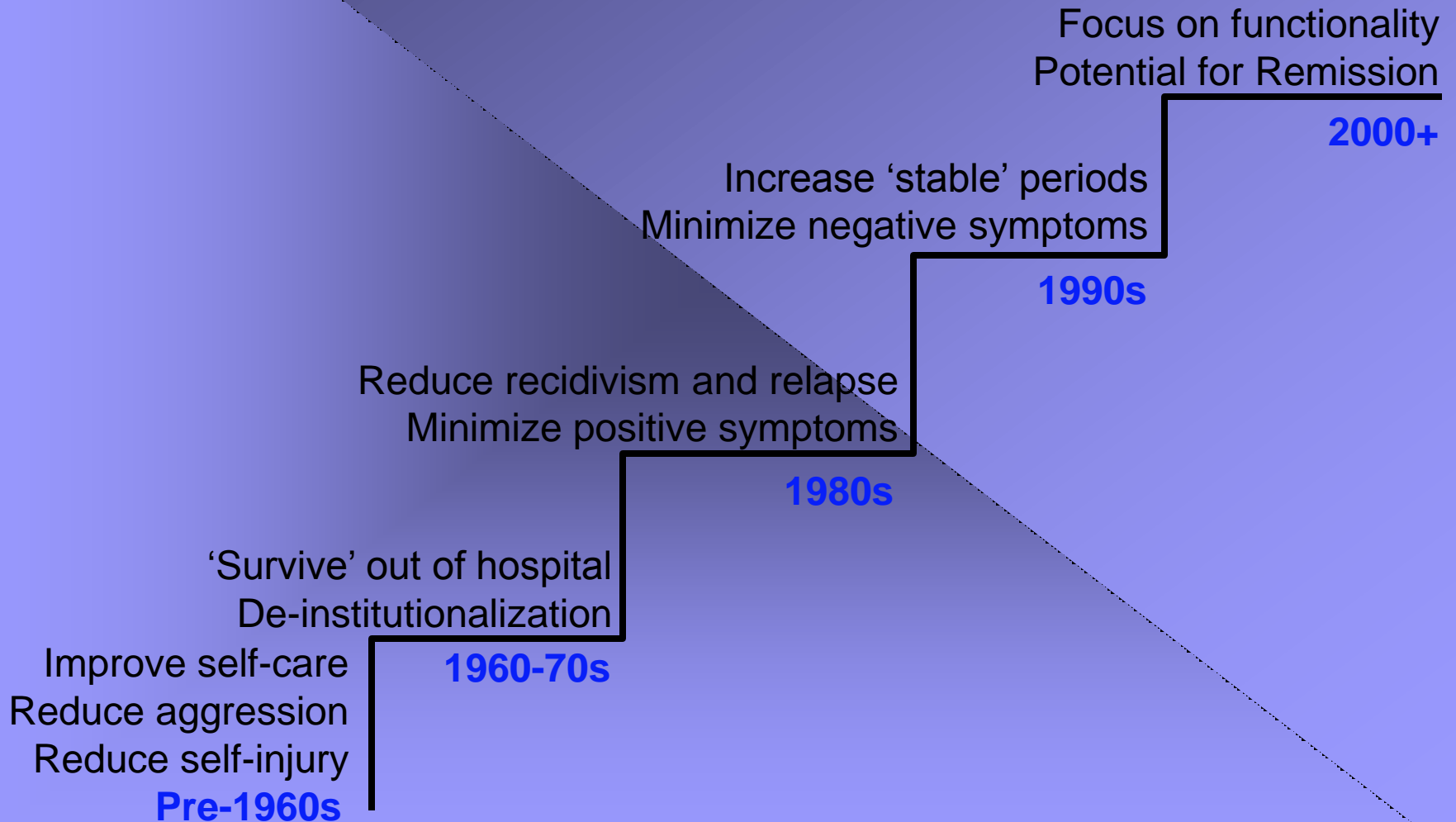


'mental health reformation and medication safety: introspective omphalism vs reality'

Harry Hustig
Director Glenside Research Unit
Director Inpatient Rehabilitation AHS



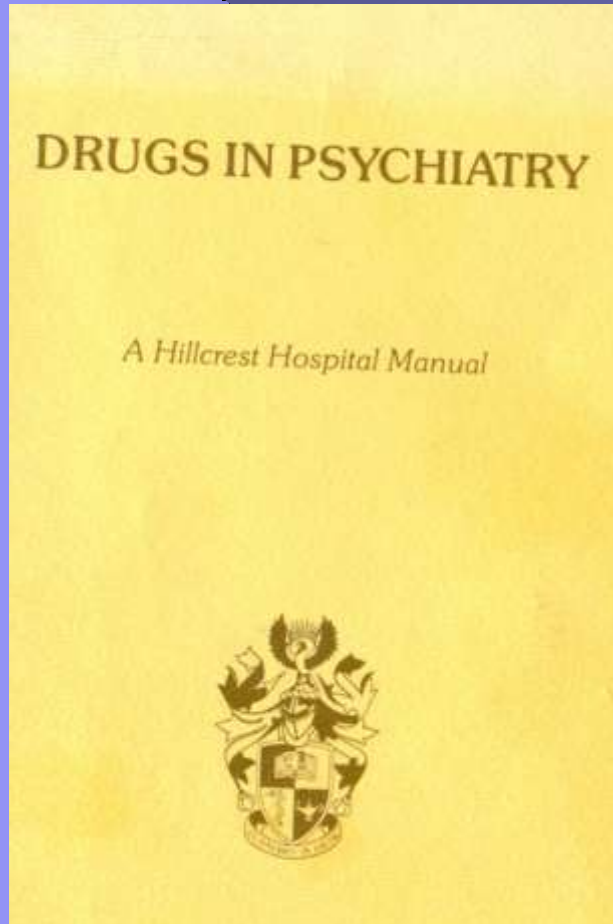
Long-term outcomes in schizophrenia



Practical target outcomes

- ◆ Acute services
 - ◆ Reduction aggression reduced inpatient care
 - ◆ Positive symptom control
 - ◆ Not too many nasty side effects, “compliance”
 - ◆ If it ain’t broke why fix it
- ◆ **Patient**
 - ◆ Symptom control including negative and cognition
 - ◆ Minimal side effects
 - ◆ Chance of a semi-ordinary life, “Survival”
 - ◆ Any change has the potential for relapse
- ◆ **“RECOVERY”**
 - ◆ Remission of all symptoms
 - ◆ No long term side effects
 - ◆ Effects of drug use minimal
 - ◆ Chance to have what we all have a relationship, a job, a future

The Masters word of A/Prof N James



FOREWORD

There is comfort in having knowledge about drugs presented didactically. The clinician requires a portable *vade-mecum* which offers synoptic guidance in a style not totally devoid of prose.

In moments of therapeutic uncertainty the treater is also treated by being 'spoken' to rather than challenged by lists of the potential consequences of his prescription.

The trainee psychiatrist for whom this manual is primarily intended will readily associate the clarity of this presentation with the erudite voice of its author. Herein he will find succour, and will emerge from his readings better equipped

to prescribe not only a 'drug', but also 'himself'.

DAVID RAMPLING

Director of Training

Hillcrest Hospital

Clinical Senior Lecturer in Psychiatry

The University of Adelaide

Kumar & Clark in their textbook of “Clinical Medicine “
define an adverse drug reaction as
‘the unwanted effect of a drug
under normal conditions of use’

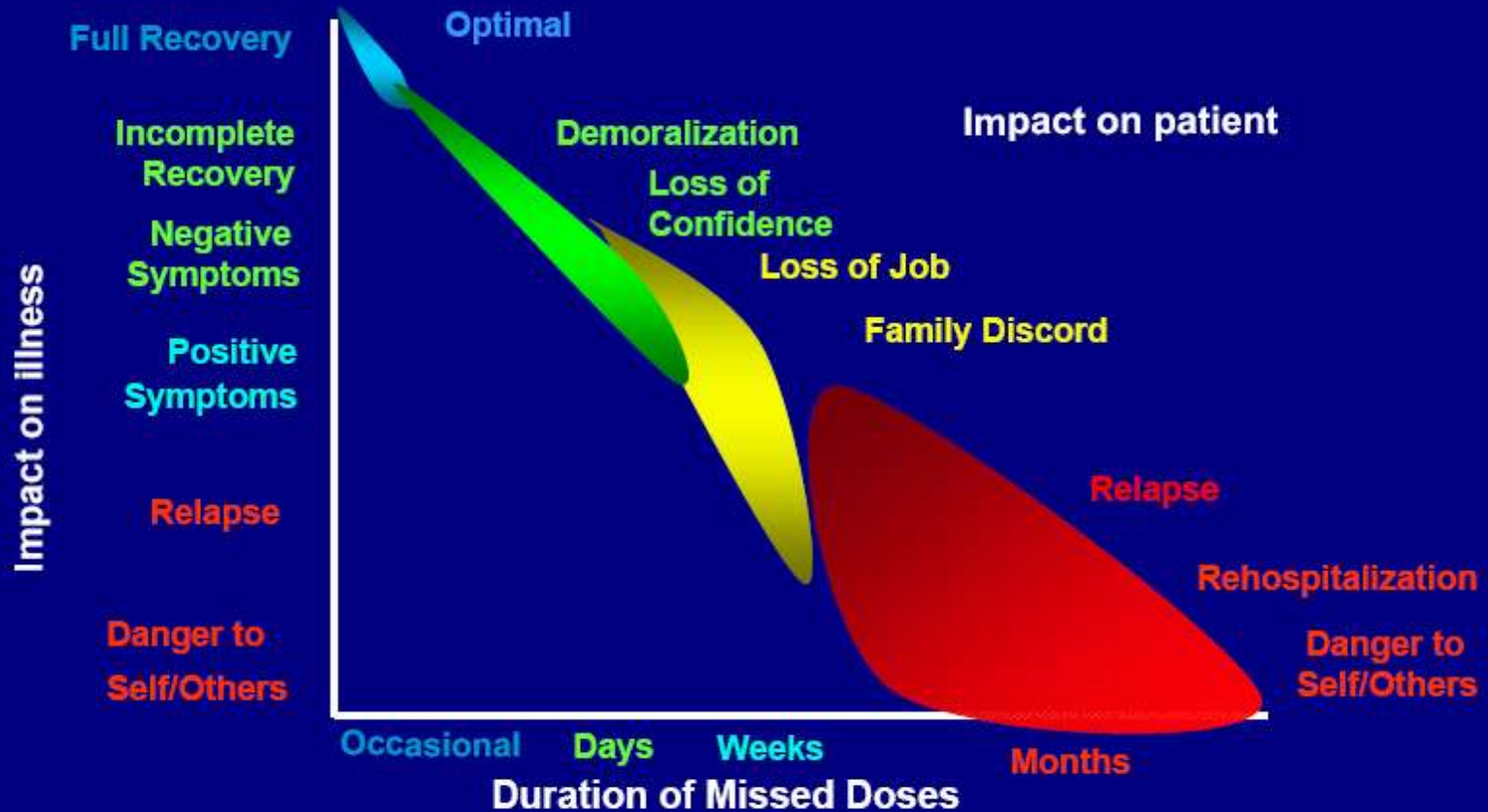
These reactions account for 5% of acute medical
emergency admissions and around 10-20% of
patients suffer such events during their stay

