Antipsychotic Adverse Effects in Children and Adolescents

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Question 1

Recent research suggests that this antipsychotic may actually result in a decrease in prolactin levels:

A. Paliperidone
B. Risperidone
C. Quetiapine
D. Olanzapine
E. Aripiprazole

Question 2

For monitoring children and adolescents on antipsychotics, weight, height and BMI should be monitored on:

A. Every visit
B. Every second visit
C. Every 3 months
D. Every 6 months
E. Every 12 months

Question 2

FDA recently advised a labeling change to consider the increased potential for weight gain and hyperlipidemia in adolescents (compared to adults) with this atypical antipsychotic:

A. Quetiapine

B. Olanzapine

C. Risperidone

D. Ziprasidone

E. Aripiprazole

Speaker Disclosure of Financial Relationship

Consultant, Advisory Board, Data Safety Monitoring Board and/or Speaker's Bureau member for:

Add information

Grant support from:

Add information

Discussion of off-label or investigational use:

Yes _X_ No __

Teaching Points

- Review the effect of different antipsychotics on extrapyramidal side effects, prolactin-related side effects, sedation, weight gain and metabolic abnormalities in youth

- Describe the adequate monitoring and intervention strategies to minimize adverse effects, particularly weight gain and metabolic abnormalities associated with antipsychotics

Outline

- General Comments
- Extrapyramidal Side Effects
- Prolactin Effects
- Sedation/Somnolence
- Weight Gain
- Metabolic Effects
- Monitoring and Management
- Conclusions

General Comments

Psychotropic Adverse Events In Children and Adolescents vs. Adults

Increased risk for acute and intermediate adverse effects:

- Sedation
- EPS (except for akathisia)
- Withdrawal dyskinesia
- Prolactin-related AEs (especially postpubertal females)
- Weight gain and dyslipidemia
- Suicidal ideas/behavior

Decreased (delayed?) risk for:

- Persistent TD
- Diabetes mellitus

Adapted from: Correll CU et al. Child Adolesc Psychiatr Clin N Am. 2006;15(1):177-206.

Time Course of Antipsychotic Adverse Effects

Receptor	Acute ≤1 wk	Consequence	Early <3 mo	Consequence	Late: ≥3 mo	Consequence
α 1	Hypotension*	Falls non-adherence	Hypotension *	Falls non-adherence	Hypotension	Falls non-adherence
D 2	Dystonia * Parkinsonism*	Pain non-adherence	Parkinsonism* Akathisia *	↓ cognition non-adherence	TD	Stigma ↓ socialization ↓ quality of life
	↑ Prolactin (*)	Sexual Dysfunction non-adherence	↑ Prolactin (*)	Sexual Dysfunction Hypogonadism non-adherence	↑ Prolactin	Osteoporosis ? CHD ? breast cancer
H 1	Sedation *	↓ cognition ↓ functioning non-adherence	Sedation *	↓ cognition ↓ functioning non-adherence	Sedation	↓ cognition ↓ functioning non-adherence
	↑ Weight	↑ lipids/ glucose	↑ Weight	↑ lipids/glucose non-adherence	Diabetes dyslipidemia CHD	↓ functioning ↓ quality of life early death
M 1-4	Blurry vision* dry mouth *	Discomfort non-adherence	↓ cognition Blurry vision * dry mouth * constipation *	↓ functioning discomfort non-adherence	↓ cognition Blurry vision * dry mouth * constipation *	↓ functioning discomfort non-adherence

Acute (<1 week) Early (<3 months) Late

*= Tolerance may develop; CHD= Coronary heart disease

Correll CU. CNS Spectr. 2007;12(12) (Suppl 21):10-14.

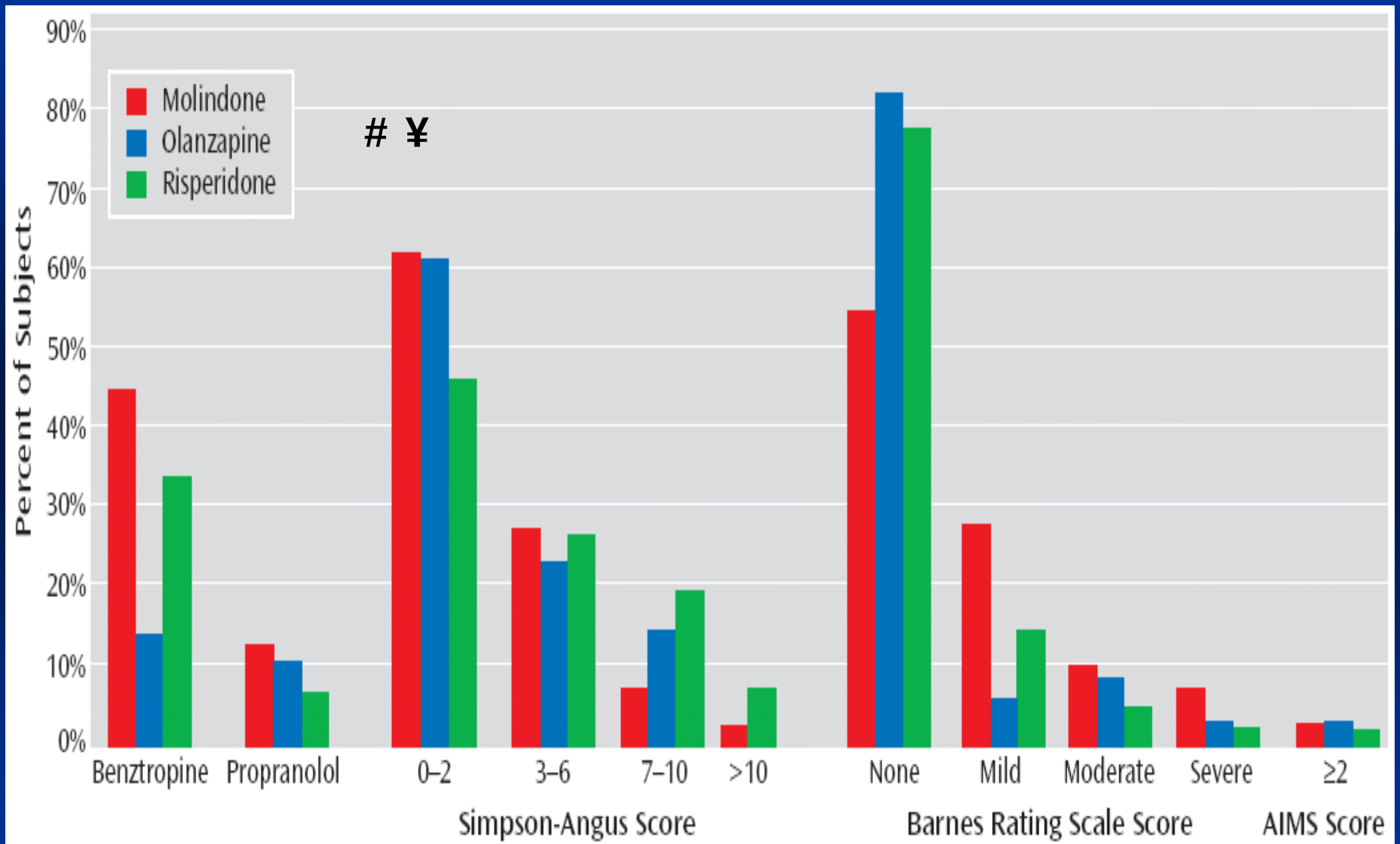
Methodology Matters

- Most data are based on spontaneous reports
  - +: Individually meaningful events are captured
  - -: Underreporting
- Categorical data presented as period incidence rates
  - -: Inability to determine time course
  - -: Inability to determine likelihood of tolerance
  - -: Inability to determine severity / functional impact
- Continuous data analyzed with OC methodology
  - -: Pseudo-tolerance due to early high-risk drop outs
- Continuous data analyzed with LOCF methodology
  - -: Underestimation of time-dependent effects (eg, weight gain)
  - -: Artificial lack of difference between treatments if higher risk drug leads to earlier drop outs
  - -: Artificial relationship between efficacy and time-dependent adverse effect (responders treated longer and more adherent)

Modified from: Correll CU. J Clin Psychiatry;68(9): 1441-2

Extrapyramidal Effects

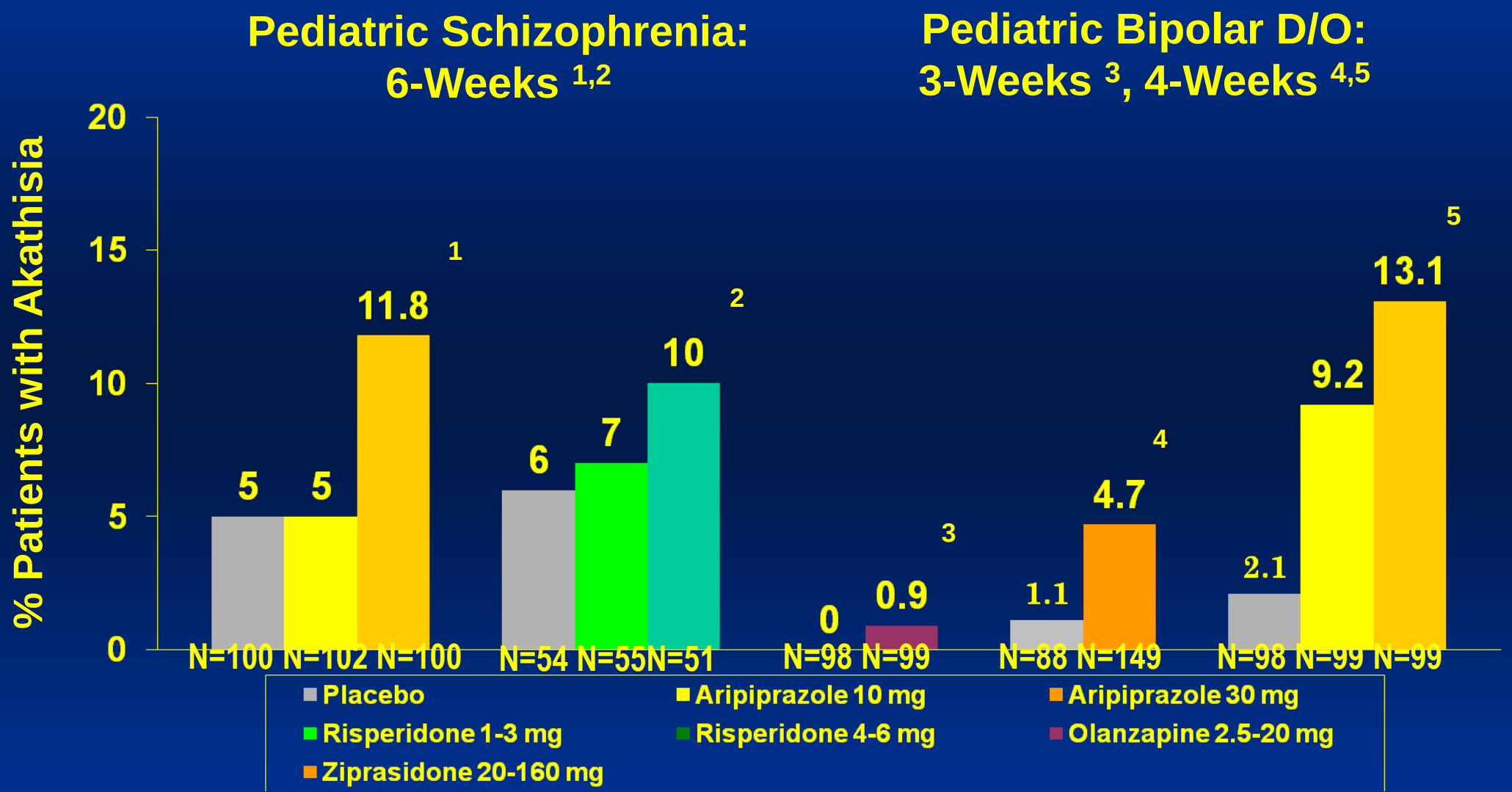
Neuromotor Changes in the TEOSS Trial



# p<.05 within group; ¥ p<.05 across groups; ¥ ¥p<.05 across groups

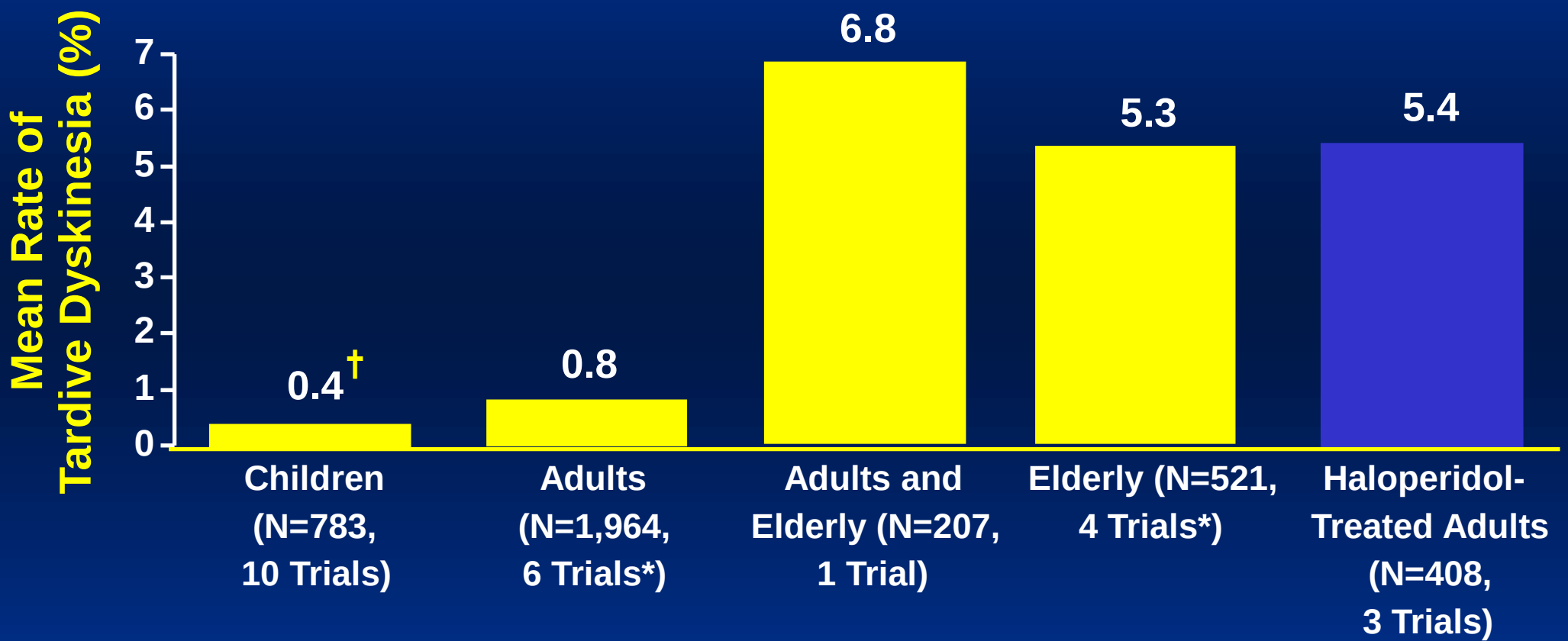
Sikich L, et al. Am J Psychiatry 2008;165(11):1420-31

Akathisia in DBRPC Trials of Aripiprazole and Risperidone in Pediatric Schizophrenia and Bipolar D/o



[1] Findling RL et al., Am J Psychiatry 2008;165:1432-41; [2] Haas M et al. NCDEU 2007, Boca Raton; [3] Tohen M et al. Personal Communication 2008; [4] DelBello M et al., APA 2008; [5] Findling RL et al. J Clin Psychiatry. 2009 Oct;70(10):1441-51

