Tourette syndrome in adults

Tamara Pringsheim, MD FRCPC Neurology

Professor, University of Calgary

Objectives

To define the clinical features of tics and Tourette syndrome

To describe the evolution of symptoms over time from childhood to adulthood

To review the evidence for treatment of tics

Tic definition

- Movements or vocalizations
- Intermittent
- Often brief
- Repetitive and recurrent
- Non-rhythmic and stereotyped
- Often preceded by premonitory urges or sensations
- May be temporarily suppressible

Tourette's Disorder: DSM 5

A. Both multiple motor and one or more vocal tics have been present at some time, although not necessarily concurrently.

B. The tics may wax and wane in frequency but have persisted for more than 1 year since first tic onset.

C. Onset is before age 18 years.

D. The disturbance is not attributable to the physiological effects of a substance or another medical condition

Tourette Disorder

Pediatric onset persistent tic syndrome

Characterised by

- Motor and phonic tics
- Predominately affect the craniofacial region
- More simple than complex tics at onset
- Begin gradually, with waxing and waning
- Onset is almost exclusively in childhood, usually before age 12
- Duration of at least one year

Supportive features

- Perceived sense of agency
- Suppressibility
- Comorbid ADHD and OCD
- Family history

Etiology

- Idiopathic neurodevelopmental condition

Comorbid Conditions in Tourette Disorder

- Neuropsychiatric and neurodevelopmental comorbid conditions are very common
- 80% of clinically referred patients meet diagnostic criteria for at least one comorbidity
- ADHD and OCD most common (50%)
- Anxiety disorders
- Disruptive behaviour disorders
- Depression
- Autism

Yale Global Tic Severity Score (YGTSS)

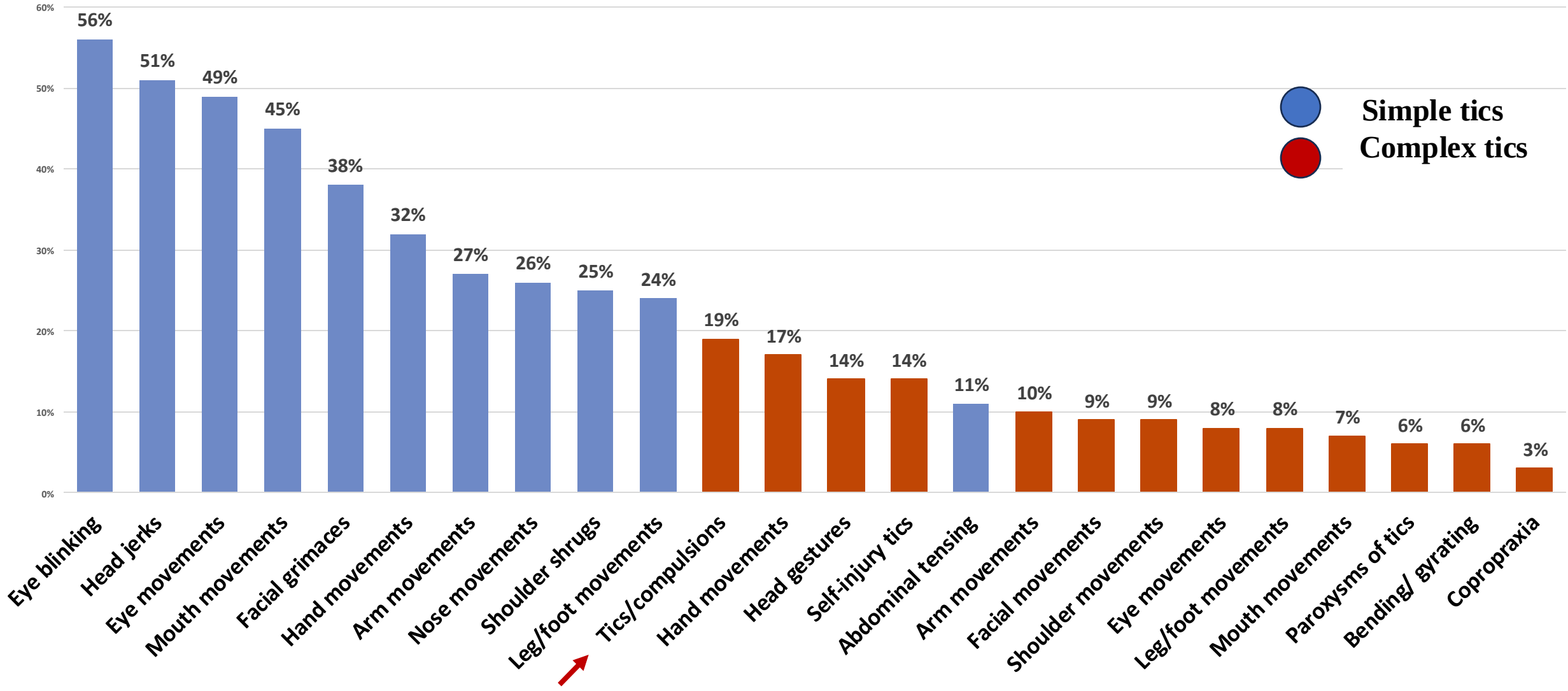
- Detailed tic inventory – different types of simple and complex tics, both motor and phonic, collected with reference to the past week
- Motor and phonic tics are rated separately on a 0-5 scale across five dimensions
  - Number
  - Frequency
  - Intensity
  - Complexity
  - Interference
- Total Tic Severity score (range 0-50) is calculated based on the sum of the motor tic score (0-25) and phonic tic score (0-25)
- Tic related impairment is assessed based on the impact that the tics have on the patient's social life, schoolwork, family life and self-esteem (0-50, by 10-point thresholds)
- Global Tic Severity Score (0-100) is the sum of the total tic severity and tic related impairment scores

