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# Potentially disabling factors of newly diagnosed leprosy patients in southwest China: a retrospective observational study

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## Abstract

**Background** With the prevalence of leprosy dramatically declining, the focus of leprosy control has gradually shifted from the implementation of multidrug therapy (MDT) to accelerating the reduction of the disease burden and preventing disability. Southwestern China currently bears the highest leprosy burden in China and more than half of the disability cases reported every year are from this region. However, the potential risk factors of leprosy disability in this area remain unknown.

**Methods** In this study, we evaluated the physical disabilities of 4578 leprosy patients in southwest China from 2010 to 2020. Clinical and epidemiological factors associated with physical disability resulting from leprosy were identified using multinomial logistic regression.

**Results** A total of 4578 leprosy cases with complete information were reported in southwestern China during the 11 years. Among them, 1126 (24.60%) patients were diagnosed with grade 2 disability (G2D), and 737 (16.10%) were confirmed with grade 1 disability (G1D) at diagnosis. The potential factors associated with G2D are as follows: nerve damage, male, leprosy reaction, older age of the patient, the longer delay in diagnosis, and more skin lesions. Furthermore, nerve damage, leprosy reaction, male, older age, and longer delayed diagnosis were the main risk factors of G1D. Among them, nerve damage, older age, longer delayed diagnosis, male, and leprosy reaction were the common risk factors for G1D and G2D.

**Conclusion** In our study, we found older age, longer delayed diagnosis, male, more skin lesions, more nerve lesions, and leprosy reactions were associated with leprosy disability. These findings provide a foundation for the development of targeted interventions aimed at the early identification of individuals at higher risk of physical disability, as well as for self-care and health education to promote timely medical consultation to prevent leprosy-related disabilities.

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**Keywords** Leprosy, Physical disability, Multinomial logistic regression analysis

## Background

Leprosy, also known as Hansen's disease, is a chronic infectious disease caused by *Mycobacterium leprae* (*M. leprae*), and it is a significant cause of disability [1]. Despite being declared as nationally eliminated in China, it persists as a notable public health concern, especially due to the disability caused by leprosy affecting the physical and psychological well-being of patients [2].

Historically, leprosy was endemic worldwide, largely due to inadequate treatment. With the introduction and widespread adoption of multi-drug therapy (MDT), the spread of leprosy has been gradually brought under control, and the number of new annual cases has significantly decreased. Nonetheless, numerous studies have found that many leprosy patients have already exhibited some form of disability by the time they are diagnosed [3, 4], complicating their treatment and long-term management. Therefore, the focus of leprosy control has gradually shifted from the implementation of MDT to accelerating the reduction of the disease burden and preventing disability. To meet the goal of “zero leprosy-related disability” proposed by the World Health Organization (WHO) [5], it is crucial to monitor the prevalence and evaluate the risk factors contributing to disability in leprosy patients.

Southwest China, which consists of Yunnan Province, Guizhou Province, and Sichuan Province, currently bears the heaviest burden of leprosy in China [6]. From 2010 to 2020, more than 50% of leprosy-associated disability in China were reported from these areas. Therefore, there is an urgent need to evaluate the potential risk factors of leprosy-related disability. Several studies have been conducted on disabilities in leprosy only in one province in China and no study has comprehensively assessed the areas consisting of these high disease burden provinces. Therefore, we conducted this study to assess the characteristics and disabling factors of newly diagnosed leprosy patients in southwest China from 2010 to 2022.

## Methods

### Data sources

This study was an observational retrospective study conducted in southwest China from January 1, 2010 to December 31, 2020. Data including clinical and epidemiological information of leprosy patients were abstracted from the Leprosy Management Information System (LEPMIS) in China. Epidemiological data such as sex, age, ethnicity, education level, and clinical characteristics such as date of diagnosis, surveillance pattern, number of skin lesions, number of nerve lesions, exposure history,

leprosy reaction, and Ridley-Jopling classification are included.

### Inclusion and exclusion criteria

From January 1, 2010, to December 31, 2020, all newly detected leprosy cases including any age group in southwest China, where patients had lived for more than six months (considered permanent residence) at the time of diagnosis, were included in our study ( $N = 4578$ ). Cases of relapse or those without permanent residence in southwest China were explicitly excluded ( $N = 162$ ). Meanwhile, new cases without complete records ( $N = 61$ ) were also excluded from this study.