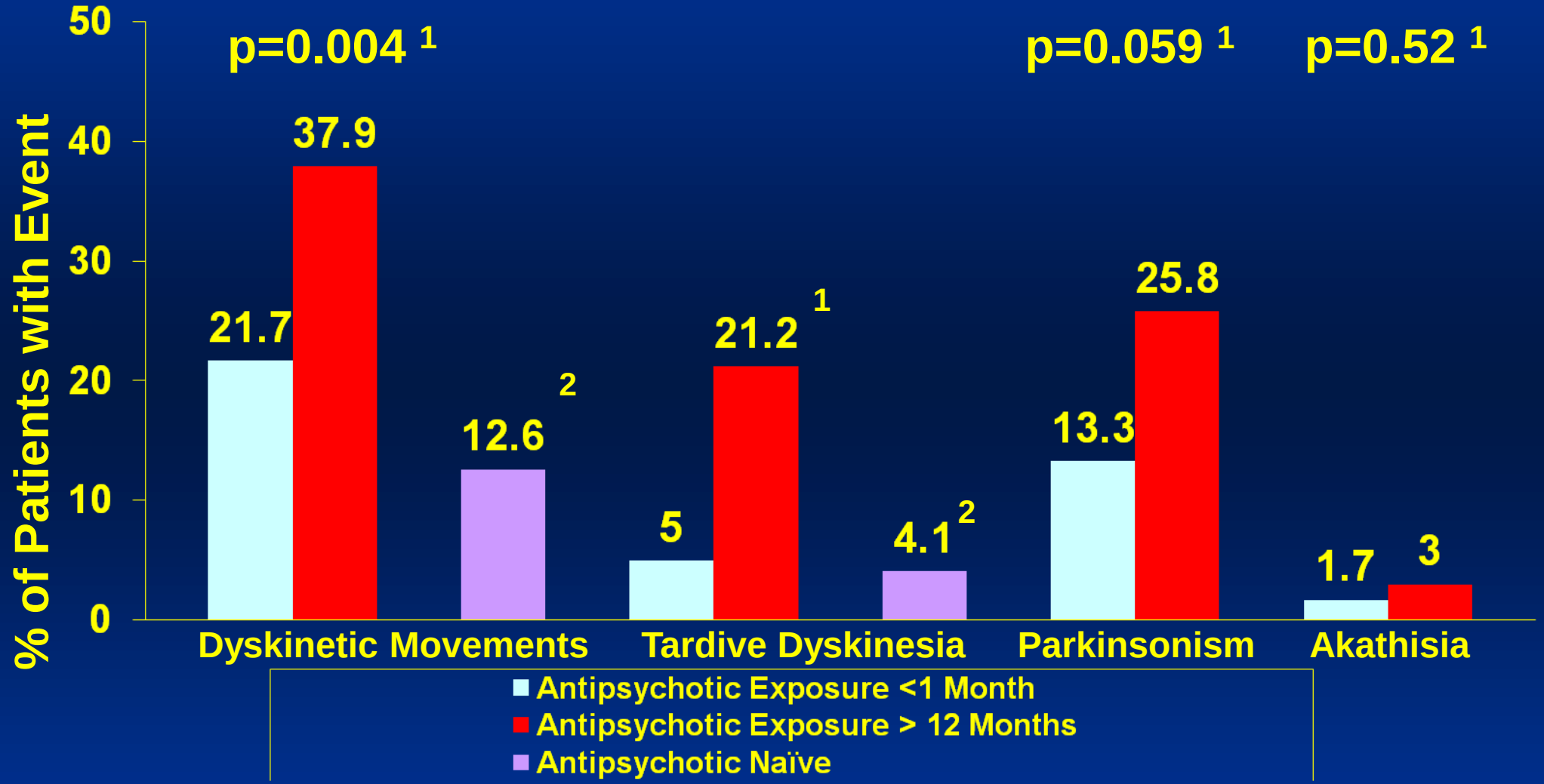
6 times lower 1-Year Incidence Rates of TD with Atypical Antipsychotics vs. Haloperidol in Adults and 50% lower Risk in Youth



Participants Treated With 2nd-Generation Antipsychotics

*1 study reported separate rates for TD in adults and in the elderly; Correll CU et al. (2004), Am J Psychiatry 161(3):414; †Correll CU & Kane JM (2007), J Child Adolesc Psychiatry;15(5):647-655.

Greater Dyskinesia and Parkinsonism Rates in Youth Exposed to Antipsychotics <1 Month (N=60) vs. >12 Months (N=66)



[1] Laita P et al. J Child Adolesc Psychopharmacol 2007;17:487-501; mean age: 15.6 yrs, 62% male, 88% White; Antipsychotics in short-/long-term group: risperidone= N:29/19; olanzapine= N: 11/12; quetiapine= N: 4/12; typical neuroleptic= N:2/5; atypical+typical antipsychotic= N:5/6; off antipsychotics= N:9/2.

[2] Magulac M et al. Can J Psychiatry 1999;44:368-73. 390 antipsychotic-naïve youth (age:3-17 yrs) in foster care

Prolactin and Related Effects

Relative Potency of Antipsychotics in Elevating Serum PRL Prolactin in Youth

- Paliperidone ≥ Risperidone > Haloperidol
> Olanzapine **>** Ziprasidone
> Quetiapine **>** Clozapine **>** Aripiprazole

- Aripiprazole has partial D2-DA agonist activity, and may suppress PRL below baseline levels

Correll and Carlson, JAACAP 2006;45: 771-791

Signs & Symptoms of Hyperprolactinemia

- Amenorrhea and oligomenorrhea in women of reproductive age
- Breast enlargement/engorgement in both women and men
- Galactorrhea, mostly in women
- Decreased libido in both genders
- Erectile dysfunction in men
- Osteoporosis due to hypogonadism in both women and men
- Failure to enter or progress through puberty
- Possibly, hirsutism in women

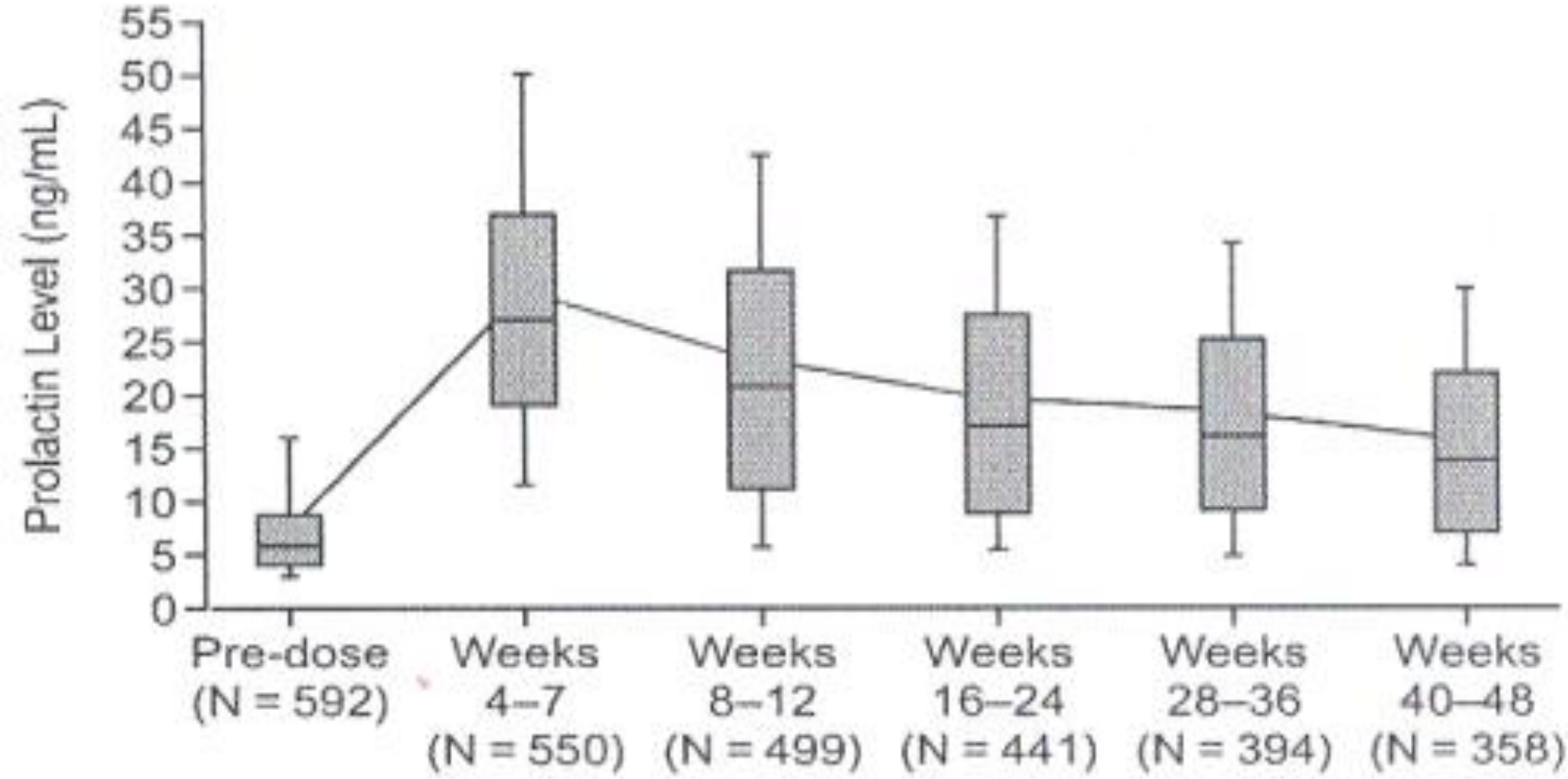
Correll CU and Carlson H. J Am Acad Child Adolesc Psychiatry. 2006 Jul;45(7):771-91.

Variable Effects of Hyperprolactinemia

- PRL levels positively correlated with having AEs
- Not all patients with hyperprolactinemia develop PRL-related signs and symptoms
- Dissociation may be due to:
  - Production of less bioactive PRL molecules
  - Differential sensitivity of receptors affected by PRL
- Prepubertal youth express PRL effects less:
  - Lower PRL levels (esp. boys)
  - Less biologically active / primed end organs
  - Not sexually active
  - ? Hypogonadism less relevant for bone maturation

Correll and Carlson, JAACAP 2006;45: 771-791

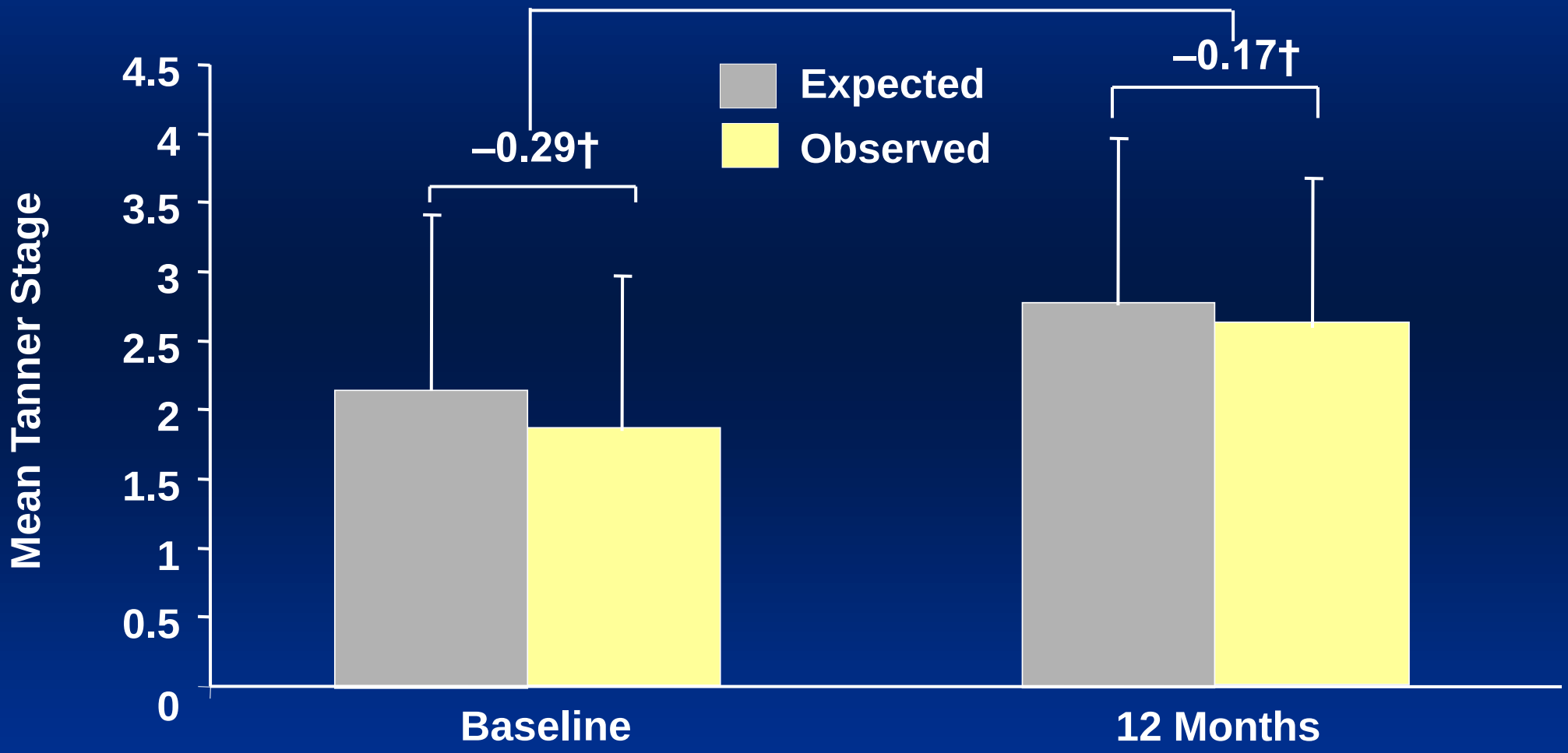
Prolactin During 1-Year Risperidone Treatment in Youth (5-15 years, N=700)



Findling et al., J Clin Psychiatry 2003;64: 1362

Observed vs. Expected Tanner Stage in Youth ≥9 years Treated with Risperidone (N=222)

Deviation from expected maturation at year 1 was 0.12 ± 0.77

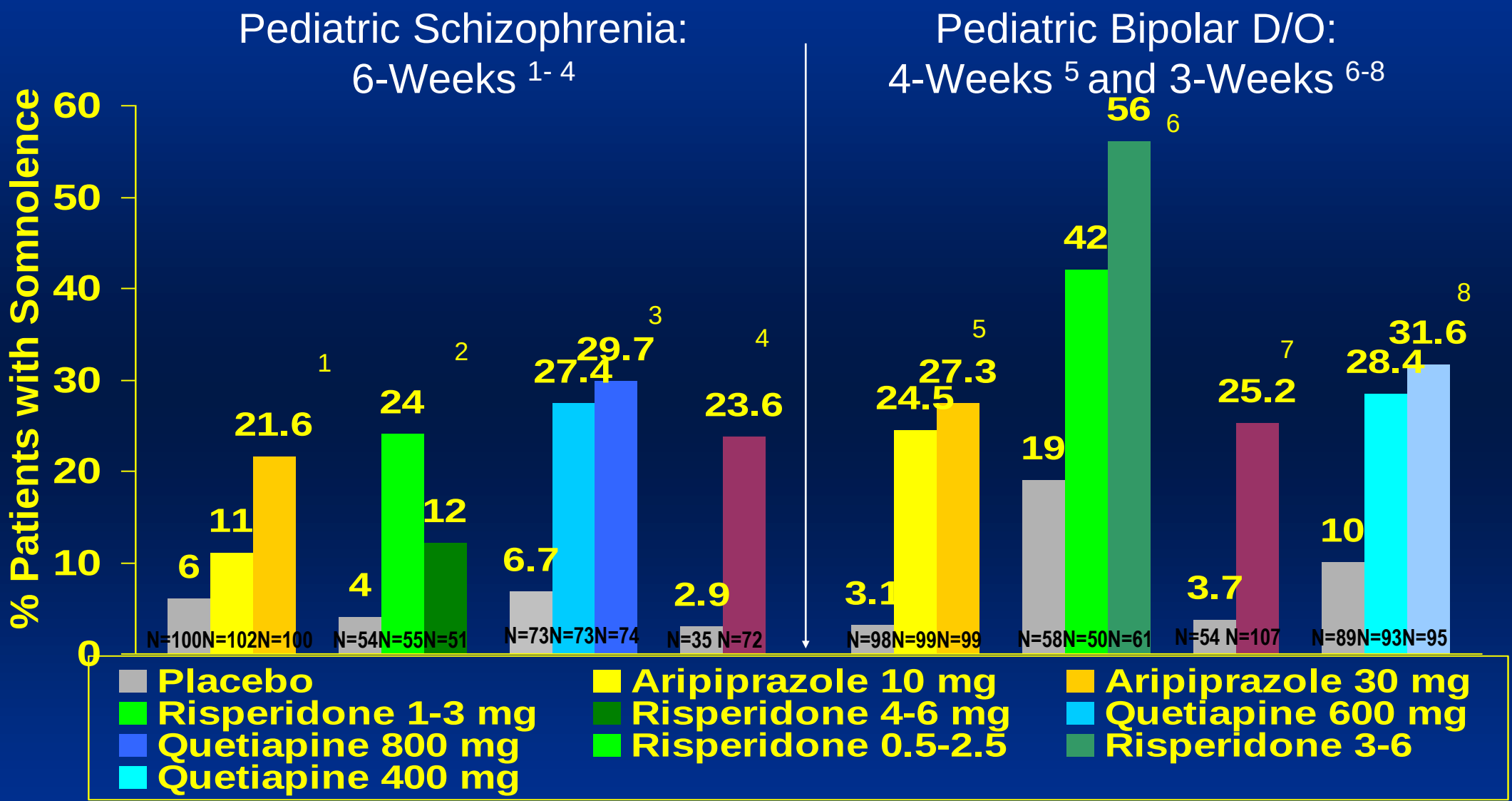


Mean age: 11.9±1.4 years; Boys (≥ 10 years): 80%; Girls (≥ 9 years): 20%; Caucasian: 88%

Dunbar et al. Am J Psychiatry 2004 May;161(5):918-20.

