Patient-Reported Outcomes

Analyzing the Pain/Discomfort and Anxiety/Depression Composite Domains and the Meaning of Discomfort in the EQ-5D: A Mixed-Methods Study

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A B S T R A C T

Objectives: The EQ-5D has 2 composite domains: pain/discomfort (PD) and anxiety/depression (AD). This study aims to explore how respondents use the composites to self-report health and what the meaning of discomfort is in the EQ-5D for the general public.

Methods: Both qualitative and quantitative data were collected in an online cross-sectional survey involving a nationally representative general population sample in Hungary (n = 1700). Respondents completed the 5-level version of EQ-5D, followed by the composites split into individual subdomains. Open-ended questions were asked to explore respondents' interpretations and experiences of discomfort.

Results: Six different response behaviors were identified in the composites: "uniform" (21%-32%), "most severe" (30%-34%), "least severe" (16%-23%), "average" (2%-4%), "synergistic" (4%-5%), and "inconsistent" (13%-15%). Compared with the individual subdomains, many respondents under-reported their problems on both composites (PD 16%-22% and AD 6%-13%, $P < .05$). In respondents who scored differently in the 2 separate domains, mainly problems with the first subdomain determined responses in the composites (PD 66% and AD 61%). The discomfort subdomain in the EQ-5D captured more than 100 different problems, including pain, nonpain physical discomfort (eg, tiredness, dizziness, and nausea), and psychological discomfort (eg, anxiety, nervousness, and sadness). Women, older adults, and those in worse general health status more often considered discomfort as pain ($P < .05$).

Conclusions: We found empirical evidence of measurement error in the composite responses on the EQ-5D, including under- and inconsistent reporting, ordering effects, potential differential item functioning, and interdomain dependency. Our findings contribute new knowledge to the development of new and refinement of existing self-reported health status instruments, also beyond the EQ-5D.

Keywords: composite domains, content analysis, discomfort, EQ-5D-5L, measurement properties, mixed-methods research, self-reported health.

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Introduction

There are a growing number of preference-accompanied generic health status measures that can be used to inform resource allocation decisions.[1] These instruments typically comprise 2 parts, a self-completed questionnaire that describes health status along different domains of health and response levels within these (ie, the descriptive system) and a value set that enables to score the questionnaire based on societal preferences, the latter enabling the calculation of quality-adjusted life-years. Composite domains, combining multiple different but related domains of health into a single domain, are a commonly used approach to keeping the potential number of health states feasible for valuation. Several instruments, including the EQ-5D, SF-6D, and 15D, use composite domains to capture physical (eg, having

pain, discomfort, or symptoms) and mental symptoms (eg, being anxious, depressed, tense, downhearted, or low).[2]

The available methodological literature on the use and interpretation of composite domains to report one's own health is scarce and mainly limited to the EQ-5D.[3–9] The EQ-5D is one of the most frequently used preference-accompanied health status measures that is recommended in several national pharmacoeconomic guidelines worldwide.[10,11] It classifies health into 5 domains, 2 of which are composite domains, pain/discomfort (PD) and anxiety/depression (AD).[12] The composites in the EQ-5D may be considered a special form of double-barreled questions. Questions using the conjunction "or" pose a variety of challenges for both respondents completing the questionnaire and researchers interpreting the responses. Undoubtedly, the complexity of these questions may cause respondents to not know which component

of the question they are supposed to answer.[13–15] This increased cognitive burden on respondents may also result in longer completion time and higher number of missing responses.[16] A further apparent difficulty with such questions is that it is impossible to disentangle which part of the question (eg, pain or discomfort) was answered.

Existing qualitative evidence suggests that respondents demonstrate a good understanding of the concepts of pain, anxiety, and depression in the EQ-5D.[17–20] By contrast, there is a lack of conceptual clarity surrounding the term "discomfort."[21–24] Some generic preference-accompanied measures give examples for discomfort in their descriptive systems; for example, the discomfort and symptoms domain of 15D mentions "pain, ache, nausea, itching, etc," whereas the EQ-5D does not mention specific examples. Nevertheless, without any specification, it is not clear what respondents think of discomfort when they describe their health or value health states. A recent concept analysis found that individuals attribute not only physical but also psychological meaning to discomfort.[23] So far, no studies have been conducted to qualitatively explore the meaning of discomfort in any generic health status measure among members of the general population.

This study aims to explore (1) how respondents use the PD and AD composites to self-report health status on the EQ-5D, (2) what the meaning of discomfort is in the EQ-5D for the general public, and (3) whether sociodemographic and health-related characteristics of people affect what they consider as discomfort.

Methods

Study Design and Data Collection

Our study adopted a convergent mixed-methods design, where quantitative and qualitative data were collected in parallel. The integration of quantitative and qualitative data was achieved at the methods level through connecting the sampling frame and at the interpretation and reporting level through data transformation.[25] In November 2020, an online cross-sectional survey was conducted involving a large general population sample in Hungary. Nonprobabilistic quota-based sampling was applied to recruit respondents aged 18 years or older from members of an existing online panel. The study sought to attain an approximate representativeness applying "soft targets" for age, gender, education, place of living, and region. Upon completion of the questionnaire, online panelists earned survey points. Data collection was approved by the Research Ethics Committee of the Corvinus University of Budapest (no. KRH/343/2020). Respondents were asked to read a brief information sheet and to provide their informed consent before starting the survey.

5-Level Version of EQ-5D

The 5-level version of EQ-5D (EQ-5D-5L) health status measure aims to capture the respondent's current health status (recall period: today).[26] It consists of 2 parts, a descriptive system and a visual analogue scale (EQ VAS) with endpoints of 0 ("the worst health you can imagine") and 100 ("the best health you can imagine"). The descriptive system assesses health status across 5 domains (mobility, self-care, usual activities, PD, and AD) with 5 response levels in each (1 = no problems, 2 = slight problems, 3 = moderate problems, 4 = severe problems, and 5 = extreme problems/unable to), therefore defining a total of 3125 health profiles.

