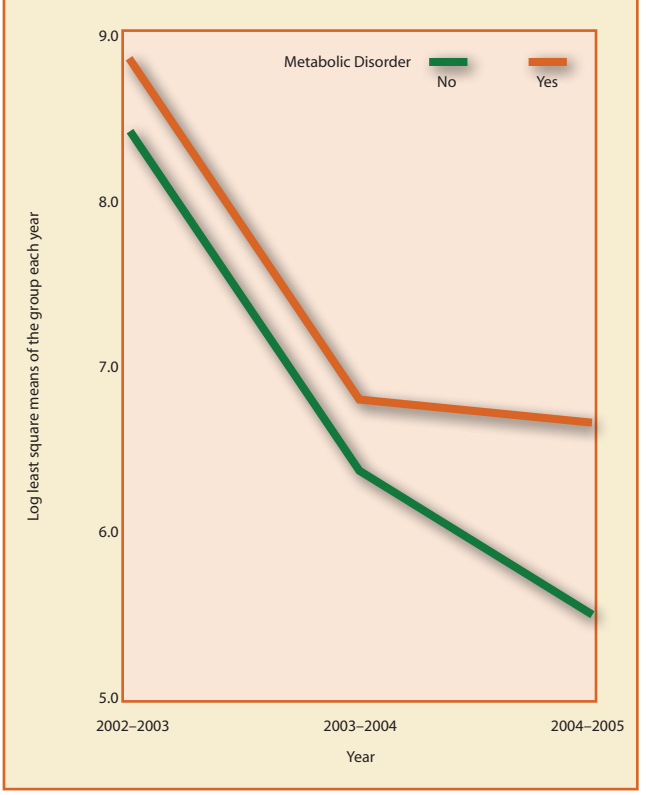
Table 4 Mean Psychiatric and Medical Costs Paid by Year

Year	N of Cases	Variable	Mean	SD
2002–2003	2,019	Psychiatric Costs Paid	$10,271.75	$18,203.71
		Medical Costs Paid	$ 5,377.74	$15,299.44
2003–2004	2,129	Psychiatric Costs Paid	$ 7,021.15	$ 9,700.07
		Medical Costs Paid	$ 702.90	$ 3,630.65
2004–2005	1,921	Psychiatric Costs Paid	$ 7,138.00	$ 9,304.45
		Medical Costs Paid	$ 437.43	$ 1,168.05

reporting of some of the conditions by psychiatric or primary care providers.

The finding that patients are *not* at higher risk of developing obesity, Type II diabetes mellitus, or dyslipidemia due to a specific antipsychotic medication diverges from the results of previous controlled and uncontrolled investigations (10, 14-18). This may be due to: 1) "sample selection" differences between controlled trial studies and routine practice settings wherein controlled trials select only those individuals with no pre-existing conditions, but routine practices must treat/manage all individuals presenting for service; 2) the effect of antipsychotic or other psychotropic medications prescribed *prior to* this selection timeframe; 3) clinical practice differences across medications, i.e., based on their personal and treatment histories, patients were prescribed agents that minimized their risk for developing various adverse effects; or, 4) the patients are not being seen by primary care physicians to diagnose and treat the conditions. A combination of these factors may be evident in these results.

Figure 1 Trend of Adjusted Total Medical Cost over Three Years after Start of Antipsychotic Treatment



In this cohort, pre-existing cardiometabolic conditions were identified separately from those which developed after the patients were prescribed the new antipsychotic medication. The medication group predictors for the pre-existing cardiometabolic conditions are consistent with expected clinical practice for anticipating and managing adverse events related to these medications, e.g., patients with obesity and diabetes were *not* being newly prescribed olanzapine. Furthermore, psychiatric providers appear to be prescribing antipsychotic medications and managing patients so that they are *not* at higher risk of developing obesity, Type II diabetes mellitus, or dyslipidemia due to the effects of specific antipsychotic medications. Finally, the high percentage of patients incurring "zero" Medical costs in the second and third years of the study period, while they continue to receive psychiatric services, may indicate a lack of access to primary care services in which Type II diabetes mellitus, dyslipidemia, or hypertension are diagnosed and treated.

To better understand the cost implications to Medicaid of the added burden of incident metabolic conditions in patient care, our analysis of the service visit and medication costs for both the Psychiatric and the Medical conditions indicated a substantial decline during the study period, with a very modest, but statistically significant, difference in the mean Medical and Total costs over the three-year follow-up period, and only one significant medication group difference in mean Psychiatric, Medical, and Total costs for those coprescribed atypical and conventional antipsychotic medications. These findings are generally consistent with Leslie and Rosenheck's findings over a fifteen-month follow-up period (21).