The risk rises sharply with number of drugs
administered

Every Day Life for persons with psychosis in Australia 1997-8

- ◆ of 91% who receive medication 75% had side effects severe enough to stop them carrying daily activities
- ◆ two thirds on older medication
- ◆ only 19% attended rehabilitation where they could meet people and enhance social skills
- ◆ many had trouble getting clinical treatment
- ◆ Those with mental illness
 - ◆ more likely abuse street drugs
 - ◆ four fold increase alcohol abuse
 - ◆ three times more likely to smoke

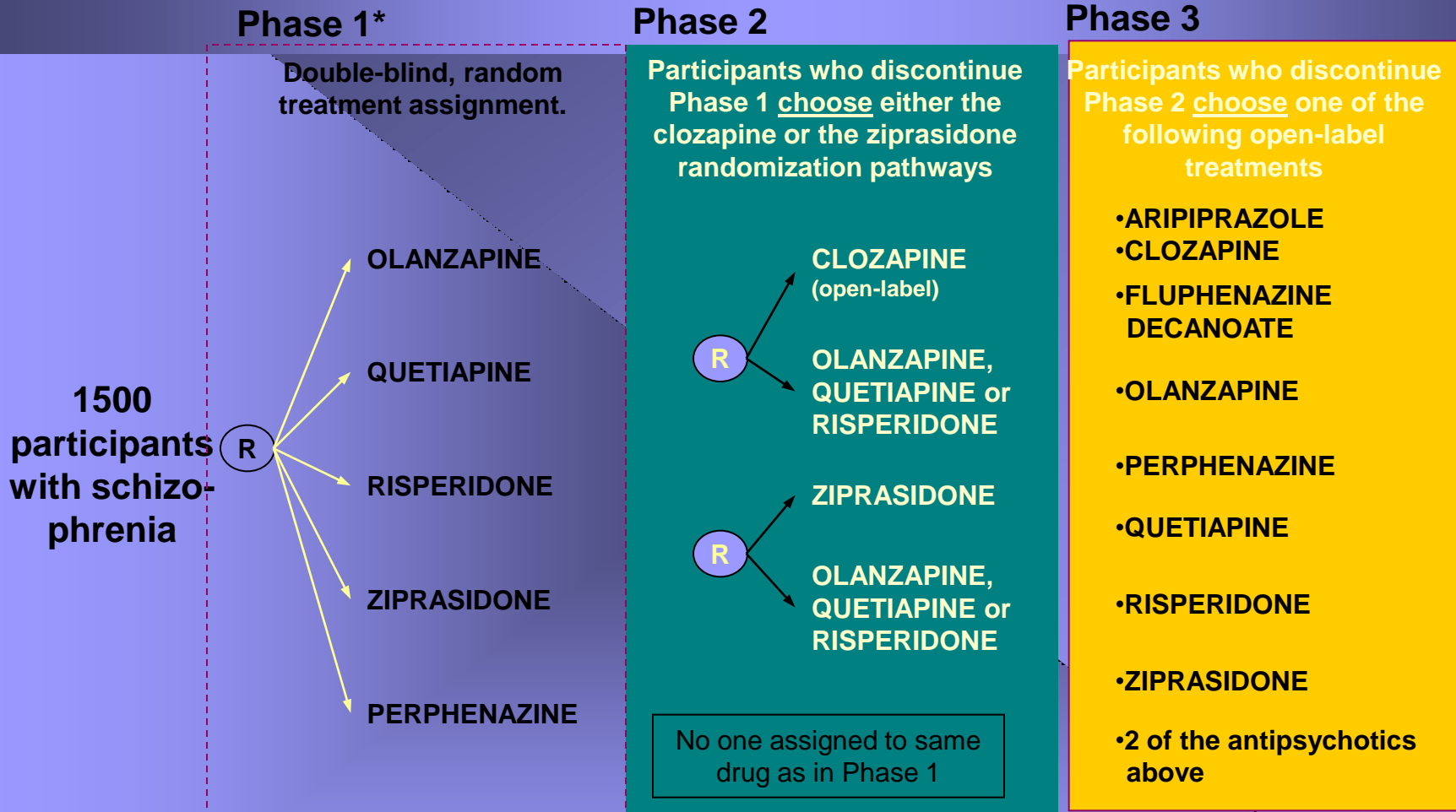
Partial compliance: impact



©Chue 06

Keith S. J Clin Psych 2003; 64:1308-15;

CATIE Schizophrenia Trial Design



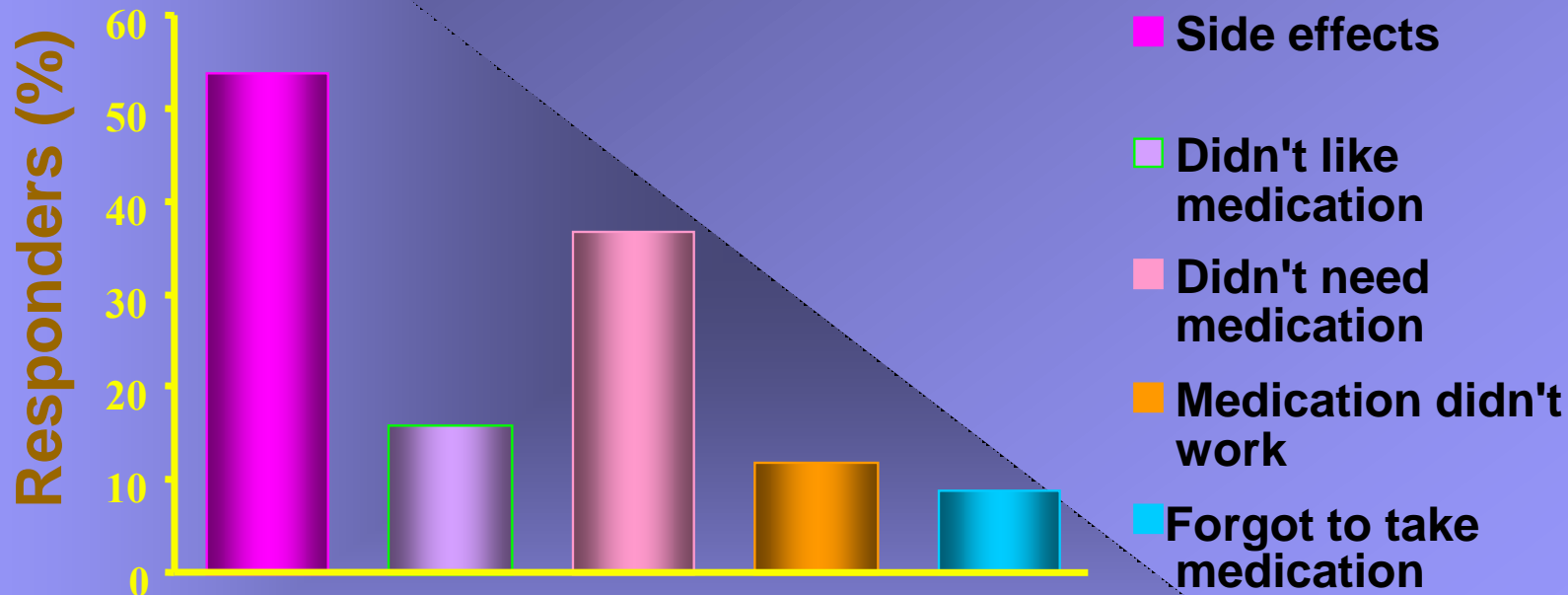
Responders stay on assigned medication for duration of 18-month treatment period

- * Phase 1A: participants with tardive dyskinesia do not get randomized to perphenazine
- Phase 1B: participants who fail perphenazine will be randomized to an atypical (olanzapine, quetiapine, or risperidone) before they are eligible for Phase 2

Effectiveness of Antipsychotic Drugs in Patients with Chronic Schizophrenia (CATIE)

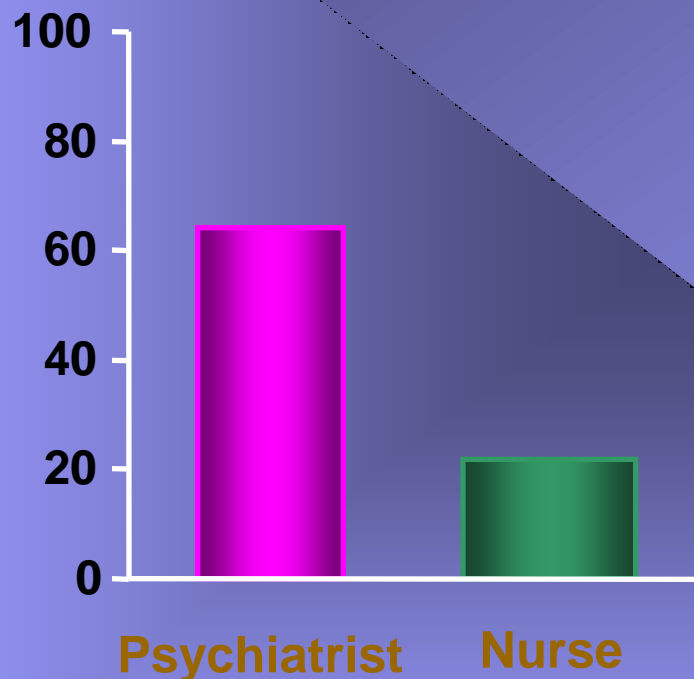
	Olanzapine	Quetiapine	Risperidone	Perphenazine
	(N=336)	(N=337)	(N=341)	(N=261)*
Discontinuation of treatment owing to intolerability – no. %				
Discontinuation	62 (18%)	49 (15%)	34 (10%)	40 (15%)
Weight gain or metabolic effects	31 (9%)	12 (4%)	6 (2%)	3 (1%)
Extrapyramidal effects	8 (2%)	10 (3%)	11 (3%)	22 (8%)
Sedation	7 (2%)	9 (3%)	3 (1%)	7 (3%)
Other effects	16 (5%)	18 (5%)	14 (4%)	8 (3%)

