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Tourette's Syndrome (Myna Yadegar and Emily Ricketts, Section Editors)

Course of tic disorders over the lifespan

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ABSTRACT

Purpose of review: To summarize and update information on the course of tic disorders from childhood through later life.

Recent findings: Tics tend to improve substantially over the first year after they appear. However, contrary to widespread opinion, tics usually last longer than one year, though usually at minimal severity. Tics often wane to clinical insignificance over the teen years, possibly resurging occasionally over the lifespan. However, in an important minority of patients, tics remain clinically relevant throughout life. Tics rarely first come to clinical attention later in adulthood, but new reports describe additional such cases.

Summary: Recent publications have shown tics to persist past a few months more often than previously thought, though often at minimal severity, and recurrence after an asymptomatic period is common. The safety and efficacy of behavior therapy for tics, together with prospective indicators of early prognosis, make feasible the possibility of bettering the lifetime course of tic disorders with early intervention.

Keywords: tic disorders; Provisional Tic Disorder; Tourette syndrome; prognosis; recurrence; spontaneous remission; adult; outcome

INTRODUCTION

Tics are sudden, brief, recurrent, non-rhythmic movements or vocalizations [1]. They occur frequently in childhood: most experts agree that at least 20% of all children will have a tic at some point, though the true lifetime prevalence is probably closer to 75% [see Appendix 3 in ref. 2]. When tics have not yet lasted a year, provisional tic disorder (PTD) can be diagnosed, while tics occurring at least a year after the first tic are generally diagnosed as persistent (chronic) motor or vocal tic disorder (CTD) or Tourette syndrome (TS) [3]. All these diagnoses require onset before age 18 years.

The earliest medical descriptions of TS in the late 19th century conceptualized it as a chronic, incurable and even degenerative illness [4 (pp. 3-10)]. However, the cases those authors described actually included various ages of onset, fluctuations in severity over time, and, often, improvement after adolescence. Later work has borne out these nuances. Here we review the existing evidence about the course of tic disorders from their earliest symptoms to their persistence into, or recurrence in, later life.

One caveat to note at the outset is that we cannot yet answer definitively some important questions about the natural history of TS. Such questions ideally require prospective, longitudinal studies, which are difficult and expensive, and hence rare. Several features of tic disorders also contribute to the difficulty in accurately describing course over the lifespan. First, much of the available information comes from studies of patient samples, *i.e.*, those with symptoms severe enough to lead them to clinical care. This recruitment approach is reasonable both from a practical standpoint and from the point of view that these are exactly the people for whom tics may be most relevant. However, this approach also biases results. Second, many people with tics are unaware of their tics, and teachers and family members may not notice them either [5, 6, Appendix 2 in ref. 2]. Third, tics fluctuate in intensity from time to time and from one situation to another, and may not be manifest during a visit to the doctor even if they

are common during the preceding week. Therefore, some studies tell us more than others about the course of tic disorders.

PREMORBID CHARACTERISTICS

Tic disorders are currently defined and diagnosed based on tics alone. However, most people with tics, especially most patients with tics, also have other symptoms. Some of these tend to predate tics, thus comprising prodromal features, or early evidence of the brain dysfunction that later will cause tics. Hirschtritt et al. retrospectively dated the onset of various psychiatric disorders in a large sample of patients with TS [7]. The median age of onset was earlier for Attention-Deficit/Hyperactivity Disorder (ADHD), disruptive behavior disorders, and elimination disorders (all around age 5) than for TS (about age 6). Anxiety disorders and obsessive–compulsive disorder (OCD) had a later median age of onset (~age 7) in these TS patients, but a quarter to half of the time began before age 6. In a retrospective study of over 500 adults, ADHD preceded TS by an average of 6.3 years [8].

TICS BEGIN: PROVISIONAL TIC DISORDER

Usually tics appear around ages 5-9. An epidemiological study found that earlier age of onset is more likely in children who will later be diagnosed with TS compared to those who will eventually be diagnosed with persistent motor tic disorder or whose tics fade within the first year after onset [9]. Patient records in a specialized TS clinic, however, showed no such relationship [10].

