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Review Article

Systematic Review and Meta-Analysis of Tourette Syndrome Prevalence; 1986 to 2022



PEDIATRIC NEUROLOGY

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A R T I C L E I N F O

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ABSTRACT

Background: Tourette syndrome (TS) is a disorder characterized by a history of multiple motor tics and the emergence of at least one vocal tic during a period of the disorder. The current investigation sought to clarify the prevalence statistics for TS using a systematic review and meta-analysis.

Methods: This systematic review and meta-analysis covered the period between 1986 and 2022. Embase, Scopus, PubMed, Web of Science, and Google Scholar were searched to locate articles pertinent to the study topic. The I^2 index was used to examine the heterogeneity of the studies, and a comprehensive meta-analysis was employed to analyze the data.

Results: Ultimately, 30 studies (39 outcomes) were included in the meta-analysis and systematic review. The results showed the global prevalence of TS to be 0.5% (95% confidence interval [CI], 0.3% to 0.8%), with the highest rate of spread observed in the Americas at 0.6% (95% CI, 0.2% to 1.6%). Analyzing the subgroups of the sample revealed that the highest prevalence was associated with the population of children and adolescents at 0.7% (95% CI, 0.4% to 1.4%) and males at 0.5% (95% CI, 0.2% to 1.0%).

Conclusions: This comprehensive review and meta-analysis revealed that the prevalence of TS worldwide is sufficiently high, such that attention of medical specialists and health policy makers is warranted. © 2022 Elsevier Inc. All rights reserved.

Introduction

Tics refer to a group of nervous developmental disorders that typically manifest during childhood and adolescence and may remain stable over time or fluctuate in intensity or severity. Even

Ethics approval and consent to participate: Ethics approval was granted by the Ethics Committee of the Department of Research and Technology at Kermanshah University of Medical Sciences (IR.KUMS.REC.1400.780).

Consent for publication: Not applicable.

Competing interests: The authors declare that they have no conflict of interest. * Communications should be addressed to: Dr. Kazeminia; Student Research Committee; Kermanshah University of Medical Sciences; Kermanshah, Iran. though tics are involuntary, some individuals can suppress them during certain periods.¹ Tics are repetitive, involuntary, discordant, and sudden movements or sounds that can involve multiple muscle groups and typically appear between the ages four and six years. Tics range from weak and gentle jerks, contractions, and grunting to significant muscle jerks that disrupt social interactions.^{2,3}

The incidence of tics is more prevalent in children than in adults. Consequently, approximately five children of every 10,000 people suffer from tics, whereas only one to two adults are affected.⁴ The literature in the field indicates that children aged seven to 11 years have the highest prevalence. In addition, Tourette syndrome (TS), the more complete and severe form of the disease, is less prevalent than transient tics. All types of tics are more prevalent in boys than in girls, and the ratio of boys to girls with TS is nearly 3:1.⁵

Tics were classified into four diagnostic groups in the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders, published by the American Psychiatric Association, including TS, constant (chronic) motor or vocal tic disorder, provisional (transient) tic disorder, and other specified or unspecified tic disorders. TS is characterized by both motor and vocal tics, whereas chronic



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Availability of data and materials: Datasets are available through the corresponding author upon reasonable request.

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TABLE 1. Search Strategies

bearen birategies			
Database	Search Strategy	Date	Number
PubMed	((((((Epidemiology[MeSH Terms]) OR (Prevalence[MeSH Terms])) OR (Epidemiology[Title/Abstract])) OR (Prevalence[Title/Abstract])) OR (Prevalence[Title/Abstract])) OR (Prevalent*[Title/Abstract])) OR ("Prevalence's"[Title/Abstract])) OR ("Prevalence s"[Title/Abstract])) AND ((("Tourette's syndrome"[Title/ Abstract]) OR ("Tourette syndrome"[Title/Abstract])) OR ("Tourette syndrome"[MeSH Terms]))	January 1, 2022	386
Scopus	(TITLE-ABS-KEY (epidemiology) OR TITLE-ABS-KEY (prevalence) OR TITLE-ABS-KEY (prevalence) OR TITLE-ABS-KEY (prevalence's) OR TITLE-ABS-KEY (prevalence's) OR TITLE-ABS-KEY (prevalence's) OR TITLE-ABS-KEY (prevalence's) OR TITLE-ABS-KEY (Tourette's syndrome'))	January 2, 2022	757
WoS	TS=(Epidemiology OR Prevalence OR Prevalence OR Prevalent* OR Prevalence OR "Prevalence s") AND TS=("Tourette syndrome" OR "Tourette's syndrome")	January 3, 2022	710
Embase	 #1: 'Epidemiology':ab,ti OR 'Prevalence':ab,ti OR 'Prevalence':ab,ti OR 'Prevalent*':ab,ti OR 'Prevalence's':ab,ti OR	January 3, 2022	585
Google Scholar	(Epidemiology OR Prevalence OR Prevalence OR Prevalent* OR Prevalence OR "Prevalence s") AND ("Tourette syndrome" OR "Tourette's syndrome")	January 9, 2022	250

