



PSYCKES QUALITY COLLABORATIVE

GNYHA-PSYCKES Learning Collaborative Information Packet

Scientific Articles (arranged in descending order by date):

1. Diabetes and Cardiometabolic Risk among individuals with Serious Mental Illness: pp. 1-7
2. CATIE, TEOSS, PSYCKES: Large multi-site studies examining difference between antipsychotics (focusing here on metabolic outcomes) pp. 8-10

Cardiometabolic Articles

Research Studies

1. **Padmavati R, McCreddie RG, Tirupati S. Low prevalence of obesity and metabolic syndrome in never-treated chronic schizophrenia.** *Schizophrenia Research* 2010, vol 121 pp 199-202
 - Researchers and clinicians have wondered whether people with schizophrenia have an increased risk for developing obesity and metabolic abnormalities independent of treatment with medications. This case-control study was done in India with 51 people with never-treated schizophrenia and 51 normal controls. 96% were vegetarians. People with schizophrenia were more likely to be unmarried and unemployed but all subjects and controls lived in extended family groups.
 - BMI was higher in the control group than the schizophrenia group.
 - Waist circumference, blood pressure, glucose, triglyceride and HDL cholesterol levels were not different between the two groups.
2. **De Hert M, Hanssens L, Van Winkel R et al. Reversibility of Antipsychotic Treatment-Related Diabetes in Patients With Schizophrenia.** *Diabetes Care* 2006, Vol 29, no 10, p2329-2330 (letter).
 - While the clinical concerns related to metabolic effects of antipsychotic treatment have been well-documented, scientific evidence regarding effect of medication changes on medical illness is just emerging. This case series reports on 7 patients who were switched from other high and moderate risk antipsychotics to aripiprazole (Abilify) after the new onset of diabetes, determined by glucose tolerance testing and fasting glucose levels. There was reduction at 3 months of glucose values at all times in the OGTT, fasting insulin, glycosylated hemoglobin, weight, waist circumference, and BMI. This prospective case series provides evidence that diabetes can be reversed with a change in antipsychotic medication.
3. **Ray WA, Chung CP, Murray KT: Atypical antipsychotic drugs and the risk of sudden cardiac death.** *New England Journal of Medicine* 360 (3):225-235, 2009
 - This study, conducted in Tennessee, found that current users of typical and atypical antipsychotic drugs had a similar, dose-related increased risk of sudden cardiac death.
 - Adjusted IRR for sudden cardiac death in relation to antipsychotic treatment was: typicals 1.99 (95% CI 1.68,2.34); atypicals 2.26 (95% CI 1.88,2.72).
4. **Baker RA, Pikalov A, Tran QV, et al: Atypical antipsychotic drugs and diabetes in the US food and drug administration adverse event database: a systematic bayesian signal detection analysis.** *Psychopharmacology Bulletin* 42(1):11-31,2009
 - In the FDA AERS database, higher associations with diabetes-related adverse events were found for olanzapine, risperidone, clozapine, and quetiapine.
 - Lower associations with diabetes-related adverse events were found with haloperidol, aripiprazole, and ziprasidone.
 - These findings support differential risk of diabetes across atypical antipsychotics and reinforce the need for metabolic monitoring of patients taking antipsychotics.