Question: "What Were the Reasons for Stopping your Medication?" (N=346)

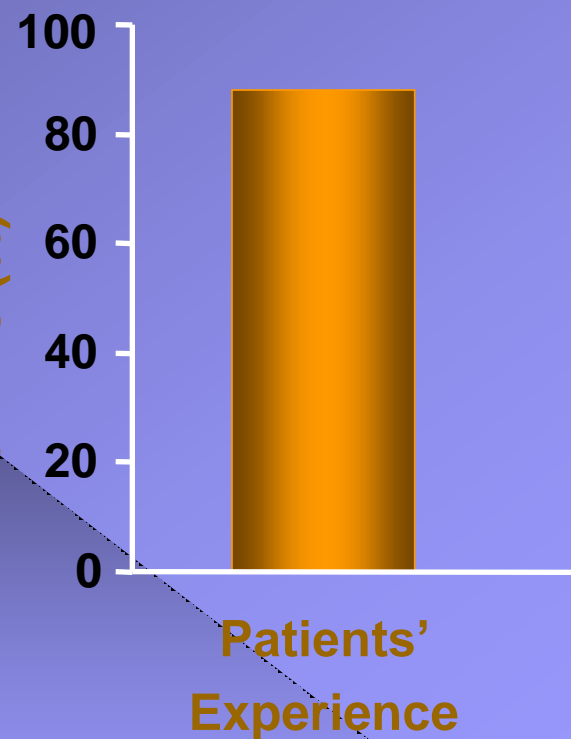


Patients Who Had Experienced EPS/ Admitted to Symptoms of EPS

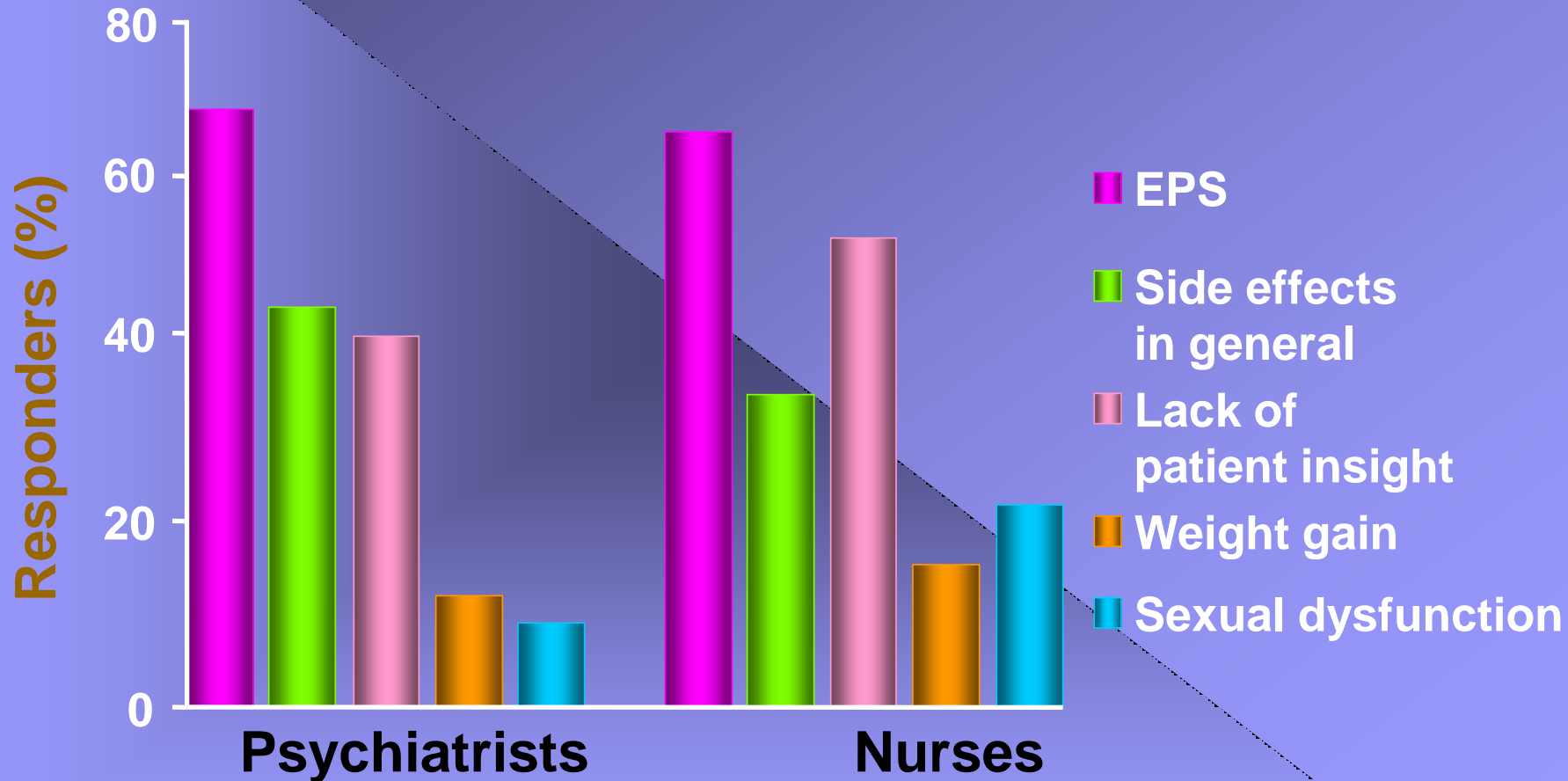
Estimated Proportion of Patients Who
Had Experienced EPS (%)



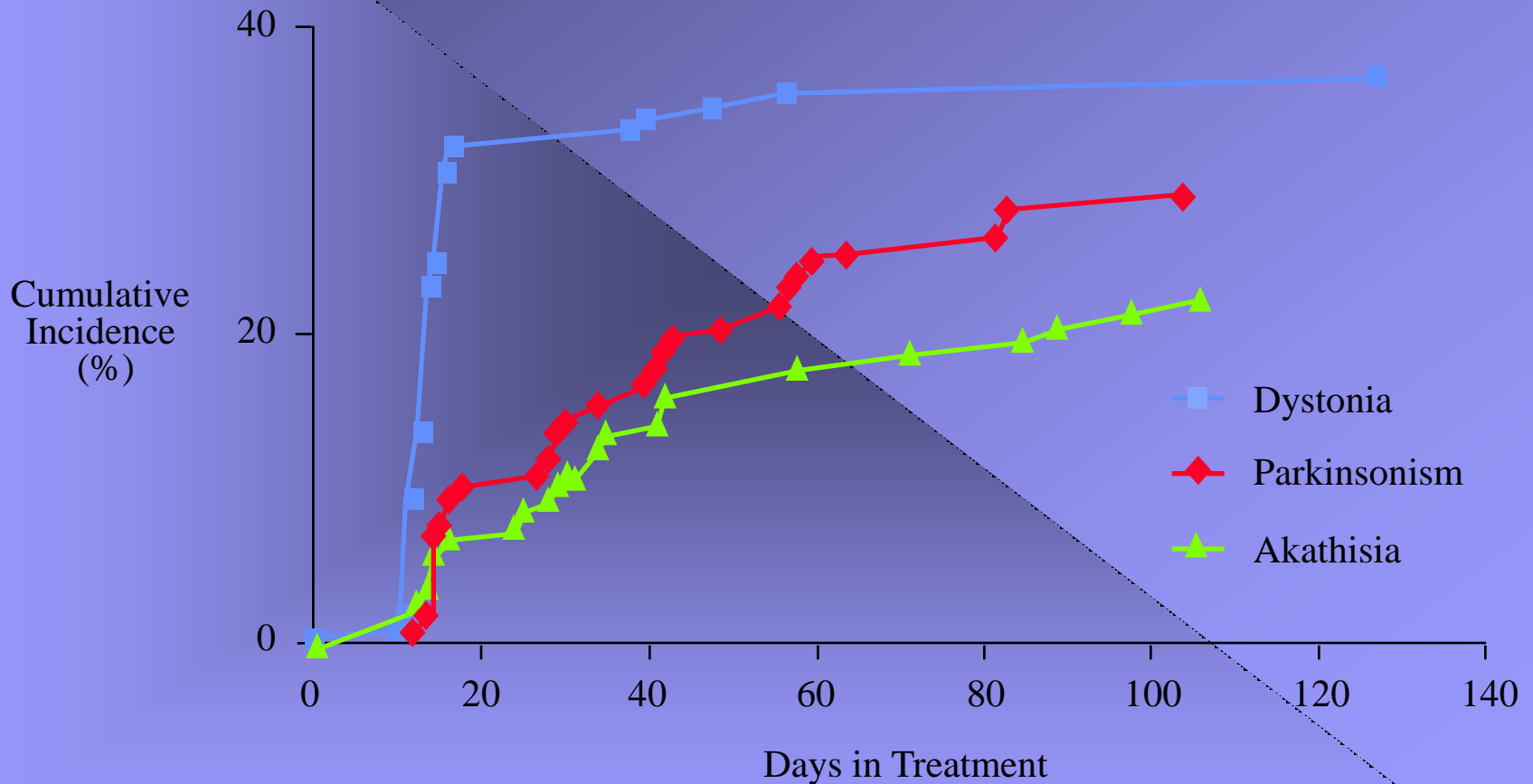
Proportion of Patients Who
Admitted to Symptoms Suggestive
of EPS (%)



Question: "What are the Main Reasons for Noncompliance?" (Psychiatrists (N=331) and Nurses (N=301))



Time to Extra-pyramidal Symptoms During Treatment of First Episode Schizophrenia



Data of J. A. Lieberman.

