

# ADHD, PERFORMANCE ENHANCEMENT, OR COSMETIC NEUROLOGY: CLINICAL AND ETHICAL ISSUES

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## **SPEAKER DISCLOSURES**

- ✓ Consultant: Supernus
- √ Genomind
- ✓ Myriad Neuroscience
- ✓ Medici

These relationships have been mitigated.



### **OBJECTIVES**

- Review history of stimulant treatment and ADHD
- Discuss diagnostic process and dilemmas leading to misdiagnosis, underdiagnosis, and overdiagnosis
- 3. Review ethical Issues
- 4. Highlight impairment and therapeutic options



# **CHARLES BRADLEY (1937)**

- "...a spectacular change in behavior...remarkably improved school performance...a large proportion became subdued without losing interest in their surroundings."
- Bradley, C. & Bowen, E. (1937).
   The behavior of children receiving benzedrine. <u>American Journal of Psychiatry</u>, 94, 577-585
- Bradley, C. (1950). Benzedrine and dexedrine in the treatment of children's behavior disorders.
   Pediatrics, 5, 24-37



"Birth of stimulant medications"



# HISTORY OF MEDICINE TRIVIA: WHAT IS THIS WOMAN'S FIRST NAME AND WHAT DOES SHE HAVE TO DO WITH ADHD?

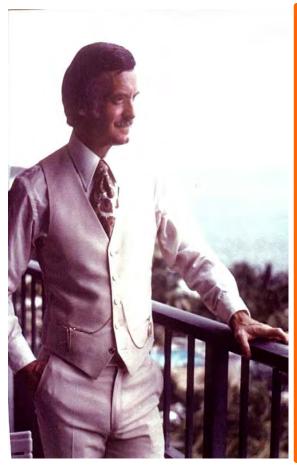
- Meet Rita, as in "Ritalin"
- In 1944 her husband, Leandro Panizzon of Swiss company CIBA (now Novartis) invented methylphenidate to help Rita improve her athletic performance

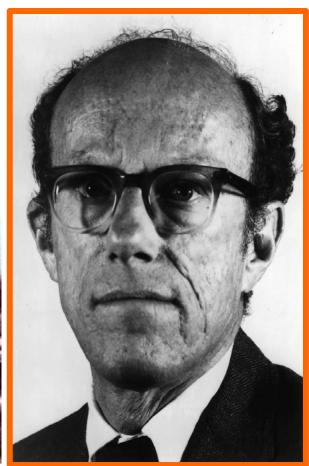




# FIRST CONTROLLED METHYLPHENIDATE TRIALS (1963)

"The decrease in impulsivity...is compatible with the hypothesis that methylphenidate enhances the action of inhibitory controlling systems... However, a second mechanism-increased alerting--is probably active here..."

