Health-Related Quality of Life with Cervical Cancer and Precancer: A Cross-Sectional Study in Yunnan Province, China

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Abstract

Objectives

Cervical cancer is the fourth most common cancer in women, with an estimated 600,000 new cases and 340,000 deaths worldwide in 2020. However, there remains limited understanding of the association between individual socioeconomic status (SES) and clinical characteristics and health-related quality of life (HRQoL) of women with cervical precancerous lesions and cancer worldwide, including in China. This study investigates socioeconomic and clinical variations in HRQoL of women with cervical precancerous lesions and cancer in Yunnan Province, China.

Methods

The present study employed a cross-sectional survey design. An EQ-5D-5L questionnaire was used to assess HRQoL of 400 patients with cervical precancerous lesions and cancer in Yunnan Province, China from 2019 to 2020. ANOVA and independent samples *t*-tests were performed to identify the independent variables associated with the EQ-5D-5L utility scores and VAS scores. Predictors of the utility scores were confirmed using a Tobit regression model.

Results

The mean of cervical precancerous lesions and cancer patients' EQ-5D-5L utility scores was 0.939 (SD, 0.104) and the mean of VAS scores was 80.84 (SD, 16.551). Patients aged 40-59 years ($\beta = -0.037$, $p = 0.005$), patients who were not aware of the human papillomavirus (HPV) vaccine ($\beta = -0.032$, $p = 0.004$), and patients who underwent radical hysterectomy ($\beta = -0.036$, $p = 0.006$) had significantly lower utility scores, whereas having high monthly household income ($\beta = 0.023$, $p = 0.033$) was significantly associated with higher EQ-5D-5L utility scores. Age ($p = 0.023$) was statistically significant in differences in patients' VAS scores. Anxiety/depression was the most frequently reported issue (35.75%) among participants.

Conclusions

Future cervical cancer prevention and treatment guidelines should focus on low-income women, women aged 40-59 years, and those lacking knowledge about cervical cancer prevention.

Introduction

Cervical cancer is the second most common female malignant cancer worldwide [1], and is a serious threat to women's health [2]: the International Agency for Research on Cancer's latest estimates on the global burden of cancer found cervical cancer is the most common cancer in women, with an estimated 600,000 new cases and 340,000 deaths worldwide in 2020 [3]. Persistent infection with specific types of human papillomavirus viruses (HPV) is a necessary factor in the development of cervical cancer, and cervical intraepithelial neoplasia (CIN) is a precancerous lesion of invasive cervical cancer. In China, there were 106,400 new cervical cancer cases in 2018 [4], an incidence rate of 10.88 per 100,000 people, and

there was a mortality rate of 3.17 per 100,000 people, which made it the 8th highest cause of female cancer mortality [5].

Women diagnosed with cervical cancer can experience both significant physical and psychological trauma as the diagnosis leads to financial burden on their families, changing body image, and altered relationships with partners, among other major life changes that result. These many changes in turn can adversely impact health-related quality of life (HRQoL) of patients and their families.

HRQoL is a patient-reported outcome that refers to individuals' subjective assessment of well-being and ability to perform social roles. It is used as a health indicator in medical settings, including clinical interventions, treatments, and health surveys [5]. Evaluation of HRQoL in cervical cancer patients can help determine the burden of disease and provide essential information to plan interventions. Thus, it is important to understand the HRQoL of patients with precancerous lesions or cervical cancer, and to explore the factors that affect it.

Based on Casper Tax's study in 2017, which provided an overview of the HRQoL tools used to measure cervical cancer patients [9], HRQoL tools were categorized as generic, cancer-specific, and cervical cancer-specific. At present, research on HRQoL of cervical cancer patients has been conducted in many countries [6–8]. However, in China, there have been few studies on HRQoL of those with cervical cancer [10–12], and even fewer among Chinese ethnic minority populations of cervical cancer survivors.