Alertness

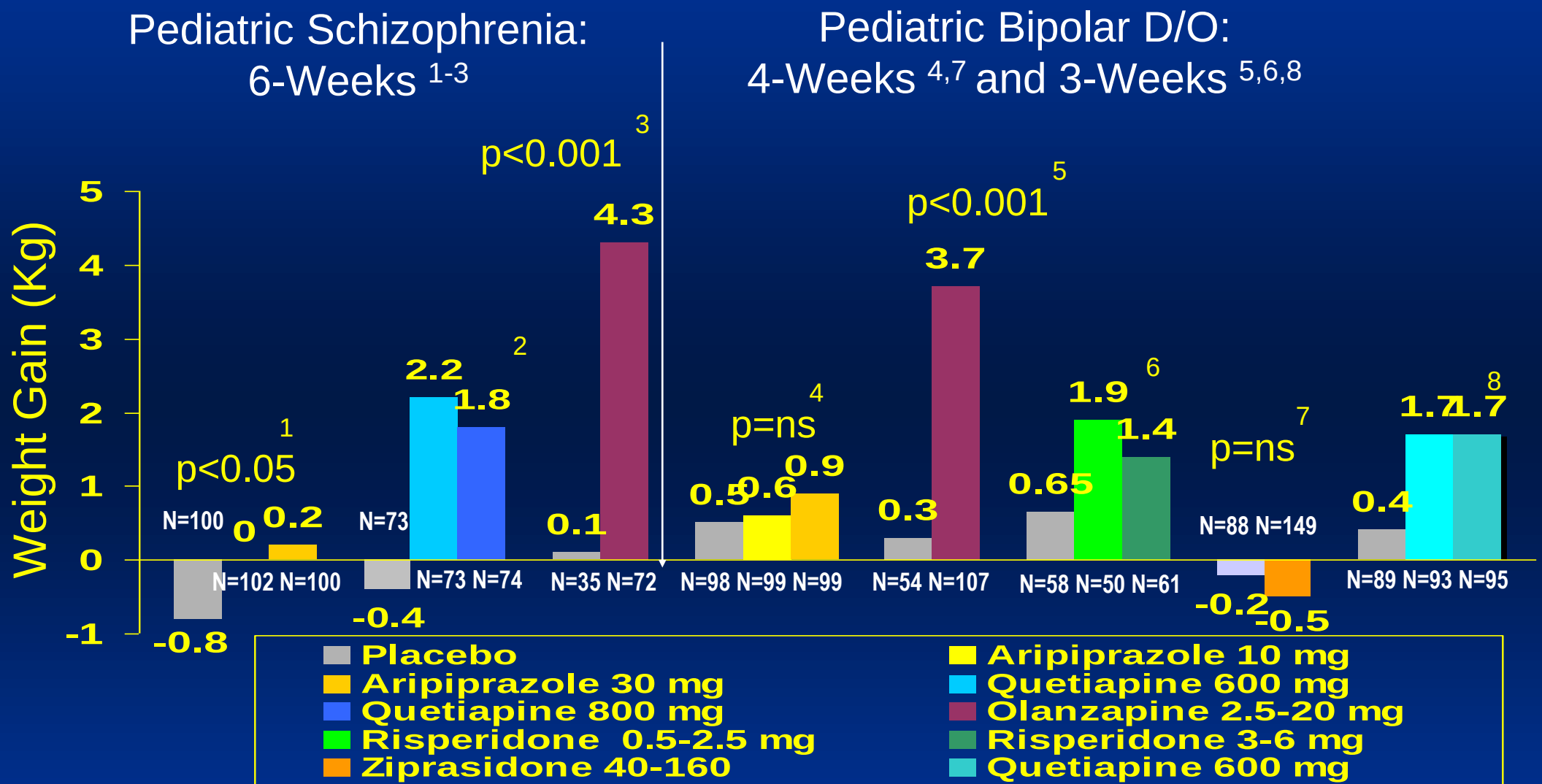
Somnolence in DBRPC Trials of Atypical Antipsychotics in Pediatric Schizophrenia & Bipolar Disorder



[1]. Findling RL et al. Am J Psychiatry. 2008 Nov;165(11):1432-41; [2]Haas M et al. (2007), APA Meeting. San Diego [3]Findling RL et al. AACAP 2008; [4] ; [4] Kryzhanovskaya L et al. J Am Acad Child Adolesc Psychiatry. 2009 Jan;48(1):60-70; [5] Findling RL et al. J Clin Psychiatry. 2009 Oct;70(10):1441-51; [6]Haas M et al Bipolar Disord. 2009 Nov;11(7):687-700; [7]Tohen M et al. (2007), Am J Psychiatry;164:1547-56. [8]DelBello M et al. (2007), AACAP Meeting. Boston. Adapted from: Correll CU. J Clin Psychiatry 2008;69 (suppl 4): 26-36

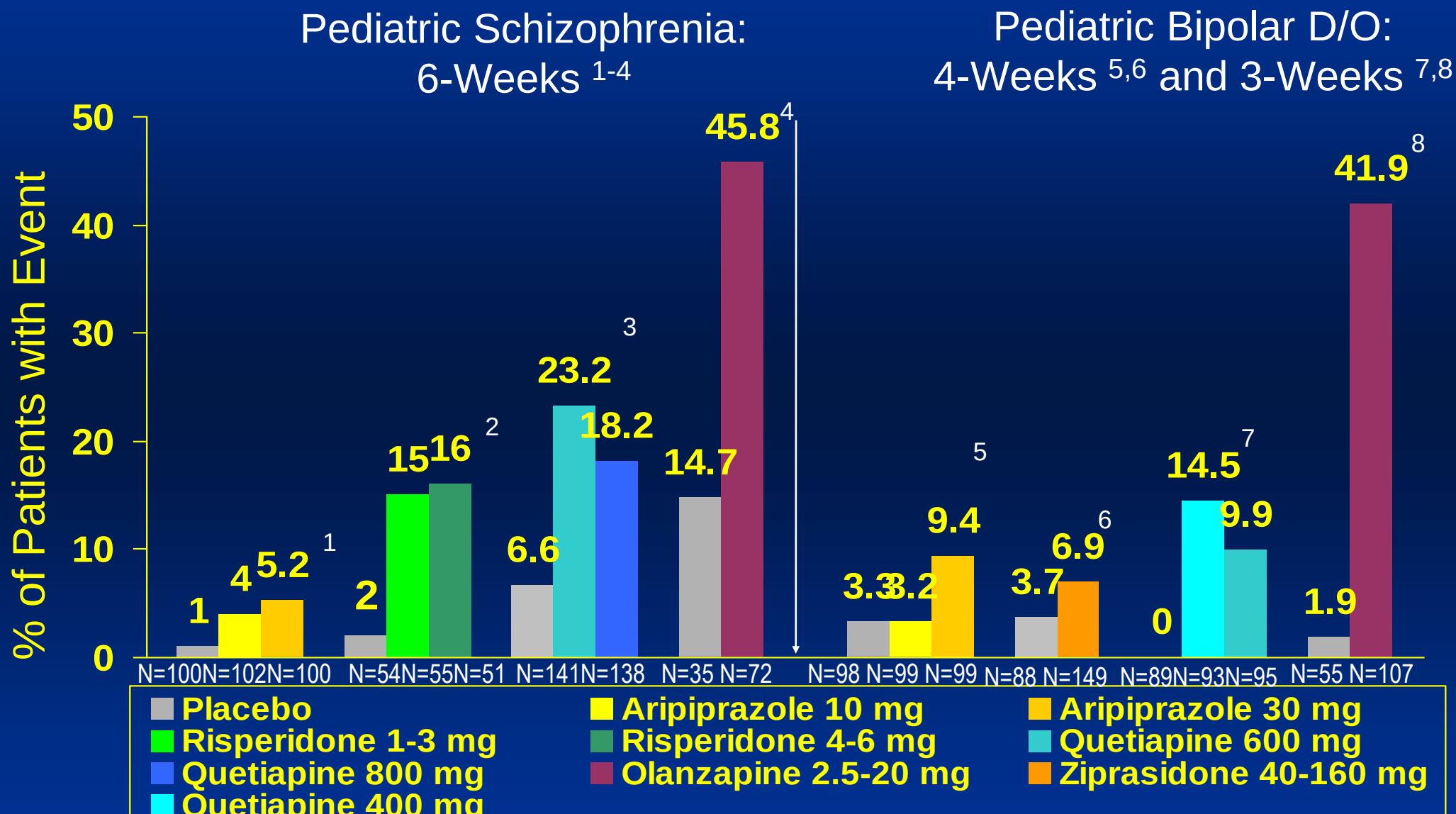
Weight Gain Associated with Antipsychotics in Youth

Weight Gain in DBRPC Trials of Atypical Antipsychotics in Pediatric Schizophrenia and Bipolar Disorder



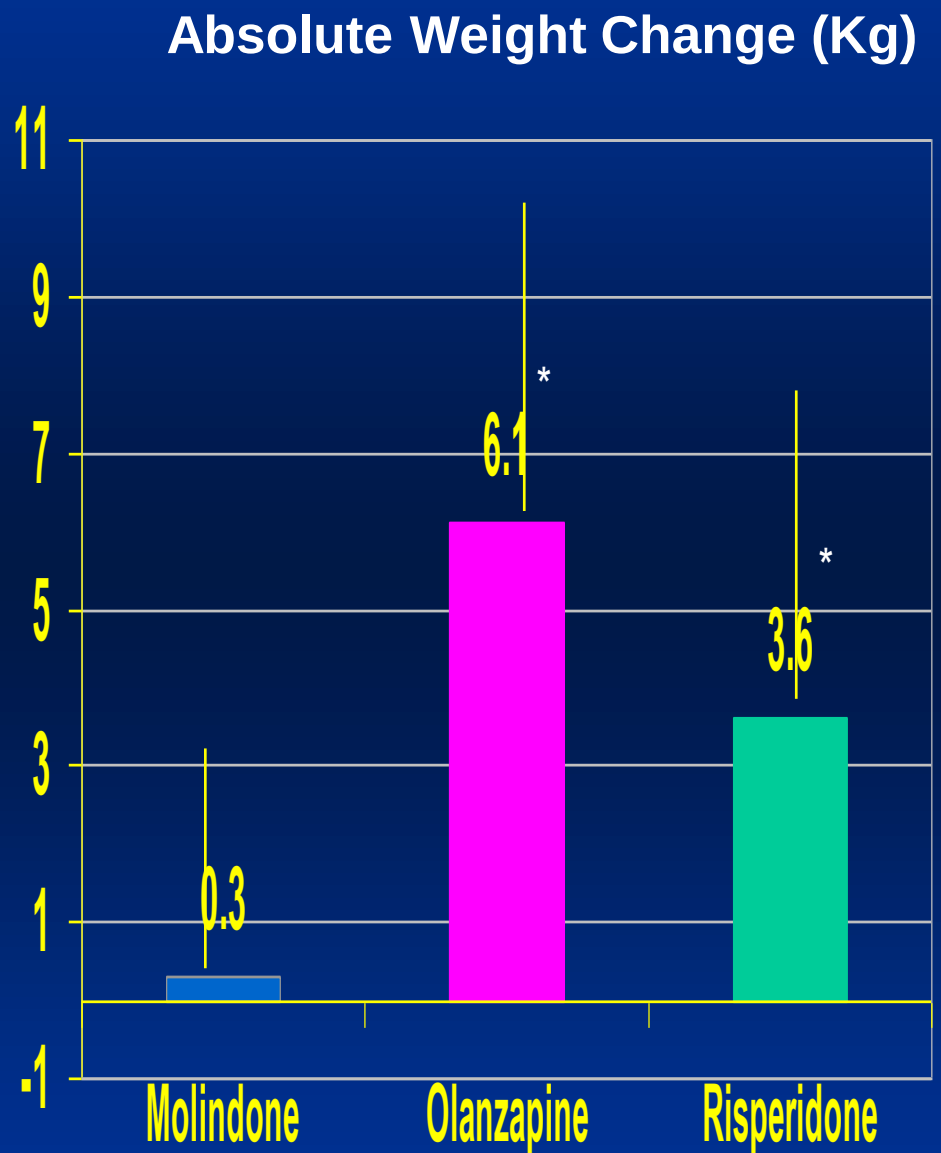
[1] Findling RL et al., Am J Psychiatry 2008;165:1432-41; [2] Findling RL; AACAP Meeting 2008; [3] Kryzhanovskaya L et al. J Am Acad Child Adolesc Psychiatry. 2009 Jan;48(1):60-70; [4] Findling RL et al. J Clin Psychiatry. 2009 Oct;70(10):1441-51; [5]Tohen M et al., Am J Psychiatry 2007;164(10):1547-56; [6]Haas M et al Bipolar Disord. 2009 Nov;11(7):687-700; [7]DelBello M et al.(2008) APA Meeting Washington DC; [8]DelBello M et al. (2007), AACAP Meeting Boston. Adapted from: Correll CU. J Clin Psychiatry 2008;69 (suppl 4): 26-36.