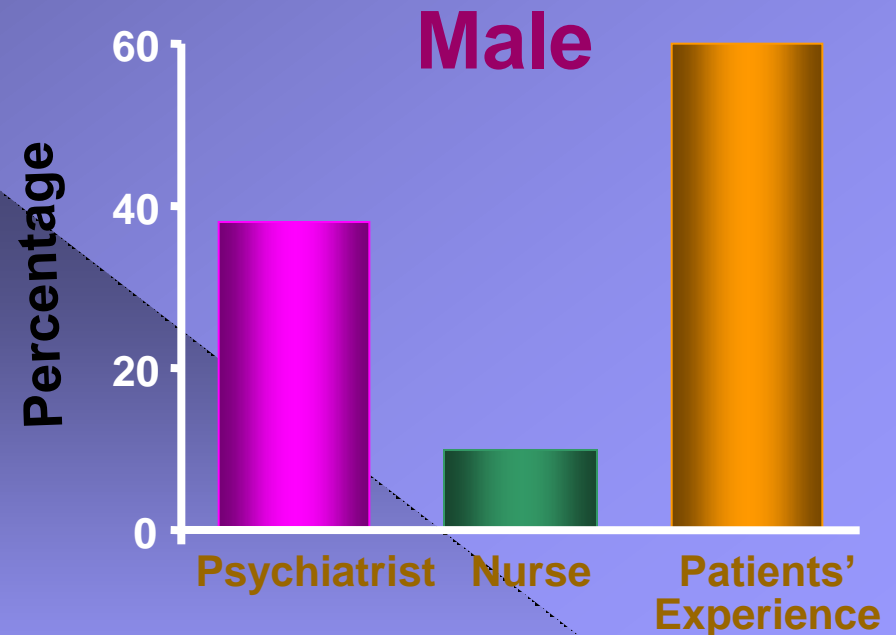
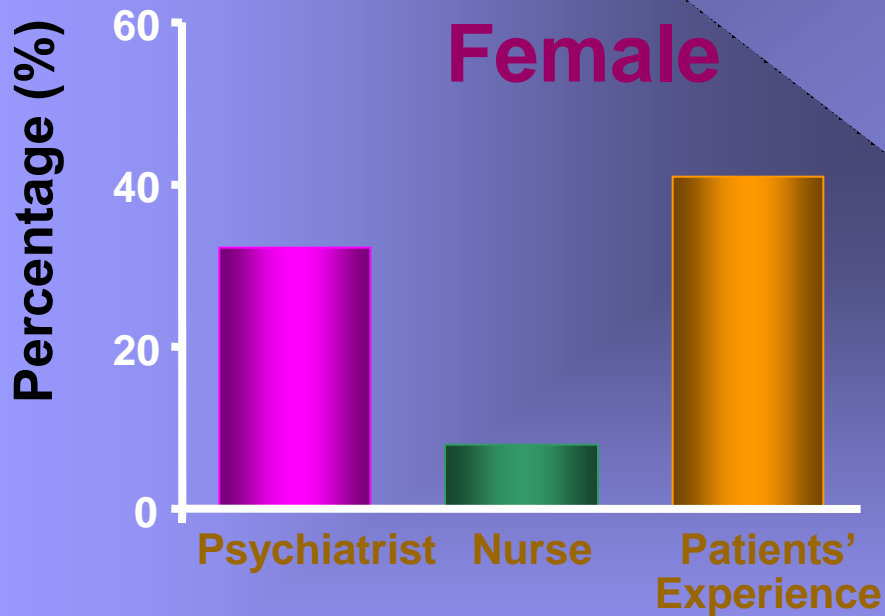


Play DVD

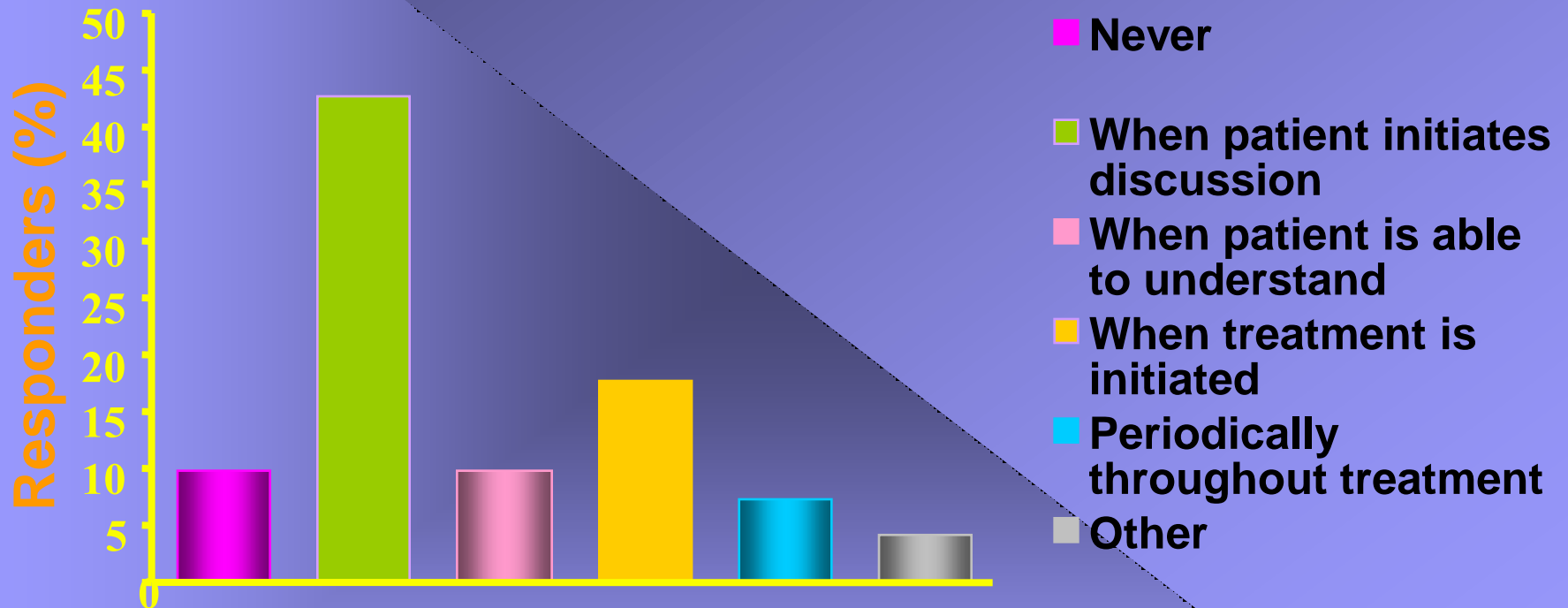
Estimated Prevalence of Sexual Side Effects and Patients' Actual Experiences

(Psychiatrists N=331, Nurses N=301)

(Female N=243, Male N=372)

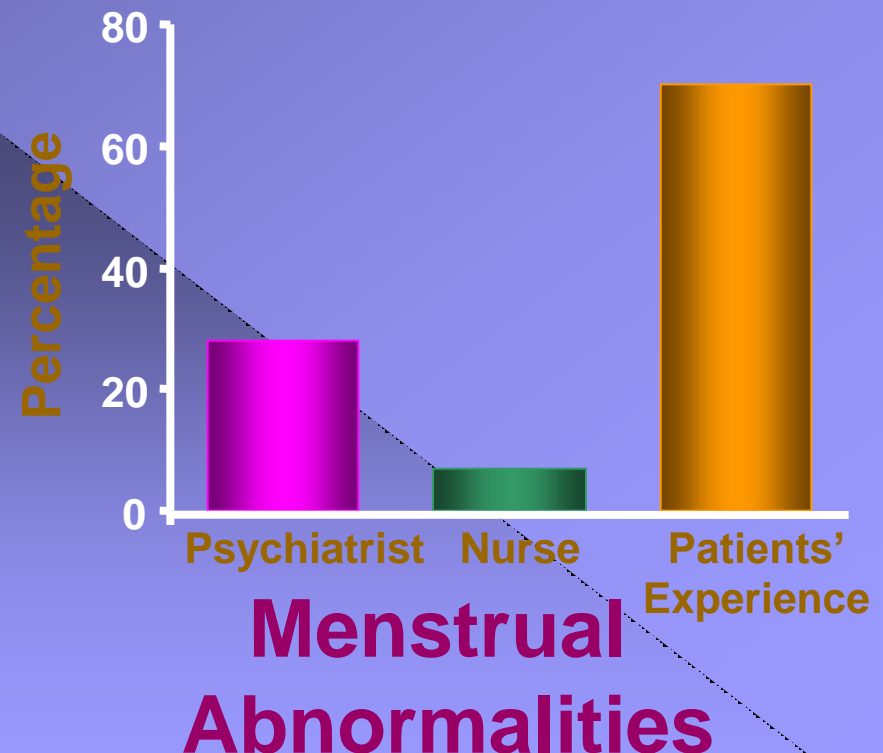
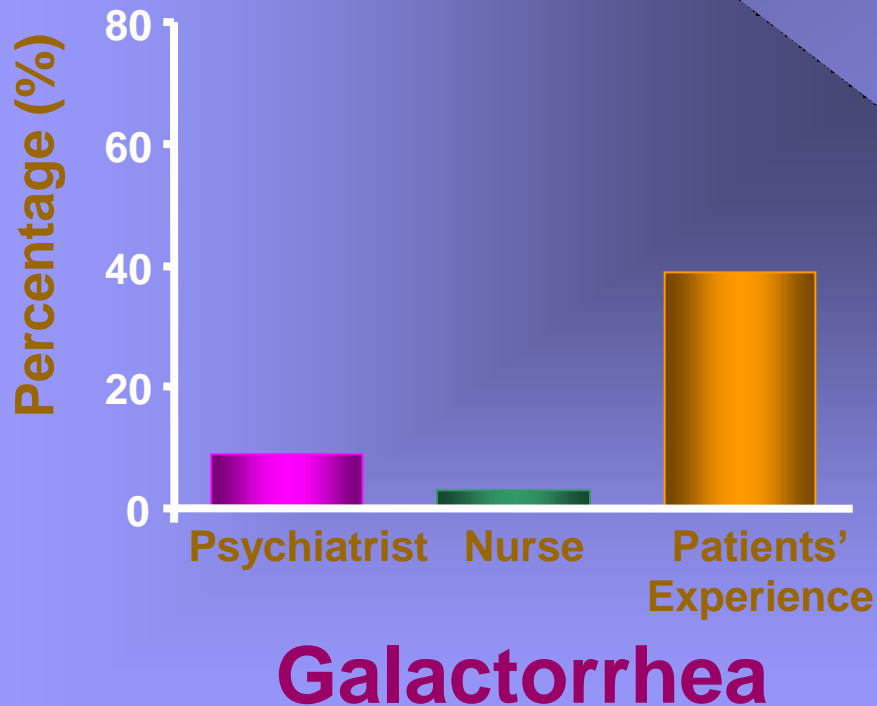


Question: "How often do you Discuss Sexual Dysfunction with your Patients?"



