Quality of Life in people with CKD: focussing on modifiable risk factors

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Abstract

Purpose of review:

With ageing populations and rising prevalence of key risk factors, the prevalence of many long-term conditions including chronic kidney disease (CKD) is increasing globally. Health related quality of life (HRQoL) is important to people living with CKD but not all HRQoL determinants are modifiable. This review summarises recently identified potentially modifiable factors affecting HRQoL for people with CKD and recent trials incorporating HRQoL as an outcome.

Recent findings

Considering a broad definition of 'potentially modifiable', many factors have been associated with HRQoL in recent observational studies. These include mental health conditions, symptoms, medications, health behaviours, weight-related issues, poor social support, lower education, limited literacy and directly CKD-

related factors such as anaemia. Some potentially modifiable factors have been tested in CKD trials, though often with HRQoL as a secondary outcome, so may be underpowered for HRQoL. Interventions with evidence of effect on HRQoL include physical activity, education, some nutritional interventions and medications targeting CKD-related anaemia.

Summary

Clinicians should consider the range of potentially modifiable factors influencing HRQoL as part of a holistic approach to CKD care. High-quality, adequately-powered trials, with HRQoL as a primary outcome, with interventions focusing on the other potentially modifiable factors identified are needed.

Keywords:

Chronic kidney disease, health-related quality of life, modifiable, risk factors

Introduction

Chronic kidney disease (CKD) is a common but heterogenous condition with many underlying causes and wide variation in severity and risk of progression and other adverse outcomes [1,2]. The health-related quality of life (HRQoL) experienced by people with CKD also varies widely depending on many factors [3]. HRQoL is affected not only by CKD severity, but therapeutic interventions, particularly dialysis, and many symptoms that change as CKD progresses and play an important role in determining individual experience [3,4]. CKD also spans the age range, though is much more common in older people, and HRQoL is known to vary with age [4,5]. Multimorbidity is common among people with CKD which also significantly influences HRQoL [6]. Many aspects affecting HRQoL are not amenable to change and it is logical to focus endeavours on those that are potentially modifiable to improve HRQoL for people living with CKD. To do this, it is worth considering what we mean by ‘modifiable’- a commonly used but poorly defined term. A potentially helpful conceptualisation recommends posing a series of questions about a risk factor:

1. Is it measurable?
2. Is it potentially changeable?
3. Are its causes modifiable in themselves?

4. Is it plausible as a cause?
5. Is there empirical evidence for its effect?

[7]. The ability to infer causality from observational studies may also benefit from a framework approach to explore issues such as the causal assumptions being made [8]. In health contexts ‘modifiable’ is often applied to individual behaviours like smoking, or clinical attributes such as anaemia, but for HRQoL a wider consideration of modifiability is important, such as the influence of health services, social support and policy.

Health-related quality of life

HRQoL has multiple definitions and the term is sometimes used interchangeably with ‘quality of life’ or ‘health-status’ [9]. Distilling from several definitions [10,11,12], HRQoL is a combination of a person’s perceived functional, physical and mental health statuses. Several different outcome measures are used to quantify HRQoL in observational studies and as patient reported outcome measures in clinical trials [13]. It is beyond the remit of this review to explore every HRQoL measure, but understanding the commonly used measures and their limitations is helpful. Several are can be used in general populations but some are condition-specific. *Table 1* summarises some common measures.

Table 1. Summary of commonly used health-related quality of life measures

Risk factors associated with HRQoL in observational studies of people with CKD

Mental health

A substantial body of work now demonstrates an association between mental health conditions and HRQoL. For example, baseline findings from the NURTuRE-CKD secondary care (referred) cohort of 2958 people with CKD study in the UK showed independent associations between poorer HRQoL and depression and anxiety [31]. Analysis of data from 160 patients (inpatients or at dialysis centres) using KDQoL in a German cohort identified depression as an independent predictor of worse physical component summary (PCS) and mental component summary (MCS) [32]. Depression was also among several independent associations with lower HRQoL among 649 non-dialysis CKD patients in the nationally-representative US medical expenditure panel survey (MEPS) [33].

Changes over time in HRQoL were evaluated in the ‘Screening for Chronic Kidney Disease among Older People across Europe’ (SCOPE) project, a multicentre 2-year prospective cohort involving people over 75 years attending outpatients clinics in Austria, Germany, Israel, Italy, the Netherlands, Poland, and Spain, with 1748 participants completing the EQ-5D-5L. Those with greater Geriatric Depression Scale-Short Form scores were more likely to show EQ-VAS decline over time [34].

