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# **Epidemiological Studies in Tourette Syndrome: Recent findings**

**Lorena Fernández de la Cruz**

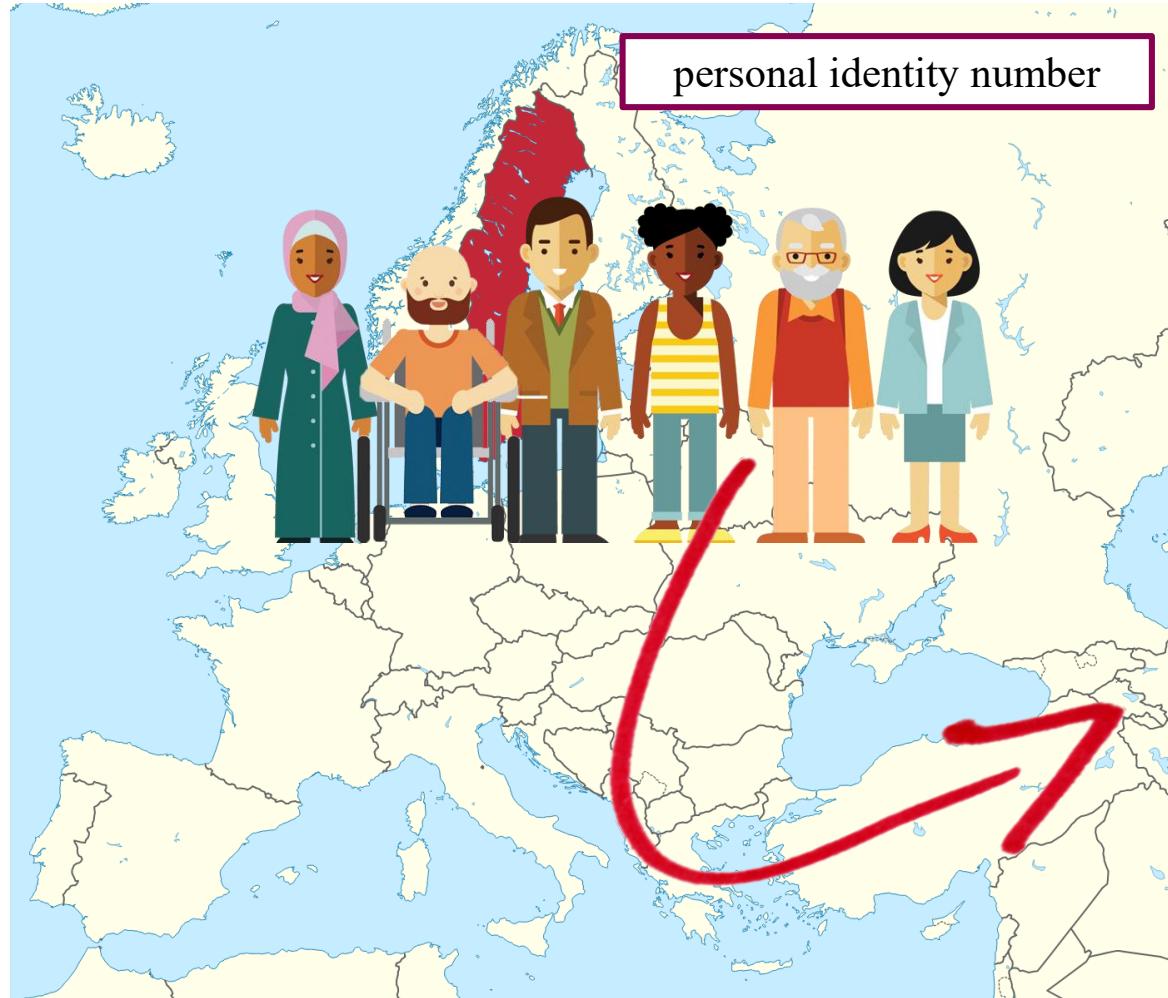
Obsessive-compulsive and related disorders across the lifespan research group  
Centre for Psychiatry Research, Department of Clinical Neuroscience

13<sup>th</sup> European Conference on Tourette Syndrome and Tic Disorders  
European Society for the Study of Tourette Syndrome (ESSTS)

# The Swedish National Registers: the entire Swedish population is a cohort



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BIRTH

MIGRATIONS

MEDICAL APPOINTMENTS  
AND DIAGNOSES

MEDICATION

EDUCATION

SOCIAL SECURITY DATA  
(E.G., UNEMPLOYMENT,  
SICK LEAVE)

MORTALITY

FAMILY MEMBERS

# The Swedish Tic Cohort: characteristics



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Tics involving the eyes, i.e., eye-blinking, are the most common tics in childhood-onset tic disorders. Patients with tic disorders frequently develop other motor tics of the head and neck, including grimacing and frowning.