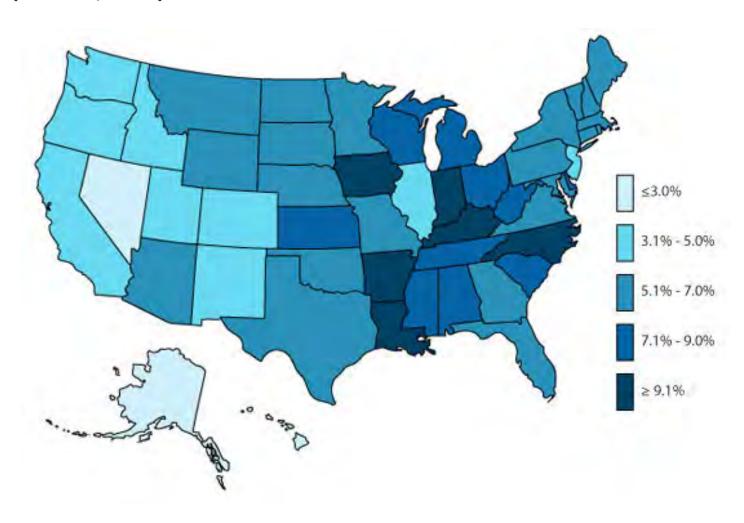






# PERCENT OF YOUTH AGED 4-17 YEARS CURRENTLY TAKING MEDICATION FOR ADHD

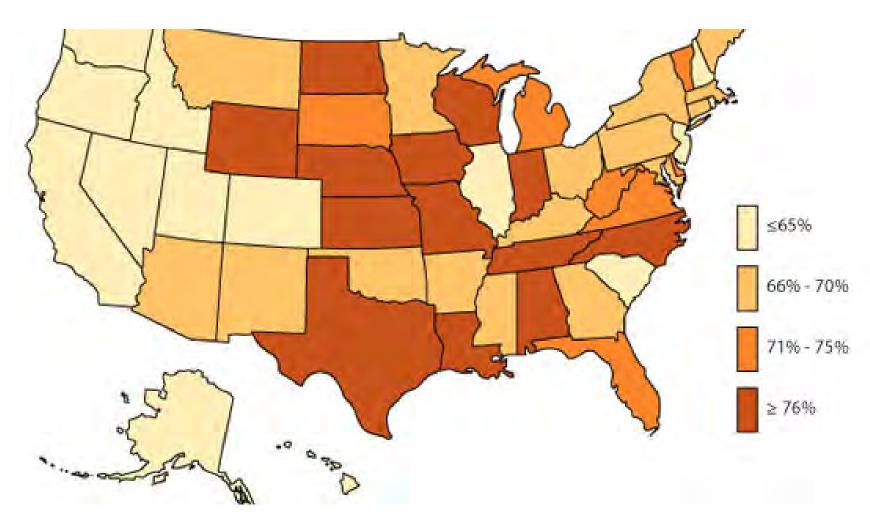
BY STATE: NATIONAL SURVEY OF CHILDREN'S HEALTH 2011 (VISSER, CDC)



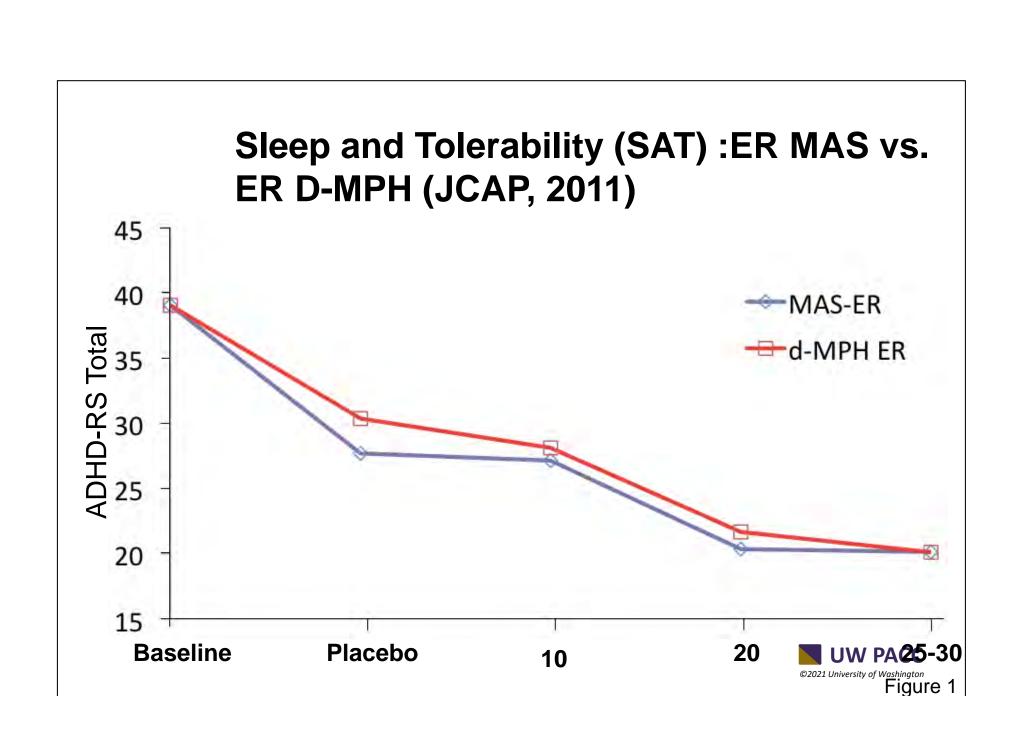


## PERCENT OF YOUTH AGED 4-17 CURRENTLY WITH ADHD RECEIVING MEDICATION TREATMENT BY STATE: NATIONAL SURVEY OF CHILDREN'S HEALTH