These results have been discussed with the SC DHHS (Medicaid agency), the ORS (Office of Statistics and Research) which provided the statistical file, and the SC Department of Mental Health (DMH), which provides the

Table 5 Treatment Rates for Cardiometabolic Conditions By Year

Metabolic Condition	2002–2003 n=2,189	2003–2004 n=2,099	2004–2005 n=1,866
Diabetes	316 (14.4%)	348 (16.6%)	298 (16.0%)
Obesity	160 (7.3%)	142 (6.8%)	80 (4.3%)
Dyslipidemia	222 (10.1%)	259 (12.3%)	205 (11.0%)
Hypertension	652 (29.8%)	696 (33.2%)	501 (26.9%)

vast majority of the psychiatric services to these patients, to explore other possible explanations of the trends identified. The compilation of the statistical file was reviewed and found to be an accurate and valid representation of all the patients meeting the study criteria and of all of the Medicaid-paid services provided to them during the three-year study period, with no change in the recording of claims and payments. No changes in reimbursement policies occurred during this three-year time period, except that some psychiatric services, which were deemed not medically necessary (clubhouse-based, day activities) were taken out of the SC DMH reimbursement regulations. This change would account for the substantial decline in Psychiatric costs during the study period, but not for the decline in Medical costs. SC DMH has, however, experienced problems identifying primary care providers willing to accept Medicaid to serve severe mentally ill adults. Starting in the early 2000s and continuing to the present, contracts that local mental health centers enacted with federally qualified primary care centers to help address the medical needs of severely mentally ill adults suffered cutbacks and terminations as the SC DMH budget was cut.

Other investigators reviewing CATIE findings have argued that mental health services researchers need to monitor and change prescriber behavior to encourage informed medication selection by identifying questionable prescriber practices and developing interventions to change them. Because the CATIE findings highlighted the prevalence of cardiometabolic disorders in this treatment population, and the potential impact of antipsychotics on these conditions, services researchers should be encouraged to use secondary data to monitor whether prescribers are providing appropriate screening and treatment (26). Based on the secondary data used herein and the results emerging from this study, it appears that psychiatric practitioners are appropriately prescribing atypical antipsychotics based on their knowledge of the patients' medical and psychiatric history to minimize adverse events. However, a gap appears to exist between their psychiatric and primary medical care, in which a lack of access to primary care, in general, is compounded by the possibility that, even when care is available, screening and treatment of the pre-existing and incident conditions by primary care practitioners is lacking or underutilized.

Limitations

Although the methods of this study were designed to minimize the factors that have plagued previous pharmacoepidemiologic investigations (e.g., short follow-up period for examining incidence, attention to only one or two metabolic conditions, length of time in the cohort, one-to-one drug comparisons, matched cohorts, and inaccurate identification of pre-existing conditions), it has several important limitations. The data were not gathered using a prospective, randomized or controlled design. These results report associations and, as a result, directions of causality cannot be inferred. Other important risk factors were not available for analysis in this data set, i.e., family history. While metabolic abnormalities are well-established risk factors for cardiovascular disorders and are associated with the use of several atypical antipsychotics, the observation period (three years) chosen may have been insufficient to observe an association between the use of some antipsychotics, the development of these metabolic conditions, and *subsequent* development of cardiovascular disorders (27). There was no research confirmation of the diagnoses examined or that the medications billed to Medicaid were the only ones prescribed to/taken by each patient, e.g., brief trials of agents received as samples or through an indigent medications program, or injectible medications given by the mental health clinic and not billed to any third-party source. However, previous studies have found that although Medicaid databases provide much less detailed information on individuals than a structured research interview, the physician diagnoses and utilization data are more reliable than client or family self-reports, and the administrative data correspond to clinical medical records reviews in 75 to 95% of the cases examined (28-31). Patients who were not diagnosed with schizophrenia, who were not eligible nine to twelve months per year for Medicaid coverage, or who had no psychiatric service visits during the year of eligibility, are not represented in this data set and their outcomes may differ from those patients who remained over time. Therefore, we cannot generalize these results to them. Finally, there is no way to estimate how representative this Medicaid cohort is in relation to those in other states and service systems.

Conclusions

Overall, about 50% of these patients had a pre-existing or incident cardiometabolic medical condition that should be treated in a primary care setting. These patients had the public insurance to access the needed primary care resources, but were not receiving them. It seems reasonable to conclude that these patients with schizophrenia and comorbid medical conditions that have been shown to increase severity, disability and mortality over time, are not receiving the amount and type of primary medical care they need.

Unfortunately, the phenomenon of excess mortality and neglect of the general health needs of patients with schizophrenia appears to be a global one (32). The reintegration of psychiatry and medicine focused on providing optimal treatment services to this vulnerable patient population may be the most important challenge for clinical psychiatry today (32). These results underscore the need for practitioners not only to be personally vigilant in assessing comorbid medical conditions in patients with schizophrenia and potential adverse events due to their antipsychotic medications, but also to advocate in the broader medical profession for more comprehensive practices which would meet the needs of patients with severe mental disorders.

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