Cohort of >7,800 cases with TS or chronic motor or vocal tic disorder

Validated diagnostic codes

Diagnosed in specialist services since 1969

Demographic and clinical characteristics comparable to other samples

## Recent findings

Alcohol- and drug-related disorders, convictions, and deaths

Insomnia

Transport accidents

Cervical spine disorders

## Recent findings

Alcohol- and drug-related  
disorders, convictions,  
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## Archival Report

Biological  
Psychiatry

# Association of Tourette Syndrome and Chronic Tic Disorder With Subsequent Risk of Alcohol- or Drug-Related Disorders, Criminal Convictions, and Death: A Population-Based Family Study

Suvi Virtanen, Anna Sidorchuk, Lorena Fernández de la Cruz, Gustaf Brander, Paul Lichtenstein, Antti Latvala, and David Mataix-Cols

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Biological Psychiatry February 15, 2021; 89:407–414 [www.sobp.org/journal](http://www.sobp.org/journal)

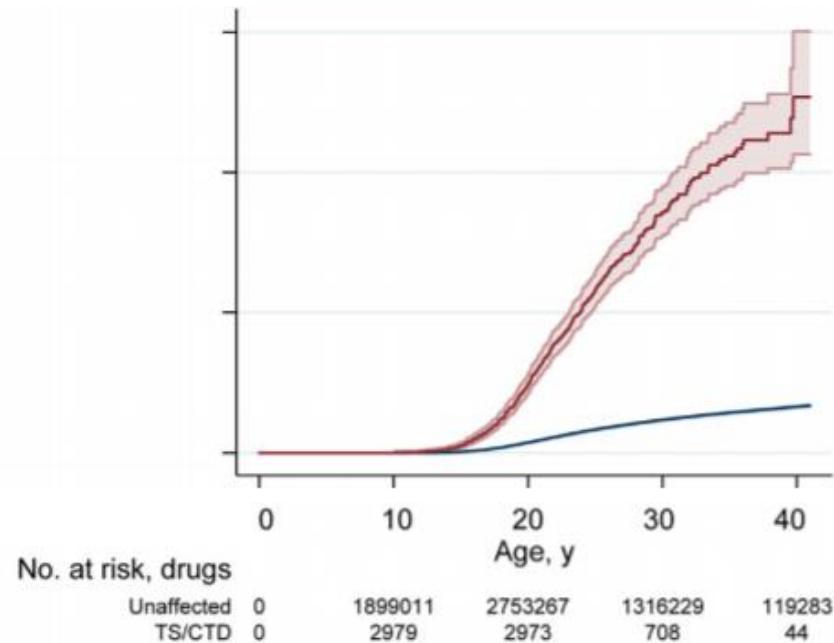
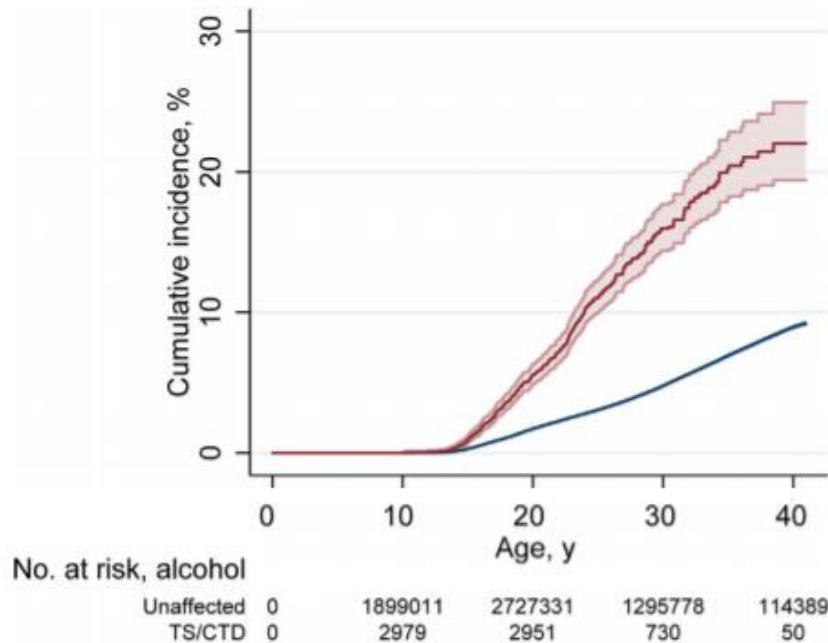
# Alcohol- or drug-related disorders, criminal convictions, and death

- Substance misuse rarely studied in tic disorders.
- Some cross-sectional studies point to an increased risks of substance use disorders, compared to the general population.
- Underlying mechanisms?

