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2	Medical and non-medical correlates of carpal tunnel
3	syndrome in a Taiwan cohort of one million
4	
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1	Background: Carpal tunnel syndrome (CTS), with unclear etiology, is the most
2	common entrapment neuropathy. Its occurrence is related to lots of medical and
3	non-medical conditions with uncertain causality. With a large population, we
4	characterized selected demographical and clinical factors to add more information on
5	CTS correlated factors and new insight into future CTS prevention.
6	Methods: A national insurance claim dataset of one million in Taiwan was used to
7	identify 15,802 CTS cases and 31,604 randomly selected controls, during a period of
8	seven years starting January 1, 2000. Statistical association with CTS was determined
9	for five sociodemographic and nine medical factors.
10	Results: Patients were predominantly female (65.6% vs. 47.7% in the control group)
11	and older (40 and above, 62.6% vs. 36.2%). Rheumatoid arthritis was found to be the
12	most significant comorbidity associated with CTS, followed by gout, hypertension,
13	diabetes, obesity, uremia, and acromegaly. For younger group age ≤ 39 , the
14	association of these comorbidities was stronger, and hypothyroidism and vitamin B_6
15	deficiency were additional comorbidities. Aging appears to reduce the relative impact
16	of the diseases commonly associated with CTS as the possible risk factors.
17	Conclusions: Identification of the CTS correlates in younger group would be of
18	greater value in timely detection and treatment of these diseases. Correcting these
19	disorders may aid in removing possible causes of CTS. This is the first report on the

1	effect of aging on probable CTS risk factors. How factors associated with aging
2	contribute to the development of CTS remains to be determined.
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6	
7	Key words: carpal tunnel syndrome, case-control study, comorbidities,

8 statistical association.

1 Introduction

2	Carpal tunnel syndrome (CTS) is known to be the most common entrapment
3	neuropathy [1]. It is produced by compression of the median nerve inside the carpal
4	tunnel due to overuse or strain in hand activities [2]. Over one half of the patients
5	have symptoms in both hands, with the remainder having symptoms more in the
6	dominant hand than in the non-dominant hand [3].
7	The prevalence of CTS was estimated to be around 5% in the general population
8	[4]. CTS can occur at any age, and it is most common among females in the fifth and
9	sixth decades of life [3]. The etiology of CTS is unclear though strong association has
10	been observed between CTS and a number of occupational and non-occupational
11	factors. Nerve compression has been correlated with occupations that involve
12	repetitive wrist movements, awkward wrist positions, and the use of vibrating
13	machinery [5]. Non-occupational or personal correlates of CTS include age, gender,
14	pregnancy, obesity, diabetes mellitus (DM), hypothyroidism, rheumatoid arthritis
15	(RA), hemodialysis, and acromegaly [6,7].
16	In the present population-based study, we took advantage of the large size of a
17	National Health Insurance (NHI) claim dataset available in Taiwan to examine more
18	precisely the independent association between CTS and each of its medical and
19	non-medical correlates in a randomly selected cohort of one million enrollees for a

- 1 period of seven years starting January 1, 2000. Among CTS comorbidities, some are
- 2 more health-threatening than CTS. Upon statistical confirmation, these graver
- 3 disorders should be considered along with CTS for their early detection and timely
- 4 treatment.

1 Methods

2	The NHI program of Taiwan was instituted in 1995, which has now covered over 96%
3	of the entire national population of some 23 million. We obtained a set of NHI claim
4	data for the period of 1996-2007 of up to 1,000,000 enrollees randomly selected by
5	the National Health Research Institute in 2005. From this cohort of one million, we
6	identified new patients as cases who received care for CTS for at least 3 times during
7	a period of 7 years starting January 1, 2000. Controls were randomly selected from
8	among the cohort who did not have a record of CTS, at a control to case ratio of 2:1.
9	The International Classification of Diseases, 9 th Revision, Clinical Modification
10	(ICD-9-CM) code 354.0 or A-code 229 was used to identify CTS cases and
11	comorbidities (Table 1). Patient identification numbers were scrambled, and hence no
12	ethics board approval was needed because the researchers were blinded to the patient
13	identities.
14	
15	Data analysis
16	From the cohort of one million, 15,802 cases and 31,604 controls were identified in
17	the dataset for the seven years specified. Among the 15802 cases, 7,575 (47.9%)
18	received nerve electrophyiological studies and 969 (6.13%) underwent surgical
19	interventions for CTS. Non-medical, sociodemographic characteristics including