Four years ago, we reviewed evidence about how often PTD permanently remitted [2]. The best available estimate of permanent remission of tics after tics initially appeared was only 32%. About half the data for that estimate (*N*=58) came from the follow-up study of Bruun and Budman [11]. Since that review appeared, the "New Tics" project in our lab has produced important, surprising information on this topic [12]. This study recruits children who have exhibited tics for an average of only 3-4 months, via extensive advertising in addition to clinical referrals. Initial follow-up occurs at the 12-month anniversary of the first tic. The most relevant finding is that all of the first 39 children to return for follow-up still had tics at 12 months, so

that all now had DSM–5 Tourette's Disorder or CTD [13]. These results disproved the previous consensus that recent-onset tic disorders usually disappear within a few months. However, in several of these children, tics were apparent only when observing the child alone via remote video. In these children, doctors would not note tics at a typical clinical visit. In addition, in some cases the child or parent was unaware of the tics. Finally, tic severity had diminished in the majority of participants, even those who were still aware of the tics. Only 10% of families were planning to seek any further clinical care for the tics. Thus these results do not contradict the previous clinical observations, once one considers the ascertainment bias and limited observation inherent in clinical follow-up.

OUTCOME AFTER DIAGNOSIS OF TOURETTE SYNDROME

Typical course in adolescence and early adulthood

On average, tics in TS peak in severity around age 10-12 and tend to improve gradually through adolescence, but individuals differ substantially in symptom progression [14, 15]. Singer summarized adolescent prognosis in the "rule of thirds," *i.e.*, by age 20 symptoms disappear in one third of patients, improve in one third, and continue in the other third [16]. The underlying data tell a somewhat more complex story.

At first blush, tics would appear to be rare in adults. A recent review of 3 studies over the past 35 years involving over 2 million participants found an overall rate of TS in adulthood of just over .01% [17]. This represents an improbable 99.8% remission rate estimated from a childhood TS prevalence of .5%. Individual follow-up studies of pediatric patients tell a different story. These studies appear in the Table, and show substantial symptomatic improvement, but a large fraction of patients with tics continuing into adulthood.

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Some studies followed up TS children/adolescents and reported the outcome in early adulthood, but the remission rates differ substantially between studies (Table). This heterogeneity may be partially due to different methods employed to assess tic outcome. One study that used a clinical interview at follow-up reported remission of tics by adulthood in more than half of the individuals [8]. By contrast, studies with direct observation tell a different

story. Müller-Vahl points out that although tics usually improve with age and impairment usually fades, most patients still have mild tics which they often may not notice [18, p. 69]. Other experts agree [11, 16, 19]. In other words, some adults with tics are unaware of their tics, so will not report them in an interview. Three studies that directly observed adults at follow-up found tics in 82%, 90% and 100% of TS patients previously diagnosed in childhood or adolescence [15, 20, 21]. Some adults reported themselves to be tic-free, but half of these still had tics on video when recorded alone [20]. Assessment in the study that reported tics in 100% of adult patients included video recording of tics while the person was seated alone [21].

Similarly, in a longitudinal study of TS, tic severity did not differ significantly at 2-year follow-up from baseline, but the proportion of participants with at least moderately severe tic-associated impairment in a life role declined from 30% to 14% [22]. Large adult epidemiological studies find TS 12 times as often if they do not require distress or impairment for diagnosis [17]. Therefore, the remission rate reported by previous studies will differ depending on the diagnostic criteria used. DSM–IV required marked distress or impairment in a life role to diagnose TS, while DSM–IV–TR and DSM–5 diagnose tic disorders regardless of impairment. The remission rate will appear much higher if diagnosis requires impairment.

To summarize this section, although tics often improve over adolescence in patients with TS, and may lose clinical importance, tics usually persist into adulthood.

Intermittent tics and remission of TS

In a large clinical sample, 97% experienced "substantial fluctuation in severity of tics" over time [4 (pp. 169-175)]. How often does "substantial fluctuation" include a temporary complete remission? In a longitudinal study that observed elementary school children monthly over 8 months, tics were observed in many children at two classroom visits separated by one or more tic-free visits [23]. We have observed a similar on-again, off-again phenomenon in an independent school setting [12]. These results may merely reflect imperfect sensitivity of brief observations to tic disorders [24], but may also reflect intermittent tics interrupted by brief remissions. In fact, the most common course (62%) in a group of children with clinically problematic tics followed to age 15-29 was one of occasional "relapses persisting for several

days" [25]. Bruun and Budman's experience led them to conclude that, rather than complete, lifelong remission of TS, "the more common course is one of occasional recurrences of mild tics throughout adult life" [11]. Data from Shapiro et al., who followed 666 patients diagnosed with DSM–III TS, support this conclusion [4 (pp. 169-175)]. Twenty-seven percent had experienced a spontaneous complete remission for at least a week. However, these remissions were generally brief: they lasted less than 6 months in two thirds of these patients, and only 3 of the first 50 patients with adequate follow-up had experienced a remission lasting more than 7 years.

