Outcomes and care priorities for older people living with frailty and advanced chronic kidney disease: a multi-professional scoping review

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Key Words

Chronic Kidney Disease (CKD); Chronic Renal Failure; Renal replacement therapy; Dialysis; Transplantation; Older people; Aged; Frailty; Comprehensive Geriatric Assessment

Key points:

- The prevalence of frailty in advanced chronic kidney disease (ACKD) is greater than in the general population.
- Understanding care priorities and outcomes relevant to individuals living with frailty and advanced chronic kidney disease (ACKD) is important.
- Providing interventions that reflect improvements in outcome measures that matter to patients is essential.
- Poor health outcomes in individuals living with frailty and advanced chronic kidney disease (ACKD) is of concern.

Abstract

Background

The growing older population with advanced chronic kidney disease (ACKD stages 4-5) poses a challenge for healthcare worldwide. The high prevalence of frailty and associated adverse health outcomes highlights concerns for management and interventions specific to this population.

Objectives

The aim was to objectively review the evidence relating to older people ($\geq$65years) living with frailty and ACKD. More specifically how frailty is identified, what interventions have been studied and what outcomes have been reported including outcomes important to patients, families and carers.

Methods

A scoping review was undertaken following the PRISMA-Scr guidelines. Nine databases were searched and a review team of five people followed a process using defined inclusion and exclusion criteria. Data was then analysed to answer the specific questions of the review. The World Health Organisation (WHO)'s International Classification of Functioning Disability and Health (ICF) was used to map outcomes across the domains.

Results

A total of 90 studies were included. The most reported frailty measure was the Frailty Phenotype. The most reported outcomes were mortality, hospitalisation and healthcare utilisation. Health related quality of life was the most common patient reported outcome measure. There were few intervention studies and limited evidence of patient and carer perspectives.

Conclusion

This scoping review highlights important areas for further research in older people living with frailty and ACKD. This includes a ‘gold standard’ measure for identifying frailty, interventions and improvements in outcome measures that matter to patients (including studies that focus on carers and carer burden) and priority setting for future research.

Introduction

By 2066 there will be a predicted 20.4 million people over the age of 65 years living in the United Kingdom [1]. Generally, someone over the age of 65 might be considered an older person accepting also that people can biologically age at different rates [2]. With advancing years comes the increased likelihood of living with multimorbidity, frailty and associated risk of adverse outcomes, including falls, hospitalisation, institutionalisation, and death [3]. Evidence-based health care services are essential to mitigate these risks. The advanced chronic kidney disease (ACKD) population is aging rapidly. 17% to 45% of people accepted for renal replacement therapy (RRT) are now >75 years old [4]. Nephrology services are therefore not exempt from the challenge, with the prevalence of frailty being greater in advanced chronic kidney disease (ACKD) than in the general population [5-7]. Action is especially important within Nephrology given that interventions such as renal replacement therapy, which have the potential to prolong life, may not promise improved wellbeing [8-12].

To inform and direct the development of appropriate and effective management strategies for older people living with frailty and ACKD, we must first understand the care priorities of this group. Moreover, to effectively evaluate proposed interventions, we need to identify outcomes that are important and meaningful to these groups. The James Lind Alliance [13] and the Standardised Outcomes in Nephrology (SONG) initiative [14] highlight important research priorities and outcomes in ACKD generally; however, neither have explored priorities and outcomes specifically pertinent for older people living with frailty and ACKD.

Using scoping review methodology our aims were to: (1) identify and map the available evidence relating to older adults living with ACKD, and (2) identify knowledge gaps [15].

Following discussion with a stakeholder group, comprising older people living with ACKD, their caregivers and relatives, we identified four research questions:

1. Is frailty formally identified in studies involving older people living with ACKD and if so what methods are used?
2. What interventions have been reported and how might they enhance both care and outcomes for older people with ACKD?
3. What outcomes have been reported in studies involving older people living with frailty and ACKD?
4. What outcomes matter most to older people living with frailty and ACKD?

Methods

The review was guided by Arksey and O'Malley's framework [16] and the PRISMA-ScR guidelines (Appendix 1 checklist), as per protocol [17]. The research team provided expertise in frailty, kidney care and scoping review methodology.