motor or vocal tic disorders are distinguished by either motor or vocal tics; they may be simple, such as blinking, shrugging one's shoulders, clearing one's throat, and sniffing, or more complex, such as turning one's head and shrugging one's shoulders or rehashing an action.^{6,7}

Tics decrease significantly during sleep and increase dramatically in stressful, exciting, and tiring situations. Unfortunately, symptoms of TS and other tic disorders can be socially inappropriate, and as a result, many people are victimized and isolated from social environments.⁸ The diminished self-esteem and accompanying psychiatric issues can expose individuals to additional potential problems.^{8,9} Studies suggest that certain psychiatric disorders, such as mood disorders and self-injurious behavior, share a genetic basis with TS.¹⁰ The symptoms of anxiety and depression accompanying TS pose a greater threat to patients' social and functional performance than tics themselves.¹¹ In patients with autism,¹² attention-deficit/hyperactivity disorder,¹³ obsessive-compulsive disorder,¹⁴ and Down syndrome,¹⁵ the prevalence of TS



FIGURE 1. Article selection flowchart under PRISMA 2020. The color version of this figure is available in the online edition.

TABLE 2.

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Summary of Studies Included in the Systematic Review/Meta-Analysis

First Author, Year, (Reference)	Country (Continent)	nt) Sample Size (n)		Age (year)	Type of Study	Diagnostic Tool	nostic Tool Prevalence			Population	Quality	
		Total	Male	Female				Total	Male	Female		Score
Charania, 2022 ²⁶	USA (America)	51,001	-	-	6-17	A national population-based study	NSCH	0.3	-	-	Children and adolescents	5
Scharf, 2012 ²⁷	UK (Europe)	6768	-	-	13	Cohort	DSM-IV-TR	0.3	-	-	Children and adolescents	5
Yang, 2016 ²⁵	Canada (America)	122,884	55,579	67,305	>12	A national population-based	NSCH	0.01	0.09	0.04	General population	9
0.	· · · ·					study						
Scahill, 2009 ²⁸	USA (America)	123,520	64,032	59,488	6-17	A national population-based study	NSCH	0.3	0.44	0.15	Children and adolescents	6
Burd-1, 1986 ²³	USA (America)	448,556	223,557	224,999	>19	Cross-sectional study	DSM-III	0.05	0.09	0.001	Adults	5
Khalifa, 2003 ²⁹	Sweden (Europe)	4479	2321	2158	7-15	Cross-sectional study	DSM-IV	0.6	0.9	0.1	Children and adolescents	7
Alves, 2014 ³⁰	Brazil (America)	762	388	374	11 (7-21)	Cross-sectional study	DSM-IV-TR	0.43	0.6	0.2	Children and adolescents	6
Kraft, 2012 (age = $9-11$) ³¹	Denmark (Europe)	33	-	-	9-11	Cohort	DSM-IV-TR	0.6	-	-	Children and adolescents	5
Kraft, 2012 (age = $11-12$) ³¹	Denmark (Europe)	31	-	-	10-12	Cohort	DSM-IV-TR	0.5	-	-	Children and adolescents	5
Kraft, 2012 (age = $13-15$) ³¹	Denmark (Europe)	27	-	-	13-15	Cohort	DSM-IV-TR	0.5	-	-	Children and adolescents	5
Eapen, 2001 ³²	UK (Europe)	200	-	-	-	Cross-sectional study	DSM-III-R	1.0	-	-	Adults	7
Giraldo, 2013 ³³	Colombia (America)	346	151	172	9 ± 1.5 (6-12)	Cross-sectional study	DSM-IV-TR	3.4	5.53	1.27	Children and adolescents	8
Jin, 2005 ³⁴	China (Asia)	9742	5304	4438	7-16	Cross-sectional study	The Apter Questionnaire itself	0.43	0.74	0.07	Children and adolescents	7
Heiervang 2007 ³⁵	Norway (Furone)	9155	_	_	8-10	Cross-sectional study	DSM_IV	0.16	_	_	Children	5
