



ANTIPSYCHOTICS: Clinical Pharmacology

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Pre-Lecture Test

Question 1

1. Which of the following is an antipsychotic dose that is in excess of the optimal?
 - A. Aripiprazole 15 mg/day
 - B. Ziprasidone 80 mg bid
 - C. Haloperidol 20 mg qd
 - D. Risperidone 4 mg/day
 - E. Quetiapine 300 mg bid

Question 2

2. Which of the following antipsychotics must be taken with food in order to prevent significant loss of absorption?
- A. Ziprasidone
 - B. Olanzapine
 - C. Clozapine
 - D. Aripiprazole
 - E. Risperidone

Question 3

3. Which of the following is the recommended starting dose for clozapine?
- A. 25 mg twice a day
 - B. 12.5 mg
 - C. 25 mg
 - D. 50 mg

Question 4

4. All of the following are true of a patient on risperidone who gets parkinsonian side effects, except:
- A. D2 receptor occupancy is 75% or more
 - B. The patient is above the “neuroleptic threshold”
 - C. Patient is at risk for secondary negative symptoms
 - D. Raising the dose is likely to be helpful

Question 5

5. What is the drug of choice for a schizophrenia patient with polydipsia?
- A. Olanzapine
 - B. Thirodazine
 - C. Ziprasidone
 - D. Pimozide
 - E. Clozapine

Question 6

The NNT for antipsychotics is lower for

- A. Schizophrenia
- B. Schizoaffective disorder
- C. Bipolar disorder
- D. Aggressive behaviour in autism
- E. Depression

Question 7

Which one of these antipsychotics has a longer half life?:

- A. Olanzapine
- B. Haloperidol
- C. Chlorpromazine
- D. Aripiprazole
- E. Quetiapine

Question 8

Which one of these antipsychotics is the only one that does not have affinity for the D2 receptor?

- A. Paliperidone
- B. Quetiapine
- C. Chlorpromazine
- D. Aripiprazole
- E. None

Question 9

When do we have plasma levels similar to oral risperidone with Risperidone consta (25 mg)

- A. Day 1
- B. Day 5
- C. Day 10
- D. Day 15
- E. Day 30

Question 10

What antipsychotic would you not recommend for a 16 year old with a first psychotic episode

- A. Aripiprazole
- B. Risperidone
- C. Quetiapine
- D. Olanzapine
- E. Haloperidol (low dose)

Question 11

For what drug do guidelines (e.g PORT) recommend to measure plasma levels (therapeutic window)?

A. Aripiprazole

B. Clozapine

C. Quetiapine

D. Olanzapine

E. Haloperidol

Question 12

Most of the weight gain with antipsychotics takes place in:

- A. First month
- B. 3 months
- C. 6 months
- D. 1 year
- E. 2 years

Question 13

The half life of LAI (depot) antipsychotics is:

- A. 2 weeks
- B. 4 weeks
- C. 12 weeks
- D. A and B are correct
- E. A, B and C are correct

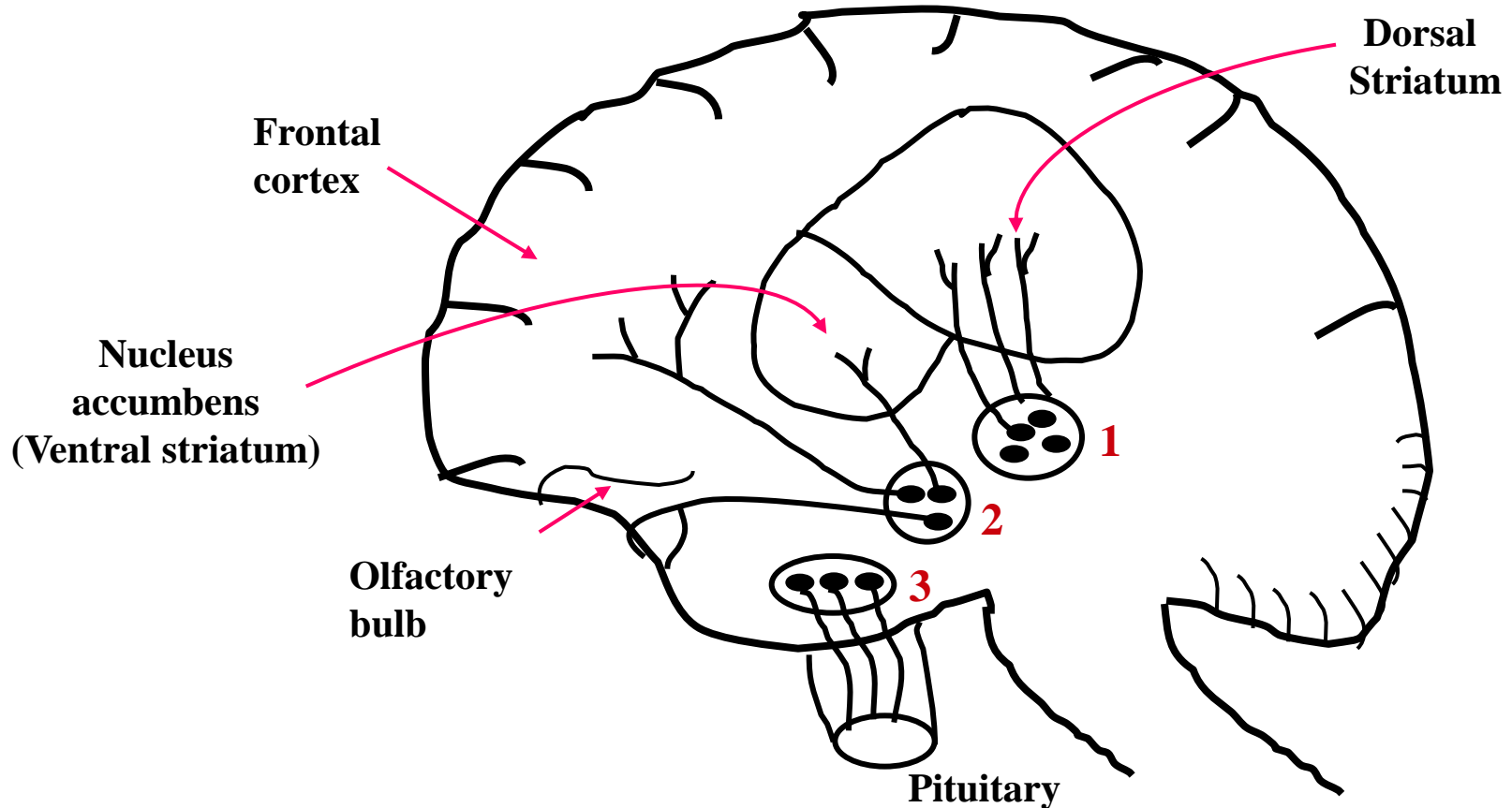
Outline of Lecture

- Introduction
- Algorithm for selecting antipsychotics
- What do they treat and what they do not treat
- Most common antipsychotics: minimal facts we should know about them
- Efficacy
- Safety and tolerability

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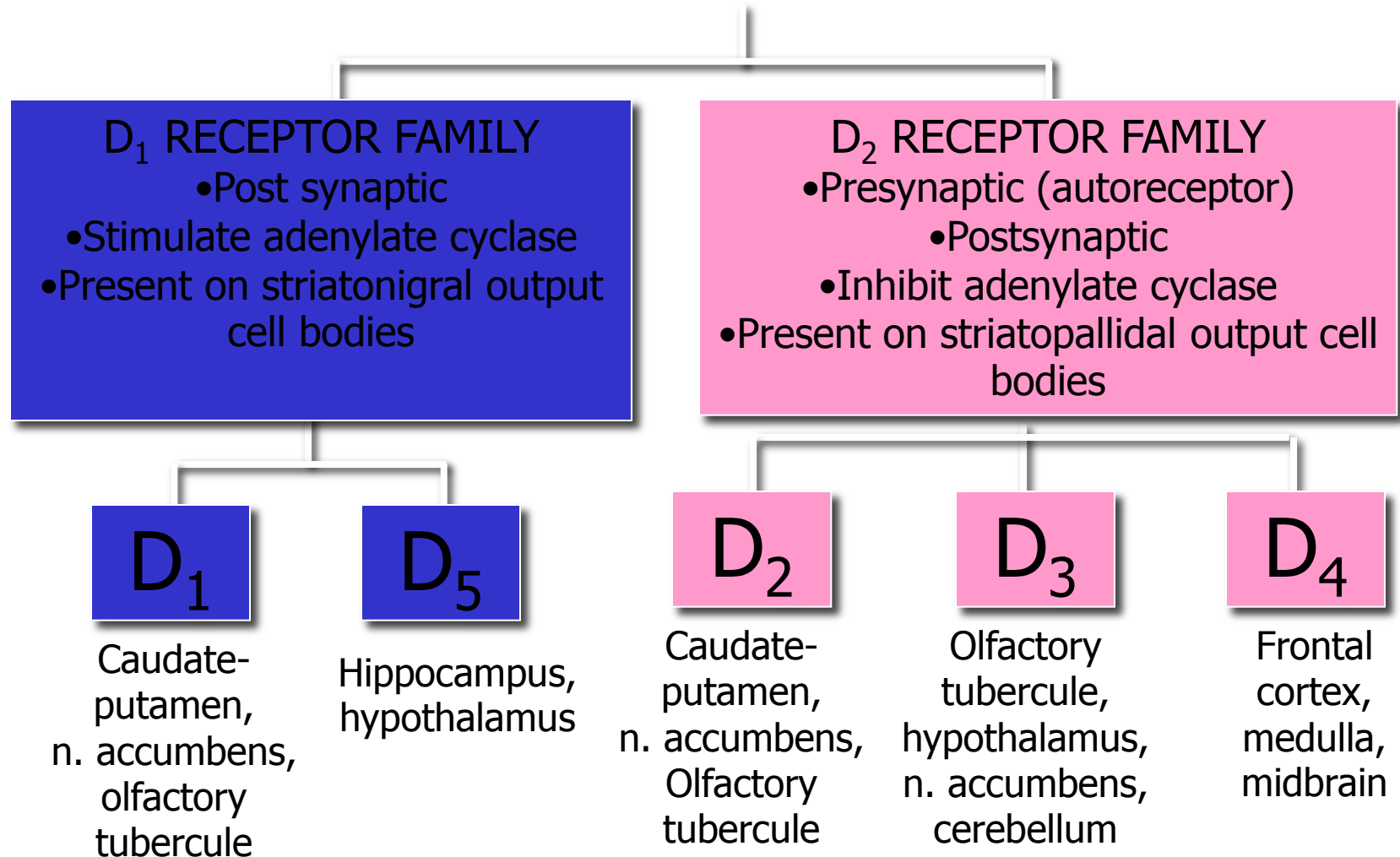
Dopamine pathways



