



## Epidemiologic study of pterygium in Taiwan

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### Abstract

**Purpose** To investigate the incidence, prevalence, and factors related to pterygium in Taiwan.

**Study design** An ecological study

**Methods** We analyzed a random sample of 1 million individuals in Taiwan drawn from the National Health Insurance Database (NHIRD), established in 2005, for the period 2000 to 2011. Patients with pterygium were identified using ICD-9-CM diagnostic codes. The prevalence and annual age- and gender-adjusted incidence of pterygium were calculated for each county in Taiwan. The risk factors including ultraviolet (UV) exposure, outdoor occupation, educational level, and average socioeconomic status of each county of each index year were identified. Univariate and backward elimination multivariate selection by the mixed-effects model were performed to identify significant risk factors related to the incidence of pterygium in Taiwan.

**Results** A total of 22,063 individuals with pterygium (10,125 men and 11,938 women) were identified in this study. The prevalence of pterygium was 2.14% in the overall population and 3.48% in the population aged 40 years or older. The occurrence of pterygium was greater in women. In addition, this study demonstrated that UV exposure and low educational level are correlated with the age- and gender-adjusted incidence of pterygium.

**Conclusion** Our study is the first to use the NHIRD to determine the prevalence (2.14%) and annual age- and gender-adjusted incidence of pterygium among the general population of Taiwan. The relationship of pterygium with UV exposure and educational level suggests a complex and multifactorial etiology for this disease.

**Keywords** Epidemiology · Pterygium · Taiwan · Ultraviolet exposure

### Introduction

Pterygium is a common fibrovascular proliferative disease characterized by a wing-shaped growth from the conjunctiva over the ocular surface [1]. In addition to obvious cosmetic concerns, it can result in ocular irritation, visual

disturbances, corneal astigmatism, and other complications [2, 3]. Many previous reports have shown the prevalence of and risk factors for pterygium in population-based studies [1, 4–12]. However, prevalence and incidence rates may vary considerably depending on different diagnostic criteria, sampling methods, and demographic factors. The prevalence of pterygium varies from 1.4% to 33% in different geographic regions, with higher rates generally in regions where sun radiation is more intense—such as near the equator or at high altitudes—as well as among darker-skinned individuals [1]. The proposed causative mechanisms of pterygium formation include alterations in limbal stem cells or conjunctival fibroblasts resulting from chronic ultraviolet light exposure and altered expression of p53, transforming growth factor- $\beta$ , and matrix metalloproteinases [13]. The definitive causative mechanisms, however, are unknown [9]. Although the exact etiology of pterygium is unknown, there seems to be an association between pterygium formation and aging, gender, ultraviolet (UV) radiation, and outdoor work [1, 14].

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Moreover, a higher geographic latitude, higher educational level, and higher socioeconomic status are associated with a reduced pterygium incidence [8, 15–17].

Taiwan is located in the Western Pacific, between Japan and the Philippines off the southeast coast of China, from which it is separated by the Taiwan Strait. Taiwan's latitude and longitude are 10–26°N and 114–124°W. Crossed by the Tropic of Cancer, Taiwan has a subtropical climate with the exception of its extreme southern tip, which is tropical. Although advances have been made in the knowledge of the distribution and associations of pterygium, to date a national, population-based study on the prevalence and incidence of pterygium has not been conducted anywhere in the world; in addition, before this study, no documented, large-scale studies of pterygium had been conducted in Taiwan. Furthermore, the factors responsible for the variation observed among studies performed in similar latitudes remain elusive. In Taiwan, some population-based studies have been conducted focusing on the prevalence of pterygium in certain populations of southern and eastern Taiwan and the outlying islands, with the incidence ranging from 25.2% to 53.1% [18–21]. However, the actual incidence and prevalence in the general population of Taiwan remains unknown. In this study, we used Taiwan's National Health Insurance Research Database (NHIRD), which contains health care data of virtually all the residents of Taiwan, to provide an estimate of the nationwide prevalence and age- and gender-adjusted annual incidence of pterygium from January 2000 through December 2011 and to examine the factors possibly related to the development of pterygium.

