

# Gilles de la Tourette syndrome: the complexities of phenotype and treatment – further information

This document contains three additional tables (Tables 1, 4 and 5) and their references for the article Robertson MM (2011) Gilles de la Tourette syndrome: the complexities of phenotype and treatment. *Br J Hosp Med* 72(2): 100–7

The author conducted a survey among UK Tourette specialists asking which drugs they prescribed for Tourette syndrome patients: the author ranked the replies (indicating which was commonly prescribed and how many ‘points’ each drug scored in the ranking). Results were as follows: aripiprazole (53 points) was the most commonly prescribed by far, followed by clonidine (41 points), then risperidone (39 points), haloperidol (23 points), amisulpiride (10 points), pimozide (6 points), tetrabenazine (4 points) and finally clonazepam (1 point). This

information is highlighted in a column in *Table 4*. A large unpublished survey in Europe undertaken on behalf of the European Society for the Study of Tourette Syndrome also demonstrated that aripiprazole is by far the most commonly prescribed medication for the tics.

Haloperidol is the only drug licensed worldwide for Tourette syndrome, but few use it as first line in USA, UK and Western Europe because of its many unacceptable side effects. It is also worth noting national differences. For example, tiapride is available in all Europe apart from the UK, while sulpiride is available in only the UK and neither drug is available in the USA: the author knows of several American or Canadian practitioners who import sulpiride for use in their (private) practices. Tiapride is the most prescribed medication in Russia. [BJHM](#)

**Table 1. Standardized schedules and rating scales used to assess aspects of Tourette syndrome**

Scale (abbreviation)	Reference	Comments
Yale Global Tic Severity Scale (YGTSS)	Leckman et al (1989)	Clinician-rated severity scale gold standard
MOVES (MOVES)	Gaffney et al (1994)	Self-report, not useful in young children
Hopkins Motor and Vocal Tic Severity Scale (Hopkins Scale)	Walkup et al (1992)	Clinician-rated severity scale
Premonitory Urges Scale (PUTS)	Woods et al (2005)	Self-report – giving information about premonitory sensations
Tourette syndrome-specific health related-quality of life scale (GTS-QOL)	Cavanna et al (2008)	Self-report Tourette syndrome-specific quality of life scale (adults only)
Diagnostic Confidence Index (DCI)	Robertson et al (1999)	Clinician-rated, gives lifetime probability of diagnosis
National Hospital Interview Schedule (NHIS)	Robertson and Eapen (1996)	Standardized interview to obtain family history and to diagnose Tourette syndrome, attention deficit hyperactivity disorder, obsessive compulsive behaviours, obsessive compulsive disorder, oppositional defiant disorder, conduct disorder
Tourette syndrome Videotaped Scale (Rush Video)	Goetz et al (1987)	Mainly used in research as standardized videos are used
Obsessive–Compulsive Inventory – revised (O-C Inventory (R))	Foa et al (2002)	Self-report inventory to measure obsessive compulsive symptoms
Social and communication disorders checklist	Skuse et al (2008)	Useful screening scale for presence of social communication disorders
Beck Depression Rating scale (BDRS)	Beck et al (1961)	Self-report adult depression scale
Birleson Child Depression Rating scale (Birleson)	Birleson (1981)	Self-report young person’s depression scale