Estimated Prevalence of Galactorrhea and Menstrual Abnormalities Among Female Patients (N=243)

Hellewell JSE, 1999





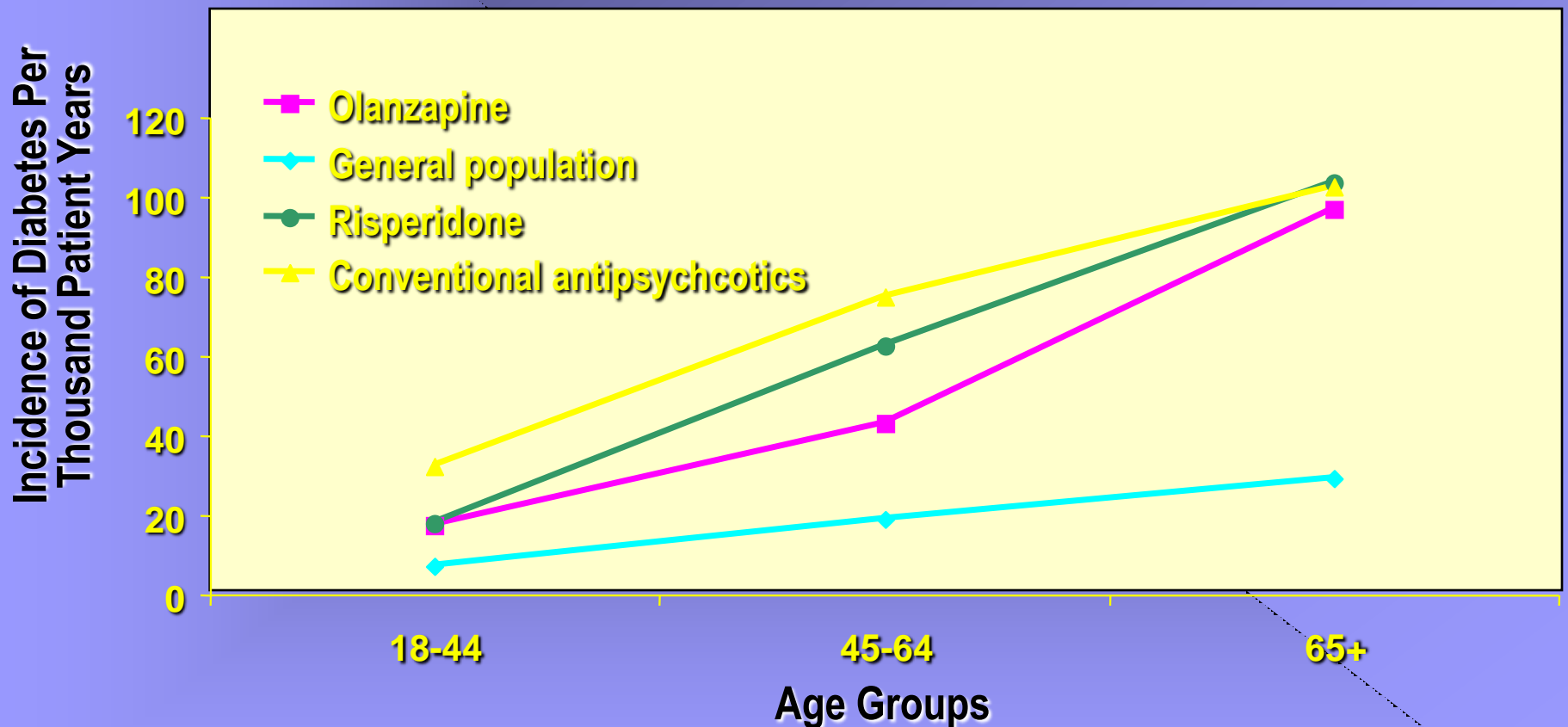
Upsizing finally reaches Africa.

Prevalence of Diabetes and Impaired Glucose Tolerance Are High in Schizophrenia and Bipolar Disorder

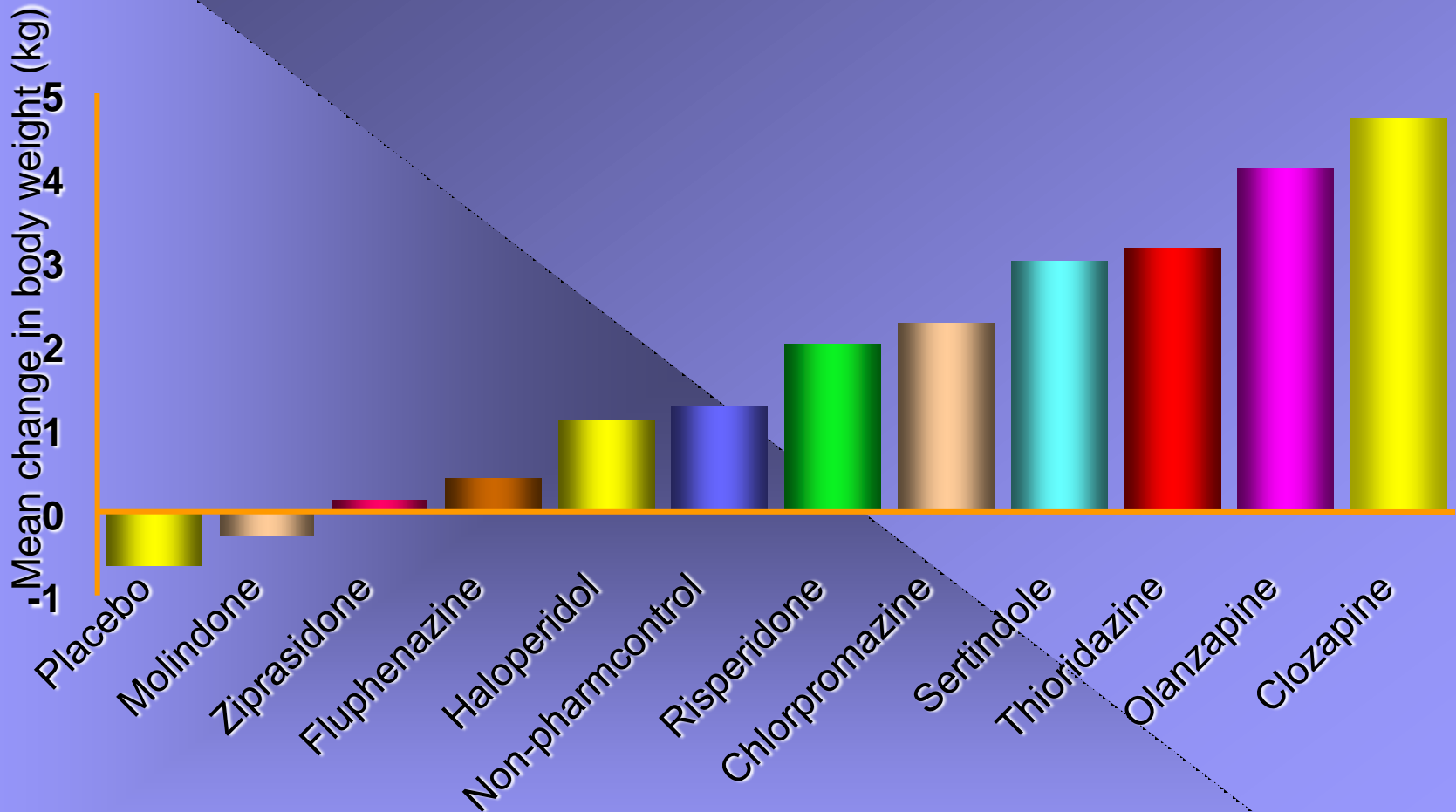
- ◆ The prevalence of type 2 diabetes mellitus is 2-4 times greater among patients with schizophrenia than reference populations (Keskiner et al, 1973; McKee et al, 1986; Mukherjee et al, 1996).
- ◆ The rate of type 2 diabetes among hospitalized bipolar patients is reported to be 2-3 times the general population (Cassidy et al, 1999).
- ◆ Increased rates of insulin resistance and glucose dysregulation were noted in psychiatric patients even before the introduction of antipsychotics or mood stabilizers (Braceland, 1945; Freeman, 1946; Langfeldt, 1952; Lorenz, 1922) and

