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Appropriate care for older people approaching kidney failure: design and implementation of geriatric assessment in kidney care

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Citation
Voorend, C. G. N. (2025, January 21). *Appropriate care for older people approaching kidney failure: design and implementation of geriatric assessment in kidney care*. Retrieved from https://hdl.handle.net/1887/4176401

Version:	Publisher's Version
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Note: To cite this publication please use the final published version (if applicable).

APPROPRIATE CARE FOR OLDER PEOPLE APPROACHING KIDNEY FAILURE

DESIGN AND IMPLEMENTATION OF GERIATRIC ASSESSMENT IN KIDNEY CARE



CARLIJN G.N. VOOREND

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Carlijn G.N. Voorend

The work described in this thesis was performed at the Department of Internal Medicine, Leiden University Medical Center, The Netherlands.

The work presented in this thesis was supported by grants from the Dutch Kidney Foundation (A1D3P04) and the Nephrosearch Foundation.

Cover design: Karolien Rijksen, based on the art work *Conscious Choice* (2023, karolienrijksen.com)
Layout and design: Karin Jansen, persoonlijkproefschrift.nl
Printing: Ridderprint
ISBN: 978-94-6506-594-6

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Appropriate Care for Older People approaching Kidney Failure

Design and implementation of geriatric assessment in kidney care.

Proefschrift

ter verkrijging van
de graad van doctor aan de Universiteit Leiden,
op gezag van rector magnificus prof.dr.ir. H. Bijl,
volgens besluit van het college voor promoties
te verdedigen op dinsdag 21 januari 2025
klokke 14:30 uur

door

Carlijn Gabriëlle Nicolette Voorend
geboren te Zegveld
in 1986

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chapter 1

General introduction

GENERAL INTRODUCTION

Healthcare is increasingly embracing a more person-centred approach, aiming for treatment tailored to each patient's preferences and needs. This shift is accelerated by the increasing number of chronically ill individuals and people with multiple conditions and the ageing population. Generally, as individuals get older, health needs become more complex, and priorities may change and differ between individuals. Specific care needs of older people often remain unseen and unaddressed.[1] These ageing-related challenges are among the factors that pressure the accessibility, quality and affordability of healthcare. To address these challenges, the Dutch healthcare sector is committed to providing appropriate healthcare.[2] Appropriate care includes the right care at the right place and is value-driven to patients and society using outcomes that matter to patients. Geriatric care provides a scheme for such a patient-centred approach beyond solely the somatic domain, and can facilitate the process of adapting care to what matters most for the patient and to the individual's situation and capacity.[3] Could such a holistic approach be integrated into routine care settings? In this dissertation I provide insights into practical knowledge on integrating geriatric principles into routine nephrology care. Before presenting this dissertation's aims and outline, I first describe the challenges of the growing and ageing population with chronic kidney disease, the need for appropriate kidney care, and the potential role of geriatric assessment.

Chronic kidney disease

Increasing and ageing chronic kidney disease population

People with Chronic Kidney Disease (CKD) suffer from gradual loss of their kidney function, which is crucial for filtering waste and excess fluids from the blood. CKD is frequently caused by lifestyle diseases such as diabetes and hypertension. Also, ageing goes along with the loss of kidney function. The worldwide population with all-stages CKD is estimated at 10% to 13% and growing rapidly and getting older due to the increasing global burden of lifestyle diseases, population growth and ageing.[4-6] In the Netherlands, the average age of people with CKD is 72 years.[7] Each year almost 2000 new patients require kidney replacement therapy (KRT), of whom more than half are above 65 years of age and almost a quarter are above 75 years of age.[8] The expected increase of the older population in The Netherlands is amongst the highest in Europe, as the number of adults aged 80 or older is projected to rise by 135% over the next three decades.[9] It is thus inevitable that the number of age-related diseases, including CKD, will also increase.

The ageing CKD population imposes new challenges for clinical treatment. Older patients more frequently experience multiple diseases, impaired cognition, and physical decline compared to younger patients. In turn, CKD accelerates ageing processes and increases the risk for other diseases. Complications of CKD may include anaemia, mineral bone disease, inflammation, and small vessel disease, which are attributable to cognitive and physical decline in patients with CKD.[10] Particularly the older advanced CKD population represents a heterogeneous group. As of moderate CKD (stage 3b; estimated glomerular filtration rate [eGFR] <45mL/min/1.73m2) the risk of being frail is multiplied by six, as compared to a general population.[11] Among those with dialysis treatment, studies report 30% to 80% of the patients

classified as frail.[12] Cognitive decline and malnutrition are highly prevalent but often go unrecognised, despite its concurrent higher risk for hospitalisation and mortality.[13-16] Next to somatic complaints, the CKD population have also shown to be more vulnerable to mental health problems such as depression and anxiety.[17] Symptoms of anxiety and depression, but also other emotional symptoms, including sleep disorders, reduced social interactions, and worrying, have not only been associated with poorer clinical outcomes and increased mortality, but mainly affect patients' health-related quality of life (HRQoL).[18-23] Awareness and knowledge within nephrology teams about such mental problems is increasing but still limited.[24]

Treatment options for kidney failure patients

When a patient's kidney function has severely decreased and approaches almost complete loss of kidney function (i.e. kidney failure, eGFR <15mL/min/1.73m2), difficult decisions are faced. Generally, four medical treatments can be considered, although choices are often restricted. All options require timely preparations for shared decision-making for the treatment that best fits the patient's health status and their outcome priorities. The first option is kidney transplantation, which is preferred when a patient is fit enough and a donor kidney is available. Second, haemodialysis is a method of two to four times per week that filters the blood from waste products and can be performed either in-centre or at home. Third, peritoneal dialysis is another way of using the peritoneal membrane as a dialysis filter. This treatment can be done at home by a patient independently or with nurse assistance. Fourth, patients could also choose to forgo dialysis treatment, so-called conservative kidney management or conservative care. Conservative care includes the best effort to support a patient with medications and dietary restrictions to offer a comfortable life for as long as possible, generally more focused on maintaining HRQoL. Currently, this is a well-established treatment approach in several Western countries, as guidelines recommend presenting conservative care as a valid alternative for older vulnerable patients.[25,26]

The burden and impact on patient's daily lives during these treatments remain substantial. Kidney transplantation requires patients to take lifelong immunosuppressive medications, which often have considerable side effects. Transplantation also comes with a higher risk of complications and mortality with higher age, multimorbidity and geriatric impairments. With dialysis treatment, hospitalisations are frequent, symptom and treatment burden is high and health-related quality of life low.[27-30] In the Netherlands, the mortality rate within the first year of dialysis treatment amongst older people is high (i.e. on average 26% amongst those aged 75 years or older, compared to 3% in those aged below 45 years), primarily due to dialysis withdrawal.[31] The knowledge on outcomes on conservative care is increasing, but are not systematically measured.[32]

Although the rate of CKD progression towards kidney failure highly differs between individuals, the decision-making process generally starts early (e.g. from eGFR <20-30 ml/min/1.73m2), allowing time for education, dialogue, and preparation for kidney replacement therapy. The shared decision-making process involves the patient, their relatives, nephrologists and other members of the nephrological treatment team.[33] The trajectory of kidney function and ageing effects on outcomes are hard to predict and often unknown for the individual patient. Though reliable estimation of outcomes concerning survival, HRQoL

and symptoms of dialysis and conservative care helps to inform patients and healthcare professionals in shared decision-making. Average outcomes are available, but due to the groups' heterogeneity, lacking detail to provide individual prediction of treatment choices. Over time, patients' preferences and circumstances may change and, with that, their choice of future kidney replacement therapy may also change. To what extent patients switch their treatment choices is unknown.

Appropriate kidney care

Joint nephrology associations recently warranted that the increasing burden of kidney disease in the foreseeable future will have serious implications for survival, quality of life and healthcare spending worldwide.[34] Moreover, the ageing population puts pressure on healthcare systems regarding accessibility, affordability and quality. In response to the increasing societal healthcare burden and workforce shortages, the Dutch healthcare sector recently committed to work towards appropriate care. Appropriate care encompasses the right care at the right place, value-driven to both patients and society.[2] Patient-centred care is therefore essential, and may involve treating individuals differently to address their unique needs.[35]

Healthcare is traditionally focussed on longevity, but especially to older individuals with CKD quality of life can become more important.[36] On average, half of the older patients with advanced CKD prioritised maintaining independence in daily life highest, followed by staying alive and reducing symptom burden.[37] Fatigue, cramping and insomnia are common prioritised physical symptoms, and anxiety and depression are important mental symptoms in the pursuit of a better quality of life with CKD or haemodialysis.[38,39] However, individuals' priorities change depending on the patient's life goals, views and situation.

Remarkably, healthcare professionals' and patients' health outcome priorities poorly align. A study in the United States showed that only 35% of the time agreement between providers' perceptions and patients' actual health outcome priorities.[37] Qualitative studies also showed that patients often prioritise additional outcomes that their healthcare professionals may overlook.[40] To improve awareness on symptoms and patients' HRQoL in individual management of dialysis treatment, and monitor these on a larger scale, recently patient-reported outcomes measures (PROMs) were integrated in Dutch dialysis and transplantation, but not yet in pre-dialysis care.[41,42]

Providing appropriate treatment and prognostic information for older patients with advanced CKD is challenging. Sufficient evidence for risk stratification and individualised treatment prognosis of KRT options for older patients is lacking. The diverse health needs, patient preferences, and multifaceted vulnerabilities of these patients make selecting the most appropriate treatment pathway an individualised and complex process.

Integrating the geriatric approach in kidney care

Comprehensive geriatric assessment

Geriatricians are experts in clinical complexity. These specialists look at age-related problems using a systematic approach to identify and address individual care needs in diverse patient groups. In the Netherlands, clinical geriatricians or internist-geriatricians fulfil this role, together with specialised (advanced practice) nurses. They use comprehensive geriatric

assessment (CGA), which is geriatric medicine's cornerstone and is defined as *'a multidimensional, multidisciplinary process which identifies medical, social and functional needs, and the development of an integrated/co-ordinated care plan to meet those needs'*.[43] CGA facilitates tailored therapy adjustments and improvement of outcomes such as the likelihood of patients remaining at home, mitigating decline, and averting mortality.[44,45] Full CGA encompasses the involvement of a geriatrician in the (i) thorough assessment of impairments in multiple domains and (ii) development and further evaluation of an integrated treatment plan to meet patients' needs. This makes full CGA a time-consuming process for both patients and healthcare providers and poses logistical difficulties for use to all patients that may benefit from CGA.[46]

In recent decades, new forms of delivery of geriatric assessment have emerged in hospital settings, for example in acute and emergency care, oncology care and before surgical and pre-operational decisions. In such specialty settings, a modified geriatric assessment was conducted to identify multi-domain vulnerabilities without the traditional involvement of geriatricians in diagnosis and follow-up care plan needed for full CGA.[46] This approach is particularly interesting for nephrology since brief frailty screening tools have shown to be insufficient for thorough identification of geriatric impairments or frailty among older individuals with CKD.[47] Implementing a modified geriatric assessment is anticipated to integrate geriatric evaluation more seamlessly into existing nephrology care pathways.

Nephrology-tailored geriatric assessment

Geriatric evaluation is important to better cater to the needs of older patients with kidney disease in these decision-making processes. The importance was underscored by the 2017 European guideline for management of older patients with moderate or more advanced CKD.[25] Dutch and British guidelines advocate specifically the use of geriatric assessment for individuals identified as frail or at high risk of mortality.[48,49] Despite these guideline recommendations and several efforts to integrate geriatric assessment into nephrology populations,[50-55] consistent and widespread adoption of standardised geriatric assessment in routine nephrology care remains elusive. There is a lack of a golden standard set of instruments and evidence on the best approach to perform geriatric assessment in nephrology care.

Employing a standardised set of instruments suitable to assess geriatric impairments in kidney care is important to clinical practice and of scientific significance.[14,55-58] Firstly, due to the chronic nature of kidney diseases, nephrologists seek a comprehensive understanding of their patients' geriatric status, but without objective measurements impairments may go unnoticed. These instruments should be sensitive to address vascular problems that frequently affect nephrology patients, such as vascular cognitive impairment, and often significantly affect the geriatric phenotype. Secondly, broader awareness of geriatric impairments is crucial for making (future) treatment decisions and establishing goals for ongoing care for these vulnerable patients. Thirdly, a modified geriatric assessment tailored to kidney care may offer a practical solution to overcome implementation barriers of full CGA effectively. Designing an appropriate set and examining the implementation process, including barriers and facilitators, may aid in successfully integrating this complex intervention into clinical practice. Scientific significance of conducting geriatric assessment

lies in their ability to contribute valuable outcomes to scientific evidence, particularly where there is a dearth of information, such as mental well-being, HRQoL, symptom management, and cognitive impairments. Collecting data from the geriatric assessment can offer insights into new risk factors for adverse outcomes, clues to uncover etiological pathways for impairments, and the prognostic capabilities and interactions with treatments for other diseases.

Aims and outline of this dissertation

In this dissertation I aim to describe if and how structured geriatric assessment contributes to appropriate/patient-centred care and decision-making for the older population approaching kidney failure (CKD, stage G4/G5). We hypothesise that geriatric assessment provides a useful and feasible scheme for the treatment of the increasingly older population approaching kidney failure. The specific objectives for this thesis are as follows:

I. To add knowledge about outcomes of treatment options for kidney replacement therapy.
II. To design and implement geriatric assessment prior to treatment-decision making about kidney replacement therapy in older people.
III. To address unveiled, previously unrecognised, challenges and vulnerabilities faced by the older CKD population.

This dissertation is structured in three parts. In the first part, I delve into outcomes relevant to the decision-making process for kidney replacement therapy in older individuals: whether to start dialysis or not? **Chapter 2** reports a literature review examining the mortality risk among patients opting for dialysis versus conservative care, which is crucial for shared decision-making. Analogous we investigated the impact on HRQoL, reported by Verberne *et al.*,[59] which is highlighted in the summary and general discussion of this dissertation (chapter 10) rather than included as a separate chapter. Subsequently, in **chapter 3** we looked into the robustness of this decision, whether or not patients switch their chosen therapy.

The second part of this thesis reports our efforts to integrate geriatric assessment in nephrology care: a project named *Pathway for older patients reaching end-stage renal disease (POLDER).* We held focus groups with patients and healthcare professionals on the value and considerations for implementing geriatric assessment in nephrology, being discussed in **chapter 4**. In addition, **chapter 5** reports our exploration of patients' and providers' perspectives on geriatric assessment as a valuable tool to the decision-making process on kidney replacement therapy. Afterwards, we studied an appropriate set of instruments for geriatric assessment in nephrology. **Chapter 6** proposes a consensus-based nephrology-tailored geriatric test set to routinely identify impairments across somatic, cognitive, functional and social domains. **Chapter 7** outlines the implementation process of this test set in multiple Dutch hospitals. Our investigations on the contribution of geriatric assessment to the process of shared-decision making are discussed in this dissertation's general discussion (chapter 10).

The final part of the thesis explores some of the clinical outcomes and implications of geriatric assessment in nephrology. **Chapter 8** investigates symptoms of anxiety and

depression, and HRQoL during the COVID-19 pandemic, using data gathered in the POLDER cohort. **Chapter 9** delves into the occurrence of apathy symptoms in the CKD population, particularly relevant due to its hypothesised association with vascular impairments and its link to depression, physical- and cognitive decline. We used data from the *Cognitive decline in Older Patients with End stage renal disease (COPE)* cohort for this.

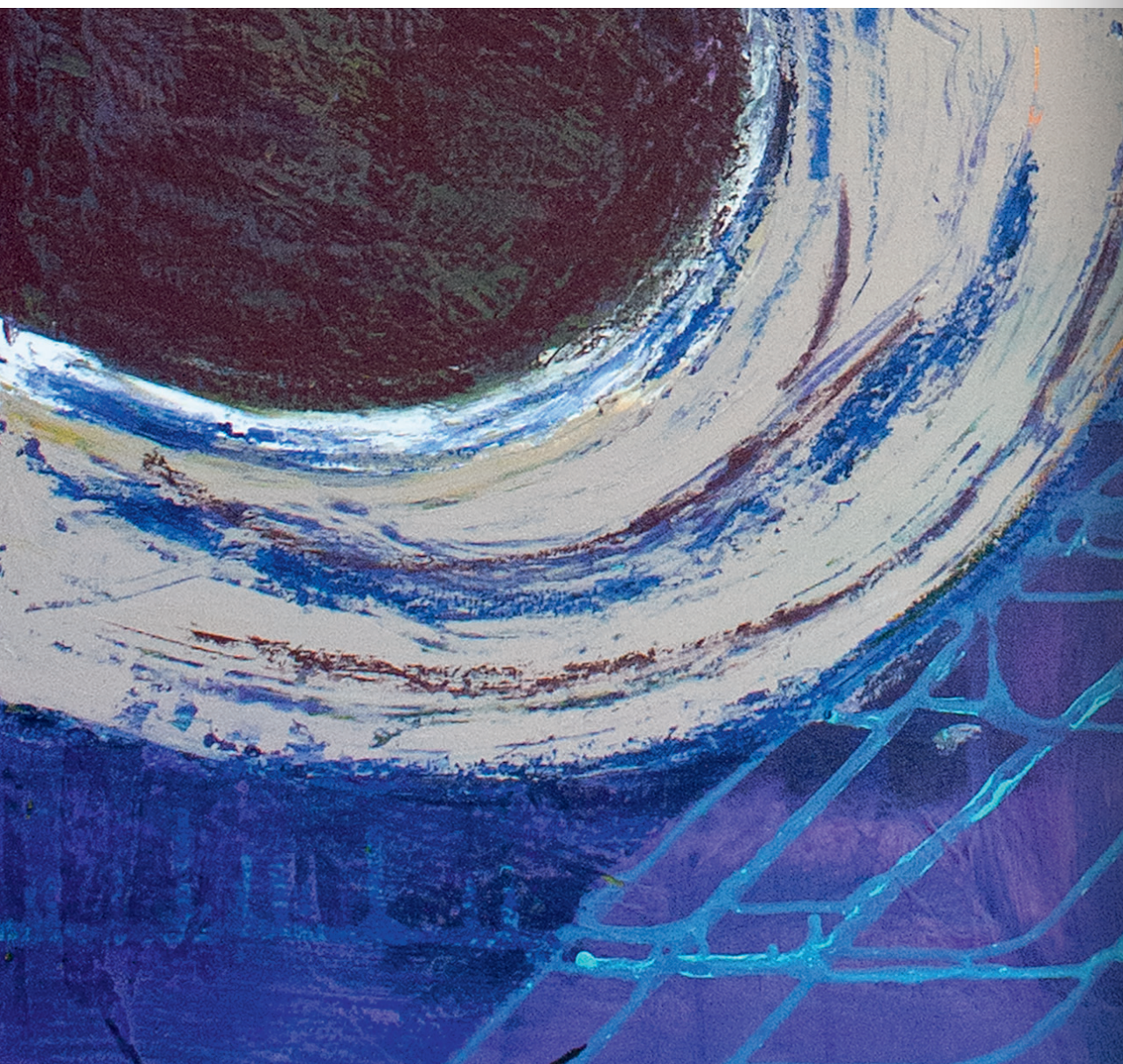
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PART I



INCREASE THE KNOWLEDGE ON OUTCOMES OF DECISIONS FOR KIDNEY FAILURE TREATMENT





chapter 2

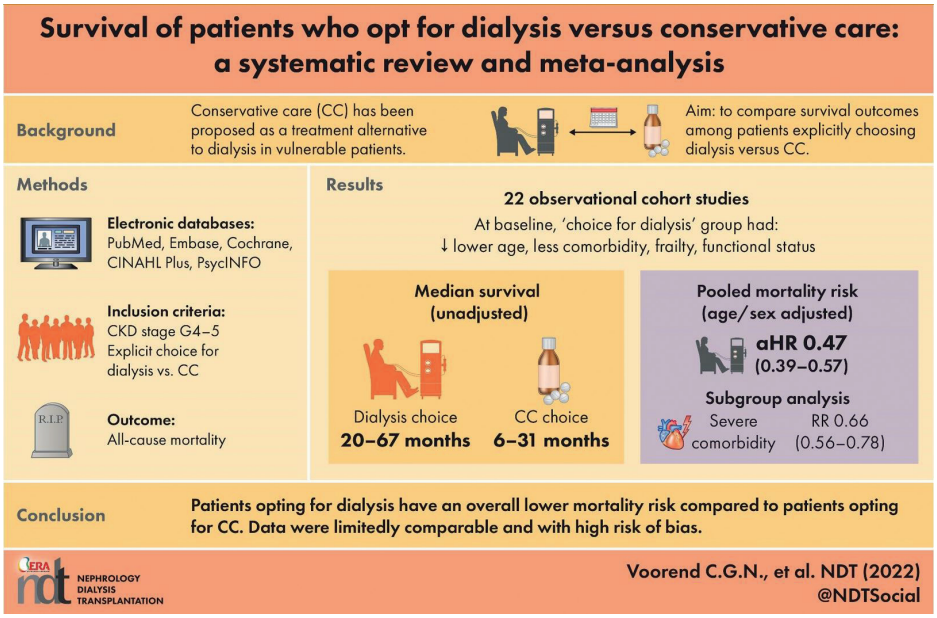
Survival of patients who opt for dialysis versus conservative care: a systematic review and meta-analysis.

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Nephrology Dialysis Transplantation 2022;37(8):1529-44.

GRAPHICAL ABSTRACT



ABSTRACT

Background: Non-dialytic conservative care (CC) has been proposed as a treatment option for patients with kidney failure. This systematic review and meta-analysis aims at comparing survival outcomes between dialysis and CC in studies where patients made an explicit treatment choice.

Methods: Five databases were systematically searched from origin up to February 25th, 2021 for studies comparing survival outcomes among patients choosing dialysis versus CC. Adjusted and unadjusted survival rates were extracted and meta-analysis performed where applicable. Risk of bias analysis was performed according to the Cochrane Risk Of Bias In Non-randomized Studies of Interventions.

Results: A total of 22 cohort studies were included covering 21 344 patients. Most studies were prone to selection bias and confounding. Patients opting for dialysis were generally younger, had fewer comorbid conditions, fewer functional impairments and less frailty than patients who chose CC. The unadjusted median survival from treatment decision or estimated glomerular filtration rate <15mL/min/1.73m^2 ranged from 20 and 67 months for dialysis and 6 and 31 months for CC. Meta-analysis of 12 studies that provided adjusted hazard ratios (HRs) for mortality showed a pooled adjusted HR of 0.47 (95% CI 0.39-0.57) for patients choosing dialysis compared with CC. In subgroups of patients with older age or severe comorbidities, the reduction of mortality risk remained statistically significant, although analyses were unadjusted.

Conclusions: Patients opting for dialysis have an overall lower mortality risk compared to patients opting for CC. However, a high risk of bias and heterogeneous reporting preclude definitive conclusions and results cannot be translated to an individual level.

INTRODUCTION

Dialysis is the most frequently chosen treatment in patients with kidney failure. Current guidelines recommend presenting comprehensive conservative care (CC) as a treatment alternative to vulnerable patients.[1,2] CC captures a range of pharmacological, clinical and lifestyle interventions, except dialysis, to delay the progression of kidney disease, minimize risk and complications, and to provide active symptom management and psychosocial support.[1] Although CC is generally more focused on maintaining health-related quality of life (HRQoL) than potentially increasing survival, reliable estimation of survival outcomes of both CC and dialysis might help to inform patients and healthcare professionals in shared decision making.

Previous attempts have been made to systematically compare survival data for kidney failure patients choosing between dialysis and CC.[3-6] Most recent reviews suggested a survival benefit for dialysis over CC but highlighted heterogeneity of included studies.[5,6] Comparability between both groups is hampered due to confounding by indication, which occurs when CC is more often chosen by or offered to patients deemed to have a worse prognosis, e.g. older or more frail patients. Additionally, the start of CC is difficult to define, compared with dialysis, potentially resulting in selection bias.[7] Using both the explicit treatment decision and aligning the starting point for survival analysis is therefore critical.

The aim of this systematic review was to compare survival of patients with kidney failure who made an explicit choice for a dialysis pathway versus CC, e.g. excluding studies where dialysis was withheld on medical grounds, in line with a recently published systematic review on HRQoL.[8] Additionally, we looked at subgroups of patients above 80 years of age and with severe comorbidity and frailty. We aimed at including studies that evaluated outcomes from predefined time points, preferably the moment of treatment decision, as an equivalent time point for treatment start itself is difficult to identify in both treatment pathways.[9]

METHODS

We conducted a systematic review according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[10] The protocol was announced in advance on PROSPERO (CRD42018103379).[9]

Search strategy

Electronic databases PubMed, Embase, Cochrane, CINAHL Plus, and PsycINFO were systematically searched from origin up until February 25th 2021. Potentially relevant citations were derived with use of a structured search strategy, tested and reviewed by a clinical librarian, using search terms related to or describing the patient population of interest (i.e. chronic kidney disease with severely reduced glomerular filtration rate [KDIGO stage G4] or kidney failure [stage G5]), the intervention (any form of maintenance dialysis), and the comparative intervention (CC). Full search strategy is provided in Supplementary Table S1. Additional studies were identified by checking reference lists and citations of the included studies via Scopus, and consultation of experts.

Study selection

All records were screened by title and abstract by a minimum of two authors independently (WV, IW, CV and MO). Consecutively, full-text articles were screened for eligibility by the same authors using predefined eligibility criteria (Table S1).

All studies that reported and compared survival outcomes of patients choosing either dialysis or CC were considered for inclusion. Ideally, included studies should use a randomized-controlled design and assess survival from the moment of the decision for either CC or dialysis is made using an intention-to-treat approach, at an average equal kidney function between both groups, to rule out selection bias (Figure 1A). In such an ideal trial, as opposed to observational studies, confounding factors such as age, comorbidities, frailty, functional status and cognitive status are expected to be equal in both groups due to randomization. In observational studies, confounding by indication affects this ideal comparison. In our review, at minimum, both treatment strategies should be presented as reasonable options and an explicit choice for either dialysis or CC had to be made. CC had to be applied as non-dialytic care for kidney failure intended to be provided until death and not just to delay the start of dialysis.[1] We defined dialysis pathway as a choice for haemodialysis (HD) and/or peritoneal dialysis (PD), both including patients who would eventually start dialysis or were yet to start. For patient selection within the studies, where reported data allowed to do so, we excluded patients with short-term dialysis for acute kidney injury or where the decision to withhold dialysis was done on the nephrologists' decision based on medical grounds only. Articles were excluded if non-English, or when the study solely reported on patients approaching kidney failure who did not decide on preferred treatment yet. In case of disagreements, we strived for consensus with a third reviewer (WB). If necessary, authors of original studies were approached for additional information. In case of overlapping study populations, we aimed to include the study with longest follow-up and most patients.

Data extraction

Data were extracted on bibliography, study design, risk of bias, (definitions of) exposure(s), outcomes, characteristics of study participants, numerical results, and effect estimates by three authors (WV, IW and CV) using a predefined and pilot tested data extraction form. Disagreements in screening for inclusion and data extraction were resolved though consensus discussion.

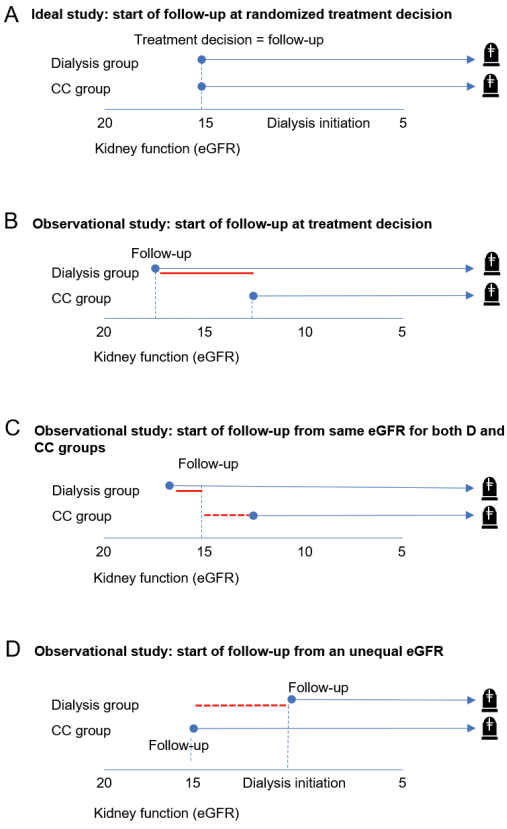
Risk of bias assessment

The risk of bias of the included studies was assessed by two authors (CV and MO) independently, using the Cochrane Risk Of Bias In Non-randomized Studies - of Interventions (ROBINS-I).[11,12] ROBINS-I addresses seven domains of potential bias. Risk of confounding was assessed for the most relevant confounding factors: age and comorbidities. Selection bias was considered if follow-up time was missing due to selection of patients, e.g. because not all eligible patients were included or if follow-up time was inequal between both groups, and may lead to selection bias (Figure 1). In addition, ROBINS-I defines risk of bias on classification of interventions, deviations from the intended interventions, missing data, measurement of outcomes, and selection of the reported results. All domains address internal validity as

distinct from issues of generalizability. Discrepancies in risk of bias assessment were resolved through discussion with a third author (WB).

Data synthesis and analysis

The main outcome of interest was the hazard ratio (HRs) and 95% confidence intervals (CIs) for mortality. The median survival (in months), and one-, two-, and five-year survival in both groups were extracted to estimate absolute survival. If necessary, outcomes were reconstructed from graphs (Kaplan-Meier), using the software WebPlotDigitizer v4.2.[13] Three predefined subgroup analyses were conducted. First, we aggregated the results from studies using four starting points for survival analyses: (1) estimated glomerular filtration rate (eGFR) <20 mL/min/1.73m^2, (2) treatment decision, (3) eGFR <15 mL/min/1.73m^2, and (4) eGFR <10 mL/min/1.73m^2 or the putative start of dialysis (as dialysis is, on average, commonly initiated around eGFR 10 mL/min/1.73m^2). Second, unadjusted survival outcomes were, when possible, assessed according to different age groups (70+, 75+, 80+, 85+ years). Third, if available, separate analysis was intended for patients with severe comorbidity, by using the study's own definition of severe comorbidity, and for frail patients. Patients were analyzed as a combined 'choice for dialysis' group, assuming the best fitted modality was chosen.



A: Ideal study: a design where therapy decision is randomized at a similar eGFR (on average). In an ideal observational study follow-up starts from treatment decision, which should be at a similar eGFR for all patients (on average). Please note that in observational studies, even when the start of follow-up is aligned at the treatment decision, other biases, such as indication bias, remain an important limitation.

B. Follow-up from treatment decision. Selection bias occurs in observational studies when the time between, in this example, eGFR 17 and 12 mL/min/1.73m^2 is immortal for CC patients: individuals who died soon after treatment decision will be missing from analyses. If not adequately discounted, the CC group has a survival advantage (i.e. over- or underestimation of the effect).

C: Follow-up from a specific eGFR threshold (e.g. eGFR of 15 mL/min/1.73m^2 for both the dialysis and CC groups). Selection bias of the dialysis group and CC group is reduced but still present. For the dialysis group, follow-up time (from, in this example, eGFR 17 to 15mL/min/1.73m^2 on average), and individuals who died soon after their treatment decision, will be missing from analyses. For the CC group, patients have had to survive up until the moment of start of treatment decision.

D: Follow-up does not start at an equal time point for both groups; at dialysis initiation versus eGFR <15 mL/min/1.73m^2 for CC group**.** Selection bias occurs when patients choosing dialysis, but dying before dialysis is initiated, are not included in the cohort.

Figure 1: Visualization of selection bias. In this figure, the course of eGRF also reflects the course of time.

Statistical analysis

We conducted random-effects meta-analysis using DerSimonian and Laird's method[14] to estimate pooled adjusted HR. If HRs were presented for (choice of) HD and PD modalities only separately, these ratios from a single study were pooled using a weighted fixed-effects model. Publication bias was considered low by means of a funnel plot (Figure S1). The I^2 statistic was used to describe the percentage of variation between the studies due to heterogeneity (values of <25%, 25-50% and >50% indicating respectively low, moderate, and high heterogeneity).[15] To estimate the effect of adjustment for confounding, we compared the adjusted HR with unadjusted risk ratios (RR) for one- and two-year mortality, which were calculated using random-effects Mantel-Haenszel method.[16,17] Meta-analysis of unadjusted one- and two-year survival data was performed for subgroups of patients above 80 years of age and with severe comorbidity.

RESULTS

Search results

The search resulted in 7634 records, of which 353 full-text articles were assessed for eligibility (Figure 2). Authors of five studies were contacted for clarification of the CC definition, of whom four responded. Based on their answers, patient groups did not match our definition of explicit choice for CC, and all five articles were excluded (Table S2). One study was excluded that stopped follow-up at dialysis start,[18] and two because of overlapping study populations.[19,20] Two other studies partly overlapped, the smaller study[21] was excluded for the main (meta)analyses. Our analyses were performed on 22 cohort studies, no randomized controlled trials were found.

Study characteristics

Table 1 presents the characteristics of the 22 included studies.[21-42] Sample size varied from 87 to 14,071 patients,[40,42] resulting in a total of 21,344 patients. Proportion of patients opting for CC varied between 6% and 77% (median 31%).[35,40] Majority of the studies were restricted in age, varying from ≥65 to ≥80 years old.[18,21,23,26,27,30,31,33-37,39,41,42] Mean age in the studies ranged from 61 to 86 years (median 78 years).

Choice for dialysis included mostly combined HD and PD treatment,[21-23,26,30,31,35,38,39] occasionally together with choice for pre-emptive transplantation (encompassing <5% of study population).[25,29,32,41] Four studies did not specify dialysis modalities.[28,33,36,40] CC comprised ongoing care of a multidisciplinary team, symptom control, and medication management, and some form of palliative care or advanced care planning. Eight studies did not specify the CC strategy.[25-27,30,31,38,40,41]

The reference point for survival analysis in most studies was the time when eGFR dropped below 15 mL/min/1.73m^2 (n=10),[21,24,29,32,35-38,40,42] followed by eGFR <10 mL/min/1.73m^2 or putative dialysis start (n=6),[23,25,27,28,31,34] eGFR <20 mL/min/1.73m^2 (n=1),[30] and treatment decision (n=1).[41] Four studies assessed multiple starting points for their survival analyses.[22,26,33,39]

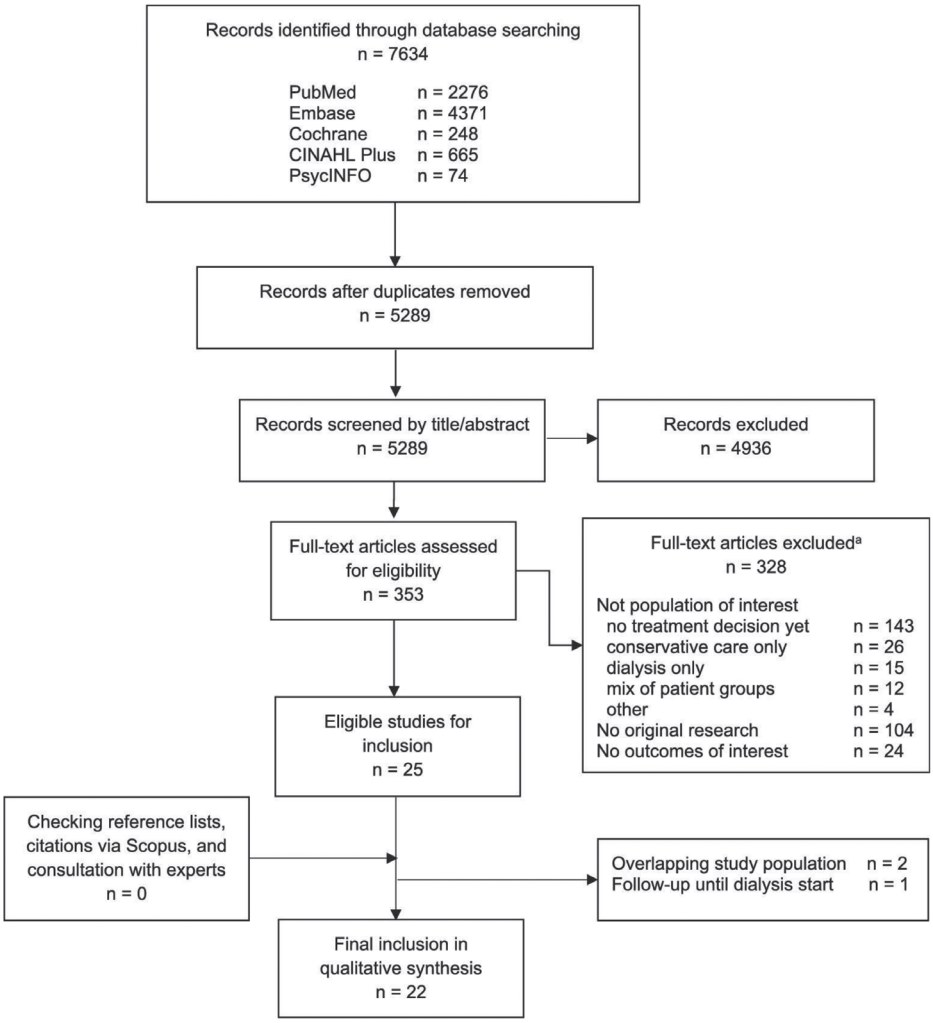


Figure 2. Study inclusion and exclusion flowchart.

[a]explanation of reasons for exclusion: no treatment decision yet includes patients with advanced chronic kidney disease who did not, or did not have to, decide on preferred treatment yet (commonly referred to as "pre-dialysis patients", or "non-dialysis dependent CKD patients"), including five studies discussed with the authors to clarify their patient groups (Supplementary Table S2); Mix of patient groups means a mix of different patient categories into one patient group without subgroup analyses (e.g. mix of patients who have not made a decision yet and patients who chose conservative care); No original research, for example reviews, opinion papers, or study protocols.

Table 1. Characteristics of studies included in the systematic review

Study	Design[a]	Cohort era	*n*	Inclusion criteria	Dialysis patient group	Reported CC strategy	Starting point survival analysis	Follow-up
Brown *et al.*,[22] Australia	Prospective	2009-2013	395	CKD stage G4/G5 No age criterion	Choice D, 34% started during follow-up (HD 60%, PD 40%)	Usual nephrology care and renal supportive care clinic	From first attendance to clinic after decision; and from eGFR<15	Until death or study end, median 10 (4-21) months
Carson *et al.*,[23] United Kingdom	Prospective	1997-2003	202	Dialysis start or eGFR <10.8 (CC) ≥70 years	On D (HD 69%, PD 31%)	Active medical treatment, multidisciplinary care, dietary input, and end-of-life care	(Putative) dialysis start: eGFR 10.8	Until death, study end, transplantation, referral to other centre, loss to follow-up, maximum 107 months.
Chandna *et al.*,[32] United Kingdom	Retrospective	1990-2008	844	eGFR <15, >10 No age criterion	Mix of choice D and on D, 97% started (HD, PD, KTx)[d]	Active medical treatment and multidisciplinary care	From first eGFR<15	Over period of 18 years. Until death or study end
Chandna *et al.*,[21] United Kingdom	Retrospective	1995-2010	250	eGFR <15 >75 years	Mix of choice D and on D, 91% started (HD, PD)[d]	Active medical treatment and multidisciplinary care	From first eGFR<15	Until death, transfer to other centre or study end. Minimum 3 years, maximum 8 years over period of 18 years.
Da Silva-Gane *et al.*,[24] United Kingdom	Prospective	2005-2007	154	Late stage G4/G5 No age criterion	Choice on HD (65%; 59% started) or PD (35%; 52% started)	Active medical treatment and multidisciplinary care	From date of recruitment (duration to decision up to 15 months)	Until death, study end, or transplantation. Minimum 30 months, median 31.9 months (IQR 25.1)
García-Testal *et al.*,[42] Spain	Retrospective	2014-2017	87	CKD stage G5, ≥ 80 years	On HD	Medical and nursing consultation, including symptom control, active medical treatment and dietary advise.	Date that eGFR <15 (diagnosed ESKD)	Minimal 3.5, maximal 51.5 months
Hussain *et al.*,[33] United Kingdom	Retrospective	2006-2010	441	eGFR <20 >70 years	Choice on D, 44.6% started [d]	Supportive care by a palliative medicine consultant	eGFR<20, eGFR<15, eGFR<12	Until death or study end (May 2011)
Joly *et al.*,[34] France	Retrospective[b]	1989-2000	144	eGFR <10 >80 years	On HD	Continued palliative care strategy: i.e. management of fluid overload, relief of uremic symptoms and pain, nonpharmacologic supportive measures	Start dialysis (first session), or date of written decision for CC	Until death or study end (April 2001)

Table 1. Continued

Study	Design[a]	Cohort era	*n*	Inclusion criteria	Dialysis patient group	Reported CC strategy	Starting point survival analysis	Follow-up
Kwok *et al.*,[35] Hong Kong	Retrospective	2005-2013	558	eGFR <15 ≥65 years	Choice on D, 98.4% started (HD 23%, PD 77%)	Multidisciplinary care in palliative care clinic, and symptom control	Date of advanced care planning interview (median duration until decision was 10 days)	Until death, loss to follow-up or study end (minimum 1 year, max 10 years)
Moranne *et al.*,[30] France	Prospective (*n* = 24)	2009-2010	269	eGFR <20 for at least 3 months >75 years	Choice HD or PD (mostly HD), 50% started	NR	Date of inclusion in cohort (approximates date of treatment decision)	5-year follow up (median 34.5 [±21] months)
Morton *et al.*,[25] Australia	Prospective (*n* = 66)	2009	721[e]	eGFR <15 No age criterion	On HD (77%), PD (23%), 96% started, or KTx (4%)	Differed per renal unit, not further specified	Start dialysis, or decision for CC	3 years, until study end (2012)
Murtagh *et al.*,[36] United Kingdom	Retrospective, (*n* = 4)	2003-2004	129	CKD stage G5 >75 years	Choice on D, 53.8% started [d]	Active multidisciplinary care, including educational, dietary, social and psychological support	First eGFR<15	Until death or study end (2005)
Pyart *et al.*,[41] United Kingdom	Retrospective	2004-2016	1216	eGFR <20mL/min ≥ 70 years	Choice HD (79%), PD (21%), home HD (2%), pre-emptive transplant (1%), 50.5% started	Maximal conservative management (not specified)	Final choice	5 years
Raman *et al.*[26] United Kingdom	Prospective [c]	NR	204	eGFR <15 ≥75 years	Choice D, 42.3% started (HD, PD)[d]	NR	eGFR<15; eGFR<10	Until death or study end (2015), mean 35.1 (± 22.1) months
Seow *et al.*,[27] Singapore	Prospective	2007-2009	101	eGFR 8-12 ≥75 years or age-adjusted CCI≥8	Choice D, 100% started [d]	NR	Random moment (time of inclusion) at renal ward or outpatient clinic	24 months
Shum *et al.*,[37] Hong Kong	Retrospective	2003-2010	199	eGFR<15 ≥65 years	Choice on PD, 71.8% started	Optimization of medical management and syptom control	First eGFR<15	Until death or minimum 1.5 years until study end (2011), median 2.0 years (IQR 0.9-3.6)
Smith *et al.*,[28] United Kingdom	Prospective	1996-2000	321[e]	Approaching ESKD No age criterion	Choice / recommendation on D, 72% started [d]	Active medical treatment and multidisciplinary care.	(Putative) start of dialysis: eGFR 10	Until death or study end (2000)

Table 1. Continued

Study	Design[a]	Cohort era	*n*	Inclusion criteria	Dialysis patient group	Reported CC strategy	Starting point survival analysis	Follow-up
Teo *et al.*,[38] Singapore	Retrospective	2005	159	Diagnosed ESKD[f] No age criterion	Choice HD (71%), PD (29%); all started	NR	Date of diagnosis with ESRD	One year (after ESKD diagnosis)
Teruel *et al.*,[29] Spain	Prospective (registry) & retrospective	2013-2014	232	eGFR <15 No age criterion	Choice HD (57%), PD (39%), KTx (4%); 44.4% started	Chronic renal disease division (similar care protocol as dialysis group) or palliative care unit.	Date of inclusion in the registry (i.e. first visit to the Nephrology Service)	Maximum one year. Mean 4.9 (± 3.2) months for CC, 7.2 (± 3.7) for D.
Van Loon *et al.*,[31] The Netherlands	Prospective (*n* = 17)	2014-2017	281	Starting dialysis or eGFR<15 (CC) ≥ 65 years	On HD (77%), PD (23%)	Maximal conservative management (not specified)	Start of dialysis, or decision for CC	12 months
Verberne *et al.*,[39] The Netherlands	Retrospective	2004-2016	366	CKD stage G4/G5 ≥70 years	Choice HD (79%), PD (21%), 60.8% started	Active medical treatment and multidisciplinary care.	Date of decision, date of first eGFR<20, eGFR<15, eGFR<10	Until death, KTx (censored), loss to follow-up or study end (2016)
Wong *et al.*,[40] USA	Retrospective, (registry)	2000-2009	14,071	eGFR <15 (second measure drawn after minimum 90 days) Adults	On D (group 1) Choice on D (group 2)	NR	eGFR<15 (sustained; second measurement after 90 days)	Until death or study end (2011)

[a]Study setting is single centre or indicated if otherwise. All were observational cohort studies. [b] Retrospective analysis of a mostly prospectively followed cohort. [c]Retrospective selection of patients; but data prospectively collected. [d] (Number of patients for) the specific treatment modalities were unknown. [e] Less patients were included in the survival analysis, respectively n=663 [25] and n=222 [28] [f]serum creatinine concentration ≥880 µmol/L. [g] n=222 patients were included in the survival analysis, but no separate baseline data was provided.

CC, conservative care; Choice D, patients who had chosen but not yet started dialysis; D, dialysis (including all dialysis modalities); eGFR, estimated glomerular filtration rate in mL/min/1.73m^2; HD, haemodialysis; PD, peritoneal dialysis; NA, not applicable; NR, not reported; KTx, pre-emptive kidney transplantation[25,32] or preferred pre-dialysis living donor renal transplantation[29]

Risk of bias assessment

The risk of confounding was serious in the majority of the studies (Figure 3 and Table S3). In eleven studies results were not adjusted for age and comorbidity status.[23,25,27-30,33-35,38,40] Seven studies were of serious or critical risk of selection bias[25-27,31,34,40,42] as start of follow-up probably not coincided for the included patients, leading to a risk of lead time- or immortal time bias. The risk of bias due to unclear classification of interventions was considered serious in two studies where the intervention was not well-defined.[25,42] The risk of bias on missing data could often not be assessed, because nine studies lacked a statement on number of patients lost-to-follow up or missing data.[21,22,25-27,29,32,38,39,41] The risk of selective reporting of results was at least moderate since none of the studies prespecified survival outcomes in a published protocol. Bias on other domains (deviations of intended interventions, missing data, and measurements of outcomes) were in general low or unclear, and moderate in some instances.

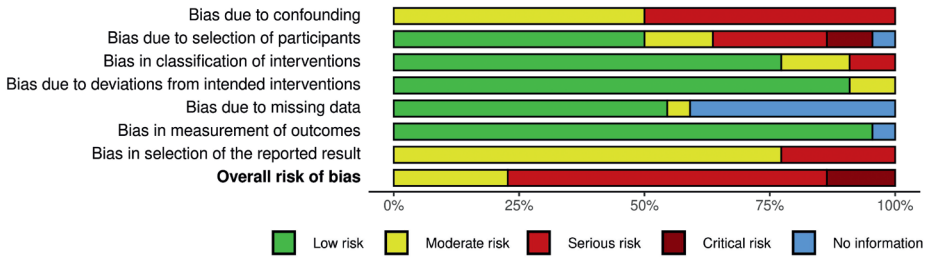


Figure 3: Risk of bias as assessed with the ROBINS-I for all 22 included studies

Characteristics of study subjects

Patients opting for CC were generally older than patients who chose dialysis treatment in all studies (Table 2; median 7.0 years, range 1.0-21.6 years). Both groups consisted of more men than women. Half of the studies reported more comorbidities in the CC group than the dialysis group.[21,22,24,27-29,32,33,35,40] In the other studies no clear difference in overall comorbidity score was found[23,31,34,36,37,39,41,42] or not presented.[25,26,30,38] CC patients had a lower functional and cognitive status, as reported in seven (out of nine) and five (out of seven) studies, respectively (Table S4). Correspondingly, frailty was more common in patients choosing CC, although assessed in two studies only.[31,41]

Table 2: Characteristic of the dialysis and conservative kidney management patients in the included studies

Study	Number of patients		Mean age (years)		Female (%)		Mean eGFR at baseline		Severe comorbidity		Median follow up time, months (IQR)	
	D	CC	D	CC	D	CC	D	CC	D	CC	D	CC
Brown *et al*[22]	273	122	67	82	33	45	16	16	18% ≥3 comorbidities [f]	38% ≥3 comorbidities [f]	16 (7-26)	10 (4-21)
Carson *et al.*[23]	173	37	76	82	31	41	11[c]	NR	mean CCI 4.0 (sd 1.6)	mean CCI 3.7 (sd 1.8)		
Chandna *et al.* (2011)[32]	689	155	59	76	33	41	13	13	17% high comorbidity [g]	50% high comorbidity [g]	NR	NR
Chandna *et al.* (2016)[21]	92	158	79	82	21	40	13	13	29% high comorbidity [g]	44% high comorbidity [g]	NR	NR
Da Silva-Gane *et al.*[24]	HD: 80 PD: 44	30	61 48	78	24 50	30	13 14	14	35% high comorbidity [h] 14% high comorbidity [h]	74% high comorbidity [h]	NR	NR
García-Testal *et al.*[42]	33	54	83	87	70	33	NR	NR	Mean CCI 9.6 (1.9)	Mean CCI 9.4 (1.9)		
Hussain *et al.*[33]	269	172	77	82	40	49	NR	NR	mean CCI 7.7 mean Davies score 1.9	mean CCI 8.3 mean Davies score 2	NR	NR
Joly *et al.*[34]	101	43	83	84	45	62	NR	NR	21% ≥3 comorbidities [i]	32% ≥3 comorbidities [i]		
Kwok *et al.*[35]	126	432	74	80	49	58	9	10	mean CCI 7.8	mean CCI 9.0	NR	NR
Moranne *et al.*[30]	215	54	81[c]	85[c]	40	56	12[c]	12[c]	[p]	[p]	NR	NR
Morton *et al.*[25]	619[a]	102[a]	61	79	40	49	NR	NR	*j*	*j*	NR	NR
Murtagh *et al.*[36]	52	77	80[c]	83[c]	35	34	NR	NR	19.2% high (Davies grade 2)	18.2% high (Davies grade 2)	19 (2-72)	18 (0-72)
Pyart *et al.*[41]	841	375	76[c]	83[c]	64	56	16[c]	15[c]	Median CCI 5 (IQR 3-6)	Median CCI 4 (IQR 3-5)	NR	NR
Raman *et al.*[26]	123	81	79	84	33	44	13	13	*k*	*k*	35.1 (± 22.1) [r]	
subgroup: eGFR <10	73	42	80	85	36	52	9	9	*k*	*k*	26.9 (± 23.4) [r]	
Seow *et al.*[27]	38	63	71[c]	78[c]	47	44	10[c]	10[c]	Median CCI 5 (IQR 3-5) [l]	Median CCI 5 (IQR 5-6) [l]		
Shum *et al.*[37]	157	42	73	75	48	57	6	7	Mean CCI 4.3 (sd 1.5)	Mean CCI 4.6 (sd 1.8)	NR	NR
Smith *et al.*[28]	258[b]	63[b]	59	71	43	38	NR	NR	Mean score: 2.1 (2.4) [g]	Mean score: 4.7 (sd 3.0) [g]		
Teo *et al.*[38]	HD: 102 PD: 41	16	59 61	67	44 66	63	NR	NR	[m]	[m]	NR	NR

Study	Number of patients		Mean age (years)		Female (%)		Mean eGFR at baseline		Severe comorbidity		Median follow up time, months (IQR)	
	D	CC	D	CC	D	CC	D	CC	D	CC	D	CC
Teruel *et al.*[29]	142	90	68[c]	83[c]	37	42	12	11	mean CCI 4.7 (SD 2.1)[l]	mean CCI 5.8 (SD 1.9)[l]	7.2 (±3.7)[r]	4.9 (±3.2)[r]
Van Loon *et al.*[31]	192	89	75	82	33	44	8	12	41% high comorbidity[q]	44% high comorbidity[q]	NR	NR
Verberne *et al.*[39]	240	126	76	83	33	46	13	16	30% severe (Davies ≥3)	32% severe (Davies ≥3)	NR	NR
Wong *et al.*[40]	503 (not started)	812	<65yr: 34% 65-74: 29% 75-84: 30% ≥85: 7%	<65yr: 18% 65-74: 21% 75-84: 43% ≥85: 18%	1	1	12	12	33.2% high comorbidity[o]	43.1% high comorbidity[o]		
	12756 (started)		<65yr: 37% 65-74: 31% 75-84: 28% ≥85: 3%		1		11		23.7% high comorbidity[o]			

CCI, Charlson Comorbidity Index; CIRS-G, Cumulative Illness Rating Scale-Geriatric; D, patients who chose or started with dialysis; IQR, inter-quartile range.

[a] For dialysis and conservative care respectively n=571 and n=92 were included in the survival analysis, but no separate baseline data was provided.

[b] For survival analysis, n=186 dialysis patients and n=26 conservative care patients were included but no separate baseline data was provided.

[c] Median presented.

[d] 48% female in overall sample size.

[e] Creatinine clearance instead of eGFR measurement.

[f] Comorbidities included ischemic heart disease or cardiac failure, cerebrovascular or peripheral vascular disease, chronic liver or lung disease, diabetes and dementia.

[g] Scores of 0 (no disease) to 4 (advanced disease) were attributed to the following condition categories: cardiac disease, peripheral vascular disease, cerebrovascular disease, respiratory disease and cancer, cirrhosis was scored as a 4. Scores were summed. High comorbidity was designated to patients with scores of 4 in one condition category or with total scores >4.

[h] Same scoring as described under ***d***, but 'high comorbidity' was defined when patients had summed scores >3, or a score of 3 derived from a single category.

[i] Comorbidities included malignancy, ischemic heart disease, cardiac failure, dysrhythmia, peripheral vascular disease, sequelae of stroke and/or overt, dementia and diabetes.

[j] Data on comorbidities were not systematically recorded.

[k] No overall score presented. Patients choosing D over CC were less likely to have peripheral vascular disease (33% versus 15%, p=0.005). Percentage of patients suffering from coronary artery disease, heart failure, COPD, diabetes and CVA did not significantly differ.

[l] non-age adjusted.

[m] No overall score presented.

[n] The Davies comorbidity score was used, based on the presence of seven comorbid conditions: ischemic heart disease, left ventricular dysfunction, peripheral vascular disease, malignancy, diabetes mellitus, systemic collagen vascular disease, and other significant disorder (e.g., chronic obstructive pulmonary disease). The score assigns one point for each present condition and produces three groups: no comorbidity (Davies score =0), intermediate comorbidity (Davies score =1–2), and severe comorbidity (Davies score ≥3).

[o] Comorbid burden was categorized by tertile of Gagne comorbidity score as having low (score < 4), moderate (score = 4-6), or high (score > 6).

[p] No overall score presented. No significant differences in diabetes, cancer, congestive heart failure, dysrhythmia, cerebrovascular disease, and chronic respiratory disease.

[q] The Cumulative Illness Rating Scale–Geriatrics was used, in which ≥2x score 3 or ≥1x score 4 was considered high comorbidity.

[r] Mean follow up (for total group)

Adjusted mortality outcomes

Twelve studies reported adjusted HRs for mortality and were included in this analysis (Figure 4a and Table 3). The study of Moranne *et al*.[30] was excluded as dialysis start was used as a censoring event in their adjusted survival analysis. All outcomes were adjusted for age. Two studies did not adjust for comorbidity[25,38]. Meta-analysis shows a pooled adjusted HR for mortality of 0.47 (95% CI 0.39-0.57) comparing choice for dialysis to CC, with high heterogeneity between studies (Figure 4a, I^2=55%). For an impression of the effect of adjustment for confounding by the variables age and comorbidity, the unadjusted effect for the same studies was RR 0.38 (95% CI 0.27-0.52) for one-year survival (Figure 4b) and RR 0.41 (95% CI 0.32-0.53) for two-year survival.

Outcomes on median, one-, two-, and five-year survival

Absolute median survival was longer in all studies for choice of dialysis compared to CC, approximating 22 months (2.3 times) longer median survival (Figure 5). Survival was shorter with a lower kidney function (i.e. eGFR <10 mL/min/1.73m^2) compared to higher kidney function (i.e. from treatment decision, eGFR <20mL/min/1.73m^2 or eGFR<15mL/min/1.73m^2)), especially for CC patients. Unadjusted one-, two- and five-year survival ranged widely between studies (Table 4, Table S5), but was consistently higher in the population choosing for dialysis compared to those opting for CC.

Survival for patients of older age

Studies appraising survival at age >80 years were limited in numbers, had small sample sizes, and mostly outcomes unadjusted for confounding variables. Despite this heterogeneity, the lower mortality risk for dialysis seems to decline with higher age (Figure S2). For patients aged >80 years, most studies reported a lower mortality risk for patients opting for dialysis, albeit statistically non-significant.[26,31,33,35,39] In two studies, this difference was statistically significant.[34,42] Pooled unadjusted survival analysis indicated a lower mortality risk for dialysis in the five studies available (Figure S3a,b).[33-35,39,42]

Survival for patients with severe comorbidities or frailty

Eight studies presented a subanalysis for patients with high comorbidity scores, using different definitions of high or severe comorbidity (Table S6). Although all studies concluded that with severe comorbidity the lower mortality risk for patients choosing dialysis is substantially reduced or lost, pooled unadjusted RR from seven studies suggested that the lower mortality risk for these patients from an eGFR <15mL/min/1.72m^2 was still present, i.e. for one-year (unadjusted RR 0.55, 95% CI 0.42-0.73) and two-year (unadjusted RR 0.66, 95% CI 0.56-0.78, Figure 6) mortality.

The mortality risk of severe comorbid patients adjusted or restricted for age was only limitedly reported, sample sizes were small and findings were contradictory (Table S6). Two studies observed a lower mortality risk for patients choosing dialysis [22,41] while one study found no decreased risk.[21] Heterogeneity across and within studies is potentially high as none of the studies provided separate baseline tables for these subgroup analyses. Survival data specifically in frail patients were presented in one study only. Survival did not statistically

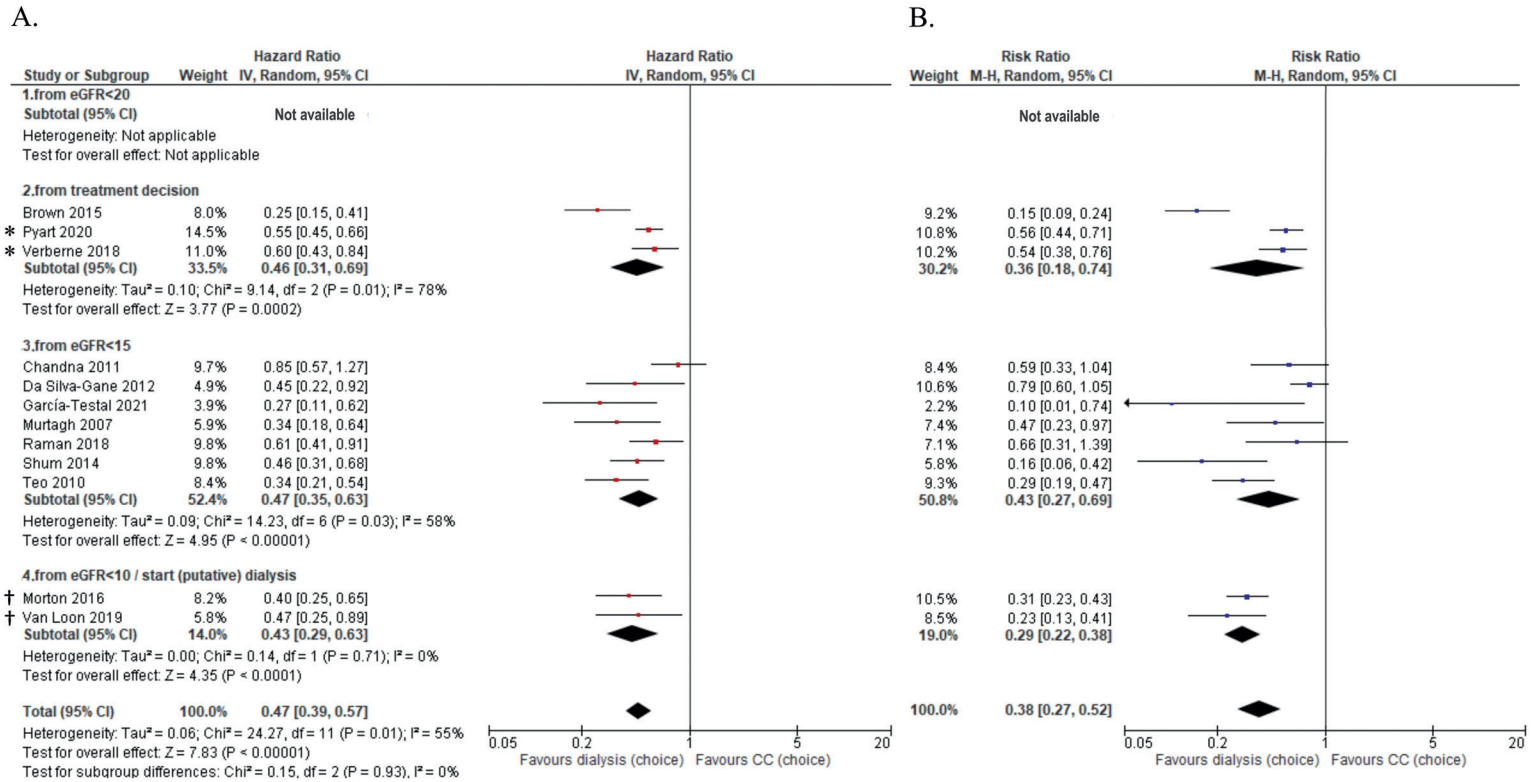


Figure 4: Meta-analysis of (A) adjusted survival and (B) unadjusted 1-year survival comparing choice of dialysis with choice of conservative care.

*Considered as the best studies in addressing confounding and selection bias.

†These studies used a different starting point for the dialysis (initiation of dialysis) versus the CC group (eGFR <15 mL/min/1.73 m2)

differ between frail patients (Clinical Frailty Scale score ≥6) choosing dialysis or CC (HR 1.2 [95% CI 0.69-2.06, p=0.52] adjusted for sex, comorbidity and age) in this study.[41]

DISCUSSION

This systematic review and meta-analysis shows an overall lower mortality risk for patients choosing dialysis compared to those opting for CC: dialysis is associated with half the risk for mortality and a longer (unadjusted) median survival from the time of treatment decision for this group. Our data suggests that in patients with severe comorbidity and/or high age, the lower risk for mortality was still present, albeit more limited. It is important to note that the included 22 observational cohort studies were heterogeneous for age distribution, comorbidities, and the starting point and/or reference kidney function from which survival was assessed. Additionally, risk of selection bias and (residual) confounding was high. Results on lower mortality risk for dialysis should therefore be interpreted cautiously and cannot be translated into an individual level.

Our analysis updates and extends a previously published systematic review of survival outcomes for dialysis versus CC pathways with five studies.[5] More importantly, our scope was to only include studies where patients made an explicit treatment choice, e.g. choice for CC rather than patients who did not receive dialysis treatment. Therefore, after consultation of authors, three studies[43-45] – which were included in the review of Fu *et al.*[5] – were omitted.

Regardless of these differences, we found an adjusted risk for mortality (HR 0.47, 95% CI 0.39-0.57) comparable to findings of Fu *et al.* (HR 0.47, 95% CI 0.32-0.69) and Wongrakpanich *et al.* (HR 0.53, 95% CI 0.30-0.91), yet, with less – but still high – heterogeneity (lower I^2 statistic).[5,6] Similar to Foote *et al.*[4] we also found a lower mortality risk for patients opting for dialysis when only assessing patients with higher age or severe comorbidity. Studies that did not find any difference could have been underpowered. Median survival in our analysis was similar to findings of Wrongapanic *et al.*[6]: 20 to 67 months for patients choosing dialysis and 6 to 31 months for those opting for CC. Interestingly, in a review published a decade ago, the median survival for CC patients ranged only up to 23 months.[3] Our results, adding five studies with higher median survival for CC, may indicate that CC has evolved as a treatment option over time.

