Tuesday, 12:30 – 2:00, B2

The Use of Psychotropic Medications in Intellectual and Developmental Disabilities: The Good, the Bad and the Costly

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Objectives:

1. Identify effective methods for the practical application of concepts related to improving the delivery of services for persons with developmental disabilities
2. Identify advances in clinical assessment and management of selected healthcare issues related to persons with developmental disabilities

Notes:

The Use of Psychotropic Medications in Intellectual and Developmental Disabilities: The Good, the Bad and the Costly

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Developmental Disabilities Conference
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Professional Information

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Disclosure Statement

- Dr. Calles has no financial relationships related to the topic of this presentation.

Preface

- Compared to child, adolescent and adult psychiatric populations, there has been relatively little psychopharmacologic research conducted in individuals with intellectual and developmental disabilities (IDDs).
- Therefore, some of the information in this presentation has been extrapolated from the general psychiatric literature.

Selected medications (generic & trade names) mentioned in this presentation

- Antipsychotics
  - aripiprazole (Abilify©)
  - clozapine (Clozaril©)
  - olanzapine (Zyprexa©)
  - quetiapine (Seroquel©)
  - risperidone (Risperdal©)
  - ziprasidone (Geodon©)

Selected medications (generic & trade names) mentioned in this presentation

- Antidepressants
  - citalopram (Celexa©)
  - fluoxetine (Prozac©)
  - fluvoxamine (Luvox©)
  - sertraline (Zoloft©)
  - venlafaxine (Effexor©)

Psychotropic Medications in IDDs: Background

Psychotropic Medications in IDDs: Background

- The two most common reasons for use of psychotropic medications in individuals with intellectual and developmental disabilities (IDDs) are to treat psychiatric disorders and/or to try to reduce/eliminate behaviors that are variously described as *challenging, disruptive, aggressive, self-injurious, repetitive,* or otherwise *inappropriate*.

Psychotropic Medications in IDDs: Background

- There has been an ongoing debate as to the extent of overlap between mental health problems and problem behaviors. There have been numerous studies showing that psychiatric morbidity among people with IDDs is associated with higher levels of behavioral problems.
- However, other studies have not found any association between psychiatric morbidity and problem behaviors.
- It needs to be kept in mind that oversimplified, "either-or" conceptualizations do not address the complexities of the systems surrounding all the various factors that impact on a person's mental health and behavior.

Psychotropic Medications in IDDs: Background

- In the U.K., the National Institute for Health and Care Excellence (NICE) recently published (January, 2014) their Quality Standards: Autism (http://www.nice.org.uk/guidance/qs51).
- In Quality statement 6, it's stated that "Drug treatments have been shown to be ineffective in addressing the core features of autism."
- In Quality statement 7, readers are reminded that "The causes of behaviour… can involve physical health conditions, mental health problems and environmental factors…"

Psychotropic Medications in IDDs: Background

- NICE Quality Standards: Autism (cont.):
- In Quality statement 8, it follows that "People with autism and behaviour that challenges are not offered antipsychotic medication for the behaviour unless it is being considered because psychosocial or other interventions are insufficient or cannot be delivered because of the severity of the behaviour."
- In Quality statement 6, it's noted that "in certain circumstances, medication may be appropriate for the short-term treatment of challenging behaviour."

Psychotropic Medications in IDDs: Background

- Emerson, et al (2010), using a nationally representative sample of young Australian children, found that children with limited intellectual functioning make a disproportionate contribution to overall child psychiatric morbidity.
- Implications for public health and child and adolescent mental health services are discussed in the article.

Prevalence and odds ratios of "abnormal" scores on the SDQ* for intellectual status among 6-7-year-old Australian children

	Intellectual disabilities	BD	TD
Percentages			
Total difficulties (%)	24	17	5
Conduct difficulties (%)	24	19	8
Emotional difficulties (%)	13	15	6
Hyperactivity (%)	26	15	8
Peer problems (%)	35	21	11
Pro-social behaviour (%)	14	8	3
Odds ratios			
Total difficulties	5.58***	3.36***	1.00
Conduct difficulties	3.39***	2.29***	1.00
Emotional difficulties	2.23**	2.53***	1.00
Hyperactivity	3.71***	1.98***	1.00
Peer problems	4.38***	2.25***	1.00
Pro-social behaviour	5.33***	2.86***	1.00

ID intellectual disability; *BD* borderline intellectual functioning; *TD* typically developing

* Strengths and Difficulties Questionnaire

** $p < 0.01$

*** $p < 0.001$

Emerson, et al, 2010

Psychotropic Medications in IDDs: Background

- In a study by Rosenberg, et al (2011), the lifetime prevalence of a psychiatric disorder by age 16 in youth with autism spectrum disorders (ASDs) was determined to be 49% in contrast to reported rates for the general population of 37%.

