

Wisconsin Department of Health Services



Wisconsin Public Psychiatry Network Teleconference (WPPNT)

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Antipsychotic Medications

The Good, the Bad and the Ugly



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Four out of five doctors recommend. . .²

Evidence Based Practice (Modified from PORT Recommendations)

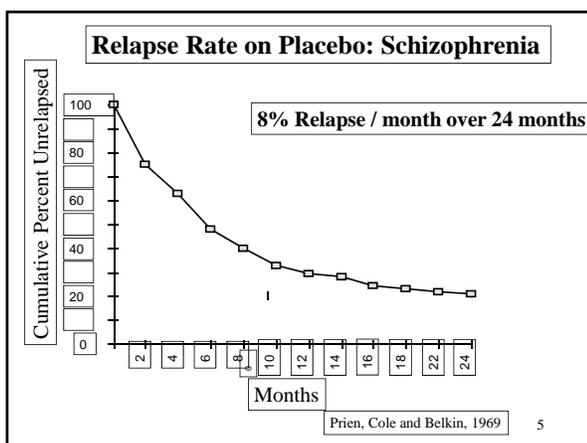
- Family psycho-education
- ACT and Clubhouse psychosocial programs
- Integrated supported work programs
- Skill training
- Integrated Mental Health and AODA Treatment
- Cognitive Behavioral Therapy
- Cognitive Remediation

Dixon L, et al. *Schizophr Bull.* 2010;36:48-70. 3
 Clubhouse not part of current PORT recommendations

Using medication as a tool to recovery

- What does the consumer want this medication to do? What problem can it help to fix?
- What else has the consumer tried to also help deal with this problem?
- How would the consumer and others know if the medication was helping?

Modified from Pat Deegan



Medication prices

Generic ziprasidone 80 mg # 60 tabs:	\$99.08
Brand name Geodon 80 mg # 60 tabs:	\$1106.52
Generic olanzapine 10 mg # 30	\$17.91
Brand name Zyprexa 10 mg #30	\$635.57
Generic quetiapine 100 mg # 100	\$16.32
Brand name Seroquel 100 mg # 100	\$740.98

We prescribe medications so that our client's "get better"...
 But what do we mean by "getting better"?

- Feel better
- Decrease symptoms
- Increase function
- Increase stability/stay out of hospital

- Improve subjective sense of well-being
- Improve quality of life

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All medication has risks

- Balance potential benefits Vs risks
 - What risks or benefits are most important
 - Question of values
 - Who gets to decide

- When is a risk "worth it"
 - What is the risk of NOT taking medication

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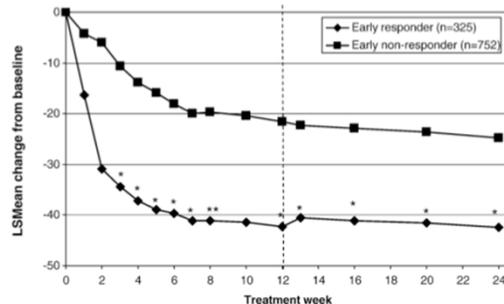
Need to develop "target list"

- What is the "target" of the medication: what behavior/feeling or experience do we hope will change?
 - What is the consumer hoping medication will do
 - What are others hoping medication will do

- Must be detailed, specific and concrete
- Based on observable behavior

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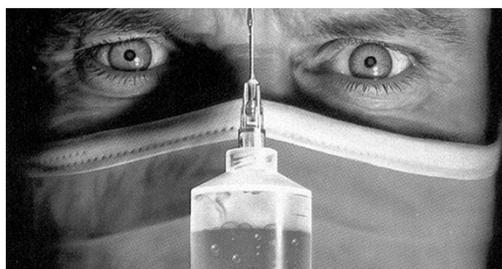
Predicting Antipsychotic Response from Early Treatment Response



Kinon et al Schiz Res 102 (2008) 230-240

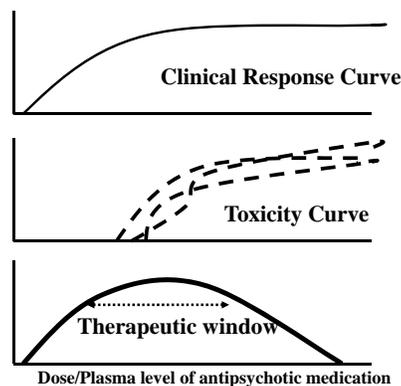
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Treatment Adherence



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Antipsychotic Dose-Response Curve



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Antipsychotic Medications: Indications

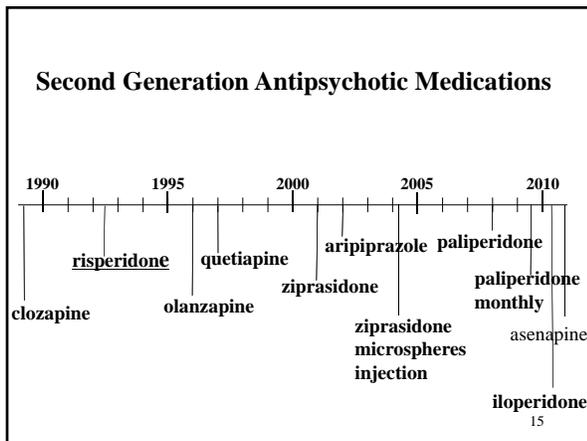
- Schizophrenia: + positive symptoms
 ? Negative symptoms
 ? Cognitive dysfunction
- Depression + psychotic depression
 ? Some (quetiapine)
- Bipolar disorder + anti-manic
 + mood stabilizer (some)
- OCD
- Autism related behaviors
- Aggression

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Antipsychotic Medications: What do we really know?

