Original article

Acta Medica Academica 2017;46(2):133-144
DOI: 10.5644/ama2006-124.198

Assessment of inpatient psychiatric readmission risk among patients discharged on an antipsychotic polypharmacy regimen: A retrospective cohort study

Esad Boskailo[1,2], Aldin Malkoc[2,3,4], Dustin B. McCurry[5], Jacob Venter[6], David Drachman[2], Gilbert M. Ramos[2]

[1,2]College of Medicine – Phoenix, The University of Arizona, Phoenix, Arizona USA, [2]Department of Psychiatry, Maricopa Integrated Health System, Phoenix, Arizona, USA, [3]School of Biological and Health Systems Engineering, Arizona State University, Tempe, Arizona, USA, [4]St. George's University School of Medicine True Blue, Grenada, [5]Department of Internal Medicine, University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania USA, [6]Department of Psychiatry Cambridge Health Alliance, Cambridge Massachusetts & Harvard Medical School Boston, Massachusetts, USA

Correspondence:
esad_boskailo@dmgaz.org
Tel.: + 1 602-344-5813
Fax.: + 1 602 344 1211

Received: 21 November 2017
Accepted: 30 November 2017

Key words: Antipsychotics ▪ Polypharmacy ▪ Readmission.

Objective. Patients are frequently prescribed multiple antipsychotic medications, leading to higher healthcare costs and increased risk for side effects. The efficacy of multiple versus single antipsychotics to prevent acute relapse, measured by incidence of inpatient readmission, is investigated in Arizona, USA. **Method.** A retrospective chart review compared socio-demographic and clinical data from 1,010 patients discharged on a single and 377 discharged on multiple antipsychotic medications. Case management records were reviewed for readmission within one year of discharge. **Results.** Younger age, diagnosis of Schizophrenia or Schizoaffective Disorder, prescription of mood stabilizer, shorter length of stay, and discharge to residential treatment or crisis recovery unit were associated with multiple antipsychotics at discharge. Readmission rates of the single (13.7%) versus multiple (15.9%) antipsychotic groups were not statistically different ($P = 0.286$). Logistic regression analysis established that only age (younger) and the prescription of a mood stabilizer at discharge were significant predictors for increased risk for readmission (p=0.010 and p=0.049, respectively). A Cox survival analysis supported these findings. **Conclusions.** Concomitant antipsychotic polypharmacy at discharge did not reduce readmission risk over a one-year period. Given the increased risk of side effects and financial costs of polypharmacy, this study did not provide evidence to support this practice. Strikingly, only two variables predicted readmission risk, younger age and prescription of mood stabilizer. Although practitioners should follow practice guidelines more closely to prevent unnecessary exposure to potentially lethal side effects of antipsychotic polypharmacy, further studies are needed to better identify patients at high risk for readmission.

Introduction

The concomitant use of multiple antipsychotic medications or antipsychotic polypharmacy (APP) is a routinely utilized treatment modality in the psychiatrist's armamentarium (1). In the Clinical Antipsychotic Trial of Intervention Effectiveness (CATIE) study, six percent of patients were taking two antipsychotics upon study entry (2). Additional studies indicate that the rates of APP in the United States may be as high as 50%, depending on the treatment setting and population being evaluated (3-7). The tendency to initiate multiple antipsychotics does not seem to be limited to country of

training or practice setting, as one Canadian study indicated that 27.5% of patients were prescribed an APP regimen at discharge from a tertiary care psychiatric service (8). Furthermore, long-term prescription surveys report increased use of APP in the same treatment setting over time, and the advent of second-generation antipsychotics is associated with an increase in the rates of APP (1, 4, 9).

While the pharmacologic factors driving the widespread use of APP are unclear, there are many postulated rationales, including combining high and low potency antipsychotics or paring more and less sedating medications (1). However, it is uncertain how combining antipsychotic medications is correlated with clinical improvement. There is some evidence to support that the efficacy of antipsychotic medications is correlated with other factors. For example, multiple studies indicate that the occupancy of the dopaminergic D_2 receptor is a determinant of antipsychotic efficacy. In these studies, a range of 65%-75% occupancy was needed to produce efficacy; at over 80% occupancy there was increased risk of extrapyramidal side effects and tardive dyskinesia (10-12). Given the high clinical efficacy of clozapine and its low affinity for D_2 receptors, it is unclear whether D_2 affinity and occupancy are correlated or if there are other potential undiscovered mechanisms of clozapine's therapeutic efficacy (13). In either case, current evidence for APP combinations grounded upon pharmacologic principles is limited.

