

Table S1. Rate ratio* for tonsillectomy in the first year after tonsillectomy in a relative, by type of tonsillectomized relative, Denmark, 1977-2013.

Type and number of tonsillectomized relatives†	Tonsillectomy		
	Person-years x 10 ³	Number of events	Rate ratio [95% confidence Intervals]
TWINS			
No	662.40	2037	1 [Reference]
Yes [same-sex twin]	1.70	308	39.09 [34.67, 44.07]
No	347.14	1247	1 [Reference]
Yes [different-sex twin]	1.17	49	7.74 [5.82, 10.3]
First-degree relatives			
SIBLINGS			
No	29050.40	89798	1 [Reference]
Yes, 1	114.86	1809	5.23 [4.99, 5.48]
PARENTS††			
No	1500.65	5057	1 [Reference]
Yes, 1	4.16	45	2.65 [1.97, 3.55]
Yes, both	-	-	-
Second-degree relatives			
MATERNAL HALF SIBLINGS			
No	5001.56	17872	1 [Reference]
Yes, 1	24.40	214	2.46 [2.15, 2.81]
PATERNAL HALF-SIBLINGS			
No	5769.94	19393	1 [Reference]
Yes, 1	29.16	167	1.67[1.43, 1.94]
UNCLES/AUNTS			
No	3330.29	12771	1 [Reference]
Yes, 1	10.86	66	1.58 [1.24, 2.02]
Third-degree relatives			
COUSINS			
No	20658.13	71811	1 [Reference]
Yes, 1	261.32	1396	1.52 [1.45, 1.61]
HALF UNCLES/AUNTS			
No	2433.84	10333	1 [Reference]
Yes, 1	12.92	73	1.27 [1.01, 1.6]

[Table S1 continued]

Type and number of tonsillectomized relatives†	Tonsillectomy		
	Person-years x 10 ³	Number of events	Rate ratio [95% confidence Intervals]
<i>Fourth-degree relatives</i>			
HALF COUSINS			
No	3521.07	14776	1 [Reference]
Yes, 1	41.17	239	1.34 [1.18, 1.53]

* Rate ratios adjusted for calendar-period, number of relatives of the considered type, and the interaction between attained age and sex. Rate ratios are based on tonsillectomy at any age in cohort member and relatives including after 20 years of age. For simplicity we show rate ratios only for *one* tonsillectomized relative of a given type while rate ratios for two, or more, tonsillectomized relatives are not shown.

† "No" means that although the person had relatives of the given type and number, none of these relatives had been tonsillectomized.

†† Numbers are small because few individuals are tonsillectomized after age 20 years when most child births take place, and thus even fewer children are tonsillectomized in the first year after a parent is tonsillectomized.

Methods

Detailed explanation of the definition of the study population

Using the Civil Registration System, we established a cohort of persons in Denmark who were alive in 1977, or born later, for whom any relatives were born in Denmark since 1977. The year 1977 was used as cut-off because national registration of surgeries, e.g. tonsillectomy, started in 1977 with establishment of the National Hospital Discharge Register. Thus, with this definition, information on tonsillectomy, both for the index persons and his/hers identified relatives, would be complete during the entire follow-up period starting in 1977 or later. This also means that the cohort does not include the entire Danish population (5.615 million individuals in 2013) but about half of the population.

Statistical model

To evaluate to what degree the observed familial aggregation could be ascribed to shared genes or shared environment the observed RR_h for family history h were modelled as the product of a genetic component and a shared environmental component: $RR_h = G_h \cdot E_h$.

The genetic component, G_h , was modelled as $G_h = A^{2r(h)}$, with $r(h)$ as the coefficient of relatedness with a relative of type h (e.g. $r(\text{siblings})=0.5$). The structure of this simple genetic model is inspired by Risch et al (1992).* The parameter A can be interpreted as the relative increase in risk of tonsillectomy due to genetics in individuals with and without a tonsillectomized sibling.

The environmental component (E_h) was allowed to differ for relatives with and without same mother (as a marker of sharing household), i.e. $E_h = B_1$ when having the same mother as the relative, and $E_h = B_2$ when not having the same mother. E_h can be interpreted as the relative increase in risk of tonsillectomy due to the shared environment in individuals with and without a tonsillectomized relative.