Table 1 outlines the inclusion and exclusion criteria.

Table 1. Study Eligibility Criteria.

Inclusion Criteria

- Population: Older people (aged ≥65 years) with ACKD stages 4 and 5 living with frailty, who may be receiving Renal Replacement Therapy (RRT), conservative care or have received a renal transplant, and carers/families of these individuals.
- Studies: all study designs that include older people with ACKD, carers/families in line with the population inclusion criteria.
- Interventions: where interventions are described, all types of interventions will be included
- Outcomes: examples such as health-related quality of life (HRQoL), symptom burden, patient experience, functional and cognitive ability, life participation.

Exclusion criteria:

- Studies not including ≥65-year-old population and studies where subgroup analysis was not performed in this age group
- Studies not published in English
- Studies prior to 1995

Literature searching

Nine databases were searched covering multiple disciplines and grey literature; full list included in the protocol (15). Search results were managed using Endnote web reference management software (online). Each search strategy was recorded in full (see Appendix 2 which provides an example record of one of the searches). This search approach was replicated across all databases, changing thesaurus terms and search operators as appropriate. Searches were completed in 2019 and updated in 2021.

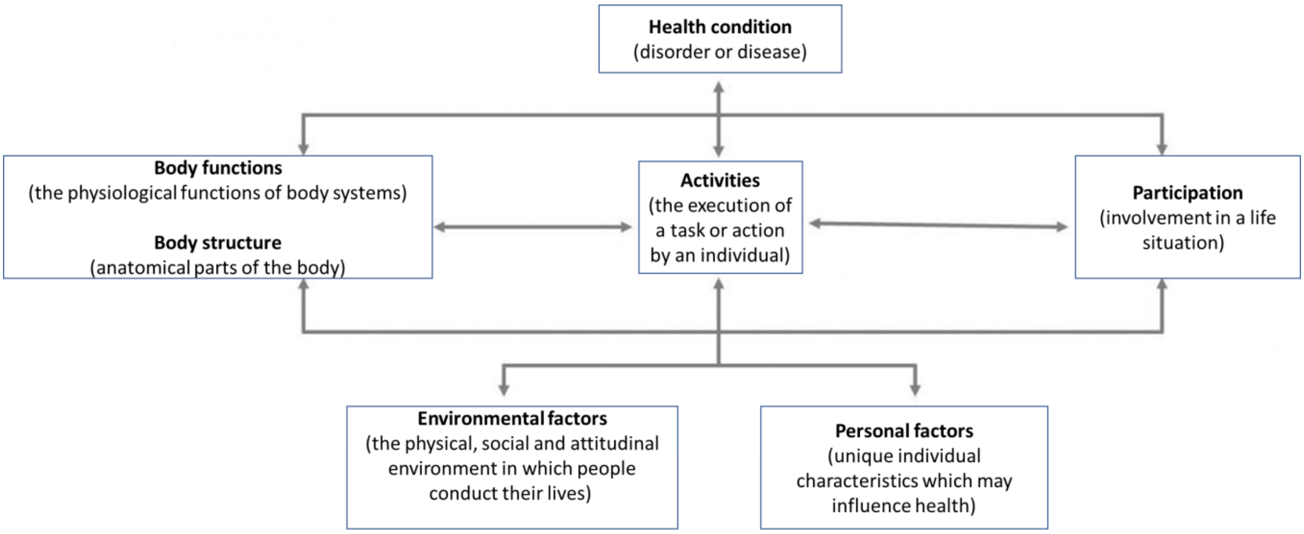
Study selection

Five members of the review team used the eligibility criteria to identify potentially relevant studies by title. Three members (HH, HY, AN) then independently sifted by abstract, and subsequently by full text to create the final list of included studies.

Data charting

The final set of papers included in the review are summarised in Appendix 4. Initial charting was piloted and completed by two reviewers (HH, HY). No authors were contacted for information or clarity. Outcomes were charted using the World Health Organisation (WHO)'s International Classification of Functioning Disability and Health (ICF). The ICF provides a comprehensive conceptual framework for understanding and organising health functioning and disability (see Figure 1) [18], which facilitated the comparison of outcome use between studies and provided a structure for reporting findings [17, 18].