# 2011 (VISSER ET AL)





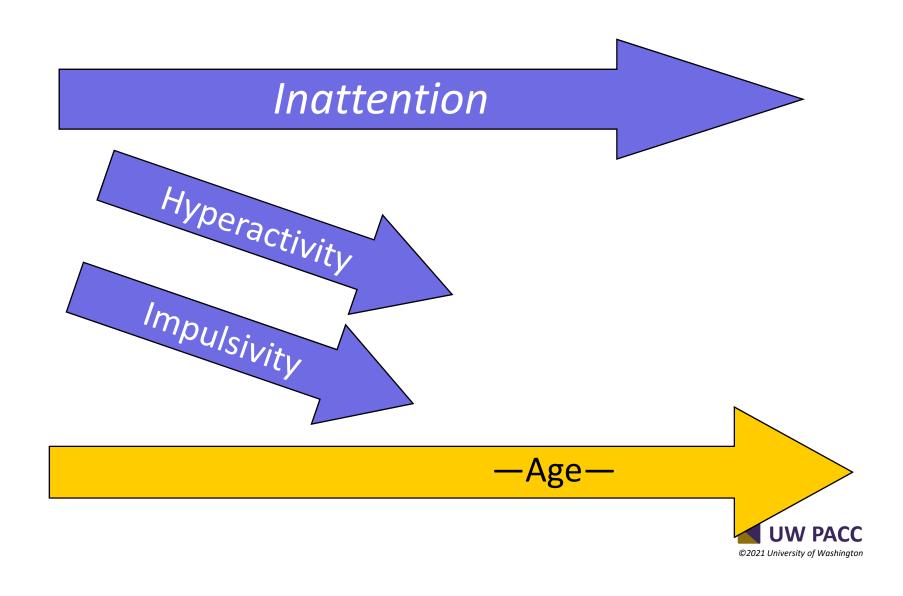


# TREATMENT BEGINS WITH AN EVALUATION AND A DIAGNOSIS...

- Current Symptoms (DSM V)
  - Screening does not = diagnosis
- Impairment (e.g., academic/vocational, social adaptive and executive functioning)
- Mimics
  - Psychiatric
  - Biological
  - Social
- Co-Morbidities and Associated Problems (Psychiatric, Developmental, Medical)
- Strengths (Social, Cognitive, Familial)
- Diagnostic Process: A Personalized Approach (Nayakkara., Hans, & Stein MA. Assessment of ADHD. L Adler, T. Spencer, T. Wilens: ADHD in Children, Adolescents and Adults. Cambridge University Press (2014)



## **ADHD: COURSE OF THE DISORDER**



# MEDICAL MIMICS (PEARL, WEISS, AND STEIN, 2002 & 2014)

- Sensory impairments (hearing, vision, motor)
- Sleep deprivation, poor nutrition (breakfast)
- Medication effects (e.g., steroids, anticonvulsants)
- Chronic and acute illness (hypothyroidism, seizures)
- Genetic syndromes (Fragile X, Williams)
- Environmental toxins (Pb, FAE)
- Post-traumatic encephalopathy
- Constipation/encopresis



# LACK OF AWARENESS OF SOCIAL MIMIC OR EXACERBATING FACTORS— MOST COMPLEX

Poor fit between temperament, expectations
Beverly Hills, Glencoe, Mercer Island, Potomac ADHD
Marital dissatisfaction/confict
ivialital dissatisfaction/connect
Montessori schools, home schooling,
Widitlessoft schools, notifie schooling,
Chaotic environments
COVID-19



## **COMMON DIAGNOSTIC PITFALLS**

#### Truncated evaluation-e.g. "positive Vanderbilt"

- Confusion of symptoms versus diagnosis
- Rater Bias -False positive and False negative
  - Parents, fathers, teachers
  - Self report bias

#### Over-extensive evaluations

- no correction for multiple comparisons
- Interviews with prompts
- Neuropsychological evals