Studies seeking to understand the clinical motivators of APP have implicated a wide number of factors: intent to minimize potential side effects induced by a specific compound (for instance clozapine-induced weight gain), short term combinations that are extended beyond original intent, such as the use of both a typical and atypical antipsychotic as a bridge to a new treatment regimen, the use of APP when it is reasonable to try different compounds as monotherapy, and failure of or patient refusal to continue monotherapy (1, 9). Given that schizophrenia and schizoaffective disorder are chronic and disabling, it is possible that the severity and persistence of symptoms of psychosis contribute to the use of multiple antipsychotics (14, 15). Additional factors associated with APP include diagnostic inaccuracy, a need to make decisions under time constraints due to short hospital stays, inadequate knowledge of receptor pharmacology, and poor understanding of the differences among antipsychotics (16).

Despite use of APP, there is ample evidence of its potential harm. APP is associated with a greater risk for side effects, adverse reactions and drug-drug interactions (17). For example, investigations of mortality in schizophrenia implicate APP as a significant predictor of reduced survival (18, 19). Antipsychotic combinations may also increase QTc intervals, especially when ziprasidone is used (20). Other potential side effects of antipsychotics, such as sedation and anticholinergic toxicity, may be potentiated when two or more antipsychotics are used concomitantly, or when anticholinergic medications are used to alleviate extrapyramidal side effects (17). Combinations of first and second generation antipsychotics may further increase the risk of tardive dyskinesia posed by the first generation agent (21). Furthermore, the high prevalence of APP is costly for patients and insurers. A one year follow up study comparing patients with treatment initiated on quetiapine, risperidone or olanzapine, reported that each dollar spent on the index antipsychotic was accompanied by an additional $1.31, $0.64 and $0.38 cost for concomitant antipsychotics for these medications, respectively (22).

These factors have led to evidence-based guidelines that recommend using more than one antipsychotic only after at least four trials of antipsychotic monotherapy have been

tried, one of which must have been clozapine (1, 23-25). The apparent discrepancy between clinical practice and evidence-based guidelines suggests that ongoing empirical research is needed to place the implied benefits and drawbacks of APP into perspective (26).

We sought to compare both socio-demographic and clinical variables of two cohorts of patients discharged on either antipsychotic monotherapy or polypharmacy, and their associated acute relapse rates, as measured by readmissions to an acute inpatient facility within one year. Logistic regression and Cox survival analyses helped to address confounders and other clinical or demographic factors associated with acute relapse, as measured by readmission.

Methods

Study setting

The study was completed at the Maricopa Integrated Health System (MIHS), which operates the county hospital and related healthcare safety net facilities within greater Phoenix and Maricopa County, Arizona. MIHS also receives all persons within Maricopa County who are petitioned to undergo an involuntary inpatient psychiatric evaluation. If these patients are then placed on court ordered treatment (COT), inpatient care is provided at MIHS inpatient psychiatric facilities and outpatient care is provided by a provider agency contracted by the state as the county's Regional Behavioral Health Authority (27). Value Options (VO) was the contracted outpatient provider at the time of the study. Within Arizona, persons may be placed on COT for up to one year across both inpatient and outpatient settings. Additionally, it should be noted only patients placed on COT were assessed in this study in order to accurately keep track of discharges and readmission from the provider agency contracted by the state. The study was approved by the MIHS Institutional Review Board (IRB 2006-016).

Study design

An inquiry of the MIHS electronic health record for patients discharged from psychiatric units over a two-year period (2003-2005) yielded 2,587 discrete inpatient stays coded with one of the following inclusion diagnoses: Schizophrenia, Schizoaffective Disorder, and other Psychotic Disorders (Psychotic Disorder and Brief Psychotic Disorder). Each admission and discharge primary diagnosis was confirmed by chart review, with repeat hospitalizations during the study period dropped and only the most recent stay retained. Outpatient treatment data from the Regional Behavioral Health Authority's case management database was queried to identify patients who were readmitted to an acute psychiatric inpatient facility within one year of discharge. Each patient had to be prescribed at least one antipsychotic medication at discharge and receive outpatient case management to be included in the study. The final sample size (n=1,387) included 377 unique records of subjects discharged on multiple antipsychotics and 1,010 discharged on a single antipsychotic medication.

