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REVIEW ARTICLE

Oral leukoplakia in China: a review

Xiaolin Zhang · Chengjie Li · Yi Song · Peter A. Reichart

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Abstract
Background Most prevalence studies on oral leukoplakia (OL) in China have been published in the Chinese language. The present review on the literature in Chinese aimed at making the data available to colleagues who are not familiar with the Chinese language.
Methods The overall rate and 95% confidence interval of OL were calculated using Excel 2003.
Results Overall prevalence of OL was 9.18% (95%CI=9.06-9.30%). Gender ratio of prevalence was 8.03:1 (males/females). Prevalence was high in age groups over 40 years with the highest in the group aged 60-69 years (21.04%, 95%CI=19.95-22.13%). The buccal mucosa was most commonly affected (47.08%, 95%CI=46.52-47.64%), followed by lip (39.09%), palate (9.85%), gingiva (1.80%), and tongue (1.46%). The prevalence in smokers was 23.43% and in non-smokers 1.93%. Among three variants of smoking, the traditional Hanyan pipe smoking carried the highest risk for the development of OL followed by cigarette and Shuiyan water pipe smoking. The rate of alcohol drinkers with OL was 54.50% and 22.21% in individuals without OL. No case of oral cancer was found in six surveys.
Conclusions The present data on the prevalence of OL in China are comparable to those in other parts of the world. Some traditional smoking habits, however, are particular to certain regions of China.

Keywords Oral leukoplakia · Oral cancer · Tobacco · Alcohol · PR China

X. Zhang · C. Li
School and Hospital of Stomatology, Peking University,
Beijing, People's Republic of China

Y. Song
School of Public Health, Peking University,
Beijing, People's Republic of China

P. A. Reichart
University of Bern, Department of Oral Surgery and Stomatology,
Bern, Switzerland

X. Zhang (✉)
Department of Oral Biology, School and Hospital of Stomatology,
Peking University,
Zhongguancun Nandajie 22,
Beijing 100081, People's Republic of China
e-mail: xlz45@yahoo.com.cn

Introduction

Oral leukoplakia (OL) is a prevalent lesion of the oral mucosa with a premalignant potential occurring worldwide including China. The first study on OL published in the Chinese language was published in 1964 [1], followed by studies on the epidemiology of OL. In 1978 and 1983 the National Collaborating Center for Oral Leukoplakia and Oral Lichen Planus proposed definitions of OL based on those suggested by WHO [2, 3]. In 1983, the center subsequently made a revision. The number of prevalence and longitudinal follow-up studies of OL from China is limited. The aim of the present review was to introduce the results of surveys on OL from China. This review is focused on data on the prevalence of OL in China and is presented in the English language thus enabling colleagues not familiar with the Chinese language to study the data presented.

Materials and methods

The literature reviewed for this article was retrieved from journals published in the Chinese language. Three

reviewers (XLZ, CJL, and YS) collected and studied the literature from an internet database including Chinese journal full-text database, China Academic Library and Information System and Chinese Journal database. Some earlier literature was collected from printed publications.

References were searched by using and combining the following search terms: oral leukoplakia, oral precancerous condition, oral precancerous lesion, oral mucosal lesion, oral mucosal diseases, and oral cancer. References were selected for this review finally by using the following inclusion criteria:

1. All studies had to be in keeping with the definitions of OL, which were established by the National Collaborating Center in 1978 or 1983 as mentioned earlier.
2. The surveys had to be carried out in unselected groups of the general population.
3. Studies which contained information on OL such as age, gender, type of lesion, localization, smoking, alcohol, data on transformation, and histology were included. Retrospective studies with follow-up were searched for in particular.

Data analysis

The overall rate and 95% confidence interval (95% CI) of OL were calculated by merging all included studies in the present review, the overall sample as denominator, and the individuals with OL as numerator. The figure of overall rate provided an estimated parameter on OL in China, and 95% CI shown in tables was used to indicate the reliability of an estimate. Data were all calculated by using Excel 2003.

