

Estimating Disability Weight of Human Neurocysticercosis in Dali, Yunnan province, China

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Research

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Abstract

Background

Human cysticercosis, caused by the liver parasite *Taenia solium*, remains an important neglected tropical disease in China. In Yunnan province, a large proportion of in-patients with cysticercosis suffer from neurocysticercosis. Neurocysticercosis, though preventable, is a cause of epilepsy globally. Disability weight is an important parameter when estimating neurocysticercosis disease burden and assessing disability-adjusted life years. However, there is a paucity of information on disability weight in patients with neurocysticercosis.

Methods

Participants were separated into 2 groups and were interviewed by EQ-5D+C questionnaire in Dali prefecture, Yunnan province. Statistical analysis was performed using SPSS 20.0.

Results

Compared to those in the first-visit group, health barriers were less frequently reported in all six dimensions in the follow-up group, except for the cognitive dimension. Disability weights in both the first-visit and follow-up groups were 0.3.

Conclusions

The health-related quality of life of NCC patients was seriously impaired, and cognitive competence is the most prominent health barrier. Psychological medical care should be taken as one component in the treatment of NCC patients.

Background

Human cysticercosis is a tissue infection caused by larvae of the parasite *Taenia solium* [1–6]. The Food and Agriculture Organization (FAO) categorized cysticercosis as a neglected zoonotic disease in 2014 after it was classified by the World Health Organization (WHO) as a neglected tropical disease in 2010 [7–9]. Cysticercosis has been identified as a major health problem in Asia and is also endemic in developing countries of Latin America and Africa [1]. In addition, it has also been recently identified as an emerging infectious disease in some developed countries due to increasing international communications [2, 10]. The World Health Assembly passed the WHA66.12 resolution in 2013, targeting elimination of cysticercosis as a public health problem [11]. Cysticercosis can damage any tissue in the human body, including the central nervous system, subcutaneous tissues, eyes, and muscles [1, 2]. Symptoms vary by location. When the larvae invade central nervous system, it can cause neurocysticercosis (NCC). NCC accounts for the major proportion of human cysticercosis patients. Clinical symptoms of NCC can result in serious health complications [4, 5, 7, 12, 13]. The parasite causes a large number of NCC-associated epilepsy and deaths, with 2.79 million disability-adjusted life years

(DALYs) [14]. Following increasing global concern, disease burden studies have been carried out in many countries [9, 15–17]. In these studies, NCC disability weight (DW) is a key parameter in estimation of NCC burden [18]. However, the DW of epilepsy or headache was used to estimate NCC DALYs rather than that of NCC directly [9, 16, 17]. Moreover, not all NCC patients manifest symptoms of epilepsy or headache [4]. It is, therefore, imperative to obtain NCC DW in the research of disease burden.

Between 1987 and 1991, an inter-disciplinary, five-country group developed the EuroQol instrument to measure and evaluate health status [19–21]. The five-dimensional, three-level generic measuring instrument was subsequently termed the 'EQ-5D'. A cognitive dimension was later added to the initial questionnaire, making the tool EQ-5D plus or EQ-5D + C [19, 22].

This study aimed to obtain NCC DW using EQ-5D + C tool in Dali, Yunnan province. Estimating NCC DW will not only provide basic scientific evidence in cysticercosis disease burden research, but also inform control strategies in this area.

Methods

Study area

This study was carried out in the Dali Prefectural Institute of Research and Control on Schistosomiasis, located in the Dali Bai Autonomous Prefecture, Yunnan, China. Dali prefecture is located in the central western part of Yunnan, 350 km northwest of Kunming, the capital of Yunnan province. It has a territory of 29,459 square kilometres and a population of 3,400,000. The prefecture is subdivided into 12 county-level divisions: one county-level city, eight counties, and three autonomous counties. In China, Dali is a hotspot for cysticercosis endemicity due to the local dietary habit of eating undercooked pork. For years, the Dali Prefectural Institute of Research and Control on Schistosomiasis has served as a reference hospital for cysticercosis patients in Yunnan province.

Study design

Participants were separated into 2 groups, the first-visit group and the follow-up group. The first-visit group were those patients who received standard anti-cysticercosis treatment for the first time in the hospital while the follow-up group were those who received subsequent treatment in the hospital. A survey was administered to both groups in 2018. It consisted of three parts: part one, demographical characteristics including age, sex, occupation, ethnic status, education, and marriage status; part two, case diagnosis and treatment information, including diagnosis basis, case classification, previous medical story, and clinical manifestations; and part three, the EQ-5D + C survey, which included 6-domains and a visual analogue scale.