Figure 1. International Classification of Functioning Disability and Health



For all studies reporting information on outcomes, details of the measures used and what the selected measure aimed to capture was extracted. For studies which used measures with multiple components, each component was charted. Studies which included questionnaires, each question item was included.

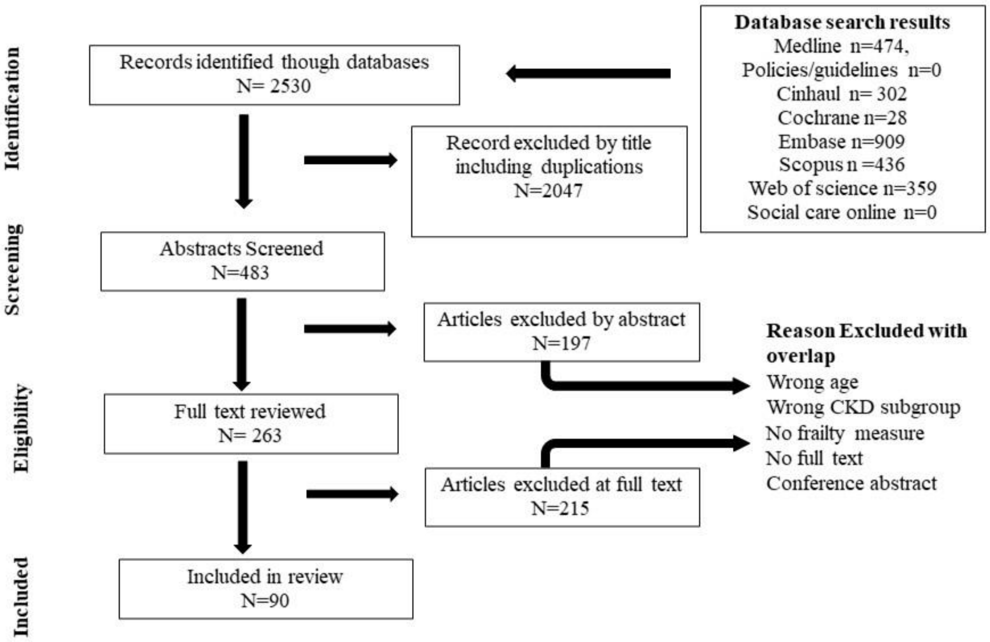
Synthesis of results

Results were synthesised using descriptive statistics and/or narrative summaries where appropriate. For outcome data, two reviewers familiar with the ICF (HY, AN) used published linking rules to map outcomes to the ICF [19, 20]. Meaningful concepts for each measure, component (for composite measure) or question item and responses (for questionnaires) were identified and linked to the most precise category, using the ICF browser [21]. Where this was unclear, an interpretative approach was used, based on the study aims, and using supporting literature that described the tests in detail [19]. Agreement on these interpretations was reached via discussion, including decisions regarding whether a measure was related to activity or participation, using operational definitions by Whitehead and Dejeckers [22].

Results

Ninety papers, from 69 studies, were included in this review (see Figure 2). The manuscripts were categorised as: observational (n=61, 88%), cohort (n=37, 53%), cross-sectional (n=24, 35%), protocols (n=11, 16%), systematic reviews (n=7, 10%), qualitative (n=4, 6%), quality improvement and program evaluations (n=3, 3%), randomised controlled trials (RCT) (n=2, 3%), convenience series (n=1, 1%) or where described as a 'comparative' design (n=1, 1%). The populations most studied were people receiving haemodialysis (HD) (n= 45, 65%), ACKD (n=34,50%), peritoneal dialysis (PD) (n= 15,22%), transplant (n=5,7%) and conservative management (n= 4,6%).

Figure 2. Scoping Review Consort Diagram.



Is frailty formally identified in this population and if so, what methods are used to identify frailty?

Across included studies frailty was identified using 37 different assessments, with a median of 3 per study (IQR 1-6). Appendix 3 describes all assessments. The use of frailty measures varied according to the objectives of included studies. Twelve studies specifically compared self-reported frailty with other frailty measures to examine correlations and comparability.

