



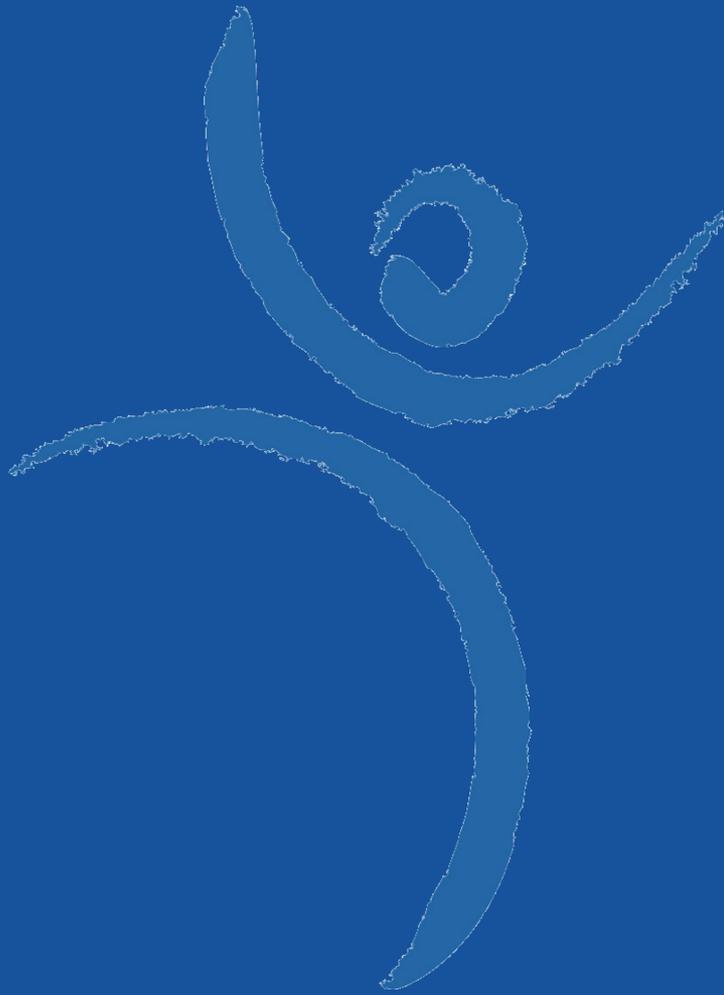
Safe Medication Use as an Essential Component of Wellness Among People with Mental Health Problems

JULY 20, 2010



Disclaimer

The views expressed in this training event do not necessarily represent the views, policies, and positions of the Center for Mental Health Services (CMHS), Substance Abuse and Mental Health Services Administration (SAMHSA), U.S. Food and Drug Administration (FDA), the National Institutes of Health (NIH), or the U.S. Department of Health and Human Services.



FOCUS ON ATYPICAL ANTIPSYCHOTICS, HEALTH COMPLICATIONS, AND POLYPHARMACY

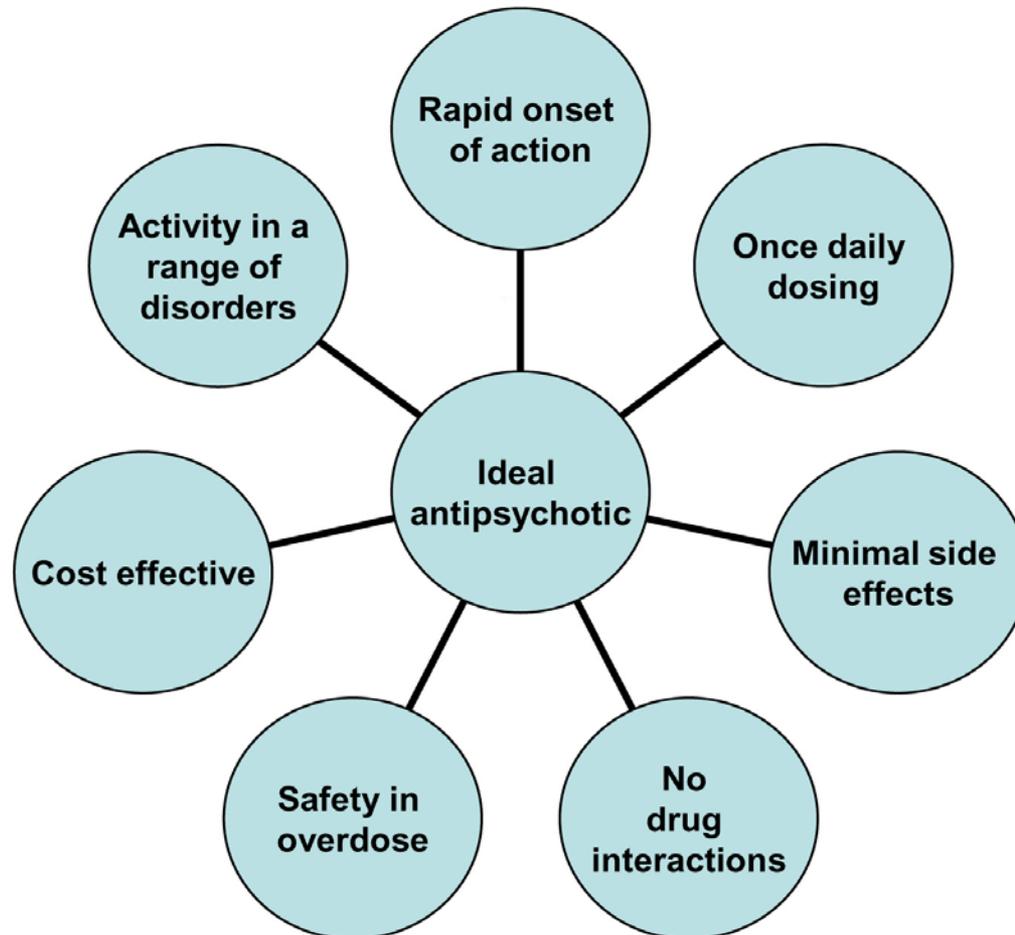
Jerry Overman, Pharm.D.,
B.C.P.P.

Clinical Pharmacy Specialist
National Institutes of Health

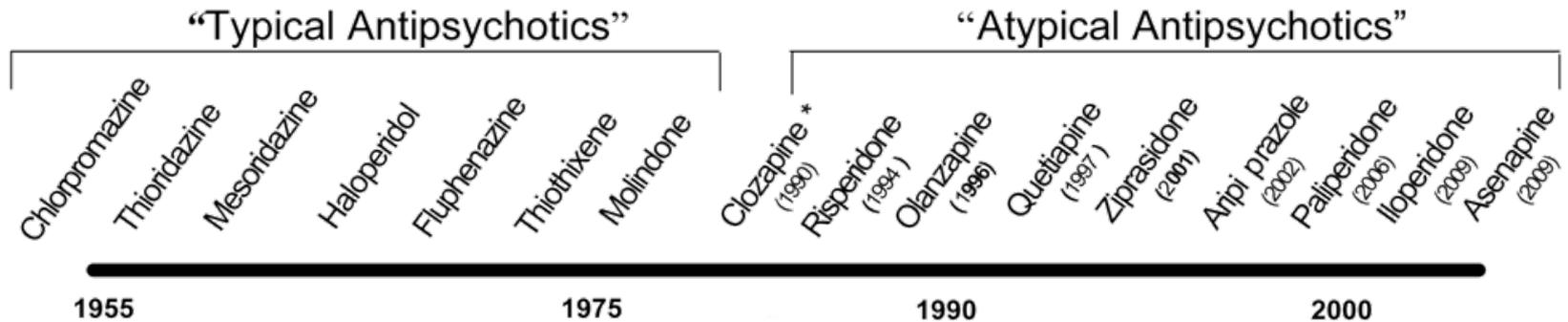
What is Polypharmacy and Why do We Care?

- **Polypharmacy vs. rational polypharmacy:**
 - Increased risk of medication related side effects
 - Increased risk of drug interactions
 - Long term risks remain largely unknown
 - Increased risk with decrease in coordinated care

Ideal Antipsychotic



Antipsychotic Drugs: Development Timeline

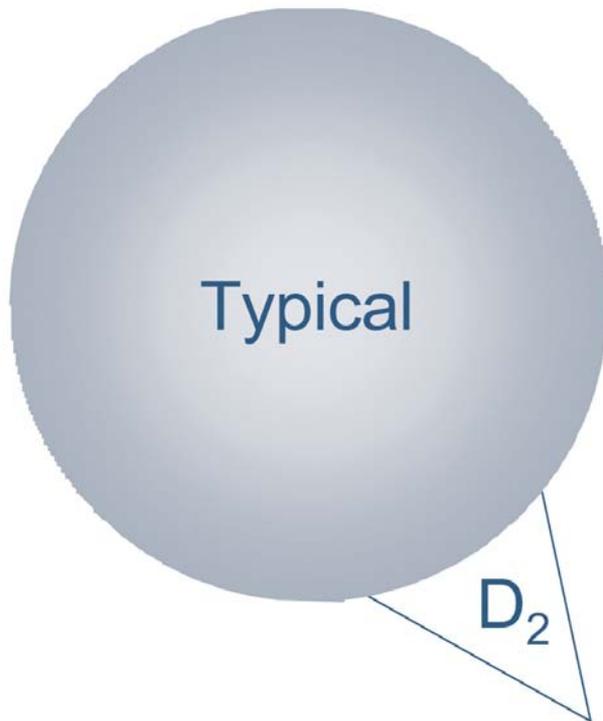


- Minimal efficacy with regard to positive symptoms in 20-30 percent of patients
- Much weaker effect on negative symptoms than positive symptoms
- Significant parkinsonian symptoms and anticholinergic effects (poor compliance and potentially disabling)
- Tardive dyskinesia in a minimum of 20 percent of patients who receive chronic neuroleptic treatment. Cumulative incidence five percent per year of exposure.

