







# ADHD Dx, Rx & MISINFORMATION

### CHOOSING WISELY IN PAEDIATRICS COMMUNITY OF PRACTICE WEBINAR

February 13th, 2024 1 PM-2 PM ET Format: Zoom

### Mark Feldman MD FRCPC

Professor, University of Toronto, (Paediatrics) Director, Continuing Education & Community Paediatrics, Staff, SickKids (Toronto), Unity Health (SJHC), & Point in Time (Haliburton)

# Learner Objectives

- Discern SCREENING / TESTING that should NOT be done to diagnose ADHD nor help to decide about suitability of meds
- 2. Describe consequences of over (and under) diagnosis of ADHD
- 3. List *unproven therapies* that should *NOT* replace evidence-based treatment
- 4. Describe true risks & benefits of evidence-based Rx for ADHD



"The Number of Diagnoses Soared Amid a 20-Year Drug Marketing Campaign"



### **Disclosure – Conflict of Interest Statement**

• No conflicts of interest / no financial relationship with industry

# Is ADHD really a problem?

### More likely to be injured

Pediatrics 1998 102(6):1415-142 & Osteoporosis International 2016, 27 (7): 2223-2227

### More likely to try drugs and to become dependent

Am J Addict. 1998 Spring;7(2):156-63 & AJP in Advance (doi: 10.1176/appi.ajp.**2017**.16060686)

Obesity

Curr Psychiatry Rep (2017)19:4 & J.of Child Psychology & Psychiatry, & Allied Disciplines 2017, 58(6):711-718

- School Failure
- Job Failure
- Early pregnancy / Sexually Transmitted Infections
   J Am Acad Child Adolesc Psychiatry 2006 Feb;45(2):192-202.
- Social Problems
- Divorce
- Arrests / Incarceration (jail)
  - □ J Clin Psychiatry 2006 Apr;67(4):524-40.
- More likely to smoke cigarettes and drink alcohol in pregnancy
  - BIOL PSYCHIATRY 2009;66:722–727 & J Child Psychol Psychiatry. 2009 Sep;50(9):1073-83. Epub 2009 Feb 27.
- More likely to be involved in a motor vehicle accident
  - JAMA Psychiatry. 2014 Mar;71(3):319-25. doi: 10.1001/jamapsychiatry.2013.4174.
- More likely to die young (increased risk of MVA, Suicide, Overdose, Poisonings)
  - Lancet 2015 May 30, 385 (9983): 2190-6 & BMJ 2014;348:g3769 doi: 10.1136/bmj.g3769

# What can we do about it?

Short Term <u>RCT's</u> (Randomized Controlled Trials) with Methylphenidate:

- Improved handwriting
  - Lerer et al 1977
- Improved MOTHER-CHILD RELATIONSHIP
  - Barkley et al. 1979
- Improved TEACHER-PUPIL RELATIONSHIP
  - Whalen et al. 1981
- Improved MATH AND READING
  - Firestone et al. 1981
- Improved PEER RELATIONSHIPS
  - Cunningham et al.1985
- Improved BEHAVIOUR
  - Cunningham et al. 1985
- Let's talk about more recent evidence on Rx outcomes

## What does Stimulant Rx of ADHD lead to?

- Reduced likelihood of injuries
- Reduced likelihood of drug dependency
- Reduced likelihood of Obesity
- Reduced likelihood of School Failure
- Reduced likelihood of Early pregnancy / Sexually Transmitted Infections
- Reduced likelihood of Relationship problems
- Reduced likelihood of Arrests / Incarceration (jail)
- Reduced likelihood of smoking cigarettes & drinking alcohol in pregnancy
- Reduced likelihood of being involved in a motor vehicle accident
- Reduced likelihood of dying young (via MVA, Suicide, Overdose, Poisonings)

### Examples of old-school evidence to support stimulant Rx

Children with ADHD > greater risk of fractures

# Children Rx'd with stimulants < fracture risk</li>

- BMC Pediatr. 2021 Aug 19;21(1):354.
- Acta Orthop Belg. 2021 Mar;87(1):159-166.
- Arch Osteoporos. 2021 Jun 2;16(1):81.
- J Orthop Res. 2018 Dec;36(12):3328-3333.
- Child Care Health Dev. 2018 Nov;44(6):871-878.

