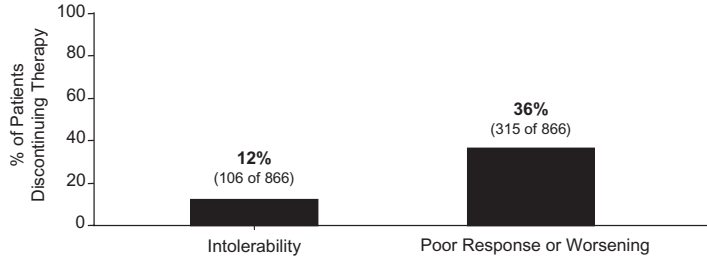


Management of Psychiatric Illness and Medical Comorbidities: Part 2

A Case Study Approach

Reasons for Early Discontinuation from Antipsychotic Therapy^{1,2}



Study Methodology

- 4 randomized, double-blind, actively controlled trials (N=1627, n=866 discontinued)
- Duration of 24 to 28 weeks
- Schizophrenia indication
- Pooled results from all treatment arms

Other Reasons for Discontinuation

- Criteria Not Met (12.12%)
- Lost to Follow-Up (11.89%)
- Patient Decision (19.98%)
- Physician Decision (3.93%)
- Noncompliance (1.96%)
- Sponsor Decision (1.27%)
- Satisfactory Response (0.2%)

1. Liu-Seifert H, et al. *Schizophr Bull.* 2005;31(2):487.
2. Data on file, Lilly Research Laboratories.

Chart #5

Lilly

Diabetes in Patients With Serious Mental Illness Is Not a New Problem

- Rates of type 2 diabetes in schizophrenia are 2-4 times that in the general population¹⁻⁴
- Rates in hospitalized bipolar patients are 2-3 times that in the general population⁵
- The link between schizophrenia and diabetes was first postulated in the 1920s⁶
- A temporal association between first-generation antipsychotic drug treatment and hyperglycemia was first reported in the 1950s⁷

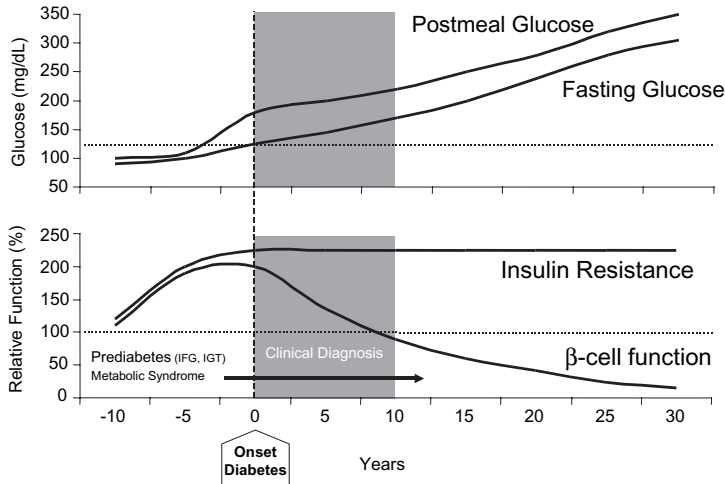
1. Keskiner A, et al. *Psychosomatics*. 1973;14(3):176-181.
2. McKee HA, et al. *J Clin Hosp Pharm*. 1986;11(4):297-299.
3. Mukherjee S. *Schizophr Res*. 1995;15(1-2):195.
4. Mukherjee S, et al. *Compr Psychiatry*. 1996;37(1):68-73.

5. Cassidy F, et al. *Am J Psychiatry*. 1999;156(9):1417-1420.
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Chart #8