Basic demographic and additional clinical information were retrieved, including additional diagnoses, discharge disposition location (i.e., home, residential placement, or sub-acute psychiatric facility), presence and severity of substance use, and medications prescribed at discharge (antipsychotic, anti-manic, anti-anxiety, and/or anti-depressants). Clinical case management records were reviewed and admission to one of the county's two emergency psychiatric facilities within one year of discharge was recorded as a psychiatric readmission. For readmitted patients, the number of days until readmission was recorded.

Statistical analysis

The sample was separated into two cohorts: those subjects prescribed a single antipsychotic and those prescribed multiple antipsychotics at discharge. Descriptive statistics for the socio-demographic and clinical characteristics between the two cohorts were assessed by two-tailed t-tests, Mann Whitney U tests, and chi-square tests where indicated. Differences between rates of readmission for the two cohorts were calculated. To identify variables associated with readmission and potential confounders, multivariate logistic regression models and a Cox regression survival analysis were conducted. All analyses were conducted with the Statistical Package for the Social Sciences (SPSS) version 15.0 (SPSS Inc, Chicago, IL) software, unless otherwise indicated, and p values less than 0.05 were considered statistically significant.

Results

Socio-demographic and clinical characteristics associated with the concomitant use of multiple antipsychotics

We sought to determine the baseline socio-demographic and clinical characteristics to determine if these variables are associated with antipsychotic mono- or polypharmacy. The study sample (n=1,387) consisted of 60% males and 36% non-white ethnicities. The average age of the subjects was 38.5 years. At discharge, 72.8% of the sample (1,010 subjects) was prescribed a single antipsychotic, and 27.2% (377 subjects) of the sample was prescribed multiple antipsychotics. The rate of APP was consistent with values reported elsewhere (1-8).

Unsurprisingly, due to the lack of randomization associated with retrospective cohort studies, differences in the treatment cohorts were seen. For socio-demographic variables, younger age was significantly associated with polypharmacy, while gender and ethnicity were not (p=0.008, p=0.080, and p=0.212, respectively, Table 1). These differences were expected, as younger age has also previously been associated with polypharmacy (15).

Substance use can be an important confounder in psychiatric symptoms and clinical assessment and might contribute to treatment decisions. We therefore examined the prevalence of substance use between the two cohorts, including abuse, dependence and those with insufficient data recorded to determine the severity of their substance use in this group. Surprisingly, there was no statistical difference amongst the study cohorts (p=0.518, Table 1). As with socio-demographic factors, significant differences were seen for clinical variables. Multiple clinical diagnoses were significantly associated with either mono or polypharmacy. Both Schizophrenia and Schizoaffective Disorder were associated with polypharmacy (p<0.0005 and p=0.008, respectively, Table 1) though the prevalence of Schizophrenia was nearly one in three of the patients in the monotherapy group (32.8% vs 44.3% of patients in the mono or polypharmacy groups, respectively, Table 1). Interestingly, the diagnosis of Psychotic Disorder was significantly associated with monotherapy (p<0.0005, Table 1). Neither the diagnosis of a personality disorder nor intellectual disability was significantly associated with one treatment modality (P = 0.265 and p=0.056, respectively, Table 1).

Additional treatment variables were associated with polypharmacy. Interestingly, both the concomitant use of a mood stabilizer and a decreased length of inpatient stay (LOS) were associated with APP (p<0.0005 and p<0005, respectively, Table 1). However, the concomitant prescription of an anxiolytic or antidepressant was not (p=0.069 and p=0.793, Table 1). Finally, each discharge disposition was significantly associated with either mono or polypharmacy. Discharge

Table 1 Socio-demographic and clinical variables by single and multiple antipsychotic discharge cohorts[a]

