Quality of Life in Early-Stage Chronic Kidney Disease: A Targeted Literature Review

Authors: James Fotheringham[1], Suzy Paisley[2], Kevin Erickson[3], Maarten Postma[4], John FP Bridges[5], Cornelis Boersma[6], Amit Ahuja[7], Tanya Madan[7], Rishabh Verma[7], Ron Akehurst[2] and Wolfgang Winkelmayer[3]

Contact: James Fotheringham; j.fotheringham@sheffield.ac.uk

Affiliations: [1]School of Population Health, University of Sheffield, Sheffield, UK, [2]Lumanity, London, London, UK, [3]Baylor College of medicine, Houston, TX, USA, [4]Health-Ecore, Zeist, UT, Netherlands, [5]The Ohio State University College of Medicine, Columbus, OH, USA, [6]University of Groningen, Department of Health Sciences, UMCG; Open University, Heerlen, Department of Management Sciences and Health-Ecore Ltd, Zeist, The Netherlands, Zeist, UT, Netherlands,[7]Lumanity, Gurugram, India

INTRODUCTION

- Chronic kidney disease (CKD) is characterized loss of kidney function, ranging from initial risk or damage to mild, through to severe stages and kidney failure. It affects approximately 10% of the global population[1] and has established links to cardiovascular morbidity and mortality;
- The Kidney Disease: Improving Global Outcomes (KIDGO) guidelines categorize CKD based on the estimated glomerular filtration rate (eGFR) values and albuminuria[2]. CKD stage 1: ≥90 ml/min/1.73 m², CKD stage 2: 60-89 ml/min/1.73 m², CKD stage 3a: 45-59 ml/min/1.73 m², CKD stage 3b: 30-44 ml/min/1.73 m², CKD stage 4: 15-29 ml/min/1.73 m² and CKD stage 5: <15 ml/min/1.73 m²
- Significant reductions in QoL are well documented in late-stage CKD (e.g. CKD stage 4 (15-29 ml/min/1.73 m² and stage 5 (<15 ml/min/1.73 m²), but the effect of early stages (CKD1 (>90 ml/min/1.73 m²) and CKD2 (89-60 ml/min/1.73 m²) is relatively unexplored[3]
- QoL has a crucial role in health technology assessment (HTA) submissions and is an important measure of a treatment's value beyond clinical efficacy and safety[4]
- Currently, two out of three CKD patients are underdiagnosed. Understanding how early-stage CKD affects QOL may improve screening and diagnosis[5]

OBJECTIVES

- To synthesize the current evidence on QoL in early-stage CKD (eGFR > 60 mL/min/1.73 m²) and compare it with that of individuals in advanced stages and those without CKD
- To summarise the factors influencing QoL in patients with early-stage CKD