### Problem with this type of research

### **Confounders?**

 Maybe families that take medication are different than families that choose not to – the difference might account for the # risk and medication is simply a marker of that difference

# Rx, Driving & ADHD

# Prospective Studies

- Driving *skills* demonstrably improved with Rx in RCTs
  - Pediatrics. 2006
     Sep;118(3):e704-10. Cox DJ,
     Merkel RL, Moore M,
     Thorndike F, Muller C,
     Kovatchev B.
- DURING MEDICATED HOURS!!!!!!

#### **Original Investigation**

### Serious Transport Accidents in Adults With Attention-Deficit/Hyperactivity Disorder and the Effect of Medication A Population-Based Study

Zheng Chang, PhD; Paul Lichtenstein, PhD; Brian M. D'Onofrio, PhD; Arvid Sjölander, PhD, Henrik Larsson, PhD

**IMPORTANCE** Studies have shown that attention-deficit/myperactivity disorder (ADHD) is associated with transport accidents, but the magnitude of the association remains unclear. Most important, it is also unclear whether ADHD medication reduces this risk.

Scale document up

**OBJECTIVES** To estimate the association between ADHD and the risk of serious transport accidents and to explore the extent to which ADHD medication influences this risk among patients with ADHD.

**DESIGN, SETTING, AND PARTICIPANTS** In total, 17 408 patients with a diagnosis of ADHD were observed from January 1, 2006, through December 31, 2009, for serious transport accidents documented in Swedish national registers. The association between ADHD and accidents was estimated with Cox proportional hazards regression. To study the effect of ADHD medication, we used stratified Cox regression to compare the risk of accidents during the medication period with the risk during the nonmedication period within the same patients.

MAIN OUTCOMES AND MEASURES Serious transport accident, identified as an emergency hospital visit or death due to transport accident.

**RESULTS** Compared with individuals without ADHD, male patients with ADHD (adjusted

#### Supplemental con jamapsychiatry.com

 CME Quiz at jamanetworkcme.
 CME Questions patients

#### JAMA Psychiatry | Original Investigation

### Association Between Medication Use for Attention-Deficit/ Hyperactivity Disorder and Risk of Motor Vehicle Crashes

Invited Commentary

Supplemental content

Zheng Chang, PhD, MSc: Patrick D, Quinn, PhD; Kwan Hur, PhD; Robert D. Gibbons, PhD; Arvid Sjolander, PhD; Henrik Larsson, PhD; Brian M. D'Onofrio, PhD

**IMPORTANCE** Motor vehicle crashes (MVCs) are a major public health problem. Research has demonstrated that individuals with attention-deficit/hyperactivity disorder (ADHD) are more likely to experience MVCs, but the effect of ADHD medication treatment on the risk of MVCs remains unclear.

**OBJECTIVE** To explore associations between ADHD medication use and risk of MVCs in a large cohort of patients with ADHD.

DESIGN, SETTING, AND PARTICIPANTS For this study, a US national cohort of patients with



#### **ORIGINAL ARTICLE**

### Medication for Attention Deficit– Hyperactivity Disorder and Criminality

Paul Lichtenstein, Ph.D., Linda Halldner, M.D., Ph.D., Johan Zetterqvist, M.Ed., Arvid Sjölander, Ph.D., Eva Serlachius, M.D., Ph.D., Seena Fazel, M.B., Ch.B., M.D., Niklas Långström, M.D., Ph.D., and Henrik Larsson, M.D., Ph.D.

ABSTRACT

#### BACKGROUND

al Epide-..H., J.Z., oscience ckholm: Attention deficit-hyperactivity disorder (ADHD) is a common disorder that has been associated with criminal behavior in some studies. Pharmacologic treatment is available for ADHD and may reduce the risk of criminality.

### **ADHD Medication and Substance-Related Problems**

Patrick D. Quinn, Ph.D., Zheng Chang, Ph.D., Kwan Hur, Ph.D., Robert D. Gibbons, Ph.D., Benjamin B. Lahey, Ph.D., Martin E. Rickert, Ph.D., Arvid Sjölander, Ph.D., Paul Lichtenstein, Ph.D., Henrik Larsson, Ph.D., Brian M. D'Onofrio, Ph.D.