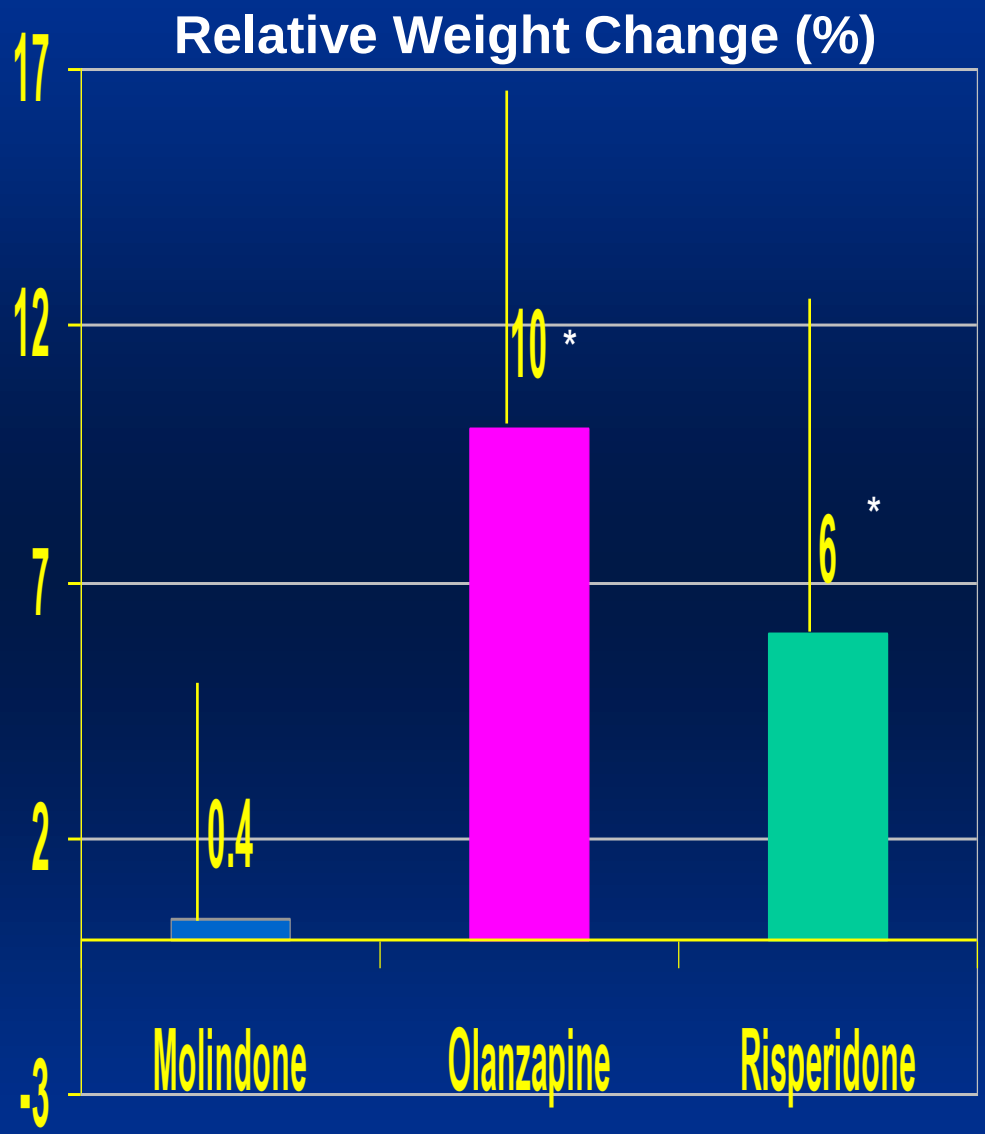
≥7% Weight Gain in DBRPC Trials of Atypical Antipsychotics in Pediatric Schizophrenia & Bipolar Disorder



[1] Findling RL et al., Am J Psychiatry 2008;165:1432-41; [2] Haas M et al. NCDEU 2007, Boca Raton; [3] Findling RL; AACAP Meeting 2008; [4] Kryzhanovskaya L et al. J Am Acad Child Adolesc Psychiatry. 2009 Jan;48(1):60-70; [5] Findling RL et al. J Clin Psychiatry. 2009 Oct;70(10):1441-51; [6] DelBello M et al., APA 2008, [7] DelBello M et al., AACAPP 2007; [8] Tohen M et al., Am J Psychiatry 2007;164(10):1547-56. Adapted from: Correll CU. J Clin Psychiatry 2008;69 (suppl 4): 26-36

TEOSS: 8-Week Weight Change

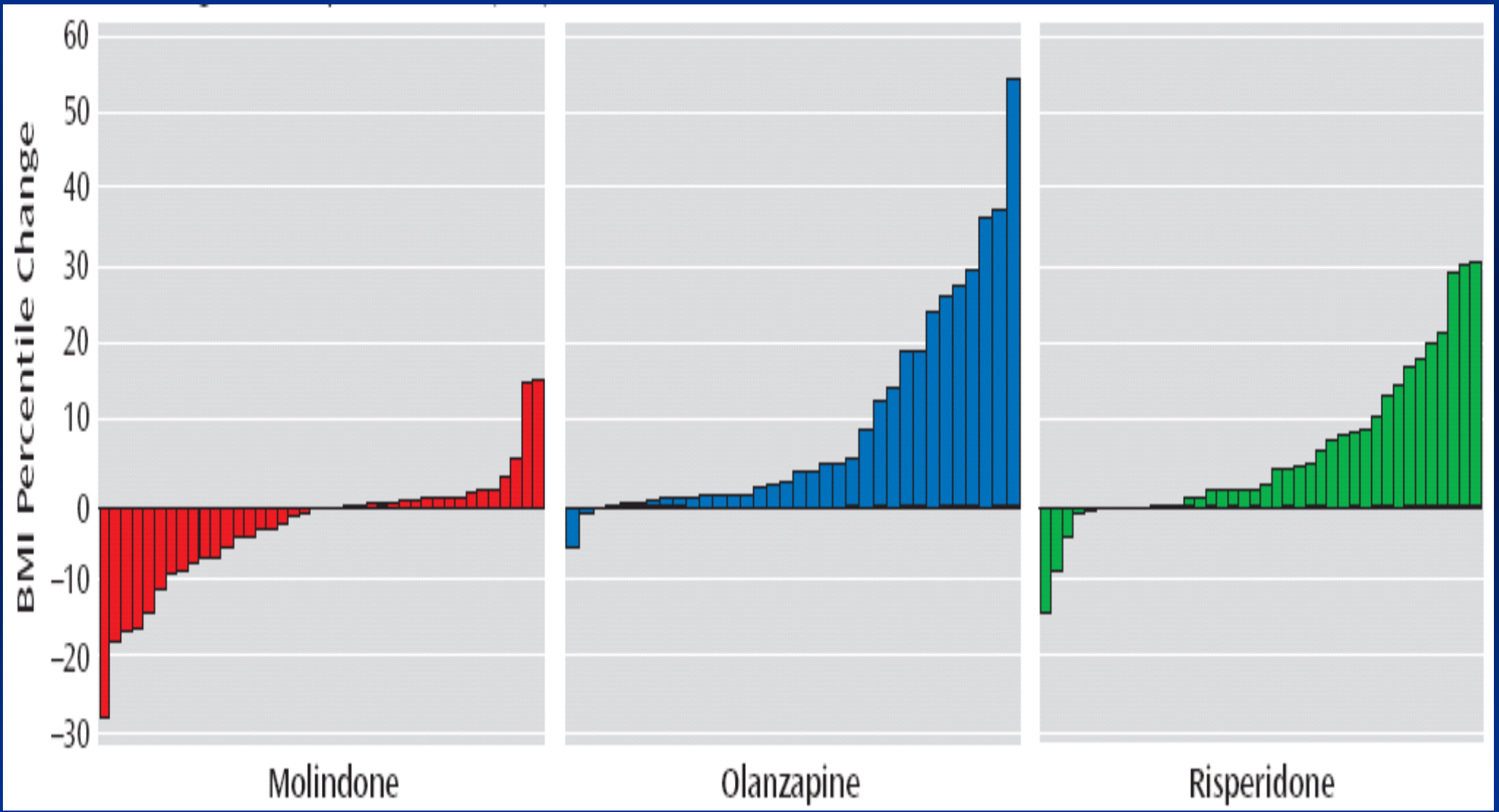




•= p<0.0001 for within subject comparison: 3 group comparison significant at p <0.0001, O>M,R; R>M

Sikich L, et al. Am J Psychiatry 2008;165(11):1420-31

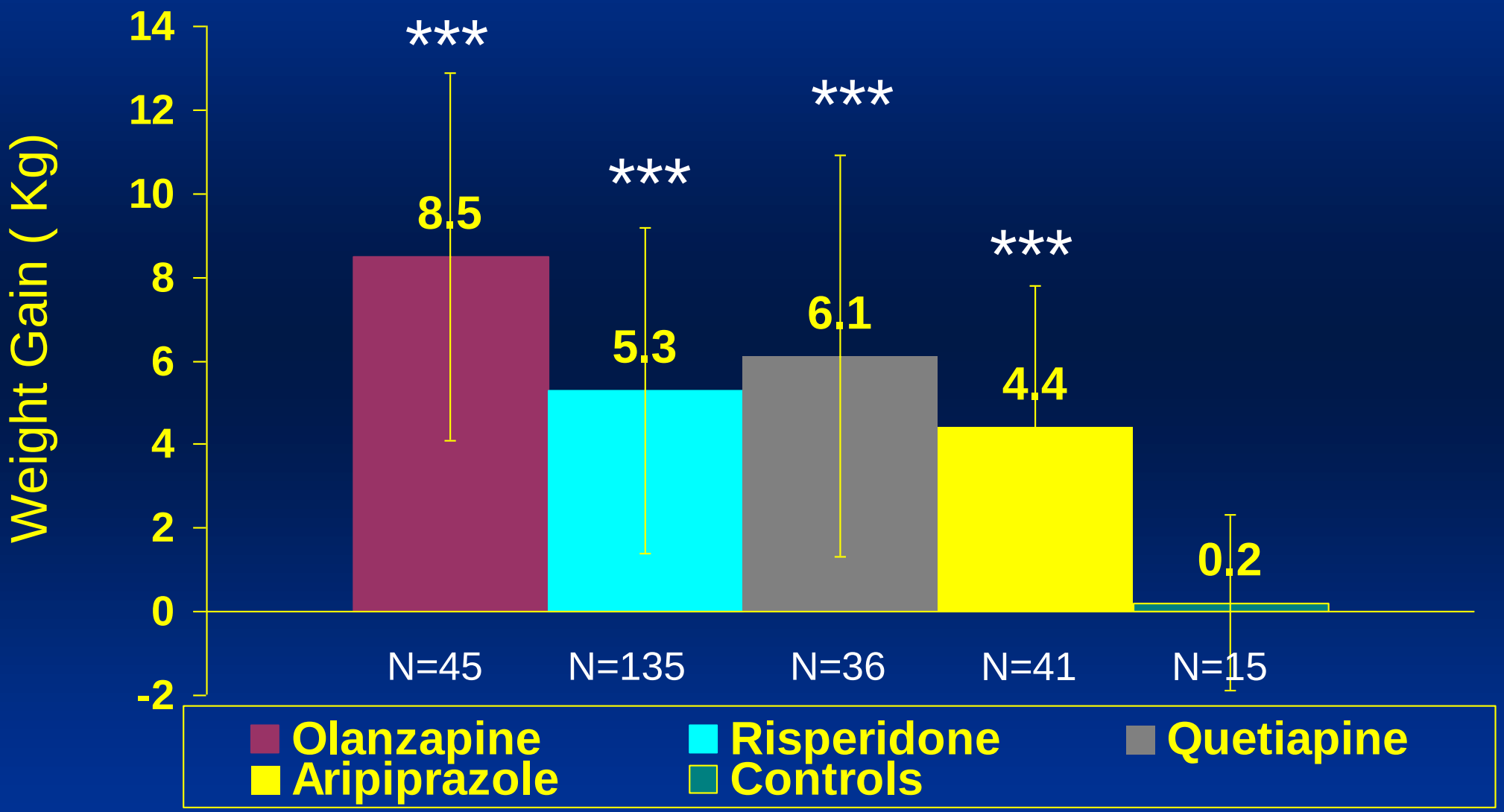
TEOSS: 8-Week Weight Change in BMI Percentiles per Subject



Mean weight gain: OLA: 6.1 kg (10%), RIS: 3.6 kg (6%), MOL: 0.3 Kg (0.4%)

Sikich L, et al. Am J Psychiatry 2008;165(11):1420-31

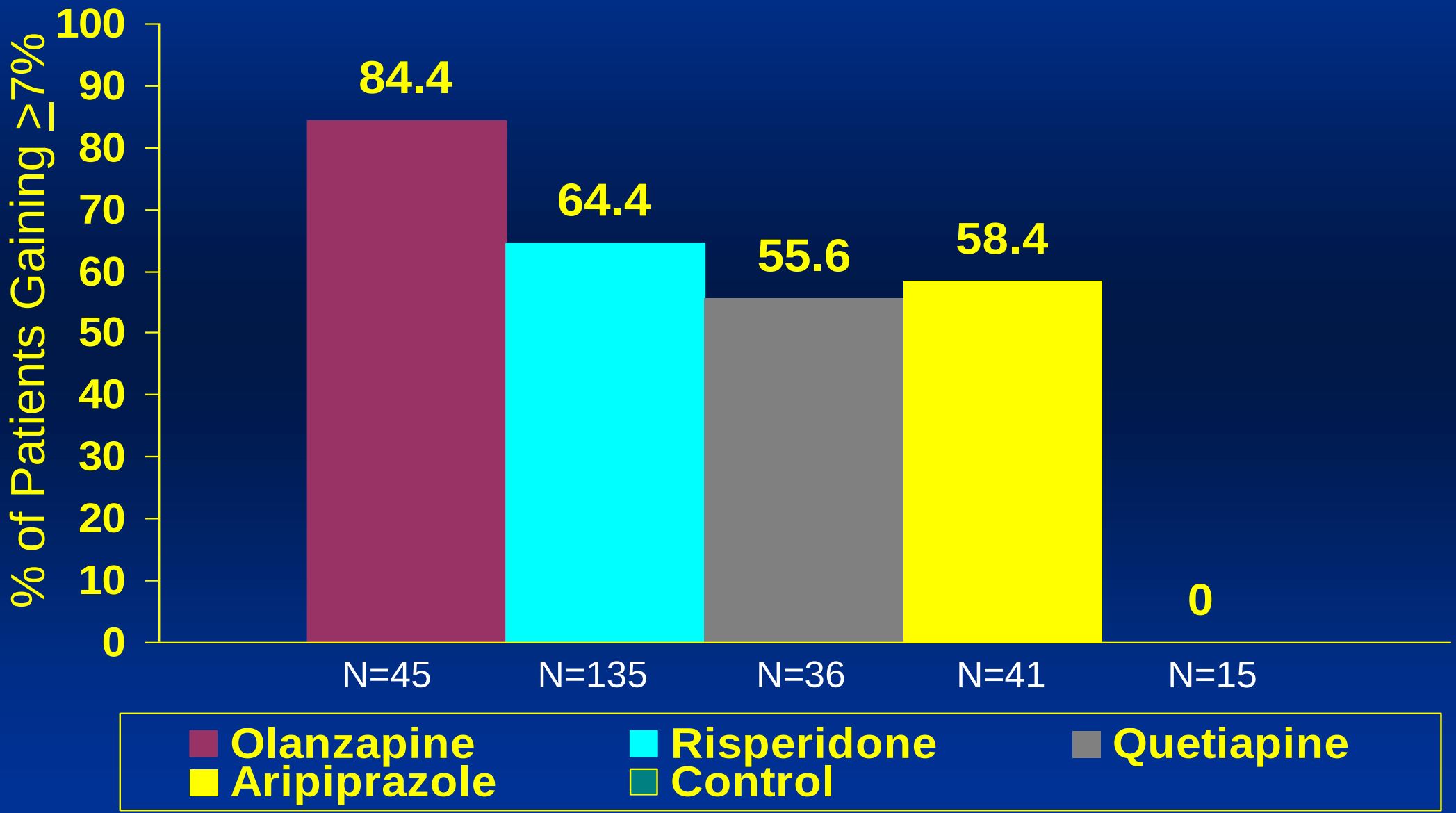
Weight Gain (kg) over 3 Months in Antipsychotic-Naïve Youth (N=272)