METHODS

- A targeted literature review (TLR) of studies measuring QoL in CKD was undertaken from 2013–2023. Structured searches were conducted in Embase.com across Embase® and MEDLINE® databases
- Title/abstracts and full-text papers were screened according to the pre-defined inclusion criteria (Table 1)
- A single reviewer performed the title/abstract and full-text screenings, with a 20% random quality check by a second, senior reviewer on completion of the screening process At the full-text screening stage, studies that reported QoL data for early-stage CKD (CKD stages 1–2) were prioritised for extraction
- SF-36 and KDQOL scores are interpreted on a 0–100 scale, with higher scores indicating better QoL. EQ-5D scores range from 0 (equivalent to death) to 1 (perfect health).
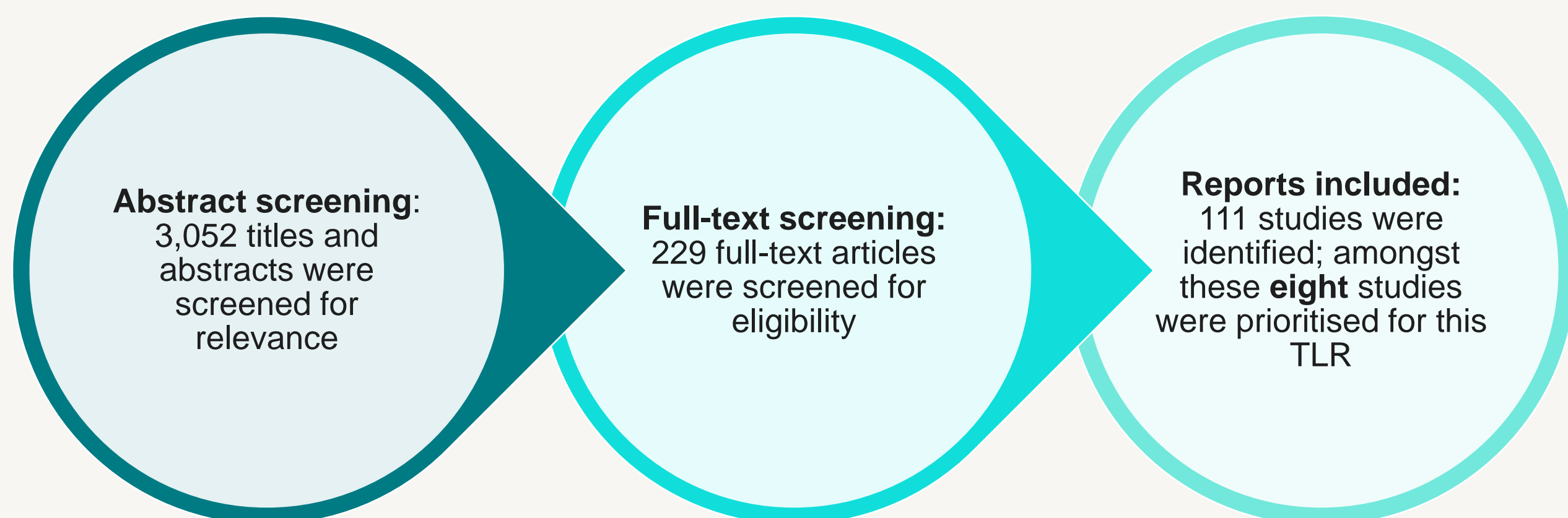
Table 1. Study inclusion criteria

Category	Inclusion criteria
Population	Adult patients with CKD (emphasising CKD1–2)
QoL scales	EQ-5D, SF-36, KDQOL*
Outcomes	QoL data associated with CKD stage; prioritising early-stage disease
Study design	All study types reporting QoL data
Time frame	2013–2023

Key: CKD, chronic kidney disease; HRQL, health-related quality of life; HTA, health technology assessment; KDQOL kidney disease quality of life; QoL, quality of life.
Note: * These QoL measures were identified and chosen through primary research and are suitable for use in assessing HRQL in HTA submissions.

RESULTS

- The titles and abstracts of the identified papers were screened, leading to a full-text review of selected studies, with priority given to those reporting QoL evidence in CKD Stages 1–2. Figure 1 summarizes the flow of study inclusion

Figure 1: Study selection flowchart

Abstract screening: 3,052 titles and abstracts were screened for relevance

Full-text screening: 229 full-text articles were screened for eligibility

Reports included: 111 studies were identified; amongst these **eight** studies were prioritised for this TLR

- Table 2 summarizes the study and patient characteristics of eight studies in CKD. Among the included studies, one used the KDQOL, three used the EQ-5D, and four used the SF-36. Two studies were conducted in both the UK and Germany, with one each in India, Ethiopia, Korea and Australia. Population sizes ranged from 160–5,159, with mean ages between 44.6–74.5 years. Baseline eGFR values ranged from 19.1 to 77.3 ml/min/1.73m²

### Table 2. Study and patient characteristics

Study name	Population size	CKD stage	Region	QoL scale	Age, mean (SD)	Baseline eGFR, mean (SD)
Aggarwal 2016[6]	200	CKD 1–5	India	SF-36	49	NR
Busa 2022[7]	857	CKD 2–4	UK	EQ-5D	74.5 (6.9)	63.8 (15.5)
Faulhaber 2022[8]	5,159	CKD 1–5	Germany	SF-36	NR	NR
Kefale 2019[9]	256	CKD 1–5	Ethiopia	SF-36	52.5 (16.8)	NR
Nguyen 2015[10]	357	CKD 1–5	UK	EQ-5D	CKD 1: 44.6 (18.2) CKD 2: 60.0 (17.4) CKD 3 without albuminuria: 65.3 (14.8) CKD 3 with albuminuria: 74.1 (13.4) CKD 4/5: 72.2 (10.3)	NR
Park 2016[11]	2,568	CKD 1–5	Korea	EQ-5D	45.4	NR
Wirkner 2022[12]	160	CKD 2–5D	Germany	KDQOL-36	66.6 (14.2)	19.1 (18.0)
Wyld 2021[13]	841	CKD 1–5	Australia	SF-36	63.2 (15.9)	77.3 (25.5)

