

# **Cardiometabolic Risk Factors and Antipsychotic Medications**

**Changing Prescribing Practices  
Promoting Wellness**

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# Cardiometabolic Indicator

## ■ Focus:

- Clients who have at least one cardiometabolic risk factor  
*and*
- are on a high or moderate risk antipsychotic or are considering starting one

## ■ Cardiometabolic Risk Factors:

- Type 2 Diabetes
- Hypertension
- High Triglycerides/Low HDL (high-density lipoprotein)
- Obesity
- Preexisting Cardiovascular Disease

# Antipsychotics Classified by Risk: Adults

High / Moderate Risk	Lower Risk
<b>Olanzapine</b> (Zyprexa) <b>Quetiapine</b> (Seroquel) <b>Chlorpromazine</b> (Thorazine) <b>Thioridazine</b> (Mellaril)	<b>Aripiprazole</b> (Abilify) <b>Paliperidone</b> (Invega) <b>Risperidone</b> (Risperdal) <b>Ziprasidone</b> (Geodon) <b>All other first generation antipsychotics.</b>

# Antipsychotics Classified by Risk: Youth

High/ Moderate Risk	Lower Risk
<p><b>Olanzapine (Zyprexa)</b> <b>Quetiapine (Seroquel)</b> <b>Paliperidone (Invega)</b> <b>Risperidone (Risperdal)</b> <b>All first generation antipsychotics except molindone (Moban)</b></p>	<p><b>Aripiprazole (Abilify)</b> <b>Ziprasidone (Geodon)</b> <b>Molindone (Moban)</b></p>

# Scope of the Problem

*In the general population:*

- 68% of adults overweight or obese
- 31% of children overweight or obese
- Obesity doubles mortality rates
- Medical costs: \$1500 more per year for obese persons
- 10% of all adults have Type 2 diabetes, and 23% over 60 have it.
- DM (diabetes mellitus) doubles mortality risk
- Medical costs: \$2257 more per year for people with DM. \$1 out of \$10 health care dollars spent for DM; \$174 billion in 2009.

# The Metabolic Syndrome:

## 3 out of 5 risk factors

- Criteria:
  - Hypertension
  - Hyperlipidemia
  - Low HDL (good cholesterol)
  - Obesity (waist circumference or BMI)
  - Type 2 Diabetes
- People who have Metabolic Syndrome have double the risk of developing cardiovascular disease.
- 10-20% of the general population in the US have Metabolic Syndrome.

# Criteria for the Metabolic Syndrome\*

Criterion	Adults	Adolescents
High triglyceride level, mg/dl	≥150 mg/dl fasting	≥110 mg/dl fasting
Low HDL-Chol level, mg/dl Males Females	<40 mg/dl fasting <50 mg/dl fasting	≤40 mg/dl fasting for boys and girls
Abdominal obesity, waist circumference Males Females	> 40 inches > 35 inches	≥90 <sup>th</sup> percentile for boys and girls
High fasting glucose level, mg/dl	≥110 mg/dl	≥110 mg/dl
High blood pressure, mm HG	≥ 130/85 mmHg	≥90 <sup>th</sup> percentile for boys and girls

*Cook S, Weitzman M, Auinger P, et al. Prevalence of a metabolic syndrome phenotype in adolescents: findings from the third National Health and Nutrition Examination Survey, 1988–1994. Arch Pediatr Adolesc Med 2003;157(8):821 – 7.*

\* At least three criteria must be met

# ADA Consensus Monitoring Protocol for Individuals on SGAs

	Start	4 wks	8 wks	12 wks	Every 3 mos.	Every 12 mos.	Every 5 yrs.
<b>History</b>	X					X	
<b>Weight (BMI)</b>	X	X	X	X	X		
<b>Waist circumference</b>	X					X	
<b>Blood pressure</b>	X			X		X	
<b>Fasting glucose</b>	X			X		X	
<b>Fasting lipids</b>	X			X			X