Estimation

The three parameters A , B_1 , B_2 were estimated using a meta-analytic approach. More specifically, the logarithm of the family-history-specific RR estimates were summarized in a simple linear model using inverse-variance weighting (RR and standard error presented in figure 1), i.e.:

$$\log(RR_h) = \begin{cases} 2 \log(A) r + \log(B_1) & \text{If } h = \text{twins, siblings or maternal halfsiblings} \\ 2 \log(A) r + \log(B_2) & \text{Otherwise} \end{cases}$$

Where r instead of $r(h)$ is used for simplicity. Thus, the steeper the trend, the larger the genetic component, and the larger the difference between the intercept and 0 the larger the environmental component. All three parameters were assumed to be larger or equal to 1. The model was estimated for persons being less than 10 years and being 10 to 19 years. The two models were based on RRs where both the index person and the relative were in the specified age-interval. The model was also estimated for each year between 0 and 19 based on the age-interval including the two adjacent age groups on each side, i.e. a “moving average” approach with overlapping age-intervals of 5 years. For age 0 and 1 the estimation intervals were 0-2 and 0-3, respectively, while for age 18 and 19 the estimation was also based on data for ages >19 years.

The difference between the observed and estimated $\log(RR)$, i.e. the goodness of fit, was evaluated by visual inspection of how well the observed $\log(RR)$ s followed the linear form.

*Risch N, et al. Linkage strategies for genetically complex traits. I. Multilocus models. Am J Hum Genet 1990;46:222-8.

Estimates

Table e1 below shows the model estimates for the age-group 0-9 years and 10-19 years. The genetic component for the two age-groups is similar: 2.91 and 2.39. This can be seen as very similar slopes for the lines in Figure 1A compared to 1B. In contrast, the environmental component was strongest in the young group for relatives with the same mother, 1.83 vs. 1.19, and without the same mother, 1.13 vs. 1.00. In Figure 1 this can be seen as larger intercepts in Figure 1A compared to 1B.

Table e1: Estimates used to produce the lines in Figure 1A and Figure 1B. Age-specific estimated sibling rate ratio (RR).

Age-group	A	B_1	B_2	Estimated sibling RR*	Observed sibling RR
0-9	2.91	1.83	1.13	4.73	4.80
10-19	2.39	1.19	1.00	2.83	2.88

*Note that the estimation is not only based on the sibling RR, but on all types of family relations reported in Figure 1.

Table e2 below shows the model estimates for ages 0, 1, 2..., 19 years.

Table e2: Estimates for Figure 2. Age-specific estimated sibling rate ratio (RR).

Age-group	A	B_1	B_2	Estimated sibling RR	Observed sibling RR
0	4.84	3.55	1.70	17.20	17.08
1	3.58	2.69	1.41	9.63	9.91
2	3.62	2.02	1.21	7.29	7.47
3	3.21	1.92	1.21	6.16	6.28
4	3.05	1.86	1.17	5.67	5.78
5	2.77	1.82	1.17	5.03	5.15
6	2.52	1.73	1.14	4.37	4.44
7	2.55	1.58	1.09	4.02	4.10
8	3.00	1.27	1.05	3.80	3.92
9	2.98	1.27	1.04	3.77	3.91
10	3.10	1.25	1.01	3.88	3.91
11	2.85	1.38	1.02	3.93	3.87
12	3.11	1.24	1.00	3.86	3.83
13	2.64	1.34	1.00	3.53	3.53
14	2.70	1.14	1.00	3.08	3.13
15	2.65	1.10	1.00	2.93	3.03
16	2.84	1.00	1.00	2.85	2.93
17	2.67	1.00	1.00	2.67	2.75
18	2.48	1.02	1.02	2.54	2.53
19	2.34	1.05	1.00	2.45	2.43

Table S2. Age-specific rate ratio* for tonsillectomy according to type and age of tonsillectomized relatives, Denmark, 1977-2013.

Type and age of tonsillectomized relatives*	Tonsillectomy	
	Age <10 years	Age 10-19 years
	Rate ratio [95% confidence Intervals]	Rate ratio [95% confidence Intervals]
First-degree relatives		
SIBLINGS		
No	1 [Reference]	1 [Reference]
Yes, aged <10 years	5.03 [4.89, 5.17]	2.42 [2.33, 2.52]
Yes, aged 10-19 years	3.43 [3.00, 3.92]	2.80 [2.63, 2.97]
PARENTS		
No	1 [Reference]	1 [Reference]
Yes, aged <10 years	3.31 [3.11, 3.53]	2.16 [1.41, 3.32]
Yes, aged 10-19 years	2.19 [2.05, 2.34]	2.46 [1.73, 3.50]
Second-degree relatives		
MATERNAL HALF-SIBLINGS		
No	1 [Reference]	1 [Reference]
Yes, aged <10 years	2.80 [2.62, 2.99]	1.70 [1.56, 1.86]
Yes, aged 10-19 years	2.24 [1.95, 2.58]	1.58 [1.37, 1.83]
PATERNAL HALF-SIBLINGS		
No	1 [Reference]	1 [Reference]
Yes, aged <10 years	1.80 [1.67, 1.95]	1.46 [1.33, 1.60]
Yes, aged 10-19 years	1.43 [1.23, 1.66]	1.22 [1.04, 1.44]
UNCLES/AUNTS		
No	1 [Reference]	1 [Reference]
Yes, aged <10 years	1.98 [1.86, 2.10]	1.49 [1.22, 1.82]
Yes, aged 10-19 years	1.50 [1.40, 1.60]	1.52 [1.27, 1.82]
Third-degree relatives		
COUSINS		
No	1 [Reference]	1 [Reference]
Yes, aged <10 years	1.62 [1.58, 1.66]	1.25 [1.21, 1.30]
Yes, aged 10-19 years	1.36 [1.29, 1.44]	1.25 [1.19, 1.32]
HALF-UNCLES/AUNTS		
No	1 [Reference]	1 [Reference]
Yes, aged <10 years	1.54 [1.44, 1.65]	1.05 [0.91, 1.23]
Yes, aged 10-19 years	1.27 [1.17, 1.38]	1.20 [1.03, 1.40]