Results

A total of over 350 references in Chinese language were retrieved from the literature of which 14 articles were considered to fulfill selection criteria (Table 1) shows prevalence according to gender of cases with OL which were reported by seven surveys with a total of 225,513 urban or rural individuals [4–10]. Prevalence of OL ranged from 15.56% (95%CI=15.01-16.11%) [4] to 1.46% (95%CI= 1.05-1.87%) [10]. Out of 225,513 individuals 20,694 cases with OL were found, the overall prevalence was 9.18% (95% CI=9.06-9.30%). Prevalence of OL in males ranged from 22.70% [4] to 2.13% [10]. Overall prevalence of OL in males was 13.90% (19,182 cases in 137,965 individuals). Prevalence of OL in females ranged from 2.12% [5] to 0.18% [10]. Overall prevalence of OL in females was 1.73% (1,512 cases in 87,548 individuals). Gender ratio of the prevalence of OL was males/females=8.03:1 [4–10].

In Table 2, the prevalence of OL according to age distribution is shown [4, 5, 7–10]. The overall highest prevalence of OL was found in the age group 60-69 years (21.04%). In three surveys the highest prevalence of OL (32.99%) was found in the group aged 50-59 years [4, 8, 9], while an additional three surveys showed that the highest prevalence of OL was in the group aged 60-69 years [5, 7, 10].

Fang et al. reported on gender distribution in different age groups. The highest prevalence of OL was found in males over 70 years (33.99%) followed by the group of 50-59 years (28.77%), and in females the highest prevalence of OL was in the 60-69 year group (8.61%), followed by the group of over 70 years (6.40%) [5]. Data of all the six surveys showed a decrease of prevalence of OL: 40-49 years >30–39 years>20–29 years>10–19 years [4, 5, 7–10].

Table 3 shows sites of lesions in OL cases in four surveys. Of the lesions of OL, 30,639 were found in a total of 17,517 cases. The buccal mucosa was most commonly affected (47.08%) followed by lower and upper lip, respectively; then hard and soft palate, respectively; and the following sites in decreasing frequencies of occurrence: gingiva, tongue, alveolar process, vestibule, floor of mouth, pharyngeal arch, and lastly the retromolar pad. No lesions located to the labial commissures were recorded in the four surveys [5, 7, 9, 10].

In four surveys, there were 73,159 smokers (34.46%) among a total of 212,271 individuals (Table 4) of which 52.49% were males and 6.04% were females. The overall prevalence of OL in four studies in smokers was 23.43% as against 1.93% non-smokers. The ratio of prevalence of smokers compared to non-smokers was 12.14:1. Prevalence of OL in male smokers was 24.16%, in female smokers it was 13.41%. The ratio of prevalence of OL in male smokers to female smokers was 1.80:1 (Table 4) [4, 5, 8, 9].

There are three main types of smoking habits in China. The most prevalent type is to smoke cigarettes. The other two are known as the Hanyan and Shuiyan types, respectively, which are characteristic pipe-smoking habits. The habit of Hanyan smoking is more commonly practiced Northern areas of China (Fig. 1a; Han means “dry” and “Yan” is tobacco.). In the survey by Fang et al., the prevalence of OL in 4,019 Hanyan smokers was 43.72%; whereas in 43,836 cigarette smokers, it was only 23.31% [5]. In contrast to the habit of Hanyan smoking, Shuiyan smoking is the characteristic habit practiced South-eastern areas of China. (Shui stands for water, Yan is tobacco.) This is a type of water pipe, and it is made of copper or bamboo (Fig. 1b).

Few articles reported on alcohol consumption in OL cases. One survey showed that 54.50% were drinkers in 2,631 OL cases compared to 22.21% of drinkers in 14,278 individuals without OL. The ratio of drinkers with OL and