Selection of participants

Participants were inpatients in the Dali Prefectural Institute of Research and Control on Schistosomiasis from September 2017 to September 2018. According to the national standardized diagnostic criteria for

NCC (WS381-2012) [23], patients were classified into three categories, suspected cases, clinically diagnosed cases, and confirmed cases. Only confirmed cases were eligible for inclusion in the survey. Exclusion criteria were: (i) patients who did not finish the questionnaire, (ii) cysticercosis other than NCC, (iii) patients with other underlying diseases, (iv) mixed cysticercosis, (v) patients younger than 5 years old.

Sampling

The sample size (n) was determined using the statistical formula:

$$n = \frac{z^2 \pi (1 - \pi)}{\sigma^2}$$

Where α is the type I error rate (0.05) and $\alpha = 0.05$ (two-sided), π is the population rate and if $\pi = 0.5$, the maximum sample size can be obtained. σ is the allowable error (0.1), N reaches to 96. Considering the cluster sampling power as 2, then the required sample size was 192. The study participants were then selected by systematic random sampling using selected participants as a sampling frame. As a result, a total of 210 participants were enrolled in the study (Fig. 1).

Data collection

Surveys were conducted face-to-face and data collected by trained investigators. Data were double-entered and logic correction was conducted using EpiData3.1 (The EpiData Association, Odense, Denmark).

Statistical analyses

Descriptive analysis was used to show the demographic characteristics and clinical symptoms of NCC patients; the χ^2 test was used to compare the differences in clinical symptoms between the first-visit and follow-up groups. Descriptive analyses were used to show the distribution of patients' six-dimensional and EQ-VAS scores. T-test or analysis of variance was used to compare the EQ-VAS scores for normally distributed data, while Mann-Whitney U or Kruskal-Wallis test was used for non-normally distributed data. The χ^2 test or Fisher's exact probability method was used to compare the proportion of health difficulties in the six dimensions. DW was determined by the formula $DW = 1 - VAS/100$, with VAS as the patient's EQ-VAS self-assessment. SPSS 20.0 software (IBM, Armonk, NY, US) was used for statistical analysis. DW was compared using t-test or analysis of variance when data were normally distributed. Bonferroni test was used to make pairwise comparisons between groups when the difference was statistically significant. Mann-Whitney U test or Kruskal-Wallis test was used to compare DW for non-normally distributed data. Bonferroni test was performed when the difference was statistically significant.

Results

Socio-demographic findings

A total of 210 participants with age range of 7 to 74 years old were included. The mean age was 38.9 ± 15.5 . The largest number of study participants, 69 (32.9%) was from the age group 30–44 years. The sex ratio (M/F) was 1.9 with 138 males and 72 females. Bai was the predominant ethnic group (29.1%), followed by Yi with 17.2%. Out of the 210 participants, 84 were in the first-visit group and 126 were in the follow-up group. Respondents' demographic and socioeconomic characteristics are summarised in Table 1.

Table 1
Social demographic characteristics in patients

Characteristic	No.	Distribution(%)
Age		
5–14	10	4.76
15–29	51	24.29
30–44	69	32.86
45–59	61	29.05
≥ 60	19	9.05
Gender		
male	138	65.71
female	72	34.29
Marital status		
unmarried	49	23.33
married	156	74.29
divorced/widoerd	5	2.38
Occupation		
farmer	133	63.33
preschooler	7	3.33
student	24	11.43
worker	21	10.00
civil servant	7	3.33
others	18	8.57
Education		
no school graduation	22	10.48
primary school	76	36.19
junior high school	76	36.19
high school	23	10.95
college and/or above	13	6.19

Clinical symptoms

The most prominent clinical symptoms in the first-visit group and follow-up group were headache (64 cases) and hypomnesia (85 cases), respectively. Headache, epilepsy, and hypomnesia were the most frequently reported manifestations by the first-visit group while hypomnesia, headache, and muscle paraesthesia were more common in the follow-up group. The percentage of epilepsy was 54.76% in the first-visit group compared to 25.40% in the follow-up group ($\chi^2 = 18.52$, $P < 0.001$), and headache was 76.19% in the first-visit group compared to 62.70% in the follow-up group ($\chi^2 = 8.52$, $P < 0.05$), respectively. However, the proportion of patients with hypomnesia was significantly higher in the follow-up group (67.46%) than that in the first-visit group (52.38%; $\chi^2 = 8.76$, $P < 0.05$) (Table 2).