[Table S2 continued]

Type and age of tonsillectomized relatives*	Tonsillectomy	
	Age <10 years	Age 10-19 years
	Rate ratio [95% confidence Intervals]	Rate ratio [95% confidence Intervals]
<i>Fourth-degree relatives</i>		
HALF COUSINS		
No	1 [Reference]	1 [Reference]
Yes, aged <10 years	1.22 [1.14, 1.29]	1.11 [1.02, 1.21]
Yes, aged 10-19 years	0.99 [0.88, 1.12]	1.02 [0.88, 1.17]

To increase the reader's overview of the table, number of events and person-years is not shown in this table.

* Rate ratios were estimated using the same model as in main analysis and included rate ratios for more than one tonsillectomized relative of a given type. "No" means that although the person had relatives of the given type and age, none of these relatives had been tonsillectomized.

Table S3. Rate ratio* for tonsillectomy stratified by total number of relatives, according to type and number of tonsillectomized relatives, Denmark, 1977-2013.

Type and number of tonsillectomized relatives*	Tonsillectomy				
	1 relative	2 relatives	3 relatives	4 relatives	5 relatives
	Rate ratio [95% confidence Intervals]	Rate ratio [95% confidence Intervals]	Rate ratio [95% confidence Intervals]	Rate ratio [†] [95% confidence Intervals]	Rate ratio [†] [95% confidence Intervals]
First-degree relatives					
SIBLINGS					
Yes, 1	3.16 [3.08, 3.24]	3.12 [3.01, 3.24]	2.75 [2.54, 2.98]	3.00 [2.54, 3.55]	2.72 [2.05, 3.61]
Yes, 2		6.58 [6.06, 7.15]	5.27 [4.59, 6.05]	6.49 [5.07, 8.30]	5.60 [3.77, 8.32]
Yes, 3			11.93 [9.05, 15.74]	11.36 [7.35, 17.56]	7.97 [4.22, 15.05]
Yes, 4				14.12 [5.86, 34.06]	18.99 [8.43, 42.79]
Yes, 5+					44.78 [14.32, 140.03]
PARENTS [not calculated]					
Second-degree relatives					
MATERNAL HALF-SIBLINGS					
Yes, 1	1.89 [1.78, 2.00]	1.95 [1.8, 2.12]	2.05 [1.73, 2.42]	1.71 [1.20, 2.44]	0.85 [0.36, 2.03]
Yes, 2		3.41 [2.88, 4.05]	3.27 [2.46, 4.34]	1.79 [0.88, 3.66]	2.00 [0.61, 6.52]
Yes, 3			5.17 [2.77, 9.66]	6.04 [2.47, 14.73]	6.67 [1.60, 27.78]
Yes, 4				-	19.79 [6.07, 64.53]
Yes, 5+					42.29 [10.15, 176.26]

[Table S3 continued]