1	gender, age, occupation code, income, and urbanization levels of residence area were
2	compared between cases and controls. With quartiles of population densities, the
3	urbanization levels were stratified into 3 levels: low (lowest 50%, < 662 persons/km ²),
4	moderate (median 25%, 662-1822 persons/km ²), and high (highest 25%, >
5	1822 persons/km ²). The univariate analysis was used as a screening test for
6	preliminary assessment of correlation between the sociodemographic or medical
7	characteristics and CTS. Once found significantly correlated, each of the variables
8	was then tested with the multivariate logistic regression analysis in order to estimate
9	the association strength of the individual variables to CTS in terms of odds ratios
10	(OR).
11	Based on literature review, we selected nine medical conditions including
11 12	Based on literature review, we selected nine medical conditions including hypertension, DM, obesity, gout, uremia, vitamin B ₆ deficiency, RA, hypothyroidism,
12	hypertension, DM, obesity, gout, uremia, vitamin B ₆ deficiency, RA, hypothyroidism,
12 13	hypertension, DM, obesity, gout, uremia, vitamin B_6 deficiency, RA, hypothyroidism, and acromegaly, as possible comorbidities of CTS [1], for analyses. The A-codes and
12 13 14	hypertension, DM, obesity, gout, uremia, vitamin B_6 deficiency, RA, hypothyroidism, and acromegaly, as possible comorbidities of CTS [1], for analyses. The A-codes and ICD-9-CM codes of these comorbidities are listed in Table 1. The association strength
12 13 14 15	hypertension, DM, obesity, gout, uremia, vitamin B ₆ deficiency, RA, hypothyroidism, and acromegaly, as possible comorbidities of CTS [1], for analyses. The A-codes and ICD-9-CM codes of these comorbidities are listed in Table 1. The association strength of each of these medical conditions to CTS was estimated based on significance of
12 13 14 15 16	hypertension, DM, obesity, gout, uremia, vitamin B ₆ deficiency, RA, hypothyroidism, and acromegaly, as possible comorbidities of CTS [1], for analyses. The A-codes and ICD-9-CM codes of these comorbidities are listed in Table 1. The association strength of each of these medical conditions to CTS was estimated based on significance of differences in the prevalence of each comorbidity between cases and controls by the

1 logistic regression analyses were performed for age and for gender difference.

1 Results

2	The sociodemographic characteristics of cases and controls were compared as shown
3	in Table 2. There was a female predominance in cases and a male predominance in
4	controls. Individuals at age 40-59 (49.5% vs. 26.2%), higher income earners (20.2%
5	vs. 15.5%), and high urbanization living (70.5% vs. 68.5) were in greater proportions
6	in cases than in controls. Female gender and age range stood out to be the most
7	significant non-medical factors associated with CTS.
8	Comparison between cases and controls of the prevalence of nine possible
9	comorbidities associated with CTS (Table 3) revealed that the most prevalent
10	comorbidities were, in descending order, RA, acromegaly, hypertension, gout, DM,
11	uremia, hypothyroidism, obesity, and vitamin B_6 deficiency. This ranking is similar to
12	that seen in the group of age 40-59 (Table 4), the most vulnerable group of CTS
13	(Table 2). However, the relative significance of these comorbidities in the younger
14	group of age ≤ 39 was quite different (Table 4). In the younger group, the most
15	significant comorbidities were gout, followed by RA, obesity, DM, hypertension,
16	hypothyroidism, vitamin B ₆ deficiency, uremia, and acromegaly (Table 4). Also, the
17	strength of association was considerably greater in the younger group than in the older
18	group, indicating that age did not have a strong confounding effect. Vitamin B_{12}
19	deficiency is a potential cause of CTS. In the present study, it is not found to be a

1 significant contributing factor (data not shown).

2	The results of univariate analysis confirmed that RA, DM, obesity, gout,
3	hypertension, hypothyroidism, vitamin B_6 deficiency, uremia, and acromegaly were
4	more prevalent in cases than in controls (Table 5). Multivariate logistic regression
5	analysis revealed most significant correlates of CTS being age at 40-59, obesity, gout,
6	RA, male gender, and DM.
7	Further analysis by gender indicated that the association between comorbidities
8	and CTS was similar between males and females (Table 6).