## Materials and methods

### Data source

The study was approved by the institutional review board of Chang Gung Memorial Hospital. Taiwan's NHIRD is a publicly released and deidentified research database that covers virtually all of Taiwan's population (coverage rate in 2011, 99.6%) since 1996 [22]. In 2005, the National Health Research Institute (NHRI) provided a database of 1 million random individuals, about 4% of the population, to be available for research purposes [23]. The data contain information about 495,804 men (49.58%) and 504,171 women (50.42%). No significant differences in age and sex were found between the sample group and all enrollees [24, 25]. To help ensure privacy, individual and hospital identifiers are unique to the research database and cannot be used to trace individual patients or health service providers [26]. In this study, we used outpatient claims data collected during the 2000–2011 period to investigate

the prevalence, age- and gender-adjusted incidence, and demographic characteristics of pterygium in Taiwan.

### Identification of patients with pterygium

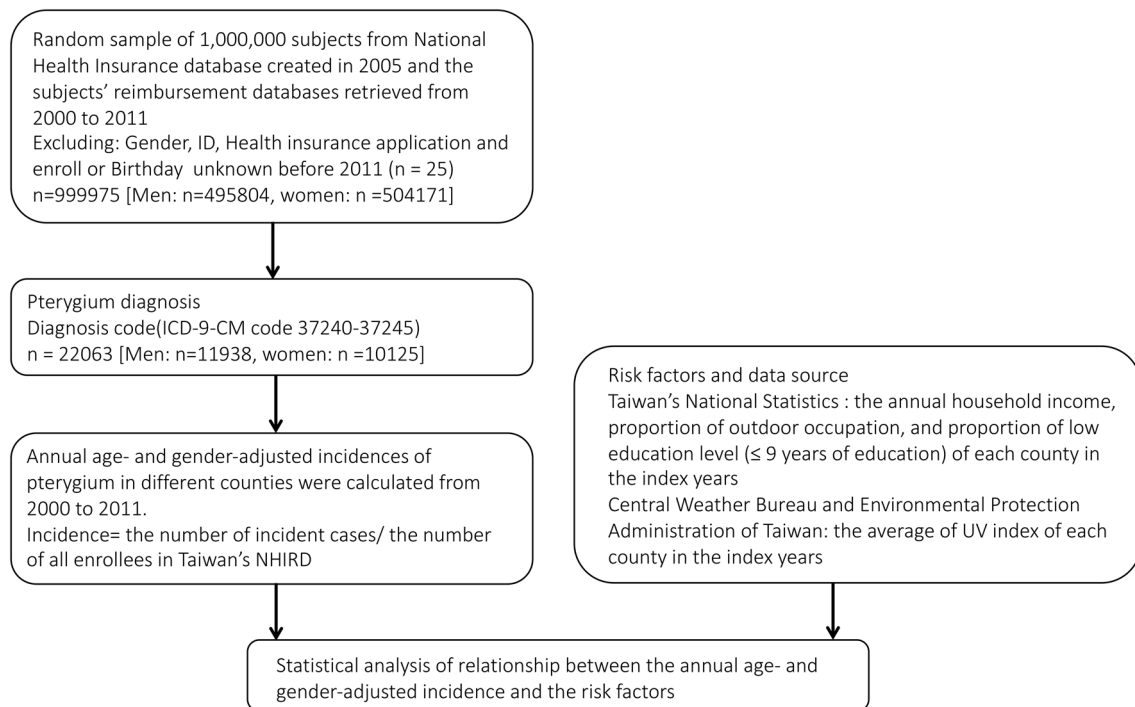
Within Taiwan's national health insurance (NHI) scheme, medical claims are sent to the Bureau of National Health Insurance (BNHI) of Taiwan for cross-checking and validation with the aim of ensuring the accuracy of the diagnostic coding. The diagnostic coding of the NHI in Taiwan is conducted according to the International Classification of Disease, 9th Revision, Clinical Modification (ICD-9-CM) diagnostic criteria. A recent validation study supported the reliability of the NHIRD diagnostic codes [27]. We searched the Taiwan's NHIRD for the source population during the 2000–2011 period and used outpatient claims to find any visit for pterygium (ICD-9-CM code 37240–37245) in each county of Taiwan (Fig. 1).

