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314: Incorporating Patient-Reported Outcomes in Drug Pricing and Reimbursement Decision-Making: Development and Validation of Chrome System in China

The Development of the China Health Related Outcomes Measures: Generic Version (CHROME-G)

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Disclosure

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ORIGINAL RESEARCH ARTICLE

China Health Related Outcomes Measures (CHROME): Development of a New Generic Preference-Based Measure for the Chinese Population

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Abstract

Background and Objectives Existing generic preference-based measures were all developed in Western countries. Evidence shows that the Chinese population may have different perceptions about health and health-related quality of life. This study aimed at developing a descriptive system of a new generic preference-based measure under the initiative of China Health Related Outcomes Measures (CHROME).

Methods Qualitative data were collected through semi-structured interviews conducted in-person or online. Respondents were recruited from both the general public and populations with chronic diseases. Open-ended questions about the respondent's perception of general health and important aspects of health-related quality of life were asked. Probing questions based on a systematic review of existing generic preference-based measures were also used. The framework analysis was used to synthesize the qualitative data. Candidate items for the descriptive system were selected following the ISPOR and COSMIN guidelines. Expert panel review and cognitive debriefings were conducted for further revisions.

Results Qualitative interviews were conducted among 68 respondents, with 48.5% male and a mean age of 47.8 years (range 18–81 years). In total, 1558 codes were identified and then aggregated to 31 sub-themes and corresponding six themes to inform the development of the initial version of the descriptive system. Feedback from the expert panel survey and meeting (n = 15) and the cognitive debriefing interviews (n = 30) was incorporated into the revised version of the measure. Finally, the generic version of CHROME (CHROME-G) included 12 items across six domains, namely, pain, fatigue, appetite, mobility, vision, hearing, sleeping, daily activities, depression, worry, memory, and social interactions. The descriptive system used a mix of four-level and five-level response options and a 7-day recall period.

Conclusions The CHROME-G is the first generic preference-based measure to be developed based on the inputs from the Chinese populations.

1 Introduction

Economic evaluations of healthcare technologies generate key cost-effectiveness evidence to inform coverage decision making [1, 2]. A cost-utility analysis with the outcome measure of quality-adjusted life-years is recommended in many countries, including China [1, 2]. China's latest version of economic evaluation guidelines published in 2020 recommends the use of generic preference-based measures (PBMs) in measuring health utilities for quality-adjusted life-years [3]. Instead of recommending a specific instrument, the guidelines prefer the use of the instruments with a value set developed from a representative sample of the Chinese general population [1, 4–6]. Currently, among the commonly used generic PBMs are the EQ-5D (including EQ-5D-3L and EQ-5D-5L) and SF-6D (the latest version SF-6Dv2), which have Chinese versions and corresponding value sets available [4–7].

All existing generic PBMs were developed in Western countries [8, 9]. Evidence shows that the Chinese population might have different perceptions about health and health-related quality of life (HRQoL) compared with people in Western countries [10–12]. Socio-cultural adaptation may

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Objective of our study

- **The China Health Related Outcomes Measures – generic version (CHROME-G) was an initiative aimed at developing a GPBMs specifically for Chinese populations.**
  - ✓ For more comprehensive and accurate measurement of the HRQoL or health utility of the general Chinese population

Sample for the qualitative interviews

- **Basic inclusion criteria**
  - ✓ age≧18; Chinese nationality; had lived in China for the past 5 years; were able to read and communicate in Chinese; without cognitive impairment
- **Total 68 respondents**
  - ✓ **40 general population**
    - Stratified by gender, age, education, urban/rural residence
  - ✓ **28 patients population**
    - Select 15 types of health conditions with the heaviest disease burden in China according to the Global Burden of Diseases, Injuries, and Risk Factors Study 2017
    - Stratified by gender
- **Content saturation was reached after 63 interviews**

