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ADHD, Tics and Tourette's Disorder

Child and Adolescent Psychopharmacology
March 18, 2023

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Disclosures

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My spouse/partner and I have the following relevant financial relationship with a commercial interest to disclose:

- American Academy of Child and Adolescent Psychiatry: Honoraria
- Emalex: Research Support
- Harvard Medical School /Psychiatry Academy: Honoraria
- New Venture Fund: Research Support
- NIMH/NINDS: Research Support
- Partners Healthcare: Honoraria
- Skyland Trail: Advisory Board
- Teva/Nuvelution: Research Support; Scientific Advisory Board
- Tourette Association of America: Co-Chair, Medical Advisory Board; TAA-CDC Partnership

Off-label indications will be discussed

"Young man, go to your room and stay there until your cerebral cortex matures."

WEDNESDAY
JUNE 18

ADHD, Tics and Tourette's Disorder Learning Objectives

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- At the end of this session, the participant should be able to:
- 1) Describe what is known about **boundaries and overlapping phenomenology of** ADHD and tic disorders, including Tourette's Disorder (TD)
- 2) Discuss importance of **disentangling** ADHD and tic symptoms, as this may help guide treatment
- 3) Interpret relevance of these findings **for application to treatment of patients** with ADHD and tic disorders

The FAR SIDE®

March

4

SATURDAY

MGH 1811 MASSACHUSETTS GENERAL HOSPITAL

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"I need you to line up by attention span."

THURSDAY
MAY 15

ADHD and TD/Tic Disorders: Neurocircuitry

(Leckman, J. et al; JCAP, 2010; 20 (4); 237-247; Robertson, M. Nature Reviews; 2017 (3); 1-20; Malhany, N. et al Eur J Pediatr 2015; 174; 279-288)

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- **Inhibition**: core deficit in both disorders; thought to result from fronto-striatal and frontal-parietal network dysfunction in **Cortical-Striatal-Thalamic-Cortical (CSTC)** tracts**.**
- **ADHD:** Imaging studies: Reductions in total cerebral volume, PFC, BG, dACC, CC, and cerebellum reported in ADHD patients are consistent with **fronto-striatal models**. Some studies also showed reduction in right cerebral volume, and right caudate nucleus in ADHD.
- **TD:** Mixed results; reduced caudate nucleus volume frequently reported.
- Individuals with TD+ADHD have smaller caudate nuclei.
- **TD+ADHD:** hyper-functioning/overactive circuits in BG in TD result in motor/cognitive/emotional disinhibition, worsened by frontal hypo-activity in ADHD.
- **Both TD and ADHD** tend to improve with time, which may be a result of increased myelinization of prefrontal regions.

Table 3 Main brain regions implicated in the pathogenesis of TS and ADHD

Brain areas	TS	ADHD	Ref.
Prefrontal areas	+	+	[19, 29, 56]
Inferior frontal gyrus	+	+	[100]
Sensorimotor areas	+	+	[19, 29, 55]
Anterior cingulated cortex	+	+	[19, 29, 55]
Posterior cingulated cortex	+	+	[91]
Basal ganglia	+/—	+	[19, 29, 73]
Cerebellum	—	+	[29]

(+) implicated region, (—) not implicated region, (+/—) findings contradictory

El Malhany, N. at al. Tourette syndrome and comorbid ADHD: causes and consequences. 2015; Eur J Pediatr 174; 279-288

Table 1 Pre-perinatal risk factors implicated in the pathogenesis of TS and ADHD

Pre-perinatal risk factors	TS	ADHD	Ref.
Alcohol during pregnancy	+	+	[78]
Smoking during pregnancy	+	+	[9, 53]
Prematurity	+	+	[36]
Low birth weight	+	+	[41]

(+) implicated factor

El Malhany, N. at al. Tourette syndrome and comorbid ADHD: causes and consequences. 2015; Eur J Pediatr 174; 279-288

Course of ADHD and Tic Disorders: What Happens to Tics in the Context of ADHD Over Time?

(Spencer, T. Biederman, J. Coffey, B. et al. Arch Gen Psych 1999, 56: 842-847)

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- **Design: Prospective ADHD Follow-up**
- **Objective**: To evaluate the prevalence and impact of tic disorders at baseline and at follow-up on the course of ADHD.
- **Methods**: N=128 boys with ADHD; N=110 controls.
- Duration of follow-up: 4 years; mean ages 9-13.
- **Results:**
  - ***Proportion of ADHD youth with tics: 34%***
  - ***Remission rate for tics over 4 years: 65%***
  - **Remission rate for ADHD: 20%**
- **Conclusion:** Tic remission rate is independent of ADHD.
- Tic disorders did not impact ADHD course.

Onset of ADHD and Tic Disorders in ADHD Probands

(Spencer, T. Biederman, J. Coffey, B. et al. Arch Gen Psych 1999, 56: 842-847)