Yunnan Province, a high altitude region located on the Yunnan-Guizhou Plateau in southwestern China, has the largest concentration of ethnic minorities in China [13]. According to a 2018 study, the incidence of cervical cancer in Yunnan Province was 11.42 per 100,000 people and the mortality rate was 3.77 per 100,000 people, both metrics higher than the national average [14]. The mean age of onset of cervical cancer in Yunnan Province has also gradually risen in the past five years [15]. However, few studies have evaluated HRQoL among precancerous or cervical cancer patients in Yunnan. In turn, it remains unclear what effect cervical lesions and cancer has on HRQoL of women, independent of age, socio-economic status, and other important confounders, such as clinical stage, therapeutic regimen, and degree of differentiation.

This study thus examined HRQoL of women with cervical precancerous lesions and cancer and its socio-demographic and clinical determinants in order to guide cervical carcinoma prevention and treatment efforts in Yunnan Province, China.

Methods

Instruments

Internationally, several instruments have been developed to evaluate the HRQoL of patients with cervical precancerous lesions and cancer, including EQ-5D [8], SF-36 [12], EORTC QLQ-CX24 [16], and FACT-Cx [10, 17]. Of these, EQ-5D is one of the most commonly used instruments to describe and assess HRQoL [18].

This instrument has been translated into Chinese and has shown to have satisfactory psychometric properties [19]. The simplified Chinese version of the EQ-5D-5L questionnaire consists of 2 key components: the EQ-5D descriptive system and the EQ visual analogue scale (EQ VAS). The EQ-5D-5L descriptive system is a preference-based HRQoL measure with one question for each of the 5 dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression [18]. In this study, each of these 5 dimensions in turn had 5 scoring levels: no problems, slight problems, moderate problems, severe problems, and extreme problems. Each health status can be assigned a weighted utility score based on different scoring systems. In this study, we used the Chinese EQ-5D-5L value set to calculate the quality of life utility score of individual health states, which ranged from - 0.391 (the worst state) to 1.000 (the second-best state) [19]. We also leveraged EQ-VAS, a 20 cm vertical line with clearly defined endpoints within which respondents can report their present health status with a grade ranging from 0 (worst possible health status) to 100 (best possible health status). The simplified Chinese version of the EQ-5D-5L questionnaire employed in this study can be downloaded from the EQ-5D website (www.euroqol.org).

Participants and procedures

The Third Affiliated Hospital of Kunming Medical University in Kunming, the capital of Yunnan Province in southwest China, was selected through a convenience sampling method. It is a cancer hospital in Yunnan with integrated medical services, scientific research, teaching, and cancer prevention programs. More than 1,000 patients with cervical cancer receive treatment at the hospital annually. All patients with cervical precancerous lesions and cervical cancer who previously received or currently receive treatment at this hospital were considered eligible for participation in this study. The following inclusion criteria were used to select participants among this population: age ≥ 18 years, a positive cervical tissue biopsy diagnosis of cervical precancerous lesions or cervical cancer (diagnosed by a gynecologist), not having received any treatment from another hospital, able to read, write and speak in Mandarin Chinese, and willing and able to give informed consent to participate in the study. All diagnoses and treatment of cervical cancer were carried out in accordance with the cervical cancer clinical practice guidelines put forth by the National Comprehensive Cancer Network of the United States (NCCN). The following criteria led to exclusion from the study: having severe co-morbidities (including mental illness or cognitive impairment), the presence of other non-cervical cancer malignant tumors, and contraindications before radiotherapy, chemotherapy, and surgery. The survey was conducted through face-to-face interviews during participants' hospital stays.

Data collection and measurement

The cross-sectional survey was performed from 2019 through 2020. All participants who consented to participate signed informed consent forms and were individually interviewed, face-to-face, by trained interviewers using a simplified Chinese version of the EQ-5D-5L questionnaire. Demographic data was collected along with the questionnaire survey, including age, sex, ethnicity (e.g., Han majority or ethnic minority), occupation (e.g., farmer), level of education (primary school or below, junior high school, senior high school, or college or above), marital status (unmarried, married, widowed, divorced, or separated),

monthly household income, health insurance type (e.g., basic medical insurance for urban employees, basic medical insurance for urban and rural residents), and awareness of the HPV vaccine (yes or no). Monthly household income was separated into two classifications (low and high), with the median value as the cutoff point. Low income referred to an approximate monthly household income <\$500 USD, while high referred to a monthly household income $\geq$ \$500 USD.