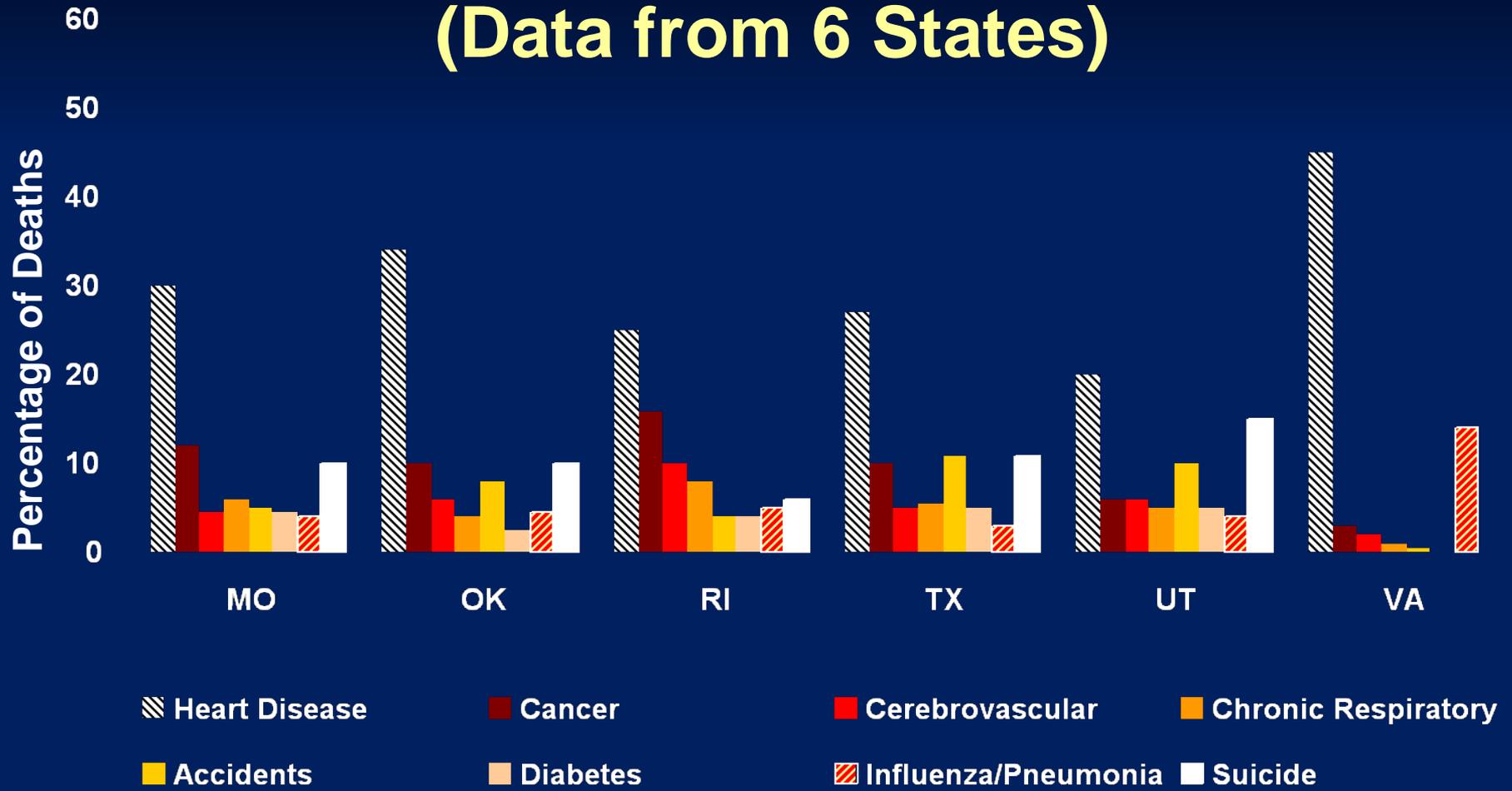
# Metabolic Syndrome in People with Mental Illness

- People with serious and persistent mental illness (SPMI) die 25 years earlier than the general population! 60% of the increased mortality is due to cardiovascular disease.
- In NYS, Type 2 diabetes is twice as common in people with mental illness on Medicaid compared to the general Medicaid population.
- In a study of over 10,000 clients with depression, schizophrenia or depression, 52% had metabolic syndrome, and 92% had at least one risk factor
- 43% of clinical antipsychotic trials of intervention effectiveness (CATIE) participants had metabolic syndrome on enrollment.