Type and number of tonsillectomized relatives*	Tonsillectomy				
	1 relative	2 relatives	3 relatives	4 relatives	5 relatives
	Rate ratio [95% confidence Intervals]	Rate ratio [95% confidence Intervals]	Rate ratio [95% confidence Intervals]	Rate ratio [†] [95% confidence Intervals]	Rate ratio [†] [95% confidence Intervals]
PATERNAL HALF-SIBLINGS					
Yes, 1	1.5 [1.4, 1.6]	1.35 [1.24, 1.47]	1.26 [1.08, 1.48]	1.40 [1.05, 1.87]	1.55 [0.97, 2.46]
Yes, 2		2.13 [1.76, 2.57]	2.05 [1.52, 2.77]	1.37 [0.75, 2.51]	0.93 [0.34, 2.53]
Yes, 3			1.86 [0.83, 4.14]	2.05 [0.66, 6.40]	-
Yes, 4				-	-
Yes, 5+					-
UNCLES/AUNTS					
Yes, 1	1.62 [1.53, 1.72]	1.66 [1.53, 1.80]	1.62 [1.42, 1.85]	1.47 [1.17, 1.84]	1.54 [1.12, 2.10]
Yes, 2		2.78 [2.28, 3.38]	2.65 [2.12, 3.32]	2.26 [1.59, 3.21]	2.90 [1.92, 4.40]
Yes, 3			4.45 [2.57, 7.70]	3.40 [1.68, 6.85]	3.64 [2.02, 6.58]
Yes, 4				2.70 [0.38, 19.22]	9.62 [3.94, 23.50]
Yes, 5+					23.95 [8.85, 64.77]
Third-degree relatives					
COUSINS					
Yes, 1	1.42 [1.29, 1.58]	1.35 [1.28, 1.43]	1.36 [1.28, 1.44]	1.39 [1.32, 1.46]	1.33 [1.29, 1.36]
Yes, 2		1.83 [1.57, 2.12]	1.91 [1.68, 2.18]	1.55 [1.37, 1.74]	1.60 [1.54, 1.67]
Yes, 3			1.69 [1.08, 2.65]	2.03 [1.47, 2.80]	1.79 [1.65, 1.93]
Yes, 4				2.51 [0.94, 6.68]	2.26 [1.97, 2.60]
Yes, 5+					2.85 [2.36, 3.43]

[Table S3 continued]

Type and number of tonsillectomized relatives*	Tonsillectomy				
	1 relative	2 relatives	3 relatives	4 relatives	5 relatives
	Rate ratio [95% confidence Intervals]	Rate ratio [95% confidence Intervals]	Rate ratio [95% confidence Intervals]	Rate ratio† [95% confidence Intervals]	Rate ratio† [95% confidence Intervals]
HALF-UNCLES/AUNTS					
Yes, 1	1.30 [1.20, 1.41]	1.36 [1.23, 1.50]	1.23 [1.09, 1.40]	1.36 [1.14, 1.62]	1.31 [1.07, 1.60]
Yes, 2		1.71 [1.33, 2.19]	1.97 [1.55, 2.50]	1.81 [1.34, 2.46]	1.63 [1.22, 2.19]
Yes, 3			1.74 [0.83, 3.65]	2.17 [1.08, 4.37]	1.12 [0.53, 2.37]
Yes, 4				-	9.34 [3.48, 25.06]
Yes, 5+					-
Fourth-degree relatives					
HALF COUSINS					
Yes, 1	1.07 [0.90, 1.27]	1.12 [1.00, 1.25]	1.12 [0.99, 1.26]	1.16 [1.02, 1.32]	1.08 [1.00, 1.16]
Yes, 2		1.45 [1.12, 1.89]	1.36 [1.05, 1.76]	1.05 [0.77, 1.43]	1.11 [0.98, 1.25]
Yes, 3			2.06 [1.20, 3.56]	1.14 [0.51, 2.55]	1.26 [1.00, 1.57]
Yes, 4				3.56 [0.50, 25.26]	1.08 [0.66, 1.77]
Yes, 5+					0.83 [0.35, 2.00]

To increase the reader's overview of the table, number of events and person-years is not shown in this table.

* Rate ratios adjusted for calendar-period, number of relatives of the considered type, and the interaction between attained age and sex. Rate ratios are based on tonsillectomy at any age in cohort member and relatives including after 20 years of age.

† Due to small numbers rate ratios in this table were not calculated when only 0-5 events occurred.

Table S4. Rate ratio* for tonsillectomy according to tonsillectomized half-cousins by type of parental line, Denmark 1977-2013.

Number of tonsillectomized half cousins**	Tonsillectomy		
	Person- years x 10 ³	Number of events	Rate ratio [95% confidence Intervals]
<i>Fourth-degree relatives</i>			
MATERNAL HALF COUSINS†			
No	723.5	3372	1 [Reference]
Yes, in 1	39.48	189	1.08 [0.93, 1.25]
Yes, in 2	38.79	167	0.98 [0.84, 1.15]
Yes, in 3+	11.05	69	1.42 [1.11, 1.82]
PATERNAL HALF COUSINS††			
No	617.71	2483	1 [Reference]
Yes, in 1	28.31	94	0.86 [0.70, 1.06]
Yes, in 2	26.38	108	1.08 [0.89, 1.32]
Yes, in 3+	5.36	24	1.24 [0.82, 1.88]
OTHER HALF COUSINS			
No	2947.65	12310	1 [Reference]
Yes, in 1	173.48	756	1.08 [1.00, 1.17]
Yes, in 2	181.05	859	1.21 [1.12, 1.30]
Yes, in 3+	57.29	271	1.26 [1.11, 1.43]

* Rate ratios adjusted for calendar-period, number of half cousins, and the interaction between attained age and sex. Rate ratios are based on tonsillectomy at any age in cohort member and relatives including after 20 years of age.