- At least as effective as typical neuroleptics with regard to positive symptoms
- More effective than typical agents with regard to negative symptoms
- Lower incidence of parkinsonian symptoms and anticholinergic effects than typical agents
- TD does occur but at much lower incidence
- Elevated risk of metabolic side effects

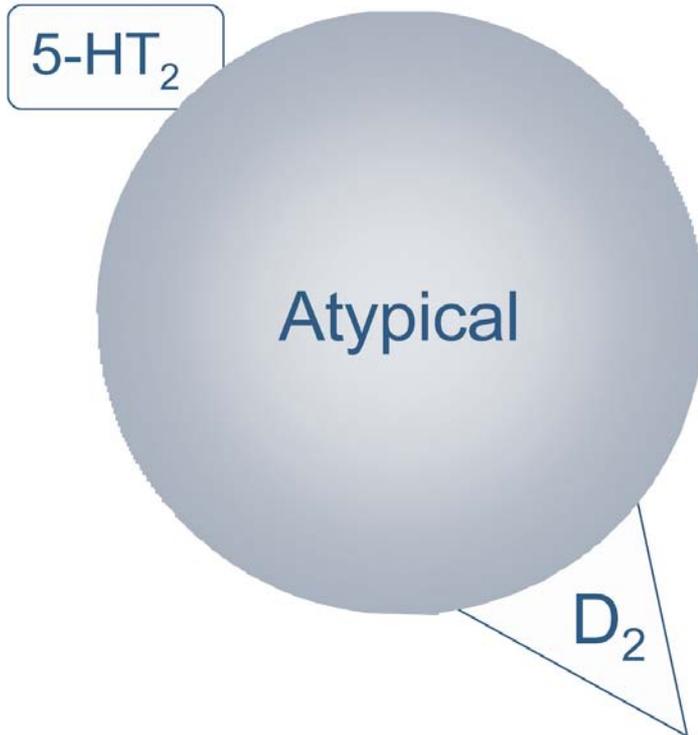
**1-2 percent incidence of agranulocytosis; CBC monitoring required by FDA*

Typical Antipsychotics (the older agents)



- Examples:
 - Chlorpromazine (Thorazine[®])
 - Thioridazine (Mellaril[®])
 - Mesoridazine (Serentil[®])
 - Haloperidol (Haldol[®])
 - Fluphenazine (Prolixin[®])
 - Thiothixene (Navane[®])
 - Molindone (Moban[®])

Atypical Antipsychotics (the newer agents)



- Examples:
 - Clozapine (Clozaril[®])
 - Olanzapine (Zyprexa[®])
 - Risperidone (Risperdal[®])
 - Quetiapine (Seroquel[®])
 - Aripiprazole (Abilify[®])
 - Ziprasidone (Geodon[®])
 - Paliperidone (Invega[®])
 - Asenapine (Saphris[®])
 - Iloperidone (Fanapt[®])

Adverse Effects of Receptor Blockade

RECEPTOR	ASSOCIATED ADVERSE EFFECTS
Dopaminergic(D ₂)	EPS, prolactin elevation
Histaminergic (H ₁)	Sedation, weight gain
Muscarinic (M ₁)	Dry mouth, urinary retention, blurred vision, constipation, sinus tachycardia, cognition and memory problems
α_1 -adrenergic	Orthostatic hypotension, reflex tachycardia, sexual dysfunction

The Old Concerns and the New Ones in Schizophrenia Management

ISSUE	OLD ERA	NEW ERA
EPS	Major patient tolerability issues, effects on medication compliance	Infrequent Not major concerns
Tardive dyskinesia	Major long-term risk	Seems rare Not major concern
Social, cognitive, and vocational efficacy	Disappointment Accepted	New hope and expectations
Negative symptoms and refractory patients	Disappointment Accepted	New hope and expectations
Poor patient adherence	Common	Expected improvement

The Old Concerns and the New Ones in Schizophrenia Management

ISSUE	OLD ERA	NEW ERA
Cardiovascular health	Not on the radar screen	Major public health issue
Glucose and lipid problems	Not on the radar screen	Major public health issue
Weight gain	Never thought of	Major public health concern
Cognitive dysfunction	Lack of progress Accepted	New hope for improvement
Depression	Assumed to be part of the illness	New hope and expectations

Identification of Metabolic Syndrome

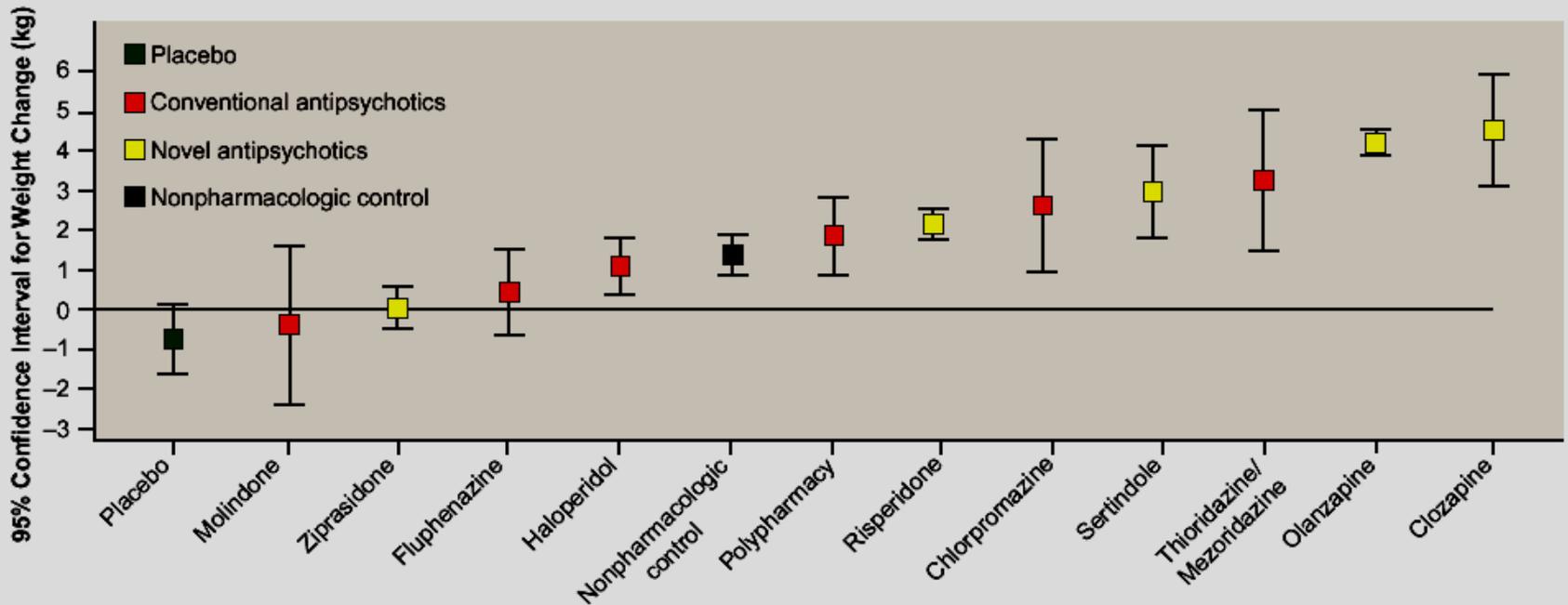
≥ 3 RISK FACTORS REQUIRED FOR DIAGNOSIS

Risk Factor	Defining Level
Abdominal obesity Men Women	Waist circumference >40 in >35 in
Triglycerides	≥150 mg/dL
HDL cholesterol Men Women	<40 mg/dL <50 mg/dL
Blood pressure	130/85 mmHg
Fasting blood glucose	≥100 mg/dL

HDL = high density lipoprotein; BP = Blood pressure
NCEP III (2002). *Circulation*, 106:3143-3421