Key: CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; KDQOL, Kidney Disease Quality of Life; NR, not reported; QoL, quality of life; SD, standard deviation; SF-36, Short Form 36 Health Survey.
Note: CKD stage 1: ≥90 ml/min/1.73 m2, CKD stage 2: 60-89 ml/min/1.73 m2, CKD stage 3a: 45-59 ml/min/1.73 m2, CKD stage 3b: 30-44 ml/min/1.73 m2, CKD stage 4: 15-29 ml/min/1.73 m2 and CKD stage 5: <15 ml/min/1.73 m2
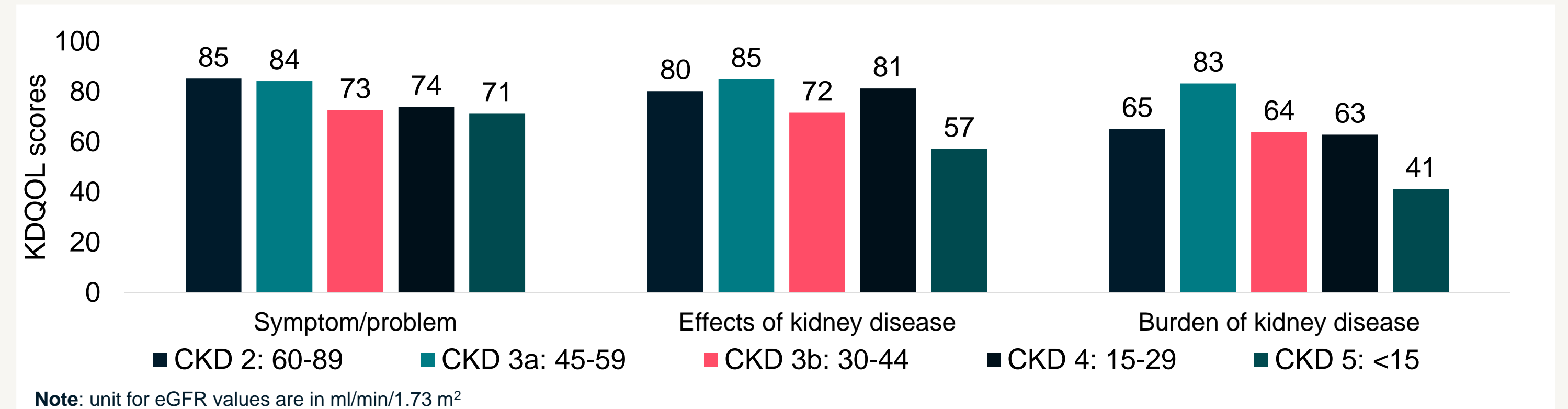
QoL across CKD stages

- Four studies[8, 10, 11, 12] reported a decline in QoL as CKD disease progresses from early to late stages
- Wirkner et al.[12] reported SF-36 Qol values across CKD 2–5 and compared them with the general population. Patients with CKD 2 have higher scores in physical functioning, pain, and general health compared with those with CKD 5. However, these scores are lower than the general population. This study indicates a decline in QoL as kidney function worsens from CKD 2 to CKD 5, with both groups scoring lower than the general population in all domains. Physical Component Summary (PCS) declined from 36.7 (CKD 2) to 30.9 (CKD 5), while Mental Component Summary (MCS) remained stable (47.4 to 47.2). Figure 2 summarizes the QoL scores across all domains as reported in the Wirkner study[12]

Figure 2. SF-36 scores across different domains[12]