** "No" means that although the person had relatives of the given type and number, none of these relatives had been tonsillectomized.

† Half cousins through female line of relatives only, i.e. mother, grandmother, and aunt.

†† Half cousins through male line of relatives only, i.e. father, grandfather, and uncle.

Table S5. Rate ratio* for tonsillectomy stratified by age-intervals, according to type and number of tonsillectomized relatives,[§] Denmark, 1977-2013.

Type and number of tonsillectomized relatives [†]	Tonsillectomy					
	Age <10 years			Age 10-19 years		
	Person-years x 10 ³	Number of events	Rate ratio ^{††} [95% confidence Intervals]	Person-years x 10 ³	Number of events	Rate ratio ^{††} [95% confidence Intervals]
TWINS						
No	367.59	1368	1 [Reference]	196.29	456	1 [Reference]
Yes [same-sex twin]	3.32	77	5.94 [4.72, 7.47]	1.19	22	5.98 [3.90, 9.18]
No	207.11	928	1 [Reference]	99.23	229	1 [Reference]
Yes [different-sex twin]	2.88	64	4.55 [3.53, 5.86]	0.63	6	3.72 [1.65, 8.36]
<i>First-degree relatives</i>						
SIBLINGS						
No	12326.99	49347	1 [Reference]	7489.87	22736	1 [Reference]
Yes, 1	283.21	5275	4.80 [4.66, 4.94]	121.35	1042	2.88 [2.7, 3.06]
Yes, 2	14.1	494	11.15 [10.19, 12.21]	2.04	26	5.09 [3.46, 7.49]
Yes, 3+	0.99	58	20.38 [15.69, 26.46]	0.05	2	-
PARENTS						
No	1586.28	6231	1 [Reference]	76.34	184	1 [Reference]
Yes, 1	86.28	1075	3.28 [3.08, 3.50]	6.15	36	2.45 [1.71, 3.5]
Yes, both	1.16	31	8.15 [5.72, 11.61]	0.04	1	-

[Table S5 continued]

Type and number of tonsillectomized relatives [†]	Tonsillectomy					
	Age <10 years			Age 10-19 years		
	Person-years x 10 ³	Number of events	Rate ratio ^{††} [95% confidence Intervals]	Person-years x 10 ³	Number of events	Rate ratio ^{††} [95% confidence Intervals]
Second-degree relatives						
MATERNAL HALF SIBLINGS						
No	1578.64	7542	1 [Reference]	884.27	3527	1 [Reference]
Yes, 1	72.23	918	2.63 [2.46, 2.82]	31.13	186	1.61 [1.39, 1.86]
Yes, 2	4.09	105	5.81 [4.78, 7.08]	0.7	4	-
Yes, 3+	0.27	13	12.69 [7.29, 22.09]	0.03	0	-
PATERNAL HALF-SIBLINGS						
No	1699.34	8104	1 [Reference]	908.37	3409	1 [Reference]
Yes, 1	79.93	678	1.75 [1.62, 1.89]	34.28	151	1.24 [1.05, 1.46]
Yes, 2	4.81	68	2.97 [2.34, 3.78]	0.68	2	0.83 [0.21, 3.33]
Yes, 3+	0.38	1	-	0.01	0	-
UNCLES/AUNTS						
No	2893.14	12314	1 [Reference]	595.17	1585	1 [Reference]
Yes, 1	143.48	1122	1.89 [1.78, 2.01]	30.62	122	1.53 [1.27, 1.84]
Yes, 2	7.72	101	3.36 [2.75, 4.09]	0.48	2	-
Yes, 3+	0.87	18	5.48 [3.44, 8.72]	0.02	1	-
Third-degree relatives						
COUSINS						
No	10894.97	45498	1 [Reference]	6305.09	19722	1 [Reference]
Yes, 1	874.58	5516	1.52 [1.48, 1.57]	374.49	1470	1.26 [1.19, 1.32]
Yes, 2	151.18	1288	2.08 [1.97, 2.20]	31.78	147	1.51 [1.29, 1.78]
Yes, 3+	32.49	354	3.24 [2.91, 3.60]	3.13	25	3.01 [2.03, 4.46]

[Table S5 continued]