Zeitlin 2001 ³⁶	IIK (Furone)	1012	483	529	13.7 ± 0.45	Cross-sectional study	Self_report	0.10	_		Adolescents	6
2001	OR (Europe)	1012	-105	525	(13-14)	cross-sectional study	questionnaires	0.70			Adolescents	0
Cubo 2011 ³⁷	Spain (Furone)	1158	753	405	109 ± 285	A population-based study	Screening and	5.26	_	_	Children and adolescents	7
	Spani (Barope)	1100	700	100	1010 1 2100	n population based stady	diagnosis ascertainment	5.20				
BSc 1998 ²⁴	LIK (Furone)	166	93	73	13-14	Cross-sectional study	DSM-III-R	0.03	0.032	0.027	Adolescents	6
Janik 2014 ³⁸	Poland (Furone)	268	221	47	4-54	Cross-sectional study	DSM-IV-TR	0.02	-	-	General population	5
Apter 1993 ³⁹	Israel (Asia)	28 037	18 364	9673	-	Population-based	DSM-III-R	0.04	0.05	0.03	Children and adolescents	5
		20,007	10,001	5075		epidemiologic study			0.00	0.00		
Amiri, 201240	Iran (Asia)	1658	-	-	-	Cross-sectional study	DSM-IV-TR	1.3	-	-	Children	6
Liu, 2013 ⁴¹	China (Asia)	4062	-	-	6-12	Cross-sectional study	DSM-IV	1.21	-	-	Children	5
Zheng, 2004 ⁴²	China (Asia)	9742	5456	4286	7-16	Cross-sectional study	DSM-III-R	1.04	1.66	0.29	Children and adolescents	5
Kurlan, 2001	USA (America)	1596	1063	533	7-16	Cross-sectional study	DSM-IV	3.8	-	-	Children and adolescents	6
Caine, 1988	China (Asia)	142,636	-	-	/-16	Cross-sectional study	DSM-III-R	0.03	-	-	Children and adolescents	5
Burd-2, 1986-5	USA (America)	142,636	60,910	81,726	-	Cross-sectional study	DSM-III	0.03	0.05	0.001	Children	5
Comings, 1990 ¹⁰	Georgia (Europe)	3034	-	- 170	-	Cross-sectional study	DSM-III	0.46	-	-	Children and adolescents	5
Gadow, 2002 (age = $3-5$) ¹³	USA (America)	413	237	1/6	4.2 ± 0.7	Cross-sectional study	DSIVI-IV	12.34	14.34	9.7	Children and adolescents	7
Gadow, 2002 (age = $6-12$) ¹³	USA (America)	1520	/8/	/33	8.2 ± 1.9	Cross-sectional study	DSM-IV	3.28	5.33	1.50	Children and adolescents	7
Gadow, 2002 (age = $13-18$) ⁴⁷	USA (America)	10/3	5/3	500	14.4 ± 1.8	Cross-sectional study	DSIVI-IV	1.3	2.1	0.4	Children and adolescents	/
wong, 1992	Hong Kong (Asia)	/18	347	371	9.2 ± 1.2	Cross-sectional study	diagnosis	0.4	0.54	0.2	Children	5
							by a neurologist					
Wang, 2003 ⁴⁸	China (Asia)	2000	_	_	6-12	Cross-sectional study	DSM-IV	0.56	_	-	Children	6
Schlander, 2011 (age = $0-6$) ⁴⁹	Germany (Europe)	2681	1789	892	0-6	Cross-sectional study	DSM-IV	0.007	0.008	0.005	Children	8
Schlander, 2011 (age $= 7-12$) ⁴⁹	Germany (Europe)	8230	6029	2201	7-12	Cross-sectional study	DSM-IV	0.04	0.06	0.02	Children and adolescents	8
Schlander, 2011 (age = $13-18$) ⁴⁹	Germany (Europe)	2636	2021	615	13-18	Cross-sectional study	DSM-IV	0.04	0.06	0.02	Adolescents	8
Schlander, 2011 (age = $19-79$) ⁴⁹	Germany (Europe)	481	318	163	19-29	Cross-sectional study	DSM-IV	0.01	0.02	0.001	Adults	8
Schlander, 2011 (age = $30-49$) ⁴⁹	Germany (Europe)	794	369	425	30-49	Cross-sectional study	DSM-IV	0.006	0.008	0.004	Adults	8
Schlander, 2011 (age $= 50 + 13^{9}$	Germany (Europe)	886	338	548	50+	Cross-sectional study	DSM-IV	0.003	0.003	0.003	Adults	8
Kadesjö, 2000 ⁵⁰	Sweden (Europe)	598	352	246	7-11	Cross-sectional study	DSM-IV	1.1	1.7	0.5	Children	5
Nomoto, 1990 ⁵¹	USA (America)	830	445	385		Cross-sectional study	DSM-III-R	0.5	0.7	0.1	Children and adolescents	5

Abbreviations:

DSM = Diagnostic and Statistical Manual of Mental Disorders NSCH = National Survey of Children's Health

TABLE 3.