Survey Instrument

Respondents were asked to rate their own health at the time of the survey (ie, current health) on the EQ-5D-5L.[26] In addition, 3 modified versions of the EQ-5D-5L were also used to collect data on self-reported health. The selected modifications and some of their combinations have been used in earlier studies.[3,4,27] After completing the EQ-5D-5L and EQ VAS, the first adaptation asked respondents to fill in the composites split into 4 individual subdomains (the first 3 domains were not used). The second modification changed the recall period of the EQ-5D-5L and EQ VAS to the time when respondents felt the worst because of their health (ie, worst recalled health), and the third one combined the first 2 modifications; thus, the recall period was also changed for the 4 individual subdomains. The inclusion of worst recalled health was expected to increase variability in responses in the composite domains. The sequencing of EQ-5D-5L and EQ VAS modifications within the questionnaire is presented in Appendix 1 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2022.06.012.

Rather than imposing our preconceptions about the meaning of discomfort, we opted to explore the respondents' own interpretations of discomfort by open-ended questions. To avoid priming participants to focus on discomfort when filling in the EQ-5D-5L, all open-ended questions were asked after completing the EQ-5D-5L and the individual subdomains. The exact wording and placement of these questions are presented in Appendix 1 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2022.06.012. All respondents were asked 2 open-ended questions about the theoretical meaning of discomfort. Only those respondents who experienced any problems in the individual discomfort subdomain for current health or worst recalled health received open-ended questions about their experienced discomfort, respectively. Those reporting any pain in the individual pain subdomain were asked about their pain to further understand what the PD domain captures (eg, type, duration, and possible cause of pain).

Respondents were asked to identify their age, gender, level of education, place of living, geographical region, employment status, marital status, self-perceived health status (excellent to poor scale), and the presence of any chronic conditions or chronic consequences of acute conditions.

Data Analysis

Quantitative and qualitative data were first analyzed separately. Then, respondents' answers to the open-ended questions were transformed into numeric counts using content analysis and merged with the quantitative data for the mixed-methods analyses.

Quantitative analyses

Descriptive statistics were used to provide an overview of the sample's demographic and health-related characteristics. All analyses on EQ-5D-5L responses were first conducted for current health and then were repeated for worst recalled health. A series of cross-tabulations were created to explore the distribution of responses across the individual subdomains and composites. Chi-square test was used to compare (1) the proportion of respondents reporting problems in the composite versus problems in individual subdomains and (2) the proportion of respondents underreporting problems for PD and AD (ie, did not score the composite but did score an individual subdomain).

To explore variations in response behavior for each composite, we restricted the main analysis sample to those respondents who reported any health problems either in the composite or in any of the 2 individual subdomains. For respondents scoring at different levels in the 2 individual subdomains, we examined the presence of any ordering effect (ie, if the responses in the composite were mainly driven by the first mentioned [pain or anxiety] or the

second mentioned [discomfort or depression] subdomain). Two sensitivity analyses were conducted to evaluate the impact of potential inconsistencies in the data (Appendix 2 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2022.06.012). Correlations among EQ-5D-5L domains, the 4 individual subdomains, and EQ VAS were analyzed by Spearman's rank-order correlations. Correlation coefficients were interpreted as very weak (< 0.20), weak (0.20-0.39), moderate (0.40-0.59), strong (0.60-0.79), and very strong (≥ 0.80).[28] Statistical analyses were performed using Stata 14 (StataCorp. 2015, College Station, TX).

Qualitative content analysis

Text responses on the 4 open-ended questions about discomfort were analyzed using inductive content analysis in Microsoft Excel 2016 (Microsoft Corporation, Redmond, WA).[29] Four separate analyses were conducted: (1) theoretical examples for discomfort, (2) theoretical descriptions of discomfort, (3) examples for discomfort experienced on the day of the survey, and (4) examples for discomfort for worst recalled health.

For the first, third, and fourth parts of the analysis, the unit of analysis was a single word or a few words, whereas in the second analysis a clause or a sentence. First, we read all the 1700 respondents' text answers multiple times. Then, we constructed an initial coding framework using open coding. For coding examples for discomfort, subcategories of related content were grouped together as generic categories that were further grouped to form main categories. Descriptions of discomfort were categorized based on a shared meaning. Few examples that did not fit into any of these main categories were placed in an "other" category. Examples and quotes were selected to support each subcategory. Coding was performed by one researcher, and any uncertainties were resolved through discussion with the other researcher.

Mixed-methods analyses

Three sets of mixed-methods analyses were conducted. First, the sample was divided into subgroups based on how participants interpreted discomfort (considering their responses to all open-ended questions), and then we examined whether respondents' demographic characteristics and health status were associated with belonging to any of these particular groups. Second, we analyzed whether there was an association between the type of discomfort reported for current health and worst recalled health (considering responses on each open-ended question separately) and self-reporting it in the PD composite. Finally, we explored whether there was an association between respondents' overall interpretations of discomfort (considering their responses to all open-ended questions) and self-reporting discomfort in the individual subdomain. Proportions were compared using chi-square tests.

Results

Characteristics of the Study Population

Overall, 2502 individuals initiated the survey, 423 of whom (17%) were screened out because they did not consent and 379 (15%) did not finish the questionnaire. A total of 1700 respondents (68%) completed the survey. The sample was roughly representative of the Hungarian adult general population for age, gender, employment and marital status, place of residence, geographical region, and the presence of any chronic illness (Table 1).

Self-Reported Health in the Composites and Individual Subdomains

The distribution of responses across the composites and individual subdomains is presented in Table 2. In self-reporting current health, 44% of respondents reported problems in the composite PD, whereas 53% reported problems in either of the 2 individual subdomains ($P < .001$). In contrast, there was only a very small difference between self-reporting problems in the composite AD (34%) and in its 2 individual subdomains (36%) ($P = .350$). For worst recalled health, 78% reported any problems in the composite PD, whereas 87% separately and 52% reported problems in the AD composite and 60% separately ($P < .001$ for both).

In the composite, more respondents under-reported discomfort than pain (22% vs 16%, $P = .019$) and anxiety than depression (13% vs 6%, $P < .001$). In contrast, for worst recalled health, almost the same proportion of participants under-reported discomfort as pain (9% and 8%, $P = .224$), whereas again more respondents under-reported anxiety than depression (15% vs 11%, $P = .006$). The sensitivity analyses confirmed the robustness of these findings (Appendix 2 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2022.06.012).

Analysis of Response Behaviors

When describing current health, 968 and 674 subjects reported any problems in either the individual or corresponding composite domains of PD and AD, respectively. Six different response

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BOX 1. Response behaviors in the composite domains of EQ-5D.