Table 1 Prevalence of OL and gender

Study	Individuals *n*			OL *n* (%)					
	Males	Females	Total	Males	95%CI	Females	95%CI	Total	95%CI
Su et al. [4]	11,054	5,855	16,909	2,509 (22.70)	21.92-23.48	122 (2.08)	1.71-2.45	2,631 (15.56)	15.01-16.11
Fang et al. [5]	88,668	45,824	134,492	13,143 (14.82)	14.59-15.05	970 (2.12)	1.99-2.25	14,113 (10.49)	10.33-10.65
Lin et al.[6]	2,613	1,941	4,554	378 (14.47)	13.12-15.82	38 (1.96)	1.34-2.58	416 (9.13)	8.29-9.97
Zhang et al. [7]	3,311	2,089	5,400	317 (9.57)	8.57-10.57	43 (2.06)	1.45-2.67	360 (6.67)	6.00-7.34
Wang [8]	783	1,237	2,020	123 (15.71)	13.16-18.26	7 (0.57)	0.15-0.99	130 (6.44)	5.37-7.51
Chen et al. [9]	29,380	29,470	58,850	2,666 (9.07)	8.74-9.40	330 (1.12)	1.00-1.24	2,996 (5.09)	4.91-5.27
Yu [10]	2,156	1,132	3,288	46 (2.13)	1.52-2.74	2 (0.18)	−0.07-0.43	48 (1.46)	1.05-1.87
Total	137,965	87,548	225,513	19,182 (13.90)	13.72-14.08	1,512 (1.73)	1.64-1.82	20,694 (9.18)	9.06-9.30

individuals without OL was 2.45:1.4. Chen et al. reported that 31.17% of 2,996 cases with OL were drinkers who drank 50~100 ml/day of Samshu (strong traditional liquor made of rice) [9]. Samshu has been a common alcoholic drink 20-30 years ago, which now largely has been replaced by beer and wine. In another study of 48 OL cases, 52.08% were drinkers [10]. Guli reported 150 cases of OL of whom 52.00% were drinkers of 100-200 ml of Samshu per day [11].

In six out of seven surveys, no cases of oral cancer (OC) have been reported in 6,581 cases with OL [4, 6–10]. One survey reported 15 cases (0.11%) of OC which were diagnosed clinically among 14,113 OL cases [5].

Four clinical studies reported on the site of OC in OL cases. The highest rate of OC development in OL was found in the alveolar process (28.57%), followed by floor of mouth (21.05%), tongue (11.21%), palate (10.00%), lip (6.54%), buccal mucosa (3.53%), and gingiva (3.13%). No case of OC was found in other sites [12–15].

Discussion

There is a vast body of literature on the epidemiology of OL and its association with tobacco and alcohol usage from many geographic areas of the world. Prevalence of OL varies greatly according to tobacco habits (smoking and/or chewing), alcohol consumption, infection of the oral mucosa with human papilloma virus and diet, or nutritional factors [16, 17].

In China, epidemiologic studies on OL have been carried out in the 1970s when OL was recognized as the most prevalent precancerous lesion of the oral mucosa. In the present review, the overall prevalence of OL was 9.18% in 225,513 individuals of seven surveys with a 95% CI calculated providing a range around the estimate that conveys how precise the estimate is. A wide range of prevalence of OL from 15.56% to 1.46% was reported in these studies [4, 5, 7–10]. In India, a similarly wide range of prevalence of OL has been found ranging from 11.7% in 57,518 industrial workers [18] to 0.7% in 101,761 villagers [19]. Surveys from Europe reported prevalence of OL in 8.0% (USSR) [20], 3.6% (Sweden) [21], 0.9% (Germany) [22], and 0.2% (The Netherlands) [23]. One of the main reasons for the relatively high overall prevalence of OL (9.18%), compared to most other studies worldwide, may well be the high prevalence of cigarette smoking and pipe smoking habits (Hanyan and Shuiyan). Traditional pipe smoking (Hanyan or Shuiyan) associated with the occurrence of OL is on the decline in China and therefore may become less important for the development of epithelial precursor lesions in the future.

The present data on age and presence of OL in China showed similar findings as most studies worldwide and thus confirm that OL must be regarded as a lesion of the elderly [24].

The present review revealed that the buccal mucosa is a predilection site for the development of a finding comparable to other studies [24, 25]. Other less frequent affected sites were the lips, palate, gingiva, and tongue (Table 3). The ventral tongue and the floor of mouth which are generally considered as predilection sites for OL with a great potential to transformation to cancer were in this review rarely involved (0.01% and 0.06%).