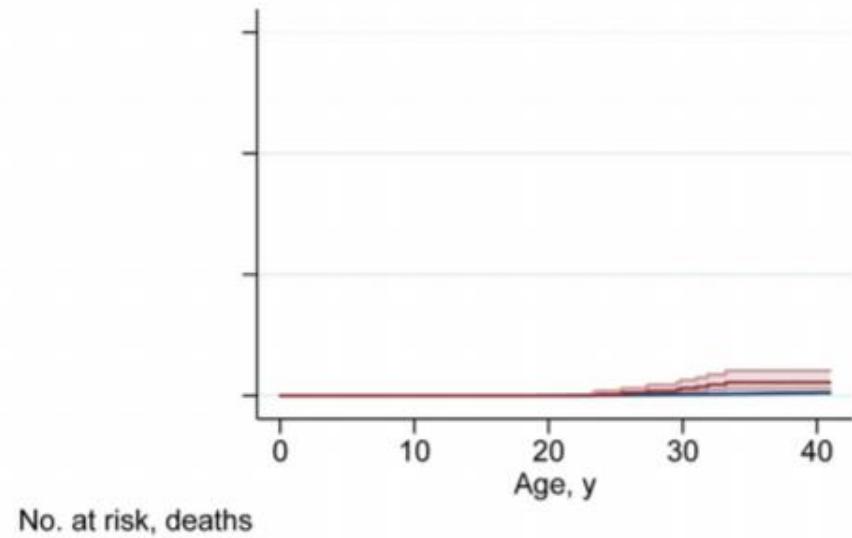
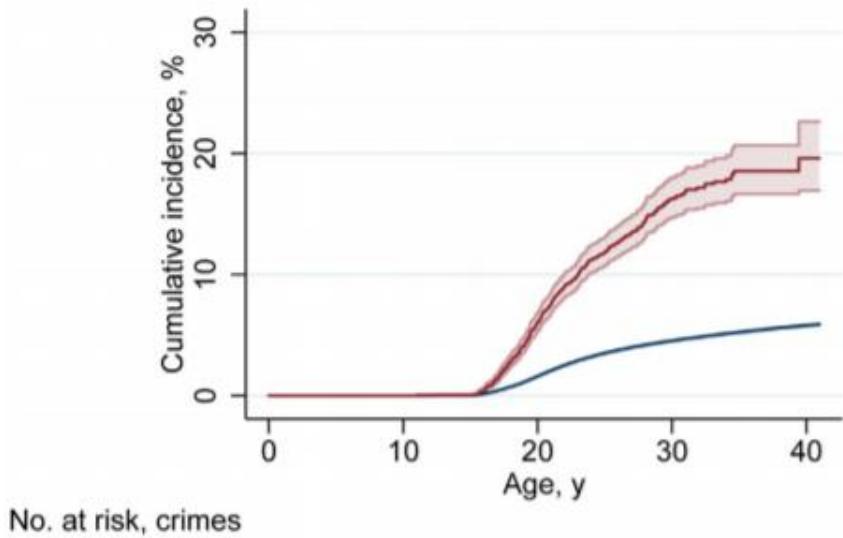
# Alcohol- or drug-related disorders, criminal convictions, and death

- 7,832 individuals with TS/CTD, compared to >14 M individuals from the general population.
- 16% of individuals with TS/CTD and 7% of individuals from the general population presented with substance misuse outcomes.
- Individuals with TS/CTD had a significantly increased risk of:
  - Any substance misuse-related outcome (aHR 3.11; 95% CI, 2.94-3.29)
  - Alcohol-related disorders (aHR, 3.45; 95% CI, 3.19–3.72)
  - Drug-related disorders (aHR, 6.84; 95% CI, 6.32–7.40)
  - Substance-related criminal convictions (aHR, 2.56; 95% CI, 2.36–2.77)
  - Substance-related deaths (aHR, 2.54; 95% CI, 1.83–3.52)

# Alcohol- or drug-related disorders, criminal convictions, and death



# Alcohol- or drug-related disorders, criminal convictions, and death



# Alcohol- or drug-related disorders, criminal convictions, and death

- TS/CTD are associated with increased risk of substance misuse outcomes in their own right, but individuals with comorbid ADHD seem to be at particularly high risk.

**Table 2. Risk of Substance Misuse Outcomes in Individuals With Tourette Syndrome or Chronic Tic Disorder, Compared With Unaffected Individuals From the General Population, Excluding Psychiatric Comorbidities**