Table 2
Comparison of symptoms between first-visit group and follow-up group

Variate	No. of NCC	Epilepsy***		Headache**		Hypomnesia*		Muscle paraesthesia*		Uncomfortable of eye*	
		NO.	ratio	NO.	ratio	NO.	ratio	NO.	ratio	NO.	ratio
First-visit group	84	46	54.76	64	76.19	44	52.38	26	30.95	12	14.29
Follow-up group	126	32	25.40	79	62.70	85	67.46	37	29.37	11	8.73
Total	210	78	37.14	143	68.10	129	61.43	63	30.00	23	10.95
Note: * $P > 0.05$; ** $P < 0.05$; *** $P < 0.01$											

Health-related life quality

The results collected through the EQ-5D + C questionnaire are summarized in Tables 2 and 3. Out of the 210 patients, 93.33% (196) complained of at least one impairment. The number of patients that claimed moderate and severe impairments were 175 (83.33%) and 21 (10.00%), respectively. Barriers in cognitive competence was the most frequently reported in patients (71.9%, 151/210) (Table 3).

In terms of the six-dimensional distribution, pain and/or discomfort ranked highest (77.38%) in the first-visit group while cognition was highest in the follow-up group (74.60%). Compared to those in the first-visit group, health barriers were less frequently reported in all six dimensions in the follow-up group, except for cognitive dimension (Table 4).

Table 3
Study population EQ-5D + C six-dimensional and three-level distribution

Dimension	Degree of health barriers			No of having any health barriers (%)
	None (%)	Moderate (%)	Extreme (%)	
Mobility	201(95.71)	9(4.29)	0(0.00)	9(4.29)
Self-care	204(97.14)	6(2.86)	0(0.00)	6(2.86)
Usual activities	124(59.05)	83(39.52)	3(1.43)	86(40.95)
Pain/discomfort	61(29.05)	147(70.00)	2(0.95)	149(70.95)
Anxiety/depression	80(38.09)	118(56.19)	12(5.71)	130(61.90)
Cognitive competence	59(28.1)	144(68.57)	7(3.33)	151(71.90)
Any dimension	14(6.67)	175(83.33)	21(10.00)	196(93.33)

Table 4
Proportion of patients with health barriers in six dimensions

Dimension	First-visit group		Follow-up group		<i>P</i>
	No. of health barriers ^a	ratio	No. of Health barriers ^a	ratio	
Mobility*	5	5.95	4	3.17	>0.05
Self-care*	2	2.38	4	3.17	>0.05
Usual activities	38	45.24	48	38.1	1.06 >0.05
Pain/discomfort	65	77.38	84	66.67	2.81 >0.05
Anxiety/depression	53	63.1	77	61.9	0.03 >0.05
Cognitive competence	57	67.86	94	74.6	1.14 >0.05
Note: *Fisher exact probability method; ^a "Problem" = moderate or extreme health barriers					

The findings indicated that age, occupation, usual activities, pain/discomfort, anxiety/depression, and cognition were predisposing factors for the EQ-VAS score (Table 5). Multiple linear regression analysis was applied by using EQ-VAS score as the dependent variable. The results of a multiple linear regression model showed a significant difference ($F = 16.99$, $P < 0.001$). R^2 was equal to 0.46, indicating that the variables included could account for 46% of the total DW variation. Multivariate analysis found that EQ-VAS score was negatively correlated with daily activities, pain/discomfort, anxiety/depression, and

cognitive ability. The standardized regression coefficients showed that cognitive ability had the greatest impact on EQ-VAS score (-0.32), followed by daily activities (-0.27), and pain/discomfort (-0.25) (Table 6).

