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ORIGINAL ARTICLE

Cross-cultural adaptation of the connective tissue disease screening questionnaire and development of a Chinese version in a multi-ethnic Asian population

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Abstract

Objectives To cross-culturally adapt the Connective Tissue Disease (CTD) Screening Questionnaire (CSQ) in a multi-ethnic Asian population in Singapore.

Methods An expert panel of accredited rheumatologists evaluated the content validity of the original CSQ. Consenting participants newly referred from primary care to a rheumatology specialist outpatient clinic for evaluation of possible CTDs were studied. Cognitive debriefing interviews (CDIs) using the original CSQ were conducted with English-speaking participants, with modifications made based on their inputs and in discussion with a second expert panel (rheumatologists and the CSQ developers). Forward and back translations of the adapted English version were reviewed by the second expert panel. The common translation produced was tested in CDIs with Chinese-speaking participants. Adapted English and Chinese versions were pilot tested in a separate group of newly referred patients.

Results Content validity of the original CSQ was confirmed by the expert panel. A total of 30 and 15 participants were recruited for English and Chinese CDIs, respectively. Alternative terms and explanatory notes were added to difficult medical terms in the adapted English CSQ. A further explanatory note was added to one difficult item, and English medical terms were retained in the Chinese version. Pilot testing of the adapted CSQ was performed on 116 participants, which exhibited an overall sensitivity and specificity of 71% and 58%, respectively, in identifying CTDs.

Conclusions The adapted CSQ demonstrated satisfactory sensitivity in the pilot testing and appears to be a promising tool for facilitating early identification of CTDs in the multi-ethnic Asian population.

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Key Points

- *Early identification and management of patients with CTDs is crucial given their high disease burden and short "windows of opportunity."*
- *High reliability and validity of original CSQ and its cross-culturally adapted versions have been reported; however, the CSQ has not been validated in Southeast Asia where CTDs are associated with higher morbidity and mortality compared to other countries.*
- *Our cross-culturally adapted CSQ demonstrated satisfactory sensitivity in identifying CTDs in the multi-ethnic Asian population.*

Keywords CTDs · Mass screening · Rheumatoid arthritis · Self-assessment · Systemic lupus erythematosus · Systemic sclerosis

Introduction

Despite their low prevalence, connective tissue diseases (CTDs) such as rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), and spondyloarthritis are among the leading causes of disability worldwide, often affecting patients in the prime of life (1, 2). Early intervention in CTDs with a "window of opportunity" following the onset of symptoms, which is about 12 weeks for RA (3, 4), has been found to significantly improve patient outcomes and reduce healthcare costs (4–10). Given the high disease burden and the short window of opportunity, early identification and management of patients with CTDs is crucial. Despite this, delays exist in the diagnoses and treatments of all CTDs, occurring most often from symptom onset to being seen in primary care and from primary care to rheumatology referral (11–14). Importantly, self-administered screening questionnaires that require low cost and minimal intervention from healthcare professionals have been shown to facilitate early identification of CTDs in various settings (15–19).

The most widely used CTD screening questionnaire, the connective tissue disease screening questionnaire (CSQ), was developed by Karlson et al. in the USA for identifying RA, SLE, systemic sclerosis (SSc), Sjögren's syndrome (SS), polymyositis, dermatomyositis, and mixed CTD (MCTD) (20). It comprises 30 items that were selected from then current American College of Rheumatology (ACR) criteria for RA and SLE, preliminary ACR criteria for SSc, and published classification criteria for SS, myositis, and MCTD. High reliability and validity have been reported for screening for CTDs using both original and its cross-culturally adapted versions in Korea and Germany (15, 16, 20).

The CSQ, however, has not been validated in Southeast Asia, where the clinical presentation of CTDs may vary from that in Western countries. For example, higher prevalence of SLE and more severe hematological, serosal, neurological, and renal manifestations have been reported in Asian populations (21–27). This may affect the sensitivity and specificity of the CSQ in screening for CTDs. A pilot study from our group done in 2016 found an overall sensitivity of 72% in identifying patients with CTDs using the original CSQ in Singapore (unpublished data, manuscript under review). This result was promising but also highlighted the need for cross-cultural validation of the CSQ so that it could be used in Asian populations (28). Singapore, the setting of this study, is a multi-ethnic and multi-lingual country with 95% of its population literate in English and/or Chinese (29). As part of a larger effort to facilitate early identification of CTDs in Singapore, this study aimed to cross-culturally adapt the CSQ English version and develop a Chinese version for use in the Singapore population.

Materials and methods

Study design

This is a cross-sectional study consisting of two phases: (1) cross-cultural adaptation of the original CSQ into Singapore English and Singapore Chinese and (2) pilot testing of the adapted versions in order to evaluate their ease of comprehension and performance in identifying CTDs.