### Incidence and prevalence

Incident cases were defined as patients who had their first contact with the services and received a diagnosis of pterygium during a given year and who had not received such a diagnosis previously. The annual age- and gender-adjusted incidence from 2000 to 2011, adjusted by the standardized population at each index year, was calculated separately. The numerator was the number of incident cases in the given year, and the denominator was the number of all enrollees in Taiwan's NHIRD in the corresponding year. The data were further grouped according to the patient's location of residence at the county level (20 data of incidence at county level each year and totally 240 data of incidence at county level from 2000 to 2011). In addition, prevalence in 2011 was defined as the incident cases collected from 2000 to 2011, excluding individuals who died in or before 2011, divided by the number of all enrollees in Taiwan's NHIRD in 2011.

### Risk factors

To estimate the socioeconomic status, occupation, and educational level of the Taiwanese population, we searched the average annual household income, proportion of outdoor occupations, and proportion of low education level ( $\leq 9$  years of education) of each county in the database of Taiwan's National Statistics from 2000 to 2011. The UV index was provided by the Central Weather Bureau and the Environmental Protection Administration of Taiwan.



**Fig. 1** Flowchart showing the selection procedure of the study participants and data analysis

## Statistical analysis

Trend analysis was performed to examine the decrease in age- and gender-adjusted incidence of pterygium from 2000 to 2011. With the age- and gender-adjusted incidence and risk factors of each county at each index year, univariate and backward elimination multivariate analyses by the mixed-effects model with the selection criterion of a probability value less than 0.05 were performed to identify the independent significant factors related to the occurrence of pterygium in Taiwan. The statistical analyses were performed using SPSS 22 (SPSS). A 2-tailed level of 0.05 was considered significant.

## Results

### Patients' characteristics

The study participants comprised 22,063 patients (10,125 men and 11,938 women) with claims of a primary diagnosis of pterygium during the 12-year study period. The prevalence of pterygium in Taiwan in 2011 was 2.14% (95% confidence interval [CI], 1.65%–2.63%); among those aged 40 years or older, it was 3.48% (95% CI 2.85%–4.11%). In addition, in 2011, the prevalence for men was 1.96% (95% CI 1.54%–2.38%) and the prevalence for women was 2.32% (95% CI 1.78%–2.86%). A modest

decrease in the annual age- and gender-adjusted incidence of pterygium during the study period was observed ( $P$  for trend  $< 0.001$ ). The annual age- and gender-adjusted incidence of the whole population decreased from 3.7% (95% CI 2.79%–4.60%) in 2000 to 2.0% (95% CI 1.50%–2.49%) in 2011 (Table 1).

**Table 1** Annual age- and gender-adjusted incidence of pterygium in Taiwan, 2000–2011

Index year	Incident cases	Incidence (%)	95% confidence interval (%)	
			Lower bound	Upper bound
2000	2469	3.70	2.79	4.60
2001	2207	3.09	2.48	3.70
2002	2153	3.43	2.59	4.27
2003	1869	2.83	2.15	3.52
2004	2060	2.79	2.13	3.45
2005	1915	2.56	1.98	3.14
2006	1776	2.53	2.01	3.05
2007	1726	2.61	2.04	3.19
2008	1646	2.66	1.86	3.45
2009	1480	2.39	1.79	2.99
2010	1394	1.97	1.57	2.37
2011	1368	2.00	1.50	2.49

## Incidences of pterygium in different counties

The average annual age- and gender-adjusted incidence of pterygium and the geographic characteristics in the study years in each county of Taiwan are shown in Table 2. Among these counties, the average annual age- and gender-adjusted incidence was highest in Penghu (6.22%; 95% CI 2.56%–9.88%), one of Taiwan's outlying islands, and was lowest in Keelung (0.79%; 95% CI 0.23%–1.35%), located in northern Taiwan. No difference in the age- and gender-adjusted incidence was found between the east and west side of Taiwan (Fig. 2). In addition, the geographic characteristics including the average annual UV index, the proportions of the population engaged in outdoor occupations, lower education level (<9 years of education), and annual household income of each county are also illustrated in Table 2 and Fig. 2.