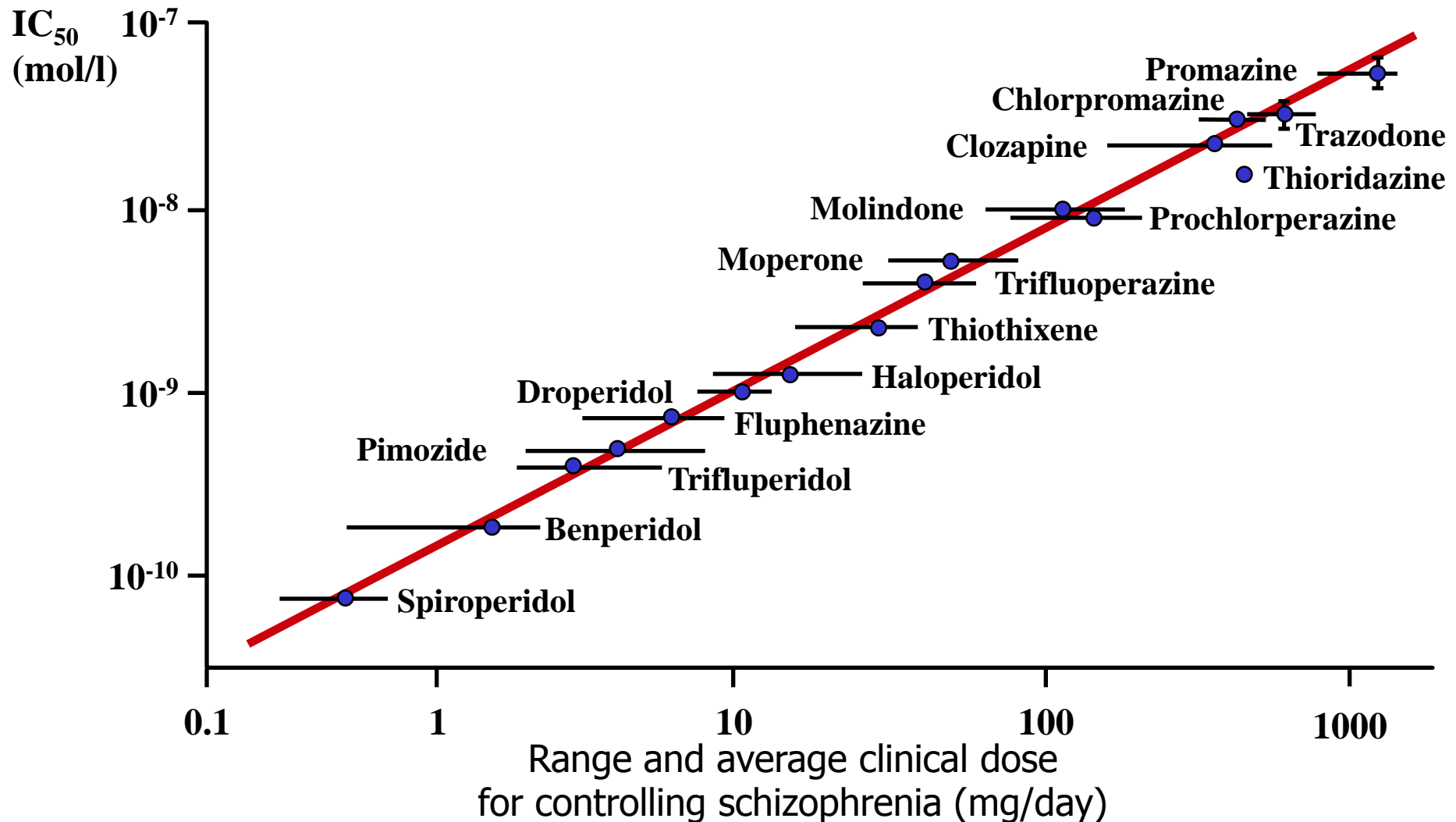
1. Nigrostriatal pathway (substantia nigra)
Parkinson's disease, initiation of motor plans
2. Mesocortical and mesolimbic pathways (Ventral tegmental area: VTA)
Psychosis, reward and motivation
3. Tuberoinfundibular pathway (Median eminence)
Prolactin release

CLASSIFICATION OF DOPAMINE RECEPTORS

DOPAMINE



AFFINITY FOR D₂ RECEPTORS & CLINICAL POTENCY

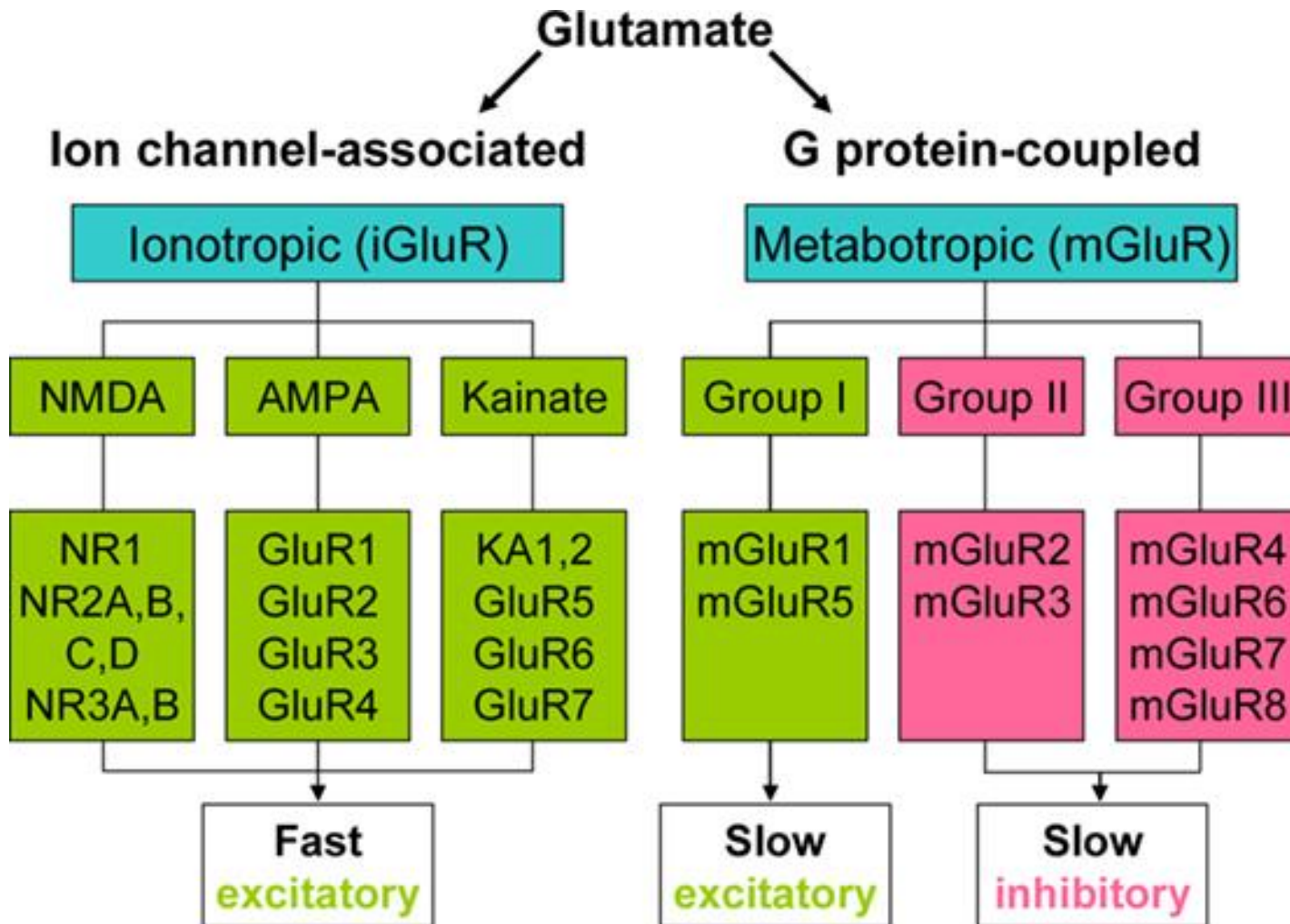


Barriers to Drug Discovery: Reasons for Minimal Progress since 1952

Adherence to single disease paradigm where psychosis represents the latent disease structure.

Discovery platforms produce dopamine antagonists.

CLASSIFICATION GLUTAMATERGIC RECEPTORS



Glutamatergic neurotransmission modulators under evaluation for schizophrenia treatment

NMDA receptor

Glycine site full agonists (glycine, D-serine, D-alanine)

Glycine site partial agonists (D-cycloserine)

Glycine type I transporter inhibitors (N-methylglycine, Bitopertin:negative studies, AMGEN: stopped)

D-serine transport inhibitors

AMPA receptor

Positive allosteric modulators (AMPAkines)

Metabotropic receptors

mGluR_{2/3} activators (N-acetylcysteine)

mGluR_{2/3} agonists (Pomaglumetad: failed)