Note: unit for eGFR values are in ml/min/1.73 m²
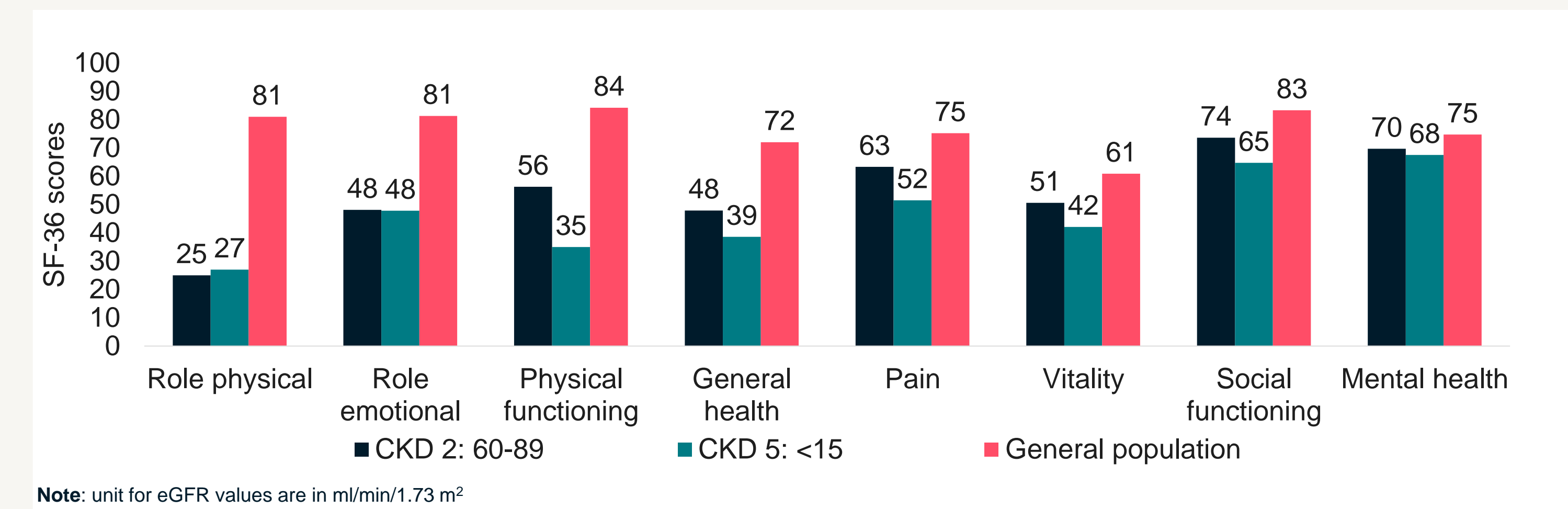
- The same study[12] reported KDQOL scores across CKD 2–5 (Figure 3). The study found no significant differences across CKD categories for work status, cognitive function, social interaction, sexual function, sleep, and social support. Patients in CKD 2 and CKD 3a had higher kidney disease symptoms and problems score compared with others

Figure 3. Kidney Disease Quality of Life Instrument subscales among patients followed longitudinally as CKD progressed[12]

Note: unit for eGFR values in ml/min/1.73 m²

- Faulhaber et al.[8] reported SF-36 scores across CKD 1–5. PCS scores decreased and MCS scores remained stable as the disease progressed (Figure 4)
- Park et al.[11] reported EQ-5D index values for CKD stages 1–5, showing a decline from 0.955 in stage 1 to 0.901 in stage 2, and 0.793 in stages 4/5. EQ-5D values begin to drop from stage 2 compared to the non-CKD population

Figure 4. Physical Component Summary and Mental Component Summary scores among patients followed longitudinally as CKD progressed[8]

Key: PCS, Physical component summary; MCS, Mental component summary Note: unit for eGFR values are in ml/min/1.73 m²
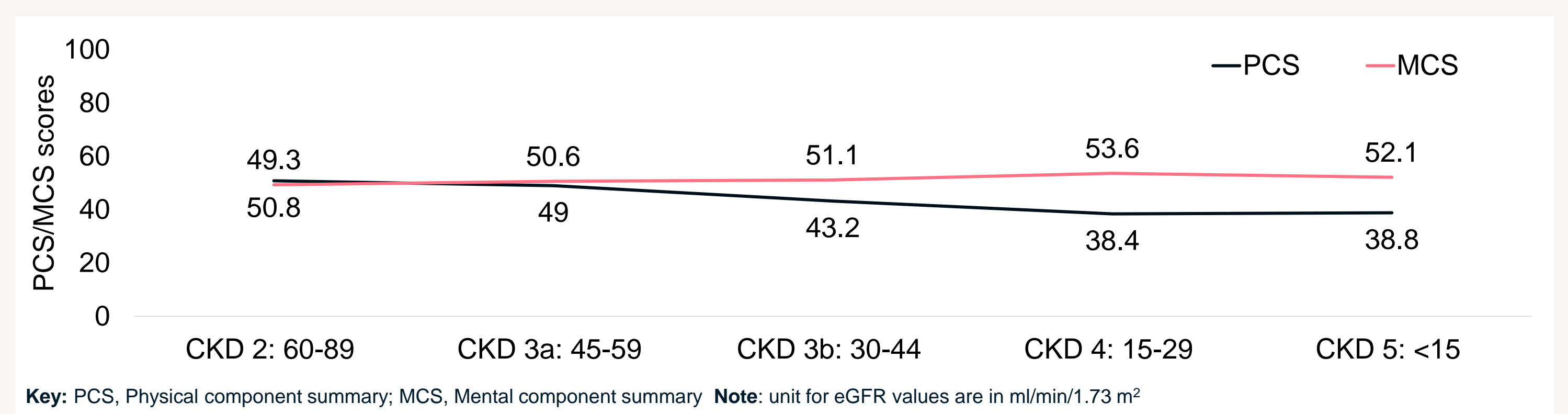
Factors influencing QoL of CKD patients

