IMPORTANCE There are limited data concerning the risk of metabolic and cardiovascular disorders among individuals with Tourette syndrome (TS) or chronic tic disorder (CTD).

OBJECTIVE To investigate the risk of metabolic and cardiovascular disorders among individuals with TS or CTD over a period of 40 years.

DESIGN, SETTINGS, AND PARTICIPANTS This longitudinal population-based cohort study included all individuals living in Sweden between January 1, 1973, and December 31, 2013. Families with clusters of full siblings discordant for TS or CTD were further identified. Data analyses were conducted from August 1, 2017, to October 11, 2018.

EXPOSURES Previously validated International Classification of Diseases diagnoses of TS or CTD in the Swedish National Patient Register.

MAIN OUTCOMES AND MEASURES Registered diagnoses of obesity, dyslipidemia, hypertension, type 2 diabetes, and cardiovascular diseases (including ischemic heart diseases, arrhythmia, cerebrovascular diseases and transient ischemic attack, and arteriosclerosis).

RESULTS Of the 14,045,026 individuals in the cohort, 7,804 individuals (5,964 males [76.4%]; median age at first diagnosis, 13.3 years [interquartile range, 9.9-21.3 years]) had a registered diagnosis of TS or CTD in specialist care. Of 2,675,482 families with at least 2 singleton full siblings, 5,141 families included siblings who were discordant for these disorders. Individuals with TS or CTD had a higher risk of any metabolic or cardiovascular disorders compared with the general population (hazard ratio adjusted by sex and birth year [aHR], 1.99; 95% CI, 1.90-2.09) and sibling controls (aHR for any disorder, 1.37; 95% CI, 1.24-1.51). Specifically, individuals with TS or CTD had higher risks for obesity (aHR, 2.76; 95% CI, 2.47-3.09), type 2 diabetes (aHR, 1.67; 95% CI, 1.42-1.96), and circulatory system diseases (aHR, 1.76; 95% CI, 1.67-1.86). The risk of any cardiometabolic disorder was significantly greater in males than in females (aHR, 2.13; 95% CI, 2.01-2.26 vs aHR, 1.79; 95% CI, 1.64-1.96), as was the risk of obesity (aHR, 3.24; 95% CI, 2.83-3.70 vs aHR, 1.97; 95% CI, 1.59-2.44). The risks were already evident from childhood (the groups were significantly different by age 8 years) and were significantly reduced with the exclusion of individuals with comorbid attention-deficit/hyperactivity disorder (aHR, 1.52; 95% CI, 1.42-1.62), while excluding other comorbidities did not significantly affect the results. Compared with patients with TS or CTD who were not taking antipsychotics, patients with a longer duration of antipsychotic treatment (>1 year) had significantly lower risks of metabolic and cardiovascular disorders.

CONCLUSIONS AND RELEVANCE The findings of this study suggest that TS and CTD are associated with a substantial risk of metabolic and cardiovascular disorders. The results highlight the importance of carefully monitoring cardiometabolic health in patients with TS or CTD across the lifespan, particularly in those with comorbid attention-deficit/hyperactivity disorder.
Tourette syndrome (TS) and chronic tic disorder (CTD) are neurodevelopmental movement disorders characterized by multiple motor and phonic tics in TS and multiple motor or phonic tics in CTD, lasting more than 1 year in both disorders.17-20 Although these disorders are associated with multiple adversities, including an increased risk of premature death.4 However, very little is known about the factors that contribute to these adverse outcomes.

Previous research has shown that individuals with neuropsychiatric disorders are more prone to develop health complications,5-12 which in turn are known to increase the risk of mortality.13-15 Among these complications, metabolic syndrome, a group of risk factors that generally includes abdominal obesity, increased triglyceride concentrations, reduced high-density lipoprotein cholesterol concentrations, hypertension, and hyperglycemia,16 together with cardiovascular problems, have received the most attention.