1 Discussion

2	CTS is a common disorder of the peripheral nervous system and a cause of
3	considerable hand dysfunction. Literature review [5] reveals that both occupational
4	(industrial) and non-occupational (personal) factors were related to the development
5	of CTS, but there is controversy regarding the etiological contributions of these
6	factors [5]. The most significant socio-demographic characteristics associated with
7	CTS were female gender, advance in age (\geq 40 years), and higher income [1,6]. The
8	most significant concurrent medical conditions were RA, DM, obesity, gout,
9	hypertension and hypothyroidism [1]. Our results from Taiwan populations are not in
10	full agreement with what was reported in the literature.
11	
12	Sociodemographic characteristics
13	A number of studies, including our own, have found that development of CTS is
14	increasing with age [3,4,6,8]. The prominently high prevalence of CTS in the age
15	group of 40 to 59 (Table 2) coincided with this group being the major constituent of
16	workforce, suggesting the correlation between occupational factors and CTS. The
17	relatively high rate of CTS in the age group of > 60 can probably be attributed to
18	age-related carpal tunnel changes.
19	Correlation of female gender with CTS has been well documented [1,3,4,6,8].

1	Blandetal et al. reported that CTS was more prevalent in females although its severity
2	was greater in males and in the elderly [3]. Among the elderly, the prevalence in
3	females was almost four times of that in males [6,8]. Our results indicate that CTS
4	was twice as prevalent in females as in males (Table 2). This ratio differs from those
5	found in the literature, being from 1.4:1 to 6.0:1 [1,3,6,9-12] averaging 3:1 [2].
6	Several factors may have contributed to this difference, including ethnic
7	characteristics and varying gender distributions of sociodemographic factors and
8	comorbidities, which were closely associated with CTS. In Taiwan, we found males
9	had higher employment rate, older mean age, and higher income than females (data
10	not shown). Also, males tend to be more susceptible to uremia, hypertension, gout and
11	acromegaly (data not shown).
12	The relationship between income and CTS was evaluated by a study of Tanaka,
13	et al. [6], in which an annual family income of \geq 20,000 U.S. dollars was shown to be
14	associated with CTS (adjusted $OR = 1.5$). A similar correlation between higher
15	income (\geq 30,000 New Taiwan Dollars per month) and CTS (adjusted OR = 1.15,
16	Table 5) was found in our study. Certain blue-collar occupations were reported to be
17	associated with CTS in both males and females [9-11]. We found a similar association
18	between blue-collar occupations and increased risk of CTS ($OR = 1.25$).
19	So far, we have found no study in the literature addressing the relationship

1	between urbanization of living and CTS. We are the first to observe that people living
2	in a relatively urbanized area had a higher risk for CTS ($OR = 1.07$).
3	
4	Comorbidities
5	RA is a well documented condition associated with CTS [12-14]. In a systematic
6	review, van Dijk et al. reported that the prevalence of concurrent RA, DM, and
7	hypothyroidism was higher in CTS cases than in controls [13]. In our study, we found
8	that RA had, among the comorbidities tested, the strongest association with CTS. This
9	association was stronger in males than in females.
10	Positive correlations between obesity and CTS [6,8,12,13] and between DM
11	alone and CTS [8,12-14] have been observed in a number of studies. These positive
12	correlations were also found in our study (Table 5).
13	Hypertension is a common medical problem associated with CTS. It can occur as
14	a solitary disorder or in combination with medical conditions concurrent with CTS,
15	such as acromegaly [15], vitamin B_6 deficiency [16], and metabolic syndrome [14,17].
16	According to Edwards, et al. [18], hypertension could impair the sensory nerve
17	conduction through elevation of cutaneous sensory thresholds and reduction of
18	sensory action potential amplitudes. The causal link of these conditions is unclear.
19	Our results confirm a strong association between hypertension and CTS (Table 5) and

thus suggest that hypertension-related conduction impairment of the sensory nerves
 might be a risk factor.

3	The relationship between gout and CTS has been well documented [19,20]. Kang,
4	et al. [20] reported that tophus deposition in the carpal tunnel can lead to CTS. In
5	addition, imaging studies have shown the presence of tophi in the floor of the carpal
6	tunnel, carpal bones, radiocarpal joint, and extensor tendons or tendon sheaths of the
7	wrist [19]. Our results confirm the strong association between gout and CTS (OR =
8	2.29).
9	Numerous findings have suggested that hypothyroidism is a significant risk
10	factor for CTS [6,8,21,22]. In a study by Duyff et al. [22], 29% of hypothyroid
11	patients were found to have CTS. In our study, we found a positive correlation
12	between hypothyroidism and CTS ($OR = 1.38$). Primary hypothyroidism is an
13	autoimmune disorder, which is more prevalent in younger populations. It follows that
14	the association between hypothyroidism and CTS should be strongest among
15	individuals younger than 40. Our results indicate that the association was more than
16	thrice stronger (OR = 3.43 vs. 1.05 , Table 4) in this group than in the older ones.
17	Though vitamin B_6 is widely found in foods, a considerable number of people
18	suffer a vitamin B_6 deficiency [16], maybe due to abnormalities in vitamin B_6
19	metabolism [16] or uptake. It has been documented that CTS was associated with