CONVENTIONAL ANTIPSYCHOTICS

Classification: Chemical type Representative drug

Phenothiazines

Aliphatic

chlorpromazine

Piperidine

thioridazine

Piperazine

trifluoperazine

Thioxanthines

flupenthixol

Butyrophenones

haloperidol

Diphenylbutylpiperidines *pimozide*

Dibenzoxapines

sulpiride

Indoles

oxypertine

NEW ANTIPSYCHOTICS

Classification: Chemical type Representative drug

Dibenzazepines

Dibenzodiazepine

clozapine

Thienobenzodiazepine

olanzapine

Dibenzothiazepine

quetiapine

Benzisoxazoles

risperidone

Benzamides

amisulpride

Benzisothlazoylpiperazines

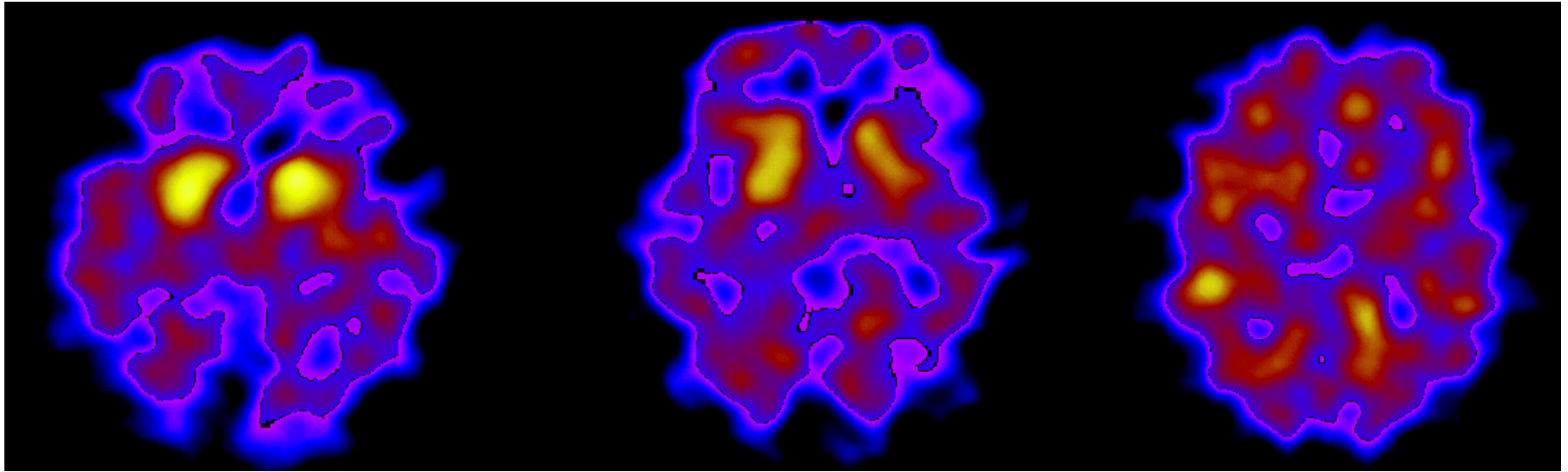
ziprasidone

Imidazolidinone

sertindole

NNN

asenapine



Healthy Volunteer

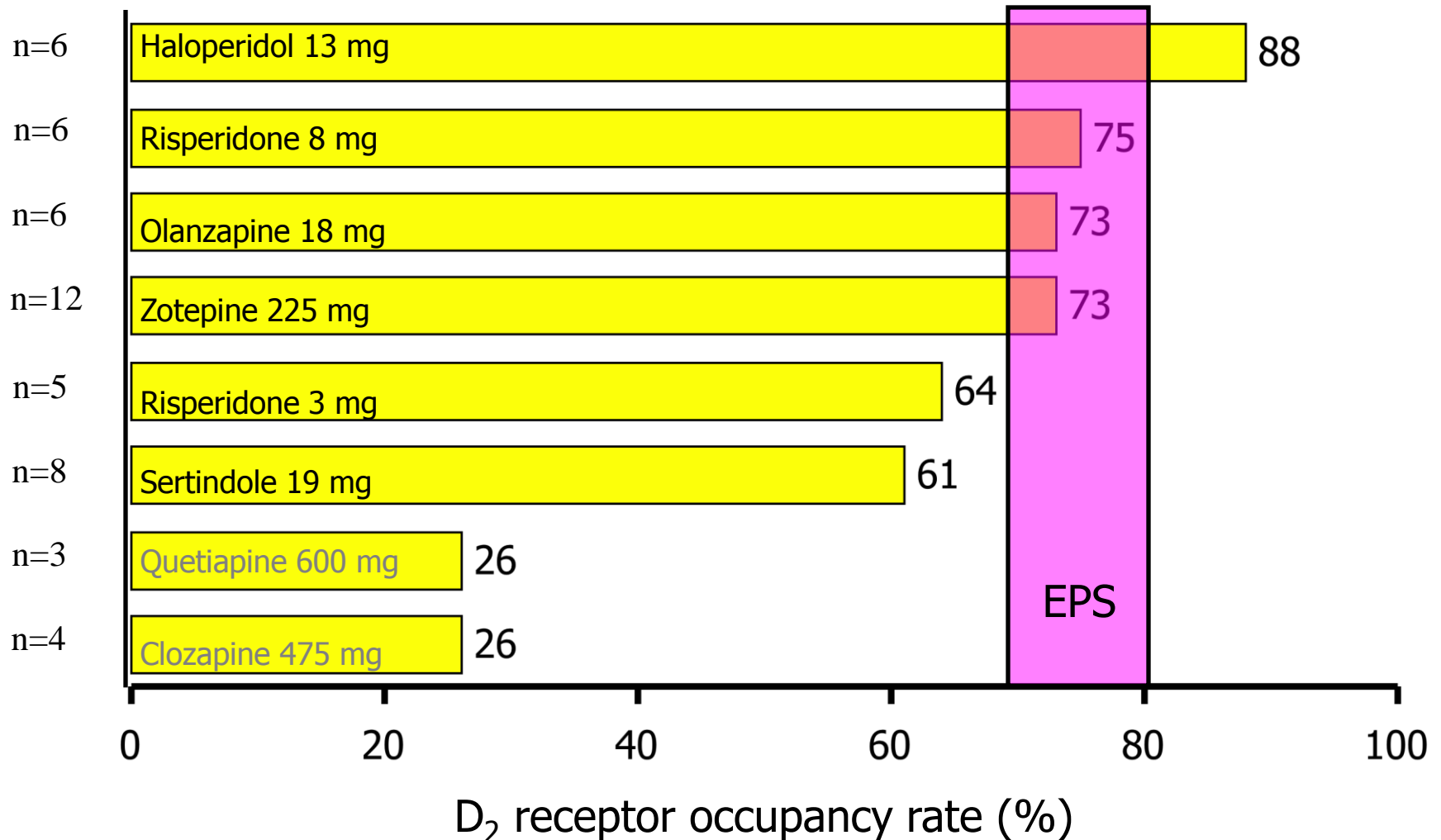
Clozapine treated
Schizophrenia patient

Typical antipsychotic
treated schizophrenia patient

¹²³I-IBZM SPET scans of striatal D₂ receptor occupancy
(Pilowsky et al 1992)

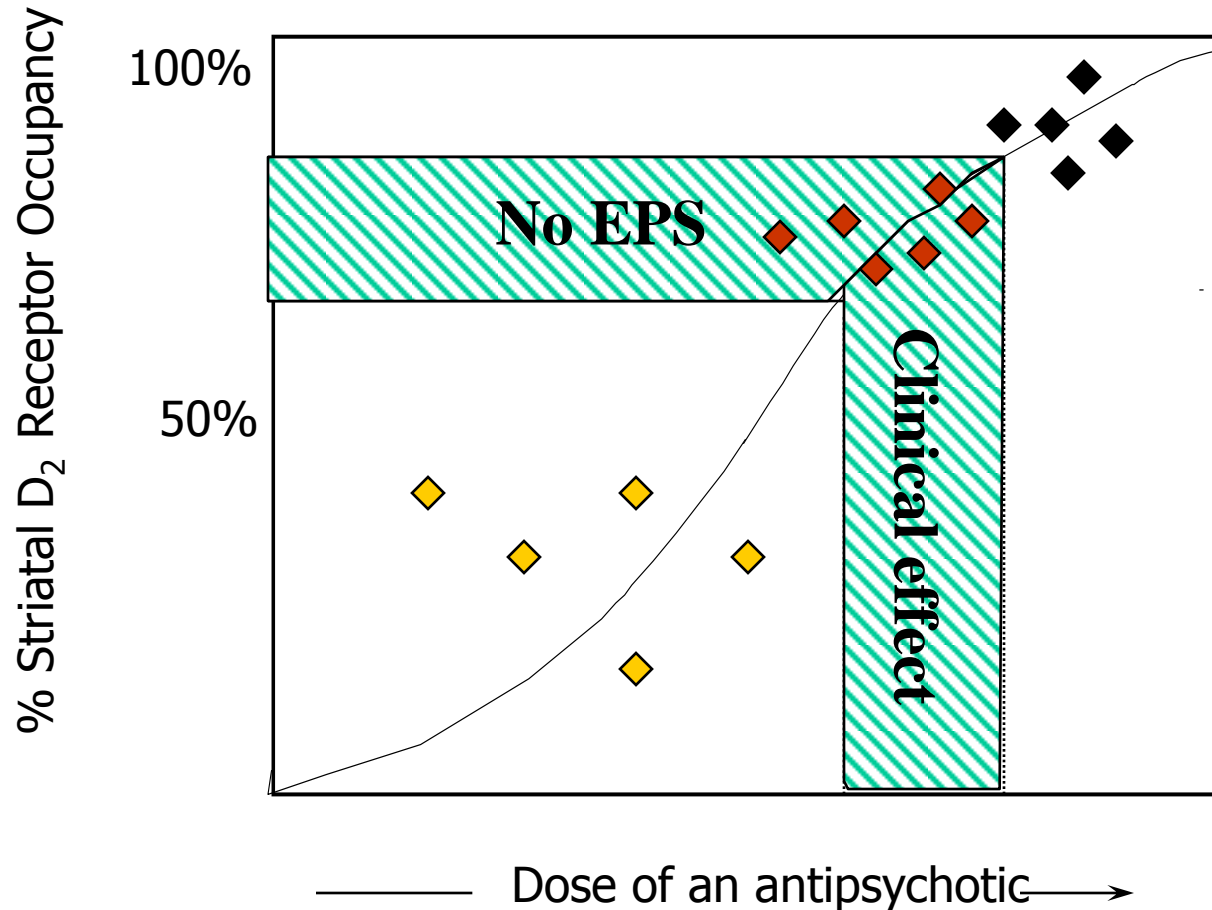
CONVENTIONAL & NEW ANTIPSYCHOTICS

Striatal D₂ receptor occupancy rates



(Kasper et al 1999)

RELATIONSHIP BETWEEN D₂ RECEPTOR OCCUPANCY, EPS AND RESPONSE



(after, Farde et al, 1992, Nyberg et al 1996, Pickar et al 1996 & Kapur et al 2000)

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Initial challenge: diagnosis

Potential psychotic disorders

- Schizophrenia
- Schizophreniform disorder
- Schizoaffective disorder
- Bipolar disorder
- Psychotic depression
- Brief psychotic disorder
- Psychotic disorder due to general medical condition
- Substance-induced psychotic disorder
- Post-psychotic depressive disorder of schizophrenia
- Delusional disorder
- Simple deteriorative disorder (simple schizophrenia)
- Shared psychotic disorder
- Postpartum psychosis
- Culture-bound psychotic syndromes
- Atypical psychotic disorders

Basic Algorithm For Selection of Antipsychotics

- Begin with antipsychotic that causes the less side effects or no side effects feared by **the patient you are treated**
- If patient had 4-6 week trial with full dose, but response unsatisfactory, try another antipsychotic
- If patient intolerant/unable to complete trial of initial agent, try another and then another until you get an adequate trial
- If treatment resistant positive symptoms after 2 adequate monotherapy trials try clozapine

CAUTION!! PROBLEMS WITH GENERALIZABILITY

Males	82%
Mean age (years)	37
Age of onset (years)	22
>6 hospitalisations	65%

Characteristics of patients participating in pivotal trials of new antipsychotics

Antipsychotics dosing

- Chinese and other East Asian ethnic individuals (and many Africans) usually need somewhat lower doses of antipsychotics metabolized by 2D6.
- 35-50% have a less active form of the 2D6 enzyme, rendering them "Slow Metabolizers" (SM's)

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The science of
pain control



PSYCHOSIS AND FEVER

There are other things besides positive symptoms!!

Antipsychotic drugs versus placebo for relapse prevention in schizophrenia: a systematic review and meta-analysis

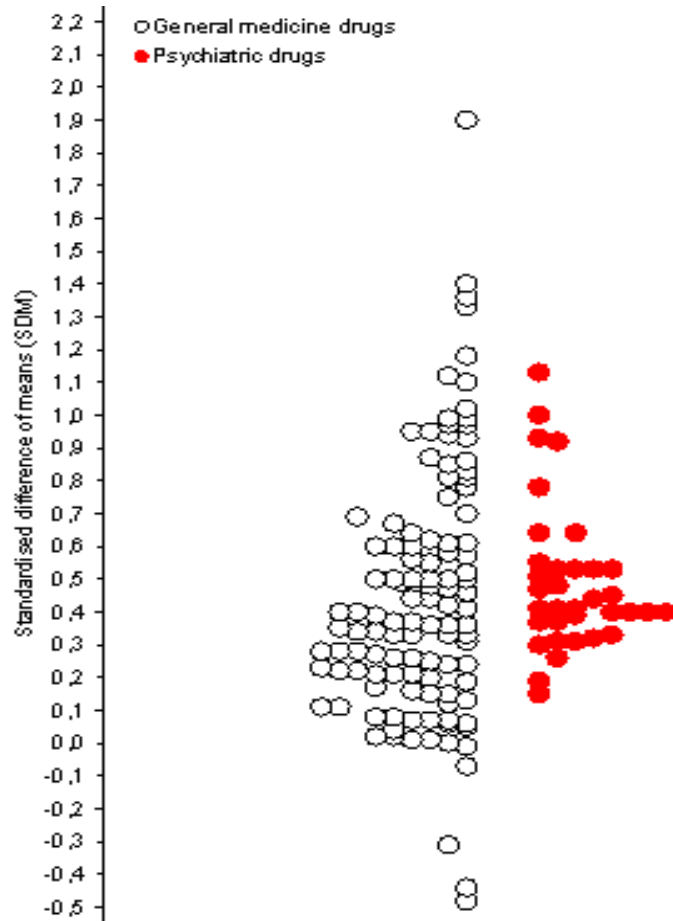
Stefan Leucht, Magdolna Tardy, Katja Komossa, Stephan Heres, Werner Kissling, Georgia Salanti, John M Davis