- Across the included studies, key factors influencing QoL in CKD patients (assessed using the SF-36, KDQOL and EQ-5D scales) include age, eGFR and CKD stage, haemoglobin levels, comorbidities, depression, and medication count. These factors significantly impact physical and mental health outcomes. Table 3 summarizes the factors reported across the studies

Table 3: Factors influencing QoL in CKD patients

Study name	Type of care	SF-36 PCS	SF-36 MCS	KDQOL	EQ-5D
Aggarwal 2016[6]	Unclear	Age, MAP, Hb, CRP, blood urea, serum creatinine, uric acid, calcium, phosphorus, eGFR		NE	NE
Busa 2022[7]	Primary care	NE	NE	NE	Age, BMI, diabetes, smoking status, eGFR, no. of comorbidities
Faulhaber 2022[8]	Primary care	CKD 3a/3b, gender, age, BMI, comorbidities	CKD 1 and 4/5, gender, age, BMI, comorbidities	NE	NE
Kefale 2019[9]	Secondary care	CKD stage, number of medications, number of comorbidities, complications, Hb		NE	NE
Nguyen 2015[10]	Unclear	NE	NE	NE	CKD stage, gender, age
Park 2016[11]	Unclear	NE	NE	NE	Age, proteinuria, diabetes, comorbidities
Wirkner 2022[12]	Unclear	Age, depression, HbA1c		NE	NE
Wyld 2021[13]	Unclear	Age, hypertension, smoking, BMI, high cholesterol, low Vitamin D, hyperuricemia	Age, smoking, low Vitamin D	NE	NE

Key: BMI, body mass index; CKD, chronic kidney disease; CRP, C-Reactive Protein; eGFR, estimated glomerular filtration rate; ESR, erythrocyte sedimentation rate; Hb, haemoglobin; KDQOL, Kidney Disease Quality of Life; MAP, mean arterial pressure; MCS, Mental Component Summary; NE, not evaluated; PCS, Physical Component Summary; SF-36, Short Form 36 Health Survey.

CONCLUSIONS

- Early-stage CKD impacts physical functioning, general health, and pain perception, which remain lower than in the general population. Physical health (PCS) declines as CKD progresses, while mental health (MCS) remains more stable, suggesting a greater toll on physical health in advanced stages. The evidence is limited and not all studies reviewed showed consistent decline across CKD stages
- Key factors affecting QoL in patients with CKD include age, eGFR, haemoglobin levels, comorbidities, CKD stage, depression, and medication
- There is a poor relationship between disease stages and some QoL domains. If treatments for early-stage CKD are to be assessed, more appropriate instruments for the measurement of QoL in trials or greater confidence in existing ones, are needed for reimbursement decision-making

REFERENCES
1. Kovesdy. KI Supplements 12(1): 7-112022. 2. Stevens et al. Kidney International 105(4): S117-S3142024. 3. Sharma et al. Medicina (Kaunas) 59(10)2023. 4. Nicod et al. Eur J Health Econ 23(4): 645-692022. 5. Vart et al. Lancet Reg Health Eur. 20, 2022. 6. Aggarwal et al. Qjm 109(11): 711-62016. 7. Busa et al. PLoS One 17(10): e02755722022. 8. Faulhaber et al. Kidney Blood Press Res 47(1): 13-222022. 9. Kefale et al. PLoS One 14(2): e02121842019. 10. Nguyen et al. PLoS One 13(11): e02079602018. 11. Park et al. Am J Kidney Dis 67(6): 851-602016. 12. Wirkner et al. J Clin Med 11(16)2022. 13. Wyld et al. Nephrol Dial Transplant 36(6): 1048-562021.

An electronic version of the poster can be viewed by scanning the QR code.