1	vitamin B ₆ deficiency [1,8,16], and supplements of the vitamin have proved to be a
2	successful treatment in some cases [1,16]. Although vitamin B ₆ deficiency was rare in
3	Taiwan, our results indicate its significant association with CTS in females especially
4	at age 20-39 (OR = 2.57).
5	Uremia is a metabolic disorder caused by chronic renal dysfunction. Studies have
6	shown that uremia is associated with CTS in patients undergoing hemodialysis [23, 24]
7	and peritoneal dialysis [24]. In our study, uremia was found associated with CTS,
8	more in males than in females.
9	Acromegaly is a rare disease caused by over-secretion of growth hormone [25].
10	Its relationship with CTS has been well documented [13,15,25]. Colao, et al. [15]
11	reported that 20-64% of acromegaly patients suffered from symptomatic CTS. In our
12	study, a similar relationship between acromegaly and CTS was found in both genders.
13	
14	Features of study
15	One strength of the present study is that cases and controls were identified from a
16	dataset of one million enrollees in a national insurance program covering over 96% of
17	the entire population in Taiwan. Insurance claims of consecutive cares for CTS
18	ensured the diagnosis of CTS. The demographic profiles and comorbidities noted in
19	this cohort are in accord with those reported in the literature. The large sample size

1	gave adequate power for statistical analyses and enabled us to ascertain important
2	associations between comorbidities and CTS. However, we could not rule out the
3	possibility of over-diagnosing CTS since only 6.13% of the patients with CTS were
4	operated. It is also possible that some in the control group with asymptomatic or mild
5	CTS might have escaped the diagnosis. Thus, the risks derived from the present study
6	may be underestimated. Even though surgery is covered by the NHI system, low
7	operation rate is noted in the present study because surgery is entertained as the last
8	resort among CTS patients in Taiwan. It should be noted that our study was designed
9	only to demonstrate statistical associations but not causal relationships. Further
10	studies are needed to elucidate the etiological relationships and the mechanisms of
11	these associations of interest.
12	Our results indicate that the most significant non-medical correlates of CTS were
13	female gender, age > 40, higher income, blue-collar occupations, and high
14	urbanization level of living (Table 2). In females in general, most significant
15	comorbidities of CTS were RA, DM, obesity, and gout (Table 6), while at the most
16	vulnerable age range of 40-59, these were RA, hypertension, DM, and gout (Table 4).
17	CTS thus serves to alert the possible presence of these related comrobidities for timely
18	treatment, some of these are more health-threatening such as RA and DM.
19	Correlation of the comorbidities chosen in this study with CTS has been reported

1	in a large number of studies. But most of these reports were based on relatively small
2	number of CTS patients. With a large patient number in our study, we were able to
3	discern a hitherto obscure aging-related dilution of correlation strength between most
4	of these comorbidities and CTS as shown in Table 4. For the younger population, the
5	comorbidities were more strongly associated with CTS, and CTS would be of greater
6	value to serve as a precautionary sign to alert for timely diagnosis and treatment of
7	more serious concurrent disorders. In older populations, although the correlation
8	between the comorbidities and CTS still existed, it became less important (Table 4).
9	The factor that caused this dilution effect is unclear and warrants further mechanistic
10	studies for its elucidation.
11	
12	Author contributions

Drs. Tseng, Liao, Sung, Hsieh and Tsai designed the study and developed the
manuscript; data analysis was performed by Kuo, Liao and Sung.