Multivariate logistic regression odds ratios (95% CI) of overall and individual parent-reported lifetime psychiatric comorbidities in ASD (n=2219)

	Any comorbidity	Any anxiety disorder	Any mood disorder (depression and/or bipolar disorder)	Depression	Bipolar disorder	AD/HD or ADD
Female Gender	ns	ns	ns	ns	.5 (.3, .9)*	.8 (.6, 1.0)*
Autism spectrum diagnosis (reference: autistic disorder)						
PDD-NOS	2.1 (1.6, 2.6)	1.9 (1.5, 2.5)	2.8 (2.0, 4.2)	2.3 (1.5, 3.7)	3.6 (2.0, 6.3)	2.1 (1.6, 2.6)
Asperger	2.8 (2.2, 3.5)	2.5 (1.8, 3.3)	3.9 (2.7, 5.7)	3.5 (2.3, 5.1)	2.9 (1.6, 5.1)	2.4 (1.9, 3.0)
SRS *t* score, per 10-point increase	1.3 (1.1, 1.5)	1.3 (1.1, 1.5)	1.4 (1.1, 1.8)	1.4 (1.1, 1.9)	1.4 (1.1, 1.7)	1.2 (1.1, 1.3)
Reported ID	Ns	ns	Ns	.6 (.4, .9)*	ns	ns
History of skill loss[a]	.8 (.6, 1.0)*	ns	.7 (.5, 1.0)*	ns	ns	.7 (.5, .8)

SRS= Social Responsiveness Scale

[a] Moderate to severe loss of communication and/or social skills between ages of 12 and 36 months

* P< .05; all others P< .001

Rosenberg, et al 2011

Psychotropic Medications in IDDs: Background

- Davies & Oliver (2013) statistically analyzed published data regarding the age-related prevalence of aggression and self-injury in persons with IDDs.
- The analysis indicated that the relative risk of self-injury, and to a lesser extent aggression, increased with age until mid-adulthood, with some indication of a curvilinear relationship for self-injury (significantly increasing with age up to about ages 30-40, with notable decrease after the age of 50).

Prevalence of aggression (%/n) by age bands (years) for the eleven studies identified meeting selection criteria

Study	Prevalence of aggression % (n) by age band (years)														
Tavormina *et al.* (1976) n = 52	*2-4* 0 (0)	*4-6* 35 (6)	*8-12* 15 (2)	*12-17* 33 (3)											
Eyman & Call (1977) n = 6,870	*0-12* 28.5 (464)				*13+* 27.5 (1442)										
Ando & Yoshimura (1978) n = 128		*6-9* 11.1 (5)		*11-14* 1.4 (1)											
Jacobson (1982) n = 30,578	*0-21* 8.5 (669)				*22+* 11.3 (2164)										
Harris (1993) n = 901		*2-9* 10.6 (5)	*10-14* 14.9 (10)	*15-19* 20.2 (17)	*20-24* 24.7 (19)	*25-29* 16.5 (22)	*30-34* 11.9 (10)	*35-39* 28.9 (20)	*40-44* 18.6 (13)	*45-49* 21.8 (12)	*50-54* 6 (3)	*55-59* 22.9 (8)	*60-64* 11.8 (4)	*65-69* 16 (4)	*70+* 12 (6)
Rojahn *et al.* (1993) n = 135,102	*0-10* 7.09 (2095)		*11-20* 11.62 (2991)		*21-45* 14.13 (11274)										
Smith *et al.* (1996) n = 2,202					*20-29* 22.45 (183)		*30-39* 21.5 (116)		*40-49* 18.1 (73)		*50-59* 20.45 (48)		*60+* 22.5 (47)		
Cooper (1998) n = 207					*20-64* 6.8 (5)								*65+* 5.2 (7)		
Deb *et al.* (2001) n = 101			*16-29* 31 (11)				*30-45* 21.5 (116)				*46-64* 14.7 (5)				
Crocker *et al.* (2006) n = 3,165			*18-29* 26.8 (194)				*30-39* 24.5 (190)		*40-49* 28.5 (258)		*50-59* 15.1 (72)		*60+* 22.4 (64)		
Tyrer *et al.* (2006) n = 3,062				*19* 24 (57)	*20-29* 16 (105)		*30-39* 17 (122)		*40-49* 13 (82)		*50-59* 9 (38)		*60-69* 9 (23)		*70+* 6 (9)

Davies & Oliver, 2013

Prevalence of self-injury (%/n) by age bands (years) for the ten studies identified meeting selection criteria (cont.)

Study	Prevalence of self-injury % (n) by age band (years)										
Tavormina *et al.* (1976) n = 52	*2-4* 0 (0)	*4-6* 17.6 (3)	*8-12* 30.8 (4)	*12-17* 22.2 (2)							
Eyman & Call (1977) n = 6,870	*0-12* 14.9 (243)		*13+* 15.2 (797)								
Ando & Yoshimura (1978) n = 128		*6-9* 6.7 (3)		*11-14* 4.2 (3)							
Jacobson (1982) n = 30,578	*0-21* 7.7 (551)		*22+* 9.3 (1723)								
Kebbon & Windahl (1986) n = 28,215	*< 1* 0 (0)	*2-11* 4.8 (152)	*12-21* 20.5 (1360)	*22-31* 32.5 (1928)	*32-41* 22.1 (1073)	*42-51* 10.4 (303)	*52-61* 5.5 (131)	*62-71* 2.8 (43)	*72-81* 1.3 (8)	*82+* 0 (0)	
Rojahn *et al.* (1993) n = 135,102	*0-10* 7.1 (2100)		*11-20* 8.4 (2167)	*21-45* 9.05 (7212)							
Smith *et al.* (1996) n = 2,202				*20-29* 21.2 (173)	*30-39* 19.45 (105)	*40-49* 16.1 (65)	*50-59* 9.3 (22)	*60+* 9.2 (19)			
Cooper (1998) n = 207				*20-64* 2.7 (2)				*65+* 3 (4)			
Deb *et al.* (2001) n = 101			*16-29* 20 (7)	*30-45* 35.5 (11)		*46-64* 17.6 (6)					
Crocker *et al.* (2006) n = 3,165			18-29 22 (159)	30-39 28.4 (220)	40-49 26.6 (240)	50-59 20.2 (96)	60+ 19.9 (57)				

Davies & Oliver, 2013

Psychotropic Medications in IDDs: Background

- The atypical antipsychotics (AAs) are commonly prescribed for the management of serious behavioral disturbance in individuals with ASDs and/or IDDs.
- Risperidone (for ages 5-16 years) and aripiprazole (for ages 6-17 years) are the only two FDA-approved medications for irritability (aggression, self-harm, tantrums and/or mood lability) in children and adolescents with autism.