Age Adjusted Incidence

Incidence of diabetes by age groups and antipsychotic exposure



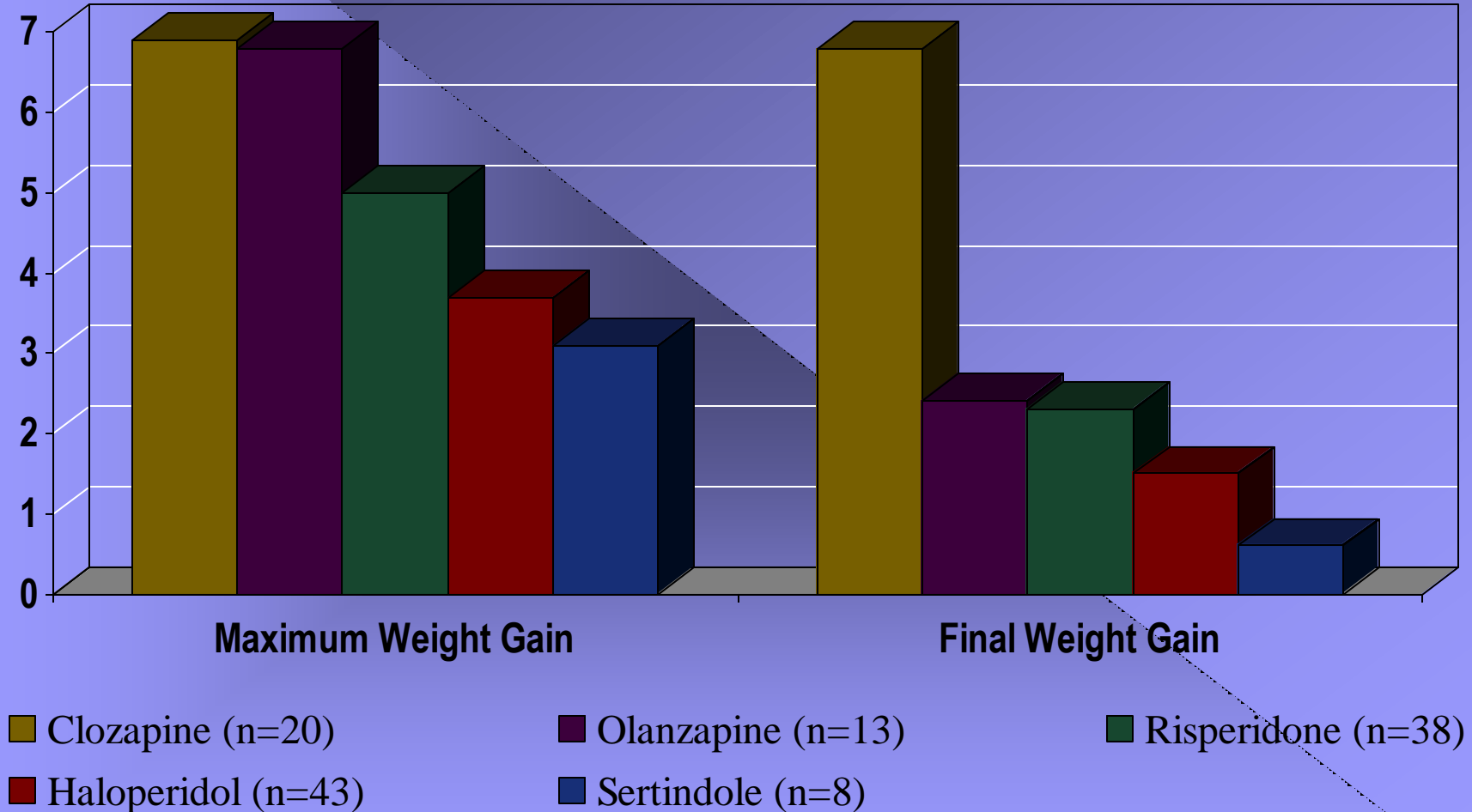
Estimated Mean Weight Gain at 10 Weeks



Allison DB, Mentore JL, Heo M, et al.: Weight gain associated with conventional and new antipsychotics: a meta-analysis.

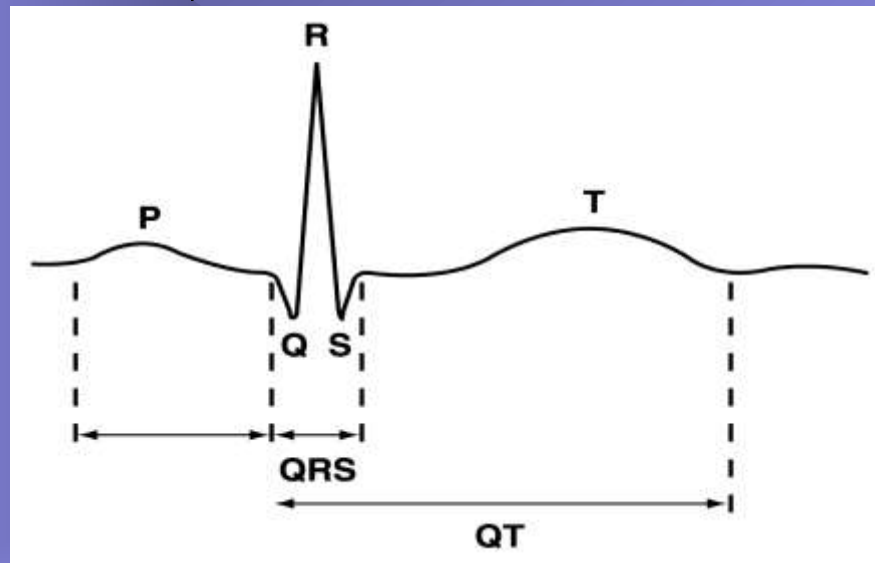
Behavioral Interventions

Weight gain by antipsychotic



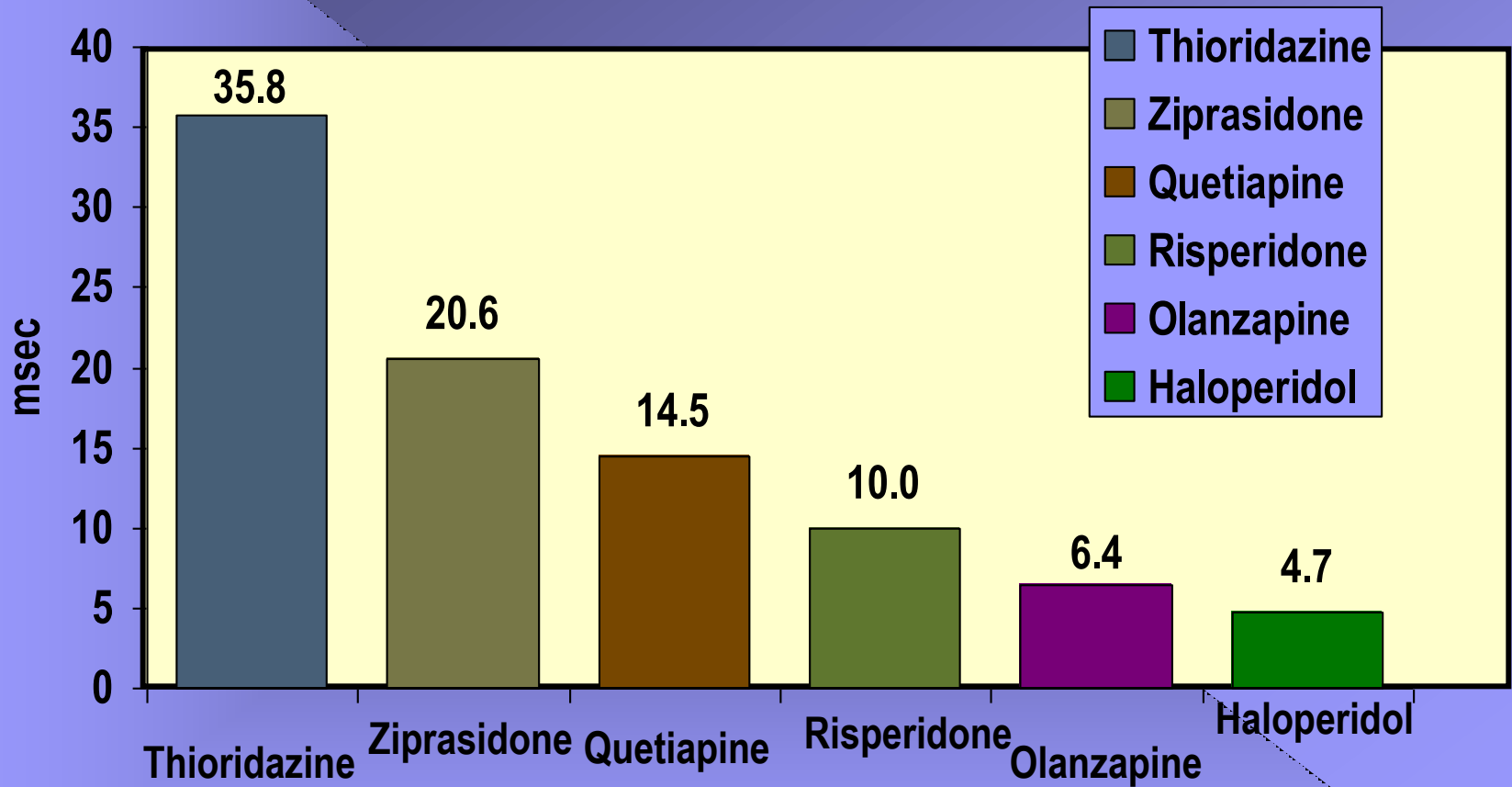
What We Know about QTc Intervals

- ◆ The QTc interval is the clinically significant ECG measure of QT prolongation that is corrected for heart rate