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3 Disclosure

4 The authors disclose no conflicts of interest.

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6 **References**

7	1.	Stewart JD. Focal peripheral neuropathies, 3rd edn. Philadelphia:
8		Lippincott Willians & Wilkins, 2000.
9	2.	Werner RA, Andary M. Carpal tunnel syndrome: pathophysiology and
10		clinical neurophysiology. Clin Neurophysiol 2002; 113: 1373-1381.
11	3.	Bland JD, Rudolfer SM. Clinical surveillance of carpal tunnel syndrome
12		in two areas of the United Kingdom, 1991–2001. J Neurol Neurosurg
13		Psychiatry 2003; 74: 1674-1679.
14	4.	Bickel KD. Carpal tunnel syndrome. J Hand Surg [Am] 2010; 35A: 147-
15		152.
16	5.	Maghsoudipour M, Moghimi S, Dehghaan F, et al. Association of
17		occupational and non-occupational risk factors with the prevalence of
18		work related carpal tunnel syndrome. J Occup Rehabil 2008; 18:152-156.
19	6.	Tanaka S, Wild DK, Cameron LL, et al. Association of occupational and
20		non-occupational risk factors with the prevalence of self-reported carpal
21		tunnel syndrome in a national survey of the working population. Am J Ind
22		<i>Med</i> 1997; 32: 550-556.
23	7.	Bahou YG. Carpal tunnel syndrome: a series observed at Jordan
24		University Hospital (JUH), June 1999-December 2000. Clin Neurol
25		Neurosurg 2002; 104: 49-53.
26	8.	Thurston A. Aetiology of the so-called 'idiopathic' carpal tunnel
27		syndrome. Curr Orthop 2000; 14: 448-456.
28	9.	Roquelaure Y, Ha C, Pelier-Cady M-C, et al. Work increases the
29		incidence of carpal tunnel syndrome in the general population. Muscle
30		Nerve 2008; 37: 477-482.
31	10.	Roquelaure Y, Ha C, Nicolas G, et al. Attributable risk of carpal tunnel
32		syndrome according to industry and occupation in a general population.
33		Arthritis Rheum 2008; 59: 1341-1348.
34	11.	Mattioli S, Baldasseroni A, Curti S, et al. Incidence rates of surgically
35		treated idiopathic carpal tunnel syndrome in blue- and white-collar
36		workers and housewives in Tuscany, Italy. Occup Environ Med 2009; 66:

1 299-304.

1		<i>277</i> 501.
2	12.	Geoghegan JM, Clark DI, Bainbridge LC, et al. Risk factors in carpal
3		tunnel syndrome. J Hand Surg [Br] 2004; 29B: 315-320.
4	13.	van Dijk MA, Reitsma JB, Fischer JC. Indications for requesting
5		laboratory tests for concurrent diseases in patients with carpal tunnel
6		syndrome: a systematic review. Clin Chem 2003; 49: 1437-1444.
7	14.	Balci K, Utku U. Carpal tunnel syndrome and metabolic syndrome. Acta
8		Neurol Scand 2007; 116: 113-117.
9	15.	Colao A, Auriemma RS, Pivonello R, et al. Medical consequences of
10		acromegaly: what are the effects of biochemical control? Rev Endocr
11		Metab Disord 2008; 9: 21-31.
12	16.	Aufiero E, Stitik TP, Foye PM, et al. Pyridoxine hydrochloride treatment
13		of carpal tunnel syndrome: a review. Nutr Rev 2004; 62: 96-104.
14	17.	Chiou WK, Lin JD, Weng HF, et al. Correlation of the dysmetabolic risk
15		factors with different anthropometric measurements. Endocr J 2005; 52:
16		139-148.
17	18.	Edwards L, Ring C, McIntyre D, et al. Cutaneous sensibility and
18		peripheral nerve function in patients with unmedicated essential
19		hypertension. Psychophysiology 2008; 45: 141-147.
20	19.	Chen CK, Chung CB, Yeh LR, et al. Carpal tunnel syndrome caused by
21		tophaceous gout: CT and MR imaging features in 20 patients. Am J
22		Roentgenol 2000; 175: 655-659.
23	20.	Kang HJ, Jung SH, Yoon HK, et al. Carpal tunnel syndrome caused by
24		space occupying lesions. Yonsei Med J 2009; 50: 257-261.
25	21.	El-Salem K, Ammari F. Neurophysiological changes in neurologically
26		asymptomatic hypothyroid patients: a prospective cohort study. J Clin
27		<i>Neurophysiol</i> 2006; 23: 568-572.
28	22.	Duyff RF, Van den Bosch J, Laman DM, et al. Neuromuscular findings in
29		thyroid dysfunction: a prospective clinical and electrodiagnostic study.
30		J Neurol Neurosurg Psychiatry 2000; 68: 750-755.
31	23.	Al-Hayk K, Bertorini TE. Neuromuscular complications in uremics: a
32		review. Neurologist 2007; 13: 188-196.
33	24.	Copley JB, Lindberg JS. Nontransplant therapy for dialysis-related
34		amyloidosis. Semin Dial 2001; 14: 94-8.
35	25.	Mestrón A, Webb SM, Astorga R, et al. Epidemiology, clinical
36		characteristics, outcome, morbidity andmortality in acromegaly based
37		on the Spanish Acromegaly Registry (Registro Español de Acromegalia,
38		REA). Eur J Endocrinol 2004; 151: 439-446.