#### Un-validated etiological assumptions

- Is it ADHD in the presence of trauma history or ETOH exposure not ADHD?
- TBI

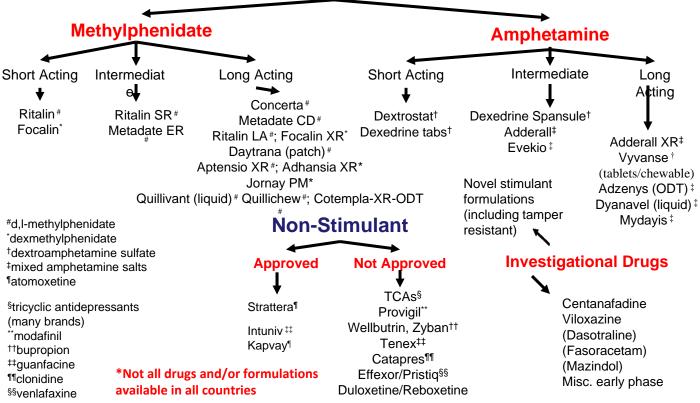
#### Failure to re-evaluate over time



# ADHD MEDICATIONS WORLDWIDE\* (APPROVED AND INVESTIGATIONAL)



#### **Stimulants**





## Comparative efficacy and tolerability of medications for attention-deficit hyperactivity disorder in children, adolescents, and adults: a systematic review and network meta-analysis

Samuele Cortese, Nicoletta Adamo, Cinzia Del Giovane, Christina Mohr-Jensen, Adrian J Hayes, Sara Carucci, Lauren Z Atkinson, Luca Tessari, Tobias Banaschewski, David Coghill, Chris Hollis, Emily Simonoff, Alessandro Zuddas, Corrado Barbui, Marianna Purqato, Hans-Christoph Steinhausen, Farhad Shokraneh, Jun Xia, Andrea Cipriani

#### Summary

Background The benefits and safety of medications for attention-deficit hyperactivity disorder (ADHD) remain Lan controversial, and guidelines are inconsistent on which medications are preferred across different age groups. Put We aimed to estimate the comparative efficacy and tolerability of oral medications for ADHD in children, adolescents, and adults.

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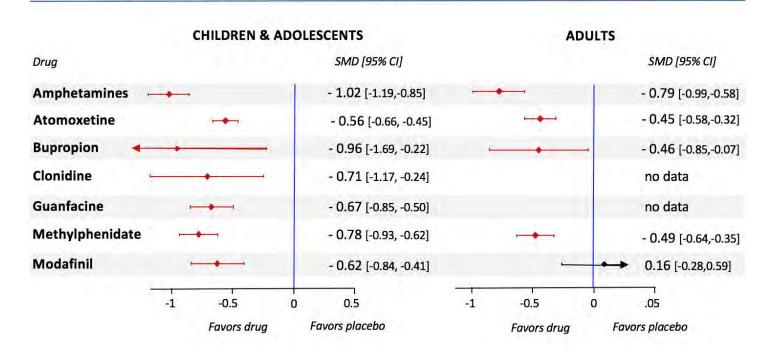
522

Cortese et al., Lancet Psychiatry 2018



#### **DRUGS VS PLACEBO- 12 WEEKS**

#### Mean change in ADHD symptoms - rated by clinicians





## QUESTIONS

- How do you decide to treat when the impairment is mild or unclear?
- Should we, and what are the costs/risks of using meds when other treatments are not available
- Should we continue treating those who are doing well and may not need medication?
- Should we treat beyond well?
- Should we be treating subclinical ADHD or performance enhancement only for those who ask?
- Is treating some patients fair to others who do not have access to resources, including evaluation, ADHD medications, or accommodations?
- Is the risk-benefit ratio for performance enhancement different than for mild ADHD?



## **EMILY**

- Dr. and Mrs. Jones want you to see their 10-year old daughter
  - ♦ Does well in school and is in a gifted and talented program
  - + Has been taking an intermediate duration stimulant since third grade
  - After school, she does competitive gymnastics 4 days/week, 2 days/week, performance declining in regional competitions
- Her parents note that the she resists practicing her piano and does not excel in all her studies
  - ♦ They would like to increase her medication
  - ♦ ADHD ratings are positive from parents, but not from teachers
- You meet with her, she looks tired and she starts describing how she is disappointing her parents and starts to cry