Demographic characteristics of the study sample

Characteristics	Qualitative interviews (N = 68)	
	Respondents from the general population (N = 40)	Respondents with chronic diseases (N = 28)
Gender		
Female	20 (50.0%)	15 (53.6%)
Age, mean±SD	46.0 ± 15.7	50.5 ± 18.8
Age group, years		
18-29	8 (20.0%)	4 (14.3%)
30-39	8 (20.0%)	8 (28.6%)
40-49	8 (20.0%)	1 (3.5%)
50-59	7 (17.5%)	4 (14.3%)
≥60	9 (22.5%)	11 (39.3%)
Education		
Primary or lower	10 (25.0%)	2 (7.1%)
Junior high school	16 (40.0%)	3 (10.7%)
Senior high school	7 (17.5%)	8 (28.6%)
College or higher	7 (17.5%)	15 (53.6%)
Residence		
Urban	24 (60.0%)	24 (85.7%)
Rural	16 (40.0%)	4 (14.3%)

Number of respondents representing the 31 provinces of mainland China

* 15 types of selected conditions were neck pain, depressive disorders, anxiety disorders, blindness and visual impairment, stroke, headache disorders, oral conditions, chronic obstructive pulmonary disease, diabetes mellitus, chronic kidney disease, dermatitis, maternal disorders, upper digestive system diseases, breast cancer, and colorectal cancer.

Data collection for the qualitative interviews

- **Semi-structured qualitative interviews (2020.05-2020.11)**
  - ✓ Two interviewers completed all the interviews
  - ✓ 10 (14.7%) interviews were face to face and the rest online
- **Interview guide**
  - ✓ Informed consent form
  - ✓ Demographic information
  - ✓ **Open-ended questions**

    - To identify factors that respondent proposed on his/her own initiative

    "Why do you think your health status is not in a good condition?"

    "How does XXX (factors that the respondent mentioned) affect your health-related quality of life?"

    - To identify factors that respondents proposed after probing

    "What about social relationships?"

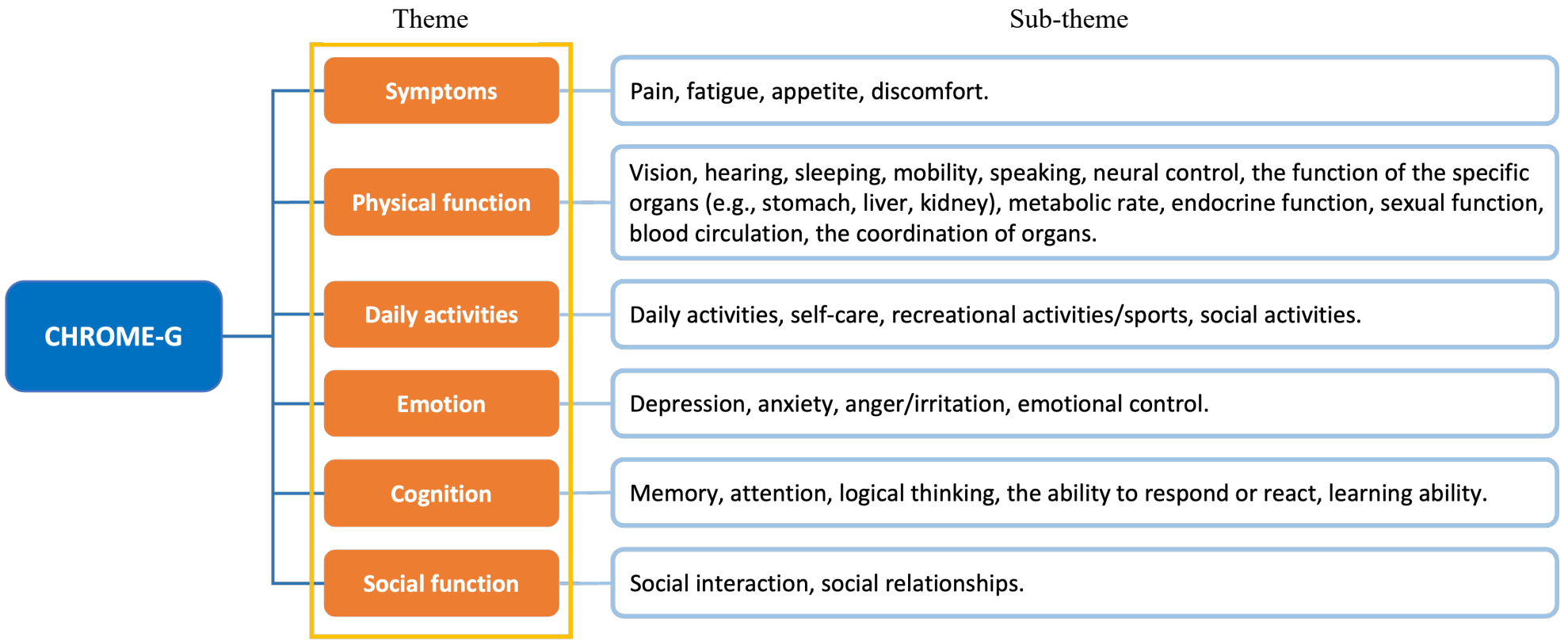
    "How does appetite affect your health-related quality of life?"
  - ✓ Summary question