Psychotropic Medications in IDDs: Background

- Coury, et al (2012), found that, in a sample of youth from the Autism Treatment Network, the use of AAs was common in ASDs:
  - 4% of 3- to 5-year-olds;
  - 14% of 6- to 11-year-olds; and
  - 23% of 12- to 17-year-olds…

  were taking atypical antipsychotic medications.

Psychotropic Medications in IDDs: The Good

Psychotropic Medications in IDDs: The Good

- Ching & Pringsheim (2012) concluded that "Evidence from two randomized controlled trials suggests that aripiprazole can be effective in treating some behavioral aspects of ASD in children. After treatment with aripiprazole, children showed less irritability, hyperactivity, and stereotypies (repetitive, purposeless actions)."

Psychotropic Medications in IDDs: The Good

- In the first prospective randomized clinical trial comparing the safety and efficacy of aripiprazole and risperidone (Ghanizadeh, et al, 2013), both lowered Aberrant Behavior Checklist (ABC) scores.
- The safety and efficacy of aripiprazole (mean dose 5.5 mg/day) and risperidone (mean dose 1.12 mg/day) were comparable.

Psychotropic Medications in IDDs: The Good

- In a recent update, Baribeau & Anagnostou (2014) "… suggested that atypical antipsychotic medications ought only to be considered when behavioral interventions have been tried and failed, and when the physical risks associated with disruptive behavior exceed the risk of harm from medication."

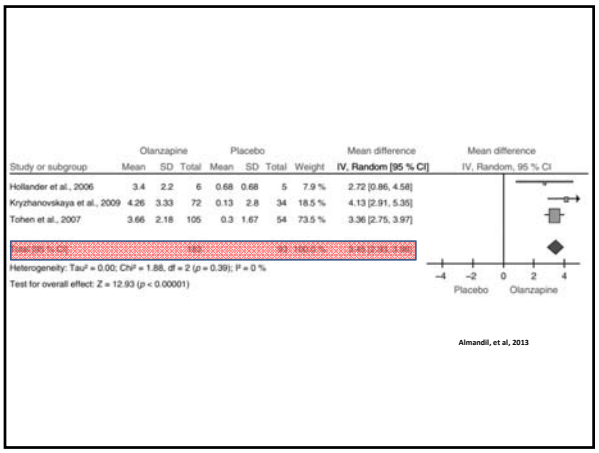
Psychotropic Medications in IDDs: The Bad

Psychotropic Medications in IDDs: The Bad

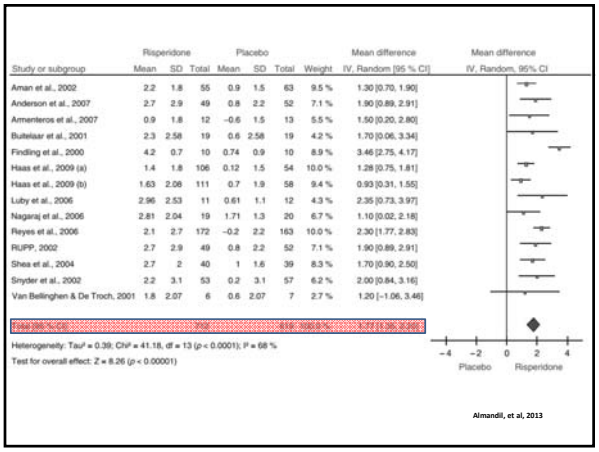
- There are several well-known adverse effects of psychotropic medications. The most common ones that are of especial concern are:
  - Metabolic abnormalities (weight gain, hyperglycemia and/or hyperlipidemia);
  - Hyperprolactinemia;
  - Extrapyramidal symptoms.

Metabolic Abnormalities: Weight Gain

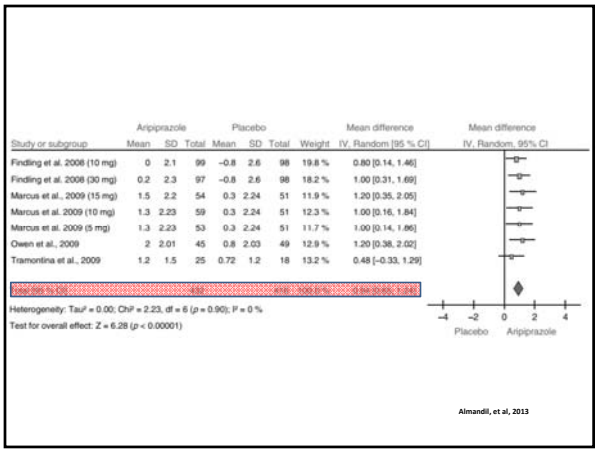
- Almandil, et al (2013), conducted a review and meta-analysis of double-blind, randomized, controlled trials (RCTs) investigating the metabolic adverse effects associated with AA use in children and adolescents, with weight gain as the primary objective.
- Olanzapine, risperidone, and aripiprazole were all associated with statistically significant weight gain. Olanzapine was associated with the most weight gain and aripiprazole the least.