Results of the Meta-Analysis Fixed and Random Effects Models

Model	Number of Results	Prevalence % (95% CI)	P Value	Q Value	P Value	I^2	Tau Squared	Standard Error	Tau
Fixed Random	39 39	0.3 (95% Cl, 0.3-0.4) 0.5 (95% Cl, 0.3-0.8)	0.000 0.000	3668.92	0.000	98.96	2.64	1.21	1.62

Abbreviation:

CI = Confidence interval

has increased. In terms of its etiology, genetic, neurochemical, neuroanatomic, immunologic, and consequently infectious factors (among others) have been discussed.¹⁶⁻¹⁸

Several early studies on the prevalence of TS worldwide were conducted in small environments with smaller sample sizes. Scharf et al. and Levine et al. conducted the most recent meta-analyses regarding the prevalence of TS.^{19,20} Scharf et al. conducted their study in 2015 but did not include studies conducted before that year. In addition, this study did not examine the studies conducted from 2015 to 2022. In contrast, the study by Levine et al. focused solely on the prevalence of TS in adults and analyzed only three articles.

Furthermore, none of the studies examined the effects of potential variables such as the year, sample size, qualitative assessment score, diagnostic instruments, and gender. In addition, the studies failed to report the prevalence rate by population subgroup (i.e., specific information for each continent and age group). Moreover, there are contradictions between their findings. Consequently, the purpose of the present study was to determine the global prevalence of TS using a systematic review/meta-analysis approach.

Methods

The current systematic review/meta-analysis was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) 2020 identification, screening, eligibility, and inclusion criteria.²¹ To reduce the effects of publication bias and errors, researchers independently performed the phases of searching, evaluating, selecting articles, and collecting data (F.J. and

M.K.). Moreover, conflicts were resolved initially through discussion and subsequently through the mediation of a third party.

Study identification

Embase, PubMed, Scopus, and Web of Science were searched to identify articles relevant to the research questions (i.e., the global prevalence of TS). A set of keywords including "Epidemiology," "Prevalence", "Prevalence," "Prevalent*" "Prevalences," "Prevalence's," "Tourette's Syndrome," and "Tourette Syndrome" were validated using MeSH and were combined with the OR and AND operators to determine the search strategy for the current study in the aforementioned databanks. There was no time limit on the search; thus, all studies conducted until January 2020 were retrievable. Finally, Google Scholar and the references of all articles relevant to the aims of the current study were manually researched to maximize the search's efficiency (Table 1).

Inclusion criteria

- (1) Original scientific articles
- (2) Observational studies
- (3) Access to the article's complete text
- (4) Reporting the prevalence rate for TS

Exclusion criteria

(1) Being irrelevant to the study's objectives



Funnel Plot of Standard Error by Logit event rate

FIGURE 2. The funnel plot of the results corresponding to a global estimate of the prevalence of Tourette syndrome (TS).