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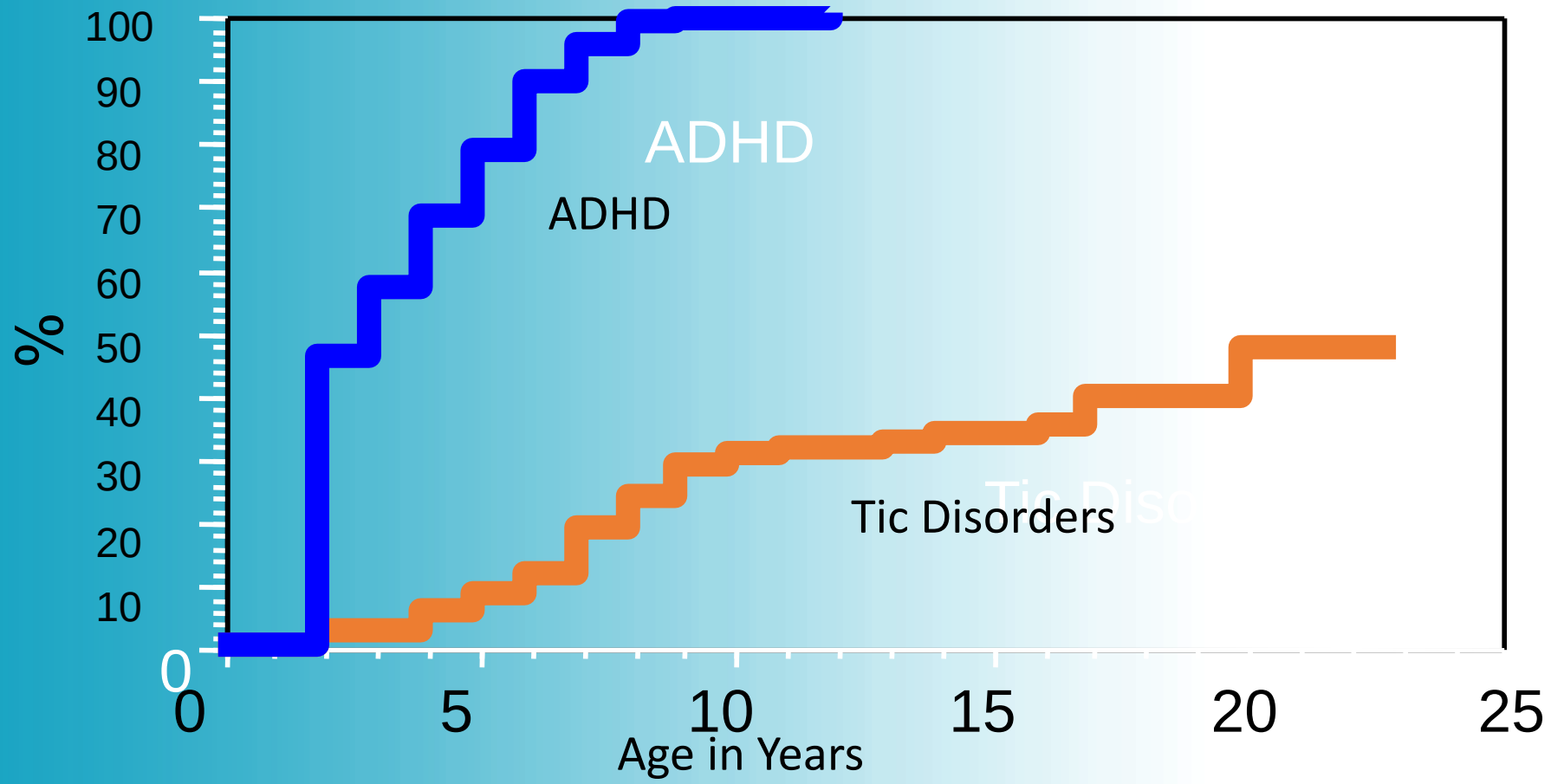

Offset of ADHD and Tic Disorders in ADHD Probands

(Spencer, T. Biederman, J. Coffey, B. et al. Arch Gen Psych 1999, 56: 842-847)

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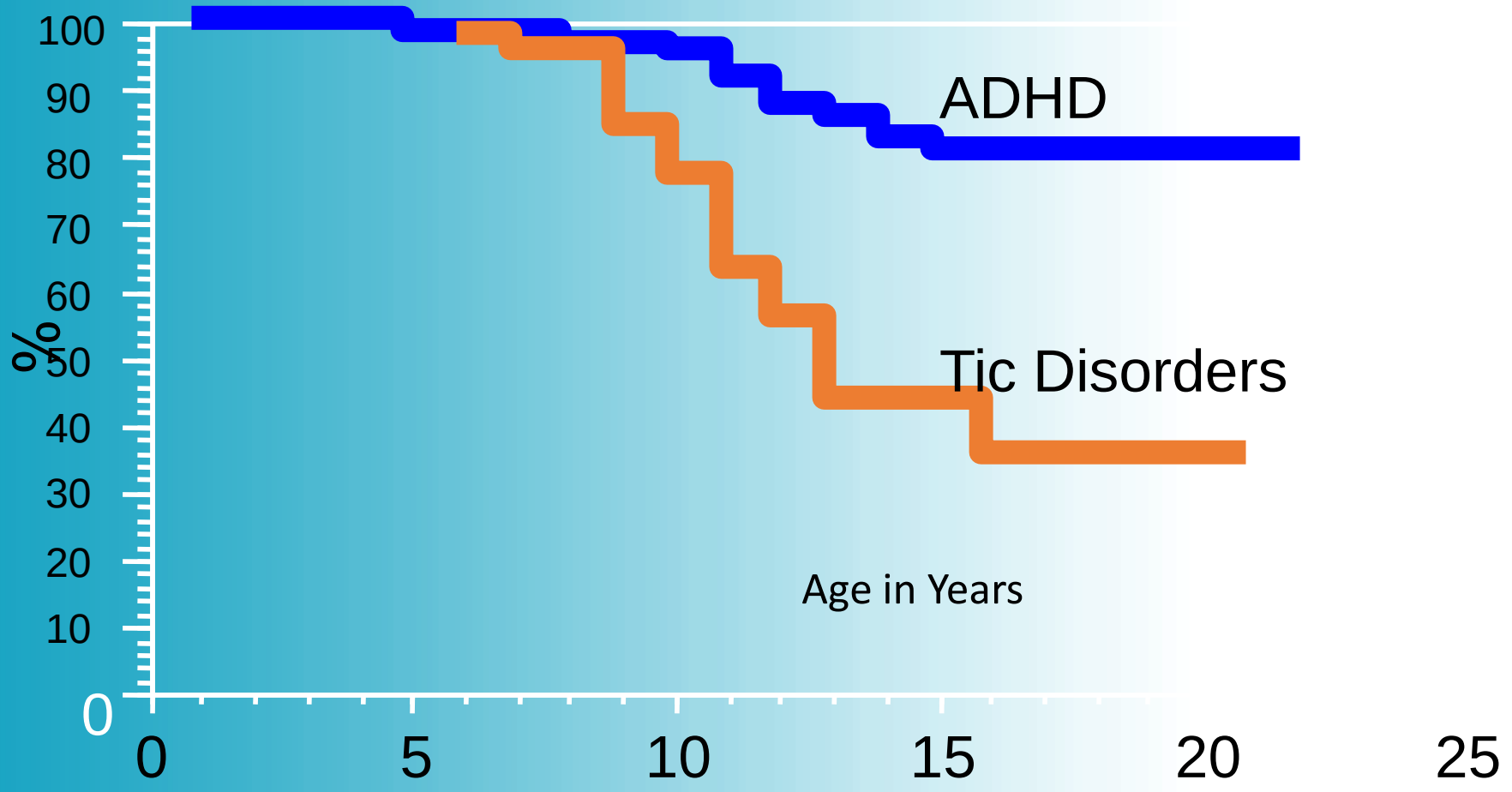

Chronic Tic Disorders (CTD) in Children with ADHD

(Poh, W., Payne, J. et al. Arch Dis Child; 2018; 0; 1-6)

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Aim: To examine: 1) prevalence of chronic tics in a community-based cohort in children with ADHD compared to children with non-ADHD at ages 7 and 10 and 2) additional psychiatric and functional burden of CTD in ADHD.