In TS and CTD, cardiometabolic disorders have been explored mainly as potential adverse effects of pharmacologic treatment, particularly antipsychotics.17-20 Although these studies were valuable, they were small, had short follow-up periods, and lacked control groups of unexposed individuals, thus limiting the generalizability of the results. In addition, previous studies could not examine the role of other potential variables, such as psychiatric comorbidity or familial factors, that may influence both the disorder and the outcomes, such as shared environment or genetic factors.21

In this longitudinal population-based cohort study, we aimed to study the risk of cardiometabolic disorders in almost 8000 individuals with TS or CTD identified in the Swedish national registers over 4 decades. We also aimed to explore whether common psychiatric comorbidities contribute to the risk of cardiometabolic disorders. To rule out alternative explanations of the association between TS and CTD and metabolic and cardiovascular disorders (eg, genetic or shared environmental factors), we used a full sibling comparison design that controlled for possible shared familial confounders. In addition exploratory analyses, we examined whether pharmacologic treatment with antipsychotics was associated with the risk of cardiometabolic disorders in patients who received a diagnosis of TS or CTD.

### Methods

This study largely follows the methods and reports on the same outcomes examined in a previous study in which the exposure was obsessive-compulsive disorder.12 The study was approved by the Regional Ethical Review Board in Stockholm (reference number 2013/862-31/5). The requirement for informed consent was waived because the study is register based and the individuals are not identifiable at any time.

### Data Sources

Data were obtained by linking several Swedish nationwide administrative registers through the unique personal national identification numbers assigned to Swedish citizens.22 Registers included (1) the Swedish Total Population Register, containing data on all Swedish inhabitants since 1968, from which demographic data were obtained; (2) the Migration Register, which contains a record on all migration flows in and out of Sweden; (3) the Multi-Generation Register, which connects every person born in Sweden since 1933 and ever registered as living in the country after 1960 with their parents, allowing for the identification of siblings and other relatives; (4) the Cause of Death Register, which contains information on all deaths since 1952; (5) the National Patient Register (NPR), which includes data on all diagnoses given in both inpatient (since 1969, with good coverage for psychiatric disorders since 1973)24 and outpatient specialist services (since 2001) based on the *International Classification of Diseases (ICD)* in its eighth (ICD-8; 1969-1986), ninth (ICD-9; 1987-1996), and tenth (ICD-10; 1997-2013) revisions; and (6) the Prescribed Drug Register, which includes, since July 1, 2005, a record of all dispensed medications in Sweden, registered using the codes from the *Anatomical Therapeutic Chemical Classification System*.25

### Study Cohort and Exposure Variables

The study cohort included all individuals living in Sweden at any given time between January 1, 1973, and December 31, 2013. Individuals were followed up from birth or 1973, whichever came last, until the date of the outcomes of interest (ie, metabolic or cardiovascular disorders), emigration, death, or December 31, 2013 (end of the study period), whichever came first.

Individuals with a lifetime diagnosis of TS or CTD between January 1, 1973, and December 31, 2013, were identified from the NPR (ICD-8 code 306.2, ICD-9 code 307C, and ICD-10 codes F95.0 [transient tic disorder], F95.1 [chronic motor or vocal tic disorder], F95.2 [TS], F95.8 [other tic disorders], or F95.9 [unspecified tic disorder]). The Swedish TS and CTD codes have been previously validated.26 As in previous works,27-30 we used an algorithm to minimize the inclusion of individuals with only transient tics.

### Lifetime comorbid psychiatric diagnoses were obtained from the NPR and included (1) organic disorders (organic brain disorder and epilepsy), (2) obsessive-compulsive disorder, (3) attention-deficit/hyperactivity disorder (ADHD), (4) conduct disorders, (5) pervasive developmental disorders, etc.
(6) depressive and bipolar disorders, (7) anxiety disorders, and (8) psychotic disorders. All disorders were defined as at least 1 registered diagnosis in the NPR during follow-up (eTable 1 in the Supplement).

Antipsychotic drugs (Anatomical Therapeutic Chemical Classification System code N05A) were identified from the Prescribed Drug Register. Individuals were classified as receiving antipsychotics if they had been dispensed between July 1, 2005, and December 31, 2013. For each individual with TS or CTD, follow-up time was divided into treatment periods (when the patients were taking antipsychotics) and nontreatment periods. The duration of an individual’s treatment period was estimated as the length of time between the first and the final dispensation. As the Swedish pharmaceutical benefits allow for a maximum 3-month medication supply per prescription, the duration of each treatment period was extended by 91 days to ensure capturing the full length of treatment.31 Treatment periods consisted of single dispensations or 2 or more consecutive dispensations within a 6-month period. If there were gaps extending beyond 6 months, the next dispensation was considered as the initiation of a new period of treatment. Thus, each person could have more than 1 individual period of treatment of different duration during the follow-up. For each individual, the cumulative number of days of all treatment periods was summed and categorized into no antipsychotic medication, antipsychotic medication up to 1 year, and antipsychotic medication for more than 1 year.