While patients who choose dialysis live generally longer than those who choose CC, treatment choice is not based on survival outcomes alone. Our recent review on HRQoL and symptoms concluded that, despite a higher burden of kidney disease after dialysis start, no distinct advantage was found for either one of the treatment options.[8] Taken together, these reviews show that overall dialysis patients live longer while HRQoL is comparable. Ultimately, patients' treatment decisions are the result of shared decision-making between the nephrologist, patient, and caregiver, tailored on patients' individual situation. For individual patient goals of care social arguments may play an important role next to medical conditions. Also, reasons for choosing either dialysis or CC are likely to differ between patients, caretakers, and physicians,[33,46,47,48] and decisions may change over time. Therefore, a well-informed continuous shared decision making process between the patient, caretakers, and healthcare professionals is needed.[49,50]

Table 3: Adjusted HR for mortality per starting point comparing dialysis with CC

Authors, year	Age, in years	Kidney function at start of survival analysis	Comparison	Adjusted Hazard ratio (95% CI)	Adjustment variables
Brown *et al.*[22]	>75	eGFR <15	D vs CC	0.22 (0.11-0.45)	Age, sex, diabetes and ischemic heart disease
	-	TD	D vs CC[a] D-started vs CC D-not started vs CC	0.25 (0.15-0.42)[a] 0.3 (0.13-0.67) 0.23 (0.12-0.41)	Age, sex, diabetes and ischemic heart disease
Chandna *et al.*[32]	>75	<15 eGFR >10	D vs CC	0.85 (0.57-1.27)	Age, diabetes, high/low comorbidity, sex, and ethnicity
Da Silva-Gane *et al.*[24]	-	Late stage G4/ G5	D vs CC HD vs CC PD vs CC	0.45 (0.22-0.91)[a] 0.47 (0.2-1.1) 0.39 (0.10-1.48)	Age, comorbidity, performance score, physical health score and propensity score
García-Testal *et al.*[42]	>80	eGFR <15	D vs CC	0.27 (0.11-0.62)	Age, sex, CCI, diabetes mellitus
Moranne *et al.*[30]	>75	eGFR<20	D vs CC[d]	0.61 (0.37-0.99)[c]	Age, sex, systolic blood pressure, BMI, diabetes, active cancer, chronic respiratory failure, congestive heart failure, dysrhythmia, cerebrovascular disease, peripheral vascular disease, behavioural disorders, mobility, living at home, haemoglobin and proteinuria.
Morton *et al.*[25]	-	eGFR <15 / on dialysis	D vs CC (on 3years mortality)	0.40 (0.25-0.65)	Age, sex, home language, marital status, socio-economic status, remoteness, health insurance, late referral to a nephrologist, serum albumin and hemoglobin.
				0.46 (0.29-0.72)	Age, sex, baseline serum albumin (other model)
Murtagh *et al.*[36]	>75	Stage G5	D vs CC	0.34 (0.18-0.63)	Age, Davies score, Ischemic heart disease, modality choice
Pyart *et al.*[41]	>70	TD	D vs CC	0.55 (0.45-0.66)	Age, sex, CCI
Raman *et al.*[26]	>75	eGFR <15	D vs CC	0.61 (0.41-0.91)	Age, living alone, peripheral vascular disease
	>75	eGFR <10	D vs CC	0.36 (0.21-0.62)	Age, peripheral vascular disease
	>85	eGFR <15	D vs CC	0.72 (0.25-2.08)	Age, living alone, peripheral vascular disease?
	>85	eGFR <10	D vs CC	0.15 (0.02-1.19)	Age, peripheral vascular disease?
Shum *et al.*[37]	>65	Stage G5	PD vs CC	0.46 (0.31-0.68)	Age, modified CCI, basic activities of daily living impairment
Teo *et al.*[38]	-	ESRD (creatinine 880 umol/L)	D vs CC PD vs CC HD vs CC	0.34 (0.21-0.54)[a] 0.44 (0.22-0.86) 0.26 (0.13-0.51)[d]	Age, sex, race, ejection fraction >50%, type of therapy centre (charities/private)
Van Loon *et al.*[31]	≥65	Start dialysis / decision CC	D vs CC	0.47 (0.25-0.89)	Age, comorbidity level and GFR category

Table 3: Continued

Authors, year	Age, in years	Kidney function at start of survival analysis	Comparison	Adjusted Hazard ratio (95% CI)	Adjustment variables
Verberne *et al.*[39]	>70	TD	D vs CC	0.60 (0.42-0.84)	Age, sex, Davies comorbidity score

Bold HRs were used for the meta-analysis.

[a] The HR given for multiple dialysis groups (i.e. HD and PD group, [24,38] or patients who started on dialysis and who did not start yet [22]) were pooled using a fixed-effects model.

[b] The CC group was defined as 'no-dialysis by patient'

[c] The HR and CI were calculated by dividing HR of 'dialysis indication'-group by 'no-dialysis patient'-group and using standard error of 'no-dialysis patient'-group by 'no-dialysis nephrologist' group. Study is not included in meta-analysis since dialysis initiation was a competing event.

[d] The HR was calculated using standard errors of the hazard ratio of PD vs CC.

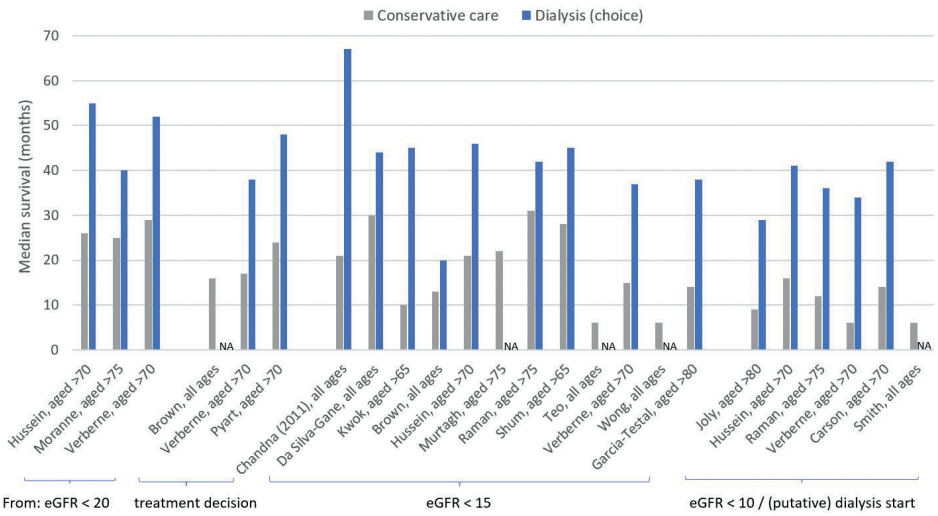


Figure 5: Unadjusted median survival outcomes, grouped per reference point of survival analysis.
The minimum age for inclusion in each study is shown if applicable. Note that as these data are unadjusted, (sometimes large) imbalances between the dialysis and conservative care groups may exist, including older age, greater presence of severe comorbidity, more frailty, worse functional performance and worse cognitive performance in the group opting for CC. Please refer to Table 2 and Supplementary data, Table S4 for more details.

Table 4: Ranges of unadjusted survival outcomes between studies.

	From treatment decision (if not available: eGFR<20, or <15mL/min/1.73m^2)			From start dialysis (or eGFR<10mL/min/1.73m2)		
	N	D	CC	N	D	CC
Median (months)	14	20 – 67	6 – 31	6	29 – 42	6 – 16
One-year (%)	13	72 – 97 %	31 – 85 %	8	74 – 92 %	29 – 66 %
Two-year (%)	11	46 – 89 %	13 – 64 %	7	60 – 79 %	13 – 41 %
Five-year (%)	8	11 – 55 %	1 – 20 %	2	32 – 43 %	4 – 21 %

Abbreviations: CC, (choice for) conservative care; D, (choice for) dialysis; eGFR, estimated glomerular filtration rate; N, number of studies.

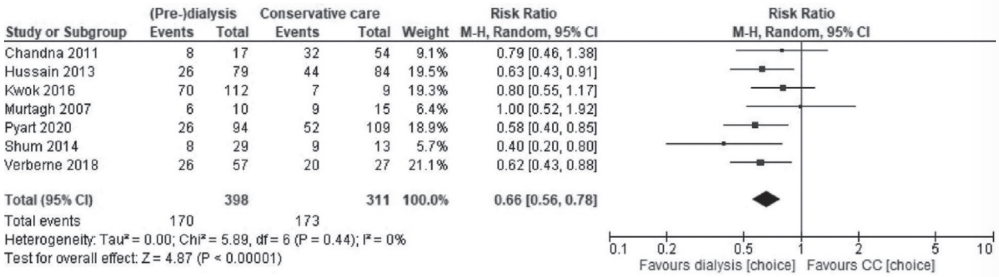


Figure 6: Unadjusted 2-year RRs for patients with severe comorbidity.

The strength of our systematic review is the wide-ranging search in multiple databases directed by the PRISMA guidelines. Also, we focussed on studies reporting an explicit choice for either dialysis or CC treatment pathways, and comparing survival (from intention to treat) between both groups. Authors were contacted if the population of interest or the presence of an explicit treatment decision was not clear. Our approach limited the risk of including selected patients for whom the nephrologist decided that dialysis was not appropriate. A limitation of our systematic review is that not all articles could be included in the formal meta-analysis due to clinical and methodological heterogeneity among the studies, and primarily, lacking adjustment for confounders. Additional heterogeneity was introduced by inclusion of a small number of as-treated analyses.[28,35,40] Besides the likely significant (residual) confounding when comparing groups, we could not assess the validity of the assumptions of the models used in the included studies. All studies reporting adjusted HRs used Cox proportional hazards models but only two studies reported checking any of its assumptions.[39,41]

Using observational data, it is important to consider risk of bias and generalizability, for multiple reasons. First, our results on both unadjusted and adjusted survival should be taken with caution because of (residual) confounding. Patients opting for dialysis were younger and had fewer comorbid conditions. Adjustment for these factors showed only a relatively small effect, likely explained by other confounding factors. Several other geriatric impairments, including frailty, have been associated with increased mortality in prior studies.[51-53] Although numerous studies showed a higher prevalence of frailty and functional- and cognitive impairments in the CC group,[22,24,28-31,33-35,40,41] none adjusted for these discrepancies. The study by Pyart *et al.*[41] showed that frailty better predicts outcomes compared to comorbidity. This would imply that the lower mortality risk found in patients treated with dialysis could be partly explained by the severity of disease in the CC group, meaning that (due to residual confounding) the actual survival benefit of dialysis may be less. This is also illustrated by two studies[39,41] in which significantly more patients choosing CC, compared to those choosing dialysis, die before they would (putative) have started dialysis. For a more adequate comparison of survival between CC and dialysis, future non-randomized studies should take factors such as frailty, cognitive impairment and other confounders, e.g. functional status,[35] and the rate of decline of kidney function,[21,54] into account.

Second, the moment of treatment decision differs between patients, potentially leading to selection bias. Ideally, to limit this bias, our review would have focused solely on treatment

decision as the starting point for survival analysis. However, as this was only available in three studies,[22,39,41] we chose to also present results of other starting points. Furthermore, although guidelines suggest to start education on different treatment modality options early,[1,2] it has been reported that older patients may articulate their decision at a late stage of disease course, or switch from their initial intention to treat.[30,49]

Third, generalizability of the study findings may be an issue for interpretation of our outcomes, particularly on absolute survival, because of stringent in- and exclusion criteria in several studies (e.g concerning severe comorbidities[26], reduced life expectancy[27], acute referrals[38], sex[40], or high numbers of transplanted patients[29]). The percentage of patients undergoing CC in the different studies varied widely (6-77%), illustrating differences in study populations and/or the delivery and acceptability of CC as a viable treatment options among countries.[55,56]

Future studies reporting survival comparison between dialysis and CC should include a clear definition of CC (i.e. distinguishing between CC and delaying the dialysis decision with a stable clinical status in terms of eGFR and limited clinical uraemic symptoms), report outcomes on multiple and comparable starting points of survival analysis, and ensure comparability of groups. Randomized controlled trials, such as the ongoing Prepare for Kidney Care study[57], are the ideal study design for this, however study populations in randomized trials tend to differ significantly from real-world populations due to (explicit or implicit) selection. Non-randomized studies should prospectively look at intention-to-treat analysis, not only adjusting for the common confounding factors such as age and comorbidities, but also use essential data on the impact of frailty and functional and cognitive status.[31,33,41] One study, which incorporates geriatric assessment for this purpose, is ongoing in the Netherlands.[58] Furthermore, including patients opting for CC in national renal registries may provide opportunities to further comprehend the prognosis and outcomes, guide tailored treatment decisions, and stimulate research improving their management.[33]

CONCLUSIONS

In conclusion, our systematic review and meta-analysis demonstrate that patients opting for dialysis have an overall lower mortality risk compared with patients opting for CC, even patients with severe comorbidity and high age, granting that data were limitedly comparable, and the current evidence is insufficient to provide conclusions on absolute survival benefit. High-quality prospective studies are needed to substantiate and extend these methodologically conditional findings and to extend findings for individual prediction of survival outcomes in clinical practice.

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SUPPLEMENTARY FILES

Supplementary Table S1. Search strategy and selection criteria

Search terms[a]	Pubmed database: ("Renal Insufficiency, Chronic"[Mesh] OR ESRD[tiab] OR ESRF[tiab] OR ESKD[tiab] OR ESKF[tiab] OR ((end-stage[tiab] OR endstage[tiab] OR advanced[tiab] OR stage 4[tiab] OR stage 5[tiab] OR stage IV[tiab] OR stage V[tiab]) AND (CKD[tiab] OR kidney disease[tiab] OR renal disease[tiab] OR kidney failure[tiab] OR renal failure[tiab] OR kidney insufficiency[tiab] OR renal insufficiency[tiab]))) AND ("Renal replacement therapy"[Mesh] OR renal replacement therap*[tiab] OR dialysis[tiab] OR kidney replacement therap*[tiab] OR hemodialysis[tiab] OR haemodialysis[tiab] OR hemofiltration[tiab] OR haemofiltration[tiab] OR hemodiafiltration[tiab] OR haemodiafiltration[tiab] OR HD[tiab] OR PD[tiab] OR CAPD[tiab] OR CCPD[tiab]) AND ("Palliative Care"[Mesh] OR "Palliative Medicine"[Mesh] OR "Watchful Waiting"[Mesh] OR conservative[tiab] OR palliative[tiab] OR nondialytic[tiab] OR non-dialytic[tiab] OR supportive care[tiab] OR non-dialysis[tiab] OR watchful waiting[tiab])
Inclusion criteria	• Patients with advanced chronic kidney disease (stage 4/5) • Comparison of non-dialytic conservative care *versus* a dialysis pathway • Conservative care: patients in whom a decision was made to treat end-stage kidney disease conservatively, including all interventions except dialysis, with the intention to provide it until death (not just to postpone dialysis; irrespective of how or by whom the decision was made) • Dialysis pathway: patients in whom a decision was made to treat end-stage kidney disease with dialysis, including patients who had chosen but not yet started dialysis, and patients being treated with dialysis • Study design: randomised controlled trials, observational studies including prospective cohorts, retrospective cohorts, case-control studies, or case reports with >5 patients included per patient group • Outcomes of interest: patient-reported outcomes on health-related quality of life and/or symptoms
Exclusion criteria	• Patients with acute kidney injury • No comparison group: not including both a conservative care patient group and dialysis patient group • No treatment decision yet: patients with advanced chronic kidney disease in whom no decision was made on intended treatment for end-stage kidney disease • No outcomes of interest, including: patient education, pharmocokinetics, economic evaluations, and studies on treatment decision-making • No original research, including: reviews, letters, opinion papers, abstracts only, and study protocols • Pediatric (<18 years) • Not human • Not English
Searches performed up to February 25th, 2021, in PubMed, EMBASE, The Cochrane Library, CINAHL Plus, and PsycINFO.	

[a] A proposal on search terms and databases to be searched was reviewed and pilot tested by an external clinical librarian.

Table S2. Results of contact with authors to clarify their patient group designated as conservative care or non-dialysis group

Study	Response	Authors' explanation of their non-dialysis or conservative care-like patient group	Decision on inclusion
Bonner; Journal of Renal Care 2018. [1]	Yes	Mix of patients in stage 4 chronic kidney disease (too early to make a decision), and patients in stage 5 chronic kidney disease where a decision had been made into one non-dialysis group; no subgroup analysis	Excluded
Martinez Echevers; Nefrologia 2016. [2]	No	-	Excluded; most likely patients being not on dialysis yet, no reporting on treatment decision-making
Reindl-Schwaighofer; PloS One 2017. [3]	Yes	No patient had been started on dialysis; no data on treatment decision-making	Excluded; most likely patients who died before dialysis was initiated or a treatment decision was made
Kurella Tamura; JASN 2018. [4]	Yes	Medical management included all patients who were not treated with dialysis	Excluded; time prior to dialysis initiation was designated as "conservative care"
Tam Tham; Kidney Int 2018. [5]	Yes	No data on treatment decision-making; not aware if a treatment decision had been made	Excluded

First three studies identified through database searching; last two studies identified through checking citations via Scopus.

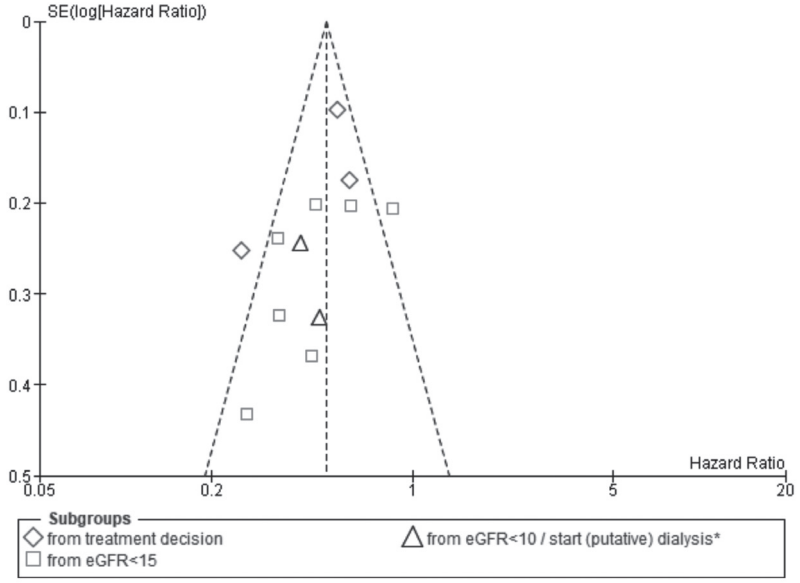
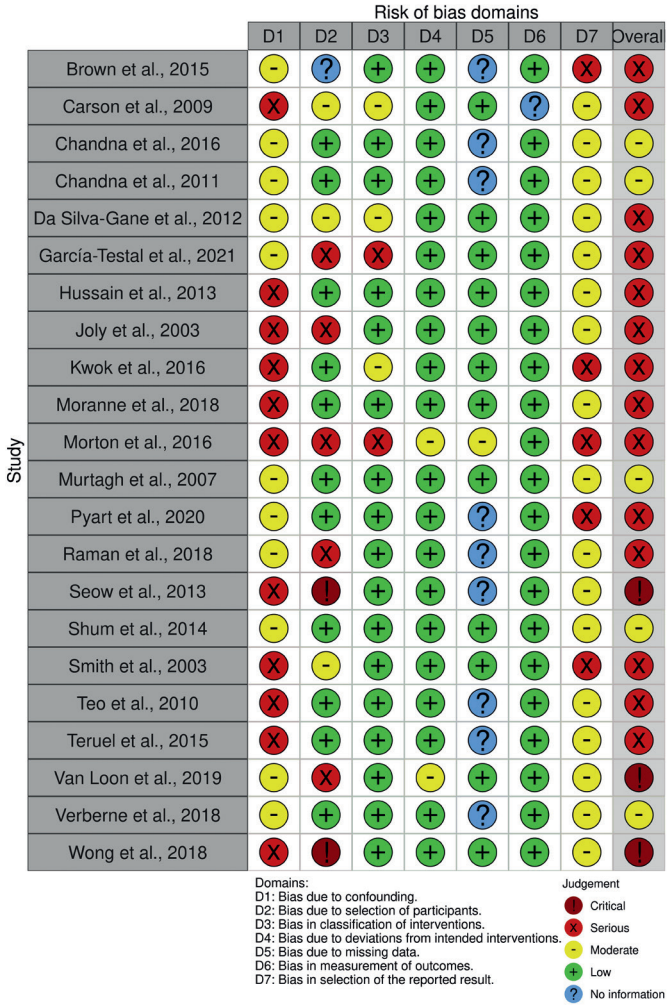


Figure S1: Funnel plot to assess publication bias in effect estimates in adjusted mortality outcomes.
In this figure we used fixed-effects to allow presenting 95% confidence intervals.

Table S3. Risk of bias assessment per included study, the Risk Of Bias In Non-randomised Studies -of Interventions (ROBINS-I)[6,7]



Domains:

D1: **Bias due to confounding**, to assess whether confounding is expected, appropriately measured and controlled for. Confounding was expected in all studies and therefore moderate at minimum. If outcomes were not controlled for age, sex and/or comorbidities, it was deemed serious at minimum.

D2: **Bias due to selection of participants**, to assess whether all eligible patients were included and start of follow up and intervention coincided. If a potential important amount of follow-up time was missing from analysis (lead time or immortal time bias), it was deemed serious.

D3: **Bias in classification of interventions**, to assess whether intervention status was well defined, including risk of misclassification.

D4: **Bias due to deviations from intended interventions**, to assess if any deviations from usual practice were likely to impact on the outcome, including switches to an intervention that was not of interest for the research question (such as kidney transplantation).

D5: **Bias due to missing data**, to assess how missing data and loss-to-follow-up were handled.

D6: **Bias in measurement of outcomes**, to assess whether methods of outcome assessment were comparable across groups, and objectively measured.

D7: **Bias in selection of the reported result**, to assess whether outcomes were described as planned per published protocol, and defined similarly in methods and results. If there was no available protocol it was deemed moderate at minimum.

Table S4: Baseline characteristic of frailty, functional- and cognitive status in the included studies

Study	Number of patients		Functional status %, mean(sd), median (iqr)			Frailty % or mean (sd)			Cognitive status % or mean (sd)		
	D	CC	D	CC	definition	D	CC	definition	D	CC	definition
Brown *et al.* [8]	273	122	NR	NR		NR	NR		0.4% *	11.5% *	Clinical dementia
Carson *et al.* [9]	173	37	NR	NR		NR	NR		NR	NR	
Chandna *et al.* (2011) [10]	689	155	NR	NR		NR	NR		NR	NR	
Chandna *et al.* 2016 [11]	92	158	NR	NR		NR	NR		NR	NR	
Da Silva-Gane *et al.*[12]	HD: 80 PD: 44	30	18% * 2% *	66% *	Karnofsky score<70	NR	NR		5.5 (3.6) * 4.7 (4.0) *	5.2 (3.3) *	HADS-Depression
García-Testal *et al.*[13]	33	54	NR	NR		NR	NR		NR	NR	
Hussain *et al.*[14]	269	172	2.0 (0.7)*	2.4 (0.7) *	WHO score	NR	NR		1% *	7% *	Dementia
Joly *et al.* [15]	101	43	63 (20) *	55 (18) *	Karnofsky score				6%	8%	Overt dementia
Kwok *et al.* [16]	126	432	65% * 29% * 6% *	38% * 40% * 23% *	Independent walker assisted walker chairbound/bedridden	NR	NR		2% * 96% * 4% * 0% *	13% * 73% * 18% * 9%*	Dementia Mental status: full, limited, incapacitated
Moranne *et al.* [17]	215	54	95% *	85% *	Walks without help	NR	NR		3%*	13% *	Behavioural disorder or dementia
Morton *et al.* [18]	619[a]	102[a]	NR	NR		NR	NR		NR	NR	
Murtagh *et al.* [19]	52	77	NR	NR		NR	NR		NR	NR	
Pyart *et al.* [20]	841	375	NR	NR		5 (4-5) [c] 20% *	5 (4-6) [c] 42% *	CFS [c] CFS ≥ 6	NR	NR	
Raman *et al.* [21]	123	81	88 (8)	88 (9)	Karnofsky score	NR	NR		NR	NR	
Seow *et al.* [22]	38	63	60 (50-80)	60 (40-70)	Karnofsky score	NR	NR		NR	NR	
Shum *et al.* [23]	157	42	78% 22% 91% 5% 2%	76% 24% 90% 7% 5%	Independent BADL Impaired BADL Independent walker assisted walker chairbound/bedridden	NR	NR		2.5%	2.4%	Dementia

Table S4: Continued

Study	Number of patients		Functional status %, mean(sd), median (iqr)			Frailty % or mean (sd)			Cognitive status % or mean (sd)		
	D	CC	D	CC	definition	D	CC	definition	D	CC	definition
Smith *et al.* [24]	258[b]	63[b]	85 (14) *	55 (9) *	Karnofsky (modified)	NR	NR		NR	NR	
Teo *et al.* [25]	HD:102, PD:41	16	NR	NR		NR	NR		NR	NR	
Teruel *et al.* [26]	142	90	0% * 1% * 3% * 96% * 0% * 9% * 91% *	9% * 12% * 18% * 61% * 18% * 34% * 48% *	Barthel index: full dep. severely dependent moderately dep. non-relevant dep. Gait acute disorder moderate (FAC2/3) non-relevant (FAC 4/5)	NR	NR				
Van Loon *et al.* [27]	192	89	NR	NR		77%	88%	≥2 geriatric impairments	NR	NR	
Verberne *et al.* [28]	240	126	NR	NR		NR	NR		NR	NR	
Wong *et al.* [29]	503 (not started) 12756 (started)	812	NR	NR		NR	NR		3.6% * 1.8% *	9.0% *	Dementia

BADL, basic activities of daily living; CC, conservative care group; CFS, Clinical Frailty Scale; D, patients who chose or started with dialysis; FAC, FAC scale for gait abnormalities (acute discorder: patient cannot walk [0] or walks with difficulty held by another person [1], moderate: needs support from another person to walk [2] or can walk only under supervision [3], non-relevant: patient can walk independently anywhere [5] or on level ground, but requires help on stairs [4]); FFI, Fried frailty index; HADS, Hospital Anxiety and Depression Scale; HD, haemodialysis; IQR, inter-quartile range; NR, not reported; PD, peritoneal dialysis; SD, standard deviation; IQR, inter-quartile range.

* $p<0.05$

[a] For dialysis and conservative care respectively n=571 and n=92 were included in the survival analysis, but no separate baseline data was provided. [b] For survival analysis, n=186 dialysis patients and n=36 conservative care patients (including n=10 patients with a conservative care recommendation that were eventually dialysed) were included but no separate baseline data was provided.[c] Only a subgroup had enough data available to estimate Clinical Frailty Scale in choice for dialysis group (n=288) and choice for CC group (n=198).

Table S5. Study results on unadjusted survival (median, one- two- five- year survival) by kidney function

CKD stage	Study	Age	Kidney function at start of survival analysis	Number of patients		Median survival time, months		One year survival, %		Two year survival, %		Five year survival		Notes:
				D	CC	D	CC	D	CC	D	CC	D		
eGFR <20ml/min/1.73m^2														
	Hussain *et al.* [14]	>70	eGFR <20	164	142	55	26	72	58	46	20	50[a]	20[a]	unadjusted
	Verberne *et al.* [28]	≥70	eGFR <20	226	109	52	29	91[a]	84[a]	79[a]	60[a]	47[a]	18[a]	unadjusted
	Moranne *et al.* [17]	>75	eGFR <20	215	54	40	25	87	74	72	54	31	20	unadjusted
Treatment decision														
	Brown *et al.* [8]	NA	stage G4/G5	273	122	NA 33 (32-34)[d]	16 (7-39) 20 (17-23)[d]	93	53	89[a]	38[a]	NA	NA	adjusted for ?
	Pyart *et al.* [20]	≥70	stage G4/G5	841	375	48 (43-53)	24 (21-28)	NR	NR	NR	NR	87	63	unadjusted
	Verberne *et al.* [28]	≥70	stage G4/G5	240	126	38	17	81[a]	64[a]	65[a]	40[a]	30[a]	15[a]	unadjusted
eGFR<15ml/min/1.73m^2														
	Brown *et al.* [8]	NA	eGFR<15	118	53	20[d]	13[d]	NA	NA	NA	NA	NA	NA	
	Chandna *et al.* [10]	NA	eGFR<15	689	155	67	21	92[a]	76[a]	81[a]	45[a]	55[a]	12[a]	unadjusted
	Da Silva-Gane *et al.* [12]	NA	recruitment[b] (late stage G4/G5)	HD: 80 PD: 44	30	HD: 43 PD: 46	30	88[a] 90[a]	76[a]	73[a] 77[a]	51[a]	NA	NA	adjusted for high comorbidity, dependency, age >75, propensity scores
	García-Testal *et al.*[13]	>80	eGFR<15	33	54	38 (21-52)	14 (6-31)	97[a]	71[a]	87[a]	43[a]	54[a]	7[a]	unadjusted
	Hussain *et al.*[14]	>70	eGFR <15	264	169	46[a]	21[a]	79[a]	68[a]	67[a]	46[a]	40[a]	14[a]	unadjusted
	Kwok *et al.* [16]	>65	eGFR<15 (TD)	126	432	45	10	79	40	54	13	11	1	unadjusted
	Murtagh *et al.* [19]	>75	eGFR<15	52	77	NR	22[a]	84	68	76	47			unadjusted
	Raman *et al.* [21]	≥75	eGFR<15	123	81	42 (33-50)	31 (21-41)	90[c]	85[c]	76[c]	64[c]	31[c]	14[c]	adjusted for age, peripheral vascular disease, and living alone
	Shum *et al.* [23]	≥65	eGFR<15	157	42	45	28	96[a]	77[a]	86[a]	55[a]	48[a]	18[a]	unadjusted
	Teo *et al.* [25]	NA	ESKD diagnosis	HD:102 PD: 41[b]	16	NA	6[a]	80 78	31	NA	NA	NA	NA	unadjusted

Table S5. Continued

CKD stage	Study	Age	Kidney function at start of survival analysis	Number of patients		Median survival time, months		One year survival, %		Two year survival, %		Five year survival		Notes:
				D	CC	D	CC	D	CC	D	CC	D		
	Teruel *et al.* [26]	NA	eGFR<15	142	90	NR	NR	96[e]	60[e]	NA	NA	NA	NA	unadjusted mortality rate: 0.6 vs. 8.2 per 100 patients-months (p<0.001)
	Verberne *et al.* [28]	≥70	eGFR<15	191	84	37	15	85[a]	61[a]	69[a]	41[a]	35[a]	11[a]	
	Wong *et al.* [29]	adults	eGFR<15	not started: 503 started: 12.756	812	7 32	6	NR	NR	NR	NR	NR	NR	Patients who survived were excluded
eGFR around <10ml/min/1.73m^2/ (putative) start dialysis														
	Morton *et al.* [18]	NA	eGFR<15 / start dialysis	571	92	NR	NR	86	55	79	36	NR	NR	unadjusted HR 4.07 (3.08-5.37)
	Van Loon *et al.* [27]	≥65	eGFR<15 / start dialysis	192	89	NA	NA	92	66	NA	NA	NA	NA	adjusted for age, comorbidity, eGFR
	Carson *et al.* [9]	>70	(putative) start dialysis	121	29	42	14	79[a]	56[a]	67[a]	17[a]	39[a]	NR	unadjusted
	Hussain *et al.*[14]	>70	eGFR <12	172	110	41[a]	16[a]	74[a]	59[a]	64[a]	41[a]	43[a]	21[a]	unadjusted
	Joly *et al.* [15]	>80	Start dialysis vs decision	101	43	29 (24-38)	9 (4-10)	74	29	60	15			unadjusted
	Raman *et al.* [21]	≥75	eGFR <10	73	42	36 (25-47)	12 (0-5)	89[c]	53[c]	65[c]	31[c]	32[c]	4[c]	Adjusted for age, peripheral vascular disease
	Seow *et al.* [22]	>75 or CCI≥8	Started on dialysis or chose CC	38	63	NR	NR	NR	NR	62	13	NR	NR	unadjusted
	Smith *et al.* [24]	16-92	'from putative dialysis'	186	26	NA	6							
	Verberne *et al.* [28]	≥70	eGFR<10	132	42	34	6	75[a]	30[a]	62[a]	19[a]	29[a]	NR	

Abbreviations: TD: treatment decision; NR: not reported; NA: not applicable. [a] derived from Kaplan Meier curve; [b] decisions on modality choice took place throughout the recruitment phase an up to an additional 15 months. Survival analysis was based on planned modality group composition after this 15 month-period. [c] derived from cumulative incidence curve [d] mean survival time was given [e] derived from number of deceased persons after one year follow-up.

Table S6: Survival outcomes for severe comorbidity

Study	Age	Survival from	Definition severe comorbidity	Number of patients		Median survival time, months			One year survival (%)		Two year survival (%)		HR (95% CI): D vs CC	Adjusted for
				D	CC	D	CC	p-value	D	CC	D	CC		
Brown *et al.* [8]	-	eGFR<15	≥2	58	37								0.16 (0.08-0.34, p<0.001)	Age, sex, diabetes, IHD
	>75	eGFR<15	≥2, incl. CHF/IHD	18	52								0.48 (0.21-1.09, p=0.08)	Age, sex, diabetes?
Chandna *et al.*[11]	>75	eGFR<15	Score of 4[a]	27	69								0.65 (0.47-0.89, p=0.093)	Age, gender, ethnicity, diabetes
Chandna *et al.* [10]	>75	eGFR<15	Score of 4[a]	17	54	26	20	p=0.83	80[b]	73[b]	56[b]	41[b]		unadjusted
Hussein *et al.* [14]	>70	eGFR<15	CCI >8	79	84	53[b]	22[b]	p=0.01	76[b]	63[b]	67[b]	47[b]		unadjusted
Kwok *et al.* [16]	≥65	eGFR<15	mCCI ≥11	112	9	24[b]	7[b]	p=0.09	67[b]	37[b]	37[b]	17[b]		unadjusted
Murtagh *et al.* [19]	>75	eGFR<15	Davies 2	10	14	23[b]	22[b]	p=0.98	60[b]	63[b]	45[b]	40[b]		unadjusted
Pyart *et al.* [20]	>80	TD	CCI >4	94	109				88[d]	72[d]	72[d]	52[d]	0.64 (0.47-0.88, p=0.007)	unadjusted
Shum *et al.* [23]	≥65	eGFR<15	mCCI≥6	29[c]	13[c]	34[b]	20[b]	p=0.08	97[b]	54[b]	72[b]	31[b]		unadjusted
Verberne *et al.* [28]	≥70	eGFR<15	Davies ≥ 3	57	27	25[b]	10[b]	p=0.03	69[b]	39[b]	54[b]	27[b]		unadjusted
Range						**23-53**	**10-22**		**67-97**	**39-73**	**37-72**	**17-52**		

Abbreviations: CC, choice for conservative care; CCI, Charlson comorbidity index; CHF, cardiac failure; D, choice for dialysis; eGFR, estimated glomerular filtration rate in mL/min/1.73m^2; IHD, ischemic heart disease; mCCI, modified Charlson Comorbidity Index; TD, treatment decision.

[a] Scores of 0 (no disease) to 4 (advanced disease) were attributed to the following condition categories: cardiac disease, peripheral vascular disease, cerebrovascular disease, respiratory disease and cancer, cirrhosis was scored as a 4. Scores were summed. High comorbidity was designated to patients with scores of 4 in one condition category or with total scores >4.[30]

[b] derived from Kaplan Meier curve

[c] personal information from author

[d] derived from supplementary data-file

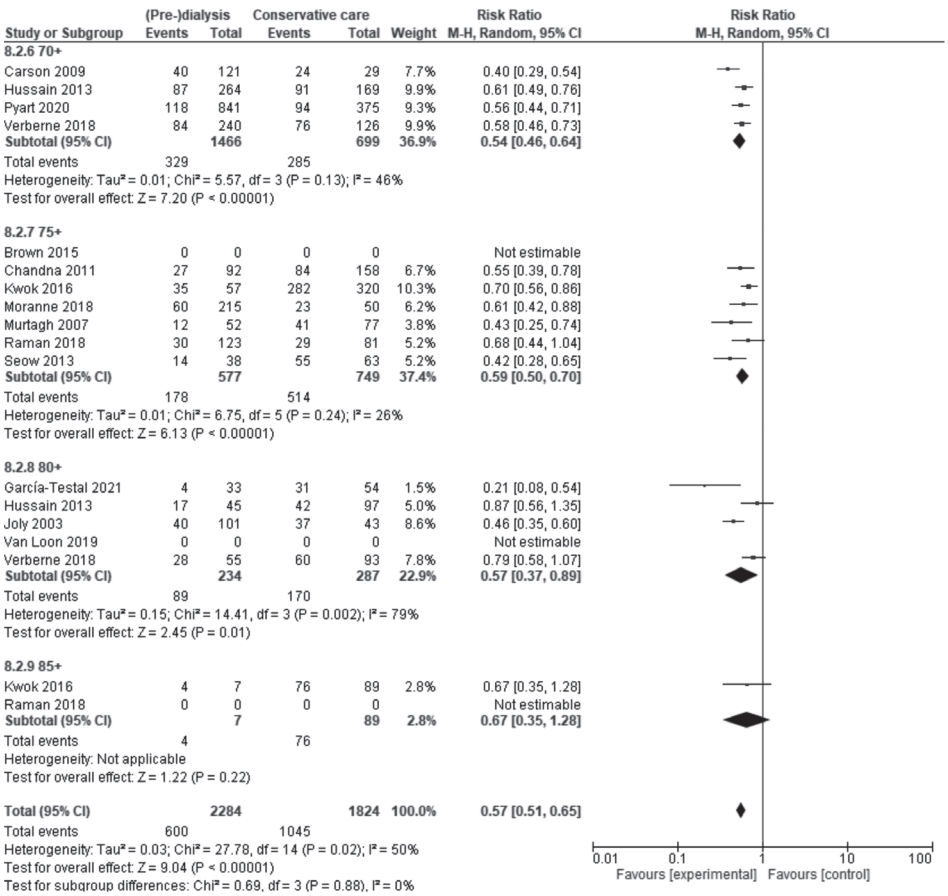
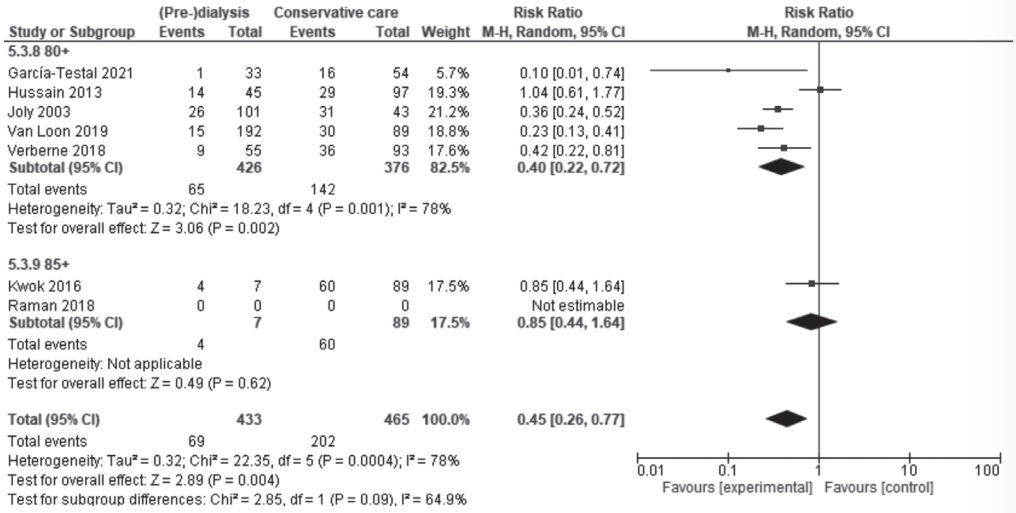


Figure S2: Age stratified risk ratio's for mortality, based on two-year survival.

A: RR for mortality among patients 80 years or older, based on one-year survival



B: RR for mortality among patients 80 years or older, based on two-year survival

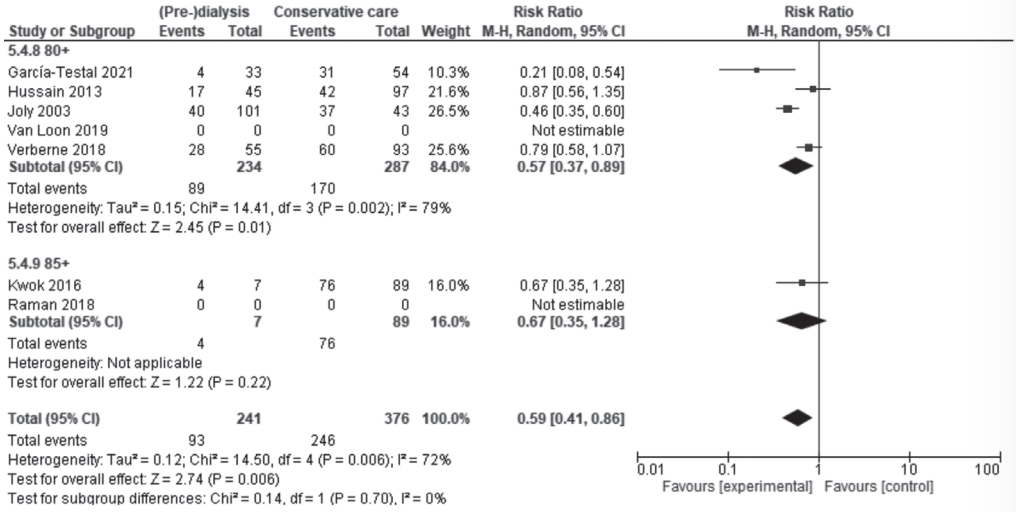


Figure S3: Unadjusted risk ratio's (RR) restricted to high age

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chapter 3

Changing the choice from dialysis to conservative care or vice versa in older patients with advanced chronic kidney disease.

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Nephrology Dialysis Transplantation 2021;36(10):1958-61.

INTRODUCTION

Maintenance dialysis is the most commonly chosen treatment for kidney failure in older patients. Current guidelines recommend presenting conservative care (CC) as a valid alternative to older patients who do not want to start dialysis.[1] While the survival benefit of dialysis is distinct, it appears to be reduced for the oldest patients and those with multiple comorbid conditions.[2] Also, the risk of treatment burden and the impact on daily life increase after dialysis initiation.[2,3] In terms of health-related quality of life (HRQoL) and symptom burden, both treatment pathways have the potential to achieve similar outcomes.[3]

Determining the most appropriate treatment pathway—often a difficult process—results from a dialogue between healthcare professionals, patients and their relatives on the goals of care, possible treatment options and risks and patients' values and preferences. This process of shared decision making (SDM) may start as early as from an estimated glomerular filtration rate (eGFR) of 20–30 mL/min/1.73 m^2, allowing time for dialogue, education and preparation for kidney replacement therapy. Reasons for choosing either dialysis or CC are based on aspects other than mortality and HRQoL and are likely to differ between patients, their relatives and physicians.[4] Furthermore, as patients' circumstances and preferences may change over time, the choice of therapy might also be subject to change.

When kidney function declines, clinical condition often deteriorates and symptoms increase. Intuitively, one may think that increasing uraemic complaints may result in more patients changing their initial choice from CC to dialysis than vice versa. However, no studies have been published presenting aggregated numbers of patients switching their treatment choice. Therefore we aim to assess the number of patients with chronic kidney disease (CKD) who made an explicit choice for dialysis or CC and switched their decision afterwards, either from dialysis to CC or from CC to dialysis.

METHODS

We systematically searched five databases from inception to 25 February 2021 for studies in patients with severely reduced eGFR or kidney failure (CKD stage G4–G5) and choosing either dialysis or CC that compared patient-reported outcomes (HRQoL and symptoms),[3] survival and treatment burden.[5] Detailed methods on search strategy and predefined selection criteria are described elsewhere.[3,5] For the present analysis we included studies reporting the number of patients switching their (initial) treatment choice in either direction. Studies that started their observations at the (putative) start of dialysis were excluded. Screening of 7634 records resulted in 10 studies.[2,6–14] that reported the number of patients changing their treatment choice from dialysis to CC or vice versa (Figure 1). (Sub)groups where the decision to withhold dialysis was based on medical grounds only were excluded from the analysis; e.g. patients who started acute dialysis or when their nephrologist decided that dialysis was not appropriate.[9] This was done to ensure that our results reflected a patient group that was allowed to make a treatment choice. Three studies were omitted because of (partly) overlapping study populations; we excluded the studies first published and with the lowest number of CC patients[10,11] or shortest follow-up duration.[12]

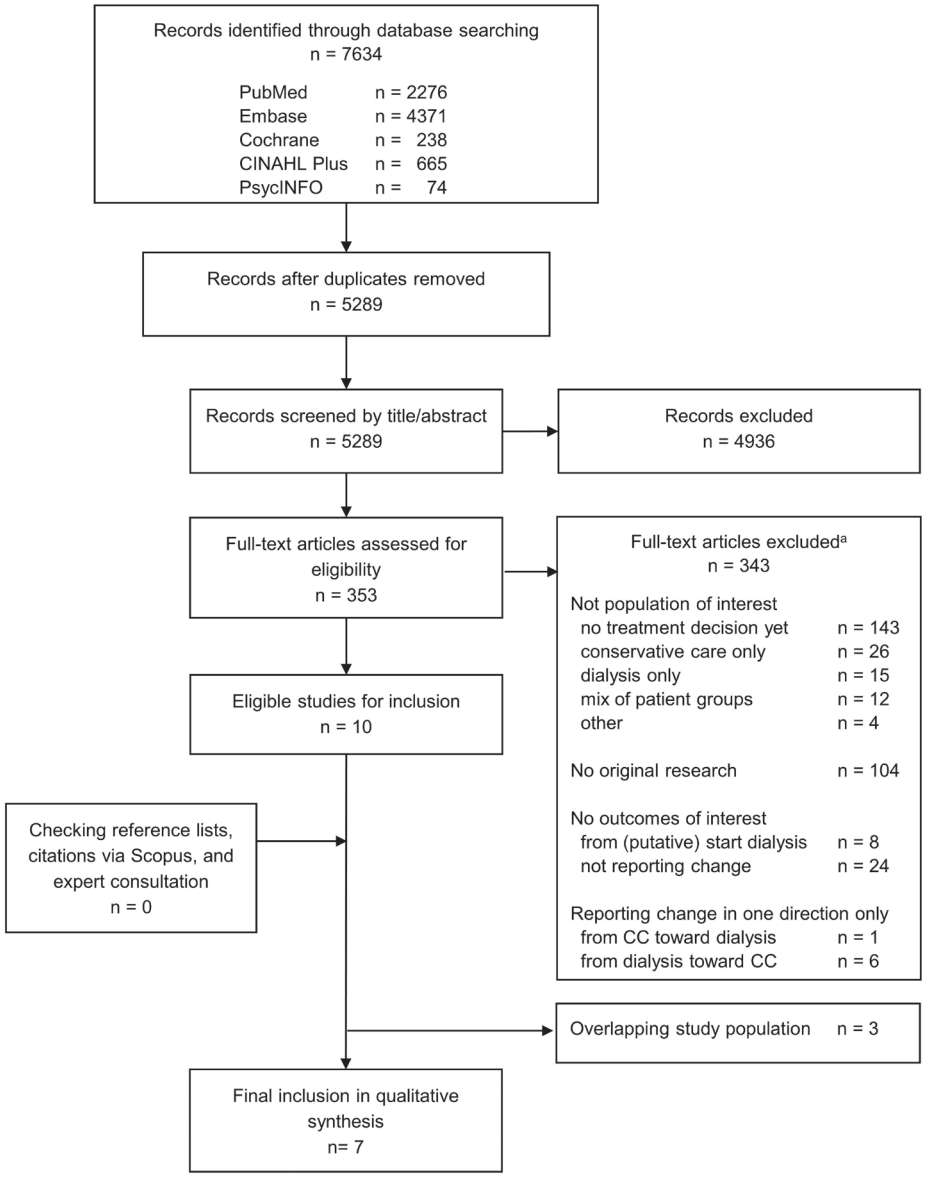


Figure 1. Study inclusion and exclusion flow diagram.

[a] Explanation of reasons for exclusion: No treatment decision yet includes patients with advanced chronic kidney disease who did not, or did not yet have to, decide on preferred treatment (commonly referred to as "non-dialysis dependent chronic kidney disease patients"), including 4 studies discussed with the authors to clarify their conservative care-like patient group (Verberne et al., 2020, Supplementary Table S2)[3]; Mix of patient groups means mix of different patient categories into one patient group without subgroup analyses (e.g., mix of patients who have not made a treatment decision yet and patients who chose conservative care); No original research, for example reviews, opinion papers, or study protocols; No outcomes of interest for the initial systematic reviews, i.e. on health-related quality of life, symptoms, hospitalization and/or mortality.

RESULTS

Seven observational cohort studies were included, mostly single centre and with a retrospective design. The sample size varied from 269 to 1216 patients per study (3527 patients overall: 2217 with an initial treatment plan for dialysis and 1310 for CC). Within these highly heterogeneous study populations, treatment plans changed among 0.0–8.9% of the patients. Table 1 shows that 0.0–12.1% (weighted mean 5.3%) of patients changed their choice from dialysis to CC, whereas 0.0–3.9% (weighted mean 2.7%) of patients changed their choice from CC to dialysis. Reported reasons to change from dialysis to CC were based on a change in personal preference or due to deterioration of their clinical condition.[7,10] Reported reasons to change from CC to dialysis were physical complaints after a sudden decline in kidney function[10] or secondary to intercurrent illness for which urgent dialysis was offered.[7]

Table 1. Studies reporting a change in initial choice for either dialysis or CC pathway

	Country	**Design**	**Inclusion criteria**		**Dialysis choice**		**CC choice**	
Study			CKD stage	Age (years)	Initial, n	Changed, n (%)	Initial, n	Changed, n (%)
Brown et al.[6]	Australia	P, S	G4–G5	–	273	33 (12.1)	122	2 (1.6)
Hussain et al.[7]	UK	R, S	eGFR <20 mL/min/1.73 m2	>70	269	19 (7.1)	172	3 (1.7)
Kwok et al.[8]	Hong Kong	R, S	eGFR <15 mL/min/1.73 m2	>65	126	7 (5.6)	432	17 (3.9)
Moranne et al.[9]	France	P, M	eGFR <20 mL/min/1.73 m2	>75	215[a]	14 (6.5)	54[a]	1 (1.9)
Pyart et al.[14]	UK	R, S	eGFR <20 mL/min/1.73 m2	>70	841	29 (3.4)	375	8 (2.1)
Verberne et al.[2]	Netherlands	R, S	G4–G5	>70	240	15 (6.3)	126	4 (3.2)
Salat et al.[13]	USA	P, S	G4–G5	>60	253[b]	0 (0.0)	29[b]	0 (0.0)
Total					2217	117 (5.3)	1310	35 (2.7)

Abbreviations: G4, severely reduced eGFR of 15–29 mL/min/1.73 m2); G5, kidney failure, eGFR <15 mL/min/1.73 m2; M, multicentre; n, number of patients; P, prospective study; R, retrospective study; S, single centre.

[a] Excluding patients with nephrologist's decision that dialysis is not appropriate and patients postponing the decision about dialysis because of stable clinical condition.

[b] Estimation of the number of patients; due to rounding differences, no exact number could be derived from the percentages given.

DISCUSSION

Within the few studies that reported a change in (initial) treatment choice, older patients more often switched from a choice of dialysis to CC than vice versa. The studies did not specify any difference in change between patients with an initial choice for haemodialysis versus peritoneal dialysis in switching to CC. One study[14] found that all eight patients changed their choice from CC to haemodialysis (instead of peritoneal dialysis, home haemodialysis or pre-emptive transplant). The data do not describe the patient characteristics of switchers, i.e. whether patients with more advanced disease and comorbid conditions switched back to CC, while patients with better clinical conditions and faster disease progression decided to initiate dialysis. When foregoing dialysis, this most likely is a more well-informed decision, well-discussed between the patient, the medical team and the patient's relatives, compared

with a choice for dialysis, which might be the default option. Previous studies have reported that doubts are more apparent in older patients who choose dialysis rather than CC,[4] and substantial numbers of patients report decisional regret after starting dialysis.[15,16] Education programmes have been reported to reduce changes in treatment decisions.[17] We hypothesize that the smaller number of switches from CC to dialysis reflects a more thorough consideration of the treatment decision for CC.

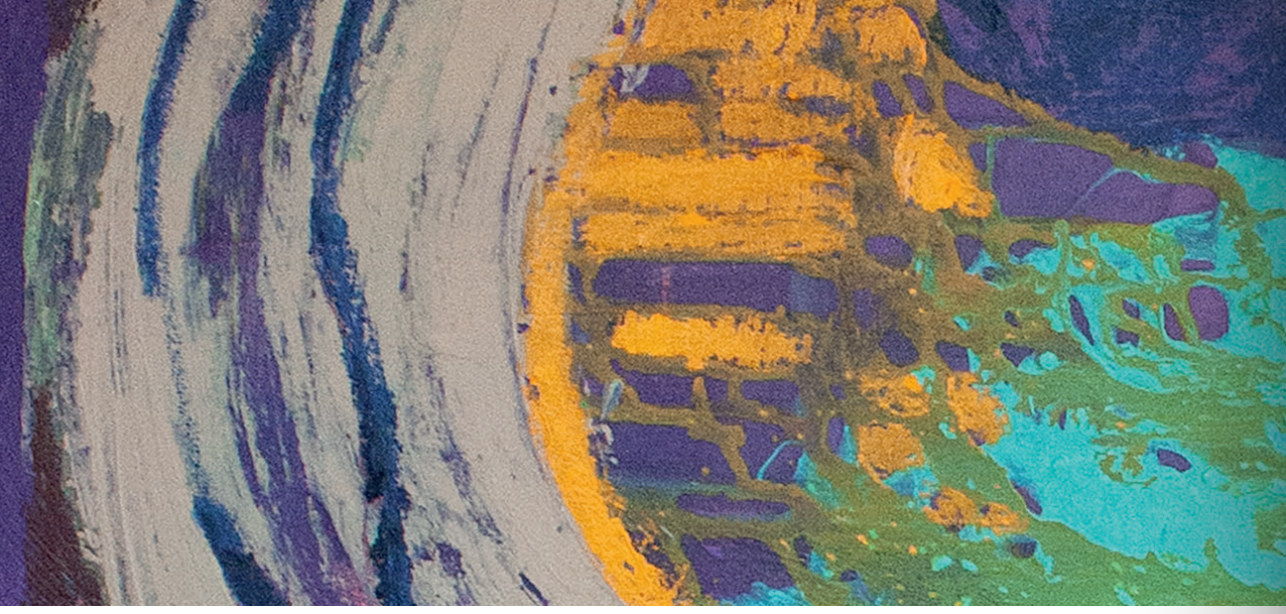
Our review has several major limitations. First, only a small number of studies reported a change in treatment decision in both directions, suggesting that results may be biased by publication. Second, studies were heterogeneous and had a high risk of confounding and selection bias, e.g. for heterogeneity between treatment groups, incomplete outcome data and missing information,[3] which warrants careful interpretation. Third, data are based on practices of nephrologists who are experienced and have a special interest in the CC pathway and may not reflect SDM practices elsewhere. Fourth, this study does not account for patients who withdraw from dialysis early in favour of CC, which may potentially lead to a greater number of patients ultimately switching from dialysis to CC. Fifth, as our systematic data search was primarily focused on survival, HRQoL and treatment burden, other research articles on therapy choice switches[17] may have been missed.

CONCLUSIONS

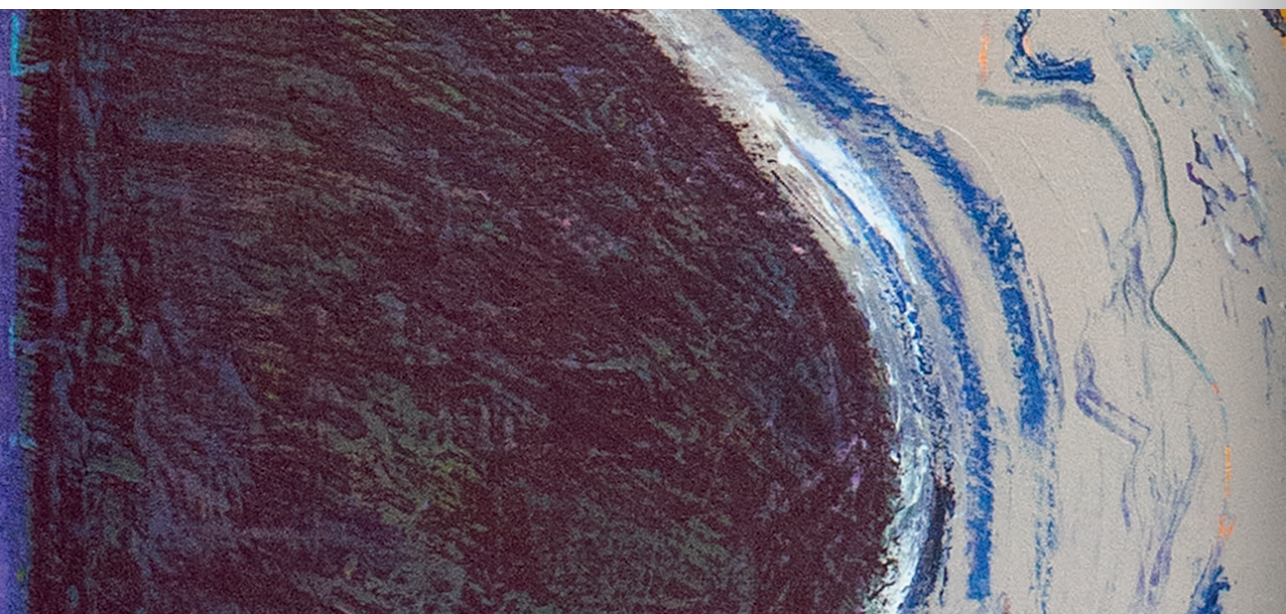
In conclusion, little attention has been paid to the topic of older patients switching their choice of therapy between dialysis and CC. The few studies that have been conducted show that older patients with CKD stage G4–G5 more often change their decision from dialysis to CC than vice versa, although treatment groups are heterogeneous and outcomes are highly susceptible to bias and confounding. Our findings underline that SDM is a continuous process rather than a static point in time. Patients may benefit from an exhaustive education process on all treatment options, including centre and home haemodialysis, peritoneal dialysis, incremental dialysis and CC, in the management of advanced CKD. This management should include active and ongoing evaluation of treatment decisions and the patient's goals for care. Prospective studies should pay more attention to changing treatment choices for kidney failure by reporting controlled clinical observations. Both characterizing the group of patients who switch their treatment choice and gaining insights into reasons for decision changes may help nephrologists to better inform older patients with CKD in future SDM processes.

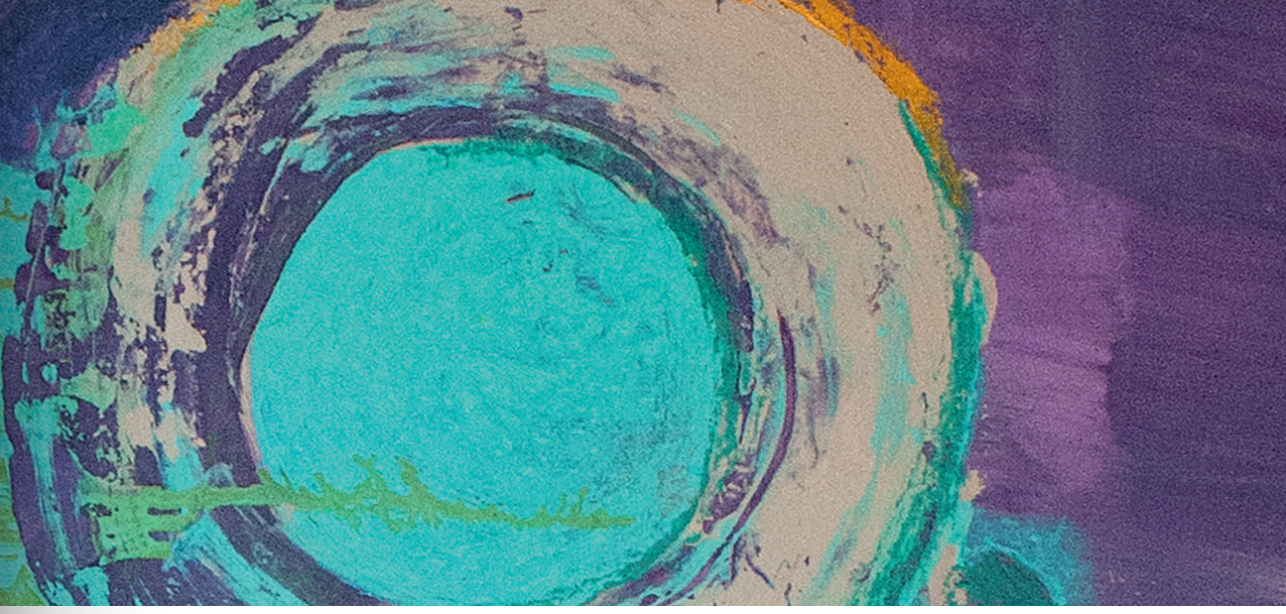
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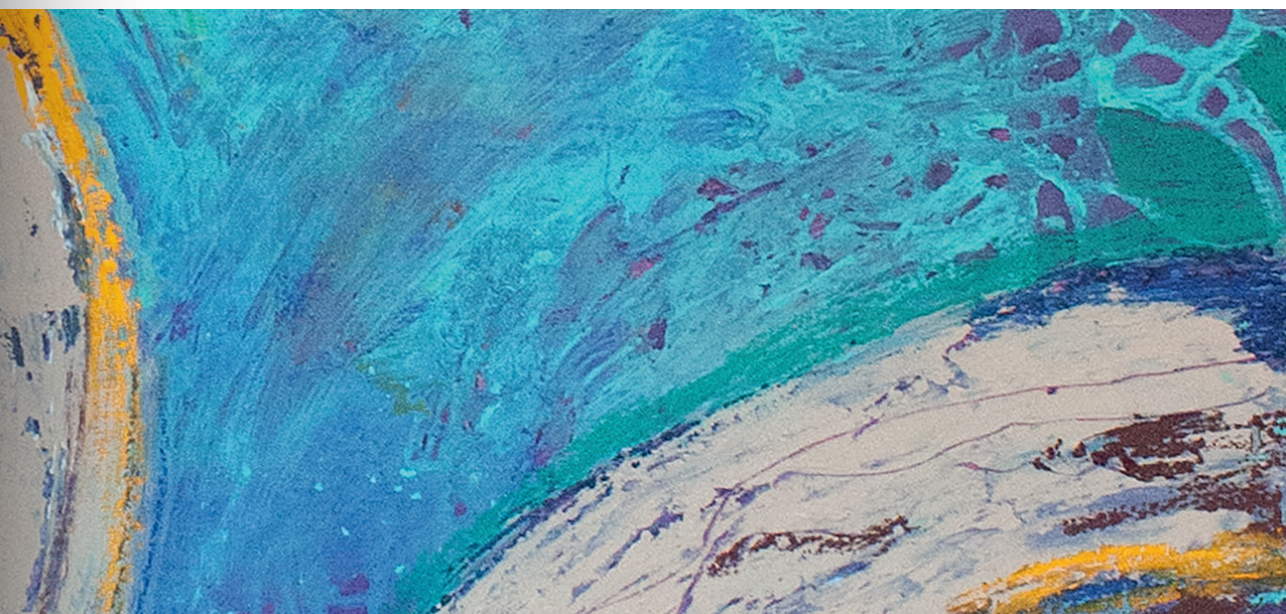


PART II





DESIGN AND IMPLEMENTATION OF GERIATRIC ASSESSMENT





chapter 4

Perspectives and experiences of patients and healthcare professionals with geriatric assessment in chronic kidney disease: a qualitative study.

Carlijn G. N. Voorend, Noeleen C. Berkhout-Byrne, Yvette Meuleman, Simon P. Mooijaart, Willem Jan W. Bos and Marjolijn van Buren

BMC Nephrology 2021;22(1):9.

ABSTRACT

Background: Older patients with end-stage kidney disease (ESKD) often live with unidentified frailty and multimorbidity. Despite guideline recommendations, geriatric assessment is not part of standard clinical care, resulting in a missed opportunity to enhance (clinical) outcomes including quality of life in these patients. To develop routine geriatric assessment programs for patients approaching ESKD, it is crucial to understand patients' and professionals' experiences with and perspectives about the benefits, facilitators and barriers for geriatric assessment.

Methods: In this qualitative study, semi-structured focus group discussions were conducted with ESKD patients, caregivers and professionals. Participants were purposively sampled from three Dutch hospital-based study- and routine care initiatives involving geriatric assessment for (pre-)ESKD care. Transcripts were analysed inductively using thematic analysis.

Results: In six focus-groups, participants (n = 47) demonstrated four major themes: *(1) Perceived characteristics of the older (pre)ESKD patient group*. Patients and professionals recognized increased vulnerability and (cognitive) comorbidity, which is often unrelated to calendar age. Both believed that often patients are in need of additional support in various geriatric domains. *(2) Experiences with geriatric assessment*. Patients regarded the content and the time spent on the geriatric assessment predominantly positive. Professionals emphasized that assessment creates awareness among the whole treatment team for cognitive and social problems, shifting the focus from mainly somatic to multidimensional problems. Outcomes of geriatric assessment were observed to enhance a dialogue on suitability of treatment options, (re)adjust treatment and provide/seek additional (social) support. *(3) Barriers and facilitators for implementation of geriatric assessment in routine care.* Discussed barriers included lack of communication about goals and interpretation of geriatric assessment, burden for patients, illiteracy, and organizational aspects. Major facilitators are good multidisciplinary cooperation, involvement of geriatrics and multidisciplinary team meetings. *(4) Desired characteristics of a suitable geriatric assessment* concerned the scope and use of tests and timing of assessment.

Conclusions: Patients and professionals were positive about using geriatric assessment in routine nephrology care. Implementation seems achievable, once barriers are overcome and facilitators are endorsed. Geriatric assessment in routine care appears promising to improve (clinical) outcomes in patients approaching ESKD.

INTRODUCTION

In older patients with end stage kidney disease (ESKD) frailty, malnutrition, cognitive impairments, depression and impaired health-related quality of life are highly prevalent[1-3] and often underdiagnosed.[4,5] Geriatric impairments are strongly associated with adverse health outcomes such as hospitalisation and mortality in (pre-)ESKD patients.[3,6] Recently published ESKD guidelines recommend to frequently measure different geriatric domains and to use these outcomes in the decision making process[7,8] but this is not part of standard clinical care.[9]

The gold standard to geriatric appraisal is the Comprehensive Geriatric Assessment (CGA); a multidisciplinary process to identify older patients' medical, psychosocial and functional needs, and to develop a coordinated integrated care plan.[10] CGA has been shown to improve outcomes including hospitalisation and mortality, and may potentially also reduce costs.[11,12] However, for implementation in standard clinical care, full CGA often poses logistical difficulties.[10] Contrarily, short frailty screening tools are insufficiently discriminative for clinical use in ESKD patients.[13] In medical areas such as oncology, acute hospital settings and perioperative care, new models and settings of geriatric assessment are being explored,[10] but limited attempts in nephrology are reported.[4,14-17] So far, no standardized approach exists and thus, the search for the optimum use of geriatric assessment in routine care of older patients approaching ESKD continues.[9]

To develop a nephrology-tailored routine geriatric assessment (NGA), it is crucial to understand patients' and professionals' perspectives on current practices of geriatric assessment in nephrological care. Until now, this has not yet been properly investigated.[14] Qualitative research can provide valuable insights into stakeholders' perceived effectiveness of care pathways.[18] The primary aim was to elicit perspectives and experiences of patients and professionals with geriatric assessment in the care for older (≥65 years) patients approaching ESKD (estimated glomerular filtration rate < 20 ml/min/1.73m2), and to identify benefits, facilitators and barriers for implementation into routine nephrological care.