5. **Weiden PJ, Newcomer JW, Loebel AD, et al: Long-term changes in weight and plasma lipids during maintenance treatment with ziprasidone.** *Neuropsychopharmacology* 33:985-994, 2008
 - Clinically significant sustained improvements in weight, BMI, total cholesterol, and triglycerides were found in patients switched to ziprasidone from risperidone or olanzapine.
6. ***Correll CU, Frederickson AM, Kane JM, et al: Equally increased risk for metabolic syndrome in patients with bipolar disorder and schizophrenia treated with second-generation antipsychotics.** *Bipolar Disorders* 10:788-797, 2008
 - Patients with bipolar disorder and schizophrenia who are treated with SGAs have similarly high rates of metabolic syndrome.
 - These findings suggest a shared susceptibility to antipsychotic related metabolic dysregulation that is not primarily related to psychiatric conditions or concomitant mood stabilizer treatment.
7. **Kreyenbuhl J, Medoff JR, Seliger SL, et al: Use of medications to reduce cardiovascular risk among individuals with psychotic disorders and type 2 diabetes. *Schizophrenia Research* 101:256-265, 2008**
 - Use of cardioprotective medications in patients with diabetes and serious mental illness increased over the study period. However, a considerable number of patients remained inadequately managed despite considerable cardiac risk.
 - African Americans were less likely than Caucasians to receive statins but more likely to receive ACE-inhibitors or ARB's.
8. **Haupt DW, Fahnestock PA, Flavin KA et al: Adiposity and insulin sensitivity derived from intravenous glucose tolerance tests in antipsychotic-treated patients.** *Neuropsychopharmacology* 32:2561-2569, 2007
 - This study used IV glucose tolerance tests to quantify whole-body insulin sensitivity in patients treated with either an FGA or an SGA.
 - Adiposity levels occurring during antipsychotic treatment are strongly related to insulin resistance. This confirms that antipsychotic-induced weight gain can contribute to increased cardiometabolic risk in patients with schizophrenia and schizoaffective disorder.
 - There were no consistent effects of medication group on either insulin sensitivity or secretion, independent of adiposity.
9. **Goethe JW, Szarek BL, Caley CF, et al: Signs and symptoms associated with the metabolic syndrome in psychiatric inpatients receiving antipsychotics: a retrospective chart review.** *Journal of Clinical Psychiatry* 68:22-28, 2007
 - 69.3% of the study sample had at least one correlate of metabolic syndrome (BMI >30 kg/m², dyslipidemia, and/or a diagnosis of hypertension or diabetes).
 - The risk for symptoms of metabolic syndrome is particularly high in those >50 years, those taking clozapine, or those on more than one antipsychotic.
 - These findings support the call for routine screening for metabolic syndrome in patients on antipsychotics.

10. **Bobes J, Arango C, Aranda P, et al: Cardiovascular and metabolic risk in outpatients with schizophrenia treated with antipsychotics: results of the CLAMORS study.** *Schizophrenia Research* 90:162-173, 2007
- Patients treated with antipsychotics (either an SGA or haloperidol) had CHD risk and prevalence of metabolic syndrome in the same range as the Spanish general population who were 10-15 years older than the study population.
11. **Correll CU, Frederickson AM, Kane JM, et al: Does antipsychotic polypharmacy increase the risk for metabolic syndrome?** *Schizophrenia Research* 89:91-100, 2007
- Antipsychotic polypharmacy was present in 19.2% of the study population.
 - Compared to patients receiving monotherapy, patients on antipsychotic polypharmacy have higher rates of metabolic syndrome and lipid markers of insulin resistance.
 - Logistic regression analysis showed that metabolic syndrome was significantly associated with co-treatment with an FGA ($p < .0001$).
 - However, antipsychotic polypharmacy dropped out of multivariate regression models, indicating that antipsychotic polypharmacy is not independently associated with the prevalence of metabolic syndrome and lipid markers of insulin resistance, which are related to known demographic, clinical, and anthropometric risk factors.
12. **Citrome LL, Holt RIG, Zachry WM, et al: Risk of treatment-emergent diabetes mellitus in patients receiving antipsychotics.** *Annals of Pharmacotherapy* 41:1593-1603, 2007
- This was a Medline and PSYCInfo search for antipsychotics and diabetes that was undertaken for the years 1966-2005.
 - Comparing antipsychotics and diabetes, little observable difference was noted between individual SGAs vs. FGAs.
 - Avoidance of diabetes as an outcome cannot be predictably achieved with precision by choice of an SGA vs. an FGA.
 - Risk assessment for new-onset diabetes requires assessment of established risk factors (family history, non-white ethnicity, diet, central obesity, level of physical activity).
13. **Strassnig M, Miewald J, Keshavan M et al: Weight gain in newly diagnosed first-episode psychosis patients and healthy comparisons: one year analysis.** *Schizophrenia Research* 2007, 93(1-3): 90-98
- In the CATIE trial patients had on average been on antipsychotics for 14 years. This study demonstrates that antipsychotic naïve people treated for the first time for psychosis with antipsychotic medications are significantly more susceptible to weight gain. This data comes from an ongoing study of first episode psychosis at the University of Pittsburgh. There were 98 subjects, including patients with and without mood symptoms, and 30 controls matched for age and gender. There was a small group of people with first episode of psychosis on no medication. Average antipsychotic exposure was 303 days, and there was no antipsychotic polypharmacy. Excessive weight gain was defined as an increase of $\geq 7\%$ of body weight.
 - Factors associated with more weight gain: younger patients, more negative symptoms.