Participants

Between October 2017 and June 2018, we approached patients who were newly referred for evaluation of possible CTDs from primary care clinics to the Rheumatology Specialist Outpatient Clinic in a tertiary referral center in Singapore. We included these subjects because they were representative of the intended users of the screening questionnaire—individuals with early CTD symptoms seen in primary care settings. The inclusion criteria were 21 years of age or over, Singapore citizens or permanent residents, newly referred to the clinic, no previous diagnosis of CTD, and able to read and speak English or Chinese. Participants were recruited separately for the two phases.

We used purposive sampling to represent a range of ethnicities and education levels in phase 1. We oversampled patients with fewer years of education as they might have more difficulty understanding the questionnaire.

Written informed consent was sought from all participants. This study was approved by the SingHealth Centralised Institutional Review Board (CIRB reference: 2016/3138).

Content validity

We convened a panel of accredited rheumatologists ($n = 7$) to examine the relevance of the original CSQ in the light of the changes in CTD classification criteria since the CSQ was developed. The classification criteria used in examining the relevance of the CSQ were (1) RA—ACR/European League Against Rheumatism (EULAR) Criteria (2010) (30), (2) SLE—Systemic Lupus International Collaborating Clinics (SLICC) Criteria (2012) (31), (3) SSc—ACR/EULAR Criteria (2013) (32), (4) SS—ACR/EULAR Criteria (2016) (33), (5) Myositis—EULAR/ACR Criteria (2017) (34), and (6) MCTD—Alarcon-Segovia Criteria (1987) (35).

Cross-cultural adaptation

We first adapted the original CSQ into Singapore English. We conducted cognitive debriefing interviews (CDIs) with English-speaking participants before they saw an attending rheumatologist to avoid any change of perception arising from their consultation, which might influence their answers to questionnaire items. All participants were instructed to complete the questionnaire by themselves in a separate room at the clinic, during which any hesitation or skipping of questionnaire items were noted by the interviewers (LX and EPST). We used retrospective probing in the CDIs to identify items whose meaning was unclear to participants and to solicit suggestions to address these issues and refine wording of the CSQ. We discussed possible changes to improve understandability of the questionnaire in Singapore with the CSQ developers and tested these changes iteratively until participants reported no significant difficulty in the CDIs. As the questionnaire items had been phrased in relatively simple terms, we did not foresee major changes to the original CSQ and expected 10 CDIs to be sufficient to achieve data saturation.

We then translated the cross-culturally adapted English version into Singapore Chinese and adapted it following the guidelines recommended by Beaton et al. and the COnsensus-based Standards for the selection of health status Measurement INstruments (COSMIN) checklist (28, 36). Forward translation of the adapted questionnaire was performed by two independent bilingual translators (one rheumatologist and one research staff) whose primary language was Singapore Chinese. Back translation was done by another two independent translators who had no knowledge of CTDs and whose primary language was Singapore English. Inconsistency in different translations was reviewed by an expert panel made up of four rheumatologists, one sociologist, and the forward and back translators, the majority of whom were fluent in both Singapore English and Singapore Chinese. The resulting translation and modifications proposed by the panel were discussed with the CSQ developers, after which a common translation was produced. Similarly, we conducted CDIs with the common translation with Chinese-speaking participants. We iteratively modified the common translation based on findings in CDIs via discussions with the expert panel and the CSQ developers until participants reported no significant difficulty in comprehension. As this group of Chinese-speaking patients was deemed more homogeneous in terms of their literacy level due to their relatively older age and fewer years of education (37), we also anticipated CDIs with up to 10 respondents would be sufficient.

Pilot testing of the adapted CSQ

All eligible participants were invited to answer the adapted CSQ in their preferred language while they were waiting to see the attending rheumatologist for the first time. Feedback on ease of comprehension and time needed for completion of the adapted questionnaire were recorded. The adapted questionnaire was scored according to the algorithm provided by the developers (20).

We followed all participants' cases until a definitive CTD diagnosis or a conclusive ruling out of a CTD condition could be made. The diagnosis of CTDs was made based on chart review by study team members (LX and JT), using the criteria stated above.

As part of the adaptation process, we performed a pilot assessment of the performance of the adapted CSQ by calculating the overall sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratio (LR+), and negative likelihood ratio (LR-) along with corresponding 95% confidence intervals (CIs) for identifying any CTD in a separate group of newly referred patients.

The planned sample size was 113, including 17 CTDs (assuming a prevalence of 15% among the new referrals in the Rheumatology Specialist Outpatient Clinic based on our hospital data), to achieve a power of 83% to detect a change in sensitivity from 0.5 to 0.8 and a power of 100% to detect a change in specificity from 0.5 to 0.8 at a significance level of 0.1 using a two-sided binomial test.

All analyses were performed using Stata 14.