METHODS

Study design and participants

We conducted a qualitative study, approved by the Medical Research Ethics Committee United (MEC-U, Nieuwegein, The Netherlands, reference W17.127), using focus group discussions. The study population comprised of (pre)ESKD patients, caregivers and healthcare professionals who were experienced with hospital-based geriatric assessment practices in nephrology. The three different practices included (i) a yearly one-hour geriatric assessment in routine care for patients approaching ESKD performed in a University hospital, (ii) a three-hour geriatric assessment for patients approaching ESKD in a study setting, of which results were used in routine-care,[15] and (iii) a single-time point geriatric assessment among patients starting with or withholding from dialysis for study purposes, to be measured in a home-visit.[4] Table 1 shows detailed information on the geriatric assessment practices, population of interest, and different instruments that were used. For each of the three assessment

Table 1. Overview of geriatric assessment practices, from which participants were recruited, including geriatric testing methods

Practices	COPE study[15]	GOLD study[4**]	Routine care pathway, UMCG
Focus group number	1, 2	3, 4	5, 6
Type of practice	Prospective multicentre observational cohort study 4 year follow up	Prospective multicentre observational cohort study (cross-sectional geriatric assessment)	Routine care practice
Aim of geriatric assessment	Examine the severity of cognitive impairment in older patients reaching ESKD before dialysis and the rate of decline after dialysis or CCM initiation	Assess the association of geriatric measures between start of dialysis and after 6 months	Guide patients to the best treatment choice and to define supplementary care to optimize quality of life and reduction of illness-related symptoms
Population at inclusion	≥65 years, eGFR ≤ 20 ml/min/1.73m^2	≥65 years, initiating dialysis or conservative kidney management	≥70 years (or younger if indicated), eGFR ≤ 20 ml/min/1.73^{m}2
Measurements	Baseline: at inclusion Follow-up: yearly (four times), and after six months of start dialysis treatment	Baseline: within 4 weeks of initiating dialysis or 4 weeks after final decision to withhold Follow-up: after 6 months by phone	Yearly assessment divided over 2 or 3 visits
Conducted by	Nurse practitioner or geriatric nurse	Research nurse	Nurse practitioner
Duration	3 hours	60-90 minutes	2 x 30 minutes
Location	Outpatient clinic	Home visit, follow-up by telephone	Outpatient clinic
Use of outcomes of assessment	For study purposes and discussed in multidisciplinary meeting and with patient, if necessary referred for geriatric consult	Collected for study purposes only, at home or in dialysis centre	Discussed in multidisciplinary meeting and with patient
Geriatric measures:			
Functional status (ADL/ iADL)	GARS* Lawton*	Katz-6* Lawton*	Katz*
Mobility	Gait speed* Hand grip strength* Short Physical Performance battery*	Timed up and go Falls* Four Test Balance Scale	Timed up and go*** Falls***

Table 1. Continued

Practices	COPE study[15]	GOLD study[4**]	Routine care pathway, UMCG
Cognition	Mini Mental State Examination* Clock drawing* 15- WVLT* Stroop Colour Word Test * Trail making test (A&B) * Visual Association Test* Letter Digit Substitution Test* Assessment of numeracy*	Mini Mental State Examination Clock drawing Enhanced Cued Recall Semantic Fluency Test	MOCA*
Mood	Geriatric Depression Scale*	Geriatric Depression Scale	Geriatric Depression Scale *
Nutritional status	Subjective Global Assessment or SNAQ*	Mini-Nutritional Assessment	(anamnesis by dietician)*
Comorbidity	Charlson Comorbidity Index*	CIRS-G	(anamnesis)*
Quality of Life	RAND-36*	EuroQol-5D*	EuroQol-5D* Visual Analogue Scale*
Frailty	Fried frailty indicator*	Groningen Frailty Index* Fried Frailty Index (includes 4 meter walking test and Handgrip strength)	Rockwood Clinical Frailty score***
Caregiver burden	EDIZ-plus*	EDIZ*	[hetero]amnesis by social worker*
Estimation of nephrologist		VAS: overall condition Surprise question	Surprise question***
Other	Cantril's ladder, Pain score, Anxiety score Illness perceptions questionnaire*	Additional subjective cognition tests (by caregiver): IDDD* IQCODE* Neuro-Psychological Inventory*	Outcome Prioritization Tool (treatment goals)*

Abbreviations: ADL, activities of daily living; iADL, instrumental activities of daily living; GARS, Groningen Activity Restriction Scale; 15-WVLT, 15-Word Verbal Learning Test, immediate and delayed; SNAQ, Short Nutritional Assessment Questionnaire; CIRS-G, Cumulative illness rating scale for geriatrics; EDIZ, 'Ervaren Druk door Informele Zorg' Self perceived burden from informal care; IDDD, Interview of Deterioration in Daily life Dementia; IQCODE, Informant Questionnaire on COgnitive DEcline.

*Reassessed measures at follow up,

** Next to the study measures, two hospitals used additional instruments in routine care practice. St. Antonius hospital: a pre-dialysis decision making trajectory, including a home visit by a social worker and assessment of different domains (Katz, Lawton, MMSE, sometimes depression score (GDS), receiving care and living situation). Maasstad hospital: patients ≥70 years, if considered frail by nephrologist, are seen in a separate appointment with a nurse practitioner and assessed with multiple instruments (including: Katz ADL, Lawton iADL, Mini Mental State Examination, Geriatric Depression Scale, Charlson Comorbidity Index, Groningen Frailty Indicator, Timed up and go, Hand grip strength, fall risk, caregiver burden, wellbeing measurement) outcomes are discussed in MDTM and with the patient.

***Measures assessed at each visit to the outpatient clinic.

practices we initially planned one focus group for the patient-perspective (including caregivers) and one professional group.

Patients were purposively sampled when meeting the inclusion criteria: i.e. aged ≥65 years, chronic kidney disease (CKD; stages 4/5/5D or recent transplantation, eGFR < 20 ml/min/1.73m^2), and experienced with either one of above mentioned geriatric assessment practices. We invited patients who had positive as well as negative experiences with NGA and with different (future) choices of treatment modality. Patients were asked by phone or face-to-face to participate by the (principal) investigator or treating nurse practitioner, and subsequently sent an information letter and informed consent form per mail. The letter included an invitation for a caregiver to participate, in case patients were unable or unwilling to come to the site on their own. Professionals were recruited per face-to-face, phone or e-mail through a combination of purposive and snowball sampling, if meeting the inclusion criteria: i.e. medical profession involved in providing care for older CKD patients, and involved in one of above mentioned geriatric assessment practices. We purposively invited professionals from various disciplines (i.e. nephrologists, geriatricians, nurse practitioners, dialysis nurses, social workers, dieticians) to ensure representation of all disciplines in geriatric nephrological care. Professionals received an information letter on study purpose, procedure, and confidentiality. Participants were excluded if they were not available at the date of the focus group or unable to get to the interview site. In total, four patients and five professionals declined their invitation, another two patients and two professionals did not show up at the day of the focus groups. Main reasons for decline were inability to attend or for personal reasons. Informed consent was given before start of the focus groups. The Consolidated Criteria for Reporting Qualitative Studies (COREQ) checklist was used as reference for reporting.

Data collection

Researchers (MB, NB, CV) developed a semi-structured interview topic guide (Supplementary item S1) which was informed by literature[3,4,6,14,15,19] and clinical experiences, and reviewed by nephrologists and geriatricians (HJ, WB, CG, SM). Guiding questions were designed to prompt for views on:

1. Perceptions on the value of geriatric assessment in routine practice
2. Barriers and facilitators to the implementation of geriatric assessment in routine practice

All groups were led in Dutch language by a nurse practitioner (NB) with 40 years' experience in clinical nephrology and 7 years in geriatric nephrology. It was ensured that none of her own patients were included in groups. The interviewer was trained to conduct focus groups. Each group was held in a quiet and comfortable hospital meeting room, and lasted for a maximum of 3 h, including half an hour break. The interviewer began by clarifying reasons for doing the interviews (i.e. research to develop a nephrology-tailored routine geriatric assessment), explaining confidentiality, introducing herself and observers, and asking participants to introduce themselves. Participants were encouraged to speak freely and discuss their shared opinions as well as differences. One observer (CV) experienced in qualitative research took notes of nonverbal communication and group dynamics. At patient-

groups, another observer (NG, RK, KC) was present to provide background information on geriatric assessment practices or feedback to the interviewer.

Data analysis

Focus groups were audio-recorded, transcribed verbatim, and analysed using inductive thematic analysis, which is a widely used descriptive approach for identifying, analysing and reporting patterns (themes) in qualitative data.[20] A brief summary of discussed topics was given to participants at the end of the focus group, transcripts were not returned for comments or correction. Initial coding and analysis was done by C.V. and N.B. separately, followed by a discussion of meaning of quotes, to confirm and agree on initial codes and (sub)themes. Consistency of the code scheme was checked by M.B. and Y.M. after which some changes were made. Further analysis was done by C.V in close collaboration with N.B. No qualitative research software was used, although coding, memo's and analyses were documented digitally. Interpretations were iteratively reviewed and critically discussed until consensus was reached within the multidisciplinary research team. Data saturation was assessed by the research team at different stages of analysis, after conducting the groups, coding and analysis, until agreement was reached on sufficiency of information power and no new themes emerged.[20-22] The research team consisted of different backgrounds (i.e. nurse practitioner, health scientist, nephrologists, psychologist, and geriatrician), of whom most were experienced in conducting geriatric assessment in nephrology (except for CV and YM). Selected illustrative quotes were translated from Dutch to English by a native speaker (NB), using back-translation.

RESULTS

Six focus groups were conducted (n = 47, mean 7.8, range 7–9) from November 2017 to January 2018 until data saturation was reached (i.e., until no new information was obtained, or new themes emerged). Three groups concerned the patient-perspective (n = 22; i.e. 18 patients [aged 67–88 years] and four caregivers) and three were held with healthcare professionals (n = 25). Participant characteristics are shown in Table 2. We identified four themes: (i) perceived characteristics of the older (pre)ESKD patient group, (ii) experiences with geriatric assessment, (iii) barriers and facilitators for implementation of NGA, and (iv) desired characteristics of a suitable geriatric assessment. Illustrative quotations are provided in the results below and additional quotations are shown in Supplementary Item S2.

Perceived characteristics of the older patient group approaching ESKD

Patients and professionals recognized that becoming older is often accompanied by increasing vulnerability and co-morbidity, including polypharmacy and reduced cognition. Both believed that older (pre)ESKD patients need additional support in various domains.

> *"In older patients, problems arise that do not occur in younger patients. In many cases, cognitive impairment and life goals also change when life expectancy is shortened. So this does, I think, require extra attention" (Geriatrician, woman 35-40 years)*

Table 2: Participant characteristics

	Patients (N=18)	**Caregivers (N=4)**	**Professionals (N=25)**
Age, mean (range)	79 (67-88)	60 (51-76)	48 (29-61)
Sex, male	9 (50%)	0 (0%)	4 (16%)
Children, yes	17 (94%)		
Civil status			
married/living together with partner	10 (56%)		
widow/no partner	8 (45%)		
Living situation			
independent	12 (67%)		
independent with care facilities (e.g. care at home, alarm bell, or assistance in housework)	6 (33%)		
Education level			
Primary or secondary education	6 (34%)		
Secondary vocational education	5 (28%)		
Higher professional/ university education	7 (39%)		
Treatment status			
Haemodialysis / peritoneal dialysis, n (months since start)	5 (2-21, mean 11.6)		
Transplantation, n (months since transplantation)	3 (4-32; mean 15.3)		
CKD stage 4/5 not on KRT, n	10		
Future choice (if in CKD stage 4/5, not on KRT)			
Haemodialysis / peritoneal dialysis	3		
Transplantation	2		
Conservative kidney management	2		
Multiple modalities open or no decision made	3		
Time since last geriatric assessment, in months, median (range)	5.5 (0.6-14.3)*		
Experience in care for 65+ CKD patients, in years, median (range)			5.5 (0.5-28.3)
Clinical role			
Nephrologist			7 (28%)
Geriatrician			4 (16%)
Nephrologist/geriatrician			2 (8%)
Nurse practitioner			2 (8%)
Nurse (nephrology)			3 (12%)
Nurse (other)			2 (8%)
Social worker			4 (16%)
Dietician			1 (4%)
Initiative and medical centre			
COPE study	7 (39%)	-	9 (36%)
Haga hospital, The Hague	4		5
Jeroen Bosch hospital, Den Bosch	-		1
Leiden University Medical Centre	3		2
Reinier de Graaf hospital, Delft	-		1

Table 2: Continued

	Patients (N=18)	Caregivers (N=4)	Professionals (N=25)
GOLD study	6 (33%)	1 (25%)	8 (32%)
Academic Medical Centre, Amsterdam	1		-
Gelderse Vallei Hospital, Ede	1		-
Leiden University Medical Centre	1		-
Maasstad Hospital, Rotterdam	-		1
St. Antonius Hospital, Nieuwegein	-		2
University Medical Centre, Utrecht	3		5
Routine care pathway (University Medical Centre Groningen)	5 (28%)	3 (75%)	8 (32%)

Abbreviations: CKD, chronic kidney disease; KRT, kidney replacement therapy.
* Time since last geriatric assessment was substantially longer for patients from the GOLD study (median 11.8 months) versus other initiatives (median 2.2 months), because we reported the time since initial formal geriatric assessment. Additionally, patients had a follow-up after 6 months by telephone

"You grow old, so things go wrong here and there. Yes, that should be taken into account" (Woman 80-85 years, on peritoneal dialysis)

Patients described that their goals in life may be different in comparison to younger patients (e.g. more focus on independence, care for a sick partner or the ability to spend time with their grandchildren) and their treatment options as more limited, whereas impact of dialysis on daily life may be less invasive.

"Being on dialysis three days a week for four hours, that is much more invasive for a young patient than for an old patient." (Woman 80-85 years, on haemodialysis)

Professionals observed that older patients more often suffer from loneliness and grief compared to younger patients, and had impaired ability to process information due to reduced functional and cognitive functioning. However, they stressed that above mentioned factors are not only related to age but also vary according to individual fitness and social environment. Multiple professionals reported that they wrongly presume to have comprehensive knowledge of their nephrology patients due to the chronic care pathway, and that they realize that without NGA certain geriatric impairments remain underrecognized.

"As doctors we tend to concentrate on somatic aspects, patient vigour and medical history. We have too little time to explore things like cognition, quality of life, and expectations [...] Perhaps we should do things differently." (Nephrologist, man, 45-50 years)

Experiences of using a geriatric assessment

(Providers' perceptions of) patients' experiences with a geriatric assessment

Patients appreciated the attention during geriatric assessment for multiple aspects of health and daily functioning. They particularly valued the (extra) time and attention they received from professionals. Consequently, patients were able to share more fears and concerns about treatment choices.

"It was an eye-opener for me. Fortunately, and much to my relief, I discovered that, in spite of my age, I'm able to do things that many peers are not able to do anymore."
(Man 80-85 years, on haemodialysis)

"I do notice that when they [patients] are at the geriatrician, they dare to admit more honestly what their fears are. They do not dare to share these fears with a nephrologist because they think that he/ she might not want to treat them anymore. With involvement of a very different person or function [the geriatrician] quite different things sometimes come to the surface."
(Nephrologist-geriatrician, woman 40-45 years)
"Or the other way around: people who do not want a treatment [..] who almost do not dare to say to me [nephrologist] that they are afraid that they will undermine my role when refusing the treatment". (Nephrologist, woman 60-65 years)

Patients experienced the NGA as comparable to a school examination or brain games, either having a strong positive or negative association: some patients felt positively challenged because of the competition with themselves while others were apprehensive. Professionals believed that some patients also experienced tests and subsequent outcomes as confrontational.

"You want to perform well [patient 5 and 6 mumble in consent]. It is a kind of exam, you do want to get a good grade." (Woman 70-75 years, transplanted) "Yes, obviously you want to do well." (Woman 75-80 years, pre-dialysis phase)

"If a patient himself thinks he functions good and then he realizes that he does not actually perform well, it can be incredibly confrontational for that patient."
(Nurse practitioner, woman 60-65 years)

Potential benefits of a repetitive NGA are recognised among most patients, except when treatment was already started, if they were still active in working life, or when cognitive or functional limitations were experienced shortly after a surgery. Interestingly, even the few patients who were negative about testing and to whom the value of doing these tests was unclear, acknowledged the potential of repeating measures to see any progress or decline and to deploy targeted interventions.

"So you do not understand the purpose [of doing the test]?" (Interviewer). "No, not at all" (Woman 80-85 years, on peritoneal dialysis)."Well, I do! They look at your condition. And after a year, one can off course notice any decline. That is the purpose!"
(Man 70-75 years, transplanted after haemodialysis).

"I would like to know: are the test-results shared with the treating nephrologist? That should be the case, so they can respond to it – in spheres of social and daily life – and provide more support. Make sure that support is there." (Woman 80-85 years, on peritoneal dialysis).

Professionals' experiences with a geriatric assessment

Professionals also considered repeating NGA important; not only to detect changes in patients' medical situation, but also the social situation. NGA is perceived to be a very important tool to enhance their knowledge of the patient and to identify trends of functioning

on geriatric domains over time. Especially cognitive problems and frailty are identified more often when using NGA.

> *"And the blind spot: [..] On the ward we had two patients who had just undergone AV-fistula placement, and both turned out to have dementia. In one patient, the diagnosis was missed due to a language barrier. The other was very well educated and was able to camouflage difficulties. Both cases developed a serious delirium after the operation [for which geriatric follow-up was indicated] [..] And that's when I thought: okay, yes, cognition is indeed something that I don't specifically look for. So there are other domains that need to be appraised" (Nephrologist-geriatrician, woman 35-40 years)*

Measuring these geriatric domains initiates dialogue on treatment decision and -goals, and provides reason to set targeted interventions. According to most professionals, NGA improves awareness among the whole treatment team to (re)consider different treatment options like conservative kidney management and home dialysis. Notably, caregivers also accredited the importance of NGA in decision making, for safety and competence reasons.

> *"Those tests that were done [..] we saw these as very positive, enabling you to make a better choice [..]. If I had memory problems that could cause me to make mistakes, then [test-results] could support me in making a more suitable choice or make a different decision. Your choice becomes more subtle." (Daughter of male 80-85 years pre-dialysis patient)*

Professionals acknowledged that they themselves should be cautious of labelling patients based merely on test scores. Also, difficult dilemmas may arise when a patient is unexpectedly diagnosed with dementia without a formal request to do so, or when a patient appears to be unable to decide on his/her own treatment. Professionals believed that more evidence is needed on geriatric outcomes after initiating kidney replacement therapy.

> *"There is a scientific gap on the course of physical functioning and the course of cognition after start of dialysis therapy in older patients. It has not yet been well-researched. So yes, you cannot inform patients properly either." (Nephrologist, woman 30-35 years)*

Barriers and facilitators for implementation of geriatric assessment in routine care

Barriers:

Lack of communication about goals and interpretation of tests

A clear explanation of the NGA' purpose and outcomes is important for patients. To some the tests were unexpected and they felt unprepared whilst other patients recognised benefits of being unprepared.

> *"Undoubtedly there may be good reasons to confront patients unexpectedly with a test, but I know my father experienced it as being somewhat unpleasant." (Daughter of male 80-85 years pre-dialysis patient)*

Furthermore, patients mentioned that they did value discussing personal NGA-results and implications, but that in some hospitals feedback on NGA-results was lacking. Shortcomings in communication about the purpose of NGA in routine care were acknowledged by some

professionals. Possible explanations were mentioned, including a sensitive topic and attempts not to worry patients beforehand.

Burden for patients

Professionals mentioned that a multi-hour extensive set was more burdensome for frail patients and patients on dialysis, and that in some cases the expected burden was a reason to refrain from testing. A few patients described their tiredness after doing tests for hours. Extra hospital visits were also mentioned by patients as a barrier, especially for those who depend on family for transportation.

Masked illiteracy

Professionals warned that masked illiteracy may affect interpretation of test-results of patients with a low education level or a non-Dutch background.

Lack of time and budget

Most professionals mentioned that a lack of time was a barrier for implementation of routine NGA. Sufficient time – in duration and consult frequency – is needed to get to know patients and their preferences, and to collect and provide sufficient information for a treatment decision.

In relation to time, professionals perceived limited budget as a barrier, despite that some believed that NGA would potentially save future dialysis treatment costs.

> *"Apart from better patient-centred care, it will be more cost effective in my view. When a CGA is performed, you are better informed on the patient's choice, and this could result in a less expensive treatment choice." (Nephrologist-geriatrician, woman 40-45 years)*

Resistance to involve geriatrics

Both geriatricians and nephrologists reported that nephrologists may feel resistance to consult a geriatrician, partly due to nephrologists' lack of knowledge on added value of geriatric care.

> *"I think that part of the problem is due to the feeling of having to hand over one's position as leading physician, this feeling that one is not capable of doing this oneself. Perhaps it was more a question of not knowing exactly what the added value of the geriatrician could be." (Geriatrician, woman 25-30 years)*

Loss of knowledge

Professionals reported that, due to a high turnover of young doctors and other team changes, teams often face a loss of knowledge about geriatric nephrology, hindering general awareness for geriatric problems.

Facilitators:

Conducting geriatric assessment: trained nurses and home visits

Professionals reported positive experiences when tests were conducted by a trained (specialized) nurse (practitioner) from either the geriatrics or the nephrology department. Additional tests were often conducted by a dietician, social worker or occupational therapist.

Professionals believed they played an important role in providing valuable insights into the patients' situation, for example by conducting home visits.

> *"You see a lot during a home visit, for example: you observe the interaction between husband and wife, and between parents and concerned children. When standing at the door, you can already estimate how long you will have to wait. Do you get a cup of coffee or is someone actually up to nothing? These are very subtle signs and observations."*
> *(Social worker, woman 60-65 years)*

Multidisciplinary cooperation: involvement of geriatrics

Cooperation between geriatric- and nephrology departments is indispensable to complete non-somatic aspects of frail patients and to support treatment (decisions). Nephrologists experienced the involvement of a geriatrician as supportive in interpreting results, for example: patients had a 'second opinion'. Most patients confirmed a positive experience with geriatric consultation referring to the given extra attention and additional information.

> *"I had a nice conversation with the geriatrician: I was able to discuss my personal experience, real experiences! And I got a lot of information." (Woman 70-75 years, pre-dialysis phase)*

> *".. at an earlier stage, doubts [about suitability for RRT] have been discussed. That's just extra support [..] it is a way to share the burden with the geriatrician. It [geriatric impairment] has been objectively tested and that's the reality. You can then build on that."*
> *(Nephrologist, woman 60-65 years)*

Professionals emphasized that not all older patients need to be referred to a geriatrician and suggested that the NGA could particularly be used to identify patients with (pre)ESKD who may benefit from a geriatric consultation.

Multidisciplinary team meetings and reports

Professionals considered a regular multi-disciplinary team meeting (MDTM) of utmost importance to discuss NGA-results and to formulate treatment options.

> *"[In a multi-disciplinary team meeting] you can explain how the assessment went, what was striking in conjunction with the numerical results. Sharing this [test-results and striking observations] will give us a better picture, I think." (Nephrologist, man 45-50 years)*

> *"Otherwise, there is a risk that the fragmentation of knowledge will not be brought together into a decision at the multidisciplinary team meeting. Therefore it is very important to have a distinct format with all the aspects of NGA included, and to schedule the discussion of new patients' test-results and observations." (Geriatrician, woman 35-40 years)*

Meeting-reports provide useful information for all (future) therapists and general practitioners, and electronic patient records have the potential to facilitate efficient information gathering. However, logistic difficulties were perceived to incorporate all disciplines in the MDTM.

Care planning

Professionals reported that care planning could be facilitated by a prolonged first consultation, and combining appointments at multiple disciplines in one hospital visit, immediately followed by a MDTM. Yet, it may be challenging to schedule all appointments in one day.

Forerunner and management support

To facilitate multidisciplinary cooperation, professionals reported that it is important to have good informal contact between all disciplines, management support and an enthusiastic forerunner.

Desired characteristics of a suitable nephrology-tailored geriatric assessment

Patients and professionals described desired characteristics of a NGA suitable for use in practice, relating to the scope and use of test and timing of assessment. Besides, proper execution of tests should include good legibility (reported by patients to lack in instances), and take into account illiterateness and patients' different cultural backgrounds (mentioned by professionals). No remarkable disparities were observed in assessment preferences for patient groups different in age, gender and educational status.

Scope and use of tests

Both patients and professionals stressed the importance to explore beyond the somatic domain, including health-related quality of life, cognitive and social functioning, and other domains such as nutritional status, fall-risk, medication, co-morbidity, mood, home situation and -care, educational level, pain score, life goals and spirituality. Additionally, many professionals indicated that collecting information from caregivers or family members (hetero-anamneses) provides very valuable information.

There was a large variability in how different tests were experienced by patients. For example: mathematics tests were less favoured by patients and sometimes experienced as challenging, whereas others associated them with enjoyable brain games. Professionals favoured specific tests because of familiarity and scientific reasons. For example, among cognitive tests, most professionals agreed that the Montreal Cognitive Assessment (MOCA) was, compared to the Mini-Mental State Examination (MMSE), more appropriate for CKD patients as it would unveil vascular risk. Also, the Stroop Colour and Word Test (i.e. neuropsychological test assessing the ability to inhibit cognitive interference) received little support from professionals. In contrast, clock drawing was considered simple and informative according to most professionals. Patients mentioned recognition of a recurrent Visual Association Test as 'funny', and emphasised the need to avoid repetition of tests within and between hospitals.

Timing of assessment

To patients ideal testing duration differed from 30 min up to 3 h. The more time the better, applied to some patients. Other patients said they were more concentrated in the morning and preferred to combine appointments for testing with a routine doctor's consultation. Professionals indicated that it would take between 45 and 90 min to conduct a proper NGA and assess all domains, if necessary divided over disciplines. In addition, several professionals

believed that follow-up conversation with the patient to discuss test-results was most important.

> *"In my personal opinion, I still think the conversation with the patient matters the most, by far. Usually I'm just not so much into clinimetry but in the long run I do think it is good to have numbers for future comparisons, especially when other doctors become involved." (Geriatrician, woman 35-40 years)*

Regarding frequency of assessment, most patients said that conducting an NGA once or twice per year is doable. However, opinions varied as some patients would like to take tests frequently while others disagreed. Follow-up measurements were perceived useful by patients to provide insights in decline. But, patients also emphasized that too much repetition of tests within but also between hospitals needs to be avoided.

> *"Yes, I do have a bad memory, but I remember the tests. Because in another hospital the same tests were conducted again. Then I thought: Well, they use the same things. [..] and makes it hilarious really, I'm sorry to have to say." (Woman 81 years, on haemodialysis).*

DISCUSSION

In this qualitative study, we elicited perspectives about and experiences with hospital-based geriatric assessment in (pre)ESKD patients, by conducting focus group discussions with patients, caregivers and healthcare professionals. We also identified benefits, facilitators and barriers for implementation into routine nephrological care. Although the need for geriatric appraisal for patients approaching ESKD in the hospital setting is widely recognised in guidelines[7,8] and research,[9,17,23] the lack of routine assessment practices discloses the need for understanding barriers and preferences of geriatric assessment practices. Our study is the first to explore these important questions using focus group discussions with both patients and professionals.

Our findings show that both patients and healthcare professionals have predominantly positive attitudes about use of a NGA in clinical care of older (pre)ESKD patients. Information provided by NGA creates the much-needed awareness[4] of cognitive and social problems among the whole treatment team, hereby shifting their focus from mainly somatic problems to multidimensional issues. Consistent with previous qualitative studies,[14,16] professionals reported being unaware of deficits in geriatric domains in some patients and that NGA often revealed unidentified cognitive impairments. Nephrologists considered cognitive impairments most important in deciding if a patient is eligible for dialysis.[24] The pivotal role of geriatric assessment in treatment plans and decisions has been reported in oncology.[11,14,25] Correspondingly, our study illustrates that discussing NGA-results starts a dialogue about suitability of treatment options between patient and professionals. As a result, patients were able to share more of their fears and concerns. Consistent with a previous study,[16] patients reported to highly appreciate the extra time spent on NGA and the attention for impact of CKD on daily functioning. Together with caregivers, patients recognised the benefits of (recurrent) NGA. Outcomes of NGA could enable patients and professionals to assess where supportive interventions may be beneficial. Hence, good multidisciplinary cooperation between nephrology,

geriatrics and supportive disciplines is of the utmost importance.[26] Our study illustrates that geriatricians have a complementary function to nephrologists, with the latter knowing the patient and the disease, and the geriatrician having valuable expertise on clinical judgement of frailty and appropriate interventions for older patients.

Despite a growing awareness of the need for geriatric screening among older patients approaching kidney failure,[17,23,24] implementing NGA in standard care, as recommended in nephrology guidelines,[7,8] remains complicated [9]. Difficulties may relate to lack of a widely-used and trusted test-sets and to implementation hitches. Our study identified several barriers and facilitators for successful implementation of geriatric assessment into routine care. First and foremost, clear communication about the purpose and interpretations of NGA-results with patients is essential. Barriers for interpretation of NGA-results include legibility and masked illiteracy. Since assessment is more burdensome for frail patients,[9,16] an individual approach is recommended. This requires allocated time to perform tests, to interpret test-results and to cautiously present results without overwhelming ill and worried patients.[27] Insufficient time was mentioned as important barrier in our and previous studies.[16,26,28] Our findings suggest that between 45 min and 1,5 h is needed, and should be feasible to accomplish a complete picture.

Second, for selecting the right test set, although a full CGA remains the gold standard approach,[29] our study confirms that adaptation of CGA into a smaller set is necessary and feasible to reduce both provider and patients' burden.[9] Our study provides some arguments in favour of using specific instruments in nephrology (e.g. Montreal Cognitive Assessment) but there was no outspoken preference for a particular set. Our participants agreed that caregivers provide important information on the patients' geriatric domains facilitating to provide additional insights in the patients' situation.[14]

Third, barriers for successful interdepartmental cooperation[26,30] were identified, including: limited availability of geriatricians,[9] sparse knowledge and use of geriatric tools among nephrologists,[9] and a tension among nephrologists to lose their span of control. Hall et al.[14] have previously described two models of conducting NGA: by a geriatric-trained and experienced nephrologist/nurse practitioner, or by partnership between geriatric medicine and nephrology. Our study supported their findings that both models may work, if tests are conducted by trained and experienced professionals.

Fourth, our findings also highlight the importance of a multidisciplinary team meeting. In oncology, MDTMs led to significant changes in diagnostic findings and altered management plans for more than 10% of cancer patients, including increased likelihood of appropriate staging.[31] More general, (multidisciplinary) geriatric evaluation has led to a primarily less intensive treatment plan in a third of oncology patients, recommendations of non-oncologic interventions in 72% of the patients,[11] and, although evidence is sparse, suggests an improvement in clinical outcomes.[11,31] Finally, sufficient management support and budget was found vital to facilitate resources and to actively support clinicians to efficiently report findings.[32,33]

Strength of our study included the purposive sampling of patients and professionals across (multiple hospitals linked to) three different initiatives performing geriatric assessment in nephrology care. Although one might argue that the experiences with the different practices may have had an impact on our results, it was not our aim to compare the

perspectives between the three practices. We rather focussed on the overall perspectives about geriatric assessment among patients approaching ESKD, towards our ultimate goal to develop a generic routine geriatric assessment. Any striking differences between practices were highlighted throughout the results. However, our findings should be interpreted in the light of known limitations related to generalizability and potential for bias. Patients who gave informed consent may potentially be relatively healthier and have a more positive attitude towards their healthcare and NGA. Moreover, patients who lack decisional capacity were not included. Recall bias might have been an issue for some patients since time had passed since they underwent the assessment. A final limitation is research reflectivity: although the whole research team with different backgrounds have judged the results, we cannot rule out that interpretation of the data is coloured by theoretical preconceptions and a pre-set aim and involvement (except for YM) to implement NGA in routine care.

Further quantitative research is needed on the clinical- and cost-effectiveness[10] of NGA, and the beneficial effects on treatment decision making and supportive interventions, as well as on the feasibility and acceptability of implementation of NGA in routine care.[32] This may give insight into how new diagnoses of cognitive defects and frailty lead to changes in treatment plans and avoidance of hospitalization, and on the necessity of test repetition. Furthermore, consensus on a tool set and long-term systematic collection of data may enhance clinical- and research comparability, enabling individual predictions in disease progression. We hope that our lessons and recommendation described (please also see Table 3) help to successfully integrate NGA into regular clinical care.

Table 3: Lessons learned and considerations for NGA implementing into routine clinical practice

Patients' involvement and potential benefits
• Clear communication of goals and outcomes (and interpretation) of tests • Consider the burden for patients individually, pay attention to results that might be confrontational • Spending 45 – 90 minutes in total to complete the NGA is acceptable and feasible • Repeated measurements to assess progression and to identify the need for additional supportive interventions • Caregivers can provide important information about patients' situation at home
Selecting the right test set
• Legibility and masked illiteracy can be important barriers • Adaptation of CGA into a smaller set for nephrology (NGA) is possible and feasible • Different instruments are suitable for usage in routine clinical practice, as long as all geriatric domains (i.e. somatic, social, functional and cognitive) are covered • Uniform implementation of NGA is necessary in response to the need for scientific evidence of geriatric measures on outcomes to predict individual progress of the disease.
Sufficient expertise and multidisciplinary cooperation
• Collaboration between nephrology and geriatrics departments is of utmost importance to provide complementary patient care • Multidisciplinary team meetings are key to success • Assessment of geriatric domains can be done by either the nephrology and geriatrics department, once professionals are trained and experienced • Barriers for successful cooperation between the geriatric and nephrology department include: apprehension among nephrologists about loss of span of control, sparse knowledge and use of geriatric tools, and a high turnover of doctors
Supporting structures
• Sufficient management support providing essential resources (e.g. time and money) for innovations • Securing the appropriate workforce, especially the availability of geriatricians • Value of NGA should be proven, resulting in evidence and directive guidelines

CONCLUSIONS

In conclusion, we observed that both patients and professionals experienced a great potential for hospital-based standardized geriatric assessment to improve (pre)ESKD patient care and clinical outcomes by identifying, discussing and targeting multidimensional problems. Implementation into routine care seems promising and achievable, once barriers and facilitators are recognized, but future studies are needed to investigate the effects of implementing geriatric assessment.

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SUPPLEMENTARY FILES

Item S1: Semi-structured interview topic guide.

Semi-structured interview topic guide (questionnaire) developed for this research and used in the focus group discussions.

Welcome (purpose and procedure of focus group discussion, confidentiality, introducing)

1 **How does care differ for patients approaching ESKD above 65 years of age, compared to patients of a younger age?**
   Probe for aspects missing in pre-ESKD care of older patients.
2 **What does a patient [and professional] need in order to enhance the treatment decision making process?**
   Write down a number of points, please explain.
3 **How did you experience doing the geriatric tests [from patient and professional perspective]?**
   Probe for: factors of patient-impact and feasibility (frequency, setting, caretakers, way of assessing, specific tests), psychological experience or burden
4 **To what extent do you think geriatric care (i.e. geriatric tests, consultation and advice of geriatrician) contributed to the regular nephrology care?**
   Probe for: collaboration between nephrology and geriatric department, contact with the geriatrician, impact of the tests, including effect on renal replacement therapy (RRT) choice.
5 **Which factors play an important role for older patients in pre-ESKD care and decision making for RRT?**
   Probe for: factors in geriatric domains (social, psychological, somatically, functional), role of partner and family, other influences and crucial aspects in decision making.
6 **To what extent did the results of the geriatric assessment influence treatment choice (RRT) [from a patient and professional view]?**
   Probe for: experience with specific tests
7 **Which barriers would you expect if a geriatric assessment is introduced in routine care of older patients with pre-ESKD? Which facilitators could you foresee?** Please write down three main barriers and three main facilitators.
   Probe for: general aspects (psychological, social, organizational barriers and facilitators) and specific aspects (intrinsic/extrinsic psychological barriers and facilitators)
8 **If you had the chance to design your own program to screen older patients with ESKD, which tests would you definitely include?**
   Probe for: reasons for specific preferences, practical issues, patient-related factors, what is needed for successful implementation.
9 **Did you miss a topic in this conversation on nephro-geriatric care? Is there anything you would like to add?**

Questions were asked to both patients and professionals, with minor adjustments in form of address for the group of interest. Parts between squared brackets were only used in the interview protocol for professionals. The interview guide was not pilot tested but minor changes were conducted after each focus group.

Item S2: Additional illustrative quotations.

Additional illustrative quotations by theme and subtheme.

Theme 1: Characterisations of the older ESKD patient group

"What I often hear from older people, is that – when becoming older – they have to deal much more frequently with bereavement. Relatives they have lost and the inherent loneliness which follows." (Social worker, woman 30-33 years)

"In my view, older patients are often more settled in life. The older patients over 70 years of age who visit us are sometimes fitter compared to the 40-50 year old's who have all kinds of cardio-vascular problems and diabetes. [..] I find it difficult to generalize and to put a label on all older patients, since it depends very much on each individual" (Nephrologist, man 45-50 years)

"Some nephrology patients we know for over 10 years [..] and some of them are fit. But I think that, particularly in the field of cognition, we do not look close enough."
(Nephrologist, woman 30-35 years)

Theme 2: Experiences of use of a geriatric assessment

Experiences

"I am very positive about the tests, because I want to know about my situation. When you get tested, you know where you stand. I like that. It's nice when they ask me as many questions as possible about things that I can still do." (Man 85-90 years in pre-dialysis phase)

"If your test-results are positive, it gives you a boost." (Woman 70-75 years transplanted)

"Yes, it gives you courage. Yes, it is really encouraging."
(Woman 75-80 years, on haemodialysis; in response)

Benefits

"Geriatricians are especially good at interpreting the CGA results of comprehensive geriatric assessment [especially the comprehensive aspect of the assessment] and generating a treatment plan to ensure that dialysis goes as well as possible"
(Geriatrician, woman, 45-50 years)

Concerns

"The thing I find difficult [..] is when patients themselves do not make the medical request because of memory problems, but when I myself suspect dementia. So it is not the reason for their visit, not their own requisition. That's sometimes a difficult dilemma, what do you do in that case?" (Geriatrician, man 45-50 years)

Theme 3: Potential barriers and facilitators to implementation of geriatric assessment

Barrier: communication on goals and interpretation of tests

"People are very sensitive if, based on their age or functional impairments alone, they are discounted up front and feel unworthy." (Social worker, woman 60-65 years)

Barrier: burden for patients

"Most patients [on dialysis] do not want to continue [geriatric assessment] anymore. They think it is a hassle and they really say it is too burdensome. They really do not want to stay at the dialysis department for a minute longer than the dialysis itself."
(Dialysis nurse, woman 40-45 years)

"So, you must take into consideration that it should not become an extensive test battery, that is too time consuming and therefore unsuitable in the outpatient clinic."
(Nephrologist, woman 35-40 years)

Barrier: masked illiteracy

"I sometimes wonder whether we should screen for illiteracy, since this is a neglected problem." (Nephrologist-geriatrician, woman 40-45 years)

"Yes, patients are very well able to mask that…[illiteracy]." (Dialysis nurse, woman 40-45 years)

"They are well able to partake in discussions, so you overestimate them and the information you provide – and think you deliver well – just isn`t comprehended."
(Nephrologist-geriatrician, woman 40-45 years; again)

Barrier: Resistance to involve geriatrics

"There is probably also some tension – at least that is what I notice in my hospital – between the specialists internal medicine and geriatricians. That they would prefer to keep those geriatricians out." (Nephrologist, woman 35-40 years)

Barrier: loss of knowledge

"I see one other obstacle [..] that has to do with knowledge and transferability of information. Frequently, fellows [nephrologists in training] perform the consultations, however we [nephrologists] may fail to properly inform them about the procedures and protocols involving these [older] patients. Consequently, the fellows will do it in their own way. So I think that is a learning point for us." (Nurse practitioner, woman 50-55 years)

Facilitator: Care planning

"In our practice, patients 70 years and older are triaged into our nephrology-geriatric care pathway and therefore receive more consultation time. [..] One hour is allocated for first consultations with patients 70 year of age or older, and routine visits are allocated half an hour."
(Nurse practitioner, woman 50-55 years)

Theme 4: Desired characteristics of a suitable nephrology-tailored geriatric assessment

"For me as often as possible. So at every visit. I think that is fine."
(Man 75-80 years pre-dialysis phase)

"I would find it terrible to have to do a repeat of the tests: an inspection every year."
(Woman 80-85 years on haemodialysis)



chapter 5

Nephrology-tailored geriatric assessment as decision-making tool in kidney failure.

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Journal of Renal Care 2024;50(2):112-27.

ABSTRACT

Background: Dialysis might not benefit all older patients with kidney failure, particularly those with multimorbid conditions and frailty. Patients' and healthcare professionals' awareness of the presence of geriatric impairments could improve outcomes by tailoring treatment plans and decisions for individual patients.

Objective: We aimed to explore the perspectives of patients and healthcare professionals on nephrology-tailored geriatric assessment to fuel decision-making for treatment choices in older patients with kidney failure.

Design: In an exploratory qualitative study using focus groups, participants discussed perspectives on the use and value of nephrology-tailored geriatric assessment for the decision-making process to start or forego dialysis.

Participants and Measurements: Patients (n = 18) with kidney failure, caregivers (n = 4), and professionals (n = 25) were purposively sampled from 10 hospitals. Interviews were audio-recorded, transcribed verbatim and inductively analysed using thematic analysis. Results: Three main themes emerged that supported or impeded decision-making in kidney failure: (1) patient psycho-social situation; (2) patient-related factors on modality choice; (3) organisation of healthcare. Patients reported feeling vulnerable due to multiple chronic conditions, old age, experienced losses in life and their willingness to trade longevity for quality of life. Professionals recognised the added value of nephrology-tailored geriatric assessment in three major themes: (i) facilitating continual holistic assessment, (ii) filling the knowledge gap, and (iii) uncovering important patient characteristics.

Conclusions: nephrology-tailored geriatric assessment was perceived as a valuable tool to identify geriatric impairments in older patients with kidney failure. Integration

INTRODUCTION

Dialysis is an extremely burdensome therapy that considerably impacts patients' lives. Older patients with chronic kidney disease (CKD) stage G4-G5, eGFR <20 mL/min/1.73 m^2 with multiple chronic conditions are particularly at risk for cognitive and functional decline which leads to a high risk of mortality and poor quality of life (QOL).[1-3] Within this group, it remains unclear who might benefit from dialysis and for whom conservative care can be an acceptable alternative.[4] In addition, there is a high incidence of withdrawal from dialysis in this older group.[5-8]

Literature review

Decision-making about kidney replacement therapy (KRT) in older patients with CKD stage G4-G5 is highly complex because of multiple health issues such as multimorbidity, increased mortality, loss of functional status, cognitive impairment and diminished QOL. Discussions about KRT can be very stressful and nephrology multidisciplinary teams are tasked with helping patients decide which treatment fits an individual's preferences and goals alongside weighing the benefits against the burdens of KRT.[9]

Fundamental to the decision-making process is collaboration between all those involved and provision of trustworthy information about all options whereby personal circumstances, concerns and contexts of patients and their families are taken into account.[10-11]

Multidisciplinary assessment of older people with CKD stage G4-G5 is recommended in guidelines.[12] This recommendation includes assessing frailty, cognitive function, comorbidities, nutritional, psycho-social and physical function domains. These domains are all part of comprehensive geriatric assessment (CGA), the quintessence of geriatric medicine and governed by a geriatrician[13] (for details about CGA, see Figure 1). However, full CGA is time-consuming and challenging to implement into routine care of older patients with CKD stage G4-G5 as it takes about 2 h, the involvement of a geriatrician and an integrated treatment plan.[14] So new initiatives have emerged to screen outpatients for impairments in all domains without involvement of Geriatric Medicine.[14] In nephrology, several initiatives reported on using a modified (nephrology-tailored) geriatric assessment (NGA) (for details about NGA, see Figure 2).[15-20] Such a modified assessment could help to recognise patient-led and patient-driven goals, identify patients who would benefit from referral to a geriatrician for full CGA and contribute to a complete holistic patient portrayal. Yet it is unknown if and how these geriatric assessments facilitate decision- making about choices for KRT.

Previous qualitative studies have revealed perspectives of older patients with CKD stage G4-G5 about treatment choices[21-25] and professionals perspectives on factors influencing decision-making.[17] To our knowledge, patients' and professionals' perspectives on how NGA can play a role in decision-making about KRT have not yet been studied.

The aim of the present study was first to describe patients' and professionals' perspectives on decision-making about KRT in older patients with kidney failure while using NGA. Second, to identify factors which support or impede decision-making and thirdly to explore the experienced added value of NGA in decision-making. Such in-depth knowledge could improve decision-making for older patients with CKD stage G4-G5 and benefit potential future implementation of NGA.

Domain	Sub domain	Instrument used for CGA
Functional	Functional status Mobility	ADL; iADL Gait speed ;Handgrip strength; Timed up and go; Falls
Cognitive	Cognition Neuropsychological assessment	MMSE; MOCA;Clock drawing 15- WVLT; Stroop Colour Word Test; Trail making test (A&B); VAT; LDST
Psychological	Mood	GDS
Somatic	Comorbidity Frailty Nutritional status Polypharmacy	Charlson Comorbidity Index; CIRS-G Fried frailty indicator; Canadian clinical frailty scale SGA or SNAQ
Social	Caregiver burden	EDIZ-plus
Other	Quality of life	RAND-36; EQ-5D; Cantril's ladder; Pain score, Anxiety score

Figure 1: Comprehensive geriatric assessment (CGA). An Illustration of core elements of CGA carried out by geriatrician and multidisciplinary geriatric team with examples of assessments which may be used.
Abbreviations: 15-WVLT, 15-word verbal learning test, immediate and delayed; ADL, activities of daily living; CIRS-G, cumulative illness rating scale for geriatrics; EDIZ, 'Ervaren Druk door Informele Zorg' selfperceived burden from informal care; EQ-5D, EuroQol Instrument; GDS, 15-item geriatric depression scale; iADL, instrumental activities of daily living; LDST, letter digit substitution test; MMSE, mini mental state examination; MOCA, Montreal cognitive assessment; RAND-36, the RAND36-item health survey 1.0; SGA, subjective global assessment; SNAQ, short nutritional assessment questionnaire; VAT, visual association test.

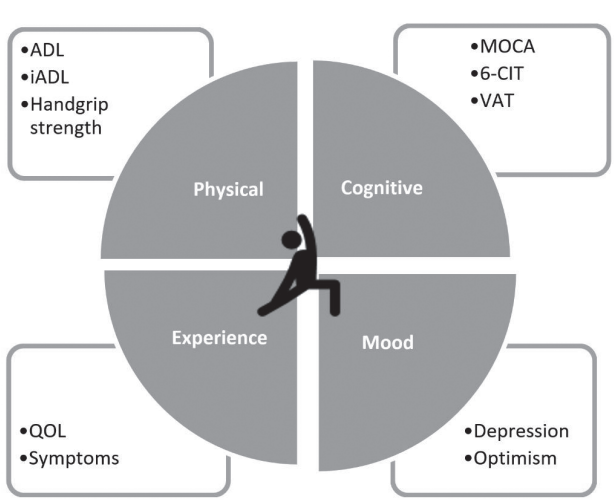


Figure 2: Nephrology-tailored geriatric assessment (NGA). An illustration of a NGA with examples of assessments which may be used.
Abbreviations: 6-CIT, six-item cognitive impairment test; ADL, activities of daily living; DSI, dialysis symptom index; GDS, 15-item geriatric depression scale; iADL, instrumental activities of daily living; MNA, mini nutritional assessment; MOCA, Montreal cognitive Assessment; QOL, quality of life, usingSF-12: The Short Form (12) health survey. Nutritional assessment; SGA, subjective global assessment; VAT, visual association test.

METHODS

We performed an exploratory qualitative study approved by Medical Research Ethics Committee.[26] The study population covered healthcare professionals and older people with CKD stage G4- G5, who experienced geriatric assessment during (their) build-up to KRT decisions. We use the term 'geriatric' only when referring to the 'tool' or speciality of 'geriatrics'. To enable discussions and interaction between patients and caregivers and between professionals and to understand commonalities and differences in perspectives we conducted focus groups.[26]

Population and sampling

Patients were purposively sampled and eligible when exposed to NGA during their build-up to KRT decisions, aged ≥65 years, with CKD stage G4-G5 eGFR ≤20 mL/min/1.73 m2, or a recent kidney transplantation. Caregivers who usually accompanied a patient were also invited to join the focus groups. The sampling methods were described previously in Voorend et al.[26] In short, participants were approached from three different NGA initiatives.[16,27] All three practices used various geriatric measures in multiple domains (e.g., functional, cognitive, psycho-social, and somatic status) for study- or routine-care purposes. All initiatives included patients above 65 years of age with CKD stage G4-G5, (either eGFR <20 or <15 mL/min/1.73 m2). Patients were approached by their treating (study) physician and purposively sampled with different (future) choices of treatment modality that is, KRT or CKD G5 without KRT or CKD G1T-G5T after transplantation (maximum variation sampling). Professionals were recruited through a combination of purposive and snowball sampling related to these same initiatives. We aimed to include all multidisciplinary perspectives (i.e., nephrologists, geriatricians, nurse practitioners, dialysis nurses, social workers and dieticians) (see Table 1 for participant characteristics). The study's purpose, procedure and confidentiality was written in an information letter and sent to all potential participants, after which informed consent was given.

Relationship with participants

We ensured that none of the patients were being treated by the interviewer. The interviewer defined her role as researcher at the start of all interviews. Although the interviewer is an advocate of NGA the research team agreed that there were clear benefits to her conducting the interviews as opposed to a person with no experience with NGA.

Data collection (interview design and procedure)

A semi-structured interview topic guide was developed comprising questions from a brainstorming session between two experienced researchers in nephro-geriatric care and one in qualitative research (see Table 2). The topic guide was further informed by literature[1,3,18,28] and approved by a group of nephrologists and geriatricians with extensive experience in the field of older patients with CKD G4-G5. Guiding questions were designed to prompt views on:

1. Patients' and professionals' needs to enhance the treatment decision process.
2. Factors that play a role in decision-making for KRT.
3. Consequences of NGA on treatment choice and decision-making process (see Table 2).

Table 1. Participant characteristics

	Patients (N=18)	Caregivers (N=4)	Professionals (N=25)
Age in years, mean (range)	79 (67-88)	60 (51-76)	48 (29 – 61)
Sex, male	9 (50%)	0 (0%)	4 (16%)
Children, yes	17 (94%)		
Civil status			
married/living together with partner	10 (56%)		
widow/no partner	8 (45%)		
Living situation			
independent	12 (67%)		
independent with care facilities (e.g. care at home, alarm bell, or assistance in housework)	6 (33%)		
Education level			
Primary or secondary education	6 (34%)		
Secondary vocational education	5 (28%)		
Higher professional/university education	7 (39%)		
Treatment status			
Haemodialysis/peritoneal dialysis, n (months since start)	5 (2-21, mean 11.6)		
Transplantation, n (months since transplantation)	3 (4-32; mean 15.3)		
CKD stage 4/5 not on KRT, n	10		
Future choice (if in CKD stage 4/5, not on KRT),n			
Haemodialysis/peritoneal dialysis	3		
Transplantation	2		
Conservative kidney management	2		
Multiple modalities open or no decision made	3		
Time since last geriatric assessment, in months, median (range)	5.5 (0.6-14.3)		
Experience in care for 65+ CKD patients*, in years, median (range)			5.5 (0.5-28.3)
Profession			
Nephrologist			7 (28%)
Geriatrician			4 (16%)
Nephrologist/geriatrician			2 (8%)
Nurse practitioner			2 (8%)
Nurse (nephrology)			3 (12%)
Nurse (other)			2 (8%)
Social worker			4 (16%)
Dietician			1 (4%)
Academic hospital	13 (72%)	3 (75%)	15 (60%)
Regional hospital	5 (28%)	1 (25%)	10 (40%)

Note: For more details about the time since last geriatric assessment see Chapter 4.
Abbreviations: CKD, chronic kidney disease; KRT, kidney replacement therapy.
[a] The self-reported number of years professionals were involved in the care of patients with chronic kidney disease, particularly with patients CKD without KRT, or kidney failure with or without KRT.

The topic guide was further elaborated in an instruction manual that contained detailed information on objectives, planning, focus (for moderator and observer), introduction and different types of questions for example, key questions, transition questions etc. At three centres, two focus groups were held: one with patients and one with professionals. A female nurse practitioner (NB) with 40 years of experience in clinical nephrology and 7 years in geriatric nephrology was trained to conduct focus groups and led all discussions. The focus groups lasted for 2.5 h including a break. An observer was present and took notes. Finalising each focus group, the interviewer provided a summary of the conversation to the participants verifying their different views on the main topics. In addition, sociodemographic data (for patients: date of birth, gender, civil status, living situation, education level, treatment modality or future modality choice, the treating hospital; for healthcare professionals: date of birth, sex, profession, hospital of origin, years of experience in nephrology/geriatric care) was collected on the day of the focus groups.

Data analysis

All interviews were audio-recorded, transcribed verbatim and inductively analysed using thematic analysis.[29] Two authors coded separately (Noeleen C. Berkhout-Byrne and Carlijn G. N. Voorend) followed by a discussion of the themes. Additional checks on the consistency of the coding scheme was performed by two other authors (Marjolijn Van Buren and Yvette Meuleman) and inconsistencies were discussed and adjusted afterwards. Further analysis was done by the first author in close collaboration with the other authors. Throughout the entire analysis process the research team iteratively reviewed and critically discussed interpretations until they reached consensus. Data saturation was assessed at different stages of the analysis until agreement was reached (i.e., until no new information was obtained or new themes emerged).[30] Translation of selected illustrative quotes was performed by a native English speaker (Noeleen C. Berkhout- Byrne) using back-translation. No qualitative software package was used for coding transcripts. Coding books, memo's and analyses were documented digitally and all data was saved on a secure server at the leading centre. To describe patients' characteristics, descriptive statistics were computed using SPSS (IBM, version 25). Recommended guidelines and checklists (e.g., the Consolidated Criteria for Reporting Qualitative Studies) were used to conduct and report this study[31,32] (see extra information in Supplement 1. Methodology).

RESULTS

Six focus groups were carried out with in total 47 participants (7–9 participants per focus group), with a response rate for professionals 83%, for patients 85%. Reasons for nonparticipation included travel restrictions, not being available on the focus group date and personal reasons. Professionals (n = 25) related to three academic and seven regional hospitals represented all disciplines of the nephrogeriatric team. Three groups were held with patients (n = 22) and caregivers (n = 4) whereby five patients had started dialysis and three patients had received kidney transplantation. Baseline participant characteristics are listed in Table 1.

Table 2. Focus group topic guide

Following welcoming of participants, clarification of purpose and procedure including confidentiality of focus group discussion was given. Purpose of focus groups: There is a need of standardized tests and questionnaires which can support patients with CKD stage G4-G5 > 65 years and professionals in decision making process about kidney replacement therapy (KRT) in kidney failure

Type question	Question	Probe
Opening question	1.In what way should care differ for patients with kidney failure above 65 years of age, compared to patients of a younger age?	Probe for aspects missing in kidney failure care of older patients.
Transition question	2. What does a patient [and professional] need in order to enhance the treatment decision making process?	Probe for type of information & education needed, who is important in decision making process in kidney failure?
Central questions (3- 8) Experiences performing tests & questionnaires	3. How did you experience doing the geriatric tests [from patient and professional perspective]?	Probe for: Impact: confrontation with results, stress, worry, psychological experience or burden Feasibility: frequency, setting, caretakers, way of assessing, specific tests, setting (home or hospital), presence of family/caregiver; questionnaires digital/paper?
Added value to decision making process	**4.To what extent do you think geriatric care (i.e. geriatric tests, consultation and advice of geriatrician) contributed to the regular nephrology care?**	**Probe for: collaboration between nephrology and geriatric department, contact with the geriatrician, impact of the tests, including effect KRT choice.**
	5. Which factors play an important role for older patients in kidney failure care and decision making for KRT?	**Probe for: factors in geriatric domains (social, psychological, somatically, functional), role of partner and family, other influences and crucial aspects in decision making. Further line of inquiry: What is crucial in your decision? Give specific examples e.g. does your partner agree with your choice for PD?**
	6. To what extent did the results of the geriatric assessment influence treatment choice (KRT) [from a patient and professional view]?	**Probe for: experience with specific tests**
Potential barriers & facilitators	7. Which barriers would you expect if a geriatric assessment is introduced in routine care of older patients with kidney failure? Which facilitators could you foresee? Please write down three main barriers and three main facilitators.	Probe for: general aspects (psychological, social, organizational barriers and facilitators) and specific aspects (intrinsic/extrinsic psychological barriers and facilitators)
The ideal test battery	8. If you had the chance to design your own program to screen older patients with kidney failure, which tests would you definitely include?	Probe for: reasons for specific preferences, practical issues, patient-related factors, what is needed for successful implementation
Closing question	9. Did you miss a topic in this conversation on nephro-geriatric care? Is there anything you would like to add?	

Note: Interview questions relevant to decision-making about KRT are highlighted in bold.

Perspectives on factors which play an important role in decision-making about KRT options

We identified three main themes and 12 subthemes that play an important role in patients with CKD stage G4-G5 and could both support or impede decision-making about KRT. Figure 3 gives an overview of identified themes and subthemes. In addition to the illustrative quotations provided in the results below, Table 3 provides a selection of quotes from participants and explanations offered by the authors to illustrate each theme.

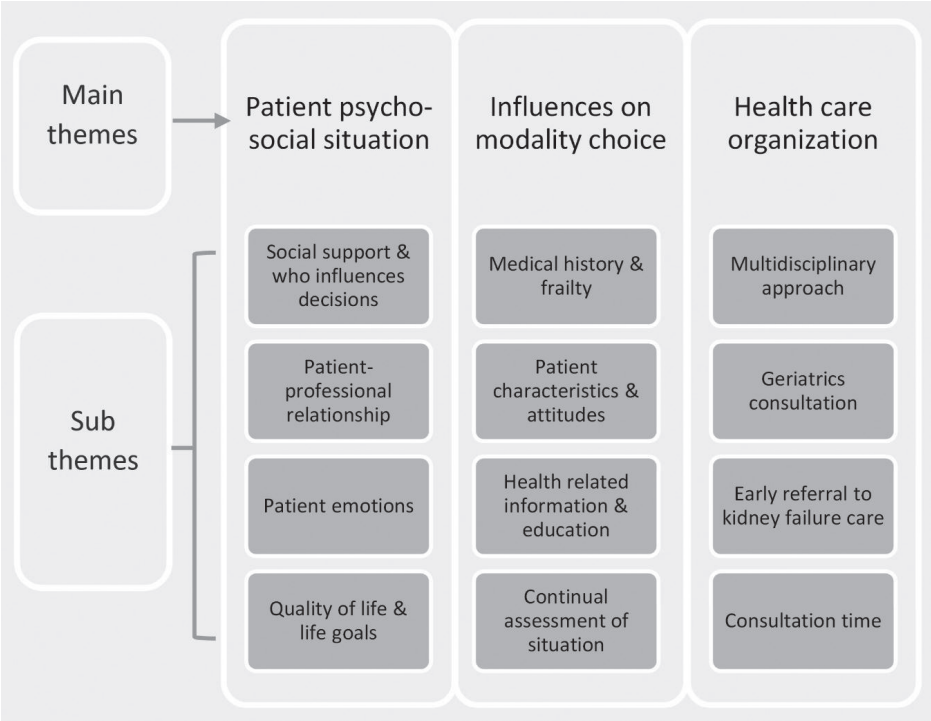


Figure 3: Supporting and impeding factors to decision-making in CKD G4-G5.

THEME 1. PATIENT PSYCHO-SOCIAL SITUATION

Under the main theme patient psycho-social situation four subthemes were identified, that is: social support and who influences decision- making; patient-professional relationships; patient emotions; QOL and life goals.

Social support and who influences decision-making

Patients and professionals recognised that a patient's social support system can act as a double-edged sword supporting or impeding KRT-modality choices. Civil status in conjunction with a patient's level of (in)dependence or caregiver support can influence modality decisions.

"Your children can influence your choice. I had a very passive attitude, I just didn't want to go on dialysis. But my children said 'no Mom, that [not going on dialysis] is not going to happen. You are going to go on dialysis' And I am very glad I did go on dialysis[…] I have three sons and they were in agreement with each other, they even came to the doctor with me. I am very happy and thankful." (Patient, 79 years)

Lack of support or too much interference from family can persuade patients towards certain decisions (Table 3). Both professionals and patients reported that family were often involved in decision-making and that some patients choose (the setting) to dialyze due to family pressure:

"I did discuss it [choice KRT] with my children. And they said: 'Mom please do not start dialysis at home, you are alone, -my husband died 2 years ago- If something happens in the middle of the night! Just go to the hospital'. They felt it would be a safer option." (Patient, 86 years)

Patient-professional's relationship

Across all groups, both patients and professionals reported the importance of having a trusting patient-professional relationship partnered by good guidance by the nephrologist, particularly for older patients, as a key supporting factor in decision-making.

"If people choose a conservative treatment and know that they may remain in the care of their trusted nephrologist then they are able to make this decision with more confidence." (nurse practitioner)

Patients stated that care for older patients differs from younger patients because older patients often live alone, have a shorter life expectancy which affects life goals and are more willing to trade longevity for QOL (Table 3). Patients reported feeling more vulnerable due to multiple chronic conditions, needing more time to process complex information about KRT and therefore greatly appreciate counselling and advice from trusted professionals other than support and advice from direct family and friends.

"I think it's very important that older people are given good guidance. Whatever you choose, that you are supported by your nephrologist and nurses." (Patient, 77 years)

Patient emotions

Patients reported feeling worried about their future on dialysis and the prospect of dialysis was even described as 'Damocles' sword'. A recurring concern of patients was their anxiety about existing in a debilitated state, being a burden to family and society and loss of independence:

"I hope that I can delay [KRT]as long as possible, whatever happens it mustn't go to the extreme, that one exists in a vegetative state." (Patient, 85years)

"I don't want to be resuscitated either. As long as I can take care of myself. But I don't want to be dependent on others." (Patient, 79 years)

"That [being dependent on others] would certainly be the limit for me too." (Patient, 79years)

Professionals described patient fear of failure in the NGA cognitive domain tests and patient anxiety about the possible impact cognitive impairment might have on options for KRT:

"I notice that when we discuss cognition and a patient, or partner tell me that there are problems and I suggest we do a MMSE, then I notice patients concern 'what happens if I don't perform well?'" (nurse practitioner)

QOL and life goals

Patients reported the importance of maintaining QOL juxtaposed with their concern about a diminishing QOL following the initiation of dialysis treatment. Patients recognised that growing old can mean functional impairment and loss of independence for some people and that this impacts choices and decisions about KRT. They questioned whether dialysis in very old individuals contributes in any positive way to QOL and longevity. A number of patients expressed that there are limits to an acceptable QOL (Table 3).

"[…] the younger you are the more likely you are inclined to accept treatment more so than when you are much older […] I did dialysis myself and it is an extremely burdensome treatment. So if when you are much older, you can function relatively normally and you can manage without dialysis I would consider this a better option. The question really is about whether dialysis in older age has any benefit to quality of life or lifespan." (Patient 73 years)

THEME 2. INFLUENCES ON MODALITY CHOICES

Under the main theme, influences on modality choice, the following four subthemes were identified: medical history and frailty; patient character and attitude; health-related information and education; continual holistic assessment of situation.

Medical history and frailty

Both patients and professionals described medical history and frailty, including cognitive functioning, as significant factors influencing decision-making about KRT. Patients reported that experiences with other illnesses and experienced losses in life, all play a role in one's attitude about KRT-decisions (Table 3). Many professionals reported that NGA has the potential to uncover individual frailty (somatic, cognitive, functional and psycho-social frailty) and can enhance a well-informed choice regarding KRT:

"Where is the focus of our attention with ≥ 70- year old's? As doctors we tend to concentrate on somatic aspects, patient vigour and medical history. We have too little time to explore things like cognition, quality of life, and expectations […] Perhaps we should do things differently." (nephrologist)

Patient character and attitude

Patients and professionals believed that a patient's character (i.e., optimistic or pessimistic view of life, ability to deal with life's challenges) determines an individual's attitude towards a specific modality and can support or impede decision-making:

"I have a very positive attitude to life. I have loving children and very loving grandchildren whom I see regularly. Therefore I wouldn't be inclined to say: 'I'll do nothing, leave me be'. So, if I have to go on dialysis I will do it, even though I'm fairly old." (Patient, 72 years)

Table 3. Additional selection of illustrative quotes.