# Cardiometabolic Risk and Prescription of High/Moderate Risk Antipsychotics in New York State

- 46.24% of consumers with cardiometabolic risk factors who are also on antipsychotic medications take ***high-to moderate-risk antipsychotics***

# Cardiovascular Disease is Primary Cause of Death in Persons with Mental Illness (Data from 6 States)



Colton CW, Manderscheid RW. Congruencies in increased mortality rates, years of potential life lost, and causes of death among public mental health clients in eight states. *Prev Chronic Dis* [serial online] 2006 Apr [Apr 10, 2009]. Available from: URL: <http://www.cdc.gov/pcd/issues/2006/>

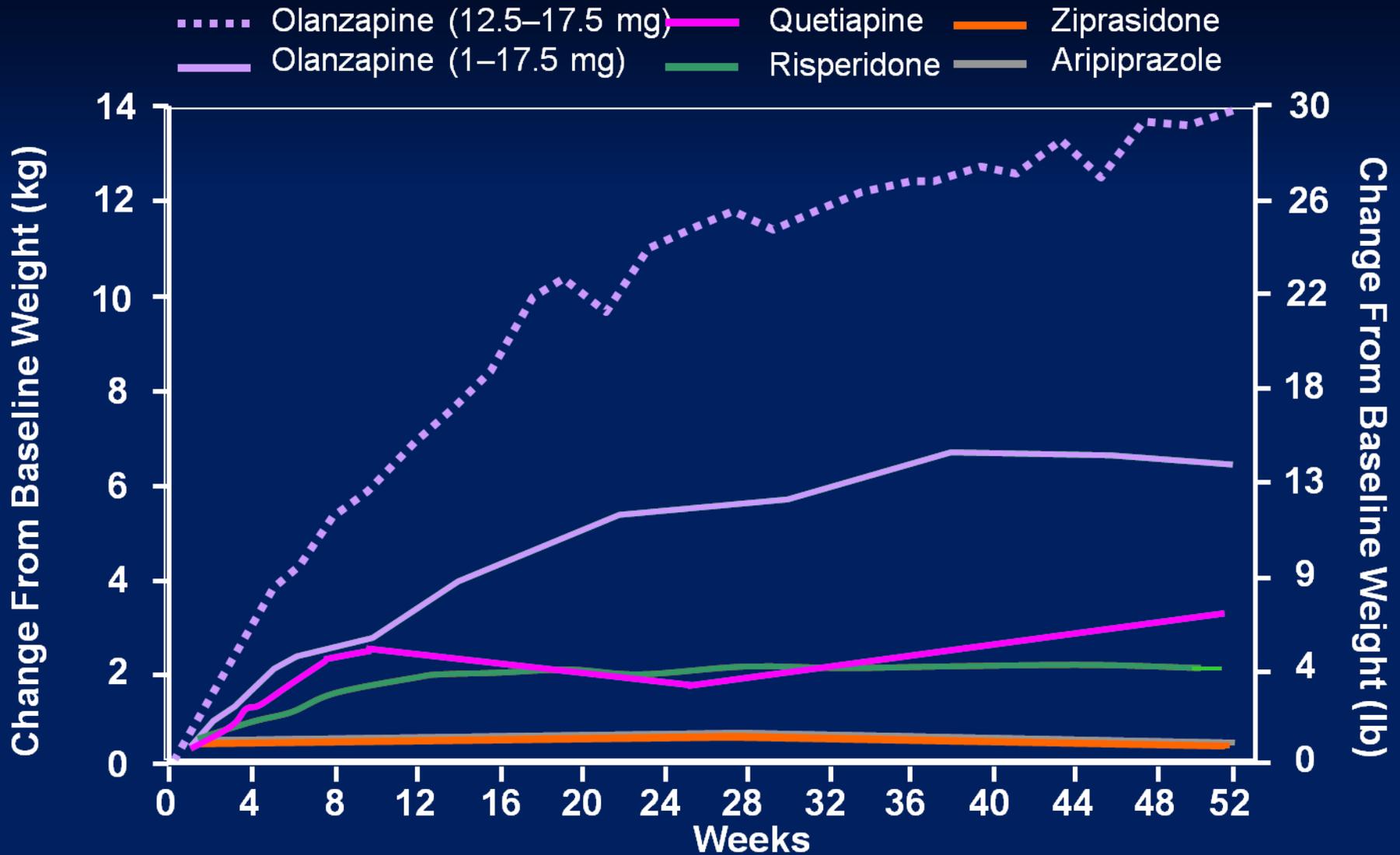
# Cardiometabolic Risk is Modifiable

- Smoking cessation
- Diet changes: portion control, less fat, less glucose
- Increased physical activity
- Routine medical care