### Diagnostic criteria and variable definitions

The diagnostic criteria of leprosy and disability caused by leprosy [7] remain almost unchanged during the study period. The detailed diagnostic criteria of disability associated with leprosy are described below:

Grade 0 disability (G0D): hands and feet: no protective sensory impairment, no visible deformity or change in appearance; eyes: no leprosy-induced eye disease, no visual impairment.

Grade 1 disability (G1D): hands and feet: protective sensory impairment, but no visible deformity or impairment; eyes: corneal sensory impairment, but no severe visual impairment and no visible deformity or impairment.

Grade 2 disability (G2D): hands and feet: visible deformities or impairments; eyes: severe visual impairment or blindness and other visible eye impairments.

Diagnostic delay: The time interval between the onset of symptoms and the confirmation of diagnosis.

### Statistical analysis

Data were cleaned and managed using Microsoft 2019. For quantitative information, mean  $\pm$  standard deviation (Mean, SD), median  $\pm$  interquartile range (Median, Interquartile range) were used to describe the data. For qualitative data, the number of cases (percentage) was used to describe the data. For the univariate analysis of the data, the chi-square test and Fisher's exact probability method were used. As the test of parallel lines was  $P < 0.05$ , the multivariate analysis of the data was done by multinomial logistic regression analysis. The multivariate analysis was used to determine potentially disabling factors of leprosy patients. All statistical analysis tests were conducted using SPSS (Version 24.0) software at the significance level of  $P < 0.05$ .

## Results

### Description of leprosy data

A total of 4801 cases, of which 4578 cases were recorded with complete information on disability. As shown in Tables 1, 1126 (24.60%) patients were diagnosed with G2D; 737 (16.10%) patients were diagnosed with G1D and G0D occurred in 2715 (59.30%) patients. The mean age at diagnosis was 40 years; 42.90% patients were aged 30–49 years. Disability was more common in male patients than females, with 823 (73.09%) patients with

G2D and 535 (72.59%) patients with G1D. Among all patients, 49.58% (2270) were Han Chinese. 2706(59.11%) patients were detected by active surveillance. 192(4.19%) patients had no skin lesions; 788 (17.21%) patients had no nerve lesions. The mean delay in diagnosis was 31.48 months; the median delay in diagnosis was 17 months. The mean delay in diagnosis for patients with G2D was 61.63 months, and the median delay in diagnosis was 37 months. The mean delayed diagnosis time for patients with G1D was 27.27 months, and the median delayed