Characteristic	Single antipsychotic discharge group (n=1,010)[b]	Multiple antipsychotic discharge group (n=377)[b]	p[c]
Total readmission rate	1,010 (13.7%)	377 (15.9%)	0.286
Age, mean years	39.0	37.1	0.008
Gender, male	58.2 (588)	63.4 (239)	0.080
Ethnicity, non-white	35.9 (357/994)	39.6 (148/374)	0.212
Substance use	53.7 (535/996)	55.7 (206/370)	0.518
Schizophrenia	32.8 (331)	44.3 (167)	<0.0005
Schizoaffective disorder	35.9 (361)	43.8 (165)	0.008
Psychotic disorder	32.0 (323)	11.9 (45)	<0.0005
Personality disorder	16.6 (168)	19.4 (74)	0.265
Intellectual disability	4.2 (42)	6.6 (25)	0.056
Mood stabilizer	34.1 (344/1008)	47.9 (179/374)	<0.0005
Anxiolytic	26.6 (266/1000)	31.6 (118/374)	0.069
Antidepressant	29.3 (294/1005)	28.5 (107/375)	0.793
Length of stay, mean days	38.3	36.6	<0.0005
Discharge home	59.7 (603/1010)	43.8 (165/377)	<0.0005
Discharge to residential treatment	19.4 (196/1010)	26.5 (100/377)	0.004
Discharge to crisis recovery unit	12.9 (130/1010)	22 (83/377)	<0.0005

[a]All results presented as % of n unless otherwise noted; [b]Single group n=1,010; Multiple group n=377, unless otherwise noted.; [c]Age analyzed with independent-groups t test, Length of stay analyzed with Mann-Whitney U test; all other comparisons with Chi-square test.

to home was associated with monotherapy (p<0.0005, Table 1), while both discharge to residential treatment or a crisis recovery unit was associated with polypharmacy (p=0.004 and p<0.0005, respectively, Table 1). Taken as a whole, these cohorts display expected differences in socio-demographic and clinical variables due to the nature of the study. However, even for variables that displayed significant differences across the cohorts, such as age, the diagnosis of Schizophrenia, Schizoaffective Disorder, Psychotic Disorder, or discharge disposition, the differences between the groups did not exceed fourteen percent (or three years or days, for mean age or length of stay, respectively), except for the diagnoses of Psychotic Disorder and discharge to home (20.1% and 15.9%. respectively, Table 1).

Reduced inpatient psychiatric readmission rates are not associated with APP

After assessing the socio-demographic and clinical variables of the cohorts, we sought to determine if the polypharmacy group had either increased or decreased incidence of readmission following discharge. Given the n of the two cohorts, the study yielded sufficient statistical power to detect a difference in rate of readmission of 5.8% with 95% confidence and 80% power. The overall incidence of readmission was 14.3% of patients. Readmission occurred at a rate of 13.7% for those on a single antipsychotic compared to 15.9% for the multiple antipsychotic group, a 2.2% difference (Table 1). This small percentage difference tended to favor the use of a single antipsychotic, but did not meet statistical significance given the scope of the study.

Younger age and concomitant use of a mood stabilizer are predictive of increased risk of readmission

Due to the unequal distribution of socio-demographic and clinical variables between the cohorts, and the potential for these differences to act as cofounders in determining readmission rates amongst the groups, a logistic regression was performed.

Consistent with the univariate analysis (Table 1) demonstrating no significant difference in readmission rate between cohorts, a predictive logistic regression model did not find concomitant antipsychotic to be associated with either increased or decreased incidence of readmission (Table 2).

Two socio-demographic and clinical variables which were significantly associated with either the mono- or polypharmacy treatment groups were also found to be predictors of readmission. Specifically, increased age was found to predict a decreased incidence of readmission (OR=0.982, 95% Cl=0.968-0.996, p=0.010, Table 2), and the concomitant use of a mood stabilizer in addition to at least one antipsychotic was found to predict increased risk of readmission (OR=1.418, 95% Cl=1.001-2.010, p=0.049, Table 2). Having a personality disorder and discharge to residential treatment (OR=7.596, 95% Cl=0.968-59.591, p=0.054, and OR=1.911, 95% Cl=0.916-3.988, p=0.085, respectively, Table 2) approached statistical significance favoring increased readmission risk. Based upon this logistic regression model, for each additional year of age, the odds of being readmitted decreased by 12%. However, if a mood stabilizer was prescribed, the odds of being readmitted increased by 42%.