Table 5
Single factor analysis of DW

Parameter		No.	M(P25-P75)	Mean Rank	Z/χ^2	P
Type of patients	first-visit	84	0.3(0.2–0.4)	101.78	-0.74	>0.05
	follow-up	126	0.3(0.2–0.4)	107.98		
Gender	male	138	0.3(0.2–0.4)	105.06	0.15	>0.05
	female	72	0.3(0.2–0.4)	106.34		
Marital status	unmarried	49	0.25(0.2–0.4)	114.92	1.65	>0.05
	married	155	0.3(0.2–0.4)	99.26		
Age	5-14 ^a	10	0.2(0.1–0.2)	163.7	13.25	<0.05
	15-29 ^b	51	0.3(0.2–0.4)	111.51		
	30–44 ^b	69	0.3(0.2–0.4)	104.79		
	45–59 ^b	61	0.3(0.2–0.4)	97.93		
	≥ 60 ^b	19	0.3(0.2–0.3)	85.58		
Education	No school graduation	22	0.4(0.25–0.4)	79.71	5.53	>0.05
	Primary school	76	0.3(0.2–0.4)	108.28		
	Junior high school	76	0.3(0.2–0.4)	106.26		
	High school	23	0.3(0.2–0.4)	119.04		
	College degree or above	13	0.3(0.2–0.4)	104.5		
Occupation	Farmer	133	0.3(0.2–0.4)	93.12	3.97	<0.001
	Nofarmer	77	0.2(0.2–0.3)	126.88		
Mobility	No Problem	201	0.3(0.2–0.4)	106.94	-1.66	>0.05
	Problem	9	0.4(0.25–0.5)	73.28		
Self-Care	No Problem	204	0.3(0.2–0.4)	106.19	-0.98	>0.05
	Problem	6	0.4(0.2–0.5)	82		
Usual Activites	No Problem	124	0.23(0.2–0.3)	127.31	-6.39	<0.001

Parameter		No.	M(P25-P75)	Mean Rank	Z/χ^2	P
Pain/Discomfort	Problem	86	0.4(0.3–0.5)	74.06	5.66	<0.001
	No Problem	61	0.2(0.2–0.3)	141.8		
	Problem	149	0.3(0.2–0.4)	90.64		
Anxiety/Depression	No Problem	80	0.2(0.2–0.3)	139.36	6.41	<0.001
	Problem	130	0.3(0.25–0.4)	85.08		
	Problem	130	0.3(0.25–0.4)	85.08		
Cognitive ability	No Problem	59	0.2(0.1–0.25)	156.25	7.74	<0.001
	Problem	151	0.3(0.25–0.4)	85.67		
	Problem	151	0.3(0.25–0.4)	85.67		

Table 6
Linear regression parameter estimation of DW predisposing factors

Parameter		Partial regression co-efficient	Standard error	<i>t</i>	<i>P</i>	Standardized regression coefficient
Intercept						
Age(group)						
	15– 29	-1.39	3.47	-0.40	>0.05	-0.05
	30– 44	-0.33	3.43	-0.10	>0.05	-0.01
	45– 59	-0.09	3.48	-0.03	>0.05	0.00
	≥ 60	-3.20	3.90	-0.82	>0.05	-0.07
Occupation		2.62	1.56	1.68	>0.05	0.10
Mobility		-0.38	3.43	-0.11	>0.05	-0.01
Self-Care		-6.19	4.16	-1.49	>0.05	-0.08
Usual activities		-7.13	1.46	-4.88	<0.001	-0.27
Pain/discomfort		-6.97	1.50	-4.66	<0.001	-0.25
Anxiety/depression		-5.42	1.52	-3.56	<0.001	-0.20
Cognitive		-9.12	1.65	-5.52	<0.001	-0.32
$R^2 = 0.46$						

Disability weights

According to the normality test, DW did not conform with the normal distribution (Shapiro-Wilk test $W = 0.73$, $P < 0.001$). The DW in the first-visit and follow-up groups were both 0.3 (0.2–0.4) (Table 7, Table 8), without statistical significance ($Z = 0.74$, $P > 0.05$) (Table 9). No significant significance was found in the proportion of gender ($\chi^2 = 2.87$, $P > 0.05$) or age ($\chi^2 = 2.08$, $P > 0.05$) between the two groups. Therefore, DWs in both groups were combined and analysed as a whole. The overall DW of NCC was 0.3 (0.2–0.4), without significant difference between genders ($Z = -0.15$, $P > 0.05$). However, DWs were not equal among age groups ($\chi^2 = 13.25$, $P < 0.05$). DW tended to increase with age. Pairwise comparison showed no significant differences between the age groups except for the 5–14 age group (Table 10).