Type and number of tonsillectomized relatives [†]	Tonsillectomy					
	Age <10 years			Age 10-19 years		
	Person-years x 10 ³	Number of events	Rate ratio ^{††} [95% confidence Intervals]	Person-years x 10 ³	Number of events	Rate ratio ^{††} [95% confidence Intervals]
HALF UNCLES/AUNTS						
No	1774.23	8343	1 [Reference]	649.95	2284	1 [Reference]
Yes, 1	126.31	882	1.49 [1.39, 1.60]	41.54	179	1.23 [1.06, 1.44]
Yes, 2	10.06	103	2.16 [1.77, 2.63]	1.37	2	-
Yes, 3+	1.12	9	1.80 [0.93, 3.47]	0.04	0	-
Fourth-degree relatives						
HALF COUSINS						
No	1932.06	9582	1 [Reference]	830.33	3088	1 [Reference]
Yes, 1	160.26	933	1.16 [1.08, 1.24]	48.89	184	0.99 [0.85, 1.15]
Yes, 2	26.39	197	1.49 [1.29, 1.72]	3.21	13	1.08 [0.63, 1.87]
Yes, 3+	5.49	43	1.65 [1.22, 2.24]	0.35	3	-

Pyr, person years at risk in thousands; SST, same sex twins; DST, different sex twins.

§ Both cohort members and relatives [of the given number and type] were of same age in each comparison in the table.

† No tonsillectomized relatives is indicated by "No" and includes only persons with the given number of relatives of that type and age.

* Rate ratios adjusted for calendar-period, number of relatives of the considered type, and the interaction between attained age and sex.

†† Due to small numbers rate ratios in this table were not calculated if only 0-5 events occurred.

Table S6. Rate-ratio* of tonsillectomy stratified by age-intervals and sex, according to sex of tonsillectomized sibling, Denmark, 1977-2013.

Sex of tonsillectomized sibling	Sex of the cohort member [index]	Tonsillectomy					
		Age <10 years			Age 10-19 years		
		Person-years x 10 ³	Number of events	Rate ratio [95% confidence Intervals]	Person-years x 10 ³	Number of events	Rate ratio [95% confidence Intervals]
Male	Female	84.2375	1387	4.75 [4.50, 5.01]	19,0547	231	2.91 [2.56, 3.32]
	Male	84.8077	1659	4.59 [4.37, 4.82]	21,1111	129	3.37 [2.83, 4.01]
Female	Female	56.9343	1043	5.28 [4.96, 5.62]	38,2134	476	2.98 [2.72, 3.26]
	Male	57.235	1186	4.86 [4.58, 5.15]	42,9697	206	2.62 [2.28, 3.01]

* Rate ratios adjusted for calendar-period, number of siblings, and the interaction between attained age and sex. The reference groups are male or female with no tonsillectomized siblings in the given age interval. For simplicity, the analysis was performed for cohort members with only one tonsillectomized sibling.

Table S7. Rate ratio* of tonsillectomy by type and number of tonsillectomized relatives, restricted to tonsillectomies indicated by acute or chronic tonsillitis during admission, Denmark, 1977-2013.**

Type and number of tonsillectomized relatives [†]	Tonsillectomy		
	Person-years x 10 ³	Number of events	Rate ratio [‡] [95% confidence Intervals]
TWINS			
No	671.38	905	1 [Reference]
Yes [same-sex twin]	6.85	44	4.27 [3.15, 5.77]
No	353.81	513	1 [Reference]
Yes [different-sex twin]	4.63	19	2.42 [1.53, 3.83]
First-degree relatives			
SIBLINGS			
No	29720.09	50870	1 [Reference]
Yes, in 1	757.82	3485	2.98 [2.88, 3.08]
Yes, in 2	22.27	180	5.90 [5.09, 6.83]
Yes, in 3+	0.7	16	18.11 [11.08, 29.62]
PARENTS			
No	1563.93	1016	1 [Reference]
Yes, in 1	191.19	356	2.84 [2.51, 3.2]
Yes, in both	4.63	16	5.86 [3.55, 9.67]
Second-degree relatives			
MATERNAL HALF SIBLINGS			
No	5162.61	10988	1 [Reference]
Yes, in 1	202.27	716	1.96 [1.82, 2.12]
Yes, in 2	6.97	38	3.25 [2.36, 4.47]
Yes, in 3+	0.23	2	-
PATERNAL HALF-SIBLINGS			
No	5963.07	11788	1 [Reference]
Yes, in 1	246.48	597	1.46 [1.35, 1.59]
Yes, in 2	10.63	38	2.23 [1.62, 3.07]
Yes, in 3+	0.56	0	-
UNCLES/AUNTS			
No	3447.09	3543	1 [Reference]
Yes, in 1	297.84	489	1.68 [1.53, 1.85]
Yes, in 2	12.67	27	2.63 [1.79, 3.86]
Yes, in 3+	0.89	2	-

[Table S7 continued]