Baseline to endpoint change: ***p<.0001

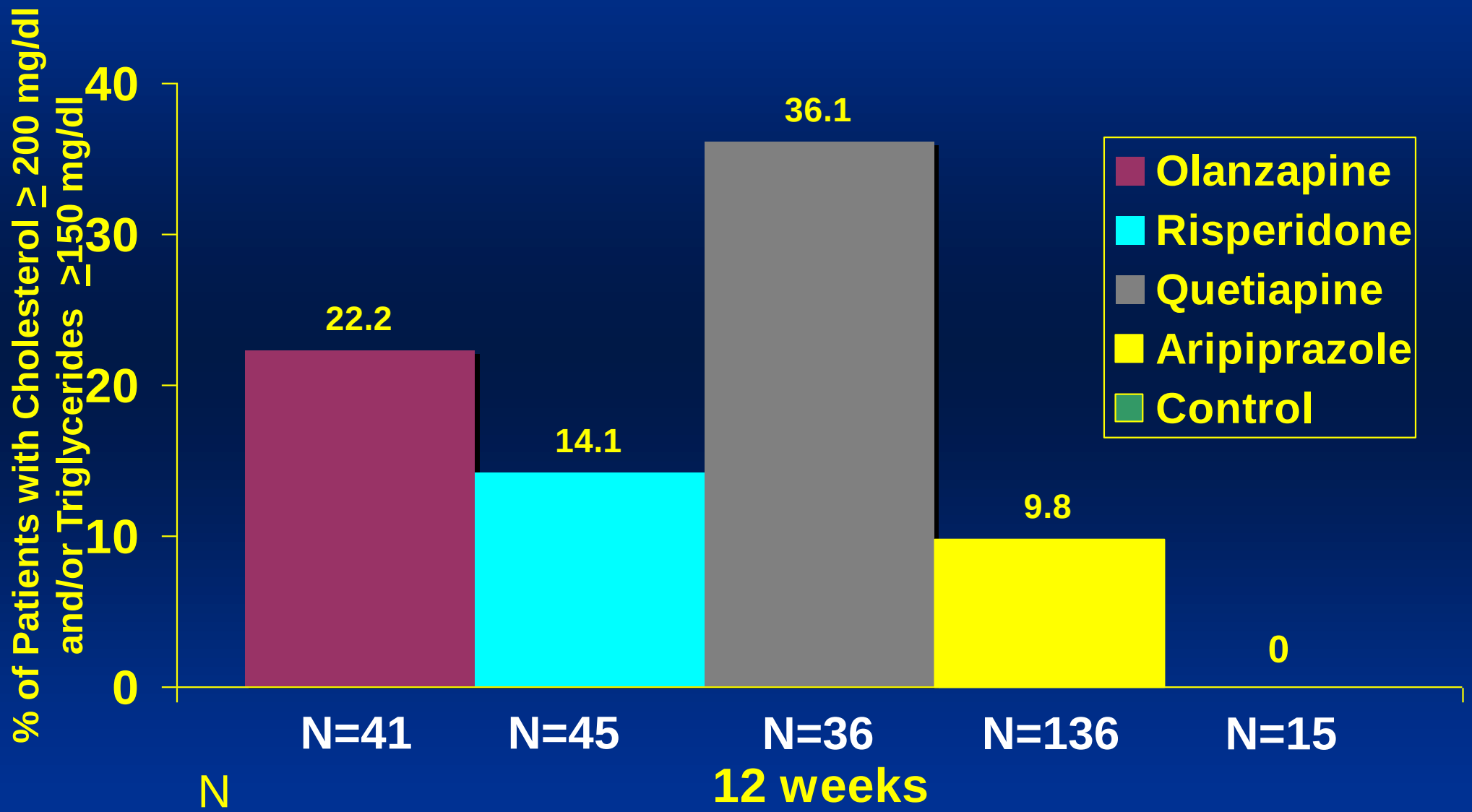
Correll CU et al. JAMA 2009;302(16):1763-1771.

Weight Gain ≥7% over 3 Months in Antipsychotic-Naïve Youth (N=272)



Correll CU et al. JAMA 2009;302(16):1763-1771.

% Of Drug-naïve Youth With New-onset Shift to Obese or Overweight over 3 Months (N=272)



Corrected P< 0.05

Correll CU et al. JAMA 2009;302(16):1763-1771.

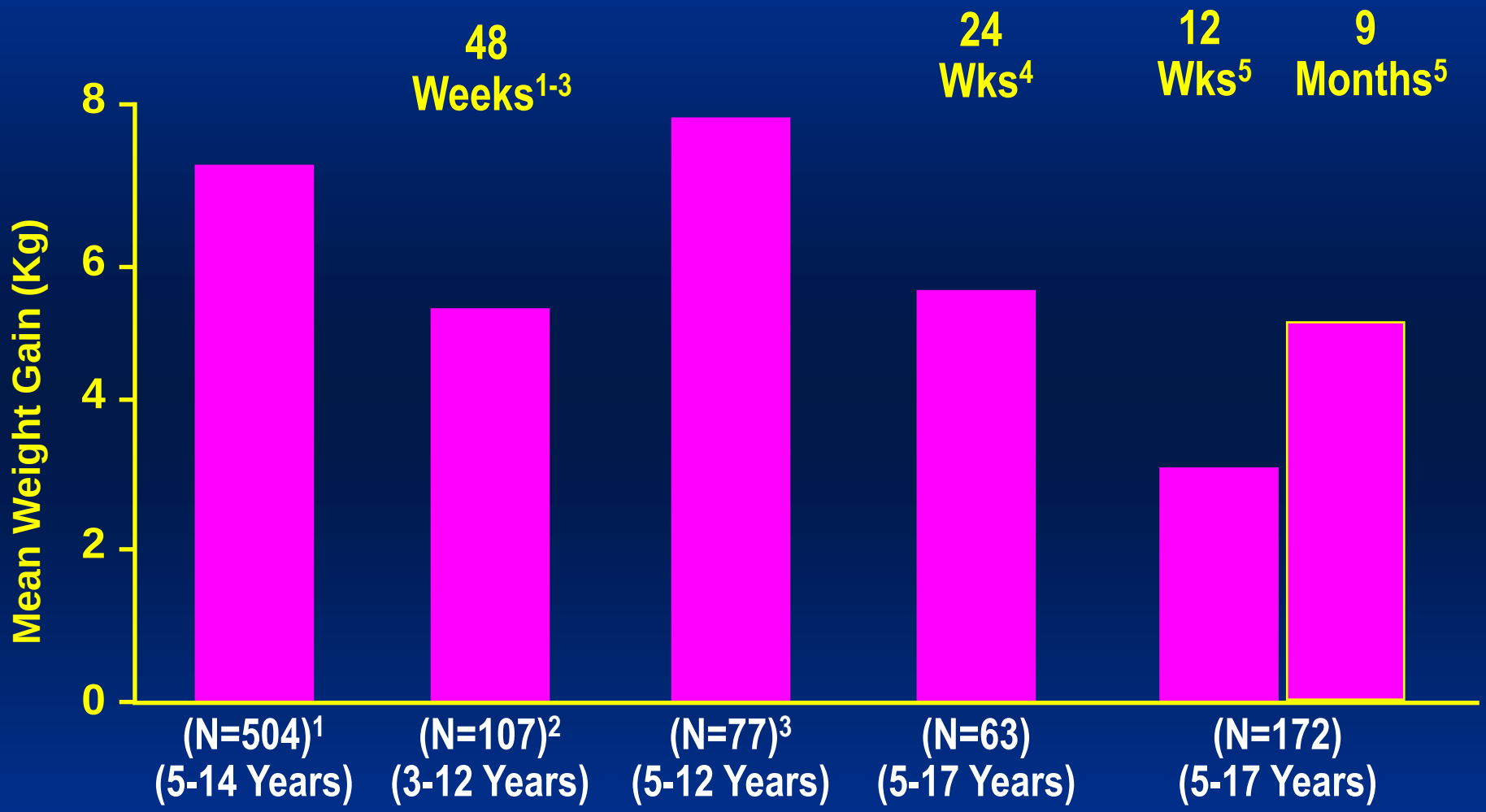
Numbers-Needed-to-Treat for Adverse Body Composition or Metabolic Outcomes in Antipsychotic-Naïve Youth Treated for 3 Months (N=272)

Outcome Variable	Aripiprazole (n=41)	Olanzapine (n=45)	Quetiapine (n=36)	Risperidone (n=135)
Weight Gain ≥7%	2 (1-3)	1 (1-2)	2 (1-3)	2 (1-3)
Weight Gain ≥14%	6 (3-∞)	2 (1-4)	3 (2-14)	4 (2-31)
Weight Gain ≥21%	20 (6-∞)	4 (2-38)	18 (6-∞)	15 (5-∞)
>10% BMI	5 (2-97)	1 (1-2)	3 (2-7)	3 (2-9)
>20% BMI	14 (5-∞)	5 (2-86)	18 (6-∞)	17 (6-∞)
>0.5 BMI z-Score	5 (2-97)	2 (1-3)	3 (2-8)	2 (1-5)
>1.0 BMI z-Score	20 (6-∞)	3 (2-9)	7 (3-∞)	5 (3-∞)
Hypercholesterolemia	14 (5-∞)	4 (2-23)	7 (3-∞)	6 (3-∞)

Antipsychotic naïve sample
Hypercholesterolemia: >/=170 mg/dL

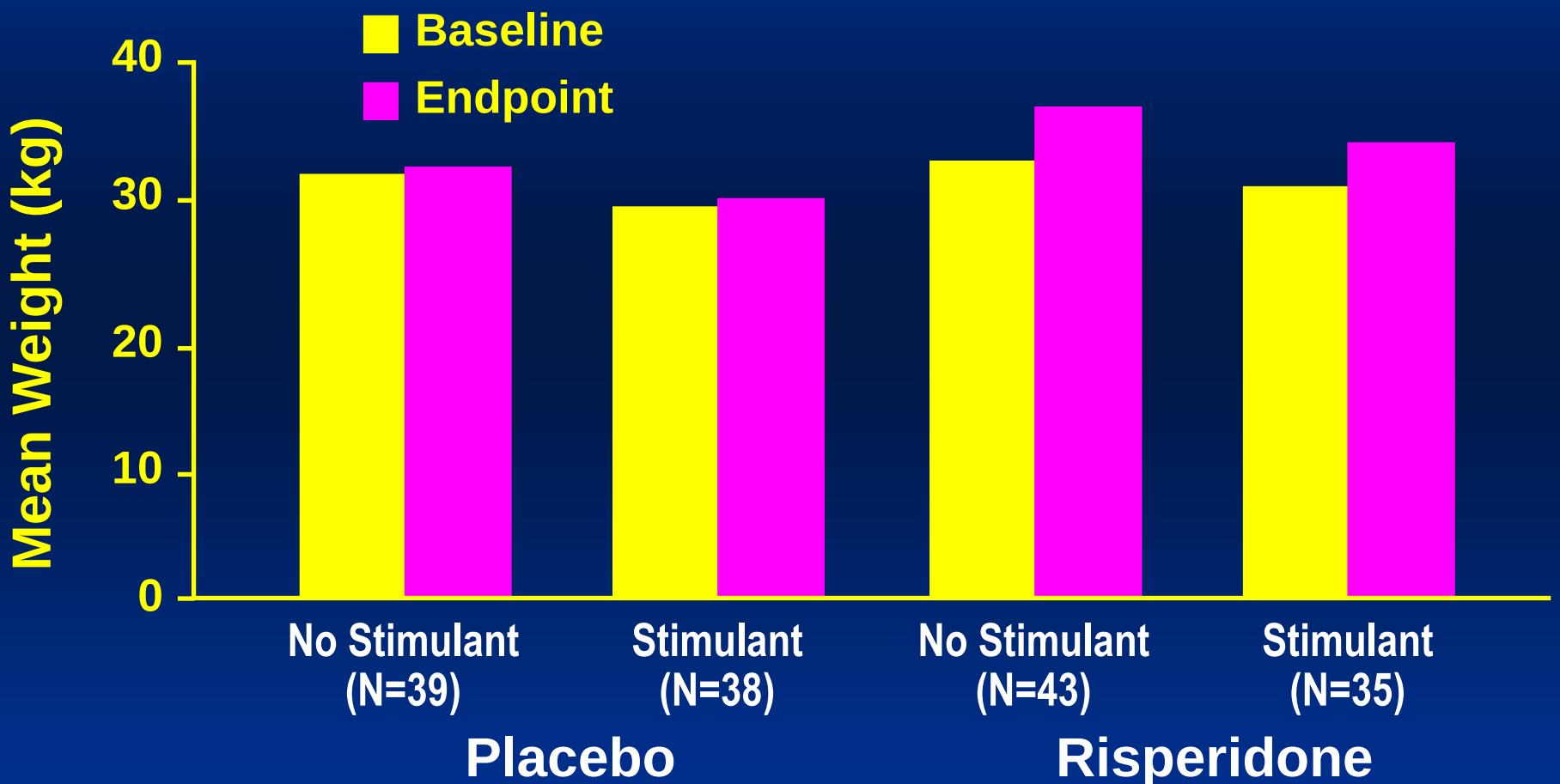
Data are presented as NNT +/- 95% Confidence Interval
Correll CU et al. JAMA 2009;302(16):1763-1771

6-12 Month Risperidone: Weight Gain in Disruptive Disorders [1-3, 5], Autism[4]



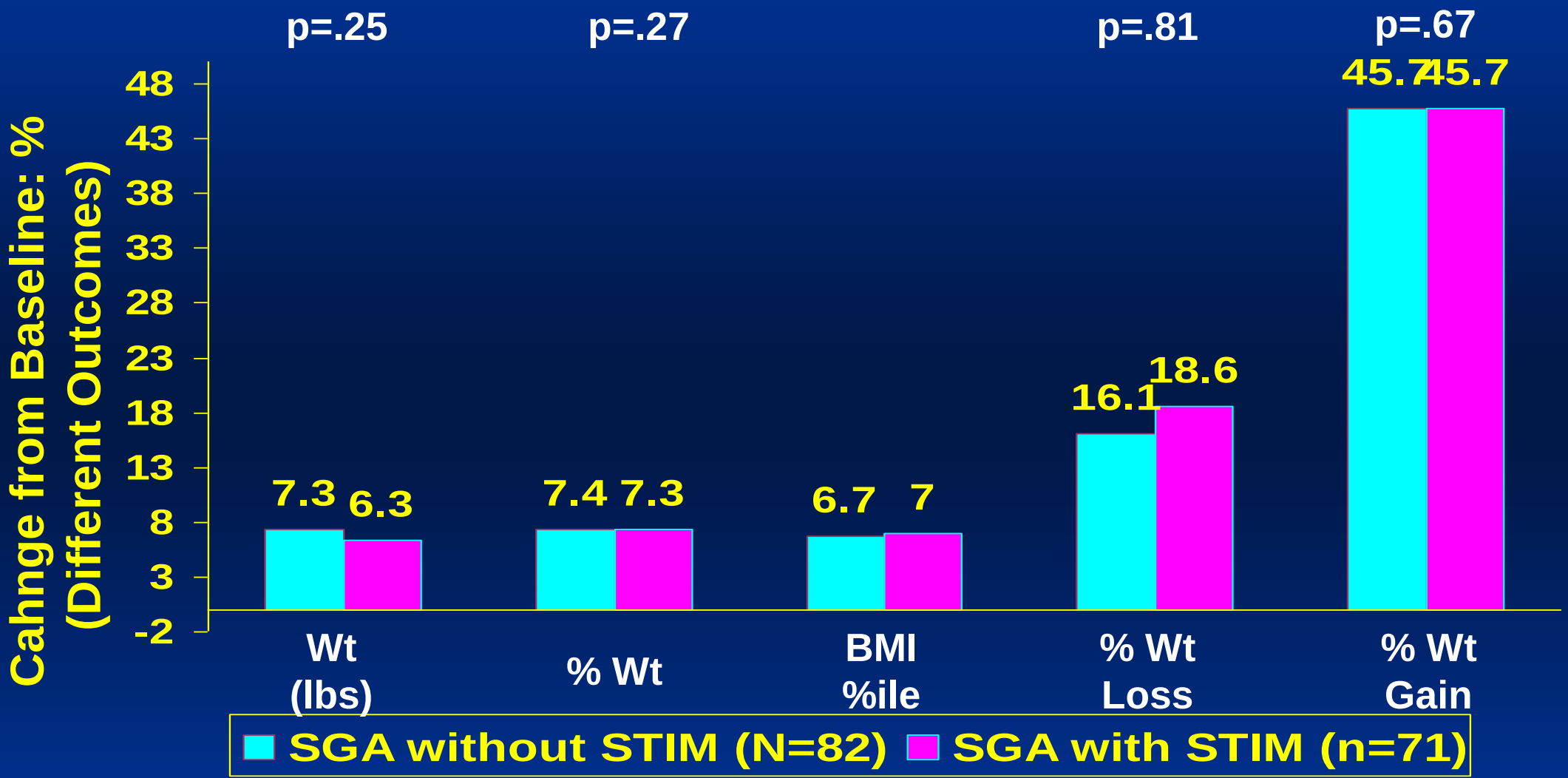
[1]Croonenberghs J at al. (2005), J Am Acad Child Adolsc Psychiatry 44(1):64-72; [2]Findling RL et al. (2004), Am J Psychiatry 161(4):677-684; [3]Turgay A et al. (2002), Pediatrics 110(3):e34, [4]Martin A et al. (2004), Am J Psychiatry 161(6):1125-7; [5]Reyes M et al. (2006) Am J Psychiatry 163(3):402-10