# . WHAT WOULD YOU RECOMMEND?

- Continue to follow and monitor for impairment (e.g self esteem)
- Treat with stimulant medication
- Do something else (504 plan, tutoring, career counseling, psychotherapy,coaching)
- Complimentary or Alternative treatment with some efficacy
  - Supplement
  - Exercise
  - Caffeine
- Other



## **JARED**

- 17-year-old boy with 3.9 GPA at a suburban public school
- taking MAS since 8<sup>th</sup> grade
- 31 on ACT, not good enough for Ivy League
- wants a 34
- already gets test accommodations



#### WHAT WOULD YOU RECOMMEND?.

- Continue to follow and monitor for impairment (e.g self esteem)
- Treat with stimulant medication
- Do something else (504 plan, tutoring, career counseling, psychotherapy,coaching)
- Complimentary or Alternative treatment with some efficacy
  - Supplement
  - Exercise
  - Caffeine



#### **SOPHIE-14 YEAR OLD FRESHMAN**

- 50 mg. LDX, 10 mg MAS at 4
- Always an A student and talented soccer player
- 8<sup>th</sup> grade, grades declined, demoted in soccer, family arguments, COVID restrictions, negative mood symptoms
- Parents "walking on eggshells"



#### WHAT WOULD YOU RECOMMEND?.

- Continue to follow and monitor for impairment (e.g self esteem)
- Treat with stimulant medication
- Do something else (504 plan, tutoring, career counseling, psychotherapy,coaching)
- Complimentary or Alternative treatment with some efficacy
  - Supplement
  - Exercise
  - Caffeine



# NO DX

Richard,-27 year old recent law school graduate studying for bar and working

"I know I don't meet diagnostic criteria for ADHD, but I sometimes have trouble concentrating and staying organized, and it would help me to have some Ritalin on hand for days when I really need to be on top of things at work."



#### WHAT WOULD YOU RECOMMEND?.

- Continue to follow and monitor for impairment (e.g self esteem)
- Treat with stimulant medication
- Do something else (504 plan, tutoring, career counseling, psychotherapy,coaching)
- Complimentary or Alternative treatment with some efficacy
  - Supplement
  - Exercise
  - Caffeine



## **JOHN**

- 17-year-old at public high school
- has 1.7 GPA
- Says can't pay attention in class or get hw done, has 3 inattentive symptoms on parent Vanderbilt Scale, 1 on teacher
- would like to go to college
  - school not concerned, will not do evaluation
  - no insurance coverage for evaluation
- single parent family with limited finances
- pediatrician calls and wonders about trying a stimulant



# **QUESTIONS**

 How do you decide to treat when the impairment is mild or unclear?



# THERAPEUTIC DILEMMAS INCREASE WHEN DX CRITERIA ARE NOT MET, IMPAIRMENT IS UNCLEAR, OR LIMITED ACCESS TO TREATMENT.



# CENTRAL ROLE OF IMPAIRMENT IN TREATMENT

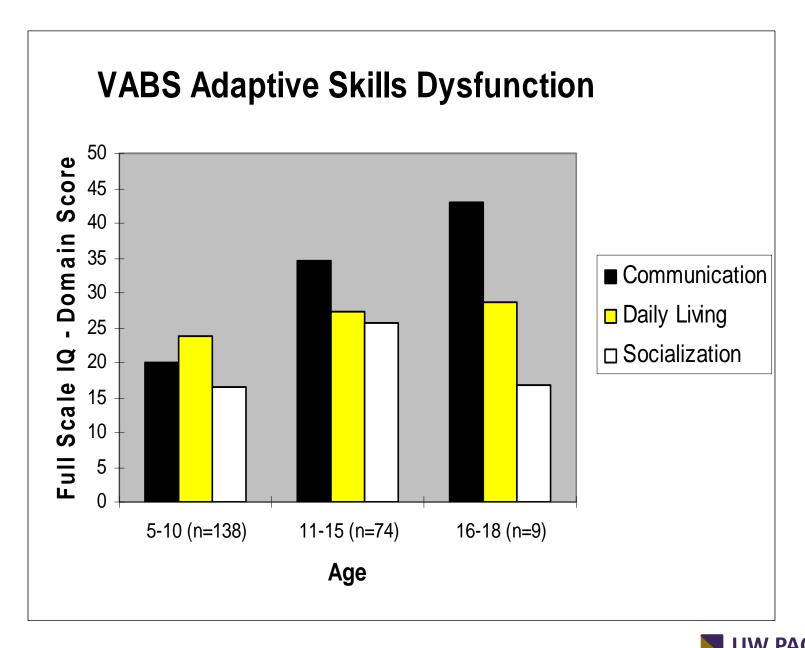
- Impairment--that is, problems in daily life functioning that result from symptoms--rather than symptoms themselves-is what should be targeted in treatment
- Therefore, assessment of impairment in daily life functioning is a fundamental aspect of initial evaluation
- Ongoing assessment of impairment in critical domains is necessary to determine the impact of and need for modifications in treatment
- Normalization or minimization of impairment in daily life functioning is the goal of treatment