Almandil, et al, 2013



Almandil, et al, 2013



Almandil, et al, 2013

Metabolic Abnormalities: Weight Gain

- An additional concern is that children with IDDs may already be at higher risk for weight gain.
- An Australian study (De, et al, 2008) found that children (ages 2-18 years) with IDDs, vs. those in the general school population, were more likely to be overweight (24% vs. 17%) or obese (15% vs. 6%).
- Differences were statistically significant for overweight (p=.05) and obesity (p=.0003).

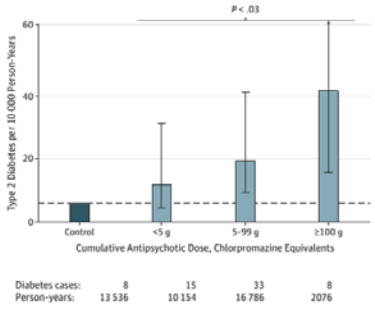
Metabolic Abnormalities: Hyperglycemia

- Bobo, et al (2013), conducted a retrospective cohort study of the Tennessee Medicaid program.
- The objective was to compare the risk of type 2 diabetes in children and youth (6 to 24 years of age) for recent initiators of antipsychotic drugs vs. controls who had recently initiated another psychotropic medication.

Metabolic Abnormalities: Hyperglycemia

- Bobo, et al (cont.): In the cohort of children 6 to 17 years of age, antipsychotic users had more than a 3-fold increased risk of type 2 diabetes (HR= 3.14 [95% CI = 1.50-6.56]).
- The risk increased significantly with increasing cumulative dose (P< .03).
- The risk was increased for use restricted to AAs (HR= 2.89 [95% CI = 1.64-5.10]) or to risperidone (HR= 2.20 [95% CI = 1.14-4.26]).

Adjusted Annual Incidence of Type 2 Diabetes Mellitus Among Children and Youth 6 to 17 Years of Age, According to Cumulative Antipsychotic Dose



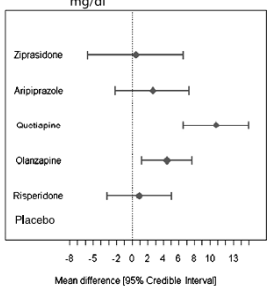
Bobo, et al, 2013

Metabolic Abnormalities: Hyperlipidemia

- In a meta-analysis of short-term adverse effects of AAs in children and adolescents, Cohen, et al (2012), found that:
  - Quetiapine and olanzapine significantly increased cholesterol rates compared with placebo;
  - Olanzapine and quetiapine also significantly increased triglyceride levels compared with placebo.

10 studies
27 arms - 1784 patients cholesterol gain; compared to placebo

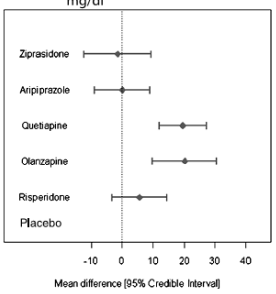
Arm (N)	Patient (N)
3	212
3	243
5	371
4	259
4	187
8	512



Cohen, et al, 2012

10 studies
27 arms - 1655 patients triglycerides gain: compared to placebo
mg/dl

Arm (N)	Patient (N)
3	212
3	243
6	388
3	152
4	187
8	473



Cohen, et al, 2012

Hyperprolactinemia

- Prolactin is a hormone produced in the anterior pituitary. Its most prominent actions are the stimulation of mammary gland development and milk production.
- Its secretion is stimulated by serotonin.
- Most antidepressants and newer antipsychotics have serotonergic activity. Therefore, use of those agents can increase secretion of prolactin (mildly for the antidepressants).

Hyperprolactinemia

- Prolactin secretion is inhibited by dopamine and gamma-aminobutyric acid (GABA).
- Antipsychotics (except clozapine and aripiprazole) increase secretion of prolactin by blocking the effects of dopamine on the pituitary gland.
- Benzodiazepines (e.g. clonazepam) enhance the effect of GABA.

Effect of Psychotropic Medications on Prolactin: Severity and Mechanism

Drug name	Drug class	Effect on PRL	Mechanism
Clozapine	Atypical AP	↔	$D_1/D_2/D_4$, histamine, and 5-HT_2 R antagonism[2]
Butyrophenone/haloperidol	Typical AP	↑↑/↑↑↑	D_2R antagonism[2]
Phenothiazine/fluphenazine/thioridazine	Typical AP	↑↑/↑↑↑	D_2R antagonism[2]
Thioxanthines/flupenthixol	Typical AP	↑↑ (reversible)	D_1/D_2, serotonin, and H_1 R antagonism[2]
Risperidone	Atypical AP	↑↑↑	D_{2H}-HT_2 R antagonism[2]
Amisulpride	Atypical AP	↑↑↑	D_2/D_{3H}-HT_7 R antagonism
Olanzapine	Atypical AP	↑	D_{2H}-HT_2 R antagonism[2]
Quetiapine	Atypical AP	↑ (transient)	D_{2H}-HT_{2A} R antagonism[2]
Aripiprazole	Atypical AP	↔/↓	D_{2H}-HT_{1A} partial agonist and 5-HT_{2A}R antagonism[2]
Ziprasidone	Atypical AP	↑ (transient)	5-HT_{1A}
Amitriptyline/desipramine	TCAs	↑	
Imipramine	TCAs	↑	
MAOIs		↑/↑↑	Increases serotonin, dopamine, and norepinephrine
Fluoxetine	SSRI	↑	Serotonin reuptake inhibitor
Sertraline	SSRI	↑	Serotonin reuptake inhibitor
Citalopram	SSRI	↑	Serotonin reuptake inhibitor
Venlafaxine	SNRI	↑	Serotonin/norepinephrine reuptake inhibitor