Phenomenology of motor tics

- Simple
  - Clonic
  - Tonic
  - Sudden, brief, purposeless
- Complex
  - More purposeful or sustained in appearance
  - Dystonic
  - Blocking
  - May occur in orchestrated bouts
  - Rarely seen in absence of simple motor tics

- *Most patients with TS have a greater number of simple tics than complex tics, and more motor tics than vocal tics*

Prevalence of motor tics by type/location - children



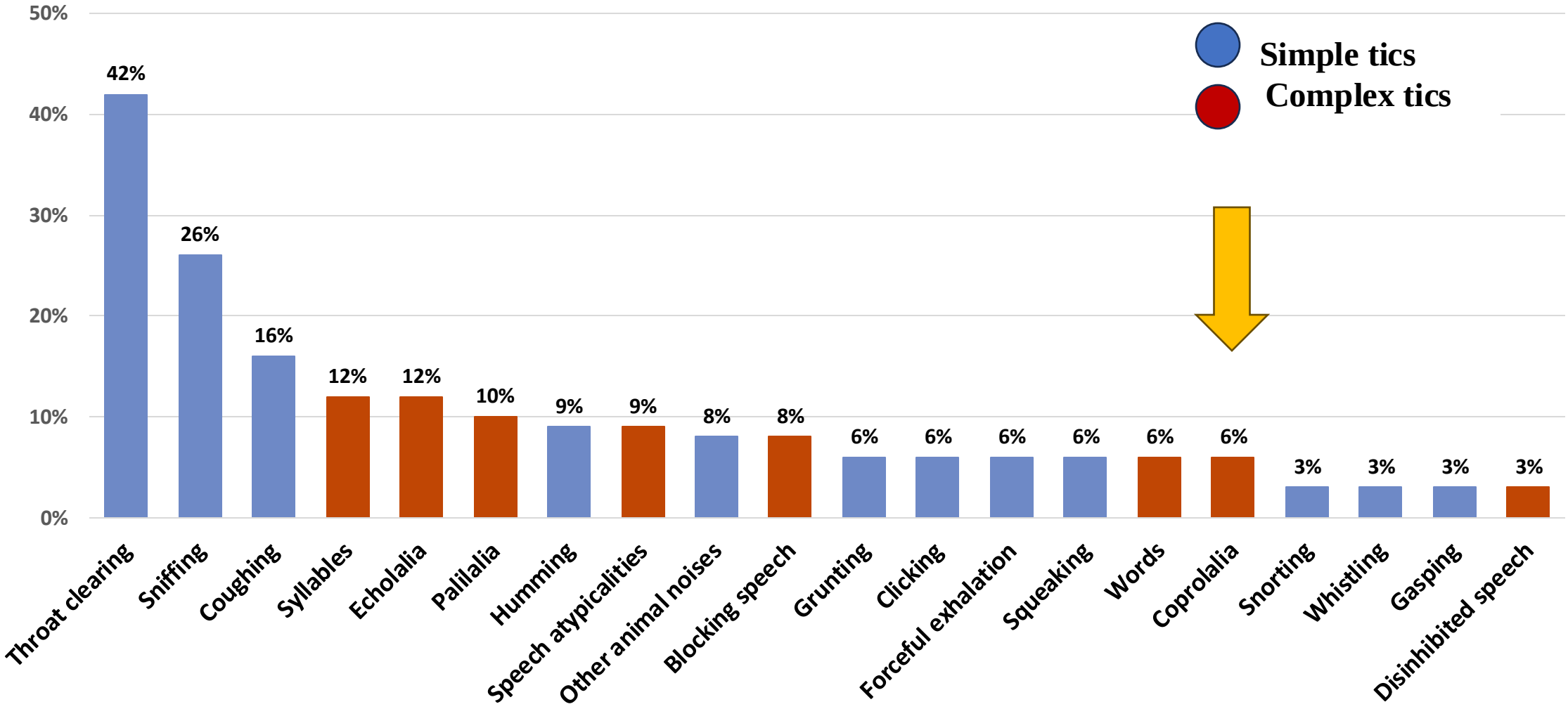
** simple tics predominate*

Data from Calgary Child Tic Disorder Registry; Nilles, Martino, Fletcher &. Pringsheim MDCP 2023

Phenomenology of Vocal Tics

- Simple vocal tics
  - Sudden, meaningless sounds or noises
- Complex vocal tics
  - Syllables, words, phrases or statements
  - Sudden changes in rate, rhythm, or volume
  - Echolalia
  - Palilalia
  - Coprolalia
    - Obscene, inappropriate and aggressive words or statements

Prevalence of vocal tics by type - children



Data from Calgary Child Tic Disorder Registry; Nilles, Martino, Fletcher & Pringsheim MDCP 2023