Substance Misuse Outcome	Without Exclusion	Excluding ADHD	Excluding Conduct Disorder	Excluding Pervasive Developmental Disorders	Excluding OCD	Excluding Anxiety Disorders	Excluding Depressive Disorders	Excluding Psychotic and Bipolar Disorders	Excluding All Psychiatric Comorbidities at the Same Time
Any Substance Misuse Outcomes <sup>a</sup>	3.11 (2.94–3.29)	2.00 (1.82–2.19)	2.93 (2.76–3.11)	3.10 (2.91–3.31)	3.03 (2.84–3.23)	2.52 (2.32–2.74)	2.74 (2.54–2.95)	2.97 (2.78–3.16)	1.43 (1.20–1.79)
Alcohol-Related Disorder <sup>b</sup>	3.45 (3.19–3.72)	2.19 (1.94–2.48)	3.27 (3.02–3.55)	3.42 (3.13–3.74)	3.34 (3.06–3.64)	2.69 (2.39–3.03)	3.16 (2.85–3.51)	3.33 (3.05–3.64)	1.64 (1.28–2.10)
Any Drug-Related Disorder <sup>c</sup>	6.84 (6.32–7.40)	4.44 (3.86–5.10)	6.54 (6.01–7.11)	6.58 (5.98–7.24)	6.46 (5.89–7.09)	6.24 (5.63–7.32)	6.81 (6.02–7.62)	6.58 (5.99–7.23)	2.76 (1.86–4.08)
Substance-Related Convictions <sup>d</sup>	2.56 (2.36–2.77)	1.55 (1.35–1.77)	2.40 (2.20–2.61)	2.75 (2.51–3.00)	2.62 (2.40–2.86)	2.30 (2.07–2.57)	2.39 (2.16–2.64)	2.53 (2.31–2.77)	1.31 (1.03–1.67)

# Alcohol- or drug-related disorders, criminal convictions, and death

- Comparison of the TS/CTD cohort with their unaffected full siblings: significant attenuation of the estimates.

**Table 3. Sibling Comparison for the Risk of Substance Misuse Outcomes**

Substance Misuse Outcome	HR (95% CI) Adjusted for Sex and Birth Year
Any Substance Misuse Outcomes <sup>a</sup>	1.74 (1.53–1.97)
Alcohol-Related Disorder <sup>b</sup>	1.94 (1.65–2.29)
Any Drug-Related Disorder <sup>c</sup>	3.17 (2.60–3.86)
Substance-Related Convictions <sup>d</sup>	1.64 (1.36–1.98)

# Alcohol- or drug-related disorders, criminal convictions, and death

- The majority of individuals with TS/CTD do not have substance misuse problems, but the risk is higher when compared to individuals without TS/CTD.
- Screening for drug and alcohol use should become part of the standard clinical routines, particularly in TS with comorbid ADHD.
- Importance of implementing preventive and early intervention strategies to preclude the onset and minimize the consequences of substance misuse.

## Recent findings

Alcohol- and drug-related  
disorders, convictions,  
and deaths

Insomnia

Transport accidents

Cervical spine disorders

# Insomnia

- Sleep problems very prevalent in tic disorders across the lifespan, limited methodological quality of the studies
- Insomnia: imprecise prevalence estimates (range 0.3% to 77%)
- Role of comorbidities is unclear