It should be noted that the types of mood stabilizers recorded for this study were lithium and divalproex sodium.

We also sought to correlate our analysis for the total study duration with a Cox regression

Table 2 Socio-demographic and clinical variables as predictors of readmission (Logistic regression analysis of readmission incidence)[a]

Predictor	Odds Ratio	95% CI	p
Increased age	0.982	0.968-0.996	0.010
Gender, male	0.784	0.556-1.105	0.164
Ethnicity, non-white	0.836	0.596-1.173	0.301
Substance use	0.906	0.635-1.293	0.587
Schizophrenia	1.141	0.722-1.803	0.573
Schizoaffective disorder	1.263	0.813-1.964	0.299
Psychotic disorder	3.160	0.420-23.795	0.264
Personality disorder	7.596	0.968-59.591	0.054
Intellectual disability	1.708	0.192-15.230	0.632
Mood stabilizers	1.418	1.001-2.010	0.049
Anxiolytic	1.175	0.832-1.659	0.360
Antidepressant	1.080	0.764-1.528	0.663
Increased length of stay	1.004	0.997-1.010	0.280
Discharge home	1.518	0.754-3.059	0.243
Discharge to residential treatment	1.911	0.916-3.988	0.085
Discharge to crisis recovery unit	1.077	0.486-2.387	0.856
Multiple antipsychotics at discharge	1.098	0.767-1.572	0.609

[a]Total cases analyzed=1,329. A Hosmer-Lemeshow test indicated that model fit was good (chi-square with 8 df=10.12, p=0.257).

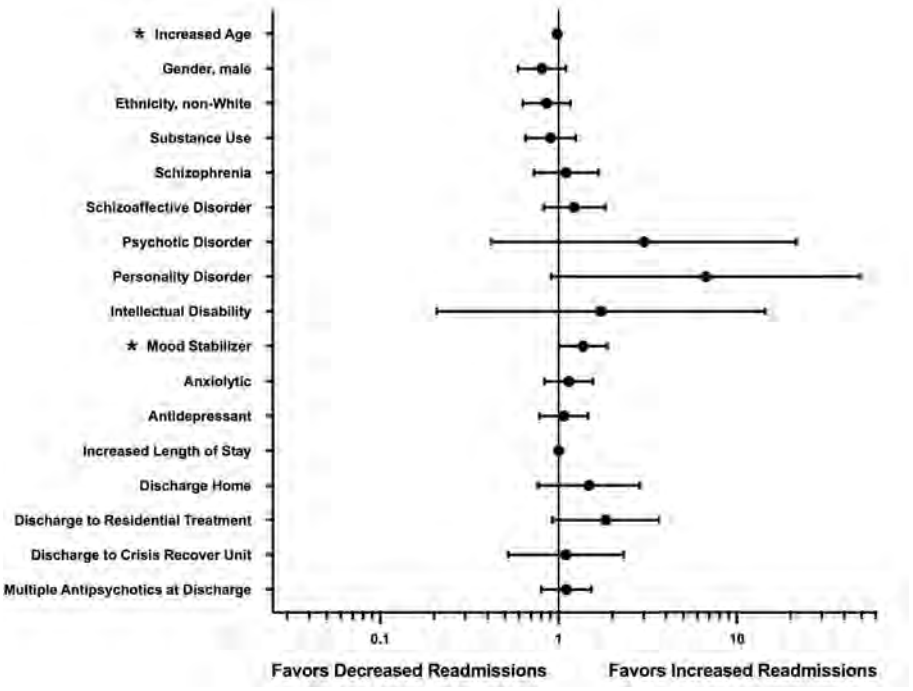

Figure 1 Forest Plot of Cox regression socio-demographic and clinical variables as predictors of survival days until readmission: Total cases analyzed=1,329. – 2Log Likelihood=2434.30, indicating that model fit was good. Mean Hazard Ratios shown with 95% confidence intervals are displayed. Statistically significant predictors are indicated by *, where p<0.05.