**Table 1** Epidemiological information on disability caused by leprosy in southwest China

		G0D (%)	G1D (%)	G2D (%)	Physical disability (%)	Total	P-value
Total		2715	737	1126	1863	4578	
Gender	Male	1791 (65.97)	535 (72.59)	823 (73.09)	1358 (72.89)	3149 (68.79)	< 0.001
	Female	924 (34.03)	202 (27.41)	303 (26.91)	505 (27.11)	1429 (41.21)	
Age(y)	Median (IQR)	36 (25–48)	41 (31–51)	49 (37–60)	45 (34–58)	40 (28–52)	
	Mean $\pm$ SD	37.44 $\pm$ 15.49	41.75 $\pm$ 14.84	48.54 $\pm$ 15.72	48.86 $\pm$ 15.73	40.86 $\pm$ 16.13	
Ethnic Group	Han	1200 (44.20)	409 (55.50)	661 (58.70)	1070 (57.43)	2270 (49.58)	< 0.001*
	Minority	1504 (55.40)	326 (44.23)	455 (40.41)	781 (41.92)	2285 (49.91)	
	Unknown	11 (0.41)	2 (0.27)	10 (0.89)	12 (0.64)	23 (0.50)	
Education	Illiterate	554 (20.41)	176 (23.88)	335 (29.75)	511 (27.43)	1065 (23.29)	< 0.001
	Primary school or below	1058 (38.97)	277 (37.58)	482 (42.81)	759 (40.74)	1817 (39.69)	
	Junior high school	825 (30.39)	226 (30.66)	242 (21.49)	468 (25.12)	1293 (28.24)	
	Senior high school	135 (4.97)	36 (4.88)	24 (2.13)	60 (3.22)	195 (4.24)	
	University or above	78 (2.87)	13 (1.76)	18 (1.60)	31 (1.66)	109 (2.38)	
	Unknown	65 (2.39)	9 (1.22)	25 (2.22)	34 (1.83)	99 (2.16)	
Detection mode	Active	1660 (61.14)	456 (61.87)	590 (52.40)	1046 (56.15)	2706 (59.11)	< 0.001
	Passive	1028 (37.86)	269 (36.50)	519 (46.09)	788 (42.30)	1816 (39.67)	
	Other ways	27 (0.99)	12 (1.63)	17 (1.51)	29 (1.56)	56 (1.22)	
Skin lesion	0 skin lesion	75 (2.76)	19 (2.58)	98 (8.70)	117 (6.28)	192 (4.19)	< 0.001
	1 skin lesion	222 (8.18)	56 (7.60)	154 (13.68)	210 (11.27)	432 (9.44)	
	2–5 skin lesion	681 (25.08)	156 (21.17)	353 (31.35)	509 (27.32)	1190 (25.99)	
	> 5 skin lesion	1516 (55.84)	474 (64.31)	470 (41.74)	944 (50.67)	2460 (53.74)	
	Unknown	221 (8.14)	32 (4.34)	51 (4.53)	83 (4.46)	304 (6.64)	
Nerve lesion	0 nerve lesion	668 (24.60)	50 (6.78)	70 (6.22)	120 (6.44)	788 (17.21)	< 0.001
	1 nerve lesion	365 (13.44)	105 (14.25)	153 (13.59)	258 (13.85)	623 (13.61)	
	> 1 nerve lesion	1652 (60.85)	574 (77.88)	901 (80.02)	1475 (79.17)	3127 (68.30)	
	Unknown	30 (1.10)	8 (1.09)	2 (0.18)	10 (0.54)	40 (0.87)	
Delayed time in diagnosis(m)	Median (IQR)	13 (6–24)	18 (10–34)	37 (19–79)	26 (13–59)	17 (8–35)	
	Mean $\pm$ SD	20.11 $\pm$ 27.97	27.27 $\pm$ 29.41	61.63 $\pm$ 69.98	48.04 $\pm$ 59.86	31.48 $\pm$ 45.93	
Leprosy reaction	Absent	2375 (87.48)	599 (81.28)	981 (87.12)	1580 (84.81)	3955 (86.39)	0.002
	T1R	135 (4.97)	54 (7.33)	63 (5.60)	117 (6.28)	252 (5.50)	
	T2R	154 (5.67)	60 (8.14)	60 (5.33)	120 (6.44)	274 (5.99)	
	Mixed reaction	30 (1.10)	11 (1.49)	8 (0.71)	19 (1.02)	49 (1.07)	
	unknown	21 (0.77)	13 (1.76)	14 (1.24)	27 (1.45)	48 (1.05)	
Ridley-Jopling Classification	TT	251 (9.24)	89 (12.08)	294 (26.11)	383 (20.56)	634 (13.85)	< 0.001
	BT	495 (18.23)	109 (14.79)	289 (25.67)	398 (21.36)	893 (19.51)	
	BB	233 (8.58)	64 (8.68)	67 (5.95)	131 (7.03)	364 (7.95)	
	BL	1050 (38.67)	278 (37.72)	249 (22.11)	527 (28.29)	1577 (34.45)	
	LL	647 (23.83)	190 (25.78)	220 (19.54)	410 (22.01)	1057 (23.09)	
	I	39 (1.44)	7 (0.95)	7 (0.62)	14 (0.75)	53 (1.16)	
BI	Positive	2003(73.78)	563(76.39)	577(51.24)	1140(61.20)	3143(68.65)	0.001
	Negative	712(26.22)	174(23.61)	549(48.76)	723(38.80)	1435(31.35)	

P-value calculated by chi-square test; \* calculated by Fisher's exact probability method