Atypical Antipsychotics: Clinically Significant Weight Gain

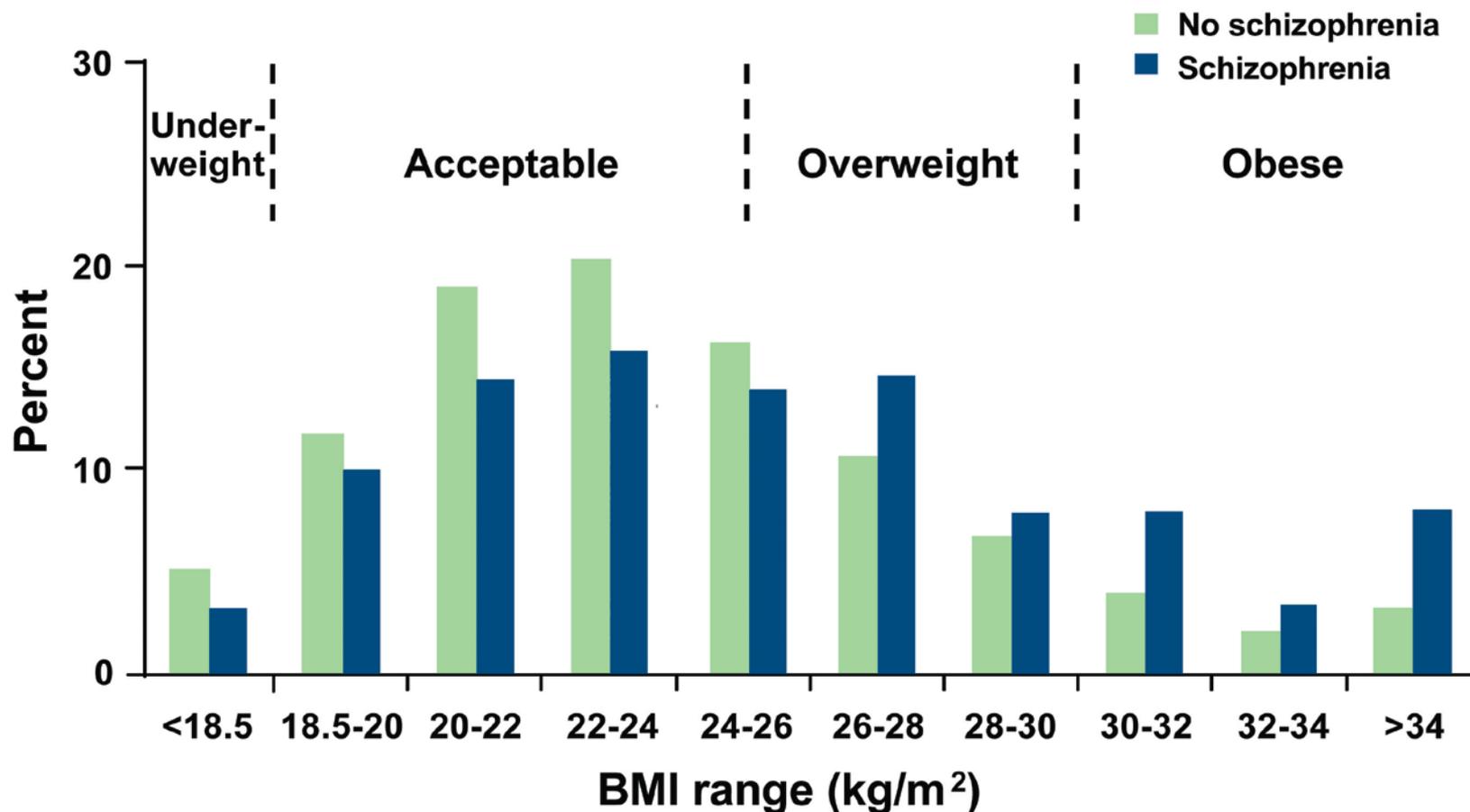
FIGURE 1. 95% Confidence Intervals for Weight Change After 10 Weeks on Standard Drug Doses, Estimated From a Random Effects Model



Body Mass Index

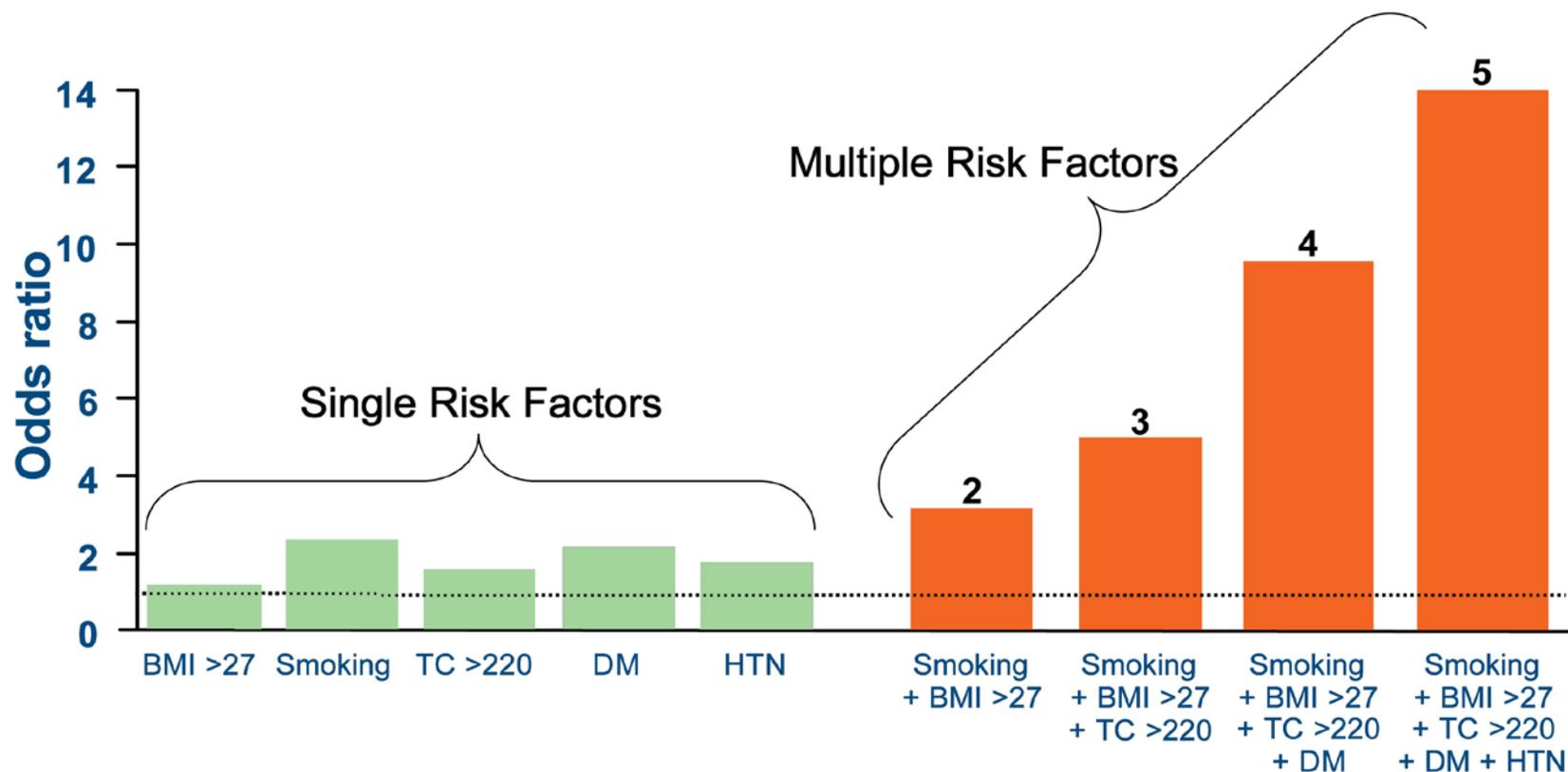
- Is a measure of body fat based on height and weight that applies to both adult men and women
- To calculate: Weight in kilograms/height in meters²
 - Underweight = <18.5
 - Normal weight = 18.5–24.9
 - Overweight = 25–29.9
 - Obesity = 30 or greater

BMI Distributions in General Population and in Patients with Schizophrenia



Allison et al. (1999). *J Clin Psychiatry*, 60:215.

Risk Factors for Heart Disease in the General Population



BMI = body mass index (kg/m²); TC = total cholesterol (mg/dL); DM = diabetes mellitus; HTN = hypertension.

Wilson et al. (1998). *Circulation*, 97:1837.