Metabolic and Cardiovascular Disorders
The diagnosis of metabolic syndrome as such generally requires laboratory tests and medical examinations16 that are not recorded in the population health registers. As a proxy and in accordance with previous work,12 we selected several medical conditions known to be associated with the diagnostic criteria of metabolic syndrome (eTable 2 in the Supplement). In addition, because type 2 diabetes and cardiovascular diseases are strongly associated with metabolic syndrome,16 these diagnoses were also included as outcome variables. The study outcomes were defined by means of 2 different methods. First, diagnoses of obesity, hypertension, type 2 diabetes, and cardiovascular diseases (which included ischemic heart diseases, arrhythmia, cerebrovascular diseases, and transient ischemic attack, and arteriosclerosis) were retrieved from the NPR (ICD codes are listed in eTable 2 in the Supplement). Individuals with a diagnosis of type 2 diabetes who also had a diagnosis of type 1 diabetes (ICD-10 code E10) were excluded to avoid these cases being confounded with a disorder that, etiologically, would be distinct. Second, in an attempt to improve the coverage of the outcomes, individuals who were dispensed drugs generally prescribed to treat dyslipidemia, type 2 diabetes, hypertension, or cardiovascular disorders (eTable 2 in the Supplement shows the specific drugs and corresponding Anatomical Therapeutic Chemical Classification System codes) were also considered as having these outcomes. Because the drugs prescribed to treat hypertension and cardiovascular problems usually overlap (eg, diuretics are prescribed for both conditions), the 2 categories were merged into a broader category called circulatory system diseases, as classified in ICD-10. For individuals having both an ICD diagnosis and 1 of the relevant drug prescriptions, the date of the first event was used as the censoring date for the survival analysis.

Statistical Analysis
Analyses were performed from August 1, 2017, to October 11, 2018, using SAS, version 9.4 for Windows (SAS Institute Inc). We used Cox proportional hazards regression analyses to estimate hazard ratios (HRs) and corresponding 95% CIs for metabolic and cardiovascular disorders in exposed individuals (those with a lifetime diagnosis of TS or CTD) compared with unexposed individuals (those without a diagnosis of TS or CTD), taking into account the time at risk, with days since the start of follow-up as the underlying time scale. Analyses were adjusted for birth year (used as a continuous variable) and sex. The main analyses were also stratified by sex.

As a sensitivity analysis, the same models were repeated in the subgroup of individuals who entered the cohort at birth to ensure complete follow-up time, thus avoiding issues with left truncation (ie, exposure, outcome, or death occurring before the register started, which may lead to missing observations or individuals). In addition, the expected cumulative incidence of cardiometabolic disorders for exposed and unexposed individuals was calculated using Kaplan-Meier survival estimates in the subgroup of individuals with data available from birth.

In a further step, we implemented a fixed-effects model in the subsample of full siblings included in the cohort, also using stratified Cox proportional hazards regression models. This analysis compares all full siblings within a family with each other in a way that exposed siblings (those who have received a diagnosis of TS or CTD) have their unexposed full siblings as comparison. These models control for potential familial confounders that are shared by full siblings, including unmeasured shared environmental factors, such as parental socioeconomic status, and about 50% of the genetic factors.32 To determine how the presence of other psychiatric disorders was associated with the risk of cardiometabolic disorders in the cohort, the main analyses were repeated excluding different groups of comorbid psychiatric disorders, one at a time.

An exploratory analysis aimed to study the association of antipsychotic drugs with cardiometabolic disorders in individuals with TS or CTD. We excluded all individuals who had developed any cardiometabolic disorder before July 1, 2005 (start of the follow-up period in the Prescribed Drug Register). Then we performed Cox proportional hazards regression analyses (adjusted for birth year and sex) comparing individuals with a registered TS or CTD diagnosis who were not receiving antipsychotic drugs (reference group) with those receiving antipsychotic drugs as a cumulative time-varying exposure using the above-described duration categories.