- All are much more effective for positive sx than for negative sx or cognitive dysfunction
- Clozapine is more effective than any other, but has the most side effects and risks
- None of the others is clearly more effective than any other, but they are different and different people respond differentially
- The data on lifetime need is problematic and may be wrong, at least for some patients

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Clozapine

A diagram of a clozapine molecule (a dark sphere) with several receptors attached to it, represented by different shapes and colors. The receptors are labeled: 5HT2A, 5HT2C, 5HT3, 5HT1b, 5HT1, D4, D3, D2, D1, M1, and A1. The clozapine molecule is shown interacting with all these receptors.

- Other side effects
 - Agranulocytosis
 - Heat Related Deaths
 - Heart related problems
 - Diabetes
 - Drooling
 - Seizures
- **Very effective**
 - positive and negative
 - good mood stabilizer
 - very low EPS
 - very low TD

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Risperidone (Risperdal)

A diagram of a risperidone molecule (a dark sphere) with several receptors attached to it. The receptors are labeled: 5HT2A, 5HT1, and D2. The risperidone molecule is shown interacting with these receptors.

- Dose related EPS
- Less is better
- Prolactin Elevation
- Weight Gain
- Positive and negative efficacy
- Mood stabilizer
- Decreased TD
- Has a 2 week injection: Consta

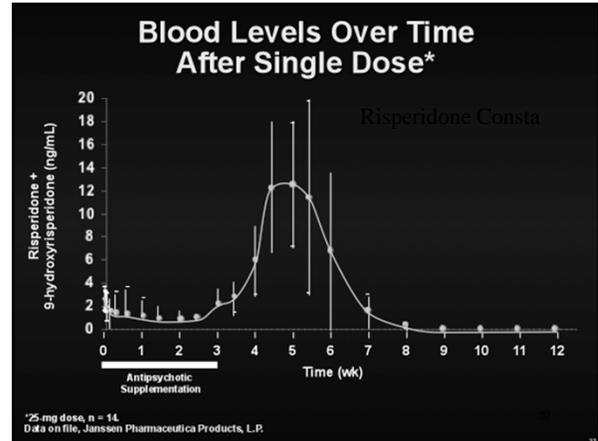
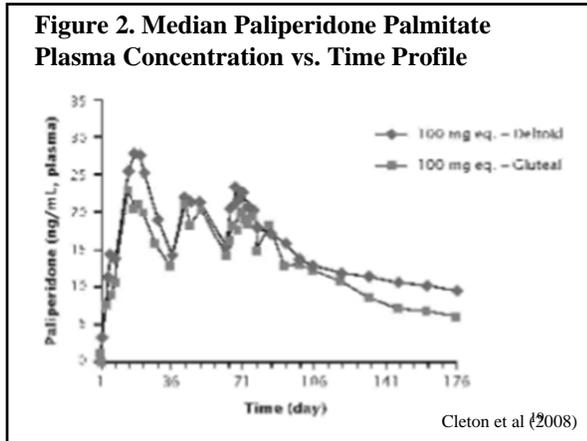
Adapted from Stahl
 Essential Psychopharmacology

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Paliperidone (Invega)

- Major metabolite of risperidone
- Similar prolactin elevation to risperidone
- Similar weight gain to risperidone
- Has a 4 week injection: Invega Sustenna

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Olanzapine (Zyprexa)

- **Big Weight Gain**
- **Diabetes risk**
- **Somewhat sedating**
- **Positive and negative efficacy**
- **Mood stabilizer**
- **Can be given in full dose in crisis situation**

Adapted from Stahl
 Essential Psychopharmacology

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Quetiapine (Seroquel)

- **More is Better**
- **400 mg up to 1200 mg**
- **Very low EPS**
- **Very low TD risk**
- **Some weight gain**
- **Sedating**
- **Needs dose titration to decrease dizziness**
- **Low dose may be useful in people with borderline disorder**