Results

Content validity

The rheumatologist panel ($n = 7$) compared the 30 items in the original CSQ to the current classification criteria for RA, SLE, SSc, SS, and myositis. The panel agreed that the original CSQ had content validity to identify these CTDs using current criteria.

Cross-cultural adaptation

Participants

Of the 64 patients we approached, 55 (86%) consented to participate in the study and 45 (70%) completed the CDIs (Table 1). The main reason for refusing participation and withdrawing from the study was that these patients felt most items in the CSQ were irrelevant to them.

Participants had a mean age of 48 years and were mostly female (69%), Chinese (80%), with more than 10 years of education (above secondary education: 64%), and symptomatic (89%) at the time of study enrollment as identified in their answers to the CSQ. Participants who were recruited for Chinese CDIs were relatively older than those recruited for English CDIs (mean age: 55 years vs 45 years) with more females (80% vs 63%), fewer years of education (secondary education or below: 40% vs 27%), and more symptoms (93% vs 87%).

Findings from cognitive debriefing interviews

English version

Twenty-one English-speaking participants answered all items in the original CSQ. All participants reported no/ minimum difficulty with four items (Q8 (Raynaud's phenomenon), Q10 (malar rash), Q13 (alopecia), and Q15 (finger swelling)) and thus no modifications were made to these items (Table 2).

Multiple participants reported difficulty understanding the medical terms in five items (Q14 (seizure), Q16–17 (skin thickening), Q27 (proteinuria), and Q28 (discoid rash)). However, no modifications were made after discussion with the expert panel and the CSQ developers as it was deemed that (1) participants who had these symptoms would likely respond affirmatively to the current terms and (2) there was no clearer way to explain these medical terms. In order to understand the comprehensiveness of these difficult items in patients who may have experienced skin thickening and related symptoms, we interviewed nine patients with established SSc. Their opinion on comprehensiveness of Q7 (cold sensitivity), Q8 (Raynaud's phenomenon), and Q16–17 were sought. We also tested the feasibility of adding photographs of Raynaud's

Table 1 Demographics of participants

	Cognitive debriefing interviews			Pilot testing				
	English version ($N = 30$)	Chinese version ($N = 15$)	Overall ($N = 45$)	English version ($N = 93$)	Chinese version ($N = 23$)	CTD ($N = 17$)	Non-CTD ($N = 99$)	Overall ($N = 116$)
Age, mean (SD)	44.7(13.6)*	55.2(11.4)*	48.2(13.7)	48.4(15.1)**	58.6(10.6)**	58.3(11.2)*	49.1(15.0)*	50.4(14.9)
Male, *n* (%)	11(36.7)	3(20.0)	14(31.1)	20(21.5)	7(30.4)	4(23.5)	23(23.2)	27(23.3)
Ethnicity, *n* (%)								
Chinese	21(70.0)	15(100.0)	36(80.0)	66(71.0)	23(100.0)	15(88.2)	74(74.8)	89(76.7)
Malay	4(13.3)	–	4(8.9)	13(14.0)	–	1(5.9)	12(12.1)	13(11.2)
Indian	2(6.7)	–	2(4.4)	8(8.6)	–	–	8(8.1)	8(6.9)
Others	3(10.0)	–	3(6.7)	6(6.4)	–	1(5.9)	5(5.1)	6(5.2)
Education level, *n* (%)								
Secondary or lower (<= 10 years education)	8(26.7)	6(40.0)	14(31.1)	17(18.3)**	14(60.9)**	8(47.1)	23(23.2)	31(26.7)
Diploma (11–14 years education)	9(30.0)	3(20.0)	12(26.7)	41(44.1)**	7(30.4)**	6(35.3)	42(42.4)	48(41.4)
Degree or above (>= 15 years education)	11(36.7)	6(40.0)	17(37.8)	35(37.6)**	2(8.7)**	3(17.6)	34(34.3)	37(31.9)
Unknown	2(6.7)	–	2(4.4)	–	–	–	–	–
Presenting symptoms, *n* (%)	26(86.7)	14(93.3)	40(88.9)	91(97.9)	23(100.0)	17(100.0)	97(98.0)	114(98.3)

*$p < 0.05$, **$p < 0.01$

Table 2 Difficulties encountered in answering the original CSQ and modifications made to improve understandability