Getting the History of Tics

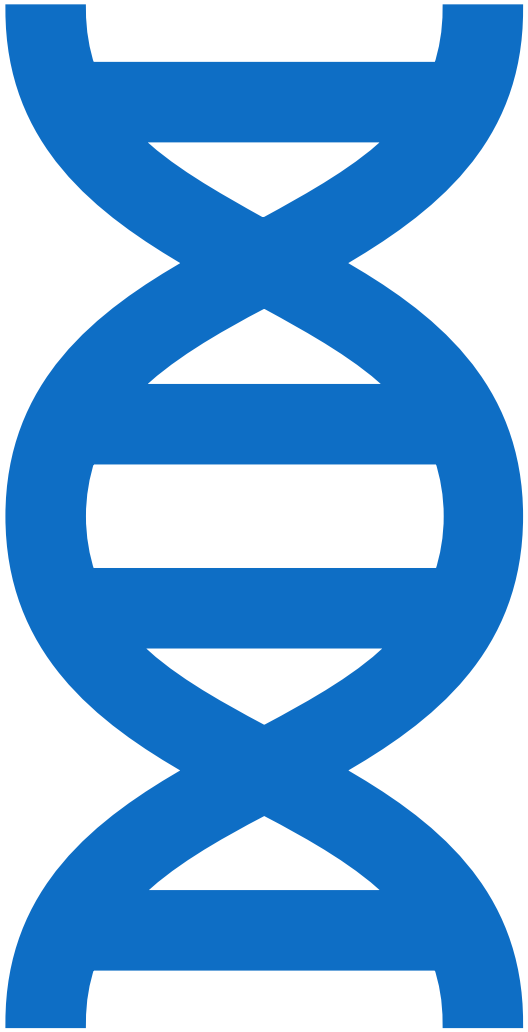
- Exacerbating factors
  - Major transitions
  - Being tired
  - Stress
  - Caffeine
  - Alcohol
- Relieving factors
  - Engagement in quiet hobbies
  - Exercise/sports
  - Playing music/singing (alone)

Neurological Examination

- Intermittent tics
  - Stereotyped/faithfully reproduced
- Distractibility
  - During examination of eye movements, visual fields, finger-nose
- Suggestibility
  - During tic inventory
- Suppressibility
  - 1 minute suppression test

Neurobiology of tic disorders

- Neurochemical and neuroimaging studies suggest dysfunction of the dopaminergic pathways in the cortico-striato-cortico-frontal circuitry
- Other neurotransmitter systems implicated – glutamatergic, GABA-ergic, noradrenergic, histaminergic pathways
- Highly heritable but genetically heterogenous condition
- Environmental factors may play a contributory role
    - Autoimmune dysfunction
    - Pre/perinatal adversity



Epidemiology of Tourette Disorder

- 7.7 per 1000 of school age children (based on meta-analysis of population-based prevalence studies)
- Male to female ratio 3:1
- Prevalence in adolescents and adults
  - Canadian population-based study of diagnosed Tourette syndrome, using the Canadian Community Health Survey
    - Youth 12-17
      - Males 6 per 1000
      - Females 0.48 per 1000
    - Adults
      - Males 0.89 per 1000
      - Females 0.44 per 1000
  - Prevalence risk ratio for males 5.31 (95% CI 2.38-11.81) in youth, compared to 1.93 (95% CI 1.21-3.08) in adults (p=0.03)

The Prevalence of Diagnosed Tourette Syndrome in Canada: A National Population-Based Study

Jaeun Yang, BSc,[1] Lauren Hirsch, BSc,[2] Davide Martino, MD, PhD,[3,4] Nathalie Jette, MD,[2,5] Jodie Roberts, BSc,[2,5] and Tamara Pringsheim, MD[2,5,6*]

NEW RESEARCH

Course of Tourette Syndrome and Comorbidities in a Large Prospective Clinical Study

Camilla Groth, MD, Nanette Mol Debes, MD, PhD, Charlotte Ulrikka Rask, MD, PhD, Theis Lange, PhD, MSc, Liselotte Skov, MSc

- Prospective follow-up study describes the clinical course of tics and co-morbidities during adolescence
- Clinical cohort from the Danish National Tourette Clinic
- Data collected at baseline (n=314, age 5-19 years) and at follow-up 6 years later (n=227), to establish the persistence and severity of tics and comorbidities

Groth 2017, Course of TS

- Prospective study conducted in two phases
- T1 2005-2007
  - All children meeting diagnostic criteria for TS invited to participate; 314/376 entered study
- T2 2011-2013
  - 227/314 participants re-examined
  - No significant differences in age, sex, socioeconomic status, tic and OCD severity, IQ, presence of OCD or ADHD or family history in those who participated at T2 and those who declined

Groth 2017, Course of TS

- Assessments at T1 and T2
  - Tics – YGTSS
    - Minimal tics 1-9
    - Mild tics 10-19
    - Moderate tics 20-39
    - Severe tics 40+
- T1 occurred at mean age of 12.4 years (SD 2.8, range 5.3-19.8)
- T2 occurred 4 to 8 years later (median 5.6), at mean age of 18.5 years (SD 2.8, range 11.1-25.9)
- 227 of 314 re-examined; 212 in clinic, 15 by telephone
  - Females 18%
  - Caucasians 98%

Groth 2017, Course of TS

- Tics
- Between the ages of 6 and 26 years, tics showed an age-related yearly decline of 0.8 points (95% CI 0.58-1.01, p <0.001) on the YGTSS
- Tic severity assessments at age > 16 years
  - Absent 18%
  - Minimal 22%
  - Mild 37%
  - Moderate 22%
  - Severe 1%

Behav Ther. 2022 November ; 53(6): 1250–1264. doi:10.1016/j.beth.2022.07.002.

Childhood Predictors of Long-term Tic Severity and Tic Impairment in Tourette's Disorder

Emily J. Ricketts, Ph.D.[a], Douglas W. Woods, Ph.D.[b], Flint M. Espil, Ph.D.[c], Joseph F. McGuire, Ph.D.[d], Jordan T. Stiede, M.S.[b], Jennifer Schild, M.S.[e,f], Mina Yadegar, Psy.D.[g], Shannon M. Bennett, Ph.D.[e], Matthew W. Specht, Ph.D.[e], Susanna Chang, Ph.D.[a], Lawrence Scahill, M.S.N., Ph.D.[h], Sabine Wilhelm, Ph.D.[i], Alan L. Peterson, Ph.D.[j], John T. Walkup, M.D.[k,l], John Piacentini, Ph.D.[a]

- 80 adolescents and adults aged 16 to 30 who participated in a long-term follow-up evaluation of the randomized controlled comparison of CBIT and Psychoeducation & Supportive Therapy in childhood
- Follow-up occurred 11.17 years after treatment
- Mean age at follow-up of 22.9 years; 75% male, 86% Caucasian