The most frequently used assessment was the Frailty Phenotype, employed in 40 (44%) studies. In identifying frailty 36 (43%) studies used one objective measure of frailty: Frailty Phenotype (n=17,16%) the Clinical Frailty Scale (CFS n=10, 14%), Edmonton Frailty Scale (n=4, 4%) and the Frail Scale (n=5 4%). All other studies used multiple assessments, either directly or by proxy measure. For example, functional and cognitive assessments were used as a proxy measure of frailty. The majority of the assessments have all been used in the general population, specific CKD measures were the CKD frailty index (n=6, 5%) and the DMMS (Dialysis Morbidity Mortality Study n=1, 1%).

Five self-assessments of frailty were identified in 11 (16%) studies (see appendix 3). Information gathered was used in conjunction with assessments undertaken by the researcher/healthcare professional. The perception of frailty by an individual did not always correlate with the healthcare professional [23]. Eighteen studies (19%) included a cognitive assessment, using four different assessments. Eleven studies (13%) included in-depth assessment of related geriatric domains including cognition, depression, falls and nutrition Six types of functional assessments were used across 18 studies. Nutritional assessments were completed in eight studies (9%). Only two studies (2%) included social isolation as part of the assessment process. Caregiver burden was included in two studies (2%), with a further study including caregiver perspective using the Frailty Advanced Care Tool [24].

Seven systematic reviews highlighted issues with the consistency of the identification of frailty across CKD studies. Van Loon et al (2016) examined the prevalence of frailty and geriatric impairments in people greater than 70 years old commencing dialysis [25]. Twenty-seven studies were included. Three studies focused on frailty specifically, others focused on domains of frailty, including: impairment of cognitive function, mood, performance status or (instrumental) activities of daily living, mobility (including falls), social environment, and nutritional status. Malnutrition and frailty were the most systematically assessed [25]. Four reviews included studies which did not use a measure of frailty [4, 26-28] and most included all age ranges. Corroborating the findings of the current review, Mei et al [29] found that the Frailty Phenotype was the most used frailty assessment across studies included within their review.

What interventions have been reported and how might they enhance both care and outcomes specifically for older people with ACKD?

Few studies reported interventions (N=5, 6%). Those that did broadly evaluated two types of interventions: comprehensive geriatric assessment (CGA) and exercise. CGA is a model of health care based upon comprehensive multi-disciplinary assessment taking account of medical, psychological, functional, social and environmental problems [30]. Four studies (6%) reported on the implementation of CGA in practice, with variability in the populations included (HD, PD, pre-dialysis ACKD), the domains assessed, and methodology used (qualitative, quality improvement, comparative, cross sectional) to evaluate implementation

[31-34]. CGA appeared to enhance education, training and awareness of the holistic and palliative needs of this population, facilitating appropriate onward referrals and advance care planning [32, 34, 35]. Barriers to CGA included lack of communication about goals, interpretation of geriatric assessments by clinicians, assessment burden for patients, poor health literacy and organisational challenges [34]. The latter related to the time needed to complete CGA and additional costs of involving geriatricians and additional multi-disciplinary team members (34). Although not formally measured, some studies observed an improvement in discussions about treatment options and adjustments in addition to increased advice seeking relating to social support [31, 34, 35]. These findings suggest that CGA may enhance decision making and facilitate informed person-centred interventions for older people living with ACKD and frailty [34]. Other interventions included exercise. Two included papers (the protocol and completed study) referred to the same intervention [36, 37]. This was a pilot RCT evaluating a multicomponent home-based exercise programme for pre-frail and frail older adults with CKD. Seventy-three percent completed the programme of two exercise sessions per week, leading to potential improvements in both function and symptoms [37]. The other included intervention studies were all protocols of ongoing trials of exercise, focusing on hospitalised individuals with ACKD [38], and the effects of muscle stimulation during HD [39]. Finally, a protocol by Chang et al [40] described an RCT evaluating intervention individualised according to the findings of CGA [40].

What outcomes have been reported in older people living with frailty and ACKD?