Items		Difficulties understanding the original CSQ questionnaire	n/N	Modifications and difficulties understanding them
Q1	Arthritis	Difficulty understanding "arthritis" due to unfamiliarity with the medical terms	4/21	"Arthritis" was changed to "joint pain or joint swelling"
		Unsure if the question was asking whether they had been diagnosed with arthritis or they had arthritis symptoms	9/21	
		Unsure if the symptom should be continuous or could be on and off	1/21	"Persistent" was added in front of the symptom as per discussion with developers
Q2	Morning stiffness of joint	Associated "joint stiffness" with "pain" because they felt pain when trying to move the affected joint	3/21	An explanatory note "difficulty in moving the joint" was added to "joint stiffness"
				"In the morning" was changed to "for most mornings" as per discussion with developers
		Ignored "lasting at least one hour" and/or "for more than 6 weeks"	4/21	Symptom duration was underlined to emphasize
Q3	Rheumatoid nodules	Difficulty understanding "nodules" and used the alternative "bumps" to comprehend	6/17	None
		Difficulty understanding both "nodules" and "bumps" due to unfamiliarity with the medical terms	1/17	An alternative term "lumps" was added
Q4	Joint swelling	Ignored "lasting more than 6 weeks" in the main question	1/21	Symptom duration was underlined to emphasize
		Associated "swelling" with "numbness"	1/21	None
		Difficulty understanding "finger (but not the joints nearest the fingernails)" due to unfamiliarity with the joints in the hand	2/21	A photograph of hand showing referred hand joints and wrist was added
Q5	Blood test results for RA	Difficulty understanding "rheumatoid arthritis" due to unfamiliarity with the medical terms	7/21	None
		Unsure of the tests for "rheumatoid arthritis"	4/21	Two most common tests for RA (rheumatoid factor (RF) and anti-CCP) were added
		Unsure of the criteria for a "negative" or "positive" result because they were not informed by their doctors	2/21	A response option "Do not know" was added
Q6	Blood test results for lupus	Difficulty understanding "lupus" due to unfamiliarity with the medical terms	8/17	None
		Difficulty understanding "antinuclear antibody", "ANA", "FANA" and "LE prep"	15/17	"FANA" and "LE prep" were removed as they are not commonly done in Singapore
Q7	Cold sensitivity	Difficulty understanding "unusually sensitive" and interpreted it based on their own experiences such as "the first person to feel cold" and "only feel cold in −25 degree celsius"	9/21	"Unusually sensitive" was changed to "get cold easily" and two examples ("reaching into the freezer" and "air-conditioning") were added
		Interpreted "fingers" as "whole hand"	1/21	None
Q8	Color change in cold	Interpreted "fingers" as "whole hand"	1/21	None
Q9	Oral/ nasal ulcer	Unsure what "sores" are but associated "sores" with "pain"	1/17	An alternative term "ulcers" was added to "sores" as "ulcers" is more commonly used in Singapore
		Difficulty understanding "sores"	3/17	
Q10	Malar rash	None		
Q11	Photosensitivity	Difficulty understanding "skin break out" and used the alternative "rash" to comprehend	1/17	"Skin break out" was removed as per discussion with developers
		Couldn't tell the difference between "rash" and "sunburn"	4/17	None

Table 2 (continued)

Items		Difficulties understanding the original CSQ questionnaire	n/N	Modifications and difficulties understanding them
Q12	Serositis	Difficulty understanding "pleurisy" and used the alternative "chest pain made worse with deep breaths" to comprehend	14/17	None
		Ignored "made worse with deep breaths"	3/17	"Pleurisy" was shifted in brackets after "chest pain made worse with deep breaths" as an explanatory note
Q13	Alopecia	Associated "rapid" with "constant"	1/17	None
Q14	Seizure	Difficulty understanding "seizure", "convulsion" and "fit" due to unfamiliarity with the medical terms	4/21	None
Q15	Finger swelling	Skipped "puffy" and used "swollen" to comprehend	2/17	None
Q16	Skin thickening over face, neck, trunk and limbs	Difficulty understanding "trunk"	9/21	"Trunk" was changed to "other parts of the body" – 2 out of 9 participants considered "fingers" as "other parts of the body". "Except hands and feet" was added to emphasize as per discussion with developers
		Difficulty understanding "thickening" or "tightening"	6/21	None (no modification was done as there's no clearer way to explain)
		Associated "thickening" and "tightening" with "stiffness"	3/21	
Q17	Skin thickening over fingers and toes	Difficulty understanding "thickening" or "tightening"	4/17	
		Associated "thickening" and "tightening" with "stiffness"	2/17	
Q18	Digital scars	Difficulty understanding "sores"	4/17	"Sores" was changed to "ulcers or blisters" which are more commonly used in Singapore
		Ignored "sores"	1/17	"Leaving scars" was changed to "that result in scars" – 1 out of 9 participants reported difficulty understanding "scars", no modification was done as the majority of participants and the team deemed that the current wording was clear
		Ignored "leaving scars"	2/17	
Q19	Muscle weakness	Associated "weakness" with "pain"	2/17	An explanatory note "lack of strength without pain" was added to "muscle weakness"
		Associated "weakness" with "pain" and "stiffness"	2/17	
		Difficulty understanding "muscle weakness"	2/17	
Q20	Lower extremity proximal muscle weakness	Associated "weakness" with "pain"	4/17	
		Associated "weakness" with "stiffness from sitting down for too long"	2/17	
		Associated "weakness" with "giddiness"	2/17	
		Misinterpreted the question as "sitting down for 3 months", "weight loss from illness", and "having problems standing up" respectively	3/17	
Q21	Upper extremity proximal muscle weakness	Associated "weakness" with "pain"	3/17	
		Associated "weakness" with "pain" and "stiffness"	1/17	
		Couldn't imagine which part of the body was affected when combing the hair	1/17	
Q22	Dry eyes	Difficulty understanding "gritty" and used the alternative "sandy" to comprehend	4/21	An alternative term "persistent dry eyes" was added and "gritty or sandy sensation" was shifted in brackets as an explanatory note
		Associated "gritty or sandy sensation" with dryness or soreness	4/21	