Table 7
DW values of NCC patients in untreated group

Variate	Category	No.	DW			Z/χ^2	P
			M	P ₂₅ -P ₇₅	Mean Rank		
Gender	male	52	0.3	0.20–0.40	44.58	0.62	>0.05
	female	32	0.3	0.20–0.40	41.22		
Age group	5–14	8	0.2 ^a	0.10–0.25	19.75	10.93	<0.05
	15–29	19	0.3 ^b	0.20–0.40	44		
	30–44	27	0.3 ^b	0.20–0.40	41.24		
	45–59	23	0.3 ^b	0.20–0.40	45.93		
	≥ 60	7	0.3 ^b	0.30–0.50	58		
Total		84	0.3	0.20–0.40			
Note: statistical difference between a and b (Bonferroni test, $P < 0.01$)							

Table 8
DW values of NCC patients treatment group

Variate	Category	No.	DW			Z/χ^2	P
			M	P ₂₅ – P ₇₅	Mean Rank		
Gender	male	86	0.3	0.20–0.40	64.94	-0.66	>0.05
	femal	40	0.28	0.20–0.38	60.4		
Age	5–14	2	0.15 ^a	0.10–0.20	19.5	8.23	<0.05
	15–29	32	0.25 ^b	0.20–0.38	56.56		
	30–44	42	0.30 ^b	0.20–0.40	65.26		
	45–59	38	0.30 ^b	0.20–0.40	67.92		
	≥ 60	12	0.30 ^b	0.25–0.38	69.17		
	Total	126	0.3	0.20–0.40			
Note: statistical difference between a and b (Bonferroni test, $P < 0.01$)							

Table 9
Comparison of DW values of NCC patients with first visit group and follow-up group

Variate	No.	DW			Z	P
		M	P ₂₅ -P ₇₅	Mean Rank		
first-visit group	84	0.3	0.20-0.40	109.22	0.74	>0.05
follow-up group	126	0.3	0.20-0.40	103.02		

Table 10
DW values in NCC patients

Variate	Category	No.	DW			Z/χ^{22}	P
			M	P ₂₅ -P ₇₅	Mean Rank		
Gender	Male	138	0.3	0.20–0.40	109.44	-0.15	>0.05
	female	72	0.3	0.20–0.40	101.66		
Age group	5–14	10	0.20 ^a	0.10–0.20	47.3	13.25	<0.05
	15–29	51	0.30 ^b	0.20–0.40	99.49		
	30–44	69	0.30 ^b	0.20–0.40	106.2		
	45–59	61	0.30 ^b	0.20–0.40	113.07		
	≥ 60	19	0.30 ^b	0.30–0.40	125.42		
	Total	210	0.3	0.20–0.40			
Note: statistical difference between a and b (Bonferroni test, $P<0.01$)							

Discussion

Cysticercosis has historically been widely distributed in China [3, 10, 24–25]. However, the prevalence has recently decreased gradually in parts of southwestern China due to improvements in social and economic development. Nevertheless, a large proportion of residents, especially in Yunnan province, are accustomed to consuming raw or undercooked pork [3, 13, 25–27].

Previous studies showed that seizures were the most common clinical manifestation among NCC patients [4, 6, 13, 28–32]. However, the main clinical symptom among patients in this study was headache, followed by hypomnesia and seizure. This may be because the period of epilepsy symptoms in this study was defined as whether there was epilepsy in the last month, rather than whether there was epilepsy at any time prior. In addition, some of the patients received standardized treatment, indicating that treatment may effectively alleviate symptoms of seizures [5, 33–35].

The EQ-5D + C is a valid tool widely used to measure health-related quality of life [20, 36–38]. It was found that pain/discomfort and cognitive disorders were the most prominent symptoms attributable to NCC. Patients with NCC develop cognitive impairment, with mild to moderate cognitive dysfunction reported in about 88% [39], indicating that they suffer cognitive problems which may be due to changes such as partial seizures, mass effect of cysts, and increased intracranial pressure [39–41]. Hypomnesia is rarely mentioned in previous studies, but is commonly reported in cysticercosis cases [42–43]. In this study, over 60% NCC patients had symptoms of hypomnesia. Hypomnesia has been identified as a cause

of cognitive disorders and is therefore an important parameter in assessing cognitive ability [39]. Long-term hypomnesia causes patients great psychological pressure and seriously affects their quality of life. Early detection and diagnosis are important for cysticercosis and taeniasis treatment [33, 44–45]. It can not only improve the prognosis of cysticercosis, reduce the burden of the patients themselves, but also reduce the risk of the patients as a source of infection to others [35]. In order to improve the case detection and reduce the risk of NCC [44], local residents should be informed to seek urgent medical attention whenever they experience unexplainable headache or epilepsy. Also, health workers should consider the possibility of NCC and arrange for further diagnosis.

