

Supplementary Material

Baseline Characteristics of the DISCOVER CKD

Prospective Cohort

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Supplementary Methods

International Classification of Diseases, 10th Revision (ICD-10) codes used to identify patients with chronic kidney disease (CKD)

- I12.0
- I13.11
- I13.2
- N18.3
- N18.4
- N18.5
- N18.6
- N18.9
- Z99.2

Scoring of patient-reported outcomes (PRO) questionnaires

- The 36-item Short Form questionnaire consists of eight sections, which are the weighted sums of the questions in their section.
- Rapid Assessment of Physical Activity (RAPA) Part 1: Aerobic scoring was as follows:
 - Sedentary
 - 1. I rarely or never do any physical activities
 - Under-active:
 - 2. I do some light or moderate physical activities, but not every week
 - Under-active (light):
 - 3. I do some light physical activity every week
 - Under-active (regular):
 - 4. I do moderate physical activities every week, but < 30 min/day or < 5 days/week
 - 5. I do vigorous physical activities every week, but < 20 min/day or < 3 days/week
 - Active:
 - 6. I do ≥ 30 min/day of moderate physical activities, ≥ 5 days/week
 - 7. I do ≥ 20 min/day of vigorous physical activities, ≥ 3 days/week
- RAPA Part 2: Strength and flexibility scoring was as follows:
 - Only strength
 - 1. I do activities to increase muscle strength, such as lifting or calisthenics, once a week or more
 - Only flexibility

2. I do activities to improve flexibility, such as stretching or yoga, once a week or more
 - Both (3)
 - None (0)
- The Work Productivity and Activity Impairment chronic kidney disease (WPAI-CKD) questionnaire includes the following questions:
 1. Currently employed
 2. Hours missed due to specified problem
 3. Hours missed due to other reasons
 4. Hours actually worked
 5. Degree problem affected productivity while working
 6. Degree problem affected regular activities
 - Scoring instructions are as follows:
 1. Multiply scores by 100 to express in percentages
 2. Percent work time missed due to problem: $Q2/(Q2 + Q4)$
 3. Percent impairment while working due to problem: $Q5/10$
 4. Percent overall work impairment due to problem:

$$Q2/(Q2 + Q4) + [(1 - (Q2/(Q2 + Q4))) \times (Q5/10)]$$
 5. Percent activity impairment due to problem: $Q6/10$
 - The symptom questionnaire includes the following questions:

Patient Symptom Information

To be completed once per week as directed. Please select the option that best describes your experience of symptoms in the last 7 days.