Of all individuals with OL studied, 33.46% were not surprisingly smokers. Of the male individuals, 52.49% were smokers while only 6.04% of females smoked. This is in marked difference to smokers in Europe where 18.2-17.8% of women, particularly young women, smoke [26]. The present data showed that Shuiyan water pipe smoking

Table 2 Prevalence of OL and age distribution

Study		10-19 years	20-29 years	30-39 years	40-49 years	50-59 years	60-69 years	70 years	Total
[4]	*n*	1,766	6,241	4,396	2,981	1,164	277	84	16,909
	OL *n*	32	598	779	782	384	45	11	2,631
	OL (%)	1.81	9.58	17.72	26.23	32.99	16.25	13.1	15.56
	95%CI	1.19-2.43	8.85-10.31	16.59-18.85	24.65-27.81	30.29-35.69	11.91-20.59	5.88-20.32	15.01-16.11
[5]	*n*	0	45,398	34,582	35,392	15,091	3,520	509	134,492
	OL *n*	0	1,911	2,971	4,919	3,356	839	117	14,113
	OL (%)	0	4.21	8.59	13.9	22.24	23.84	22.99	10.49
	95%CI	-	4.03-4.39	8.29-8.89	13.54-14.26	21.58-22.90	22.43-25.25	19.33-26.65	10.33-10.65
[7]	*n*	602	1,514	1,400	1,176	506	202	0	5,400
	OL n	3	37	52	109	105	54	0	360
	OL (%)	0.5	2.44	3.71	9.27	20.75	26.73	0	6.67
	95%CI	−0.06-1.06	1.66-3.22	2.72-4.70	7.61-10.93	17.22-24.28	20.63-32.83	-	6.00-7.34
[8]	*n*	167	547	564	649	93	0	0	2,020
	OL *n*	1	11	26	68	24	0	0	130
	OL (%)	0.6	2.01	4.61	10.48	25.8	0	0	6.44
	95%CI	−0.57-1.77	0.83-3.19	2.88-6.34	8.12-12.84	16.91-34.69	-	-	5.37-7.51
[9]	*n*	2,465	22,520	12,009	13,568	6,694	1,329	265	58,850
	OL *n*	5	180	397	1,206	1,005	189	14	2,996
	OL (%)	0.2	0.8	3.31	8.89	15.01	14.22	5.28	5.09
	95%CI	0.02-0.38	0.68-0.92	2.99-3.63	8.41-9.37	14.15-15.87	12.34-16.10	2.59-7.97	4.91-5.27
[10]	*n*	194	808	984	857	402	43	0	3,288
	OL *n*	0	2	5	19	19	3	0	48
	OL (%)	0	0.25	0.51	2.22	4.73	6.98	0	1.46
	95%CI	-	−0.09-0.59	0.06-0.96	1.23-3.21	2.65-6.81	−0.64-14.60	-	1.05-1.87
Total	*n*	5,194	77,028	53,935	54,623	23,950	5,371	858	220,959
	OL *n*	41	2,739	4,230	7,103	4,893	1,130	142	20,278
	OL (%)	0.79	3.56	7.84	13.00	20.43	21.04	16.55	9.18
	95%CI	0.55-1.03	3.43-3.69	7.61-8.07	12.72-13.28	19.92-20.94	19.95-22.13	14.06-19.04	9.06-9.30