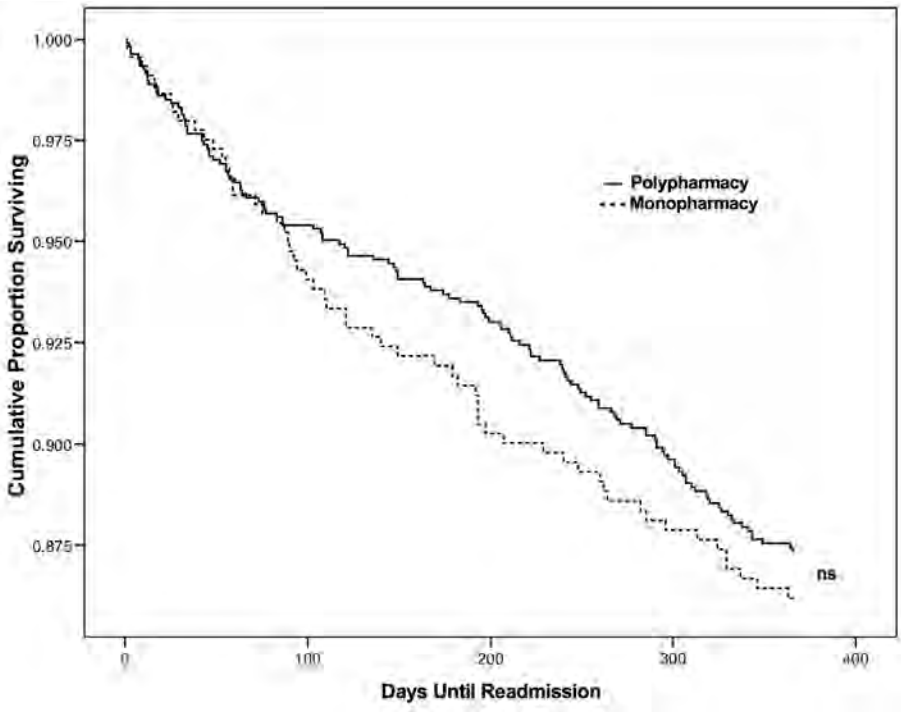

Figure 2 Cox regression days until readmission for mono or polypharmacy cohorts (adjusted for covariates): Total cases analyzed=1,329. – 2Log Likelihood=2434.30, indicating that model fit was good. The difference between the two groups was not statistically significant, p=0.542.

Table 3 Cox regression of socio-demographic and clinical variables as predictors of survival days until readmission[a]

Predictor	Hazard ratio	95% CI	p
Increased age	0.983	0.971-0.996	0.010
Gender, male	0.808	0.593-1.101	0.177
Ethnicity, non-white	0.857	0.630-1.167	0.328
Substance use	0.901	0.652-1.245	0.527
Schizophrenia	1.103	0.724-1.681	0.648
Schizoaffective disorder	1.224	0.822-1.824	0.319
Psychotic disorder	3.019	0.421-21.646	0.272
Personality disorder	6.714	0.909-49.597	0.062
Intellectual disability	1.729	0.207-14.472	0.613
Mood stabilizer	1.372	1.003-1.878	0.048
Anxiolytic	1.141	0.837-1.557	0.405
Antidepressant	1.072	0.784-1.464	0.663
Increased length of stay	1.003	0.997-1.008	0.325
Discharge home	1.480	0.766-2.859	0.244
Discharge to residential treatment	1.839	0.926-3.653	0.082
Discharge to crisis recovery unit	1.097	0.520-2.313	0.809
Multiple antipsychotics at discharge	1.106	0.800-1.528	0.542

[a]Total cases analyzed = 1,329. -2Log Likelihood = 2664.20, indicating that model fit was good.

(survival analysis) model that predicts the variables that modify daily risk of readmission. For each subject readmitted, the number of days between discharge and readmission was calculated. If a subject was not readmitted within the one-year period, the number of days were treated as censored observations with survival times of 365 days (Figure 1).

As with all prior analyses, there was no significant difference between mono- or polypharmacy cohorts (HR of polypharmacy=1.106, 95% Cl=0.800-1.528, p=0.542, Figure 1, Figure 2, and Table 3). Consistent with the logistic regression analysis only increased age (HR=0.983, 95% Cl=0.971-0.996, p=0.010, Figure 1 and Table 3) and the concomitant use of a mood stabilizer (HR=1.372, 95% Cl=1.003-1.878, p=0.048, Figure 1 and Table 3) were statistically significant predictors of days until readmission. Having a personality disorder and discharge to residential treatment again approached significance (HR=6.714, 95% Cl=0.909-49.597, p=0.062, and HR=1.839, 95% Cl=0.926-3.653, p=0.082, respectively, Figure 1 and Table 3). The Cox regression analysis found that for each additional year of age, the risk for readmission on any given day decreased by 12% and if the subject was prescribed a mood stabilizer, the odds of being readmitted on any given day increased by 37%.