Methods: N=179 children ages 6-8 with ADHD and 212 healthy controls

Recruited through 43 schools using parent and teacher Conners followed by case confirmation with DISC-IV.

Baseline and 36 month follow up evaluations: tic measures; CBCL; academic performance; quality of life.

Results: Compared with controls, **children with ADHD were 4 times more likely to have CTD at age 7 and 5.9 times more likely at age 10.**

Concurrent CTD symptoms contribute to **higher rates of internalizing disorders, more peer problems and reduced quality of life in children with ADHD**.

Conclusions: Clinicians should be aware of and manage both symptoms.

Table 1 Sample characteristics for ADHD+CTD and ADHD-only children

	ADHD+CTD (n=23)	ADHD-only (n=92)	P
ADHD			
Combined subtype, n (%)	7 (30.4)	31 (33.7)	0.79
Inattentive subtype, n (%)	7 (30.4)	30 (32.6)	0.60
Hyperactive/impulsive subtype, n (%)	5 (21.7)	3 (3.3)	0.005
Symptom severity, parent report, mean (SD)	13.7 (5.7)	12.1 (5.5)	0.23
Symptom severity, teacher report, mean (SD)	10 (6.1)	11.0 (6.5)	0.51
Medications			
Medication use (any), n (%)	5 (21.7)	27 (29.3)	0.43
ADHD medication, n (%)	4 (17.4)	16 (17.4)	0.98
ASD symptoms			
SCQ score >15, n (%)	4 (17.4)	7 (7.6)	0.48
Primary caregiver characteristics			
Single parent family, n (%)	4 (17.4)	18 (19.6)	0.49
Did not complete high school, n (%)	7 (30.4)	25 (27.2)	0.83
Completed high school, n (%)	7 (30.4)	26 (28.3)	0.92
Completed higher education, n (%)	6 (26.1)	26 (28.3)	0.75
SEIFA score, mean (SD)	1018.1 (40.3)	1016.6 (46.5)	0.61

ADHD, attention-deficit/hyperactivity disorder; ASD, autism spectrum disorder; CTD, chronic tic disorder; SCQ, Social Communication Questionnaire; SEIFA, Socio-Economic Indexes for Areas.

Poh W, *et al*. *Arch Dis Child* 2018;**0**:1–6. doi:10.1136/archdischild-2017-314139

Table 2 ADHD+CTD versus ADHD-only—psychiatric outcomes

	ADHD+CTD (n=23)	ADHD-only (n=92)	Mean difference* (95% CI)	P
Psychiatric outcomes, n (%)				
Internalising disorder	11 (52.4)	20 (23.8)	28.3 (6.1 to 50.6)	0.007
Generalised anxiety disorder	4 (19.1)	3 (3.2)	13.4 (−2.6 to 29.6)	0.03
Separation anxiety disorder	4 (19.1)	9 (10.7)	8.3 (8.5 to 25.1)	0.26
Social anxiety	3 (14.3)	6 (7.1)	5.3 (−9.7 to 20.3)	0.44
Obsessive compulsive disorder	3 (14.3)	7 (8.3)	6.5 (−8.3 to 21.4)	0.31
Post-traumatic stress disorder	0 (0)	0 (0)	-	-
Dysthymia	1 (4.4)	1 (1.1)	3.2 (−5.6 to 11.8)	0.36
Major depression	1 (4.4)	1 (1.1)	3.2 (−5.6 to 11.8)	0.36
Hypomania	0 (0)	0 (0)	-	-
Mania	0 (0)	0 (0)	-	-
Externalising disorder	14 (66.7)	37 (44.0)	11.5 (−11.3 to 34.4)	0.33
Oppositional defiant disorder	14 (66.7)	38 (41.3)	19.6 (−11.3 to 34.4)	0.33
Conduct disorder	3 (13.0)	5 (5.4)	7.6 (−8.3 to 21.3)	0.32

*Difference in mean prevalence (ADHD+CTD minus ADHD).
ADHD, attention-deficit/hyperactivity disorder; CTD, chronic tic disorder.

Poh W, *et al*. *Arch Dis Child* 2018;**0**:1–6. doi:10.1136/archdischild-2017-314139