Themes	Perspective	Relative to interview question & discussion	Quote
Main Theme 1. Patient psycho-social situation			
Sub theme: Social support & who influences decisions	Patient	Decisions about KRT were influenced by age alongside personal situations,	*For instance, if I don't want a new kidney or I don't want to dialyze. However, I do have responsibility towards my husband and if I`m younger, for my family. I believe, that is the crux, in the decision that you make.(patient, 79 years)*
	Patient	Assuming an active and participatory role rather than a passive role alongside the importance of making decisions independent of what others might think, was described by patients as an essential part in KRT decision making.	*However, in the end you have to make the decision yourself. You can get all the information and then you have to read it and think about it but in the end you must make the decision yourself. (patient, 71 years)*
Sub theme: Patient-professional relationship	Professional	An open and honest relationship between doctor and patient was described as essential in supporting patient decisions.	*If people choose a conservative treatment and know that they may remain in the care of their trusted nephrologist, then they are able to make this decision with more confidence. (nurse practitioner)*
Sub theme: Patient emotions	Professional	Professionals described patients fear of failure in the NGA cognitive domain tests and patients` anxiety about the possible impact cognitive impairment might have on options for KRT.	*When a patient, or partner tell me that there are memory problems and I suggest we do a MMSE, then I notice patients concern "what happens if I don't perform well". (nurse practitioner)*
Sub theme: QOL & life goals	Patient	Patients consider QOL versus longevity and expressed that there are limits to what an acceptable QOL is.	*Does dialysis, in very old age, have any additional value to quality of life? (patient, 72 years)* *If I see that my situation worsens, and I`m confined to bed, then life would have no purpose for me anymore. (patient, 79 years)*
Main theme 2. Influences on modality options			
Sub theme: Medical history & frailty	Patient	Patients reported that experiences with other illnesses and accumulated experiences, all play a role in ones attitude to decisions about KRT.	*I think your medical history and all of life`s losses, all counts up in your attitude towards future choices. (patient, 77 years)*
Main theme 3. Healthcare organization			
Sub theme: Early referral and consultation time	Professional	Early referral to kidney failure care, enough consultation time to facilitate NGA, interpret, discuss results and to enable patients to process and interpret information on KRT is important. It is conducive to building a trusting relationship with the nephrologist which lays the basis for open decision making discussions	*You need a lot of time and the discussion about whether to dialyze or not must begin in an earlier stage. Not as dialysis is fast approaching. When patients attend the kidney failure clinic for a longer period of time, have a good relationship with their nephrologist, then the atmosphere is conducive to discussions about KRT. (social worker)*

Note: Supporting and impeding factors to decision-making in older patients with CKD stage G4-G5.
Abbreviations: KRT, kidney replacement therapy; MMSE, mini mental state examination; NGA, nephrology-tailored geriatric assessment; QOL, quality of life.

Health-related information and education

Both patients and professionals believed that comprehensive information which is tailored to an individual's needs on all KRT options, including conservative care, is fundamental to decision- making. This could be supported by the opportunity to undergo a time trial, peer-to-peer discussions and a visit to a dialysis centre.

> *"I have no experience with hemodialysis, but I was offered the opportunity to visit the dialysis unit and talk to a patient on dialysis. He told me he was very, very tired with it all and he was only 50 years old! He said to me: 'if I were you I wouldn't start on it [dialysis]'." (Patient 77 years)*

Furthermore, professionals observed that information about KRT in conjunction with NGA creates awareness of a patient's possibilities but also of their limitations.

> *"We gain a better, more objective insight [NGA] which helps us to anticipate the treatment's impact. This information helps to make decisions about a less invasive therapy instead of dialysis which might offer no benefits to the patient." (nurse practitioner)*

Professionals believed in the importance of continually assessing a patient's need for information and checking whether the information was processed and understood. However, contrary to professionals, some patients reported that they received too much information and experienced it as being overloaded:

> *"I also got all the necessary information; you get one of those books. You can even keep a record in it. I thought it was a bit over the top!" (Patient, 79 years)*

Professionals agreed about the importance of unbiased information delivery. However, it was suggested that a nephrologists' personal preferences often tips the balance in favour of a treatment modality:

> *"Doctors who are motivated for peritoneal dialysis (PD) convince more patients to do PD. Yes, they tend to give a more positive picture. The patients are more inclined to think this is a suitable treatment." (nephrologist)*

Continual holistic assessment of the situation

Professionals reported the need for continual assessment of a patient's situation in all geriatric domains. A broader knowledge of all domains and not merely biomedical factors is deemed necessary for insight into the patient's condition and healthcare needs.

> *"[...] The work-up for kidney transplantation includes an evaluation by the cardiologist. If transplantation occurs only after three years, then re-evaluation must be performed. And of course you can understand that re-evaluation should also apply to NGA." (nephrologist)*

Early recognition of frailty has the potential to facilitate interventions which support a patient's needs (e.g., physiotherapy for balance training and muscle strengthening, case management in the home situation, home help etc.) (Table 4 provides a selection of quotes from participants about the added value of NGA).

"When we see patients with an eGFR below 20 ml/min then we ask ourselves 'is this person frail?' The next step is to determine what can we do about it? Is support from specialist care for older patients in general practice services available? Is extra home help available, or are tools needed to support living at home? In my experience, many people don't have a clue about the possibilities to improve their home situation." (social worker)

THEME 3. HEALTHCARE ORGANISATION

Under the main theme healthcare organisation, the following four subthemes were identified: multidisciplinary approach, geriatrician consultation, early referral and consultation time.

Multidisciplinary approach

Professionals recognised the importance of multidisciplinary care with regular meetings to discuss NGA results and their impact on KRT decisions. Furthermore, including other partners, such as a district nursing/care team, an occupational therapist together with the geriatrician and nephrology team, were mentioned as a supporting factor to decision-making for KRT. Professionals stated this wider collaboration as an added value in decision- making:

"I think it is very important to work in a multidisciplinary team. Together with the geriatrician, we can discuss which aspects of ageing play a role by a patient with kidney failure? (nurse practitioner)"

Geriatrician consultation

Most professionals considered a consultation with a geriatrician of additional value as a support to decision-making in kidney failure:

"I think it's very important to collaborate with the geriatrician [...] to discuss which aspects of ageing are playing a role in a particular patient. To be able to understand which problems are caused by ageing and not necessarily due to kidney failure because it does get mixed up." (nurse practitioner)

"Being a geriatrician, you think about the consequences of dialysis, even if there are limitations, about possible interventions and actions which can be taken to ensure dialysis goes as well as possible." (geriatrician)

Patients also reported their appreciation of a consultation with the geriatrician in particular, the time given to discuss their personal situation was valued.

"I had a nice chat with the geriatrician which included an exchange of very personal information. Real life experiences and also information gained." (Patient 71 years)

Discussing the options for KRT and the broader impact of such decisions with another doctor, other than the trusted nephrologist, enhanced patient involvement in decision-making and supported decisions about treatment choices:

"[...talking with the geriatrician] you become much more involved in your own personal situation. Also more involved about the decisions that have to be made about further treatments." (Patient 72 years)

Early referral and consultation time

Professionals expressed the importance of early referral to kidney failure care as a supporting factor to decision-making, preferably when eGFR is under 20 mL/min/1.73 m^2 with progression to kidney failure and when KRT is expected to be imminent within a year. One professional described the transition from CKD to kidney failure for patients as 'a pressure cooker moment' when postponed decisions must be finally addressed. Guidelines recommend referral to kidney failure care of at least 4 months. However, professionals stated that this time was far too short (Table 3). Patients are mostly referred when the eGFR has fallen below 20 mL/min/1.73 m^2 or even 15 mL/min/1.73 m^2, which acts as a barrier to effective decision-making when progression to kidney failure is rapid:

> *"When we have little time (in kidney failure care) then we see patients frequently with shorter intervals between visits so that we can be as efficient as possible. And that is often, for this patient group, very burdensome." (consultant geriatric nurse)*

Benefits of NGA in decision-making

The added value of NGA for decision-making was found in three major themes: (1) facilitating continual holistic assessment; (2) filling the knowledge gap, and (3) uncovering important patient characteristics. Figure 4 illustrates these three themes about the added value of NGA. Table 4 provides a selection of quotes from participants about the added value of NGA and explanations offered by the authors to illustrate each of these themes.

Overall, by performing NGA professionals believed that not only somatic frailty is unearthed but in-depth knowledge is obtained about a patient's social system and psychological wellbeing – information they consider vital for good quality decision-making about KRT.

Professionals noted that NGA performed before KRT decisions and repetition of NGA uncovers changes in geriatric domains and this can lead to a change in former KRT decisions.

> *"If it is your ambition to choose wisely [...] then you need to repeat NGA in the immediate time before the final choice is made. [...] because a CVA or other major event can have an enormous impact on a patients' functionality but, also in a patients priorities. If the reason for choosing dialysis was mainly for your partner and your partner has in the meantime passed away." (nephrologist)*

The benefits of NGA as a tool to support decision-making in KRT were recognised by some patients although less explicit. Caregivers reported that information about KRT in conjunction with NGA results creates awareness of one's possibilities but also of one's limitations which could benefit a nuanced KRT choice.

> *"We saw the tests that were done, alongside the information that was given, as very positive enabling you to make a better choice [. .]. If I had memory problems that could cause me to make mistakes, then [test results] could support me in making a more suitable choice or make a different decision."(caregiver, 60 years)*

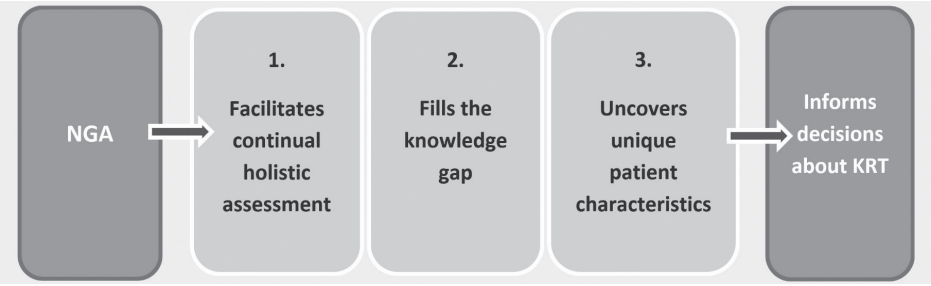


Figure 4: Added value of nephrology-tailored geriatric assessment in decision-making about KRT.

Table 4. Perspectives on the added value of NGA as an aid to decision making about KRT

Perspective	Added value NGA	Illustrative Quote
Theme 1. Facilitates continual holistic assessment		
Professional	NGA questionnaires offer the opportunity to open conversations on sensitive topics e.g. mapping mood and loneliness, information which informs decision making.	*What I really like is the frailty assessment tool because questions are posed about loneliness, mood etc. and as it is part of routine care you are able to ask without patients feeling ambushed. (nephrologist in training, 34 years)*
Theme 2. Fills the knowledge gap		
Professional	Consultation with a geriatrician after or as part of NGA helps identify frail patients and thus informs decisions about KRT.	*Yes, we have an unmet need. We realize that we are unable to identify those who would benefit or not with a kidney transplant. We sometimes reject patients who perhaps would have benefitted from kidney transplant, or accepted patients who in hindsight should have been rejected. […] and we are searching for a method to do this better. And of course you want to consult the expert in the organization and that is [in this case] the geriatrician. (nephrologist)*
Caregiver	Information about KRT in conjunction with NGA tests creates awareness of one's possibilities but also of one's limitations.	*We saw the tests that were done, alongside the information that was given, as very positive, enabling you to make a better choice [..]. If I had memory problems that could cause me to make mistakes, then [test-results] could support me in making a more suitable choice or make a different decision" (caregiver, 60 years)*
Patient	NGA also satisfies patients wish to know how they perform within their own unique situation and to recognized the benefits of NGA as a tool to be more involved in decision making about KRT.	*I think it is very interesting to see whether each year it [my condition] deteriorates or stabilizes as improvement is less expected at this age. (patient, 79 years)* *Due to the tests you gain more insight into your own situation and that stimulates more self-examination […] in this way the patient is more involved in his/her own situation and importantly, the decisions about further treatment. (patient, 71 years)*
Theme 3. Uncovers unique patient characteristics		
Patient	NGA uncovers important patient concerns about loneliness, being a burden to society and the limits to treatment, issues which should be addressed during decision making conversations about KRT.	*We grow old but the loneliness gets worse too and I think it's important to consider this as well. I mean should we continue to treat endlessly… the financial consequences…I mean who is going to pay the bill? (patient,72 years)*
Professional	NGA reveals more in-depth knowledge of an individual patients` character which can be a barrier to a certain modality choice.	*It depends enormously on the patient […]. There are patients who I would consider very suitable to a home dialysis therapy. But the patient has sleepless nights just thinking about a dialysis machine at home. Yes, and these patients choose for in-center dialysis. (nephrologist)*

Abbreviations: NGA, Nephrology-tailored Geriatric assessment; KRT, Kidney replacement therapy.

DISCUSSION

In this qualitative study, we uncovered perspectives about the added value of NGA in decision-making about KRT during focus groups with patients, caregivers and healthcare professionals. We elicited in-depth information about supporting and impeding factors to decision-making for KRT in older patients with kidney failure and identified three main themes: patient psycho-social situation, influencing factors on modality choice and healthcare organisation. Importantly, this is the first study which sheds light on patient, caregiver and professionals' perspectives on the added value of NGA as a tool in decision-making for KRT.

Professionals unanimously reported the benefits of NGA as a tool to identify geriatric impairments and how integration of its outcomes can inform decision-making for KRT, namely: it facilitates continual holistic assessment, it fills the knowledge gap – information that would otherwise remain unknown and it uncovers important patient characteristics. The advantages of geriatric assessment in decision-making has been reported in oncology,[33-36] and has been recommended by the American Heart Association.[37] However, geriatric assessment has not yet been implemented in routine kidney failure practices. By performing NGA a more complete picture of the patient is portrayed and medical, psycho-social, cognitive and functional frailty can be identified. Early detection of impairments such as frailty offers opportunities for interventions to improve outcomes and such improvement has been reported in other studies. [38-41] Furthermore, NGA may offer the opportunity to have open discussions on sensitive topics and this dialogue facilitates a more holistic approach, is conducive to good decision-making about KRT and to the development and management of personalised and coordinated care plans.

Drawbacks of NGA practices were mentioned by professionals and related to time constraints, potential labelling of patients based on NGA results, masked illiteracy affecting interpretation of tests and dilemmas around an unsought diagnosis of dementia.[26]

Patients had predominantly positive attitudes towards NGA, but compared to professionals, the purpose and role which NGA could play in decision-making about KRT was less clear. This discrepancy between perspectives of professionals and patients could be explained in two ways. First, in one initiative NGA had been performed following decision-making about KRT. Second, due to lack of communication about the reason for performing NGA may not have been explained in all hospitals. This underscores the importance of clear patient-professional communication throughout the CKD trajectory, consistent with findings from studies about patient dissatisfaction with information and involvement in decision-making about KRT.[42,43] Our study also showed that patients wished to know how they perform in their unique situation. It is plausible that being able to recognise their vulnerabilities before a decision about KRT will prepare and improve patients' engagement in discussions about the possible impact of future treatments in their daily lives. In a number of studies, patient involvement in decision-making was shown to be associated with improved satisfaction, QOL and treatment adherence.[44-48] Moreover, confirming other studies, we found that knowledge about cognitive or functional decline could potentially facilitate managing and tempering of unrealistic patient expectations about life on dialysis and in turn may limit regret about KRT decisions.[49-51]

Consistent with other studies, we found an overlap between patients' and professionals' perspectives about supporting and impeding factors for decision-making about KRT.[23,52] These included: a trusting relationship with the nephrologist, maintenance of QOL, comprehensive information and education, timely referral to kidney failure care and medical history, frailty and age. In addition, some perspectives were reported as bidirectional, for example, where the role of the family can endorse or embargo a patient's preferred treatment. Previous research corroborates our findings about the role of informal caregivers in decision-making.[23,53-57] Recognition of bidirectional aspects of specific perspectives may enhance awareness of the complexity of decision-making about KRT in older patients approaching kidney failure and underline the importance of tailoring discussions to suit each patient. Professionals considered early referral conducive to building a trusting relationship with the nephrologist and multidisciplinary team which lays the basis for open decision-making discussions.[58] Early referral offers more opportunities for interactions with professionals to help patients understand, process and discuss complex information and to weigh benefits and burdens of all options against patient's life goals, values and preferences which has been reported as an important and modifiable factor to aid decisions.[45,59]

The strength of our study was the novel insight into patients' and professionals' perspectives on the role of NGA in decision-making about KRT which is to our knowledge the first of its kind. Patients and professionals were purposively sampled from experienced multidisciplinary kidney failure nephrology teams, from multiple hospitals across The Netherlands using three different NGA practices at major university institutions.[26] This diversity yielded a kaleidoscope of perspectives from participants about NGA and its added value to decision-making about KRT and improved transferability of our findings.

Our findings should be interpreted in light of recognised limitations. First, in the patient focus groups, recall bias might have been an issue for some patients as time had passed since they underwent the assessment. This could mean that participants gave 'appropriate' answers rather than their perspective or remained silent in other discussions. For professionals, we expected this to be less of an issue as NGA was an ongoing procedure in their nephrology practice. Second, the selection of patients who gave informed consent may have been relatively healthy since non- motivated patients and those with physical and mental disabilities may have refused to participate or may not have been approached. Therefore, results might have been biased towards a more positive attitude on their healthcare and NGA, potentially affecting transferability. For this reason, we included patients with a broad range of perspectives using purposive sampling methods from three different practices. Third, although we strived to achieve a broad and varied research group, we cannot rule out that interpretation of the data may possibly be influenced by our experience, ideas and preconceptions.

Our study addresses the relevance of geriatric assessment in nephrology care. Clinicians should perform NGA and discuss results before decision-making for a better-informed decision process. Recently our groups have published a suggested test-set appropriate for use in outpatient nephrology.[20] Further research is required to gain insights into the feasibility and acceptability of implementation in routine care. Also, the prognostic capacity of NGA instruments and determinants of adverse outcomes requires further research.[60] Our study did not set out to discuss the shared decision-making (SDM) model as proposed by Elwyn

et al.[61] and later adapted by Elwyn and Vermunt.[62] However, we recognise that there is potential to incorporate the outcomes of NGA in the SDM model.

CONCLUSIONS

Both patients and professionals had positive attitudes towards NGA, describing it as a useful tool to identify geriatric impairments in older patients with kidney failure. Integration of NGA outcomes facilitates a more holistic approach to inform choices and decisions about KRT based on patient characteristics, values, expectations and goals.

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SUPPLEMENTARY FILE

Supplement Methodology

Data collection (Interview design and procedure)

Additional information not in the main text:

Following the welcoming of participants, clarification of purpose and procedure including confidentiality was given. The participants were encouraged to speak freely and discuss their shared opinions as well as differences. All questions were open-ended and the interviewer probed for understanding their experiences, opinions about treatment decisions and the NGA. An observer (CV) took notes of nonverbal communication and group dynamics. During the focus groups with patients, background information on geriatric assessment was given and afterwards feedback for the interviewer was provided by observers (KC, CV).

Data Analysis

Additional information not in the main text:

- The final interviews were checked for quality by (NB,CV). Content analysis was conducted with an integrated approach. Initial coding was done by (NB,CV) individually, followed by a discussion of main themes and the meaning of quotes, to confirm and agree on initial codes and themes.
- These discussions were positively impacted by the composition of the research team (nurse practitioner, health scientist, nephrologists, geriatrician and medical psychologist) and strengthened the process of analysis and theory building.
- Data are presented as mean with standard deviation (SD) for normally distributed continuous variables and as median with range for skewed continuous variables. Count (percentage) was used for categorical variables.



chapter 6

Design of a consensus-based geriatric assessment tailored for older chronic kidney disease patients: results of a pragmatic approach.

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European Geriatric Medicine (2021) 12:931–942

ABSTRACT

Purpose Unidentified cognitive decline and other geriatric impairments are prevalent in older patients with advanced chronic kidney disease (CKD). Despite guideline recommendation of geriatric evaluation, routine geriatric assessment is not common in these patients. While high burden of vascular disease and existing pre-dialysis care pathways mandate a tailored geriatric assessment, no consensus exists on which instruments are most suitable in this population to identify geriatric impairments. Therefore, the aim of this study was to propose a geriatric assessment, based on multidisciplinary consensus, to routinely identify major geriatric impairments in older people with advanced CKD.

Methods A pragmatic approach was chosen, which included focus groups, literature review, inventory of current practices, an expert consensus meeting, and pilot testing. In preparation of the consensus meeting, we composed a project team and an expert panel (n = 33), drafted selection criteria for the selection of instruments, and assessed potential instruments for the geriatric assessment.

Results Selection criteria related to general geriatric domains, clinical relevance, feasibility, and duration of the assessment. The consensus-assessment contains instruments in functional, cognitive, psychological, somatic, patient preferences, nutritional status, and social domains. Administration of (seven) patient questionnaires and (ten) professional-administered instruments, by nurse (practitioners), takes estimated 20 and 40 min, respectively. Results are discussed in a multidisciplinary meeting including at least nephrology and geriatric expertise, informing nephrology treatment decisions, and follow-up interventions among which comprehensive geriatric assessment.

Conclusion This first multidisciplinary consensus on nephrology-tailored geriatric assessment intent to benefit clinical care and enhance research comparability for older patients with advanced CKD.

INTRODUCTION

Functional and cognitive impairment, frailty, and depression are highly prevalent in patients with advanced chronic kidney disease (CKD stage G4-G5; estimated glomerular filtration rate [eGFR] ≤ 30 mL/min/1.73 m^2),[1-5] but are often unidentified.[6] These impairments are strongly associated with adverse health outcomes such as hospitalization and mortality,[5-7] and therefore relevant for risk stratification. Incorporating geriatric evaluation in routine nephrology care could better address older patients' needs[8-11] and is recommended in recently published guidelines.[12-13]

Nephrology-specific geriatric assessment could be meaningful, first because the geriatric phenotype is often severely impacted by vascular problems, such as vascular cognitive impairment,[14] which necessitates the use of instruments that are sensitive to these impairments. Second, due to the chronic nature of kidney diseases, nephrologists perceive to have a full geriatric picture of their patients' status, but without objective measurements, impairments may still be overlooked.[6] Third and most importantly, broader knowledge of these impairments is important for (future) decisions regarding treatment for these vulnerable patients, and determining goals of ongoing care. Existing pre-decision care pathways mandate a geriatric assessment tailored to the older advanced CKD population. Fourth, a compromise between a full comprehensive geriatric assessment (CGA) and a brief screening (i.e., a modified geriatric assessment) might be a feasible solution to overcome practical barriers of implementation.[8]

Comprehensive geriatric assessment (CGA), the cornerstone of geriatric medicine, has to conducted by a geriatrician and includes three elements; (i) thorough assessment of an older patient's physical, functional, cognitive, and social capabilities, uncovering otherwise unnoticed impairments and detection of frailty, (ii) development of an integrated treatment plan, and (iii) evaluation of the progression of impairments and accordingly adjustment of the plan. CGA has shown to enable therapy adjustments and estimation of outcomes such as patient's likelihood of living at home, limiting deterioration, and avoiding death.[15,16] Yet, this systematic interdisciplinary process is time-consuming and therefore impracticable to use routinely in older CKD patients. Contrarily, geriatric screening with brief questionnaires is conduced to assess frailty and potential need for geriatric referral. However, this approach has lacked discriminating abilities to adequately recognize geriatric impairments or frailty in CKD patients.[17]

Instead, we direct towards a geriatric assessment that aims to assess patients on all geriatric domains using validated questionnaires without necessary involvement of a geriatrician. Such a modified nephrology-specific geriatric assessment could be conducted by a trained nephrology nurse and be discussed in a multidisciplinary meeting, informing nephrology treatment decisions and follow-up interventions among which geriatric assessment identifies those patients who may benefit from CGA. In this model, the geriatrician adds valuable expertise on clinical judgement of frailty and appropriate interventions for older patients in addition to the nephrologists' knowledge of the patient and the disease.[18] Clinicians have recognized that a standardized set of instruments could benefit these clinical purposes.[5,19]

In the absence of consensus on a uniform geriatric assessment for patients with advanced CKD, our aim was to propose a nephrology-tailored geriatric assessment, based on

multidisciplinary consensus, useful in routine clinical care for older patients with advanced CKD.

METHODS

The current study aimed to reach agreement on a nephrology-tailored geriatric assessment (NGA) suitable to routinely identify major geriatric impairments in the target population, which was defined as older patients (≥65 years of age) with stage G4–G5 CKD. Ultimately, the test set should be ready to be implemented and evaluated in routine practice. Therefore, a pragmatic approach was chosen, which included focus group meetings to identify criteria for the assessment, literature review to identify potential instruments, questionnaires to inventory currently used instruments, an expert consensus meeting to ensure that the selection of tests was based on input from patients, clinical experience in nephrology and geriatrics, and pilot testing to ensure practicability. In preparation of the consensus meeting, we composed a project team and an expert panel, drafted selection criteria for the selection of instruments, and assessed potential instruments for the test set. After the consensus meeting, the set was pilot tested.

Composition of the project team and expert panel

A multidisciplinary project team was formed, consisting of nephrologists (MB, WB, and CF), a geriatrician (SM), a nephrologist-geriatrician (HJ), nurse practitioners in nephrology (AD and NB), and a project leader (CV), to guide and prepare the consensus process. A multidisciplinary expert panel of 33 healthcare professionals was selected by an open purposive invitation for a meeting to find consensus on a preliminary test set. We invited medical doctors, nurses, and supportive disciplines experienced in t-he care for older kidney patients and/or with scientific experience in geriatric nephrology (Table 1).

Table 1: List of participants of the expert meeting 31st of January, and input via round of comments.

Discipline	Number of participants (n = 33)
Nephrologist (i.t)	12
Geriatrician (i.t)	5
Medical doctor (otherwise)	1
Nephrologist/geriatrician	2
Nurse practitioner (nephrology)	6
Nurse (nephrology)	3
Social worker	1
Physician assistant (i.t)	1
Other: medical information officer, project leader	2

i.t. in training

Identifying potential selection criteria

A list of basic principles for geriatric assessment in nephrology was drafted by the project group, based on clinical and scientific expertise of the project team and general principles of geriatric assessment. The latter includes a holistic view of the patients' unique needs and preferences, and assessment of health status in four domains (i.e., physical, cognitive, functional, and social), aiming to maximize self-reliance and quality of life.

In-depth input from older patients with advanced CKD, caregivers, and healthcare professionals experienced with conducting geriatric assessment in nephrology care was gathered in six focus group meetings. Purposively sampled CKD patients were included if aged ≥ 65 years, had an eGFR < 20 ml/min/1.73 m^2), and had experience with geriatric assessment practices. Both patients with positive and negative experiences with NGA and with different (future) choices of treatment modality were invited, as were their caregivers. Detailed methods and overall results of these focus groups are published elsewhere.[18] Findings were included in the list of basic principles for geriatric assessment in nephrology which was presented and discussed in the expert meeting described below.

Selection of potential instruments

Scientific use of geriatric tests was enumerated in published nephrology literature. We critically appraised previous systematic reviews[5,7] and experience from (national ongoing) research cohorts in older patients with CKD G4-G5(D).[3,6,8,11,20,21] Tests with evidence-based associations with outcomes in older (CKD) patients were prioritized. In preparation of the consensus phase, two potential test sets were created to illustrate how the selection criteria and preconditions could work out in a practical test set.

Potential instruments for NGA were selected on the basis of current clinical and research practices. Clinical use was inventoried in 14 large Dutch academic and peripheral nephrology centers (comprising 25% of all Dutch nephrology centers). The centers were purposively selected based on their interest in implementation of geriatric assessment practices in nephrology. A questionnaire was sent to a nephrologist of each of the 14 centers by e-mail to ask for current and preferred geriatric screening instruments or assessment practices.

Consensus meeting

The expert panel was invited to a meeting (January 31st 2018) to discuss and reach consensus on a preliminary test set. Main aims of the meeting was to agree on (1) the proposed selection criteria, (2) the geriatric and clinical domains to be appraised, and (3) the selection of potential instruments. After the meeting, the preliminary test set was sent for a final round of comments to all attendees of the meeting, to experts who could not attend the meeting, and to a clinical neuropsychologist. Their feedback was discussed within the project group.

Final test set

The final geriatric assessment was subsequently pilot tested by two experienced nurse practitioners from the project team (NB, AD), in two patients from different hospitals (patients aged 74 and 78 years, estimated glomerular filtration rate 18 and 26 ml/min/1.73 m^2, respectively), to estimate administration time and patient and provider acceptability.

Ethics information

This study is a narrative of a pragmatic consensus approach to improve routine clinical care, for which ethical approval is not applicable. Except for the qualitative part of the research using focus group discussions, which was approved by the Medical Research Ethics Committee United (MEC-U, Nieuwegein, The Netherlands, reference W17.127).

RESULTS

Selection criteria

Table S1 presents the description of the generic purposes of the geriatric screening, criteria for selection of tests and questionnaires, criteria for feasibility, and duration of the assessment. Results of the focus group meetings[18] yielded five additional essential points: i.e., awareness of illiteracy, burden for patients, learning effect in case of repeated measurements over time, feasibility to conduct the NGA next to other local preferred instruments, and unpracticality of performing walking tests in the outpatient-clinic.

Selection of instruments

The inventory of current geriatric screening instruments or assessment practices had a response rate of 100%. Supplementary Table S2 shows that 8 out of the 14 hospitals incorporated some form of geriatric screening or assessment in routine care for CKD G4–G5 patients, of which three for study purposes only. Among the hospitals, different screenings tests were used. Table S3 provides an overview of geriatric assessments as used in these hospitals and described in nephrology literature.[3,6,8,11,20,21]

Reaching consensus on the domains and measures

In the expert panel meeting, first, the panel agreed on the selection criteria as proposed (i.e., basic principles for geriatric assessment in nephrology; Table S1), and underlined that feasibility was of utmost importance for use in routine care. Possible barriers were discussed: e.g., burden for patients, desirable answers, over testing, illiteracy and multi-ethnical patient population, duplication of locally used tests, unavailability of geriatricians, availability of time for conducting the assessment, and conflicting interests between pragmatic routine care and science. Second, the panel suggested three major changes after discussing two potential test sets. Primary, the panel agreed on including items of health-related quality of life (HRQoL) and patient preferences that correspond with the recently implemented Dutch patient-reported outcome measures (PROMs) for nephrology.[22] Secondary, the Montreal Cognitive Assessment (MoCA) was preferred over Mini-Mental State Examination (MMSE) for identifying mild cognitive impairment within the CKD population, especially because the latter is less in-depth and less discriminating.[23,24] Tertiary, difficulties were recognized in standardized measurement of social domain. At the end of the meeting, consensus was reached on a preliminary test set including instruments for functional status, cognitive functioning, mood/psychological functioning, patient preferences, and frailty.

After the subsequent round of comments, the test set was changed on three aspects: instruments for assessing nutritional status and fall risk were added, and the Visual Association Test (VAT) was substituted by the Letter Digit Substitution Test (LDST) for the need of a

more specific executive function test. The assessment comprises of patient questionnaires (seven instruments, including one caregiver questionnaire) and a test set administered by a professional (ten instruments).

Items of the final consensusbased test set

Instruments are described below, and the main characteristics and cut-off points are summarized in Table 2. Supplementary Table S4 shows the predictive and diagnostic performance of tests in chronic kidney disease patients.

Table 2: Instruments and scoring of the consensus-based nephrology-tailored geriatric assessment

Domain	Instrument	Executed by	Explanation	Score / cut-off	Duration (minutes)
Functional status	Activities of daily living (Katz ADL-6) [25]	P	Grading of dependency on 6 functions, e.g. bathing, dressing, feeding.	0-6 [b], ≥2 indicates dependency.	2
	Instrumental Activities of daily living (Lawton) [26]	P	Grading of dependency on 8 more complex functions, e.g. ability to use telephone, housekeeping, medication.	0-8 for women, 0-5 for men. Higher scores indicate more independency, no cut-off point.	2
	Handgrip strength	I	Best of 3 repetitive measurements with dominant hand (i.e. no vascular access).	Reference value depending on age and gender. [62]	4
	Fall risk assessment	I	One-year fall history and fear of falling.	Yes/no; 1 ('no fear') to 10 ('very afraid').	1
Cognitive functioning	Montreal Cognitive Assessment [29]	I	Screening for mild cognitive impairment in 8 domains (i.e. visuospatial, naming, memory, attention, language, abstraction, delayed recall, orientation).	0-30, < 26 indication of cognitive impairment.	10
	6-item Cogninitive Impairment Test [31]	I	6-item screening for dementia, assessing orientation, attention and memory.	0-28, ≥11 indication of cognitive impairment.	2-3
	Letter Digit Substitution Test [30]	I	Speed dependent task to measure speed of processing by matching letters to corresponding numbers provided in the key.	Number of correct substitutions at 60s; reference values depend on age, gender, education level. [63]	5
Psychological status/mood	Whooley-questions / Geriatric Depression Scale-15 [33,34]	I [a]	Two initial question on depressed mood and anhedonia in the past month. If yes on at least one question, 15-item GDS assesses presence and degree of depressive symptoms.	Yes/no 0-15, (≥6 indicative of depression) [64]	1 5-7
	Life Orientation Test-Revised [35]	P	Dispositional optimism is measured by 10 items (including 4 filler items). Calculation of a total score, or the pessimism (reversed score on items 3, 7, 9) and optimism (items 1 ,4, 10) constructs separately.	0 ('strongly disagree') to 4 ('strongly agree') 0-24 total score, or 0-12 per construct. Higher scores indicate more optimism, reference values depend on age and gender. [65]	<3

Table 2: Continued

Domain	Instrument	Executed by	Explanation	Score / cut-off	Duration (minutes)
Patient reported outcome measures	HRQoL: 12-item Short Form Health Survey [41]	P	12 items on HRQoL providing a mental component summary (MCS) and physical component summary (PCS), using 3- or 5-point Likert scales.	0-100, higher scores indicating better HRQoL.	≤2 [c]
	Dialysis Symptom Index [42]	P	Measuring symptom burden, by indicating presence of 30 or any other additional symptoms. If present, patients are asked to specify for the degree of bothersome.	Yes/no, if yes 1 ('not at all') to 5 ('very much')	2-15 [c]
Somatic status	Surprise question [40]	C	Clinicians response to the question: *"Would I be surprised if the patient died in the next 12 months?"* assessed by nephrologist, geriatrician and/or nurse (practitioner).	Yes/no	1
	Clinical Frailty Score [36]	C	Clinical judgement on a visual and written chart with 9 graded pictures. [d]	1 ('very fit') to 9 ('terminally ill')	<1
	Charlson Comorbidity Index [37]	C	Comorbid conditions weighted for increased severity of the condition.	1 to 6 points per condition, total range of 0-33.	4
	Polypharmacy	C	Assessed by means of the total number of different medication for chronic use (i.e. for more than two weeks).	Use of five or more medications daily.	2
Nutrition	Patient-Generated Subjective Global Assessment [45]	P P/I	Short Form includes 4 self-reported items on weight development, food intake, symptoms, and activities. Complete PG-SGA: 5 additional items to be filled in by a clinician or dietician (diagnosis, age, metabolic stress, physical examination) to assess numerical score.	Short Form only, range: 0-36 (≥6 indicates malnutrition). 0-52 (≥9 indicates malnutrition)[46]	1 5-10
Social	Caregiver burden: EDIZ-plus [47]	CG	Self-perceived burden from informal care measured in 15-statements to 'agree', 'neither agree / nor disagree' or 'disagree'.	1 point per question answered with 'agree'; 0 ('no burden'), 1-3 ('minor burden'), 4-8 ('moderate burden'), 9-15 ('severe burden')	5

Abbreviations: P, patient; I, interviewer; C, clinician; CG, caregiver; NA, not available; HRQoL, health-related quality of life; EDIZ, Ervaren Druk door Informele Zorg [Self-perceived burden from informal care]. [a] GDS can be either self-administered or by an interviewer, for more in-depth assessment interviewer-administered is preferred. [b] Score range 0-12 for the ternary-answering version, [c] 12 minutes on average for both measures, [d] The initial 7-point scale version was expanded to a 9-point scale by the authors

Functional and performance status

Two instruments were selected to assess functional dependency. Katz Activities of Daily Living score (Katz-ADL-6)[25] was included to measure self-reported task for self-care on six functions of daily living activities; such as dressing and bathing. Whereas the Lawton scale for instrumental Activities of Daily Living (Lawton-iADL or $IADL_8$)[26] measures more complex

skills required for independent living in the community, such as handling finances and medication. Third measure of functional status is handgrip strength, which was considered important as it is associated with risk of commencing dialysis, and higher physical domain QOL scores.[27] Measure of gait speed was also considered as a sensitive and often used measure, but eventually not preferred above handgrip strength for practical reasons (i.e., gait speed assessment requires four to six meters of free space).

Fourth, it was considered important to assess a person's fall risk, as among older dialysis, patients falls are frequent and negatively impact HRQoL.[28] Two short questions were included on 1-year fall history and fear of falling. In summary, physical functioning is assessed by Katz-ADL-6, Lawton iADL, handgrip strength, and falls questionnaire in this final NGA.

Cognitive functioning

Three cognitive tests were included (i.e., MoCA, LDST, and six-item cognitive impairment test [6-CIT]), to ensure all unidentified cognitive deficits were captured. Besides, multiple tests allow future selection of the best fitting instrument to our population. The MoCA[29] is developed to measure cognitive decline in multiple cognitive domains, such as executive function, orientation, recall, and visuospatial ability. The LDST [30] is used in CKD G4-G5 patients[14] to measure the speed of processing general information. The 6-CIT [31] is a screening instrument for dementia, assessing only six items on orientation, attention, and memory. The 6-CIT is a feasible, acceptable, short, and simple instrument,[32] which was a key reason for incorporating the test in the NGA set, and allowing further research to potentially replace MoCA and LDST by a shorter instrument.

Psychological functioning/mood

Depression is assessed in two steps. First, a validated two-item case-finding instrument is used, asking about depressed mood and anhedonia in the past month ('Whooley-questions').[33] If at least one question is answered positive, the binary 15-item Geriatric Depression Scale (GDS-15)[34] will be assessed. GDS-15 is specifically designed for older people by putting less weight into somatic symptoms as these may be part of comorbidity. The 10-item Life Orientation Test-Revised (LOT-R)[35] is used to assess dispositional optimism and pessimism. In summary, psychological functioning is assessed by the LOT-R and 'Whooley-questions' and GDS-15 in this final NGA.

Somatic status/clinical judgement

Consensus was reached about the inclusion of three different predictive measures of mortality: frailty, comorbidity, and the surprise question. Frailty is measured using the Clinical Frailty Scale (CFS),[36] i.e. clinical judgement score on a visual and written chart with nine graded pictures, varying from very fit tot terminally ill. Second, comorbidity is assessed with the Charlson Comorbidity Index,[37] a score calculated by the patient's comorbid conditions weighted for increased severity of the condition. It is the most common used validated prognostic index to predict mortality for CKD patients starting dialysis.[38] Finally, the surprise question (i.e., *'Would I be surprised if the patient died in the next 12 months?'*) was included, since it performs as a predicter for death in CKD populations and because it is a simple and feasible instrument.[39,40]

Patient preferences and HRQoL

The 12-item Short Form (SF-12) and the Dialysis Symptom Index (DSI) were recently introduced as PROMs in Dutch Nephrological Care by the Dutch Kidney Patients' Association, Dutch Federation of Nephrology, and Nefrovisie Foundation. SF-12 is a measure of eight domains of HRQoL, comprising of a mental and a physical component summary score.[41] The DSI is a measure of symptom burden.[42] Patients are asked to indicate and rate the presence of 30 possible symptoms during the past week. Discussing symptoms could provide insights and guidance in symptom burden and management.[43,44]

Other domains: nutrition, caregiver burden, and polypharmacy

Nutritional status is assessed by the Patient-Generated Subjective Global Assessment (PG-SGA).[45] The PG-SGA contains a patient-questionnaire on intake, symptoms and physical activities (i.e., PG-SGA Short Form), and a professional part on subjective clinical judgement. The instrument can be used as a triage tool for nutritional interventions and to identify malnourished patients.[46]

Caregiver burden is measured (optional) with a 'self-perceived burden of informal care' 15-item questionnaire (EDIZ-plus),[47] which can indicate overburdening of caregivers. Polypharmacy, defined by use of five or more medications daily, is assessed by means of the total number of different medications for chronic use (i.e., for more than 2 weeks).

Pilot testing

The geriatric assessment was pilot tested and took 20–30 min for the patient questionnaire and 30–45 min for the professional-administered set. Patient and professional acceptability was ensured as both nurse practitioners and patients did not have any remarks.

DISCUSSION

We propose a consensus-based nephrology-tailored geriatric assessment (NGA) suitable to routinely identify major geriatric impairments in older patients with advanced chronic kidney disease. The NGA contains instruments in functional, cognitive, psychological, somatic, patient preferences, nutritional status, and social domains. Selection of instruments resulted from focus group meetings with patients and professionals, literature evidence, inventory of current geriatric screening practices, consensus between clinicians from nephrology and geriatrics, and pilot testing. This first consensus-based geriatric assessment is intended for use in nephrology clinical practice, and can be seen as a first pragmatic step towards implementation of standardized geriatric practices in nephrology.

Other fields, such as oncology, have previously reported studies on the pivotable role of geriatric assessment for treatment decisions and plans,[20,48,49] the development of new approaches for geriatric assessment,[50-52] and consensus trajectories for these new approaches.[53-55] However, such initiatives are relatively new to the field of nephrology, where only a few NGA practices have been published. One example is the Renal Elderly Care Integration Project[8,10] which presented a 'modified geriatric assessment' using similar domains compared to our proposed geriatric assessment. The main difference to our set is the choice of patient experiences (Renal Treatment Satisfaction Score and Distress

thermometer) compared to our inclusion of PROMs measures,[43] and the addition of instruments on nutritional status and caregiver burden. Compared to other geriatric assessment initiatives in nephrology, our set is more holistic than the presented set for the CGA-4-CKD and Renal Silver Program,[20] and the Multi Prognostic Index,[56] and more compact, benefitting use in routine practice, than sets designed for research.[3,6,21] Another recent initiative presented positive results on quality improvement by combined frailty screening and geriatric assessment practices.[57]

For both the somatic and social domain, limited instruments were selected, under the assumption that regular anamnesis already addresses most somatic deficits. Our final consensus NGA may be considered a minimum data set, but is not all-inclusive. Additional domains and instruments may be of local interest and beneficial for the patient to assess; e.g., spiritual beliefs, life goals, physical fitness, cumulative illness rating scale, self-efficacy, health-literacy assessment, and patients' outcome prioritizations. The proposed set consists of instruments that have been established in clinical or scientific use in aged populations, although some instruments (e.g., 6-CIT, LDST, LOT-R, CFS) should be further tested for use in CKD G4-G5 patients, as illustrated in Table S4. The geriatric assessment is aimed complementary to routine data collection as part of nephrology care (including, e.g., CKD classification, metabolic and cardiovascular parameters, cohabitation status, and history of smoking/alcohol use).

Implementation of geriatric assessment may differ locally, since health settings and structures diverge. Contrary to a time and labor-intensive CGA, the proposed NGA in this article is feasible within 1 h and could be assessed without involvement of a geriatrician. Rather, results are discussed in a multidisciplinary meeting, informing nephrology treatment decisions and follow-up interventions among which CGA and consultation of a geriatrician. The NGA could be conducted by a geriatric-trained nephrology nurse (practitioner) or by a partnership between geriatric medicine and nephrology (i.e., geriatrician co-management after screening for eligibility by geriatrician or triage nurse) as described elsewhere.[18-20] However, appropriate geriatric training for clinicians to assess and manage geriatric conditions is advocated.[3,6,8,10,20,21] Also, at least minimal geriatric involvement is recommended.[55,58] Logistical difficulties of implementing geriatric assessment in new settings, like involving geriatricians and other team members being added to existing services, should not be under-estimated.[50] Factors, such as stretching budgets,[50] shortage of geriatricians,[55] and lack of knowledge on geriatric tools,[8,59] may hamper practical implementation.

Controversy still exists regarding the selection of patients for whom NGA is beneficial.[50] Due to considerable heterogeneity in the aging process, actual age may not always be useful. In oncology, patients' age cut-off for assessment is often ≥ 70 years,[53] but also those who are younger with age-related issues or concerns were recommended for assessment.[55] In nephrology, assessment has been reported from age of 65 [3,6,11,21] or 70 years [8,20] or younger if a patient is considered frail. Furthermore, timing of assessment is subject to further investigation. To optimally benefit the decision-making process, we advocate geriatric assessment in (late) CKD stage-G4, [20,21] rather than at initiation or during dialysis.[6,8]

Strengths of our presented NGA test set is that it is a first consensus-proposal, based on current routine practices, with input from patients and a multidisciplinary expert panel. There are several limitations. First, this appraisal was neither based on a formal Delphi-

method or nominal group technique, nor a systematic review of literature. Rather, our pragmatic consensus approach was seen as a first step to implementation of a standardized geriatric assessment in nephrology care. After evaluation of the NGA, subsequent Delphi-method may be useful in further implementation and development, as was done in oncology.[54] Second, bias is an inherent risk in consensus approaches, e.g., in selection of our expert panel. Although we aimed to represent all disciplines involved in CKD G4-G5 care, the panel was a selected group of Dutch professionals with special interest in the field of nephrogeriatrics, and may not reflect the general nephrology opinion. A third limitation is that the test set is less suitable in illiterate patients. Furthermore, although CGA has demonstrated benefits in other medical fields,[15,16] studies on its effectiveness are lacking. Though, use of a geriatric assessment was suggested to identify often undiagnosed problems,[6] raise awareness for these problems among healthcare professionals,[3,18,20] and enables treatment adjustment or tailored supportive interventions.[48] Besides, the information derived from standardized geriatric assessment can potentially be used to stratify patients into risk categories to better predict their outcomes on kidney replacement therapy or conservative care.[5]

Future research is needed to evaluate the effectiveness and feasibility of implementation of the set. Also, value of NGA for decision-making, which is an extremely complex process, should be further explored. Therefore, insights in determinants of adverse outcomes and exploration of the prognostic capacity on outcomes are needed. Furthermore, (cost) effectiveness of geriatric assessment on key outcomes such as quality of life, hospitalization, treatment, and survival needs to be investigated in the older nephrology population. Along with the identification of standardized (preventive) clinical interventions for the management of geriatric impairments. As a first step, the NGA is currently implemented in 11 Dutch hospitals. In a pilot study,[60] we will explore feasibility of implementation of the NGA in routine nephrology care and evaluate the included instruments (outcomes are expected in 2021). Experience and data from succeeding prospective cohort studies[61] could ultimately lead to prediction models to guide tailored treatment decisions or preventive interventions.

CONCLUSIONS

In conclusion, we propose a consensus-based nephrology-tailored geriatric test set to assess frailty, cognitive and functional status for older patients approaching kidney failure (CKD G4-G5), in accordance with (inter)national guidelines and suitable to routinely identify major geriatric impairments. Future research should investigate feasibility of implementation of this NGA and its value for decision-making trajectories for kidney replacement therapy, providing insights in determinants of adverse outcomes, and for improvement outcomes for older kidney failure patients.

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SUPPLEMENTARY FILES

Table S1: Basic principles of geriatric screening in nephrology.

Basic principles of geriatric screening	• Is aimed at creating improved awareness of geriatric focus areas for care providers and patients • Provides input for the decision-making process and the conversation surrounding the treatment • There is sufficient scope to complete this set in addition to the instruments already implemented locally • Deviating results can form a reason to refer to the "geriatric specialist" for further investigation • Significant changes over time can form a reason to re-evaluate treatment decisions with patients and their caregivers
Substantive selection of questionnaires and tools based on:	• Providing insight into all four of the classical geriatric domains (somatic disease and physical, cognitive/mental and social functioning) • A combination of questionnaires and at least 1 objectively measurable physical parameter • At least 1 measurement instrument/tool that provides insight into patient preferences and values (to be determined via focus groups) • A sufficiently broad evaluation of the cognitive/mental domain (i.e. in several areas) • Alignment with nationally implemented instruments, such as a safety management system • Clinical experience from previous studies and/or care pathways involving the older persons • Evidence from literature, preferably validated instruments in populations with CKD G4-G5, or from (older) populations from other specialisms (oncology/haematology, surgery, palliative care, etc.), including instruments required for the prediction of negative outcomes • Clinical relevance (expert opinion, to be determined via focus groups and healthcare providers with experience of COPE study /GOLD study / best practice Groningen care pathway) • Where possible, the experience from existing studies and care pathways in The Netherlands is used in the selection of tests: GOLD study, COPE study, Groningen care pathway and ICHOM • Limitation of the learning effect where possible (considering the repetition factor over time)
Practical feasibility entails that the geriatric assessment:	1 Can be completed in an outpatient setting 2 Does not form too much of a burden for the patient (to be determined via focus groups) 3 Aforementioned objective measurements are physically feasible for the CKD G4-G5 population 4 Can be completed uniformly in all participating Dutch centres 5 Can be completed by a trained nephrology nurse (after training), geriatric nurse or physician assistant in no more than [30-45-60] minutes (consult with focus groups and pilot centres) 6 In theory, a medically substantive consultation geriatric doctor should not be necessary for each screening (be aware: funding)
Considerations:	• What is the maximum time frame within which the geriatric screening should be able to take place? • 30-45-60 minutes (in 2 sessions if necessary) • In theory, perform geriatric assessment once a year: • at start of dialysis • monitor annually or biannually for a wait-and-see approach • complete an extra screening set in the interim if indicated • Geriatric medicine consultation is indicated in case of abnormal screening • To be integrated based on the local capabilities and working arrangements
Input from focus groups:	• Pay attention to functional illiteracy in screening • Take into consideration the taxability of older CKD G4-G5 patients • Walking test impractical in outpatient setting • Be wary of learning effect due to repetition factor • Must be feasible in addition to the local instruments/preferences

CKD, chronic kidney disease; ICHOM, International consortium for health outcomes measurement;
[Translated from Dutch by an certified (ISO 9001 and ISO17100) medical translation company.]

Table S2: Short questionnaire for inventory of current geriatric screening and assessment practices.

No.	Question	Answers	Hospitals (n=14)
1	Is a geriatric assessment currently performed in the pre-dialysis care?	Yes, in routine care Yes, study in routine care setting No, geriatric assessment is done for study purposes only No	n=5 n=3 n=3 n=3
	If yes, who performs this assessment (pre-dialysis nurse, geriatric nurse, physician, ...)	Geriatric department Nephrology department Combined	n=2 n=5 n=1
	If yes, which tests are used for this assessment?	*See Table S3*	
	If yes, how is this assessment integrated in the standard pre-dialysis care?	Integrated/combined with regular visit to outpatient clinic Separate patient visit	n=5 n=3
2	What cooperation currently takes place between geriatric care and nephrology?	1. Internist-geriatrician and nurse (practitioner) are part of a multi-disciplinary kidney failure team, or the multi-disciplinary consultation of the pre-dialysis outpatient clinic 2. By nurses/nursing specialists in pre-dialysis and geriatric care 3. Geriatric outpatient clinic separate from kidney failure carousel, but the plan is to combine these 4. Short communication lines with clinical geriatric care and separate slots at clinical geriatrics outpatient clinic 5. No structural consultation, referral from nephrology department 6. None at the moment, agreement to have older pre-dialysis patients seen by geriatric specialists in the near future 7. Good cooperation, set-up of pre-dialysis outpatient clinic supported by both geriatric specialists and nephrologists	n=2 n=2 n=1 n=1 n=4 n=5 n=1
	Are there nursing specialists and specialist dialysis nurses employed by the department who play a role in the pre-dialysis care?	Nephrology nurse practitioner Pre dialysis nurse Geriatric nurse Geriatric nurse practitioner	n=4 n=7 n=1 n=2
3	Do you expect any logistical problems in the implementation of a standard geriatric assessment in pre-dialysis care? (based on the duration of the assessment of maximum 1 hour, for patients aged 65+ years)		
	If yes, which problems?	1. Staffing, particularly in clinical geriatrics 2. Logistics: Outpatient planning and spaces 3. Time: 1 hour for a first intake is long 4. Multi-disciplinary consultation too full for discussion of assessment, need to create inventory of the number of patients 5. Extra appointment for patient, carousel outpatient appointments not possible 6. Nurse and nephrologist are not trained 7. Database entry	

Table S2: Continued

No.	Question	Answers	Hospitals (n=14)
	If no, what is the plan of action?	1. Expansion of standard geriatric assessment from patients 70+ to 65+ 2. Information supplied by nephrology, screening by nursing specialist under supervision (resident) geriatric specialist, discussion in multi-disciplinary meeting 3. Same as COPE study: combined appointment with pre-dialysis and geriatrics, testing by geriatric nurse or pre-dialysis nurse 4. Consultation with internist-geriatrician in kidney failure carousel, nursing specialist provides information, specialised nurse performs GA 5. Probably as part of standard patient care 6. Possibly delegate care from clinical geriatrics to dialysis nurse and social worker, evaluation with clinical geriatrics in multi-disciplinary meeting 7. Separate appointment for extra geriatric assessment and open outpatient clinic for this purpose 8. Plan will be worked out with geriatric specialists	
4	Do you foresee any problems with online data entry in the RENINE database? (assuming 1/2 hour time budget per patient, aim to see at least 20 patients per hospital over a period of one year)	No Possible Yes Missing	n=10 n=1 n=2 n=1

Table S3: Inventory of use of instruments for geriatric screening and assessment in nephrology practice, study initiatives and published literature.

	Proposed nephrology-tailored geriatric assessment (POLDER)	**Renal Elderly Care Integration Project[1]**	**Parlevliet et al. [2]**	**CGA-4-CKD Program[3]**	**Renal Silver Program[3]**
Characteristics:					
Duration	One hour or less	One hour	One hour (+ one hour q.)	<10 minutes	45 minutes
Assessed by	NP, dialysis/geriatric nurse, team	Specialized nurse (team)	Research nurse	Geriatrician or nurse	Nephrologist or NP
Target population	CKD G4-G5 >70 years of age	Dialysis patients (HD/PD) >70 years, 60-70 years at indication, (n=118)	Dialysis patients (HD/PD) >65 years, (n=50)	CKD, not in geriatrics clinic, >70 years, (n=33)	Advanced CKD >75 years, (n=35)
Setting	Routine practice	Routine practice: outpatient clinic / dialysis unit	Home visit	In CKD clinic	In CKD clinic
Domain:					
Functional status	*Katz Activities of Daily Living (6 item)* *Lawton i-ADL*	*Personal care: help required for Activities of Daily Living*	*Katz Activities of Daily Living* *Modified Katz index for iADL* *Neurosensory impairments*	*Activities of Daily Living [a]* *i-ADL [a]*	*Activities of Daily Living [a]*
	Handgrip strength *Fall risk: 1-year fall history, fear of falling.*	*Mobility: aids* *Fall history*	*Walking aid* *≥Two falls in past three months*	*Mobility (walking ability)* *Falls (prior 12 months)*	*Mobility (walking aid)* *Falls (prior 12 months)*
Cognitive functioning	*Montreal Cognitive Assessment* *Six-item Cognitive Impairment Test* *Letter Digit Substitution Test*	*Abbreviated Mental Test Score* *Clock drawing*	*Mini Mental State Examination* *IQCODE-SF* *NPI-q* *Confusion Assessment Method*	*Dementia diagnosis or Mini-Cog test*	*Dementia diagnosis or Mini-Cog test*
Mood	*Geriatric Depression Scale* *Optimism check*	*Distress thermometer* *Social: (anamnesis)* *Environmental: (anamnesis)*	*Geriatric depression scale-15* *Loneliness: De Jong-Gierveldschaal*		
Quality of life and patient preferences	*Short Form-12* *Dialysis Symptom Index*	*Renal Treatment Satisfaction Score (Patient experience)*	*EuroQol-6D, including VAS*		
Somatic functioning (Clinical judgement)	*Surprise question* *Clinical Frailty Score* *Charlson Comorbidity Index* *Polypharmacy*	*Clinical Frailty Score*	*Charlson comorbidity index* *Polypharmacy: number of different medications.*	*SOF (Frailty)*	
Nutrition	*PG-Subjective Global Assessment*	-	*Short Nutritional Assessment Questionnaire* *Body Mass Index*		
Caregiver burden	*EDIZ-plus*	-	***EDIZ***		
Other:			*Pain (VAS)* *Decubitus, Constipation, Incontinence*	*Urinary incontinence*	

Purple coloured: indicates a different test than included in the proposed nephrology-tailored geriatric assessment
Abbreviations: ADL, Activities of Daily Living; iADL, instrumental Activities of Daily Living; CIRS-G, Cumulative Illness Rating Scale-Geriatric version; CKD, chronic kidney disease; EDIZ, Ervaren Druk door Informele Zorg [Self-perceived burden from informal care];

	Soysal et al.[4]	COPE [5]	GOLD[6]	Clinical nephrology practice in the Netherlands
Characteristics:				
Duration	Not specified	3 hours	60-90 minutes	*(see supplementary Table S1)*
Assessed by	Not specified	Nurse practitioner or geriatric nurse	Research nurse	
Target population	Dialysis patients (HD) >65 years, (n=121)	CKD patients with eGFR<20 >65 years, (n=157)	Initiating dialysis or CC >65 years, (n=285)	
Setting	In clinic, after dialysis session	In CKD clinic	Home visit	
Domain:				
Functional status	*Basic ADL* *IADL*	*Groningen Activity Restriction Scale* *Lawton iADL*	*Katz-ADL* *Lawton iADL*	*Katz-ADL* *Lawton iADL*
		Handgrip strength *Gait speed* *Short Physical Performance Battery*	*Handgrip strength* *Falls* *Four meter walking test* *Timed up and go* *Four Test Balance Scale*	*Timed up and go* *Falls* *Gait speed* *Handgrip strength* *Short physical performance battery*
Cognitive functioning	*Mini Mental State Examination*	*Mini Mental State Examination* *Clock drawing* *15- WVLT* *Stroop Colour Word Test* *Trail making test (A&B)* *Visual Association Test* *Letter Digit Substitution Test* *Assessment of numeracy*	*Mini Mental State Examination* *Clock drawing* *Enhanced Cued Recall* *Semantic Fluency Test* *Interview of Detoriation in Daily life* [c] *IQCODE* [c] *Neuro-Psychological Inventory (mood)* [c]	*Mini Mental State Examination* *Montreal Cognitive Assessment (MoCA)* [b] *Cambridge Cognitive Examination* *Six-item Cognitive Impairment Test*
Social functioning / Mood	*Geriatric Depression Scale-15*	*Geriatric Depression Scale-15*	*Geriatric Depression Scale-15*	*Geriatric Depression Scale-2/15*
Quality of life and patient preferences		*RAND-36*	*EuroQol-5D*	*Outcome Prioritization Tool (treatment goals)* *EuroQol-5D* *Visual analogue scale*
Somatic functioning (Clinical judgement)		*Fried frailty indicator* *Charlson comorbidity index*	*Surprise question* *Groningen Frailty index* *Fried Frailty index* *CIRS-G* *Overall condition (VAS)*	*Rockwood Clinical Frailty Score* *Groningen Frailty Indicator* *Geriatric-8* *Charlson Comorbidity Index* *Surprise question*
Nutrition	*Mini Nutritional Assessment* *Body Mass Index*	*Short Nutritional Assessment Questionnaire*	*Mini Nutritional Assessment*	*Mini-Nutritional Assessment* *Body Mass Index* *(Anamnesis by dietician)*
Caregiver burden		*EDIZ-plus*	*EDIZ*	*(Hetero-anamnesis)*
Other:		*Cantril's ladder, Pain score,* *Anxiety score* *Illness perceptions questionnaire*		

eGFR, estimated glomerular filtration rate; HD, hemodialysis; VAS, visual analogue scale; IQCODE, Informant Questionnaire on COgnitive DEcline.

[b] Clock drawing is included in the Montreal Cognitive Assessment, [c] subjective cognition tests filled in by caregiver.

Table S4: Diagnostic and predictive performance of consensus nephrology-tailored geriatric assessment test set for CKD G4-G5.