Comorbidity	A-codes	ICD-9-CM codes
Rheumatoid arthritis (RA)	A430	714.0, 714.1, 714.2, 714.30, 714.31,
		714.32, 714.33
Acromegaly	A189	253.0
Hypertension	A260, A269	401.0, 401.1, 401.9, 402.00, 402.01,
		402.10, 402.11, 402.90, 402.91,
		403.00, 403.01, 403.10, 403.11,
		403.90, 403.91, 404.00, 404.01,
		404.02, 404.03, 404.10, 404.11,
		404.12, 404.13, 404.90, 404.91,
		404.92, 404.93, 405.01, 405.09,
		405.11, 405.19, 405.91, 405.99
Gout	A189	274.0, 274.10, 274.11, 274.19,
		274.81, 274.82, 274.89, 274.9
Diabetes mellitus (DM)	A181	250.00, 250.01, 250.02, 250.03,
		250.10, 250.11, 250.12, 250.13,
		250.20, 250.21, 250.22, 250.23,
		250.30, 250.31, 250.32, 250.33,
		250.40, 250.41, 250.42, 250.43,
		250.50, 250.51, 250.52, 250.53,
		250.60, 250.61, 250.62, 250.63,
		250.70, 250.71, 250.72, 250.73,
		250.80, 250.81, 250.82, 250.83,
		250.90, 250.91, 250.92, 250.93
Uremia	A350	585
Hypothyroidism	A180	243, 244.0, 244.1, 244.2, 244.3,
		244.8, 244.9
Obesity	A183	278.00, 278.01
Vitamin B ₆ (Vit. B ₆) deficiency	A193	266.1

 Table 1
 A-codes and ICD-9-CM codes of comorbidities of CTS

ICD-9-CM, International Classification of Diseases, 9th Revision, Clinical Modification.

CTS, carpal tunnel syndrome.

	Cor	ntrols	Ca	ises	Tot	al	
	N=3	1,604	N=1	5,802	N=47	,406	
Variable	n	(%)	n	(%)	n	(%)	p Value
Gender							< 0.0001
Female	15,085	(47.7)	10,370	(65.6)	25,455	(53.7)	
Male	16,519	(52.3)	5,432	(34.4)	21,951	(46.3)	
Age, years							< 0.0001
≤19	8,951	(28.3)	630	(4.0)	9,581	(20.2)	
20-39	11,217	(35.5)	5,278	(33.4)	16,495	(34.8)	
40-59	8,284	(26.2)	7,823	(49.5)	16,107	(34.0)	
≥ 60	3,152	(10.0)	2,071	(13.1)	5,223	(11.0)	
Occupation							< 0.0001
White collar	17,273	(54.7)	7,714	(48.8)	24,987	(52.7)	
Blue collar	9,195	(29.1)	5,567	(35.2)	14,762	(31.1)	
Others	5,136	(16.3)	2,521	(16.0)	7,657	(16.2)	
Urbanization							< 0.0001
Low	3,781	(12.0)	1,805	(11.4)	5,586	(11.8)	
Moderate	6,165	(19.5)	2,852	(18.1)	9,017	(19.0)	
High	21,658	(68.5)	11,145	(70.5)	32,803	(69.2)	
Income							< 0.0001
< 30,000 NTD	26,704	(84.5)	12,605	(79.8)	12,605	(82.9)	
≥ 30,000 NTD	4,900	(15.5)	3,197	(20.2)	3,197	(17.1)	

 Table 2
 Baseline sociodemographic characteristics of CTS cases and controls in Taiwan,
 2000-2007

Cases in 2000-2007 used outpatient services for CTS treatment.

CTS, carpal tunnel syndrome; NTD, New Taiwan Dollars.