Discussion

In spite of evidence-based guidelines limiting the use of APP to specific situations, multiple antipsychotics were prescribed for 27.2% of patients at discharge in the study. The rate of prescription of multiple antipsychotic medications was similar to that for a sample of patients with schizophrenia discharged from a Canadian tertiary care psychiatric facility (8). The rate of polypharmacy in the study was surprising, given that the sample was obtained from a psychiatry residency training program where it is ex-

pected that evidence-based medicine will be followed more closely. However, it is theoretically possible that every prescription for multiple antipsychotics followed evidence-based recommendations, though that is unlikely given the previously reported clinical factors which are associated with polypharmacy are also likely to exist in an academic setting (1, 9, 14-17).

Multiple studies indicate that APP is related to variables that can be proxies for greater illness burden, such as diagnosis of schizophrenia or schizoaffective disorder, COT, longer length of inpatient hospitalization, prescription of additional psychiatric medications, and comorbidities such as substance use (15). This study found areas of overlap with previously reported proxy variables of illness severity, such as the diagnosis of schizophrenia and prescription of additional psychiatric medications. In contrast, in this study a shorter duration of hospitalization was associated with APP. This discrepancy may be related to the overall increased length of stay in the study compared to nationwide hospital statistics for similarly diagnosed patients (28). It is unclear why patients in this study had an overall increased LOS, but this may be due to the legal process for commitment in Arizona where length of inpatient treatment is not factored into whether someone is ordered to receive COT (27). Given that shortened time constraints for rapid stabilization are associated with APP, an increased LOS may in turn lead to less hurried treatment decisions, and therefore also reduce other forms of polypharmacy.

Another illness severity variable, aggression, is difficult to assess via a specific quantifiable measure, and the effect of this variable on prescribing tendencies or readmission risk could not be assessed. However, the prescription of a mood stabilizer, which may be used to treat aggression, was associated with APP. These patients may be more emotionally and/or behaviorally dysregulated, and present with more challenging behavior on inpatient units. The study did not include other measures to quantify behavior, such as mania, preventing a comparison of the presence and severity of these symptoms between the two cohorts.

While APP may be associated with proxy measures for greater disease burden, it is critical to determine if APP effectively treats the increased disease burden by preventing the risk of inpatient readmission, given APP's greater cost and increased risk for side effects. In this study, there was no statistically significant difference in the readmission rates over a one-year period following discharge for patients prescribed APP. Inpatient readmission functioned as a proxy measure for acute relapse, though the nature of COT in Arizona requires that relapsing patients receive an appropriate higher level of care, which would include inpatient admission. It is possible that patients discharged on multiple antipsychotics may be switched to a single antipsychotic, and vise-versa, in the outpatient setting. Given the nature of the study, as an intention to treat study based upon polypharmacy at discharge, these outpatient treatment changes could dilute the differences between the groups. However, the historical trend of patients remaining on a polypharmacy regimen over time, even when the polypharmacy regimen is first initiated as a short-term treatment plan, makes it unlikely that cohort crossover was a significant variable in the study (1, 4, 9, 15).

Critically, when evaluating the factors predicting increased risk of readmission, very few factors were identified. These findings suggest that it is challenging to risk-stratify which patients are likely to relapse: a task that has proven difficult and is of urgent clinical need to reduce morbidity from psychiatric illness (29). This study further reinforces that many proxy measures for disease severity that have been associated with APP are not associated with relapse risk, and

should alter perceived risk of relapse in patients thought to have greater illness severity. It is possible that with a larger study size, other variables, such as discharge to a residential treatment facility, which approached statistical significance, may become statistically significant. Interestingly, discharge to a sub-acute facility, which was the highest discharge level of care in the study, was not predictive of relapse, indicating that disease burden may not predict relapse if treated in the appropriate setting.