#### **COMMON MEASURES OF IMPAIRMENT**

- Academic Underachievement
  - GPA
  - Achievement tests (WIAT, WJ, WRAT, KTEA)
  - Discrepancy between achievement and ability
- Executive Functioning
  - Neuropsychological tests
    - Poor ecological and diagnostic validity
  - Scales
    - ADHD symptoms embedded
- Adaptive Functioning (Vineland, ABAS)





Stein, M. A., Szumowski, E., Blondis, T. A., & Roizen, N. J. (1995). Adaptive skills dysfunction in ADD and ADHD, of Washington children. Journal of child psychology and psychiatry, and allied disciplines, 36(4), 663-670.

### **MEASURES OF FUNCTIONAL IMPAIRMENT IN**

**ADHD** (SASSER, SCHOENFELDER, STEIN, CNS DRUGS 2017)

ADHD-FX  Parent or teacher  Parent, 19 for peer, family, overall  Barkley Functional Impairment Scale (BFIS)  Impairment Rating Scale (IRS)  Parent or teacher  Parent or teacher  To overall, home-school, community-leisure  Parent or parent, 5 for parents, family, selfesteem,  Parent or teacher  Academic, peer, family, overall  No data available English  Purchase  Purchase  Public	Measure	Rater	# of items	Subscales	Sensitive to medication / behavioral treatment?	Languages	Availabil ity
Impairment Scale (BFIS)  Impairment Rating Parent or 7 for Academic, Yes English Public Scale (IRS)  Scale (IRS)  Parent or 7 for Academic, Yes English Public parent, 5 peer, siblings, for parents, teacher family, self-esteem.	ADHD-FX		parent, 19 for	peer, family,	No data available	_	•
Scale (IRS)  teacher parent, 5 peer, siblings, for parents, teacher family, self- esteem.	Impairment Scale	Parent	15	home-school, community-	No data available	English	Purchase
overall	•		parent, 5 for	peer, siblings, parents, family, self- esteem,	Yes	English	

#### WEISS FUNCTIONAL IMPAIRMENT RATING SCALE – PARENT REPORT (WFIRS-P)

Your name:	Relationship to child:
Circle the number for the rating that hest describes how your child's emotiona	alorhebayiouralnrohlemsbaye affectedeachiteminthelastmonth

		Never or not at all	Sometimes or somewhat	Often or much	Very often or very much	n/a
A	FAMILY					
15	Having problems with brothers & sisters	0	0	0	0	
2	Causing problems between parents	0	0	0	0	
3	Takes time away from family members' work or activities	0	0	0	0	
4	Causing fighting in the family	0	0	0	0	
5	Isolating the family from friends and social activities	0	0	0	0	
6	Makes it hard for the family to have fun together	0	0	0	0	
7	Makes parenting difficult	0	0	0	0	
8	Makes it hard to give fair attention to all family members	0	0	0	0	
9	Provokes others to hit or scream at him/her	0	0	0	0	
10	Costs the family more money	0	0	0	0	
В	SCHOOL			237 02		7h
	Learning					
1	Makes it difficult to keep up with schoolwork	0	0	0	0	
2	Needs extra help at school	0	0	0	0	
3	Needs tutoring	0	0	0	0	
4	Receives grades that are not as good as his/her ability	0	0	0	0	
	Behaviour			254.50		
1	Causes problems for the teacher in the classroom	0	0	0	0	
2	Receives "time-out" or removal from the classroom	0	0	0	0	
3	Having problems in the school yard	0	0	0	0	
4	Receives detentions (during or after school)	0	0	0	0	
5	Suspended or expelled from school	0	0	0	0	
6	Misses classes or is late for school	0	0	0	0	
C	UFE SKILLS					
1	Excessive use of TV, computer, or video games	0	0	0	0	
2	Keeping clean, brushing teeth, brushing hair, bathing, etc.	0	0	0	0	
3	Problems getting ready for school	0	0	0	0	