Domain	Subdomain	Instrument	Validated in CKD patients	Purpose and construct to assess	Performance	Validation cohort / source
Functional	Functional dependency	Katz ADL-6[7]	Partly: in HD patients	Assesses activities of daily living Predicting mortality	- Despite frequent use of Katz' index, evidence on validity and reliability is limited [8, 9], terminology inconsistently used, and different versions (5/6/7 items) exist.[8] - Reliability rated questionably positive, validity and responsiveness both moderate or unknown for Katz 6-item version.[8] - Construct validity is established with SF-36 physical and mental function domains at 1-month. Criterion predictive validity on short-term mortality but not longer-term mortality 3-6 months.[10] - Good internal consistency (Cronbach's alpha's: 0.93 and 0.94) for 10-item and 5-item version[11], good acceptability and reasonable criterion validity for the former version.[9] - Limited utility because of ceiling effects[12]	Generally widely used [8, 13, 14] Older patients (55-74 years)[9] Systematic review in older (>60 year) community-dwelling population [8] Systematic review in critically ill [10] General population sample[9] Hemodialysis patients[11, 12]
		i-ADL$_8$ Lawton [15]	Partly: in HD patients	Assesses instrumental activities of daily living Predicting mortality	- Good internal consistency (Cronbach's alpha 0.87).[11] Limited utility due to ceiling effects.[12] - Predicting post-hospital and cumulative mortality, conflicting results for in-hospital mortality.[10] - Dependency (combined Katz ADL-5 and Lawton iADL$_8$ scales) were predictor of mortality in HD and associated with dialysis withdrawal and HRQoL[16]	Generally widely used [13] Hemodialysis patients [11, 12, 16]
	Hand grip strength	Hand grip strength	Yes	Assesses muscle strength Predicting mortality and outcomes	- Good to excellent test-retest reliability (ICC >0.80). High variability of minimal detectable change between studies (14.5-98.5%)[17] - Predictive for functional status (pooled ratio 1.78 [95% CI 1.28–2.48] for high vs low handgrip strength, and 0.95 [95% CI 0.92–0.99] for handgrip strength as a continuous variable) and mortality (pooled HR 1.79 [95% CI 1.26–2.55] for high vs low handgrip strength and 0.96 [95% CI 0.93–0.98] for continuous handgrip strength).[18] - Predictive for lower all-cause mortality (low versus high hand grip strength [RR 1.88, 95%CI 1.55-2.33], and per 1kg increase [RR 0.95, 95%CI 0.93-0.97]) in dialysis patients.[19] - Associated with HRQoL scores (+0.13 [95%CI 0.01-0.24] in total score per 1kg) and decreased risk for commencing dialysis in CKD patients (aHR 0.89 [95%CI 0.84-0.96]) [20] or reaching composite end points in male CKD G3b-G5 patients (aHR 3.72 [95%CI 1.03-13.41)[21] - Sensitivity of outcome predictability was 95% and 88%, and specificity 50% and 58%, for cut-off scores of 20.15kg and 10.15kg in resp. men and women [21]	Systematic review including older patients[17] Systematic review: older patients (60+ years)[18] Systematic review: HD/PD patients[19] CKD G1-G5 not on dialysis[20, 21] CKD G3b-G5[21]
	Fall risk	Fall risk assessment	No	Fall history and fear of falling	No appropriate fall risk screening tool is available[22]	Systematic review[22]

Table S4: Continued

Domain	Subdomain	Instrument	Validated in CKD patients	Purpose and construct to assess	Performance	Validation cohort / source
Cognitive	Cognitive decline	MoCA[23]	Yes	Assesses (mild) cognitive impairment	- Good internal consistency (Cronbach alpha 0.83). High test-retest reliability (correlation coefficient =0.92 over mean 35 ±17.6 days). Content validity established with Mini-Mental State Examination (r = 0.87, p<0.01)[23], and concurrent validity established with a neuropsychological test battery in HD patients.[24] - No consensus on the best cutoff point[25]. Original instrument uses cut-off of ≤25 for detecting mild cognitive impairment (sensitivity 90%, specificity 87%, PPV 89%, NPV 91%)[23] In HD patients: good sensitivity (77% and 87%) and specificity (79% and 57%) for cutoff scores of ≤24 and ≤25 respectively. AUC was optimal for cutoff scores of ≤24 (76%, 95%CI 0.60-0.87), with PPV 0.88, NPV 0.61.[24] Similar to findings in meta-analysis for older patients (best cutoff ≤24 yielded sensitivity 80%, specificity 81%, AUC 0.85 95%CI 0.82-0.87; while cutoff ≤25 yielded sensitivity 90%, specificity 57%)[26]	Patients with mild cognitive impairment and healthy controls[23] Hemodialysis patients[24] Systematic review: CKD including pre-dialysis populations [25] Systematic review: older patients (60+ years)[26]
		LDST[27]	No	Assesses psychomotor speed	- High test-retest correlation (r=0.88) and manageable by older persons[28].	Older persons (70-82 years)[28] CKD late G4-G5 patients [29]
		6-CIT[30]	No	Assesses cognitive impairment	- Concurrent validity established with MMSE[31, 32] and expert diagnosis of delirium/dementia[33] - Adequate to good sensitivity (73%-83%) and good specificity (>90%), excellent AUC (>0.91) for cognitive impairment (cutoff score ≥11) according to the MMSE.[31, 34] PPV (0.83), NPV (0.98)[31] - Promising instrument, but further robust validation studies are required, including the best cutoff [32] - Associated with adverse outcomes, and a predictor of length of stay (adjusted OR 1.54, 95%CI 1.1-2.1), new institutionalization (adjusted OR 3.45, 95%CI 1.9-6.3) and in-hospital mortality (adjusted OR 3.11, 95%CI 1.2-8.0) for older acutely hospitalized patients[35]	>70 year old general hospital patient population[31] Review of primary and secondary care settings[32] Referrals to outpatient dementia service[34] Emergency department attendees (>70 years)[33] Older (>70 year) acutely hospitalized or emergency department patients[35]
	Depression	'Whooley-questions'[36]	No	Screening for / diagnosing depression	- Adequate to high sensitivity (79-96%), but low specificity (54-57%), LR+ 1.9-2.2, LR- 0.07-0.37, AUC 72-82% [36] [37]	Adult primary care patients [36] Older primary care and hospitalized patients (60+ years)[37]

Table S4: Continued

Domain	Subdomain	Instrument	Validated in CKD patients	Purpose and construct to assess	Performance	Validation cohort / source
Mood		GDS-15[38]	No		- Adequate sensitivity (79%, 95%CI 0.70-0.86), specificity (77%, 0.73-0.81) in meta-analysis. Test accuracy LR+ 3.41, LR- 0.29. Diagnostic odds ratio of 12.4, AUC 84%, at a cutoff score of 5/6.[39] - Pooled sensitivity (0.89 95%CI 0.80-0.94) and specificity (0.77, 0.65-0.86) for a cutoff score of 5.[40]	Meta-analysis of studies among older in-patients (60+ years) from general hospitals[39] Older population (55+ years) in primary care, secondary care, and community settings[40]
	Optimism	LOT-R[41]	No	Assessing optimism and pessimism	- Acceptable reliability for subscales of optimism and pessimism (Cronbach alpha 0.70, and 0.74 respectively), questionable for the total score (alpha 0.68). Convergent validity is assessed with other psychological scales for depression, anxiety, pain, disability, self-reported state of health and multiple domains of life satisfaction (Pearson correlations presented)[42] - Optimism was associated with pro-health behaviours in kidney transplantation patients[43]	General population[42] Kidney transplantation patients[43]
PROMs	HRQoL	SF-12[44] SF-12 (continued)	Yes	Assessing HRQoL (physical and mental component scale) Predicting mortality and hospitalization	- Validated to detect change in HRQoL physical component score (PCS) and mental component score (MCS) (ICC with SF36 0.83 and 0.90 respectively).[45] - Good evidence for reliability for PCS and MCS (Cronbach alpha=0.89 and 0.90, respectively) and test-retest reliability (ICC 0.76 and 0.74 respectively). No floor and ceiling effects. Acceptable convergent validity assessed. Higher HRQoL PCS and MCS were associated with decreased mortality (resp. aHR -2.4% and -1.2% per incremental point) and first hospitalization (resp. aHR -1.2% and -0.6% per point).[45,46]	HD/PD patients[45] Hemodialysis patients[46,47]
	Symptoms	DSI[48]	Yes	Assessing symptom burden	- Content validity established, and reliable (Cronbach alpha 0.90).[49] Good test-retest reliability (total agreement mean 0.80±0.09). Kappa statistics for the items ranged from 0.06 to 0.90 (mean 0.48±0.22).[48] - Responsiveness, smallest detectable change and minimal important change need further investigation[49].	Advanced CKD[49] and hemodialysis patients[48]

Table S4: Continued

Domain	Subdomain	Instrument	Validated in CKD patients	Purpose and construct to assess	Performance	Validation cohort / source
Somatic	Clinical judgement	Surprise question (binary)[50]	Yes	Predicting mortality	- Poorly to modestly predictive performance for death at 6 to 18 months. - Pooled prognostic characteristics: sensitivity 67% (95%CI 0.56–0.77), specificity 80% (0.73–0.86), positive likelihood ratio 3.4 (2.8–4.1), negative likelihood ratio 0.41 (0.32–0.54), positive predictive value 37% (0.30–0.45) and negative predictive value 93% (0.91–0.95). Adequate discrimination in patients with noncancer illness (AUC = 0.77, 0.73–0.81)[51]	Meta-analysis (including 7 dialysis populations out of 11 noncancer illness studies, additional to 5 cancer studies)[51]
					- Sensitivity 66% (95% CI, 0.49-0.80), specificity 68% (0.63-0.73). Predictor of mortality (aHR 3.3; 95% CI, 1.8-6.0). Moderate inter-rater reliability (Krippendorff's alpha = 0.58, 0.42-0.72), good test-retest correlation (Pearson coefficient = 0.66, 95% CI, 0.58-0.75)[52]	Outpatient CKD G4-G5 not on dialysis, aged ≥ 60 years. [52]
	Frailty	CFS[53]	No	Predicting mortality, entry into institutional facility and length of stay	- Confirmed construct validity with multiple tools for measuring degree of frailty (Pearson coefficient 0.80, p < 0.01). High reliability between 2 ratings (ICC 0.97, p < 0.001). Interrater reliability not assessed. Adequate prediction of entry into institution (AUC = 0.75), and 18- month (AUC = 0.77) and 5-year mortality (AUC = 0.70). Calibration not assessed.	Community-dwelling older people[53]
					- Adequate prediction of in-patient mortality (AUC = 0.72, 95%CI 0.69 – 0.75, p<0.001). Moderate prediction of transfer to geriatric ward (AUC = 0.68, 0.66 to 0.71, P<0.001) and length of stay ≥10 days (AUC = 0.62, 0.61 to 0.64, P<0.001). [54]	Emergency admissions of people aged ≥75 years[54]
					- Associations between CFS and mortality in pre-dialysis (aHR 1.35, 95%CI 1.16 – 1.57) [55] and incident dialysis patients (aHR 1.32; 95%CI, 1.15 to 1.52)[56] indicates potential prognostic significance.	Patients referred to pre-dialysis education[55] Adult patients on incident dialysis in tertiary centre[56]
	Comorbidity	CCI[57]	Yes	Predicting mortality	- Acceptable discrimination performance (c-statistic = 0.74, 95%CI 0.65-0.83). Calibration was lacking reporting. Among prognostic indices, CCI delivered best and most discrimination performance, and is most commonly used. [58]	Patients starting dialysis (meta-analysis) [58]
					- Poor discrimination (c-statistic = 0.63, 0.63-0.64) for one year mortality, calibration not reported. [59] - Association between CCI and mortality in pre-dialysis patients (aHR 1.18, 1.05-1.34). [55]	Patients eGFR≤45ml/min/1.73m^2 (large retrospective cohort) [59] Patients referred to pre-dialysis education[55]

Table S4: Continued

Domain	Subdomain	Instrument	Validated in CKD patients	Purpose and construct to assess	Performance	Validation cohort / source
	Polypharmacy	Five or more medications daily	NA	NA	Polypharmacy definitions are variable, ranging from ≥2 to ≥ 11 medications daily. Most commonly definition is: the use of ≥5 medications daily.[60]	Systematic review of definitions[60]
Nutrition		PG-SGA[61]	Yes	Assessing malnourishment	PG-SGA score (cut off score ≥4, defined by PG-SGA global rating B=moderately malnourished or C=severely malnourished): AUC 93% (95%CI 0.90-0.97), sensitivity 90%, specificity 83%, accuracy 85%. [62] Complete PG-SGA (cut-off score ≥9, as defined by SGA≥9): sensitivity 83%, specificity 92%, PPV 71%, NPV 96%., poor reliability (Cronbach alpha=0.52), satisfactory internal reliability (standardized item alpha coefficient=0.73). [63] PG-SGA Short Form as stand-alone questionnaire (using cut-off score ≥6, as defined by a complete PG-SGA≥9): sensitivity 78% (95%CI 0.64-0.88),specificity 94% (0.86-0.98), PPV 91% (0.79-0.98), NPV 84% (0.74-0.92), overall accuracy (AUC: 87%).[64]	CKD patients (inpatients, outpatients combined, including dialysis patients) [64] and HD patients [62, 63]
Social	Caregiver burden	EDIZ-plus[65]	No	Assessing self-perceived pressure of informal care	Validated: average scalability (H= 0,46), good reliability (Rho=0,87) and a good convergent validity (r=0,70)[65]	Informal carers for older persons (65+ years of age), physically disabled, institutionalized patients, mentally disabled, psychiatric problems [66]

Abbreviations: NA, not applicable; (i)-ADL, (instrumental) activities of daily living; AUC, area under the curve; aHR, adjusted hazard ratio for mortality; CCI, Charlson comorbility index; CFS, clinical frailty scale; CKD, chronic kidney disease; DSI, dialysis symptom index; EDIZ, Ervaren Druk door Informele Zorg [Self-perceived pressure from informal care]; eGFR, estimated glomular filtration rate; GDS-15, geriatric depression scale 15-item; H, Loevinger's coefficient H for scalability; HD, hemodialysis; PD, peritoneal dialysis; HRQoL, health-related quality of life; ICC, intra-class correlation coefficient; LDST, letter-digit substitution test; LOT-R, life orientation test-revised; LR, likelihood ratio; MCS, mental component score; MoCA, Montreal cognitive assessment; MMSE, mini-mental state examination; NPV, negative predictive value; OR, odds-ratio; PCS, physical component score; PG-SGA, patient-generated subjective global assessment; PPV, positive predictive value; PROMs, patient reported outcome measures; r, correlation coefficient; RR, risk ratio; 6-CIT, 6-item Cognitive Impairment Test; SF-12, 12-item short-form; 95%CI, 95% confidence interval.

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chapter 7

Geriatric assessment in CKD care: an implementation study.

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Kidney Medicine 2024;6(5):100809.

ABSTRACT

Rationale & Objective: Older people with progressive chronic kidney disease (CKD) have complex healthcare needs. Geriatric evaluation preceding decision making for kidney replacement is recommended in guidelines, but implementation is lacking in routine care. We aimed to evaluate implementation of geriatric assessment in CKD care.

Study Design: Mixed methods implementation study.

Setting & Participants: Dutch nephrology centers were approached for implementation of geriatric assessment in patients aged ≥70 years and with an estimated glomerular filtration rate of ≤20 mL/min/ 1.73 m^2.

Quality Improvement Activities/Exposure: We implemented a consensus-based nephrology-tailored geriatric assessment: a patient questionnaire and professionally administered test set comprising 16 instruments covering functional, cognitive, psychosocial, and somatic domains and patient-reported outcome measures.

Outcomes: We aimed for implementation in 10 centers and 200 patients. Implementation was evaluated by (i) perceived enablers and barriers of implementation, including integration in work routines (Normalization Measure Development Tool) and (ii) relevance of the instruments to routine care for the target population.

Analytical Approach: Variations in implementation practices were described based on field notes. The postimplementation survey among healthcare professionals was analyzed descriptively, using an explanatory qualitative approach for open-ended questions.

Results: Geriatric assessment was implemented in 10 centers among 191 patients. Survey respondents (n = 71, 88% response rate) identified determinants that facilitated implementation, ie, multidisciplinary collaboration (with geriatricians) -meetings and reports and execution of assessments by nurses. Barriers to implementation were patient illiteracy or language barrier, time constraints, and patient burden. Professionals considered geriatric assessment sufficiently integrated into work routines (mean, 6.7/10 ± 2.0 [SD]) but also subject to improvement. Likewise, the relevance of geriatric assessment for routine care was scored as 7.8/ 10 ± 1.2. The Clinical Frailty Score and Montreal Cognitive Assessment were perceived as the most relevant instruments.

Limitations: Selection bias of interventions' early adopters may limit generalizability.

Conclusions: Geriatric assessment could successfully be integrated in CKD care and was perceived relevant to healthcare professionals

INTRODUCTION

Among the increasing population of older patients with kidney failure,[1,2] unrecognized geriatric impairments are highly prevalent. Such impairments, including cognitive and functional decline, comorbid conditions, frailty, depression, and malnutrition,[3-5] are associated with adverse health outcomes such as mortality, hospitalization, and reduced health-related quality of life.[6,7] Understanding geriatric impairments can be valuable for decision making for kidney replacement therapy choices and for risk stratification. Therefore, Dutch and British guidelines recommend geriatric assessment for those at high risk of death or those identified as being frail, respectively.[8,9] For this, clinicians have recognized the clinical and scientific value of a standardized set of instruments.[7,10]

In the absence of a gold standard for geriatric assessment, a group of Dutch healthcare professionals recently reached a consensus on a geriatric assessment tailored for nephrology care (nephrology-tailored geriatric assessment [NGA]).[11] This set of instruments takes less than 1 hour to perform and could be routinely conducted by trained nephrology or geriatric nurses. In contrast to comprehensive geriatric assessment, this modified approach of geriatric assessment is therefore expected to be less challenging to embed in existing routines in nephrology care pathways. Furthermore, unlike short frailty screening instruments,[12] the set would enable adequate recognition of geriatric impairments or frailty in the older chronic kidney disease (CKD) population. After NGA, if needed, a patient could be referred to a geriatrician for full comprehensive geriatric assessment, which includes a more extensive multidisciplinary diagnostic and treatment process that identifies medical, psychosocial, and functional impairments that may necessitate development of an integrated care plan.

Although some previous attempts at incorporating a geriatric assessment in nephrology populations have been reported,[3,4,13-16] consistent and widespread implementation of standardized geriatric assessment in routine nephrology care has yet to be achieved. Analysis of the process of implementation (including barriers and facilitators) may help to successfully incorporate this complex intervention in clinical practice.[17] The current study, therefore, aimed to evaluate multicenter implementation of geriatric assessment in routine nephrology care.

METHODS

Design

In this implementation study, we used a mixed methods approach, combining quantitative data collection with a partially qualitative postimplementation survey involving healthcare professionals.

Context

This study was part of the Pathway for Older Patients Reaching End-Stage Renal Disease (POLDER) initiative, aimed at designing, implementing, and evaluating geriatric assessment in Dutch nephrology clinics. In October 2017, we approached 16 Dutch university and non–university hospital–based nephrology centers on their interest in implementing geriatric assessment. This interest was evidenced either by partaking in previous studies involving

geriatric assessment or by showing interest in the topic at conferences. Following an email survey to assess current practices,[11] 10 centers chose to participate, representing 18% of all Dutch nephrology centers. Although the geriatric assessment protocol was new for all participating centers, some had previously participated in studies using geriatric assessment in patients with CKD stage G4 or G5 (N = 3) or CKD G5 or G5D (N = 2).[3,18] Additionally, 2 centers used geriatric assessment in their routine care on referral, whereas the remaining 3 centers had not previously used geriatric assessment in CKD care.

Table 1. Instruments included in the nephrology-tailored geriatric assessment.

Nephrology-tailored geriatric assessment: domains and instruments			**Type of assessment**	
Domain	Subdomain	Instrument	(I) patient-questionnaire	(II) provider-administered test set
Functional status	Activities of daily living	Katz Activities of Daily Living-6 [19]	X	
	Instrumental activities of daily living	Lawton instrumental Activities of Daily Living [20]	X	
	Handgrip strength	Handgrip strenght		X
	Fall risk assessment	One-year fall history, fear of falling		X
Cognitive status	Cognitive functioning	Montreal Cognitive Assessment [21]		X
		6-item Cognitive Impairment Test [22]		X
		Letter Digit Substitution Test [23]		X
Psychological status/mood	Depression	Whooley-questions / Geriatric Depression Scale-15 [24,25]		X
	Optimism	Life Orientation Test-Revised [26]	X	
Patient reported outcome measures	Health-related quality of life	12-item Short Form Health Survey [27]	X	
	Symptoms	Dialysis Symptom Index [28]	X	
Somatic status	Clinical judgement	Surprise question [29]		X
	Frailty	Clinical Frailty Score [30]		X
	Comorbidity	Charlson Comorbidity Index [31]		X
	Polypharmacy	Polypharmacy (≥5 medications)		X
	Nutritional status	Patient-Generated Subjective Global Assessment [32]	X	X
Social	Caregiver burden	Self-perceived pressure from informal care-plus [33]	Caregiver	

This nephrology-tailored geriatric assessment, and its consensus-based development, has been described in more detail by Voorend *et al.,* [11].

Intervention description

Previously, we developed a consensus-based nephrology-tailored assessment (NGA).[11] NGA consists of a patient questionnaire and professionally administered tests that can be completed within 1 hour by a trained nurse or medical specialist. NGA includes instruments covering various domains, including functional, cognitive, psychosocial, somatic, and patient-reported outcomes. Table 1 presents the included instruments[19-33] and by whom they were completed. NGA was developed to enhance routine care and research in older patients with advanced CKD, aiming to identify known and unknown geriatric impairments

in older patients with CKD stage G4-G5. If needed, NGA could lead to appropriate supportive interventions (eg, physiotherapy, referral to geriatrician) and is beneficial to decision making in patients with kidney failure.

Target population

NGA was implemented among patients aged ≥70 years with an estimated glomerular filtration rate (eGFR) of ≤20 mL/min/1.73 m^2 and the ability to read and understand the questionnaire. Patients were excluded in case of a history of dementia or lack of mental capacity assessed by a geriatrician.

Implementation strategy

An educational program was developed to enhance awareness of geriatric impairments in the advanced CKD G4-G5 patient population and improve knowledge about geriatric assessment among involved healthcare professionals. The program existed of a plenary education and onsite training session, described in Figure 1. Participating centers had the flexibility to determine how they would embed the intervention in the care process. This encompassed decisions regarding who would conduct the NGA, the extent of geriatrics department's involvement, and the organization of multidisciplinary team meetings for discussion of NGA outcomes and managing identified geriatric impairments. Additionally, optional digital entry of the patient questionnaires was offered, and a summary of NGA results was made available (after July 2020) for download after data entry in the online dashboard for data collection (see Supplementary File 1).

I. Plenary session

- General aspects of aging* (lecture given by a geriatrician)
- Relationship between kidney failure and geriatric measures: relevance for daily nephrology practice* (lecture given by nephrologist)
- Two examples of routine care pathways integrating NGA in nephrology practice* (lecture given by two nurse practitioners)
- Case discussion

*video recorded and made available online afterwards.

II. On-site training for the multidisciplinary team

- Explanation of the protocol and instruments included in NGA
- Practical exercises for all instruments
- Principles of good clinical research

Figure 1: Educational program as part of the implementation strategy

Outcome

A priori, we aimed for 10 participating centers, each including 20 patients. We aimed to gain insights in variation of implementation practices, contextual changes that affected hospital participation and patient inclusion, and completeness of the NGA instruments.

Determinants of successful implementation were evaluated on 2 aspects. First, we assessed the presence of enablers and barriers to implementation and integration in work routines. A list of potential barriers and enablers was used as previously identified in a focus group study.[34] To understand "integration in work routines" we employed the validated Dutch version of the Normalization Measure Development (NoMAD) tool,[35,36] which has been

previously used in the implementation of complex interventions in nephrology.[37,38] Four processes of integration in work routines (ie, normalization) were assessed: sense making, cognitive participation, collective action, and reflexive monitoring (Table S1).[39] Second, we investigated the perceived relevance of the NGA instruments to CKD care, specifically whether NGA achieved the intervention objective (enabling identification of known and unknown geriatric impairments), facilitated supportive interventions, and supported decision making for kidney failure treatment.

Data collection

An overview of data collection is presented in Table 2. We collected data at the hospital level using field notes to capture information on the administration of the provider-administered test set, multidisciplinary team meetings, the involved disciplines, and any contextual changes that affected hospital participation or patient inclusion. At healthcare provider level, a postimplementation survey was conducted among partaking healthcare professionals. The survey (Supplementary File 2) included questions about respondents' characteristics, the presence of enablers and barriers to implementation, the NoMAD tool, the perceived relevance of NGA practices and its individual components, and the intervention's ideal target group. Additionally, explanatory open-ended questions probed for deeper understanding of implementation determinants. Data were collected on the number of patient inclusions, conducted NGAs, digital patient questionnaires entries, and instrument completeness. Patient characteristics were extracted from the database managed by Nefrovisie, the Dutch quality institute for nephrology.

Survey sampling

Participants for the postimplementation survey were purposively sampled by asking each center's contact person to list at least 5 colleagues from various disciplines involved in the care of older patients with CKD. The survey was disseminated after study inclusion closed in May 2021. Eighty-one professionals received a personal email invitation to participate in an online survey using Qualtrics software (Qualtrics, version 2021). Nonresponders received reminders 2 weeks later. We assured confidentiality through pseudonymized analyses of the data.

Data analysis

Feasibility of implementation was assessed by analyzing per center the implemented components of the intervention, patient inclusion and completeness of NGA instruments. Demographic and clinical patient data, along with survey respondent characteristics and quantitative survey responses, were presented descriptively. To assess integration into routine work (ie, normalization), we used paired t tests to compare current and anticipated future use of NGA. Average construct scores were calculated for each participant, excluding "nonapplicable" items. Higher scores signified better-perceived implementation.[37,39] A mean subconstruct score <4 indicated potential for improvement. The overall perceived relevance of the NGA set was appraised by the sample mean of the respondents' judgment on 3 intervention objective achievement questions. A score of ≥7 was considered relevant (ie, successful in reaching the intervention objective). For the specific instruments, we strived

Table 2: Overview of data collected for evaluation of NGA implementation according to the implementation outcomes.

Aim	Implementation outcome	Data collected	Units or score (range)	Source
Feasibility of implementation	Hospital participation	Number of participating hospitals that implanted NGA practices	Percentage of aimed hospitals	Field notes (hospital level)
		Implemented components of the intervention: - Who executed the provider-administered test set, - When the provider-administered test set was done - Outcomes discussed in multidisciplinary team meetings - Who attended multidisciplinary team meetings - Contextual changes that affected hospital participation and patient inclusion	Discipline Single or multiple visit Yes/no Disciplines -	
	Patient inclusion	-Number of patient participants -Patient characteristics	Count Gender Age eGFR	Database collection (patient level)
		-Completeness of the NGA (i.e. provider-administered test-sets and patient questionnaire) -Completeness of items of each NGA instrument	Percentage completed test-sets and questionnaires Percentage complete instruments	
Determinants of (un)successful implementation	Enablers and barriers to implementation	-Rating of the presence of potential barriers and enablers identified in a preceding study[34] -Respondents' three perceived most important enablers and barriers for successful implementation in their center.	10-point Likert presence scale Top 3 given by respondent	Post-implementation survey among partaking healthcare professionals
	Integration in work routines	NoMad tool:[a] - Three general normalization items on the past, current, and likelihood of future use of the intervention - Eighteen questions were used to measure the normalization-subconstructs	0-10 visual analogue scale; higher scores indicating more use. 5-point Likert scale (1-disagree to 5-agree).	
	Perceived relevance of the NGA	Agreement of relevance of NGA practices as a whole: Rating three aspects of the intervention objective; *i.e. NGA supports in:* *1. identification and objectivation of impairments,* *2. adjusting or supplementing current treatment strategies,* *3. informing future treatment decision for kidney replacement therapy (KRT).*	10-point Likert scale: 0-'strongly disagree' to 10-'strongly agree'	
		Rating all 17 individual NGA instruments for their relevance to the intervention objective (see above).	5-point Likert scale: 1 (not at all relevant) to 5 (very relevant).	
		Appraisal of the target group by rating: age limit (70+ y) kidney function limit (eGFR <20mL/min/1.73m^2)	3 options: 'too extended', 'sufficient' or 'too narrow'	
	Explanatory qualitative information	Understanding on determinants of implementation	Open questions	
Additional information		Survey respondents' characteristics	discipline, years' experience in current function and department, affiliated hospital	

Abbreviations: eGFR, estimated glomerular filtration rate; NGA, nephrology-tailored geriatric assessment; NoMAD, Normalization MeAsure Development

for a rating of ≥4 (ie, "relevant" or "very relevant") among 70% of the respondents. IBM SPSS statistics for Windows (version 25) was used for quantitative analysis.

Explanatory qualitative data analysis involved open-ended survey responses, initially coded by 2 authors independently (ie, project lead [CV] and an uninvolved author [LB]). Codes were discussed to ensure agreement on the final interpretations. We did not use qualitative research software. Triangulation of the quantitative and qualitative data was done by exploring (dis)agreements within and between hospitals in the survey responses and participants or centers with notable normalization levels. The Revised Standards for Quality Improvement Reporting Excellence (SQUIRE 2.0)[40] and Consensus-Based Checklist for Reporting of Survey Studies guided reporting of our results.[41]

Ethical considerations

The POLDER study's protocol was approved by the Medical Research Ethics Committee Leiden-Den Haag-Delft (reference NL65322.098.18) to facilitate patient data collection and analyses, and the study was conducted according to the principles of the Declaration of Helsinki and the Dutch Medical Research Involving Human Subjects Act. The POLDER study is registered in the Netherlands Trial Registry (trialsearch.who.int: NTR7310).

RESULTS

Hospital participation

Ten of the 16 initially approached centers implemented NGA practices, while 5 declined because of a lack of reimbursement and personnel shortages. Two nephrology units independently agreed to participate but later merged into one. Implementation started between October 2018 and March 2020, with the study start and inclusion period extended because of logistic and COVID-19–related challenges, and patient inclusion concluded in April 2021.

Geriatric tests were conducted by a nephrology nurse (practitioner) (N=6 centers, 60%), a geriatrician or geriatric nurse (N=3, 30%), or a research nurse (N=1, 10%), see Table S2. Visits for the geriatric tests were combined with regular nephrology appointments at most centers (N=9, 90%). Patient questionnaires were sent in advance of their visit for at-home completion or given afterward. Approximately 15% (n=28) of patients digitally entered their questionnaires; this was done at 7 centers (ranging from 8%-38% per center). At 9 centers, outcomes were discussed in multidisciplinary team meetings with geriatric expertise involved in 7 settings. One center conducted meetings if geriatric impairments that needed further involvement of a geriatrician were detected.

Patient inclusion and -characteristics

A total of 194 patients gave informed consent, with 3 unable to participate because of deteriorating health status (n=2, 1%) or no-show (n=1, 0.1%). NGA was performed in 191 patients. Participation varied between n=10 and n=30 per hospital. Most participants were men (n=135, 71%). Median age was 77.5 (interquartile range, 74.3-81.9) years, and mean eGFR at the time of NGA was 15.0 ± 4.4 (SD) mL/min/1.73 m^2.

Completeness of NGA

In total, 187 patients (98%) returned the patient questionnaire. All but one patient (n=190, 99%) finalized the provider-administered test set. Table S3 reports completeness of the NGA instruments.

Somatic instruments were completed by all patients. Over 90% of the patients completed measures for activities of daily living, fall risk, 6-item Cognitive Impairment Test, Montreal Cognitive Assessment (MoCA), Letter Digit Substitution Test, and depressive mood. Measures of caregiver burden and nutritional status were conducted in 64% (n=121) and 82% (n=156) of the patients and were less often completed (60% and 66%, respectively).

Survey respondents' characteristics

Of 81 invited healthcare professionals, 71 responded (88% response rate). Table 3 summarize the survey respondent characteristics, with a median of 6 professionals (range, 5-12) participating per hospital.

Table 3: Survey responders' characteristics and outcomes

Survey participant characteristics	n= 71
Respondents per participating hospital, median (range)	6 (5-12)
Working experience (y), median (range)	
in current profession	9 (1-30)
in current department	8 (1-39)
Clinical role, n (%)	
Nephrologist	27 (38)
Geriatrician	10 (14)
Nurse practitioner [a]	10 (14)
Nurse (nephrology)	11 (16)
Nurse (geriatrics / geriatrics-nephrology)	2 (3)
Physician assistant (nephrology)	1 (1)
Social worker	7 (10)
Dietician	2 (3)
Research nurse	1 (1)

[a] Including one respondent in training.

Enablers and barriers to implementation

The most frequently cited top 3 enablers for successful implementation included collaboration with geriatric department (n=45, 76%), multidisciplinary meetings and reports (n=39, 66%), assessment performed by nurses (practitioners) (n=26, 44%), and discussion of purpose and outcomes of the test with patients (n=26, 44%). Common barriers to implementation included patient illiteracy or non-Dutch speaking (46% of respondents' top 3 barriers, n=25), lack of time (n=20, 37%), burden for patients (n=20, 37%), and lack of patients' willingness or eagerness to participate in NGA (n=17, 31%). The open-ended questions showed concerns on patient burden: difficulty of NGA questions (Table S4, Q41), the toll (ie, time and burden) of hospital visits (Table S4, Q42), and the negative connotation of "geriatric assessment" (Table S4, Q43 and Q44). Table 4 presents the respondents' agreement on the presence of

implementation enablers and barriers. Interestingly, respondents reported that patients were often willing to participate in NGA (mean score as enabler, 6.9/10 ± 1.68), although this was frequently cited as a top 3 barrier.

Integration in work routines

The general NoMAD questions indicated that NGA was not fully embedded at the time of the survey (mean, 6.9/ 10 ± 2.01 versus mean, 6.7 ± 1.42; P < 0.001). Figure 2 presents responses to each of the NoMAD questions. Although 97% (n=69) recognized the potential value of NGA and 96% (n=49) continued to support it, there were opportunities to enhance integration, according to 97% (n=65). Table S4 and Figure S1 show the mean NoMAD (sub-) construct scores and qualitative analysis of the open-ended survey questions. Respondents found NGA meaningful (Sense Making mean score, 4.6 ± 0.59) and were committed to making it work (Cognitive Participation mean score, 4.6 ± 0.50). To a somewhat lesser extent, the respondents acknowledged the efforts of working together to make NGA work (Collective Action mean score, 4.1 ± 0.66) and appraised the effect of NGA (Reflexive Monitoring mean score, 4.3 ± 0.64). Concurrently, respondents recognized the potential improvement of sufficient training, resources, and knowledge about the effects of NGA, indicated by mean scores of <4 for the subcon-structs of skill set workability, contextual integration, and systemization (Figure S1). The open-ended questions showed that nurses' lack of time and availability hampered integration in routine work (Table S3, Q12), and suggested improvements such as reducing the number of tests (Table S3, Q36-Q39), and improvement of interdisciplinary cooperation (Table S3, Q28 and Q29).

Perceived relevance of the NGA instruments to CKD patient care

Healthcare professionals perceived NGA instruments as successful in reaching the intervention objective and its aimed effects, with an overall score of 7.8/10 ± 1.16. The relevance of each included instrument is shown quantitatively in Table 5 and qualitatively in Table S5. Providers rated the relevance of the MoCA and the Clinical Frailty Score as high (mean, 4.5/5 ± 0.60 and mean, 4.4 ± 0.69, respectively), while they appraised polypharmacy and the Life Orientation Test as less relevant (mean, 3.5 ± 0.98 and mean, 3.6 ± 0.79, respectively). Less than 70% of the users were convinced of the relevance of the latter 2 instruments and handgrip strength, Letter Digit Substitution Test, and the Patient Generated-Subjective Global Assessment.

Perceived relevance to the target group.

Survey respondents had varying opinions on age and kidney function cutoffs for NGA practices. Cutoffs of >70 years and eGFR of <20 mL/min/1.73 m2 were too narrow for 24% (n=16) and 18% (n=12), good for 67% (n=44) and 69% (n=45), and too broad for 9% (n=6) and 12% (n=8), respectively. Several respondents qualitatively addressed that NGA should be tailored to each patient's situation, considering the progression of CKD, clinical judgment, and biological age rather than calendar age or kidney function.

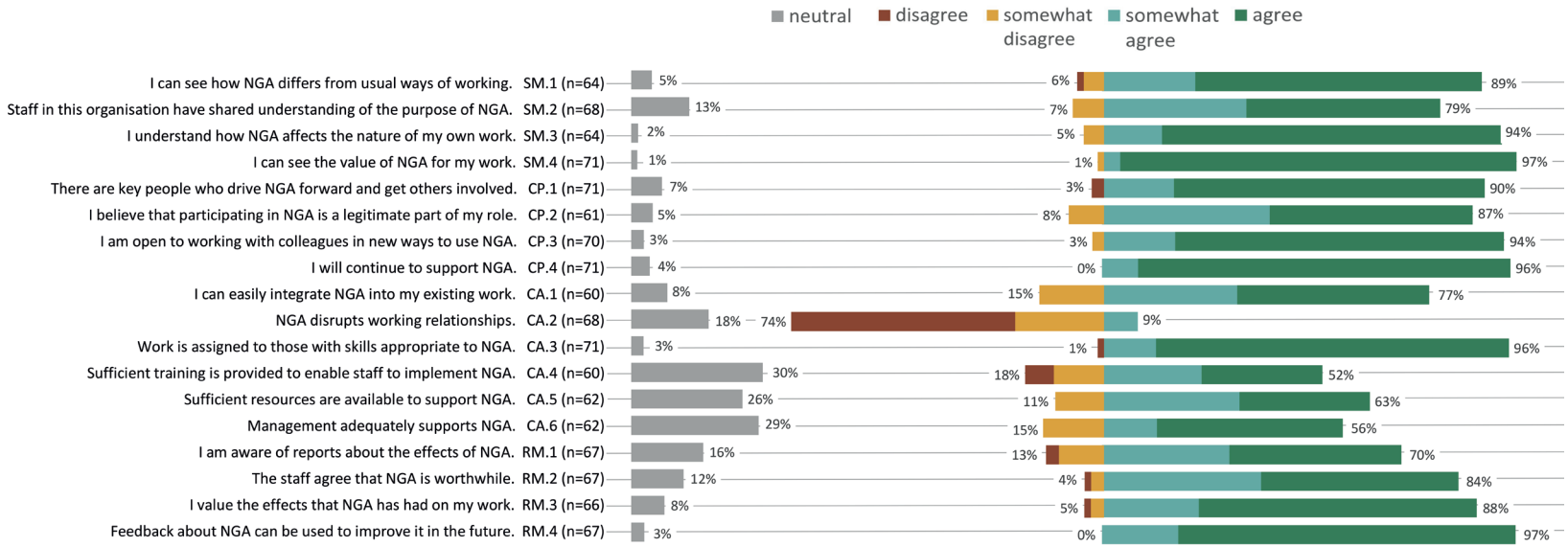
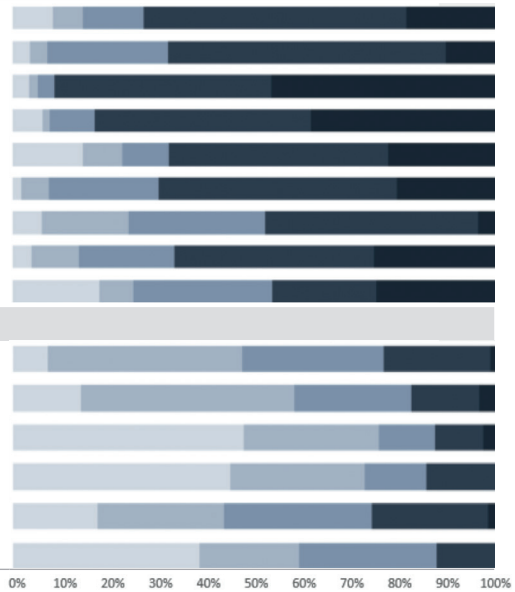


Figure 2. Response to statements on normalization of NGA.

Figure bars show the percentage of respondents reporting their agreement with the NoMAD statements. The number of respondents lower than n=71 bypassed the statement by indicating "not relevant for my role." Questions relate to the constructs of the NPT framework, ie, SM: sense making, CP: cognitive participation, CA: collective action, and RM: reflexive monitoring. Abbreviations: NGA, nephrology-tailored geriatric assessment; NoMAD, Normalization measure development; NPT, normalization process theory.

Table 4: Presence of enablers and barriers of implementation of the NGA, and those most frequently rated for successful implementation.

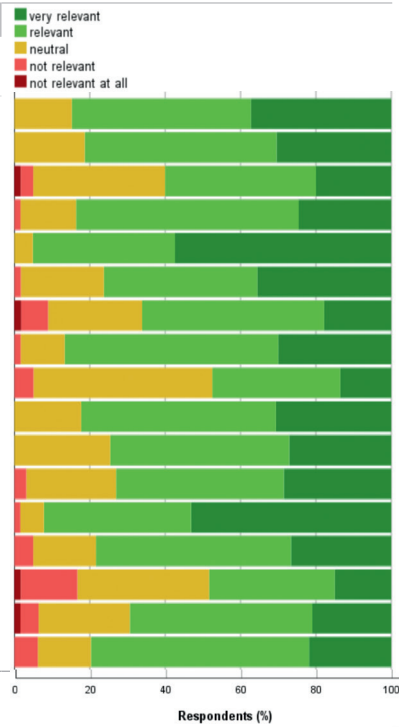
	The following reasons may have led to good or less good implementation. In your experience, were these reasons present in your hospital's NGA performance?	N	Agreement, mean ± SD	Presence
	Enablers			Totally disagree (1) — Totally agree (10)
☺	**The purpose and results of the tests were discussed in detail with the patient**	48	6.8 (2.09)	
☹	**Patients were willing and available for the geriatric assessment**	56	6.9 (1.68)	
☺	**Good cooperation with geriatrics department**	58	8.1 (1.79)	
☺	**Multidisciplinary consultation and reports in which NGA outcomes and treatment policy were discussed**	65	7.7 (2.03)	
	Support from other disciplines (e.g. dietitian, social worker) in the administration and interpretation of NGA	62	6.6 (2.77)	
☺	**Suitable (and trained) personnel were sufficiently available to administer the NGA**	53	7.2 (1.91)	
	The outpatient schedule was easy to adjust for NGA administration	50	6.0 (2.04)	
	Management supports the implementation of the NGA	51	6.9 (2.22)	
	The sum-score forms in the dashboard (available from July 2020) were helpful	28	6.1 (2.81)	
	Barriers			
☹	**The NGA is too much of a burden for many patients**	55	4.8 (1.81)	
☹	**NGA was performed to a limited extent because many patients had low health literacy or due to a language barrier**	50	4.5 (1.88)	
	Reluctance in the Nephrology department to involve geriatrics/elderly care in routine care	61	3.3 (2.35)	
	Loss of geriatric knowledge and practical skills (for example due to team changes)	47	3.3 (2.25)	
☹	**Time constraints restricted carrying out the NGA**	46	4.7 (2.32)	
	Lack of budget is a reason to carry out NGA less often or adequately.	39	3.6 (2.28)	



Notes: Both enablers and barriers are sorted by respectively: patient-related, multidisciplinary cooperation and organizational aspects. Score range: 1 (totally disagree) to 10 (totally agree). Four enablers (☺) and 4 barriers (☹) that were most frequently in respondents' top 3 for successful implementation. One enabler was mentioned as determinant in the top 3 barriers for implementation.
Abbreviations:NGA,nephrology-tailored geriatric assessment.

Table 5: Appraisal of relevance of the instruments included in the NGA.

		Survey outcomes				
Domain	**Instrument**	**Respondents (n)**	**Relevance score* mean (SD)**	**Not relevant n (%)**	**Neutral n (%)**	**Relevant n (%)**
Functional status	Activities of daily living (Katz ADL-6)	59	4.2 (0.70)	0 (0%)	9 (15%)	50 (85%)
	Instrumental Activities of daily living (Lawton)	59	4.1 (0.70)	0 (0%)	11 (19%)	48 (81%)
	Handgrip strength	60	3.7 (0.88)	3 (5%)	21 (35%)	36 (60%)
	Fall risk assessment	61	4.1 (0.68)	1 (2%)	9 (15%)	51 (84%)
Cognitive functioning	Montreal Cognitive Assessment	61	4.5 (0.60)	0 (0%)	3 (5%)	58 (95%)
	6-item Cognitive Impairment Test	59	4.1 (0.80)	1 (2%)	13 (22%)	45 (76%)
	Letter Digit Substitution Test	56	3.7 (0.90)	5 (9%)	14 (25%)	37 (66%)
Psychological status/mood	Whooley-questions / Geriatric Depression Scale-15	60	4.2 (0.81)	1 (2%)	7 (12%)	52 (87%)
	Life Orientation Test-Revised	59	3.6 (0.79)	3 (5%)	28 (47%)	28 (47%)
PROM's	HRQoL: 12-item Short Form Health Survey	62	4.1 (0.69)	0 (0%)	11 (18%)	51 (82%)
	Dialysis Symptom Index	59	4.0 (0.73)	0 (0%)	15 (25%)	44 (75%)
Somatic status	Surprise question	63	4.0 (0.81)	2 (3%)	15 (24%)	46 (73%)
	Clinical Frailty Score,	64	4.4 (0.69)	1 (2%)	4 (6%)	59 (92%)
	Charlson Comorbidity Index	60	4.0 (0.80)	3 (5%)	10 (17%)	47 (78%)
	Polypharmacy	60	3.5 (0.98)	10 (17%)	21 (35%)	29 (48%)
Nutrition	Patient-Generated Subjective Global Assessment	62	3.8 (0.88)	4 (6%)	15 (24%)	43 (69%)
Social	Caregiver burden: SPICC-plus	64	4.0 (0.79)	4 (6%)	9 (14%)	51 (80%)



Note: The percentages in the fifth to seventh column do not add up to exactly 100% due to rounding differences.
Abbreviations: HRQoL, health-related quality of life; PROMs, patient-reported outcome measures; SPICC, self-perceived pressure from informal care.
* Scoring was done on a 5-point Likert scale: 1 (not at all relevant) to 5 (very relevant).

DISCUSSION

Our findings demonstrate the feasibility of implementing NGA in older patients with advanced CKD. Furthermore, they offer recommendations for extending guidance on how to integrate geriatric assessment in nephrology care. We identified determinants of successful implementation and barriers. Collaborative involvement from the geriatrics department, nurse practitioners, and multidisciplinary meetings enhanced implementation, while limited collective action, lack of time and personnel, and patient-related factors, such as burden and low literacy, hampered it. Integration of NGA into work routines could be enhanced because it was not yet fully integrated. Nonetheless, healthcare professionals recognized its relevance in care of patients with CKD.

Our findings contribute to the emergence of models for integrating geriatric care into hospital practices,[42,43] gaining recognition for geriatric assessment as a predictive and rehabilitative instrument for older patients across various medical disciplines. Compared with oncology[42] and acute care patients, care of patients with CKD involves longer-standing patient–provider relationships and generally longer-lasting decision trajectories. However, impairments, primarily cognitive problems, often go unnoticed in patients with CKD.[3] Therefore, geriatric assessment should focus on detecting and managing such impairments and also on adapting how education and information on treatment selection is delivered. Similar to other medical fields, substantial implementation barriers were recognized, mainly concerning practicalities and resources such as time constraints and unavailability of healthcare personnel.[42,44,45]

Our study provides a practical example of the previously recognized need to integrate standardized geriatric assessment into routine nephrology practice.[3,46-50] Our insights extend the paucity of guidance on the incorporation of geriatric assessment in nephrology care.[13,51] Predominantly, collaboration with the geriatric department appears to be essential because it provides expertise for advice and referrals for management of identified impairments.[13,15,16] Although the extent of geriatrics involvement may vary from overseeing all NGA practices to availability for referrals only, both are viable approaches.[13]

To improve integration of NGA in work routines, our results showed that collective action (ie, how people work together to make NGA practices work) deserves attention. Our study found that implementation often relied on one or a few key persons, which makes maintenance of NGA practices vulnerable. Evidence regarding the benefits and use of NGA would help to improve collective action. Related to the latter, discussion of carefully summarized results of NGA in multidisciplinary team meeting (including geriatric healthcare professionals) is essential.[34,44,52] This will help to create awareness on the presence and relevance of detected cognitive and functional impairments and implications for treatment and supportive care.

A potential facilitator for implementation into routine nephrology care may be the integration of summarized NGA outcomes in electronic patient files. This may increase multidisciplinary use of recurring geriatric assessment and support its interpretation. In oncology, a tailored geriatric assessment summary with guided recommendations has facilitated and improved patient care,[53] and web-based applications for geriatric assessment seem promising.[54,55] Involvement of older (CKD) patients in future research and development of digital tools is desired.[56]

The negative effect of patient burden on implementation was noted, as in previous studies.[34,42,57] Therefore, it is essential to integrate NGA in regular nephrology hospital visits and limit the frequency and duration of prolonged hospital visits. Adjustments to NGA practices for individual cases may be necessary and helpful, whereas refinement of the assessment by modifying the test set can also improve acceptance and implementation.

In absence of a gold standard,[58] our test set was derived in a foregoing pragmatic consensus trajectory.[11] If time for assessment practices is limited, some instruments could be considered for omission or substituted with shorter instruments, preferably only after the discriminative and predictive value of the tests is investigated in the CKD stage G4-G5 population. For example, polypharmacy was irrelevant to a substantial part of our NGA users, potentially because of overlap with repeated attention to this topic in routine medical care. The instrument on nutrition (Patient Generated-Subjective Global Assessment) showed considerable incompleteness and perceived irrelevance in our study, potentially because of inconvenient usage and overlapping practices of dieticians who already have a clearly defined role in multidisciplinary management of patients with CKD in routine care. In addition, the Life Orientation Test, Letter Digit Substitution Test, and handgrip strength were perceived less relevant to the professionals. Based on our evaluation and other literature,[15,59-62] both the Clinical Frailty Score[30] and MoCA[21] are a relatively new to outpatient nephrology care but may be promising instruments. The caregiver burden (Self-Perceived Pressure from Informal Care) questionnaire, though perceived relevant to professionals, reported considerable incompletion, which was to a large extent explained by those patients that did not need caregiver support.

Further development of NGA should focus on inclusiveness by incorporating linguistic and cultural factors.[34,42,57] Although illiteracy was an exclusion criterion for the present study, apparently, healthcare professionals determined that assessment was still too elaborate for some patients. In our view, low health literacy as a barrier to implementation of geriatric assessment has been underreported in scientific studies.

Flexibility in adapting the abovementioned fixed parts of NGA according to organizational circumstances, resource constraints, and patient profile has proven advantageous for successful implementation.[45,63]

A strength of our study is that we are among the first to explore and report multicenter implementation of geriatric assessment in routine CKD care quantitatively, enriched by an explanatory qualitative analysis. Although NGA implementation was feasible for hospital participation, we fell short of our patient inclusion goal in half of the centers. This was due to incomplete integration of NGA practices, the effect of the COVID-19 pandemic, and scientific study formalities. However, the subsequent DIALOGICA (Dialysis or Not: Outcomes in Older Kidney Patients With Geriatric Assessment) study64 now involves 35 centers and >600 patients, showcasing widespread feasibility.65 Limitations of our study are that we did not structurally collect data on the management plan of identified geriatric impairments (eg, outcomes of multidisciplinary team meetings and follow-up of patients). We also did not include an economic component or use a randomized controlled or pre- or postsurvey design. This prevents us from drawing conclusions regarding efficacy, effectiveness, and efficiency of NGA practices. Furthermore, survey responders were committed to this topic, which may have led to bias toward positive outcomes. However, no financial incentives or

inclusion fees were provided. Activities were organized in daily practices. Although some hospitals made use of local research departments for data entry and study-related logistics, this was outside the scope of the current implementation study but may have influenced implementation.

Future research should evaluate implementation of management of geriatric impairments and establish the efficacy of geriatric practices in nephrology,[66] as was done in other medical fields.[67,68] Also, the acceptability from patient perspective[34] and the use of cross-cultural in-struments[57] needs further investigation.

CONCLUSIONS

In conclusion, geriatric assessment could successfully be integrated in CKD care and is perceived as relevant by partaking healthcare professionals.

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SUPPLEMENTARY FILES – Item S1: Visualization of individuals' NGA results summary.

An individual's NGA results summary for (A) the provider-administered test set and (B) the patient questionnaire has been available for download after data entry in the online dashboard since July 2020.

A

Geriatric assessment scores

Below you will find an overview of the scores of the professional-administered tests used in the POLDER study. Please note, the explanation in the third column (interpretation) is not intended as a clinical cut-off point for diagnosis or the use of interventions. Always take into account the overall picture and clinical judgment.

Patient: 9002, female, 81 jaar (+/- 1 jaar), education level: low

Inclusion date: 12-12-2020

Measurement: baseline (date: 16-2-2021)

Clinical judgement	Score	Score range (interpretation)
Surprise question	1x ja / 3x nee	
Clinical frailty scale	6 (moderate frailty)	1 - 9 (1=very fit, 9=terminally ill)
Comorbidity		
Charlson score (not age-adjusted)	6	0 - 33
Mental functioning		
MOCA score	26	0 - 30 (≥26 is considered not impaired) [1]
Six Item Cognitive Impairment Test	10	0 - 28 (≥11 suggest moderate to severe impairment of cognitive functioning) [2]
Letter digit substitution test Correct after 60 sec	25 (=p76)	Percentile based on age, gender and education level [3]
Depression / mood		
GDS-2/Whooley questions, count 'yes'	1	0 - 2 (if score is 0, GDS-15 is not assessed)
GDS-15 score	6	0 - 15 (≥6 possible depression) [4]
Physical functioning		
Maximum handgrip strength	32 (=p90)	0-60 kg, higher indicates more strength. Percentile based on age and gender [5]
Fall history	Yes	Past year ≥1 times fallen
Fall anxiety score	8	1-10 (1=no fear, 10=very afraid)
Nutritional status (PG-SGA)		
Total worksheet 1 to 4	24	0-52 (≥9 possible nutritional interventions needed) [6]
Global staging	A (well nourished)	Stage A (well nourished) Stage B (moderately malnourished) Stage C (severely malnourished)

References: [1] MOCA: Nasreddine et.al. (2005, J Am Geriatr Soc), [2] 6-CIT: Van Tuijl et al. (2002, Int J Ger Psych), [3] LDST: Van der Elst et al. (2006, J Clin Exp Neuropsychol), [4] GDS-15: Dennis et al. (2012, Age Ageing), [5] Handgrip strenght: Dodds et al. (2014, Plos One), [6] PG-SGA: Koster et al. (2020, Nutrition)

B

POLDER

Patient questionnaire scores

Below you will find an overview of the scores from the patient questionnaire of the POLDER study.

Study id: 9002

Inclusion date: 12-12-2020

Measurement: baseline (date: 16-2-2021)

Heath-related quality of life	Score	Score range (interpretation)
SF12 – physical component	40,4	Higher score indicates better well-being (50,3 general Dutch population [1] 35,6 dialysis patients [2])
SF12 – mental component	41,6	Higher score indicates better well-being (52,9 general Dutch population [1] 47,7 dialysis patients [2])
DSI - Dialysis Symptom Index:count 'yes'	6 symptoms	See specific symptoms on next page
Mental functioning		
Optimism (Life-orientation test)	Not calculated due to missing items	0-24 (higher scores indicates higher optimism, average score general population: 16.2) [3]
Physical functioning		
Katz-ADL6	2, somewhat dependent (≥2)	0-6 (≥2: somewhat, ≥4: moderately, 6: complete dependent)
IADL-Lawton	5	0-8 for females (higher score is less dependent)
Nutritional status (PG-SGA)		
Nutritional status (patient part)	8	0-36 (≥ 6 indicates malnutrition) [4]
Caregiver burden		
Caregiver burden (SPICC-plus)	2, minor burden	0-15 (0: no burden (21%), 1-3: minor burden (33%), 4-8: moderate burden (27%), 9-15: severe burden (19%) [5]

References: [1] CBS Statistics Netherlands (2009), [2] Pilot PROMs-NNL, Nefrovisie (2017), [3] Optimism (LOT-R): Hinz et al. (2017, J Clin Health Psychol), [4] PG-SGA-SF: Kosters et al. (2020, Nutrition), [5] SPICC-plus: De Boer et al. (2012, Tijdschr Gerontol Geriatr)

Symptoms experienced in past week	Symptom presence, burden
1. Constipation	No
2. Nausea	No
3. Vomiting	No
4. Diarrhea	No
5. Decreased appetite	No
6. Muscle cramps	No
7. Swelling in legs	No
8. Lightheadedness or dizziness	No
9. Shortness of breath	No
10. Restless legs or difficulty keeping legs still	No
11. Numbness or tingling in feet	Yes, a little bit
12. Feeling tired or lack of energy	No
13. Cough	No
14. Dry mouth	No
15. Bone or joint pain	No
16. Chest pain	No
17. Headache	No
18. Muscle soreness	No
19. Difficulty concentrating	No
20. Dry skin	No
21. Itching	No
22. Worrying	No
23. Feeling nervous	No
24. Trouble falling asleep	No
25. Trouble staying asleep	No
26. Feeling irritable	Yes, a little bit
27. Feeling sad	Yes, a little bit
28. Felling anxious	Yes, somewhat
29. Descreased interest in sex	Yes, a little bit
30. Difficulty becoming sexually aroused	Yes, a little bit
Other symptom 1:	
Other symptom 2:	
Other symptom 3:	

Item S2: Post-implementation survey distributed among health-professionals; translated from Dutch

Supplement File 2: Post-implementation survey amongst health care professionals
Translated from Dutch.

POLDER Evaluation: implementation of NGA

Start of Block: Consent

Consent Form

Thank you for participating in the evaluation of the nephro-geriatric assessment (NGA) in the POLDER study. Your opinion on this innovation in kidney failure care is essential!

This POLDER sub-study aims to:

1. Evaluate the implementation of nephro-geriatric assessment (NGA) in routine care for patients with kidney failure
2. Improve the test set.

The questionnaire consists of 6 parts: *integration of NGA in routine care (using the validated NoMAD questionnaire), contribution of NGA to routine care, reasons for successful or limited implementation, evaluation of the specific instruments in the NGA, improvements for NGA practices, and general data.*

It takes about 15 minutes to complete the multiple choice questions and scoring statements. Optionally, you can provide us additional explanations. We process your data in such a way that the answers cannot be traced back to you personally. This applies to both the report to the funder (Kidney Foundation) and the scientific article.

Would you like to have more information? Please see full information letter at our website: *www.polderstudie.nl/nl/over-polder/evaluatie*

Do you give permission for the use of your answers for this research and their (scientific) publication?

○ Yes, I give permission

○ No, I don't give permission < end of questionnaire>

Supplement File 2: Post-implementation survey amongst health care professionals
Translated from Dutch.

Explanation:

Definition Nephro-Geriatric Assessment (NGA):
he questionnaire is about 'embedding NGA in routine care'. This includes the patient questionnaire and the professional-administered test set of POLDER study, and using the results of these tests in CKD-care.

The NGA test set comprised of different domains and instruments:

- physical functioning: hand grip strenght, (instrumental) Activities of Daily Living, risk of falling,
- cognitive functioning: MoCA, 6-CIT, Letter Digit Substitution Test,
- mood: geriatric depression scale, optimism,
- somatic: Clinical Frailty Scale, Charlson Comorbidy Index, polypharmacy,
- nutritional status: PG-SGA,
- PROMs: quality of life, symptoms,
- caregiver burden: EDIZ-plus.

Assessment may have been done with interference of the geriatrician. Ideally, the results should be discussed with the patient in a multidisciplinary consultation.

End of Block: Consent

Supplement File 2: Post-implementation survey amongst health care professionals
Translated from Dutch.

Start of Block A: General data

Q1 What is your profession?

- ○ Nephrologist
- ○ Geriatrician / internist-geriatrician
- ○ Nurse practitioner, discipline: _____
- ○ Nephrology nurse
- ○ Geriatric nurse
- ○ Dietician
- ○ Social worker
- ○ Research nurse
- ○ Other, please specify: _____

Q2 How many years of work experience do you have in this position?

_____

Q3 How many years have you been working for this department in this hospital?

_____

Q4 Through which hospital are you connected to POLDER?

<multiple choice answer option for all 10 hospitals>

Q5 Have you been directly involved in the design and/or implementation of the NGA in your hospital?

Yes / No

End of Block A: General data

Start of Block B: Integration in routine care (NoMAD questionnaire)

Supplement File 2: Post-implementation survey amongst health care professionals
Translated from Dutch.

Q6 When you use the nephro-geriatric assessment, how familiar does it feel?

Not at all familiar — Neutral — Feels completely familiar

(0) (1) (2) (3) (4) (5) (6) (7) (8) (9) (10)

Q7 Do you feel the nephro-geriatric assessment is currently a normal part of your work in care for older CKD patients?

No, not at all — Neutral — Yes, completely

(0) (1) (2) (3) (4) (5) (6) (7) (8) (9) (10)

Q8 Do you feel the nephro-geriatric assessment will become a normal part of your work in care older CKD patients?

No, not at all — Neutral — Yes, completely

(0) (1) (2) (3) (4) (5) (6) (7) (8) (9) (10)

Q10 For each statement please select an answer that best suits your experience. If the statement is not relevant to you please select *'not relevant to my role'*.

	Disagree (1)	Somewhat disagree (2)	Neither agree nor disagree (3)	Somewhat agree (4)	Agree (5)	Not relevant to my role
1. I can see how the NGA differs from usual ways of working in the kidney failure outpatient clinic.	○	○	○	○	○	☐
2. Staff in this organization have a shared understanding of the purpose of NGA.	○	○	○	○	○	☐
3. I understand how the nephro-geriatric assessment affects the nature of my work at the kidney failure outpatient clinic.	○	○	○	○	○	☐
4. I can see the potential value of the nephro-geriatric assessment for my work in older CKD patient care.	○	○	○	○	○	☐

Q11 Could you briefly elaborate your answers? (optional)

_____

_____

Supplement File 2: Post-implementation survey amongst health care professionals
Translated from Dutch.

Q12

	Disagree (1)	Somewhat disagree (2)	Neither agree nor disagree (3)	Somewhat agree (4)	Agree (5)	Not relevant to my role
5. There are key people who drive the NGA forward and get others involved.	○	○	○	○	○	☐
6. I believe that participating in the NGA is a legitimate part of my role.	○	○	○	○	○	☐
7. I'm open to working with collegues in new ways to use the NGA.	○	○	○	○	○	☐
8. I will continue to support the NGA.	○	○	○	○	○	☐

Q13 Could you briefly elaborate your answers? (optional)

Who are the key people?
Why do you support the NGA, or not?
What is your motivation for performing the NGA?

_____

_____

Supplement File 2: Post-implementation survey amongst health care professionals
Translated from Dutch.

Q14

	Disagree (1)	Somewhat disagree (2)	Neither agree nor disagree (3)	Somewhat agree (4)	Agree (5)	Not relevant to my role
9. I can easily integrate the NGA into my existing work.	○	○	○	○	○	☐
10. The NGA disrupts working relationships.	○	○	○	○	○	☐
11. Work is assigned to those with skills appropriate to the NGA.	○	○	○	○	○	☐
12. Sufficient training is provided to staff to implement NGA.	○	○	○	○	○	☐
13. Sufficient resources are available to support the NGA.	○	○	○	○	○	☐
14. The management adequately supports NGA.	○	○	○	○	○	☐

Q15 Could you briefly elaborate your answers? (optional)

If the nephro-geriatric assessment is not easy to integrate; Why not?
Why does NGA disrupt working relationships? What do you run into?
What additional support would you need to make NGA implementation feasible?
How relevant, necessary and complete did you find the training?

_____

_____

Supplement File 2: Post-implementation survey amongst health care professionals
Translated from Dutch.

Q16

	Disagree (1)	Somewhat disagree (2)	Neither agree nor disagree (3)	Somewhat agree (4)	Agree (5)	Not relevant to my role
15. I am aware of the reports about the effects of NGA.	○	○	○	○	○	□
16. The staff agree that the NGA is worthwile.	○	○	○	○	○	□
17. I value the effects that the NGA has had on my work.	○	○	○	○	○	□
18. Feedback about the NGA can be used to improve it in the future.	○	○	○	○	○	□

Q17 Could you briefly elaborate your answers? (optional)

If colleagues do not agree with the NGA, where is the discussion?
If NGA is worth it, what are the most important points of added value?
What adjustments to the NGA would you like?

_____

_____

End of Block B: integration in routine care (NoMAD questionnaire)

Supplement File 2: Post-implementation survey amongst health care professionals
Translated from Dutch.

Start of Block C: *contribution of NGA to routine care*

Q18 The NGA supports in..:

1. ..the identification and objectivation of, otherwise unnoticed, impairments
[if not applicable for your role: plaese leave score blank]

Strongly disagree (0) (1) (2) (3) (4) (5) (6) (7) (8) (9) (10) Strongly agree

2. .. adjusting or supplementing treatment strategies.

Strongly disagree (0) (1) (2) (3) (4) (5) (6) (7) (8) (9) (10) Strongly agree

3. ..inform in decision-making for choice of therapy.

Strongly disagree (0) (1) (2) (3) (4) (5) (6) (7) (8) (9) (10) Strongly agree

End of Block C: *contribution of NGA to routine care*

Supplement File 2: Post-implementation survey amongst health care professionals
Translated from Dutch.

Start of Block D: instruments of the NGA

Q19 Starting from the 3 just mentioned objectives of the NGA (identifying and objectifying impairments, determining supportive treatment strategies, informing decision-making for choice of kidney replacement therapy).

How relevant are the specific instruments from the test set for your role in kidney patient care?

(Please fill in your judgment and motivation)

	Not relevant at all	Not relevant	Neutral	Relevant	Very relevant	motivation:	Not relevant to my role:
Handgrip strenght	O	O	O	O	O	....	☐
Fall risk assessment	O	O	O	O	O	....	☐
MoCA (cognition)	O	O	O	O	O	....	☐
6-CIT (6-item cognitive impairment test)	O	O	O	O	O	....	☐
Letter Digit Subsitution Test (cognition)	O	O	O	O	O	....	☐
Depression-questions (GDS2/15)	O	O	O	O	O	....	☐
Surprise question *("I would be surprised if patient died after 12 months")*	O	O	O	O	O	....	☐
Frailty score	O	O	O	O	O	....	☐
Comorbidity index (Charlson)	O	O	O	O	O	....	☐
Polypharmacy (>5 medications)	O	O	O	O	O	....	☐
Nutritional status (PG-SGA)	O	O	O	O	O	....	☐
Caregiver burden (Ediz-plus)	O	O	O	O	O	....	☐

Supplement File 2: Post-implementation survey amongst health care professionals
Translated from Dutch.

Q20 Starting from the 3 just mentioned objectives of the NGA (identifying and objectifying impairments, determining supportive treatment strategies, informing decision-making for choice of kidney replacement therapy).

How relevant are the specific tools of the patient-questionnaire for your role in kidney patient care?

(Please fill in your judgment and motivation)

	Not relevant at all	Not relevant	Neutral	Relevant	Very relevant	motivation:	Not relevant to my role:
Katz ADL-6 (functioning)	O	O	O	O	O	....	☐
Lawton iADL (functioning)	O	O	O	O	O	....	☐
Optimism check	O	O	O	O	O	....	☐
Quality of Life (SF-12)	O	O	O	O	O	....	☐
Dialyse symptom index	O	O	O	O	O	....	☐

End of Block D: instruments of the NGA

Supplement File 2: Post-implementation survey amongst health care professionals
Translated from Dutch.

Start of Block E: Reasons for successful or limited implementation

Q21 The reasons below may have been reason for good or limited implementation. Please indicate, from your experience, were these reasons present when the NGA was performed in your hospital?

Patient-related factors

	Not at all present 1 2 3 4 5 6 7 8 9 10 Strongly present	Not applicable to my role
The purpose and results of the tests were discussed in detail with the patient		☐
Patients were willing and available for the geriatric assessment		☐
The NGA is too much of a burden for many patients		☐
NGA was performed to a limited extent because many patients had low health literacy or due to a language barrier		☐

Multidisciplinary cooperation

	Not at all present 1 2 3 4 5 6 7 8 9 10 Strongly present	Not applicable to my role
Good cooperation with geriatrics department		☐
Reluctance in the Nephrology department to involve geriatrics/elderly care in routine care		☐
Multidisciplinary consultation and reports in which NGA outcomes and treatment policy were discussed		☐
Support from other disciplines (e.g. dietitian, social worker) in the administration and interpretation of NGA		☐
Loss of geriatric knowledge and practical skills (for example due to team changes)		☐

Supplement File 2: Post-implementation survey amongst health care professionals
Translated from Dutch.

Organizational factors

	Not at all present 1 2 3 4 5 6 7 8 9 10 Strongly present	Not applicable to my role
Suitable (and trained) personnel were sufficiently available to administer the NGA		☐
The outpatient schedule was easy to adjust for NGA administration		☐
Management supports the implementation of the NGA		☐
Time constraints restricted carrying out the NGA		☐
Lack of budget is a reason to carry out NGA less often or adequately.		☐
The sum-score forms in the dashboard (available from July 2020) were helpful		☐

Q22 Do you have any additional explanation about reasons for successful or limited implementation? (optional)

_____

_____

_____

Q23 What are the 3 most important for limited and successful implementation of NGA in your hospital?

Choose from the above reasons or fill in yourself. Please drag the reasons to the boxes.

Discuss purpose and goal with patient
Patient burden
Low health literacy or language barrier
Patient willingness to participate
Cooperation with geriatrics department
Multidisciplinary meetings and repots
Execution of NGA by nurses or nurse practitioners
Execution of NGA other disciplines: e.g social work, dietician, ...
Loss of knowledge (e.g. due to team changes)
Outpatient schedule could (not) be adjusted
Involved key person, i.e. discipline…
Management support
Time (constraints)
Budget (constraints)
(non) availability of digital forms with NGA scores
Other reasons:....

3 reasons for limited implementation:

1.
2.
3.

3 reasons for successful implementation

1.
2.
3.

End of Block: Deel E: Redenen voor goede of minder goede implementatie van NGA in routine zorg

Supplement File 2: Post-implementation survey amongst health care professionals
Translated from Dutch.

Start of Block F: verbeteringen van het geriatrisch assessment

Q24 What is your opinion on the frequency and target group of the geriatric assessment in the POLDER study?

	too little/narrow	just right	too expanded
Frequency: once a year	○	○	○
Target group: age limit 70+	○	○	○
Target group: kidney function <20mL/min/1.73m2	○	○	○

Q25 Please elaborate briefly (optional):

_____

_____

_____

Q26 Finally, do you have any other suggestions or comments about the nephro-geriatric assessment or the POLDER study?

_____

_____

_____

This is the end of the questionnaire. If you have any questions or comments, please refer these to <email address>.

Thank you very much for your cooperation!

End of Questionnaire:

Table S1: Constructs of integration in work routines, assessed with the NoMAD tool

Construct	Explanation	Contains subconstructs (question number)[a]	Question label in survey [b]
Sense making	how people make sense of what needs to be done.	*Differentiation (*SM1), *Communal specification* (SM2), *Individual specification* (SM3), *Internalization* (SM4)	Q10
Cognitive participation	how relationships with others influence outcomes	*Initiation* (CP1), *Legitimation* (CP2), *Enrolment* (CP3), *Activation* (CP4)	Q12
Collective action	how people work together to make practices work	*Interactional workability* (CA1), *Relational integration* (CA2/3), *Skill set workability* (CA4), *Contextual integration* (CA5/6)	Q14
Reflexive monitoring	how people assess the impact of NGA	*Systemization* (RM1), *Communal appraisal* (RM2), *Individual appraisal* (RM3), *Reconfiguration* (RM4)	Q16

[a] Refers to the questions as shown in Figure 2.
[b] Refers to the questions as shown in Supplemental file 2.

Table S2: Implementation outcomes per center

Center number	Patient inclusion	Intervention components			
		Execution of provider-administered NGA instruments		Multidisciplinary team meeting	
	(n)	Conducted by disciplines	combined with regular hospital visit *or* separate visit	NGA outcomes discussed	Disciplines involved
1	10	RN	combined	At indication [a]	N, NP, NN, G, SW, D
2	22	GN, D	combined	Yes	N, NN, G, GN, SW, D [b]
3	21	NP/NN, D	combined	Yes	N, NP, NN, G, SW, D
4	30	NP	combined & separate [c]	Yes	N, NP, NN, SW, D
5	19	NN	separate /combined [d]	Yes	N, NN, G
6	10	G	combined & separate [c]	Yes	N, NP, NN, G [b], SW, D,
7	26	NP, G	combined	Yes	N, NP, NN, G, SW, D
8	15	NP	combined	Yes	N, NP, G, SW
9	13	GN/G [e]	separate	Yes	N, NP, NN, G, P, SW
10	25	NN/GN [f]	combined	No/Yes [g]	N, NP, NN, SW, D
Total	191				

Abbreviations: D: dietician; G: geriatrician (or internist-geriatrician); GN: geriatric nurse; N: nephrologist; NN: nephrology nurse; NP: advanced nurse practitioner (nephrology); P: psychiatrist; PQ: patient-questionnaires; RN: research nurse; SW: social worker.
[a] Only for patients in whom there were doubts on physical and cognitive functioning.
[b] Discipline not always present at multidisciplinary team meeting.
[c] Either combined or in a separate visit, often in combination with educational- and/or doctors' consultation.
[d] Initially separate visits but later these were combined.
[e] Initially conducted by geriatric nurse, later by internist-geriatrician, in future disposition to be done by a nephrology nurse (practitioner).
[f] Geriatric practices were conducted by a geriatric nurse who took over from the nephrology nurse.
[g] During/subsequent to the study period a multidisciplinary team meeting was developed.