Table 2 (continued)

Items		Difficulties understanding the original CSQ questionnaire	n/N	Modifications and difficulties understanding them
		Associated "gritty or sandy sensation" with "poor vision"	2/21	
Q23	Dry mouth	Ignored "awakening you"	4/21	"Awakening you and requiring a drink of water" was changed to "that wakes you up"
		Associated "dry mouth" with "sore throat or pain"	1/21	None
Q24	Anemia	Difficulty understanding "anemia" due to unfamiliarity with the medical terms	6/17	An explanatory note "lack of red blood cells" was added
Q25	Leukopedia	Difficulty understanding "white cell count" due to unfamiliarity with the medical terms	2/17	An explanatory note "lack of white blood cells" was added
Q26	Low platelet count	Difficulty understanding "platelet count" due to unfamiliarity with the medical terms	4/17	An explanatory note "lack of blood clotting component" was added
Q27	Proteinuria	Difficulty understanding "protein in your urine" due to unfamiliarity with the medical terms	5/17	None
		Associated "protein in your urine" with "diabetes"	1/17	
Q28	Discoid rash	Difficulty understanding "discoid lupus" due to unfamiliarity with the medical terms	15/17	None
Q29	Pulmonary fibrosis	Difficulty understanding "pulmonary fibrosis" and used the alternative "scarring of the lungs" to comprehend	3/17	None
		Difficulty understanding both "pulmonary fibrosis" and "scarring of the lungs"	10/17	An alternative term "hardening" was added to "scarring"
Q30	Elevated muscle enzyme	Difficulty understanding "CPK" and used the alternative "muscle enzyme" to comprehend	2/17	"CPK" was changed to "creatine kinase (CK)" and shifted in brackets as an explanatory note for "muscle enzyme" as per discussion with developers
		Difficulty understanding "CPK" and "muscle enzyme" due to unfamiliarity with the medical terms	10/17	

phenomenon. All SSc patients reported no difficulty understanding any items but half of them would change their answers to Q8 as their symptoms were not as severe as what were shown in the photographs. As such, no photographs of Raynaud's phenomenon were added to the CSQ.

Difficulties encountered by the 21 CDI participants when answering the original CSQ and the changes we made to improve its understandability are shown in Table 2. In brief, the reported issues fell into three main categories: (1) Difficulty understanding/misinterpretation of medical terms/symptoms. To address this, we added alternative terms, explanatory notes, and photograph, as summarized in Table 2. Some of the alternative terms were elicited from participants with probing. For example, out of the 21 participants, 2 reported difficulty understanding "arthritis" in Q1 and 9 were unsure if the item was asking whether they had been diagnosed with arthritis or they had arthritis symptoms. We therefore changed "arthritis" to "joint pain or joint swelling" after clarifying the original intent of the item with the developers. Also, two participants reported difficulty understanding "finger (joints) but not the joints nearest the fingernails" (Q4). We therefore added a photograph of a hand with markings for the metacarpophalangeal (MCP), proximal interphalangeal (PIP) joints, and wrist to aid comprehension. (2) Ignoring the duration and/or location of symptoms. To address this, we underlined the symptom durations and locations. (3) Unsure of the tests for rheumatic conditions and the interpretation of test results. To address this, we added examples of tests and a response option "Do not know".

The above-mentioned modifications were tested on nine subsequent English-speaking participants. Two of them included "fingers" as "other parts of the body" when answering Q16 (skin thickening over face, neck, limbs, and other parts of the body); we thus added "except hands and feet" in the question to avoid misinterpretation as per discussion with the developers (Table 2). All nine participants reported ease of comprehension with the remaining changes in the CDIs and thus no further modifications were made.