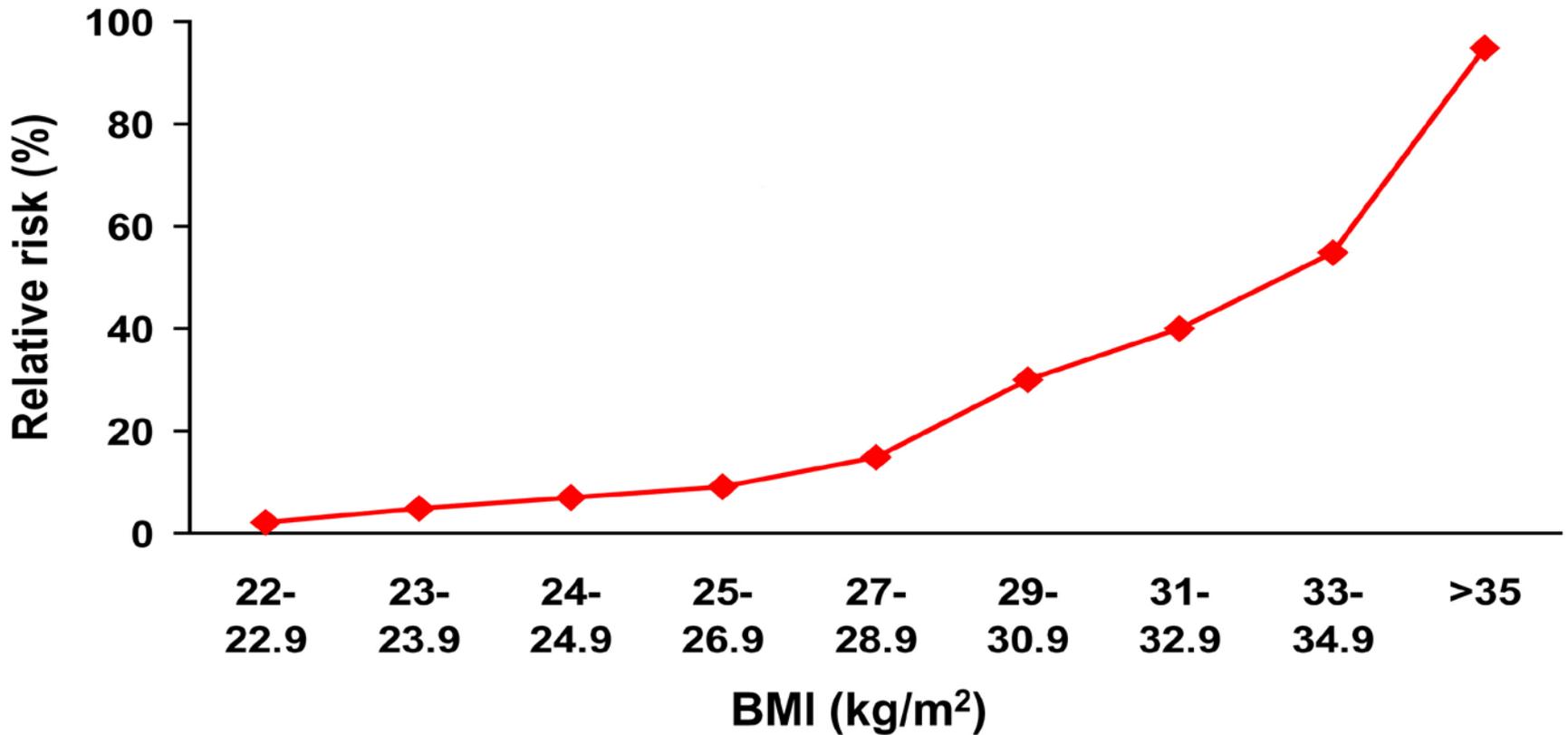
Schizophrenia and Diabetes

- Prevalence of adult-onset diabetes in schizophrenia populations is about 13 percent¹
- Increased risk for diabetes predates arrival of antipsychotics^{1,2}

1. Dixon et al. (2000). *Schizophr Bull*, 26:903.

2. Newcomer et al. (2002). *Arch Gen Psychiatry*, 59:337.

Body Mass Index and Diabetes Risk



Hyperglycemia/Diabetes

Drug	Weight Gain	Risk for Diabetes	Worsening Lipid Profile
Clozapine	+++	+	+
Olanzapine	+++	+	+
Risperidone	++	D	D
Quetiapine	++	D	D
Aripiprazole*	+/-	-	-
Ziprasidone*	+/-	-	-

+ = increase effect - = no effect D = discrepant results

* newer drugs with limited long-term data

Monitoring for Metabolic Syndrome

	Baseline	4 weeks	8 weeks	12 weeks	Quarterly	Annually	Every 5 years
Personal/ family history	X					X	
Weight (BMI)	X	X	X	X	X		
Waist circum- ference	X					X	
Blood pressure	X			X		X	
Fasting plasma glucose	X			X		X	
Fasting lipid profile	X			X			X



**SAFE USE:
COLLABORATING TO
REDUCE
PREVENTABLE HARM
FROM MEDICATIONS**

**Karen D. Weiss, M.D., M.P.H.
Associate Director for Medical
Affairs FDA/CDER**

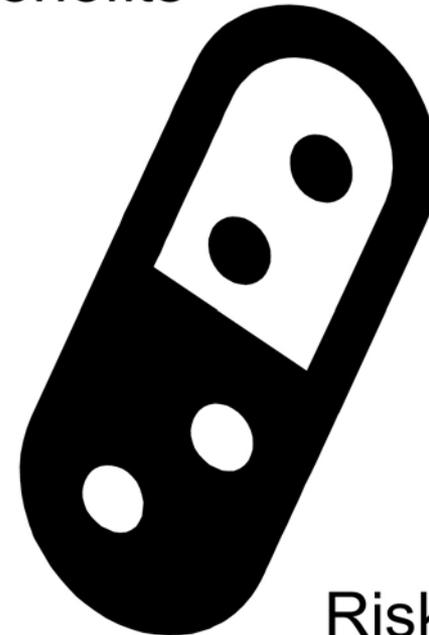
The Yin and Yang of Medications

Good



Bad

Benefits



Risks

Preventable and Unavoidable Risks

Preventable Risks

Accidental/Unintended Exposure

Intentional Misuse, Abuse or Self-harm

Drug Quality Defect

Medication Error

Unavoidable Risks

Gaps in Knowledge

Unknown Risks

from new drugs
not detected in clinical trials

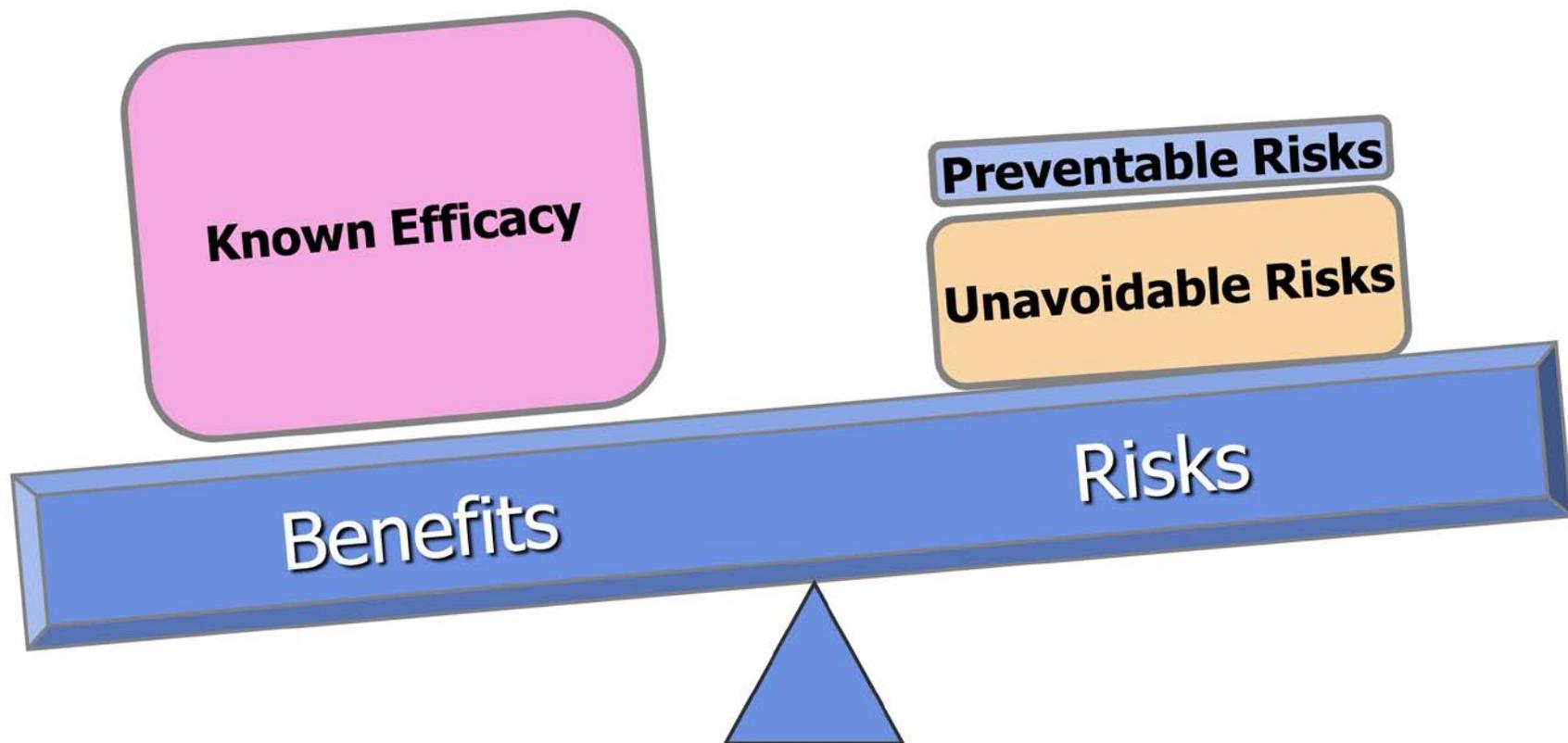
- Rare events
- Use with other healthcare products
- Use off-label