Fifty-two papers, from 41 studies, reported outcome measures. A total of 121 separate outcomes were identified, with a median of two outcomes per study (IQR 1-7) (see Figure 3). Three (2%) measures were not reported in sufficient detail to enable classification. Thirty-two (26%) outcomes could not be classified according to the ICF domains. Of these, most reported mortality (n=24, 58%), and hospitalisation and healthcare utilisation (n=13, 32%).

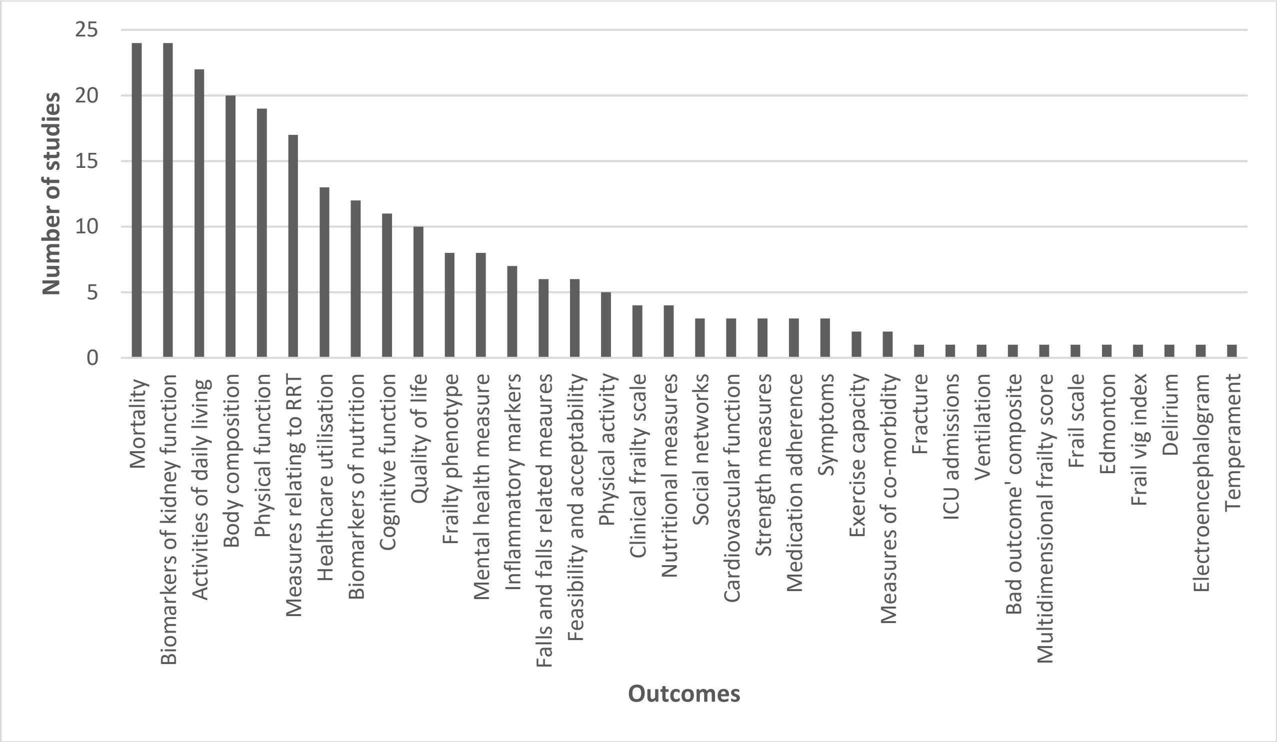


Figure 3. Reported Outcome Measures.

RRT, Renal Replacement Therapy; ICU, Intensive Care Unit.' Bad outcome' refers to delayed graft functioning of greater than 14 days, never functioning kidney, readmission before day 90, surgical complications, discharge to a care facility or death.

Most outcomes (n=86, 71%) were classified according to the ICF. Most (n=47, 55%) were objective tests or appraisals from the perspective of the healthcare professional/researcher; the remainder were patient-reported outcomes (PROMS; n=21, 24%), and biomarkers (n=18, 21%). The most frequently reported objective measures examined capacity, performance or dependency related to activities of daily living (ADL) (n=21, 22%), physical function (n=19, 20%), cognition (n=11, 12%), and body composition (n=10, 11%). No measures clearly predominated, however grip strength and gait speed (both n=6, 6%) were most frequently used measures of function, and the Lawton and Barthel most frequently used ADL measures (n=9, 10%; n=7, 7% respectively). The Mini Mental State Examination was most frequently used measure of cognition (n=5, 5%). Frailty was measured as an outcome within 11 (27%) studies, primarily using the Frailty Phenotype (n=8, 50%) or the Clinical Frailty Scale (n=4, 25%).