Dimension	Item
Physical aspect	
Physical movement	Mobility (going outside and walking); climbing stairs; body inclining; bending over; squatting; kneeling; jumping; dexterity; vigorous activities (such as running, lifting heavy objects, laboring in the field); moderate activities (such as moving table, pushing vacuum cleaner, playing golf, riding bike)
Daily activity	Going to work; going to school; housekeeping; self-care (such as eating, bathing, dressing, grooming); doing things with friends and family; usual activities; ability of life; medical need
Pain/ Discomfort	Pain; discomfort; symptom
Physical function	Sense (vision, hearing, speaking, voice); fertility; breathing; sleeping; urination and defecation; sexual function; diet (appetite, taste); digestion; body constitution (hot palms and feet, afraid of cold, easy to catch a cold); sweating; the function of five internal organs (heart, liver, spleen, lungs, kidneys)
Vitality	Energy; tired/ feeble; physical power; spirit
External image	Complexion (face and lips); spirit of eyes
Lifestyle	Diet habit; drinking and smoking
Mental aspect	
Negative emotion	Sad/ depressed/ downhearted/ unhappy; worried/anxiety/ nervous; fear; annoyed; disappointed; despair; fretful; angry/irritable; shock; complaining; hesitent; confused; lonely; helpless; listless; lossing of confidence; feeling worthless; sense of burden; sense of defect; sense of insecurity; willing to give up
Positive emotion	Happy/joyful; passionate; grateful; confident; self-esteeming; satisfied; well-being/happiness; calm; carefree; joy of life; full of expectation; sense of security
Cognition	Learning; memory; thinking; solving problems; concentration; judgment; clear-headed
Life attitude	Optimistic; peace
Emotion control	Emotion control; emotion venting
Social aspect	
Social activities	Visiting family or friends; shopping; doing hobby activities, recreational activities, and religious activities; social and collective activities
Social relationship	Close relationships (with family and friends); interpersonal relationships (with colleagues, superior and subordinate); social integration/social isolation; social roles (roles in community and roles in sporting, church or cultural activities; taking social responsibility)

Probing: items extracted from the existing generic PBMs

Data analysis for the qualitative interviews

- **The process of the framework analysis identified 1558 unique codes across 129 code categories, which were subsequently grouped into 31 sub-themes and 6 theme.**