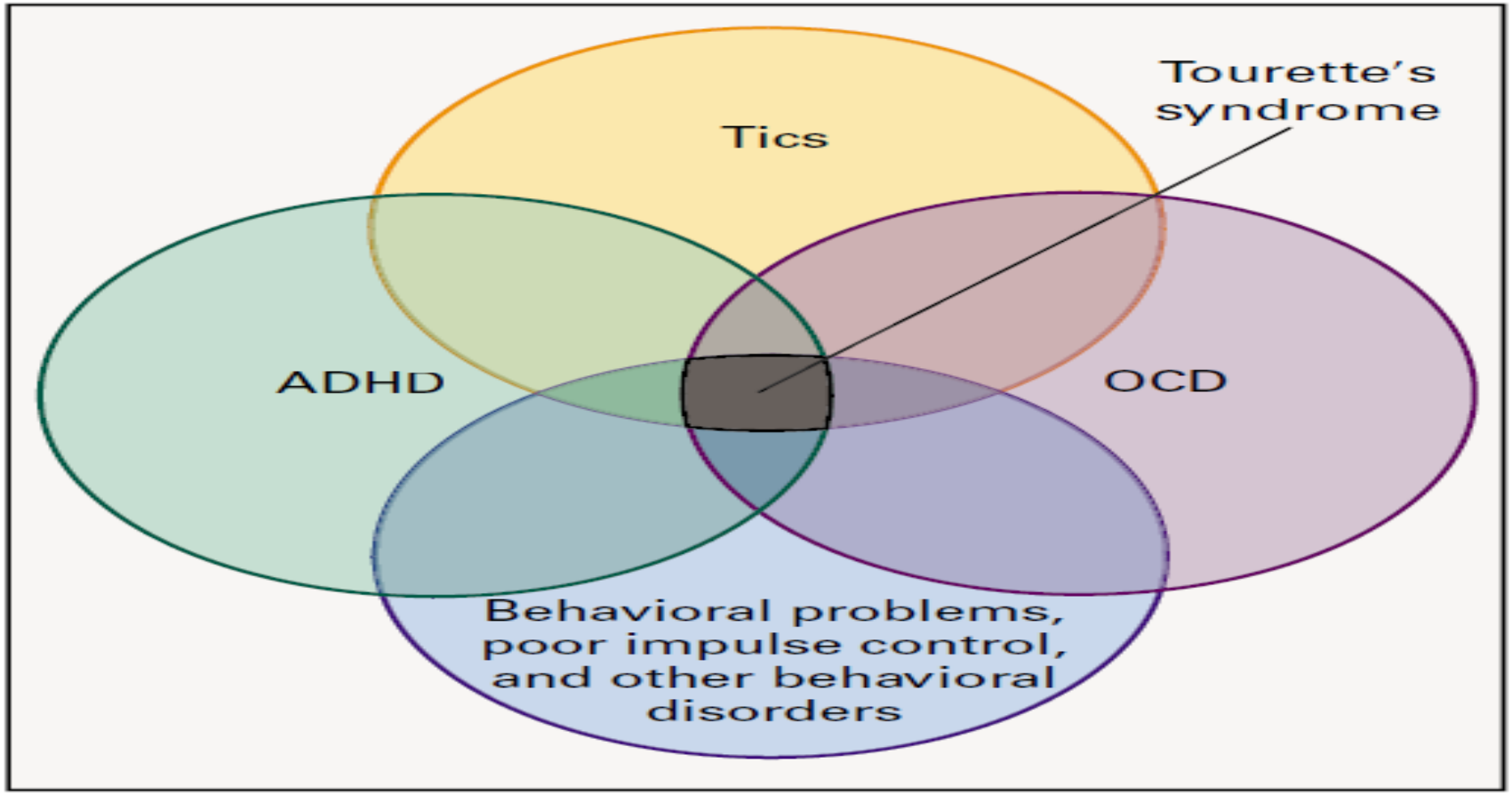

Figure 1. Clinical Hallmarks of Tourette's Syndrome.
The diagnosis is based on the occurrence of tics along with behavioral disorders, including attention-deficit–hyperactivity disorder (ADHD) and obsessive–compulsive disorder (OCD). Other behavioral disorders include anxiety and mood disorders, learning disorders, sleep disorders, conduct and oppositional behavior, and self-injurious behavior.

Jankovic J. NEJM; 2001.

Phenotype Development in Adolescents with Tourette Syndrome: A Large Clinical Longitudinal Study

(Groth, C. Mol Debes, N. et al ; Journal of Child Neurol; 2017; 32 (3) 1047-1057)

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Aim: Description of TS phenotype development and tic-related impairment in a longitudinal study of 226 children and adolescents followed up after 6 years.

Methods: Participants examined for tic severity, impairment, OCD and ADHD.

Results: Phenotype development changed toward **less comorbidity:**

at baseline 40% had TS only (no OCD or ADHD); 55% TS only at follow up.

Tic related impairment scores did not reflect tic decline. Sex, vocal and motor tics, OCD and **ADHD severity** were highly significantly correlated with tic related impairment score.

Conclusion: Knowledge of phenotype development may be useful in clinical settings.

Table 1. Baseline Characteristics of Participants and Nonparticipants at Follow-Up.

Characteristics	Participants	Nonparticipants	*P* value
Sample size	227	87	—
Age, years, mean(SD)	12.5 (2.7)	12.3 (2.9)	.69
Male, number (%)	185 (81.5)	72 (82.8)	.87
IQ, mean (SD)	90.0 (18.4)	85.3 (16.1)	.07
SES, mean (SD)	2.5 (1.0)	2.7 (1.0)	.10
ADHD, number (%)	93 (41.2)	42 (48.3)	.31
OCD, number (%)	89 (39.2)	33 (37.9)	.90
OCD, CY-BOCS score, mean (SD)	8.4 (8.0)	8.2 (7.9)	.82
Tics YGTSS score, mean (SD)	24.5 (18.2)	25.6 (17.6)	.68

There were no significant differences ($P < .05$) between any of the demographic variables examined between participants and nonparticipants using Fisher's exact test for sex, SES, ADHD, OCD, and CY-BOCS; and *t*-test for age, tic severity, OCD severity, IQ, and YGTSS.[25] Abbreviations: ADHD, attention-deficit/hyperactivity disorder; CY-BOCS, Children's Yale-Brown Obsessive Compulsive Scale; IQ, intelligence quotient; OCD, obsessive compulsive disorder; SES, socioeconomic status; YGTSS, Yale Global Tic Severity Scale.