Results

Descriptive Statistics
We identified 14 045 026 individuals who lived in Sweden during the period 1973-2013. The mean (SD) length of the follow-up was 22.2 (13.7) years (median, 22.8 years; range, 0-41
Table 1. Risk of Metabolic and Cardiovascular Disorders Among Individuals With Tourette Syndrome or Chronic Tic Disorder, Compared With Unaffected Individuals From the General Population

<table>
<thead>
<tr>
<th>Metabolic and Cardiovascular Disorders</th>
<th>Tourette Syndrome or Chronic Tic Disorder Cohort (n = 7804)</th>
<th>Unaffected General Population (n = 14,037,222)</th>
<th>HR (95% CI), Adjusted for Sex and Birth Yeara</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any disorder, all</td>
<td>1572 (20.1)</td>
<td>4,933,345 (35.1)</td>
<td>1.99 (1.90-2.09)</td>
</tr>
<tr>
<td>Male</td>
<td>1067 (17.9)</td>
<td>2,344,448 (33.2)</td>
<td>2.13 (2.01-2.26)</td>
</tr>
<tr>
<td>Female</td>
<td>505 (27.5)</td>
<td>2,588,897 (37.2)</td>
<td>1.79 (1.64-1.96)</td>
</tr>
<tr>
<td>Obesity, all</td>
<td>301 (3.9)</td>
<td>196,158 (1.4)</td>
<td>2.76 (2.47-3.09)</td>
</tr>
<tr>
<td>Male</td>
<td>217 (3.6)</td>
<td>66,883 (1.0)</td>
<td>3.24 (2.83-3.70)</td>
</tr>
<tr>
<td>Female</td>
<td>84 (4.6)</td>
<td>129,275 (1.9)</td>
<td>1.97 (1.59-2.44)</td>
</tr>
<tr>
<td>Dyslipidemia, all</td>
<td>180 (2.3)</td>
<td>1,122,174 (8.0)</td>
<td>0.87 (0.75-1.00)</td>
</tr>
<tr>
<td>Male</td>
<td>111 (1.9)</td>
<td>592,355 (8.4)</td>
<td>0.79 (0.65-0.95)</td>
</tr>
<tr>
<td>Female</td>
<td>69 (3.8)</td>
<td>529,819 (7.6)</td>
<td>1.04 (0.82-1.31)</td>
</tr>
<tr>
<td>Type 2 diabetes, all</td>
<td>147 (1.9)</td>
<td>426,448 (3.0)</td>
<td>1.67 (1.42-1.96)</td>
</tr>
<tr>
<td>Male</td>
<td>98 (1.6)</td>
<td>228,344 (3.2)</td>
<td>1.63 (1.34-1.99)</td>
</tr>
<tr>
<td>Female</td>
<td>49 (2.7)</td>
<td>198,104 (2.8)</td>
<td>1.83 (1.38-2.42)</td>
</tr>
<tr>
<td>Circulatory system diseases, all</td>
<td>1291 (16.5)</td>
<td>4,790,365 (34.1)</td>
<td>1.76 (1.67-1.86)</td>
</tr>
<tr>
<td>Male</td>
<td>846 (14.2)</td>
<td>2,288,283 (32.4)</td>
<td>1.81 (1.69-1.94)</td>
</tr>
<tr>
<td>Female</td>
<td>445 (24.2)</td>
<td>2,502,082 (35.9)</td>
<td>1.70 (1.55-1.87)</td>
</tr>
</tbody>
</table>

Abbreviation: HR, hazard ratio.

a Percentages for male and female individuals are based on the total numbers by sex in each group (Tourette syndrome or chronic tic disorder: 5964 male individuals and 1840 female individuals; unaffected general population: 7,070,359 male individuals and 6,966,863 female individuals).

Risk of Cardiometabolic Disorders

Individuals with TS or CTD had nearly double the risk of any cardiometabolic disorder compared with unaffected individuals from the general population (HR adjusted for sex and year of birth [aHR], 1.99; 95% CI, 1.90-2.09 (Table 1). Similarly, the risk for each specific disorder was also significantly higher in those with TS or CTD except for dyslipidemia (aHR, 2.76; 95% CI, 2.47-3.09; type 2 diabetes: aHR, 1.67; 95% CI, 1.42-1.96; circulatory system diseases: aHR, 1.76; 95% CI, 1.67-1.86; and dyslipidemia: aHR, 0.87; 95% CI, 0.75-1.00)). The risk of any cardiometabolic disorder was significantly greater in males than in females (aHR, 2.13; 95% CI, 2.01-2.26 vs aHR, 1.79; 95% CI, 1.64-1.96), as was the risk of obesity (aHR, 3.24; 95% CI, 2.83-3.70 vs aHR, 1.97; 95% CI, 1.59-2.44) (Table 1).