	Cor	ntrol	C	ase	Tot	al	
	N=3	1,604	N=1	5,802	N=47	,406	
Variable	n	(%)	n	(%)	n	(%)	p Value
Uremia							< 0.0001
No	31,280	(99.0)	15,433	(97.7)	46,713	(98.5)	
Yes	324	(1.0)	369	(2.3)	693	(1.5)	
Vit. B ₆ deficiency							< 0.0001
No	31,546	(99.8)	15,732	(99.6)	47,278	(99.7)	
Yes	58	(0.2)	70	(0.4)	128	(0.3)	
Rheumatoid arthritis							< 0.0001
No	31,202	(98.7)	15,093	(95.5)	46,295	(97.7)	
Yes	402	(1.3)	709	(4.5)	1,111	(2.3)	
Hypothyroidism							< 0.0001
No	31,357	(99.2)	15,482	(98.0)	46,839	(98.8)	
Yes	247	(0.8)	320	(2.0)	567	(1.2)	
Obesity							< 0.0001
No	31,475	(99.6)	15,589	(98.6)	47,064	(99.3)	
Yes	129	(0.4)	213	(1.4)	342	(0.7)	
Hypertension							< 0.0001
No	31,217	(98.8)	15,247	(96.5)	46,464	(98.0)	
Yes	387	(1.2)	555	(3.5)	942	(2.0)	
Diabetes							< 0.0001
No	31,364	(99.2)	15,380	(97.3)	46,744	(98.6)	
Yes	240	(0.8)	422	(2.7)	662	(1.4)	
Gout							< 0.0001
No	31,289	(99.0)	15,307	(96.9)	46,596	(98.3)	
Yes	315	(1.0)	495	(3.1)	810	(1.7)	
Acromegaly							< 0.0001
No	31,056	(98.3)	15,197	(96.2)	46,253	(97.6)	
Yes	548	(1.7)	605	(3.8)	1,153	(2.4)	

 Table 3
 Prevalence of comorbidities in CTS cases and controls in Taiwan, 2000-2007

Cases in 2000-2007 used outpatient services for CTS treatment.

CTS, carpal tunnel syndrome; Vit. B₆, vitamin B₆.

	Age, years					
	≤ 3 9	40-59	≥ 60			
Variable	Odds ratio (95% CI)	Odds ratio (95% CI)	Odds ratio (95% CI)			
Uremia						
No	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)			
Yes	2.63 (1.86-3.70)	1.48 (1.15-1.85)	1.30 (0.99-1.69)			
Vit. B ₆ deficiency						
No	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)			
Yes	2.73 (1.43-5.23)	1.09 (0.62-1.94)	1.66 (0.84-3.28)			
Rheumatoid arthritis						
No	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)			
Yes	4.22 (2.99-5.95)	2.48 (2.03-3.02)	1.67 (1.36-2.05)			
Hypothyroidism						
No	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)			
Yes	3.43 (2.52-4.67)	1.05 (0.82-1.34)	0.85 (0.56-1.28)			
Obesity						
No	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)			
Yes	3.72 (2.67-5.18)	1.70 (1.19-2.42)	2.44 (1.18-5.04)			
Hypertension						
No	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)			
Yes	3.59 (2.43-5.29)	2.03 (1.66-2.49)	1.42 (1.14-1.78)			
Diabetes						
No	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)			
Yes	3.69 (2.40-5.67)	2.00 (1.58-2.55)	1.82 (1.37-2.41)			
Gout						
No	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)			
Yes	5.17 (3.67-7.26)	2.16 (1.74-2.70)	1.79 (1.38-2.31)			
Acromegaly						
No	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)			
Yes	2.15 (1.60-2.88)	1.43 (1.19-1.71)	1.41 (1.14-1.75)			

Table 4Estimated risk and 95% confidence interval of CTS by age in relation to comorbiditiescontrolling sociodemograhic characteristics in multivariate logistic analysis in Taiwan, 2000-2007

CTS, carpal tunnel syndrome; CI, confidence interval; Vit. B₆, vitamin B₆.