- Increases after one year in body weight by drug: olanzapine 37 lbs, risperidone 28 lbs, haloperidol 9 lbs, perphenazine 3.4 lbs, psychotic on no meds 3.3 lbs, healthy controls 2.4 lbs.
- Regarding polypharmacy, the total number of medications (regardless of class) and the use of antidepressants were predictors of weight gain.

14. Joukaama M, Heliövaara M, Knecht P, et al: Schizophrenia, neuroleptic medication, and mortality. British Journal of Psychiatry 188:122-127, 2006

- This study utilized comprehensive medical exams at baseline and at 17 year follow-up.
- The number of neuroleptics used at baseline survey showed a graded relationship to mortality. Adjusted for age, gender, somatic diseases, and other potential risk factors for premature death, RR was 2.50 (95% CI 1.46,4.3) per increment of neuroleptic.

15. Honer WG, Thornton AE, Chen EY, et al: Clozapine alone vs. clozapine and risperidone with refractory schizophrenia. New England Journal of Medicine 354(5):472-82, 2006

- In this randomized, double-blind study, patients with schizophrenia and poor response to clozapine received augmentation with risperidone.
- Addition of risperidone to clozapine did not improve symptoms in patients with severe schizophrenia.
- There was an increase in fasting blood glucose in the group treated with risperidone.

16. Citrome L, Jaffe A, Levine J, et al: Incidence, prevalence, and surveillance for diabetes in New York State psychiatric hospitals 1997-2004. Psychiatric Services 57:1132-1139, 2006

- From 1997-2004, the doubling of the IR of treated diabetes (from 0.9% to 1.8%; RR=2.03, 95% CI 1.51,2.73), and the increased prevalence of identified diabetes cases (from 6.9% to 14.5%; RR=2.11, 95% CI 1.93,2.31) among psychiatric inpatients in NYSOMH facilities mirrors that of the general population, but at higher absolute rates.

17. Citrome L, Jaffe A, Levine J, Allingham B, Robinson J: Relationship between medication treatment and new cases of diabetes among psychiatric inpatients. Psychiatric Services 55:1006–1013, 2004

- Exposure to SGA polypharmacy, to clozapine monotherapy, or to quetiapine monotherapy significantly increased risk of treatment emergent diabetes.

Reviews and Metanalyses

1. Newcomer JW: Antipsychotic medications: metabolic and cardiovascular risk. Journal of Clinical Psychiatry 68(Suppl 4):8-13, 2007

- This article reviews evidence in the literature for increased mortality, cardiovascular risk factors, diabetes, obesity, and metabolic syndrome in people with serious mental illness and the associations of antipsychotics with these health problems.
- Also provides a discussion on various strategies for monitoring cardiometabolic risk factors in patients with mental illness.

2. **Newcomer JW: Metabolic considerations in the use of antipsychotic medications: a review of recent evidence.** Journal of Clinical Psychiatry 68(suppl):20-27, 2007
 - There is a critical need for psychiatrists and primary care professionals to increase awareness of and attention to the physical health problems of people with mental illness, including appropriate management of metabolic adverse effects associated with psychiatric medications.

3. **Cohn TA, Sernyak MJ. Metabolic monitoring for patients treated with antipsychotic medications.** Canadian Journal of Psychiatry 51:492-501, 2006
 - This is a review of major published consensus guidelines for metabolic monitoring of patients treated with antipsychotics.
 - Also provides a selective review of practice guidelines for management of diabetes, dyslipidemia, and hypertension.
 - There is considerable consensus in the published guidelines.
 - Monitoring, but not necessarily treatment, falls within the scope of psychiatric practice and should include screening for metabolic disorders and tracking of effects of antipsychotic treatment.

4. **Hennekens CH, Hennekens AR, Hollar S: Schizophrenia and increased risks of cardiovascular disease.** American Heart Journal 50:1115-21, 2005
 - This article reviews absolute and relative impacts of major causes for mortality among patients with schizophrenia.
 - The chief cause of premature mortality among patients with schizophrenia is CHD, caused mainly by increased adverse risk profiles.
 - Patients with schizophrenia have a 20% decreased life expectancy compared to the general US population.
 - More than two-thirds of patients with schizophrenia die of CHD, compared to one-half of the US population.