1. In the last 7 days, have you experienced any fatigue?

None 0 1 2 3 4 5 6 7 8 9 10 Worst possible

2. In the last 7 days, have you experienced any pruritus (itching)?

None 0 1 2 3 4 5 6 7 8 9 10 Worst possible

3. In the last 7 days, have you experienced any problems with sleep?

None 0 1 2 3 4 5 6 7 8 9 10 Worst possible

4. In the last 7 days, have you experienced any numbness or tingling?

None 0 1 2 3 4 5 6 7 8 9 10 Worst possible

5. In the last 7 days, have you experienced any chest pain?

None 0 1 2 3 4 5 6 7 8 9 10 Worst possible

6. In the last 7 days, have you experienced any shortness of breath?

None 0 1 2 3 4 5 6 7 8 9 10 Worst possible

7. In the last 7 days, have you experienced any nausea?

None 0 1 2 3 4 5 6 7 8 9 10 Worst possible

8. In the last 7 days, have you experienced any muscle cramping?

None 0 1 2 3 4 5 6 7 8 9 10 Worst possible

9. In the last 7 days, have you had depressed or unhappy feelings?

None 0 1 2 3 4 5 6 7 8 9 10 Worst possible

10. In the last 7 days, have you had anxious or worried feelings?

None 0 1 2 3 4 5 6 7 8 9 10 Worst possible

11. Overall, how do you feel about your health today?

Best Possible 0 1 2 3 4 5 6 7 8 9 10 Worst possible

Supplementary Table S1. Study sites and ethics committees

Country	Study site	Ethics committee
Italy	Istituto Clinico Humanitas Rozzano, IRCCS	IRCCS Istituto Clinico Humanitas
	AOU Università degli studi della Campania Luigi Vanvitelli, Policlinico di Napoli	Comitato Etico Università degli Studi della Campania "Luigi Vanvitelli" - Azienda Ospedaliera Universitaria "Luigi Vanvitelli" - AORN "Ospedali dei Colli"
	Alma Mater Studiorum Università di Bologna	Comitato Etico Indipendente di Area Vasta Emilia Centro c/o Azienda Ospedaliero – Universitaria di Bologna, Policlinico S.Orsola-Malpighi
	Umberto I Policlinico di Roma, Università La Sapienza	Comitato Etico dell'Università "Sapienza" Policlinico Umberto I c/o Ufficio locale sperimentazioni cliniche
	AO S. Andrea, Università degli Studi di Roma La Sapienza	Comitato Etico dell'Università "Sapienza" Policlinico Umberto I
Japan	Kumamoto University Hospital	Kumamoto University Hospital Clinical Research Review Committee
	Nagoya University Hospital	Observational Study Review Committee, Nagoya University Graduate School of Medicine, Nagoya University Hospital
	Nara Medical University Hospital	Nara Medical University Hospital
	Niigata University Medical and Dental Hospital - Second Internal Medicine	Niigata University Medical and Dental Hospital
	Osaka City University Hospital - Nephrology	Osaka Metropolitan University Medical Research Ethics Review Committee
	Saitama Medical University Hospital	Ethics Committee of Saitama Medical University
	Teikyo University Hospital	Teikyo University Ethics Committee for Medical and Health Research
	Okayama University Hospital – Division of Kidney, Diabetes, and Endocrine Diseases	Okayama University Hospital
	Kawasaki Medical School	Kawasaki Medical School Hospital

Spain	Hospital Vithas Nisa Sevilla Aljarafe	CEIm Comité Coordinador de la Ética de Investigación Biomédica de Andalucía
	Hospital Fundació Althaia	Fundació la Unió Fundació Catalana d'Hospitals
	Hospital Universitari Arnau De Vilanova De La Gerencia Territorial De Lleida	CEIm Hospital Universitari Arnau de Vilanova de la Gerència Territorial de Lleida – GSS
	Hospital de La Santa Creu i Sant Pau	CEIm Fundacio de Gestio Sanitaria Hospital de la Santa Creu i Sant Pau
	Complejo Hospitalario Universitario de Ferrol	CEIm de Galicia
	Complexo Hospitalario Universitario de Santiago	CEIm de Galicia
	Hospital do Meixoeiro	CEIm de Galicia
Sweden	Hospital General Universitario Gregorio Marañón	CEIm Hospital General Universitario Gregorio Marañón
	Hospital Universitario Donostia	CEIm de Euskadi
	Capio Citykliniken Lund	Etikprövningsmyndigheten
	Karolinska University Hospital, Institute for Medicinal Kidney Disease	Etikprövningsmyndigheten
UK	Linköping University Hospital	Etikprövningsmyndigheten
	Danderyd Hospital Nephrology Clinic	Etikprövningsmyndigheten
	Nottingham University Hospitals NHS Trust - Nottingham City	Yorkshire and The Humber - South Yorkshire Research Ethics Committee
	St Bartholomew's Hospital	Yorkshire and The Humber - South Yorkshire Research Ethics Committee
	Hope Hospital	Yorkshire and The Humber - South Yorkshire Research Ethics Committee
	St James's University Hospital	Yorkshire and The Humber - South Yorkshire Research Ethics Committee
	Hull and East Yorkshire Hospitals NHS Trust - Hull Royal Infirmary	Yorkshire and The Humber - South Yorkshire Research Ethics Committee
	Royal Free and University College Medical School	Yorkshire and The Humber - South Yorkshire Research Ethics Committee

	Rowden Hill Surgery	Yorkshire and The Humber - South Yorkshire Research Ethics Committee
	South Shore Nephrology	Advarra
	Pioneer Research Solutions, Inc.	Advarra
	Accel Research Sites - Avail Clinical Research	Advarra
	Bassetti Medical Research, Inc. - Research	Advarra
	Apex Research of Riverside	Advarra
	Kidney and Hypertension Center	Advarra
USA	Zuckerberg San Francisco General Hospital and Trauma Center	Advarra
	MedResearch, Inc.	Advarra
	University of Texas Health Science Center at San Antonio - Internal Medicine	Advarra
	Albert Einstein College of Medicine - Jack and Pearl Resnick Campus	Biomedical Research Alliance of New York
	North Shore University Hospital	Advarra