Recurrence in adult life

Even TS patients with long (years to decades) remissions can experience a recurrence of tics. Schaefer and colleagues describe 16 people with TS who had experienced a clinical remission or marked improvement lasting more than 1 year, followed by symptomatic worsening as adults that led them to seek treatment again [26]. On average the "latent period" (defined by the absence or substantial reduction of tics) had lasted 16 years. Seven of the 16 had worse tics when returning for care than they recalled having as children. Five reported new substance use as a trigger for exacerbation. In some patients, childhood TS can recur even after age 60 [27, 28].

Adult-onset tics

The three common DSM–5 tic disorders (PTD, CTD, TS) require onset before age 18. However, adults sometimes present for clinical care of recent-onset tics. Some of these individuals have simply failed to recollect earlier tics. Transient childhood tics were identified after thorough questioning in 9 of 22 patients who first presented for medical care for tics reporting tic onset after age 21 [29]. These patients had tic phenomenology, family history and comorbid OCD similar to patients with known childhood onset of TS. Alternatively, those with apparent onset around age 18-25 may represent the upper tail of the distribution of age of onset of a primary chronic tic disorder. In fact, some relatives of typical TS probands report tics beginning after age 21 [30].

However, occasionally tic disorders seem truly to begin later in life [31]. Such presentations should spur a search for a neurological or systemic illness causing tics [32]. Adult patients in

whom a childhood history of tics could not be elicited were more likely to have an identified secondary cause (e.g. infection, trauma, cocaine use) [29]. Rarely, adult-onset tic disorders may be primary, but a systematic review in 2017 identified only 26 such cases in the medical literature [33]. Even these cases may not represent a different illness, as 10 (38%) of them had a family history of tics.

Quality of life

In recent years, researchers have increasingly studied quality of life in tic disorders [34]. The YGTSS impairment score correlates with the total tic score: those with more severe tics show more impairment. However, surprisingly, impairment score changes did not correlate tightly with the improvement in tics [15]. For example, in a 2-year follow-up of children with persistent tic disorder, tic impairment statistically improved, even though tic scores remained unchanged on a group level [22]. Similarly, Singer and colleagues noted that many patients' lives improve even though tics persist [16]. In one adult follow-up study of pediatric TS, "in spite of a high frequency of school and behavioral problems during development, 98% graduated high school and 90% were full-time students or fully employed" [21].

COURSE OF SYMPTOMS OTHER THAN TICS IN TS

Singer et al. also pointed out that symptoms other than tics often contribute more to quality of life than does tic severity [16, 35]. Almost 60 years ago, Torup noted that "nervous disorders were seen in from 80-100% of the children at their first visit and in about 50-80% at follow-up" [36]. "Nervous disorders" here meant "all types of behavior disturbances," including anxiety, delinquency, insomnia, nail-biting and stuttering. She found that tics were more common at follow-up in patients who still had these other disorders. Similarly, both internalizing and externalizing behavior problems improved as adolescents aged [37]. Larger studies with modern psychiatric methods further clarify the outcome of non-tic symptoms in TS. A large, 4-year study of boys with ADHD showed tics in about half by study end, and the remission rate was much higher for tics (age-adjusted rate of 65%) than for ADHD (20%) [38]. The same group obtained similar results in 36 adults with a history of tics and ADHD: tics usually improved, but

ADHD remitted even by age 60 in only ~20% [8]. A 7.6-year (mean) prospective study of 46 children with TS showed that OCD symptom severity peaked about 2 years after peak tic severity and remitted less often than did tics [39]. A large prospective study tracked tics and other symptoms for 6 years [15]. In most patients tics had improved, but not disappeared, and OCD and ADHD significantly improved during adolescence. Patients with TS also commonly report sleep problems, but these studies are generally cross-sectional [4 (pp. 286-288), 40]. Finally, recently a population registry study demonstrated suicide to be more common in adults with TS than in the general population; suicidality was not explained by other psychiatric illnesses such as major depression, but was more common in those whose tics persisted past young adult life [41].

