

Supplementary materials

Socioeconomic factors

The residence for each individual was assigned as one of 369 towns or districts in Taiwan,[1] each classified as urban, suburban or rural. Because of the high prevalence of gout in Taiwanese aborigines,[2] 55 towns/districts with a predominant aboriginal population (according to the Council of Indigenous People) were categorised as aboriginal areas, regardless of the corresponding urbanisation levels. Occupations were classified into 5 categories: (1) civil servants, teachers, military personnel and veterans; (2) non-manual workers and professionals; (3) manual workers; (4) other and (5) the unemployed/dependents. Income levels were approximated based on the payroll-related amount, which was determined by the payroll of the employees and civil servants and the business income of employers. We categorised income levels into sex-specific income quartiles.

Threshold liability model

This model assumes a normally distributed liability of disease resulting from a large number of unspecified genes and environmental factors, each with small and additive influences. The liability of the affected individuals is greater than a critical threshold, which value can be determined with the information of the disease prevalence in the affected and the general population. The familial transmission is the function of the difference of normal deviation of the threshold from the mean liability between individuals with affected relatives (T_1) and the normal population (T_0). Since the environmental factors such as diet and alcohol consumption may be shared by family members, common environmental component may substantially contribute to familial transmission, in addition to heritability. To separate the effects of genes and common environment, we used individuals with affected spouses as a control since spouses shares the family environment but not the genes with the individuals

and his/her biological relatives. Assuming that there is no inbreeding or assortative mating effects, the magnitude of the spouse RR provide an estimate of the importance of the familial environment.[3] Therefore, the heritability is the function of the difference of normal deviation of the threshold from the mean liability between individuals with affected relatives (T_1) and individuals with affected spouses (T_s).

References

1. Liu CY HY, Chuang YL, Chen YJ, Weng WS, Liu JS, Liang KY. Incorporating development stratification of Taiwan townships into sampling design of large scale health interview survey. *J health Manag* 2006;14:1-22.
2. Chou CT, Lai JS. The epidemiology of hyperuricaemia and gout in Taiwan aborigines. *Br J Rheumatol* 1998;37:258-262.
3. Rice TK. Familial resemblance and heritability. *Adv Genet* 2008;60:35-49.

Table S1. Demographic characteristics and gout prevalence of the study population by gender and relatives' affected status of gout

	Men		Women	
	≥1 affected relatives (n = 879,852)	General population (n= 11,360,576)	≥1 affected relatives (n = 784,052)	General population (n = 11,283,172)
Age (years) (mean ± standard deviation)	29.8 ± 18.4	34.9 ± 20.8	30.0 ± 19.8	35.2 ± 20.5
Gout (%)	10.79	7.07	3.13	2.15
Place of residence (%)				
Urban	60.16	57.53	61.39	59.40
Suburban	30.86	32.15	29.39	30.39
Rural	5.75	7.49	5.75	7.40
Aboriginal	3.23	2.83	3.47	2.81
Income levels (%)				
Quartile 1	24.27	27.68	24.49	27.77
Quartile 2	25.37	27.52	26.44	30.18
Quartile 3	22.20	19.60	18.79	16.84
Quartile 4	28.16	25.20	30.28	25.21
Occupation (%)				
Dependents of the insured individuals	41.07	34.49	49.97	42.39
Civil servants, teachers, military personnel and veterans	5.25	4.39	4.09	3.04
Non-manual workers and professionals	30.53	29.33	27.17	25.81
Manual workers	14.50	20.28	12.52	21.57
Other	8.65	11.51	6.25	7.19

Foot note: Income levels (in new Taiwan dollars [NTD]): Quartile1, 0 to 16500 NTD (both genders); Quartile 2, 16,501 to 19,200 NTD (both genders); Quartile 3, 19,201 to 33,300 NTD (men) and 19,201 to 28,800 NTD (women); Quartile 4, higher than 33,301 NTD (men) and higher than 28,801 NTD (women).

Table S2. Sensitivity analysis of adjusted relative risks of gout according to family exposure, age, place of residence, income levels and occupations, using primary and alternative gout case definition.

Risk factors	Adjusted relative risks (95% confidence interval)	
	Men	Women
<i>Age-adjusted model</i>		
Affected relatives of gout		
No relative affected	1	1
≥1 affected relatives	1.92 (1.91–1.93)	1.91 (1.89–1.93)
<i>Multivariate-adjusted model</i>		
Affected relatives of gout		
No relative affected	1	1
≥1 affected relatives	1.91 (1.90–1.93)	1.97 (1.94–1.99)
Place of residence		
Urban	1	1
Suburban	1.00 (1.00–1.01)	1.05 (1.04–1.05)
Rural	1.03 (1.02–1.04)	1.10 (1.09–1.12)
Aboriginal	1.34 (1.33–1.36)	1.58 (1.55–1.61)
Income levels		
Quartile 1	1	1
Quartile 2	1.14 (1.13–1.16)	1.03 (1.02–1.05)
Quartile 3	0.98 (0.97–0.99)	1.05 (1.03–1.07)
Quartile 4	1.10 (1.09–1.11)	0.95 (0.94–0.97)
Occupation		
Dependent	1	1
Civil servants, teachers and military servicemen	1.14 (1.13–1.16)	0.64 (0.62–0.66)
Non-manual workers and professionals (%)	0.98 (0.97–0.99)	0.73 (0.72–0.74)
Manual workers(%)	1.13 (1.13–1.14)	1.08 (1.07–1.09)
Other (%)	1.10 (1.09–1.11)	1.01 (0.99–1.02)

Footnote: adjusted for age and family size. all RR estimates were statistically significant (p<0.01).