Ricketts 2022, Childhood Predictors

- Participants completed initial baseline assessment as part of clinical trial
- Independent evaluators performed assessments of
  - Psychiatric diagnoses
  - Tic severity (YGTSS)
  - Tic impairment (YGTSS)
- Parents provided demographic information, medical history, rated tic severity (Parent Tic Questionnaire), and internalizing and externalizing symptoms (CBCL)
- Youth rate premonitory urge severity (PUTS) and family functioning (BFAM-III)

Ricketts 2022, Childhood Predictors

- 80 of the original 126 participants in the trial participated in the follow-up study
- YGTSS administered
- Multiple linear regression with backward elimination was performed to identify the most important baseline variables predicting clinician-rated tic severity and tic impairment at 11-year follow-up, after controlling for tic treatment effects

Ricketts 2022, Childhood Predictors

- Baseline predictors determined a priori
- Sex
- Medication status
  - Tic medication
  - Stimulant medication
- Tic phenomenology
  - PTQ, PUTS
- Comorbidity
  - CBCL internalizing and externalizing totals
- Family functioning
  - B-FAM-III total

Ricketts 2022, Childhood Predictors

- Baseline predictors of tic severity at 11-year follow-up
  - Female sex and having higher parent-reported tic severity in childhood were associated with greater clinician-rated tic severity in adulthood
- Baseline predictors of tic impairment at 11-year follow-up
  - Female sex, no stimulant medication use, and having higher parent-reported tic severity and poorer family functioning in childhood were the most relevant predictors of tic impairment in adulthood

Phenomenology of tics in adults

- Very few descriptions of phenomenology in adult patients
- Small samples (40-60 patients), retrospective designs

Adult tics in Gilles de la Tourette's syndrome:
Description and risk factors

C.G. Goetz, MD; C.M. Tanner, MD; G.T. Stebbins, PhD; G. Leipzig, MD; and W.C. Carr, MD

Comparison of Tic Characteristics Between Children and Adults

Esther Cubo,* MD, PhD,[1,2] Teresa Chmura, BS,[1] and Christopher G. Goetz, MD[1]

Tourette's Syndrome in Adults

Joseph Jankovic, MD,* Rose Gelineau-Kattner, BS, and Anthony Davidson, BS

Adult tics in Gilles de la Tourette's syndrome:

Description and risk factors

C.G. Goetz, MD; C.M. Tanner, MD; G.T. Stebbins, PhD; G. Leipzig, MD; and W.C. Carr, MD

- Studied 58 adults with TS diagnosed during childhood
- Cross-sectional study, with retrospective assessment of childhood features
- Tics caused minimal to mild impairment; no one with extreme disability
- Only 26% continued to receive medical care for tics
- Factors associated with mild tics in adulthood were mild tics at worst period, mild tics in adolescence

Table 1. Adult manifestations of Gilles de la Tourette's syndrome (58 subjects): Data derived from Historical section of the Unified Tic Rating Scale

	Motor tics	Vocal tics
Presence of any tics	91%	66%
Tics multiple in type	79%	34%
Tics continual throughout the day	21%	12%
Tics draw attention to subject	21%	7%
Tics inappropriate, bizarre, obscene	9%	4%
Tics frequently interrupt actions	12%	29%
Tics complex in character	63%	84%
UTRS Historical score: median	10.5	5.0

Disability	Adult
LeWitt scale: median	80
Yale scale: median	10
Shapiro scale: median	0

Comparison of Tic Characteristics Between Children and Adults

Esther Cubo,* MD, PhD,[1,2] Teresa Chmura, BS,[1] and Christopher G. Goetz, MD[1]

- Video and chart retrospective longitudinal review
- Compared 40 children to 31 adults
- Tic phenomenology and severity in adults were similar to children
- More adults received treatment for tics

	Children N = 40	Adults N = 31	Comparison of adults vs. children *P* value
Gender			
Male/female	33/7	28/3	–
Diagnosis frequency (%)			
TS syndrome	31 (78)	24 (77)	0.56
Chronic motor tics	1 (2)	2 (7)	–
Chronic vocal tics	0	1 (3)	–
Secondary tics	0	4 (13)	–
Transitory motor/vocal tics	8 (20)	0	–
Comorbidities (%)			
OCD	11 (28)	14 (45)	0.10
ADHD	22 (55)	8 (26)	0.02
Anxiety/depression	8 (20)	16 (52)	0.011
Sleep disorders	2 (5)	7 (23)	–
Bipolar disorders	0	1 (3)	–
Treatment (%)			
Clonidine	6 (15)	1 (3)	–
Tetrabenazine	0	0	–
Pimozide	4 (10)	4 (13)	–
Haloperidol	1 (2)	3 (10)	–
Risperidone	5 (12)	3 (10)	–
Quetiapine	1 (2)	2 (6)	–
Aripiprazole	0	0	–
Olanzapine	0	0	–
Fluphenazine	0	2 (6)	–
Ziprasidone	1 (2)	0	–
Antidepressants/Anxiolitics	11 (28)	18 (58)	0.014
ADHD drugs	12 (30)	3 (10)	0.04
No treatment for tics	20 (50)	6 (19)	0.012
Baseline tic severity			
YGTSS score, mean (SD)	27.6 (10.9)	34.4 (16.4)	0.23
MRVRS score, mean (SD)	6.41 (3.10)	7.71 (3.93)	0.11
Tic localization (%)			
Eyes	24 (62)	17 (55)	0.37
Nose	16 (41)	12 (39)	0.54
Mouth	20 (51)	14 (45)	0.37
Neck	18 (46)	18 (58)	0.15
Shoulders	22 (56)	14 (45)	0.21
Arms	6 (15)	6 (19)	–
Hands	6 (15)	3 (10)	–
Trunk	7 (18)	9 (29)	–
Pelvis	1 (3)	2 (6)	–
Legs	6 (15)	4 (13)	–
Feet	3 (8)	0	–
Number of anatomical regions affected by tics			
Mean (SD)	3.31 (2.17)	3.20 (1.72)	0.94
Median (range)	3 (0–9)	4 (0–6)	
Vocal/motor tic severity			
Mean (SD)	2.64 (1.38)	2.78 (1.35)	0.51
MRVRS, Motor Tics subscore	0.48 (0.79)	0.97 (1.34)	0.10
MRVRS, Vocal Tics subscore			