Similarly, in a German population-representative study of 5159 adults using the SF-36, depression was negatively associated with both PCS and MCS scores. However, while poorer kidney function was associated with most dimensions relating to physical HRQoL, there was no clear association for mental HRQoL [35]. An Irish study among 268 people with a range of CKD severities (including non-dialysis dependent CKD, those using different dialysis modalities and transplant recipients) using SF12 and the Hospital Anxiety and Depression Scale (HADS) showed that mental health conditions were common with depression, anxiety and having a mental health diagnosis all associated with lower HRQoL [36]. A small cross-sectional study among people with non-dialysis dependent CKD tested for cognitive function, frailty and HRQoL also showed that cognitive impairment was associated with poorer HRQoL (SF-36) [37].

Education and work

Several recent studies have demonstrated association between education, work and HRQoL in a variety of settings. Baseline analyses from the NURTuRE-CKD cohort found that those with lower educational attainment were more likely to report poorer HRQoL and that being in work was associated with better HRQoL [31]. A cross-sectional study in secondary care setting in Nigeria including 220 people with CKD stages 1 to 4 used the 15-dimensional HRQoL questionnaire and showed that lower education level and unemployment or self-employment were independently associated with poor HRQoL [38]. A cross-sectional study of 300 people with CKD at two Ethiopian hospitals using KDQoL-36 identified that poorer PCS was independently associated with lower levels of literacy [39].

Illness denial and patient activation

A survey of 14 renal units in England of 3013 people with non-dialysis dependent CKD, dialysis, and kidney transplant, used latent class analysis to determine HRQoL and symptom burden subgroups. Lower patient activation levels were associated with higher symptom burden and reduced HRQoL across CKD stages and treatment modalities [40]. An interesting cross-sectional study of 100 people with CKD in an outpatient setting

in a single hospital in Italy investigated the link between illness denial, specific personality traits (‘Big-Five’) and HRQoL using the KDQOL-SF. Illness denial was associated with better HRQoL and certain personality traits (extraversion, agreeableness, conscientiousness, neuroticism and openness) were associated with better HRQoL in certain domains [41]. A Dutch cohort study of 180 older adults with eGFR ≤ 20 mL/min/1.73 m^2 assessed apathy symptoms using a subscale of the Geriatric Depression Scale. Apathy was common (36% of older patients with CKD) and presence of apathy symptoms was associated with lower physical and cognitive functioning and HRQoL at baseline [42].

Health behaviours

Physical activity has been linked to HRQoL in several observational studies. An analysis of step count among 558 adults with CKD suggested that walking between 7,000 and 12,000 steps daily was associated with high HRQOL and step count demonstrated an inverse U-shaped relationship with SF-36 subscale scores; lower than 7,000 was associated with lower PCS and MCS scores and higher than 12,000 with lower MCS score [43]. Lower physical activity was also associated with worse HRQoL in the MEPS study described above [33].

A propensity score matching approach was used among 1618 patients from the KNOW-CKD study to estimate the effect of physical activity on HRQoL. ‘Health-enhancing physical activity’ (150 min of moderate-intensity or 75 min of vigorous-intensity aerobic physical activity a week) was associated with better HRQoL [44].

Smoking has been implicated in worse HRQoL. The NURTuRE-CKD HRQoL study found that being an ex-smoker was associated with worse HRQoL by EQ-5D-3L mapped index value [31]. The cross-sectional Ethiopian study mentioned above also found previous smoking to be independently associated with poorer PCS [39].

Diet, specifically low protein diet, was associated with both depression and poor HRQoL (EQ-5D-5L index) after adjusting for relevant confounders in a cross-sectional study of 571 people with CKD in South Korea [45]. In a secondary analysis from a randomised trial of an exercise intervention in 99 people with CKD stage 3b-4, poor appetite was a component of baseline ‘geriatric syndromes’ (including cognitive impairment, poor appetite, dizziness, fatigue, and chronic pain) that were associated with lower HRQOL (SF-36 and EQ-5D-5L)

[46]. Among 100 people with autosomal dominant polycystic kidney disease in a cross-sectional study, a positive relationship was observed between dietary adherence and HRQoL (EQ-5D-3L) [47].