Chinese version

The common Chinese translation was administered to six Chinese-speaking participants who completed all items. All 6 participants reported no/minimum difficulty in understanding 13 items and thus no modifications were made (Table 3). The main issue with the remaining items was the difficulty reading the Chinese translation for medical terms, while the corresponding English terms were easily understood during the CDIs. We thus decided to retain the original English medical terms in the Chinese version. We tested these modifications on another nine Chinese-speaking participants. All these participants reported no difficulty understanding the modifications except one participant with less than 6 years of education who had difficulty understanding some of the body parts in both English and Chinese, which was deemed to be specific to this participant. As such, no further modifications were made to the Chinese version.

Pilot testing

Participants

We approached 192 newly referred subjects who fulfilled the inclusion criteria, of which 117 (61%) consented and 116 (60%) completed the cross-culturally adapted questionnaire in their preferred language (Table 1). Participants had a mean age of 50 years and were mostly female (77%), Chinese (77%), with more than 10 years of education (above secondary education: 73%), and symptomatic (98%) at the time of study enrollment.

Ninety-three participants (80%) completed the Singapore English version and 23 (20%) completed the Singapore Chinese version. Compared to participants who completed the English version, those who completed the Chinese version were relatively older (mean age: 59 years vs 48 years) and had fewer years of education (secondary or below: 61% vs 18%). Participants spent a mean duration of 6.5 and 7.5 min answering the English and the Chinese version, respectively. All participants reported ease of comprehension with both adapted versions.

A total of 17 participants (15%) were diagnosed with a CTD (13 RA, 2 SLE, 1 SSc, and 1 SS). Sixteen were diagnosed on the first visit, and one was diagnosed on the second visit to the clinic. These 17 participants who had CTDs were relatively older than participants who were not diagnosed with CTDs (mean age: 58 years vs 49 years). Out of the remaining 99 participants, 14 were diagnosed with rheumatologic conditions not screened for by the CSQ (deemed as non-CTD for purpose of assessing the performance of the adapted CSQ): 1 with seronegative arthritis, 2 with palindromic rheumatism, 2 with psoriatic arthritis, 1 with axial spondyloarthritis, 8 with undifferentiated CTD, and 85 were deemed to have no features of CTD.

Performance of the adapted CSQ

The overall sensitivity and specificity of the adapted CSQ to identify a CTD were 71% (95% CI 44–90%) and 58% (95% CI 47–68%), respectively (Table 4). The PPV was 22% (95% CI 12–36%), NPV was 92% (95% CI 82–97%), LR+ was 1.7 (95% CI 1.1–2.4), and LR− was 0.5 (95% CI 0.2–1.1). One participant who was diagnosed with RA scored negative for RA but positive for SSc and was deemed to have been classified as having a CTD by the adapted CSQ. The adapted versions failed to identify individual CTD in 6 out of 17 participants (3 with RA, 1 with SLE, 1 with SSc, and 1 with SS). A

Table 3 Difficulties encountered in answering the adapted CSQ questionnaire Chinese version and modifications made to improve understandability

Items		Difficulties understanding the common Chinese translation	n/ N	Modifications and difficulties understanding them
Q1	Arthritis	Unsure which joint the question was referring to	1/6	None
Q2	Morning stiffness of joint	Difficulty understanding the Chinese translation for "stiffness"	1/6	None
Q3	Rheumatoid nodules	Difficulty understanding the Chinese translation for "nodules/ bumps/ lumps"	3/6	The original English terms were retained—1 out of 9 participants reported difficulty understanding "elbow" and "ankle" in both English and Chinese, no modification was done as the majority of participants and the team deemed that the current wording was clear
		Difficulty understanding the Chinese translation for "elbow"	4/6	
		Difficulty understanding the Chinese translation for "ankle"	3/6	
Q4	Joint swelling	Associated "swelling" with "pain"	2/6	None
		Difficulty understanding the Chinese translation for "elbow"	3/6	The original English terms were retained—1 out of 9 participants reported difficulty understanding "elbow" in both English and Chinese, no modification was done as the majority of participants and the team deemed that the current wording was clear
		Difficulty understanding the Chinese translation for "knee"	1/6	
Q5	Blood test results for RA	Difficulty understanding "rheumatoid arthritis" and its tests	3/6	None
		Unsure of the criteria for a "negative" or "positive" result because they were not informed by their doctors	3/6	
Q6	Blood test results for lupus	Difficulty understanding "lupus" and its tests	3/6	None
Q7	Cold sensitivity	None		
Q8	Color change in cold	None		
Q9	Oral/ nasal ulcer	Difficulty understanding the Chinese translation for "ulcers/ sores"	4/6	The original English terms were retained—1 out of 9 participants reported difficulty understanding "ulcer" in both English and Chinese, no modification was done as the majority of participants and the team deemed that the current wording was clear
Q10	Malar rash	Difficulty understanding the Chinese translation for "cheeks"	2/6	The original English term was retained
		Difficulty understanding "rash"	1/6	None (no modification was done as the majority of participants and the team deemed that the current wording was clear)
Q11	Photosensitivity	Difficulty understanding "sunburn"	1/6	None (no modification was done as the majority of participants and the team deemed that the current wording was clear)
		Couldn't tell the difference between "rash" and "sunburn"	2/6	
Q12	Serositis	Ignored "made worse with deep breaths" as no chest pain present	2/6	None
Q13	Alopecia	None		
Q14	Seizure	Difficulty understanding the Chinese translation for "seizure/convulsion/fit"	3/6	The original English terms were retained—1 out of 9 participants reported difficulty understanding "seizure" in both English and Chinese, no modification was done as the majority of participants and the team deemed that the current wording was clear