Of the PROMS, ten (30%) related to HRQOL, eight (24%) to mental health outcomes, particularly anxiety and depression, and three (9%) to physical activity. None examined the impact of ACKD and frailty upon carers or significant others. Again, no preferred PROMs emerged, but the SF-36 appeared to be the most frequently used HRQOL measure (n=4, 12%). Most biomarkers were related to the management of kidney disease (n= 24, 73%), but 12 (36%) were markers of nutrition. The tests most commonly reported were albumin (n=8, 22%) and haemoglobin (n=5, 13%).

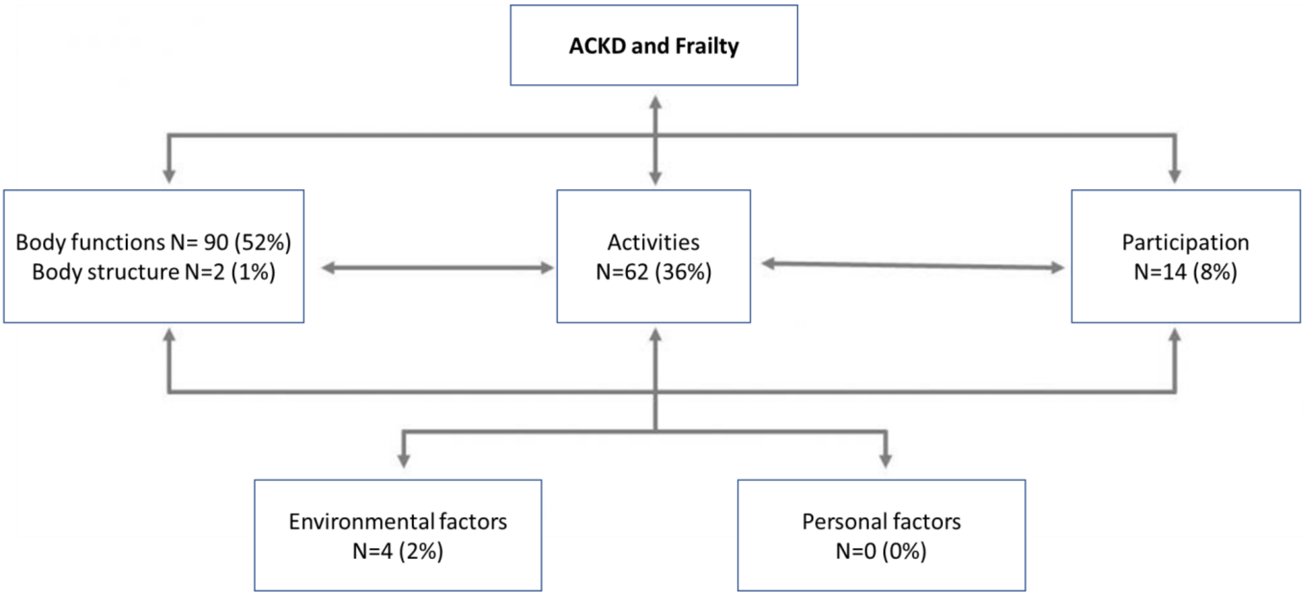


Figure 4. ICF Categorisation of Outcome Measures.

Overall, outcomes mapped to 172 categories within the ICF (summarised in Figure 4). Categories of body function most frequently examined related to mental functions (n=99, 46%), digestive and metabolic functions (n=41, 19%), cardiovascular, haematological, immunological and respiratory functions (n=30, 14%), and genitourinary and reproductive functions (n=14, 6%). Categories of activity and participation most frequently examined related to mobility (n=80, 40%), self-care (n=37, 19%) and domestic life (n=29, 15%). Categories of body structures examined related only to movement, specifically muscle (n=7, 78%) and bone (n=2, 22%). Categories of environment related only to products and technology; specifically financial assets and medications (n=10, 91%) and support and relationships (n=1, 9%).