AP = antipsychotic; D = dopamine; H = histamine; 5-HT = 5-hydroxytryptamine; MAOIs = monoamine oxidase inhibitor; PRL = prolactin; R = receptor; SNRIs = serotonin/norepinephrine reuptake inhibitors; SSRIs = selective serotonin reuptake inhibitors; TCAs = tricyclic antidepressants; ↑ = mild; ↑↑ = moderate, ↑↑↑, strong; ↓ = inhibition; ↔ = no affect.
(Lined-out medications are not available in the U.S.)

Ajmal, et al, 2014

Hyperprolactinemia

- Elevated levels of prolactin, especially if prolonged, can cause some physical problems:

Common Signs and Symptoms of Hyperprolactinemia

Men	Women	Both
Gynecomastia	Hirsutism	Decreased libido
Erectile dysfunction	Acne	Infertility
	Vaginal dryness	Galactorrhea
	Irregular menses (oligomenorrhea and amenorrhea)	Osteopenia
		Osteoporosis
		Fracture

Ajmal, et al, 2014

Hyperprolactinemia

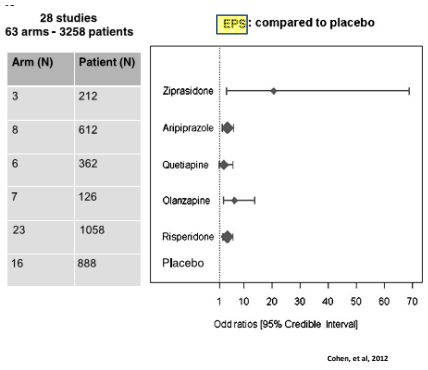
- Elevated prolactin levels can cause decreased estrogen levels in females, lower testosterone levels in males.
- Lower sex hormone levels can cause decreased bone mineral density (BMD).
- Decreased BMD can lead to an increased risk of fractures. This can be exacerbated by certain lifestyle factors, such as smoking, physical inactivity, and poor nutrition (especially lower calcium and vitamin D intake.)

Extrapyramidal Symptoms (EPS)

- Extrapyramidal symptoms (EPS) are neurologic adverse effects of antipsychotic medications.
- All antipsychotic medications, including AAs, can cause EPS.
- The four possible, major EPS patterns seen are:
  - acute dystonia;
  - acute akathisia;
  - parkinsonism;
  - tardive dyskinesia.

Extrapyramidal Symptoms (EPS)

- In the previously cited Cohen article, odds ratios (OR) of developing EPS were calculated for the AAs (clozapine was not included in the study).
- All AAs (except quetiapine) significantly increased the risk of EPS compared with placebo.



AA Adverse Effects: Summary

Summary of SGAs' Secondary Effects Reported in Controlled Short-Term Studies

	Aripiprazole	Clozapine	Olanzapine	Quetiapine	Risperidone	Ziprasidone
↗ Weight	+	++++	++++	+++	++	+/−
↗ Glucose	+/−	?	+	+/−	++	0
↗ Cholesterol	0	?	+++	++++	0	0
↗ Triglycerides	0	+++*	++++	++++	+/−	0
Hyperprolactinemia	0	?	+++	+/−	++++	++
Sedation	++	++++	++	+	++	++
EPS	+	0?	++	+/−	+	++++

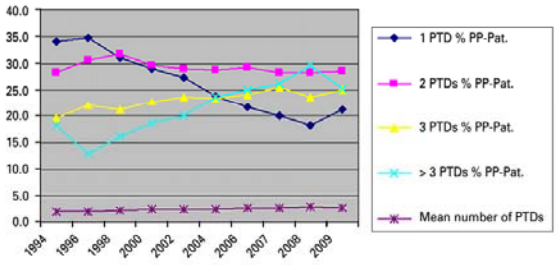
*Based on the calculation of ORs for the percentage of patients with a significant increase in triglycerides. This analysis included 11 studies, 26 arms, and 1668 patients, including 30 treated with clozapine (data not shown).
? indicates unknown.

Cohen, et al, 2012

Psychotropic Polypharmacy

- According to the National Library of Medicine-Medical Subject Headings, polypharmacy is defined as "the use of multiple drugs administered to the same patient, most commonly seen in elderly patients. It includes also the administration of excessive medication."
- In recent years, polypharmacy has become more common, even in countries in which psychotropic prescribing has traditionally been conservative.

Prevalence of co-medication/polypharmacy with psychotropic drugs (PTD) in inpatients treated with psychopharmaca (PP) in Germany



Möller, et al, 2013

Psychotropic Polypharmacy

- Rates of polypharmacy differ, depending on how it's defined.
- The National Association of State Mental Health Program Directors, in 2001, issued its "Technical Report on Psychiatric Polypharmacy," in which it delineated five types of polypharmacy:
  1) *Same-Class Polypharmacy*: The use of more than one medication from the same medication class (e.g. two SSRIs, such as fluoxetine plus paroxetine).