1. **"Uniform":** respondent reports the same level of problems in both individual subdomains and the composite, for example, slight pain, slight discomfort, slight problems in the composite;
2. **"Nonuniform":** respondent reports different levels of problems in the 2 individual subdomains or same level of problems but a different level in the composite;
   A **"The most severe problem":** respondent reports the most severe problem across the subdomains in the composite, for example, no pain, slight discomfort and slight problems in the composite;
   B **"The least severe problem":** respondent reports the least severe problem across the subdomains in the composite, for example, no pain, slight discomfort and no problems in the composite;
   C **"Average":** respondent reports the average of problems across the subdomains in the composite, for example, no pain, moderate discomfort and slight problems in the composite;
   D **"Synergistic":** respondent reports more severe problems in the composite than in the subdomains, for example, slight pain, slight discomfort and moderate problems in the composite;
   E **"Inconsistent":** paired responses (composite vs the nearest individual subdomain) not belonging to any other nonuniform category and differing at least one level were defined as "inconsistent," with a size of inconsistency ranging from 1 to 4, for example, moderate pain, slight discomfort and no problems in the composite (one-level inconsistency).

Table 1. Characteristics of the study population.

Variables	General population reference (%)*	Total sample		Considered discomfort "pain"		Considered discomfort "nonpain, physical"		Considered discomfort "psychological"		P value (χ² test)[†]
		n	%	n	%	n	%	n	%	
Total[‡]	100	1700	100	1122	66	396	23	113	7	-
Gender										< .001
Female	53	957	56	686	61	192	48	55	49	
Male	47	743	44	436	39	204	52	58	51	
Age (years)										.016
18-54	61	1054	62	673	60	255	64	82	73	
55+	39	646	38	449	40	141	36	31	27	
Highest level of education										.566
Primary or secondary	79	1150	68	749	67	267	67	81	72	
College/university	21	550	32	373	33	129	33	32	28	
Marital status										.479
Married/domestic partnership	59	1078	63	719	64	254	64	66	58	
Single/widowed/ divorced/other	41	622	37	403	36	142	36	47	42	
Employment status										.388
Employed	53	865	51	580	52	189	48	56	50	
Not employed	47	835	49	542	48	207	52	57	50	
Place of residence										.939
Capital	18	380	22	256	23	86	22	23	20	
Other town	53	820	48	533	48	196	49	55	49	
Village	30	500	29	333	30	114	29	35	31	
Geographical region										.052
Central	30	572	34	383	34	138	35	30	27	
Western	30	493	29	331	30	140	35	57	50	
Eastern	40	635	37	408	36	118	30	26	23	
Self-perceived health[§]										.005
Excellent/very good/ good	83	1222	72	777	69	299	76	91	81	
Fair/poor	17	478	28	345	31	97	24	22	19	
History of chronic illness[‖,¶]										< .001
Yes	48	1146	74	813	78	256	71	51	51	
No	52	410	26	233	22	103	29	49	49	

*Hungarian Central Statistical Office (KSH), Microcensus 2016.
[†]Comparison across the 3 groups.
[‡]Sixty-nine respondents are not included in these groups who indicated "don't know" or "refused to answer" in all open-ended questions or their responses did not allow to include them in any of the 3 groups.
[§]Reference population: Rencz et al.[30]
[‖]Don't know or refused to answer n = 144.
[¶]Hungarian Central Statistical Office (KSH), Health at a Glance 2019.

behaviors were identified that are summarized and defined in Box 1. Overall, 21% and 32% of the participants reported the same level of problems in both individual subdomains and the corresponding composites of PD and AD, respectively ("uniform responses") (Table 2). Among respondents who scored at different levels on the 2 individual subdomains ("nonuniform responses"), for PD 34% and for AD 30% used the composite to report their most severe problem across the subdomains. These proportions were lower for those scoring according to their least severe problem (PD 23% and AD 16%). A minority of respondents reported the average rating across the 2 subdomains in the composite (PD 4% and AD 2%). Some respondents considered that problems of the subdomains could strengthen each other ("synergistic") in the composite (PD 4% and AD 5%). Proportion of inconsistent responses was 13% for PD and, slightly higher, 15% for AD. The average size of

inconsistency in terms of difference in levels was generally low (1.22 for PD and 1.23 for AD). In most respondents scoring different levels in the 2 individual subdomains, responses in the composite were driven by their problems in the first subdomain (PD 66% and AD 61%). The sensitivity analyses reduced the proportion of inconsistent responses, but otherwise showed little change in results (Appendix 2 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2022.06.012).

Self-Reported Pain

In total, 728 respondents reported pain in the individual subdomain, 91% of whom had physical pain (Appendix 3 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2022.06.012). Notably, 37% of respondents with any pain reported to have psychological pain (9% without coexisting physical pain).

Table 2. Self-reported health in the EQ-5D-5L composites and individual subdomains.

Responses	Pain/discomfort				Anxiety/depression			
	Current health		Worst recalled health		Current health		Worst recalled health	
	n	%	n	%	n	%	n	%
Self-reported responses (A)	1700	100	1700	100	1700	100	1700	100
Any problems in the composite (B, proportion B/A)	756	44	1333	78	585	34	892	52
Any problems in the 1st or 2nd subdomain (C, proportion C/A)*	908	53	1471	87	611	36	1021	60
Difference composite vs subdomains (B vs C, χ^2 test P value)	< .001		< .001		.350		< .001	
Any problems in both the 1st and 2nd subdomains (D, proportion D/A)	424	25	1271	75	357	21	734	43
Any problems in the 1st subdomain (E, proportion E/A)	728	43	1382	81	563	33	987	58
Not reported in the composite (F, proportion F/E)	120	16	111	8	76	13	148	15
Any problems in the 2nd subdomain (G, proportion G/A)	604	36	1360	80	405	24	768	45
Not reported in the composite (H, proportion H/G)	130	22	127	9	24	6	81	11
Under-reporting 1st vs 2nd subdomain (F vs H, χ^2 test P value)	.019		.224		< .001		.006	
Response behavior in the composite (I)	968	100	1483	100	674	100	1060	100
Uniform responses (J, proportion J/I)	205	21	448	30	213	32	305	29
Nonuniform responses (K, proportion K/I)	763	79	1035	70	461	68	755	71
Most severe problem (L, proportion L/I)	328	34	408	28	199	30	268	25
Most severe problem (1st subdomain) (M, proportion M/L)	242	74	297	73	164	82	243	91
Most severe problem (2nd subdomain) (N, proportion N/L)	86	26	111	27	35	18	25	9
Least severe problem (O, proportion O/I)	227	23	240	16	109	16	208	20
Least severe problem (1st subdomain) (P, proportion P/O)	122	54	136	57	23	21	30	14
Least severe problem (2nd subdomain) (Q, proportion Q/O)	105	46	104	43	86	79	178	86
Average (R, proportion R/I)	43	4	77	5	13	2	56	5
Synergistic (S, proportion S/I)[†]	40	4	63	4	37	5	50	5
Inconsistent (T, proportion T/I)[‡]	125	13	247	17	103	15	173	16
Average size of inconsistency[‡]	1.22	-	1.53	-	1.23	-	1.43	-
Ordering effect (U)[§]	613	100	804	100	343	100	567	100
Composite response driven by the 1st subdomain (V, proportion V/U)*	404	66	507	63	209	61	312	55
Composite response driven by the 2nd subdomain (W, proportion W/U)*	209	34	297	37	134	39	255	45