**Table 2** Multinomial logistic regression analysis of disabling factors of leprosy in southwest China

Variables		G1D		G2D	
		OR (95%CI)	P-value	OR (95%CI)	P-value
Age		1.018(1.015–1.020)	< 0.001	1.031(1.029–1.034)	< 0.001
Delay diagnosis		1.010(1.009–1.011)	< 0.001	1.024(1.023–1.025)	< 0.001
Gender	Male	1.292(1.190–1.403)	0.009	1.389(1.281–1.507)	< 0.001
	Female	1		1	
Detection mode	Active	0.954(0.884–1.029)	0.223	1.003(0.932–1.079)	0.942
	Passive	1		1	
Source of infection	Inside	0.813(0.750–0.881)	< 0.001	0.807(0.747–0.873)	< 0.001
	Outside	1		1	
Skin lesion	> 5 skin lesions	1.086(0.861–1.369)	0.485	0.365(0.309–0.432)	< 0.001
	2–5 skin lesions	0.865(0.683–1.094)	0.226	0.428(0.362–0.507)	< 0.001
	1 skin lesion	1.001(0.781–1.310)	0.931	0.543(0.450–0.656)	< 0.001
	0 skin lesion	1		1	
Nerve lesion	> 1 nerve lesion	4.856(4.016–5.238)	< 0.001	5.646(4.956–6.432)	< 0.001
	1 nerve lesion	4.144(3.533–4.860)	< 0.001	3.313 (2.833–3.875)	< 0.001
	0 nerve lesion	1		1	
Leprosy reaction	Yes	1.388(1.255–1.536)	< 0.001	1.323(1.187–1.474)	< 0.001
	No	1		1	

diagnosis time was 18 months. 3955 patients, or 86.39%, had no leprosy reaction. 49(1.07%) patients had both leprosy type I and II reactions; in both G1D and G2D, more than 80% of the patients had no leprosy reaction. According to Ridley and Jopling classification, 294(26.11%) cases of G2D were classified by TT; 289 (25.67%) were BT; 67 (5.95%) were BB 249 (22.11%) were BL; and 220 (19.54%) were LL. Among the G1D, 89(12.08%) cases were classified by TT, 109(14.79%) were BT, 64 (8.68%) were BB, 278(37.72%) were BL, and 190 (25.78%) were LL.

#### Risk factors of Grade 2 disability

Table 2 summarizes the risk factors associated with physical disability in patients with G1D and G2D.

The results revealed that age, delayed diagnosis time, gender, household infection, skin lesions, nerve lesions were the influencing factors for G2D. The older the patients were (OR=1.031, 95%CI: 1.029–1.034,  $P<0.001$ ), the possibility of G2D increased. The longer patients delayed diagnosis (OR=1.024, 95%CI: 1.023–1.025,  $P<0.001$ ), the greater possibility of G2D occurred. Male patients (OR=1.389, 95%CI: 1.281–1.507,  $P<0.001$ ) had an increased possibility compared to female patients. There was no statistically significant difference in passive detection mode (OR=1.003, 95%CI: 0.932–1.079,  $P=0.942$ ) compared to active detection mode. The difference was statistically significant for patients with household infection (OR=0.807, 95%CI: 0.747–0.873,  $P<0.001$ ) compared to extra-household infection. Skin lesions greater than 5 (OR=0.365, 95%CI: 0.309–0.432,  $P<0.001$ ), 2–5 (OR=0.428, 95%CI: 0.362–0.507,  $P<0.001$ ), and 1 (OR=0.543, 95%CI: 0.450–0.656,  $P<0.001$ ) compared to no skin lesions, The differences

in the occurrence of G2D were all statistically significant. Patients with nerve lesions greater than or equal to 2 (OR=5.646, 95%CI: 4.956–6.432,  $P<0.001$ ) and 1 (OR=3.313, 95%CI: 2.833–3.875,  $P<0.001$ ) were more likely to develop G2D compared to leprosy patients without nerve lesions. There was statistically significant difference in patients with leprosy reaction (OR=1.323, 95%CI: 1.187–1.474,  $P<0.001$ ) compared to those without leprosy reaction.)

#### Risk factors of Grade 1 disability

The results showed that age, delayed diagnosis time, gender, household infection, nerve lesions and leprosy reaction were influencing factors of patient with G1D. The older the patient was, the more likely occurrence in G1D (OR=1.018, 95%CI: 1.015–1.020,  $P<0.001$ ). The longer patients delayed diagnosis, the more likely they were diagnosed with G1D (OR=1.010, 95%CI: 1.009–1.011,  $P<0.001$ ). Male patients (OR=1.292, 95%CI: 1.190–1.403,  $P=0.009$ ) had an increased possibility of G1D compared with female patients. There was no statistically significant difference in the passive mode of detection (OR=0.954, 95%CI: 0.884–1.029,  $P=0.223$ ) compared to the active mode of detection. The difference was statistically significant for patients with household infection (OR=0.813, 95%CI: 0.750–0.881,  $P<0.001$ ) compared to extra-household infection. Skin lesions greater than 5 (OR=1.086, 95%CI: 0.861–1.369,  $P=0.485$ ), 2 to 5 (OR=0.865, 95%CI: 0.683–1.094,  $P=0.226$ ), and 1 (OR=1.001, 95%CI: 0.781–1.310,  $P=0.931$ ) compared to no skin lesions were all no statistical significance. There were statistically significant in patients with two or more nerve lesions (OR=4.856, 95%CI: 4.016–5.238,  $P<0.001$ )