Medications

The NUTuRE-CKD HRQoL study identified that polypharmacy was independently associated with worse overall HRQoL and problems in most dimensions, possibly linked to greater comorbidity. Some individual medications were also associated with HRQoL measures. Taking prednisolone was associated with worse HRQoL in the self-care dimension. In contrast, treatment with renin-angiotensin system inhibitors was associated with fewer reported problems in mobility and usual activities dimensions [31].

Polypharmacy was also negatively associated with HRQoL in the MEPS study [33]. Over 2/3 had ‘major polypharmacy’ (5–9 medication classes), and ‘hyperpolypharmacy’ (≥10 medication classes). Mean PCS score was lower among those with major compared to minor polypharmacy. Age, income, health insurance coverage, lower physical activity, census region, number of comorbidities, depression, diabetes, arthritis, and cardiovascular disease were also negatively associated with HRQoL [33].

Weight

Several studies have identified associations between overweight and obesity and lower HRQoL. For example, in the German population-based study described above, higher BMI, was associated with lower perceived general state of health [35]. This was also the case in the NURTuRE-CKD HRQoL baseline analyses, where obesity was independently associated with poorer HRQoL [31].

Symptoms

A major systematic review and meta-analysis including 449 studies and a total of 199,147 participants from 62 countries identified the high symptom and HRQoL burden experienced by people with CKD [3]. Fatigue, poor mobility, drowsiness, and pain (especially bone or joint pain) were particularly common. HRQoL was reported in 361 of the studies confirming that HRQoL scores were lowest in people on dialysis, better for those receiving a kidney transplant and higher for those not requiring kidney replacement therapy [3].

Other recent studies exploring symptoms and HRQoL have identified the following:

- Pain and frailty in NURTuRE-CKD HRQoL [31].
- ‘Geriatric syndromes’ (cognitive impairment, poor appetite, dizziness, fatigue, and chronic pain) in secondary analysis of a randomised trial of an exercise intervention [46].

- Reduced physical function and physical performance in a cross-sectional study of 61 older people with CKD stages 3-5 in Japan and in the SCOPE study described above [34,48].
- Sleep disorders in a cross-sectional study of 172 people with non-dialysis CKD [49].
- Constipation in a systematic review and meta-analysis exploring gastrointestinal symptoms among people with non-dialysis CKD [50].
- Difficulty with usual activities, drowsiness and shortness of breath in a UK cross-sectional study among 216 people with conservatively-managed CKD stage 5. Variables independently associated with poorer EQ-VAS were difficulty performing usual activities, self-rated drowsiness and shortness of breath [51].

Kidney function

Several studies have linked kidney function with HRQoL. For example, in the population-representative German study, poorer kidney function was associated with most dimensions relating to physical HRQoL while for mental HRQoL there was no clear association with different eGFR categories [35]. In NURTuRE-CKD HRQoL, higher eGFR was independently associated with a higher self-reported VAS score [31]. By contrast, the SCOPE study findings suggested that decrease in kidney function did not contribute to EQ-VAS decline over a two-year period in early CKD [34]. Rapid kidney function decline was, however, linked to rapid HRQoL deterioration in the KNOW-CKD study (610 participants with non-rapid decline and 360 with rapid decline). The PCS score decreased significantly in both rapid and non-rapid decline groups, while the MCS score decreased significantly only in the rapid kidney function decline group [52].

Potentially modifiable conditions closely linked to CKD

A cross-sectional study of 423 10-year long term survivors in the Frontier of Renal Outcome Modifications in Japan study found that baseline systolic blood pressure and history of hyperuricemia were predictors of HRQOL [52]. Similarly in the population-representative German study, hypertension was associated with lower perceived general state of health, as was heart failure [35].

Several studies identify anaemia as contributing to poor HRQoL. These include a cross-sectional Sri Lankan study in 886 people with CKD of varying severity using a structural equation modelling approach to identify factors contributing directly or indirectly to HRQoL (EQ-5D-3L) [54]. Symptoms were strongly negatively

associated with HRQoL and decreased kidney function, lower haemoglobin and greater number of comorbidities directly contributed to increased symptoms, therefore indirectly influencing HRQoL. The NURTuRE-CKD HRQoL study identified haemoglobin <100 g/L as independently associated with worse HRQoL [31]. An online US survey of 410 patients and 258 care partners exploring the burden experienced by people with anaemia and CKD found that patients with anaemia reported lower average HRQoL and partners reported severe burden [55].