EQ-5D-5L indicates 5-level version of EQ-5D.
*1st subdomain, pain or anxiety; 2nd subdomain, discomfort or depression.
[†]Problems in the 2 subdomains strengthen each other.
[‡]Paired responses (composite vs the nearest individual subdomain) not belonging to any other nonuniform category and differing at least one level were defined as "inconsistent," with a size of inconsistency ranging from 1 to 4, for example, moderate pain, slight discomfort, and no problems in the composite (one-level inconsistency).
[§]Computed only for those respondents where this could be unambiguously assessed.

Table 3. Content analysis of the examples for discomfort.

Categories	Examples	Theoretical (n = 1700)		Current health (n = 604)		Worst recalled health (n = 1360)		Total responses (n = 3664)	
		n	%	n	%	n	%	n	%
(A) Physical discomfort due to pain		923	54.3	237	39.2	543	39.9	1703	46.5
(1) Pain									
Pain (in general)	Pain, something hurts, physical pain	404	23.8	44	7.3	274	20.1	722	19.7
Headache	Headache, migraine	500	29.4	93	15.4	89	6.5	682	18.6
Musculoskeletal pain	Low back pain, muscle pain, joint pain	201	11.8	88	14.6	104	7.6	393	10.7
Abdominal pain	Stomach ache, abdominal pain	86	5.1	21	3.5	50	3.7	157	4.3
Toothache	Toothache	26	1.5	10	1.7	18	1.3	54	1.5
Pain in other body part	Ear pain, eye pain	13	0.8	8	1.3	26	1.9	47	1.3
Chest pain	Chest pain, tightness in the chest	6	0.4	8	1.3	27	2.0	41	1.1
Sore throat	Sore throat	7	0.4	5	0.8	12	0.9	24	0.7
Kidney pain	Kidney stones, kidney stone attack	0	0.0	0	0.0	15	1.1	15	0.4
(B) Nonpain physical discomfort		1147	67.5	266	44.0	893	65.7	2306	62.9
(2) Illness		165	9.7	31	5.1	183	13.5	379	10.3
Illness (in general)	Illness, being sick	137	8.1	26	4.3	171	12.6	334	9.1
Health problem	Health problem	40	2.4	5	0.8	4	0.3	49	1.3
Start of illness	As if something is hiding in me, sickening for something, the start of a disease	32	1.9	0	0.0	0	0.0	32	0.9
(3) Homeostasis-related		120	7.1	16	2.6	116	8.5	252	6.9
Fever	Fever, low-grade fever	68	4.0	3	0.5	96	7.1	167	4.6
Shivering	Shivering	18	1.1	0	0.0	11	0.8	29	0.8
Cold/warm	To be cold, to be warm	14	0.8	7	1.2	4	0.3	25	0.7
Sweating	Sweating	6	0.4	0	0.0	15	1.1	21	0.6
Hunger or thirst	Hunger, thirst	7	0.4	4	0.7	1	0.1	12	0.3
Hot flush	Hot flush	8	0.5	1	0.2	1	0.1	10	0.3
(4) Gastrointestinal		382	22.5	27	4.5	161	11.8	570	15.6
Nausea	Nausea	235	13.8	10	1.7	82	6.0	327	8.9
Loss of appetite	Loss of appetite	92	5.4	6	1.0	48	3.5	146	4.0
Digestive problems (unspecified)	Bad or upset stomach, digestive problems	52	3.1	7	1.2	10	0.7	69	1.9
Vomiting	Vomiting	3	0.2	0	0.0	42	3.1	45	1.2
Diarrhea or constipation	Diarrhea, constipation	19	1.1	0	0.0	25	1.8	44	1.2
Bloatedness	Bloatedness	22	1.3	5	0.8	1	0.1	28	0.8
Heartburn	Heartburn, acid reflux symptoms	11	0.6	0	0.0	1	0.1	12	0.3
Overeating	Eating too much, overeating	8	0.5	1	0.2	3	0.2	12	0.3
(5) Respiratory		82	4.8	24	4.0	50	3.7	156	4.3
Common cold	Having a common cold, runny nose	46	2.7	11	1.8	10	0.7	67	1.8
Breathing problems	Breathlessness, rapid breathing	22	1.3	5	0.8	33	2.4	60	1.6
Coughing or sneezing	Coughing, sneezing	13	0.8	7	1.2	12	0.9	32	0.9
Nasal congestion	Stuffy nose	8	0.5	3	0.5	0	0.0	11	0.3
(6) Neurological		320	18.8	42	7.0	101	7.4	463	12.6
Dizziness	Dizziness	251	14.8	28	4.6	72	5.3	351	9.6
Concentration or memory problems	Difficulty concentrating, deconcentrated	53	3.1	3	0.5	5	0.4	61	1.7
Numbing	Numbing	14	0.8	3	0.5	15	1.1	32	0.9
Trembling	Trembling, shaking hands	13	0.8	4	0.7	12	0.9	29	0.8