5. **Newcomer JW: Second generation (atypical) antipsychotics and metabolic effects: a comprehensive literature review.** CNS Drugs 19(suppl):1-94, 2005
 - This review covers eight separate SGAs available in USA or Europe.
 - Clozapine and olanzapine are associated with the greatest risk of clinically significant weight gain, as well as the greatest risk of diabetes and dyslipidemia.
 - Limited controlled studies support the hypothesis that clozapine and olanzapine may have a direct effect on glucose regulation independent of adiposity.
 - The rank order of risk observed for SGAs suggests that the differing weight gain liability of atypical agents contributes to the differing relative risk of insulin resistance, dyslipidemia and hyperglycemia between SGAs.

Pediatrics (Cardiometabolic)

1. **Fraguas D, Merchan-Naranjo J, Laita P et al: Metabolic and hormonal side effects in children and adolescents treated with second generation antipsychotics.** Journal of Clinical Psychiatry 69: 1166-1175, 2008
 - After six months of treatment with either risperidone, olanzapine, or quetiapine, the number of patients at risk for adverse health outcomes

- increase from 16.7% (n=11) to 37.9% (n=25, p=.018). The number of subjects at risk for adverse health outcomes increased significantly only for olanzapine (p=.012).
- Total cholesterol increased significantly for patients receiving olanzapine (p=.047) and quetiapine (p=.016)
 - At six month follow-up, 50% (n=33) of subjects showed significant weight gain. Significant increases in BMI z scores were seen in those treated with olanzapine and risperidone.
 - Metabolic and hormonal side effects of SGAs in children and adolescents should be carefully monitored when prescribing these drugs.

2. **McIntyre RS, Jerrell JM: Metabolic and cardiovascular adverse events associated with antipsychotic treatment in children and adolescents.**

Archives of Pediatric and Adolescent Medicine 162(10):929-935, 2008

- This rich study highlights the increased effects of both antipsychotic polypharmacy as well as polypharmacy involving antipsychotic plus another class of medication on cardiovascular and metabolic illness in youth under 18. It is designed as a retrospective cohort study using Medicaid data in a single state (SC), and compares the incidence/prevalence of metabolic, cardiovascular, and cerebrovascular events in a group of youths treated with antipsychotics (n=4140) to a random sample of youth (n=4500) without antipsychotic exposure over a 10 year period. The study compared risks between the exposed and unexposed groups, and then looked at which factors increased the risk of cardiometabolic health problems in both groups. Potential factors examined including gender, ethnicity, age, antipsychotic polypharmacy, and other drug classes prescribed concomitantly with the antipsychotic. Preexisting cardiovascular, cerebrovascular, and metabolic disorders were factored out.
- 42% of individuals youth received **antipsychotic polypharmacy**.
 - The antipsychotic-treated cohort had higher prevalence of **obesity** (OR 2.13), **type 2 diabetes** (OR 3.23), and **cardiovascular conditions** (OR 2.70). The control sample, interestingly, had a higher prevalence of dyslipidemia (OR 3.01) and hypertension (OR 2.35)
 - Odds of **obesity and/or weight gain** were greatest for youth receiving **antipsychotic polypharmacy** (OR 2.28), **polypharmacy including mood stabilizers** (OR 1.78), **polypharmacy including high risk antidepressants** (amitriptyline, nortriptyline, mirtazapine, and paroxetine) (OR 1.66). Female gender (OR 1.75), and for youth ≥ 13 (OR 1.34) were also significant.
 - The odds of developing **Type 2 diabetes** were higher for youth on **antipsychotic polypharmacy** (OR 2.36), **for girls** (OR 1.79), and **youth ≥ 13** (OR 1.52)
 - The mean age of **initiation of antipsychotic treatment was 11.4**; the mean **age of onset of incident type 2 diabetes was 13.8**. Youth taking aripiprazole (Abilify), compared to other psychotropics had significantly longer time to diagnosis of DM (OR 35.92).
 - Odds of **dyslipidemia** were higher for **antipsychotic polypharmacy** (OR 5.26), girls (OR 2.08) and youth ≥ 13 .
 - Hypertension was unrelated to which antipsychotic was used.
 - **Incident cardiovascular conditions** were more likely with the use of **haloperidol** (Haldol)(OR 4.34) and **multiple antipsychotics** (OR 1.57).