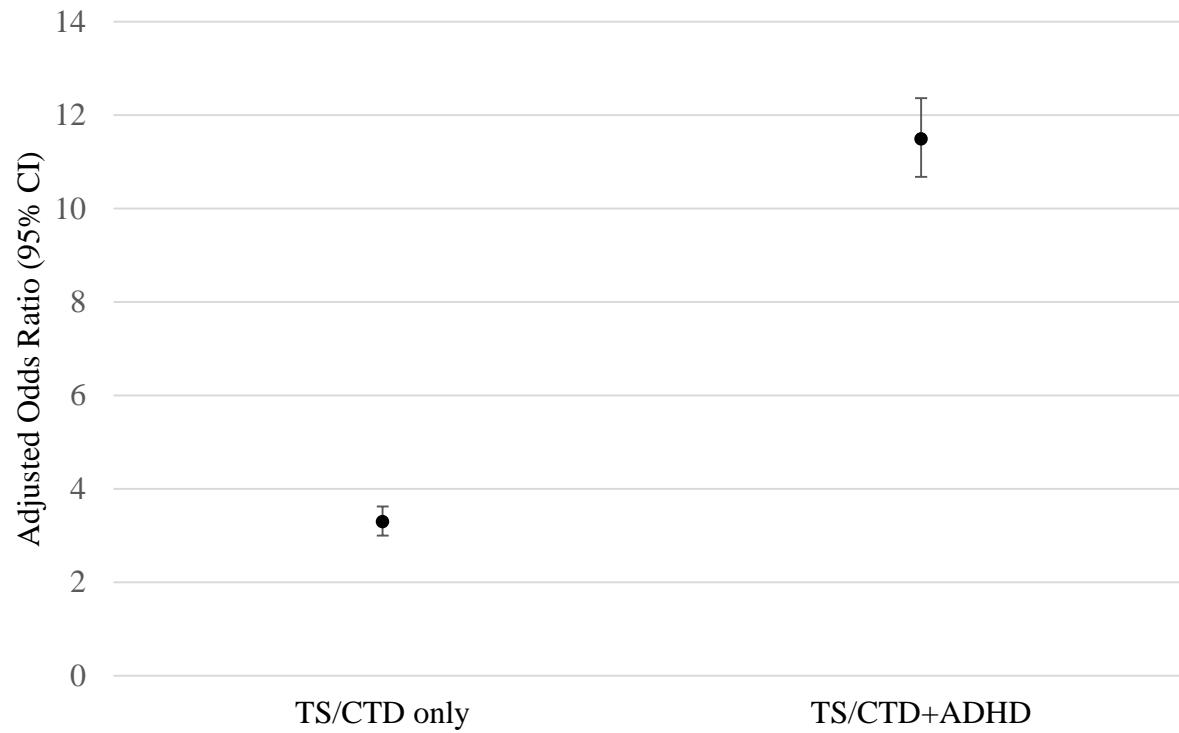
# Insomnia

- 5,877 individuals with a diagnosis of TS/CTD, compared to unexposed individuals from the general population (>10M) and their unaffected siblings.
- Period-prevalence of insomnia:
  - TS/CTD: 32.16%
  - Unexposed: 13.70%
- Likelihood of insomnia:
  - Population comparison: aOR=6.74; 95% CI, 6.37–7.15
  - Sibling comparison: aOR=5.41; 95% CI, 4.65–6.30

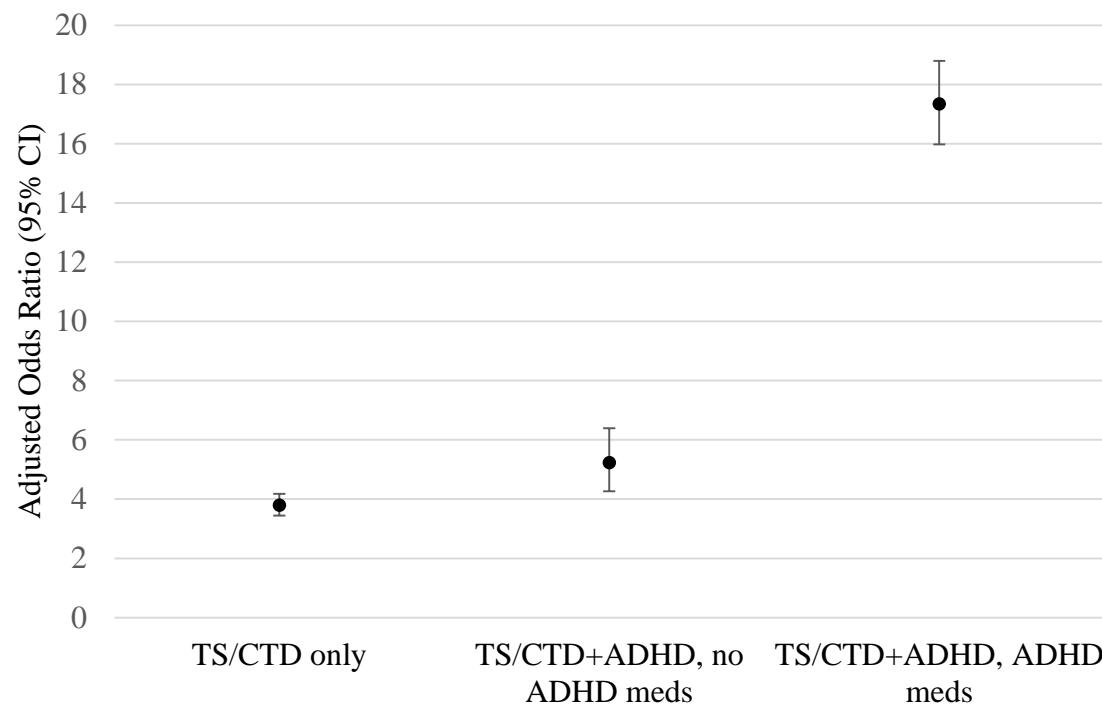
# Insomnia

- When excluding individuals with pervasive developmental disorders and learning disabilities and individuals with ADHD, the association between TS/CTD and insomnia remained statistically significant, but the magnitude significantly decreased.
- Likelihood of insomnia for individuals with TS/CTD with comorbid ADHD and with comorbid ADHD on medication was higher.

# Insomnia



# Insomnia



# Insomnia

- Insomnia should be systematically evaluated in individuals with tic disorders and managed according to the available evidence in order to minimize its potential negative impact.
- This is particularly important for those individuals with comorbid neurodevelopmental disorders, especially ADHD/ADHD medication.