Tourette's Syndrome in Adults

Joseph Jankovic, MD,* Rose Gelineau-Kattner, BS, and Anthony Davidson, BS

- Retrospective review of all patients (n=43) diagnosed with tics who were 19 years or older, presenting in the last 5 years
  - 35/43 had tic onset in childhood
- Comparison with 100 children
- Adults with tics had more facial and truncal tics

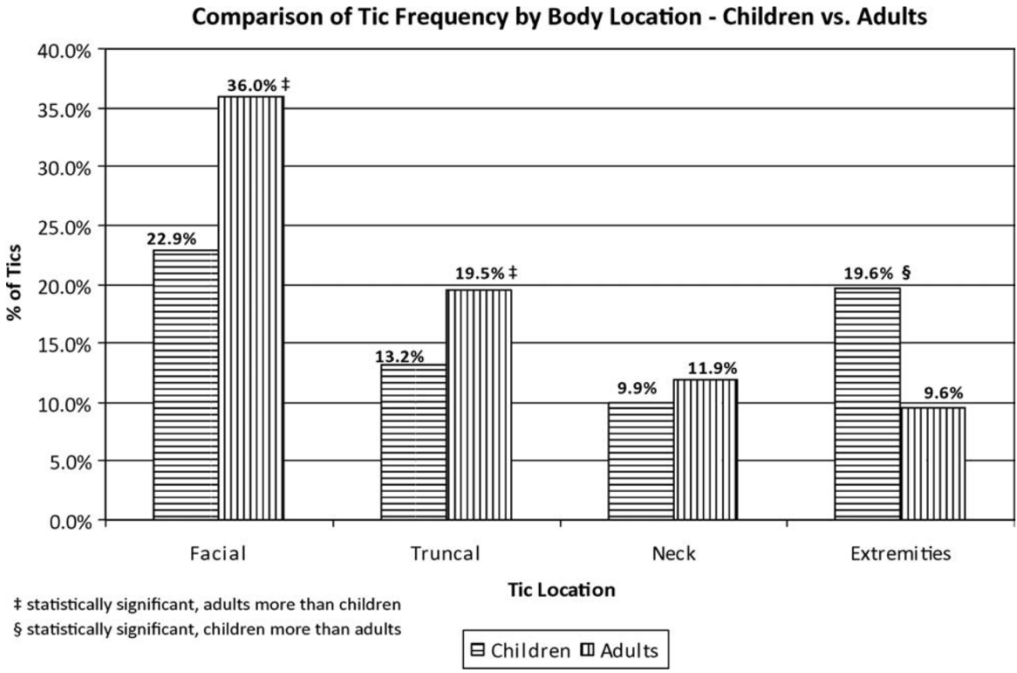


FIG. 2. Frequency of tics according to anatomic distribution.

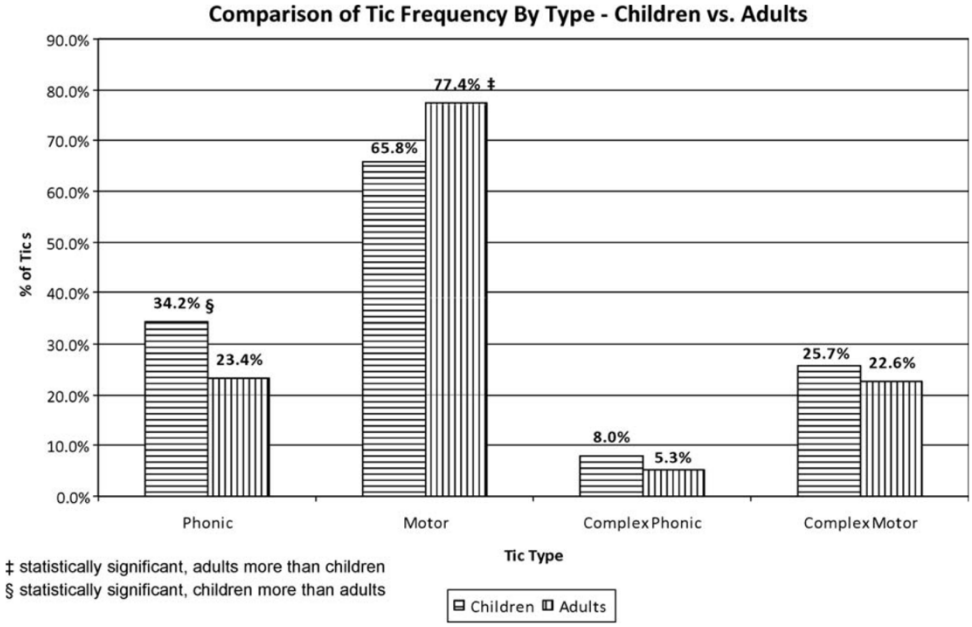


FIG. 3. Frequency of tics by type.