A total of 6245 individuals with TS or CTD and 4,244,718 individuals from the general population cohort had full data available from birth. When the analysis was limited to this cohort to ensure complete follow-up time, the risks for cardiometabolic disorders remained overall unchanged for any disorder (aHR, 2.06; 95% CI, 1.93-2.19) and for all the specific diagnoses (obesity: aHR, 2.88; 95% CI, 2.55-3.25; type 2 diabetes: aHR, 1.85; 95% CI, 1.50-2.29; and circulatory system diseases: aHR, 1.95; 95% CI, 1.81-2.10) except for dyslipidemia, which became statistically significant (aHR, 1.58; 95% CI, 1.06-2.36) (eTable 3 in the Supplement).

The cumulative incidences of any cardiometabolic disorder at the end of follow-up (under the assumption of no competing risks estimated as 1 – the Kaplan-Meier estimate of survival function, with the oldest individual being 41 years) were 52.5% (95% CI, 47.7%-57.4%) for those with TS or CTD and 29.5% (95% CI, 29.3%-29.6%) for the general population cohort (Figure). The differences between the 2 cohorts for any cardiometabolic disorder were already significant (nonoverlapping 95% CIs) from childhood (age, 8 years).

Sibling Comparison

Of the 2,675,482 families who had at least 2 singleton children, 5,141 families included clusters of full siblings who were discordant for TS or CTD. Those with TS or CTD had a higher risk of any cardiometabolic disorder compared with their unaffected full siblings without TS or CTD (aHR, 1.37; 95% CI, 1.24-1.51) (Table 2). The risks of obesity (aHR, 1.57; 95% CI, 1.25-1.98) and circulatory system diseases (aHR, 1.39; 95% CI, 1.25-1.56) were also significantly increased among individuals with TS or CTD compared with their full siblings (Table 2) but with lower risk estimates compared with the general population.

Effect of Comorbidities

Frequencies of comorbid conditions in the cohort with TS or CTD and in the general population are displayed in eTable 4 in the Supplement. When different groups of psychiatric comorbidities were excluded from the analyses, the risk estimates for metabolic and cardiovascular disorders remained largely similar. The only exception was ADHD; the risks were reduced, but remained substantial, when individuals with this disorder were excluded (aHR, 1.52; 95% CI, 1.42-1.62) (Table 3).

Effect of Antipsychotic Use

A total of 6324 individuals in the cohort with TS or CTD with data in the Prescribed Drug Register were used in these exploratory analyses. Use of antipsychotic medication for up to 1 year was not associated with a significantly increased risk of metabolic and cardiovascular disorders (aHR, 0.83; 95% CI,
However, use of antipsychotic medication for more than 1 year was associated with a significantly decreased risk of these disorders (aHR, 0.27; 95% CI, 0.17-0.43).

**Discussion**

To our knowledge, this is the first study to report on the risk of cardiometabolic disorders among individuals with TS or CTD at the population level. The results expand our understanding of the broader health consequences of TS and CTD and have direct clinical implications across health services, including neurology, pediatrics, psychiatry, and primary care.

The main finding was that individuals who received a diagnosis of TS or CTD were nearly twice as likely to develop at least 1 cardiometabolic disorder, compared with individuals from the general population without TS or CTD. In particular, the risks of obesity, circulatory system diseases, and type 2 diabetes were significantly elevated. The risks of any cardiometabolic disorder and obesity were significantly greater in 0.56-1.24). However, use of antipsychotic medication for more than 1 year was associated with a significantly decreased risk of these disorders (aHR, 0.27; 95% CI, 0.17-0.43).
males than in females. By the end of the follow-up (age, 41 years), 29.5% of the general population cohort were expected to have developed at least 1 cardiometabolic disorder, well in line with the literature.\textsuperscript{33,34} The corresponding figure in those with TS or CTD was 52.5%. The risk for any disorder was already significantly higher from childhood.