Statistical analysis

Descriptive analyses were used to calculate absolute and relative frequencies (%). Counts and percentages were used to present categorical variables. Mean values of EQ-5D-5L utility scores and VAS scores were expressed as mean $\pm$ standard deviations ($\bar{X} \pm S$). *T*-tests and ANOVA were used to determine differences in the utility scores and VAS of the respondents with different characteristics. Regarding censored data for outcome variables, as health utility scores ranged from - 0.391 to 1.000 in this study, a Tobit regression model was used to examine the associations between the EQ-5D-5L utility score and other independent variables. All data analyses were conducted using SPSS 22.0 software and STATA V.12.0. All statistical significance decisions were based on two-tailed *P* values of less than 0.05.

Results

400 patients participated in the study. Participants were classified as CIN (*n* = 136) or cervical cancer (*n* = 264). The demographic and clinical characteristics of the study population are described in Table 1. Participant ages ranged from 23 years to 75 years, with the majority of participants between the ages of 40 to 59 years. The percentage of Han majority ethnicity participants was 76%. The majority of participants were farmers (64%). More than half of the participants had a low education level (primary school or below). More than 80% of patients were married while 1% were single. All participants were covered by social health insurance, although across two different insurance schemes. 54% of participants were low-income (monthly household income <\$500 USD).

Table 1
Demographic and clinical characteristics of the study population

Characteristics	n	%
Age (years)		
≤ 39	83	20.75
40–59	267	66.75
≥ 60	50	12.5
Ethnicity		
Han ethnicity	304	76.00
Ethnic minorities	96	24.00
Occupation		
Farmer	256	64.00
Other	144	36.00
Level of education		
Primary school or below	217	54.25
Junior high school	107	26.75
Senior high school	36	9.00
College or above	40	10.00
Monthly household income (US\$)		
Low	217	54.2
High	183	45.8
Marital status		
Unmarried	5	1.25
Married	362	90.5
Widowed	22	5.5
Divorced or separated	11	2.75
Type of health insurance		
Basic medical insurance for urban employees	67	16.75

Characteristics		n	%
	Basic medical insurance for urban and rural residents	333	83.25
Awareness of the human papilloma virus (HPV) vaccine			
	Aware	131	32.75%
	Unaware	269	67.25%
Degree of differentiation			
	Undifferentiated	172	43.00
	Well differentiated	20	5.00
	Moderately differentiated	103	25.75
	Poorly differentiated	105	26.25
Clinical stages			
	CIN	136	34.00
	I	133	33.25
	II	88	22.00
	III	32	8.00
	IV	11	2.75
Type of disease			
	CIN	136	34.00
	Cervical cancer	264	66.00
Therapeutic regimen			
	Loop electrosurgical excision Procedure (LEEP)	118	29.5
	Radical hysterectomy	141	35.25
	Concurrent radiochemotherapy	105	26.25
	Surgery followed by adjuvant therapy	36	9.00

Regarding degree of differentiation, the proportion of patients in undifferentiated, well differentiated, moderately differentiated, and poorly differentiated categories were 43.00%, 5.00%, 25.75%, and 26.25%, respectively. Most participants were in clinical stages CIN or I (136 and 133, respectively). The most common intervention received by participants was radical hysterectomy (35.25%), followed by loop

electrosurgical excision procedure (LEEP) (29.5%), concurrent radiochemotherapy (26.25%), and surgery followed by adjuvant therapy (9.00%).

Table 2 compares the summary statistics for participants' EQ-5D-5L utility scores and VAS scores based on their socio-demographic and clinical characteristics. The mean of cervical precancerous lesions and cancer patients' EQ-5D-5L utility scores was 0.939 and VAS scores was 80.84. Han ethnicity patients had significantly lower EQ-5D-5L utility scores than ethnic minorities ($P = 0.027$). Patients aged 40–59 years had the lowest EQ-5D-5L utility scores ($P = 0.012$). Low monthly household income also correlated with lower utility scores ($P = 0.013$). Patients with cervical cancer had lower utility scores than patients with CIN ($P < 0.047$). Participants who were aware of the HPV vaccine had higher utility scores ($P = 0.001$). The difference in utility scores was statistically significant among different therapeutic regimens ($P = 0.038$). The characteristic of age ($P = 0.023$) was statistically significant in patients' VAS scores. No significance was found among the other variables with utility scores and VAS scores ($P > 0.05$).