- 65 included randomised controlled trials with 6,493 patients
- Patients with schizophrenia, stabilised on antipsychotic drugs
- Published over long period, 1959–2011
- Any antipsychotic drug versus placebo (antipsychotics continued or withdrawn)
- 63 double-blind, 2 open randomised controlled trials

Relapse at 7–12 months

- Drug 27%
- Placebo 64%

Effect sizes of general medicine and psychiatric drugs



- Review of
 - 94 meta-analyses of 48 general medicine drugs
 - 33 meta-analyses of 16 psychiatric drugs

Negative symptoms of schizophrenia

Primary negative symptoms

- **Direct causality**
- **Primary manifestation of schizophrenia**
- **Enduring symptoms**

Secondary negative symptoms

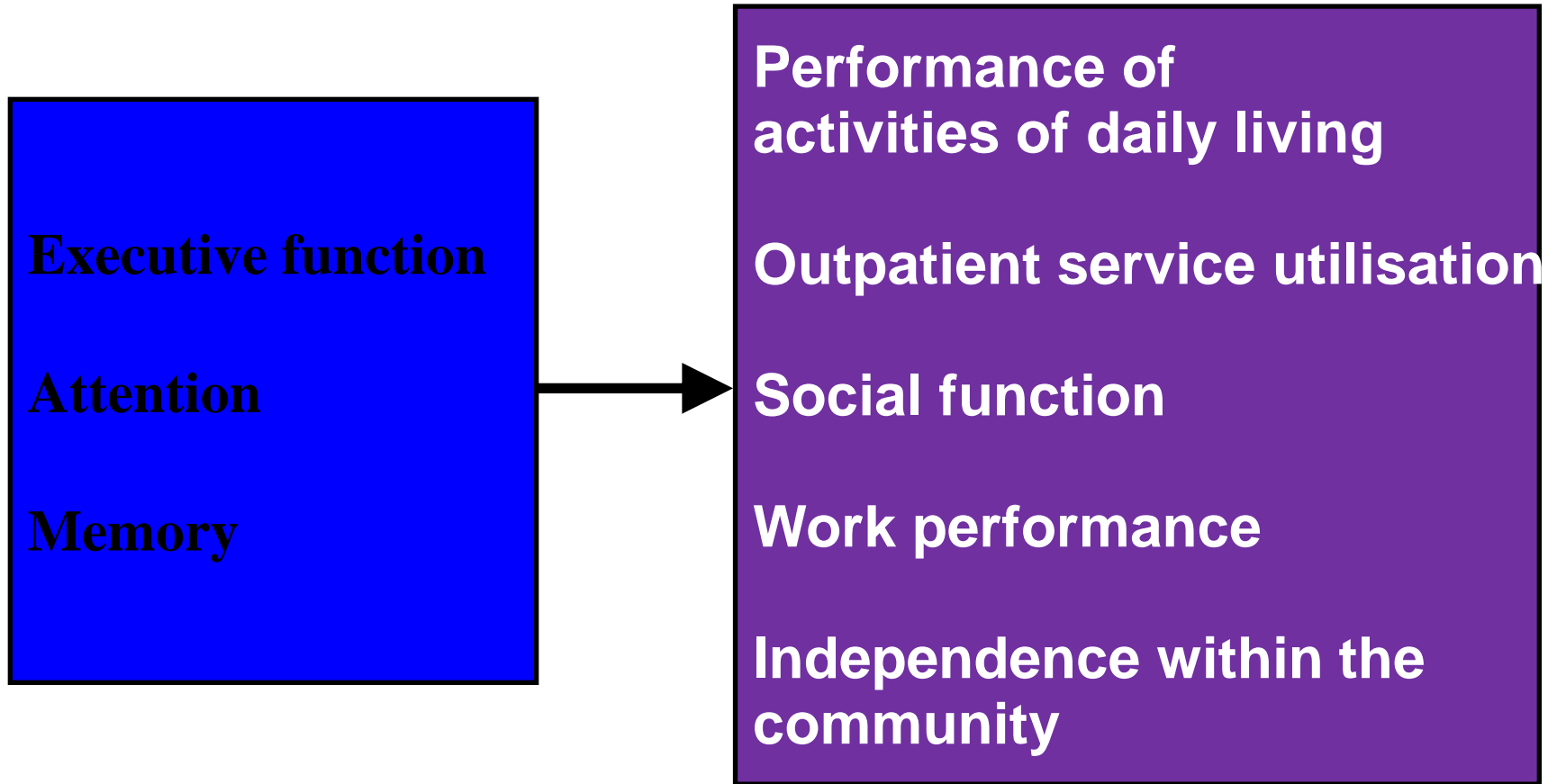
- **Consequence of EPS**
- **Depressive symptoms**
- **Disorganised or paranoid withdrawal**

D2 blockade impairs negative symptoms

Antipsychotics and negative symptoms

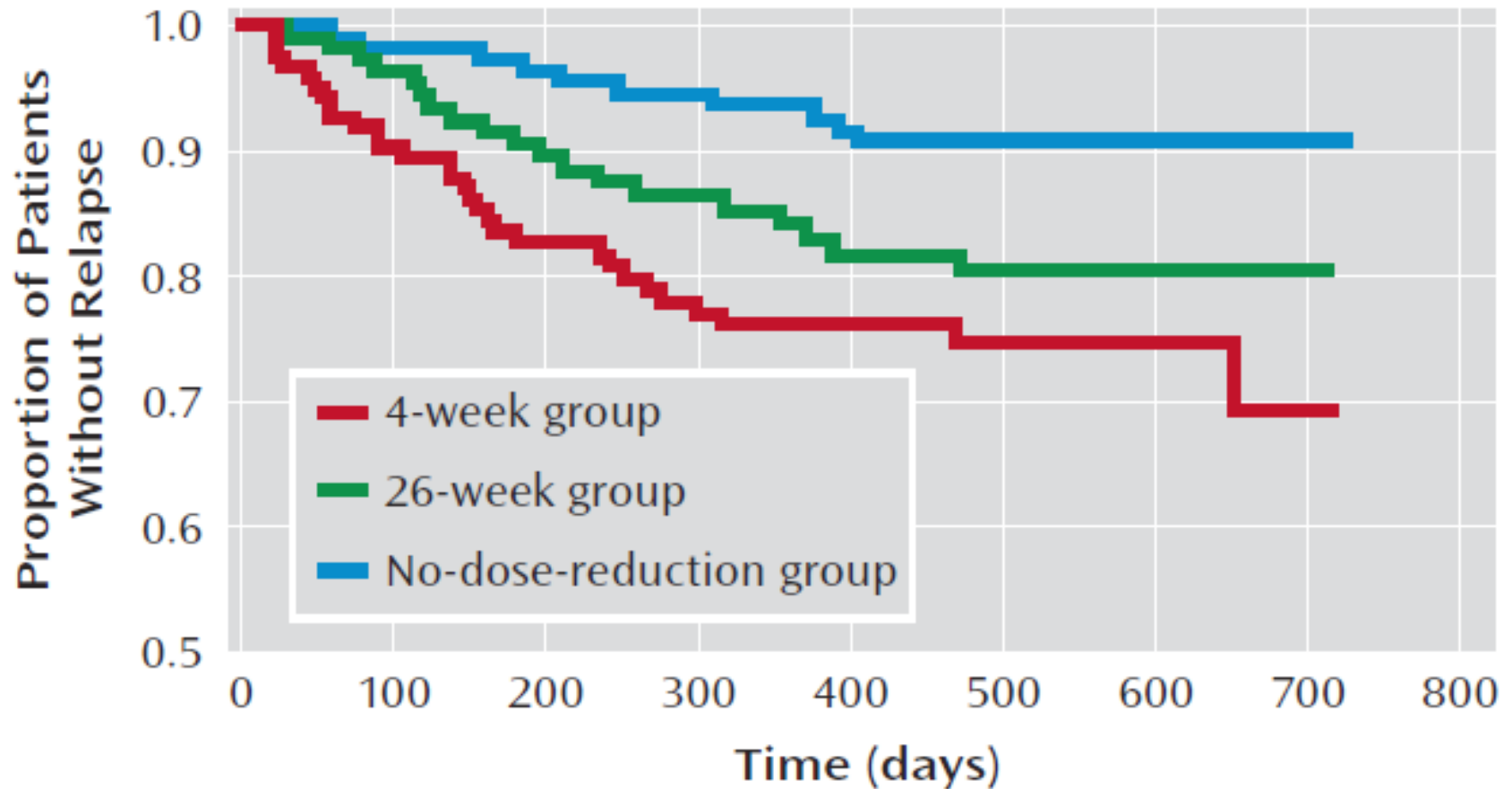
- SGA do not seem to improve primary enduring negative symptoms (Arango et al 2004)
- Some FGA and SGA cause negative symptoms in healthy controls (Artaloytia, Arango et al 2006)
- Patients with negative symptoms are at higher risk to develop Metabolic Syndrome (Arango et al 2008)

Cognitive deficits predict functional outcomes



D2 blockade impairs cognition

50% dose reduction after four weeks or 26 weeks was associated with significantly more relapses than keeping the initial dose



Starting dose: risperidone 4-8mg/day

Wang et al. AJP 2010

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Haloperidol Dosing

- With acute treatment, check for cogwheel rigidity daily as haloperidol, started at 1-2 mg per day, is increased by 1-2 mg every other day.
- For antipsychotic purposes no need to go above 6-8 mg/day. Maintenance: 2-4 mg/day
- Oral, acute IM, depot

Risperidone Dosing

- 3-6 mg per day for 3-6 weeks as an antipsychotic
- A dose that produces parkinsonian side effects is probably too high a dose
- First exposure: 0.5 mg bid, then 1 mg bid
- Acute exacerbation: 1 mg bid, then 2 mg bid
- Elderly: 50% of above, or less
- P450 Drug Interactions: 2D6 substrate

Olanzapine Dosing

- Works most quickly when *started* at 10-20 mg/d*
- Smoking increases clearance by 40%** (58-88% of patients with schizophrenia smoke)
- Female gender decreases clearance by 30%**
- Should you exceed the PDR max. dose of 20 mg? (the *average* dose used in CATIE) Not routinely.

* Osser (2001)

**Package Insert, Weiss (2005), Carrillo (2003)

Metabolic Issues w. Olanzapine

- More than 50% of olanzapine patients gain $> 7\%$ body wgt (naïve: 75%)
- Elevated triglycerides – highest with olanzapine
- HgbA1C – increased the most with olanzapine
- Triglycerides v. strongly correlated with insulin resistance (IR)

Ziprasidone

- Half-life 10 hours
- Avoid ziprasidone if EKG shows QTc is >500 milliseconds
- On medications that might prolong the QTc since this EKG was done? (tricyclics, quetiapine, thioridazine, floxacins.) If so, repeat EKG
- Risk for electrolyte problems? (alc. Dependent, purging bulimic) If so, get K^+ , Mg^{++} and follow

Dosing of Ziprasidone - 1

- Package insert recommends starting at 20 mg twice daily, but 3/4 acute treatment studies in patients with schizophrenia failed to show superiority of 20 mg bid to placebo
- Stable outpatient being switched: could start with 40 mg bid. Continuation with the other drug is recommended (at least 1 week)
- Absorption is reduced by 40% if not taken with food

Dosing of Ziprasidone - 2

- Raise the dose, as tolerated, every 1-2 days to 80 bid for the routine case of an acutely ill hospitalized patient with schizophrenia
- If this is a first episode patient, try perhaps half the routine dose
- Major clinical concern: difficult to find the right dose!