Calgary & Paris Adult Tic Disorder Registry

- Launched in 2021
- Prospective longitudinal study over 1 year
- Joint project with the Tourette National Reference Centre in Paris
- Purpose:

1. Characterize the relationship between tic severity and tic-related impairment in women compared to men
2. Describe tic phenomenology in adults
3. Standardize screening methods for comorbid conditions
4. Create a source of potential participants for research studies

Calgary Adult Tic Disorder Registry

- Total participants recruited to date n=165
- Sex
  - Males 77 (46.7%)
  - Females 88 (53.3%)
- Mean age at enrolment 29.5 years, range 17-72
- Primary tic disorder n=108 (65%)
- Tic disorder diagnosis
  - Tourette syndrome 93 (56.4%)
  - Persistent motor tic disorder 14 (8.5%)
  - Persistent vocal tic disorder 1 (0.6%)
  - Functional tic like behaviours 51 (30.9%)
  - Adult-onset tic disorder 5 (3%)
  - Secondary tic disorder 1 (0.6%)

Primary Tic Disorders (n=108)

Mean age at enrolment 32.2 years, range 17-72

Precise age at onset (available for 82/108) 8.3 years, range 3-16

Sex

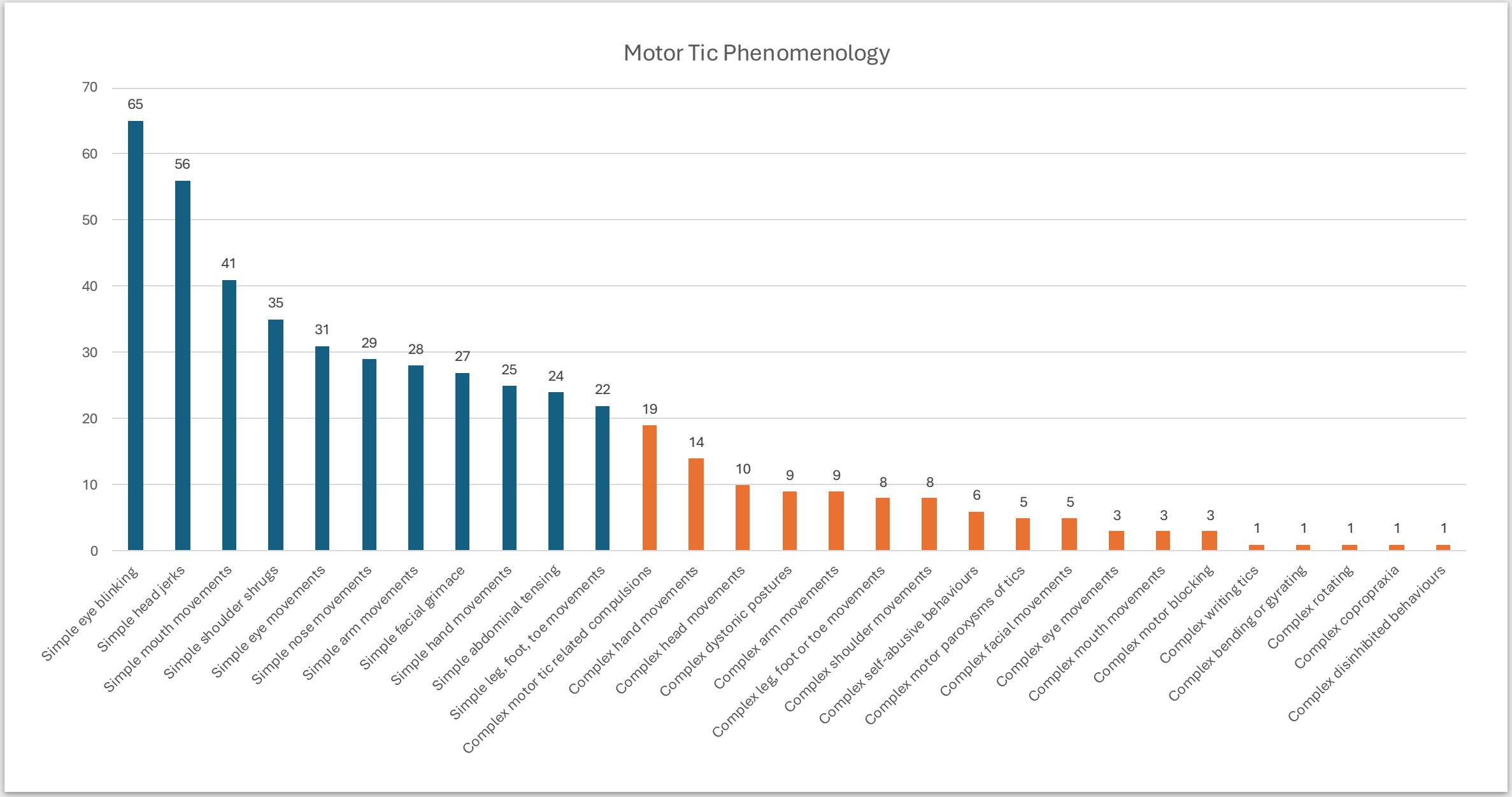
- Males 69 (63.9%)
- Females 39 (36.1%)

Comorbid disorders

- ADHD 48 (44.4%)
- OCD 27 (25%)
- Depression 37 (34.3%)
- Anxiety (45.4%)
- Autism (6.5%)

Depression & anxiety in adults vs children with Tourette syndrome

- Both anxiety disorders and depression increase in adults with TS compared to children
- From the Calgary registries
  - Adults
    - Depression 34%
    - Anxiety 45%
  - Children
    - Depression 4%
    - Anxiety 19%