PREDICTING AND EXPLAINING OUTCOME IN TS

Prognostic indicators present at tic onset

The New Tics project has identified several prognostic predictors of the degree of improvement between initial ascertainment and the tics' 1-year anniversary. As predicted, baseline tic severity correlated significantly with tic severity at follow-up [13]. Additional baseline clinical features predicting worse outcome included higher (but subsyndromal) scores on a rating scale for autism spectrum features (Social Responsiveness Scale [SRS]), a greater number of classic features of TS, higher scores on a measure of emotional dysregulation, presence of an anxiety disorder, and a history of three or more phonic tics. In fact, tic severity, SRS score and an anxiety disorder at baseline together explained nearly half the variance in 12-month tic severity. Also, children who at baseline suppressed tics more successfully when immediately rewarded had lower clinically rated tic severity at the 12-month follow-up visit [42]. More recently, we have identified a larger hippocampus at baseline as a significant predictor of greater tic severity at follow-up [43]. Other predictive features present near tic onset include earlier onset, phonic tics, tics below the neck, and ADHD [4 (pp. 373–374), 9, 38, 44, 45]. Each of these features is associated with greater tic severity at follow-up. Only baseline tic severity and 3 or more phonic tics in the first year have been replicated in an independent sample [2].

Prognostic indicators after diagnosis of TS

Several researchers have reported variables during adolescence that predict outcome in early adult life. The relevant studies are cited in detail elsewhere [46, 16, 47, 18, p. 69, 2]. Prospective, follow-up studies identify the following as prognostic factors present when children or adolescents with tic disorders present for care: lesser manual dexterity [48], worse performance on a "weather prediction" probabilistic classification test [49], reduced caudate volume [50], ADHD, OCD or simple phobias [45], lower socioeconomic class [4 (p. 175)], and more severe family history of TS [36, 51]. Greater tic severity in adolescents with TS may predict less improvement in tics in adulthood [39, 21], though severity *in childhood* may not predict adult outcome [21, 52].

Pathophysiology of tic improvement with age

Despite increasing efforts to understand the underlying pathophysiology of tics and tic disorders, our understanding of the mechanisms involved in the *progression* of tic symptoms with development is woeful. We can garner some clues from cross-sectional studies of children and adults with TS, generating testable hypotheses for future research. Based on these cross-sectional studies, there is some evidence that brain differences between TS and tic-free individuals vary by age. For example, one of the largest structural MRI studies of children and adults with TS revealed larger dorsal prefrontal volume in children with TS, yet smaller dorsal prefrontal volume in adults with TS (among other differences) [53]. Two studies examining brain function (fMRI) during cognitive control tasks in TS found differential age-related changes in activity in frontal and striatal brain regions [54, 55]. Using transcranial magnetic stimulation (TMS), another study found differences between children with TS and tic-free controls in measures of motor cortical excitability, but no differences in adults [56]. All of these age-related findings could reflect changes in the brain—perhaps maladaptive or perhaps compensatory—that occur over development with years of living with tics. Alternatively, such results could reflect a difference between the children whose tics persist into adulthood and the children whose tics are likely to improve into adulthood. Thus, without a longitudinal design it is difficult to assess if these brain differences truly reflect symptom progression. One

longitudinal study has examined brain volume in adolescents (11-19 years old) with and without TS, and measured brain volume again 4 years later [57]. They found that left putamen volume decreased with age in the controls, but not in TS. Interestingly, they did not detect significant differences between those individuals with TS whose tics improved with age and those whose tics did not improve. It should be noted, however, that the sample size of this study was fairly small (n=22) and the age range was wide. Thus, while this study was an important step in measuring brain changes within individuals with TS, its limitations leave important questions about the relationships between brain changes and symptom progression unanswered.