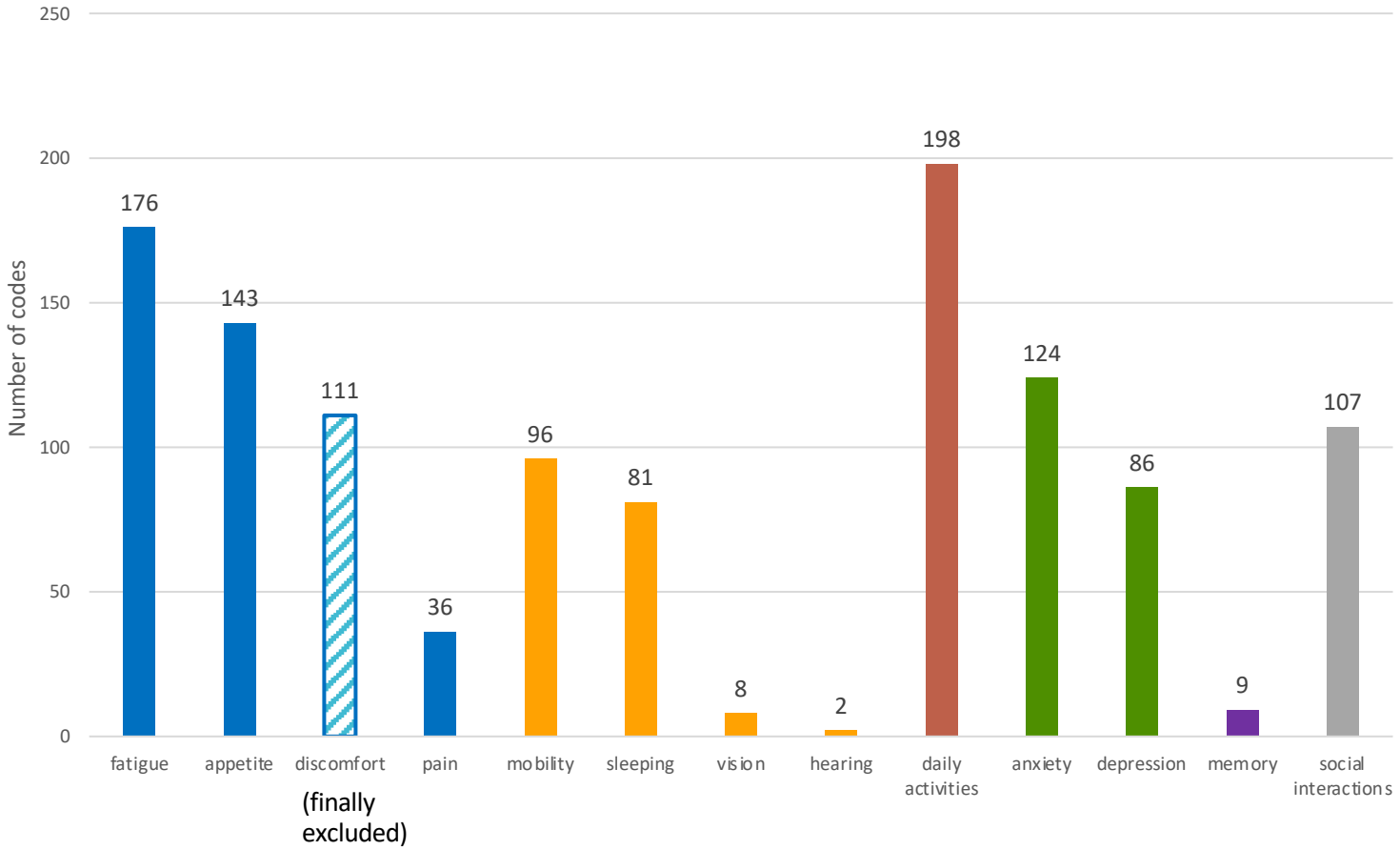


* Codes related to two non-health-related themes were excluded, namely, well-being (e.g., freedom, satisfaction, disappointment) and background (e.g., life rules/habits, social and financial status, ecological environment).

CHROME-G's domain identification

- **According to 7 principles, 13 sub-themes were selected to form the domains.**

- ✓ Capturing the constructs measured by the instrument under development
- ✓ Relevant to all members of the target population
- ✓ Worded in a clear manner and consistent with the expressions used by the target population
- ✓ Measuring a single construct, rather than a multi-dimensional concept
- ✓ Not likely to be prone to the ceiling or floor effects within the target population
- ✓ Appropriate for the recall period
- ✓ Appropriate for self-reporting