CEIm, Comité de Ética da Investigación con Medicamentos; GSS, Gestió de Serveis Sanitaris

Supplementary Table S2. Patient demographics and disease characteristics by patients who responded to PRO questionnaires versus those who did not respond

Characteristic	PRO completers ^a	PRO non-completers
	(N = 661)	(N = 391)
Age, years, mean (SD)	60.9 (13.6)	65.3 (13.1)
Missing	0	0
Sex, female, n (%)^b	234 (35.4)	154 (39.4)
Missing	0	0
Geographical location, n (%)^b		
United Kingdom	91 (13.8)	94 (24.0)
Italy	31 (4.7)	73 (18.7)
Japan	219 (33.1)	4 (1.0)
Spain	89 (13.5)	40 (10.2)
Sweden	57 (8.6)	33 (8.4)
United States	174 (26.3)	147 (37.6)
Missing	0	0
Race, n (%)^b		
White	352 (53.3)	292 (74.7)
Asian	222 (33.6)	13 (3.3)
Black/African American	49 (7.4)	30 (7.7)
Other	2 (0.3)	2 (0.5)
Missing/not reported	36 (5.4)	54 (13.8)
BMI, kg/m²		
n	385	274
Mean (SD)	29.6 (7.7)	30.6 (6.9)
Missing, n (%) ^b	276 (41.8)	117 (29.9)
BMI, kg/m², n (%)^b		
< 18.5 kg/m ²	9 (1.4)	7 (1.8)

18.5 to < 25 kg/m ²	107 (16.2)	48 (12.3)
25 to < 30 kg/m ²	111 (16.8)	76 (19.4)
≥ 30 kg/m ²	158 (23.9)	143 (36.6)
Alcohol use, <i>n</i> (%)^b		
Current	394 (59.6)	232 (59.3)
Former	79 (12.0)	26 (6.6)
Never	188 (28.4)	133 (34.0)
Missing	0 (0)	0 (0)
Nicotine usage, <i>n</i> (%)^b		
Current smoker	77 (11.6)	41 (10.5)
Former smoker	220 (33.3)	115 (29.4)
Never smoked	342 (51.7)	216 (55.2)
Missing	22 (3.3)	19 (4.9)
CKD stage, <i>n</i> (%)^b		
Stage 2	65 (9.8)	22 (5.6)
Stage 3a	195 (29.5)	137 (35.0)
Stage 3b	201 (30.4)	107 (27.4)
Stage 4	18 (2.7)	66 (16.9)
Stage 5	82 (12.4)	59 (15.1)
Missing	0	0
Dialysis status, <i>n</i> (%)^b		
Any	49 (7.4)	39 (10.0)
Haemodialysis	46 (7.0)	36 (9.2)
Peritoneal dialysis	3 (0.5)	3 (0.8)
Speciality of enrolling physician, <i>n</i> (%)^b		
Cardiology	16 (2.4)	9 (2.3)
Nephrology	534 (80.8)	302 (77.2)
General practice	25 (3.8)	38 (9.7)
Other ^c	86 (13.0)	42 (10.7)

Missing	0	0
Employment status, <i>n</i> (%)^b		
Employed	229 (34.6)	78 (19.9)
Unemployed	94 (14.2)	43 (11.0)
Retired	229 (34.6)	185 (47.3)
Self-employed	40 (6.1)	7 (1.8)
Other	69 (10.4)	78 (19.9)
Marital status, <i>n</i> (%)^b		
Married	414 (62.6)	218 (55.8)
Divorced	37 (5.6)	27 (6.9)
Widowed	29 (4.4)	27 (6.9)
Never married	104 (15.7)	44 (11.3)
Other	77 (11.6)	75 (19.2)
Health insurance coverage, <i>n</i> (%)^b		
Private	46 (7.0)	42 (10.7)
Public/governmental	563 (85.2)	299 (76.5)
Mixed	8 (1.2)	4 (1.0)
No insurance	43 (6.5)	30 (7.7)
Unknown/missing	1 (0.2)	16 (4.1)
Systolic blood pressure, mmHg		
<i>n</i>	557	274
Median (Q1, Q3)	133.0 (121.0, 146.0)	135.0 (121.0, 150.0)
Missing, <i>n</i> (%) ^b	104 (15.7)	43 (11.0)