**Objective:** Substance use disorders are major contributors to excess mortality among individuals with attention deficit hyperactivity disorder (ADHD), yet associations between pharmacological ADHD treatment and substance-related problems remain unclear. This study investigated concurrent and long-term associations between ADHD medication treatment and substance-related events.

**Method:** The authors analyzed 2005–2014 commercial health care claims from 2,993,887 (47.2% female) adolescent and adult ADHD patients. Within-individual analyses compared the risk of substance-related events (i.e., emergency department visits related to substance use disorders) during months in which patients received prescribed stimulant medication or atomoxetine relative to the risk during months in which they did not.

**Results:** In adjusted within-individual comparisons, relative to periods in which patients did not receive ADHD medication, male patients had 35% lower odds of concurrent

substance-related events when receiving medication (odds ratio=0.65, 95% CI=0.64–0.67), and female patients had 31% lower odds of concurrent substance-related events (odds ratio=0.69, 95% CI=0.67–0.71). Moreover, male patients had 19% lower odds of substance-related events 2 years after medication periods (odds ratio=0.81, 95% CI=0.78–0.85), and female patients had 14% lower odds of substance-related events 2 years after medication periods (odds ratio=0.86, 95% CI= 0.82–0.91). Sensitivity analyses supported most findings but were less consistent for long-term associations among women.

**Conclusions:** These results provide evidence that receiving ADHD medication is unlikely to be associated with greater risk of substance-related problems in adolescence or adulthood. Rather, medication was associated with lower concurrent risk of substance-related events and, at least among men, lower long-term risk of future substance-related events.

Am J Psychiatry 2017; 174:877–885; doi: 10.1176/appi.ajp.2017.16060686

# BMJ



BMJ 2014;348:g3769 doi: 10.1136/bmj.g3769 (Published 18 June 2014)

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### RESEARCH

# Drug treatment for attention-deficit/hyperactivity disorder and suicidal behaviour: register based study

COPEN ACCESS

Qi Chen *PhD student*<sup>1</sup>, Arvid Sjölander *associate professor*<sup>1</sup>, Bo Runeson *professor*<sup>2</sup>, Brian M D'Onofrio *associate professor*<sup>3</sup>, Paul Lichtenstein *professor*<sup>1</sup>, Henrik Larsson *associate professor*<sup>1</sup>

<sup>1</sup>Department of Medical Epidemiology and Biostatistics, Karolinska Institute, Box 281, 17177 Stockholm, Sweden; <sup>2</sup>Department of Clinical Neuroscience, Karolinska Institute, Stockholm, Sweden; <sup>3</sup>Department of Psychological and Brain Sciences, Indiana University, Bloomington, IN, USA

Research

JAMA Psychiatry | Original Investigation

### Association Between Medication Use and Performance on Higher Education Entrance Tests in Individuals With Attention-Deficit/Hyperactivity Disorder

Yi Lu, PhD; Arvid Sjölander, PhD; Martin Cederlöf, PhD; Brian M. D'Onofrio, PhD; Catarina Almqvist, PhD; Henrik Larsson, PhD; Paul Lichtenstein, PhD

# Is stimulant medication for the treatment of ADHD really that effective? Face Validity?

"This doctor was our last hope after we tried behaviour courses, naturopathic supplements, dye-free and gluten-free diets, etc. etc. I did not want to try medication but can't deny the huge improvement from day 1. There has been steady improvement from then on and I can't believe how my son is handling (himself) socially, emotionally and academically. If you had told me three years ago the successes my son has had I would not have believed you. Thank you Dr Feldman (and his nurse Susan is also awesome)."



### The New York Times

By <u>ALAN SCHWARZ</u> DECEMBER 14, 2013

"Few dispute that classic A.D.H.D., historically estimated to affect 5 percent of children, is a legitimate disability that impedes success at school, work and personal life. Medication often assuages the severe impulsiveness and inability to concentrate, allowing a person's underlying drive and intelligence to emerge...But even some of the field's longtime advocates say the zeal to find and treat every A.D.H.D. child has led to too many people with scant symptoms receiving the diagnosis and medication."