What outcomes matter most to older people (living with frailty and ACKD), their relatives and carers?

Two studies explored HRQOL outcomes important to people living with frailty and receiving HD [41, 42]. Hall et al [41] collected qualitative data to compare with domains measured in validated HRQOL questionaries. Two themes were identified from the qualitative data: physical well-being and social support. Physical wellbeing related to symptom control, being alive and maintaining health status, whilst social support related to practical and emotional support and socialisation (41). In Young et al's [42] study, maintaining mobility, the ability to undertake a range of ADLs, and participation in social roles were viewed as key outcomes. The qualitative findings from Hall et al's (40) study did not correspond with domains in the Kidney Disease Quality of Life Instrument and WHO Quality of Life for Older Persons Questionnaire instruments, suggesting that a bespoke HRQOL measure is needed for this population [41]. Interestingly in Young et al's study, only 13 (52%) participants agreed to complete a falls diary, many preferred falls information to be collected during HD treatment. The majority who had fallen rarely reported them to healthcare professionals, believing that they were an expected consequence of HD or having experienced their concerns about falls being overlooked. Consequently, falls prevention was not viewed as a key outcome from the patient perspective (41).

Reporting of patient and public involvement was noticeably absent from the studies reviewed; the four qualitative studies explored patient and carer perspectives. The scoping review findings, in particular outcome measurements, were presented to a patient focus group with five participants. The group raised concerns regarding use of HRQOL tools as outcome measures due to the language used, limited options available for selection and lack of inclusion of aspects group members felt to be important. Overall, members of the focus group stressed that they felt interviews were the most appropriate method to gain an in-depth patient perspective regarding the impact of interventions, though they acknowledged that this is not always feasible for studies involving large numbers of participants.

Discussion

The aim of this review was to identify and map available evidence relating to older adults living with ACKD and frailty, specifically addressing frailty assessments used, interventions reported and outcomes. Of the studies included, the majority were observational, reporting on incidence, prevalence, and associations of frailty with outcomes such as mortality and hospitalisation. The measurement of frailty was inconsistent and varied across studies. The small number of intervention studies add little to our understanding of which outcomes are a priority and are meaningful to this population. There was an underrepresentation of carers' perspectives and measures of carer burden, both are important considering carers often have great involvement with this population.

The high prevalence of frailty across many chronic diseases and associations with the frailty phenotype is now being recognised [43-45]. The importance of frailty and how it may change the prognosis and therapeutic approaches to several conditions has also been documented [43, 44]. A wide range of measures were used to identify frailty in the ACKD population. Whilst the purpose of this review was not to examine validity of assessments used, several studies have demonstrated the diagnostic and prognostic accuracy of assessments in ACKD including the Frailty Phenotype and the CFS [46-49]. The Frailty Phenotype was most common across the studies, and is also a popular frailty assessment used in the general population [50]. Some studies described modifications to the Frailty Phenotype, adding a further complexity. A lack of standardised approach makes the comparison and synthesis of studies difficult. Arguably, some of the assessments used are not validated measures of frailty, or serve only as proxy measures, with moderate specificity for the identification of frailty [51]. This challenge has been identified in previous reviews of older people with ACKD and within the general population [4, 25, 50, 52, 53]. To provide guidance on use of assessments in research and practice, existing recommendations suggest considering the context and purpose when selecting a frailty measure; for example, if risk prediction is the goal, then frailty assessments validated for this purpose should be selected [53]. Different assessments are recommended for research and practice; for example, the Frailty Phenotype is commonly used in research and but less so in practice [50, 53], and the

CFS is now gaining traction in clinical practice. In support of this, a consensus process by Voorend et al [54] recommended the CFS be used within nephrology.