BMI body mass index, *CKD* chronic kidney disease, *PRO* patient-reported outcome, *Q₁* quartile 1, *Q₃* quartile 3,

SD standard deviation

^aPRO completers include patients who completed PROs either at baseline or during follow up

^bPercentages are based on the total number of patients within each cohort: PRO completers (*N* = 661); PRO non-completers (*N* = 391)

^cIncludes any specialty other than nephrology, cardiology or general practitioner

Supplementary Table S3. Baseline PROs by CKD stage

Key PRO domain	Patients with early-stage CKD, <i>n</i>	Patient with early-stage CKD, <i>LS mean (SE)</i>	Patients with advanced-stage CKD, <i>n</i>	Patients with advanced-stage CKD, <i>LS mean (SE)</i>	P-value
Outcomes in patients with early-stage CKD (stage 2–3b) versus those with advanced-stage CKD (stage 4–5) inclusive of dialysis					
Work productivity and activity impairment: CKD					
Work time missed, %	124	6.0 (3.1)	56	10.1 (3.3)	0.104
Impairment at work, %	130	14.3 (4.6)	57	23.6 (4.8)	0.013
SF-36 outcomes					
Physical functioning scale	297	67.1 (3.3)	141	57.2 (3.5)	< 0.001
General health scale	298	49.1 (2.3)	144	39.1 (2.5)	< 0.001
Mental health scale	297	70.6 (2.3)	143	70.0 (2.5)	0.790
Patients symptoms					
Fatigue	300	4.5 (0.3)	144	4.9 (0.4)	0.159
Problems with sleep	301	3.2 (0.4)	144	3.9 (0.4)	0.041
Chest pain	301	0.8 (0.2)	144	1.0 (0.2)	0.304
Shortness of breath	301	1.9 (0.3)	144	2.1 (0.3)	0.512
Depression	301	2.2 (0.3)	144	3.1 (0.3)	0.871
Anxiety	301	2.4 (0.3)	144	2.3 (0.4)	0.751
Overall quality-of-life	301	26.9 (2.1)	144	30.3 (2.2)	0.068
Outcomes in patients with early-stage CKD (stage 3a–3b) versus those with advanced-stage CKD (stage 4–5) without dialysis					
Work productivity and activity impairment: CKD					
Work time missed, %	103	4.4 (3.1)	48	6.9 (3.3)	0.333
Impairment at work, %	108	14.1 (4.9)	49	22.0 (5.2)	0.048
SF-36 outcomes					

Physical functioning scale	258	65.5 (3.5)	103	58.3 (3.8)	0.017
General health scale	259	48.1 (2.4)	104	39.7 (2.6)	< 0.001
Mental health scale	258	70.0 (2.4)	104	71.6 (2.6)	0.428
Patients symptoms					
Fatigue	258	4.6 (0.3)	106	4.7 (0.4)	0.688
Problems with sleep	259	3.1 (0.4)	106	3.5 (0.4)	0.360
Chest pain	259	0.7 (0.2)	106	0.8 (0.2)	0.691
Shortness of breath	259	1.9 (0.3)	106	2.0 (0.4)	0.736
Depression	259	2.3 (0.3)	106	1.9 (0.3)	0.148
Anxiety	259	2.5 (0.3)	106	2.1 (0.4)	0.150
Overall quality-of-life	259	27.1 (2.1)	106	27.0 (2.3)	0.971

CKD, chronic kidney disease; *PRO*, patient-reported outcome; *SF-36*, 36-item short form survey