Stimulant-Risperidone Cotreatment Does Not Reduce Gain In Youth With ODD, ADHD and Low IQ



*Change calculated as endpoint minus baseline; †p<0.02, paired t-test; ‡p=0.03, paired t-test; §p<0.001, paired t-test; STIM = stimulant; ODD = oppositional defiant disorder; Aman MG et al. (2004), J Child Adolesc Psychopharmacol 14(2):243-254

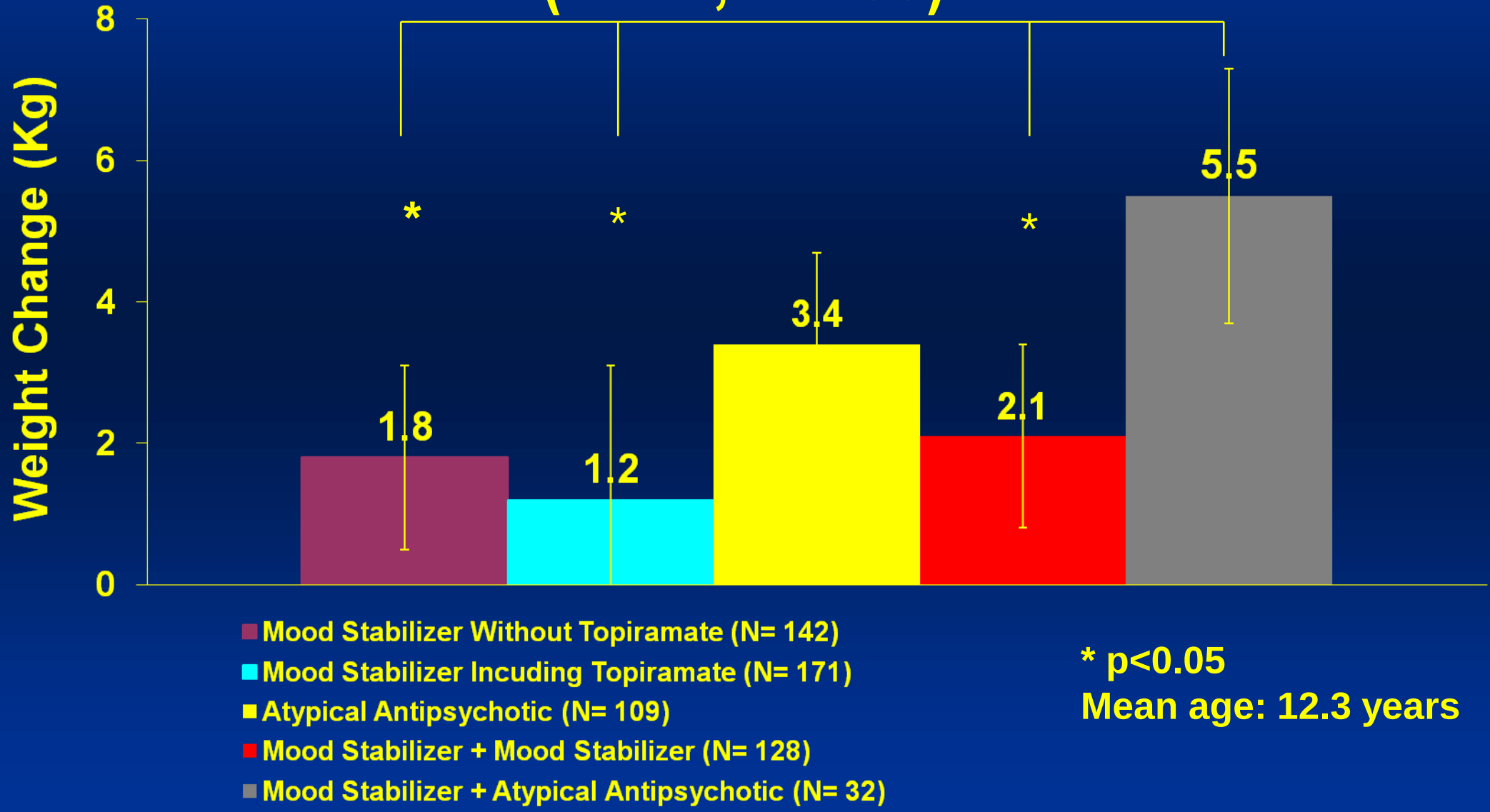
Effects of Stimulant-AP Co-Treatment: 153 SGA Trials for Disruptive Behaviors



Mean age: 11.3 y; ODD: 45.0%, PDD: 30.7%, Autism: 14.4%, other DBDs: 9.2%; ADHD Comorbidity: 57.5%; mean BMI z score at baseline: 0.5+/-1.5, 47.1% overweight/obese ; AP-naïve: 39.2%; RIS: 33.3%; ARI: 29.4%; QUE: 18.3%; OLA: 11.8%; ZIP: 5.9%

Penzner J et al. J Child Adolesc Psychopharmacol. 2009 Oct;19(5):563-73.

Antipsychotic-Mood Stabilizer Cotreatment Increases Weight Gain in Youth with Bipolar d/o (N=11, n=433)



* p<0.05
Mean age: 12.3 years

Correll CU. J Am Acad Child Adolesc Psychiatry. 2007;46(6):687-700.

Metabolic Effects

BMI Status and Lipid Profiles in Hospitalized Children and Adolescents (N=95)

Variable	*Classification of total sample (n = 95)*		
BMI percentile	Acceptable (<85th percentile) 30 (32%)	At risk for overweight (Between 85th and 94.9th percentiles) 15 (16%)	Overweight (≥95th percentile) 50 (53%)
TC	Acceptable (<170 mg/dL) 53 (56%)	Borderline high (170–199 mg/dL) 27 (28%)	High (≥200 mg/dL) 15 (16%)
LDL	Acceptable (<110 mg/dL) 63 (66%)	Borderline high (110–129 mg/dL) 21 (22%)	High (≥130 mg/dL) 11 (12%)
HDL	Acceptable (>40 mg/dL) 49 (52%)	Low (≤40 mg/dL) 46 (48%)	
TG	Acceptable (<110 mg/dL) 47 (49%)	High (≥110 mg/dL) 48 (51%)	

Mean age: 14.0 (5-18) years. Bipolar disorder: 52%, DBD: 46%, Anxiety Disorder: 39%; Developmental Disorders: 21%; Psychotic Disorders: 14%

Patel N et al. J Child Adolesc Psychopharmacol 2007 17:303-11.

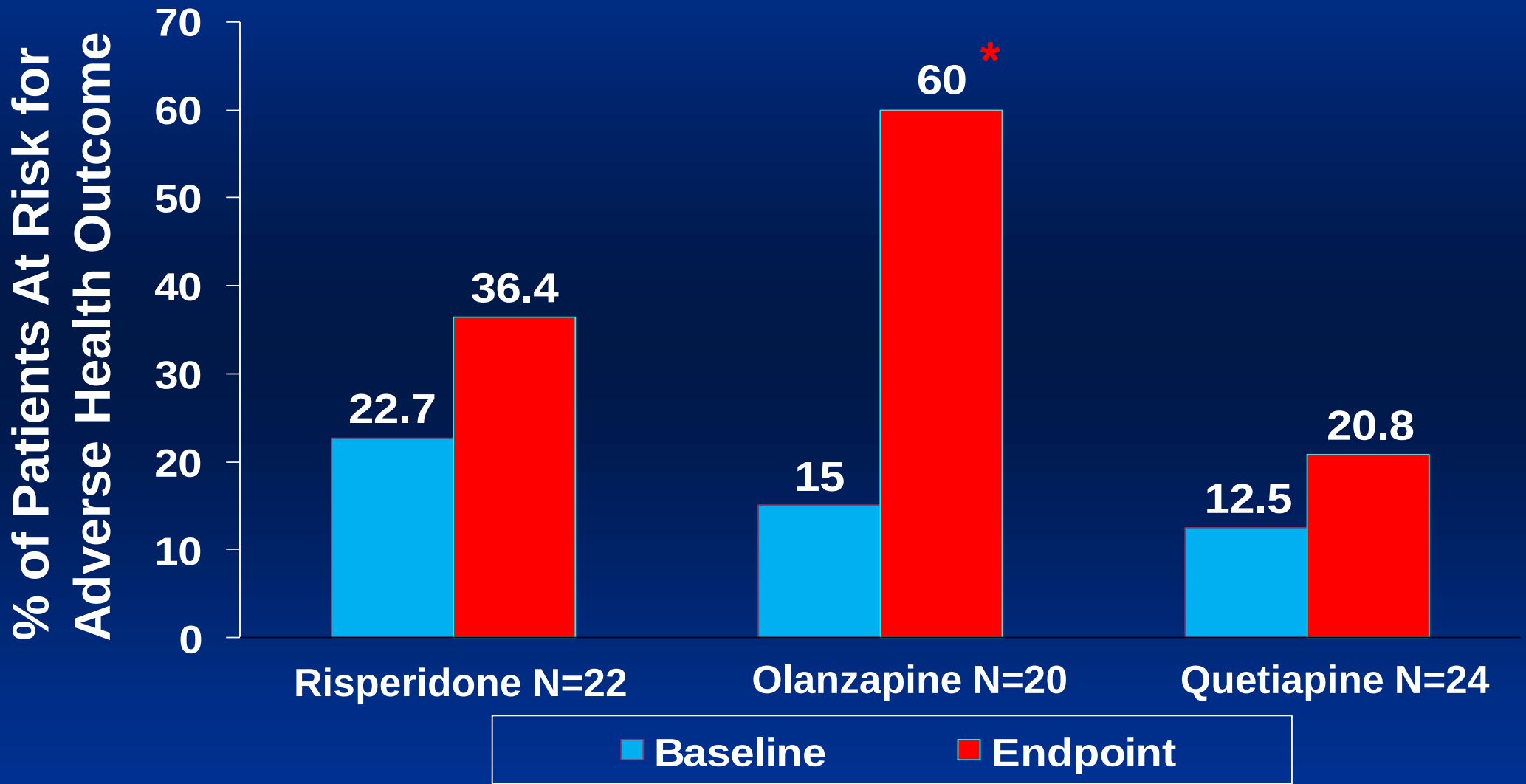
6-Month Change in Cardiometabolic Parameters during Naturalistic Treatment with Risperidone, Olanzapine, Quetiapine in Psychotic Youth (N=68)

Value	Risperidone N=22	Olanzapine N=20	Quetiapine N=24	Statistics
Body weight	5.0 ± 4.8**	11.1 ± 7.8**	2.5 ± 6.8	O>R,Q
BMI z-score	0.48 ± 0.73**	1.0 ± 0.82**	0.27± 0.86	O>Q
Fasting glucose	0.6 ± 10.8	3.1 ± 10.4	1.2 ± 10.3	ns
Total cholesterol	-1.5 ± 23.3	10.4 ± 30.4*	14.8 ± 30.9*	ns
LDL	-2.2 ± 18.2	6.9 ± 22.6	5.4 ± 22.4	ns
HDL	-2.9 ± 8.2	2.6 ± 13.2	4.3 ± 13.3	ns
Triglycerides	10.7 ± 74.4	17.3 ± 14.0	10.5 ± 56.5	ns
HBA1C (%)	0.3 ± 0.8	0.2 ± 0.8	0.9 ± 1.6	ns
Systolic BP	1.3 ± 25.0	7.4 ± 11.0	5.6 ± 31.6	ns
Diastolic BP	5.5 ± 12.7	2.0 ± 8.3	0.4 ± 12.1	ns

* p <.05; ** p <.01

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

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

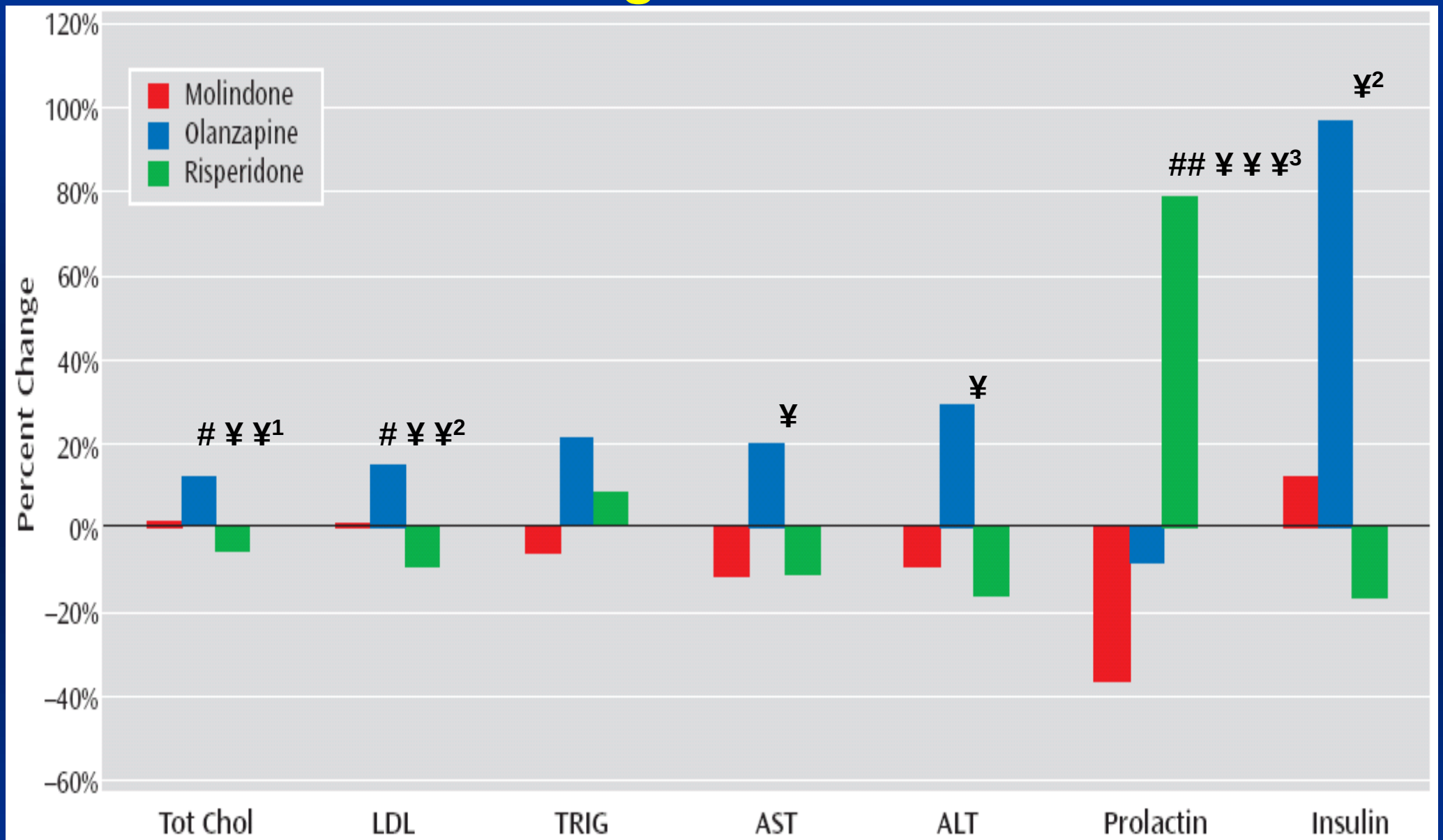


At risk for adverse health outcome: obesity or overweight plus at least one metabolic, blood pressure or other weight related health problem