### **ORIGINAL ARTICLE**

# ADHD Drugs and Serious Cardiovascular Events in Children and Young Adults

William O. Cooper, M.D., M.P.H., Laurel A. Habel, Ph.D.,
Colin M. Sox, M.D., K. Arnold Chan, M.D., Sc.D., Patrick G. Arbogast, Ph.D.,
T. Craig Cheetham, Pharm.D., Katherine T. Murray, M.D.,
Virginia P. Quinn, Ph.D., M.P.H., C. Michael Stein, M.B., Ch.B.,
S. Todd Callahan, M.D., M.P.H., Bruce H. Fireman, M.A.,
Frank A. Fish, M.D., Howard S. Kirshner, M.D., Anne O'Duffy, M.D.,
Frederick A. Connell, M.D., M.P.H., and Wayne A. Ray, Ph.D.

This article (10.1056/NEJMoa1110212) was published on November 1, 2011, at NEJM .org.

N Engl J Med 2011. Copyright © 2011 Massachusetts Medical Society. **Conclusions** This large study showed:

NO evidence that current use of an ADHD drug was associated with an increased risk of serious cardiovascular events

Canadian Paediatric Society recommends routine blood pressure monitoring but does NOT recommend baseline EKG JAMA Psychiatry | Original Investigation

### Attention-Deficit/Hyperactivity Disorder Medications and Long-Term Risk of Cardiovascular Diseases

Le Zhang, PhD; Lin Li, PhD; Pontus Andell, MD, PhD; Miguel Garcia-Argibay, PhD; Patrick D. Quinn, PhD; Brian M. D'Onofrio, PhD; Isabell Brikell, PhD; Ralf Kuja-Halkola, PhD; Paul Lichtenstein, PhD; Kristina Johnell, PhD; Henrik Larsson, PhD; Zheng Chang, PhD

IMPORTANCE Use of attention-deficit/hyperactivity disorder (ADHD) medications has increased substantially over the past decades. However, the potential risk of cardiovascular disease (CVD) associated with long-term ADHD medication use remains unclear.

OBJECTIVE To assess the association between long-term use of ADHD medication and the risk of CVD.

DESIGN, SETTING, AND PARTICIPANTS This case-control study included individuals in Sweden aged 6 to 64 years who received an incident diagnosis of ADHD or ADHD medication dispensation between January 1, 2007, and December 31, 2020. Data on ADHD and CVD diagnoses and ADHD medication dispensation were obtained from the Swedish National Inpatient Register and the Swedish Prescribed Drug Register, respectively. Cases included individuals with ADHD and an incident CVD diagnosis (ischemic heart diseases, cerebrovascular diseases, hypertension, heart failure, arrhythmias, thromboembolic disease, arterial disease, and other forms of heart disease). Incidence density sampling was used to match cases with up to 5 controls without CVD based on age, sex, and calendar time. Cases and controls had the same duration of follow-up.

EXPOSURE Cumulative duration of ADHD medication use up to 14 years.

MAIN OUTCOMES AND MEASURES The primary outcome was incident CVD. The association between CVD and cumulative duration of ADHD medication use was measured using adjusted odds ratios (AORs) with 95% CIs.

RESULTS Of 278 027 individuals with ADHD aged 6 to 64 years, 10 388 with CVD were identified (median [IQR] age, 34.6 [20.0-45.7] years; 6154 males [59.2%]) and matched with 51 672 control participants without CVD (median [IQR] age, 34.6 [19.8-45.6] years; 30 601 males [59.2%]). Median (IQR) follow-up time in both groups was 4.1 (1.9-6.8) years. Longer cumulative duration of ADHD medication use was associated with an increased risk of CVD compared with nonuse (0 to  $\leq$ 1 year: AOR, 0.99 [95% CI, 0.93-1.06]; 1 to  $\leq$ 2 years: AOR, 1.09 [95% CI, 1.01-1.18]; 2 to ≤3 years: AOR, 1.15 [95% CI, 1.05-1.25]; 3 to ≤5 years: AOR, 1.27 [95% CI, 1.17-1.39]; and >5 years: AOR, 1.23 [95% CI, 1.12-1.36]). Longer cumulative ADHD medication use was associated with an increased risk of hypertension (eg, 3 to ≤5 years: AOR, 1.72 [95% CI, 1.51-1.97] and >5 years: AOR, 1.80 [95% CI, 1.55-2.08]) and arterial disease (eg, 3 to ≤5 years: AOR, 1.65 [95% CI, 1.11-2.45] and >5 years: AOR, 1.49 [95% CI, 0.96-2.32]). Across the 14-year follow-up, each 1-year increase of ADHD medication use was associated with a 4% increased risk of CVD (AOR, 1.04 [95% CI, 1.03-1.05]), with a larger increase in risk in the first 3 years of cumulative use (AOR, 1.08 [95% CI, 1.04-1.11]) and stable risk over the remaining follow-up. Similar patterns were observed in children and youth (aged <25 years) and adults (aged  $\geq$  25 years).