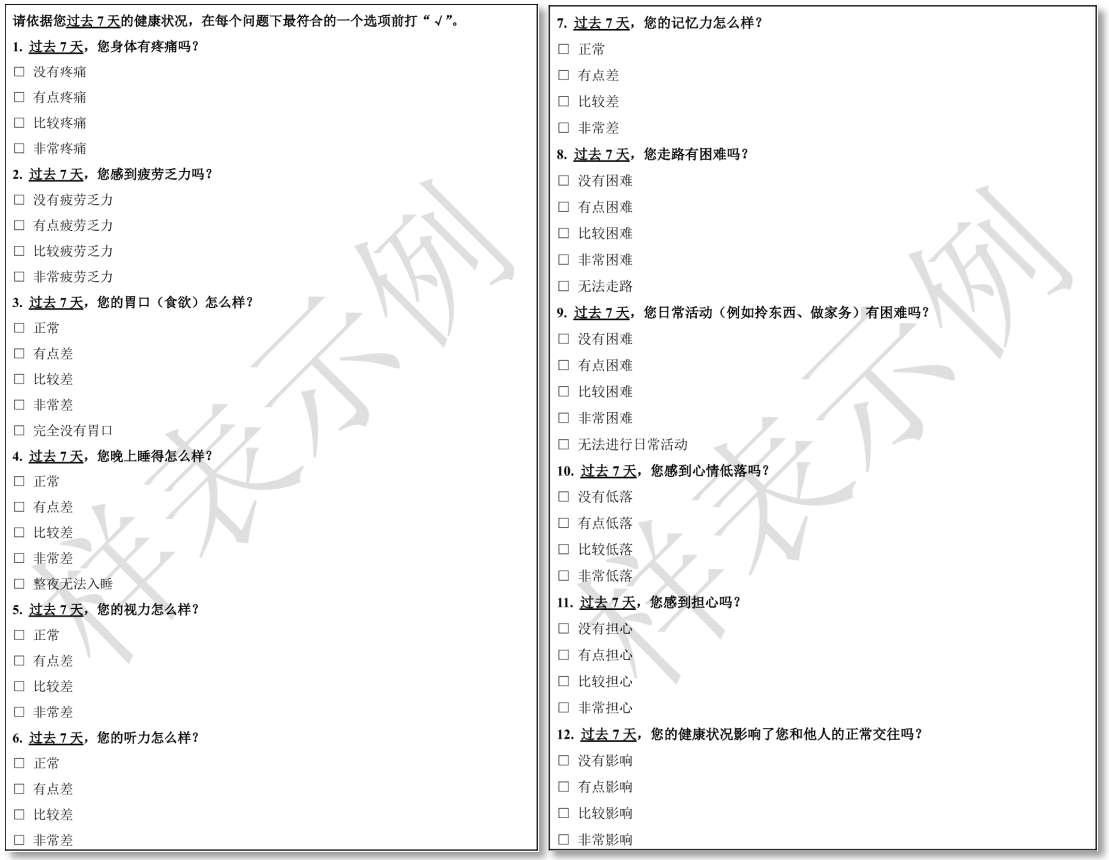


CHROME-G's item generation

- **Once written by the project team, items were modified through the expert advisory panel and the cognitive debriefing.**
  - ✓ Expert advisory panel: **15 experts** in the field of instrument development, pharmacoeconomics, clinical, and healthcare policy decision-making
  - ✓ Cognitive debriefing: **30 Chinese general population respondents**; conducted in Tianjin, Nanjing, Xi'an, Chengdu and Fuzhou

No.	Qualitative interview	Expert panel review	Cognitive debriefing interview		
	Version 1 (initial version)	Version 2	Version 3	Version 4	Version 5 (final version)
Recall period	Now/ the last week	Today/ the past 7 days	Today/ the past 7 days	The past 7 days	The past 7 days
1	Pain	RETAIN	REVISE (wording)	RETAIN	RETAIN
2	Fatigue	REVISE (wording)	REVISE (wording)	RETAIN	RETAIN
3	Mobility	RETAIN	REVISE (wording)	RETAIN	RETAIN
4	Daily activities	RETAIN	REVISE (adding examples)	REVISE (adding examples)	RETAIN
5	Vision	REVISE (wording)	REVISE (adding examples)	REVISE (wording)	REVISE (removing examples)
6	Hearing	REVISE (wording)	REVISE (adding examples)	REVISE (wording)	REVISE (removing examples)
7	Appetite	RETAIN	REVISE (wording)	REVISE (wording)	RETAIN
8	Sleeping	REVISE (wording)	REVISE (wording)	RETAIN	RETAIN
9	Depression	RETAIN	RETAIN	RETAIN	REVISE (wording)
10	Worry	RETAIN	RETAIN	RETAIN	RETAIN
11	Memory	RETAIN	RETAIN	RETAIN	RETAIN
12	Social interactions	REVISE (wording)	REVISE (wording)	REVISE (wording)	RETAIN
13	Discomfort	REVISE (wording)	REVISE (wording)	RETAIN	REMOVE