Psychotropic Polypharmacy

- NASMHPD types of polypharmacy (cont.):
  2) *Multi-Class Polypharmacy*: The use of full therapeutic doses of more than one medication from different medication classes for the same symptom cluster (e.g. the use of lithium along with an atypical antipsychotic, such as fluoxetine plus olanzapine for treatment of mania).
  3) *Adjunctive Polypharmacy*: The use of one medication to treat the side effects or secondary symptoms of another medication from a different medication class (e.g. the use of trazodone, along with bupropion, for insomnia).

Psychotropic Polypharmacy

- NASMHPD types of polypharmacy (cont.):
  4) *Augmentation*: The use of one medication, at a lower than normal dose, along with another medication from a different medication class, at its full therapeutic dose, for the same symptom cluster (e.g. the addition of a low dose of haloperidol in a patient with a partial response to risperidone) or the addition of a medication that would not be used alone for the same symptom cluster (e.g. the addition of lithium in a person with major depression who is currently taking an antidepressant).

Psychotropic Polypharmacy

- NASMHPD types of polypharmacy (cont.):
  5) *Total Polypharmacy*: The total count of medications used in a patient, or total drug load. Consideration of total polypharmacy should include all prescription medications, over-the-counter medications, alternative medical therapies, and illicit pharmacological agents (e.g., marijuana).

Psychotropic Polypharmacy in IDDs

- In a 1999 study, Martin, et al, examined prescribing patterns in the treatment of higher-functioning pervasive developmental disorders (HFPDDs).
- Results showed that:
  - 55% were currently on a psychotropic drug;
  - 22.9% were on 2 psychotropic drugs;
  - 4.6 % were on 3 psychotropic drugs;
  - 1.8 % were on 4 psychotropic drugs;
  - 29.3 % were on ≥ 2 psychotropic drugs.

Psychotropic Polypharmacy in IDDs

- Martin, et al (cont.):
- Antidepressants were the most commonly used agents (32.1 %), followed by stimulants (20.2%) and neuroleptics (antipsychotics) (16.5%).
- The most common drugs, per category, were:
  - SSRIs: fluoxetine, sertraline and fluvoxamine;
  - Stimulants: methylphenidate and dextroamphetamine;
  - AAs: risperidone and olanzapine.

Subjects Taking Psychotropic Medications on Date of Survey (N = 109)

Drug Type	No.	%
Any antidepressant	35	32.1
SSRI	29	26.6
Stimulant	22	20.2
Any neuroleptic	18	16.5
Atypical neuroleptic	14	12.8
Mood stabilizer	10	9.2
Anxiolytic	7	6.4
Antihypertensive	7	6.4
Tricyclic antidepressant	7	6.4
Traditional neuroleptic	5	4.6
Any psychotropic (current)	60	55.0
One drug	28	25.7
Two drugs	25	22.9
Three drugs	5	4.6
Four drugs	2	1.8
Any psychotropic (lifetime)	75	68.8

Note: Separate percentages will not necessarily add to the tabulated totals, as some subjects took more than one agent simultaneously. SSRI = selective serotonin reuptake inhibitor.

Martin, et al, 1999

Psychotropic Polypharmacy in IDDs

- Spencer, et al (2013), examined rates and predictors of psychotropic use and multiclass polypharmacy (i.e., concurrent medication fills across ≥2 classes for at least 30 days) among commercially insured children with ASDs.
- Among 33,565 children with ASD, 35% had evidence of psychotropic polypharmacy (≥2 classes), and 15% used medications from ≥3 classes concurrently.

Psychotropic Polypharmacy in IDDs

- Spencer, et al (cont.): Among children with polypharmacy, the median length of polypharmacy was 346 days.
- Older children, those who had a psychiatrist visit, and those with evidence of co-occurring conditions (seizures, ADHD, anxiety, bipolar disorder, or depression) had higher odds of psychotropic use and/or polypharmacy.

Psychotropic Polypharmacy in IDDs

- Spencer, et al (cont.): Common combinations of classes were:
  - antidepressants and ADHD medications;
  - antipsychotics and ADHD medications;
  - antipsychotics and antidepressants; and,
  - all 3 (antipsychotics, antidepressants, and ADHD medications).

Psychotropic Polypharmacy in IDDs

- Freudenreich, et al (2012), have suggested that there are four broad etiological categories that can contribute to psychiatric polypharmacy (see the next slide):

Differential Diagnosis of Psychiatric Polypharmacy by Four Etiological Factors That Can Lead to Polypharmacy

Disease Factors ("Biology"): What Kind of Disease?

- Refractory disease
- Suboptimal treatment
- Side-effect management
- Misdiagnoses
- Missed diagnoses

Patient Factors ("Psychology I"): What Kind of Patient?

- Insufficient adherence
- Personality style
- Consumer-choice paradigm
- Illness behavior

Physician Factors ("Psychology II"): What Kind of Physician?

- Pharmacological hedonism or Calvinism
- Early or late adopter
- Symptom-based prescribing
- Self-image as powerful healer
- Fear of patient dissatisfaction

Systems ("Sociology"): What Kind of Society?

- Market-based system with consumer choice
- Fragmented health care system
- Outside pressures (other stakeholders)

Freudenreich, et al, 2012

Psychotropic Medications in IDDs: The Costly

Psychotropic Medications in IDDs: The Costly (Background)

- There are approximately 10.2 million people who are eligible for both Medicaid and Medicare and individuals with disabilities under the age of 65 comprise about 41% (4.1 million) of that number.
- About 7% of duals are individuals with IDDs (People who are dually eligible for Medicare and Medicaid frequently are referred to as “dual eligibles” or “duals.”)