Common Events

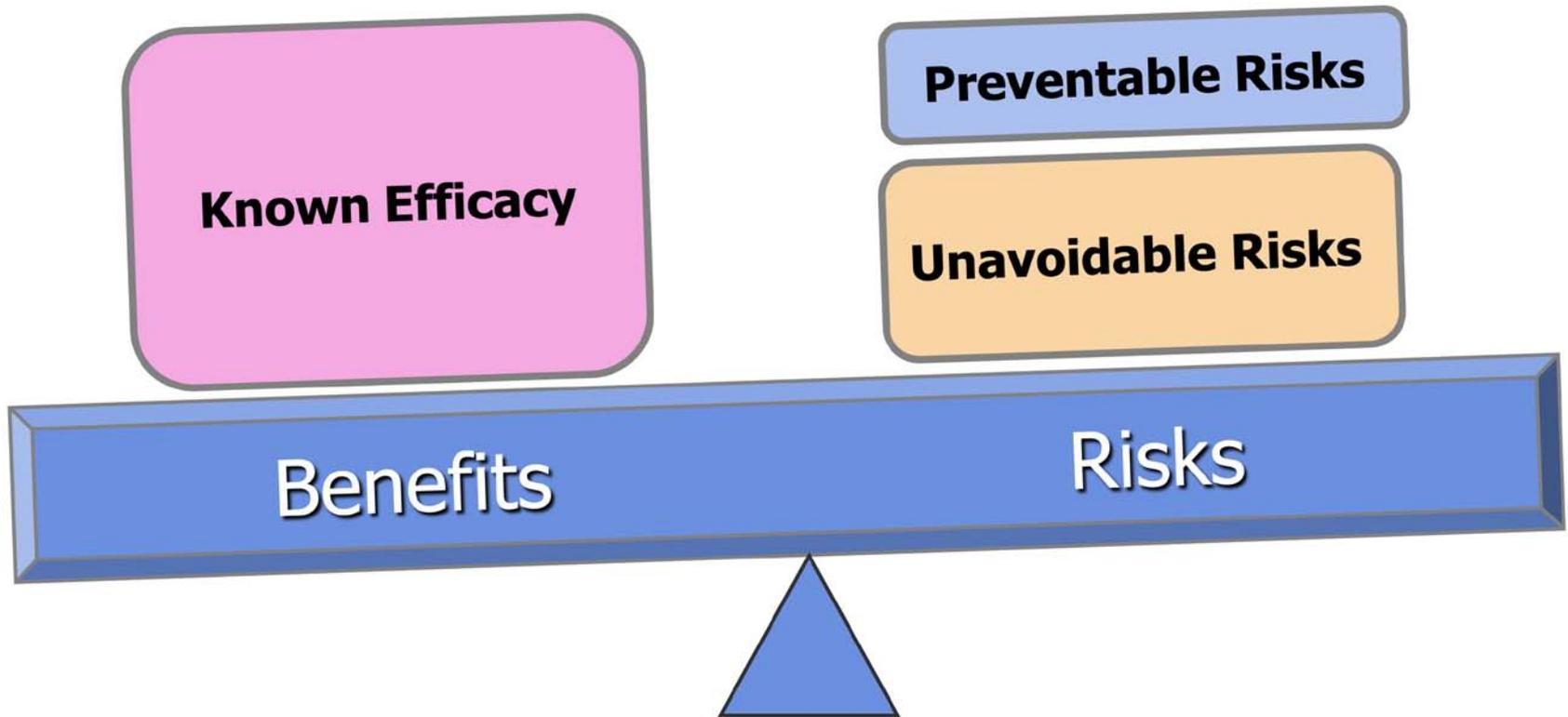
not recognized
as side effects

Known Side Effects

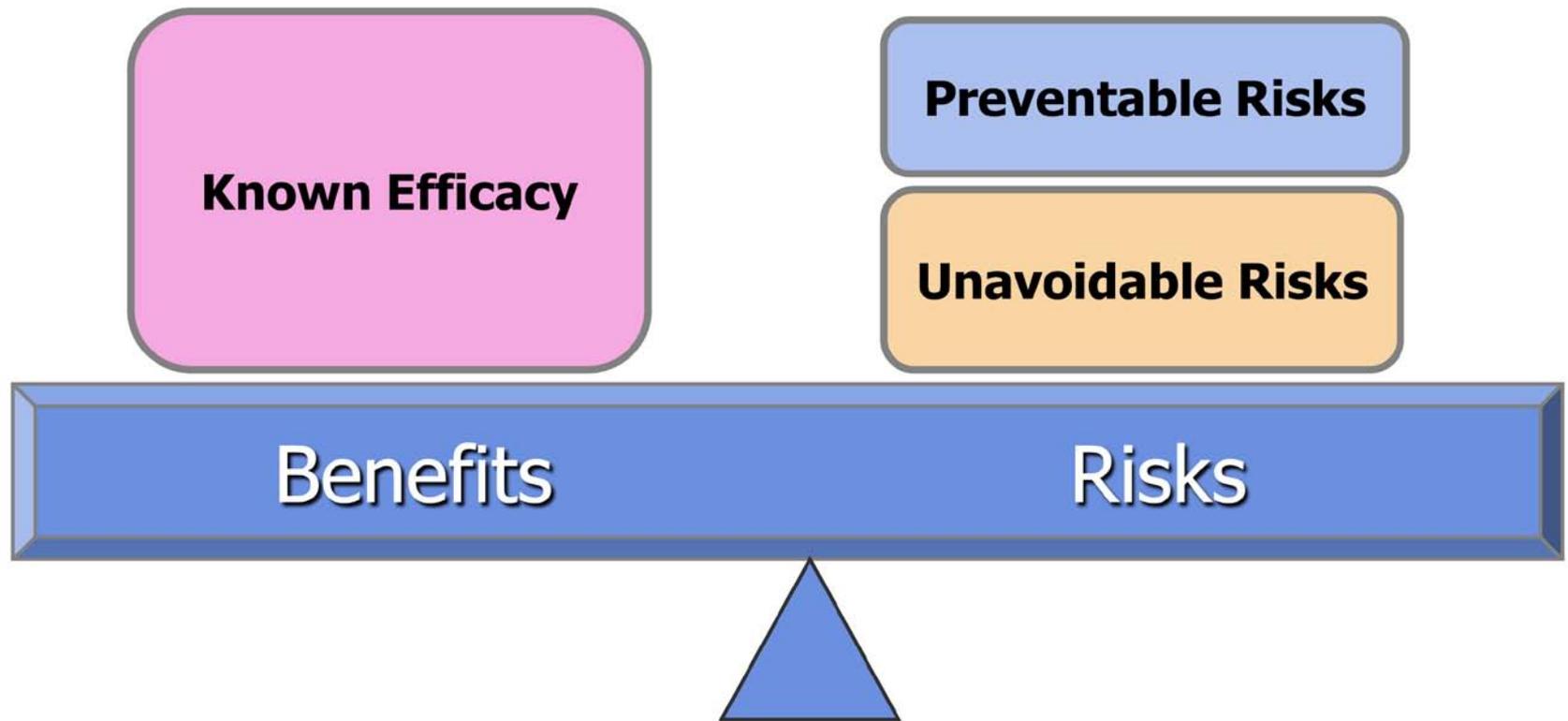
At Approval



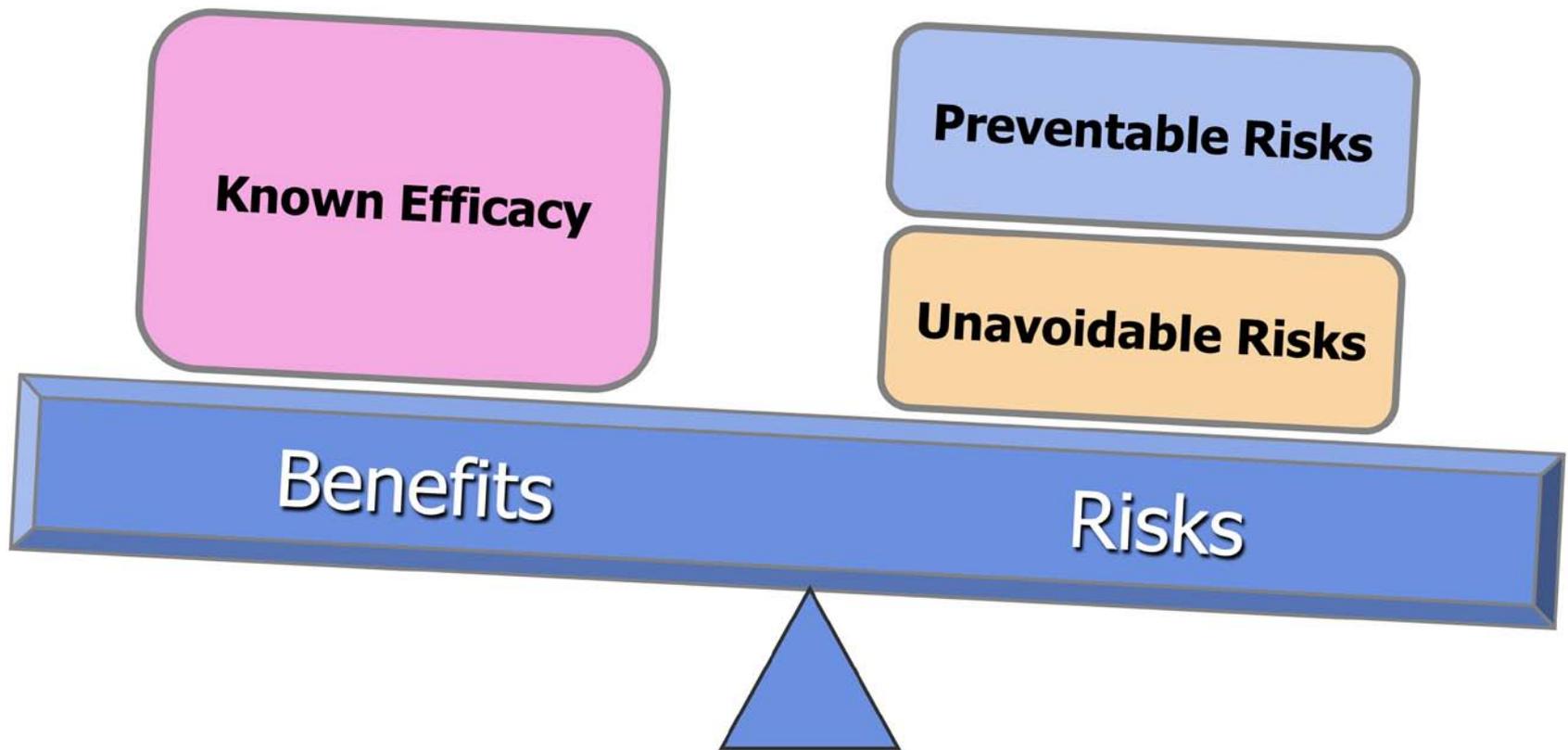
Exposure Increases



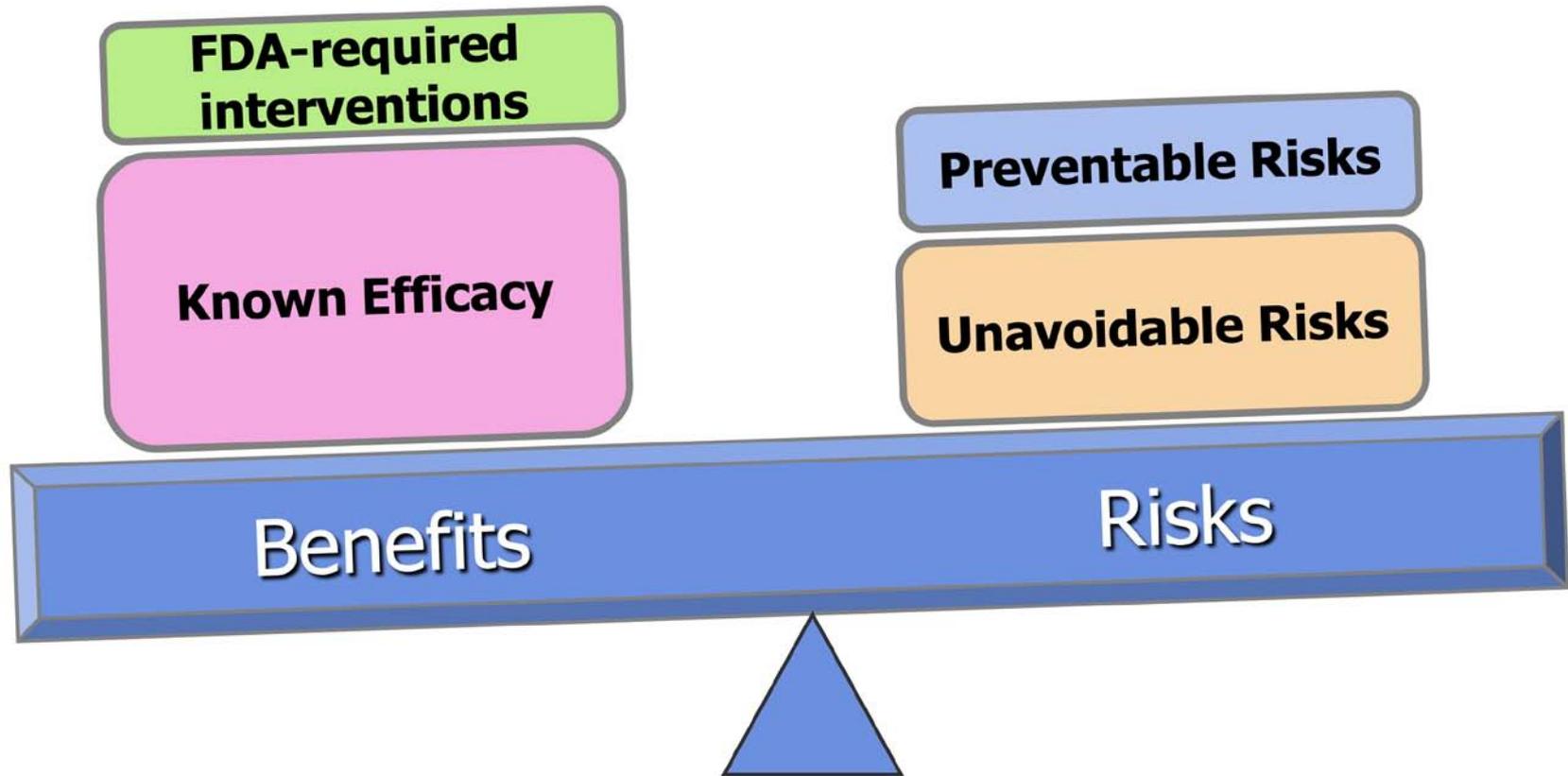
Exposure, Misuse, Errors



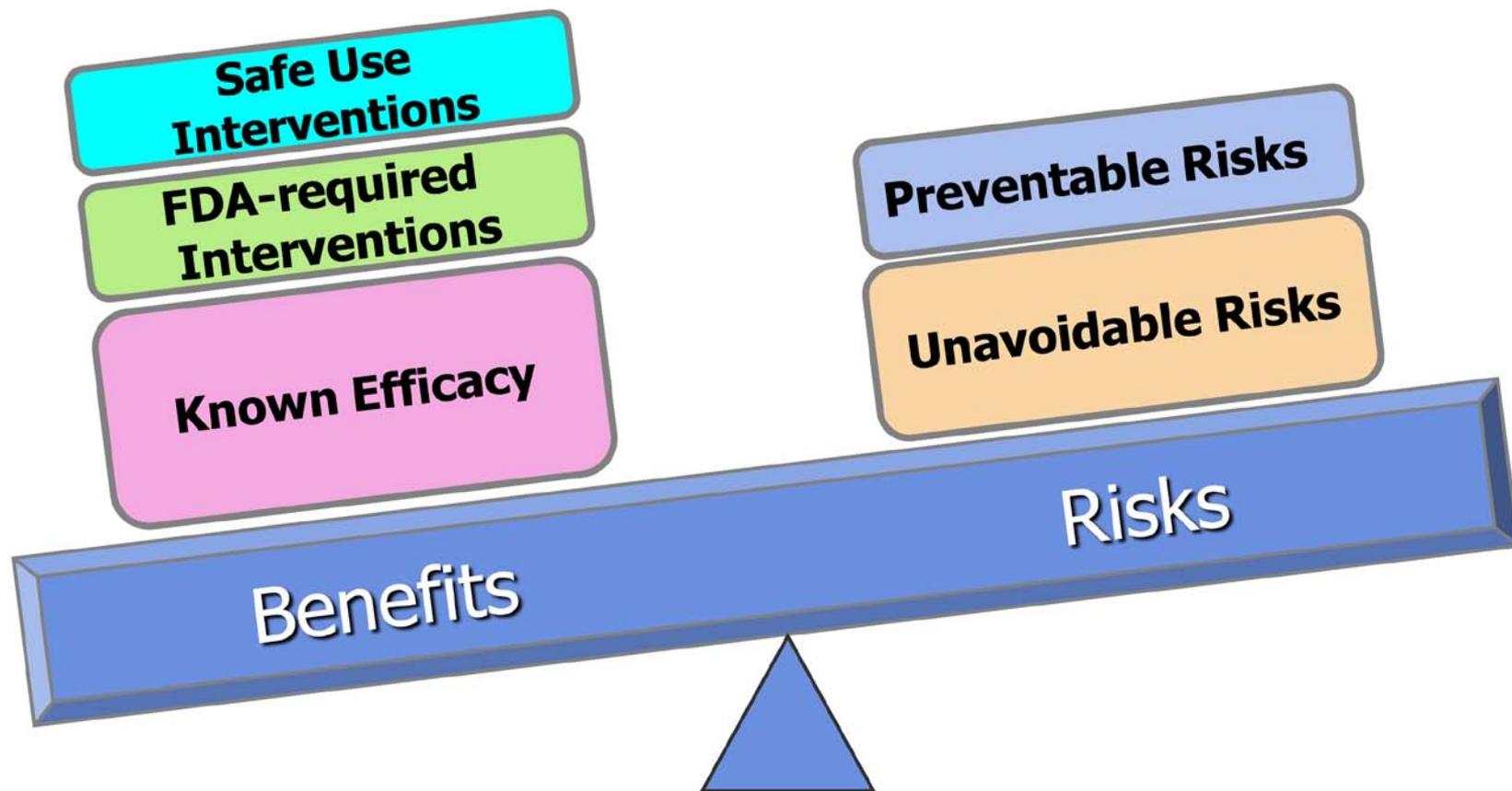
Misuse, Errors Increase



FDA can Require Interventions to Help Manage Risks (Regulatory Activities)



Safe Use Collaborations: Further Tip the Balance



Safe Use: Non-regulatory

- **What?** FDA's voluntary (non-regulatory) activities to reduce risks (*preventable* harm) from Rx and OTC drugs
- **Why?** FDA's regulatory authority alone is not sufficient to prevent harm
- **How?** Partnering with those involved in healthcare who can control, modify or influence behavior and practices
- **When?** Now

Regulatory & Safe Use Actions

Regulatory

- Require new warnings or other labeling changes
- Issue a drug safety communication
- Issue a guidance for industry
- Bring an issue to an advisory committee
- Require new studies to assess safety signals
- Require Risk Evaluation and Mitigation Strategy (REMS)

Safe Use

- Convene stakeholder workshop
 - Identify drug safety issue (s)
 - Discuss barriers to safe use medications
 - Develop interventions
- Form public-private partnerships
- Support health literacy efforts and HIT activities
- Work with standard-setting organizations