CHROME-G's descriptive system



请依据您过去 7 天的健康状况，在每个问题下最符合的一个选项前打“ √ ”。

1. 过去 7 天，您身体有疼痛吗？
☐ 没有疼痛
☐ 有点疼痛
☐ 比较疼痛
☐ 非常疼痛

2. 过去 7 天，您感到疲劳乏力吗？
☐ 没有疲劳乏力
☐ 有点疲劳乏力
☐ 比较疲劳乏力
☐ 非常疲劳乏力

3. 过去 7 天，您的胃口（食欲）怎么样？
☐ 正常
☐ 有点差
☐ 比较差
☐ 非常差
☐ 完全没有胃口

4. 过去 7 天，您晚上睡得怎么样？
☐ 正常
☐ 有点差
☐ 比较差
☐ 非常差
☐ 整夜无法入睡

5. 过去 7 天，您的视力怎么样？
☐ 正常
☐ 有点差
☐ 比较差
☐ 非常差

6. 过去 7 天，您的听力怎么样？
☐ 正常
☐ 有点差
☐ 比较差
☐ 非常差

7. 过去 7 天，您的记忆力怎么样？
☐ 正常
☐ 有点差
☐ 比较差
☐ 非常差

8. 过去 7 天，您走路有困难吗？
☐ 没有困难
☐ 有点困难
☐ 比较困难
☐ 非常困难
☐ 无法走路

9. 过去 7 天，您日常活动（例如拎东西、做家务）有困难吗？
☐ 没有困难
☐ 有点困难
☐ 比较困难
☐ 非常困难
☐ 无法进行日常活动

10. 过去 7 天，您感到心情低落吗？
☐ 没有低落
☐ 有点低落
☐ 比较低落
☐ 非常低落

11. 过去 7 天，您感到担心吗？
☐ 没有担心
☐ 有点担心
☐ 比较担心
☐ 非常担心

12. 过去 7 天，您的健康状况影响了您和他人的正常交往吗？
☐ 没有影响
☐ 有点影响
☐ 比较影响
☐ 非常影响

CHROME-G	*EQ-5D-5L*	*SF-6Dv2*
Pain	Pain/discomfort	Pain
Fatigue		Vitality
Appetite		
Sleeping		
Vision		
Hearing		
Memory		
Mobility	Mobility	
Daily activities	Usual activities	Role limitation
Depression	Anxiety/ depression	Mental health
Worry		
Social interactions		Social functioning
	Self-care	Physical functioning

Psychometric testing and comparative performance

- **Sample**
  - ✓ **1000 respondents** for the first survey, **328 respondents** for the retest survey (two weeks after the first survey)
  - ✓ Stratified by age, gender, education, urban/rural residence, and region of residence

- **Data collection (2021.12-2022.01)**
  - ✓ Self-completed online survey via mobile phone or computer
  - ✓ **First survey:** informed consent, quota screening, CHROME-G (including feedback), EQ-5D-5L and SF-6Dv2 (random order), basic information
  - ✓ **Retest survey:** quota screening, CHROME-G, EQ-5D-5L and SF-6Dv2 (same order as the first survey)
  - ✓ Quality control: time & IP address

Characteristics	First survey (N=1000) N (%)	Retest survey (N=378) N (%)	Chinese general population (%)
Gender			
Male	511 (51.1%)	206 (54.5%)	51.1%
Female	489 (48.9%)	172 (45.5%)	48.9%
Age, mean ± SD	44.69 ± 14.79	47.77 ± 13.34	N/A
Age group, years			
18-29	189 (18.9%)	45 (11.9%)	18.9%
30-39	195 (19.5%)	49 (13.0%)	19.6%
40-49	199 (19.9%)	95 (25.1%)	19.8%
50-59	191 (19.1%)	96 (25.4%)	19.1%
≥60	226 (22.6%)	93 (24.6%)	22.6%
Education			
Primary or lower	269 (26.9%)	109 (28.8%)	26.9%
Junior high school	390 (39.0%)	165 (43.7%)	39.1%
Senior high school	175 (17.5%)	60 (15.9%)	17.2%
College or higher	166 (16.6%)	44 (11.6%)	16.8%
Residence			
Urban	606 (60.6%)	217 (57.4%)	60.6%
Rural	394 (39.4%)	161 (42.6%)	39.4%
Region			
Northeast	80 (8.0%)	36 (9.5%)	7.7%
East	300 (30.0%)	110 (29.1%)	29.5%
North	120 (12.0%)	42 (11.1%)	12.5%
Central	160 (16.0%)	56 (14.8%)	16.0%
South	120 (12.0%)	44 (11.7%)	12.4%
Southwest	150 (15.0%)	56 (14.8%)	14.5%
Northwest	70 (7.0%)	34 (9.0%)	7.4%