Lilly

Natural History of Type 2 Diabetes¹

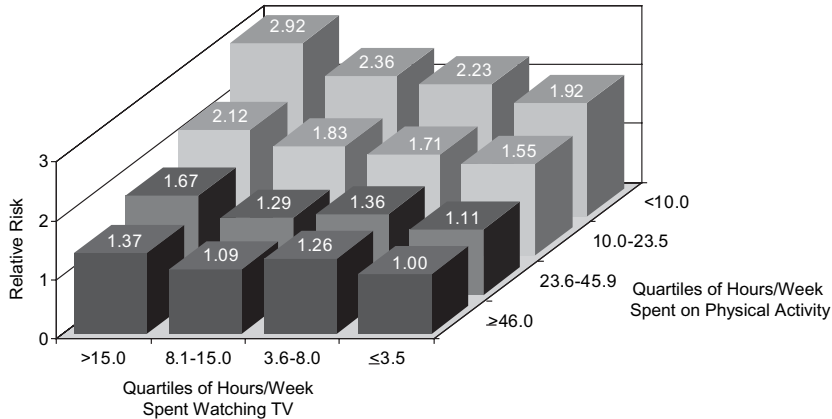


1. Kendall DM, Bergenstal RM. © 2003 International Diabetes Center, Minneapolis, MN. All rights reserved.

Chart #9

Lilly

Sedentary Lifestyle Increases the Risk for Development of Diabetes¹

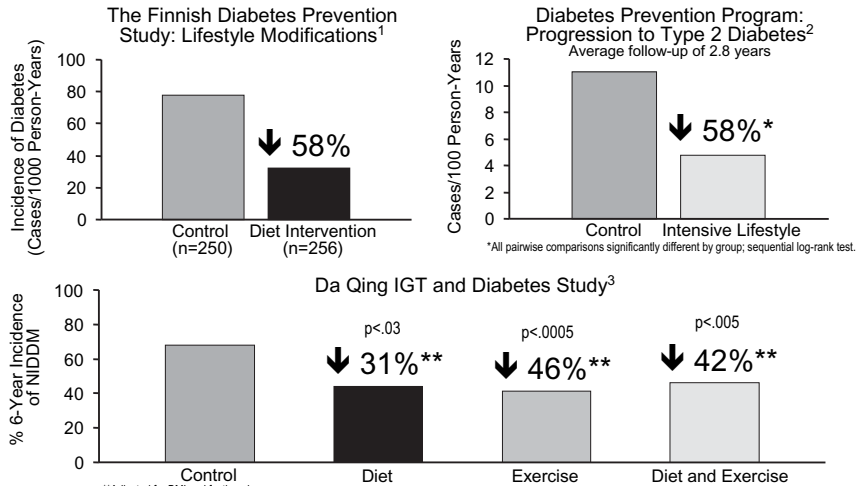


1. Hu FB, et al. *Arch Intern Med.* 2001;161(12):1542-1548.

Chart #16

Lilly

Diabetes Prevention Studies

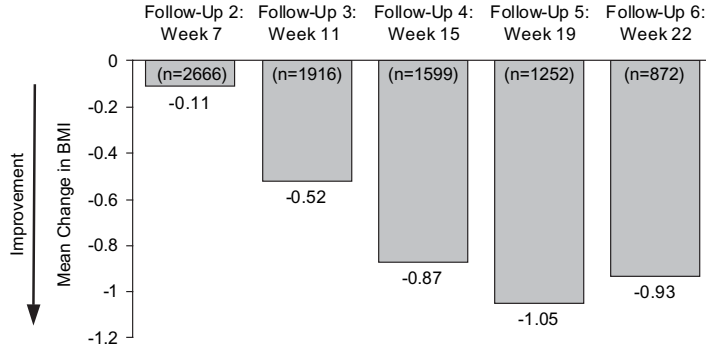


1. Tuomilehto J, et al. *N Engl J Med.* 2001;344(18):1343-1350.
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3. Pan XR, et al. *Diabetes Care.* 1997;20(4):537-544.

Chart #17

Lee

Patients Enrolled in a 24-Week Personalized Wellness Program Lost Weight¹



- Based on changes in weight as reported on returned follow-up surveys
- Individual results may vary

1. Hoffman VP, et al. *J Clin Psychiatry*. In press.

Chart #19

Lilly

Pharmacoepidemiologic Studies of Diabetes and Antipsychotic Medications: Summary of Findings*

- Studies that include nonpsychiatrically ill controls report higher rates of diabetes among patients with psychiatric illness
- The difference in risk of developing diabetes associated with the atypicals vs the conventional antipsychotics is inconsistent; some studies find a difference and others do not
- The difference in risk of developing diabetes among the atypicals is inconsistent; some studies find a difference and others do not

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4. Cavazzoni P, et al. Presented at: International Conference on Pharmacoepidemiology and Therapeutic Risk Management; Aug 22-25, 2004; Bordeaux, France.
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*Colors indicate sponsors of studies: Lilly, BMS, AstraZeneca, Janssen, Novo, independent.

Chart #22



NCEP ATP III Classification of Total Cholesterol, LDL, HDL, and Triglycerides

Total Cholesterol	
<200 mg/dL	Desirable
200-239 mg/dL	Borderline high
≥240 mg/dL	High

Triglycerides	
<150 mg/dL	Normal
150-199 mg/dL	Borderline high
200-499 mg/dL	High
≥500 mg/dL	Very high

LDL Cholesterol ¹	
<100 mg/dL	Optimal
100-129 mg/dL	Near or above optimal
130-159 mg/dL	Borderline high
160-189 mg/dL	High
≥190 mg/dL	Very high
HDL Cholesterol	
<40 mg/dL	Low
≥60 mg/dL	High