CONCLUSIONS AND RELEVANCE This case-control study found that long-term exposure to ADHD medications was associated with an increased risk of CVDs, especially hypertension and arterial disease. These findings highlight the importance of carefully weighing potential benefits and risks when making treatment decisions about long-term ADHD medication use. Clinicians should regularly and consistently monitor cardiovascular signs and symptoms throughout the course of treatment.

Author Affiliations: Author affiliations are listed at the end of this article.

+ Editorial

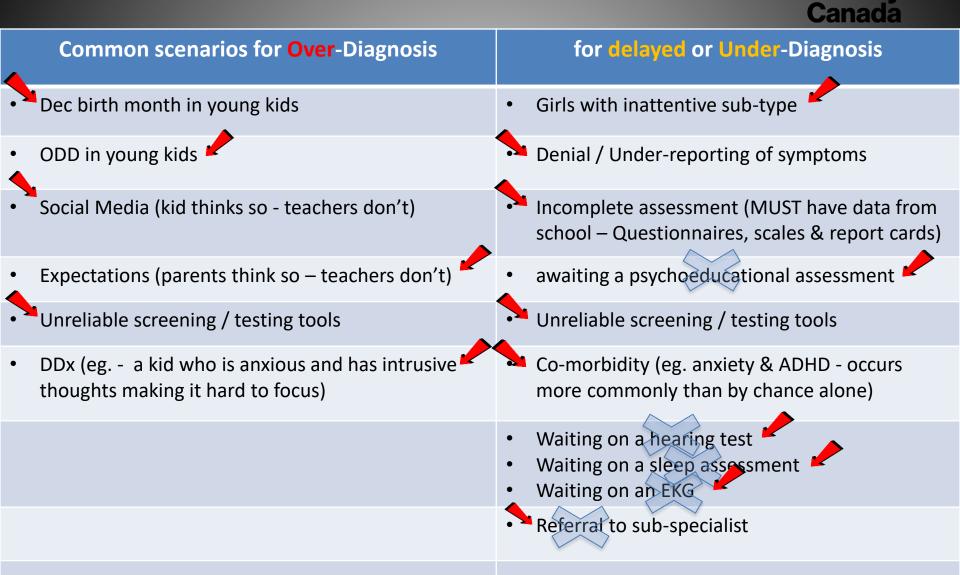
Supplemental content

Corresponding Authors: Zheng Chang, PhD (zheng; chang@kl.se) and Le Zhang, PhD (le:zhang@kl.se), Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Nobels väg 12A, 171 65 Stockholm, Sweden. Slightly higher rate of hypertension long-term but (in my opinion) inconclusive.

[Double the rate at study onset of obesity and substance use among 'cases']

JAMA Psychiatry. doi:10.1001/jamapsychiatry.2023.4294 Published online November 22, 2023.

# Don't Over-, or Under-, Diagnose ADHD



Choosi

# The New England Journal of Medicine

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**FEBRUARY 3**, 1994

Number 5

#### EFFECTS OF DIETS HIGH IN SUCROSE OR ASPARTAME ON THE BEHAVIOR AND COGNITIVE PERFORMANCE OF CHILDREN

MARK L. WOLRAICH, M.D., SCOTT D. LINDGREN, PH.D., PHYLLIS J. STUMBO, PH.D., LEWIS D. STEGINK, PH.D., MARK I. APPELBAUM, PH.D., AND MARY C. KIRITSY, M.Sc., R.D.

Abstract Background. Both dietary sucrose and the sweetener aspartame have been reported to produce hyperactivity and other behavioral problems in children.