Many studies have reported NCC DALYs globally, but few provide information on NCC DW [9, 14–17, 46]. This study showed a way to report NCC DW using EQ-5D + C. The general NCC DW was 0.30 in both the first-visit and follow-up groups. Except for hypomnesia, other clinical symptoms were alleviated in follow-up patients. Nevertheless, there was no statistical significance of DW between the two groups. This may be because that treatment did not help improve the patients' subjective health-related quality of life. Result showed that cognitive ability has the greatest impact on EQ-VAS score. In general, cognitive ability include memory, observation, and imagination [47]. Compared with first-visit patients, hypomnesia may be responsible for its DW in follow-up patients. The WHO [48] defines health as a "state of complete physical, mental, and social well-being, and not merely the absence of disease or infirmity". With this in mind, changes in clinical symptoms alone cannot effectively improve a patient's overall health. It is recommended that psychological treatment be incorporated into the treatment strategy for NCC patients. Therefore, it is proposed that in treating NCC patients, psychological counseling should be considered to help reduce emotional burden and psychological pressure caused by memory loss.

Based on the EQ-VAS score, patients rated themselves after getting to know their own health status. However, this method is highly subjective and may easily be affected by the patients' mood and other factors, which may lead to unstable result [49].

Conclusions

The health-related quality of life of NCC patients was seriously impaired, and cognitive competence is the most prominent health barrier. Psychological medical care should be taken as one component in the treatment of NCC patients.

List Of Abbreviations

NCC, neurocysticercosis; DALYs, disability-adjusted life years; DW, disability weight; VAS, visual analogue scale

Declarations

Ethics approval and consent to participate

This study was reviewed and approved by the Ethics Committee of the National Institute of Parasitic Disease (NIPD), Chinese Center for Disease Control and Prevention (No. 20180814). The objectives and procedures were explained to all participants. Written informed consent was also obtained from each participant or a literate relative. No animal work was carried out as part of this study.

Consent for publication

Not applicable.

Availability of data and materials

The data supporting the conclusions of this article are included within the article and its additional files. The datasets generated and/or analysed during the current study are available from the corresponding author upon reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

SZL, MBQ and YJQ designed the study and revised the manuscript. XZZ wrote the draft of the manuscript. HZL, HKL and YHL examined the patients and conducted a questionnaire survey. CHZ and YDC critically revised the article for the important intellectual content. All authors read and approved the final manuscript.