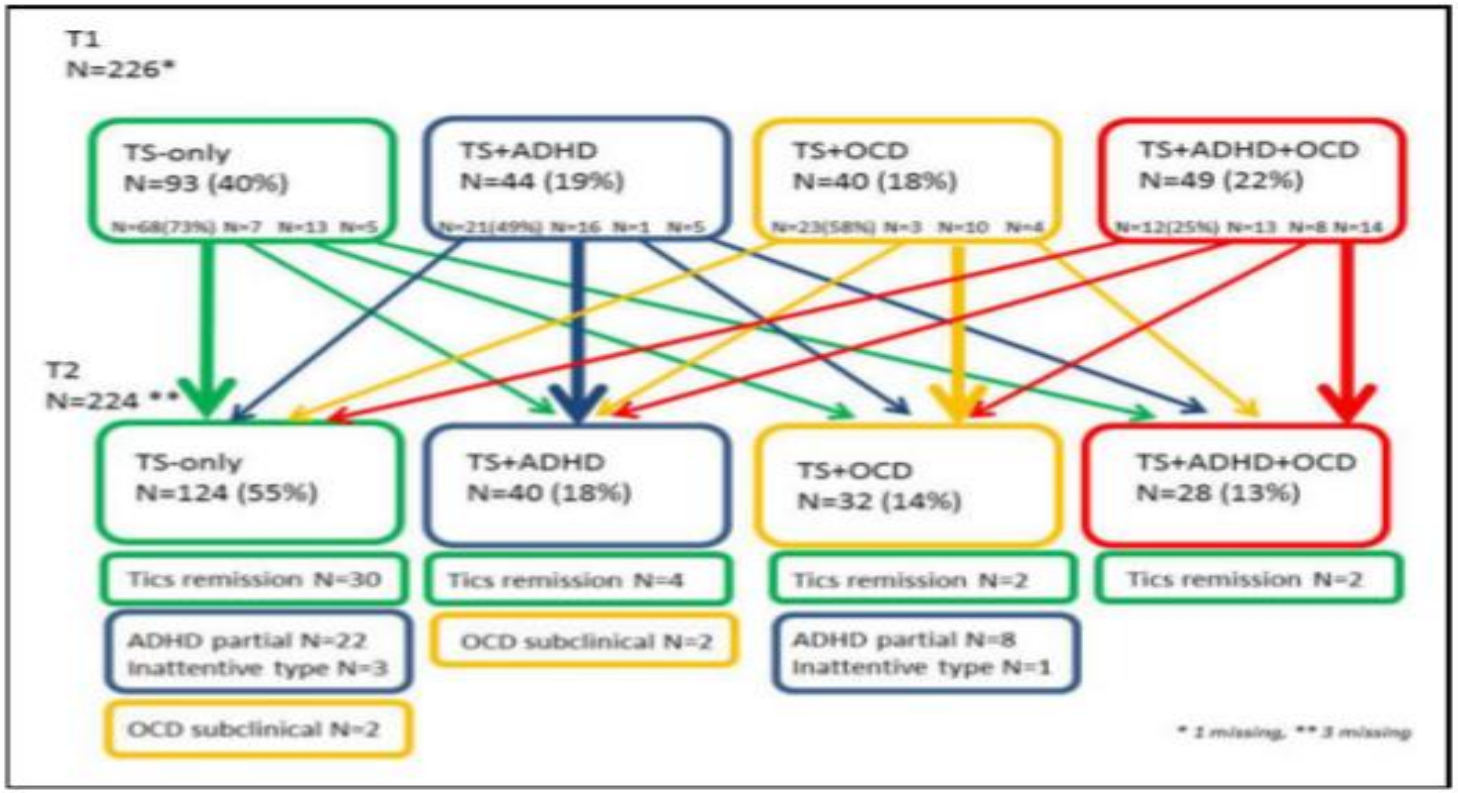
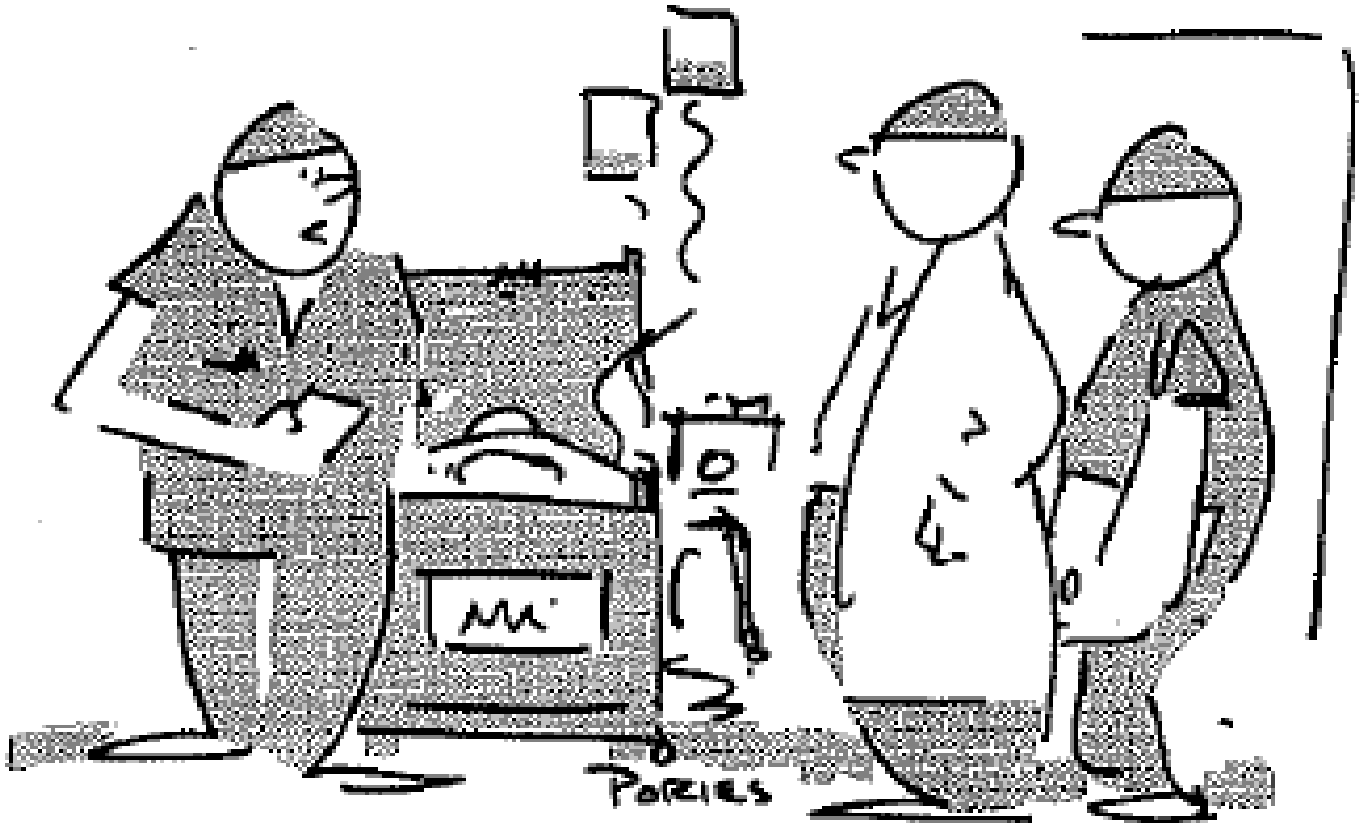


Figure 1. The development of phenotypes from baseline (T1) to follow-up (T2). At follow-up, the groups were subdivided illustrating the subclinical symptoms into full tic remission (tic score on YGTSS = 0), partial ADHD remission (subthreshold symptoms and impairment according to DSM-IV), inattentive type (ADHD predominantly inattentive type), and subclinical OCD (OCD-score8-9 on Y-BOCS). No participants fulfilled criteria at T2 for ADHD predominantly hyperactive/impulsive type. Abbreviations: ADHD, attention-deficit/hyperactivity disorder; OCD, obsessive compulsive disorder; TS, Tourette syndrome.



"After the lab studies, angiograms, MRI, and the full body CT scans, the physical examination revealed the knife in his back."

Neurodevelopmental Disorders: Diagnostic Evaluation: Tic Disorders and ADHD

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- **Diagnoses** of both disorders are made on basis of **classical history.**
- **Structured or semi-structured diagnostic interviews,** such as the DISC or K-SADS can improve classification and assessment of comorbidity.
- **Standardized rating scales** have improved diagnostic reliability in research studies; helpful in clinical care.
- The **Yale-Global Tic Severity Scale (YGTSS**) (Leckman, Riddle, Hardin, Ort, Swartz, Stevenson, et al., 1989); the "gold standard" assesses domains of: tic number, frequency, intensity, complexity and interference (0-50), and tic related impairment (0-50). **Tic Symptom Self Report** (TSSR) derived.
- **SNAP, ADHD-RS and Conners** (Parent and Teacher) are helpful for quantitative evaluation of ADHD symptoms.
- ***Quantitative ratings of tics and ADHD can facilitate 1) disentanglement and 2) prioritization for overall treatment planning and use of targeted combined pharmacotherapy.***