Studies among people requiring kidney replacement therapy (KRT)

From studies among people requiring KRT, there are many similar themes to the non-dialysis dependent population. These are summarised in *Table 2.*

Table 2. Exposures associated with worse health-related quality of life among people requiring kidney replacement therapy

Studies among children with CKD

A systematic review and meta-analysis of 14 studies among 5- to 18-year-old patients with kidney failure (using PedsQL 4.0 Generic Core Scale (GCS) and the PedsQL 3.0 ESRD Module) identified that kidney transplant patients reported a significantly higher HRQoL than those on dialysis [65]. Those on peritoneal dialysis reported better HRQoL than those on haemodialysis. A longitudinal study involving 692 children (median age 11.2, median 8.3 years CKD duration) using PedsQL found that longer CKD duration was associated with better HRQoL on child self-report [66]. The authors' had expected disease progression or worsening CKD to be associated with worsening HRQoL and suggested their findings may represent a degree of adaptation by children with CKD [66]. A cohort study in Australia and New Zealand assessed trajectories of HRQoL among 377 children with CKD aged 6-18 years over four years. The authors concluded that improvement in HRQoL over time for children on dialysis was likely related to transition to transplantation. Children with CKD stage 1-5 and transplant recipients at baseline experienced stable HRQoL over time [67].

Recent trials with HRQoL as an outcome measure

Relatively few of these wide-ranging potentially modifiable factors have been tested in CKD trials. *Table 3* summarises recently conducted trials that have included HRQoL as either primary or secondary outcome [68-79].

Table 3. Recent trials in people with CKD that included HRQoL as an outcome measure

Benefit to HRQoL in at least one study was shown for education interventions, physical activity interventions, medications to treat CKD-related anaemia, and nutritional interventions. No benefit to HRQoL was shown for medications aimed at slowing CKD progression and medications for depression. Of the twelve trials in Table 3, it is notable that only two included HRQoL as their primary outcome measure [68,78].
Figure 1 provides an overview, summarising the potentially modifiable factors associated with HRQoL in recent observational studies and those tested as interventions with some evidence of effect in recent trials. Follow-up analysis of an older trial (excluded from Table 3) of gastric bypass among people with diabetic kidney disease and obesity showed evidence of HRQoL improvement as a secondary outcome [80].

Conclusion

Poor HRQoL is common among people with CKD and many potentially modifiable determinants have been identified, including mental health conditions, symptoms, medications, health behaviours, weight-related issues, poor social support, lower education, limited literacy and directly CKD-related factors such as anaemia. Only some of these have been intervention targets in CKD trials with HRQoL as an outcome. Promising interventions for improving HRQoL include physical activity, education, some nutritional interventions and medications targeting CKD-related anaemia. Clinicians should consider the wide range of potentially modifiable factors that influence HRQoL as part of a holistic approach to CKD care. High-quality, adequately-powered trials, using HRQoL as a primary outcome, with interventions focusing on the other potentially modifiable factors identified are needed.

Key points -

1. Many potentially modifiable factors have been associated with HRQoL in recent observational studies among people with CKD, including mental health conditions, symptoms, medications, health

behaviours, weight-related issues, poor social support, lower education, limited literacy and directly CKD-related factors such as anaemia.

2. Only some potentially modifiable factors have been tested in CKD trials and those showing promise at improving HRQoL include physical activity, education, some nutritional interventions and medications targeting CKD-related anaemia.
3. Clinicians should consider the wide range of potentially modifiable factors that influence HRQoL as part of a holistic approach to CKD care.
4. High-quality, adequately-powered trials with interventions focusing on the other potentially modifiable factors identified are needed.