Several of the studies just described, plus others that included only one age group, have interpreted their findings in terms of altered brain maturation [56, 58, 59]. That is, the differences observed in TS may reflect delayed/immature development or even accelerated/overmature development. In a recent functional connectivity (FC) MRI study, our group used machine learning classification in a unique way to examine developmental differences in brain networks in TS [60]. Using cross-sectional data from children and adults with and without TS, we found evidence consistent with models of atypical maturation. Specifically, those functional connections that best distinguished children with and without TS (using a machine learning classifier) appeared "older" in the children with TS than in tic-free controls, suggestive of accelerated maturation. On the other hand, those functional connections that best distinguished adults with and without TS appeared "younger" in the adults with TS than in the tic-free controls, suggestive of delayed maturation. Of course, this study was cross-sectional, so inferences about brain maturation remain speculative. As mentioned above, longitudinal studies that track brain measures as well as symptoms over time are necessary to further our understanding of tic progression with development.

CONCLUSIONS

In general, the prognosis for patients with tic disorders is quite positive at the group level. Most children with tics for only a few months improve within the first year to the point of not seeking clinical care. However, tics persist in nearly all of them when observed directly or by

video alone. After tics persist for at least a year, the majority of patients even with moderately severe tics in childhood experience substantial improvement by adult years. Commonly tics wax and wane, including brief apparent remissions in many patients. Again, however, tics appear to persist in nearly all, when studies observe tics at follow-up in person or by video alone. Most patients finish secondary school and have gainful employment. Quality of life tends to improve, and often is driven more by symptoms other than tics, especially ADHD, OCD and anxiety.

On the other hand, some patients continue to experience clinically problematic tics into adulthood. Frustratingly, our ability to predict this outcome for individual patients remains quite limited. Furthermore, only a handful of studies were prospective, so that some cross-sectional features associated with tic severity may not prove to have prognostic value. However, prospective studies continue.

Further research hopefully will address these gaps in our knowledge. Additionally, the relatively recent consensus that certain behavior therapies are effective and safe treatments for tics suggests the tantalizing prospect of preventing Tourette syndrome. Specifically, when we can reasonably identify patients with recent-onset tic disorder who are most likely to experience a more severe course, intervening at that point with behavior therapy may prove to abolish tics or at least to ameliorate them. Of course, that remains a hypothesis yet to be tested.

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This article does not report new data from any studies with human or animal subjects performed by any of the authors.

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TABLE

Table. Follow-up studies of tic disorders.

Ref.	Year	N (orig.)	N (f/up)	Sample	Age (orig.) (years)	Age (f/up) (years)	Follow-up duration (y)	Assessment	Recovery	Comments
[61]	1930	49	31	Tics, C&A	n/a	n/a	(2-3)	Clinical Interview	65% free of tics.	Age of onset was ("<5"-14)
[62]	1954	53	49*	Tics, C&A	n/a	(7-18)	(1-5)	Clinical interview	24% had been free of tics for at least a year.	* "The information was sufficiently accurate for statistical analysis in only 41 cases, but since they appeared to be fairly representative of the total sample, it is doubtful whether the remaining cases would have influenced the findings to any appreciable degree." Age of onset was (3.5-12.5)

Ref.	Year	N (orig.)	N (f/up)	Sample	Age (orig.) (years)	Age (f/up) (years)	Follow-up duration (y)	Assessment	Recovery	Comments
[36]	1962	237	220	Tics, C&A	9 (2-16)	18 (6-26)	9 (1-15)	Parent interview, "most" children seen	By 6 months after first encounter: 37 remissions, 9 of which later recurred. At follow-up, tics had improved in 94%, only 20-40% had daily tics, and 50% had been tic-free for 1 year or more.	Mean age of tic cessation was "12-13 years." 90% of children with a parent who had tics in adulthood still had tics, vs. <45% of children whose parent had tics only in childhood.
[63, 64]	1976	80	78	TS, C&A	(2-16)	(6-67)	2.7 (0.6-8.6)	Clinical interview	4 patients reported a complete remission, and 6 patients experienced remission (from months to three years) followed by returning symptoms.	Those on haloperidol had a mean improvement of 79%; those on other or no medication 25%.
[65]	1987	99	58	Teens and young adults; DSM-III criteria	8 (median) ± 3.2 (2-15)	18 (median) ± 2.6 (15-25)	n/a	Self-report questionnaire	26% tics essentially gone 47% considerable improvement 14% stable 14% worsened tics	53 of 55 patients who had been treated with medications received haloperidol, and 45% of the 53 experienced major improvement.