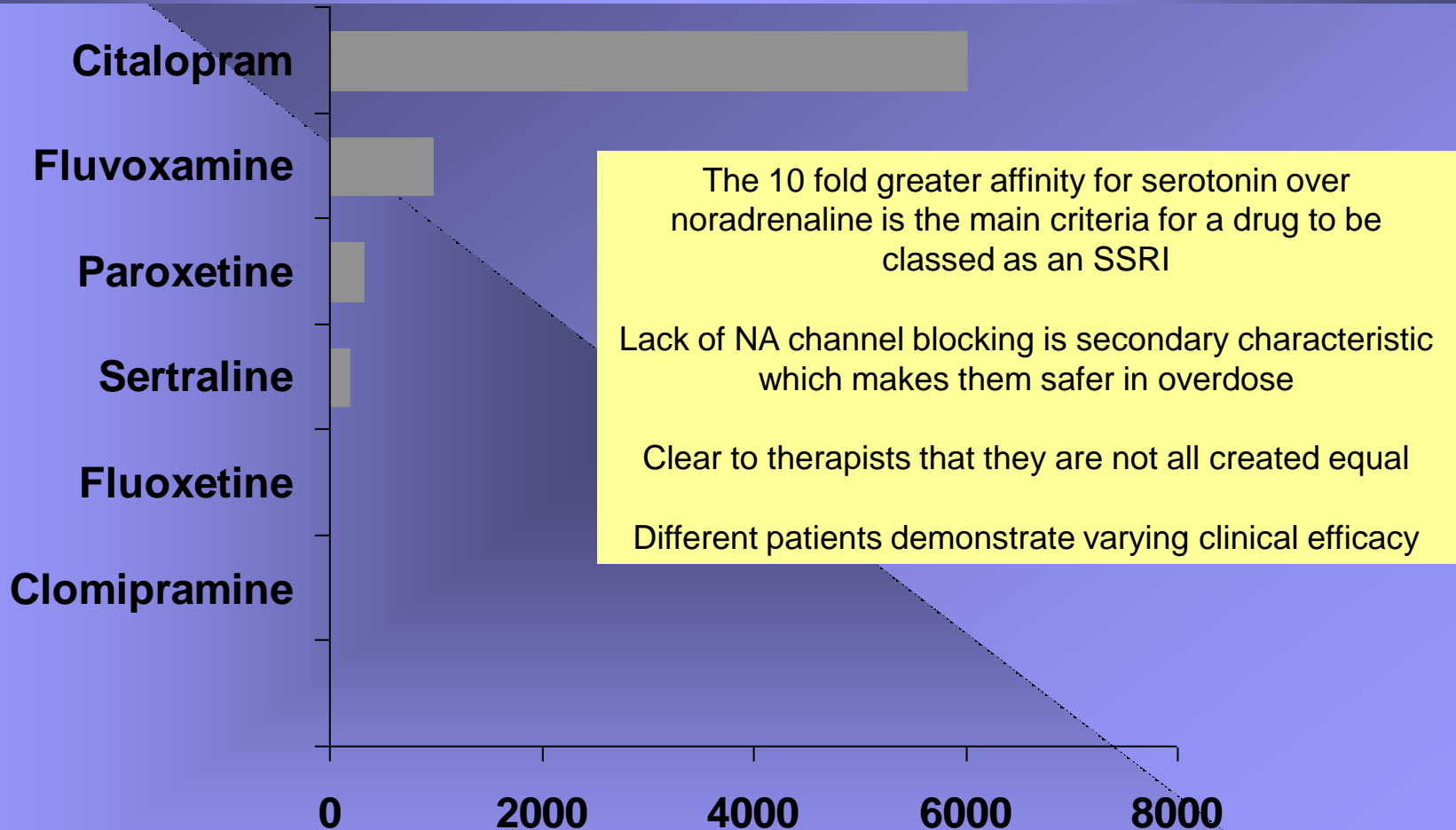
- ◆ Drug-induced lengthening QTc-interval is thought to be an important marker of arrhythmia risk by drug regulatory authorities as it often precedes arrhythmia

Mean Change in QTc from Baseline to Steady State



Pfizer, Inc. Rockville, Md: US Dept of Health and Human Services; July 19, 2000.
Psychopharmacological Drugs Advisory Committee

Selectivity for Inhibition of Serotonin vs Noradrenaline Uptake In Vitro*



*Rat brain synaptosomes

Tulloch & Johnston (1992)

Suicide / 100 000 / year

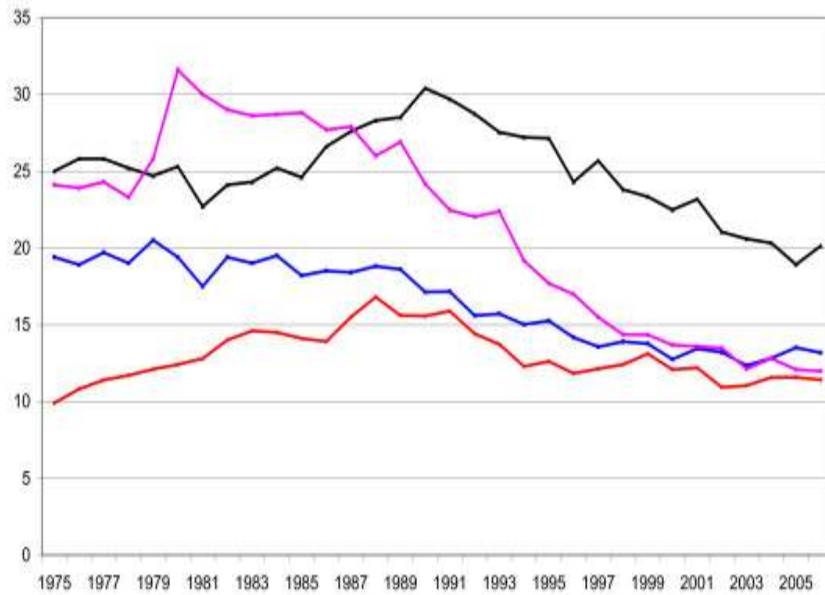


Figure 1

Suicide rates in Denmark (violet), Finland (black), Norway (red) and Sweden (blue) in the period 1975 to 2006.

From:

[BMC Psychiatry. 2010; 10: 62.](#)

Published online 2010 August 6. doi: 10.1186/1471-244X-10-62.

DDD / 1000 inh / day

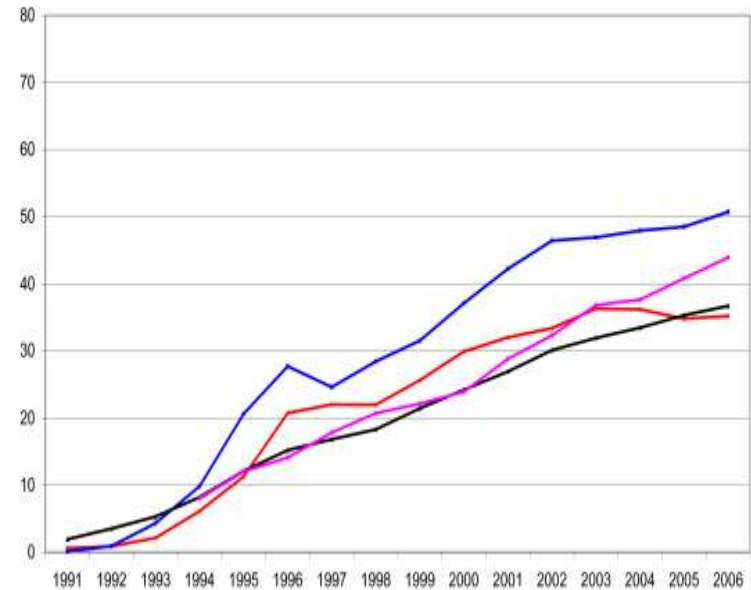


Figure 3

Sale figures of SSRIs (N06AB) in Denmark (violet), Finland (black), Norway (red) and Sweden (blue).

From:

[BMC Psychiatry. 2010; 10: 62.](#)

Published online 2010 August 6. doi: 10.1186/1471-244X-10-62

ZAHL ph

CONCLUSIONS: We found no evidence for the rapid increase in use of SSRIs and the corresponding decline in sales of TCAs being associated with a decline in the suicide rates in the Nordic countries in the period 1990-98

Selective serotonin reuptake inhibitors (SSRIs) for depressive disorders in children and adolescents. Hetrick s.

BACKGROUND: Depressive disorders are common in young people and are associated with significant negative impacts. Evidence for Selective serotonin reuptake inhibitors effectiveness in children and adolescents is not clear. Warnings against their use in this population due to concerns about increased risk of suicidal ideation and behaviour.

OBJECTIVES: To determine the efficacy and adverse outcomes, including definitive suicidal behaviour and suicidal ideation, of SSRIs compared to placebo

SEARCH STRATEGY: searched the CCDAN Trials Register, MEDLINE, PSYCHINFO and CENTRAL. letters were sent to key researchers and internet databases searched. We included published and unpublished randomised controlled trials.

MAIN RESULTS: Twelve trials were eligible for inclusion, ten providing usable data.

At 8-12 weeks, there was evidence that children and adolescents 'responded' to treatment with SSRIs (RR 1.28, 95% CI 1.17 to 1.41). There was also evidence of an increased risk of suicidal ideation and behaviour for those prescribed SSRIs (RR 1.80, 95% CI 1.19 to 2.72). Where rates of adverse events were reported, this was higher for those prescribed SSRIs.

AUTHORS' CONCLUSIONS: Caution is required to interpret the results. methodological issues, high attrition, issues instruments and clinical usefulness of outcomes,

It is unclear what the effect of SSRIs is on suicide completion. Untreated depression is associated with the risk of completed suicide, it is unclear whether SSRIs would modify this risk in a clinically meaningful way.

J Affect Disord. 2006 Aug;94(1-3):3-13. Epub 2006 May 19.

Do antidepressants t(h)reat(en) depressives? Toward a clinically judicious formulation of the antidepressant-suicidality FDA advisory in light of declining national suicide statistics from many countries.

Rihmer Z, Akiskal H.

Given that suicidality is a well-known symptom and outcome of untreated or inadequately treated depressive illness, the United States (US) Food and Drug Administration (FDA) warning of emergent suicidality in children and adolescents based on the antidepressant arm of placebo-controlled randomized trials (RCTs) has created understandable concern in clinical practice.