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Figures

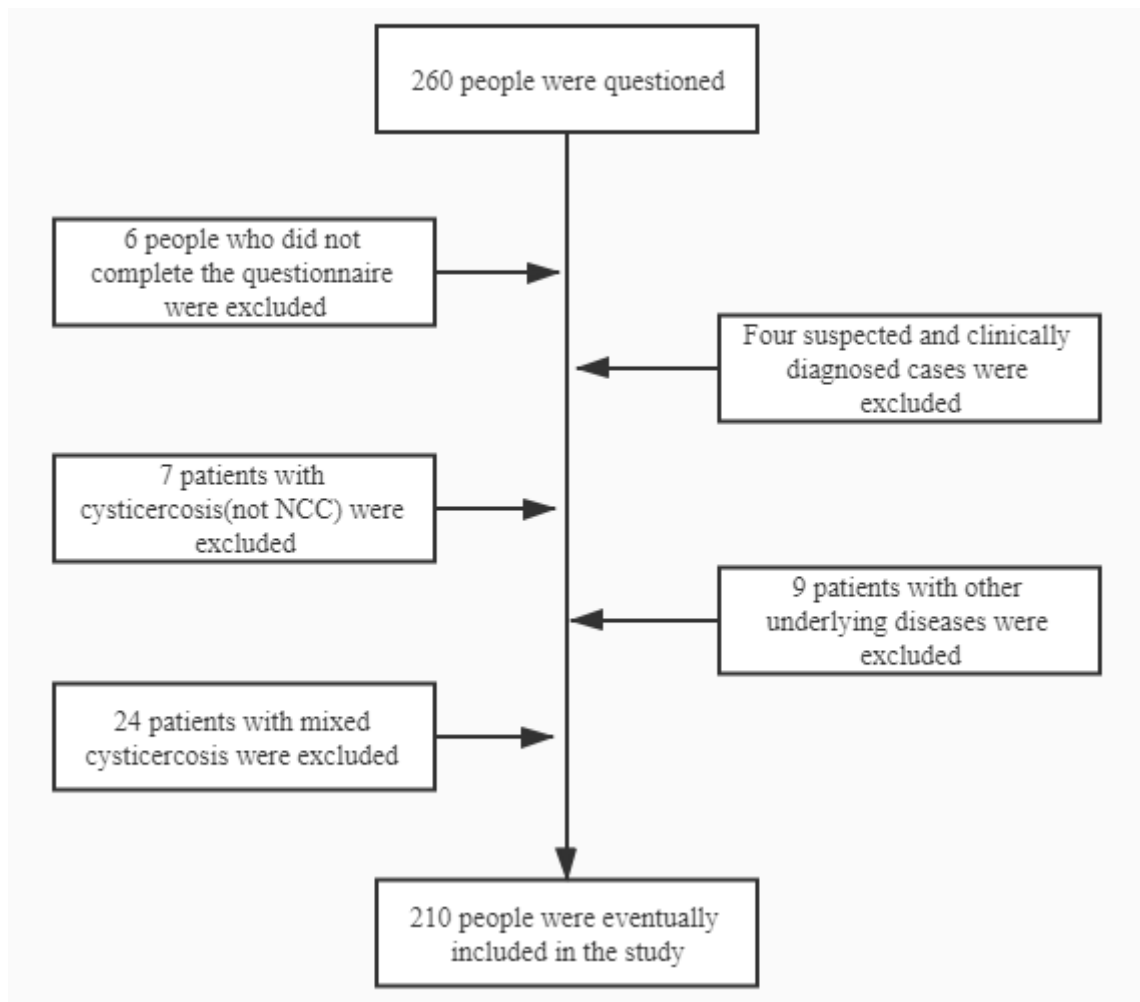


Figure 1

Flow chart of case inclusion

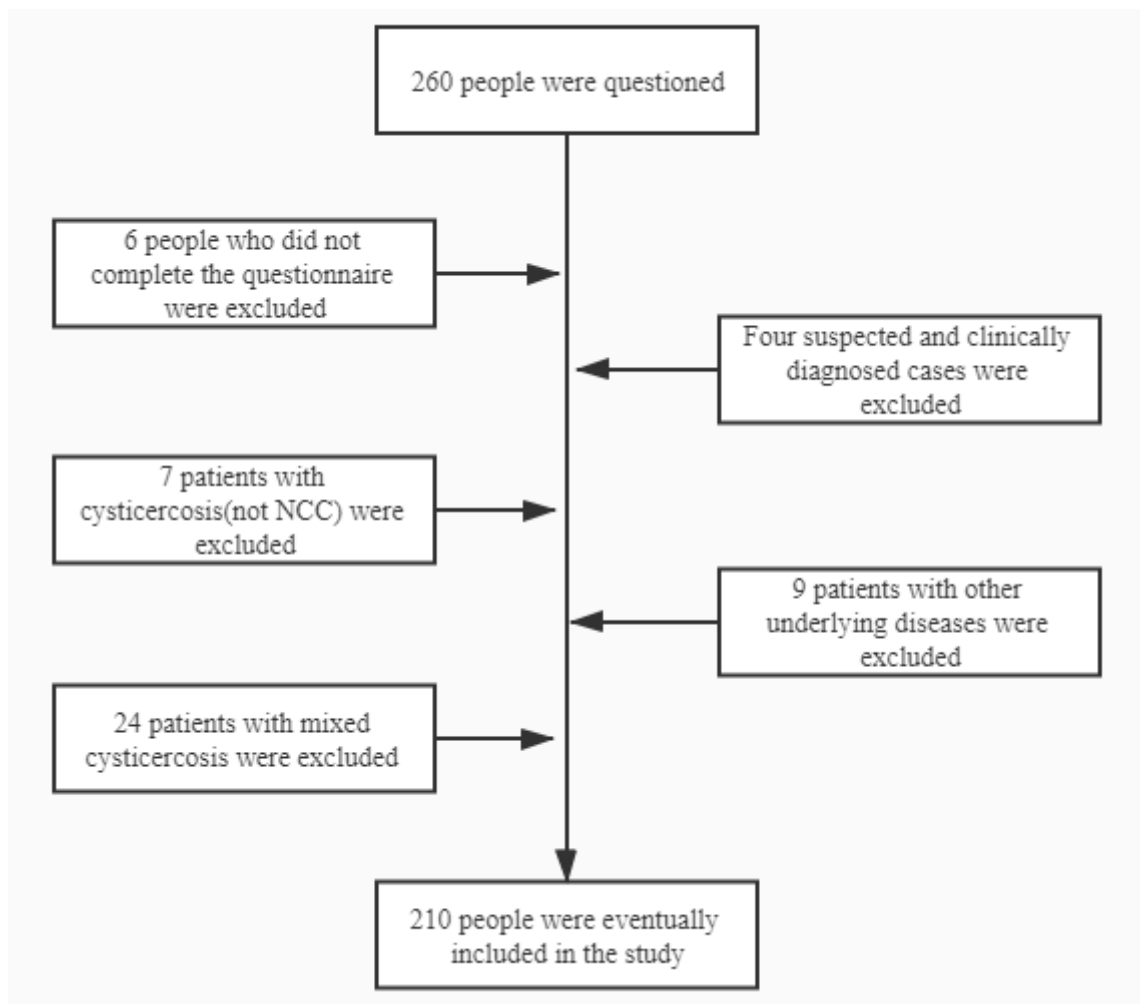