Supplementary Table S4. CKD stages of patients with missing eGFR data

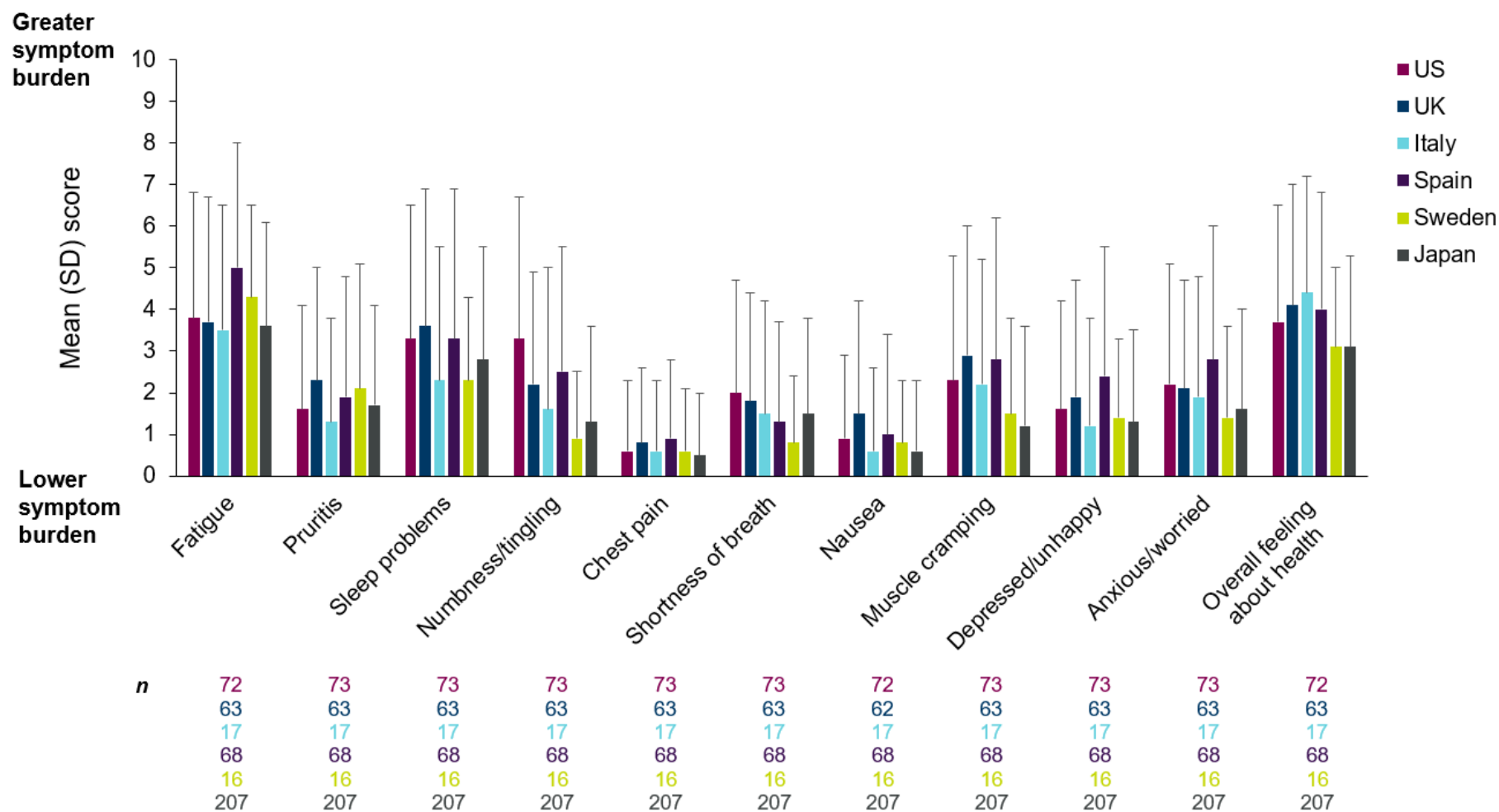
Characteristic	Patients with missing eGFR data
	(<i>N</i> = 87)
CKD stage,^a <i>n</i> (%)	
Stage 2	2 (2.3)
Stage 3a	16 (18.4)
Stage 3b	20 (23.0)
Stage 4	16 (18.4)
Stage 5	33 (37.9)

CKD chronic kidney disease, *ICD-10* International Classification of Diseases (10th Revision)