**Table 4. Management of the motor and vocal/phonic tics of Tourette syndrome**

Treatment modality	Level of empirical support*	References	Rank order (no of points scored) for UK prescription†	Comments	
<b>Antipsychotics</b>	Haloperidol	A	Ross and Moldofsky (1978) Shapiro et al (1989) Sallee et al (1997)	4 (23) Used worldwide and in many countries, Only drug licensed for Tourette syndrome Many adverse side effects	
	Risperidone	A	Dion et al (2001), Gaffney et al (2002) Bruggeman et al (2001) Scahill et al (2003)	3 (39) Randomized controlled trials in both adults and children Subsequently reports of serious adverse effects = increase in weight and glucose abnormalities (diabetes)	
	Pimozide	A	Ross and Moldofsky (1978) Sallee et al (1997)	6 (6)	Pimozide and haloperidol = efficacy Pimozide less adverse side effects than haloperidol Some reports of prolonged QTC interval with pimozide (difficult with polypharmacy)
			Regeur et al (1986) (LC)		Series of 65 cases
			Pringsheim and Marras		Cochrane Review says effective, but more studies with better methods suggested. Author suggests not an appropriate choice of treatment
	Sulpiride	B	George et al (1993) (DBT)	3 (39)	Case series on 60 patients Case series on 189 patients, sulpiride improved motor and vocal tics and significantly reduced the Yale Global Tic Severity Scale: few side effects (sedation = 16%)
			Yvonneau and Bezard (1970) (SCS)		
			Robertson et al (1990) (LC)		
			Ho et al (2009) (LC)		
	Tiapride	C	Eggers et al (1988) (DBT)		10 patients
	Ziprasidone	C	Sallee et al (2000) (DBT)		Some deaths reported subsequently
	Aripiprazole	C	See Table 5	1† (53)	Becoming first-line treatment in many dedicated Tourette syndrome clinics in UK and Europe (222 patients successfully documented to date)
	Metaclopramide	C	Nicolson et al (2005) (DBT)		Small study
	Ondansetron	C	Toren et al (2005) (DBT)		Small study
Fluphenazine	D	Goetz et al (1984)		16/21 patients, intolerant of previous haloperidol, responded well and/or had fewer side effects when taking fluphenazine	
Olanzapine	D	Stephens et al (2004)		Single blind	
		McCracken et al (2008), Van den Eynde et al (2005), Margoese et al (2002) Meyer (2002), Lucas Taracena et al (2002), Budman et al (2001), Onofrij et al (2000), Stamenkovic et al (2000)		In total less than 50 Tourette syndrome patients have been treated with olanzapine and published	
Quetiapine	D	De Jonge et al (2007), Neves Ramos et al (2007), Copur et al (2007), Mukaddes and Abali (2003), Schaller and Behar (2002), Parraga et al (2001), Matur and Uçok (2003)		All open label or small case series In total about 40 patients with Tourette syndrome have been successfully treated with quetiapine and published	
Amisulpiride	D	Trillet et al (1990) Fountoulakis et al (2004)	5 (10)	Only small case series	

\* A=good (two or three double blind trials), B = adequate (one double blind trial and other evidence, e.g. series total > 150 patients), C = fair (one double blind trial only, or open label or series, case reports (< 150 patients)), D = minimal (only case reports; small series). † for full explanation, see text on p. S1. CR = Cochrane review; DBT = double-blind trials; LC = large cohort; MA = meta-analysis; SCS = small case series. Updated and modified from Scahill et al (2006)

**Table 4. Management of the motor and vocal/phonic tics of Tourette syndrome (continued)**

Treatment modality		Level of empirical support *	References	Rank order (no of points scored) for UK prescription†	Comments	
<b>Other medications</b>	Clonidine	A	Goetz et al (1987) (DBT)	2 (41)	Tablets	
			TS Study Group (2002) (DBT)			
			Gaffney et al (2002) (DBT)			
				Hedderick et al (2009) (DBT)		
				Du et al (2008) (DBT)		Transdermal patch
				Kang et al (2009) (DBT)		
				Bloch et al (2009) (MA)		
	Botulinum toxin	B	Marras et al (2001) (DBT)		Decreased tics, decreased urges, patients not satisfied 450 patients (many responded well) 30 patients – open label – decreased tics, decreased urges, increased quality of life; hypophonia in 80%	
			Awaad (1999) (LC)			
			Porta et al (2004) (LC)			
			Scott et al (1996)			
			Salloway et al (1996) (SCS)			
			Trimble et al (1998) (SCS)			
				Kwak et al (2000) (SCS)		
				Vincent (2008) (SCS)		
Atomoxetine	B	Allen et al (2005) Spencer et al (2008)		Double blind trials (attention deficit hyperactivity disorder and tics reduced but attention deficit hyperactivity disorder more so)		
Topiramate	C	Jankovic et al (2010) (DBT)				
Nicotine	C	Silver et al (2001a) (DBT)				
		Dursun et al (1994) (SCS)				
Mecylamine	C	Silver et al (2001b) (DBT)				
		Silver et al (2000) (SCS)				
Baclofen	C	Singer et al (2001) (DBT)		Only 10 patients		
		Awaad (1999)		250/264 improved with baclofen		
Guanfacine	C	Scahill et al (2001) (DBT)				
		Chappell et al (1995) (SCS)				
Pergolide	C	Gilbert et al (2000) (DBT)		24 youngsters		
		Lipinski et al (1997)		Small open-label trial		
Naltrexone	C	Kurlan et al (1991) (DBT)		Naltrexone significantly reduced tics		
Levetiracetam	D	Smith-Hicks et al (2007) (DBT)		n=22 – not useful		
		Hedderick et al (2009) (DBT)		n=12 – not useful		
		Fernandez-Jaen et al (2009)		Open-label study; n=29		
		Awaad et al (2005)		n=60 – useful		
		Oulis et al (2008)		n=1		
		Seijo-Martinez et al (2008)		n=1		
Tetrabenazine	D	Jankovic et al (1984)	7	n=9		
		Porta et al (2008) (LC)		n= 77		
Clonazepam	D	Merikangas et al (1985)	8 (1)	Single-blind		
		Gonce and Barbeau (1987)		Add on		