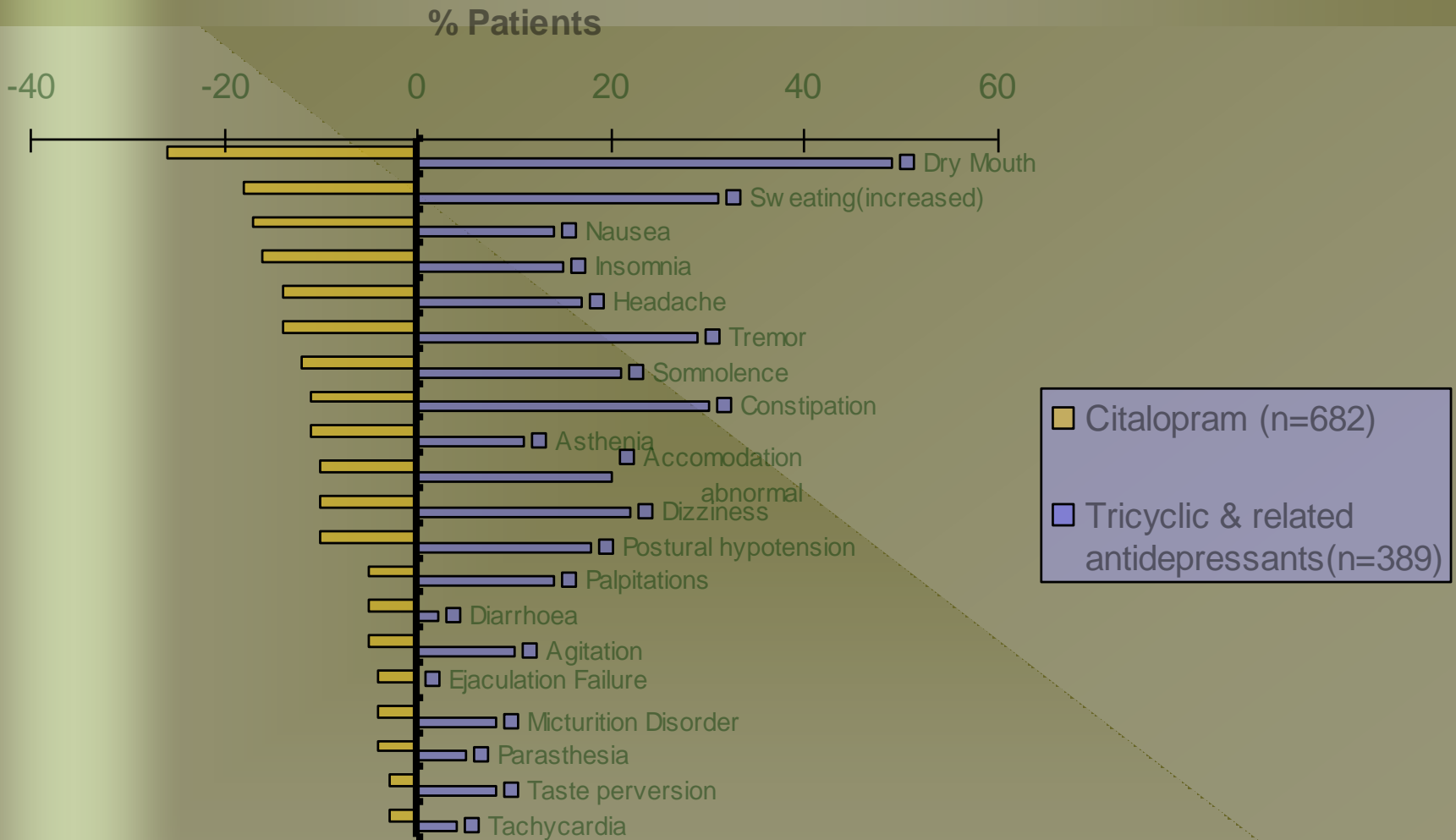
The issues involved are of broader public health importance for all age groups. As in other branches of medicine, psychiatrists must always be vigilant of the rare risk of iatrogenesis when prescribing potent agents like antidepressants for patients with depressive disorders where the risk of suicidality is inherent.

The overall evidence we review suggests that the widespread use of antidepressants in the new "SSRI-era" appear to have actually led to highly significant decline in suicide rates in most countries with traditionally high baseline suicide rates.

The decline is particularly striking for women who, compared with men, seek more help for depression.

We argue that the discrepancy between RCTs (in children) and national and clinical suicide statistics (in adults) may reside in new provocative data documenting high rates of unrecognized pseudo-unipolar mixed states particularly in juvenile, but also in adult, clinical populations. Such an interpretation accords well with equally provocative data that bipolar II (which is often "mixed" in nature) may well represent a particularly vulnerable clinical substrate for suicidality.

Citalopram vs Tricyclic & related antidepressants



CONSUMER STRATEGIES FOR COPING WITH ANTIPSYCHOTIC MEDICATION SIDE EFFECTS

Objective: *Study to investigate the strategies employed by consumers to manage the common side effects with antipsychotic medication use.*

Method: *Focus group discussions and individual interviews involving 238 consumers, 74% male and 73% diagnosed schizophrenics were employed to identify key side effects and a range of consumer coping strategies for managing these adverse effects.*

Results: *Nine side effects were selected from a total pool of 32 proposed in the group discussions. Strategies that were perceived by the participants to be useful in coping with the selected side effects were then identified.*

CONSUMER STRATEGIES FOR COPING WITH ANTIPSYCHOTIC MEDICATION SIDE EFFECTS

Table 1: Side effects ranked according to impact on client functioning (1 = 'least impact' to 5 = 'most impact')

1	Sedation, tiredness	4.6
2	Weight gain	4.3
3	Difficulty thinking/concentrating	4.2
4	Restlessness	4.1
5	Insomnia	4.0
6	Tension	3.8
7	Dry mouth	3.6
8	Dizziness	3.5
9	Drooling	3.2

Two-thirds (66.6%) were prescribed atypical medications, 15.4% were taking the older 'typical' medications and 18% had difficulty naming the medication that they were prescribed.

Some 22.7% of participants described having no side effects, 35.8% had mild side effects, 25.3% had moderate side effects and 16.2% described their side effects as being severe.

CONSUMER STRATEGIES FOR COPING WITH ANTIPSYCHOTIC MEDICATION SIDE EFFECTS

While the strategies proposed for each side effect differed, common themes included the maintenance of a balanced lifestyle, healthy eating and sleeping routines, fostering a positive outlook on life.

Understanding the strategies employed by consumers to deal with the adverse effects of their medications may help clinicians to engage more effectively with consumers in the discussion and management of side effects.

Thank you

Treatment Options

<p>Psychotic Hyper-aroused Eager to obtain reduction from subjective distress</p>	<p>Psychotic Agitated Distressed Coercible</p>	<p>Psychotic Demanding Pacing Belligerent Vocal Tormented</p>	<p>Psychotic Threatening Tormented Hostile Impulsive</p>	<p>Frankly Violent Intoxicated Floridly Psychotic Self Destructive</p>
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Oral antipsychotics

Risperidone//Olanzapine//seroquel/Chlorpromazine

IM antipsychotic

Zip,Olanzapine Clopixol acuphase Haloperidol

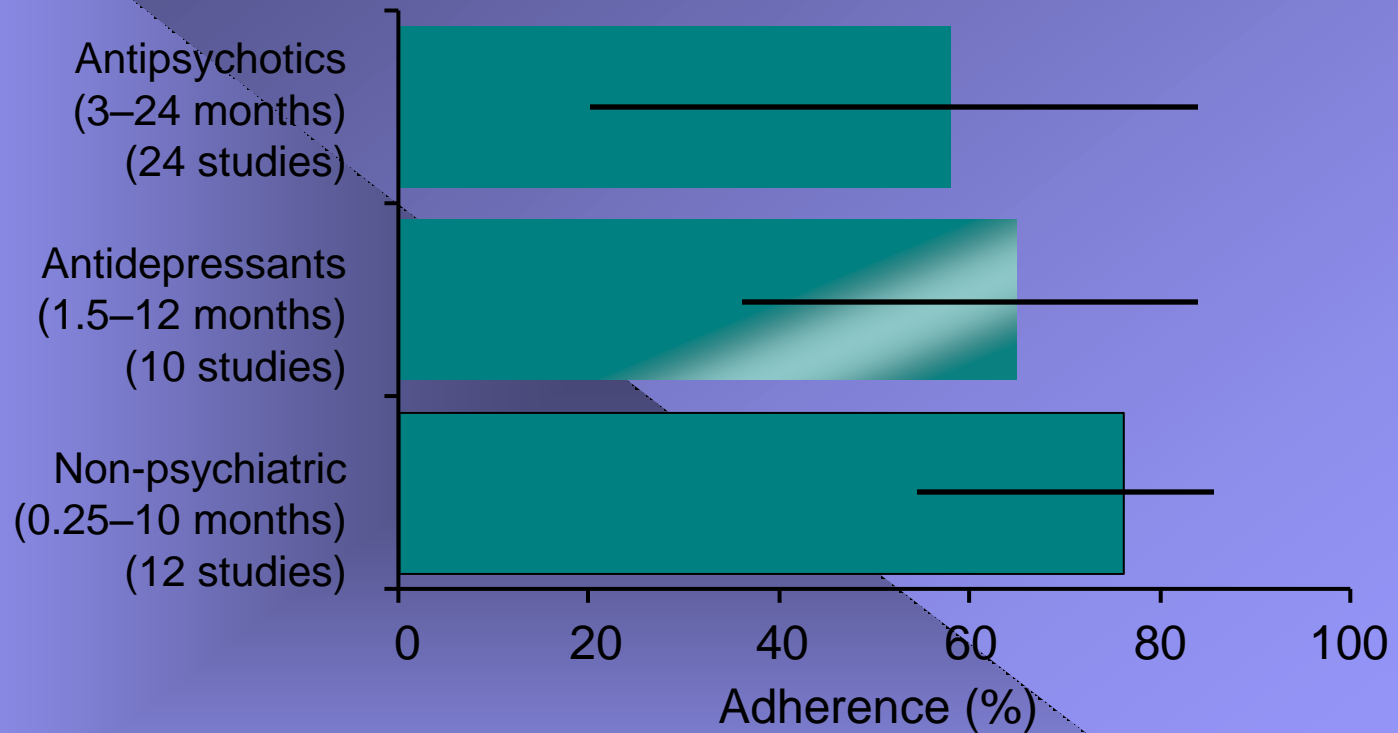
Benzodiazapines oral

Temazepam Lorazepam Diazepam Clonazepam

IM

Lorazepam Diazepam Clonazepam Midazolam

Adherence to treatment is poor



Wide range of estimates across studies may reflect difficulty of assessing covert non-adherence

Data shown are mean and range

Evolving outcomes Mood and Anxiety disorders

Early
clinical trials

1960s

Use of HAM-D in
research

1980s

HAM-D based
definition of
'response'

1990s

Consensus Groups
convene to refine
definition

2000+

Initial
conceptualization
of 'remission'

Application of
'remission' criteria
to clinical trials,
practice