Table 3 Sites of lesions of OL cases in surveys

Studies OL cases Number of lesions Lesions/cases	[5] 14,113 *n*=23,768 1.68 *n* (%)	95%CI	[9] 2,996 *n*=6,178 2.06 *n* (%)	95%CI	[7] 360 *n*=632 1.76 *n* (%)	95%CI	[10] 48 *n*=61 1.27 *n* (%)	95%CI	Total 17,517 *n*=30,639 1.75 *n* (%)	95%CI
Cheek										
Unilateral	4,557 (19.17)	18.67–19.67	863 (13.97)	13.11–14.83	303 (47.94)	44.05–51.83	28 (45.90)	33.39–58.41	5,751 (18.77)	18.33–19.21
Bilateral	6,922 (29.12)	28.54–29.70	1,734 (28.07)	26.95–29.19	0	–	18 (29.51)	18.06–40.96	8,674 (28.31)	27.81–28.81
Total	11,479 (48.30)	47.66–48.94	2,597 (42.04)	40.81–43.27	303 (47.94)	44.05–51.83	46 (75.41)	64.60–86.22	14,425 (47.08)	46.52–47.64
Lips										
Upper	277 (1.17)	1.03–1.31	72 (1.17)	0.90–1.44	2 (0.32)	−0.12–0.76	4 (6.56)	−0.68–9.80	355 (1.59)	1.45–1.73
Lower	4,596 (19.34)	18.84–19.84	2,163 (35.01)	33.82–36.20	28 (4.43)	2.83–6.03	6 (9.84)	2.37–17.31	6,793 (22.17)	21.70–22.64
Both	3,926 (16.52)	16.05–16.99	904 (14.63)	13.75–15.51	0	–	0	–	4,830 (15.76)	15.35–16.17
Total	8,799 (37.03)	36.42–37.64	3,139 (50.81)	49.56–52.06	30 (4.75)	3.09–6.41	10 (16.39)	7.10–25.68	11,978 (39.09)	38.54–39.64
Palate										
Soft	60 (0.25)	0.19–0.31	14 (0.23)	0.11–0.35	0	–	0	–	74 (0.24)	0.19–0.29
Hard	2,536 (10.67)	10.28–11.06	330 (5.34)	4.78–5.90	0	–	0	–	2,866 (9.35)	9.02–9.68
Both	0	–	15 (0.24)	0.12–0.36	0	–	0	–	15 (0.05)	0.02–0.08
No detailed	0	–	0	–	63 (9.97)	7.63–12.31	0	–	63 (0.21)	0.16–0.26
Total	2,596 (10.92)	10.52–11.32	359 (5.81)	5.23–6.39	63 (9.97)	7.63–12.31	0	–	3,018 (9.85)	9.52–10.18
Gingiva	422 (1.78)	1.61–1.95	0	–	128 (20.25)	17.12–23.38	0	–	550 (1.80)	1.65–1.95
Tongue										
Lateral	7 (0.03)	0.01–0.05	0	–	0	–	0	–	7 (0.02)	0.00–0.04
Dorsal	252 (1.06)	0.93–1.19	73 (1.18)	0.91–1.45	107 (16.93)	14.01–19.85	5 (8.20)	1.31–15.09	437 (1.43)	1.30–1.56
Ventral	4 (0.02)	0.00–0.04	0	–	0	–	0	–	4 (0.01)	0.00–0.02
total	263 (1.11)	0.98–1.24	73 (1.18)	0.91–1.45	107 (16.93)	14.01–19.85	5 (8.20)	1.31–15.09	448 (1.46)	1.33–1.59
Alveolar process	147 (0.62)	0.52–0.72	0	–	0	–	0	–	147 (0.48)	0.40–0.56
Vestibule	52 (0.22)	0.16–0.28	0	–	0	–	0	–	52 (0.17)	0.12–0.22
Floor of mouth	6 (0.03)	0.01–0.05	10 (0.16)	0.06–0.26	1 (0.16)	−0.15–0.47	1 (1.64)	−1.55–4.83	18 (0.06)	0.03–0.09
Commissure	0	–	0	–	0	–	0	–	0	–
Pharyngeal arch	4 (0.02)	0.00–0.04	0	–	0	–	0	–	4 (0.01)	0.00–0.02
Retromolar pad	0	–	0	–	0	–	3 (4.92)	−0.51–10.35	3 (0.01)	0.00–0.02