Aripiprazole Issues

- 75 hour half life
- Substrate for Cytochrome P450 3A4 and 2D6. Paroxetine and fluoxetine will raise levels (use 50% dose), carbamazepine will lower them.
- 15 mg is superior to 30 mg, at all data points and even after 1 week
- 30 mg sometimes needed in clinical practice in mania and acute schizophrenia

Aripiprazole Side Effects

- Dizziness
- **Insomnia (prescribe in the morning)**
- **Akathisia, agitation**
- Headache
- Sedation

Quetiapine

- Half-life 6-12 hours
- Starting dose 100-200 mg/day. Rapid titration if needed
- Bipolar depression: 300 mg/day
- Acute schizophrenia: up to 1200 mg/day
- Bipolar mania: 600-800 mg/day
- Maintenance: 300-500 mg/day
- Widely used outside schizophrenia

Amisulpride

- Half-life 12 hours
- Low dose: 50-200 mg/day. Block inhibitory pre-synaptic autoreceptors: facilitation of dopamine (negative symptoms)
- Dose: 400-1200 mg/day. Block D2 (partial agonist)-D3 receptors (5HT₇ antagonist)
- Activate the GHB receptor (inhibit DA release)

Paliperidone

- 9-OH- Risperidone
- Half life 23 hours
- Not metabolized by Cytochrome P450
(Patients with hepatic compromise)
- Dose between 6-12 mg/day

Asenapine

- In Europe approved only for bipolar disorder
- Sublingual
- Half-life 20 hours
- Starting dose: 10 mg bid (5 mg bid if adjunct to lithium or valproate or schizophrenia)

Sertindole

- Reintroduced in 2002 for restricted use
- Half life 72 hours
- Initiate 4 mg/day. Increase 4 mg/day
- Maximum dose 20 mg
- Extensive ECG monitoring requirement

Lurasidone

- 18.5, 37 and 74 mg
- Starting dose: 37 mg/day once a day
- Akathisia and somnolence

Clozapine Dosing

- 12.5 mg for first dose. Thereafter, divided doses
- Increase by 25-50 mg per day as tolerated, to 300-400 mg per day. Maximum is 900 mg/d
- If response unsatisfactory, check **plasma level**. Best results are with levels of parent compound greater than 400 ng/ml

No single dose should exceed 450 mg

CBC Monitoring with Clozapine

- Changes from country to country. Weekly CBC for 16 weeks. Then every 4 weeks
- If $WBC < 3.5$ or $ANC\ 1.5-2.0$, repeat CBC and get biweekly CBC until levels rise.
- If $WBC < 3.0$ or $ANC\ 1.0-1.5$, hold clozapine, get daily CBC until levels rise. Rechallenge possible
- If $WBC < 2.0$ or $ANC < 1.0$, stop clozapine. Monitor daily. Rechallenge not advised, though there are some reports.

Clozapine

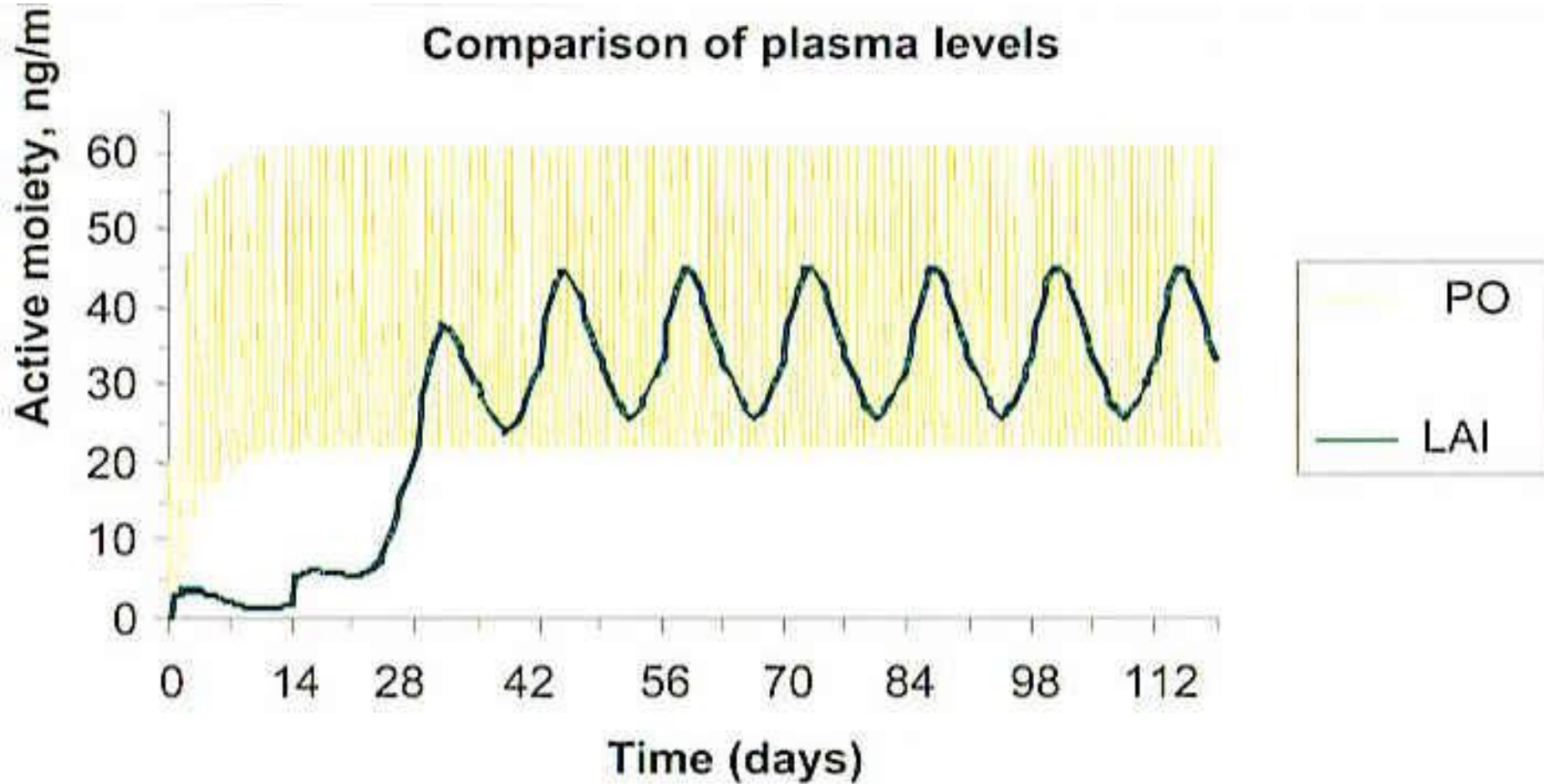
- Approved for suicide within schizophrenia
- Only antipsychotic with partial evidence for polydipsia and nicotine addiction

Other antipsychotics approved in the US or in their way

- Iloperidone
- Brexpiprazole

Depot (LAI) Neuroleptics

- Fluphenazine Decanoate: 12.5 mg to 50 mg every two weeks.
- Haloperidol Decanoate 25 mg to 200 mg every 4 weeks.
- Risperidone consta every 2 weeks (12.5 mg, 25 mg, 37.5 mg, 50mg)
- Olanzapine depot (2-4 weeks, post-injection syndrome, at least 3hour monitoring)
- Many more patients are non-compliant or not



Mannaert E et al. Poster 530. CINP. Paris, June 20-24, 2004

Paliperidone Palmitate

- Paliperidone Palmitate: (50mg, 75 mg, 100 mg) Mean doses 73.3 and 104.6 mg every four weeks
- Paliperidone palmitate (Trivecta): maintenance treatment of schizophrenia in adult patients who are clinically stable on Xeplion® (234 mg, 156 mg, 117 mg, 78 mg)

Aripiprazole LAI

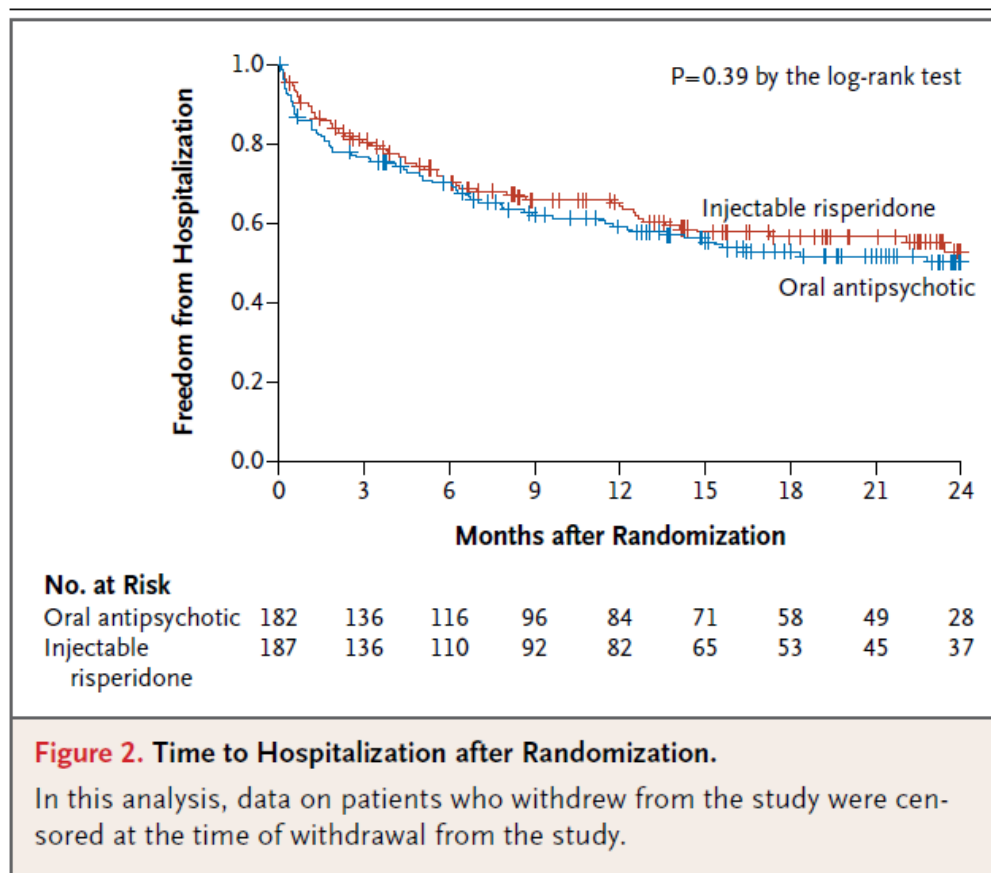
- 300/400 mg IM once a month

N Engl J Med 2011;364:842-51.