Table S3: Completeness of NGA instruments

NGA instruments			**Patient questionnaire n=187**		**Provided-administered test-set n=190**	
Domain	Instrument	Type	Filled in by n (%)	Completed by n (%)	Assessed for n (%)	Completed for n (%)
Functional status	Activities of daily living (Katz ADL-6)	P	186 (99)	183 (98) [d]		
	Instrumental activities of daily living (Lawton)	P	187 (100)	172 (92) [d]		
	Handgrip strength	T			180 (95)	164 (86) [c]
	Fall risk assessment	T			177 (93)	173 (91)
Cognitive functioning	Montreal Cognitive Assessment	T			189 (99)	189 (99)
	6-item Cognitive Impairment Test	T			184 (97)	184 (97)
	Letter Digit Substitution Test	T			185 (97)	185 (97)
Psychological status/mood	Whooley-questions / Geriatric Depression Scale-15	T			190 (100)	190 (100)
	Life Orientation Test-Revised	P	185 (99)	160 (86) [d]		
PROM's	HR-QoL: 12-item Short Form Health Survey	P	187 (100)	153 (82) [d]		
	Dialysis Symptom Index	P	187 (100)	135 (72)		
Somatic status	Surprise question	T			181 (95)	139 (73) [c]
	Clinical Frailty Score [a]	T			190 (100)	NA
	Charlson Comorbidity Index [a]	T			190 (100)	NA
	Polypharmacy (≥5 medications) [a]	T			190 (100)	NA
Nutrition	Patient-Generated Subjective Global Assessment [b]	P/T	186 (99)	76 (41)	156 (82)	125 (66) [d]
Social	Caregiver burden: EDIZ-plus	CG	121 (64)	113 (60) [d]		

Abbreviations: P, patient questionnaire; T, provider-administered test-set; HR-QoL, health-related quality of life

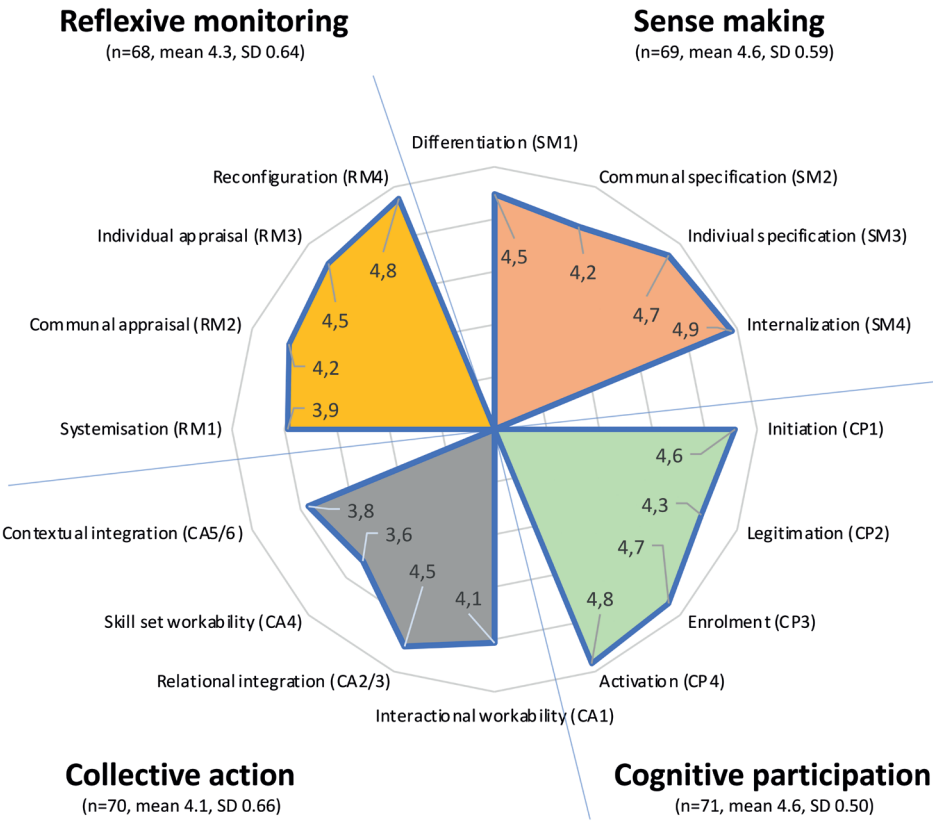
[a] Clinical Frailty Score, Charlson Comorbidity Index, Polypharmacy were instruments derived from electronic patient file.

[b] PG-SGA consists of a part filled in by the patient and a part filled in by the health-care provider.

[c] Handgrip strength: less than 3 measurements done. Surprise question: filled in by less than 3 different disciplines (nephrologist, geriatrician, nurse practitioner, dialysis nurse)

[d] Incomplete instrument restricted use of the instrument (e.g. because no total score could be generated).

Figure S1: Integration of NGA in routine care: visualization of the mixed methods approach (normalization construct scores and open-ended questions)



Notes: The petal charts presents the average score for each NPT subconstruct of normalization on a Likert scale of 1 (strongly disagree) to 5 (strongly agree). The determinants of NGA integration in routine work as derived from the qualitative analysis of open-ended questions, and supporting evidence (quotes) are presented in Supplemental Table S4.
Abbreviations: HCP, healthcare professionals; NGA, nephrology-tailored geriatric assessment; KRT, kidney replacement therapy.

Table S4: Determinants of implementation identified in qualitative analysis

Determinant / NPT-construct	Summary of qualitative content (Figure S1)	Quote	Supporting evidence [a]
Sense making			
Differentiation	NGA differs from usual care in providing objective insights, identification of unnoticed impairments. This leads to better conversations on suitable care (support) between HCW and patients, and among HCWs.	Q1	*NGA gives us the opportunity to get a more complete picture of a patient and not just medical problems. In addition we discuss life goals and the impact of treatment choices on these goals.* (nurse practitioner)
		Q2	*Being aware of a patient's functionality in all domains is a valuable tool which can enhance conversations about future KRT decisions. Patients appreciate that we assess them in this [NGA] manner and can more readily accept advice based on results.* (nephrologist)
Communal specification	In some centers the goal of NGA was widely acknowledged, but not everywhere.	Q3	*Due to the POLDER study we recognize the importance [of NGA] for this older patient group and that is why we have set up a [nephrology]geriatric committee with a geriatrician and psychiatrist.* (nurse practitioner)
		Q4	*NGA is carried out for patients with kidney failure, not yet started on dialysis. I myself am not involved further and it doesn't impact my profession. Neither are my dialysis colleagues involved in the screening. Most of them don't even know about NGA.* (nephrology nurse)
Individual specification	NGA is perceived informative for patients' decision making on KRT e.g., to dispel doubts. Although a few respondents have doubts on the relevance of NGA and its value for the decision-making process for all patients.	Q5	*It [NGA] helps us to get a better picture of a patients activities of daily living. Sometimes it helps when making KRT decisions or to dispel doubts.* (nurse practitioner)
		Q6	*Due to NGA we have a more objective picture [of a patient], previously our point of departure was instinct our "gut feeling". As a social worker I can give support to issues which are relevant within my discipline such as burdened caregiver, social isolation. Importantly, the decision making process can be impacted by NGA outcomes (social worker)*
		Q7	*In critical cases it [NGA] plays a role in decision making about whether to start or not to start KRT. We don't really know as yet how the treatment is influenced, what is reversible and what is not.* (nephrologist)
Internalization	NGA is of value for consideration of treatment options, to emphasize quality of life and provide suitable care. A minority of the respondents do not think NGA is of value; as it would not lead to concrete advices and only sporadically contributes to the decision-making process.	Q8	*The frailty which you are in practice often aware of is substantiated with NGA results in all domains. Sometimes even unexpectedly. We can take this [results NGA] into consideration and offer support where needed. Thus the quality of life of each individual patient comes first and foremost and is the point of departure [for treatment choice]* (nephrologist)
		Q9	*There was no clear feedback and particularly no specific advice (other than numeration of NGA results). Sporadically, it [NGA results] contributed to decision making, whereby before evaluation the decision had already been made.* (nephrologist)

Table S4: Continued

Determinant / NPT-construct	Summary of qualitative content (Figure S1)	Quote	Supporting evidence [a]
Cognitive participation			
Initiation	Key persons are those who execute the NGA and maintain the connection between nephrology and geriatrics; i.e. nephrology nurse (practitioner) with geriatric affinity, sometimes a nephrologist, or a geriatric nurse or -specialist. It is of risk that this often relies on one person.	Q10	*A nurse practitioner or physician assistant who has affinity with older patients plays a crucial role in building a bridge between the nephrologist and geriatrician.* (geriatrician)
		Q11	*Key figures are the ones who perform the assessment. They are responsible for feedback to the multidisciplinary team.* (social worker)
		Q12	*I was given enough time to perform NGA (particularly for the POLDER study). However I am alone and if we want to implement this [NGA] into daily practice then more colleagues are needed. The demand to carry out NGA is increasing.* (nephrology nurse)
Legitimation	While one respondent described that NGA is not for all CKD patients considered legitimate; another stated that the increasing number of frail older CKD patients legitimates standardized NGA.	Q13	*I do see the value [of performing NGA] for a specific group of patients (not based on age but on estimation of frailty), however I miss the follow-up and specific advice.* (nephrologist)
		Q14	*I see so many frail older patients who have been referred and I do think it is useful for both the practitioner and the patient to invest time in deciding together what is the best treatment.* (nephrologist)
Enrolment	Working together with the geriatrics nurses or specialists is acknowledged.	Q15	*In my hospital the goal is to employ a trained geriatric nurse on every ward so that quality of care for older patients can be improved, certainly now as the number of older patients is steadily increasing.* (nurse)
Activation	Support for the intervention is hampered by doubts about its usefulness in all patients.	Q16	*I really have difficulty with implementation of a standardized NGA for ALL patients above a certain age, and I believe that HCW who carry out NGA should be very careful about making statements about whether or not to start dialysis.* (nephrologist)
		Q17	*I support the NGA and perform it too because firstly, it offers the patient and their family better support and coaching. Secondly, it gives a lot of information about the expected treatment, degree of frailty and expected care level and prognosis.* (nurse practitioner)
		Q18	*In the meantime, more frequently geriatric assessment is requested for patients from the out-patients kidney failure clinic. We would like to see that it [NGA] becomes part of routine care. The nephrologists support the NGA and requests are becoming more frequent.* (nurse)

Table S4: Continued

Determinant / NPT-construct	Summary of qualitative content (Figure S1)	Quote	Supporting evidence [a]
Collective action			
Interactional workability	Although some stated that NGA fits well in existing outpatient care (through either standard geriatrics visit or integrated in nephrology visit with reference to geriatrics if needed), some centers needed to ask a research nurse and it was noted that not all patients were screened.	Q19	*The NGA is integrated into the outpatient clinic workflow and care pathway.* (nurse practitioner)
		Q20	*Over the past few years NGA has become more integrated into our workflow, including patients who do not participate in a study. Referral on to the geriatrician after NGA occurs regularly. The conversation with the patient and their family about KRT choice is more validated.* (nurse practitioner)
Relational integration	Confusion on focal point or which specialism is in lead may disturb working relationships. Multidisciplinary collaboration, involvement and communication is needed, and is sometimes subject for improvement. Multidisciplinary team meetings were acknowledged.	Q21	*To a degree, it disrupts work relationships because other specialists (geriatrician) discusses nephrology related treatments with the patient. I don't know precisely how these discussions go, particularly if a patient has questions [about KRT], are they then referred to the nephrologist with their questions?* (nephrologist)
		Q22	*The discussion [amongst HCW] is due to the overlap [of tasks] with other disciplines, e.g. social worker: what is the difference between NGA and PROMS or a well-being measure? Can another discipline carry out NGA, e.g. a nurse. Who decides/interprets when a geriatrician is necessary?* (nurse practitioner)
Skill set workability	Lack of knowledge and experience with NGA may hamper communal appraisal. Some said that inter-hospital knowledge exchange and (continued) training is needed, e.g. for low illiterate patients.	Q23	*Not all our colleagues have experience using NGA and because of this they don't see the advantages of the assessment. There is a lack of knowledge.* (nephrology nurse)
		Q24	*The initial training was certainly relevant, the intention was to repeat the training and the proficiency test because of the risk of faulty routine setting in. But also to carry out work visits to exchange experience with other hospitals.* (nurse practitioner)
Contextual integration	Management mostly supports NGA but not in every center. Lack of resources (i.e. time, availability of (dialysis) nurses, and budget for multidisciplinary cooperation) was noticed frequently. Information dissemination could be optimized, e.g. by software.	Q25	*The dialysis center management team does recognize the importance of good elderly care and facilitates extra education, work-shops and clinical education.* (nurse)
		Q26	*The key figures on the nephrology plus outpatients clinic are the nurses, unfortunately they are given too little time to perform their work properly and this is a recurrent issue which is discussed at meetings with the unit coordinator.* (geriatric nurse)
		Q27	*The most important missing resources are time and manpower, and shortage of dialysis nurses is the most pressing because they are needed on the kidney failure outpatients clinic*. (geriatrician)
		Q28	*During the POLDER study it became clearer what the benefits of the questionnaires, the tests, the results and extra information meant. This was all discussed at the multidisciplinary meetings. And we experienced an increasing awareness of the added value of NGA and the improvements due to consultation with the geriatrician.* (nurse practitioner)
		Q29	*There was however long term leave of absence of one HCW and that left us with only one other person who could do NGA which made things more complicated.* (nurse practitioner)

Table S4: Continued

Determinant / NPT-construct	Summary of qualitative content (Figure S1)	Quote	Supporting evidence [a]
Reflexive monitoring			
Systemization	Some noted that effectiveness of NGA has not been established. According to others effectiveness is sufficiently proven in medical fields (e.g. oncology) or from own experience.	Q30	*I'm not aware of any studies which compare the value of NGA versus the judgement/appraisal of an experienced nephrologist whether dialysis is beneficial for the individual patient.* (nephrologist)
		Q31	*The importance of performing CGA or NGA is no longer a under discussion at the geriatric out-patient clinic because we already have proof of its value, also its value in oncology.* (geriatric nurse)
Communal appraisal	Some noticed more demand for NGA, and improvement of multidisciplinary cooperation due to NGA. But the value is not seen by everyone; mostly due to needed time-investments, burden for patients, or lack of concrete outcomes.	Q32	*Colleagues do not always recognize the value [of NGA] and only see the disadvantages: the extra time it costs for patients and family.* (nephrologist)
		Q33	*Colleagues are searching for more tangible outcomes and the effect on treatment choice [of NGA results] as it's not a straightforward choice, only in extreme outcomes.* (nephrologist)
		Q34	*Colleagues from geriatrics do see the added value [of NGA] because they have experienced it in other combinations e.g. orthopedic-geriatric care; some nephrology colleagues see the added value and some recognize the limitations and time investment.* (geriatrician)
Individual appraisal	Most respondents value the effects of NGA; i.e. holistic view on frailty, improved patient-conversations and personalized care. But some noted to see no clear effect of NGA.	Q35	*There is no clear feedback and especially indisputable advice other than a summing-up of results. In practice this [NGA] contributes sporadically to decision making, whereby this information [decision about KRT] was already known prior to evaluation* (nephrologist)
		Q36	*I find it an important part of patient assessment and for individualized tailored care to support treatment choice. However it isn't as yet being performed with every patient who is eligible.* (nephrology nurse)
		Q37	*The added value is we have more insight than merely medical facts.* (nephrologist)
Reconfiguration	Some parts of NGA may not fit all patients, need for adjustments for illiterate non-Dutch speaking persons. Further development of NGA is needed said some; e.g. through multidisciplinary team meetings, availability of geriatrics, potential use of shorter screening tool for full NGA.	Q38	*The extensiveness of the assessment and the applicability in daily practice needs adjusting. Some of the assessment domains are not suitable for everyone.* (geriatrician)
		Q39	*I have been given tools to start a patient conversation. Let's hope that a DIALOGICA [study] results in an abridged version of NGA.* (nephrologist)
		Q40	*Perhaps adjustments to the test set is possible, depending on the patient and the hospital setting, e.g. targeting other languages, level of health literacy, or use of The 6-CIT versus The MoCA.* (nurse practitioner)

Table S4: Continued

Determinant / NPT-construct	Summary of qualitative content (Figure S1)	Quote	Supporting evidence [a]
Other determinants			
Patient burden		Q41	*Quite often patients found the questions too difficult. Some questions were found to be too long and these comprised different parts.* (nurse practitioner)
		Q42	*A considerable number of patients experience hospital visits as very burdensome and therefore decline to participate in a study.* (geriatrician)
		Q43	*I think that we can break the taboo of assessment and implement it more broadly, by giving it a different name or taking it out of the "geriatric" realm, and then patients will be more inclined to participate.* (nurse practitioner)
		Q44	*By less linking of it [NGA] to age you already take away the taboo, they don't want to be categorized as "geriatric patient" and are sometimes afraid of being tested for cognition.* (nephrologist)

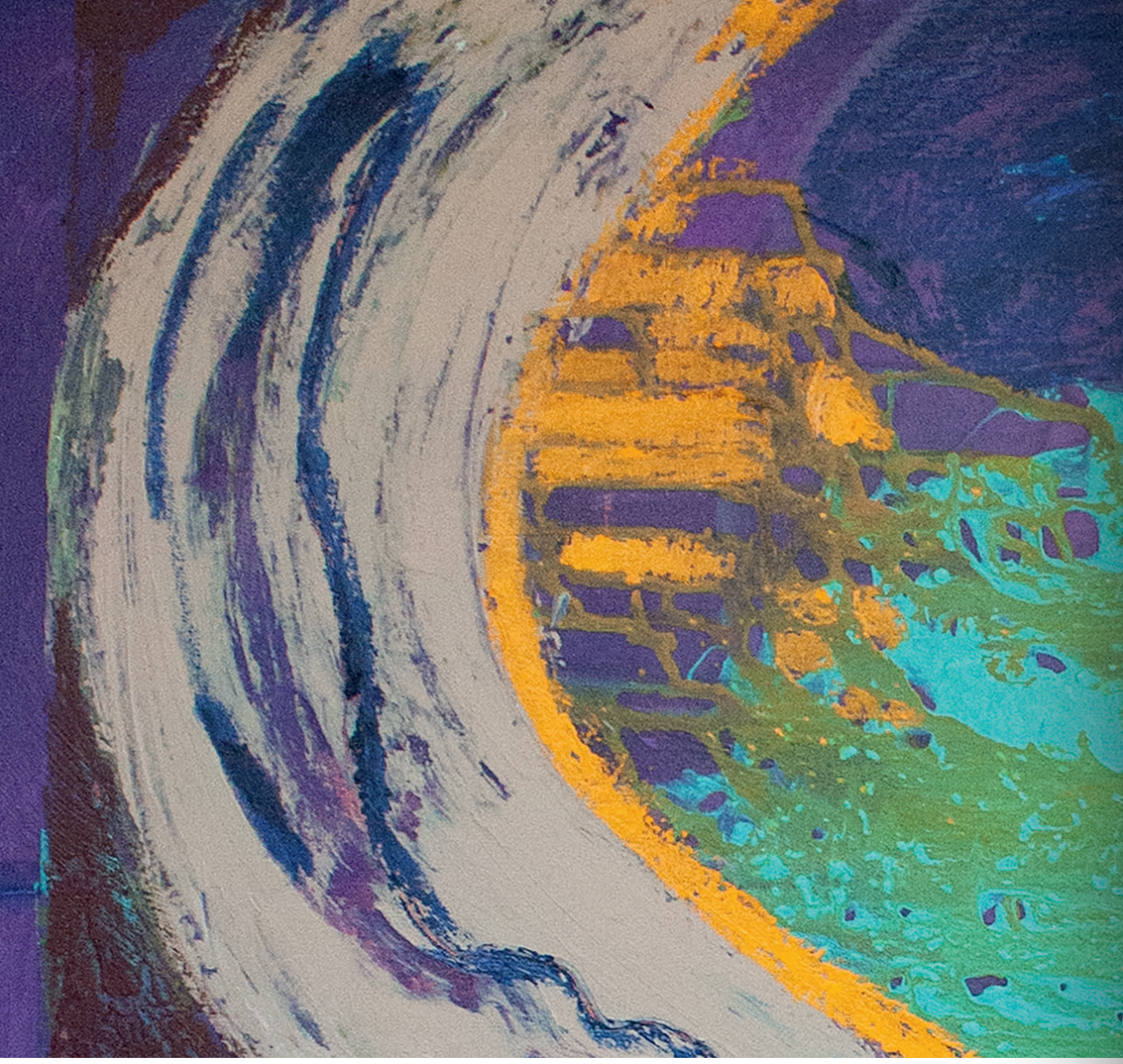
[a] All selected illustrative quotes were translated from Dutch to English by a native speaker (NB) using back-translation.
Abbreviations: 6-CIT, 6-item cognitive impairment test; HCW, healthcare worker; KRT, kidney replacement therapy; MoCA, Montreal cognitive assessment; NGA, nephrology-tailored geriatric assessment; PROMS, patient-reported outcome measure.

Table S5: Outcomes of qualitative analysis on the relevance of each NGA instrument

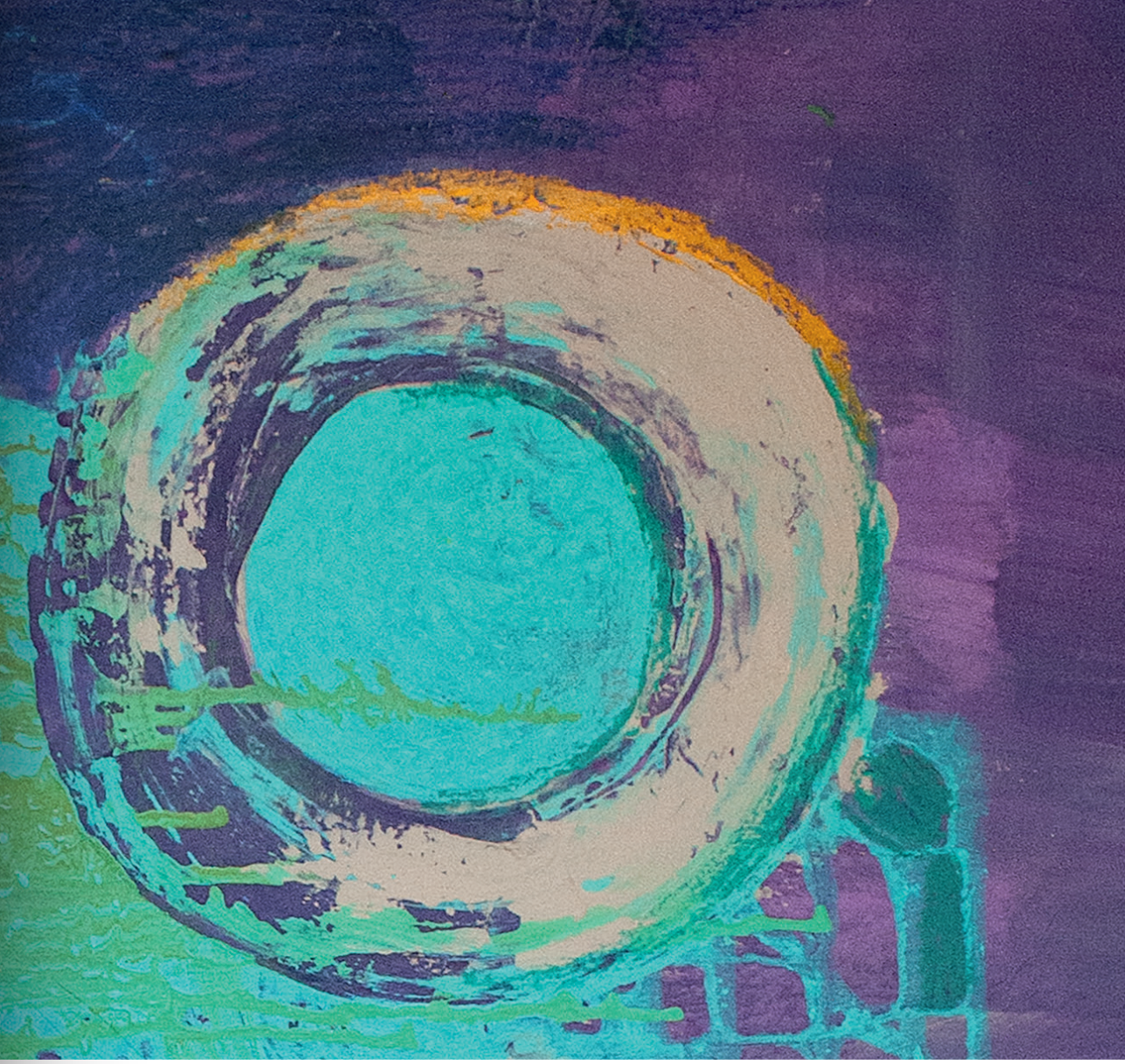
Domein	Instrument	Summary	Supporting quotes (respondents' discipline: Likert-scale rating)
Physical	KATZ-ADL & Lawton iADL	Identification of frailty and assessment of care needs	*Basic functioning is important in frailty assessment.* (geriatrician: very relevant) *This [physical functioning] domain could be targeted with supportive interventions.* (geriatrician: very relevant) *I seldom use this in my daily practice.* (nephrologist: neutral)
	Handgrip strength	Measuring deterioration of physical status, predictive value for interventions	*Indicates ability to withstand invasive procedures.* (nurse practitioner: relevant) *I don't use it at all.* (nephrologist: not relevant)
	Fall risk	Provides insights in physical functioning and need for preventive interventions	*Because of sarcopenia diagnostics.* (dietician: very relevant) *Each dialysis patient has a higher fall risk.* (nurse practitioner: neutral)
Cognitive	MoCA	Identification of unrecognized impairments, helpful in decision-making and patient care	*Provides insight into minor impairments of executive functions.* (nurse practitioner: very relevant) *Unnoticed cognitive impairments become apparent.* (nurse practitioner: very relevant) *It's not something I have experience with, in terms of interpretation and use.* (nephrologist: very relevant)
	6CIT	Provides information about cognition. Less sensitive and no added value compared to MoCA	*Sensitivity is poor/insufficient.* (geriatrician: not relevant) *It is only aimed at screening and that is insufficient in this patient group.* (nurse practitioner: neutral) *Short test, not always the same outcome in my view as the MoCA.* (nurse practitioner: very relevant).
	LDST	Limited use in practice	*Subtle indication of problems, e.g. choice for peritoneal dialysis.* (nurse practitioner: relevant) *Difficult, especially with language problems.* (nurse practitioner: neutral) *It is more research oriented.* (geriatrician: neutral)
Psychosocial	GDS	Initiating conversations and relevant for treatment choice, provides insights in need for interventions	*Being able to start a conversation about mood is important, especially when difficult choices have to be made.* (nurse practitioner: very relevant) *Useful, but sometimes language problem.* (nurse practitioner: very relevant)
	Optimism (LOT-R)	Insight into resilience and motivation. Little used in practice.	*Indicative of a patient's attitude to life is alive and whether he will be able to deal with a burdensome treatment.* (nurse practitioner: relevant) *I wonder about the added value compared to the Geriatric Depression Scale.* (nephrologist: not relevant) *Not often used in practice.* (geriatrician: neutral)

Table S5: Continued

Domein	Instrument	Summary	Supporting quotes (respondents' discipline: Likert-scale rating)
PROM's	Health-related quality of life (SF-12)	Relevant for discussion of treatment choice	*I use this too little in practice.* (nephrologist: neutral) *Especially important to start a conversation about whether or not to dialyze.* (geriatrician: relevant)
	Dialysis Symptom Index	Very useful to decide on supportive interventions and treatment choice.	*Directly applicable in outpatient clinics, focusing on specific complaints.* (nephrologist: very relevant) *Does often provides new insights.* (geriatrician: very relevant)
Somatic	Surprise question	Awareness with regard to prognosis for the healthcare provider, but the predictive value is difficult to interpret.	*Moderate predictive value.* (nephrologist: neutral) *This still feels most familiar: to listen to your 'gut feeling'* (nephrologist: very relevant)
	Clinical Frailty Scale	Relevant to decision on treatment choice and supportive interventions	*By regularly scoring this, you can see the follow-up over time and therefore notice when the patient is deteriorating.* (nurse practitioner: very relevant) *Makes this more transparent and helps to speak the same language.* (nephrologists: relevant)
	Charlson Comorbidity Index	Little used or already part of standard care. Important for choice of therapy.	*I don't need to have a score if I know the patients' history.* (nephrologist: not relevant) *Is scored anyway.* (nephrologist: very relevant) *Plays a part in the treatment choice for renal failure.* (nurse practitioner: relevant)
	Polypharmacy (≥ 5)	Creates awareness, but does not provide distinguishing information	*Side effects are point of attention due to possible negative effects on cognition/falls, etc.* (nurse practitioner: relevant) *Almost all CKD 4/5 patients, in our outpatient clinic use on average 11 drugs.* (nephrologist: not relevant)
Nutrition	Nutritional (PG-SGA)	Relevant, but no added value to routine care	*We already use this instrument, so actually regular practice is unchanged.* (geriatrician: relevant) *Nutritional status is very important for outcomes in dialysis, but the tool is very difficult to use.* (nephrologist: neutral)
Social	Caregiver (Ediz-plus)	Supports and is of relevance for treatment choice	*In my opinion, desirable answers are often given, hetero-anamnesis with social worker would help.* (nurse practitioner: relevant) *Very relevant for making choices.* (nephrologist: relevant)



PART III



REVEALING CHALLENGES AND VULNERABILITIES OF THE OLDER ADVANCED CKD POPULATION



chapter 8

Impact of the COVID-19 pandemic on symptoms of anxiety and depression and health-related quality of life in older patients with chronic kidney disease.

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BMC Geriatrics 2021;21(1):650.

ABSTRACT

Background: Older patients with advanced chronic kidney disease are at increased risk for a severe course of the coronavirus disease-2019 (COVID-19) and vulnerable to mental health problems. We aimed to investigate prevalence and associated patient (demographic and clinical) characteristics of mental wellbeing (health-related quality of life [HRQoL] and symptoms of depression and anxiety) before and during the COVID-19 pandemic in older patients with advanced chronic kidney disease.

Methods: An ongoing Dutch multicentre prospective cohort study enrols patients of ≥70 years with an eGFR < 20 mL/min/1.73m^2 from October 2018 onward. With additional questionnaires during the pandemic (May–June 2020), diseaserelated concerns about COVID-19 and general anxiety symptoms were assessed crosssectionally, and depressive symptoms, HRQoL, and emotional symptoms longitudinally.

Results: The 82 included patients had a median age of 77.5 years (interquartile range 73.9–82.1), 77% were male and none had tested positive for COVID-19. Crosssectionally, 67% of the patients reported to be more anxious about COVID-19 because of their kidney disease, and 43% of the patients stated that their quality of life was reduced due to the COVID-19 pandemic. Compared to pre-COVID-19, the presence of depressive symptoms had increased (11 to 22%; p = .022) and physical HRQoL declined (M = 40.4, SD = 10.1 to M = 36.1, SD = 10.4; p < .001), particularly in males. Mental HRQoL (M = 50.3, SD = 9.6 to M = 50.4, SD = 9.9; p = .913) and emotional symptoms remained similar.

Conclusions: Older patients with advanced chronic kidney disease suffered from diseaserelated anxiety about COVID-19, increased depressive symptoms and reduced physical HRQoL during the COVID-19 pandemic. The impact of the pandemic on this vulnerable patient group extends beyond increased mortality risk, and awareness of mental wellbeing is important.

Trial registration: The study is registered at the Netherlands Trial Register (NTR), trial number NL7104. Date of registration: 06062018.

INTRODUCTION

Older people are highly vulnerable during the coronavirus 2019 (COVID-19) pandemic: previous research showed a twenty-fold increased mortality in people aged 80 years or above compared to 50–59 year olds.[1] Besides, the emergence of the COVID-19 pandemic resulted in increased symptoms of both anxiety and depression in the general population, outpatients, and healthcare workers.[2–4] Also, mental distress during the COVID-19 outbreak was higher than before the pandemic [5] and seems to persist as the pandemic continues.[6] There are concerns that the social restrictions for COVID-19 disproportionately affect older people, mainly by increased (feelings of) social isolation and loneliness,[7,8] which, in turn, may increase patients' risk of anxiety and depressive disorders.[9]

Patients with advanced chronic kidney disease (CKD) have shown to be more vulnerable to mental health problems, such as anxiety and depression.[10] In this population, emotional symptoms, like symptoms of anxiety and depression, worrying, sleep disorders, perceived lack of social support, and reduced social interactions, affect not only health-related quality of life (HRQoL),[11–14] but have also been associated with adverse clinical outcomes and increased mortality risk.[15, 16] Above and beyond, the presence of CKD is an important risk factor for a more severe course of COVID-19, as patients with advanced CKD (stage G4/G5; severely decreased glomerular filtration rate or kidney failure) have a 2.5 times increased mortality risk, compared to those with normal kidney function.[1]

To date, no studies have been performed on mental wellbeing in older patients with advanced CKD during the COVID-19 pandemic. Therefore, our goal was to explore mental wellbeing in older patients (aged ≥70 years) with advanced CKD (estimated glomerular filtration rate [eGFR <20 mL/min/1.73m^2). First, to investigate kidney disease-related concerns about COVID-19 and general anxiety symptoms. Second, to explore changes in the presence of depressive symptoms, HRQoL, and emotional symptoms during the COVID-pandemic. Third, to examine if these (changes in) mental wellbeing are associated with patient (demographic and clinical) characteristics.

METHODS

Study population

The present study uses patients from the *Pathway for OLder patients reaching End-stage Renal disease* (POLDER) study cohort. POLDER is a currently ongoing multicentre prospective cohort study (Netherlands Trial Register identifier NL7104) which investigates the feasibility of implementing a standardised geriatric assessment into Dutch routine care for older patients with CKD stage G4/G5. Participants in POLDER are enrolled from October 2018 onwards in four non-academic and five academic Dutch nephrology units. The inclusion criteria are patients aged 70 years or older with an eGFR below 20 mL/min/1.73m^2 and the ability to read and understand the questionnaire. In POLDER, geriatric assessment is conducted at inclusion and after a one-year follow-up.

For the current study, all patients participating in the POLDER study were eligible if not lost to follow-up or deceased. An additional inclusion criterion was the completion of a baseline assessment before March 1st, 2020. This date was chosen to ensure that at least

one assessment was completed before the World Health Organisation declared the COVID-19 outbreak a pandemic (11th of March) and the Netherlands went into lockdown (15th of March), which involved the closing of restaurants, educational institutions, sporting and cultural facilities, working from home and obliged social distancing. Patients were excluded if they received a kidney transplant after enrolment into the POLDER study.

The research was conducted according to the principles of the Declaration of Helsinki and the Dutch Medical Research Involving Human Subjects Act (WMO), and approved by the Medical Research Ethics Committee Leiden-Den Haag-Delft (reference NL65322.098.18). All participants provided written informed consent when entering the POLDER study.

Study design

This current multicentre prospective cohort study consists of two parts: 1) a cross-sectional part using data derived from questionnaires that were not yet included in the POLDER study (i.e. which were specifically sent out and collected for this current study), and 2) a longitudinal part using data from questionnaires that were already included in the POLDER study.

Data collection

In the POLDER study, baseline data was collected between November 2018 and March 2020 using self-reported questionnaires, interview-based questionnaires collected in the hospital, and data from electronic patient files. Demographic and clinical characteristics collected at baseline included age, sex, living status (living together versus alone), level of education (high versus low), eGFR, Charlson comorbidity index,[17] and Clinical frailty scale.[18] For the current study, additional questionnaires were sent by mail between May 19th and June 23th 2020 (during the COVID-19 pandemic) together with an information letter about the additional study procedures. All questionnaires included are described below. If no response was received after two weeks, patients were contacted by phone and asked if they were willing to fill in the supplementary questionnaire. Also, patients' most recent eGFR, provisional dialysis initiation date and modality (haemodialysis / peritoneal dialysis) was collected from their treating physicians. All data was collected in a database managed by Nefrovisie, the Dutch quality institute for nephrology.

Outcomes measured during the COVID pandemic (cross-sectional)

Kidney disease-related concerns for COVID-19

Participants were asked to respond to four statements that were created specifically for this study: *(1) 'I am more anxious about the coronavirus because of my kidney disease', (2) 'I experience more stress from the corona-virus because of my kidney disease', (3) 'I feel more down because of the coronavirus', and (4) 'I experience a lower quality of life due to the coronavirus'.* Patients' level of agreement with the statements was rated on a five-point Likert scale, ranging from 1 'totally disagree' to 5 'totally agree'. Patients were considered to have concerns if they scored 4 'agree' or 5 'totally agree'.

General anxiety symptoms

Anxiety symptoms were assessed using the anxiety sub-scale of the Hospital Anxiety and Depression Scale (HADS-A).[19] Seven items are scored from 0 (not present) to 3 (considerably

bothersome), assessing predominantly psychological rather than somatic anxiety symptoms, for example *'I have lost interest in my appearance'*. The item scores are summed to provide the HADS-A sub-scores, with scores ranging from 0 to 21. HADS has proven reliability and validity across different ages[20] and is validated in dialysis patients.[21] A score of ≥8 is an often-used cut-off score as indication of anxiety.[22]

Outcome measures measured prior and during the COVID-19 pandemic (longitudinal)

Depressive symptoms

Depressive symptoms were assessed in two steps. First, patients were screened with two Whooley-questions (i.e. *'During the past month, have you been bothered by feeling down, depressed or hopeless?' and 'During the past month, have you often been bothered by little interest or pleasure in doing things?'*) to assess the presence of a depressed mood and anhedonia in the previous month.[23] Second, with one or two confirmative answers, the fifteen-item Geriatric Depression Scale (GDS-15) was completed as well.[24] Each binary item (e.g. *'Do you often feel helpless?'*) can be scored one point (0 'not present,' 1 'present'). The total score ranges from 0 to 15, and a cut-off score of ≥5 is often used to indicate depression.[25] Both questionnaires have been validated and widely used in older adults[25,26] and in some CKD populations.[10]

Health-related quality of life

The twelve-item Short Form Health Survey (SF-12) measures HRQoL. Using several questions on mental and physical health (e.g. *'Does your health now limit you in climbing several flights of stairs? If so, how much*?) and a scoring algorithm, the Mental Component Summary (MCS) and Physical Component Summary (PCS) scores are calculated. Scores for both Component Summaries are transformed to a scale ranging from 0 to 100, with a mean of 50 and a standard deviation (SD) of 10 in the general United States population, where higher scores reflect better HRQoL.[27] The SF-12 has proven applicability in patients with CKD and has adequate psychometric properties to display changes in HRQoL.[28]

Emotional symptoms

Six symptoms were derived from the Dialysis Symptom Index (DSI); i.e. feeling anxious, feeling sad, worrying, feeling nervous, trouble falling asleep, trouble staying asleep.[29] Per present symptom, burden was scored on a five-point Likert scale ranging from 1 'not at all bothersome' to 5 'very bothersome'.

Statistical analysis

First, descriptive statistics were computed to describe the demographic and clinical patient characteristics, concerns about COVID-19, and general anxiety symptom score (HADS-A). Proportions were reported for nominal and categorical data, means (M) with standard deviations (SD) for continuous normally distributed data, and median with interquartile range (IQR) for skewed data.

Secondly, data from prior to the COVID-19 pandemic was gathered from the most recent assessment before the pandemic, i.e. either the initial or follow-up measurement of the POLDER study. To assess whether depressive symptoms (GDS-15 score and GDS-score ≥5),

HRQoL (MCS, PCS scores), and presence of six emotional symptoms changed during COVID-19 pandemic, we conducted Wilcoxon signed-rank tests for non-normally distributed outcomes, McNemar tests for binary outcomes, and paired t-tests for normally distributed outcomes.

Third, we investigated the associations between demographic and clinical (age, sex, education, living status, frailty, comorbidity, eGFR, kidney replacement therapy, follow-up duration) patient characteristics, and disease-related COVID-19-anxiety, general anxiety symptoms, change in depressive symptoms (GDS-15 score) and change in HRQoL (MCS-12, PCS-12 scores). We tested correlation with Kendall's tau-b for continue independent variables, Mann-Whitney-U tests for binary independent variables with non-normally distributed outcomes, and used unpaired t-tests for binary independent variables with normally distributed outcomes. Overall, a two-sided significance level (alpha) of .05 was used. All analyses were conducted with SPSS 25.0.

Missing values

Missing values of SF-12 questions were, if less than 50% missing, imputed using multiple imputation techniques (i.e. maximum 50 iterations, five imputations (repetitions) and predictive mean matching[30]). Other missing variables were not imputed, as these were reasonably complete.

RESULTS

Out of the 126 patients in the POLDER study, 104 eligible participants were sent the supplementary questionnaire during the COVID-19 pandemic (Figure 1). Ninety eligible patients returned the questionnaire (response rate 87%). Non-responders did not differ in baseline characteristics from the study cohort (data not shown). Eight participants were excluded from analysis because no baseline assessment was available or they received a renal transplant. In total, 82 patients were included. Participant characteristics are shown in Table 1. The majority of participants were male (77%) and ranged in age from 70 to 95 years (median 77.5, IQR 73.9–82.1) at baseline. None of the participants had tested positive for COVID-19. In total, ten patients (12%) had started dialysis treatment; two (3%) before baseline of the current study and eight (10%) during follow up. For non-dialysis patients, eGFR declined with a mean of 1.1 (SD = 3.7, p = .012) mL/ min/1.73m^2 during follow-up. The median time between assessments prior and during the COVID-19 pandemic was 8.0 months (IQR 4.7–13.2).

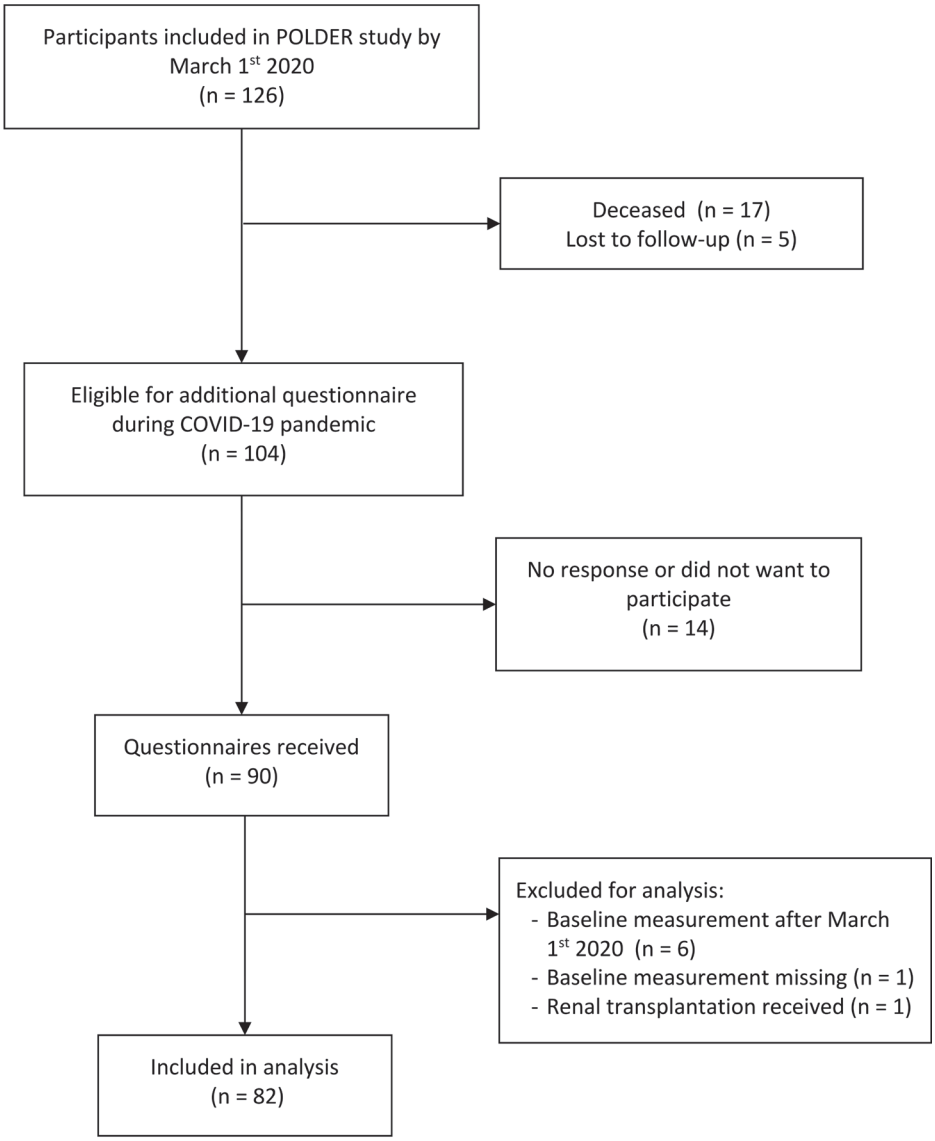


Figure 1: Sampling flow chart

Table 1: Participant characteristics prior to the COVID-19 pandemic.

Participant characteristics (n=82)	Prior COVID-19 pandemic
Age, median (IQR)	77.5 (73.9-82.1)
Sex, male (%)	63 (76.8)
Living/marital status[a]	52 (63.4)
Living together with partner / married	29 (35.4)
Living alone / widow	*1 (1.2)*
Missing	
Level of education (%)[a]	51 (62.2)
Low (none, primary, secondary education)	29 (35.4)
High (vocational, higher secondary, tertiary)	*2 (2.4)*
Missing	
Clinical frailty scale, mean (SD)[a]	3.6 (1.3)
Non-frail (score 1-3)	43 (52.4)
Vulnerable or mildly frail (score 4-5)	32 (39.0)
Moderately or severely frail (score 6-7)	7 (8.5)
Charlson comorbidity index, median (IQR)[a]	4.0 (3.0-5.0)
CCI score 2-3[b]	31 (37.8)
CCI score ≥ 4	48 (58.5)
Missing	*3 (3.7)*
eGFR, *if not on dialysis,* mean (SD)	15.7 (4.3)
Started kidney replacement therapy	2 (2.4)[c]
Haemodialysis	0 (0.0)
Peritoneal dialysis	

The following continuous variables had missing data: eGFR at baseline (2.4%).
[a] These demographic and clinical characteristics were not reassessed during COVID-19 pandemic.
[b] All patients scored minimum 2-points for *moderate to severe kidney disease.*
[c] Two patients were already on haemodialysis treatment when having the follow-up measurement of POLDER study, which has been used as reference for outcomes before COVID-19 pandemic for the current study.

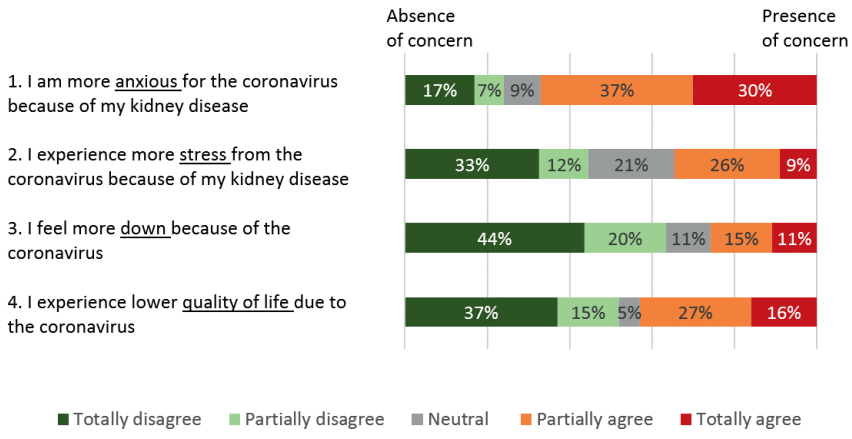


Figure 2: Respondents' agreement to the COVID-19 related statement.
Questions were scored on a scale from 1 'totally disagree' to 5 'totally agree'.

Concerns about COVID-19

Figure 2 presents responses to the four COVID-19 related statements. The majority of the respondents (*n* = 55, 67%) reported to be more anxious about COVID-19 because of their kidney disease, while 43% (*n* = 35) stated that their quality of life was reduced because of the coronavirus.

Furthermore, only 35% (*n* = 28) reported to experience more stress from the coronavirus because of their kidney disease, and 26% (*n* = 21) stated to feel more down due to the pandemic. Higher COVID-19-stress was associated with a lower education level (*p* = .036), and patients who reported to feel more down due to COVID-19 were more often female (*p* = .020). No other patient characteristics were associated with disease-related COVID-19-concerns, as shown in Supplementary Table S1.

General anxiety symptoms

The median HADS-A anxiety score was 3.0 (IQR 0.0–6.0, *n* = 80), as is shown in Table 2. In total, 15% of respondents (*n* = 12) exceeded the threshold (score > 8) indicative for anxiety. Anxiety scores were higher among females compared to males (median 4.0 [IQR 3.0–9.01 versus 2.0 [0.0–6.01, *p* = .020), and weakly associated to a decline in eGFR (correlation coefficient .197, *p* = .023). No associations were found with other patient characteristics (Supplementary Table S1).

Change in depressive symptoms

Table 2 shows that the presence of depressive symptoms (GDS-15 score > 5) increased from 11% before the COVID-19 pandemic to 22% during the pandemic (*p* = .022). No patient characteristics were associated with changes in depressive symptoms (Supplementary Table S2).

Change in HRQoL

MCS did not change from before and during the COVID-19 pandemic (*M* = 50.3, *SD* = 9.6 to *M* = 50.4, *SD* = 9.9; *p* = .913; Table 2), and no associations were found with patient characteristics (Supplementary Table S2). PCS decreased by – 4.3 (*M* = 40.4, *SD* = 10.1 to *M* = 36.1, *SD* = 10.4; *p* < .001). PCS changes were not associated with to patient characteristics except for sex (males showed a greater decline; – 5.3 (*SD* = 8.5) compared to – 0.9 (*SD* = 5.7) for females, *p* = .039).

Change in emotional symptoms

During the COVID-19 pandemic, symptoms such as feeling anxious (*n* = 23, 28%), feeling sad (*n* = 33, 41%), and worrying (*n* = 37, 46%) were often reported by patients. When compared to before the COVID-19 pandemic, presence of these symptoms did not change (from 26 to 28%, *p* = .607; 35 to 41%, *p* = .227; 50 to 46%, *p* = 1.000; respectively). Other symptoms, which were present in one third to half of the population during the pandemic, did not change either compared to before COVID-19 pandemic (i.e. feeling nervous [prior 38% and during the pandemic 37%, *p* = 1.0001, difficulty falling asleep [46 and 40%, *p* = .6781 and staying asleep [51 and 52%, *p* = 1.0001). For all symptoms, the experienced burden did not change either (Figure 3).

Table 2: Mental wellbeing prior and during COVID-19 pandemic

Cross-sectional outcomes	**Score range** [a]	**n**	**Prior COVID-19 pandemic**	**During COVID-19 pandemic**	***p*-value**
Generic anxiety symptoms					
HADS-A score, median (IQR)	0-21	80	-	3.0 (0.0-6.0)	
HADS-A score ≥ 8, n (%)		80	-	12 (15%)	
Longitudinal outcomes					
Depressive symptoms					
GDS-15 score, median (IQR) [b]	0-15	81	0.0 (0.0-3.0)	0.0 (0.0-4.0)	**.028**
GDS-15 score ≥ 5, n (%)	Yes/no	81	9 (11%)	18 (22%)	**.022**
HRQoL					
MCS, mean (SD)	0-100	80	50.3 (9.6)	50.4 (9.9)	.913
PCS, mean (SD)	0-100	80	40.4 (10.1)	36.1 (10.4)	**<.001**

Abbreviations: GDS-15, 15-item geriatric depression scale; HADS-A, anxiety subscale of hospital anxiety and depression scale; HRQoL, health-related quality of life; IQR, inter-quartile range; MCS, mental component summary; PCS, physical component summary; SD, standard deviation.

[a] Higher scores indicate more anxiety- or depressive symptoms, or better HRQoL.

[b] Where both Whooley questions were answered negative, we assumed GDS-15 score was 0.

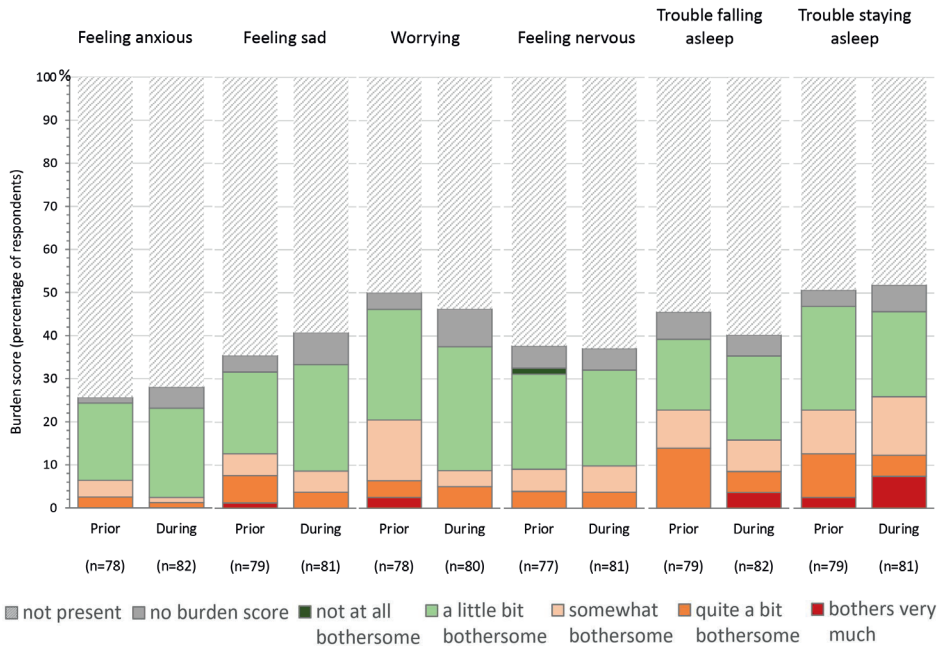


Figure 3: Symptom prevalence and burden score of six emotional symptoms (derived from DSI), prior to and during the COVID-19 pandemic.

Patients indicated whether the symptom was present (yes/no) and, for present symptoms, they subsequently rated the burden on a 5-point Likert scale ranging from 'not at all bothersome' to 'bothers very much'. Median (inter-quartile range) burden score for feeling anxious was 2.0 (2.0-3.0) prior to the pandemic and 2.0 (2.0-2.0, p = .227) during the pandemic, feeling sad 2.0 (2.0-3.5) and 2.0 (2.0-3.0, p = .314), worrying 2.0 (2.0-3.0) and 2.0 (2.0-2.3, p = .058), feeling nervous 2.0 (2.0-3.0) and 2.0 (2.0-3.0, p = .963), having trouble falling asleep 3.0 (2.0-4.0) and 2.0 (2.0-3.5, p = .594), having trouble staying asleep 2.0 (2.0-4.0) and 3.0 (2.0-4.0, p = .769).

DISCUSSION

This study investigated mental wellbeing in older patients with advanced CKD (stage G4/G5) during the COVID-19 pandemic. The majority of patients reported to be more anxious about COVID-19 because of their kidney disease, and nearly half of them stated that their quality of life was reduced because of the pandemic. We found an increase in the presence of depressive symptoms and a modest decline in physical HRQoL during the COVID-19 pandemic compared to before. Mental HRQoL and emotional symptoms did not significantly change over time. Apart from increased general anxiety symptoms in females, and a faster decline in physical HRQoL in males, no other patient characteristics were associated with validated measures of mental wellbeing.

Our findings confirm the high prevalence of disease-related worries about COVID-19 among patients with other chronic conditions, varying from 40 to 56% in type 2 diabetes[31,32] to 80% in cancer patients.[33] Interestingly, in our study, kidney disease-related COVID-19-anxiety was not associated with general anxiety symptoms (correlation coefficient .131, p =.139), suggesting that kidney disease-related COVID-19 anxiety does not directly translate into general anxiety symptoms such as restlessness, panic or tension. Also, we did not find higher HADS-A scores compared to previous studies in CKD G4/G5 patients[34,35] and dialysis patients.[21,35] Higher anxiety scores among females, one of our findings, has also been reported previously.[35] Having a male-predominant study population (77%), the anxiety scores of the study population as a whole might be an underestimation compared to populations with a more balanced sex ratio.

Regarding depressive feelings, 26% of our sample reported to feel more down because of the COVID-19 pandemic. Similarly, compared to pre-COVID-19, the presence of depressive symptoms increased significantly during the COVID-19 pandemic. However, prevalence of depression was lower compared to the average prevalence of clinical depression in CKD patients.[10] Since depression rates have been higher in dialysis patients compared to CKD population[10,36], the start of dialysis treatment during the follow-up potentially influenced the increase in depressive symptoms.

Mental and physical HRQoL during the COVID-19 pandemic in our study were comparable with previous studies in CKD G4/G5 [11,37] and the dialysis population [38,39] prior to the pandemic. In line with results of these studies, physical HRQoL was lower than the general US and the older (aged 70–79 years) Dutch population.[27, 40] We found a modest decline in physical HRQoL (– 4.3), which could be considered borderline clinically relevant, since the minimal clinical important differences for physical HRQoL in CKD patients lies between 4.5 and 6.3.[41, 42] Even though physical HRQoL was unrelated to eGFR or duration of follow-up, it is possible that disease progression influenced decline in physical HRQoL, as Wyld et al.[37] showed that patients with more advanced CKD experienced greater declines in physical HRQoL. We found a higher decline of physical HRQoL in males compared to females. At both time points scores were higher for males, particularly prior to the pandemic, which was consistent with other studies.[37,42] As our study population consisted of more men than women, the decline in physical HRQoL for sex-balanced populations might be smaller.

Taken together, our results on mental wellbeing during COVID-19 are in line with previous pre-COVID-19 studies in CKD patients. In the general population, studies on mental wellbeing

during COVID-19 show a similar picture, even though contradictory results have been found. On the one hand, absolute levels of anxiety, depression, mental health, and quality of life, during COVID-19 have been only temporarily affected or not affected at all.[43,44] whereas other studies have shown an increase[5] and persistence[6] in mental distress after the COVID-19 lockdown.

There are several potential explanations for our finding that the COVID-19 pandemic did not change the mental HRQoL or emotional symptoms of older CKD patients. First, government-imposed restrictions often restrict social gatherings and older patients are in general less socially active than younger patients. Additionally, economic uncertainty increases the risk of involuntary loss of income and older patients are often not or no longer employed. Several studies in the general population found more mental distress during the COVID-19 pandemic in both younger and employed people.[5,6,45] Second, the presence of a chronic disease may already have already had a larger effect on HRQoL of a patient than the added effect of COVID-19, as was suggested by Jeppensen et al.[33] Also, response shift may play a role, referring to a change over time in patient reported outcomes due to changes in internal standards of health and wellbeing, values and or reconceptualization of concepts such as HRQoL.[46] These cognitive changes reflect an adaptation to people's situation and could explain why HRQoL during the pandemic may remain stable while physical health declines. Third, follow-up during COVID-19 pandemic may have been too short to detect HRQoL differences. Fourth, due to the broad concept of HRQoL, potential changes in mental wellbeing during COVID-19 may have been less prominent in HRQoL compared to anxiety and depressive symptoms.

Little is known about the implications of anxiety and depression during COVID-19 in the older CKD population. Further investigation of potential mental and physical consequences is therefore required, for example on physical activity and healthcare avoidance. Additionally, ongoing studies on mental health should take the effect of the COVID-19 pandemic into account. Studies have shown that restrictions on physical activity during COVID-19 pandemic have most frequently affected people aged ≥65 years,[47] inactive individuals,[48] and those with a low HRQoL before COVID-19.[49] Furthermore, healthcare avoidance during the COVID-19 pandemic has been reported in cancer patients, among whom reluctance to consult medical care due to fear of COVID-19 infection varied between 9% and 19%.[33,50] As worrying and less social support were shown to negatively impact HRQoL,[14] and both anxiety and depression have been associated with adverse outcomes, [36] there is an urgency for awareness of mental health problems and supporting patients' needs during COVID-19 pandemic.

To our knowledge, this is the first study assessing mental wellbeing in older patients with CKD G4/G5 during the COVID-19 pandemic. Strengths of our study include the high response rate and the availability of multicentre baseline data before the COVID-19 outbreak. Our results should be interpreted in light of the limitations. First, our relatively small sample size, which most notably increases the risk of a type II error for the found absence of effect of the COVID-19 pandemic on both mental HRQoL and emotional symptoms. Second, the design of our study prevents us from drawing any causal conclusions about the effects of COVID-19 pandemic on mental wellbeing. Nonetheless, the prospective design allowed to assess changes in depression and physical HRQoL over time. Unfortunately, and this is our third limitation, for anxiety symptoms no comparison prior to the COVID-19 pandemic could

be made. Fourth, ideally, data would have been collected during or shortly after the peak of the COVID-19 infections in the Netherlands. Yet, the questionnaire was sent early June, when infection rates were stable enough to lift the stringent lockdown measures. However, most questions refer to the prior month, hereby also including the lockdown period. Still, recall bias may have affected these results.

CONCLUSIONS

In conclusion, our findings show that older patients with advanced CKD suffered from disease-related anxiety about COVID-19, increased depressive symptoms, and reduced physical HRQoL during the COVID-19 pandemic. No effect on mental HRQoL or emotional symptoms was found. The impact of the pandemic on this vulnerable patient group extends beyond increased mortality risk, and awareness of mental health problems during the pandemic is essential. More in-depth investigation on disease-related COVID-19 concerns and its implications for the CKD population is needed.

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SUPPLEMENTARY FILES

Table S1. Correlations of baseline characteristics and crosssectional outcomes of mental wellbeing.

	Kidney disease-related concerns for COVID-19**								**Anxiety symptoms**	
	anxious **(n = 82)**		***stress*** **(n = 82)**		***feeling down*** **(n = 82)**		***quality of life*** **(n = 81)**		**HADS-A (n = 80)**	
	Correlation coefficient	*p*-value	Correlation coefficient	*p*-value	Correlation coefficient	*p*-value	Correlation coefficient	*p*-value	Correlation coefficient	*p*-value
Age	-.135	.106	-.029	.725	-.032	.701	-.020	.808	.077	.335
Sex	NA	.558	NA	.074	**NA**	**.020**	NA	.546	**NA**	**.020**
Living status*	NA	.734	NA	.224	NA	.147	NA	.431	NA	.091
Level of education*	NA	.162	**NA**	**.036**	NA	.102	NA	.889	NA	.219
Clinical frailty scale*	.058	.527	.081	.369	.126	.166	.013	.885	.064	.506
Charlson comorbidity index *	.171	.063	.100	.270	.041	.657	-.073	.428	-.114	.194
eGFR, *if not on dialysis*	-.096	.295	-.094	.298	.072	.431	-.010	.913	.097	.264
Kidney replacement therapy	NA	.750	NA	.288	NA	.465	NA	.091	NA	.584
Follow-up duration	-.107	.200	-.031	.706	-.111	.183	-.004	.966	.004	.963

* Measured at baseline

** Four statements (i.e. 'I am more anxious for the coronavirus because of my kidney disease', 'I experience more stress from the coronavirus because of my kidney disease', 'I feel more down because of the coronavirus', and 'I experience a lower quality of life due to the coronavirus') for which agreement was rated on a five-point Likert scale.

Notes: The following baseline variables had missing data: Living status (1.2%), Level of education (2.4%), Charlson comorbidity index (3.7%).

Abbreviations: HADS-A, anxiety component of the Hospital Anxiety and Depression scale; NA, not applicable

Table S2. Correlations of baseline characteristics and change in longitudinal outcomes of mental wellbeing.

	Mental HRQoL Δ MCS (n = 80)		**Physical HRQoL** Δ PCS (n =80)		**Depressive symptoms** Δ GDS-15 ** (n = 81)	
	Correlation coefficient	*p*-value	Correlation coefficient	*p*-value	Correlation coefficient	*p*-value
Age	-.049	.670	-.035	.759	-.043	.606
Sex	NA	.126	**NA**	**.039**	NA	.336
Living status*	NA	.541	NA	.449	NA	.842
Level of education	NA	.841	NA	.577	NA	.275
Clinical frailty scale*	.029	.800	.188	.098	.138	.170
Charlson comorbidity index *	.233	.042	-.043	.716	-.134	.141
eGFR, *if not on dialysis*	-.049	.694	.117	.342	-.026	.774
Kidney replacement therapy	NA	.234	NA	.559	NA	.943
Follow-up duration	-.073	.535	-.005	.966	.039	.637

* Measured at baseline, ** Patients who scored zero positive Whooley questions had a GDS-15 score of '0'.
Abbreviations: GDS-15, Geriatric Depression Scale 15-item; HRQoL, health-related quality of life; MCS, mental component summary; NA, not applicable; PCS, physical component summary.



chapter

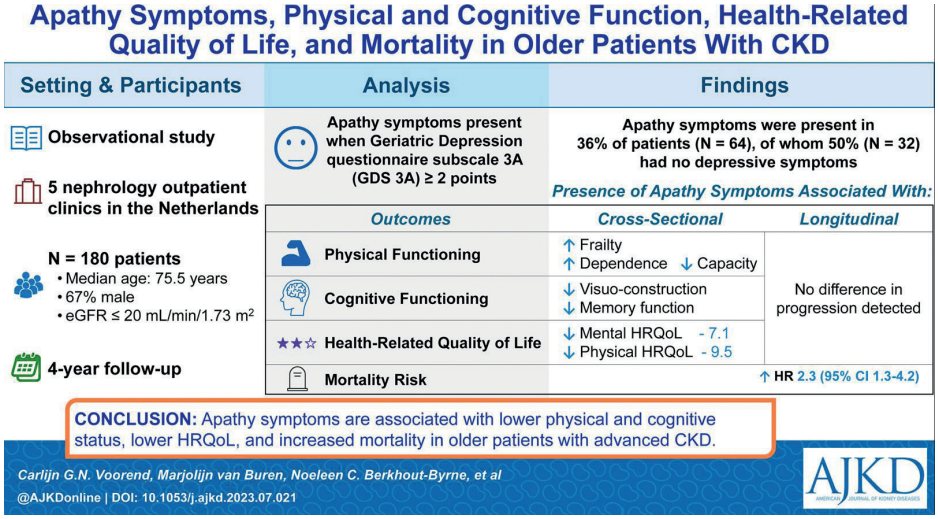
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Apathy symptoms, physical and cognitive function, health-related quality of life, and mortality in older patients with CKD: a longitudinal observational study.