Table 4 Prevalence of OL in smokers and non-smokers

Study		Individuals *n*					
		OL *n* (%)					
		Smokers	95%CI	Non-smokers	95%CI	Total	95%CI
[4]	Males	6,752 2,244 (33.23)	32.11–34.35	4,302 265 (6.16)	5.44–6.88	11,054 2,509 (22.70)	21.92–23.48
	Females	44 20 (45.45)	30.74–60.16	5,811 102 (1.76)	1.42–2.10	5,855 122 (2.08)	1.71–2.45
	Total	6,796 2,264 (33.31)	32.19–34.43	10,113 367 (3.63)	3.27–3.99	16,909 2,631 (15.56)	15.01–16.11
[5]	Males	45,998 11,613 (25.25)	24.85–25.65	42,670 1,494 (3.50)	3.33–3.67	88,668 13,107 (14.78)	14.55–15.01
	Females	1,857 362 (19.49)	17.69–21.29	43,967 607 (1.38)	1.27–1.49	45,824 969 (2.11)	1.98–2.24
	Total	47,855 11,975 (25.02)	24.63–25.41	86,637 2,101 (2.43)	2.33–2.53	134,492 14,076 (10.47)	10.31–10.63
[8]	Males	466 115 (24.68)	20.77–28.59	317 8 (2.52)	0.79–4.25	783 123 (15.71)	13.16–18.26
	Females	27 3 (11.11)	−0.74–22.96	1,210 4 (0.33)	0.01–0.65	1,237 7 (0.57)	0.15–0.99
	Total	493 118 (23.94)	20.17–27.71	1,527 12 (0.79)	0.35–1.23	2,020 130 (6.44)	5.37–7.51
[9]	Males	14,963 2,502 (16.72)	16.12–17.32	14,417 164 (1.14)	0.97–1.31	29,380 2,666 (9.07)	8.74–9.40
	Females	3,052 283 (9.27)	8.24–10.30	26,418 47 (0.18)	0.13–0.23	29,470 330 (1.12)	1.00–1.24
	Total	18,015 2,785 (15.46)	14.93–15.99	40,835 211 (0.52)	0.45–0.59	58,850 2,996 (5.09)	4.91–5.27
Total	Males	68,179 16,474 (24.16)	23.84–24.48	61,706 1,931 (3.13)	2.99–3.27	129,885 18,405 (14.17)	13.98–14.36
	Females	4,980 668 (13.41)	12.45–14.35	77,406 760 (0.98)	0.91–1.05	82,386 1,428 (1.73)	1.64–1.82
	Total	73,159 17,142 (23.43)	23.12–23.74	139,112 2,691 (1.93)	1.86–2.00	212,271 19,833 (9.34)	9.22–9.46

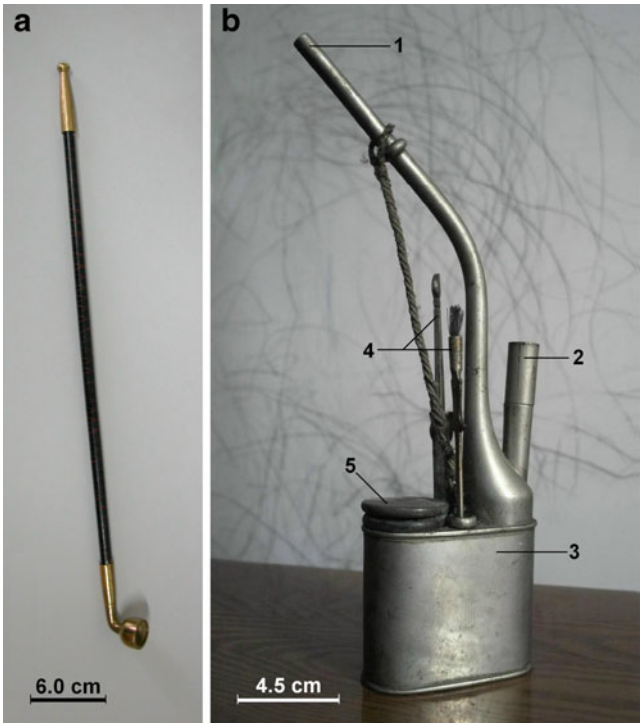

Fig. 1 **a** Shows a Hanyan pipe which is made up of three parts: mouth piece made of jade or copper, pipe bowl made of copper, and long tube made of bamboo or wood. **b** Shows a Shuiyan pipe made of copper or silver. It is made up of five main parts (1) mouth piece, (2) pipe, (3) water box, (4) tools for fire and cleaning, and (5) hole for putting water

seemed to have a lower risk for development of OL than cigarette smoking. It may be argued that the reason for this was that some of the toxic components of tobacco were removed and the temperature lowered during the passage through the water of the pipe. No scientific proof of this argument has, however been published. Hanyan pipe smoking, in contrast to Shuiyan pipe smoking revealed a higher prevalence of OL than cigarette smoking [5, 7].

Few data on consumption of alcohol and occurrence of OL in China are available. Only one article showed that there was a higher rate of drinkers among OL cases compared to individuals without OL [4].

The present review revealed that no cases of OC developing in OL were found in six surveys [4, 6–10].

Conclusions

Oral leukoplakia is a common oral mucosal lesion in China. Its relation to cigarette smoking has clearly been demonstrated. Men are affected much more commonly than women; elderly smokers have a risk of developing epithelial precursor lesions of the oral mucosa. The number of epidemiologic and follow-up studies from China is still small and more such studies are needed.

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