Table 2
EQ5D five-level utility scores and VAS scores across different characteristics

Characteristics	n	EQ-5D utility values	P values	VAS scores	P values
		$\bar{X} \pm s$		$\bar{X} \pm s$	
Age (years)			0.012		0.023
≤ 39	83	0.965 ± .0601		80.57 ± 14.354	
40–59	267	0.929 ± 0.116		79.81 ± 17.538	
≥ 60	50	0.953 ± 0.088		86.78 ± 13.196	
Ethnicity			0.027		0.436
Han ethnicity	304	0.934 ± 0.112		80.48 ± 17.254	
Ethnic minorities	96	0.956 ± 0.076		81.99 ± 14.115	
Occupation			0.115		0.945
Farmer	256	0.933 ± 0.115		80.88 ± 16.924	
Other	144	0.949 ± 0.082		80.76 ± 15.923	
Level of education			0.191		0.51
Primary school or below	217	0.931 ± 0.114		81.48 ± 16.736	
Junior high school	107	0.948 ± 0.102		78.93 ± 17.582	
Senior high school	36	0.938 ± 0.085		80.47 ± 14.858	

Characteristics	n	EQ-5D utility values	P values	VAS scores	P values
		$\bar{X} \pm s$		$\bar{X} \pm s$	
College or above	40	0.966 ± 0.059		82.80 ± 14.026	
Monthly household income (US\$)			0.013		0.311
Low	217	0.935 ± 0.111		80.08 ± 18.017	
High	183	0.958 ± 0.068		81.74 ± 14.622	
Marital status			0.944		0.198
Unmarried	5	0.959 ± 0.444		81.00 ± 12.450	
Married	362	0.940 ± 0.105		80.99 ± 16.561	
Widowed	22	0.930 ± 0.120		83.41 ± 14.751	
Divorced or separated	11	0.944 ± 0.075		70.73 ± 19.540	
Type of health insurance			0.118		0.706
Basic medical insurance for urban employees	67	0.956 ± 0.900		81.54 ± 14.830	
Basic medical insurance for urban and rural residents	333	0.936 ± 0.107		80.70 ± 16.893	
Awareness of the human papilloma virus (HPV) vaccine			0.001		0.728
Aware	131	0.961 ± 0.714		80.43 ± 15.300	

Characteristics	n	EQ-5D utility values	P values	VAS scores	P values
		$\bar{X} \pm s$		$\bar{X} \pm s$	
Unaware	269	0.929 ± 0.116		81.04 ± 17.151	
Degree of differentiation			0.066		0.259
Undifferentiated	172	0.955 ± 0.095		81.440 ± 16.434	
Well differentiated	20	0.932 ± 0.082		79.400 ± 17.795	
Moderately differentiated	103	0.927 ± 0.107		78.300 ± 17.602	
Poorly differentiated	105	0.927 ± 0.117		82.630 ± 15.315	
Clinical stages			0.406		0.281
CIN	136	0.954 ± 0.102		81.47 ± 16.332	
I	133	0.934 ± 0.097		81.63 ± 15.254	
II	88	0.931 ± 0.122		78.28 ± 18.762	
III	32	0.929 ± 0.103		83.91 ± 15.038	
IV	11	0.927 ± 0.070		75.00 ± 18.841	
Type of disease			0.047		0.585
CIN	136	0.954 ± 0.102		81.47 ± 16.332	

Characteristics	n	EQ-5D utility values	P values	VAS scores	P values
		$\bar{X} \pm s$		$\bar{X} \pm s$	
cervical cancer	264	0.932 ± 0.105		80.52 ± 16.684	
Therapeutic regimen			0.038		0.187
Conization of cervix (loop electrosurgical excision procedure (LEEP)/cold knife conization)	118	0.962 ± 0.087		82.53 ± 14.957	
Radical hysterectomy	141	0.926 ± 0.112		80.60 ± 16.134	
Concurrent Radiochemotherapy	105	0.936 ± 0.101		81.03 ± 17.991	
surgery followed by adjuvant therapy	36	0.926 ± 0.128		75.67 ± 18.291	
Total	400	0.939 ± 0.104		80.84 ± 16.551	

As shown in Table 3, among the study samples, the most frequently reported problem was anxiety/depression (35.75%), followed by pain/discomfort (24.0%), mobility challenges (9.25%), restrictions in usual activity (7.75%), and challenges to maintaining self-care (7.25%). About 53.65%(n = 228)of patients reported no problems in all five of these dimensions.