Study name		Statis	tics for e	ach study			Event i	ate and	95% CI	
	Event rate	Lower limit	Upper limit	Z-Value	p-Value					
Charania, 2022	0.003	0.003	0.004	-71.710	0.000					
Scharf, 2012	0.003	0.002	0.005	-25.995	0.000					
Yang, 2016	0.001	0.001	0.001	-76.330	0.000					
Scahill, 2009	0.003	0.003	0.003	-111.643	0.000					
Burd-1, 1986	0.001	0.000	0.001	-115.402	0.000					
Khalifa, 2003	0.006	0.004	0.009	-26.448	0.000					
Alves, 2014	0.004	0.001	0.012	-9.565	0.000					
Kraft, 2012 (age= 9-11)	0.030	0.004	0.186	-3.413	0.001					
Kraft, 2012 (age= 11-12)	0.032	0.005	0.196	-3.346	0.001					
Kraft, 2012 (age= 13-15)	0.037	0.005	0.221	-3.197	0.001			-		-
Eapen, 2001	0.010	0.003	0.039	-6.466	0.000			- I		
Giraldo, 2013	0.035	0.020	0.060	-11.321	0.000				-	
Jin, 2005	0.004	0.003	0.006	-35.193	0.000					
Heiervang, 2007	0.002	0.001	0.003	-24.815	0.000					
Zeitlin. 2001	0.008	0.004	0.016	-13.614	0.000			T		
Cubo. 2011	0.053	0.041	0.067	-21.965	0.000					
BSc. 1998	0.006	0.001	0.041	-5.091	0.000				-	
Janik. 2014	0.004	0.001	0.026	-5.577	0.000			- -		
Apter, 1993	0.000	0.000	0.001	-26.862	0.000			T.		
Amiri, 2012	0.013	0.009	0.020	-20.076	0.000					
liu. 2013	0.012	0.009	0.016	-30.652	0.000					
Zheng, 2004	0.010	0.009	0.013	-45.576	0.000					
Kurlan 2001	0.038	0.030	0.019	-24 705	0.000					
Caine 1988	0.000	0.000	0.000	-52 205	0.000				•	
Burd-2 1986	0.000	0.000	0.000	-51 721	0.000					
Comings 1990	0.000	0.000	0.000	-20.061	0.000					
Gadow 2002 (age=3-5)	0.005	0.005	0.008	-20.001	0.000			- T		
Gadow, 2002 (age=5-3)	0.123	0.000	0.133	_22 511	0.000					
Gadow, 2002 (age=0.12)	0.033	0.025	0.043	16 001	0.000					
Wong 1992	0.013	0.003	0.022	-10.001	0.000			- F		
Wang 2002	0.004	0.001	0.013	-9.401	0.000			- T		
Schlander 2011 (ago-0.6)	0.000	0.003	0.010	-17.191	0.000			- T		
Schlander, 2011 (age=0-0)	0.000	0.000	0.005	12 700	0.000			- T		
Schlander, 2011 (age=7-12)	0.000	0.000	0.001	10 1 5	0.000					
Schlander, 2011 (age=15-16)	0.001	0.000	0.005	-10.155	0.000			T.		
Schlander 2011 (age=19-29)	0.002	0.000	0.015	-0.10/	0.000					
Schlander 2011 (age=30-49)	0.001	0.000	0.009	-0.0/2 6 707	0.000			- 1 -		
Kadacia 2000	0.001	0.000	0.008	-0./82	0.000					
Nameta 1000	0.012	0.006	0.024	-11.00/	0.000					
10111010, 1990	0.005	0.002	0.013	-10.035	0.000			Δ		
	0.005	0.003	0.008	-19.034	0.000	I		1	l	I
						-0.25	-0.13	0.00	0.13	0.25
							Favours A		Favours B	

Meta Analysis

FIGURE 3. The random effects model-based forest plot of the global prevalence estimate of Tourette syndrome (TS).

- (2) Intervention studies, case reports, case series, conferencepresented articles, letters to the editor, qualitative studies, theses and dissertations, systematic reviews and metaanalyses, and animal studies.
- (3) Lack of access to the studies' complete texts
- (4) Studies that have been duplicated in multiple databases
- (5) Involvement of specific underlying conditions, such as Down syndrome, autism, and epilepsy, among others.

Study selection process

EndNote X8 was used to catalog all the studies retrieved from the analyzed databanks. Initially, all duplicate records were removed. Then, the inclusion and exclusion criteria were applied to the titles and abstracts, and irrelevant studies were eliminated. During eligibility determination, full texts of the articles were examined to eliminate records irrelevant to the study's objectives.