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References

1. Levin A, Stevens PE, Bilous RW, et al. Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. Kidney international supplements. 2013;3(1):1-150
2. Webster AC, Nagler EV, Morton RL, Masson P. Chronic Kidney Disease. Lancet. 2017 Mar 25;389(10075):1238-1252. doi: 10.1016/S0140-6736(16)32064-5. Epub 2016 Nov 23. PMID: 27887750.
3. **Fletcher BR, Damery S, Aiyegbusi OL, et al. Symptom burden and health-related quality of life in chronic kidney disease: A global systematic review and meta-analysis. PLoS Med. 2022;19(4):e1003954. doi: 10.1371/journal.pmed.1003954.
   Major review highlighting the range of symptoms experienced by people with CKD and the impact of those symptoms on HRQoL.
4. Mujais SK, Story K, Brouillette J, et al. Health-related quality of life in CKD Patients: correlates and evolution over time. Clin J Am Soc Nephrol. 2009;4(8):1293-301. doi: 10.2215/CJN.05541008.
5. Webb E, Blane D, McMunn A, Netuveli G. Proximal predictors of change in quality of life at older ages.Journal of Epidemiology & Community Health 2011;65:542-547. https://doi.org/10.1136/jech.2009.101758
6. Fraser SD, Barker J, Roderick PJ, et al. Health-related quality of life, functional impairment and comorbidity in people with mild-to-moderate chronic kidney disease: a cross-sectional study. BMJ Open. 2020;10(8):e040286. doi: 10.1136/bmjopen-2020-040286.
7. *Alwan NA, Stannard S, Berrington A, et al. Risk factors for ill health: How do we specify what is ‘modifiable’? PLOS Glob Public Health 4(3): e0002887. https://doi.org/10.1371/journal.pgph.0002887
   An important potential framework for considering which factors may be modified in chronic disease
8. Dahabreh IJ, Bibbins-Domingo K. Causal inference about the effects of interventions from observational studies in medical journals. JAMA 2024. doi:10.1001/jama.2024.7741
9. Karimi M, Brazier J. Health, Health-Related Quality of Life, and Quality of Life: What is the Difference? Pharmacoeconomics. 2016;34(7):645-9.

10. Wilson IB, Cleary PD. Linking Clinical Variables With Health-Related Quality of Life: A Conceptual Model of Patient Outcomes. Jama. 1995;273(1):59-65.
11. Torrance GW. Utility approach to measuring health-related quality of life. J Chronic Dis. 1987;40(6):593-603.
12. Ebrahim S. Clinical and public health perspectives and applications of health-related quality of life measurement. Social Science & Medicine. 1995;41(10):1383-94.
13. Kluetz PG, Slagle A, Papadopoulos EJ, et al. Focusing on Core Patient-Reported Outcomes in Cancer Clinical Trials: Symptomatic Adverse Events, Physical Function, and Disease-Related Symptoms. Clin Cancer Res. 2016;22(7):1553-8.
14. EuroQol Group. EuroQoL - a new facility for the measurement of health-related quality of life. Health Policy. 1990;16(3):199-208.
15. Rabin R, de Charro F. EQ-5D: a measure of health status from the EuroQol Group. Annals of Medicine. 2001;33(5):337-43.
16. Herdman M, Gudex C, Lloyd A, et al. Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). Qual Life Res. 2011;20(10):1727-36.
17. Janssen MF, Pickard AS, Golicki D, et al. Measurement properties of the EQ-5D-5L compared to the EQ-5D-3L across eight patient groups: a multi-country study. Qual Life Res. 2013;22(7):1717-27.
18. Stolk E, Ludwig K, Rand K, et al. Overview, Update, and Lessons Learned From the International EQ-5D-5L Valuation Work: Version 2 of the EQ-5D-5L Valuation Protocol. Value Health. 2019;22(1):23-30.
19. Devlin NJ, Shah KK, Feng Y, et al. Valuing health-related quality of life: An EQ-5D-5L value set for England. Health Econ. 2018;27(1):7-22.
20. Hernández Alava M, Pudney S, Wailoo A. Estimating the Relationship Between EQ-5D-5L and EQ-5D-3L: Results from a UK Population Study. Pharmacoeconomics. 2023;41(2):199-207.
21. Tarlov AR, Ware JE Jr, Greenfield S, et al. The Medical Outcomes Study. An application of methods for monitoring the results of medical care. Jama. 1989;262(7):925-30.
22. Stewart AL, Ware JE. Measuring functioning and well-being: the medical outcomes study approach: duke university Press; 1992.
23. Ware J, Kosinski M, Keller S. SF-36 physical and mental health summary scales. A user's manual. 2001;1994.