Table 3. Continued

Categories	Examples	Theoretical (n = 1700)		Current health (n = 604)		Worst recalled health (n = 1360)		Total responses (n = 3664)	
		n	%	n	%	n	%	n	%
Ringing in the ears	Ringing in the ears, tingling ears	4	0.2	5	0.8	2	0.1	11	0.3
Disorientation	Disorientated, confused, dopey	9	0.5	1	0.2	1	0.1	11	0.3
Feeling imbalanced	Feeling imbalanced	7	0.4	0	0.0	1	0.1	8	0.2
(7) Cardiovascular		43	2.5	5	0.8	28	2.1	76	2.1
Blood pressure	Low/high/fluctuating blood pressure	36	2.1	4	0.7	16	1.2	56	1.5
Arrhythmia	Palpitation, arrhythmia	10	0.6	1	0.2	16	1.2	27	0.7
(8) Tiredness		684	40.2	147	24.3	178	13.1	1009	27.5
Tiredness	Fatigue, tiredness	478	28.1	91	15.1	62	4.6	631	17.2
Weakness	Weak	188	11.1	19	3.1	100	7.4	307	8.4
Sleep problems	Difficulty falling asleep, insomnia	88	5.2	31	5.1	28	2.1	147	4.0
Vitality	Lack of vitality, lack of energy, laziness, slowness	89	5.2	15	2.5	11	0.8	115	3.1
Sleepiness	Sleepiness, drowsiness	61	3.6	22	3.6	10	0.7	93	2.5
(9) Women's health		10	0.6	6	1.0	32	2.4	48	1.3
Pregnancy-related	Pregnancy, morning sickness, in labor, after labor, miscarriage, cesarean section	1	0.1	2	0.3	29	2.1	32	0.9
Menstruation-related	Menstruation, premenstrual syndrome	9	0.5	4	0.7	5	0.4	18	0.5
(10) Other physical symptoms		115	6.8	20	1.2	44	2.6	179	4.9
Physical malaise	Malaise, light-headedness, fainting	34	2.0	1	0.2	14	1.0	49	1.3
Sensory symptoms	Vision problems, decreased hearing	10	0.6	1	0.2	13	1.0	24	0.7
Sensitivity to weather change	Sensitivity to weather change	18	1.1	3	0.5	0	0.0	21	0.6
Skin symptoms	Sensitive skin, itch, having a skin rash	7	0.4	0	0.0	5	0.4	12	0.3
Other physical sensations	Pounding in the head, itching throat, hangover, hygiene problems, noise	51	3.0	15	2.5	20	1.5	86	2.3
(11) Other physical problems		91	5.4	20	1.2	193	11.4	304	8.3
Mobility problems	Difficulty moving, disabled, not able to walk	46	2.7	12	2.0	137	10.1	195	5.3
Problems with usual activities	Problems with work or leisure	40	2.4	6	1.0	23	1.7	69	1.9
Confined to bed	Bedridden, confined to bed	1	0.1	1	0.2	42	3.1	44	1.2
Problems with self-care	Problems with/not able to take care oneself	2	0.1	1	0.2	25	1.8	28	0.8
Problems with physical fitness	Lack of fitness, sedentary lifestyle, gaining weight, being overweight	11	0.6	0	0.0	3	0.2	14	0.4
Problems related to aging	Getting old	6	0.4	1	0.2	1	0.1	8	0.2
(12) Specific diseases		34	2.0	24	4.0	185	13.6	243	6.6
Herniated disk	Slipped disk, spinal disk herniation	1	0.1	2	0.3	21	1.5	24	0.7
Cancer	Cancer, tumor, malignant disease	0	0.0	1	0.2	22	1.6	23	0.6
Influenza	Influenza	7	0.4	2	0.3	6	0.4	15	0.4

Table 3. Continued

Categories	Examples	Theoretical (n = 1700)		Current health (n = 604)		Worst recalled health (n = 1360)		Total responses (n = 3664)	
		n	%	n	%	n	%	n	%
Pneumonia	Pneumonia	0	0.0	1	0.2	12	0.9	13	0.4
Diabetes	Diabetes	6	0.4	2	0.3	3	0.2	11	0.3
Heart attack	Heart attack	0	0.0	0	0.0	10	0.7	10	0.3
Stroke	Stroke	0	0.0	1	0.2	8	0.6	9	0.2
Other disease	Allergy, asthma, COPD, hemorrhoids, ulcer	24	1.4	16	2.6	117	8.6	157	4.3
(13) Injury, accident	Injury, accident	4	0.2	2	0.3	129	9.5	135	3.7
(14) Medical interventions		10	0.6	4	0.7	189	13.9	203	5.5
Surgery/ anesthesia	(Post-)surgery, (post-)anesthesia	7	0.4	2	0.3	158	11.6	167	4.6
Hospital care	Staying in hospital, intensive care	0	0.0	0	0.0	30	2.2	30	0.8
Medications	Side effects of treatments	3	0.2	2	0.3	9	0.7	14	0.4
(C) Psychological discomfort		1259	74.1	339	56.1	700	51.5	2298	62.7
(15) Mental problems, emotions or feelings		1 151	67.7	251	41.6	429	31.5	1831	50.0
Mood problems	Listless, in a bad mood, downhearted	706	41.5	87	14.4	66	4.9	859	23.4
Anxiety	Anxious	179	10.5	39	6.5	62	4.6	280	7.6
Nervousness	Nervous, irritated, irritable, tense	166	9.8	27	4.5	27	2.0	220	6.0
Sadness	Sad	127	7.5	12	2.0	10	0.7	149	4.1
Depression	Depressed	82	4.8	6	1.0	38	2.8	126	3.4
Fear	Fear, fear of tomorrow/the future	57	3.4	7	1.2	49	3.6	113	3.1
Stress	Stress	66	3.9	23	3.8	10	0.7	99	2.7
Worry	Worrying	57	3.4	23	3.8	18	1.3	98	2.7
Tired of life	Apathy, lethargy, indifference, tired of life	65	3.8	11	1.8	13	1.0	89	2.4
Insecurity	Insecure	47	2.8	6	1.0	15	1.1	68	1.9
Mental problems	Mental pain, mental fatigue	32	1.9	11	1.8	22	1.6	65	1.8
Negative thoughts	Negative thoughts	47	2.8	7	1.2	5	0.4	59	1.6
Helplessness	Helpless	14	0.8	2	0.3	43	3.2	59	1.6
Irritability	Irritated	51	3.0	4	0.7	3	0.2	58	1.6
Vulnerability	Vulnerable	1	0.1	3	0.5	51	3.8	55	1.5
Loneliness	Loneliness, neglect, lack of love	28	1.6	12	2.0	14	1.0	54	1.5
Lack of prospects	Lack of prospects, aimlessness	27	1.6	10	1.7	17	1.3	54	1.5
Reference to death	Thoughts related to death	8	0.5	1	0.2	34	2.5	43	1.2
Lack of interest	Uninterested	39	2.3	1	0.2	2	0.1	42	1.1
Grief	Grief	8	0.5	5	0.8	29	2.1	42	1.1
Boredom	Bored	33	1.9	4	0.7	4	0.3	41	1.1
Motivation problems	Motivation problems, lack of motivation	35	2.1	3	0.5	1	0.1	39	1.1
Fretful	Fretful	25	1.5	3	0.5	0	0.0	28	0.8
Panic	Panic attack, panic disorder	3	0.2	2	0.3	19	1.4	24	0.7
Frustration	Frustrated	14	0.8	1	0.2	3	0.2	18	0.5
Reference to crying	Crying, being on the verge of crying	9	0.5	3	0.5	6	0.4	18	0.5
Other specific mental health condition	Obsessions, paranoia, alcohol/ drug withdrawal symptoms, bipolar disorder	3	0.2	3	0.5	10	0.7	16	0.4
Unhappiness	Unhappy	11	0.6	1	0.2	1	0.1	13	0.4
Impatience	Impatient	9	0.5	1	0.2	0	0.0	10	0.3
Failure	Failure	8	0.5	0	0.0	0	0.0	8	0.2