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

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

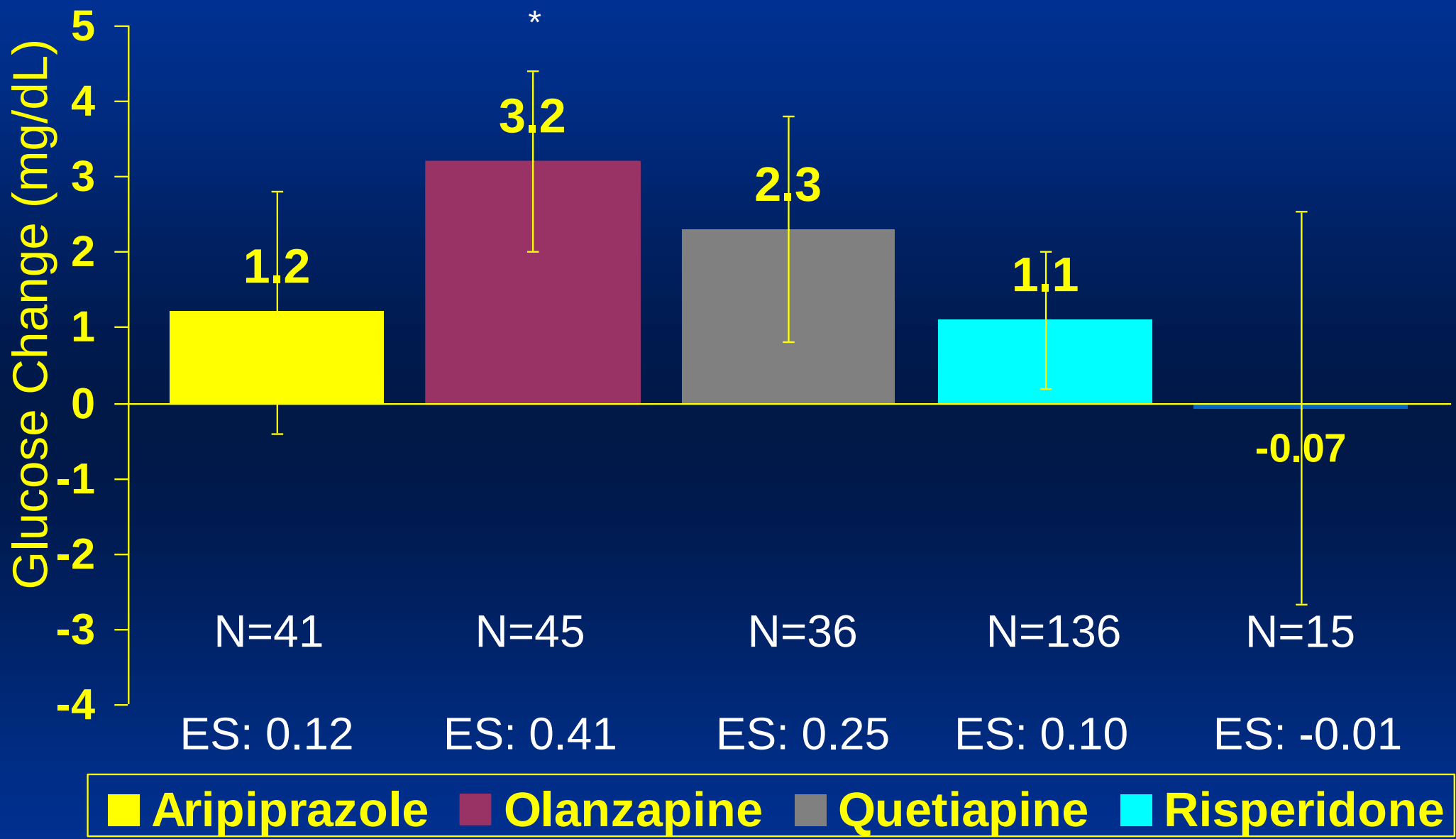
Metabolic Changes in the TEOSS Trial



# p<.05 within group; ## p<.0001 within group ; ¥ p<.05 across groups; ¥ ¥p<.005 across groups; ¥ ¥ ¥ p<.0001 across groups; 1=O>R,M; 2=O>R; 3=R>O,M; glucose and HOMA-IR changes: ns

Sikich L, et al. Am J Psychiatry 2008;165(11):1420-31

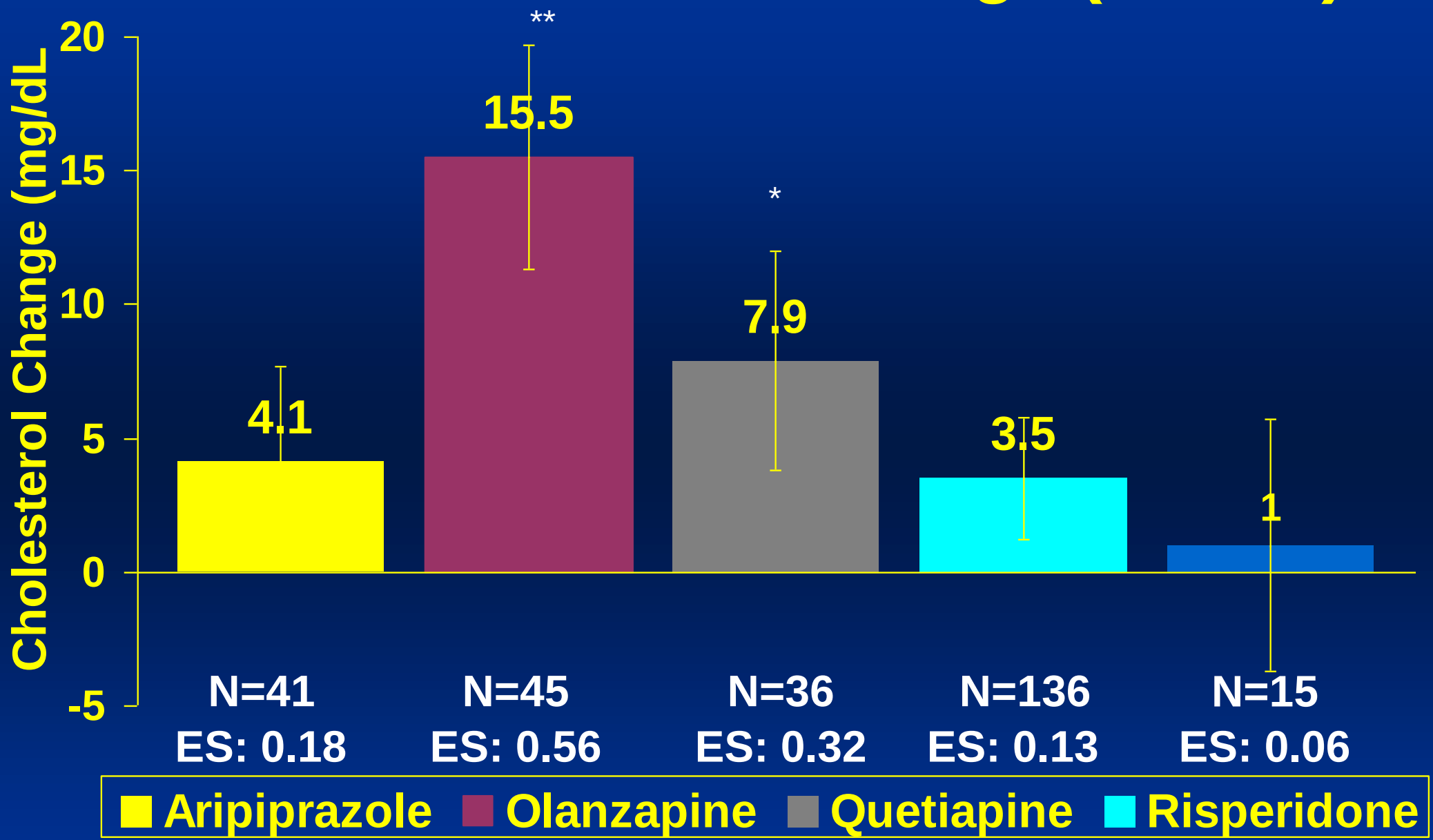
12-Week Glucose Change (N=272)



*p=0.008

Correll CU et al. JAMA 2009;302(16):1763-1771.

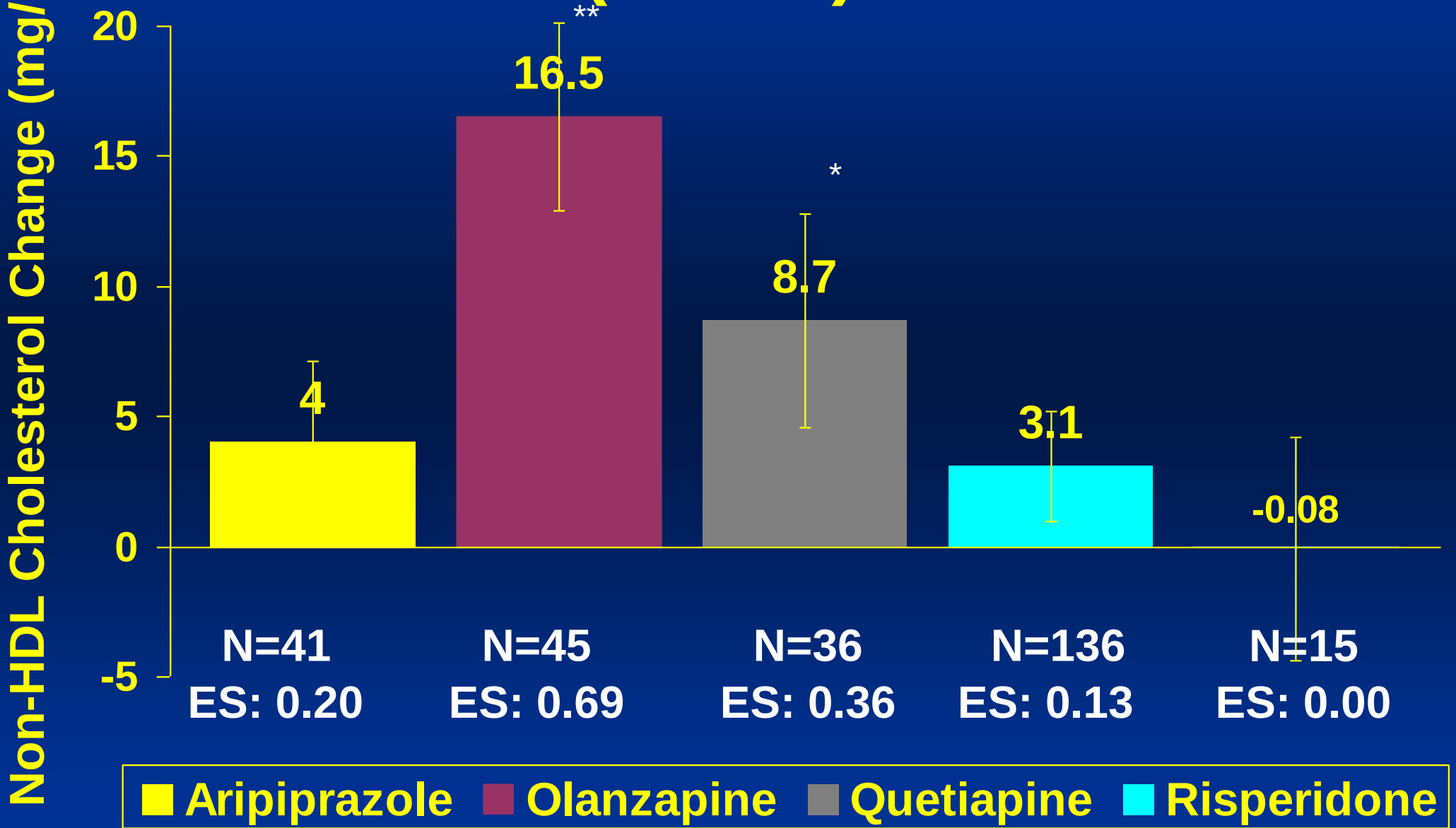
12-Week Cholesterol Change (N=272)



*p=0.046; **p=0.0004

Correll CU et al. JAMA 2009;302(16):1763-1771.

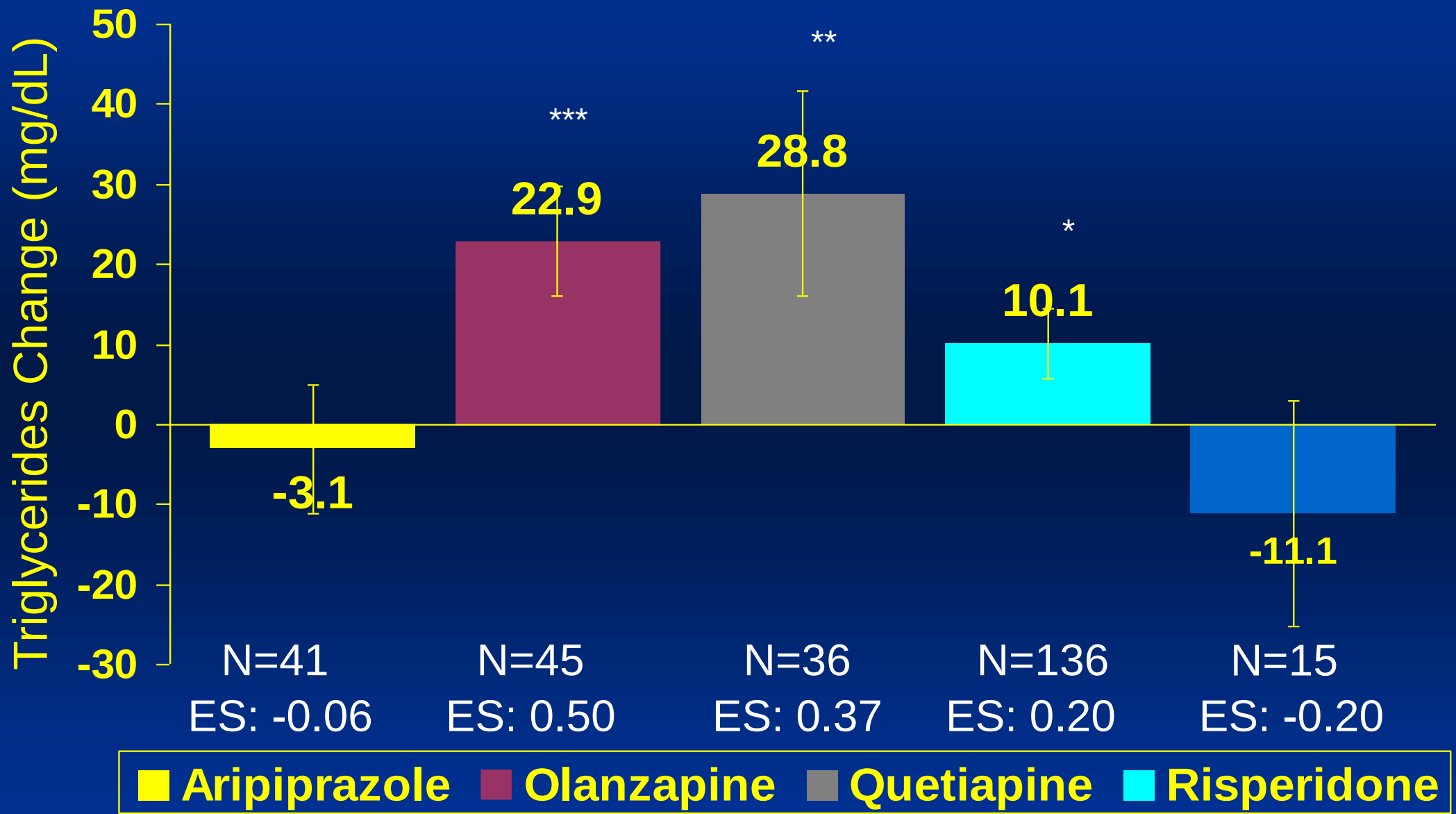
12-Week Non-HDL Cholesterol Change (N=272)



*p=0.034; **p<0.0001

Correll CU et al. JAMA 2009;302(16):1763-1771.