24. Hays RD, Kallich J, Mapes D, et al. Kidney Disease Quality of Life Short Form (KDQOL-SF™), version 1.3: a manual for use and scoring. Santa Monica: RAND. 1997:7994.
25. Taft C, Karlsson J, Sullivan M. Do SF-36 summary component scores accurately summarize subscale scores? Qual Life Res. 2001;10(5):395-404. doi: 10.1023/a:1012552211996. PMID: 11763202.
26. Saban KL, Bryant FB, Reda DJ, et al. Measurement invariance of the kidney disease and quality of life instrument (KDQOL-SF) across veterans and non-veterans. Health Qual Life Outcomes. 2010;8:120.
27. Peipert JD, Nair D, Klicko K, et al. Kidney Disease Quality of Life 36-Item Short Form Survey (KDQOL-36) Normative Values for the United States Dialysis Population and New Single Summary Score. J Am Soc Nephrol. 2019;30(4):654-63.
28. Peipert, JD, Nair D, Klicko K, et al. Kidney Disease Quality of Life 36-Item Short Form Survey (KDQOL-36) Normative Values for the United States Dialysis Population and New Single Summary Score. J Am Soc Nephrol. 2019; 30(4):654-663.
29. World Health Organisation. Programme on mental health: WHOQOL user manual. WHO 1998.
30. Development of the World Health Organization WHOQOL-BREF quality of life assessment. The WHOQOL Group. Psychol Med. 1998;28(3):551-8.
31. *Phillips T, Harris S, Aiyegbusi OL, et al. Potentially modifiable factors associated with health-related quality of life among people with chronic kidney disease: baseline findings from the National Unified Renal Translational Research Enterprise CKD (NURTuRE-CKD) cohort. Clin Kidney J. 2024;17(2):sfae010.
    A recent cross-sectional study which identified multiple potentially modifiable factors associated with HRQoL in an non-dialysis dependent CKD cohort
32. Wirkner J, Scheuch M, Dabers T, et al. Comorbid depression and diabetes are associated with impaired health-related quality of life in chronic kidney disease patients. J Clin Med. 2022;11(16):4671
33. Adjeroh L, Brothers T, Shawwa K, et al. The association between polypharmacy and health-related quality of life among non-dialysis chronic kidney disease patients. PLoS One. 2023;18(11):e0293912.
34. Artzi-Medvedik R, Kob R, Di Rosa M, et al. Quality of Life and Kidney Function in Older Adults: Prospective Data of the SCOPE Study. J Clin Med. 2023;12(12):3959.

35. Faulhaber L, Herget-Rosenthal S, Jacobs H, Hoffmann F. Health-Related Quality of Life according to Renal Function: Results from a Nationwide Health Interview and Examination Survey. Kidney Blood Press Res. 2022;47(1):13-22.
36. Cogley C, Bramham J, Bramham K, et al. High rates of psychological distress, mental health diagnoses and suicide attempts in people with chronic kidney disease in Ireland. Nephrol Dial Transplant. 2023;38(10):2152-2159.
37. Greinert R, Greinert D, Eger AL, et al. Subclinical cognitive impairment in chronic kidney disease is associated with frailty and reduced quality of life. Nephrol Dial Transplant. 2023;38(5):1151-1157.
38. Okoro RN, Adibe MO, Okonta MJ, et al. Assessment of health-related quality of life and its determinants in the pre-dialysis patients with chronic kidney disease. Int Urol Nephrol. 2022;54(1):165-172.
39. Berhe T, Tegegne GT, Berha AB. Quality of life and associated factors among chronic kidney disease patients at Zewditu Memorial and Tikur Anbessa Specialised Hospitals, Ethiopia: a cross-sectional study design. BMJ Open. 2023;13(6):e069712.
40. Magadi W, Lightfoot CJ, Memory KE, et al. Patient activation and its association with symptom burden and quality of life across the spectrum of chronic kidney disease stages in England. BMC Nephrol. 2022;23(1):45.
41. Pugi D, Ferretti F, Galeazzi M, et al. Health-Related Quality of Life in pre-dialysis patients with chronic kidney disease: the role of Big-Five personality traits and illness denial. BMC Psychol. 2022;10(1):297.
42. Voorend CGN, van Buren M, Berkhout-Byrne NC, et al. Apathy symptoms, physical and cognitive function, health-related quality of life, and mortality in older patients with ckd: a longitudinal observational study. Am J Kidney Dis. 2024;83(2):162-172.e1.
43. Xiong J, Peng H, Yu Z, et al. Daily walking dose and health-related quality of life in patients with chronic kidney disease. J Ren Nutr. 2022;32(6):710-717.
44. Oh TR, Choi HS, Suh SH, et al. The association between health-enhancing physical activity and quality of life in patients with chronic kidney disease: propensity score matching analysis. Int J Environ Res Public Health. 2022;19(3):1318.
45. Lee DY, Han SY, Lee K, et al. Association of a low protein diet with depressive symptoms and poor health-related quality of life in CKD. J Psychiatr Res. 2023;161:282-288.