Ref.	Year	N (orig.)	N (f/up)	Sample	Age (orig.) (years)	Age (f/up) (years)	Follow-up duration (y)	Assessment	Recovery	Comments
[4]	1988	†	50	TS; DSM-III criteria	18.9 ± 12.0 (4-69) ‡		13-20	Clinical exam with a large set of specified data points	3 of the 50 had remitted for >7 years. Of the whole sample, 27% had experienced a spontaneous complete remission of tics for at least a week (but in 2/3 of these it lasted <6 months).	†These are "the first 50 consecutive patients who were carefully followed up to the present time" from a total sample of 666 patients with DSM–III TS. See pp. 169–175 in ref. [4]. ‡Age and follow-up duration describe the total sample n=666; the stats for the subsample n=50 are not given.
[25]	1990	131	63	Tics, C&A	Modal age of onset is 7	(15-29)	n/a ¶	Clinical interview	38% recovered completely, 62% had occasional relapses lasting a few days, and 14% still had tics requiring treatment.	¶ 131 patients were hospitalized 1968-1988
[66]	1990	75	33	TS, C&A, adults	19 ± 14 (9-50)	25 ± 19 (13-59)	7 ± 4(1-15)	Clinical interview	All patients reported some sort of improvement, which was found in 70% of those treated with pimozide and 78% of those treated with haloperidol.	

Ref.	Year	N (orig.)	N (f/up)	Sample	Age (orig.) (years)	Age (f/up) (years)	Follow-up duration (y)	Assessment	Recovery	Comments
[21]	1992	93	58	Adults	n/a	21.2 ± 8.6 (21-62)	n/a	Clinical interview, direct observation	All adults still had tics.	Video of patient alone in the room. Age of tic onset 6.9 ± 2.8.
[67]	1994	126	23	TS, C&A, adults	17.7 ± 8 (7-61)	22.1 ± 11.3 (11-53)	About 5 (1989 to 1994)	Clinical interview	13% of subjects showed improvement in sum of tics subtypes and severity.	
[11]	1997	58	58	C&A, DSM-III transient tic disorder	n/a	n/a	2-14	Structured phone interview (62%), on-site interview (38%)	17% tics absent throughout follow-up period; 40% now chronic motor or vocal tic disorder; 43% chronic or episodic tics (either TS or tic disorder not otherwise specified).	
[52]	1998	42	38	TS, C&A	n/a ⁂	Phone follow-up: 11.0 ± 2.9 (5.9-16.9), in-person follow-up: 18.4 ± 1.0 (17-20)	7.3	Clinical interview	"By 18 years of age nearly half of the cohort was virtually tic-free."	Data available on 36 ⁂ All subjects born in 1975

Ref.	Year	N (orig.)	N (f/up)	Sample	Age (orig.) (years)	Age (f/up) (years)	Follow-up duration (y)	Assessment	Recovery	Comments
[68]	2001	54	39	TS, school-aged children	10.1 (3-17.9)	22.8 (14-28)	13	Structured phone interview, self-report questionnaire	44% "essentially symptom free"; 22% on medication.	
[45]	2001	976	Time 2 = 776, Time 3 = 760, Time 4 = 728	Tics, C&A	6.1 ± 2.8 (1-10)	Time 2: 13.7 ± 2.7 (9-20) Time 3: 16 ± 2.8 (11-22) Time 4: 22.1 ± 2.7 (17-28)	Time 2: 8, Time 3: 10, Time 4: 17	Clinical interview	Tics (and ADHD) decreased in prevalence throughout time.	At time 2, 54 families were lost so a representative supplemental sample was selected to replace them.
[8]	2001	45	45	Adults	ADHD with tics: 37.0 ± 11.8 No ADHD, some with tics: 39.7 ± 8.3	n/a	n/a	Clinical interview (retrospective data)	By age 20, "the age-adjusted rate of complete remission of the tic disorder was 62.2%; the unadjusted rate was 53% (N=19 of 36)."	This study used retrospective data and DSM-III-R. Their figure 1 shows a survival curve for tic remission in this sample.
[69]	2003	31	31	TS, Adults	22.8 ± 8.7 (4-33)	31.4 ± 7.6	7.6 ± 8.1 (0-26)	Chart review, clinical interview (retrospective data)	24 still had tics and 7 were in remission.	Excludes 2 additional patients in complete remission by chart review who did not return for follow-up.