Table 3. Continued

Categories	Examples	Theoretical (n = 1700)		Current health (n = 604)		Worst recalled health (n = 1360)		Total responses (n = 3664)	
		n	%	n	%	n	%	n	%
Other feelings	Disappointed, hopeless, desperate, missing a loved one, anger, hatred, disgust, guilt	147	8.6	40	6.6	62	4.6	249	6.8
(16) Source of psychological discomfort		199	11.7	144	23.8	59	4.3	402	11.0
Weather, time of day	Weather, time of day, seasons	66	3.9	52	8.6	3	0.2	121	3.3
COVID-19	Corona, quarantine, lockdown, restrictions	40	2.4	60	9.9	2	0.1	102	2.8
Work(place) problems	Workplace problems, one's boss	29	1.7	20	3.3	22	1.6	71	1.9
Financial problems	Lack of money, unemployment	39	2.3	18	3.0	7	0.5	64	1.7
Family problems	Family problems	29	1.7	16	2.6	13	1.0	58	1.6
Private life problems	Fight, divorce, cheating, bad company	23	1.4	8	1.3	17	1.3	48	1.3
Politics and society	News, politics, healthcare system	37	2.2	9	1.5	1	0.1	47	1.3
Bad news	Getting bad news	9	0.5	1	0.2	1	0.1	11	0.3
(D) Other		138	8.1	33	5.5	122	9.0	293	8.0
Refused to answer or nonsensical response	-, xx, "pass," "none," "I am not afraid of anything," "0"	54	3.2	22	3.6	48	3.5	124	3.4
Don't know	"I don't know", "I don't know this notion," "I've never had it"	17	1.0	4	0.7	69	5.1	90	2.5
Paraphrase	Discomfort, lack of comfort, uncomfortable feeling/sensation	67	3.9	7	1.2	5	0.4	79	2.2
Total		6163	-	1196	-	3069	-	10 428	-

COPD indicates chronic obstructive pulmonary disease.

Content Analysis of Examples for Discomfort

Respondents provided overall 10 428 examples for discomfort (6193 theoretical, 1196 for current health, and 3069 for worst recalled health). Responses were condensed into 108 sub-categories and 16 categories. These were then consolidated under 3 main categories: physical discomfort due to pain, nonpain physical discomfort, and psychological discomfort (Table 3).

Overall, 66% of respondents referred to pain as a form of discomfort, of which unspecified pain was the most common example provided (35%), followed by headache (32%) and musculoskeletal pain (18%). More than four-fifth of participants (81%) mentioned forms of nonpain physical discomfort including tiredness (31%), illness (in general) (18%), dizziness (17%), nausea (16%), and weakness (15%). Many respondents (78%) referred to psychological discomfort, of which mood problems (43%), anxiety (15%), nervousness (11%), sadness (8%), and depression (7%) were the most prevalent.

When interpreting discomfort theoretically, 204 respondents (12%) used an adjective to describe the level of discomfort in a total of 239 examples (Appendix 4 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2022.06.012). Among these, 101 examples provided by 71 respondents (4%) described

discomfort as "mild pain." Other examples included "mild headache," "small dizziness," and "strong tiredness."

Content Analysis of Descriptions for Discomfort

Overall, 595 respondents (35%) provided a description about the theoretical meaning of discomfort. These responses were synthesized in 20 subcategories and the following 5 categories: (1) the relation between pain and discomfort (ie, pain vs not pain), (2) source of discomfort, (3) time or duration of discomfort, (4) feeling/sensation of discomfort, and (5) other (Table 4).

Determinants of What is Considered Discomfort

Based on the examples and descriptions provided on all open-ended questions about discomfort, respondents were classified into 3 mutually exclusive groups. The first group comprised respondents who mentioned pain with or without other forms of discomfort (n = 1222, 66%), the second group included respondents who mentioned other forms of physical discomfort than pain with or without any psychological discomfort (n = 369, 29%), and the third group consisted of those respondents who mentioned only psychological discomfort (n = 113, 7%). Women, respondents aged 55 years or older, and those in worse health

Table 4. Content analysis of the descriptions for discomfort.