- Collaborate in coalitions to educate the public, e.g., novel efforts to disseminate safe use messages

Setting Priorities for Safe Use

- Drug safe use issue associated with preventable harm
- Public health impact
- Amenable to collaborative approach to harm reduction
- Measureable
- Complements ongoing regulatory activities

Potential Safe Use Activities and the 10x10 Wellness Campaign

- **Stimulant addiction:**
 - Misuse of methylphenidate, amphetamine, and dextroamphetamine a growing problem among students
 - from college campuses down into elementary schools
 - misperceptions about safety, benefits of Rx stimulants
 - Misuse of modafinil among drivers, pilots, and others
 - Risk of serious side effects
 - How to educate consumer/survivors, providers

Potential Safe Use Activities and the 10x10 Wellness Campaign

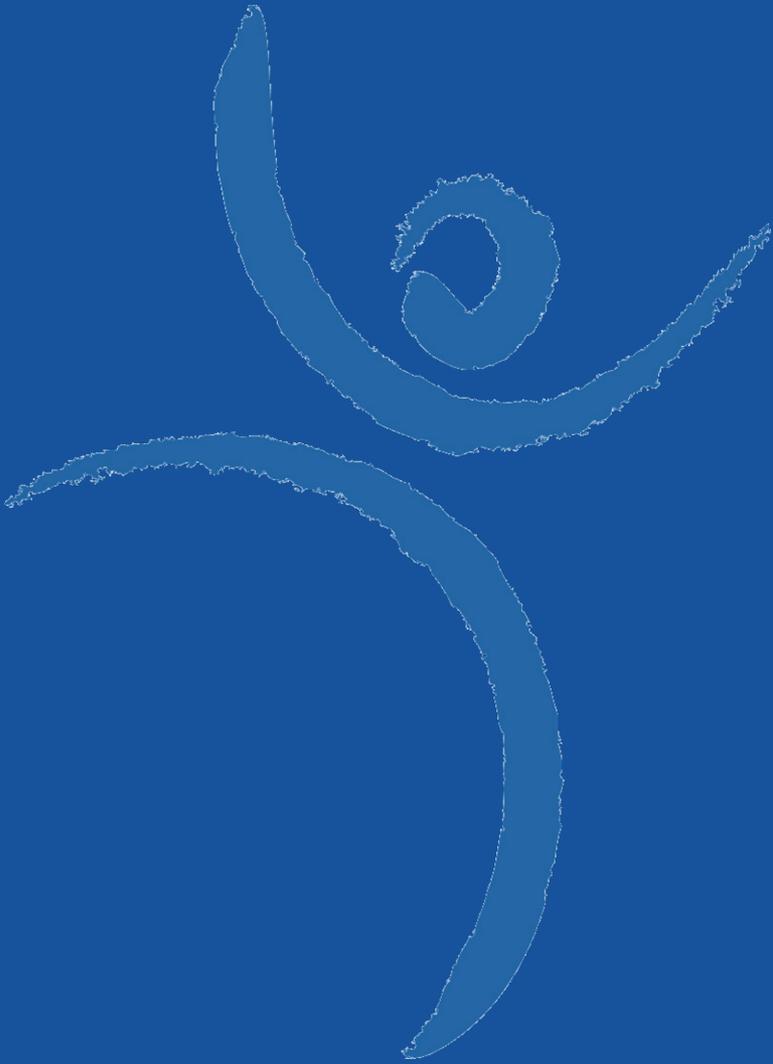
- Opioid analgesics:
 - Misuse and addiction dramatically increased since mid-1990s
 - Risk of serious side effects
 - Risk of addiction
 - Management complex:
 - DEA (diversion, illicit use)
 - FDA's regulatory activities (Risk Evaluation and Mitigation Strategy or REMS)
 - FDA's safe use activities—patient and provider education, agreements, 'take back' programs, other partnerships?

Potential Safe Use Activities and the 10x10 Wellness Campaign

- **Psychotropic and other medications:**
 - In elderly populations
 - sedatives, hypnotics, antidepressants, anticholinergics