Study name	St	atistics	with stu	udy remo	ved	Event rate (95% CI) with study removed					
	Point	Lower limit	Upper limit	Z-Value	p-Value						
Charania, 2022	0.005	0.003	0.008	-18.287	0.000						
Scharf, 2012	0.005	0.003	0.008	-19.170	0.000						
Yang, 2016	0.005	0.003	0.008	-18.845	0.000						
Scahill, 2009	0.005	0.003	0.009	-17.205	0.000						
Burd-1, 1986	0.005	0.003	0.008	-20.305	0.000						
Khalifa, 2003	0.005	0.003	0.008	-19.215	0.000						
Alves, 2014	0.005	0.003	0.008	-19.347	0.000						
Kraft, 2012 (age= 9-11)	0.004	0.003	0.008	-19.579	0.000						
Kraft, 2012 (age= 11-12)	0.004	0.003	0.008	-19.584	0.000						
Kraft, 2012 (age= 13-15)	0.004	0.003	0.008	-19.597	0.000						
Eapen, 2001	0.005	0.003	0.008	-19.457	0.000						
Giraldo, 2013	0.004	0.003	0.008	-19.647	0.000						
Jin, 2005	0.005	0.003	0.008	-19.058	0.000						
Heiervang, 2007	0.005	0.003	0.008	-19.165	0.000						
Zeitlin, 2001	0.005	0.003	0.008	-19.376	0.000						
Cubo, 2011	0.004	0.003	0.007	-20.459	0.000						
BSc, 1998	0.005	0.003	0.008	-19.443	0.000						
Janik, 2014	0.005	0.003	0.008	-19.406	0.000						
Apter, 1993	0.005	0.003	0.009	-19.158	0.000						
Amiri, 2012	0.005	0.003	0.008	-19.414	0.000						
Liu, 2013	0.005	0.003	0.008	-19.314	0.000						
Zheng, 2004	0.005	0.003	0.008	-19.077	0.000						
Kurlan, 2001	0.004	0.003	0.007	-20.127	0.000						
Caine, 1988	0.005	0.003	0.009	-19.417	0.000						
Burd-2, 1986	0.005	0.003	0.009	-19.418	0.000						
Comings, 1990	0.005	0.003	0.008	-19.263	0.000						
Gadow, 2002 (age=3-5)	0.004	0.003	0.007	-21.184	0.000						
Gadow, 2002 (age=6-12)	0.004	0.003	0.007	-19.898	0.000						
Gadow, 2002 (age=13-18)	0.005	0.003	0.008	-19.431	0.000						
Wong, 1992	0.005	0.003	0.008	-19.353	0.000						
Wang, 2003	0.005	0.003	0.008	-19.307	0.000						
Schlander, 2011 (age=0-6)	0.005	0.003	0.008	-19.242	0.000						
Schlander, 2011 (age=7-12)	0.005	0.003	0.009	-19.161	0.000						
Schlander, 2011 (age=13-18)	0.005	0.003	0.008	-19.234	0.000						
Schlander, 2011 (age=19-29)	0.005	0.003	0.008	-19.362	0.000						
Schlander, 2011 (age=30-49)	0.005	0.003	0.008	-19.325	0.000						
Schlander, 2011 (age=50+)	0.005	0.003	0.008	-19.318	0.000						
Kadesjö, 2000	0.005	0.003	0.008	-19.436	0.000						
Nomoto, 1990	0.005	0.003	0.008	-19.353	0.000						
	0.005	0.003	0.008	-19.634	0.000						
						-0.0	05 -0.	03	0.00	0.03	0.05
							Favo	urs A		Favours B	

Meta Analysis

FIGURE 4. The sensitivity analysis of the global prevalence percentage of Tourette syndrome (TS) using a random effects model.

The studies that satisfied all the inclusion criteria were then subjected to qualitative evaluation. The search team members were unaware of the authors, affiliations, and researched journals.

Qualitative evaluation of studies

The qualitative evaluation of the prevalence studies was conducted using the checklist proposed by the Joanna Briggs Institute (JBI), a well-known and standard checklist, to evaluate the studies qualitatively.²² The checklist contains nine questions regarding the sample frame, participants, sample size, study subjects and setting described in detail, data analysis, valid methods for identifying conditions, measuring the situation, statistical analysis, and an adequate response rate. Under the scoring method, "Yes" was selected if a positive record was observed, "No" indicated the absence of any records, and "NA" indicated the absence of reporting. Based on the number of "Yes" instances, the minimum and maximum possible scores were 0 and 9, respectively.

Data extraction

The data extraction process was conducted using an electronic version of the previously prepared checklist. The checklist included the first author, year, country and continent, sample size, age, study type, diagnostic tool, prevalence percentage, the population under investigation, and the qualitative evaluation score.



Regression of Logit event rate on Sample size (n)

FIGURE 5. The meta-regression of the relationship between sample size and global Tourette syndrome (TS) prevalence.

Statistical analysis

In the present study, the prevalence percentage of TS was examined, and the frequency rates reported in each study were combined to determine the overall rate. The heterogeneity between the studies was analyzed using the I² index, and the random effects model was employed due to the high heterogeneity $(I^2>75\%)$. The model is more generalizable in a heterogeneous setting than the fixed-effects model since parameter variations between the investigated studies are considered. The publication bias was investigated using funnel plots and Egger regression intercept. In addition, meta-regression was utilized to examine the association between the global prevalence of TS and the publication year, sample size, and qualitative evaluation score. Moreover, the subgroup analysis was conducted on distinct continents (Asia, Europe, and the Americas), populations, diagnostic tools, and gender. Comprehensive Meta-Analysis (v. 3) was used to analyze the data, and P < 0.05 was determined as the statistical significance of the data.

Results

A summary of the articles included in the meta-analysis

The preliminary search yielded 2688 studies employing strategies for identifying studies from various databanks. However, 1456 duplicate and overlapping studies from various databanks were eliminated. After reviewing the titles and abstracts of the remaining 1232 studies, 1182 records were determined to be irrelevant to the research topic and were therefore eliminated. Then, the full texts of the remaining 50 studies were examined, and 20 records that did not meet the inclusion criteria were eliminated. Finally, 30 studies met all of the meta-analysis's inclusion criteria. Some studies independently reported the prevalence of TS in various age groups; therefore, they were included as multiple outcomes in the meta-analysis.