Psychotropic Medications in IDDs: The Costly (Background)

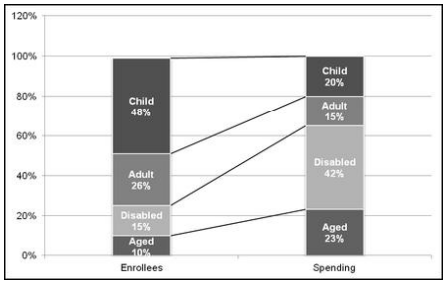
- Duals represent 21% of Medicare beneficiaries and account for 36% of Medicare costs.
- Similarly, dual eligibles constitute 15% of Medicaid enrollees, but account for 39% of the program’s costs.
- Medicaid is the largest source of financing for disabilities services in the United States.

Source: The Arc (http://www.thearc.org)

Psychotropic Medications in IDDs: The Costly

- During FY 2008, combined federal-state MCD expenditures totaled $339 billion.
- Although people under age 65 enrolled on the basis of disability made up 15% of all MCD beneficiaries that year, they accounted for 42% of program expenditures, or $142 billion.
- In contrast, children and adults under 65 years of age without disabilities accounted for approximately 75% of MCD enrollees but only about one-third of program outlays.

MCD Enrollment and Spending by Eligibility Group, FY 2008



Psychotropic Medications in IDDs: The Costly

- Source: “Prescription Drug Costs for Children with Special Health Care Needs.” In: *Quality Care for Special Kids: Profiles of Children with Chronic Conditions and Disabilities*. Mathematica Policy Research, Inc., 2006.
- This information was based on the most comprehensive data available (at the time)on a large sample of commercially insured children with special needs (chronic illnesses and/or disabilities).

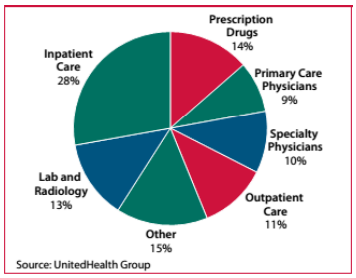
Trends in Pharmacy Costs

	1999	2000	2001
Total costs in millions	$7.4	$9.9	$13.4
PMPM* cost	$28	$34	$44
% Change from 1999	—	+21.4	+57.1
No. prescriptions per 1,000 children	9,291	9,097	10,043
% Change from 1999	—	-2.1	+8.1

Source: UnitedHealth Group

* Per-member, per-month

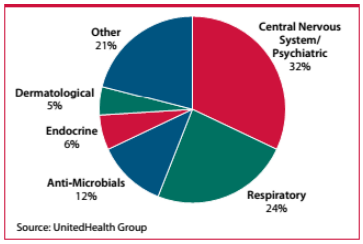
Distribution of PMPM* Costs Across Services, 2001



Source: UnitedHealth Group

* Per-member, per-month

PMPM Costs (As a Percentage of Total Costs) For Selected Drug Categories, 2001



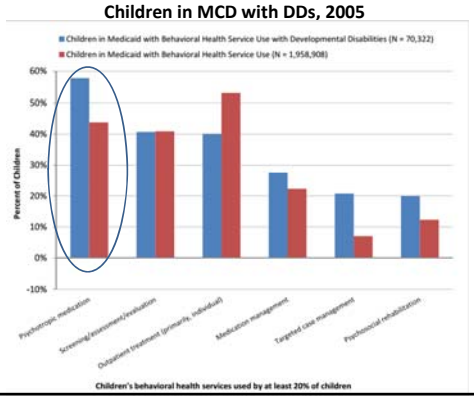
Source: UnitedHealth Group

* Per-member, per-month

Psychotropic Medications in IDDs: The Costly

- Source: *Faces of Medicaid: Examining Children's Behavioral Health Service Use and Expenditures*. Center for Health Care Strategies, Inc., December, 2013.

Most Frequently Used Behavioral Health Services among Children in MCD with DDs, 2005



Use of Psychotropic Medication among Children in MCD, by Psychiatric Diagnosis, 2005

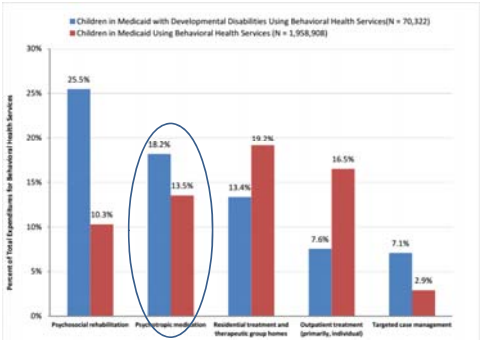
	Psychiatric Diagnosis						
Medication Category	DD	ADHD	Mood	Anxiety	COD	Psychosis	Other
Antipsychotics	66.5%	35.4%	61.8%	44.9%	54.6%	81.6%	55.7%
Anticonvulsants/mood stabilizers	14.6%	9.2%	23.5%	12.1%	16.7%	21.9%	14.2%
Lithium	4.0%	2.2%	8.1%	3.7%	4.5%	8.7%	5.7%
Anti-depressants	43.0%	31.2%	63.1%	66.8%	44.4%	52.2%	53.7%
ADHD medications	58.1%	90.5%	48.4%	49.8%	64.2%	43.4%	57.0%
Anxiety medications	8.7%	2.2%	5.0%	7.3%	4.0%	6.7%	6.0%