 - associated with falls, agitation, impaired cognition, impaired concentration, confusion, delirium, hallucination, psychosis
 - In pediatric populations
 - risk of suicide/suicidal ideation
 - risk of metabolic syndrome
 - How to improve safe use of these important medications in these populations?

Potential Safe Use Activities and the 10x10 Wellness Campaign

- Many potential opportunities to partner to improve well-being of persons with mental illness
 - Open to ideas



MAIN SIDE EFFECTS FROM A PERSON LIVING WITH PERSPECTIVE

Mark A. Davis, M.A.
Pink & Blues, Philadelphia

Hi, I'm Mark

- A proud gay asexual man:
 - living with bipolar II (the sequel)
 - in recovery from addictions to cigarettes, drugs, and alcohol
 - living long with HIV since testing positive September 27, 1988
 - profoundly deaf
 - a suicide attempt survivor
- Sample introduction at the Pink & Blues Philadelphia, a safe space to explore recovery and dualities for lesbian, gay, bisexual, transgender, questioning, intersex, and two-spirit people

I Am Who I Am

- I am a person:
 - living with
 - suffering from
 - addicted to
 - in recovery from
 - not my diagnosis or label
 - limited by
 - able to
 - proud gay asexual man
 - living with bipolar II
 - living long with HIV
 - profoundly deaf
 - a suicide attempt survivor

"I Will Survive" (Hot 100 #1, 1979), "Never Can Say Goodbye" (Hot 100 #4, 1974),
"I Have a Right" (Hot 100 #42, 1980) and "I Am What I Am" (Hot 100 #82, 1983).