TD/Tics and ADHD: Impact on Management

- **Tics:** Most patients with mild tic symptoms need only monitoring, education, and guidance. Those with moderate to severe symptoms will usually need treatment.
- ***ADHD**: Since ADHD symptoms are more likely to persist and cause significant functional impairment, treatment is recommended.
- **Comprehensive Behavioral Intervention for Tics (CBIT)** is established as **first line treatment** for tics. This may be particularly relevant to patients with tics and ADHD, since pharmacotherapy may be challenging.
- ADHD did not moderate response to CBIT. *(Sukholdosky, D. et al, Neurology, 2017)*
- **Pharmacotherapy for Tic Disorders and ADHD**:
- 1) stimulants
- 2) alpha agonists
- 3) atomoxetine
- 4) combinations

Modified Comprehensive Behavioral Intervention for Tics: Treating Children With Tic Disorders, Co-Occurring ADHD, and Psychosocial Impairment

(Greenberg,E. Albright,C. et al; DOI: 10.1016/j.beth.2022.07.007Behav Ther; 2023 Jan;54(1):51-64.Epub 2022 Jul 20).

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- **Aim:** To evaluate the feasibility and acceptability, and preliminary efficacy of a **modified comprehensive behavioral intervention for tics (MCBIT) therapy** for youth with chronic tic disorders (CTDs), co-occurring attention-deficit hyperactivity disorder (ADHD), and associated psychosocial impairment.

- **Methods:** Seventeen youth ages 10-17 with CTD and co-occurring ADHD were randomly assigned to the MCBIT group (n = 9) or to a control group where they received traditional comprehensive behavioral intervention for tics (CBIT) therapy (n = 8). Both groups received **ten 55-minute weekly treatment sessions**, and two 55-minute biweekly relapse prevention sessions. Sixteen of the 17 participants completed the study, and acceptability ratings in both treatment groups were high with no significant differences in expectation of improvement.

- **Results:** The MCBIT and CBIT groups in combination showed significant improvement in tic severity, ADHD symptom severity, and tic-related impairment. Group differences were not significant.

- **Conclusion:** MCBIT treatment is feasible and acceptable for youth with CTD and ADHD and is similarly well tolerated relative to traditional CBIT.
- **Results were not sufficiently superior to recommend MCBIT over CBIT for this population.**

Practical Tips on Treating ADHD and Tics/TD with Stimulants

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- **Methylphenidates (MPH)** are recommended.
- For children, MPH can be initiated at 5 mg (or equivalent) and titrated upward gradually.
- For adolescents, MPH can be initiated at 10 mg (or equivalent) and titrated upward gradually.
- For tic increase with upward titration: if ADHD symptoms have improved, hold the dose and monitor, or temporarily reduce the dose and re-titrate.
- There are no controlled trials of extended-release stimulants, but they may be less likely than IR to be associated with tic increase that occurs in some children?
- Guanfacine or clonidine can be added if the tic increase is sustained.

How To Decide? Systematic Review: Pharmacological Treatment of Tic Disorders: Efficacy of Antipsychotic and Alpha 2 Agonist Agents

(Weisman, H. Qureshi, I. Leckman, J. Scahill, L. Bloch, M. Neuroscience and Biobehavioral Reviews; 2013; 37; 1162-1171)

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- **Design:** Meta-analysis of RCTs in treatment of chronic tic disorders and examination of moderators
- **Results:** Significant benefit of antipsychotics vs. placebo. **SMD=0.58.**
  - No significant difference in efficacy of risperidone, pimozide, haloperidol and ziprasidone.
  - Significant benefit of alpha 2 agonists vs. placebo. Significant **moderating effect of comorbid ADHD**.
  - **With comorbid ADHD SMD: 0.68. No ADHD: 0.15.**
- **Conclusion**: Significant benefits of both medication types, but alpha 2 agonists may have minimal benefit in patients without ADHD.