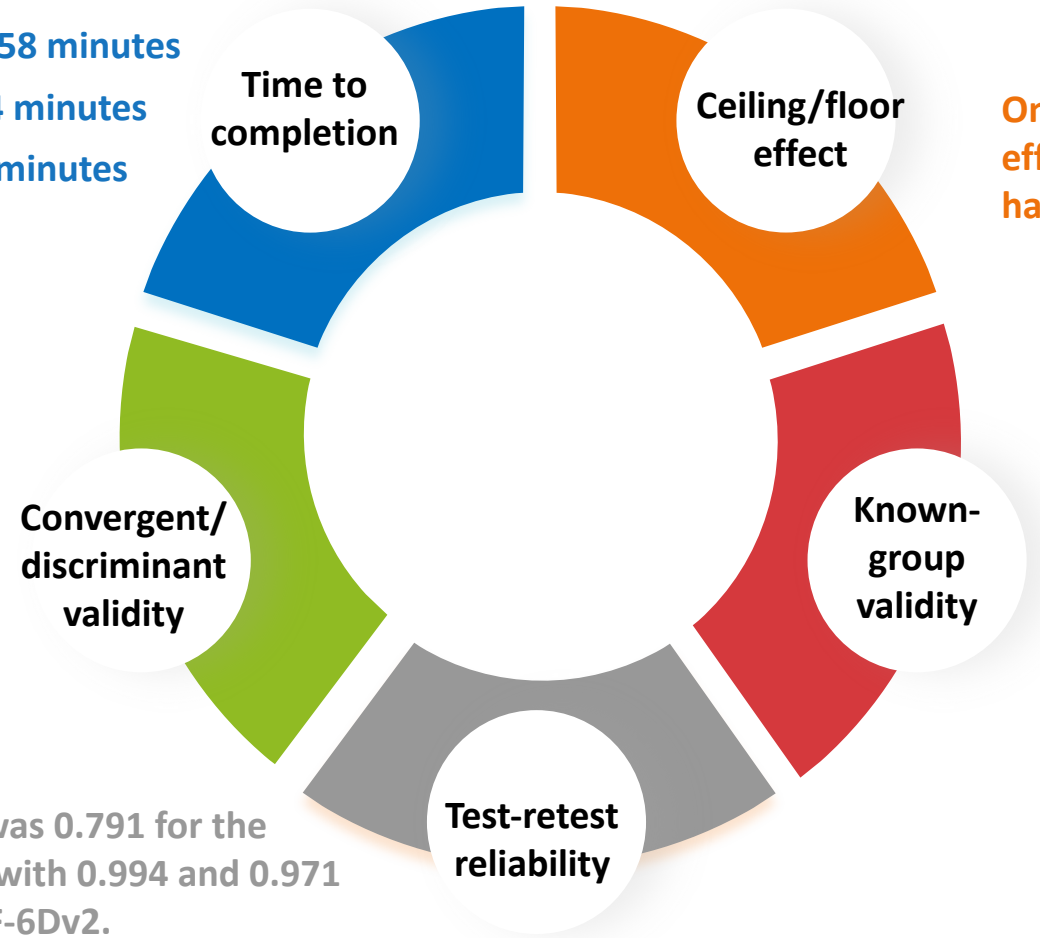
Psychometric testing and comparative performance

- **Data analysis**

CHROME-G: 2.03±0.58 minutes

EQ-5D-5L: 1.37±0.54 minutes

SF-6Dv2: 1.13±0.38 minutes



Only the EQ-5D-5L had a ceiling effect of 35.1%. No instruments had floor effect.

The range of Spearman rank's correlations was 0.45-0.62 for convergent validity and 0.14-0.46 for divergent validity.

The level sum scores of the three instruments were all significantly difference ($p<0.001$) across different health groups classified by self-reported health status, EQ-VAS scores, and number of self-reported chronic diseases.

The ICC for test-retest was 0.791 for the CHROME-G, compared with 0.994 and 0.971 for the EQ-5D-5L and SF-6Dv2.

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Thank you!

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