Consequently, the systematic review and meta-analysis included 30 researches (39 results). Figure 1 illustrates the flow diagram for PRISMA 2020.

General characteristics of the studies included in the systematic review and meta-analysis

The total sample size of the studies was 1,136,369 individuals. The earliest record was from 1986, whereas the most recent was from 2022. Most of the studies focused on the United States (11 results). In addition, the studies with the largest and smallest sample sizes were those conducted by Burd et al.²³ with 448,556 examinees and BSc et al.²⁴ with 166 examinees, respectively. More than 78% of the documents were case studies. Using the JBI checklist, the study by Yang et al.²⁵ received the highest qualitative evaluation score of 9 points. Table 2 illustrates the characteristics of the studies that met the inclusion criteria for the current systematic review and meta-analysis.

The meta-analysis of studies examining the global prevalence of TS

The results of the I^2 test concerning the global prevalence of TS indicated significant heterogeneity among the studies ($I^2 = 98.96$); therefore, the data were analyzed using the random effects model



Regression of Logit event rate on Year

FIGURE 6. The meta-regression of the relationship between year of study and global Tourette syndrome (TS) prevalence.

(Table 3). At the level of 0.1, Egger regression intercept results indicated no publication bias among the studies (P = 0.266) (Fig 2). Based on the combined results of studies employing the random effects model, the global prevalence of TS was estimated to be 0.5% (95% confidence interval [CI], 0.3% to 0.8%). The black square represents the percentage, and the line length represents the 95% CI for each study. In addition, the rhombus represents the global prevalence of TS throughout the entire study (Fig 3). The sensitivity analysis results indicated that the final results are unaffected by the exclusion of any single study (Fig 4).

The global meta-regression of TS prevalence

Meta-regression was used to examine the relationship between sample size (Fig 5), study year (Fig 6), and qualitative evaluation score based on the JBI checklist (Fig 7) and the global prevalence of TS. As the sample size increased, the prevalence of TS decreased (P< 0.05), and as the quality assessment score increased, the prevalence of TS increased (P < 0.05). The correlation between the study year and the prevalence of TS was not statistically significant (P > 0.05). In the meta-regression, each study with multiple results was entered only once (total result); therefore, 30 studies with 30 results were entered (Figs 5-7).

Subgroup analyses

Because the heterogeneity between the studies was significant ($I^2 > 95\%$), subgroup analyses were performed in terms of continents, diagnostic tools, investigated populations, and gender, and

the results are shown in Table 4. The most common percentages of TS were observed in the Americas at 0.6% (95% CI, 0.2% to 1.6%), screening and diagnosis by a neurologist at 1.6% (95% CI, 0.3% to 0.6%), children and adolescent populations at 0.7% (95% CI, 0.4% to 1.4%), and males at 0.5% (95% CI, 0.2% to 1.0%) (Table 4).

Discussion

The purpose of the present systematic review and meta-analysis was to determine the global prevalence of TS. Combining the results of 30 studies (39 results) led to the conclusion that the global prevalence of TS is 0.5%. The highest prevalence was found in a Canadian study of patients with various nervous disorders, with 17%,⁵² whereas the lowest prevalence was found in a study of adults aged 50 years and older, with 0.003%.⁴⁹ According to the JBI checklist, the study with the highest quality reported a prevalence rate of 0.1% for TS.²⁵

The prevalence rate of TS in children was estimated to be 1.7% through meta-analyses conducted in China,⁵ 0.52% by metaanalyses conducted in the United States,²⁰ and 0.11% through meta-analyses conducted in Poland.¹⁹ The following statements may be made regarding the differences between the aforementioned studies and the current systematic review/meta-analysis. The current study investigated a significantly larger number of studies (30 articles [39 results] compared with 3, 27, and 13 articles in Polish, American, and Chinese studies, respectively). In addition, the Chinese study was limited to studies conducted in China, whereas the Polish study was limited to adult population studies.



Regression of Logit event rate on Quality Score

Quality Score

FIGURE 7. The meta-regression of the relationship between qualitative evaluation scores and global Tourette syndrome (TS) prevalence.

On the other hand, the current study included participants from diverse racial and geographic backgrounds.

Depression and anxiety, as well as an increase in destructive behaviors such as mood disorders, oppositional defiance, and self-injurious behaviors, are risks for patients with TS.^{10,11} In addition,

they may have learning and motor disorders, as well as bipolar disorder and substance abuse. 53

The syndrome typically manifests between the ages four and six years, reaching its peak between age 10 and 12 years. Thus, the symptoms begin to diminish during adolescence, and many adults

TABLE 4.