and one (OR=4.144, 95%CI: 3.533–4.860,  $P<0.001$ ). Patients with leprosy reaction (OR=1.388, 95%CI: 1.255–1.536,  $P<0.001$ ) were more likely to lead to G1D compared to those without leprosy reaction.)

## Discussion

A total of 4578 patients with complete records of disability information, were included in this study, of which 2715 (59.30%) patients had no disability, 737 (16.10%) patients had G1D, and 1126 (24.60%) patients had G2D. As results showed, age, delayed diagnosis time, gender, household infection, nerve lesions and leprosy reaction were the factors affecting G1D. Age, delayed diagnosis time, gender, household infection, skin lesions, and nerve lesions influenced G2D. Among them, advanced age, longer delayed diagnosis, male, and nerve damage were common risk factors for both G1D and G2D.

In this study, we found a significantly positive association between age, delayed diagnosis, and physical disability caused by leprosy, and other studies have shown similar results [8, 9]. This demonstrates the importance of education and publicity, early detection, and early diagnosis of leprosy. Nicholls and colleagues showed that the delayed diagnosis time in patients with G2D was twice as long as in patients with G0D [10]. Previous studies have also reported a mean total delay of 19.6 and 37 months in G2D cases [11, 12]. Bekri reported a mean delay of 26 months for patients with G2D or G1D, and a mean delay of 12 months for G0D in 1998 [13]. In Nepal, the delay time from the first symptom to diagnosis was more than 18 months for 50% of the study participants [14]. The delayed time in diagnosis was longer in the present study compared to the above studies. A study from India showed that delayed diagnosis of leprosy patients was the main cause of the disability, emphasizing the significance of early detection activities for leprosy cases, such as active surveillance in areas with high leprosy burden, which could reduce the delayed diagnosis time and promote early detection [15]. Previous studies have shown that early identification and combination with appropriate chemoprophylaxis therapy are effective means to prevent disability in patients with leprosy and to reduce the severity of disability [16].

Compared to female patients, male patients were 1.292 times more likely to have G1D and 1.389 times more likely to have G2D. Similar results have also been reported in other studies. The difference that males are more prone to get physical disability caused by leprosy than females may be attributed to their social behavior, such as men being less concerned about their health and women having difficulty in accessing public health services, which could lead to underestimating the prevalence of female physical disabilities in the population [17]. Leprosy not only cause physical problems, but also cause

some psychological and economic problems. Women are a vulnerable group, and they are at a higher risk of developing depression and anxiety caused by leprosy and related disability [18], especially in developing countries, so more attention should be paid to this group [19].

We found no statistically significant difference between detection models and disability occurrence in our study, which is different than the results of a study in Brazil. In this Brazilian population-based study, the active surveillance was associated with increased risk of physical disability compared with passive surveillance, and this study used community-based surveys (collective units such as schools, nurseries, villages), which could improve the detection rate of disability caused by leprosy [20]. This reflects the fact that better training of examiners would help identify leprosy complications, such as disability. In our study, we do not find any difference in the proportion of disability between active and passive detection. Leprosy presents a low endemic situation in China, and we have made lots of efforts to eradicate disability caused by leprosy. Still, it remains difficult to find people at an early stage. Therefore, many leprosy patients have attacked disability when they are diagnosed whether they are found actively or passively. This phenomenon re-emphasized the necessity of our study. Both the active and passive detection modes should be coordinated and complemented to detect leprosy cases more effectively, thereby reducing the occurrence and further deterioration of disability [21, 22].