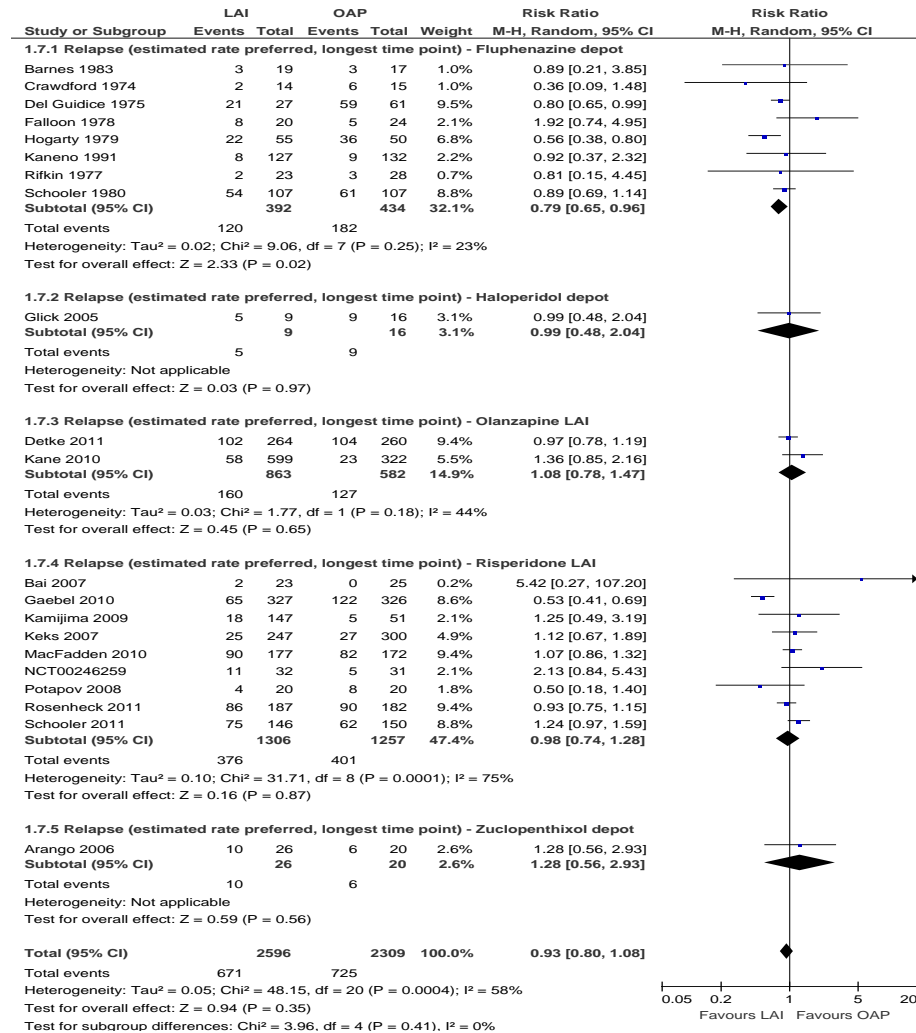
Copyright © 2011 Massachusetts Medical Society.

Long-Acting Risperidone and Oral Antipsychotics in Unstable Schizophrenia

Robert A. Rosenheck, M.D., John H. Krystal, M.D., Robert Lew, Ph.D.,
Paul G. Barnett, Ph.D., Louis Fiore, M.D., M.P.H., Danielle Valley, M.P.H.,
Soe Soe Thwin, Ph.D., Julia E. Vertrees, Pharm.D.,
and Matthew H. Liang, M.D., M.P.H., for the CSP555 Research Group*



Most recent meta-analysis...



LAI, long-acting injectable; OAP, oral antipsychotic; M-H, Mantel-Haenszel;
Random, random effects model; CI, confidence interval

A Nationwide Cohort Study of Oral and Depot Antipsychotics After First Hospitalization for Schizophrenia

TABLE 1. Pairwise Comparisons for Risk of All-Cause Discontinuation of the Initial Antipsychotic Treatment and Risk of Rehospitalization After a First Hospitalization for Schizophrenia^a

Comparison	All-Cause Discontinuation			Rehospitalization		
	Adjusted Hazard Ratio ^b	95% CI	p	Adjusted Hazard Ratio ^b	95% CI	p
Any depot injection compared with equivalent oral formulation	0.41	0.27–0.61	<0.0001	0.36	0.17–0.75	0.007
Haloperidol depot injection compared with oral haloperidol	0.27	0.08–0.88	0.03	0.12	0.01–1.13	0.06
Perphenazine depot injection compared with oral perphenazine	0.32	0.19–0.53	<0.0001	0.53	0.22–1.28	0.16
Risperidone depot injection compared with oral risperidone	0.44	0.31–0.62	<0.0001	0.57	0.30–1.08	0.09
Zuclopenthixol depot injection compared with oral zuclopenthixol	0.75	0.29–1.89	0.54	0.49	0.11–2.14	0.35

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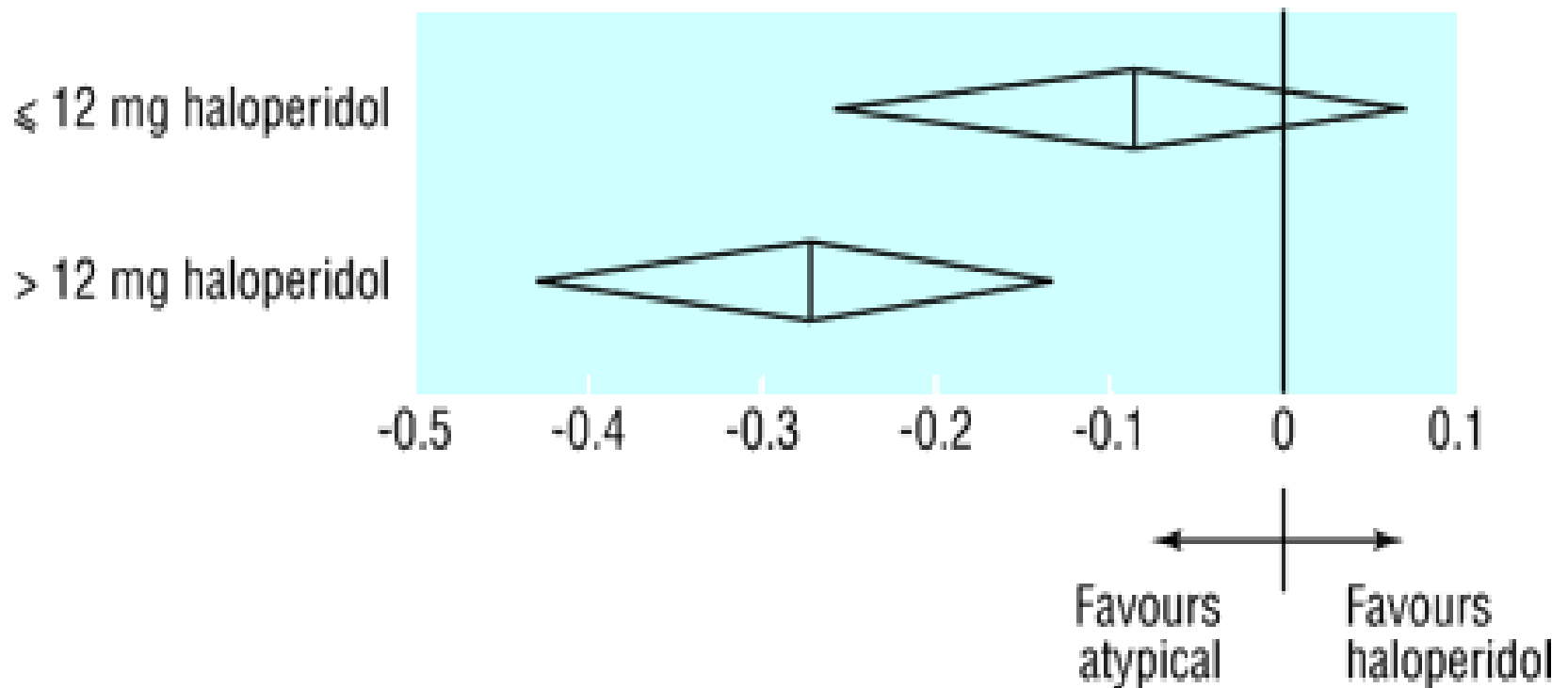
Why Olanzapine Beats Risperidone, Risperidone Beats Quetiapine, and Quetiapine Beats Olanzapine: An Exploratory Analysis of Head-to-Head Comparison Studies of Second-Generation Antipsychotics

The overall outcome reported in the abstract of head to head comparisons of atypical antipsychotics strongly depends on **the sponsor**

In a blinded analysis of the abstracts of 33 head to head comparisons of atypical antipsychotics in about 90% the overall outcome was in favour of the sponsor

Meta-analysis of atypical antipsychotics in the treatment of schizophrenia

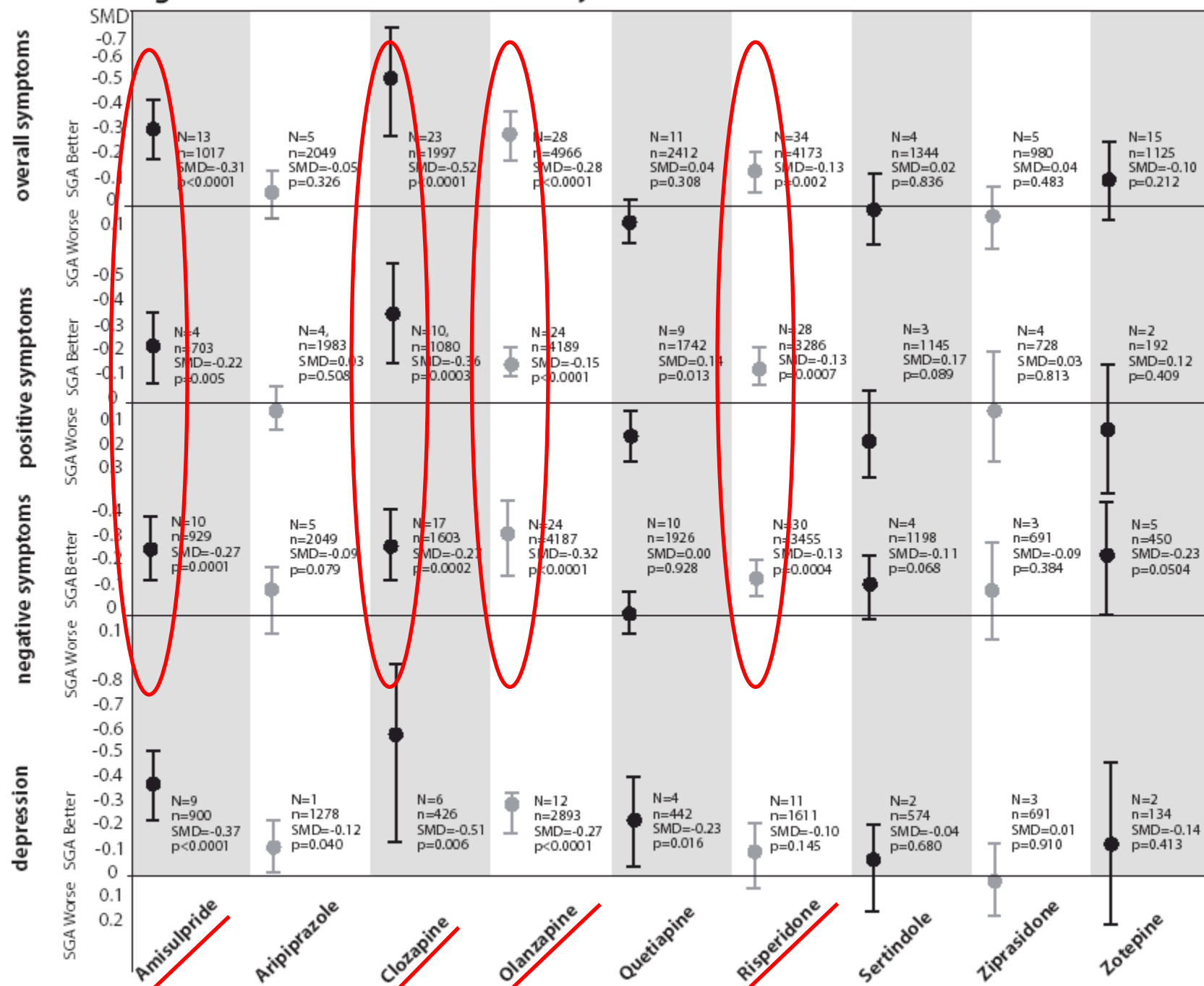
Geddes et al 2000



Overall symptom score by dose of comparator drug

Figure 2: SGA versus FGA - efficacy in various domains

Leucht et al. Lancet 2009



NNT

- Schizophrenia: 5-10
- Bipolar mania: 3-6
- Aggression in autism: 3-4

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Antipsychotic Drugs: Side effects