Motor Tic Phenomenology
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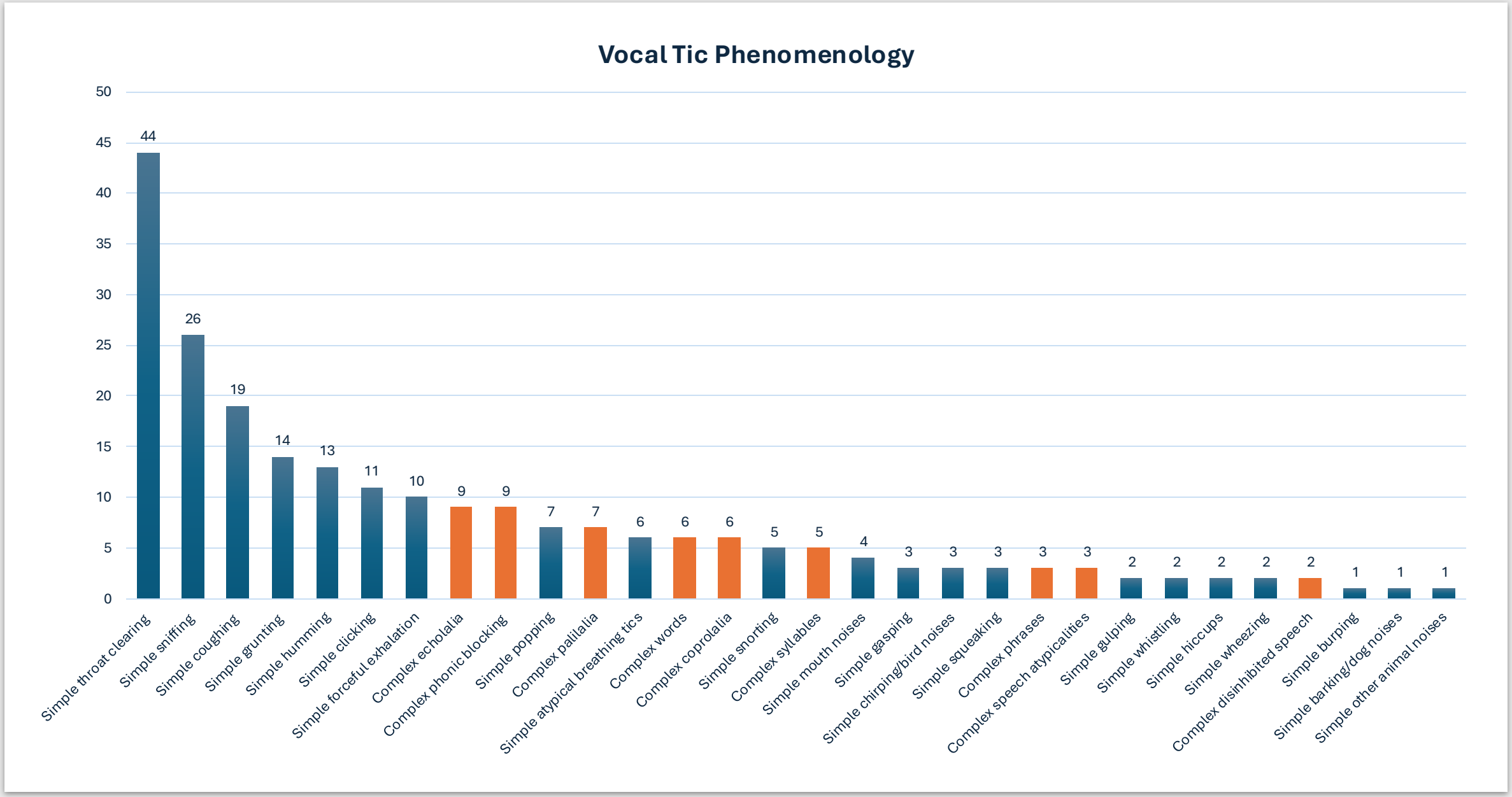
1
Simple eye blinking
Simple head jerks
Simple mouth movements
Simple shoulder shrugs
Simple eye movements
Simple nose movements
Simple arm movements
Simple facial grimace
Simple hand movements
Simple abdominal tensing
Simple leg, foot, toe movements
Complex motor tic related compulsions
Complex hand movements
Complex head movements
Complex dystonic postures
Complex arm movements
Complex leg, foot or toe movements
Complex shoulder movements
Complex self-abusive behaviours
Complex motor paroxysms of tics
Complex facial movements
Complex eye movements
Complex mouth movements
Complex motor blocking
Complex writing tics
Complex bending or gyrating
Complex rotating
Complex copropraxia
Complex disinhibited behaviours


Vocal Tic Phenomenology
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Simple throat clearing
Simple sniffing
Simple coughing
Simple grunting
Simple humming
Simple clicking
Simple forceful exhalation
Complex echolalia
Complex phonic blocking
Simple popping
Complex palilalia
Simple atypical breathing tics
Complex words
Complex coprolalia
Simple snorting
Complex syllables
Simple mouth noises
Simple gasping
Simple chirping/bird noises
Simple squeaking
Complex phrases
Complex speech atypicalities
Simple gulping
Simple whistling
Simple hiccups
Simple wheezing
Complex disinhibited speech
Simple burping
Simple barking/dog noises
Simple other animal noises

Primary Tic Disorders in Adults

Tic severity

Yale Global Tic Severity Scale (YGTSS)

Total Motor 12.3 SD 4.7

Total Vocal 8.4 SD 5.1

Total Tic 20.7 SD 7.7

Impairment 21.2 SD 10.8

Pharmacological treatment

- Alpha agonists 15%
- Antipsychotics 20%
- Botulinum toxin injections 25%
- Topiramate 6%
- CBIT 7%
- SSRIs 31%
- Psychostimulants 19%

Comparing Symptom Severity in Males and Females

	Males	Females	P value
YGTSS Total Tic Score	19.9 (18-21.8)	22.1 (19.9-24.4)	0.07
YGTSS Impairment	20 (17.3-22.7)	23.4 (20.2-26.7)	0.06
GTS QOL Total	60.6 (55-66.3)	68.6 (61.2-75.9)	0.04
GTS Visual Analogue	65.9 (60.6-71.1)	55 (47.8-62.2)	0.007
PHQ-9	9.1 (7.5-10.7)	11.3 (9.1-13.4)	0.05
GAD7	8.3 (6.9-9.8)	11 (9.1-12.9)	0.01