## Risk factors for pterygium

As shown in Table 3, univariate analysis in the mixed-effects model showed association of UV exposure, outdoor

occupation, low education, and income with the age- and gender-adjusted incidence of pterygium. After backward elimination multivariate analysis with the selection criterion of  $P < 0.05$ , we found that UV exposure and low education were the significant independent variables related to the age- and gender-adjusted incidence of pterygium.

## Discussion

To the best of our knowledge, this is the first ecological study to report the prevalence and annual age- and gender-adjusted incidence of pterygium for the entire region of Taiwan. Because 99.6% of the Taiwanese population participates in the NHI program and because no significant differences in age and sex were found between the sample group and all enrollees in the NHI program, we have reason to believe that the prevalence and the annual incidence data presented here are approximate to the true distribution of pterygium in Taiwan [22, 24, 25].

The prevalence of pterygium varies widely across studies and geographic regions—ranging from 1.4% to 33% [1].

**Table 2** Age- and gender-adjusted incidence of pterygium and geographic characteristics of 20 districts in Taiwan

District	UV index <sup>a</sup>	Outdoor occupation proportion <sup>b</sup> (%)	Low education proportion <sup>c</sup> (%)	Annual household income <sup>d</sup> (USD/y)	Incidence <sup>e</sup> (%)	95% confidence interval (%)	
						Lower bound	Upper bound
Keelung	5.564	0.66	35.8	32,403	0.79	0.23	1.35
Taipei	5.324	0.26	17.63	50,718	0.91	0.65	1.17
Taoyuan	6.082	1.97	34.92	37,726	1.03	0.74	1.32
New Taipei	5.518	0.71	35.24	36,545	1.09	0.68	1.50
Hsinchu	6.167	2.66	37.5	31,995	1.15	0.72	1.58
Taichung	5.953	3.92	32.56	33,708	1.86	0.71	3.01
Miaoli	6.167	7.83	44.48	31,035	1.94	0.61	3.27
Hualien	6.555	10.8	45.15	27,990	2.52	1.49	3.55
Tainan	7.372	8.01	40.19	29,985	2.62	1.47	3.77
Changhua	6.891	12	47.43	29,496	2.63	1.69	3.57
Yilan	6.32	7.72	49.05	29,840	2.63	1.45	3.81
Nantou	6.771	19.6	48.31	28,764	2.87	2.05	3.69
Kaohsiung	6.848	4.39	33.71	33,597	2.92	1.19	4.65
Kinmen	6.15	5.85	45.1	31,329	3.44	0.74	6.14
Chiayi	5.783	17.77	46	30,308	3.85	2.46	5.24
Taitung	7.454	24.6	56.76	24,663	4.00	1.92	6.08
Lienchiang	5.063	3.07	43.1	42,239	4.12	-3.09	11.33
Pingtung	6.977	18.78	44.66	28,93	4.43	2.44	6.42
Yunlin	6.885	23.14	53.31	26,107	4.43	2.75	6.11
Penghu	6.757	7.24	43.3	27,001	6.22	2.56	9.88