No.	Category	Subcategory	n	%	Example quote
1	The relation of discomfort and pain*	Pain	15	3	I have discomfort due to pain. When someone is in pain, they have discomfort at any level of pain.
					When something hurts that bad that I have to take medications.
					When even sounds are painful.
		Not pain*	22	4	An unnatural, tight, pressing or itchy sensation in the body which is not yet pain.
					It is a sensation when one cannot precisely tell, but feels unwell. Pain does not belong to this notion.
					When I have no particular pain, but still I don't feel well.
2	Source of discomfort	Rather physical	13	2	It is mostly of physical origin.
					To me, discomfort covers bodily symptoms.
		Rather psychological	15	3	Who has such a problem [discomfort], they have problems with their nerves.
					It is a mental state. It is like having a cold, once you've got it, you don't have the mood to do anything, you are fretful, you have discomfort.
					It is a mood characterized by dissatisfaction, restlessness, depression and anxiety. It is an unpleasant or uncomfortable feeling.
		Physical and psychological	73	12	An unpleasant physical or mental condition or state of mind, or the combination of these.
					It is a mind-body imbalance.
					It is the coexistence of larger emotional and smaller physical problems.
		Societal/ environmental	7	1	Nevertheless, discomfort might arise from political or public life reasons. I, myself, am very sensitive to the (current bad) state of the world or our country too.
					I don't feel myself. This originates from societal, workplace and private life problems.
		No (medical) or unknown reason/ inexplicable	46	8	Inexplicable symptoms that cannot be diagnosed by routine medical examinations.
					An inexplicable, unpleasant inner sensation.
					An insecure feeling of unknown source.
3	Time or duration of discomfort	Short term (moments or hours)	4	1	In my opinion, [by discomfort] we mean one's momentary mood and health status.
		Reference to the morning or getting up	36	6	In the morning I don't want to open my eyes, I barely want to get up. I don't want to start the day.
		A bad day	20	3	… on that day everything goes wrong.
					I am lost all day, I am tired despite sleeping a lot and not in the mood to get out of bed, even the smallest thing that is not how I want it to be annoys me.
		Long term/constant	38	6	A prolonged, unpleasant feeling, weakness.
4	Feeling of discomfort	Not feeling well	107	18	I am not feeling well.
		Not feeling good in one's skin	45	8	I am not feeling good in my skin.
		No mood to do anything	156	26	One is not in the mood to do anything.
		Not finding one's place	10	2	I cannot find my place.
		Something is wrong	42	7	I cannot put it into words, something is wrong.
					… when I don't know what exactly the problem is, because I have no pain, I just feel that something is not good.
					I don't feel 100% today.

Table 4. Continued

No.	Category	Subcategory	n	%	Example quote
		Everything is wrong	34	6	When nothing is good.
					Everything annoys me, I am tired of everything, I don't want to live, I find myself hopeless and helpless.
		Not as usual	35	6	Somehow I don't feel like I used to, I am not well.
					I have a feeling/sensation that I don't experience on normal days. For example, when I am ill, I don't feel well, I easily get tired…
		Withdrawal from social relationships	42	7	When one does not want to do anything or see anyone.
5	Other	Any other description that does not fit to the categories above	14	2	When one shares their discomfort with others, they [others] will also develop discomfort. It is indefinable that is why we use the word 'discomfort' for it.
Total			595	100	-

*When considering both descriptions and examples provided, there were 14 respondents who responded that discomfort can be both pain and "not pain."

status or having chronic conditions tended to consider discomfort as pain more than others (Table 1). Level of education, marital and employment status, region, and place of residence had no significant impact on what meaning participants attributed to discomfort.

The Type of Discomfort and Self-Reported Problems in the PD Composite Domain

Respondents with nonpain physical discomfort (20%) and psychological discomfort (30%) more frequently under-reported their current health problems in the composite PD domain than respondents having discomfort due to pain (16%) (P = .002). This trend was also detected for worst recalled health; nevertheless, the difference was smaller and insignificant (Appendix 5 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2022.06.012).

Respondents' Overall Interpretations of Discomfort and Self-Reported Problems in the Individual Subdomain

For current health, no significant difference was observed in the overall interpretation of discomfort between respondents with and without discomfort (Appendix 6 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2022.06.012). Nevertheless, respondents reporting discomfort for their worst recalled health more frequently considered discomfort as pain and respondents without discomfort more commonly considered discomfort as psychological (P < .001).

Correlations Between the Composites and Individual Subdomains and EQ VAS

Correlation between the individual pain and discomfort subdomains was moderate (r_s = 0.47) (Table 5). Pain showed a stronger correlation with the composite PD than discomfort

Table 5. Spearman's correlations among the 5 domains, 4 individual subdomains, and EQ VAS.

Domains		Worst recalled health (n = 1700)—above the diagonal								
		EQ VAS	MO	SC	UA	PD	AD	Pain	Disc	Anx	Dep
Current health (n = 1700)—below the diagonal	EQ VAS		−0.40	−0.45	−0.56	−0.60	−0.47	−0.50	−0.59	−0.46	−0.40
	MO	−0.41		0.66	0.59	0.56	0.33	0.47	0.33	0.26	0.22
	SC	−0.29	0.39		0.72	0.58	0.35	0.45	0.38	0.29	0.22
	UA	−0.42	0.51	0.44		0.71	0.44	0.53	0.50	0.36	0.31
	PD	−0.55	0.50	0.36	0.52		0.49	0.72	0.61	0.42	0.35
	AD	−0.39	0.21	0.20	0.33	0.44		0.34	0.55	0.80	0.74
	Pain	−0.49	0.50	0.35	0.47	0.72	0.34		0.62	0.41	0.30
	Disc	−0.51	0.25	0.26	0.38	0.56	0.60	0.47		0.65	0.54
	Anx	−0.39	0.20	0.19	0.32	0.40	0.79	0.33	0.59		0.78
	Dep	−0.37	0.20	0.21	0.31	0.38	0.74	0.32	0.54	0.69	

Note. All correlation coefficients were statistically significant (P < .05).
AD indicates anxiety/depression; Anx, anxiety; Dep, depression; Disc, discomfort; MO, mobility; PD, pain/discomfort; SC, self-care; UA, usual activities; VAS, visual analogue scale.

(r_s = 0.72 vs r_s = 0.56). Discomfort was more strongly correlated with anxiety than with pain (r_s = 0.59 vs r_s = 0.47). Among all (sub) domains, the individual discomfort subdomain demonstrated the strongest correlation with EQ VAS (r_s = −0.51). With few exceptions, correlations across domains strengthened when participants reported worst recalled health.

Discussion

In this study, we examined how respondents use the PD and AD composite domains in the EQ-5D to self-report own health. Our findings highlight several problems with the current form of the composite domains and wording of discomfort in the EQ-5D, implications of which are outlined in the discussion.