1. Adult Treatment Panel III. JAMA 2001;285(19):2486-2497.

Complications of Consistent Blood Sugar Elevation

Measurement	Normal	Impaired Glucose Tolerance (IGT)	Diabetes
Random Glucose	<140 mg/dL	140-199 mg/dL	≥200 mg/dL
Fasting Glucose	<100 mg/dL	100-125 mg/dL	≥126 mg/dL

Long-Term
Blood Sugar
Elevation



Microvascular Complications

Occur in multiple organs as the result of damage to the small blood vessels feeding those organs

- Retinopathy
- Nephropathy
- Peripheral neuropathy
- Autonomic neuropathy

Macrovascular Complications

Can include disease of the arteries/veins in the heart, extremities, and brain

- Heart attack
- Stroke

Other Complications

The condition listed below does not require long-term blood glucose elevation (it is an acute complication)

- Diabetic ketoacidosis (DKA)

Chart #24

Lilly

Additional Published Information for Physicians to Consider

Mt. Sinai Guidelines—“Physical Health Monitoring of Patients With Schizophrenia”

Domain	Level of Evidence	Recommendation
Weight gain	1	<ul style="list-style-type: none"> • Monitor BMI and weight regardless of antipsychotic prescribed • Consider relative risk of weight gain for the different antipsychotics in patients with BMI ≥ 25 • Intervene if BMI increases by 1 kg/m² (unless baseline BMI <18.5) • Monitor waist circumference; intervene if circumference ≥ 35 inches (female) or ≥ 40 inches (male) • Interventions include: closer monitoring, weight management program, adjunctive medication, switch antipsychotic
Diabetes	2	<ul style="list-style-type: none"> • All patients: assess fasting blood glucose (FBG) or HgbA1C at baseline • Patients with baseline risk factors: FBG or HgbA1C 4 months after initiation, then yearly • Patients currently gaining weight: FBG or HgbA1C every 4 months • Monitor for and inform patients of symptoms of diabetes • FBG levels between 100 mg/dL and 125 mg/dL are indicative of prediabetes and should prompt closer assessment and follow-up • FBG ≥ 126 mg/dL, random blood glucose >200 mg/dL, or HgbA1C value $>6.1\%$ suggests the possibility of diabetes and should lead to consultation with an internist or other primary care provider
Hyperlipidemia	2	<ul style="list-style-type: none"> • Follow NCEP guidelines • Obtain baseline lipid panel (total cholesterol, LDL, HDL, and triglycerides) for all patients • Obtain lipid panel every 2 years (if LDL is normal) or every 6 months (if LDL >130) • Refer patient to primary care provider or internist if LDL >130 or if patient meets criteria of metabolic syndrome

Marder SR, et al. *Am J Psychiatry*. 2004;161(8):1334-1349.

Level 1 evidence: clear evidence from multiple randomized controlled trials.

Level 2 evidence: data from cohort studies, outcomes research, or low quality randomized controlled studies.

Level 3 evidence: data from case-control studies.

Chart #25

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Additional Published Information for Physicians to Consider (*cont*)

Mt. Sinai Guidelines—“Physical Health Monitoring of Patients With Schizophrenia”

Domain	Level of Evidence	Recommendation
QTc prolongation	1	<ul style="list-style-type: none"> • Don't prescribe mesoridazine, pimozide, or thioridazine in high-risk patients • Obtain baseline ECG before treatment with ziprasidone initiated; subsequent ECG if symptoms develop
Elevated prolactin and sexual side effects	1	<ul style="list-style-type: none"> • Assess patients for clinical symptoms (before beginning treatment and subsequently if receiving non prolactin-sparing medication) • Measure plasma prolactin levels if clinically indicated • Consider switch to prolactin-sparing agent if patient symptomatic and receiving a prolactin-elevating medication
EPS, akathisia, and TD	1	<ul style="list-style-type: none"> • Assess patients for movement disorders at baseline and weekly until stable and after dose increase • Evaluate for TD every 6 months (conventionals) or annually (atypicals) • If patient is at high risk for EPS (ie, elderly), evaluate for TD every 3 months (conventionals) or every 6 months (atypicals)
Cataracts	Not graded	<ul style="list-style-type: none"> • Monitor for visual changes • Ocular evaluations annually in patients over 40, every two years in patients under 40 years old
Myocarditis in patients taking clozapine	3	<ul style="list-style-type: none"> • Health care provider (HCP) should know and monitor for signs and symptoms of myocarditis: fatigue, dyspnea, tachypnea, fever, chest pain, palpitations, other signs or symptoms of heart failure, ECG abnormalities • If myocarditis is suspected, the HCP should obtain a WBC and a plasma troponin level • If myocarditis is identified, clozapine should be stopped and the patient should be urgently evaluated by a primary care provider

Marder SR, et al. *Am J Psychiatry*. 2004;161(8):1334-1349.

Chart #26

Levy

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