		Never or not at all	Sometimes or somewhat	Often or much	Very often or very much	n/a
4	Problems getting ready for bed	0	0	0	0	
5	Problems with eating (picky eater, junk food)	0	0	0	0	
6	Problems with sleeping	0	0	0	0	
7	Gets hurt or injured	0	0	0	0	
8	Avoids exercise	0	0	0	0	
9	Needs more medical care	0	0	0	0	
10	Has trouble taking medication, getting needles or visiting the doctor/dentist	0	0	0	O	
D	CHILD'S SELF-CONCEPT					
Ý.	My child feels bad about himself/herself	0	0	0	0	- I
2	My child does not have enough fun	0	0	0	0	
3	My child is not happy with his/her life	0	0	0	0	
E	SOCIAL ACTIVITIES					
1	Being teased or bullied by other children	0	0	0	0	
2	Teases or bullies other children	0	0	0	0	
3	Problems getting along with other children	0	0	0	0	
4	Problems participating in after-school activities (sports, music, clubs)	0	0	0	0	
5	Problems making new friends	0	0	0	0	
6	Problems keeping friends	0	0	0	0	
7	Difficulty with parties (not invited, avoids them, misbehaves)	0	0	0	0	
F	RISKY ACTIVITIES		-			
1	Easily led by other children (peer pressure)	0	0	0	0	
2	Breaking or damaging things	0	0	0	0	
3	Doing things that are illegal	0	0	0	0	
4	Being involved with the police	0	0	0	O	
5	Smoking cigarettes	O	Ö	O	Ö	
6	Taking illegal drugs	0	0	0	0	
7	Doing dangerous things	O	Ö	0	Ö	
8	Causes injury to others	0	0	Ö	0	
9	Says mean or inappropriate things	0	0	0	0	
10	Sexually inappropriate behaviour	0	0	0	O	「同

#### Number of Items Scored '2' or '3'

А	Family		0	0	10
	Learning	0	0	10	
В	School	Behavior	0	0	10
С	Life skills	5	0	0	10
D	Child's s	elf-concept	0	0	10
E	Social ac	tivities	0	0	10
F	Risky act	ivities	0	0	10
		TOTAL	0	0	10

#### Total Score

A	Family		0	10
	School	Learning	0	10
В	School	Behavior	0	10
C	Life skill	S	0	10
D	Child's s	elf-concept	0	10
E	Social ac	tivities	0	10
F	Risky ac	tivities	0	10
		TOTAL	0	10

#### Mean Score

J	А	Family		0.00
١		Learning	0.00	
	В	School	Behavior	0.00
	С	Life skill	s	0.00
	D	Child's s	elf-concept	0.00
	Е	Social ac	ctivities	0.00
	F	Risky ac	tivities	0.00
l			MEAN*	0.00
	F	Risky ac		

\*Calculated from 0 answered questions.

This scale is copyrighted by Margaret Danielle Weiss, MD PhD, at the University of British Columbia. The scale can be used by clinicians and researchers free of charge and can be posted on the Internet or replicated as needed. Please contact Dr. Weiss at margaret.weiss@icloud.com if you wish to post the scale on the Internet, use it in research or plan to create a translation.





#### **RESEARCH GAPS**

How to sequence and combine treatments across the life span?

Who decides targets when there is disagreement

• parents, teachers, child, spouse?

Efficacy of Alternative/adjunctive treatments

Environmental interventions (structure, schools, after schools, monitoring)

How and when to discontinue medications if symptoms and impairment are minimal: Is it effective treatment, learning/development, maturation?



# DIAGNOSTIC PRIORITIZATION IN PHARMACOTHERAPY OF ADHD AND COMORBIDITY

Alcohol and substance abuse

**Mood disorders** 

Bipolar and MDD

**Anxiety disorders** 

Obsessive-compulsive disorder, generalized anxiety disorder, panic

**ADHD** 

Order of treatment also considers the severity of the concurrent disorders

Goodman D. Treatment and assessment of ADHD in adults. In: Biederman J, ed. *ADHD Across the Life Span: From Research to Clinical Practice—An Evidence-Based Understanding*. Hasbrouck Heights, NJ: Veritas Institute for Medical Education, Inc.2005.