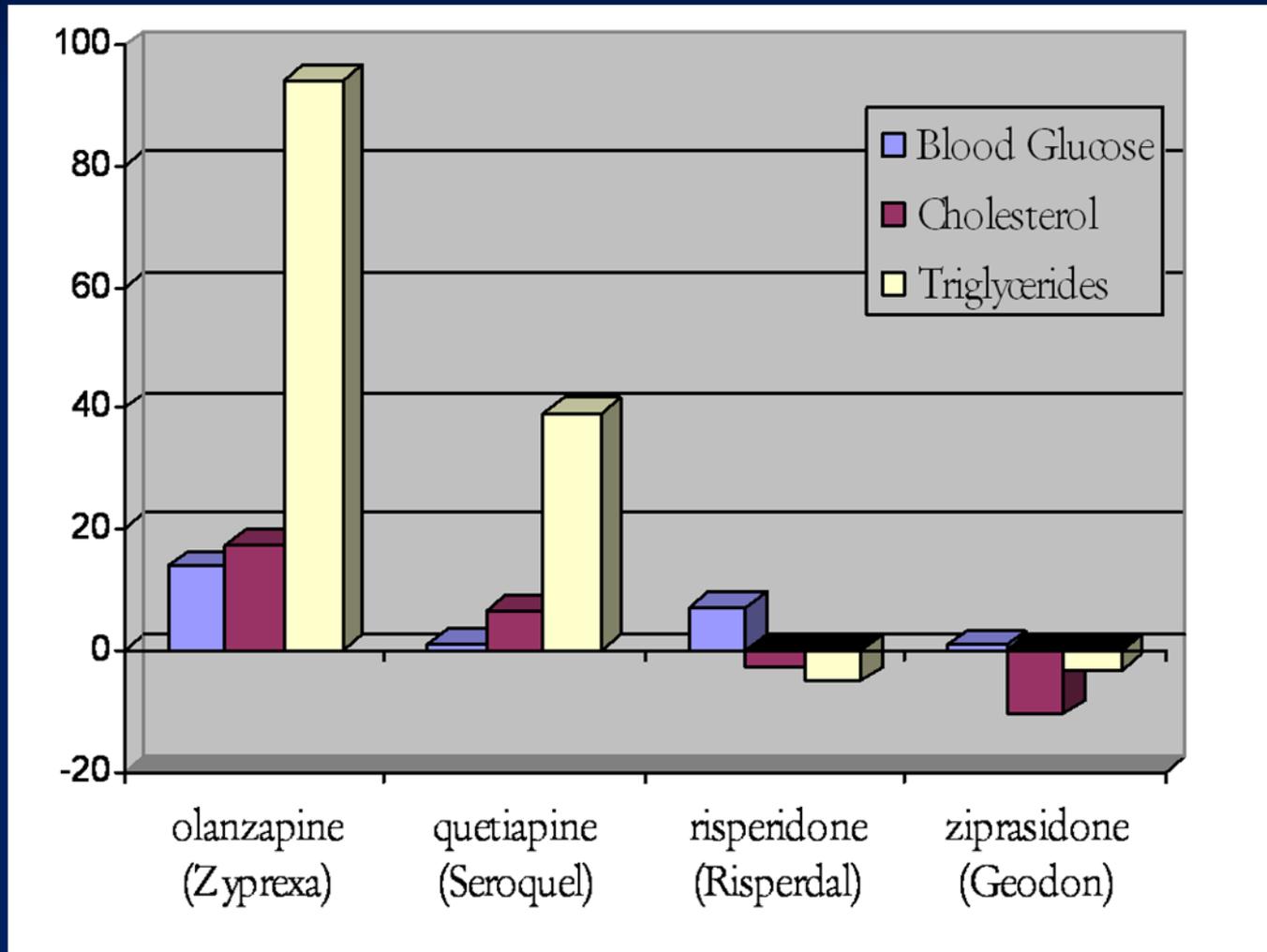
*and*

- **Choice of antipsychotic medication**

# Differential Impact of Antipsychotics on Weight



# Impact of Different Antipsychotics on Metabolic Measures



# Cardiometabolic Risk of Second-Generation Antipsychotic Medication During First-Time Use in Children and Adolescents

**Table 2.** Change in Body Composition Parameters Over Time

Outcome Variable	Weeks 0-12	
	Mean (95% CI)	P Value
Weight, kg		
Aripiprazole	4.44 (3.71 to 5.18)	<.001
Olanzapine	8.54 (7.38 to 9.69)	<.001
Quetiapine	6.06 (4.90 to 7.21)	<.001
Risperidone	5.34 (4.81 to 5.87)	<.001
Untreated	0.19 (-1.04 to 1.43)	.77