Our risk estimates remained unchanged overall in sensitivity and subgroup analyses. Exclusion of different groups of comorbidities did not significantly affect the estimates. An exception to this finding was the exclusion of individuals with ADHD from the cohort, which resulted in attenuated risk estimates, although individuals with TS or CTD without comorbid ADHD still had a 52% higher risk of developing cardiometabolic problems. This finding may indicate that a diagnosis of ADHD significantly adds to the observed risk, in line with previous research showing adverse health risk outcomes in ADHD.\textsuperscript{8} However, ADHD was the most prevalent comorbid condition within those with TS or CTD, with nearly half of the individuals with TS or CTD also receiving a diagnosis of ADHD; therefore, exclusion of such individuals results in a less representative cohort of individuals with TS or CTD.

The risk estimates were reduced, but not eliminated, in the sibling comparison analysis (from 1.99 to 1.37 for any cardiometabolic disorder). This finding is unlike that for obsessive-compulsive disorder, a closely related condition, in which the risk of metabolic and cardiovascular disorders remains intact in similar sibling analyses.\textsuperscript{12} There are several possible explanations for these findings. One possibility is that there are genetic and/or environmental risk factors that may partially influence both the disorder and the cardiovascular outcomes (eg, pleiotropic genetic effects). Another possible interpretation is that, while siblings of affected individuals did not have a diagnosis of TS or CTD, they may have had undiagnosed tic disorders or other neuropsychiatric disorders that are, in turn, known to be associated with cardiometabolic disorders.\textsuperscript{8,12} Nonetheless, the risk was still 37% higher for individuals with TS or CTD even after controlling for familial factors, which suggests that at least part of the observed health complications might be attributable to the tic disorders themselves. Individuals with TS or CTD experience a substantial number of stressors in their daily lives,\textsuperscript{35} have poorer educational outcomes,\textsuperscript{29,36} and, like individuals with other neuropsychiatric disorders, might have unhealthier lifestyles (eg, lack of physical activity and poor diet),\textsuperscript{37} which have also been shown to be associated with the development of metabolic and cardiovascular diseases.\textsuperscript{38-40}

In exploratory analyses, patients taking long-term (>1 year) antipsychotics had a lower risk of metabolic and cardiovascular diseases, compared with those who were not using antipsychotic medications. A seemingly protective effect of medication for the risk of adverse outcomes, such as cardiometabolic disorders and mortality, has also been found in other neuropsychiatric disorders, such as obsessive-compulsive disorder\textsuperscript{12} and schizophrenia.\textsuperscript{41} However, previous clinical studies, although smaller and with shorter follow-ups, found an association between use of antipsychotics and increased risk of metabolic disorders.\textsuperscript{17-20} Because this is an observational study, we are careful not to ascribe the reduction of the risk to the medication itself. Patients taking medication may represent an inherently different group than those who are not taking medication. Furthermore, patients seen in specialist services are more likely to have frequent follow-ups and receive closer monitoring of their general health. Thus, the findings might mostly reflect the indirect effects of greater medical vigilance. Our results should not be taken as evidence that antipsychotics are free from cardiometabolic adverse effects, and they should continue to be used with caution in this patient group.

Limitations
This study has some limitations. Although the Swedish registers have national coverage, the study cohort does not represent the totality of all Swedish patients with TS or CTD because many individuals with mild tics do not seek help, the register had incomplete coverage until 2001 (prior to this date, only hospital admissions were registered), and patients diagnosed in primary care by general practitioners and other nonspecialists are not included. Thus, while the patients included in our cohort resemble other patients recruited from specialist tic disorder clinics around the world, it is possible that our results do not generalize to less complex patient samples or individuals with mild tics. Similarly, it is likely that coverage is incomplete for at least some of the outcomes that are more likely to be diagnosed in primary care settings than in specialist services, such as obesity. In addition, the Prescribed Drug Register started in 2005, resulting in a relatively short follow-up time in the mediation analyses. Although many diagnostic codes in the NPR have been successfully validated,\textsuperscript{26,42-45} others (eg, conduct disorder and anxiety disorders) have yet to be validated. Despite having specific indications, some drugs used to identify specific outcomes may have been prescribed to treat more than 1 cardiovascular disorder, which means that the estimates for any cardiometabolic disorder may be more precise than those of individual disorders. Finally, the registers do not include information on other behavioral variables known to have an effect on the outcomes of interest (such as sedentary lifestyle, unhealthy eating habits, or smoking)\textsuperscript{46} or nonpharmacologic strategies to manage them (eg, behavioral interventions).

Conclusions
Tourette syndrome and CTD are associated with a substantial risk of cardiometabolic problems, even after taking into account a number of covariates and shared familial confounders and excluding relevant psychiatric comorbidities.

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