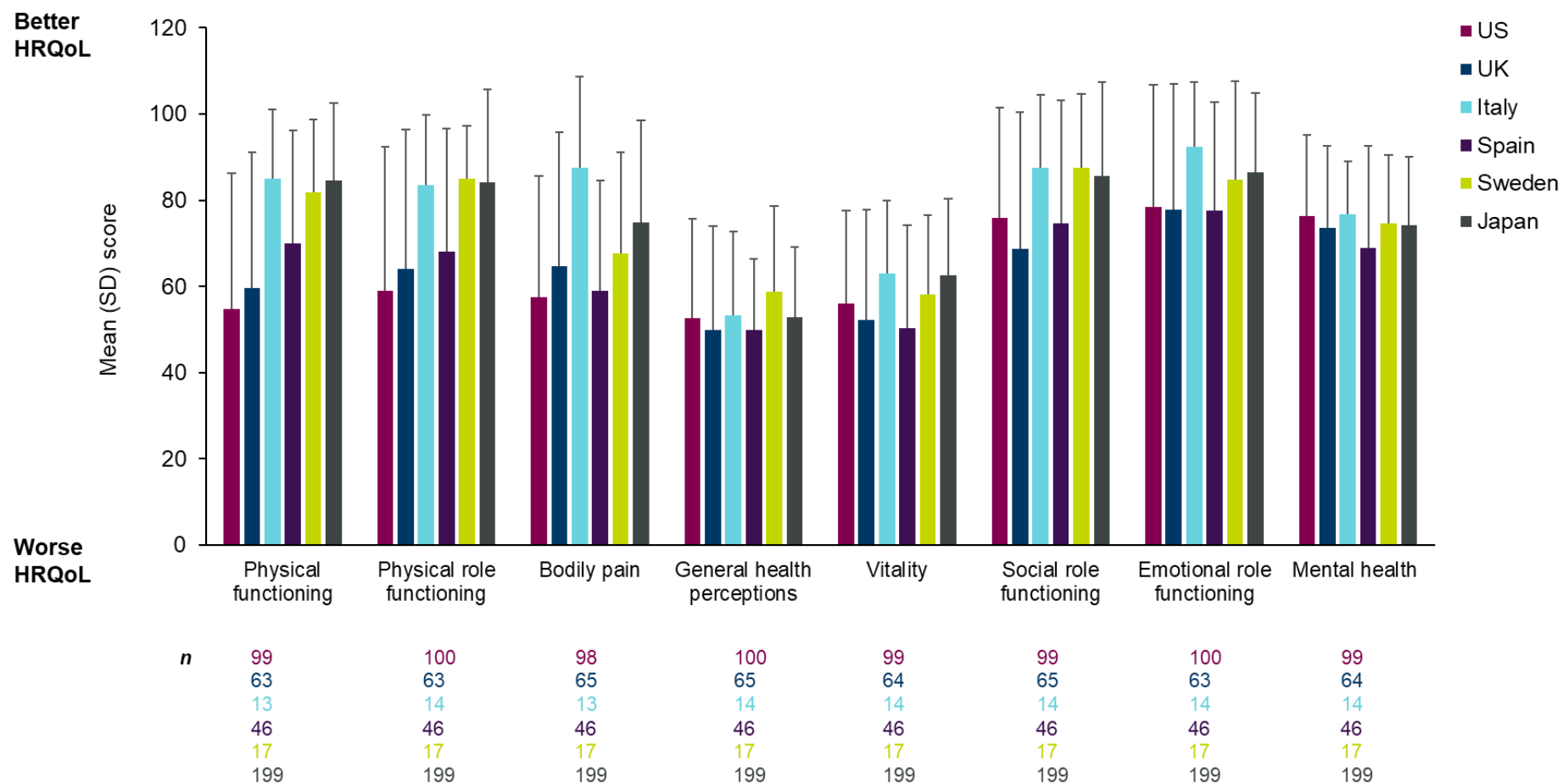
^aCKD staging of these patients was based on ICD-10 codes