Name ~ Claim ~ Tame ~ Frame ~ Sing ~ Dance It

Multiply Occurring Conditions

- Addiction recovery
- Allergies grown out & back in
- Anxiety worsening
- Bipolar II—the sequel
- Cholesterol down low, or too up
- HIV-positive
- Hypertension
- Narcolepsy
- Profoundly deaf with tinnitus distorted hearing

Surviving Conditions & Main (side) Effects

- Past surgeries include abdominal hernia, appendectomy, cervical spinal fusion
- Conditions include asthma, borderline obesity, chronic fatigue syndrome, dental decay, dyslexia, gout, pleurisy, pneumonia, shingles, spinal disk malfunctions
- Alum of community mental health system
- ECT & homelessness survivor

- Grateful to be alive to thrive
- Opposite side-effects
- Post traumatic brain injury from hate crime attack
- Suicide attempt survivor

If I did not have my work, I would not have any life. I obtain great satisfaction out of using my intellect. I am a big believer in early intervention.

—Temple Grandin

I am a MESSS

- There are many approaches to medical conditions. From these I have adopted a personal model for recovery, living with . . . and surviving from
- This is what I named a MAD Model in categories that fit holistic needs

M – edical

E – motional

S – ocial

S – piritual

S – exual

“Every day I’m housecleaning and/or cleaning up on the MESSS of life.” —Mark A. Davis (DAM Backwards)

Consumer/Survivor Movement is Broadly Representative

- Alternative healers
- Anti-psychiatry, force, ECT, involuntary commitment, medication
- Equality advocates
- Medical model cheerleaders
- Peer recovery experts, workers, and WRAP-ers
- People who choose to name, claim, tame, and frame it
- Pro-whatever works
- Psychiatric survivors, ex-patients, and inmates

I'm fine, but I'm bipolar. I'm on seven medications. This constantly puts me in touch with the illness I have. I'm never quite allowed to be free of that for a day.

—Carrie Fisher

But the main thing is that medication, too, is not all the help.

—Tanya Tucker

The Main (side) Effects

- What came first, the condition or the main (side) effects?
- Finding needle(s) in haystack (Nemo in Seaweed) only to lose it or fall off
- Missing trauma roots for the forest
- From AZT® to Xyzal®
- Toxicity or transplant?
- On mute or hold?
- Fine line between creativity and madness!
- Stigma in the name—Wellbutrin® renamed Zyban® for smoking cessation?
- $B = f(P,E)$ – Behavioral = function of Person and Environment

And while we are on the subject of medication you always need to look at risk versus benefit.

—Temple Grandin

To Be Adherent or To Be Compliant?

- Living as a person with HIV I have experienced informed consent, encouraged, educated, and supported to voluntarily take an HIV/AIDS cocktail combos with emphasis on adherence
- Living with a psychiatric diagnosis the tone is punitive, restrictive, and involuntary with a prescribed focus on compliance
- The Carter Center: Advancing Human Rights and Alleviating Suffering
 - Guided by a fundamental commitment to human rights and... Building hope through internships, job and volunteer opportunities
<http://www.cartercenter.org/homepage.html>

Informed journalists can have a significant impact on public understanding of mental health issues as they shape debate and trends with the words and pictures they convey. They influence their peers and stimulate discussion among the general public, and an informed public can reduce stigma and discrimination.

—Former First Lady Rosalynn Carter

Politics of Mass Prescription Pose Questions

- Was it parity or parody that passed? Where's the parity?
- Did you hear much discussion of mental health, addiction and suicide prevention in the Congressional healthcare debate?
- What is the future of community mental health, addiction and suicide prevention services?
- Will DSM-V do no harm, name Dx to invoice and/or better understand Tx of people with multiple conditions?
- No Child/Elder Left Un-drugged concerns
- The Reagan Administration response to HIV/AIDS

ACT UP ~ ACT OUT ~ ACT NOW!

A little rebellion now and then... is a medicine necessary for the sound health of government.

—Thomas Jefferson

Cost Rx Factors

- Name <>Generic <>On-Line<>Street<>Underground Brands or Canada Bound?
- Access or Formulary Restrictions?
- Provigil®, Nuvigil® or Just Say NOvigil Wake-up Calls
- Donut holes or Grand Canyons?
- Choosing Celebrex® or Cereal?
- Genotype Testing or Geno's Philly Cheesesteaks?
- Thankful for ADAP & PA SPBP for S.P.I.N.
- \$44,747.52 + \$22,203.00 = \$66,950.52—Bet your bottom dollar!
- No Pain, No Weight Gain?
- Co-occurring Cola
- Co-occurring systems and prescribing doctors

As soon as we find a cure, we will utilize any of the donations to go toward providing medication to those who can't afford it. That is my goal.

—Montel Williams

This is an Epidemic!

Honoring my sister, Jennifer Anne Yocom, who died by suicide in 1995 and three peers—Elaine Wilson of Pittsburgh, Stefan Hobbs of Philadelphia and Donna Wagner of Danville—who died suddenly during the 20th, 21st, and 22nd Annual PA Mental Health Consumer Conferences; a reality of people with mental illness dying 25 years too young, yet dancing and celebrating with peers forever reminding us of this call to action!

Being Resourceful

- CommonGround software:
<http://www.patdeegan.com/AboutCommonGround.html>
- Free archived webinar, " Personal Medicine in the Recovery Process: Part 1— Personal Medicine, Power Statements and Getting Active in Shared Decision Making":
<http://www.ccbh.com/providers/recoveryinstitute/webinars/webinars2008.php>
- *Mad in America: Bad Science, Bad Medicine and the Enduring Mistreatment of the Mentally Ill* (Robert Whitaker, 2001):
<http://www.amazon.com/exec/obidos/ASIN/0738207993/lawprojectfor-20>
- *Anatomy Of An Epidemic: Could Psychiatric Drugs Be Fuelling A Mental Illness Epidemic?* (Robert Whitaker, 2010): http://www.huffingtonpost.com/robert-whitaker/anatomy-of-an-epidemic-co_b_555572.html
- <http://www.psych.UIC.edu/MHSRP>, <http://www.BU.edu/CPR>,
<http://www.UPennRRTC.org>
- <http://www.mindfreedom.org/directory>, <http://www.cdsdirectory.org>

We are still mad about the mad. We still don't understand them and that lack of understanding makes us mean and arrogant, and makes us mislead ourselves, and so we hurt them.

—David Cohen, Ph.D.

FDA Resources

- Office of Women's Health:
<http://www.fda.gov/ForConsumers/byAudience/ForWomen/default.htm>
 - Safe Medication Use
<http://www.fda.gov/ForConsumers/ByAudience/ForWomen/TakeTimeToCareProgram/ucm116695.htm>
 - Medication Booklets
<http://www.fda.gov/ForConsumers/ByAudience/ForWomen/FreePublications/ucm116718.htm>
 - Medication and Pregnancy
<http://www.fda.gov/ForConsumers/ByAudience/ForWomen/ucm118567.htm>
- Safe Use Initiative:
<http://www.fda.gov/drugs/drugsafety/ucm187806.htm>
- Postmarket Drug Safety Information for Patients and Providers:
<http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/default.htm>
- Information and Adverse Event Reporting Program:
<http://www.fda.gov/Safety/MedWatch/default.htm>; 1-800-332-1088

NIMH Resources

- Guide to Mental Health Medications:
<http://nimh.nih.gov/health/publications/mental-health-medications/index.shtml>
- Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE):
<http://www.nimh.nih.gov/trials/practical/catie/index.shtml>
(abstract)

Additional Resources

- Deegan, P.E., Drake, R.E. (2006). Shared decision-making and medication management in the recovery process. *Psychiatric Services*, 57(11): 1636-1639:
<http://psychservices.psychiatryonline.org/cgi/content/abstract/57/11/1636> (abstract)
- Harm Reduction Guide to Coming Off Psychiatric Drugs & Withdrawal (The Icarus Project):
<http://theicarusproject.net/alternative-treatments/harm-reduction-guide-to-coming-off-psychiatric-drugs>

Speaker Biographies

- **Gerald "Jerry" Overman, PharmD., B.C.P.P.**, is the clinical pharmacy specialist for the National Institute of Mental Health. He served as clinical pharmacy specialist in psychiatry/substance abuse at The South Texas Veterans Health Care System, clinical assistant professor at the University of Texas Health Science Center and the UT Austin College of Pharmacy, and in the University of Illinois Departments of Pharmacy Practice and Psychiatry. His areas of interest include the pharmacological management of psychotic, mood, and substance use disorders.
- **Karen D. Weiss, M.D., M.P.H.**, is the lead for the Safe Use Initiative in the FDA's Center for Drug Evaluation and Research. In 20 years at FDA, Dr. Weiss has been involved in activities including regulation of therapeutic biologicals, pediatric and oncology drug development, and drug safety. Previously, she was an assistant professor at Georgetown University.
- **Mark A. Davis, M.A.**, is a leader in the mental health consumer/survivors, suicide attempt survivor, individuals with disabilities, and sexual and gender minority communities and has inspired the development of more than 75 peer-run groups and cross-system collaborations. He also has affected the development of culturally competent research, funding, data collection, and services. He is the founding president of the Pennsylvania Mental Health Consumers' Association and facilitates Pink & Blues, a peer-run recovery, support, and advocacy group for persons living with a mental illness who identify as LGBTIQ.

For More Information

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