This scoping review highlights a lack of interventional studies within this population. The limited number primarily reported on the implementation of CGA, the gold standard of care for older people living with frailty in the general population [30]. Although CGA has been recommended within the European Best Practice guidelines [55], existing evidence only suggests that CGA is feasible in a nephrology setting, and robust evidence that CGA improves outcomes relevant to older adults with ACKD is lacking. However, preliminary findings suggest that CGA supports enhanced decision-making and provides opportunities to embed shared decision making in practice [34]. This can improve sharing of prognostic information, facilitate discussions about advance care planning, and assist in the planning of more supportive, palliative approaches to treatment [34, 55-57].

Other interventions described related to exercise, which has been shown to be important for falls prevention and rehabilitation of older people living with frailty in the general population [58, 59]. Exercise has been shown to improve physical functioning, fatigue and HRQOL in the CKD population [60]. Whilst exercise appears to be feasible for older people with ACKD and frailty [37], further exploration of the effectiveness of tailored approaches for this group is required. This review identifies those multicomponent interventions that target all relevant parts of the CGA process are lacking, although may prove more beneficial than single interventions in this population.

Across all intervention studies, very little research has measured the impact of interventions on carer burden. A recent systematic review highlighted the high levels of burden in those caring for people with ACKD [61]. This appeared to be the result of a wide range of factors, including gender, caregiver and patient income, time providing daily care, duration of caregiving, the relationship to person, and cohabiting arrangements, reinforcing the need for further research into interventions to support this group [61]. The need to assess care giver burden with a consistent approach within standard care was highlighted. Doing so may prompt healthcare professionals to offer interventions that aim to improve caregiver wellbeing [61].

This review underlines the broad range, but limited scope, of outcomes currently utilised within existing studies. Mortality and hospitalisation were the most common reported outcomes. There was little consensus amongst the PROMs and objective measures used. Outcomes were most frequently mapped to the ICF category of activities and participation, but the majority focused on activities, rather than participation. Whilst this review exposes how little is currently known about what outcomes matter to people living with ACKD and frailty, existing evidence indicates that social support (including emotional and practical), participation in activities, maintaining mobility and being supported in decision making are all important [34, 41, 42].

The number of core outcome sets, designed to improve the consistency, relevance and reporting of outcome measures, have grown in recent years [62]. The International Consortium for Health Outcomes Measurement (ICHOM) has published core outcome sets for people with CKD and older people separately, both including different measures [63]. Matching outcomes important to individuals with measures used in assessment tools was highlighted in this review (40).

Implications For Future Research

This review highlights several priorities for future research. Two priority setting exercises have been undertaken in the general population and within the dialysis population, but neither specifically address the priorities of older people living with frailty and ACKD (11,12). The National Institute for Health Research (NIHR) also published a report of important priorities for older people living with multiple conditions, including carers, highlighting that carer burden, support and social isolation were considered important [64]. Using the results of this review as a basis for discussion, our group will undertake a consensus process using nominal group technique to better understand the key outcomes and care priorities for patients and carers. This will enable us to design studies and make recommendations which focus on areas that are meaningful and important to this group.

Limitations

This is the first scoping review to specifically examine outcomes and care priorities for older adults living with frailty and ACKD. Despite these strengths, there are limitations with this review. Scoping review methodology does not include quality assessments of included studies. This limitation was mitigated by following clear eligibility guidelines and utilising all members of the team. Mapping to the ICF was made following assessment, interpretation, and discussion between authors. Consequently, the classifications may have been assessed differently by other researchers. To mitigate this, the mapping process followed established linking rules and the procedures used described in detail to increase transparency [65]. Where the common generic patient reported outcomes (for example, the SF-36) have been mapped within other published works, the mapping decisions have been compared to increase confidence and accuracy of classification decisions. Finally, this review only included studies of people aged greater than 65 years old, therefore cannot be used to infer outcomes and care priorities for younger people living with frailty and ACKD.

Conclusion

In summary, this scoping review highlights important areas for further research in older people living with frailty and ACKD that will contribute to improvements in services and care of this population. Researchers and clinicians should use a standardised approach to measure and assess frailty whilst recognising the accumulation and interaction of geriatric domains and in particular the complicated treatment decisions required in this vulnerable population [25]. Future research should build on the evidence for the implementation of CGA into practice; and to develop and test robust holistic interventions that improve outcomes that matter to people living with frailty and ACKD. This should include studies that focus on carers and carer burden.

Declaration of Conflicts of Interest: None

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