## Recent findings

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RESEARCH ARTICLE

## Serious Transport Accidents in Tourette Syndrome or Chronic Tic Disorder

David Mataix-Cols, PhD,<sup>1,2\*</sup> Gustaf Brander, PhD,<sup>1,2,3</sup> Zheng Chang, PhD,<sup>4</sup> Henrik Larsson, PhD,<sup>4,5</sup> Brian M. D'Onofrio, PhD,<sup>4,6</sup> Paul Lichtenstein, PhD,<sup>4</sup> Anna Sidorchuk, MD, PhD,<sup>1,2</sup> and Lorena Fernández de la Cruz, PhD<sup>1,2</sup>

<sup>1</sup>Centre for Psychiatry Research, Department of Clinical Neuroscience, Karolinska Institutet, Stockholm, Sweden

<sup>2</sup>Stockholm Health Care Services, Region Stockholm, Stockholm, Sweden

<sup>3</sup>Science for Life Laboratory, Department of Medical Biochemistry and Microbiology, Uppsala University, Uppsala, Sweden

<sup>4</sup>Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm, Sweden

<sup>5</sup>School of Medical Sciences, Örebro University, Örebro, Sweden

<sup>6</sup>Department of Psychological and Brain Sciences, Indiana University, Bloomington, Indiana, USA

Movement Disorders, Vol. 36, No. 1, 2021

# Transport accidents

- Road traffic injuries are the leading cause of death in the group aged 5-29 years, and eighth cause for all age groups.
- More common in other neurodevelopmental disorders such as ADHD.
- Unknown if individuals with tic disorders also have a higher risk.
- In some countries, reporting of TS diagnosis to licensing vehicle authorities is encouraged or compulsory.

# Transport accidents

- 3,449 individuals diagnosed with TS/CTD compared to >6M unexposed individuals and their siblings, all of at least 18, on the risk of injuries or deaths attributed to transport accidents and, specifically, motor vehicle accidents

# Transport accidents

- Individuals with TS have a 50% increased risk of serious transport accidents and a 58% increased risk of motor vehicle accidents.
- Results slightly reduced in the sibling comparison.

Population Cohort	Individuals with TS/CTD (n = 3449)		Unaffected Individuals (n = 6,123,841)		HR (95% CI) Adjusted for Sex and Birth Year
	n	%	n	%	
All serious transport accidents	271	7.86	340,669	5.56	1.50 (1.33–1.69)
Men	208	7.94	190,544	6.09	1.48 (1.29–1.70)
Women	63	7.50	150,125	5.01	1.57 (1.23–2.01)
Motor vehicle accidents	189	5.48	190,376	3.11	1.58 (1.37–1.82)
Men	151	5.77	119,382	3.61	1.50 (1.28–1.77)
Women	38	4.58	70,994	2.37	1.86 (1.35–2.55)
Individuals With TS/CTD With Unaffected Full Siblings (n = 2207)		Unaffected Full Siblings of Individuals With TS/CTD (n = 3377)			
Sibling Cohort	n	%	n	%	HR (95% CI) Adjusted for Sex and Birth Year
All serious transport accidents	194	8.79	238	7.05	1.41 (1.18–1.68)
Motor vehicle accidents	132	5.98	161	4.77	1.27 (1.03–1.57)

# Transport accidents

	HR (95% CI) Adjusted for Sex and Birth Year	
	All Serious Transport Accidents	Motor Vehicle Accidents
Autism spectrum disorders	<b>1.67 (1.46–1.91)</b>	<b>1.82 (1.55–2.13)</b>
Attention deficit hyperactivity disorder	1.20 (0.99–1.44)	1.18 (0.94–1.49)
Conduct disorder	<b>1.53 (1.35–1.72)</b>	<b>1.59 (1.37–1.84)</b>
Anxiety disorders	<b>1.40 (1.20–1.65)</b>	<b>1.42 (1.17–1.72)</b>
Obsessive-compulsive disorder	<b>1.63 (1.43–1.86)</b>	<b>1.68 (1.43–1.97)</b>
Posttraumatic and other stress-related disorders	<b>1.35 (1.18–1.54)</b>	<b>1.39 (1.18–1.64)</b>
Eating disorders	<b>1.51 (1.34–1.70)</b>	<b>1.58 (1.37–1.83)</b>
Depression and other mood disorders	<b>1.39 (1.19–1.61)</b>	<b>1.44 (1.20–1.73)</b>
Bipolar disorders	<b>1.47 (1.30–1.67)</b>	<b>1.52 (1.30–1.76)</b>
Schizophrenia and other psychotic disorders	<b>1.57 (1.39–1.77)</b>	<b>1.64 (1.41–1.89)</b>
Substance use disorders	<b>1.35 (1.17–1.56)</b>	<b>1.43 (1.20–1.69)</b>
Dissocial personality disorder	<b>1.47 (1.31–1.66)</b>	<b>1.54 (1.33–1.78)</b>

- Risk of all transport accidents in those with TS/CTD + ADHD was **1.86 (1.59-2.17)** and risk of motor vehicle accidents was **2.02 (1.69-2.42)**.