3. **Correll CU: Monitoring and management of antipsychotic-related metabolic and endocrine adverse events in pediatric patients.** International Review of Psychiatry 20(2):195-201, 2008
 - Children and adolescents may be more sensitive to antipsychotic-related adverse events than adults.
 - Proactive monitoring and management of antipsychotic-related side effects should be part of clinical practice.
 - It is important to use age-appropriate thresholds for weight and metabolic measures.
4. **Correll CU: Antipsychotic use in children and adolescents: minimizing adverse effects to maximize outcomes.** Journal of the American Academy of Child and Adolescent Psychiatry, 47(1):9-20, 2008
 - This article reviews available data on antipsychotic-related adverse effects and provides a guide for evaluation and management of antipsychotic-related adverse effects in children and adolescents.
 - Antipsychotics are being used in larger and increasing quantities for a wide range of disorders in children (including psychotic, mood, and disruptive behavior disorders), and in adolescents (to treat irritability related to autism, tic disorders, OCD, PTSD, and aggression).
 - Most randomized controlled data for this population is only available for risperidone.
 - The article also has a comprehensive table that provides a comparative overview of side effects profiles for SGAs in children and adolescents, as well as suggested monitoring and management strategies in pediatric patients treated with antipsychotics.
5. **Correll CU, Carlson HE: Endocrine and metabolic adverse effects of psychotropic medications in children and adolescents.** Journal of the American Academy of Child and Adolescent Psychiatry 45:771-793, 2006
 - This is a selective review of endocrine and metabolic effects of psychotropic medications in the pediatric population with a focus on monitoring and management strategies.
 - Children and adolescents are at increased risk than adults for antipsychotic-induced hyperprolactinemia, weight gain, and related metabolic abnormalities.

Guidelines, Consensus Statements, Treatment Recommendations

1. **American Diabetes Association, American Psychiatric Association, American Association of Clinical Endocrinologists: Consensus Development Conference on Antipsychotic Drugs and Obesity and Diabetes.** Journal of Clinical Psychiatry 65(2): 267-272, 2004 Also published in: Diabetes Care 27:596-601, 2004
 - Provides consensus opinion on current use of antipsychotics and prevalence of obesity, pre-diabetes, and diabetes in the SGA population; the relationship between SGAs and obesity and diabetes; and the monitoring of these problems.
 - The prevalence of obesity, diabetes, and dyslipidemia differs depending on SGA.
 - Clozapine and olanzapine are associated with the greatest weight gain and highest occurrence of diabetes and dyslipidemia. Risperidone and quetiapine have discrepant effects. Aripiprazole and ziprasidone have little or no significant weight gain, diabetes, or dyslipidemia.

CATIE (Clinical Antipsychotic Trials of Intervention Effectiveness) Study

1. **Covell NH, Finnerty MT, Essock SM: Implications of CATIE for mental health services researchers.** *Psychiatric Services* 59: 526-29, 2008
 - The implications of CATIE for mental health services researchers are the need to monitor and change prescriber behavior to encourage informed medication selection.
 - The CATIE findings highlight the prevalence of cardiac and metabolic disorders among treatment populations and the potential impact of antipsychotics on these conditions.
 - Services researchers should use secondary data to monitor whether prescribers are providing appropriate screening and treatment.

2. **Meyer JM, Davis VG, Goff DC, et al: Change in metabolic syndrome parameters with antipsychotic treatment in the CATIE schizophrenia trial: prospective data from phase I.** *Schizophrenia Research* 101:272-286, 2008
 - The CATIE results confirm differential metabolic effects between antipsychotics.
 - At three months, metabolic syndrome increased for olanzapine but decreased for ziprasidone. Olanzapine and quetiapine had the greatest increase in waist circumference, followed by risperidone. There was no change in waist circumference for ziprasidone, and there was a decrease with perphenazine.
 - Clinicians should monitor all metabolic parameters (waist circumference, HDL, serum triglycerides), during antipsychotic treatment.

3. **Daumit GL, Goff DC, Meyer JM et al: Antipsychotic effects on estimated 10-year coronary heart disease risk in the CATIE schizophrenia study.** *Schizophrenia Research* 105:175-187, 2008
 - This paper, from Phase 1 of the CATIE trial, followed 1125 patients randomized to different antipsychotics (perphenazine, risperidone, olanzapine, quetiapine; ziprasidone added in 2002) for 18 months or treatment discontinuation. The primary outcome was the change in 10 year CHD risk using the Framingham Heart Study formula. Inputs to the equation include age, total and HDL cholesterol, blood pressure stage, presence of diabetes, presence of smoking. Results were stratified by race and gender.
 - The impact on 10-year CHD risk differs significantly between antipsychotics after only a few months of exposure. In this cohort the differences between drugs is due principally to changes in total and HDL cholesterol.
 - Olanzapine produces the largest increase in CHD risk (0.5%, SE 0.3), followed by quetiapine (0.3%, SE 0.3).
 - Risk for females was 40% lower than for men, due to lower smoking rates and higher HDL.
 - There was a risk interaction between treatment and race. Perphenazine increased HDL in Caucasians and decreased in other races. Ziprasidone decreased HDL in non-whites significantly.
 - For consumers with >10% CHD risk, perphenazine, risperidone, and ziprasidone were beneficial.