The Subgroup Analyses for Es	stimating the Prevalence Perce	entage of TS by Continent	, Diagnostic Tool, F	Population Studied, and Gender
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Subgroups	Number Results	Prevalence % (95% CI)	P Value	P Value Between	I ²	Standard Error	Tau
Continents							
America	12	0.6 (95% CI, 0.2-1.6)	0.000	0.76	99.56	1.82	1.68
Asia	8	0.3 (95% CI, 0.1-1.0)	0.000		98.66	1.59	1.53
Europe	19	0.4 (95% CI, 0.2-1.0)	0.000		94.68	1.45	1.55
Diagnostic tools							
DSM-III	3	0.1 (95% CI, 0.0-0.2)	0.000	0.001	97.56	1.03	0.93
DSM-III-R	6	0.3 (95% CI, 0.0-1.6)	0.000		98.84	5.15	0.23
DSM-IV	15	0.5 (95% CI, 0.3-1.2)	0.000		97.11	1.10	1.40
DSM-IV-TR	8	1.2 (95% CI, 0.5-2.8)	0.000		87.96	1.04	1.09
NSCH	3	0.2 (95% CI, 0.1-0.4)	0.000		98.35	0.34	0.57
Screening and diagnosis determined by a neurologist	2	1.6 (95% CI, 0.3-0.6)	0.000		94.73	4.72	1.78
Population							
Adolescents	3	0.3 (95% CI, 0.1-1.6)	0.000	0.05	77.42	2.00	1.21
Adults	5	0.2 (95% CI, 0.0-0.6)	0.000		80.40	1.82	1.30
Children	8	0.3 (95% CI, 0.1-1.2)	0.000		98.23	2.43	1.84
Children and adolescents	21	0.7 (95% CI, 0.4-1.4)	0.000		98.96	1.26	1.50
General population	2	0.1 (95% CI, 0.0-0.4)	0.000		42.51	1.24	0.61
Gender							
Male	23	0.5 (95% CI, 0.2-1.0)	0.000	0.04	98.74	1.61	1.60
Female	23	0.2 (95% CI, 0.1-0.4)	0.000		95.72	2.46	1.92

Abbreviations:

DSM = Diagnostic and Statistical Manual of Mental Disorders

NSCH = National Survey of Children's Health

TS = Tourette syndrome

with TS experience relief. This result was consistent with the findings of Edition. 53

It appears that there are no racial, ethnic, or cultural differences in the clinical characteristics, processes, or etiology of TS. However, the ethnic factors can impact the perceptions and management of TS by families and societies, as well as help-seeking patterns and treatment options.⁵³ The results of the subgroup analyses in terms of continents showed no significant differences between Asia, Europe, and the Americas in terms of the prevalence of TS.

The close to significant prevalence of TS in various populations, especially children, adolescents, and males, necessitates particular focus and attention. Owing to the severe complications and problems associated with TS and its profound impact on people's lives, authorities must pay special attention to it. Consequently, they should familiarize themselves with TS, identify suitable solutions, implement them, and conduct follow-up procedures to reduce its prevalence. Such policies will be effective when implemented on multiple levels, such as the individual, group, and organizational levels. As the prevalence values obtained using different tools are significantly different, convenient diagnostic tools and methods should be utilized to diagnose the syndrome accurately and promptly.

A contribution of the study was the estimation of the global prevalence of TS for distinct populations using a large sample (more than 1.1 million people) and the estimation of the prevalence of TS in terms of distinct continents and diagnostic tools. In addition, the significant heterogeneity (above 95%) among the studies necessitated the implementation of subgroup analyses, which reduced the level of heterogeneity to some extent and provided answers to some unanswered clinical questions. Despite this, significant heterogeneity existed between all subgroups, which may have resulted from the sample size, demographic characteristics, and study methodology. Other limitations of the study included the heterogeneous reporting of the articles, the nonrandom selection of some articles, the heterogeneous implementation method, and the inaccessibility of the full texts of the conference papers. In addition, the number of published articles about certain populations was limited. Thus, it is suggested that more research be conducted on the prevalence of TS in specific populations, such as those with Down syndrome, autism, attention-deficit/hyperactivity disorder, and obsessive-compulsive disorder (among others).

Conclusion

This comprehensive review and meta-analysis revealed that the prevalence of TS worldwide can be deemed nearly high. Therefore, it seems necessary to draw the attention of health field specialists, officials, and policymakers.

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