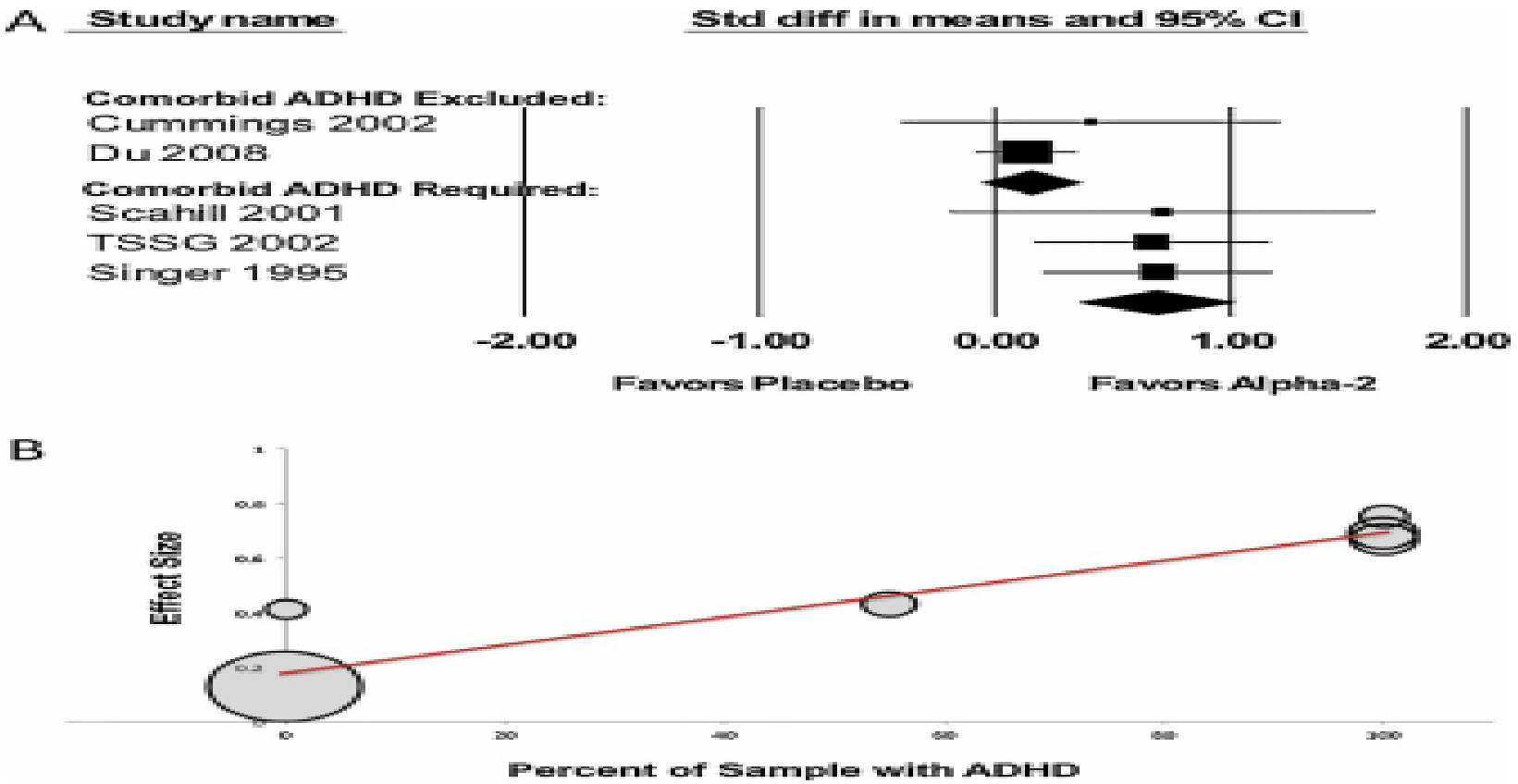

Fig. 7. (A) Efficacy of alpha2-agonists for the treatment of tics in trials stratified by ADHD comorbidity. Trials that required tic patients to have comorbid ADHD (SMD = 0.68 (95%CI: 0.36–1.01), $z = 4.10$, $p < 0.001$) demonstrated a significantly greater effect (test for subgroup differences $\chi^2 = 7.27$, df = 1, $p = 0.007$) of alpha-2 agonists in reducing tic symptoms than trials that excluded subjects with comorbid ADHD (SMD = 0.15 (95%CI: −0.06 to 0.36), $z = 1.40$, $p = 0.16$). (B) Meta-regression of alpha-2 agonist efficacy in treating tics versus percent of subjects with comorbid ADHD in trial. Meta-regression demonstrated that trials enrolling a larger proportion of subjects with comorbid ADHD reported a greater efficacy of alpha-2 agonists in treating tics ($\beta = 0.0053$ (95%CI: 0.0015–0.0091), $z = -2.72$, $p = 0.006$).

Pharmacological treatment for attention deficit hyperactivity disorder (ADHD) in children with comorbid tic disorders (Review)
(*Osland, S et al Cochrane Database of Systematic Reviews 2018, Issue 6. Art. No CD007990.*
DOI:10.1002/14651858.CD007990.pub3.

- **Summary of findings for the main comparison.**
- **Methylphenidate compared with placebo for attention deficit hyperactivity disorder (ADHD) in children with comorbid tic disorders**
- **Methylphenidate compared with placebo for attention deficit hyperactivity disorder (ADHD) in children with comorbid tic disorders**
- **Patient or population:** children with ADHD and comorbid tic disorders
- **Intervention: methylphenidate**
- **Comparison:** placebo

Outcomes	Effect of treatment	Number of participants (studies)	Quality of the evidence (GRADE)	Comments
ADHD symptom-related behavior Measured by standardized rating scales: Conners' Abbreviated Teacher Rating Scale, Conners' Abbreviated Parent Rating Scale, IOWA Conners' Teacher Rating Scale, Mothers' Objective Method for Subgrouping, Continuous Performance Task, Conners' Teacher Rating Scale, Conners' Continuous Performance Task	Tourette's Syndrome Study Group 2002 showed a significant treatment effect using the Conners' Abbreviated Teacher Rating Scale (3.3 points, 98.3% CI −0.2 to 6.8; P = 0.02). Gadow 2007 showed that all doses (0.1 mg/kg, 0.3 mg/kg, 0.5 mg/kg) of methylphenidate were superior to placebo on all rating scales (Conners' Abbreviated Teacher/Parent Rating Scale, IOWA Conners' Teacher Rating Scale, Mothers' Objective Method for Subgrouping, Continuous Performance Test), with a dose-dependent effect (F = 24.7; P = 0.001) Castellanos 1997 showed significantly decreased hyperactivity at all doses (15 mg, 25 mg, 45 mg).	229 (3 studies)	⊕⊕⊖⊖ **Low**[a]	–
Tic severity Measured by standardized rating scales: Yale Global Tic Severity Scale, Tourette Syndrome Severity Scale, Tourette Syndrome Clinical Global Impression Scale, Global Tic Rating Scale, 2-Minute Tic and Habit Count, Tic Symptom Self-Report	Tourette's Syndrome Study Group 2002 found a significant treatment effect using the Yale Global Tic Severity Scale (11.0 points, 98.3% CI 2.1 to 19.8; P = 0.003). Gadow 2007 found no difference on the Yale Global Tic Severity Scale but found an improvement in tic severity at all doses (0.1 mg/kg, 0.3 mg/kg, 0.5 mg/kg) on the Global Tic Rating Scale completed by teachers (F = 5.33; P = 0.002) Castellanos 1997 found no effect of drug on tic severity for second and third cohorts. Tic severity was significantly greater during week 2 in the first cohort (P < 0.01)	229 (3 studies)	⊕⊕⊖⊖ **Low**[a]	–

Pharmacological treatment for attention deficit hyperactivity disorder (ADHD) in children with comorbid tic disorders (Review) (*Osland, S et al Cochrane Database of Systematic Reviews 2018, Issue 6. Art. No.: CD007990. DOI:10.1002/14651858.CD007990.pub3.)*

- **Summary of findings:**
- **Clonidine compared with placebo for attention deficit hyperactivity disorder (ADHD) in children with comorbid tic disorders**
- **Clonidine compared with placebo for attention deficit hyperactivity disorder (ADHD) in children with comorbid tic disorders**
- **Patient or population:** children with ADHD and comorbid tic disorders
- **Intervention:** clonidine
- **Comparison:** placebo

Outcomes	Effect of treatment	Number of participants (studies)	Quality of the evidence (GRADE)	Comments
ADHD symptom-related behavior Measured by standardized rating scales: Conners' Abbreviated Teacher Rating Scale, Conners' Abbreviated Parent Rating Scale, IOWA Conners' Teacher Rating Scale, Conners' Continuous Performance Task, Child Behaviour Checklist, Gordon Diagnostic System, Clinical Evaluation of Language Function, Matching Familial Figures Test, Porteus Maze Test, Restricted Academic Test	Tourette's Syndrome Study Group 2002 found a significant treatment effect using the Conners' Abbreviated Teacher Rating Scale (3.3 points, 98.3% CI −0.2 to 6.8; P = 0.02). Singer 1995 found no significant difference on any ADHD outcome measures, except the nervous/overactive subscale of the Child Behaviour Checklist (boys aged 6-11 years).	170 (2 studies)	⊕⊕◯◯ **Low**[a]	–
Tic severity Measured by standardized rating scales: Yale Global Tic Severity Scale, Tourette Syndrome Severity Scale, Global Tic Rating Scale, Tic Symptom Self-Report, Hopkins Motor/Vocal Scale	Tourette's Syndrome Study Group 2002 showed a significant treatment effect using the Yale Global Tic Severity Scale (10.9 points, 98.3% CI 2.1 to 19.7; P = 0.003). Singer 1995 found no significant difference on measures of tic severity.	170 (2 studies)	⊕⊕◯◯ **Low**[a]	–