Table 3 (continued)

Items		Difficulties understanding the common Chinese translation	n/N	Modifications and difficulties understanding them
Q15	Finger swelling	None		
Q16	Skin thickening over face, neck, trunk and limbs	Difficulty understanding "thickening" Associated "thickening" and "tightening" with "stiffness"	1/6 2/6	None
Q17	Skin thickening over fingers and toes	Difficulty understanding "thickening" Associated "thickening" and "tightening" with "stiffness"	1/6 2/6	None
Q18	Digital scars	Difficulty understanding the Chinese translation for "ulcers"	4/6	The original English term was retained—1 out of 9 participants reported difficulty understanding "ulcers" but used the alternative "blisters" to comprehend, no further modification was made
Q19	Muscle weakness	None		
Q20	Lower extremity proximal muscle weakness	None		
Q21	Upper extremity proximal muscle weakness	None		
Q22	Dry eyes	None		
Q23	Dry mouth	None		
Q24	Anemia	None		
Q25	Leukopedia	None		
Q26	Low platelet count	Difficulty understanding "platelet count" due to unfamiliarity with the medical terms	2/6	None
Q27	Proteinuria	Difficulty understanding "protein in your urine" due to unfamiliarity with the medical terms	2/6	None
Q28	Discoid rash	Difficulty understanding "discoid lupus" due to unfamiliarity with the medical terms	5/6	None
Q29	Pulmonary fibrosis	Difficulty understanding "pulmonary fibrosis" and used the alternative "hardening or scarring of the lungs" to comprehend	3/6	None
Q30	Elevated muscle enzyme	Difficulty understanding "muscle enzyme" and "CK"	5/6	None

Table 4 Performance of the adapted CSQs

		Diagnosis by classification criteria		
		CTD	Non-CTD	Total
Classification by adapted CSQs	CTD	12	42	54
	Non-CTD	5	57	62
	Total	17	99	116

closer examination found that compared to the rest of the participants, these six participants had relatively fewer years of education on average and some of them spent a much longer time answering the adapted questionnaire (Table 5).

Discussion

In this study, we cross-culturally adapted the CSQ into Singapore English and Singapore Chinese. We found the adapted CSQ performing satisfactorily in identifying patients with CTDs referred for assessment. Although the performance of the adapted CSQ was relatively lower than the original CSQ studied in the USA, it was comparable to the adapted versions studied in Korea and Germany. To the best of our knowledge, this is the first study adapting the CSQ in South East Asia. Our results are promising and provide a basis for further research to screen for CTDs in the Asian populations, in which several CTDs present differently and are associated with higher morbidity and mortality than in other populations.

The cross-cultural adaptation process surfaced several issues which bear further discussion. First, it confirmed the relevance of all items in the original CSQ and identified specific modifications needed to improve respondent understanding. Second, during the CDIs, lower health literacy was observed in our participants with fewer years of education compared to those with more years of education (Tables 2 and 3). These participants had challenges understanding relatively simple medical terms that were used in the CSQ (e.g., ulcers, rashes). They were also more likely to be unaware of the relevant blood tests that had been done previously and the test results. Lower health literacy can be mitigated to some extent by refinements to the questionnaire, but cannot be totally mitigated, and this is reflected in the approach taken in this study where explanations and simplified wordings were used where possible. Third, difficulty in reading the Chinese translation of medical terms was also observed in some of our Chinese-speaking participants. No difficulty in understanding, however, was reported when the Chinese terms were read out to them. Some of these participants with fewer years of education were more comfortable with certain English terms than

Table 5 False negative cases of CTD screening using the adapted CSQ questionnaires