46. Liu CK, Miao S, Giffuni J, et al. Geriatric syndromes and health-related quality of life in older adults with chronic kidney disease. Kidney360. 2023;4(4):e457-e465.
47. Yarlioglu AM, Oguz EG, Gundogmus AG, et al. The relationship between depression, anxiety, quality of life levels, and the chronic kidney disease stage in the autosomal dominant polycystic kidney disease. Int Urol Nephrol. 2023;55(4):983-992.
48. Tabata A, Yabe H, Katogi T, et al. Factors affecting health-related quality of life in older patients with chronic kidney disease: a single-center cross-sectional study. Int Urol Nephrol. 2022;54(10):2637-2643.
49. Chen Y, Li M, Zhou L, et al. Association among sleep, depression, and health-related quality of life in patients with non-dialysis chronic kidney disease during the coronavirus disease 2019 pandemic. Ann Palliat Med. 2022;11(6):1865-1875.
50. Ruszkowski J, Majkutewicz K, Heleniak Z, et al. Prevalence and severity of lower gastrointestinal symptoms amongst non-dialysis chronic kidney disease patients: a systematic review and meta-analysis. J Clin Med. 2022;11(21):6363.
51. So S, Brown MA, Li K. Factors associated with quality of life in patients with kidney failure managed conservatively and with dialysis: a cross-sectional study. BMC Nephrol. 2023;24(1):322.
52. Kim HJ, Kim DW, Rhee H, et al. Rapid decline in kidney function is associated with rapid deterioration of health-related quality of life in chronic kidney disease. Sci Rep. 2023;13(1):1786.
53. Okubo R, Kondo M, Imasawa T, et al. Health-related Quality of Life in 10 years Long-term Survivors of Chronic Kidney Disease: A From-J Study. J Ren Nutr. 2024;34(2):161-169.
54. Yapa HE, Purtell L, Chambers S, Bonner A. Factors influencing health-related quality of life in people with chronic kidney disease: A structural equation modelling approach. J Clin Nurs. 2023;32(13-14):3445-3455.
55. Michalopoulos SN, Gauthier-Loiselle M, Aigbogun MS, et al. Patient and care partner burden in CKD patients with and without anemia: a US-based survey. Kidney Med. 2022;4(4):100439.
56. Poku E, Harnan S, Rooney G, et al. The relationship between chronic kidney disease-associated pruritus and health-related quality of life: a systematic review. Clin Kidney J. 2021;15(3):484-499.
57. Titapiccolo JI, Lonati C, Goethel-Paal B, et al. Chronic kidney disease-associated pruritus (CKD-aP) is associated with worse quality of life and increased healthcare utilization among dialysis patients. Qual Life Res. 2023;32(10):2939-2950.

58. Skoumalova I, Madarasova Geckova A, Rosenberger J, et al. Health literacy and change in health-related quality of life in dialysed patients. Int J Environ Res Public Health. 2022;19(2):620.
59. Aslam A, Shah S, Abbas G, et al. Assessment of health-related quality of life in hypertensive hemodialysis patients. PeerJ. 2022;10:e12690.
60. Király E, Szőllősi GJ, Jenei Z, Kárpáti I. Association between physical activity and quality of life in haemodialysed and peritoneal dialyzed patients in Hungary. Ren Fail. 2024;46(1):2324079.
61. Gebrie MH, Asfaw HM, Bilchut WH, et al. Health-related quality of life among patients with end-stage renal disease undergoing hemodialysis in Ethiopia: a cross-sectional survey. Health Qual Life Outcomes. 2023;21(1):36.
62. Shariff AB, Panlilio N, Kim AHM, Gupta A. Assessment of frailty and quality of life and their correlation in the haemodialysis population at Palmerston North Hospital, New Zealand. Nephrology (Carlton). 2024;29(2):93-99.
63. Morin C, Pichette M, Elftouh N, et al. Is health-related quality of life trajectory associated with dialysis modality choice in advanced chronic kidney disease? Perit Dial Int. 2024:8968608231217807.
64. Mathew N, Davies M, Kaldine F, Cassimjee Z. Comparison of quality of life in patients with advanced chronic kidney disease undergoing haemodialysis, peritoneal dialysis and conservative management in Johannesburg, South Africa: a cross-sectional, descriptive study. BMC Psychol. 2023;11(1):151.
65. Doshi K, Raina R, Ng KH, et al. Health-related quality of life for pediatric patients with end-stage kidney disease: A systematic review and meta-analysis of the Pediatric Quality of Life Inventory (PedsQL). Hemodial Int. 2024;28(2):198-215.
66. Carlson J, Gerson AC, Matheson MB, et al. Longitudinal changes of health-related quality of life in childhood chronic kidney disease. Pediatr Nephrol. 2023;38(12):4127-4136.
67. Guha C, van Zwieten A, Khalid R, et al. Longitudinal assessment of the health-related quality of life of children and adolescents with chronic kidney disease. Kidney Int. 2023;103(2):357-364.
68. **Greenwood SA, Young HML, Briggs J, et al. Evaluating the effect of a digital health intervention to enhance physical activity in people with chronic kidney disease (Kidney BEAM): a multicentre, randomised controlled trial in the UK. Lancet Digit Health. 2024;6(1):e23-e32.
    This intervention has shown benefit to HRQoL for people with either non-dialysis and kidney replacement dependent CKD, and could target several potentially-modifiable factors associated with worse HRQoL