Total Expenditures and Proportion of Behavioral Health Service Use among Children in MCD with DDs, by Service Type, 2005

Service Type	Total Expenditures	% Total Expenditures	% Users*
Psychosocial rehabilitation	$135,385,863	25.5%	20.0%
Psychotropic medication**	$96,474,188	18.2%	57.8%
Residential treatment/therapeutic group homes	$70,881,067	13.4%	3.6%
Outpatient treatment (primarily individual)	$40,141,716	7.6%	40.1%
Targeted case management	$37,599,096	7.1%	20.8%
Inpatient psychiatric treatment	$25,731,851	4.8%	3.4%
Substance use outpatient	$19,927,020	3.8%	10.5%
Case management	$18,383,326	3.5%	13.8%
Partial hospitalization/day treatment	$14,715,066	2.8%	7.4%
Behavior management consultation and training	$14,652,258	2.8%	3.8%
Wraparound	$10,679,784	2.0%	3.4%
Therapeutic foster care	$7,882,551	1.5%	0.6%
Medication management	$6,810,598	1.3%	27.6%
Screening/assessment/evaluation	$5,790,097	1.1%	40.7%
Family therapy/family education and training	$5,626,323	1.1%	17.8%
Home-based (e.g. , in-home services)	$4,462,291	0.8%	0.5%

*N = 70,322. Percentages do not sum to 100% as a child may use multiple service types.
** $96.4M reflects psychotropic medication expenditures for children who used behavioral health services.

Behavioral Health Services Accounting for the Largest Proportion of Total Expenditures for MCD Children with DDs Using Behavioral Health Services, 2005*



*Includes children with ≥ 1 claims for a behavioral health service with/without concomitant psychotropic medication use; does not include children with psychotropic medication claims and no other behavioral health service claims.

Expenditures for Psychotropic Medication among Children in MCD with DDs, by Type of Health Care Used, 2005

Type of Health Care	Children Receiving Psychotropic Medication (N)	Mean Psychotropic Medication Expenditure	Total Psychotropic Medication Expenditure
Behavioral Health Services	40,630	$2,374	$96,474,188
Indeterminate Services *	9,058	$1,808	$16,379,862
Physical Health Services Only	6,621	$1,933	$12,795,125
TOTAL	**56,309**	**$2,230**	**$125,579,175**

*Cannot determine whether service was behavioral or physical health.

Expenditures for Psychotropic Medication Use among Children in MCD, by Psychiatric Diagnosis, 2005

Medication Category	Psychiatric Diagnosis							
	DD	ADHD	Mood	Anxiety	COD	Psychosis	Other	None
Antipsychotic	$62,236,406	$285,047,522	$253,634,092	$106,002,239	$143,965,560	$68,518,457	$6,352,041	$38,670,755
Anticonvulsant/ Mood Stabilizers	$7,945,193	$34,808,726	$38,065,122	$12,873,287	$19,181,211	$6,962,950	$713,887	$8,048,276
Lithium	$258,351	$1,592,347	$2,702,399	$707,138	$893,733	$462,028	$37,110	$166,344
Anti-depressant	$6,283,006	$45,334,646	$45,423,228	$30,249,988	$19,138,913	$6,207,425	$1,292,057	$11,770,673
ADHD/ stimulant	$17,204,517	$311,658,357	$77,344,900	$47,751,161	$61,213,726	$9,412,724	$2,391,490	$25,858,505
Anxiety	$287,694	$641,370	$630,280	$529,497	$324,937	$167,255	$25,711	$381,667
Total Expenditures	$94,215,167	$679,082,968	$417,800,021	$198,113,310	$244,718,080	$91,730,839	$10,712,296	$84,896,220

Mean Behavioral Health Expenditures per User among Children in MCD with DDs Who Used Behavioral Health Services, 2005

Service Type	Children Using Behavioral Health Services (N = 1,959,908)	Children with Developmental Disabilities (N = 70,322)
Residential treatment/therapeutic group homes	$21,671	$27,976
Therapeutic foster care	$11,219	$19,855
Home-based (e.g., in-home services)	$17,191	$12,605
Inpatient psychiatric treatment	$6,652	$10,759
Psychosocial rehabilitation	$3,416	$9,627
Therapeutic behavioral support	$7,821	$8,108
Behavior management consultation and training	$1,535	$5,471
Wraparound	$3,467	$4,419
Supported housing	$2,315	$3,933
Partial hospitalization/day treatment	$5,746	$2,813
Substance use outpatient	$3,625	$2,712
Targeted case management	$1,683	$2,577
Psychotropic medication	$1,267	$2,319
Activity therapies	$1,658	$2,228
Respite	$649	$1,938
Case management	$1,233	$1,890

Conclusion

- Emotional and behavioral disorders are common in individuals with IDDs.
- Psychotropic medications are widely used in those with IDDs, despite limited research in this population.
- Individuals with IDDs, especially the young and the elderly, are at higher risk for experiencing adverse effects from psychotropic medications.

Conclusion (cont.)

- Whenever possible, non-pharmacologic interventions should be tried first.
- The best outcomes can be expected when psychotropic medications are used to treat *specific* conditions (e.g. depression) vs. non-specific conditions (e.g. aggression).
- Medications should be started at a low dose, and titrated slowly, aiming for the lowest effective dose.
- Polypharmacy should be avoided, if possible.

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