The first problem our study revealed is that respondents under- and inconsistently report their health using the composite domains. These results coincide with those of 2 previous studies that found more participants reporting problems in the individual subdomains than in the composite among the UK general public.[3,4] This may be symptomatic of confusion among respondents about how the response levels of the composites ought to be interpreted or of not accurately reading the response levels (eg, not taking the conjunction "or" into account).

Second, both for PD and AD, we detected signs of systematic order effects: mainly problems with the first subdomain determined responses in the composite in respondents who scored differently in the 2 separate concepts. In support to these findings, the first subdomains correlated more strongly with the composites. The primacy of the first subdomain was more pronounced for PD than for AD. It may be possible that, in the current form of the composite, the effects of the higher relative importance of pain in health than discomfort and the order in which it is mentioned add up. These results suggest the need for further studies testing how the order of the 2 subdomains influences respondents' answers, for example, through subdomain randomization.

The third issue is the ambiguous meaning of discomfort that could lead to differential item functioning in the composite PD domain. The variables identified to systematically influence interpretations were age, gender, and health status. This might introduce bias into direct comparisons of self-reported health across subgroups given that differences stemming from differential item functioning may be attributed to differences in underlying health.[31] Supporting this, 2 previous studies found differential item functioning for the PD domain of EQ-5D.[32,33]

The more than 100 different forms of discomfort identified imply that the EQ-5D may be able to capture a broad spectrum of forms of discomfort. Nevertheless, previous clinical studies concluded that the EQ-5D was less efficient in capturing several symptoms that this study uncovered as forms of discomfort, including respiratory symptoms (eg, shortness of breath and coughing) or gastrointestinal symptoms (eg, nausea, constipation, and diarrhea).[8,34–37] In addition, many of the existing EQ-5D "bolt-ons" (additional domains to the EQ-5D) target these specific areas of discomfort, such as breathlessness or tiredness.[38] A direction for future improvement could be to provide supportive examples for discomfort in the composite descriptor, similarly to usual activities.

Although this study explored the PD and AD composite domains and possible meanings of discomfort in the context of self-reporting own health, valuation implications of our findings remain unclear; for example, which of these examples for discomfort (if any) are considered by respondents when valuing health states. Earlier results indicated that, in valuation, respondents interpret the composite PD as pain and AD is interpreted to lie between anxiety and depression.[3] Furthermore, problems in the pain subdomain alone are considered worse than the same level of discomfort, and similar to this, depression is perceived worse than anxiety.[3] If respondents self-report discomfort in the composite but in valuation, PD is mainly interpreted as pain, then disutilities of health states actually containing discomfort and without pain might be overestimated. Moreover, for both PD and AD, the order effects in self-reporting health might also mismatch with the values attached to the composites.

The fourth problem our study revealed concerns the independence of the questionnaire domains. Our findings indicate that discomfort, to some extent, covers mental functioning and this could imply an overlap between PD and AD. Nevertheless, this observation may be subject to considerable variations across different languages. The Hungarian translation of discomfort is "rossz közérzet," whereby "rossz" means "bad" and "közérzet" refers to general state, sensation, or feeling. Furthermore, 37% of respondents reported to experience psychological pain. Therefore, the current form of the composite PD somewhat contradicts the developers' intentions that were, in fact, to capture physical pain and other forms of physical discomfort.[21] A further refinement of the PD domain could consist of focusing solely on physical symptoms; adding the term "bodily" or "physical" to the domain heading could be a solution. Interestingly, the German version of the EQ-5D already uses the expression of "körperliche Beschwerden" (bodily discomfort). Harmonization of discomfort in other languages has also been conducted; for instance, the Dutch EQ-5D-3L used the word "klachten" (complaint) that was revised as "ongemak" (discomfort) in the EQ-5D-5L. These findings provide supportive evidence for the recently developed EQ Health and Wellbeing[39] instrument that asks about physical pain and physical discomfort in 2 separate questions, with the latter being supplemented by the examples of "feeling sick, breathless, itching (not including pain)."

There are some limitations to our study. First, the study population included respondents from the general public, and it might have missed certain forms of discomfort that are relevant only to patients with specific health conditions. Second, the survey was conducted in Hungarian that might restrict the generalizability of the interpretations of discomfort to other populations. Third, positioning the individual subdomains after the composites might have enhanced the under-reporting of problems in the composites, as being repeatedly exposed to the same item might lead respondents to reconsider their previous response. Furthermore, questions about pain and discomfort preceded the EQ-5D and individual subdomains for worst recalled health in the questionnaire that might have caused overstating pain and discomfort for the worst recalled health. The association between respondents' demographic characteristics and health status and discomfort interpretation subgroups was only tested using univariate analyses, and therefore, the independence of these associations could not be tested. Finally, all coding was performed by one researcher and therefore may be prone to errors.

Some of the issues identified in this study about the composites may also arise with regard to the self-care and usual activities domains of the EQ-5D that use 2 or more examples to clarify the meaning of a single health domain. It is possible, for example, that someone has moderate problems washing oneself, while no problems with dressing. Nevertheless, given that these examples serve to clarify a single health domain, one may anticipate fewer problems, including under- or inconsistent reporting.

In spite of the limitations revealed about the PD and AD composites, the EQ-5D shows overall good measurement properties, including validity and responsiveness across different populations and settings.[40,41] It may be questioned whether

creating an EQ-7D by splitting the composites would be able to outperform the current 5-domain version.[3] Although longer questionnaires may yield a wealth of information about the respondents' health, the larger the descriptive system, the more unique health states are defined that may require more complex valuation designs placing a higher level of cognitive demand on respondents.[42] Therefore, composite domains seem to have a rightful place in generic preference-based accompanied measures. Nevertheless, our findings put forward potential future directions for improving the structure and wording of the composite domains in the EQ-5D and beyond.

Conclusions

Analyzing a mixture of quantitative and qualitative data, this study found empirical evidence of measurement error in the PD and AD composite responses on the EQ-5D in a large general population sample in Hungary including under-reporting of health problems, systematic ordering effect, potential differential item functioning, and interdomain dependency. Our findings contribute new knowledge to the future development of new and refinement of existing self-reported health status instruments.

Supplemental Materials

Supplementary data associated with this article can be found in the online version at https://doi.org/10.1016/j.jval.2022.06.012.

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