69. Bohlke M, Barcellos FC, Santos IS, et al. Effects of a 16-week physical training on clinical outcomes in patients with hypertension and chronic kidney disease: NEPHROS post-trial follow-up. Cad Saude Publica. 2022;38(5) (no pagination).
70. Thompson S, Wiebe N, Stickland MK, et al. Physical activity in renal disease and the effect on hypertension: a randomized controlled trial. Kidney Blood Press Res. 2022;47(7):475-85.
71. Sarker MH. A CKD awareness campaign and mhealth education to improve knowledge and quality of life among ckd patients in Bangladesh: a randomized controlled trial. J Am Soc Nephrol. 2022;33:48-9.
72. *Lee MC, Wu SFV, Lu KC, et al. Effect of patient-centered self-management program on blood pressure, renal function control, and the quality of life of patients with hypertensive nephropathy: a longitudinal randomized controlled trial. Biol Res Nurs. 2022;24(2):216-25.
A recent randomised trial of a physical activity intervention that considered HRQoL as the primary outcome and showed a statistically significant effect.
73. Weir MA, Walsh M, Cuerden MS, et al. The effect of micro-particle curcumin on chronic kidney disease progression: the MPAC-CKD randomized clinical trial. Nephrol Dial Transplant. 2023;38(10):2192-200.
74. Cha RH, Kang SH, Han MY, et al. Effects of AST-120 on muscle health and quality of life in chronic kidney disease patients: results of RECOVERY study. J Cachexia Sarcopenia Muscle. 2022;13(1):397-408.
75. Saleh-Arong FAH, Trisukon W, Chokemaitree N, et al. Effect of agomelatine and sertraline on major depressive disorders in patients with chronic kidney disease: A double blinded randomized controlled trial. Nephrology. 2021;26(SUPPL 1):23.
76. Greenwood SA, Oliveira BA, Asgari E, et al. A randomized trial of intravenous iron supplementation and exercise on exercise capacity in iron-deficient nonanemic patients with CKD. Kidney Int Rep. 2023;8(8):1496-505.
77. *Johansen KL, Cobitz AR, Singh AK, et al. The ASCEND-NHQ randomized trial found positive effects of daprodustat on hemoglobin and quality of life in patients with non-dialysis chronic kidney disease. Kidney Int. 2023;103(6):1180-92.
This trial demonstrated anaemia correction with daprodustat and significant HRQoL benefit, in keeping with older studies into erythropoetin stimulating agents.

78. Hamidianshirazi M, Shafiee M, Ekramzadeh M, et al. Diet therapy along with nutrition education can improve renal function in people with stages 3-4 chronic kidney disease who do not have diabetes: a randomised controlled trial. Br J Nutr. 2023;129(11):1877-87.
79. Hosojima M, Kabasawa H, Kaseda R, et al. Efficacy of low-protein rice for dietary protein restriction in CKD patients: a multicenter, randomized, controlled study. Kidney360. 2022;3(11):1861-70.
80. Cohen RV, Pereira TV, Aboud CM, et al. Gastric bypass versus best medical treatment for diabetic kidney disease: 5 years follow up of a single-centre open label randomised controlled trial. EClinicalMedicine. 2022. ;53:101725.

Figure 1. Potentially modifiable factors known to independently affect health related quality of life among people with CKD and interventions with evidence of effectiveness