Pharmacological treatment for attention deficit hyperactivity disorder (ADHD) in children with comorbid tic disorders (Cochran Review; 2018)

(Osland ST, Steeves TDL, Pringsheim T)

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- **Implications for practice**
- Drugs of the **stimulant class** have generally been thought to provide the most reliable and robust treatment responses for symptoms of ADHD in children with tics.
- Given methodological difficulties in comparing ES across studies with divergent inclusion criteria, efficacy measures, and designs, this review can provide **no evidence-based recommendations for choosing between treatment options**.
- **Stimulants will likely continue to be considered as first-line treatment for children** with moderate to-severe symptoms of ADHD in children with tic disorders.
- Although overall, stimulants have not been shown to worsen tics in most participants with tic disorders, **they may still exacerbate tics in individual cases**.
- In these instances, treatment with **alpha agonists or atomoxetine** could be considered as alternatives.

THE NEW YORKER

"I'm not going to shoot the messenger, but I'm also not going to renew his grant."

Canada Day

TUESDAY
JULY 1

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Extended-Release Guanfacine (GXR) Does Not Show a Large Effect on Tic Severity in Children with Chronic Tic Disorders

(Murphy T, Fernandez T, Coffey B, et al. JCAP. 2017;27(9):762–770.)

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- **Methods:** 8-week RCT in N=34 youth ages 6 to 17 years (mean = 11.1) with CTD.
- **Results:** At baseline, mean YGTSS total score was 26.3 for GXR group vs. 27.7 for placebo.
- GXR group: (mean final daily dose 2.6 mg.); mean YGTSS total score declined to 23; **p = 0.08; effect size = 0.35**.
- PBO group: declined to 24.7; **p = 0.08; effect size = 0.38.**
- There was **no significant difference** in the rate of positive response on CGI-I between GXR and PBO (19% vs. 22%; p = 1.0).
- **Adverse Effects (AE):** Most common: fatigue, drowsiness, dry mouth, headache, and irritability.
- **Conclusion:** This pilot study **did not confirm a clinically meaningful effect size** within GXR group. These results **do not support launch** of a larger efficacy trial for tics in youth with CTD.

Extended-Release Guanfacine (GXR) Does Not Show a Large Effect on Tic Severity in Children with Chronic Tic Disorders

(Murphy T, Fernandez T, Coffey B, et al. JCAP. 2017;27(9):762–770.)

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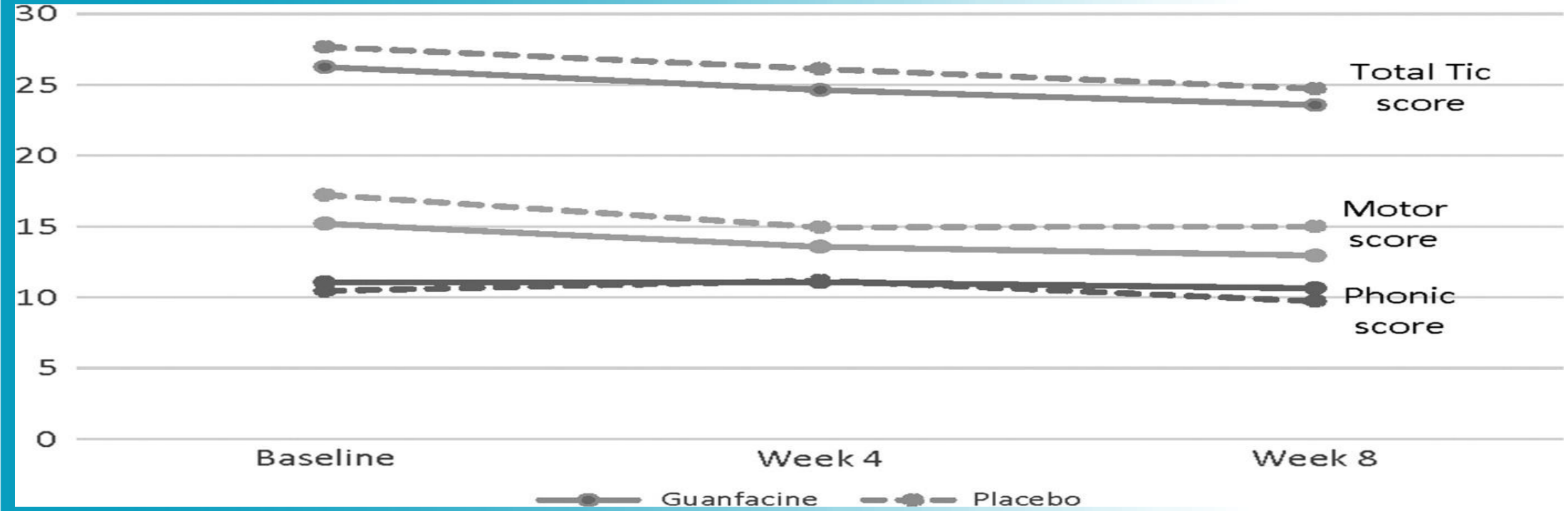

FIG. 2. YGTSS total score, motor, and phonic; Guanfacine vs. placebo. YGTSS, Yale Global Tic Severity Scale.

THE NEW YORKER

"If you're happy and you know it, stick with your dosage."

THURSDAY
SEPTEMBER 25

Summary: ADHD, Tics and Tourette's Disorder

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There is **bi-directional overlap of ADHD and Tic Disorders:** neurobiology, genetics and neurocircuitry, and phenomenology, including clinical course and psychiatric comorbidity.

ADHD symptoms tend to persist, but **tic symptoms** tend to remit over time.

Much of the **associated psychopathology (behavioral, emotional, neurocognitive**) in Tourette's Disorder is secondary to ADHD.

Children and adults with **ADHD+CTD** are more likely to have higher rates and severity of psychopathology and reduced quality of life than those with either ADHD or CTD alone.

Tic and ADHD symptoms should be carefully **disentangled,** by severity and potential outcomes, for best management and intervention.

Behavioral treatment of tics is recommended as first line; **stimulants** can be used safely for ADHD and tics, but there are several other options, including atomoxetine, and combination treatment with alpha 2 agonists.