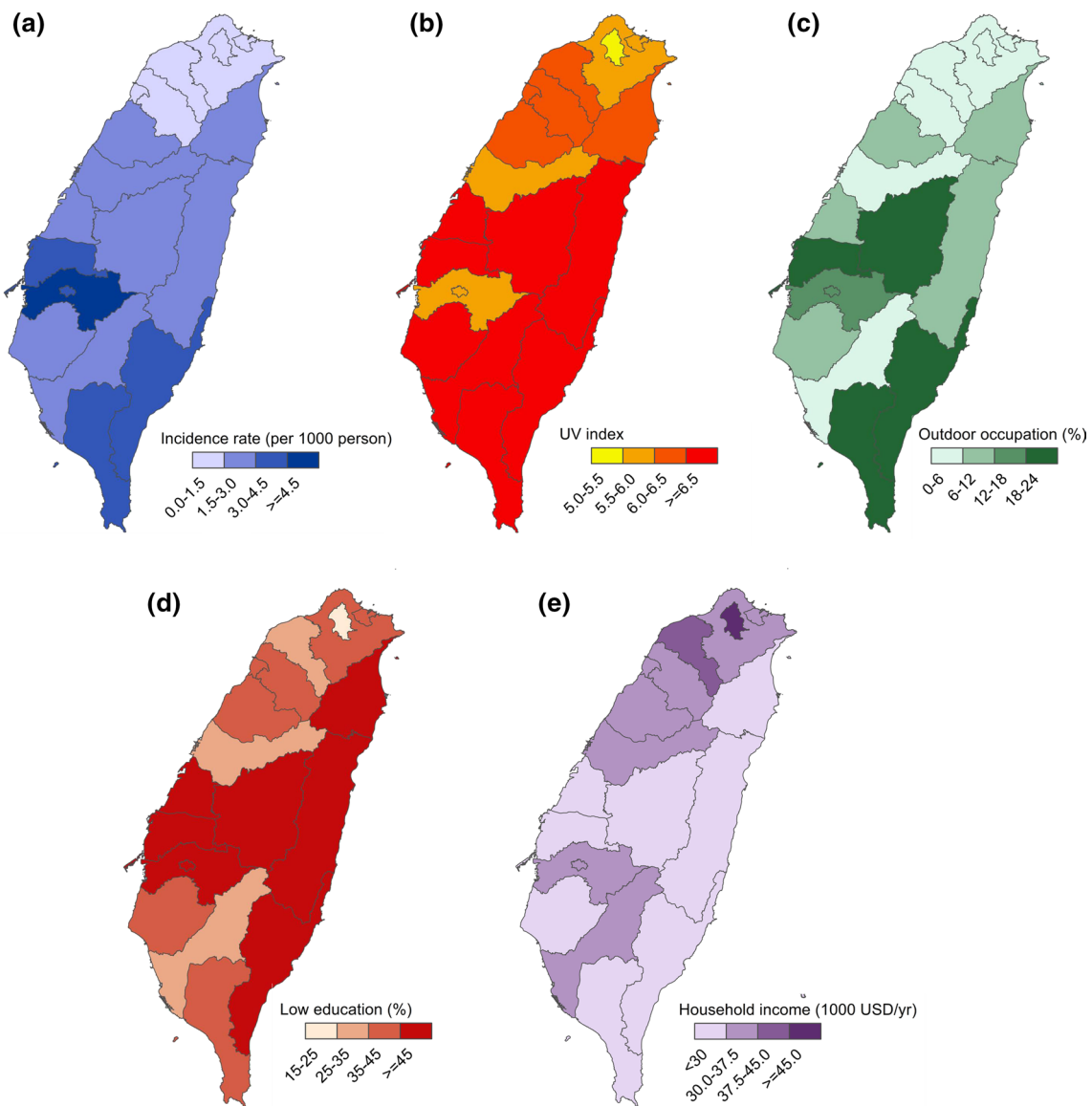
<sup>a</sup>Mean average UV index, per year (2000–2011)

<sup>b</sup>Mean proportion of residents who worked outdoors, per year (2000–2011)

<sup>c</sup>Mean proportion of residents who received less than 9 years of education, per year (2000–2011)

<sup>d</sup>Mean average annual family income (2000–2011)

<sup>e</sup>Mean annual age- and gender-adjusted incidence during the study years (2000–2011)



**Fig. 2** Geographic distribution of **a** age- and gender-adjusted incidence of pterygium, **b** UV index, **c** outdoor occupation proportion, **d** low education proportion, **e** annual household income in Taiwan

**Table 3** Significant independent variables related to the incidence of pterygium

	Univariate		Multivariate	
	B (95% CI)	P value	B (95% CI)	P value
UV exposure	0.33 (0.04, 0.62)	0.027	0.29 (0.05, 0.53)	0.017
Outdoor occupation	0.29 (0.14, 0.42)	0.001	–	
Low education	0.10 (0.07, 0.12)	< 0.001	0.10 (0.07, 0.12)	< 0.001
Annual household income	$-4 \times 10^{-6}$ ( $-6 \times 10^{-6}$ , $-2 \times 10^{-6}$ )	0.001	–	

B coefficient of the risk factors in the mixed-effects model, UV ultraviolet light