SEDATION Greater with CLOZAPINE, OLANZAPINE, QUETIAPINE

HEADACHE

SUBJECTIVE BURDEN

- | Loss of energy/drive Greater with classic
- | Dysphoria Greater with classic
- | Problems with memory and concentration

SLEEP DISTURBANCE

- | Night sleep pattern
- | Difficulty waking/daytime sleepiness
- | Insomnia Greater with ARIPIPRAZOLE

Antipsychotic Drugs: Side effects

CARDIOVASCULAR

- | Palpitations/tachycardia ? Greater with QUETIAPINE
- | Postural hypotension Greater with CLOZAPINE, LEVOMEPRMAZINE
- | ECG abnormalities
 - | QT prolongation Greater with SERTINDOLE, ZIPRASIDONE

GASTROINTESTINAL

- | Nausea/vomiting, constipation, diarrhoea

ENDOCRINE

- | Weight gain Greater with CLOZAPINE and OLANZAPINE
- | Diabetes Greater with CLOZAPINE and OLANZAPINE
- | Decreased T3 Greater with QUETIAPINE

HEPATIC DYSFUNCTION

- | Increased transaminases ? Greater with OLANZAPINE
- | Cholestatic jaundice

Antipsychotic Drugs: Side effects

HYPERALIVATION Greater with CLOZAPINE

ANTICHOLINERGIC EFFECTS

- | Dry mouth / Blurred vision / Urinary hesitancy

NOCTURNAL ENURESIS Greater with RISPERIDONE

SEXUAL SIDE-EFFECTS Greater with RISPERIDONE,
AMISULPRIDE

- | Loss of libido
- | Females: Anorgasmia/Change in menstruation
- | Males: Erectile dysfunction/Ejaculatory disturbance
 - ? Reduced ejaculatory volume with SERTINDOLE

PROLACTIN ELEVATION Dose-related with RISPERIDONE,
AMISULPRIDE

Antipsychotic Drugs: Side effects

CNS

- | Emergence of disorientation/clouding of consciousness
- | Seizures *Greater with CLOZAPINE,? Classic antipsychotics*
- | Neuroleptic malignant syndrome *Classic*

OPHTHALMOLOGICAL

- | Glaucoma
- | Corneo-lenticular opacities/pigmentary lesions

CUTANEOUS REACTIONS

- | Photosensitive skin rash
- | Pigmentation

HAEMATOLOGICAL

- | Blood dyscrasias *Greater with CLOZAPINE*

ANTIPSYCHOTIC-INDUCED MOVEMENT DISORDER

Early onset

Parkinsonism (Classic potent D2)

Acute akathisia (Classic,
aripiprazole)

Acute dystonia (Classic potent D2,
risperidone dose dependant)

Late onset

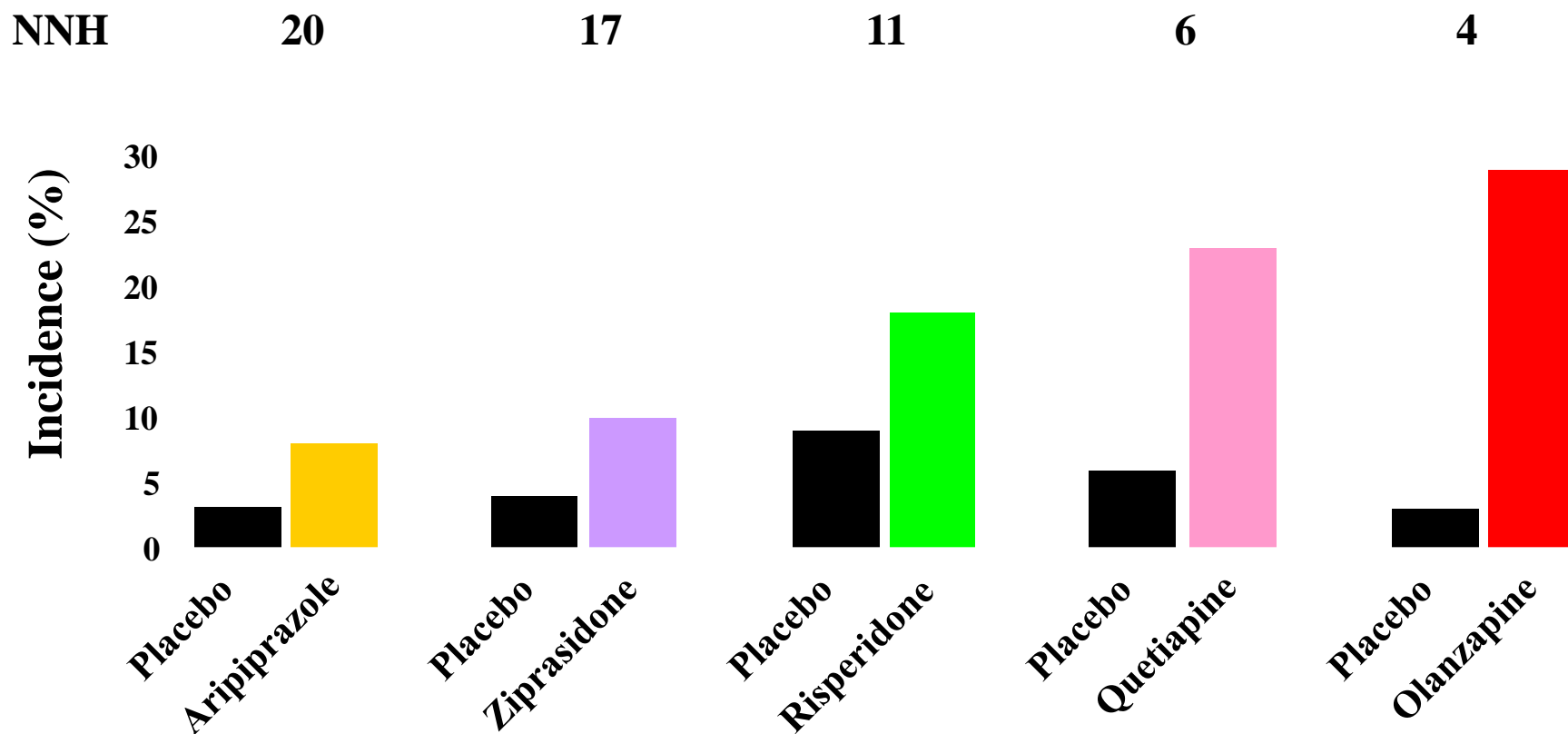
Chronic akathisia ?

Tardive dystonia ?

Tardive dyskinesia (Classic)

Clinically Significant Weight Gain ($\geq 7\%$)

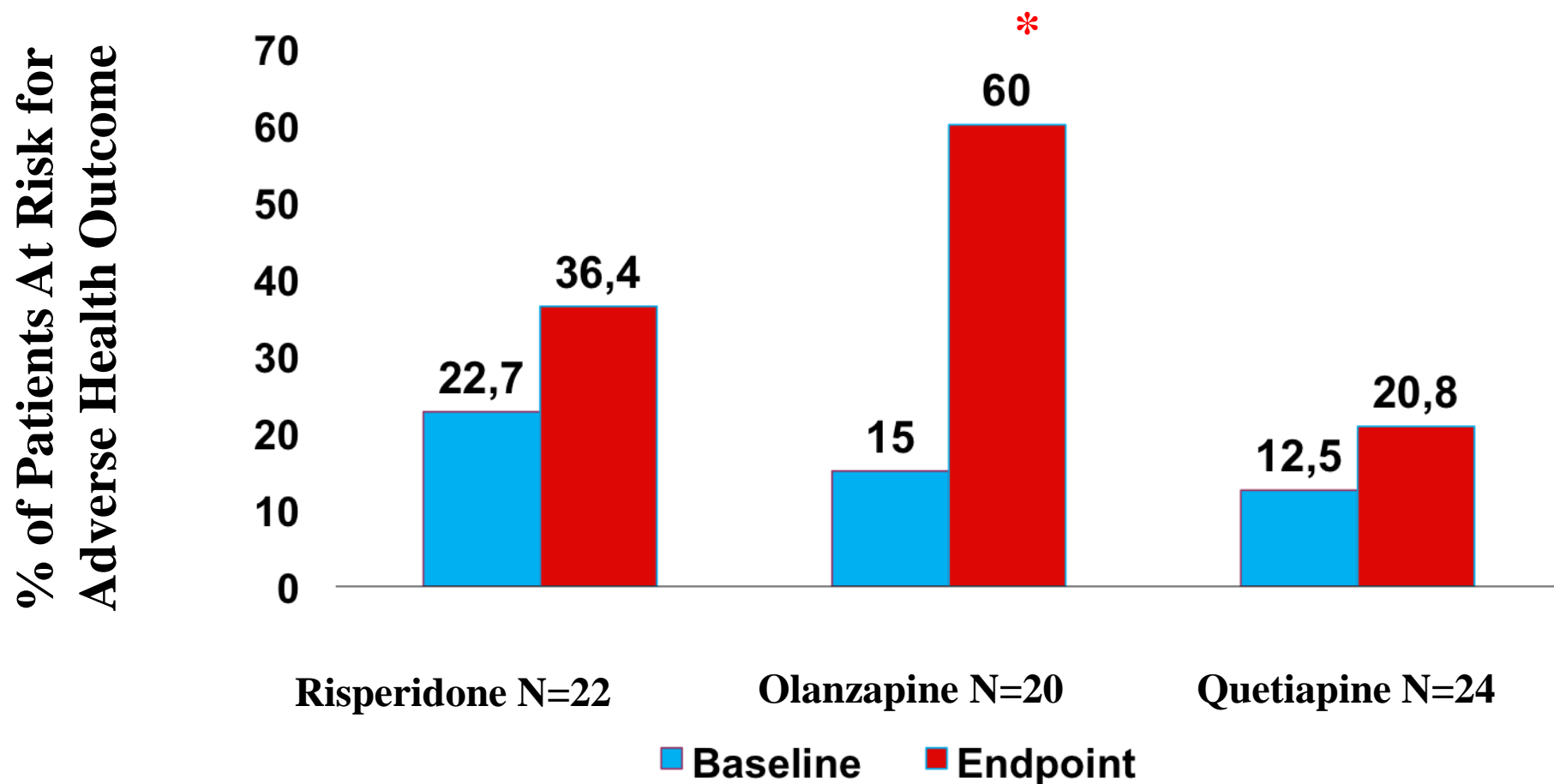
New antipsychotics vs placebo



NNH = number needed to harm

Abilify® (aripiprazole) US PI, October 2006. Geodon® (ziprasidone) US PI, August 2004. Risperdal® (risperidone) US PI, November 2006. Seroquel® (quetiapine fumarate) US PI, July 2007. Zyprexa® (olanzapine) US PI, March 2002.