# Transport accidents

- The majority of individuals with TS/CTD are able to drive safely.
- Detection and adequate management of comorbid ADHD in driving-age individuals with TS/CTD should be prioritized.
- Licensing agencies should not necessarily equate TS/CTD with an increased risk for serious transport accidents.
- Decisions should be made on individual basis.



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**Movement  
Disorders**

RESEARCH ARTICLE

CLINICAL PRACTICE

# Driving with Tic Disorders: An International Survey of Lived Experiences

Lorena Fernández de la Cruz, PhD,<sup>1</sup> Helene Ringberg, MSc,<sup>2</sup> Seonaid Anderson, PhD,<sup>3</sup> Jeremy S. Stern, FRCP,<sup>4,5</sup> and David Mataix-Cols, PhD<sup>1,\*</sup>

MOVEMENT DISORDERS CLINICAL PRACTICE 2021; 8(3): 412–419. doi: 10.1002/mdc3.13177

## Recent findings

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disorders, convictions,  
and deaths

Insomnia

Transport accidents

Cervical spine disorders



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Research

JAMA Neurology | Original Investigation

## Association of Tourette Syndrome and Chronic Tic Disorder With Cervical Spine Disorders and Related Neurological Complications

Josef Isung, MD, PhD; Kayoko Isomura, MD, PhD; Henrik Larsson, PhD; Anna Sidorchuk, MD, PhD;  
Lorena Fernández de la Cruz, PhD; David Mataix-Cols, PhD

# Cervical spine disorders

- Motor tics involving the neck region are common and bothersome.
- The neck is particularly vulnerable to severe damage due to repeated trauma.
- Single cases and case series describing a range of severe injuries to the cervical spine with neurological complications in individuals with severe forms of motor tics involving the head and the neck region.

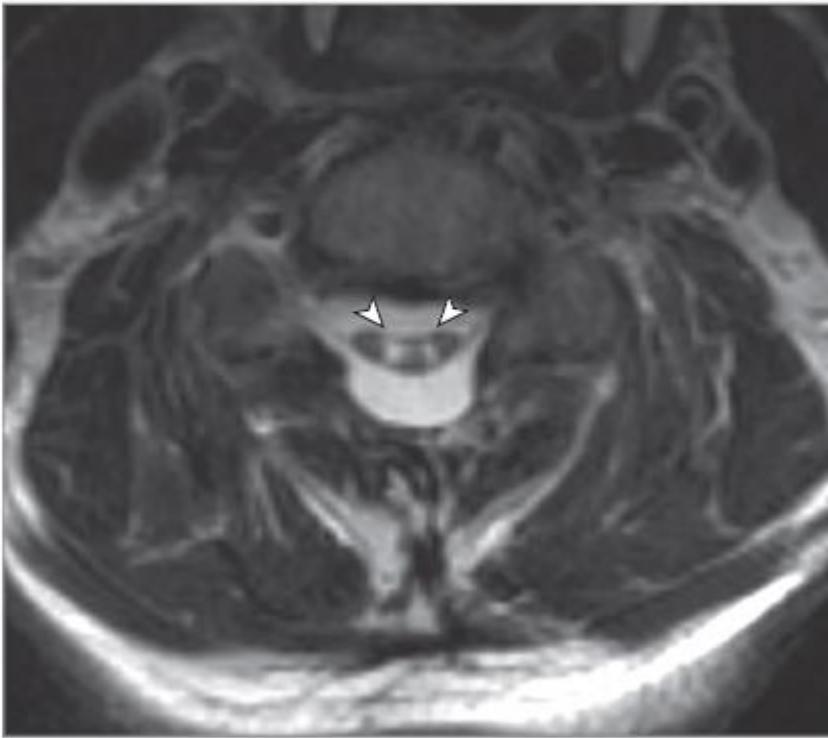
# Cervical spine disorders

**Figure 1. Magnetic Resonance Imaging (MRI) Demonstrating Extensive Injury to the Cervical Cord Secondary to Severe Motor Tics in a Patient With Tourette Syndrome**

**A** Sagittal T2-weighted MRI



**B** Axial T2-weighted MRI



- Is there an actual association between TS/CTD and severe cervical disorders?