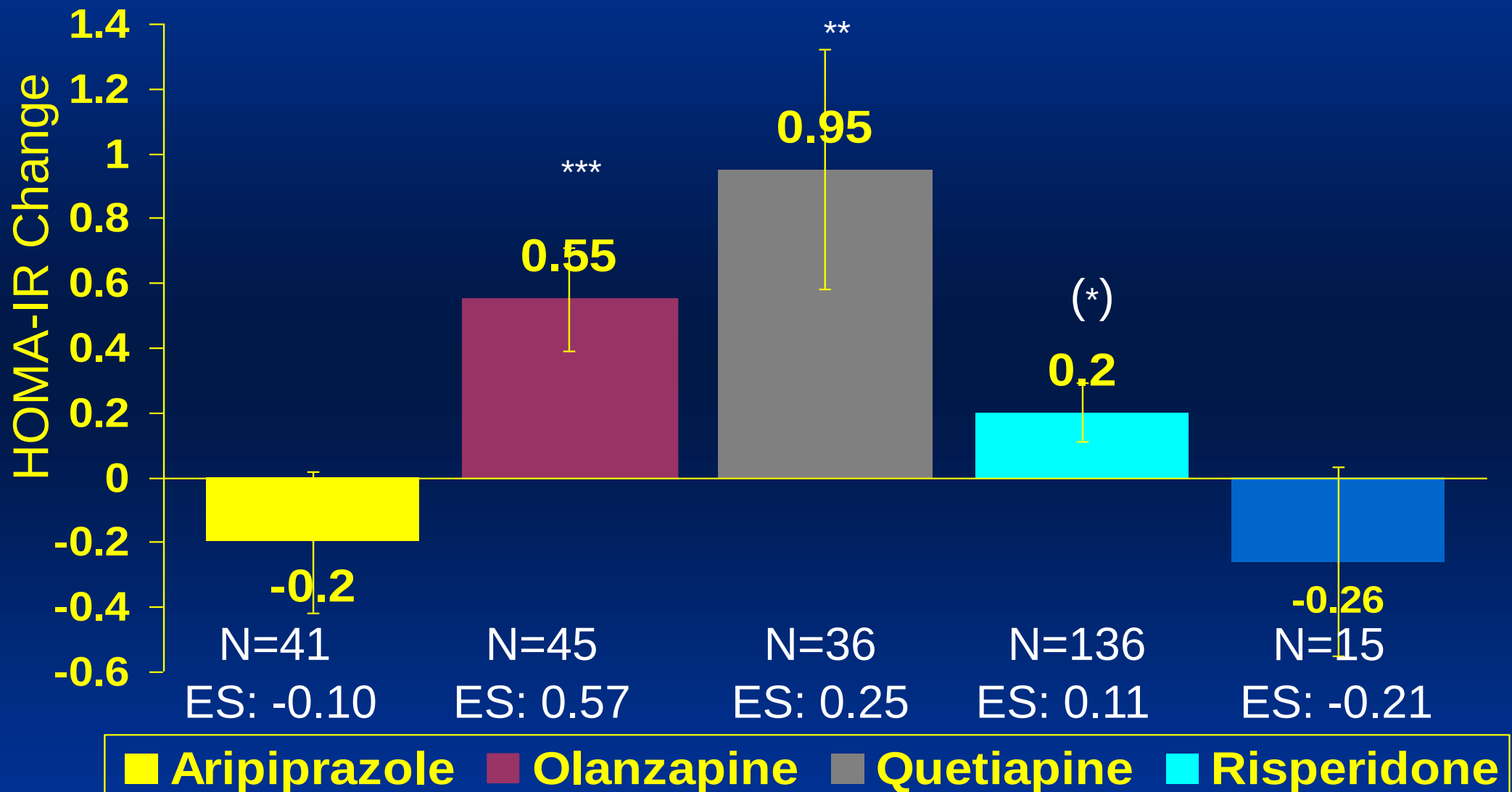
12-Week Triglyceride Change (N=272)



*p=0.03; **p=0.02; ***p=0.0013

Correll CU et al. JAMA 2009;302(16):1763-1771.

12-Week Triglyceride/HDL Ratio Change (N=272)



(*)p=0.052; **p=0.01; ***p=0.0015

Correll CU et al. JAMA 2009;302(16):1763-1771.

Monitoring and Management of Adverse Antipsychotic Effects

Adverse Effect Monitoring of Antipsychotic-Treated Children and Adolescents

Assessments	Frequency
Personal and family history	Baseline and Annually
Lifestyle monitoring	Every visit
Height, weight, BMI percentile / z-score	Every visit
Somnolence/sedation	Every visit
Sexual symptoms/signs	Baseline, during titration and q 3 mo
Blood pressure, pulse	Baseline, 3-months and 6-monthly
Fasting glucose, lipids (+/-insulin?)	Baseline, at 3 mo and 6-monthly
Liver function tests	Baseline, at 3 mo and 6-monthly
EPS, akathisia	Baseline, titration, 3 mo and annually
Dyskinesia / TD	Baseline, 3 mo and annually
Electrolytes, blood count, renal f'ction	Baseline and annually (unless on CLO)
Prolactin	Only when symptomatic
EKG	If on ZIP: during titration, at max. dose

Correll CU. *J Am Acad Child Adolesc Psychiatry*. 2008;47(1):9-20.

Assessment : Body Composition

- **Weight change: dependent on baseline weight and growth**
- **BMI: only useful within 3 months of follow up**
- **BMI %ile (sex- and age adjusted standard: 50th %ile) and BMI z-score (adjusted standard: z score of 0):**
  - Growth charts: www.cdc.gov/growthcharts/
  - Web-based calculators:
    http://www.kidsnutrition.org/bodycomp/bmiz2.html
- **BMI percentile: Definition of weight categories**
  - **Underweight: < 5th %ile; Normal: 5-<85th %ile;**
  - **Overweight: 85-<95th %ile; Obese: ≥95th %ile**
- **BMI z-score: Tracking of change over time (>3 months)**
- **Waist circumference: not recommended by AMA (difficult to asses, age dependent cut-offs uncertain)**

Correll CU. *J Am Acad Child Adolesc Psychiatry*. 2008;47(1):9-20.

Assessment : Blood Pressure and Labs

- Blood Pressure (cuff should cover >80% of the upper arm)
  - Hypertension: >90th percentile for sex and age (Calculate height %ile (https://www.nutropin.com/patient/3_5_3_growth_charts.jsp) and compare blood pressure with population norms
- Hyperglycemia: ≥100 mg/dL
- Diabetes: ≥126 mg/dL (two fasting measures)
- Insulin resistance:
  - HOMA-IR [insulin (mg/dL) x glucose (mg/dL)/405]: >4.4 (adolescent)
  - TG/HDL ratio: >3.5
- Hypertriglyceridemia: ≥110 mg/dL
- Hypercholesterolemia: ≥170 mg/dL
- High LDL: >130 mg/dL
- Low HDL: <40 mg/dL

Correll CU. *J Am Acad Child Adolesc Psychiatry*. 2008;47(1):9-20.

Assessment : Risk for Adverse Health Outcome

Duration	Threshold for Being At Risk for Adverse Health Outcome
≤3 Months	>5% of weight increase compared to baseline
Any Duration	1. ≥0.5 increase in BMI z-score
	2. Overweight (≥85-94.9 BMI %ile) plus: Hypertension (>90th percentile) or Cholesterol: ≥200 mg/dL, or LDL-cholesterol >130 mg/dL, or HDL-cholesterol <40 mg/dL, or Triglycerides ≥150 mg/dL), or Glucose ≥100 mg/dL), or Insulin >20 µmol/L), or Orthopedic disorders, sleep disorders, or gall bladder disease
	3. Obesity (≥95th BMI %ile) or abdominal obesity (≥90th waist circumference %ile)

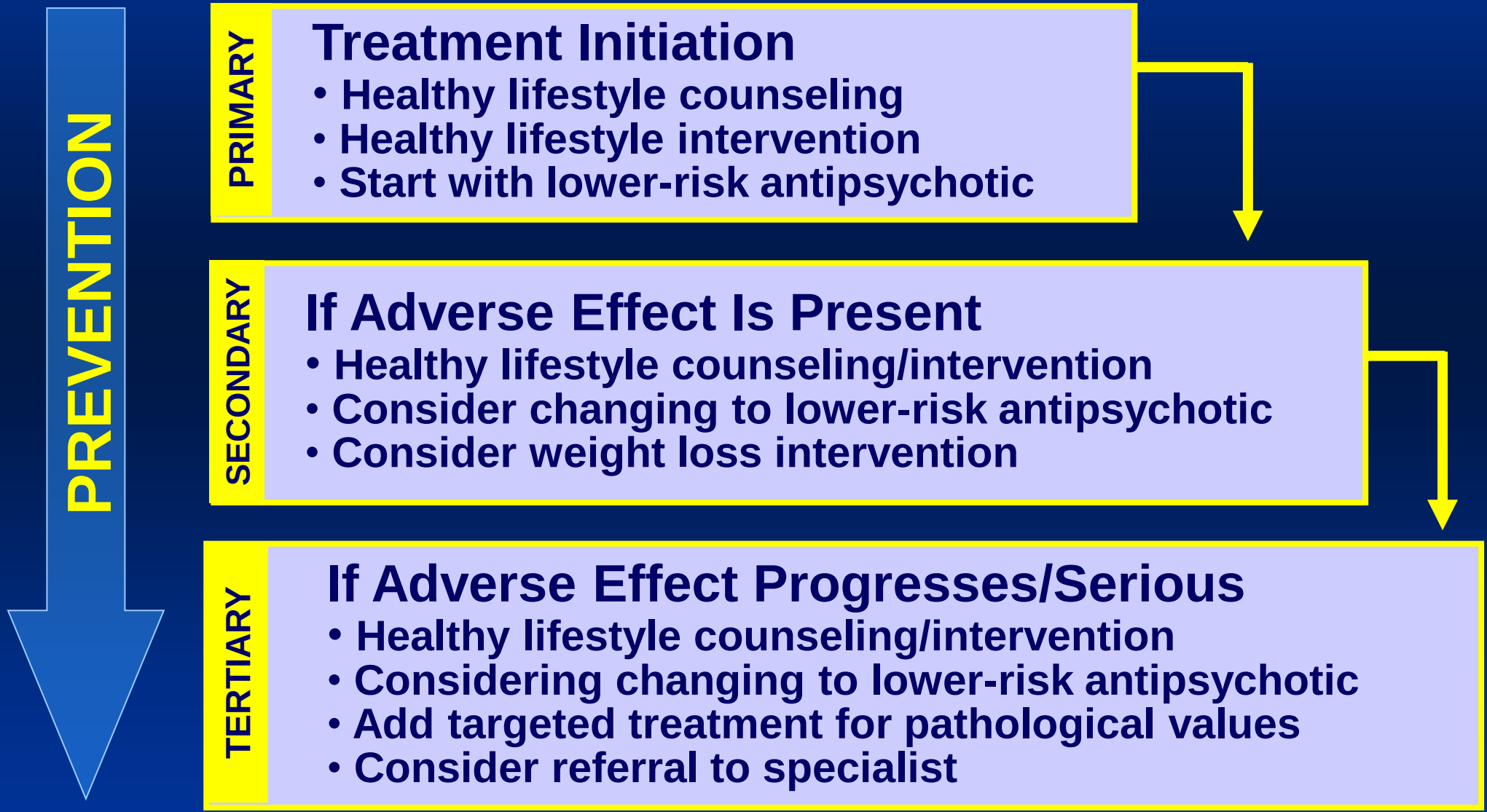
Correll CU, Carlson HE. *J Am Acad Child Adolesc Psychiatry.* 2006;45: 771-791.

Assessment : Metabolic Syndrome

Criteria (≥3 required)	Threshold[1]
1. Obesity	BMI percentile >95th percentile or waist circumference >90th percentile[2]
2. Arterial hypertension	>90th percentile for sex and age[3]
3. Hypertriglyceridemia	≥110 mg/dL
4. Low HDL-Cholesterol	<40 mg/d
5. Hyperglycemia	≥100 mg/dL

1. Cook S et al. Arch Pediatr Adolesc Med 2003;157:821-827.
2. Fourth Report on the Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents. Pediatrics 114:555–576, 2004
3 . Fernandez J et al. J Pediatr 145:439-444, 2004

Medical Risk Management Strategies in Antipsychotic-Treated Patients



Correll CU. CNS Spectr. Vol 12. No 10 (Suppl 17), 2007: 12-20,35.

12-Step Healthy Lifestyle Program

Do's:

- Replace sugar-containing drinks with water
- Eat 4 to < 6 meals, with <2 meals in the evening or night
- Serve small meal portions
- Eat slowly, drink water, take seconds only after delay
- Eat food with a low glycemic index (<55)
- Consume > 25-30 grams of soluble fiber per day
- Snack only when hungry and use fruit or vegetables
- Perform moderate physical activity for > 30-60 min/day

Do not's:

- Skip breakfast
- Consume Fast food >1 per wk
- Consume saturated or processed fat free food
- Watch TV, play computer games ≥ 2 hours/day

Correll and Carlson, J Am Acad Child Adolesc Psychiatry 2006;45: 771-791

Antipsychotic Adverse Effect Management in Children and Adolescents

Adverse Event	Selected Interventions
Sedation/ Somnolence	Wait to see if tolerance develops, ↓ dose (↑ if on quetiapine <300 mg/d); switch to lower-risk drug; add modafinil
Parkinsonism	Slow titration, ↓ dose; switch to lower-risk drug; add anticholinergic, antihistamine, benzodiazepine, etc
Akathisia	Slow titration, ↓ dose; switch to lower-risk drug; add benzodiazepine, beta-blocker, antihistamine, mirtazapine, gapabentin, anticholinergic
Tardive dyskinesia	↓ dose; ↑ dose (masking); replace with nonantipsychotic (if possible); switch to clozapine; add vitamin E

Adapted from: Correll CU. *J Am Acad Child Adolesc Psychiatry.* 2008;47:9-20.

Antipsychotic Adverse Effect Management in Children and Adolescents

Adverse Event	Selected Interventions
Hyper-prolactinemia sexual/ reproductive dysfunction	If asymptomatic: may wait. If symptomatic: ↓ dose; switch to lower-risk drug. If symptomatic despite switch to low-risk drug: MRI; add full (bromocriptine, amantadine) or partial dopamine agonist (aripiprazole); for performance: add bupropion, sildenafil, etc
Weight gain, hyperglycemia, dyslipidemia, hypertension	Switch to lower-risk drug; healthy lifestyle intervention; add weight-loss agent (metformin, orlistat, amantadine, topiramate, bupropion, etc), statin/fibrate, antihyperglycemic, antihypertensive

Adapted from: Correll CU. *J Am Acad Child Adolesc Psychiatry.* 2008;47:9-20.

Summary

- Atypical antipsychotics have proven efficacy in pediatric schizophrenia, bipolar disorder and irritability associated with autistic disorder and DBDs
- Pediatric patients are at great risk for weight gain and metabolic effects
- Ranking order of adverse effects roughly similar to adults with possible exceptions of:
  - RIS more and ? CLZ less relative weight gain
- Although frank diabetes and metabolic syndrome have been rare so far, most studies have been short-term and the marked increase cardiometabolic risk factors in youth treated with antipsychotics is of great concern

Summary cont'd

- Patients and families should be included in a careful risk-benefit assessment when choosing an AP
- Consideration of adverse effects and dietary/life style habits should be part of any AP initiation
- Routine, proactive monitoring of side effects is essential to optimize outcomes
- In case of severe early weight gain or metabolic disturbances, consider switching to a lower risk AP
- Mechanisms and long-term effects of APs on weight, glucose and lipid status and related cardio-metabolic endpoints need to be studied
- Best interventions to minimize/reverse these effects require urgent study

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Question 1

Recent research suggests that this antipsychotic may actually result in a decrease in prolactin levels:

A. Paliperidone
B. Risperidone
C. Quetiapine
D. Olanzapine
E. Aripiprazole

Question 2

For monitoring children and adolescents on antipsychotics, weight, height and BMI should be monitored on:

A. Every visit
B. Every second visit
C. Every 3 months
D. Every 6 months
E. Every 12 months

Question 2

FDA recently advised a labeling change to consider the increased potential for weight gain and hyperlipidemia in adolescents (compared to adults) with this atypical antipsychotic:

A. Quetiapine

B. Olanzapine

C. Risperidone

D. Ziprasidone

E. Aripiprazole

Answers

1) E
2) A
3) B