Type and number of tonsillectomized relatives [†]	Tonsillectomy		
	Person-years x 10 ³	Number of events	Rate ratio [‡] [95% confidence Intervals]
Third-degree relatives			
COUSINS			
No	22448.35	37683	1 [Reference]
Yes, in 1	1654.72	3661	1.35 [1.30, 1.40]
Yes, in 2	232.79	625	1.66 [1.53, 1.80]
Yes, in 3+	41.25	117	1.77 [1.48, 2.12]
HALF UNCLES/AUNTS			
No	2554.91	3923	1 [Reference]
Yes, in 1	227.73	428	1.28 [1.16, 1.41]
Yes, in 2	14.67	35	1.74 [1.24, 2.43]
Yes, in 3+	1.36	4	-
Fourth-degree relatives			
HALF COUSINS			
No	3804.43	6990	1 [Reference]
Yes, in 1	243.54	525	1.18 [1.08, 1.29]
Yes, in 2	31.03	65	1.14 [0.89, 1.46]
Yes, in 3+	4.27	6	0.79 [0.35, 1.76]

* Rate ratios adjusted for calendar-period, number of relatives of the considered type, and the interaction between attained age and sex. Rate ratios are based on tonsillectomy at any age in cohort member and relatives including after 20 years of age.

** Tonsillectomies were restricted to those performed on in- or outpatients [data from the National Hospital Discharge Register] diagnosed at admission and before surgery with either acute or chronic tonsillitis [ICD8 codes 0340.0, 4630.x, 5000.2; ICD10 codes J03x, J350]; we excluded patients diagnosed with tonsil hypertrophy [ICD8 code 5000.8, 5000.9; ICD10 code J351, J353], other diagnosis, or if surgery was performed in an otolaryngology clinic [as preoperative diagnoses for tonsillectomy are not specifically reimbursed, and thus not registered, in the National Health Service Register].

† "No" means that although the person had relatives of the given type and number, none of these relatives had been tonsillectomized.

‡ Rate ratios were not calculated if only 0-5 events occurred.

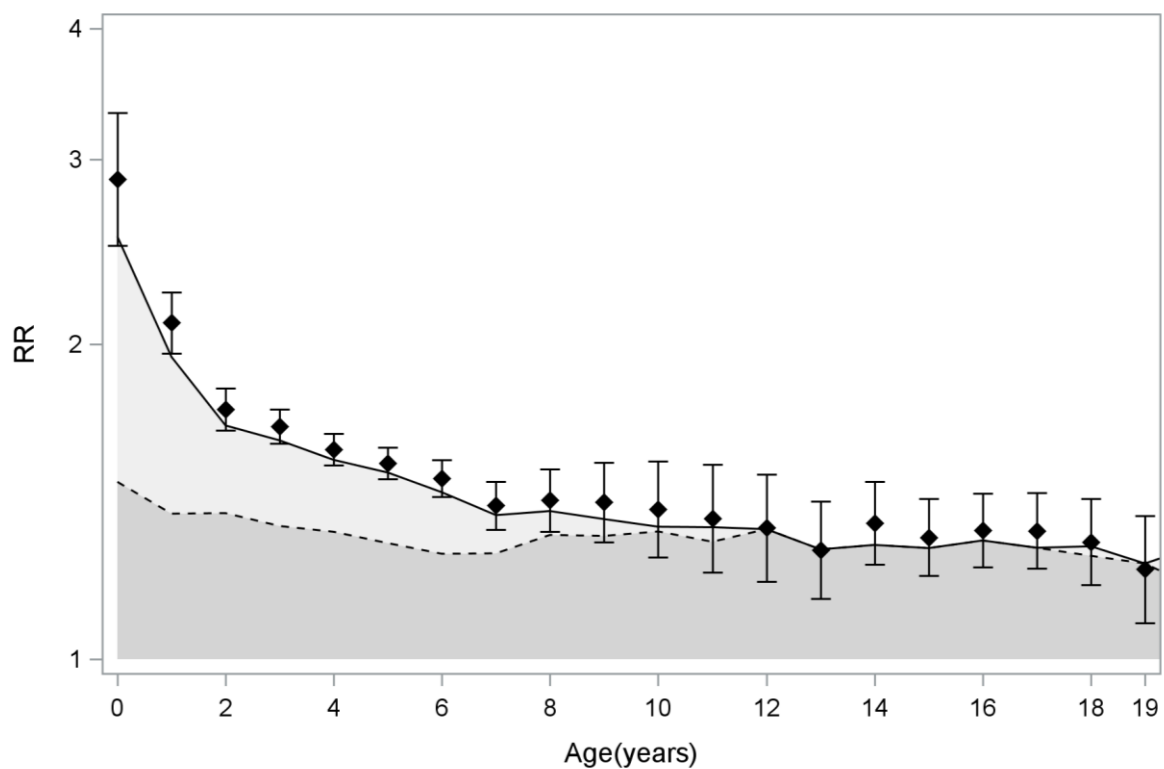


Figure S1. Age-specific rate ratio for tonsilleectomy following tonsilleectomy in a cousin among individuals with one cousin (i.e. rate ratios for pairs of cousins).