Table 3
Challenges reported by respondents in different dimensions of EQ-5D

	Mobility	Self-care	Usual activities	Pain/discomfort	Anxiety/depression
	n (%)	n (%)	n (%)	n (%)	n (%)
No problem	363(90.75)	371(92.75)	369(92.25)	304(76.0)	257(64.25)
Slight problem	31(7.75)	25(6.25)	28(7.0)	71(17.75)	116(29.0)
Moderate problem	4(1.0)	4(1.0)	3(0.75)	18(4.5)	22(5.5)
Severe problem	2(0.5)	0(0.0)	0(0.0)	7(1.75)	5(1.25)
Extreme problem	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)

The factors associated with patients' EQ-5D-5L utility scores extracted through a Tobit regression model are shown in Table 4. The model indicates that being of age 40–59 years ($\beta=-0.037$, $p = 0.005$), lacking awareness of the HPV vaccine ($\beta=-0.032$, $p = 0.004$), and having undergone radical hysterectomy ($\beta=-0.036$, $p = 0.006$) is significantly associated with lower utility scores, whereas having high monthly household income ($\beta = 0.023$, $p = 0.033$) is significantly associated with higher EQ-5D-5L utility scores.

Table 4
Results of Tobit regression model on EQ-5D five-level utility scores of respondents

Variables		Regression coefficient	95% CI	P-values
Age (Reference: ≤39 years)				
	40–59 years	-0.037	-0.062 ~ -0.011	0.005**
	≥ 60 years	-0.012	-0.049 ~ 0.024	0.502
Monthly household income (US\$) (Reference: Low)				
	High	0.023	0.002 ~ 0.044	0.033*
Awareness of human papilloma virus (HPV) vaccine (Reference: aware)				
	Unaware	-0.032	-0.053 ~ -0.010	0.004**
Therapeutic regimen (Reference: LEEP)				
	Radical hysterectomy	-0.036	-0.061 ~ -0.010	0.006**
	Concurrent radiochemotherapy	-0.026	-0.053 ~ 0.002	0.065
	Surgery followed by adjuvant therapy	-0.036	-0.075 ~ 0.003	0.072
* $p < 0.05$, ** $p < 0.01$				

Discussion

This cross-sectional study revealed a relatively high score of HRQoL in patients with cervical precancerous lesions and cancer in Yunnan Province, China, with HRQoL significantly associated with patients' socio-demographics, clinical characteristics, and awareness of cervical cancer prevention.

The mean EQ-5D-5L utility and VAS scores (0.939 and 80.84, respectively) among patients with cervical precancerous lesions and cancer in the present study was higher than in India (0.64 and 67.6, respectively) [8], Indonesia (0.76 and 75.8, respectively) [6], and Ethiopia (0.77 and 65.7, respectively) [20], while the utility scores were similar to those found in Italy (0.93) [21] and higher than in Taiwan (0.84) [11]. These differences may be related to the percentage of participants in each cancer stage: most

patients in the present study were at the cervical precancerous lesion or earlier stages (67.25% in stages CIN and I), and CIN patients have little physical discomfort, few clinical symptoms, and do not need radical surgery and radiochemotherapy, possibly explaining the overall comparatively high utility score. Moreover, the difference may also be partially attributed to the use of different HRQoL questionnaires: the use of different value sets would yield different utility scores [22], which could also explain differences in utility scores across studies.

Our study found that patients with cervical precursor lesions and cancer aged 40–59 years had the lowest HRQoL utility and VAS scores. This result was consistent with studies in Korea [23] and Thailand [24]. Previous research indicates that incidence of cervical cancer is highest in those aged 40–59 years [17]. This finding thus underscores an urgent need to perform early screening, diagnosis, and treatment of cervical cancer, particularly in those aged 40–59 years, to improve their quality of life.