## Significant Changes in Metabolic Parameters Over Time

	Total Cholesterol (mg/dl)	Triglycerides (mg/dl)	Non-HDL Cholesterol (mg/dl)	TG:HDL Ratio
Olanzapine	15.58	24.34	16.81	0.59
Quetiapine	9.05	36.96	9.93	1.22
Risperidone	NS	9.74	NS	NS
Aripiprazole	NS	NS	NS	NS

# Uses for SGAPs with RCT evidence

## On Label

- Schizophrenia
- Schizoaffective Disorder
- Bipolar Mania
- Bipolar Depression
- Bipolar Maintenance
- Major Depressive Disorder
- Autism with irritability

## Off Label

- PTSD (Post Traumatic Stress Disorder)
- OCD (Obsessive Compulsive Disorder)
- Generalized Anxiety Disorder
- Borderline Personality Disorder
- Behavioral dysregulation in children, adults, elderly, disabled

**aripiprazole, asenapine, iloperidone, lurasidone, olanzapine, paliperidone, quetiapine, risperidone, ziprasidone**

# Use of Quetiapine Contributes to Polypharmacy and Cardiometabolic Risk

- Statewide, 40% of individuals flagged for polypharmacy and 71% of those flagged for cardiometabolic risk are on quetiapine (PSYCKES, 10/1/2010).
- Low dose quetiapine for sleep is often added to psychotropic regimens, despite lack of evidence supporting its efficacy.\*
- Weight gain risk is not dose-dependent, and occurs at even low doses.

\*Wine JN et al. Effects of quetiapine on sleep in nonpsychiatric and psychiatric conditions. *The Annals of Pharmacother* 2009;43:707-13.

\*\*Cates ME et al. Metabolic consequences of using low-dose quetiapine for insomnia in psychiatric patients. *Community Ment Health J* 2009;45:251-254.

# FDA Panel Issues Mixed Decision on Quetiapine in Depression and Anxiety

“A new formulation of extended-release quetiapine, an atypical antipsychotic medication, should not be approved as monotherapy for major depressive disorder and generalized anxiety disorder because of serious cardiac and metabolic adverse events associated with the drug, according to an advisory panel to the FDA. The panel, however, voted in favor of approving more limited use of quetiapine as an adjunctive therapy in treatment-refractory depression.”

“The panel found quetiapine to be acceptably safe for adjunctive use in depression (by a vote of 6 to 3) and that the decision was not precedent-setting because the agency had previously approved the antipsychotic agent aripiprazole for such use. However, the long-term risk of patients developing metabolic syndrome and, to a lesser extent, the short-term risk of sudden cardiac death weighed heavily in the panel’s unanimous decision against recommending use of this drug as monotherapy in a wider population when other less risky drugs are available.”

**JAMA, May 27, 2009**

# Zyprexa (olanzapine): Use in Adolescents (from the FDA)

- Lilly and FDA notified healthcare professionals of changes to the Prescribing Information for Zyprexa related to its **indication for use in adolescents (ages 13-17)** for treatment of schizophrenia and bipolar I disorder . The revised labeling states that:
- Section 1, Indications and Usage: When deciding among the alternative treatments available for adolescents, clinicians should **consider the increased potential (in adolescents as compared with adults) for weight gain and hyperlipidemia**. Clinicians should consider the potential long-term risks when prescribing to adolescents, and in many cases this may lead them to **consider prescribing other drugs first** in adolescents.
- Section 17.14, **Need for comprehensive Treatment Program in Pediatric Patients:** Zyprexa is indicated as an integral part of a total treatment program for pediatric patients with schizophrenia and bipolar disorder that may include other measures (psychological, educational, social) for patients with the disorder. Effectiveness and safety of ZYPREXA have not been established in pediatric patients less than 13 years of age.

FDA January 29, 2010

# Evidence: Effects of Switching on Metabolic Parameters

- **Simpson 2004:** RCT (randomized controlled trial) comparison of olanzapine (Zyprexa) vs. ziprasidone (Geodon) in clients with schizophrenia spectrum disorder. Olanzapine caused substantially more weight gain, increase in body mass index (BMI), low-density lipoprotein (LDL), triglycerides and insulin ziprasidone.
- **Meyer J 2005:** RCT switching clients with schizophrenia spectrum disorder who had metabolic abnormality or lack of response from olanzapine (Zyprexa)→risperidone (Risperdal) with or without cognitive behavioral therapy (CBT) for weight loss: Both switch groups had significant decrease in prevalence of metabolic syndrome.