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	Univariate	Multivariate
Variable	Odds ratio (95% CI)	Odds ratio (95% CI)
Gender		
Female	2.09 (2.01-2.17)	1.00 (Reference)
Male	1.00 (Reference)	2.13 (2.04-2.22)
Age, years		
≤ 19	1.00 (Reference)	1.00 (Reference)
20-39	6.69 (6.13-7.29)	6.25 (5.72-6.83)
40-59	13.4 (12.3-14.6)	11.4 (10.5-12.5)
≥ 60	9.33 (8.46-10.3)	7.52 (6.79-8.33)
Occupation		
White collar	1.00 (Reference)	1.00 (Reference)
Blue collar	1.36 (1.30-1.42)	1.25 (1.18-1.31)
Others	1.10 (1.04-1.16)	1.06 (0.99-1.13)
Urbanization		
Low	1.00 (Reference)	1.00 (Reference)
Moderate	0.97 (0.90-1.04)	1.03 (0.95-1.12)
High	1.08 (1.02-1.15)	1.07 (0.98-1.14)
Income		
< 30,000 NTD	1.00 (Reference)	1.00 (Reference)
≥ 30,000 NTD	1.38 (1.32-1.45)	1.15 (1.09-1.22)
Uremia		
No	1.00 (Reference)	1.00 (Reference)
Yes	2.31 (1.99-2.68)	1.50 (1.28-1.76)
Vit. B ₆ deficiency		
No	1.00 (Reference)	1.00 (Reference)
Yes	2.42 (1.71-3.43)	1.51 (1.04-2.19)
Rheumatoid arthritis		
No	1.00 (Reference)	1.00 (Reference)
Yes	3.65 (3.22-4.13)	2.21 (1.94-2.52)
Hypothyroidism		
No	1.00 (Reference)	1.00 (Reference)
Yes	2.62 (2.22-3.10)	1.38 (1.16-1.65)
Obesity		
No	1.00 (Reference)	1.00 (Reference)
Yes	3.33 (2.67-4.15)	2.30 (1.82-2.91)

Table 5 Estimated risk of CTS in relation to comorbidities controllingsociodemograhic characteristics in multivariate logistic analysis, Taiwan, 2000-2007

Hypertension		
No	1.00 (Reference)	1.00 (Reference)
Yes	2.93 (2.57-3.35)	1.84 (1.60-2.11)
Diabetes		
No	1.00 (Reference)	1.00 (Reference)
Yes	3.59 (3.06-4.21)	2.04 (1.72-2.41)
Gout		
No	1.00 (Reference)	1.00 (Reference)
Yes	3.21 (2.79-3.70)	2.29 (1.97-2.67)
Acromegaly		
No	1.00 (Reference)	1.00 (Reference)
Yes	2.26 (2.01-2.54)	1.47 (1.29-1.66)

Adjusted for gender, age, occupation, urbanization, income, uremia, vitamin B_6 deficiency, rheumatoid arthritis, hypothyroidism, diabetes, obesity, gout, hypertension and acromegaly.

CTS, carpal tunnel syndrome; CI, confidence interval; Vit. B₆, vitamin B₆; NTD, New Taiwan Dollars.

	Female	Male	
Variable	Odds ratio (95% CI)	Odds ratio (95% CI)	
Uremia			
No	1.00 (Reference)	1.00 (Reference)	
Yes	1.39 (1.12-1.73)	1.62 (1.29-2.05)	
Vit. B6 deficiency			
No	1.00 (Reference)	1.00 (Reference)	
Yes	1.56 (1.01-2.42)	1.40 (0.68-2.85)	
Rheumatoid arthritis			
No	1.00 (Reference)	1.00 (Reference)	
Yes	2.06 (1.74-2.44)	2.43 (1.98-2.98)	
Hypothyroidism			
No	1.00 (Reference)	1.00 (Reference)	
Yes	1.36 (1.13-1.65)	1.36 (0.82-2.26)	
Obesity			
No	1.00 (Reference)	1.00 (Reference)	
Yes	2.27 (1.71-3.02)	2.33 (1.54-3.51)	
Hypertension			
No	1.00 (Reference)	1.00 (Reference)	
Yes	1.92 (1.57-2.35)	1.74 (1.44-2.12)	
Diabetes			
No	1.00 (Reference)	1.00 (Reference)	
Yes	2.28 (1.82-2.86)	1.78 (1.37-2.32)	
Gout			
No	1.00 (Reference)	1.00 (Reference)	
Yes	2.28 (1.76-2.95)	2.33 (1.94-2.80)	
Acromegaly			
No	1.00 (Reference)	1.00 (Reference)	
Yes	1.42 (1.17-1.72)	1.52 (1.29-1.79)	

Table 6 Estimated risk and 95% confidence interval of CTS by gender in relation tocomorbidities controlling sociodemograhic characteristics in multivariate logisticanalysis, Taiwan, 2000-2007

CTS, carpal tunnel syndrome; CI, confidence interval; Vit. B₆, vitamin B₆.