Table S3. Sensitivity analysis on the relative risk of gout among individuals with affected first- and second-degree relatives using alternative case definition for gout

Affected first- and second-degree relatives	Men at risk		Women at risk	
	RR	95% CI	RR	95% CI
Parent				
Father	1.77	1.75–1.79	2.15	2.13–2.18
Mother	1.83	1.81–1.85	1.94	1.85–2.03
Offspring				
Son	1.83	1.82–1.85	1.87	1.84–1.89
Daughter	1.79	1.73–1.85	2.34	2.24–2.44
Sibling				
Brother	2.43	2.38–2.47	2.03	1.93–2.14
Sister	2.35	2.23–2.47	3.82	3.19–4.57
Twins				
Twin brothers	6.60	5.72–7.62	2.90	0.73–11.62
Twin sisters	3.66	1.2–10.69	38.23	14.81–98.72
Grandparent				
Grandfather	1.08	1.03–1.14	1.08	0.92–1.27
Grandmother	1.20	1.14–1.27	1.21	1.04–1.41
Grandchild				
Grandson	1.22	1.16–1.28	1.39	1.33–1.46
Granddaughter	1.35	1.17–1.55	1.47	1.27–1.70
Uncle or aunt				
Uncle	1.21	1.13–1.29	1.00	0.80–1.26
Aunt	1.11	0.90–1.36	0.76	0.34–1.70
Nephew or Niece				
Nephew	1.34	1.26–1.42	1.04	0.85–1.28
Niece	1.34	1.09–1.64	0.81	0.36–1.80

Figure S1. The “dose-response” relationship between the numbers of affected first-degree relatives and relative risk of gout using alternative case definition of gout.

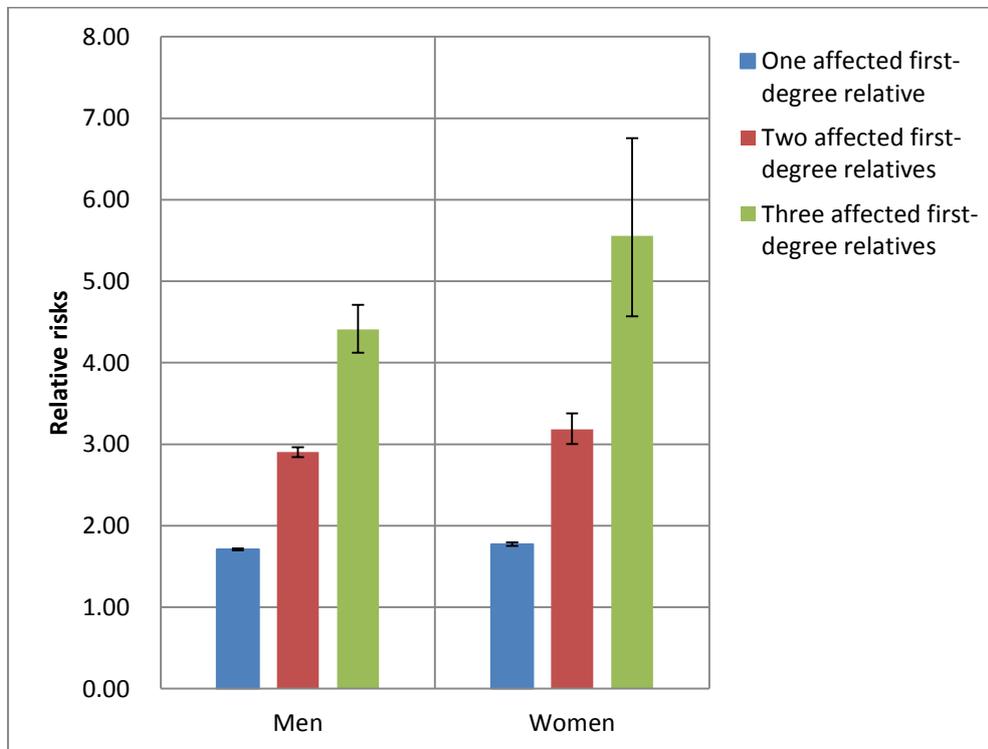


Figure S2. Relative contribution of heritability (blue), common environmental (red) and specific environmental factors (green) to phenotypic variation of gout, using alternative case definition of gout.