Change in At Risk Health Status During 6-Month Naturalistic Antipsychotic Treatment

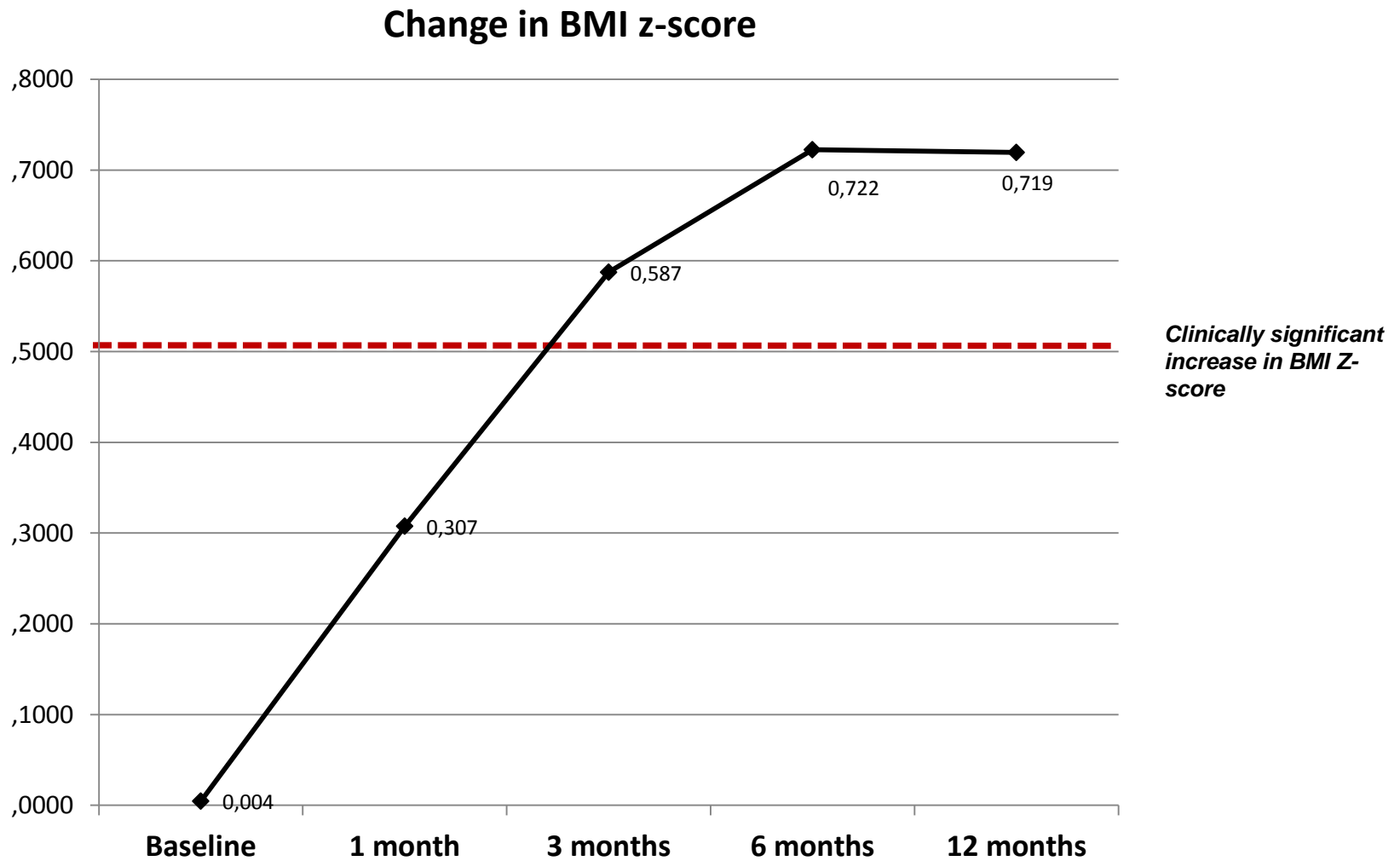


At risk for adverse health outcome: obesity or overweight plus at least one metabolic, blood pressure or other weight related health problem

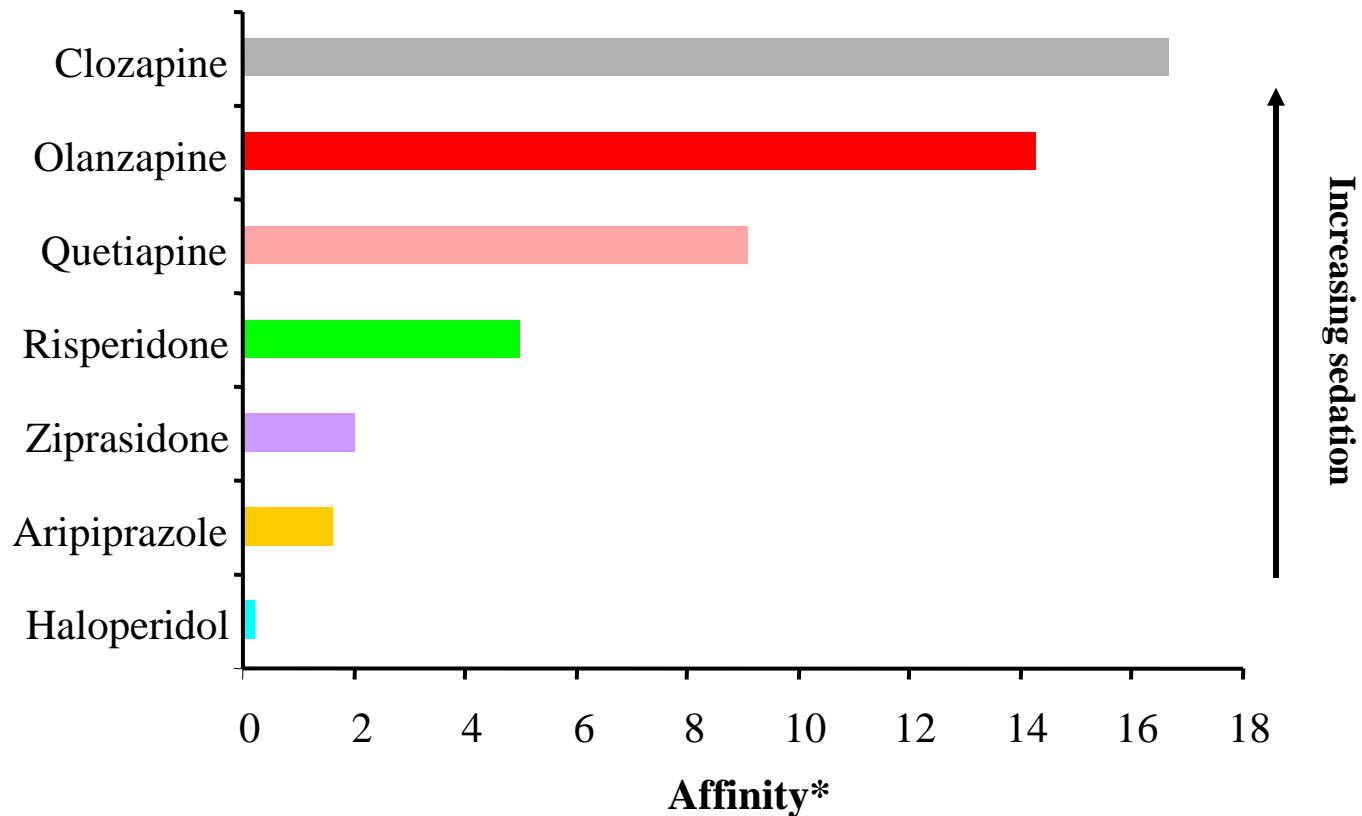
* $p < .05$; group comparison: $p = .018$

Fraguas D et al. (2008), J Clin Psychiatry ;69(7):1166-75.

One-year longitudinal study of children and adolescents treated with SGAs



Sedation may be Related to Affinity of Medications for the Histamine H1 Receptor



*Presented at $10^2 \times 1/K_i$ (nM)

**Data with cloned human receptors

Bymaster FP *et al. Neuropsychopharmacology* 1996;14:87–96;

Post-Lecture Exam

Question 1

1. Which of the following is an antipsychotic dose that is in excess of the optimal?
 - A. Aripiprazole 15 mg/day
 - B. Ziprasidone 80 mg bid
 - C. Haloperidol 20 mg qd
 - D. Risperidone 4 mg/day
 - E. Quetiapine 300 mg bid

Question 2

2. Which of the following antipsychotics must be taken with food in order to prevent significant loss of absorption?
- A. Ziprasidone
 - B. Olanzapine
 - C. Clozapine
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3. Which of the following is the recommended starting dose for clozapine?
- A. 25 mg twice a day
 - B. 12.5 mg
 - C. 25 mg
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4. All of the following are true of a patient on risperidone who gets parkinsonian side effects, except:
- A. D2 receptor occupancy is 75% or more
 - B. The patient is above the “neuroleptic threshold”
 - C. Patient is at risk for secondary negative symptoms
 - D. Raising the dose is likely to be helpful

Question 5

5. ¿What is the drug of choice for a schizophrenia patient with polydipsia?
- A. Olanzapine
 - B. Thirodazine
 - C. Ziprasidone
 - D. Pimozide
 - E. Clozapine

Question 6

The NNT for antipsychotics is lower for

- A. Schizophrenia
- B. Schizoaffective disorder
- C. Bipolar disorder
- D. Aggressive behaviour in autism
- E. Depression

Question 7

Which one of these antipsychotics has a longer half life

- A. Olanzapine
- B. Haloperidol
- C. Chlorthalidone
- D. Aripiprazole
- E. Quetiapine

Question 8

Which one of these antipsychotics is the only one that does not have affinity for the D2 receptor

- A. Paliperidone
- B. Quetiapine
- C. Chlorpromazine
- D. Aripiprazole
- E. None

Question 9

When do we have plasma levels similar to oral risperidone with Risperidone consta (25 mg)

- A. Day 1
- B. Day 5
- C. Day 10
- D. Day 15
- E. Day 30

Question 10

What antipsychotic would you not recommend for a 16 year old with a first psychotic episode

- A. Aripiprazole
- B. Risperidone
- C. Quetiapine
- D. Olanzapine
- E. Haloperidol (low dose)

Question 11

For what drug do guidelines (e.g PORT) recommend to measure plasma levels (therapeutic window)?

A. Aripiprazole

B. Clozapine

C. Quetiapine

D. Olanzapine

E. Haloperidol

Question 12

Most of the weight gain with antipsychotics takes place in:

- A. First month
- B. 3 months
- C. 6 months
- D. 1 year
- E. 2 years

Question 13

The half life of LAI (depot) antipsychotics is:

A. 2 weeks

B. 4 weeks

C. 12 weeks

D. A and B are correct

E. A, B and C are correct