In our study, the prevalence of pterygium was 2.14% in the overall population and 3.48% in the population aged 40 years or older. This was apparently lower than those found in previous studies conducted in Taiwan, i.e., a prevalence of 25.2% in Chiayi among persons aged 40 or older reported by Chen et al in 2013 [18], of 44.1% in Amis aborigines among those older than 65 reported by Huang et al in 2010 [19], and of 53.01% among residents aged 40 years or older of 3 villages exposed to arsenic reported by Lin et al in 2008 [21]. A recent epidemiologic study conducted in Kumejima island, Japan, observed that the prevalence was 30.8% (95% CI 29.3%–32.3%) in the population aged 40 years or older [9]. However, the prevalence observed in our study is more consistent with the prevalence in other tropical or subtropical areas reported previously [1]. Several factors could explain the differences in the prevalence of pterygium of our study and those of the other studies. First, our study was nationwide and involved the entire population, including persons of all ages and those living in both urban and rural areas. In previous studies, participants mostly comprised elderly individuals in areas with relatively high sun exposure intensity, such as southern Taiwan or the outlying islands. Second, the NHIRD includes patients who actively seek out medical assistance. As a result, patients who present with only mild pterygium—as well as those in whom the disease does not result in significant visual disturbance—are not included in the database unless they visit a medical facility to seek treatment.

A modest decrease in the annual incidence of pterygium, from 3.7% to 2.0% ( $P$  for trend  $< 0.001$ ), was observed over the 12-year study period (Table 1). This decrease could be explained by the continued transformation of vocations (i.e., workforce composition) that took place in Taiwan during the study years. Up until a few decades ago, Taiwan was a traditional, agriculturally based society and has since gradually shifted into an industrially and commercially based economy. As a result, the average person is exposed to less sunlight and dust during work than in the past. In addition, the use of sunglasses has continued to increase each year among the general population, resulting in a decreased incidence of pterygium over this period.

The correlation of pterygium with gender is controversial. The majority of studies reported that men are at a higher risk of developing pterygium than are women [5–7, 9, 17, 28]; a small number of other studies, however, found the opposite [4, 16]. In the current study, the prevalence of pterygium in 2011 was higher in women (2.32%; 95% CI 1.78%–2.86%) than in men (1.96%; 95% CI 1.54%–2.38%). Since the NHIRD includes patients who actively seek medical assistance, women are possibly overrepresented among pterygium patients in the database as a result of women being more sensitive to ocular irritation and/or owing to cosmetic concerns related to the disease.

A strong correlation between increased UV exposure and annual age- and gender-adjusted incidence of pterygium was found in our study; this finding is consistent with those of previous studies that demonstrated the effect of UV radiation on the prevalence of pterygium and other ocular surface diseases [29, 30]. Our result supports the UV radiation hypothesis in which pterygium formation can be attributed to alterations in limbal stem cells or conjunctival fibroblasts resulting from chronic UV light exposure [13], and this finding makes wearing sunglasses for pterygium prevention important.

In the Barbados Eye Study, logistic regression analysis indicated a positive association between pterygium and fewer years of education ( $< 12$  years) (OR 1.43; 95% CI 1.01–2.03) [31]. Lim et al also reported that a higher level of education was a protective factor against pterygium (elementary school vs college, OR 3.98; 95% CI 2.24–7.06) [17]. In the current study, we found that fewer years of education ( $\leq 9$  years) was positively correlated with pterygium formation. This result might be explained by the fact that people with a higher level of education are more likely to spend their time indoors and have relatively less exposure to wind or dust, which would infer that a higher educational level is a protective factor for preventing pterygium formation.

Our study has certain limitations that should be noted. First, either systemic bias or selection bias may exist because of the quality of the diagnostic codes used. As chart-level data were unavailable in the NHIRD, we used diagnostic codes to ascertain the diagnosis of pterygium; therefore, the prevalence of pterygium may be underrepresented here owing to a lack of correct documentation and coding. Second, detailed information such as smoking habits, alcohol consumption, family history, and ocular exam details are not included in the NHIRD, all of which may be risk factors for pterygium formation.

In conclusion, from 2000 to 2011, the prevalence of pterygium in Taiwan was 2.14% in the overall population and 3.48% in the population aged 40 years or older. The annual incidence of pterygium decreased each year of the study period, and the occurrence of pterygium was greater in women. The relationship of pterygia with UV exposure and educational level suggests a complex and multifactorial etiology for this disease.

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