Figure 1

Flow chart of case inclusion

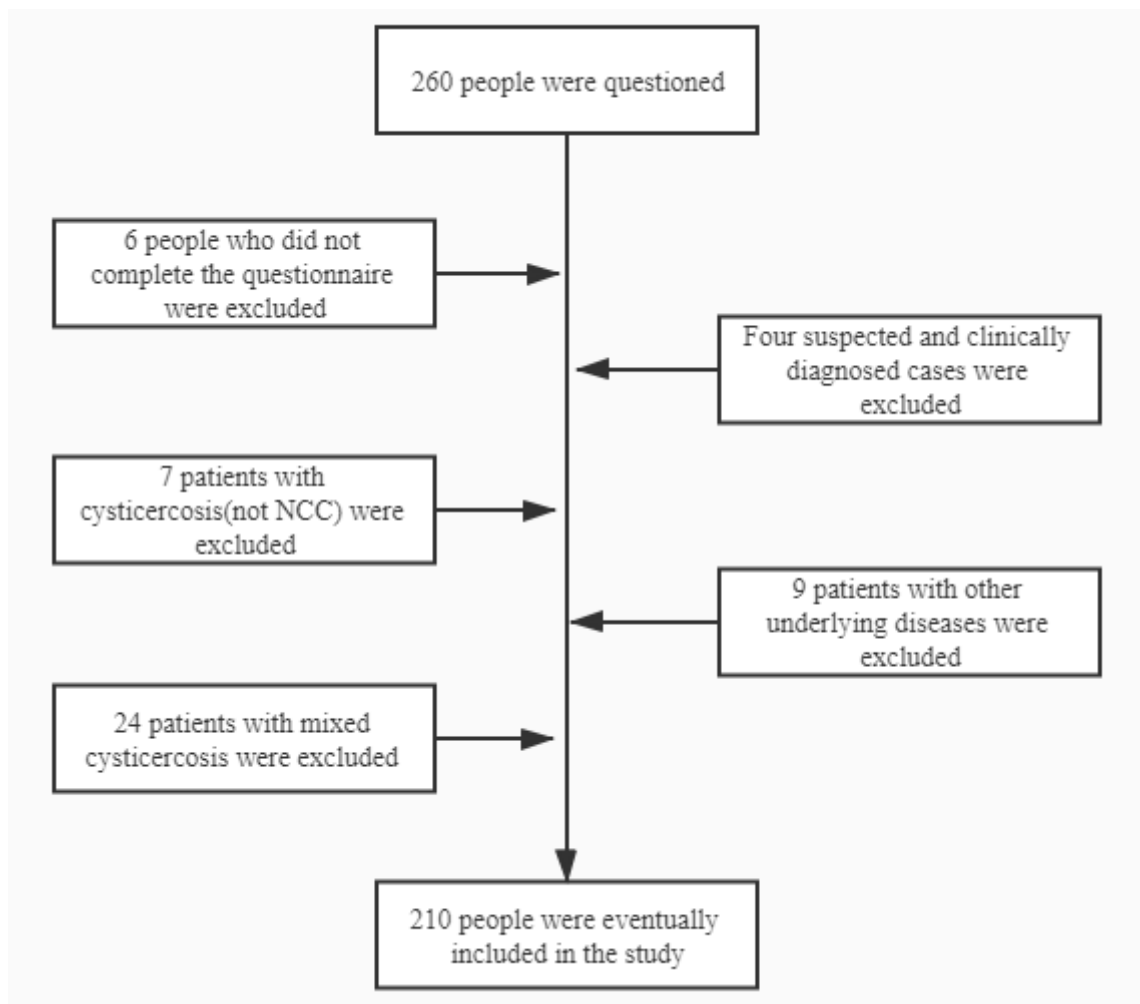


Figure 1

Flow chart of case inclusion

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