Supplementary Fig. S1 Baseline patient-reported outcomes by country

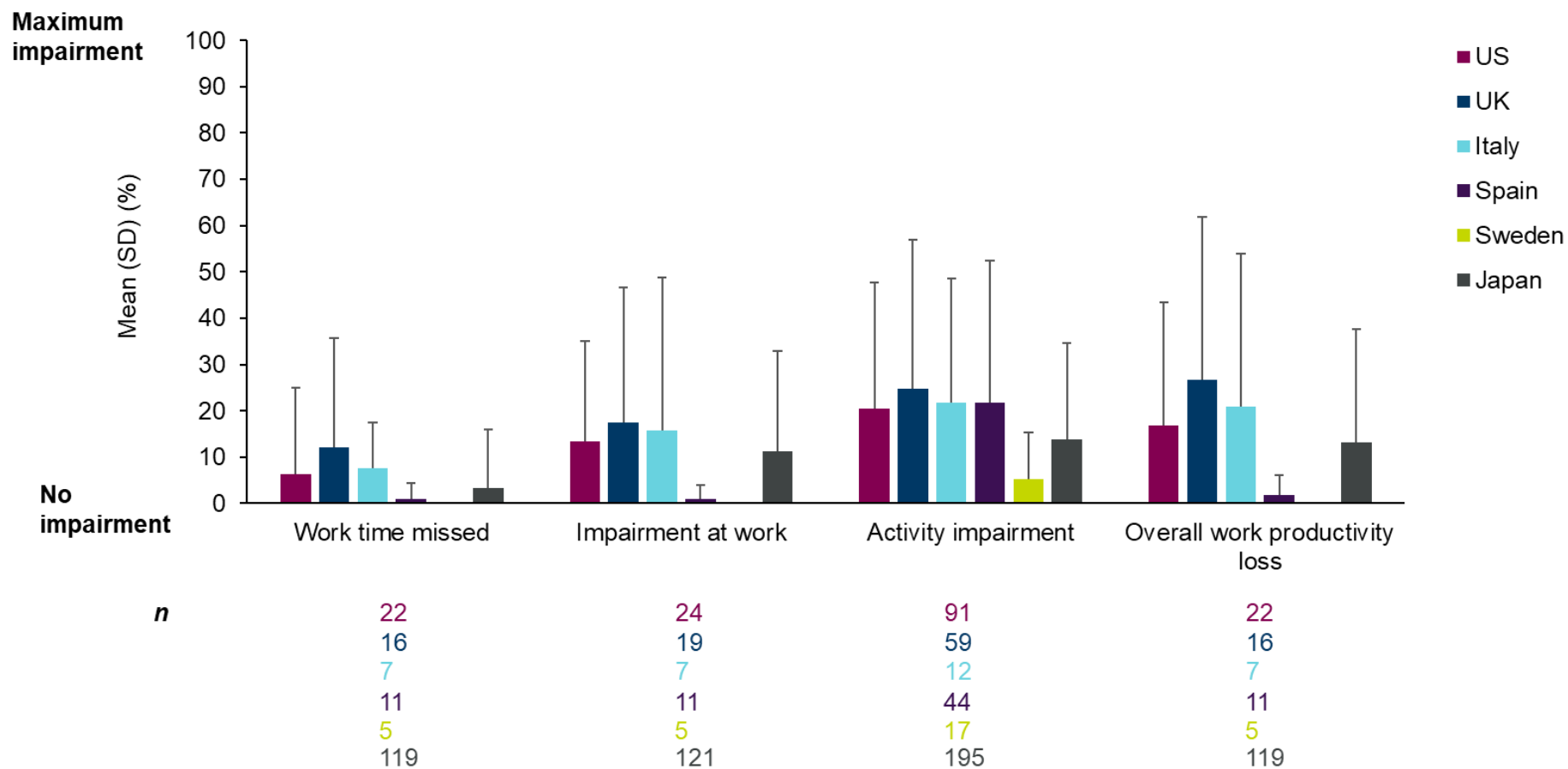
a) Symptoms



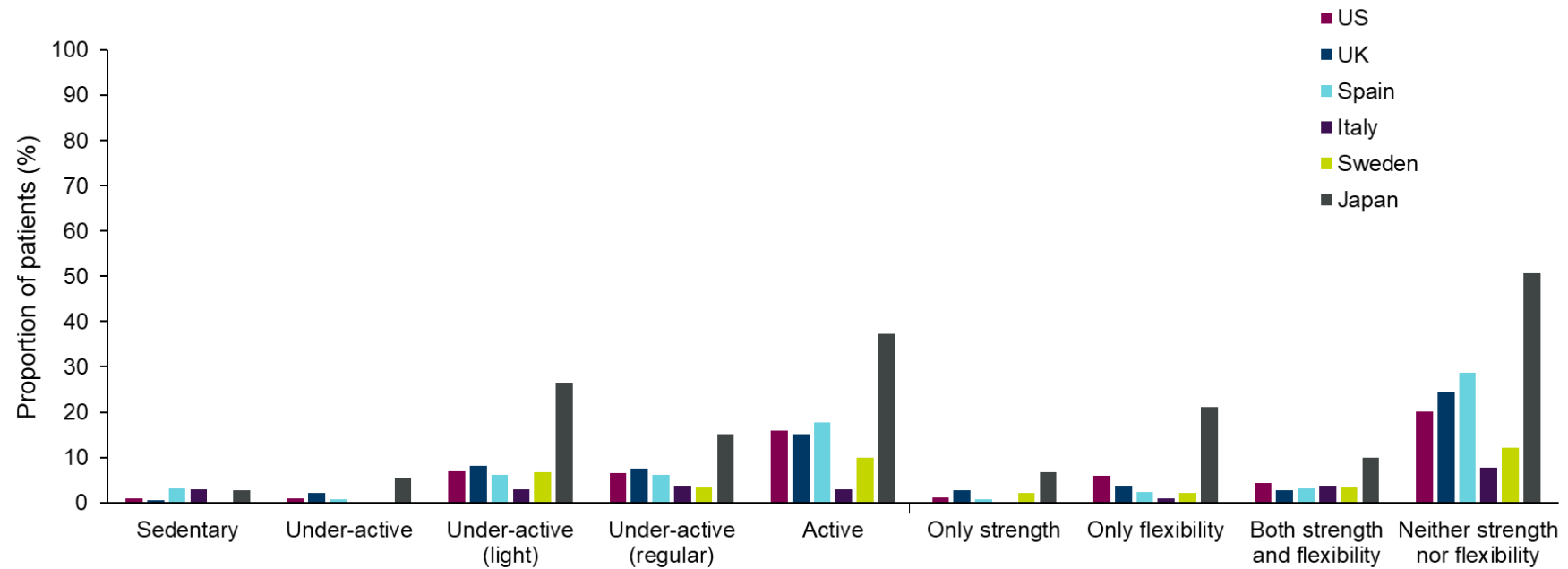
b) SF-36



c) WPAI-CKD



d) RAPA



	Part 1: Aerobic					Part 2: Strength and flexibility				
<i>n</i>	3	3	22	21	51	4	19	14	65	
	1	4	15	14	28	5	7	5	45	
	4	1	8	8	23	1	3	4	37	
	3	0	3	4	3	0	1	4	8	
	0	0	6	3	9	2	2	3	11	
	6	12	59	34	83	15	47	22	113	

Full analysis set ($N = 1052$).

- (a) Scores describe patients' experience of symptoms in the last 7 days. Individual scores are out of a maximum of 10; the overall HRQoL score is a combined score out of a maximum of 110. Higher symptom/overall scores indicate greater symptom burden.
- (b) Weighted scores from each of eight sections of the SF-36 questionnaire are converted onto a 0–100 scale, with lower scores indicating worse HRQoL.
- (c) WPAI-CKD outcomes are expressed as impairment percentages, with higher numbers indicating greater impairment and less productivity. Work time missed = percent work time missed due to problem; impairment at work = percent impairment while working due to problem; activity impairment = percent activity impairment due to problem; overall work impairment = percent overall work impairment due to problem.
- (d) Aerobic RAPA categories are scored as follows: sedentary = no/rare physical activity; under-active = some light/moderate physical activity but not on a weekly basis; under-active (light activity) = weekly light physical activity; under-active regular = < 30 min/day or < 5 days/week of moderate physical activity or < 20 min/day or < 3 days/week of vigorous physical activity; active = ≥ 30 min/day or ≥ 5 days/week of moderate physical activity or ≥ 20 min/day or ≥ 3 days/week of vigorous physical activity.

HRQoL health-related quality of life, *RAPA* Rapid Assessment of Physical Activity, *SF-36* 36-item Short Form, *UK* United Kingdom, *US* United States, *WPAI-CKD* Work Productivity and Activity Impairment – chronic kidney disease.