Adapted from Stahl
 Essential Psychopharmacology

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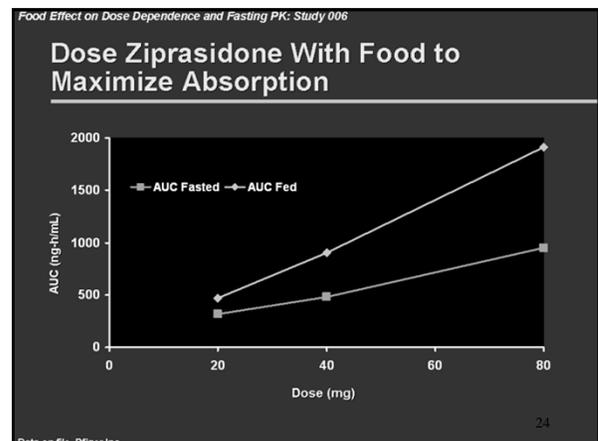
Ziprasidone (Geodon)

- **NO WEIGHT GAIN**
- **Very low diabetes risk**
- **Higher dose often better than low: rapid titration better than slow increase**
- **QTc prolongation**
- **Activating/agitating**
- **Antidepressant activity**

MUST BE TAKEN WITH FOOD!

Adapted from Stahl
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Aripiprazole (Abilify)

- Dopamine agonist/antagonist
- Some weight gain
- Some motor restlessness, dose related
- Not sedating
- Recently available as a generic

Highest Grossing Drug in U.S. 10/1/12-9/30/31
 \$6,391,050,000

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Iloperidone (Fanapt)

- “balanced” side effects
- Less weight gain than olanzapine, less EPS than risperidone, less sedation than quetiapine
- Must be titrated gradually to prevent dizziness

Expensive branded product

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Asenapine (Saphris)

- Sublingual tablet (under the tongue)
- Less wt gain than olanzapine
- VERY LITTLE data published
- Side effects: reported in clinical trials
 - Akathisia
 - Oral hypothesia
 - Somnolence
 - Dizziness
 - Weight gain (some??)

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Lurasidone (Latuda) (FDA approved Oct 2010)

- Similar to ziprasidone (Geodon)
- Weight neutral
- Some agitation
- Approved for bipolar depression
- \$2844.27 for # 120 of 40 mg tabs

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Brexipiprazole

- Partial d2 agonist
- Lower intrinsic d2 agonism affinity than aripiprazole, higher 5-HT1a/2a
- Similar to aripiprazole, but not about to become generic

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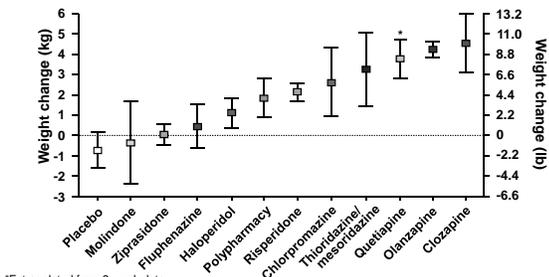
Side Effects of Antipsychotic Medications

	Clozapine	Risperidone	Olanzapine	Quetiapine	Ziprasidone	Aripiprazole	haloperidol
Weight gain	+++	++	+++	++	0	0	0
dyslidemia	+++	+	+++	+	0	0	0
Diabetes	+++	++	+++	++	+	+	+
Sedation	+++	+	++	+++	±	±	±
EPS	±	++	+	±	+	+	++
↑ Prolactin	0	+++	+	0	0	0	+++

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Mean Change in Weight With Antipsychotics

Estimated Weight Change at 10 Weeks on "Standard" Dose



*Extrapolated from 6-week data.
 Allison et al. *Am J Psychiatry*. 1999;156:1686.

Long-acting injectable antipsychotics

1st Generation

- Fluphenazine deconate [Prolixin Deconate]
- Haloperidol deconate [Haldol Deconate]

2nd generation

- Risperidone [Risperdal Consta]
- Paliperidone palmitate [Sustenna-monthly]
- Olanzapine palmoate [Relprevv-monthly]
- Aripiprazole [Maintena-monthly]

Depot antipsychotic injection

After 180 days only

- 9.7% haldol deconotate
- 5.4% still on fluphenazine dec
- 2.6% still on Consta
- More than 50% also took oral anipsychotic medication

Olison, Marcus and Ascher-Svanum *Schiz Bull* 2007;33(6)

The negative effects of medication

"Sure the drugs would do that (remove the auditory and visual hallucinations) but my ability to cognise was just totally impaired by drugs and once my ability to cognise was destroyed I would get deeper into psychosis. Yeah, deeper, less and less able to recognize myself".

Tooth, Kalyansundaram and Glover. *Recovery from Schizophrenia: A consumer perspective* 1998

Second Generation Antipsychotics: are they worth the cost?

- CATIE
- CUTLESS
- Long-term VA study

Recovery in Remitted First-Episode Psychosis at 7 Years of Follow-up of an Early Dose Reduction/Discontinuation or Maintenance

Treatment Strategy: Wunderink et al 2013

- The DR patients experienced twice the recovery rate of the MT patients (40.4% vs 17.6%).
- Logistic regression showed an odds ratio of 3.49 (P =.01).
- Better DR recovery rates were related to higher functional remission rates in the DR group but were not related to symptomatic remission rates.