CTD condition	Participant	Age	Gender	Education level	Questionnaire version	Time spent (min)	Reason
RA	QV0057	59	Female	Diploma (11–14 years)	English	8	Answered "No" to Q4a (swelling over wrist) and "Negative" to Q5a (blood test results for RA) despite swelling over bilateral wrists and positive RF and anti-CCP
	QV0099	56	Female	Diploma (11–14 years)	English	3	Answered "No" to Q4 (joint swelling) as no joint swelling
	QV0102	59	Female	No formal education (< 6 years)	Chinese	6	Answered "No" to Q4 despite swelling over multiple joints
SLE	QV0013	55	Male	Degree or above (> = 15 years)	English	6	Answered "No" to Q6 (blood tests for lupus), Q9 (oral/ nasal ulcers), Q24 (anemia), and Q25 (leukopedia) despite positive ANA, nasal ulcers, low hemoglobin/ RBC, and low WBC count
SSc	QV0051	55	Female	Secondary (7–10 years)	Chinese	7	Answered "No" to Q18 (digital scars) and Q29 (pulmonary fibrosis) despite pitting scars on fingertip and history of interstitial lung disease
SS	QV0087	70	Female	Diploma (11–14 years)	English	12	Answered "No" to Q6 and Q23 (dry mouth) despite positive ANA and dry mouth

the Chinese terms. This might be caused by the nature of the bilingual education system in Singapore where English is the medium of instruction in school and the mother tongues of different ethnic groups are only taught as academic subjects (38). It is likely that our participants have not learned these Chinese terms in school or are not using them commonly in daily conversation. Since our participants were not able to provide any alternative terms in Chinese that are easier to understand, we decided to retain the English medical terms in the Chinese version of adapted questionnaire. Fourth, we were surprised that photographs of Raynaud's phenomenon were not of additional use but could potentially mislead symptomatic respondents as they tend to compare their own symptoms with what are shown in the photographs. This could be resolved by presenting the entire spectrum of severity of the condition but would be more feasible using other approaches (e.g., digital platforms) than in the hard copy questionnaire. To avoid misleading the respondents, we decided not to add these photographs in the CSQ.

In pilot testing, the overall performance of the adapted CSQ (sensitivity 71%, specificity 58%) was relatively lower than the original paper (sensitivity 83 to 96%, specificity 83 to 93%) (20) but comparable to the adaptation studies conducted in Korea (sensitivity 78 to 100%, specificity 69 to 95%) and Germany (sensitivity 78%, specificity 80%) (15, 16) as well as our own pilot study with the original CSQ (sensitivity 72%, specificity 61%). It is worth highlighting that, in contrast to the current study, the other studies mentioned above were performed on patients with established CTDs who would have gained better knowledge on their diseases from the consultations and thus have higher health literacy compared to the new referrals in our study. Some examples of low health literacy were identified in the false negative cases in the current study (Table 5), which could have contributed to the lower performance of our adapted CSQ. This also highlights that cross-cultural adaptation can partially but not totally mitigate the impact of poor health literacy. Since health literacy was not measured in this study, we performed subgroup analyses by participants' years of education instead. We did not observe any significant association between performance of the adapted CSQ and years of education. This might be due to the fact that length of education is not a good indicator of health literacy levels (39). In addition to health literacy, the performance of the adapted CSQ might also have been negatively influenced by the following: (1) the population we studied were newly referred patients from primary care, the majority of whom were in the early stage of the disease and might have had too few symptoms to score positive on the adapted CSQ; (2) the classification of some CTDs (e.g., SS) relies heavily on the test results, which might not be available for our newly referred patients before their first visit to the rheumatology specialist outpatient clinic; and (3) small sample size in the pilot assessment. Modifying the scoring algorithm or lowering the threshold score might be able to further improve the sensitivity of the adapted questionnaire in this case. It is possible that a higher sensitivity and specificity would be achieved if the adapted questionnaire was administered by an interviewer such as a healthcare provider considering the poor health literacy observed in some of our participants whose perception may subject to errors without guidance (40). However, our ultimate goal is to facilitate early identification of potential CTDs in the population by applying the adapted CSQ in the primary care and general population settings if it is proven sensitive in screening for CTDs. We have thus decided to have our participants self-administer the adapted CSQ before they see their rheumatologists for the first time in this current study, in which the setting would be similar to the primary care or general population settings where an interviewer might not be readily available. In the next phase of our study, we plan to adopt digital platforms such as web-based and mobile applications with more explanatory text and images for screening CTDs with the adapted CSQ, which would likely improve the utility of the screening questionnaire.

Limitations

The main limitation of this study is that although we selected the study sample representative of the intended users of the CSQ—symptomatic patients seen in primary care settings, results from the study might not generalize to another intended user group, namely subjects in the general population who might be concerned that they have a CTD. The likelihood of a CTD is likely to be lower in the general population than in the primary care setting. However, this is the first step towards a larger scale pilot of these forms in the primary care setting. Second, our sample size for the pilot testing is relatively small. While the overall performance of the adapted questionnaire is promising, validation in a larger sample is required and is currently ongoing.

Conclusion

The CSQ was cross-culturally adapted into Singapore English and Singapore Chinese. The cross-culturally adapted CSQ appears to be a promising tool for facilitating early identification of potential CTDs in the multi-ethnic Asian population. Further study using a larger sample size is required and is currently ongoing.

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Compliance with ethical standards

Disclosures None.

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