Ref.	Year	N (orig.)	N (f/up)	Sample	Age (orig.) (years)	Age (f/up) (years)	Follow-up duration (y)	Assessment	Recovery	Comments
[20]	2003	56	31	TS, C&A	12.2 ± 2.2 (8-14)	16.2 ± 3.5 (20-n/a)	12	Direct observation, clinical interview	90% of adults still had tics.	
[22]	2004	50	50	TS, C&A	10.9 ± 3.4 (6-17)	n/a	2.2 ± 1.7 (0.4-5.5)	Clinical interview	82% of subjects met criteria for tic persistence (compared to 88% at baseline), but impairment was reduced substantially.	
[50]	2005	61	43	TS, C&A	11.4 ± 1.6 (8.5-13.9)	18.7 ± 1.7 (16-23)	7.5 ± 1.9 (3.8-12.8)	Clinical interview (in-person or via phone)	Few tic symptoms at follow-up, on average. 19% had tics of moderate or greater severity (YGTSS score > 20) compared to 51% initially.	Tic severity at follow-up correlated inversely with baseline caudate nucleus and right putamen volumes.
[39]	2006	64	46	TS, C&A	11.4 ± 1.6 (7.5-13.0)	19.0 ± 1.8 (16.0-22.8)	7.6 ± 1.9 (3.8-12.8)	Clinical interview	Tics had improved by adolescence in 85%. One third had a YGTSS score of 0, indicating no evidence of tics over the past week.	
[70]	2009	180	58	TS, adults	n/a	29 ± 9.8 (19-55)	n/a	Self-report questionnaire	53% improvement, 22% worsening of tics, 24% no change.	

Ref.	Year	N (orig.)	N (f/up)	Sample	Age (orig.) (years)	Age (f/up) (years)	Follow-up duration (y)	Assessment	Recovery	Comments
[71]	2015	482	83	TS, C&A	9.8 ± 3.1	25.6 ± 7.4 (18-61)	n/a	Self-report questionnaire	13.6% reported no motor tics, and 59.3% reported no vocal tics.	Initial visits were between 1972-2007
[15]	2017	314	227	C&A	12.4 ± 2.8 (5-19)	18.5 ± 2.8 (11.1-25.9)	6 (4-8)	Clinical interview	After age 16, 82% still had tics; 23% had moderate or severe tics.	
[13]	2019	43 ‖	39	PTD, C&A	8.13 ± 2.43, (5.0-10.9)	n/a	0.75 ± 0.11, (0.51-0.96)	Clinical assessment, questionnaires, video of the child alone	Every child (N=39) still had tics at the follow-up visit, though in some cases they were not aware of them, or tics manifested only when the child was alone, observed by video.	Follow-up was at the 1-year anniversary of the first tic. ‖ This line and the following line come from overlapping samples in the same study.
[42]	2019	55	45	PTD, C&A	7.74 ± 2.02 (5.03-12.9)	n/a	0.73 ± 0.13, (0.31-0.96)	Clinical assessment, questionnaires, video of the child alone		Children who were initially able to better suppress their tics in the presence of a reward showed better tic outcome at follow-up.

Ref.	Year	N (orig.)	N (f/up)	Sample	Age (orig.) (years)	Age (f/up) (years)	Follow-up duration (y)	Assessment	Recovery	Comments
[72, 73]	2020	126	80	TS; C&A	11.61 ± 2.41	n/a	Around 10 years	Clinical interview	Tics improved in both groups; acute responders to PST returned to baseline tic severity at follow-up, while CBIT responders stayed better; YGTSS impairment score was reduced in acute responders regardless of treatment and maintained at follow-up, while nonresponders eventually had similar scores as responders.	Follow-up of the large child CBIT study (preliminary reports)

Age appears as M ± SD (range) except where indicated. Ref.: reference number in bibliography. (orig.): initial sample. (f/up): at follow-up. n/a: not available. TS: Tourette syndrome. C&A: child and adolescent. PTD: Provisional tic disorder (DSM-5). CBIT: Comprehensive Behavioral Interventions for Tics. PST: Supportive psychotherapy and education.

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