### **SUMMARY AND NEXT STEPS**

- Research on impairment as a criteria for treatment
- Treatment should target impairment
- Development of impairment norms
- Guidelines for weighing impact of accommodations combined with Rx
- Safety and efficacy for subclinical, mild, and moderate ADHD
- Study of non-pharmacological alternatives (exercise, CAM)



#### **NEW DISORDERS**

#### **HEALTH LIBRARY**

#### SLEEP DISORDERS: WHEN TO SEEK HELP

- Overview
- Test Details
- •Results and Follow-Up
- Additional Details
- •Resources

#### **HEALTH & WELLNESS TIPS**

Fitness, health and wellness tips sent to you weekly

August 3, 2021 / Sleep

#### There's New Hope for People With Idiopathic Hypersomnia

#### First approved drug may soon be available to treat this rare sleep disorder

Though <u>narcolepsy</u> is fairly well-studied and well understood by medical professionals, there's far less data available on its close cousin, idiopathic hypersomnia.

<u>Classified as a rare disorder</u> by the National Institutes of Health, idiopathic hypersomnia (IH) may actually be more common than doctors previously realized — and a new medication could offer desperately needed wakefulness to those who live with this debilitating disorder.

Sleep specialist Nancy Foldvary-Schaefer, DO, MS, is an investigator in medical trials of lower-sodium oxybate, a new medication undergoing review by the U.S. Food and Drug Administration (FDA) to become the first approved treatment for IH. She talks about idiopathic hypersomnia, including why it's so understudied, and what this new medication may be able to do for people with IH.

#### What is idiopathic hypersomnia?

There's being sleepy, and then there's having idiopathic hypersomnia. IH is characterized by chronic excessive daytime sleepiness (known as EDS) that interferes with normal daily activities, such as work and hobbies

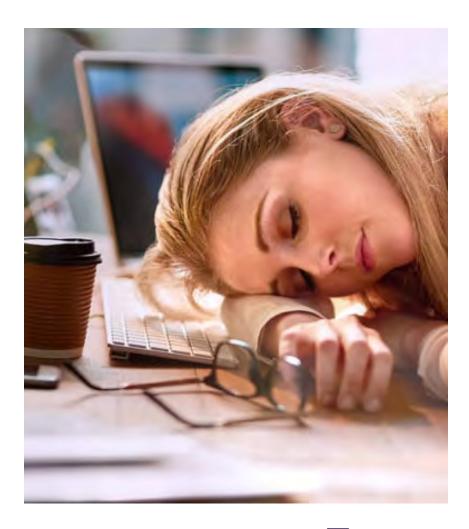
"People with IH have an irresistible need to sleep for long periods of time," Dr. Foldvary-Schaefer explains, "but their sleep is not refreshing."

#### Other symptoms include:

- •Regularly sleeping nine hours or more over a period of 24-hour periods, yet feeling unrefreshed upon waking. (Some people with IH do sleep less.)
- •Extreme difficulty awakening from sleep, sometimes known as sleep drunkenness.
- Non-refreshing daytime napping.
- •Uncontrollable desire to go back to sleep.
- •Brain fog that may impact memory, attention and concentration.
- Headaches

If you have IH, the overwhelming need to sleep may be incapacitating.

"People sometimes avoid social situations just to avoid falling asleep at inappropriate times which can be incredibly isolating," Dr. Foldvary-Schaefer says. "There can also be limitations around driving and work — the struggles really go on and on."





# ETHICAL ISSUES: FAIRNESS AND SAFETY (JOHN LANTOS)

- Fairness is a matter of convention.
- We judge fairness or unfairness based upon an agreement about the rules.
- The rules must be constantly examined.
- New developments will challenge conventional wisdom and may lead to new rules.
- Lack of safety data in non-clinical populations
- Worries are more about fairness and naturalness than about safety
- The academic world is inherently unfair. Rich kids have better schools, teachers, homes, technology.



# **THANK YOU**