As conclusive evidence in previous studies showed, an increased risk in close contact with leprosy patients, most likely through infectious aerosols produced by coughing and sneezing, but also through direct contact [23–25]. The molecular epidemiology study showed that long-term contact with those who tested positive would increase the risk of infection among household contacts and called for *Mycobacterium leprae* genome-wide analysis of the first person in the family suffering from this disease and their contacts [26]. In this study, however, we found that household infection was the protective factor of leprosy-related disability, this phenomenon may be related to the higher frequency of follow-up visits for household contacts of leprosy patients, making early detection and diagnosis relatively easier to achieve. In order to achieve the goal of zero leprosy-related disability, continuous follow-up visits for household contacts of leprosy patients are urgent.

In previous studies, both nerve damage and leprosy reactions are risk factors for the physical disability in leprosy patients [27–29]. Our present study supported previous studies, indicating that the number of nerve damage and leprosy reactions were significant risk factors for G1D and G2D. The occurrence of leprosy reactions showed a high degree of variability globally [30],



with the fluctuation between 20 %–57% [31, 32], and the proportion of leprosy reactions in the present study was also in this range. Meanwhile, it is notable that leprosy reactions can occur at any point during the disease in patients, therefore disability assessment needs to be continued despite the completion of the MDT regimen.

“The WHO Global Leprosy Strategy 2021–2030” aims to achieve zero leprosy-related disability worldwide [5], emphasizing early detection of cases before disability occurs and on early detection in high-risk populations through active surveillance in high-prevalence areas. In a sense, our study provided information on the characteristics of high-risk patients, who should be prioritized and targeted for preventive interventions. As the epidemiology of the disease varies worldwide, specific factors of disability may be present in particular populations, and there may be common factors to all populations. Different methods of statistical analysis may also cause differences in various studies. In our study, multinomial logistic regression was applied to evaluate the correlation between factors and outcome. Multinomial logistic regression could also control potential confounding factors, such as age, gender etc., thus improving the efficiency of the study [33].

It is worth noting that although some studies have shown that disability and poverty due to leprosy are not conducive to mental health [18], but the mental health dimension of individuals with leprosy infection has not been much studied. Epidemiological data in this area are not yet complete or understand how to effectively reduce the psychosocial burden caused by leprosy and the factors that contribute to it. Therefore, it is of great value to conduct research in this area. It could be one areas of future research in leprosy epidemiology.

There are also some limitations in this study. The main limitation of this study is that it is a retrospective observational study and it is difficult to avoid recall bias. The results are dependent on the accuracy and completeness of patient information records, and the data covered a long period of time and included different regions. And there may include information bias in this study.

## Conclusion

In summary, advanced age, longer delayed diagnosis time, male, number of skin lesions, nerve damages at diagnosis were risk factors for leprosy associated with disability, and the identification of these risk factors could help to prevent physical disability. These findings provide a foundation for the development of targeted interventions aimed at the early identification of individuals at higher risk of physical disability, as well as for self-care and health education to promote timely medical consultation to prevent leprosy-related disabilities.

## Abbreviations

MDT	Multidrug therapy
M. leprae	Mycobacterium leprae
WHO	World Health Organization
LEPMIS	Leprosy Management Information System in China
G0D	Grade 0 disability
G1D	Grade 1 disability
G2D	Grade 2 disability
OR	Odds ratio

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## Author contributions

H.W. and M.Y. conceived and designed the study. W.Z., H.J. and Y.S. participated in the acquisition of data. L.Q. and M.Z. analyzed the data. Y.M. gave advice on methodology. L.Q. and M.Z. drafted the manuscript. H.W. and M.Y. revised the manuscript. All authors read and approved the final manuscript.

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## Data availability

No datasets were generated or analysed during the current study.

## Declarations

### Ethics approval and consent to participate

Ethical approval for the data has been obtained from the Ethics Committee in the Institute of Dermatology, Chinese Academy of Medical Sciences & Peking Union Medical College (2022-KY-041). Informed written consent was obtained from each participant, who were ensured that data would remain confidential and used for research purposes only. All methods were carried out in accordance with the Chinese Statistical Law to ensure that participants' personal information was kept confidential. All experimental protocols conformed to the ethical standards for medical research involving human subjects, as laid out in the 1964 Declaration of Helsinki and its later amendments. Furthermore, this study was approved by the institutional review board of Institute of Dermatology, Chinese Academy of Medical Sciences & Peking Union Medical College, Nanjing, China.

### Consent for publication

Not applicable.

### Competing interests

The authors declare no competing interests.

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