# Cervical spine disorders

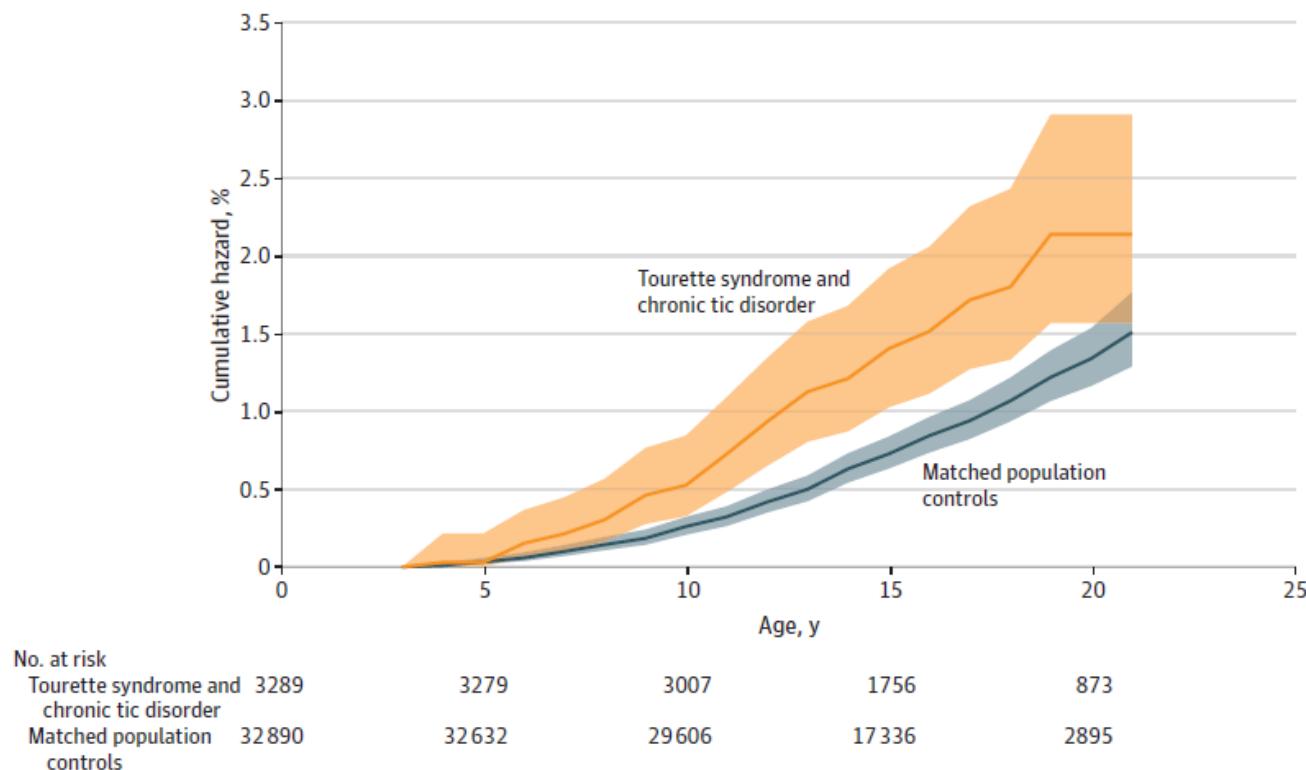
- 6,791 individuals with TS/CTD compared to matched individuals from the general population (1:10)
- Cervical spine disorders and related neurological complications:
  - Cervical vascular disorders
  - Non-vascular disorders and surgeries
- Covariates:
  - Rheumatic disorders
  - Injuries due to traffic accidents
  - Injuries due to fall- and sport-related injuries
  - ADHD diagnosis

# Cervical spine disorders

- 237 individuals (3.49%) in the TS/CTD group and 1,483 (2.18%) in the matched control group had at least one diagnosis of a cervical spine disorder
- 39% increased risk in TS/CTD (aHR=1.39; 95% CI, 1.22-1.59)
- Similar results for vascular and non-vascular groups
- Similar results when excluding individuals with ADHD (aHR=1.33; 95% CI, 1.11-1.60)

# Cervical spine disorders

Figure 2. Cumulative Incidence of Any Cervical Spine Disorders in the Subcohort of Individuals Followed Up From Age 3 Years



# Cervical spine disorders

- Individuals with TS/CTD are at increased risk of cervical spine disorders, some of which can be potentially serious and be associated with long-term disability.
- These disorders are relatively rare but may appear early in mid-childhood, highlighting the importance of increasing awareness on a potentially serious consequence of motor tics.
- Early diagnosis and management of TS/CTD and close monitoring of at-risk individuals are warranted.

## Summary 2020-2021

While in lock-down, we have learnt...

- TS/CTD are associated with various types of substance misuse outcomes.

(Virtanen et al., 2021 *Biol Psychiatry*)

- TS/CTD are associated with a higher point prevalence and higher likelihood of insomnia, particularly in those with neurodevelopmental disorders, mainly ADHD/ADHD meds.

(Isomura et al., *under review*)

# Summary 2020-2021

While in lock-down, we have learnt...

- There is a marginally increased risk for serious transport accidents in TS/CTD, which is mainly driven by ADHD comorbidity.

(Mataix-Cols et al., 2021 *Mov Disord*)

- Individuals with TS/CTD have a higher likelihood to present with cervical spine disorders and related neurological complications.

(Isung et al., 2021 *JAMA Neurol*)



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# Thank you!

**lorena.fernandez.de.la.cruz@ki.se**

 @LorenaFdeIaC

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