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American Journal of Kidney Diseases 2024;83(2):162-72.e1.

GRAPHICAL ABSTRACT



ABSTRACT

Rationale & Objective: Apathy reflects diminished motivation, goal-directed behavior, and emotions, as well as less engagement in social interactions. Apathy overlaps with depression and is associated with cognitive decline. In the older individuals with chronic kidney disease (CKD), both depression and cognitive impairments are common, but apathy symptoms have been underreported. We investigated the occurrence of apathy symptoms and their associations with physical and cognitive functioning, health-related quality of life (HRQoL), and mortality in older patients with CKD.

Study Design: Prospective observational cohort study.

Setting & Participants: 180 outpatients aged ≥65 years with estimated glomerular filtration rate ≤ 20 mL/min/1.73 m^2 from 5 Dutch nephrology centers.

Exposure: Apathy symptoms at baseline were considered present when a Geriatric Depression Scale's 3-item apathy subscale score was ≥2 points.

Outcome: Physical and cognitive functioning, HRQoL (assessed in annual geriatric assessments), and 4-year mortality.

Analytical Approach: Linear regression for cross-sectional associations, linear regression models for longitudinal associations, and Cox regression models for mortality over 4 years of observation.

Results: Apathy symptoms were present in 64 patients (36%; 67% men; median age 75.5 years), of whom 32 (50%) had no depressive symptoms. At baseline, the presence of apathy symptoms was associated with significantly more frailty, more functional dependence, less physical capacity, lower visuoconstructive performance, worse delayed recall, and lower HRQoL scores. The presence of apathy symptoms at baseline was also associated with a higher mortality risk (hazard ratio, 2.3 [95% CI, 1.3-4.2], P = 0.005 adjusted for age, sex, and high education level), but not with changes in physical and cognitive functioning or HRQoL during the follow-up period.

Limitations: Risk of selection bias and residual confounding.

Conclusions: Apathy symptoms were highly prevalent and associated with concurrent lower physical and cognitive status, lower HRQoL, and increased mortality. These findings highlight apathy as a potentially important clinical phenotype in older CKD patients.

INTRODUCTION

Apathy has been defined as a loss of motivation, reduced goal-directed behavior, diminished emotions, and less engagement in social interaction.[1] It can be a symptom of depression or cognitive impairment[2-5] but can also be observed as a syndrome in its own right.[6] Primarily in older populations, symptoms of apathy have been associated with subclinical cerebral small vessel disease.[7] Although depression and cognitive impairments, as well as vascular problems, are common in the older population with chronic kidney disease (CKD),[8-13] apathy symptoms have been underreported,[14-16] and the prevalence of apathy symptoms in CKD is unknown.

In community-dwelling older persons, apathy has been associated with poor outcomes, including functional disability,[17] reduced (non)pharmacological therapeutic response,[18] lower quality of life,[19] high caregiver distress and burden,[20,21] and a higher risk of myocardial infarction, stroke, and all-cause mortality.[22,23] The risk of incident dementia[2-4,24] and mild cognitive impairment5 was increased 2-fold among older persons with apathy symptoms. The older CKD population is growing and comprises an increasing proportion of frail and multimorbid patients.[25] It is unexplored whether apathy symptoms are associated with poor outcomes in older patients with CKD.

We investigated the occurrence of apathy symptoms in an older advanced CKD population (stages G4 to G5) and explored associations of the presence of apathy symptoms with physical and cognitive functioning, health-related quality of life (HRQoL), and mortality over time.

METHODS

Study Design and Participants

Cognitive Decline in Older Patients with End-stage Kidney Disease (COPE) is a prospective, multicenter, observational cohort study in the Netherlands.[26] The participants were included from 5 hospitals between April 2014 and December 2019. They were eligible for study inclusion if they were ≥65 years old, had an estimated glomerular filtration rate (eGFR) below 20 mL/min/ 1.73 m^2, and attended the nephrology outpatient clinic. If patients had an acute event causing a drop of eGFR ≤ 20 mL/min/1.73 m^2, they were only included when the eGFR 3 months before acute kidney injury was ≤30 mL/min/1.73 m^2. In addition, the patients initiated (or had to initiate) counseling for support in decision-making about whether to start or forego kidney replacement therapy. Patients were excluded if they were illiterate, did not speak Dutch, or were unable to provide informed consent.

After giving informed consent, the patients underwent a geriatric assessment during routine outpatient care. The assessment included neuropsychological testing and measures of physical functioning and symptoms of depression, and it has been described in more detail elsewhere.[26,27] This assessment was repeated every year for 4 years, was conducted by trained geriatric or dialysis nurses, and included a consultation with a geriatrician. The study size was predefined.[26]

The research was conducted according to the principles of the Declaration of Helsinki and the Dutch Medical Research Involving Human Subjects Act (WMO) and approved by the

Medical Ethics Committee Leiden (reference NL46389.058.13) and the participating centers accordingly. All participants provided written informed consent.

Measurements

Patient Characteristics

Demographic measures were assessed at baseline and included age, sex, living status, ethnic group, marital status/living situation, and level of education. Clinical parameters that were collected at baseline included body mass index and eGFR. The eGFR was assessed using the most common method in the different hospitals, either using the Modification of Diet in Renal Disease (MDRD) or the 2009 CKD-EPI Creatinine equation. In addition, we assessed alcohol use, current smoking status, history of diabetes mellitus, and history of vascular disease. History of vascular disease was defined as a past myocardial infarction and/or stroke and/or peripheral vascular disease. Primary kidney disease was assessed by the treating nephrologist according to the old European Renal Association coding system[28] and categorized into 2 groups: nonvascular and vascular etiology (ie, codes covering "renal vascular disease" and "diabetes mellitus"). Medication use was registered at baseline and summarized in groups, including glucose-lowering medication, antihypertensive drugs, diuretics, cholesterol-lowering drugs, vitamin D supplements, and psychiatric and sleeping medications. Polypharmacy was defined as chronic use of ≥5 drugs.

Symptoms of Apathy and Symptoms of Depression

Symptoms of apathy were assessed with the 3-item sub-scale (GDS-3A) of the 15-item Geriatric Depression questionnaire (GDS-15).[24,29-31] We defined apathy symptoms as a score of ≥2 on the 3 apathy items: *(1) "Have you dropped many of your activities and interests?"; (2) "Do you prefer to stay at home, rather than go out and doing new things?"; (3) "Do you feel full of energy?"* (reverse-coded). GDS-3A scores ≥2 have been shown to be indicative of apathy in older adults as detected with the Apathy Scale with a sensitivity of 29%-69% and a specificity of 85%-93%.[30-32] We applied this commonly used[22,32] cutoff of ≥2 to dichotomize the presence of apathy symptoms. Although research into the scale properties of the GDS-3A is limited, the GDS-3A was validated for use in research on apathy in older populations.[31] The presence of depressive symptoms was operationalized as a score ≥2 on the 12 remaining items of the GDS-15 (ie, GDS-12D). Previous studies informed these cutoffs.[22,29-31] Isolated apathy symptoms were defined as the presence of apathy symptoms and lack of depressive symptoms (GDS-3A ≥2 and GDS-12D ≤1). Patients with missing GDS items that potentially affect these cutoffs would be excluded from the analyses.

Physical and Cognitive Functioning, HRQoL, and Mortality

The annual geriatric assessment included measures of frailty, functional dependency, physical capacity to assess physical functioning, global cognition, visuoconstructive abilities, memory, executive function, and psychomotor speed for cognitive functioning. Self-reported HRQoL was assessed using the RAND 36-Item Health Survey physical health summary score and mental health summary score.[33] Table 1 provides a detailed description of the

used instruments, their score ranges, and their interpretation. Date of death was derived from the electronic patient records within 4 years of follow-up observation.

Statistical Analysis

Baseline characteristics are presented for the total sample and stratified for the presence of apathy symptoms (yes/no): in frequencies with proportions for nominal and categorical data, mean with standard deviation for continuous normally distributed data, and median with interquartile range (IQR) for skewed data. In addition, we described baseline characteristics for patients with isolated apathy symptoms and those with both symptoms of apathy and depression. Differences in percentages between groups were tested using X^2 tests.

We investigated the associations of the presence of apathy symptoms with physical and cognitive outcomes at baseline (cross-sectional) and over time (longitudinal). Cross-sectional associations between the presence of apathy symptoms and physical functioning (frailty, Groningen Activity Restriction Scale [GARS] score, handgrip strength, and walking speed), and cognitive functioning (Mini-Mental State Examination [MMSE] score, clock drawing, 15-WVLT, 15-item Word Verbal Learning Test [15-WVLT] immediate and delayed recall score, Visual Association Test [VAT] score, Trail Making Test [TMT] Δ, Stroop Color Word Test [SCWT] III-II, Letter Digit Substitution Test [LDST], TMT-A, and SCWT II) at baseline were investigated comparing mean scores using linear regression. Longitudinal analyses of up to 5 repeated measurements were conducted to investigate whether the presence of apathy symptoms at baseline was associated with a change in physical status and cognitive function over 4 years of follow-up.

Table 1. Instruments assessing physical and cognitive functioning and HRQoL.

Subdomain	Instrument	Explanation and score range
Domain: Physical Functioning		
Frailty	Fried Frailty Index (FFI)	• Assesses the frailty phenotype including weight loss, self-reported exhaustion, decreased activity, weakness, and slow mobility. Higher scores (range 0-5) indicate more frailty.
Dependency	Groningen Activity Restriction Scale (GARS)	• 18 Items about activity of daily living such as bathing and dressing, ability to cook, clean, etc; scored from 1 (without any trouble) to 4 (only with help from others). • Total score ranged from 18-72 with higher scores indicating increased dependence.
Physical capacity	Handgrip strength	• Muscle weakness is measured with a Jaymar Handheld Dynamometer. • Average of three measurements was used. More strength (kilograms) indicates more physical capacity.
	Gait speed test.	• Gait speed is measured using a timed 6-meter walking test. • Faster completion indicates more physical capacity.
Domain: Cognitive Functioning		
Global cognition	Mini-Mental State Examination (MMSE)	• Measures cognitive impairment, including functions of registration, attention and calculation, recall language, ability to follow simple commands and orientation. • Scores range from 0 to 30, with higher scores indicating better cognitive performance.

Table 1. Continued

Subdomain	Instrument	Explanation and score range
Visuo-constructive abilities	Clock drawing	• Assesses visuospatial and praxis abilities and may determine both attention and executive dysfunctions. Score ranged between 0-14 based on accuracy, with higher scores representing better performance.
Memory	15-item Word Verbal Learning Test (15-WVLT)	• Evaluates short-term auditory-verbal memory. Five presentations of a 15-word list are given, each followed by an attempted recall. • *Immediate recall* score was calculated as the mean number of correct words repeated over five trials, ranging from 0 to 15. Higher scores indicate higher auditory memory function. • *Delayed recall* was measured after a 20 minutes delay, using the same 15-word list without a representation. The number of correctly recalled words was scored (0-15 range).
	Visual Association Test (VAT)	• Evaluates visual long-term memory reproduction with the use of a brief learning task based on imagery mnemonics. Score ranged from 0 to 12 with higher scores indicate better function.
Executive function	Trail Making Test B-A (TMTΔ)	• Assesses visual attention and task switching and provides information about visual search speed, scanning, speed of processing and mental flexibility as well as executive functioning. • Trail Making Test B, corrected for the Trail Making Test-A score (i.e. TMTΔ). • Less time spent indicating better executive function.
	Stroop Color Word Test III-II (SCWT)	• Measures selective attention. It comprises 3 parts, each containing 100 elements: color names, colored patches, and color names printed in incongruously colored ink. • The SCWT-III (interference card) was corrected for the score on SCWT-II (color naming card) to discriminate between processing speed and cognitive inhibition as an explanation of the test result. • Less time spent indicates better executive function.
Psychomotor speed	Trail making Test-A (TMT-A)	• See above.
	Stroop Color Word Test II (SCWT-II)	• See above.
	Letter Digit Substitution Test (LDST)	• A speed-dependent task that requires a participant to match symbols (letters) with their corresponding digit. The LDST measures complex neuropsychological processes including sustained attention, psychomotor speed and speed of information processing. • Higher scores of correct substitutions at 60 seconds indicate better functioning.
Domain: *Health-related Quality of Life*		
Physical and mental health summary score	RAND 36-Item Health Survey	• Self-reported health-related quality of life. Both the physical and mental summary scores range from 0-100, with higher scores indicating better functioning. These scores are a weighted average normalized to a mean score of 50 and standard deviation (SD) of 10, using method of Ware et al.[33]

Further information on the used geriatric assessment, including references to the used instruments, can be was described by Berkhout et al., [26]

Linear regression models with correlated errors were used, which allow a varying number of follow-up measurements across individuals, including a single measurement. Comparable to a mixed model using random effects, generalized least squared regression models describe how the mean outcome changes in time and whether this change depends on

certain confounders while taking the within-subject correlation into account. We proceeded with this model because data were collected at approximately the same time points for all participants and follow-up is not extensively long.[34] The presence of apathy at baseline was included in the model as a fixed independent variable, the follow-up time point as a continuous fixed variable, and the previously mentioned physical and cognitive outcomes as continuous dependent variables. The interaction between apathy and follow-up time point was included, indicating the annual additional change in outcomes for patients with apathy symptoms compared with patients without apathy symptoms. Additionally, the analysis was adjusted for age, sex, and high educational level as potential confounders.

To examine the association between the presence of apathy symptoms and mortality, we plotted Kaplan-Meier survival curves for patients with and without apathy symptoms and computed Cox proportional hazards regression models to assess mortality risks. The proportional hazard assumption was checked with a time-dependent Cox model for each of the independent variables. The analysis was performed crude and adjusted for potential confounders, including age, sex, high educational level, history of diabetes mellitus, and history of vascular disease.

All analyses were conducted in SPSS Statistics version 25 (IBM Corp). $P < 0.05$ was considered statistically significant. We did not correct for multiple testing because of the exploratory character of our study. We adhered to the guidelines for reporting observational studies (ie, the Strengthening the Reporting of Observational Studies in Epidemiology [STROBE] Statement).[35]

Sensitivity Analysis

Sensitivity analyses were performed to distinguish associations of symptoms of apathy from depressive symptoms. We repeated all cross-sectional, longitudinal, and survival analyses for patients with isolated apathy symptoms (ie, excluding those with apathy and depressive symptoms) versus patients without apathy symptoms.

RESULTS

Table 2 presents the baseline characteristics of the 180 included patients. The median age was 76 years old (IQR, 71-81), and most participants were male (67%) and lived together with a partner (62%). Mean eGFR at study enrollment was 16.2 mL/min/1.73 m^2 (± 4.6 SD). The majority (61%) had a vascular cause of kidney disease, and half the participants had a history of vascular disease (50%). Polypharmacy and use of antihypertensive drugs were frequent (89% and 90%, respectively). Depressive symptoms were present in 23% (n = 58). Missing items for the GDS-12D subscale (n = 4) did not affect the used cutoff score for depressive symptoms.

GDS-3A scores were available for all patients. Apathy symptoms (GDS-3A ≥ 2) were present in 36% (n = 64) of the population. Patients with apathy symptoms more often had a vascular cause of kidney disease (n = 42, 72%) compared with the patients without apathy symptoms (n = 58, 55%, P = 0.031). Age, sex, education level, the change in kidney function in the 3 years before the study, and medication use did not differ between the groups. Depressive symptoms were significantly more prevalent in patients with apathy symptoms

(50%, n = 32) compared with the patients without apathy symptoms (23%, n = 27, P ≤ 0.001). There was no difference in baseline characteristics between the patients with isolated apathy symptoms and those with combined apathy and depressive symptoms (Table S1).

Table 2: Baseline characteristics of the study population

	Total sample	**Apathy symptoms**		
		absent	present	
	n=180	n=116 (64%)	n=64 (36%)	P value
Age, y	75.5 [71.0 – 81.0]	75.2 [70.7-81.0]	77.0 [71.7-81.0]	0.5
Male gender	120 (66.7%)	79 (68.1%)	41 (64.1%)	0.6
White	159 (89.3%)	103 (89.6%)	56 (88.9%)	0.9
Married/living together	107 (61.5%)	73 (64.6%)	34 (55.7%)	0.3
Higher education level	62 (34.6%)	40 (34.5%)	22 (34.9%)	0.9
Current smoking	23 (13.1%)	14 (12.4%)	9 (14.5%)	0.7
Alcohol consumption	90 (51.4%)	65 (57.5%)	25 (40.3%)	0.03
Body mass index, kg/m^2	27.7 ± 4.6	27.3 ± 3.9	28.5 ± 5.5	0.1
Disease-specific				
eGFR at study enrollment, mL/min/1.73m^2	16.5 ± 4.6	16.3 ± 4.6	16.7 ± 4.7	0.6
Δ eGFR [a]	- 9.5 ± 8.6	- 9.0 ± 7.7	- 10.4 ± 9.9	0.4
Vascular primary kidney disease [b]	100 (61.3%)	58 (55.2%)	42 (72.4%)	0.03
History of diabetes mellitus	74 (41.1%)	43 (37.1%)	31 (48.4%)	0.1
History of vascular disease	89 (49.7%)	52 (45.2%)	37 (57.8%)	0.1
Medication use, n (%)				
Polypharmacy (the use of ≥5 medications)	161 (89.4%)	104 (90.4%)	57 (90.5%)	0.9
Glucose-lowering medication	64 (35.6%)	37 (31.9%)	27 (42.2%)	0.2
Antihypertensive medication	162 (90.0%)	108 (93.1%)	54 (84.4%)	0.06
Diuretics	107 (59.8%)	63 (54.8%)	44 (68.8%)	0.07
Cholesterol-lowering drugs	127 (70.6%)	80 (69.0%)	47 (73.4%)	0.5
Vitamin D supplement	151 (83.9%)	94 (81.0%)	57 (89.1%)	0.2
Psychiatric medication [c]	13 (7.2%)	9 (7.8%)	4 (6.3%)	0.7
Sleep medication	18 (10.1%)	8 (6.9%)	10 (15.6%)	0.07
Depressive symptoms				
Present (GDS-12D score ≥2)	59 (32.8%)	27 (23.3%)	32 (50.0%)	<0.001

Data are presented as frequencies with proportions for nominal and categorical data, mean ± SD for continuous normally distributed data, and median [IQR] for skewed data. Missing data for apathy symptoms absent versus present: married/living together: n=3 (2.6%) vs n=3 (4.7%); White: n=1 (.9%) vs n=1 (1.6%); education level: n=0 vs n=1 (0.6%); current smoking: n=3 (2.6%) vs n=2 (3.1%); alcohol consumption: n=3 (2.6%) vs n=2 (3.1%); body mass index: n=1 (.9%) vs n=1 (1.6%); eGFR: n=3 (2.6%) vs n=4 (6.3%); Δ eGFR: n=20 (17.2%) vs n=11 (17.1%); Primary kidney disease: n=11 (9.5%) vs n=6 (9.4%) of which n=9 unknown etiology and n=8 missing data; history of vascular disease n=1 (.9%) vs n=0; polypharmacy: n=1 (.9%) vs n=1 (1.6%); diuretics: n=1 (0.9%) vs n=0; sleep medication n=2 (1.7%) vs n=0.

Abbreviations: IQR inter-quartile range; eGFR, estimated glomerular filtration rate in mL/min/1.73m^2; GDS-12D, Geriatric depression scale 12-item subscale for depressive symptoms.

[a] Δ eGFR, the decline in eGFR in the 3 years before study enrollment.

[b] Vascular primary kidney disease was defined by codes 70, 71, 72, 73, 80, 81 of the old ERA coding system [28]

[c] Psychiatric medication included anxiolytics, benzodiazepines and antidepressants.

Cross-sectional Associations of Apathy With Physical and Cognitive Functioning, and HRQoL

Table 3 shows the association of the presence of apathy symptoms with physical and cognitive performance and HRQoL at baseline. Patients with apathy symptoms had higher frailty scores (mean Fried Frailty Index 2.5 vs 1.2; P < 0.001), more functional dependency (mean GARS score 31.4 vs 26.2; P < 0.001), and lower physical capacity (mean handgrip strength 23.2 kg vs 26.7 kg; P = 0.021; mean walking speed 0.9 vs 1.1 m/ s; P < 0.001) compared with the patients without apathy symptoms. These differences remained statistically significant after adjustment for age, sex, and education level. Presence of apathy symptoms was associated with lower visuoconstructive performance (mean clock drawing score 11.2 vs 11.9; P = 0.037). Delayed memory function was significantly worse for patients with apathy symptoms only when adjusted for age, sex, and education level (mean difference in 15-WVLT delayed recall score 0.96 [95% CI, 1.9 to 0.1], P = 0.039). No statistically significant associations were found for the presence of apathy symptoms with global cognition (MMSE), visual memory (VAT), or psychomotor speed. HRQoL scores were lower for patients with apathy symptoms compared with those without, both in the physical and mental domain (9.5 [95% CI, 12.6 to 6.4] and 7.1 [95% CI, 10.0 to 4.0], respectively).

Longitudinal Associations of Apathy With Physical and Cognitive Decline, and HRQoL

The median follow-up period was 30.7 months (IQR, 13.3-48.0), and complete 4-year follow-up was reached by n=22 (12%) patients. Table 4 shows that on almost all physical and cognitive tests, mean annual change was comparable for patients with apathy symptoms to those without. Apart from the mean progression of the TMTΔ score (executive functioning) that indicated more decline in patients with apathy symptoms (ie, yearly mean 13.29 seconds less compared with those without apathy symptoms ([95% CI, 2.30-24.28], P = 0.018). Adjustment for age, sex and education level resulted in similar estimates of the difference in annual progression (13.94 [95% CI, 3.76-24.12], P = 0.008). The mean annual change in physical and mental HRQoL summary scores did not differ between the groups.

Association of Apathy With Risk of Mortality

Figure 1 presents a Kaplan-Meier survival curve showing higher mortality among patients with apathy symptoms. The crude hazard ratio [HR] was 1.88 ([95% CI, 1.053.36], P = 0.033), after adjustment for age, sex, and high education level (HR, 2.32 [95% CI, 1.29-4.17], P = 0.005). Additional adjustment for history of diabetes mellitus or vascular disease did not change the estimates (Table S4). All independent variables met the criteria for the proportional hazard assumption.

Sensitivity Analyses

To distinguish the associations of symptoms of apathy from depressive symptoms, we repeated our analysis by comparing the persons with isolated apathy symptoms with those who had no apathy symptoms. We found comparable estimates, both cross-sectionally (Table S2: physical functioning [frailty, GARS score, walking speed], executive functioning [TMTΔ], and physical HRQoL were more impaired in isolated apathy patients compared with those who had no apathy symptoms) and longitudinally (Table S3). Mortality risk was higher

in patients with isolated apathy symptoms (crude HR, 2.37 [95% CI, 1.214.63]; adjusted HR, 2.53 [95% CI, 1.29-4.96]), similar to the main analysis.

Table 3: Baseline associations of the presence of apathy symptoms with measures of physical and cognitive functioning in 180 patients with CKD aged 65 years and over.

	Apathy symptoms		Difference	
	Absent n=116	Present n=64	Unadjusted difference	Adjusted [a] Difference
Physical functioning				
Frailty, Fried Frailty Index (range 0-5) [b]	1.21 ± 1.21	2.48 ± 1.39	1.27 (.88 to 1.66)[c]	1.22 (0.84 to 1.59)[c]
Dependency, GARS-score (range 18-72) [b]	26.22 ± 9.83	31.38 ± 9.42	5.15 (2.18 to 8.13)[c]	5.05 (2.21 to 7.87)[c]
Physical capacity				
Handgrip strength, kg	26.72 ± 9.04	23.20 ± 10.59	-3.53 (-6.51 to -0.53)[c]	-2.82 (-5.12 to -0.52)[c]
Walking speed, m/s	1.11 ± 0.33	0.87 ± 0.29	-0.24 (-0.34 to -0.13)[c]	-0.23 (-0.32 to -0.13)[c]
Cognitive functioning				
Global cognition, MMSE score (range 0-30)	28.03 ± 1.88	27.70 ± 2.37	-0.32 (-0.96 to 0.31)	-0.33 (-0.95 to 0.30)
Visuo-construction, Clock drawing (range 0-14)	11.92 ± 1.79	11.17 ± 2.47	-0.75 (-.1.45 to -0.04)[c]	-0.79 (-1.42 to -0.15)[c]
Memory				
Immediate recall, 15WVLT (range 0-15)	6.35 ± 1.95	5.81 ± 2.09	-0.54 (-1.15 to 0.08)	-0.55 (-1.14 to 0.03)
Delayed recall, 15WVLT (range 0-15)	6.11 ± 3.03	5.21 ± 3.11	-0.90 (-1.86 to 0.06)	-0.96 (-1.88 to -0.05)[c]
Visual Association Test (range 0-12)	11.39 ± 1.45	10.98 ± 2.04	-0.40 (-0.93 to 0.12)	-0.42 (-0.92 to 0.08)
Executive function, Trail Making Test B-A, s [b]	105.41 ± 61.96	119.58 ± 57.24	14.17 (-4.84 to 33.18)	14.08 (-4.29 to 32.45)
Stroop Color Word Test III-II, s [b]	85.60 ± 64.10	86.60 ± 48.65	0.76 (-17.74 to 19.27)	1.11 (-15.97 to 18.20)
Psychomotor speed				
Letter Digit Substitution Test, correct/min	22.07 ± 7.22	20.10 ± 6.35	-1.97 (-4.11 to 0.17)	-2.00 (-4.06 to 0.07)
Trail Making Test-A, s [b]	67.52 ± 42.09	74.51 ± 41.99	6.99 (-6.00 to 19.98)	7.01 (-5.66 to 19.69)
Stroop Color Word Test II, s [b]	81.42 ± 29.70	87.08 ± 24.90	5.66 (-3.00 to 14.33)	5.95 (-2.66 to 14.56)
Health-related quality of life				
RAND-36 physical summary score	43.35 ± 11.25	33.83 ± 8.77	-9.52 (-12.62 to -6.42)[c]	-9.47 (-12.67 to -6.28)[c]
RAND-36 mental summary score	48.76 ± 8.71	41.66 ± 11.50	-7.09 (-10.50 to -3.69)[c]	-6.99 (-10.03 to -3.96)[c]

Figures are presented as mean ± SD for apathy symptoms and mean (95% CI) for difference. Missing data for apathy symptoms absent versus present: FFI: n=0 vs n=1 (0.6%); Handgrip strength: n=2 (1.7%) vs n=2 (3.1%); Walking speed: n=7 (6.0%) vs n=7 (10.0%); Clock: n=2 (1.7%) vs n=1 (0.6%); WVLT delayed n=2 (1.7%) vs n=3 (4.7%); VAT n=0 vs n=2 (3.1%); TMT B-A n=2 (1.7%) vs n=4 (6.3%); SCWTIII-II n=6 (5.2%) vs n=2 (3.1%); LDST, n=0 vs n=1 (1.6%); TMT-A n=0 vs n=1 (1.7%); SCWTII, n=3 (2.6%) vs n=0; RAND-36 n=7 (6.0%) vs n=5 (7.8%).

Abbreviations: 15WVLT, 15-item Word Verbal Learning Test; GARS, Groningen Activity Restriction Scale; MMSE, Mini-Mental State Examination.

[a] Adjusted for age, sex and high education level.

[b] Higher scores, mean less performance.

[c] Statistically significant values.

Table 4: Annual change in physical and cognitive functioning during follow-up for older CKD patients with and without apathy symptoms.

	Apathy symptoms		**Difference in annual decline (Presence of apathy at baseline *time)**	
Annual change	Absent at baseline n=116	Present at baseline n=64	Unadjusted model	Adjusted model [c]
Physical functioning [a]				
Frailty, Fried Frailty Index [b]	-0.00 ± 0.06	-0.03 ± 0.10	-0.03 (-0.26 to 0.21)	-0.01 (-0.24 to 0.22)
Dependency, GARS-score [b]	1.07 ± 0.34	1.88 ± 0.52	0.81 (-0.42 to 2.04)	0.80 (-0.42 to 2.03)
Physical capacity				
Handgrip strength, kg	-0.25 ± 0.31	-1.10 ± 0.46	-0.85 (-1.95 to 0.25)	-0.90 (-1.94 to 0.13)
Walking speed, m/s	-0.01 ± 0.01	-0.02 ± 0.02	-0.02 (-0.07 to 0.03)	-0.02 (-0.07 to 0.03)
Cognitive functioning [a]				
Global cognition, MMSE score	-0.01 ± 0.10	-0.14 ± 0.15	-0.12 (-0.48 to 0.24)	-0.13 (-0.49 to 0.23)
Visuo-construction, Clock drawing score	0.09 ± 0.18	0.28 ± 0.15	0.19 (-0.17 to 0.54)	0.19 (-0.16 to 0.54)
Memory				
Immediate recall, 15WVLT score	0.42 ± 0.11	0.13 ± 0.18	-0.29 (-0.72 to 0.13)	-0.25 (-0.67 to 0.17)
Delayed recall, 15WVLT score	0.74 ± 0.15	0.46 ± 0.28	-0.28 (-0.90 to 0.35)	-0.23 (-0.85 to 0.39)
Visual Association Test score	0.10 ± 0.04	0.19 ± 0.06	0.10 (-0.05 to 0.25)	0.10 (-0.06 to 0.25)
Executive function Trail Making Test B-A (seconds) [b]	-4.26 ± 2.90	9.03 ± 4.71	13.29 (2.30 to 24.28)[d]	13.94 (3.76 to 24.12)[d]
Stroop Color Word Test III-II (seconds) [b]	-6.21 ± 1.80	0.13 ± 3.18	6.35 (-0.87 to 13.57)	5.31 (-1.69 to 12.31)
Psychomotor speed				
Letter Digit Substitution Test (correct/minute)	0.06 ± 0.25	-0.36 ± 0.42	-0.42 (-1.37 to 0.54)	-0.43 (-1.36 to 0.51)
Trail Making Test-A (seconds) [b]	-1.62 ± 1.27	-1.07 ± 2.00	0.55 (-4.15 to 5.24)	0.25 (-0.98 to 4.46)
Stroop Color Word Test II (seconds) [b]	-2.38 ± 0.78	-2.58 ± 1.32	-0.20 (-3.23 to 0.83)	-0.57 (-3.58 to 2.43)
Health-related quality of life [a]				
RAND-36 physical summary score	-0.52 ± 0.45	-1.04 ± 0.72	-0.52 (-2.20 to 1.15)	-0.48 (-2.13 to 1.18)
RAND-36 mental summary score	-0.45 ± 0.47	0.76 ± 0.74	1.21 (-0.52 to 2.93)	1.25 (-0.46 to 2.95)

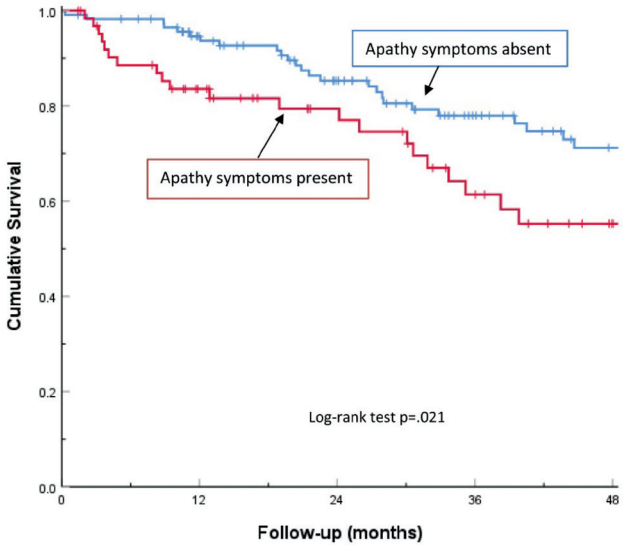
Figures are presented as mean annual change (SE) for apathy symptoms and mean difference in annual change (95% CI) for difference in annual decline. Outcome data was completely missing for: FFI: n=1 (.6%), Walking speed n=10 (5.6%) WVLT delayed: n=2 (1.5%); VAT: n=1 (.6%); TMT B-A n=5 (2.8%); SCWTIII-II n=4 (2.2%); LDST n=1 (.6%) TMT-A n=1 (.6%); SCWTII n=2 (1.1%), RAND-36 n=4 (2.2%). Abbreviations: 15WVLT, 15-item Word Verbal Learning Test; GARS, Groningen Activity Restriction Scale; MMSE, Mini-Mental State Examination.

[a] The mean number of measurements per outcome varied from 2.25 ± 1.32 SD to 2.45 ± 1.38 SD.

[b] Higher scores, means less performance.

[c] Adjusted for age, sex and high education level.

[d] Statistically significant values.



Number at risk:

No apathy	116	97	76	53	39
Apathy symptoms	64	45	33	22	12

Figure 1: Cumulative mortality depending on the presence and absence of apathy symptoms in older patients with chronic kidney disease.

DISCUSSION

The main findings of this study were 3-fold. First, symptoms of apathy were present in 36% of older patients with CKD. In half those patients the symptoms of apathy were unrelated to symptoms of depression. Second, presence of apathy symptoms was associated with lower physical and cognitive functioning and HRQoL at baseline. Third, presence of apathy symptoms was associated with a 2-fold higher risk of mortality over 4 years.

Our findings on the occurrence of apathy symptoms are in concordance with previous smaller CKD studies that have reported an occurrence of apathy of one-fifth in all stages of the CKD adult population and up to two-thirds in the adult dialysis patients.[14,36] The prevalence of apathy symptoms in our cohort was somewhat higher compared with previous estimates from community-dwelling older population cohorts[22,30,37] and older primary care pa-tients.[29-31] As in other studies, symptoms of apathy were related to depressive symptoms,[15,16,30] but they occurred without depressive symptoms in half the cases.[22,29,30] We found that apathy symptoms were associated with a vascular cause of kidney disease. This fits the vascular apathy hypothesis that apathy is caused by cerebral small vessel disease[7] and is in line with our previous finding in a subset of this cohort in which patients with a history of vascular disease showed more cerebral white matter hyperintensities on magnetic resonance imaging.[27]

Our findings on physical functioning are in line with other studies in community-dwelling older persons showing more frailty and lower functional status among patients with apathy

symptoms compared with those who had no apathy symptoms.[38-40] Although larger longitudinal studies in older adults and Alzheimer's disease patients found more decline in physical functioning in patients with apathy symptoms,[37,41,42] in our cohort we could not confirm a faster decline of dependency and physical capacity for these patients. The outcomes on cognitive functioning (visuoconstructive abilities, memory, and executive function) were consistent with earlier findings on dysfunction in critical subcortical-frontal brain circuits.[18,43] Recent systematic reviews have described the lack of evidence on apathy and cognitive decline,[5,44] but a longitudinal relationship to incident mild cognitive impairment and dementia was described.[3,5] In concordance, we found a faster decline in executive functioning in patients with apathy symptoms in our cohort, but we found no difference in other cognitive domains for patients with apathy symptoms, supporting the antithesis.

We found lower physical and mental HRQoL in those with apathy symptoms, as did other studies in stroke patients and nursing home residents.[45,46] Survival outcomes of our study were more prominent and exceed (albeit overlapping confidence intervals) the 47% higher risk for persons with apathy symptoms from a recent meta-analysis among community-dwelling older people.[22] Although residual confounding is likely, a history of diabetes mellitus and vascular disease did not explain the association between apathy symptoms and increased mortality risk in our population. Furthermore, our analysis was based on a single measurement of apathy symptoms at baseline. A patient manifesting apathy symptoms without depressive symptoms may have developed these over time or have gone through other physical and emotional events that could have contributed to the poor outcomes associated with the presence of apathy symptoms. Overall, our findings in CKD are thus consistent with other older populations.

Apathy has a particular high burden on patients and relatives,[19-21,47] and our results therefore suggest that apathy is a potentially relevant phenomenon and highlight several clinical implications for future nephrology practice. First, clinical awareness to distinguish symptoms of apathy from depressive symptoms in CKD may be desirable. Both symptoms of depression and apathy are prevalent in approximately one-third of CKD patients[8] but exist to a large extent independently of each other. One would want to prevent treating patients for depression if apathy is the problem; antidepressants may have limited effects on apathy.[48] Unfortunately, evidence on apathy treatments is scarce and may be aimed at alleviating patient disability rather than pharmacological interventions.[18,48] There are no well-powered randomized, controlled trials demonstrating any treatment effect in apathy. Also, with emerging evidence for the hypothesis of vascular apathy, studies toward depression in CKD populations may need to consider taking apathy into account as a potential common cause or confounding variable.

Second, clinical awareness for the presence of apathy symptoms may be relevant for the treatment of older CKD patients, both in the decision-making process for their upcoming choice of kidney replacement therapy and in the guidance of therapy adherence. Deficits in effort-based decision making have been associated with apathy in patients with cerebral small vessel disease.[49] One may postulate that the loss of motivation and reduced goal-directed behaviour may require a different approach compared with patients who are not experiencing apathy symptoms.[43]

Third, the presence of apathy symptoms might be an indicator of other physical and cognitive impairments. Together with the higher mortality risk among patients with apathy symptoms, it highlights the vulnerability of this patient group. The predictive value of apathy symptoms on cognitive decline may be a topic for future research in larger CKD populations. If such studies are more conclusive, apathy itself might be of interest to include in geriatric evaluation.

Strengths of our exploratory study are the unique study population, relevant outcomes for older CKD patients, and the extensive cognitive and physical tests that were conducted annually during a 4-year follow-up. This provided the opportunity to explore a broad range of physical and cognitive outcomes and progression over time. The study also had limitations. First, patient inclusion in our study cohort might have been selective, potentially limiting the generalizability of our results. Because the study was initiated from a routine care perspective to identify cognitive deficits, on the one hand, patients were more likely to be included when having a reason for geriatric workup. On the other hand, patients with worse conditions might also have been less likely to participate. Second, we conducted an observational study, and we could not make any causal interpretations. Residual confounding remains a possible explanation for the associations that were found. Nevertheless, our findings are a first step toward insights into relationships between apathy symptoms and outcomes. Third, our results are confined to the use of the GDS-3A instrument, which was used to define apathy symptoms, and dichotomization of its presence. The GDS-3A has shown high specificity and low sensitivity.[31] Because GDS-3A items closely connect to functional disability,[50] apathy symptoms might rather be an indicator of a less active and home-bound life due to an individual's chronic illness. Future research should further disentangle apathy as an independent entity by using other more dedicated instruments.[51] Fourth, we included many outcome parameters in our analyses, which might have been a risk for a statistically significant result purely by chance (ie, type I error). However, all outcomes pointed consequently in the direction of lower functioning for patients with apathy symptoms.

CONCLUSIONS

In conclusion, our study reveals that symptoms of apathy are highly prevalent in our cohort of older CKD patients, often independent of depressive symptoms. Because of the relation of apathy symptoms with mortality, physical and cognitive status, and HRQoL, symptoms of apathy could be a potentially relevant clinical entity in care for advanced CKD patients.

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SUPPLEMENTARY FILES

Figure S1: Boxplots of distributions of physical and cognitive functioning and health-related quality of life measurements over time.

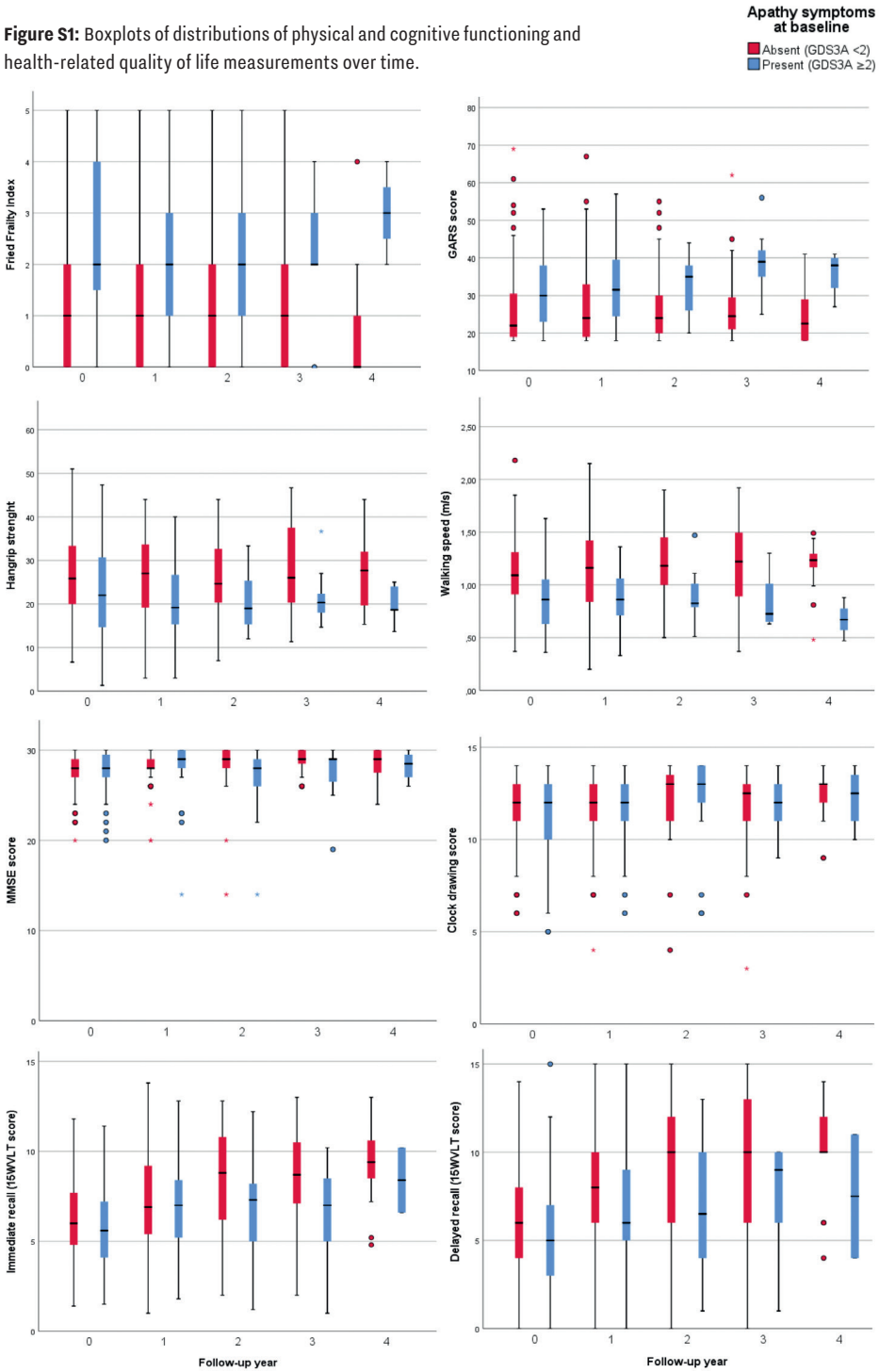


Figure S1: Continued

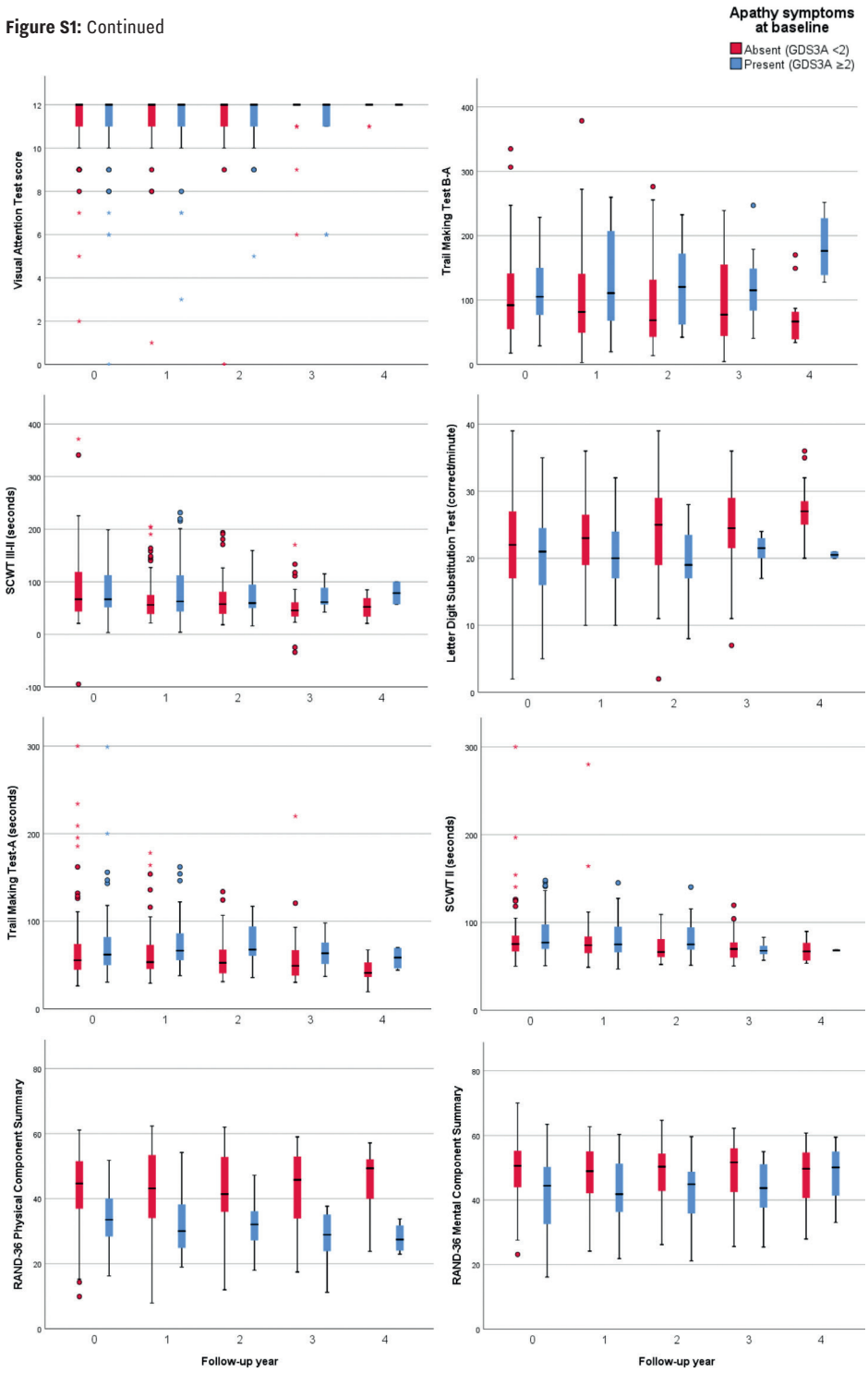


Table S1: Baseline characteristics of patients with isolated apathy symptoms and combined apathy and depressive symptoms.

	Patients with apathy symptoms		
	Isolated	With depressive symptoms	
	n=32 (50%)	n=32 (50%)	P value
Age, y	77.4 [71.3-81.9]	75.2 [72.2-80.7]	0.747
Male gender	23 (71.9%)	18 (56.3%)	0.193
Caucasian origin	28 (87.5%)	28 (90.3%)	0.722
Married/living together	16 (53.3%)	18 (58.1%)	0.710
Higher education level	13 (41.9%)	9 (28.1%)	0.250
Current smoking	5 (16.1%)	4 (12.9%)	0.718
Alcohol consumption	12 (38.7%)	13 (41.9%)	0.796
BMI	27.8 ± 5.4	29.3 ± 5.6	0.308
Disease specific			
eGFR at study enrolment, mL/min/1.73m2	16.6 ± 3.5	16.8 ± 5.6	0.899
ΔeGFR [a]	11.2 ± 11.8	9.6 ± 7.8	0.581
Vascular primary kidney disease [b]	21 (75.0%)	21 (70.0%)	0.670
History of diabetes mellitus	15 (46.9%)	16 (50.0%)	0.802
History of vascular disease	17 (53.1%)	20 (62.5%)	0.448
Medication use			
Polypharmacy (the use of ≥5 medications)	30 (93.8%)	27 (87.1%)	0.368
Glucose-lowering medication	12 (37.5%)	15 (46.9%)	0.448
Antihypertensive medication	27 (84.4%)	27 (84.4%)	1.00
Diuretics	20 (62.5%)	24 (75.0%)	0.281
Cholesterol-lowering drugs	22 (68.8%)	25 (78.1%)	0.396
Vitamin D supplement	29 (90.6%)	28 (87.5%)	0.689
Psychiatric medication [c]	1 (3.1%)	3 (9.4%)	0.302
Sleep medication	3 (9.4%)	7 (21.9%)	0.168

Data are presented as frequencies with proportions for nominal and categorical data, mean ± SD for continuous normally distributed data, and median [IQR] for skewed data. Missing data: Caucasian origin: n=1 (1.5%), married/living together: n=3 (4.7%), education level: n=1 (1.5%), current smoking: n=2 (3.1%), alcohol consumption: n=2 (3.1%), body mass index: n=1 (1.5%), blood pressure: n=1 (1.5%), eGFR: n=4 (6.3%), Δ eGFR: n=11 (17.2%); primary kidney disease: n=6 (9.4%), polypharmacy: 1 (1.5%).
Abbreviations: IQR, inter-quartile range; SD, standard deviation; eGFR, estimated glomerular filtration rate.
[a] Δ eGFR, the difference between eGFR 3 years before and at study enrolment.
[b] Vascular primary kidney disease was defined by codes 70, 71, 72, 73, 80, 81 of the old ERA coding system.
[c] Psychiatric medication included anxiolytics, benzodiazepines and antidepressants.

Table S2: Baseline associations of the presence of isolated apathy symptoms versus absence of apathy symptoms with measures of physical functioning, cognition and depressive symptoms.

	Apathy symptoms isolated (n=32) versus absent (n=116)	
	Unadjusted	**Adjusted [b]**
Physical functioning		
Frailty, Fried Frailty Index (range 0-5) [a]	0.92 (0.44 to 1.40)[c]	0.90 (0.43 to 1.36)[c]
Dependency, GARS-score (range 18-72) [a]	3.31 (-0.55 to 7.17)	3.86 (0.13 to 7.59)[c]
Physical capacity		
Handgrip strength, kg	-2.39 (-6.18 to 1.40)	-2.85 (-5.88 to 0.18)
Walking speed, m/s	-0.20 (-0.34 to -0.07)[c]	-0.20 (-0.32 to -0.08)[c]
Cognitive functioning		
Global cognition, MMSE score (range 0-30)	-0.12 (-0.88 to 0.64)	-0.17 (-0.91 to 0.58)
Visuo-construction, Clock drawing (range 0-14)	-0.08 (-0.96 to 0.81)	-0.16 (-0.92 to 0.60)
Memory		
Immediate recall, 15WVLT (range 0-15)	-0.55 (-1.33 to 0.23)	-.57 (-1.33 to 0.18)
Delayed recall, 15WVLT (range 0-15)	-1.11 (-2.31 to 0.09)	-1.13 (-2.31 to 0.05)
Visual Association Test (range 0-12)	-0.03 (-0.59 to 0.53)	-0.03 (-0.58 to 0.52)
Executive function, Trail Making Test B-A, s [a]	24.04 (-1.79 to 49.88)	26.61 (2.40 to 50.82)[c]
Stroop Color Word Test III-II, s [a]	-.36 (-24.73 to 24.00)	-.58 (-23.44 to 22.29)
Psychomotor speed		
Letter Digit Substitution Test (correct/min)	-1.32 (-4.09 to 1.45)	-1.33 (-4.00 to 1.35)
Trail Making Test-A, s [a]	.03 (-15.54 to 15.60)	-.59 (-14.87 to 16.04)
Stroop Color Word Test II, s [a]	5.91 (-5.52 to 17.34)	6.44 (-5.15 to 18.03)
Health-related quality of life		
RAND-36 physical component summary	-9.22 (-13.67 to -4.78)[c]	-9.65 (-13.93 to -5.37)[c]
RAND-36 mental component summary	-1.32 (-4.93 to 2.29)	-1.64 (-5.17 to 1.89)

Figures are presented as mean (95% CI) for difference. Missing data for isolated apathy symptoms versus absent: Handgrip strength: n=2 (1.7%) vs n=1 (3.1%); Walking speed: n=7 (6.0%) vs n=3 (9.4%); Clock: n=2 (1.7%) vs n=0; WVLT delayed n=2 (1.7%) vs n=1 (3.1%); TMT B-A n=2 (1.7%) vs n=1 (3.1%); SCWTIII-II n=6 (5.2%) vs n=1 (3.1%); SCWTII, n=3 (2.6%) vs n=0; RAND-36 n=7 (6.0%) vs n=3 (9.4%). Abbreviations: 15WVLT, 15-item Word Verbal Learning Test; GARS, Groningen Activity Restriction Scale; MMSE, mini-mental state examination.

[a] Higher scores, means less performance.

[b] Adjusted for age, sex and high education level.

[c] Statistically significant values.

Table S3: Annual change in physical and cognitive functioning during follow-up for older CKD patients with isolated apathy symptoms versus absence of apathy symptoms.

	Difference in annual decline (Presence of isolated apathy * time)	
Annual change	**Unadjusted model**	**Adjusted model [b]**
Annual change in physical functioning		
Frailty, Fried Frailty Index [a]	0.15 (-0.14 to 0.43)	0.21 (-0.06 to 0.49)
Dependency, GARS-score [a]	1.60 (0.05 to 3.17)[c]	1.59 (0.02 to 3.15)[c]
Physical capacity		
Handgrip strength, in kg	-0.87 (-2.19 to 0.45)	-1.21 (-2.48 to 0.05)
Walking speed, in m/s	-0.02 (-0.09 to 0.04)	-0.03 (-0.10 to 0.03)
Annual change in cognitive functioning		
Global cognition, MMSE score	-0.20 (-0.64 to 0.24)	-0.26 (-0.70 to 0.18)
Visuo-construction, Clock drawing score	0.30 (-0.16 to 0.03)	0.30 (-0.15 to 0.75)
Memory		
Immediate recall, 15WVLT score	-0.19 (-0.72 to 0.33)	-0.11 (-0.62 to 0.41)
Delayed recall, 15WVLT score	-0.47 (-1.25 to 0.31)	-0.40 (-1.19 to 0.38)
Visual Association Test score	-0.02 (-0.20 to 0.15)	-0.08 (-0.27 to 0.11)
Executive function Trail Making Test B-A (seconds) [a]	10.71 (-3.27 to 24.70)	13.12 (0.38 to 25.86)[c]
Stroop Color Word Test III-II (seconds) [a]	7.19 (-1.90 to 16.27)	6.75 (-2.01 to 15.50)
Psychomotor speed		
Letter Digit Substitution Test (correct/minute)	-0.61 (1.83 to 0.62)	-0.70 (-1.90 to 0.50)
Trail Making Test-A (seconds) [a]	3.42 (-2.56 to 9.39)	3.32 (-2.15 to 8.78)
Stroop Color Word Test II (seconds) [a]	0.17 (-3.77 to 4.10)	-0.14 (-4.03 to 3.75)
Health-related quality of life		
RAND-36 physical component summary	-0.09 (-2.36 to 2.19)	-0.07 (-2.33 to 2.18)
RAND-36 mental component summary	0.91 (-1.25 to 3.07)	0.68 (-1.46 to 2.82)

Figures are presented as mean difference in annual change (95% CI) for difference in annual change. Outcome data was completely missing for: Walking speed n=6e4.1%) WVLT delayed: n=1 (0.7%); TMT B-A n=2 (1.3%); SCWTIII-II n=3 (2.0%); SCWTII n=2 (1.3%), RAND-36 n=3 (2.0%).

Abbreviations: 15WVLT, 15-item Word Verbal Learning Test; GARS, Groningen Activity Restriction Scale; MMSE, mini-mental state examination.

[a] Higher scores, means less performance.

[b] Adjusted for age, sex and high education level.

[c] Statistically significant values.

Table S4: Analysis of presence of apathy symptoms on mortality risk.

		Mortality risk Exp(B), 95% CI	**p-value**
Model 1	Presence of apathy symptoms	1.88 (1.05 - 3.36)	0.033
Model 2	Presence of apathy symptoms	2.32 (1.29 - 4.17)	0.005
	Age at baseline	1.06 (1.02 - 1.11)	0.008
	Female gender	0.22 (0.09 - 0.53)	0.001
	High education level	0.85 (0.46-1.56)	0.595
Model 3	Presence of apathy symptoms	2.29 (1.27-4.14)	0.006
	Age at baseline	1.07 (1.02-1.12)	0.005
	Female gender	0.22 (0.09-0.52)	0.001
	High education level	0.88 (0.48-1.64)	0.690
	History of vascular disease	0.83 (0.45-1.52)	0.539
	History of Diabetes Mellitus	1.34 (0.72-2.50)	0.357



chapter 10

Summary and general discussion

SUMMARY OF MAIN FINDINGS

The growth of the population of older people approaching kidney failure comes with new challenges in healthcare provision. Healthcare professionals face an increasingly older and heterogeneous patient group in terms of multimorbidity, cognitive impairments and psychosocial challenges. These challenges may affect patients' healthcare provision for CKD and their treatment choices. Appropriate provision of kidney care and advance care planning should embrace a patient-centred holistic approach, focusing on the needs of individual patients, outcomes that matter to them, and adjusting treatment (choices) as the patient's health condition or preferences change.

This dissertation aims to describe if and how structured geriatric assessment contributes to appropriate/patient-centred care and decision-making for the older population approaching kidney failure (CKD, stage G4/G5). In the following paragraphs, I summarise the results of my research, following the three objectives of my dissertation: (I) To add knowledge about outcomes of treatment options for kidney replacement therapy. (II) To design and implement geriatric assessment prior to decision-making about kidney replacement therapy. (III) To address unveiled, previously unrecognised, challenges and vulnerabilities faced by the older advanced chronic kidney disease (CKD) population.

Part I: Increase the knowledge on outcomes of decisions for kidney failure treatment

In **Chapter 2** we find a lower mortality risk for patients with an explicit choice for dialysis versus those who opted for conservative care. Data from our systematic review suggest that in patients with severe comorbidity or older age, the lower risk for mortality was still present, albeit more limited. However, results should be interpreted cautiously due to the high heterogeneity between the studies. Also, the risk of selection bias and (residual) confounding was high, preventing us from drawing conclusions for individual patients. Frailty and physical and cognitive function may act as confounders but were limitedly reported and not used to adjust the mortality rates. To present a fair comparison of the survival difference between choice for dialysis and conservative care, we recommend observational studies to measure and adjust for these aspects. Concurrently, knowing that health-related quality of life (HRQoL) and symptoms are important patient outcomes, we conducted an analogous systematic review of these outcomes. While the review, written by Verberne *et al.*[1], is not included as a chapter in this dissertation, I discuss its outcomes briefly as these complement the understanding of the topic. In the article, we report that the choice of conservative care, compared to dialysis, has the potential for similar HRQoL outcomes in selected older patients. Patients who chose conservative care exhibited worse physical health outcomes and symptoms compared to those who had not yet started dialysis, but their outcomes were similar to patients already on dialysis. Mental health outcomes were consistent between patients who opted for conservative care and those who chose or initiated dialysis. Among patients choosing dialysis, the burden of kidney disease and its impact on daily life increases after the start of this treatment. While conducting both reviews, the literature assessed limitedly reported switches in treatment choices between dialysis and conservative care. In **Chapter 3** we report that available studies reported changes in treatment plans among 0 to 9% of the patients. Surprisingly, patients who chose dialysis

changed more often towards conservative care than vice versa. Our findings indicate that shared decision-making on kidney replacement therapy (KRT) is a continuous process rather than a single decision at a fixed point in time.

Part II: Design and implementation of geriatric assessment

The second part of this thesis reports on our experiences in implementing a geriatric assessment in nephrology care. This part encompasses the consultation of patients and healthcare professionals, our inquiries to find suitable instruments, and lessons learned from implementing geriatric assessment. A multidisciplinary group of health professionals participated in the *Pathway for OLDer patients reaching End-stage Renal disease (POLDER)* project. The group aimed to assess the need for nephrology-tailored geriatric assessment (NGA), agree on a suitable design, and to implement NGA to improve clinical care and strengthen scientific knowledge on geriatric impairments in advanced CKD patients.

The need for geriatric assessment in nephrology is explored among three preceding routine care and study initiatives. Using focus groups, we assessed patients' and professionals' experiences with geriatric assessment practices in nephrology care. In **Chapter 4** we report predominantly positive patient experiences with a geriatric assessment regarding the content and the time spent on the geriatric assessment. Professionals emphasised that the assessment creates awareness among the whole treatment team for cognitive and social problems, shifting the focus from mainly somatic to multidimensional problems. The benefits of geriatric assessment were perceived in three ways: identifying (mainly unknown cognitive) impairments, enhancing dialogue on the suitability of treatment options, and targeting multidimensional problems by supportive interventions. Lessons learned and considerations for implementing geriatric assessment into clinical practice concerned patients' involvement, selection of the suitable test set, multidisciplinary cooperation and supporting structures. In **Chapter 5** we describe the perspectives of these patients and professionals on the use and value of geriatric assessment for the decision-making process for KRT. We concluded that geriatric assessment was perceived as a valuable tool, and its outcomes can facilitate a more holistic approach to inform choices and decisions on KRT. In the context of geriatric assessment, decision-making in kidney failure was impeded by patients' psychosocial situation, patient-related factors on modality choice, and organisation of healthcare. Geriatric assessment adds to shared decision-making in (i) facilitating continual holistic assessment, (ii) filling the knowledge gap, and (iii) uncovering important patient characteristics.

The design of the geriatric assessment encompassed the selection of suitable tests for use in routine nephrology care, in absence of a golden standard set of instruments. In **Chapter 6** we describe practical requirements and evidence and propose a multidomain set. A multidisciplinary working group agreed on a set considered suitable for CKD care. The consensus-based set for nephrology-tailored geriatric assessment (NGA) combined instruments from traditional geriatric domains (functional, cognitive, psychosocial) with patient-reported outcomes measures (PROMs) previously selected for kidney care.[2] The consensus-based set of instruments for NGA was evaluated after implementation. In **Chapter 7** we concluded that the instruments for frailty and cognitive functioning were perceived as highly relevant by healthcare professionals. In contrast, other instruments (i.e. for caregiver

burden and nutritional status) were perceived as less relevant. The set should be further refined with a focus on improving maintenance by reducing (individual) patient burden. Also, further investigation of the use of instruments for people with low literacy, overcoming cross-cultural barriers and their relevance to outcomes is needed.

The evaluation of the implementation of NGA in ten Dutch centres is described in **Chapter 7**. We found that patient burden, lack of time, low patient literacy and low willingness to participate from patients were the most critical barriers to successful implementation. The most important enablers included multidisciplinary cooperation with geriatrics, multidisciplinary team meetings, trained personnel to assess the test set, and discussing the goals and outcomes of NGA with the patients. The findings largely corresponded with the information gathered from the focus group interviews in **Chapter 4**. Both studies suggested that maintaining flexibility in executing NGA practices is beneficial to dealing with local organisational circumstances. **Chapter 4 and 7** also conclude that involved professionals considered geriatric assessment relevant to integrate in routine care. Although integration of NGA in routine care is feasible, as reported in **Chapter 7,** implementation of NGA is subject to improvement as integration was not fully completed. Following the completion and evaluation of the POLDER project, together with the patient association, we developed a patient information flyer on geriatric assessment in kidney care. This flyer is available for general use and provided as **Supplement 1** to this dissertation. **Chapter 7** also reports that we realised broader implementation of the consensus-based NGA through the *DIALysis or not: Outcomes in older kidney patients with GerIatriC Assessment (DIALOGICA*) study.[3]

Part III: Revealing challenges and vulnerabilities of the older advanced CKD population

The third part of this dissertation describes insights into a few clinical outcomes and implications gained from geriatric assessment in nephrology, mainly related to mental health outcomes, frailty and cognitive status.

In **Chapter 9** we describe our research on the impact of the COVID-19 pandemic on mental health in the POLDER cohort. We found that older patients with advanced CKD suffered from disease-related anxiety about COVID-19 during the first wave of the COVID-19 pandemic. Compared to measures before the pandemic, we also found increased depressive symptoms and reduced physical HRQoL, but no difference in mental HRQoL or emotional symptoms. Nonetheless, symptoms of depression and anxiety have been present in a substantial part of the advanced CKD population, and the latter is more common in women compared to men.

In **Chapter 10** we found that symptoms of apathy were present in one-third of the older patients with advanced CKD included the *Cognitive decline in Older Patients with End stage renal disease* (COPE) study. The presence of apathy symptoms was associated with physical- and cognitive status and a two-times increased risk of four-year mortality in our cohort. Although we could not confirm a longitudinal decline in physical and cognitive functioning, apathy symptoms might be a potentially clinically relevant entity in care for older patients with advanced CKD. In both **Chapter 9 and 10** we recommend increasing awareness of mental health, i.e. symptoms of depression and apathy.

GENERAL DISCUSSION

The findings presented in this dissertation offer valuable insights into the potential advantages and practical application of structured geriatric assessment for enhancing tailored and patient-centred care for older patients with advanced CKD. The specific implications of each study are discussed within their respective chapters. Here, I describe my insights into the implications for clinical practice and propose future research directions based on our findings and experiences in implementing geriatric assessment in kidney care. These implications will be discussed on three dimensions: first, at the level of individual patients. Second, within the context of healthcare provision, and third, in response to prevailing societal challenges.