Methods. We conducted a double-blind controlled trial with two groups of children: 25 normal preschool children (3 to 5 years of age), and 23 school-age children (6 to 10 years) described by their parents as sensitive to sugar. The children and their families followed a different diet for each of three consecutive three-week periods. One diet was high in sucrose with no artificial sweeteners, another was low in sucrose and contained aspartame as a sweetener, and the third was low in sucrose and contained sacweight per day while on the sucrose diet,  $38\pm13$  mg of aspartame per kilogram per day while on the aspartame diet, and  $12\pm4.5$  mg of saccharin per kilogram per day while on the saccharin diet. The school-age children considered to be sensitive to sugar ingested  $4500\pm1200$ mg of sucrose per kilogram,  $32\pm8.9$  mg of aspartame per kilogram, and  $9.9\pm3.9$  mg of saccharin per kilogram, respectively. For the children described as sugarsensitive, there were no significant differences among the three diets in any of 39 behavioral and cognitive variables. For the preschool children, only 4 of the 31 measures differed significantly among the three diets, and there was no consistent pattern in the differences that were



[Intervention Review]

# Polyunsaturated fatty acids (PUFA) for attention deficit hyperactivity disorder (ADHD) in children and adolescents

Authors' conclusions

Overall, there is little evidence that PUFA supplementation provides any benefit for the symptoms of ADHD in children and adolescents.

Gillies D, Sinn JKH, Lad SS, Leach MJ, Ross MJ. Polyunsaturated fatty acids (PUFA) for attention deficit hyperactivity disorder (ADHD) in children and adolescents. Cochrane Database of Systematic Reviews 2012, Issue 7. Art. No.: CD007986. DOI: 10.1002/14651858.CD007986.pub2.

\*A novel digital intervention for actively reducing severity of paediatric ADHD (STARS-ADHD): a randomised controlled trial

- Lancet Digital "In order to cover the costs of reviewing, copy editing, layout, and online hosting and archiving, the journal will charge an article processing fee of \$5000 upon acceptance of submitted full-length papers"
- Funding Sponsored by Akili Interactive Labs.
- Declaration of interests
  - "...SHK is a consultant, principal investigator and owns stock options for Akili Interactive Labs..."
- Acknowledgments
  - "...Writing and data analysis support, under the direction of the authors, was provided by Titiimaea Alailima, an employee of Akili Interactive Labs ..."
  - …Editorial support, under the direction of the authors, was provided by Peloton Advantage, an OPEN Health company, Parsippany, NJ, with funding by Akili Interactive Labs…"