The points represent the "observed" rate ratios with 95% confidence intervals. The solid line represents the estimated areas and the area under the dotted line (the dark grey area) indicates the genetic component of the estimated rate ratios. The light grey area between the solid and dashed lines indicates the shared environment component of the estimated rate ratios. See also the Supplemental Methods and Estimates. RR, rate ratio.

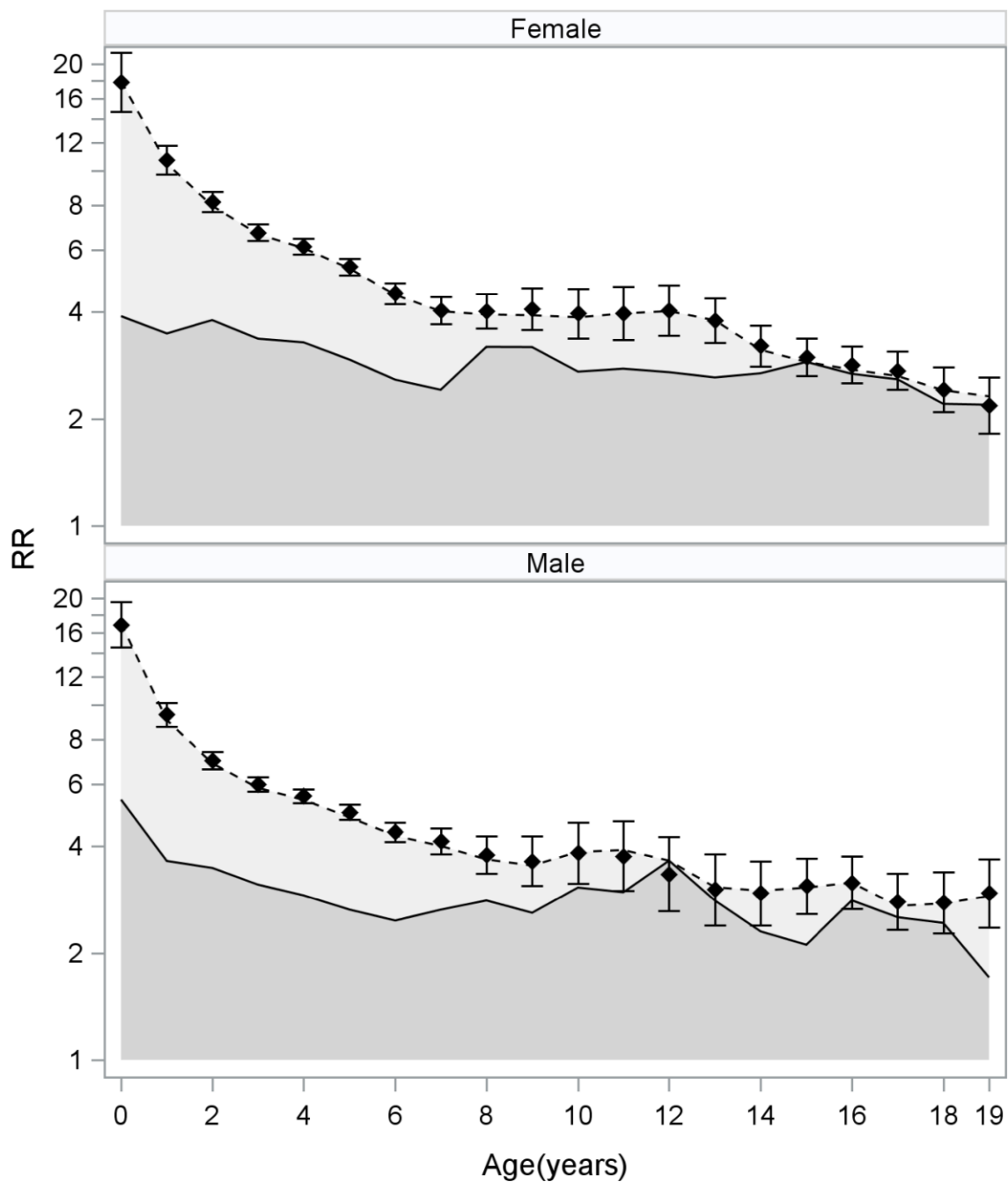


Figure S2. Age-specific rate ratios for tonsillectomy following tonsillectomy in a male (A) or a female (B) sibling among individuals with one sibling of any sex (i.e. rate ratios for pairs of siblings). The points represent the “observed” rate ratios with 95% confidence intervals. The solid line represents the estimated areas and the area under the dotted line (the dark grey area) indicates the genetic component of the estimated rate ratios. The light grey area between the solid and dashed lines indicates the shared environment component of the estimated rate ratios. See also the Supplemental Methods and Estimates. RR, rate ratio.