Implications for appropriate and patient-centered kidney care

Need for awareness of geriatric impairments

This dissertation builds upon the idea that geriatric evaluation can be used to assess individuals' medical, social and functional needs and tailor healthcare provision to these needs. Patients with advanced CKD (stage G4-5D) themselves recognised that goals in life may be different for them compared to younger people. They also perceived that a different approach, including additional support in various geriatric domains, is desirable. **(Chapter 4)** However, there is no one-size-fits-all solution to providing care appropriate to patients' needs due to heterogeneity in patients' multimorbidity, frailty and psychosocial situation, which may affect outcomes. While awaiting the prevalence of geriatric impairments in the POLDER and DIALOGICA cohorts, another Dutch study has shown that geriatric impairments are common: 48% of the older patients starting dialysis or choosing conservative care presented three or more geriatric impairments, affecting the risk of hospitalisation and tripled the risk of 12-month mortality.[4,5] Identification and awareness of geriatric impairments by healthcare professionals is essential, as its recognition can provide valuable insights for providing tailored care and risk stratification in decisions regarding KRT. **(Chapter 4 and 5)** Before I continue discussing the value of geriatric assessment, I will first highlight four interdependent key domains of vulnerabilities, their impact on advanced CKD patients, and potential ways to intervene within these domains.

i. Physical functioning and frailty

Functional dependence, affected by physical symptoms and frailty, is known to be the most frequent impaired domain in patients commencing dialysis. Studies indicate that 29% show impaired activities of daily living (e.g. dressing, transferring, eating) and 79% inability to perform instrumental activities of daily living (e.g. ability to use the phone, cooking, medication). These percentages are notably higher among patients opting for conservative care.[4] Frailty is a broader concept, mainly referred to as increased vulnerability to physical stressors, and has been reported in 7% to 43% of the pre-dialysis population,[6] and 30 to 80% of the dialysis patients.[7,8] The burden of physical symptoms is high to many patients. One of the physical symptoms most challenging for patients with CKD stage G4/G5 is fatigue.[9] We investigated 'trouble falling asleep' and 'staying asleep' in

Chapter 8. Similar to other research, 40-50% of the older advanced CKD patients experienced these symptoms, which were quite or very burdensome to 10-15%.[9]

Frailty and decline in physical functioning are crucial characteristics and outcomes for patients. These are highly relevant to patients' choice of KRT, since frailty is associated with an increased risk of hospitalisation and mortality, along with more symptoms, a higher symptom burden and poorer HRQoL.[8,10-12] Besides, the initiation of dialysis significantly impacts functional status; in nursing home residents on dialysis, it has been associated with a substantial and sustained decline. In the general older dialysis population, a significant proportion experiences a decline in functional status and has shown to increase fall injuries.[13,14] The role of functioning in decision-making is underscored by its significant impact on the recommendations made by geriatricians concerning transplantation.[15]

Various interventions to address challenges in the domain of physical functioning include home adjustments, occupational therapy, caregiver burden reduction, fall prevention, physiotherapy or exercise programs. Exercise interventions have demonstrated promising results in improving physical functioning and physical HRQoL in dialysis-dependent patients,[16,17] particularly during dialysis.[18] Additionally, exercise potentially reduces the severity of restless legs and sleep quality in people with CKD, although further research is warranted.[16,19,20] In community-dwelling older people, mobility training and home fall-risk interventions have shown promise in respectively enhancing mobility and functioning among those with frailty,[21] and in reducing both the number and rate of falls among those with high fall risk.[22]

ii. Cognitive functioning

Cognitive impairment is often underrecognised in CKD patients and is likely the domain patients most likely benefit from identification in geriatric assessments, as indicated by healthcare professionals in **Chapters 3 and 7**.[23] In CKD, cognitive impairment affects multiple domains but primarily manifests in reduced processing speed and executive function.[24,25] The prevalence of cognitive impairment in CKD patients is around 40%, varying with its definition and CKD stage.[24,26] This issue is more pronounced in older individuals with advanced CKD. In the DIALOGICA cohort, 55% of late-stage G4/G5 CKD patients aged over 65 years presented scores indicative of cognitive impairment,[27] and up to 70% of the older dialysis-dependent patients presented moderate to severe impairment.[4,28] Pre-kidney transplantation patients also show increased prevalence compared to health controls.[29] Cognitive function declines with kidney function, likely due to uremic toxins and cerebrovascular disease.[24,30] Cerebrovascular disease may also play a role in the link between apathy symptoms and reduced cognitive functioning, as explored in **chapter 9,** warranting further investigation.

Assessing cognitive impairments is crucial, as clinical awareness is low,[23] despite its association with unfavourable outcomes such as increased mortality,[31] and reduced mental HRQoL.[27] Above all, cognitive impairment and apathy symptoms affect patients' ability to participate in medical decisions and treatment adherence,[32-34] and increases caregiver burden.[35] Identification of cognitive impairments is therefore particularly

relevant to information delivery and therapy selection for KRT. For instance, home dialysis requires patients to understand and manage technical aspects; cognitive issues may necessitate extended training or assisted dialysis.[36]

Interventions to prevent cognitive decline in CKD patients are being explored, but the evidence is scarce.[37] Drew e*t al.* recommend an integrated care approach to optimise cardiovascular risk factors, strengthen family support, address depression and promote exercise.[24] A case manager could assist in coordinating integrated care. Evidence on best communication strategies for providing person-centred care to those with cognitive impairment and apathy symptoms is currently lacking.[38]

iii. Mental wellbeing

Other types of mental health problems that urge awareness include symptoms of depression, apathy and anxiety, as such issues pose a high burden on patients and their families. Although depression and anxiety disorders are more prevalent in the dialysis population, alarming prevalence has been reported in advanced CKD populations too. Depression is presented in approximately one-quarter of the adults with CKD.[39] Specific components of depression have not been well characterised in older adults with CKD, including apathy symptoms, which were found in one-third of the COPE cohort **(Chapter 9).** Elevated anxiety symptoms were presented in 31% of pre-dialysis patients, according to a recent meta-analysis.[40] For both depressive and anxiety symptoms, we found lower percentages in our cohort of advanced CKD patients **(Chapter 8).**

These mental health problems impact both outcomes and decision-making capacity. Depression and apathy symptoms have been associated with increased mortality risk **(Chapter 10)**.[41] Depression was linked to increased hospitalisation and cardiovascular events,[41] whereas apathy symptoms have associated with lower physical and cognitive function and lower HRQoL **(Chapter 10).** Another Dutch study suggested an increase in symptoms of apathy after starting dialysis, as reported by caregivers.[42] In addition, apathy was associated with an aversion to effort-based decision-making in patients with cerebral small vessel disease.[43] Although more research and confirmation of findings is needed in CKD, it seems inevitable that loss of motivation and reduced goal-directed behaviour requires adjusted communication strategies for those with apathy symptoms; namely simple, brief and include input from family and caregivers.

Treatment of depression, apathy and anxiety in CKD is still underexplored.[44] Psychotherapy appears to be a promising treatment for the reduction of depressive symptoms and improving HRQoL in dialysis patients, although the quality of evidence is currently low.[16,44,45] Whereas, an internet self-help problem-solving therapy has not proven effectiveness.[46] The content and accessibility of such interventions for CKD patients needs further research in this population, as well as the efficacy of medical treatment, exercise therapy, relaxation techniques, mindfulness-based stress reduction and dietary supplements.[44,45,47]

iv. Social status

Patients' social situation may also present challenges, particularly for informal caregivers. Research on this topic is limited, but the GOLD study showed that nearly one-third of caregivers felt burdened at the start of dialysis or conservative care, and 8% were overburdened, which increased after six months on dialysis.[4,42]. Caregivers, typically female spouses of older male dialysis patients, face higher burden levels than the general population.[48] Also, solitude may impact the social domain. Although not representative of the availability of social support, we found over one-third of the patients not living together in the POLDER and COPE cohort. **(Chapters 8 and 9)**

Maintaining strong social support is crucial for patients, as poor support is linked to higher mortality risk and lower adherence to medical care.[49] Also, the COVID-19 pandemic has shown that physical distancing led to unintended negative health consequences in CKD patients and the general population, such as increased mental distress, low willingness for telehealth, and reduced contact with caregivers living elsewhere, especially among those being vulnerable, e.g. with lower function and cognition and increased depressive symptoms.[50] Education programs and continuous case model show promise in improving caregiver burden, but further research is needed to tailor support strategies to the specific needs of CKD patients and their caregivers.[48]

Need for tailored information on outcomes of treatment options for KRT

Precise prognostic information on the treatment outcomes of KRT options is limited for older patients with advanced CKD. Recent systematic reviews, including our reviews in **Chapter 2** and Verberne *et al.*[1] on the effects of treatment choice on survival and HRQoL, report the need for studies that correct for confounding factors, including frailty and cognitive and physical functioning. Such evidence is highly relevant for information provision for conservative care as a viable treatment option. Based on our current information, we know that, on average, dialysis extends life expectancy compared to conservative care, as described in **Chapter 2.** Although we conclude that the level of evidence is low and subject to bias, recently a study using trial emulation methods confirms these findings.[51] An early step in the prediction of individuals' outcomes is a tool developed by Ramspek et al. (2020) to predict 2-year mortality for both dialysis and conservative care from the time of treatment decision. Further development and external validation are needed before the model can be used to inform the shared decision-making process.[52] Survival is undoubtedly not the sole consideration, and choice for dialysis may be at some expense of HRQoL. Although HRQoL outcomes seem comparable between dialysis and conservative care choices, after dialysis initiation the burden of kidney disease and its impact on daily life increases.[1] Recent research reported that symptom burden already significantly increases in the year preceding dialysis, and stabilises after the start of dialysis. Also the decline of HRQoL stabilizes.[9,53] Improvement of HRQoL is more frequent after transplantation compared to dialysis.[13]

Conservative care is a viable option specifically for those most vulnerable, but it is not always known to patients.[54,55] Patients who opt for conservative care provide reasons relating to maintaining quality of life, concerns about the treatment burden associated with dialysis, cost considerations, and the desire not to impose a burden on others.[55] Recently, the 'Kidney

Failure Decision Aid' has been developed to facilitate the shared decision-making process and elucidate patient preferences. The decision aid provides patients with an explanation of treatment techniques and (patients-like-me) treatment outcome information. Based on real-world data, patients can choose to see survival probabilities and average hospitalisation rates for their age group per treatment option.[56]

Two studies hold promise on the topic. First, the ongoing Prepare for Kidney Care Study compares the Quality-Adjusted Life Years (QALYs) gained over 3-years between dialysis and conservative care in older patients with CKD. This randomised controlled trial aims to enhance clinical practice by prioritising person-centred outcomes and delivering unbiased information to support shared decision-making.[57] Second, the DIALOGICA study holds promise in providing comprehensive insights into geriatric impairments and the impact of conservative care and dialysis on HRQoL, clinical outcomes, and costs. This observational study will provide evidence to assist patients and clinicians in making well-informed choices regarding the most suitable treatment for kidney failure.[3] The DIALOGICA study will also shed light on geriatric impairments and what happens during follow-up, i.e. changes in treatment choice and outcomes of care.

The choice of kidney transplantation, dialysis, or conservative care is often not easy and particularly no one-size-fits-all. Personal circumstances of older patients can change rapidly, for example, due to illness, increased dependency, loss of a partner, or shifting life goals. These conditions ongoingly shape their health outcome priorities. Given the findings in **Chapter 3** that treatment plans may alter due to such issues in up to 9% of the investigated populations, we can state that the decision-making process is continuous rather than a one-time decision. The ideal trajectory towards KRT choice would encompass frequent checks on whether a patient's choice is still appropriate and in line with their potentially changing physical, mental and social situation, as well as their individual preferences and outcome priorities.

The value of geriatric assessment for treatment support and decision-making on KRT

Ideally, care should focus on outcomes that matter most to patients. CKD patients have indicated that their main outcome priorities, next to survival, include maximizing functional capabilities, psychological health, and quality of life.[58-60] Health outcome priorities, expectations and experiences unfortunately often not align between patients and professionals.[61] NGA could benefit aligning expectations by providing firm impact, in terms of multidomain identification of vulnerabilities, and soft impact, through opening a dialogue between patients with and among clinicians. **Chapters 4 and 7** describe that NGA was perceived to create the needed awareness for impairments, open dialogue on care priorities, and enable supportive care for multidimensional issues. Recently, a project in the United Kingdom has confirmed the value of geriatric assessment for the implementation of person-centred management plans,[11] as was also described by others.[62,63] Besides, NGA is particularly of value in facilitating the shared-decision making process on KRT, as we describe **in Chapter 5.** Verberne et al. previously depicted that shared decision making in older patients with advanced CKD is often predominantly driven by a biomedical perspective, and would benefit from a shift towards a more person-centred conception.[64] Awareness and assessment of geriatric impairments enables a healthcare professional to be part of the patients' relational

context. It may therefore facilitate the shift in advanced care planning towards existential decisions based on what matters most to the patient.

Our study design **(Chapter 7)** did not allow us to gather evidence on the contribution of NGA to changes in treatment plans. Neither did we study the effectiveness (i.e. can we do it well? does NGA benefit patients?) of geriatric assessment practices in nephrology, nor the efficacy (can we do it right? does NGA work?) and efficiency (can we do it quickly and economically?). The rationale for proceeding with our work came from other fields. In oncology, for example, (comprehensive) geriatric assessments have been proven to be necessary and beneficial, and increasing evidence demonstrates the benefit of geriatric assessment-guided treatment decisions in optimising outcome of oncologic treatment in older patients.[65] The effect of CGA has been investigated in several randomised controlled trials (RCTs) in oncology, using different models of (comprehensive) geriatric assessment. Systematic review of these RCTs points towards the effectiveness of CGA for treatment completion; reduction of treatment intensity, treatment-related complications, and chemotherapy toxicity; as well as improvement of HRQoL scores and caregiver burden.[66-68] Although CGA had no impact on survival[68] or nursing home admission, low-grade evidence was found for the reduction of unplanned hospital admission risk among community-dwelling frail patients.[69]

Evidence for CGA in nephrology is currently being investigated in the GOAL study, a promising multicenter cluster RCT study in Australia. Herein, patients are included with CKD stage G3-5D (eGFR <60ml/min1.73m2) above 65 years of age who are frail. Hospitals are randomised to conduct CGA or act as controls. The trial's primary outcome is the attainment of patients' own care goals. An additional process evaluation will enable the establishment of features of CGA delivery that increase the interventions' effectiveness.[70] This would expectantly provide insights on if and how geriatric assessment might be effective in outpatient CKD care, shed light on the needed strategies after geriatric assessment, and benefit maintenance of geriatric assessment practices in nephrology.

So, what to do with the information derived from the NGA? In POLDER and DIALOGICA we advised to incorporate multidisciplinary team meetings and to involve or refer to a geriatrician for holistic advice for supportive care, rather than on specific interventions. **(Chapter 7)** Interventions after NGA were outside the scope of my research. The value and effectiveness of our modified NGA approach for advanced CKD patients – in terms of quantification of the number and type of interventions – remains to be investigated. In oncology, if geriatric-specific expertise was in place, geriatric assessment has shown to lead to less intensive treatment. Also, supportive non-oncologic interventions were recommended in over 70% of patients.[71] Self-management interventions after geriatric assessment have been described for positively targeting domains of falls/mobility, comorbidity, pain and medication and related outcomes in older people. These interventions, however, need further study on the validation, long-term effects and scalability.[72] In CKD, integration of self-management and psychosocial support has potential to enhance person-centred care, with prioritisation questionnaires and eHealth interventions serving as valuable tools in this process.[73] Although intervention studies for geriatric impairments in CKD patients are scarce, along with limited clinical guidance, the true value of NGA might lie in identifying

these impairments and tailoring care accordingly, rather than focusing solely on resolving them.

Communication and information provision on CKD and KRT.
A final value of geriatric assessment is the potential to enhance patient-centred communication and information provision on CKD and KRT options. As depicted previously, the presence of mental health issues or cognitive impairment could be a reason to alter the level of information provision. Communication and information provision on KRT options vary in quality. Recent qualitative studies conclude that identification of patient's values, needs and health outcome priorities should start early and guide patient-centred information provision in further steps of decision-making for KRT.[60,61,74] For clinicians, communication is particularly challenging due to the uncertainty of the disease course, disease complexity, clinicians' engagement with a specific treatment modality, and factors on the geriatric axes beyond the kidney disease. Barriers among healthcare professionals to convey information on kidney failure treatment include hesitation in approaching the topic, uncertainty about the benefits of conservative care, fear of the patient's reaction to suggesting conservative care, and doubts about the patient's ability to understand the information.[55] Our findings in **Chapter 4-7** indicate that a geriatric assessment will likely improve communication and focused discussions on goals of care. However, quantitative evidence is needed, as well as robust studies on how to tailor information based on patient preferences and clear delivery, especially about conservative care.[75] Herein, the continuous process of treatment decision-making should be acknowledged.

Implications on patient-level summarised
In short, to refine ongoing patient-centred care and the process of KRT decision-making for this expanding patient group, more detailed and robust data is needed on outcomes that matter to patients, extending beyond survival and quality of life. Central questions still need to be answered on how geriatric evaluation impacts these outcomes and how best to communicate with, and support patients. Improving holistic care for older CKD patients requires an interdisciplinary team approach, incorporating psychologists, social workers, exercise professionals, and geriatricians to provide active and ongoing person-centred care, addressing and managing mental health problems, cognitive impairment and social status.[38]

Implications for healthcare provision

The need for active and ongoing multifactorial assessment prior to KRT treatment decisions is increasingly recognised by nephrologists, as described in the literature and underscored in our research **(Chapter 4-6 and 8).**[4,76-80] While my focus in the POLDER project centred on dialysis preparation, the necessity for psychosocial assessment during the trajectory to identify suitable kidney transplantation candidates has also been recognised.[81-83] There is a call for concurrent further development in both domains, for which I provide considerations in the following paragraphs.

The optimal approach for geriatric assessment in CKD care

Despite several structural initiatives to investigate geriatric assessment in kidney care, there is no conclusive evidence yet on the best model for the delivery of geriatric evaluation.[11,15,62,63,84] The POLDER and DIALOGICA projects implemented a consensus-based set which was considered suitable for clinical practice as well as to inform scientific evidence. In contrast to our approach, Nixon et al. (2021) used a two-step approach applying a geriatric assessment to only those who were frail (Clinical Frailty Scale [CFS] score >5).[11] Such a simple screening tool applicable to routine care, would be a preferred way to select those that benefit from further assessment efficiently. While the Frailty phenotype is still the most commonly used frailty measure in literature,[85] the CFS has good diagnostic accuracy and is increasingly used in clinical practice since the COVID-19 pandemic.[86] However, Van Loon *et al.* previously concluded that screening tools lack the discriminative ability to rule out frailty compared with a geriatric assessment.[87] Similarly, a recent study found that sensitivity of the CFS is too low for solitary clinical use.[88] Besides, the CFS lacks an objective cognitive component, and it should be investigated how much cognitive impairments would remain unidentified. With the current knowledge, for holistic assessment of patients' needs, I therefore think that it is inevitable that some form of geriatric assessment beyond frailty screening is needed.

In selecting instruments, as described in **Chapter 6,** we proceeded in the POLDER project with a consensus-based NGA. In **Chapter 8** we investigated the perceived relevance and feasibility of this set, but we did not compare this to other models for delivery of geriatric assessment. Our considerations of the most suitable instruments are described in **Chapter 8**. Subsequently, in DIALOGICA we implemented NGA in almost 40 Dutch and Belgium hospitals, with some minor changes to the set, leaving out the test for caregiver burden and substituting the nutritional questionnaire.[3] For now, if clinical time is sparse, I would recommend a frailty assessment (CFS), cognitive test (Montreal Cognitive Assessment) and symptom assessment (Dialysis Symptom Index) at the minimum. Caregiver burden and goal-setting[89] are potentially relevant for further research and consideration. In contrast to CGA, our NGA currently lacks an explicit component to initiate existential discussions on what matters most to the patient. Further evaluation and optimisation of the consensus-based set is recommended for efficacy and efficiency reasons, targeting: 1) the discriminative and predictive value of the included instruments, 2) each instrument's value in comparison to potential short screening tools, 3) providing evidence on the optimum target population, 4) the inclusion of an instrument on health outcome prioritisation, and 5) the development and use of cross-cultural instruments for geriatric assessment, as described in **Chapter 8**.[90,91]

The organisation of geriatric assessment in kidney care entails several key requirements. Firstly, the alignment of multidisciplinary roles. Our research indicates positive attitudes from both patients and professionals towards integrating geriatric in nephrology care, although its development remains ongoing.**(Chapter 4)** Collaboration with geriatric specialists and delineating organisational responsibilities are vital, yet evidence remains limited.[92] Secondly, the crucial role of nurses and advanced nurse practitioners (in Dutch: *verpleegkundig specialist*) cannot be overstated, as they are the primary drivers behind the implementation, follow-up and maintenance of geriatric assessment.[93] Thirdly, the outcomes of geriatric

assessment should be discussed as needed within multidisciplinary team meetings in the presence of a geriatrician or geriatric internist.[94] The Dutch guidelines emphasise the importance of establishing agreements with involved medical specialists regarding responsibilities, task allocation, and content of geriatric assessment, acknowledging the limited evidence on the organisation of geriatric care. The Dutch Internists Association recently mandated each internal medicine department to incorporate geriatric expertise, underscoring the importance of integrating the geriatric perspective. Lastly, a centre should be able to tailor education trajectories for KRT based on geriatric assessment findings.

Further clinical development of geriatric assessment in nephrology may lie in establishing patient-centred pathways, transcending the single-disease-centred approach in hospital care. This entails bringing together nephrology and non-nephrology-related health professionals, including primary care physicians. Initiatives such as the ongoing GERONTE study in oncology exemplify this approach by centralising treatment recommendations based on patient's priorities.[95,96] Herein, specialised nurses serve as case managers, acting as the primary point of contact for patients to enhance coordination between specialists.[96]

Implementation of NGA is an iterative process

Integrating geriatric assessment in routine practice is a complex and ongoing process, mirroring the long-term endeavour in geriatric oncology. Over de recent decades geriatric assessment has become the cornerstone of geriatric oncology research.[97] Geriatric assessment is now being advised for every older adult who receives a new cancer diagnosis, according to recommendations from American Society of Clinical Oncology, and International Society of Geriatric Oncology (SIOG).[97] While evidence of the benefits of geriatric assessment in routine oncology care advances, the need for understanding and overcoming barriers for the broad implementation and utilisation of GA continues.[98,99] Also other fields have expressed the need for (comprehensive) geriatric assessment as part of routine assessment, e.g. in acute care[100,101], prior to hematologic stem cell transplantation,[102] surgery for aortic stenosis, and colorectal surgery.[103]

Establishing sustainable practices beyond research studies remains a challenge, also in nephrology. In POLDER and DIALOGICA standardised research procedures, limited patient enrolment and inconsistent assessment practices hindered progress (**Chapter 5 and 8**). Structured data collection should ideally be incorporated within national registries. Promisingly, the Dutch Nefodata registry was recently enhanced by integrating of PROMs (i.e. HRQoL and symptom assessments),[2] and is currently expanding its scope to CKD stages G4/G5 and conservative care. Plans to incorporate a frailty measure are being prepared. A comprehensive overview of this expansion was depicted in the report 'Samen voor Betere Nierzorg'.[104] If information on physical and cognitive functioning could also be incorporated, this would represent a significant advancement, facilitating the use of real-world data to assess treatment outcomes. Such data could then be utilised in clinical settings to provide tailored information and prognoses to patients.

Unmistakeably, ensuring the active involvement of patients in the further development of NGA is most important.[104] This particularly requires ongoing investigation of patient acceptability of NGA, alongside the potential facilitation of digital tools, including a dashboard and patient application for symptom-monitoring with self-management recommendations.

Implications for society's healthcare challenges in providing appropriate kidney care

The ageing population and anticipated rise in chronic kidney disease pose significant challenges for healthcare provision both at the hospital and societal levels. Dialysis is one of the most expensive healthcare treatments and will likely lead to escalating healthcare expenditures as demand grows. Globally, among populations with dialysis access, outcomes remain suboptimal. Recently, Himmelfarb and colleagues described in Nature Reviews the challenges and future directions of the dialysis landscape: "*While patients value longevity, reducing symptom burden and achieving maximal functional and social rehabilitation are prioritised more highly. In response, patients, payors, regulators and healthcare systems are increasingly demanding improved value, which can only come about through true patient-centred innovation that supports high-quality, high-value care.*" [105] In the Netherlands, improved prevention and increased transplantation rates turned the increase in the inflow of new dialysis patients, resulting in a stabilised number of dialysis patients, despite an ageing population.[104,106] However, government advisory bodies and news items report that shortages of qualified personnel pose a severe threat to equal access to care, while inadequate attention to diversity risks exacerbates health disparities.[107-109] To address these challenges, increasing awareness of inclusive care and enhancing knowledge about appropriate care are imperative. Which may involve treating individuals differently to address their unique needs.[110] In my view, geriatric assessment (i.e. holistic assessment and support of patient's medical, social and functional need) fits this purpose and it is a valuable tool in enhancing patient autonomy while optimising healthcare resources.

Geriatric assessment provides a scheme to assess patients' needs in multiple domains, using the inclusive approach to find out what matters most to the patient.[111] The historical scheme of CGA including a geriatrician, has been forwarded over the past decades to models that may fit into the routine care for older patients with all kinds of diseases.[101,112] A development that is still ongoing and in kidney care in its early stages. As outlined in preceding paragraphs, geriatric assessment offers substantial benefits for promoting inclusive, patient-centred kidney care by facilitating the integration of diverse perspectives within the treatment team and elucidating patients' needs and impairments across four key domains. Geriatric evaluation in oncology has shown to alter the treatment plan in one-third of the patients, primarily to a less intensive treatment option.[67,71] Conservative care as a KRT option has evolved from a strategy of "doing nothing" to providing regular active treatment (except for providing dialysis) for patients with complex conditions, increasingly emerging as a viable and acceptable alternative to dialysis with lower treatment burden and costs.[113] Leveraging insights from geriatric assessment enables healthcare providers to address patients' needs and symptoms, thus improving delivery of tailored care. Meanwhile, conservative care is being recognised as a legitimate treatment option, potentially offering comparable outcomes to dialysis in certain cases, and reducing costly dialysis treatments while increasing the quality of care. This approach further contributes to the delivery of appropriate care, and aligns with the principles of value-based healthcare, where a balance is sought between outcomes (including patient-centred outcomes), the burden of treatment for the individual patient, and societal value.[113,114]

Future of geriatric nephrology: unite forces

When this dissertation comes to press, patient inclusion in the DIALOGICA study has concluded across Dutch and Belgium hospitals. Considerations must be made regarding continuing standardised geriatric assessment in Dutch nephrology care, which is up to nephrologists, nurses and other healthcare professionals to unite forces. Conducting a survey among nephrologists and nephrology nurses on geriatric nephrology about 'where we are and what comes next' could provide valuable insights into the current landscape and guide future perspectives on care for patients approaching kidney failure, including acute kidney injury and transplantation patients.[115] International collaboration, akin to the International Society of Geriatric Oncology, could prove benefit in this regard. Establishing a consortium or working group within renal associations, similar or linked to the CONNECT research initiative which focuses on cognitive decline in brain-kidney interactions,[116] could drive scientific research agendas and elevate prominence to geriatric nephrology at scientific congresses. Furthermore, such initiatives should offer practical guidance on navigating and intervening in the increasing complexity of patient's needs in nephrology care.

Future research directions and conclusions

Future research should investigate the discriminative and prognostic value of multidimensional geriatric impairments on a broad range of outcomes, encompassing HRQoL, symptoms, cognitive impairments and mental health, with particular attention to potential sex and cross-cultural differences. Subsequent investigations should explore how this information can best inform a personalised approach, focussing on supportive treatments, particularly mental health, and providing accurate evidence on all treatment options to patients, their caregivers and health professionals. I recommend to continue research on the most suitable test set in collaboration with patients and include the development of culturally sensitive test sets. Additionally, efforts should be directed towards gathering evidence on the effectiveness of NGA, its discriminative abilities, and predictive capacity for outcomes. Enhanced scientific and clinical collaboration at national and international levels is essential for advancing the role of geriatric assessment in nephrology care.

Our research introduces a novel approach of nephrology-tailored geriatric assessment aimed at improving appropriate and patient-centered care for the increasingly heterogeneous and often vulnerable population of older CKD patients. This approach recognises the importance of treating individuals differently to address their unique needs. It also provides a practical solution to implement guideline recommendations, which we implemented broadly.

Based on our findings, I conclude that integrating NGA into routine care practices is both feasible and perceived as relevant by patients and healthcare professionals. Our research underscores shared decision-making for KRT is a continuous process, emphasising the need for active and ongoing evaluation of patients' needs and treatment decisions, whether opting to initiate or forgo high-burden and costly KRT treatment. Additionally, our research sheds light on mental well-being during COVID-19 pandemic and highlights symptoms of apathy in the ageing advanced CKD population. This dissertation contributed to a better understanding of the value, implementation and implications of a standardised holistic assessment of geriatric impairments for appropriate kidney care.

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Appendices

Nederlandse samenvatting (Dutch summary)
Patiëntenfolder (patient leaflet)
Group information
Dankwoord (acknowledgments)
Curriculum vitae
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NEDERLANDSE SAMENVATTING

Passende zorg voor oudere personen met chronische nierschade.

Naar schatting heeft 10% tot 13% van de mensen wereldwijd een vorm van nierschade, variërend van mild tot ernstig. Bij geleidelijk verlies van de nierfunctie kan het lichaam steeds minder goed afvalstoffen en overtollig vocht uit het bloed filteren. Bij gevorderde nierschade, wanneer de nierfunctie onder de 20-30% daalt, kunnen patiënten last krijgen van veel verschillende klachten, bijvoorbeeld vermoeidheid, spierkrampen, jeuk, opgezwollen voeten en armen, slaapproblemen en concentratieproblemen. Bij een nierfunctie onder de 15% spreken we van nierfalen. Daalt de nierfunctie verder, dan is behandeling nodig om de functie van de nieren over te nemen, zoals niertransplantatie, dialyse of best mogelijke ondersteuning met medicatie. Hoelang iemand leeft met deze behandelingen kan heel verschillend zijn en hangt zowel af van patiënt factoren als van de behandeling.

De gemiddelde leeftijd van mensen met chronische nierschade in Nederland is 72 jaar. Jaarlijks starten bijna 2000 nieuwe patiënten met transplantatie of dialyse als nierfunctie-vervangende behandeling. De helft hiervan is ouder dan 65 jaar en bijna een kwart ouder dan 75 jaar. Leeftijd en leefstijlziekten, zoals hoge bloeddruk en diabetes mellitus type II, zijn risicofactoren voor het ontwikkelen van nierschade. Doordat de Nederlandse bevolking gemiddeld ouder wordt (vergrijst) en door toename van leefstijlziekten, stijgt ook het aantal ouderen met chronische nierschade. Dit brengt nieuwe uitdagingen voor de gezondheidszorg met zich mee.

Vooral bij ouderen is de behandeling van chronische nierschade vaak complex, door bijkomende ziekten (comorbiditeiten), achteruitgang in cognitie (geheugen en denkvermogen) en lichamelijke beperkingen. Oudere patiënten hebben vaak specifieke zorgbehoeften die niet altijd worden herkend. De zorg voor patiënten (met een nierziekte) richt zich hoofdzakelijk op langer leven, maar voor ouderen is de kwaliteit van leven of behoud van onafhankelijkheid soms belangrijker. Informatie over de effecten van de verschillende behandelopties op deze uitkomsten voor ouderen ontbreekt vaak. De bijkomende ziektebeelden, specifieke zorgbehoeften en gebrek aan voorspellende informatie over uitkomsten, maakt de begeleiding bij chronische nierziekte en gezamenlijke besluitvorming over een mogelijke nierfunctievervangende behandeling bij ouderen uniek en complex.

Voor het bieden van passende zorg voor ouderen met gevorderde nierschade kan aanvullend onderzoek helpen. Het vakgebied van de ouderenzorg (geriatrie) gebruikt een uitgebreide geriatrische evaluatie (in het Engels: *comprehensive geriatric assessment*) om systematisch de kwetsbaarheden en zorgbehoeften van ouderen te identificeren. Dit proefschrift beschrijft hoe geriatrische principes geïntegreerd kunnen worden in de nefrologie om de zorg voor oudere CKD-patiënten te verbeteren.

Hoofdstuk 1 geeft een beknopte introductie over de aanleiding van dit onderzoek en beschrijft wat een geriatrisch assessment inhoudt. Dit aanvullende onderzoek brengt de situatie van patiënt op medisch, functioneel en sociaal gebied in kaart. Met vragenlijsten en aanvullende testen onderzoekt een arts of verpleegkundige onder andere de mate van zelfstandig functioneren, mobiliteit, sociale omstandigheden, het steunsysteem, cognitieve- of stemmingsstoornissen en de verwachtingen van de patiënt zelf. Indien nodig maakt een

geriater of internist ouderengeneeskunde een geïntegreerd zorgplan om invulling te geven aan diens specifieke zorgbehoeften. **Hoofdstuk 1** beschrijft ook de behandelopties voor nierfalen. Transplantatie van een donornier vereist een goede fysieke conditie van de patiënt, een beschikbare donornier en is niet voor iedereen mogelijk. Dialyse is een behandeling waarbij het bloed mechanisch gefilterd wordt om afvalstoffen en overtollig vocht te verwijderen, dit kan thuis of in het ziekenhuis. Dialyse is een intensieve belasting waarbij mensen gemiddeld 3 keer per week 3 tot 4 uur in het ziekenhuis moeten zijn (hemodialyse), of waarbij een dagelijkse behandeling thuis nodig is (buik dialyse). Conservatieve zorg is de behandeling waarbij zonder dialyse met behulp van medicatie en dieet zo lang en goed mogelijke kwaliteit van leven en behandeling van symptomen wordt nagestreefd. Dit proefschrift richt zich voornamelijk op de periode waarin patiënt en zorgverlener de keuze voor dialyse of conservatieve zorg moeten maken.

In dit proefschrift beschrijf ik of en hoe gestructureerd aanvullend onderzoek bij ouderen (geriatrisch assessment) kan bijdragen aan passende zorg voor mensen met gevorderde chronische nierschade en besluitvorming over behandeling bij nierfalen. Hiertoe zijn drie doelen gesteld: 1. Kennis toevoegen over de uitkomsten van behandelopties voor behandeling bij nierfalen, 2. Introduceren en implementeren van aanvullend onderzoek (geriatrisch assessment) bij oudere personen met gevorderde chronische nierschade, 3. Beschrijven van uitdagingen en kwetsbaarheden bij deze doelgroep.

Deel 1: Uitkomsten van behandelkeuzes voor behandeling bij nierfalen.

Het eerste deel beschrijft de uitkomsten van zorg bij nierfalen bij verschillende behandelkeuzes, met behulp van systematische en kritische samenvatting van onderzoeksresultaten uit bestaande studies. **Hoofdstuk 2** van dit proefschrift beschrijft *sterfterisico's* bij patiënten die kiezen voor dialyse of conservatieve zorg. Uit eerdere studies bleek dat patiënten die voor dialyse kozen over het algemeen een tweevoud lager sterfterisico hebben. Het sterfte risico met dialyse is ook bij oudere patiënten en patiënten met veel comorbiditeiten nog steeds lager dan met conservatieve zorg, hoewel het voordeel op overleving in deze groepen af lijkt te nemen. Bij interpretatie van de resultaten is voorzichtigheid geboden! Vanwege de grote variatie in de opzet van de onderzoeken is het risico op vertekening en verstoring door andere factoren (confounding) groot. De patiënten die kozen voor dialyse waren gemiddeld jonger en hadden vaker ook andere ziektebeelden (comorbiditeiten). Factoren zoals kwetsbaarheid en fysieke en cognitieve functies werden slechts beperkt gerapporteerd en niet meegenomen in de aanpassing van sterfterisico's. Om een eerlijke vergelijking te maken tussen de overlevingskansen bij dialyse en conservatieve zorg, is het belangrijk om deze aspecten in toekomstige observationele studies te meten en mee te wegen. Zoals hierboven genoemd, telt voor ouderen de kwaliteit van leven soms minstens zo zwaar. In **een andere studie**[1] (niet opgenomen in dit proefschrift) beschrijven wij de uitkomsten voor *gezondheid-gerelateerde kwaliteit van leven* en *symptoomlast*. Patiënten met een keuze voor conservatieve zorg hadden slechtere lichamelijke gezondheidsuitkomsten en meer ziekteklachten vergeleken met patiënten die nog niet gestart zijn met dialyse, maar hun uitkomsten van zorg zijn vergelijkbaar met die van patiënten die al dialyseren. Beide groepen rapporteren wel vergelijkbare mentale gezondheid. De keuze voor dialyse leidt gemiddeld echter tot een grotere ziektelast en meer impact op het dagelijks leven na de start van de

behandeling. In **hoofdstuk 3** beschrijven we dat de initiële keuze voor dialyse of conservatieve zorg soms wijzigt: bij 0 tot 9% van de patiënten volgens studies die deze switch rapporteren. Verrassende bevinding uit deze studies is dat patiënten met een initiële keuze voor dialyse vaker hun voorgenomen keuze naar conservatieve zorg wijzigen, dan andersom. Dit benadrukt dat het keuzeproces voor behandeling bij nierfalen een continu proces is, en niet louter een eenmalige beslissing. Het is dus belangrijk oog te houden voor het wijzigen van de gezondheid of sociale situatie van een patiënt.

Deel 2: Aanvullend onderzoek bij ouderen met gevorderde chronische nierschade

Het tweede deel van het proefschrift richt zich op de introductie en uitvoer (implementatie) van aanvullend geriatrisch onderzoek bij ouderen met een nierziekte. Dit onderzoek is opgezet in samenwerking met specialisten en verpleegkundigen van de nierziekten en ouderengeneeskunde, maatschappelijk werkers en diëtisten uit verschillende Nederlandse ziekenhuizen. **Hoofdstuk 4 en 5** beschrijven de noodzaak, werkwijze en waarde van aanvullend geriatrisch onderzoek bij patiënten met gevorderde nierschade. Dit is onderzocht in focusgroepen (groepsinterviews) met patiënten en zorgverleners betrokken bij drie bestaande initiatieven waar dit aanvullende onderzoek op verschillende manieren is gedaan. We vroegen hen naar hun ervaringen met het geriatrisch assessment en de waarde ervan voor het keuzeproces voor behandeling bij nierfalen. Zowel patiënten als professionals rapporteerden positieve ervaringen en gaven aan dat de zorg voor oudere patiënten anders is dan de zorg voor jongere personen met een nierziekte. Het geriatrisch assessment creëert bewustzijn onder zorgverleners over het bestaan van cognitieve en sociale problemen. De gebruikte testen en vragenlijsten werden gezien als waardevol voor het identificeren van voorheen vaak onbekende cognitieve problemen, het verbeteren van de dialoog over behandelingsopties en het aanpakken van problemen van multidimensionale aard. **Hoofdstuk 4** beschrijft geleerde lessen en overwegingen voor het gebruik van aanvullend geriatrisch onderzoek in de zorg voor oudere personen met een nierziekte. Toepassing vraagt om duidelijke communicatie met patiënten over het doel en de resultaten. Ook de belastbaarheid van patiënten is een aandachtspunt, 45 tot 90 minuten is acceptabel volgens patiënten en zorgverleners. Daarbij is het nuttig de set aan instrumenten beperkt te houden en aan te passen op de doelgroep. Mantelzorgers kunnen aanvullend nuttige informatie geven en herhaling van de metingen helpt om veranderingen te volgen. Voor het beoordelen van de uitkomsten van de testen en vragenlijsten door zorgverleners is training en ervaring nodig. Goede samenwerking tussen zorgverleners vanuit nefrologie en geriatrie kan hierbij helpen. Ook benoemen de geïnterviewden dat voldoende steun van het management en voldoende beschikbaarheid van geriaters nodig is, evenals bewijs dat geriatrisch assessment van toegevoegde waarde is.

In **hoofdstuk 5** beschrijven we hoe zorgverleners en patiënten denken over de waarde van geriatrisch assessment voor beslissingen over behandeling bij nierfalen. Patiënten gaven aan zich kwetsbaar te voelen door hun hoge leeftijd, meerdere chronische aandoeningen en verliezen in hun leven. Veel van hen waren bereid om een kortere levensduur te accepteren in ruil voor een betere kwaliteit van leven. We identificeerden thema's die van invloed zijn op het keuzeproces voor behandeling bij nierfalen, zoals het steunsysteem, de mening van naasten, patiënt-arts relatie, kwaliteit van leven en levensdoelen. Maar ook medische

geschiedenis van patiënten, of zijn/haar karakter of instelling en de informatievoorziening over de behandelopties. Ook de samenwerking van zorgverleners vanuit verschillende expertise gebieden en voldoende tijd om een keuze te kunnen maken zijn belangrijk voor een wel overwogen beslissing. Volgens zorgprofessionals is een op nefrologie afgestemde geriatrisch assessment van meerwaarde voor de beslissing over behandeling bij nierfalen: het ondersteunt de zorgverlener in een voortdurende brede blik op de patiënt, vult kennishiaten, bijvoorbeeld over cognitieve problemen en brengt belangrijke kenmerken en wensen van de patiënt naar voren.

Hoofdstuk 6 beschrijft de onderbouwing voor de gekozen set aan instrumenten voor het aanvullend onderzoek. Bij gebrek aan een gouden standaard, zijn zorgverleners een set aan vragenlijsten en testen overeengekomen relevant voor oudere personen met gevorderde nierschade, gebaseerd op beschikbare literatuur en klinische ervaring. Deze set noemen we het nefro-geriatrisch assessment. De set bevat testen voor mentaal en fysiek functioneren (zoals cognitietesten en een handknijpkrachtmeting), maar ook een kwetsbaarheid screening en surprise question voor de zorgverlener (*zou u verrast zijn als deze patiënt binnen 1 jaar overlijdt?*). Daarnaast krijgt de patiënt vragenlijsten over dagelijks functioneren, depressieve klachten, mantelzorgbelasting, optimisme, voedingsstatus, gezondheid-gerelateerde kwaliteit van leven en specifieke gezondheidsklachten (zoals vermoeidheid, angstig gevoel en misselijkheid). De laatste twee instrumenten zijn recent geselecteerd voor landelijke patiënt-gerapporteerde uitkomstmaten in de dialysezorg.

Hoofdstuk 7 beschrijft de POLDER studie waarbij in 10 ziekenhuizen het nefro-geriatrisch assessment werd afgenomen bij in totaal 191 patiënten van 70 jaar en ouder met een nierfunctie onder 20%. Na één jaar werd deze meting herhaald. Dit stelt ons in staat het mentale en fysieke functioneren te vergelijken met de basismeting. De integratie van nefro-geriatrisch assessment in de klinische praktijk werd geëvalueerd met betrokken zorgprofessionals. De zorgprofessionals gaven aan dat ze de instrumenten voor kwetsbaarheid en cognitieve functies als zeer relevant ervaren, terwijl andere instrumenten, zoals die voor mantelzorg en voedingsstatus minder relevant werden gevonden. Meer onderzoek is nodig om de belasting van het nefro-geriatrisch assessment voor patiënten te verminderen en dit aanvullende onderzoek ook geschikt te maken voor mensen met lage geletterdheid en/of culturele en taal barrières. Ons onderzoek laat zien dat het integreren van de principes van de geriatrie met gebruik van een nefro-geriatrisch assessment in de patiëntenzorg voor personen met gevorderde chronische nierschade haalbaar is. Het implementatieproces kan wel verbeterd worden. Factoren zoals belastbaarheid en lage leesvaardigheid van patiënten, evenals tijdgebrek van zorgverleners, belemmerden de integratie in routine zorg. Belangrijkste succesfactoren bij de implementatie zijn de samenwerking met de afdeling geriatrie/ouderengeneeskunde en het bespreken van de uitkomsten in gezamenlijkheid met behandelaren van meerdere disciplines. Ook is het belangrijk om het doel en de uitkomsten van het geriatrisch assessment (aanvullende onderzoek bij ouderen) duidelijk met patiënt te bespreken. Na afloop van de POLDER-studie is hiervoor samen met de Nierpatiënten Vereniging Nederland een patiëntenfolder ontwikkeld. (Zie de volgende bijlage van dit proefschrift) Het nefro-geriatrisch assessment wordt momenteel gebruikt in 35 Nederlandse en Belgische ziekenhuizen die deelnemen aan de DIALOGICA studie.

Deel 3: Kwetsbaarheden van oudere patiënten met gevorderde chronische nierschade

De uitkomsten van het geriatrisch assessment geven ook nieuwe wetenschappelijke inzichten; die zijn beschreven in **het derde deel** van het proefschrift. In **hoofdstuk 8** onderzoeken we aspecten van mentaal welzijn bij oudere personen met chronische nierschade ten tijde van de COVID-19 pandemie. Deze patiënten hebben namelijk een verhoogd risico op een ernstig verloop van COVID-19 infectie én zijn kwetsbaar voor mentale gezondheidsproblemen. Patiënten uit de POLDER-studie (hoofdstuk 7) zijn gevraagd een aanvullende vragenlijst in te vullen tijdens de pandemie. Uit het onderzoek, waaraan 82 patiënten van 70 jaar of ouder deelnamen, blijkt dat 67% zich meer zorgen maakte over COVID-19 vanwege hun nierziekte en dat 43% aangaf dat hun kwaliteit van leven achteruitging door de pandemie. In vergelijking met voor de pandemie, verdubbelde het aantal patiënten met depressieve klachten. Gemiddeld verslechterde de lichamelijke gezondheid-gerelateerde kwaliteit van leven, vooral bij mannen. Terwijl de gemiddelde score voor de mentale gezondheid-gerelateerde kwaliteit van leven vergelijkbaar was met voor de pandemie. Ons onderzoek benadrukt dat, naast het verhoogde sterfterisico bij COVID-19, ook aandacht voor het mentale welzijn van deze kwetsbare groep van groot belang is.

In **hoofdstuk 9** zijn symptomen van apathie bij ouderen met gevorderde nierschade onderzocht. Apathie weerspiegelt een verminderde motivatie, doelgericht gedrag en emoties en minder betrokkenheid bij sociale interacties. De data van de COPE studie gaf ons de mogelijkheid te kijken naar dit onderbelichte fenomeen bij 180 patiënten van 65 jaar of ouder met chronische nierschade (nierfunctie lager dan 20%) uit vijf verschillende Nederlandse ziekenhuizen. Ruim éénderde van de onderzochte groep patiënten rapporteerde symptomen van apathie, waarvan bij slechts de helft van de patiënten dit samenging met depressieve klachten. Patiënten met apathieklachten hadden ten tijde van de basismeting waren kwetsbaarder en hadden meer lichamelijke beperkingen, een slechter geheugen en een lagere gezondheid-gerelateerde kwaliteit van leven. We zagen geen snellere verslechtering van deze uitkomsten bij deze patiënten met apathieklachten gedurende de vier volgende jaren, maar wel een twee keer zo hoog sterfterisico. Klachten van apathie zijn nog maar weinig onderzocht bij patiënten met chronische nierschade. Op basis van onze resultaten bevelen we aan om meer onderzoek te doen naar, en bewustzijn te creëren voor, mentale gezondheid bij oudere patiënten met chronisch nierfalen, in het bijzonder voor symptomen van depressie en apathie.

Reflectie en conclusie

Tot slot geeft **hoofdstuk 10** een algemene beschouwing op de potentiële waarde van het integreren van de geriatrische principes in de nefrologische zorg voor de (oudere) nierpatiënt, de organisatie van deze zorg en het maatschappelijk belang.

Ons onderzoek laat zien dat het in kaart brengen van mentale en fysieke conditie en sociale omstandigheden nuttig kan zijn voor oudere patiënten met gevorderde nierschade. We hebben vastgesteld dat het opnemen van aanvullend geriatrisch onderzoek (het geriatrisch assessment) in de reguliere zorg haalbaar is. Dit is van waarde voor de herkenning van geriatrische problemen, het geven van ondersteunende zorg én bij de beslissing over behandeling bij nierfalen. Ook benadrukt ons onderzoek dat de keuze voor een behandeling soms wijzigt en dat het belangrijk is de zorgbehoeften van patiënten regelmatig in kaart te

brengen. Geriatrisch assessment kan daarbij helpen door op individueel kwetsbaarheden aan het licht brengen en wetenschappelijke inzichten te geven. Het onderzoek gebundeld in dit proefschrift helpt ons beter begrijpen hoe aanvullend geriatrisch onderzoek kan bijdragen aan betere nierzorg.

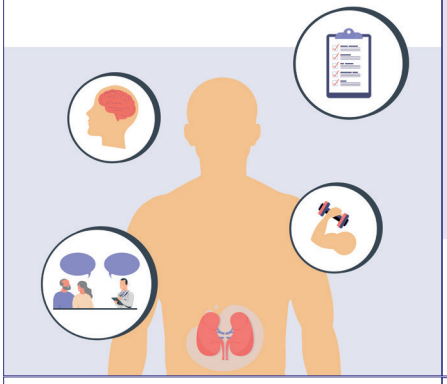
Toekomstig onderzoek zal moeten uitwijzen hoe verschillende geriatrische problemen (zoals kwetsbaarheid, geheugenproblemen, apathie, fysiek functioneren en overbelasting van mantelzorgers) invloed hebben op uitkomsten die relevant zijn voor patiënten, zoals kwaliteit van leven, dagelijks functioneren, gezondheidsklachten en mentale gezondheid. Samen met patiënten zal verder onderzocht moeten worden hoe deze informatie het beste te gebruiken om zorg en informatie op maat aan te bieden en zo bij te dragen aan het complexe keuzeproces voor de meest passende vorm van behandeling bij nierfalen.

PATIËNTENFOLDER

Deze folder voor patiënten over het geriatrisch assessment is ontwikkeld door Nierpatiënten Vereniging Nederland en de POLDER werkgroep. De folder is beschikbaar via nieren.nl/behandelingen-bij-nierproblemen/nierfalen-een-behandeling-kiezen en polderstudie.nl/nl/nieuws/patientfolder.

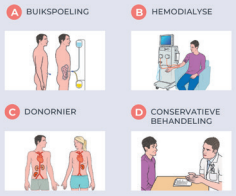
AANVULLEND ONDERZOEK WANNEER U OUDER BENT

Uw nieren werken niet meer goed.
Daarvoor zijn een aantal behandelingen mogelijk.
Met aanvullend onderzoek bekijken we welke behandeling het beste past wanneer u ouder bent.
In deze folder leest u wat dit onderzoek inhoudt.



Waarom aanvullend onderzoek?

Samen met uw arts, verpleegkundige, maatschappelijk werker en soms een diëtist kijkt u welke behandeling het beste bij u past.



Deze behandelingen hebben voordelen, maar ook nadelen. U kunt bijvoorbeeld meer moe zijn of u minder goed concentreren. Als u ouder bent, kunt u dan vaker vallen of dingen vergeten. Maar dat geldt niet voor iedereen.

Wij raden daarom mensen van 65 jaar en ouder aanvullend onderzoek aan. Zo weten we beter hoe úw situatie eruit ziet. Wat voor u belangrijk is. En wat u nog wel en niet zelf kunt doen. Dit aanvullend onderzoek noemen we een geriatrisch zorgpad.

Wat houdt het aanvullend onderzoek in?

Verschillende medewerkers kunnen het aanvullend onderzoek met u doen; de verpleegkundige (specialist), maatschappelijk werker, diëtist of een arts speciaal voor ouderen (geriater). Dit onderzoek bestaat uit de volgende stappen.

Vragenlijsten invullen
Eerst vult u vragenlijsten in. Dat kan thuis. Of soms ook in het ziekenhuis. Dat duurt ongeveer een half uur. De vragen gaan over hoe uw leven er uitziet. Bijvoorbeeld wat u graag doet, of hoe u zich voelt. En waar u in uw dagelijks leven hulp bij nodig hebt.

Onderzoeken doen
U krijgt ook een paar onderzoeken in het ziekenhuis. Uw spierkracht en uw geheugen worden dan gemeten. Deze onderzoeken duren samen ongeveer een half uur tot een uur. Meestal is deze afspraak voor of na uw poli-bezoek.





Bespreken van de resultaten
De verschillende medewerkers bespreken samen de resultaten van alle vragen en onderzoeken. Soms is dan nog extra onderzoek nodig. Daarna praten zij met u over de resultaten. Dit gebeurt bij uw volgende bezoek aan de polikliniek. En als het nodig is, overlegt uw arts ook met uw huisarts.

Tip: Neem uw partner of naaste mee
Twee mensen horen en weten meer dan één. En een nierziekte heeft niet alleen invloed op uzelf. Ook mensen in uw omgeving merken de gevolgen van de nierziekte. Bijvoorbeeld omdat u meer steun van hen nodig heeft. Neem daarom uw partner of iemand die u goed kent mee naar het bespreken van de resultaten.



Wat heeft u aan het onderzoek?

Met de resultaten kan de arts beter inschatten hoe buikspoeling, hemodialyse, een donornier of conservatieve behandeling voor u zal zijn. Zo kunt u samen met uw arts beter de behandeling kiezen die bij u past.

Als het nodig is en als u dat wilt, kan uw zorg worden aangepast. Bijvoorbeeld met een dieet, fysiotherapie of andere extra zorg. Het is belangrijk extra zorg op tijd te starten. Zo kunt u langer de dingen blijven doen die voor u belangrijk zijn.

Tenslotte
Heeft u nog vragen, of twijfelt u over het aanvullend onderzoek? Bespreek dat met uw arts, de verpleegkundige of andere medewerkers. Zij zijn ervoor om u hierbij te helpen.

Deze folder is mogelijk gemaakt door:

nvn nierpatiënten vereniging nederland

POLDER

GROUP INFORMATION FOR THE PATHWAY FOR OLDER PATIENTS REACHING END STAGE RENAL DISEASE (POLDER) STUDY GROUP

The Pathway for older patients reaching end stage renal disease (POLDER) study group is a collaboration in the Netherlands that is established to study and implement a nephrology-tailored geriatric assessment in routine care.

The POLDER investigators are (in alphabetical order): Arjan van Alphen, Maasstad Hospital Rotterdam; Noeleen Berkhout-Byrne, Leiden University Medical Center; Fenna van Breda, Amsterdam University Medical Center; Marjolijn van Buren, Haga Teaching Hospital The Hague; Henk Boom, Reiner de Graaf Hospital Delft; Willem Jan Bos, St. Antonius Hospital Nieuwegein; Adry Diepenbroek, University Medical Center Groningen; Marielle Emmelot-Vonk, University Medical Center Utrecht; Casper Franssen, University Medical Center Groningen; Carlo AJM Gaillard, University Medical Center Utrecht; Nel Groeneweg-Peeters, Reinier de Graaf Hospital Delft; Bettie Hoekstra, Maasstad Hospital Rotterdam; Nienke Hommes, Haaglanden Medical Center The Hague; Francoise Hoornaar, St. Antonius Hospital Nieuwegein; Hanneke Joosten, Maastricht University Medical Center; Joep Lagro, Haga Teaching Hospital; Elisabeth Litjens, Maastricht University Medical Center; Femke Molenaar, University Medical Center Utrecht; Simon Mooijaart, Leiden University Medical Center; Aegida Neradova, Amsterdam University Medical Center, Dianet Amsterdam; Mike Peters, Amsterdam University Medical Center; Wilma Veldman, University Medical Center Groningen; Carlijn Voorend, Leiden University Medical Center; Lidwien Westerbos, Amsterdam University Medical Center; Carlijne Westerman- van der Wijden, Haaglanden Medical Center The Hague; Judith Wierdsma, University Medical Center Utrecht.

DANKWOORD

Deze thesis was niet tot stand gekomen zonder hulp van vele anderen, aan wie ik nog een woord van dank wil richten.

Allereerst mijn (co)promotores. Prof. Bos, Willem Jan, dank voor het vertrouwen en de kans om mij tot doctor te ontwikkelen na onze eerdere samenwerking. Je oneindige enthousiasme, fijne begeleiding en inspirerende brainstormsessies waren van grote waarde voor mij en dit proefschrift. Dr. van Buren, Marjolijn, je hebt me enorm geholpen met je pragmatische adviezen en stond altijd voor me klaar. Dank voor je betrokkenheid, fijne samenwerking en het delen van je enthousiasme, kennis en ervaring over nefro-geriatrie. Prof. Mooijaart, Simon, je hebt me als gezondheidswetenschapper wegwijs gemaakt in de noodzaak en werkwijze van de ouderengeneeskunde, dank voor je goede begeleiding en schrijfadviezen.

De POLDER-werkgroep: Adry en Noeleen, jullie zijn de drijvende kracht achter dit initiatief. Deze output is te danken aan jullie visie, inzet en overtuigingskracht. Noeleen, ik kon altijd bij je terecht als ik motivatie, wijze raad of inspiratie voor een presentatie nodig had. Dank voor het delen van je passie en onze gezellige koffiemomenten. Hanneke, je beschikbaarheid en betrokkenheid bij mijn werk en daarbuiten was heel waardevol. Evenals de snelle en constructieve feedback van Casper. Bovenal wil ik alle patiënten bedanken die meewerkten aan POLDER en COPE studies.

POLDER was niet van de grond gekomen zonder hele betrokken verpleegkundigen en verpleegkundig specialisten (o.a. Nel Groeneweg-Peeters, Bettie Hoekstra, Françoise Hoornaar, Wilma Veldman, Lidwien Westerbos, Mirjam Poldervaart, Carlijne Westerman, Judith Wierdsma, Marlon van der Putte), lokale hoofdonderzoekers (Nienke Hommes, Arjan van Alphen, Fenna van Breda, Femke Molenaar, Elisabeth Litjens, Aegida Neradova, Henk Boom), nefrologen, geriaters/internist-ouderengeneeskundigen (o.a. Mariëlle Emmelot-Vonk, Joep Lagro, Mike Peters), maatschappelijk werkers en diëtisten. Ook dank aan de adviesraad en allen die hebben meegedacht tijdens de bijeenkomsten. Namiko Goto, Ria de Kleijn en Katja Cardol, dank voor de hulp bij de focusgroepen, en Helma Dolmans voor de lokale studie-coördinatie. Lara Heuveling en Martijn Leegte (Nefrovisie) bedankt voor de leuke samenwerking en mogelijk maken van dataverzameling. Karen Prantl (Nierpatiënten Vereniging Nederland) voor je waardevolle en onmisbare bijdrage vanuit het patiëntenperspectief.

Afdeling ouderengeneeskunde en het LCO, dank voor de leuke tijd tijdens het EUGMS congres in Londen en de schrijfdagen in Egmond aan Zee. De afdeling klinische epidemiologie, met name prof. Friedo Dekker en alle promovendi/deelnemers van de Nefro-journal club voor de leerzame wekelijkse discussies en tijdens cursussen zoals die op Schiermonnikoog. Prof. Ton Rabelink, dank voor het mede mogelijk maken van dit wetenschappelijke traject. Marianne dank voor je hulp hierbij.

Yvette, Mathijs, Wouter, Alferso, Leti en Margot, jullie input was van grote waarde. Yvette, je was van begin tot einde betrokken. Ik heb echt veel van je geleerd en genoten van onze

optimistische thee- en borrel momenten, veel dank voor je warme support. De woensdag-schrijfclub (Katja, Judith, Milon, Chiara, Kristell, Isra, Renée en Sara) voor de motivatie tijdens Corona-thuiswerk periode en daarna.

Het nefro-geriatrie team, Micha, Imre en in het bijzonder Mathijs; het was fijn een maatje te hebben en te kunnen sparren over inhoud en proces, ik heb veel aan je input gehad. Jullie maakten samen met de C7- en K5-collega's (Roel, Bernard, Cathelijne, Marije, Danny, Shosha, Anouk, Novella, Sophie, Suzanne en vele anderen) mijn werk bij de nierziekten een ontzettend fijne tijd. Het LUMC-fietsclubje, Franca, Rosalie, Koen en Lotte; de ochtenden op de fiets (of met de kite) waren een heerlijke start van de werkdag.

Voor ontspanning naast werk had ik mijn wekelijkse Haag-hardloopgroep en mijn vrienden. Haagse strandmatties, Yfl, Rosanne, Marije, Marga, Lieke, Marieke, Floor, Anna en Floor, onze vriendschap is me dierbaar. Karolien, dank voor je persoonlijke bijdrage aan dit werk: de POLDER-website en de voorkant laten zien welk talent je hebt. Rosa, Inge en Esther, jullie gingen mij jaren geleden al voor in het schrijven van een proefschrift en ik kon dan ook altijd bij jullie terecht voor goed advies en (schrijf)weekenden weg.

Germa & Frans, zonder jullie hulp (niet alleen tijdens Covid) was dit niet gelukt. Karen, jij bent betrokken geweest bij het begin van wetenschappelijke en andere hoofdstukken uit mijn leven. Lya, je hebt me geleerd verder te kijken dan de wereld die ik ken. Mathijs, Christiaan, Daniël en jullie wederhelften, ik weet dat ik altijd op jullie kan rekenen. Wat ben ik blij met jullie als familie.

Mam en Pap, voor jullie onvoorwaardelijke steun, stimulans om mij te blijven ontwikkelen, nieuwsgierig te zijn en de solide en liefdevolle basis. Jullie zijn fantastisch en wat ben ik jullie dankbaar.

Liefste Lune en Fedde, elke dag met jullie is een feestje, ik wens jullie veel nieuwsgierigheid en vertrouwen bij het ontdekken van jullie eigen levenspad. Lieve Freek, zonder jouw support vanaf het eerste moment dat ik dacht aan promoveren tot nu, het is zover, was dit proefschrift er niet geweest. Ik zie uit naar vele nieuwe avonturen samen.

CURRICULUM VITAE

Carlijn completed her pre-university education at the Kalsbeek College in Woerden. Her classes during high school focused on Natural Sciences and Economics. In 2004 she began studying health sciences (gezondheidswetenschappen) at the Vrije Universiteit in Amsterdam. She finished her bachelor's degree completing an internship at the Trimbos Institute on the topic of mental health in Diabetes Mellitus type II patients and epilepsy patients. Subsequently, she completed a two-year master's degree in Management Policy Analysis in Health and Life Sciences at the same university. With a particular focus on International Public Health, she conducted scientific internships at the Royal Tropical Institute in Amsterdam, the Athena Institute in Amsterdam, and at the University of the Witwatersrand in Johannesburg, South Africa.

In 2010 she started working at the Leprosy Relief and the Royal Tropical Institute in Amsterdam on guideline development for the reduction of health-related stigma, and conducted research on medication availability for a specific leprosy reaction. In 2012 she made a switch to the Dutch hospital sector, working subsequently at the financial departments of the St. Antonius hospital, Vrije Universiteit Medical Center and Alrijne hospital in internal advisory and project-leader roles. During this time she also participated in national working groups on reimbursement of expensive medications and cooperation between health care providers and insurance companies (horizontaal toezicht).

In 2017, Carlijn started at the Leiden University Medical Center as project lead for the POLDER project at the department of Nephrology, which resulted in a simultaneous PhD-trajectory as of 2018 under supervision of prof. dr. Willem Jan W. Bos. She presented her work at multiple national and international congresses in the field of nephrology and geriatrics, and received an award for the best abstracts at the ERA-EDTA congress in Budapest in 2019. During her PhD-trajectory Carlijn co-supervised a master student internship and built upon an epidemiology track-record, engaging in multiple courses and attending the weekly nephrology-related journal club at the epidemiology department.

From 2022 until 2024 Carlijn continued with a post-doctoral project named Showcase Nefrologie. On behalf of Nefrovisie and Santeon and in collaboration with the Dutch Society for Internal Medicine (NIV) and Knowledge Institute of the Federation for Medical Specialists (KIMS), she wrote a policy report '*Samen voor betere Nierzorg*'. The report describes the development and gains of 40 years of quality system in Dutch nephrology care. From this position, she also contributed to the development of a toolkit and guide for medical associations for outcome-based quality improvement and a Linnean webcast on the topic.

At the time of printing this dissertation, Carlijn is taking a sabbatical, spending time with her beloved family, while focussing on the next steps in her career.

LIST OF PUBLICATIONS

Articles included in this thesis

1. Voorend CGN, *et al.* Geriatric Assessment in CKD Care: An Implementation Study. *Kidney medicine*, 2024.
2. Berkhout-Byrne NC, Voorend CGN, *et al.* Nephrology-tailored geriatric assessment as decision-making tool in kidney failure. *Journal of Renal Care*, 2024.
3. Voorend C.G.N, *et al.* Apathy symptoms, physical and cognitive function, health-related quality of life, and mortality in older patients with CKD: a longitudinal observational study. *American Journal of Kidney Diseases*, 2024.
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5. Voorend C.G.N, *et al.* Changing the choice from dialysis to conservative care or vice versa in older patients with advanced chronic kidney disease. *Nephrology Dialysis Transplantation*, 2021.
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7. Voorend C.G.N., *et al.* Impact of the COVID-19 pandemic on symptoms of anxiety and depression and health-related quality of life in older patients with chronic kidney disease. *BMC geriatrics*, 2021.
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9. Demirhan I, van Oevelen M., Skalli Z., Voorend C.G.N, *et al.* Association between cognitive functioning and health-related quality of life and its mediation by depressive symptoms in older patients with kidney failure. *Journal of Nephrology,* 2024.
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15. Voorend CGN and Post EB. A systematic review on the epidemiological data of erythema nodosum leprosum, a type 2 leprosy reaction. *PLoS neglected tropical diseases*, 2013.
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17. Stevelink SAM, Wu IC, Voorend CGN and Van Brakel WH. The psychometric assessment of internalized stigma instruments: a systematic review. *Stigma Research and Action*, 2012.
18. Voorend CGN, *et al.* Report of the Stigma Research Workshop for the development of scientific consensus papers and field guidelines on health-related stigma, held in Amsterdam, the Netherlands from 11–14 October 2010. *Leprosy Review*, 2011

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19. Nefrovisie & Santeon. Showcase nefrologie: Samen voor betere nierzorg. (2024) Available: *https://www.nefrovisie.nl/wp-content/uploads/2024/02/ShowcaseNefrologie__rapport-met-bijlagen.pdf*
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