Treatment of Tics

- Psychoeducation and support
- Comprehensive Behavioural Intervention for Tics
- Exposure and Response Prevention
- Alpha agonists
- Antipsychotics
- Topiramate
- Botulinum toxin injections
- Deep brain stimulation

Comprehensive systematic review summary: Treatment of tics in people with Tourette syndrome and chronic tic disorders

Tamara Pringsheim, MD, MSc, Yolanda Holler-Managan, MD, Michael S. Okun, MD, Joseph Jankovic, MD, John Piacentini, PhD, Andrea E. Cavanna, MD, PhD, Davide Martino, MD, PhD, Kirsten Müller-Vahl, MD, Douglas W. Woods, PhD, Michael Robinson, Elizabeth Jarvie, MSW, LCSW, Veit Roessner, MD, and Maryam Oskoui, MD, MSc

Correspondence
American Academy of Neurology
guidelines@aan.com

Neurology® 2019;92:907-915. doi:10.1212/WNL.0000000000007467

Practice guideline recommendations summary: Treatment of tics in people with Tourette syndrome and chronic tic disorders

Tamara Pringsheim, MD, MSc, Michael S. Okun, MD, Kirsten Müller-Vahl, MD, Davide Martino, MD, PhD, Joseph Jankovic, MD, Andrea E. Cavanna, MD, PhD, Douglas W. Woods, PhD, Michael Robinson, Elizabeth Jarvie, MSW, LCSW, Veit Roessner, MD, Maryam Oskoui, MD, Yolanda Holler-Managan, MD, and John Piacentini, PhD

Correspondence
American Academy of Neurology
guidelines@aan.com

Neurology® 2019;92:896-906. doi:10.1212/WNL.0000000000007466

Comprehensive Behavioural Intervention for Tics (CBIT)

- Manualized treatment program consisting of habit reversal therapy, relaxation training, and a functional intervention to address situations that sustain or worsen tics
- RCTs in children (age 9+) and adults demonstrate efficacy of an 8-session protocol over 10 weeks, successful open-label study in children ages 5-8 (CBIT-Jr)
- Treatment through video conferencing seems as effective as face to face
- Treatment gains are maintained for at least 6 months
- High confidence in the evidence that CBIT is more effective in reducing tics than supportive psychotherapy
- SMD 0.56, 95% CI 0.31-0.82, 2 Class I studies

Exposure and Response Prevention for Tics

- Exposure to premonitory urges without performing tics can lead to habituation to the urge
- Practice tic suppression (response prevention)
- Gradually provoke premonitory urges to make tic suppression more challenging (exposure)
- Comparative trial to CBIT suggests similar efficacy
- Trial of therapist supported online remote ERP vs psychoeducation
- ERP resulted in significantly greater improvement in tics, effect size of 0.3

Antipsychotic medications for tics

Haloperidol	3 RCTs, SMD 0.59 (95%CI 0.11-1.06), moderate confidence
Pimozide	6 RCTs, SMD 0.66 (95% CI 0.06-1.25), low confidence
Risperidone	6 RCTs, SMD 0.79 (95% CI 0.31-1.27), moderate confidence
Ziprasidone	1 RCT, SMD 1.14 (95%CI 0.32-1.97), low confidence
Tiapride	1 RCT, SMD 0.62 (95% CI 0.36-0.88), moderate confidence
Aripiprazole	3 RCTs, SMD 0.64 (95%CI 0.31-0.97), moderate confidence

Other medications for tics

Clonidine	6 RCTs, SMD 0.45 (95% CI 0.13,0.77), moderate confidence
Guanfacine	3 RCTs, SMD 0.45 (95% CI 0.03-0.87), low confidence
Topiramate	1 RCT, SMD 0.91 (95% CI 0.11-1.71), low confidence
Onabotulinum toxin injections	1 RCT, SMD 1.27 (95% CI 0.51-2.03), moderate confidence
Cannabis: THC	2 RCTs, SMD 0.62 (95% CI 0.01-1.22), low confidence

Practical tips for prescribing

Start with an alpha agonist in children, botulinum toxin injections in adults

Alpha agonists

- ADHD
- Extended-release formulations preferable
- May take 8 to 12 weeks for full effect to occur
- Must monitor BP and HR

Botulinum toxin injections

- Tics migrate less in adults
- Work very well for tics involving the face and neck
- Minimal side effects

Second generation antipsychotics second line

- Used first line if you need to get control of tics quickly
- Noticeable effect within 2 to 3 weeks at appropriate dose
- Aripiprazole if comorbid OCD, anxiety or depression
- Risperidone if comorbid behavioural problems
- Must monitor for metabolic effects, hormonal effects, and drug induced movement disorders

Practical tips for prescribing

First generation antipsychotics	Topiramate	Cannabis
• Haloperidol and pimozide work but are poorly tolerated • Fluphenazine • Must monitor for metabolic effects, hormonal effects, and drug induced movement disorders • EKGs with pimozide	• Useful in patients who have become refractory to antipsychotics • Overweight patients • Use low dose in combination with aripiprazole	• Helpful but patients cannot take THC and go to work or drive • Adults only • No data for CBD but some patients report benefit

Summary

- Tic disorders often improve in adulthood, with less than 25% of patients with tics in childhood reporting moderate or severe tics after age 16
- Female sex may be a risk factor for tic persistence in adulthood, and greater tic related impairment
- Adults with tics have a greater risk of comorbid depression and anxiety than children with tics
- Treatment options include behavioural therapy and pharmacotherapy