The present study indicated that level of education, marital status, and occupation were not associated with utility scores, a finding consistent with studies in India [8], but differing from some study results [10, 25] that have found that higher education level and married status are associated with higher HRQoL scores. The reasons for this discrepancy are currently unclear.

Our findings indicate that low household income is associated with lower HRQoL utility scores, a finding consistent with study results in Thailand [24]. This association of household income with HRQoL of patients with cervical precursor lesions and cancer suggests wealthier patients may be more conscious about and able to spend money to promote their health. Previous research [17] has demonstrated that patients with cervical cancer often have serious economic problems and medical expenses contribute to the stress and negative feelings brought upon by the disease, in turn negatively impacting quality of life.

This study found that EQ-5D utility scores were higher in patients who were aware of the HPV vaccine. This awareness may indicate greater knowledge about cervical cancer more broadly. The findings suggest a need to pay more attention to health education and increasing awareness of cervical cancer prevention as this may improve their quality of life [26].

The association between HRQoL and stage of cervical precursor lesions and cancer also merits further exploration. We found a decreasing trend in HRQoL as the disease progressed, consistent with findings in India [8] and Ghana [25]. However, one study found utility score in stage IV cancer was actually higher than that found in stage II and III [6]. This may be explained by the fact that late stage patients cannot be treated so treatment complications are avoided, leading to higher quality of life scores during this stage.

The present study found that patients with cervical precursor lesions and cancer undergoing radical hysterectomy were more likely to have lower utility scores. However, no significant difference in utility scores was found between surgical treatment and concurrent chemoradiotherapy in our study, in contrast to other studies [25, 27], including one in Brazil that found women who have undergone hysterectomy present better QoL scores than those in the chemoradiotherapy treatment group [26]. Furthermore, the

utility scores of patients undergoing surgical treatment and concurrent chemoradiotherapy were higher than those undergoing cervical conization in our study.

Anxiety and depression commonly occur in cancer patients who are facing multiple biological and psychosocial stressors [28]. The EQ-5D health states of patients in our study showed anxiety/depression as the most frequently reported problem of respondents (35.75%, all levels inclusive), differing from findings in India [8] and Indonesia [22]. However, a survey of eight low- and middle-income countries in Southeast Asia revealed the proportion of patients with anxiety/depression was highest among cervical cancer patients [29], consistent with our findings. We also found that 24% of cervical precursor lesions and cancer patients face pain/discomfort. However, problems of mobility, self-care, and engaging in usual daily activities were reported by less than 10% of participants, consistent with findings in Taiwan [11]. These results together indicate that cervical precursor lesions and cancer patients have some degree of psychological and physical discomfort that can affect their quality of life. Thus, further efforts should be made to improve the management of anxiety/depression and pain/discomfort, and early assessments of anxiety, depression, and social support of women with gynecologic cancer should be conducted.

The following limitations of the present study should be noted. First, the sample size of this study is relatively small, especially for patients with stage IV cancer, and all of the participants were selected from one hospital in Yunnan Province, China. Second, as this is a cross-sectional study, causal conclusions should be made with caution. Future studies should focus on longitudinal evaluation and assessment of HRQoL of patients at different stages of cancer treatment.

In conclusion, the present study indicates patients with cervical precancerous lesions and cervical cancer in Yunnan Province, China had higher HRQoL than other countries. The results suggest that future implementation of prevention and treatment guidelines in cervical cancer should focus on low-income patients, patients aged 40–59 years, and patients lacking knowledge about cervical cancer prevention.

Declarations

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Authors' contributions

Min Zhao: Study design and Writing-original draft. Mengjiao Zhang: Formal analysis and wrote the manuscript. Lianju He and Chunmei Zuo: Conducted the survey and collected data. Songrui Ding: Performed the statistical analysis. Allison Rabkin Golden: Writing-review and editing. Le Cai: Conceptualization and Methodology. All authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Data availability

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

Compliance with ethical standards

Conflict of interest

All authors declare that there are no conflicts of interest.

Ethics approval

The Third Affiliated Hospital of Kunming Medical University Ethics Committee approved this study prior to commencement of research.

Consent to participate

Informed consent was obtained from the participants.

Consent for publication

Informed consent for publication was obtained from the authors.

Code availability

The code used in the current study is available from the corresponding author on reasonable request.

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