# Evidence: Effects of Switching on Metabolic Parameters, Continued

- **Newcomer 2008:** RCT for clients with schizophrenia spectrum disorder to stay on olanzapine or switch to aripiprazole for 16 weeks. Clients who switched had more weight loss, less weight gain, decrease in triglycerides, increase HDL. There was no difference in glycemic measures between agents. Clinical global impression (CGI) lower in olanzapine (3.09) than aripiprazole (3.74)
- **DeHert 2010:** Case series of clients switched to aripiprazole (Abilify) after developing diabetes mellitus (DM) resulted in resolution of DM.

# Medication is the last line treatment for insomnia! Diagnose and treat the problem!

## Medical Considerations

- Obstructive sleep apnea
- Restless leg syndrome
- Periodic limb movement disorder
- Pain
- Thyroid status
- Neuropathies
- Thermal regulation (socks!)
- Respiratory problems

## Psychological Considerations

- Use of electronics or TV right before trying to sleep
- Timing and type of food intake
- Timing and type of exercise
- Pets
- Anxious ruminations
- Fear of sleep/hypervigilance
- Alcohol use
- Smoking
- Noise and light
- Bedding issues
- Partner issues

# Ideas for Smarter Prescribing

1. Expand medical history taking to include more detail about family risk, including age of onset of cardiovascular disease as well as mortality.
2. Ask about weight gain history to determine trajectory. Ask about weight loss efforts and feelings about weight. Have a scale in the office.

# Ideas for Smarter Prescribing, Continued

3. Connect the dots between symptoms & complaints and function. What really matters most to the consumer?
4. Determine the primary diagnosis, and in people with complex disorders consider the hierarchy. Focus pharmacologic treatment on the primary diagnosis.
5. Explain to consumers what medications can and can't do. Build realistic expectations.

# Ideas for Smarter Prescribing, Continued

6. Treat as many symptoms as possible non-pharmacologically. Consider CBT for anxiety or sleep. If your clinic doesn't have therapist trained in these modalities, bug your clinic director to add these services. Using psychosocial treatments builds on consumer's strengths and capacity as they progress in recovery.

# Case #1

John is a 34 year old single man, intermittently employed in seasonal forestry and naturalist jobs, who had his first psychotic mania at age 18, after being diagnosed with Attention Deficit Hyperactivity Disorder (ADHD) and Generalized Anxiety Disorder (GAD) in grade school. He initially had 2-3 years between episodes, but for the last 10 years has had at least one psychotic mania/year and at least one depressive bout. He was initially on Lithium and Risperdal until he “broke through” this regimen. He is now on Depakote 2000 mg (level=108) and Zyprexa 10 mg. He has had a 30 lb weight gain, stable for the past 3 years, and has developed hypertension. Father had an MI at age 58. Despite his illness he has been able to obtain a Master’s degree in environmental conservation, and plans to start a Ph.D. He always feels moderately functionally impaired by his illness. On interview he is often slightly pressured and a bit grandiose.

## Case #2

Jane is a 42 year old married mother of 3 children; she is overweight, and has DM and hypertension. She has had depression since age 15, partially responsive to medication. Depression is severe now despite 120 mg of cymbalta and she is often unable to function. Sleep is poor. Her spouse is a physically and verbally abusive alcoholic; she also grew up in an abusive home. She endorses frequent NM, feeling numb, and high levels of fear and anxiety most of the time, with frequent panic attacks. She sometimes hears a male voice telling her she is worthless and deserves to die; AH worsen when she has to spend time with her family of origin.

## Case #3

Jim is a 43 year old married father of 2 who works in IT. He has had OCD, GAD, and ADHD since he was a small child and has taken a number of medications with partial response; he is currently on fluoxetine 60 mg/d and Adderall XR 20 mg/d. Over the past 2 years he has developed depressive symptoms and has had problems with anger attacks. His recent evaluation at work was poor. He's having trouble sleeping, with mental rituals keeping him up for hours. He doesn't like to talk about himself and hasn't participated in psychotherapy since his teens. He has high blood pressure; his father died from a heart attack at 38.

# Questions?