Concomitant use of a mood stabilizer has previously been reported as an indicator of disease severity, as is the concomitant use of an antidepressant. Why mood stabilizer use was predictive in this study is unclear, as is whether these medications were discontinued in the outpatient setting. Further studies are needed to identify why mood stabilizers were unique amongst the additional treatment medication classes and if relapse was associated with discontinuation of these medications in the outpatient setting. Additionally, it is known that younger patients are more likely to be prescribed a polypharmacy regimen, but it is not clear why younger patients are at increased risk of relapse. It is possible that elderly patients at an increased risk of relapse were placed in state hospital facilities at a younger age due to perceived risk of relapse or greater disease burden, thus presenting an age based selection bias. However, given the relatively difficult task of predicting risk of readmission, it seems unlikely that identification of these higher risk patients occurred at a younger age. Since acute relapse is associated with an inability to cope with life stressors, it may be that older patients have learned coping mechanisms to address stressors and reduce relapse risk (30).

Clinical implications

This study showed no added benefit from prescribing multiple antipsychotics over a single antipsychotic medication with regard to preventing relapse. Specifically, seen in our logistic regression data and Figures 1 and 2, our findings further support various guidelines and have the ability to protect patients from exposure to unnecessary medications by potentially changing prescriber behavior. Additionally, less medication prescribed has potentially positive financial implications.

Limitations of the study

The main outcome measure used is not a direct measure of relapse, but a proxy measure. Aggression was not assessed via a specific measure and the effect of aggressive behavior can therefore not be assessed. Additionally, the study did not take into consideration a few factors that should be addressed. For example, the study did not survey patient factors such as level of education, marital status, family status, employment, and inheritance psychotic overload. The purpose of the study was to consider the various clinical conditions patients suffered and how they responded to a single or multiple antipsychotic discharge. However, future studies would greatly benefit and bring a wider understanding by considering such other patient factors that this study did not account for.

Conclusion

APP at discharge was not found to prevent readmission to acute psychiatric inpatient facilities, supporting current guidelines recommending antipsychotic monotherapy. The study did not examine the increased risk of side effects due to exposure of higher amounts of antipsychotic medications seen with APP. This should be carefully evaluated in a future study given the lack of evidence for relapse prevention. Strikingly, many variables which are proxies for disease bur-

den were not predictive of readmission risk in statistical models. These conclusions further demonstrate that improved prediction of relapse risk is a pressing clinical need to reduce morbidity from psychiatric disease.

What is already known on this topic

Antipsychotic polypharmacy has been recorded as a routinely utilized treatment modality in a psychiatrist's armamentarium and is backed by current data from the Clinical Antipsychotic Trial of Intervention Effectiveness (CATIE) study. CATIE showed that 6 percent of patients took two or more antipsychotics upon entry to the study. High rates of APP are further confirmed from one Canadian study indicating that 27.5% of patients were placed on a polypharmacy treatment protocol upon discharge. Additionally, antipsychotic polypharmacy has shown to be associated with risk for side effects, adverse reactions and drug-drug interactions. These associations have shown the need for ongoing empirical research to place the implied benefits and drawbacks of Antipsychotic polypharmacy into perspective.

What this study adds

This investigation did not detect any difference between patients on single and multiple antipsychotic regimens at discharge and their one year readmission rates. Given the risks of side effects and financial costs of antipsychotic polypharmacy, those discharging on such prescriptions should not be considered at any less risk of relapse. However, as always, further studies would be beneficial to better identify those at higher readmission risk and the factors that may impact their pathway from stabilization to relapse.

Acknowledgements: The authors want to acknowledge Joanna Kowalik, M.D., M.P.H., Daniel Merrill, M.D., and John Kingsley, M.D., of the MIHS Department of Psychiatry for their contributions to planning the study and data collection, and Carol Olson, M.D., Chair, MIHS Department of Psychiatry, for her ideas and feedback.

Authors' contributions: Conception and design: EB; Acquisition, analysis and interpretation of data: EB, AM, DBMcC, JV, DD, and GMR; Drafting the article: EB, JV, DD, and GMR; Revising it critically for important intellectual content: EB, AM, DBMcC, JV, DD, and GMR; Approved final version of the manuscript: EB.

Conflict of interest: The authors declare that they have no conflict of interest.

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