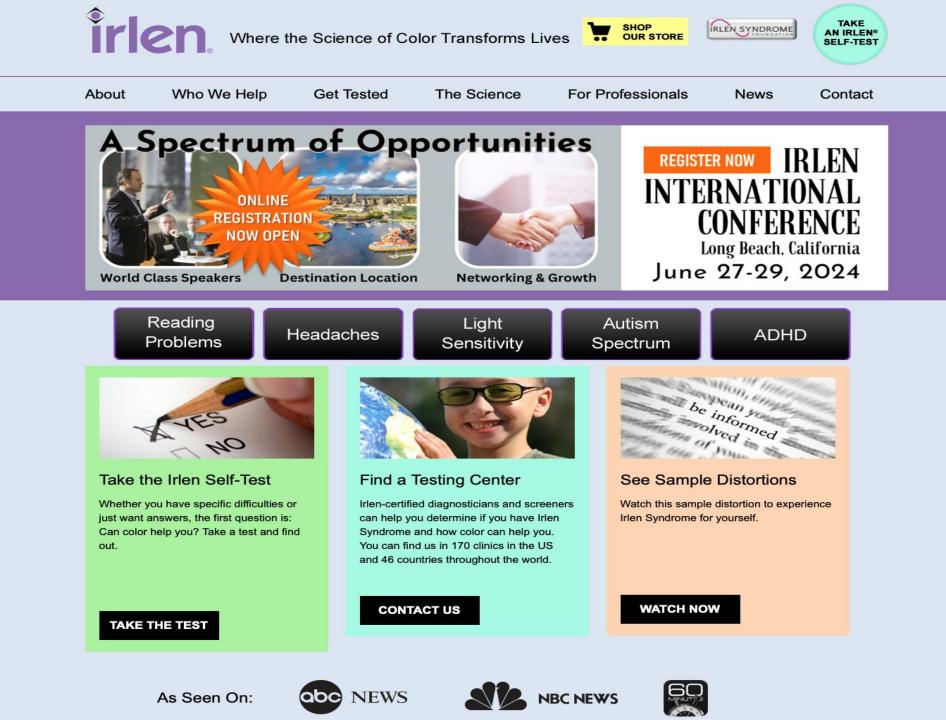


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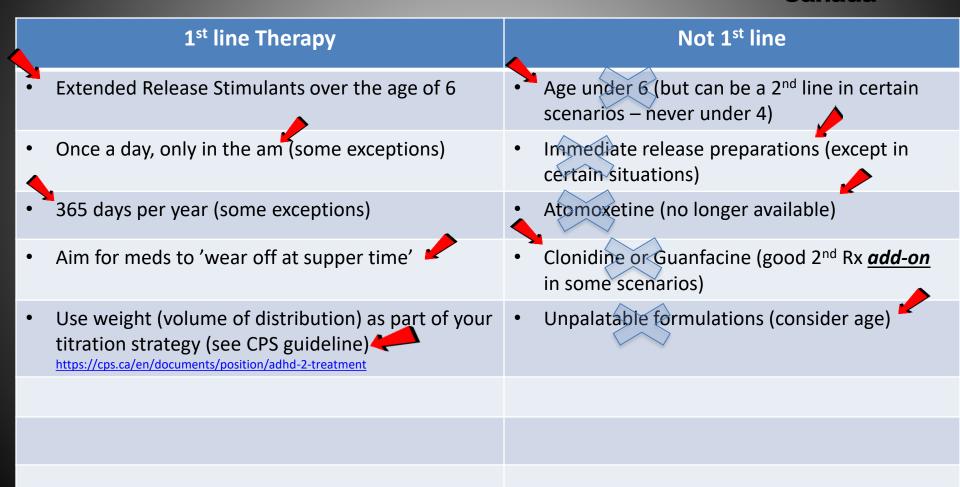
# Don't use unproven therapies:



	Non-pharmacologic Rx's that don't work		Non-pharmacologic Rx's that DO work
•	Special Diets	•	*Exercise
•	Neurofeedback J Am Acad Child Adolesc Psychiatry 2016;55(6):444–455.	•	Sleep
	Vision Tracking or Color Filter Therapy	•	Thoughtful IEP for other learning issues
•	Social skills training	<b>}</b>	Therapy for comorbidities in parallel
	Specialized therapeutic video games		
•	Unproven 'natural products'		
		the co	arger treatment effect size than behavioural erapy/ counselling / organizational training for re symptoms of ADHD. chiatr Res. 2020 Jan; 120:40-55.

# **Choosing Wisely With Proven Rx:**





### Don't stop meds that are working for misperceived A/E's

### A] Mid-day appetite suppression **V** Yes

PEDIATRICS Vol. 109 No. 3 March 2002

### B] Abdominal pain x No

PEDIATRICS Vol. 109 No. 3 March 2002 Journal of Clinical Psychopharmacology & Volume 32, Number 5, October 2012

C] Causing, unmasking or worsening of tics X No J. AM. ACAD. CHILD ADOLESC. I'SYCHIATRY, 38:8. AUGUST 1999 NEUROLOGY 58 February (2 of 2) 2002

### D] Causing, unmasking or worsening of psychosis **x** No

THE LANCET Psychiatry. VOLUME 6, ISSUE 8, P651-658, AUGUST 01, 2019

#### E] Causing, unmasking or worsening of dysrhythmia **x** No NEJM (10.1056/NEJMoall10212)November 1, 2011

### F] Addiction to stimulants or other substances x No (the opposite) Am J Psychiatry 2017; 174:877-885

G] Zombie-like flattening of affect **x** Not really

#### H] Short stature x Not if you dose & titrate correctly MTA f/u study

i] Sleep problems x Not if you dose & titrate correctly

european journal of paediatric neurology 20 (2016) 925e937 IMAJ • VOL 15 • nOVeMber 2013 J Dev Behav Pediatr. 2016 June ; 37(5): 395–404.



# Thank you for your attention!

Questions?