\* A=good (two or three double blind trials), B = adequate (one double blind trial and other evidence, e.g. series total > 150 patients), C = fair (one double blind trial only, or open label or series, case reports (< 150 patients)), D = minimal (only case reports; small series). † for full explanation, see text on p. S1. CR = Cochrane review; DBT = double-blind trials; LC = large cohort; MA = meta-analysis; SCS = small case series. Updated and modified from Scahill et al (2006)

**Table 4. Management of the motor and vocal/phonic tics of Tourette syndrome (continued)**

Treatment modality	Level of empirical support*	References	Rank order (no of points scored) for UK prescription†	Comments
Other treatments	Cannabinoids	D	Müller-Vahl et al (2001), Müller-Vahl (2003), Curtis et al (2009) (CR)	Reduced tics and did not produce cognitive impairment Systematic review showed it was not useful
	Transcranial magnetic stimulation	D	Mantovani et al (2006)	First study to show some benefit
Psychological treatments	Habit reversal training	A	Azrin and Peterson (1990) (DBT)	Double blind and randomized controlled trials indicated that habit reversal training was better than psychotherapy and the waiting list
			O'Connor et al (2001) (DBT)	
			Wilhelm et al (2003)	
			Verdellen et al (2004)	
Neurosurgery	Ablative	E		No trials – few cases
	Deep brain stimulation	C or D	Maciunas et al (2007) (DBT) Welter et al (2008) (DBT) Hariz and Robertson (2010) (review)	Two small double blind trials  50–55 cases, 19 centres, 9 targets, targets as yet under debate; ideally research based only at present

\* A=good (two or three double blind trials), B = adequate (one double blind trial and other evidence, e.g. series total > 150 patients), C = fair (one double blind trial only, or open label or series, case reports (< 150 patients)), D = minimal (only case reports; small series). † for full explanation, see text on p. S1. CR = Cochrane review; DBT = double-blind trials; LC = large cohort; MA = meta-analysis; SCS = small case series. Updated and modified from Scahill et al (2006)

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**Table 5. Aripiprazole in Tourette syndrome (2004–2010)**

Reference	No. of patients	Country
Cui et al (2010)	72	China
Frolich et al (2010)	7	Germany
Lyon et al (2010)	11	USA
Ikenouchi-Sugita et al (2009)	1	Japan
Kawohl et al (2009)	10	Switzerland and Germany
Ben Djebara et al (2008)	1	France
Budman et al (2008)	35	USA
Seo et al (2008)	15	Korea
Stenstrom and Sindo (2008)	1	Denmark
Su et al (2008)	1	Taiwan
Winter et al (2008)	1	Germany
Miranda and Castiglioni (2007)	10	Chile
Bubl et al (2006)	2	Germany
Constant et al (2006)	1	Belgium
Davies et al (2006)	11	UK
Duane (2006)	15	USA
Fountoulakis et al (2006)	1	Greece
Murphy et al (2006)	6	USA
Yoo et al (2006)	14	Korea
Dehning et al (2005)	1	Germany
Kastrup et al (2005)	2	Germany
Padala et al (2005)	2	USA
Hood et al (2004)	1	USA
Hounie et al (2004)	1	Brazil
<b>Total</b>	<b>222</b>	

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