4. **Nasrallah HA, Meyer JM, Goff DC, et al: Low rates of treatment for hypertension, dyslipidemia, and diabetes in schizophrenia: data from CATIE.** Schizophrenia Research 86:15-22, 2006
 - At baseline, rates of nontreatment for diabetes, hypertension and dyslipidemia were 30.2%, 62.4%, and 88.0%, respectively.
 - There is a high likelihood that metabolic disorders are not treated in patients with schizophrenia, especially hypertension and dyslipidemia.
 - Nonwhite women may be especially vulnerable to undertreatment of dyslipidemia and diabetes compared to nonwhite men.
5. **Lieberman JA, Stroup TS, McEvoy JP, et al (CATIE investigators): Effectiveness of antipsychotic drugs in patients with chronic schizophrenia.** The New England Journal of Medicine 353(12):1209-23, 2005
 - Olanzapine was most effective, in terms of rates of discontinuation.
 - The efficacy of perphenazine appeared similar to quetiapine, risperidone, and ziprasidone.
 - Olanzapine was associated with greater weight gain and increase in measures of glucose and lipid metabolism.
6. **McEvoy JP, Meyer JM, Goff D, et al: Prevention of the metabolic syndrome in patients with schizophrenia: baseline results from the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) schizophrenia trial and comparison with national estimates from NHANES III.** Schizophrenia Research 80:19-32, 2005
 - Metabolic syndrome is highly prevalent in US schizophrenia patients and represents an enormous source of cardiometabolic risk, especially for women.
 - Clinical attention needs to be given to monitoring for metabolic syndrome and minimizing metabolic risks associated with antipsychotic treatment.
 - In a logistic regression model using age, race and ethnicity as covariates, CATIE males were 138% more likely to have metabolic syndrome than the NHANES matched control. CATIE women were 251% more likely to have metabolic syndrome than NHANES counterparts.
 - Controlling for BMI in the logistic regression model, males were still 85% more likely and females were 137% more likely to have metabolic syndrome than NHANES counterparts.

TEOSS (Treatment of Early Onset Schizophrenia Spectrum Disorders)

1. **Sikich L, Frazier JA, McClellan J, et al: Double-blind comparison of first- and second- generation antipsychotics in early-onset schizophrenia and schizoaffective disorder: findings from the treatment of early-onset schizophrenia spectrum disorders (TEOSS) study.** American Journal of Psychiatry In Advance 1-13, Sept. 15, 2008
 - Risperidone and olanzapine did not demonstrate superior efficacy over molindone for treating early onset schizophrenia and schizoaffective disorder.
 - Adverse effects were frequent and differed among antipsychotics.
 - Olanzapine and risperidone were associated with significantly greater weight gain.
 - Olanzapine showed the greatest risk of weight gain and significant increases in fasting cholesterol, low density lipoprotein, insulin, and liver transaminase levels.
 - These results challenge the nearly exclusive use of SGAs to treat early onset schizophrenia and schizoaffective disorder.

Relevant PSYCKES Papers

1. **Uttaro T, Finnerty M, White T, et al: Reduction of concurrent antipsychotic prescribing practices through the use of PSYCKES. Administration and Policy in Mental Health and Mental Health Services Research 34:57-61, 2007**
 - Psychiatrists at South Beach Psychiatric Center achieved marked decreases in proportion of their caseloads on ≥ 2 concurrent antipsychotics after implementation of PSYCKES.
 - This suggests that PSYCKES was successful in decreasing antipsychotic polypharmacy in inpatients.
2. **Finnerty M, Altmansberger R, Bopp J, et al: Using state administrative and pharmacy data bases to develop a clinical decision support tool for schizophrenia guidelines. Schizophrenia Bulletin 28(1):95-94, 2002**
 - This paper explains and makes a case for how administrative and pharmacy data bases can be used to develop guideline-based clinical decision support tools for the treatment of schizophrenia, that may result in high physician acceptability.